Annex D. Toxicological Studies

Table D-1. Cardiovascular effects.

Study	Pollutant	Exposure	Effects
Reference: Anselme et al. (2007) **Species:** Rat **Gender:** Male **Strain:** Wistar **Age:** Adult **Weight**: 200-225 grams **n:** 10 healthy rats, 10 CHF rats	DE: monocylinder Diesel engine using Euro 4 ELF 85A reference gasoline, and clean room air	**Route:** Whole Body Inhalation **Dose/Concentration:** DE: 0.5 mg/m^3 Other emissions measured: non-methane hydrocarbons (7.7 ppm), NO_2 (1.1 ppm), CO (4.3 ppm) **Particle Size (Distribution):** 85 nm (10-500) **Time to Analysis:** Experiments started 3 months after L coronary artery ligation. ECG started at t0 and the DE exposure at t30 min for a 3h period; ventricular premature beats (VPBs) and RMSSD were calculated every 30 min during clean room air exhaust and PE periods. Early (t210-300 min) and late (t480-540 min) PE were analyzed.	Immediate decrease in RMSSD was observed in both healthy and CHF rats PE. Immediate increase in VPBs observed in CHF rats only; which lasted 4-5h after exposure ceased. Whereas HRV progressively returned to baseline values within 2.5 h post-exposure (PE); the proarrhythmic effect persisted as late as 5 h PE termination in CHF rats.
Reference: Bagate et al. (2004) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 13-15 weeks **Use:** Ex-vivo	LPS and EHC-93 (PM): Urban Air collected at the Health Effects Institute Ottawa, Canada	**Route:** Intratracheal Instillation **Dose/Concentration:** PM: 10 mg/kg of bw; LPS: 350 EU/animal **Particle Size (Distribution):** EHC-93: 0.8-0.4 μm (<3) **Time to Analysis:** 4 and 24 h post-instillation	PM and LPS elicited a significant increase in receptor-dependent vasorelaxation of the aorta compared to saline-instilled rats.
Reference: Bagate et al. (2004) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 13-15 weeks **Use:** In-vitro (aortic rings)	EHC-93 (PM), CB-V or CB-Fe, LPS	**Route:** Aortic suspension fluid **Dose/Concentration:** Cumulative concentrations of EHC-93, CB-V and CB-Fe (10, 25, 50, 75, 100 μg/mL) **Particle Size (Distribution):** EHC-93: 0.8-0.4 μm (<3) CB 1.5-2.0 nm (<5) **Time to Analysis:** Immediately post-exposure of aortic rings to cumulative concentrations of EHC-93, CB-V, CB-Fe and LPS.	CB-V particles induced more relaxation than CB-Fe particles or EHC-93 in a dose-dependent manner. PM and LPS had an acute transient effect on the receptor dependent vasorelaxation. PM and LPS attenuated ACh-elicited vasocontraction in denuded aortic rings (DARs).
Reference: Bagate et al. (2004) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 13-15 weeks **Use:** In-vitro (small mesenteric rat arteries (SMRA) and rat aortic rings)	EHC-93 (PM): Urban Air collected at the Health Effects Institute Ottawa, Canada. EHC-93 filtrate (PMF) Zn^{2+} and Cu^{2+} particles (10,000 and 845 μg PM respectively)	**Route:** SMRA and aorta segment in suspension fluid, under tension. **Dose/Concentration:** PM Suspensions (10-100 μg/mL), $CuSO_4/ZnSO_4$ (1-100 μmol)), Phe (2 μM), carbacol (10 μM) **Particle Size (Distribution):** PM: 4.6 μm (GSD = 3.2) **Time to Analysis:** Measured immediately after maximum response for each cumulative dose was achieved.	**PM-Induced Contraction:** No effect of suspension or filtrate seen on resting tension of aorta and SMRA. **PM- and Metal-Induced Vasorelaxation:** Cumulative concentrations (10-100 μg/mL) of PM suspension and its water soluble components (PMF) elicited dose-dependent relaxation in aorta. Relaxation induced by particle suspension was higher than relaxation induced by free filtrate. The difference was significant at 100 μg/mL. In SMRA, vasorelaxation similar to aorta's was observed, and the activity of the particle suspension was stronger than the filtrate, w/ the difference being significant starting at 30 μg/mL. Both Zn^{2+} and Cu^{2+} in sulfate salts (10-100 μmol) induced relaxation in pre-contracted aortic rings, w/ Cu^{2+} having a greater effect than Zn^{2+} at the same concentration. Ions didn't affect ACh relaxation. **Effect of PM on α-Adrenergic Contraction:** Phenylephrine-induced dose-response contraction, starting at 1μM w/ max at 100 μmol. Pre-treatment of SMRA didn't change the phenylephrine-induced contraction.

Study	Pollutant	Exposure	Effects
Reference: Bagate et al. (2006b) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto (WKY) and SH **Age:** 13-15 weeks **Use:** In-vitro (aortic rings)	EHC-93 (PM) EHC-93 (Filtrate) Cu^{2+} and Zn^{2+} solutions	**Route:** Exposure of normal and denuded aortic rings to EHC-93 (PM) EHC-93 (Filtrate) Cu2+ and Zn^{2+} solutions **Dose/Concentration:** PM and PMF Suspensions (10-100 μg/mL), $CuSO_4$ or $ZnSO_4$ (10-100 μmol)), Phenylephrine (2 μM), Carbacol (10 μM) **Particle Size (Distribution):** PM: 4.6 μm (GSD = 3.2) **Time to Analysis:** Measured immediately after maximum response to each cumulative dose was achieved.	PM and its soluble components elicited endothelium-independent vasodilation in rat aorta rings. This response is a result of the activation of sGC since its inhibition by NS2028 practically eliminated relaxation. PM suspensions stimulated cGMP production in purified isolated sGC. Neither receptor nor their signaling pathways played a significant role in the direct relaxation by PM or metals. Vasodilation responses were significantly higher in SH than WKY control rats.
Reference: Bagate et al. (2006a) **Species:** Rat **Gender:** Male **Strain:** SH/NHsd **Age:** 11-12 weeks **Weight:** 250-350 grams **Use:** In-vivo exposure, ex-vivo perfused hearts	EHC-93 (PM): Urban Air collected at the Health Effects Institute Ottawa, Canada. EHC-93 (Filtrate), Zinc (in PM), LPS Reference particle: Carbon coated with ammonium chloride, sodium sulfate, iron and vanadium.	**Route:** Intratracheal Instillation **Dose/Concentration:** PM: 10 mg/kg of bw; LPS: 350 EU/animal, 0.5 mL **Particle Size (Distribution):** PM: 4.6 μm (GSD = 3.2) **Time to Analysis:** 4h post-exposure	**Effect of Pretreatment on Baseline parameters of Isolated Perfused Heart:** After PM exposure a slight increase of baseline coronary flow (CF) and heart rate (HR) was noted. In contrast, a significant decrease of left developing ventricular pressure (LDVP) was observed in SH. LPS also elicited a non-significant decrease in LVDP. **Effect of Pretreatment and Ischemia on Cardiac Function:** When SH rats were pretreated with PM or LPS the isolated heart had a reduced ability to recover to baseline levels after occlusion, in comparison w/ saline treated rats. After occlusion was released CF went back to baseline values. Saline and LPS treated rats, showed a gradual decrease in CF noted during the reperfusion period. Isolated hearts from PM-exposed SH showed a complete restoration of CF and no gradual decrease. The increase of Zn2+ elicited a rapid decrease of LDVP and HR. The impairment of cardiac function measured by LDVP and HR started immediately upon Zn2+ infusion and remained the same during the perfusion period (no Zn2+ was present in the perfusate).
Reference: Bagate et al. (2006a) **Species:** Rat **Strain:** H9c2 (EACC), cardiomyocyte cells	EHC-93 (PM) Filtrate: Urban Air collected at the Health Effects Institute Ottawa, Canada, $ZnSO_4$	**Route:** In Vitro. 35-100 cells/experiment **Dose/Concentration:** 1, 50, 100 μg/mL; $ZnSO_4$ (50 μmol) **Particle Size (Distribution):** PM: 4.6 μm (GSD = 3.2); Carbon Particles: 44nm **Time to Analysis:** 30 min incubation	**Effect of EHC-93 filtrate on Ca2+ Uptake in Cardiomyocytes:** Both PMF and Zn2+ inhibited ATP or ionophore-stimulated Ca2+ influx in cardiomyocytes.
Reference: Campen et al. (2005) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6J and Apo $E^{-/-}$ **Age:** 10-12 weeks	High Whole DE (HWDE) n = 10, Low Whole DE (LWDE) n = 10, High PM Filtered (HPMF) n = 6, Low PM Filtered (LPMF) n = 5, Filtered Air (FA) n = 10	**Route:** Whole body Inhalation Chambers and Ex-vivo Exposures (isolated, pressurized septal coronary arteries) **Dose/Concentration:** HWDE: PM = 3.6 mg/m^3, NO_X = 102 ppm LWDE: PM = 0.512 mg/m^3, NO_X = 19 ppm. PM = 0.770 mg/m^3, NO_X = 105 ppm. LPMF: PM = 0.006 mg/m^3, NO_X = 26 ppm **Particle Size (Distribution):** NR **Time to Analysis:** Whole Body Exposures: DE or PFDE for 6h/day for 3 days, euthanized after 18h, at the end of last exposure. Coronary Vessels Exposure: PSS bubbled with DE to expose coronary vessels to the soluble contents of DE. Analysis occurred immediately PE.	**Whole Body Exposure on ApoE$^{-/-}$:** during DE exposure, ApoE$^{-/-}$ mice HR consistently decreased during high concentration exposures, compared to the C57BL/6J strain. **Coronary Vascular Effects on ApoE$^{-/-}$:** DE had no significant effects on the resting myogenic tone of isolated septal coronary arteries. Control coronary arteries showed constrictive responses to ET-1 and dilatory responses to SNP. DE exposed PSS vessels responses to ET-1 enhanced compared to control. SNP-induced dilation blunted in vessels resting in diesel-exposed saline.
Reference: Campen et al. (2003) **Species:** Rat **Gender:** Male and Female **Strain:** SH **Age:** 4 months	DE	**Route:** Whole body exposure **Dose/Concentration:** 0, 30, 100, 300, 1000 $\mu g/m^3$ **Particle Size (Distribution):** 0.1-0.2 μm aerodynamic diameter **Time to Analysis:** 6 h/day for 7 days; ECG measurements taken 4 days PE	**HR:** Heart Significantly higher in exposed animals and not concentration-dependent, w/ more substantial results seen in male rats. **ECG:** The PQ interval was significantly prolonged among exposed animals in a concentration-dependent manner.

Study	Pollutant	Exposure	Effects
Reference: Campen et al. (2006) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 10 weeks	Road dust from paved surfaces (Reno, NV) Gasoline engine emissions, containing PM, NO_X, CO and HC	**Route:** Whole body inhalation **Dose/Concentration:** Road dust: 0.5 and 3.5 mg/m^3; Gasoline engine emissions: dilutions of 10: 1, 15: 1, and 90: 1. Exposures from 5 to 60 μg/m^3 PM mean concentration: 61 μg/m^3, NO_X mean concentration: 18.8 ppm; CO mean concentration: 80 ppm **Particle Size (Distribution):** Road dust: 1.6 μm (Standard Deviation 2.0) Gasoline engine emissions: Average particle diameter of 15 nm **Time to Analysis:** 6h/day for 3 days. Mice were euthanized 18h post-exposure.	**ET-1:** Significantly upregulated by gasoline exhaust (dose-dependent). Increased levels in the PM filtered group. Low levels of road dust decreased ET-1. **ECG:** Consistent decreases in HR from beginning to end of exposure in all groups. No significant HR effects on road dust or gasoline exposure was observed. No significant effects on P-wave, PQ-interval, QRS-interval, or QT-interval were observed in either treatment. **T-wave:** Significant changes during exposure to whole gasoline exhaust was observed.
Reference: Cascio et al. (2007) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-10 weeks	UFPM: Ultra fine PM, EPA Chapel Hill, NC	**Route:** Intratracheal Instillation **Dose/Concentration:** 100 μg in 100 ul **Particle Size (Distribution):** <0.1 μm **Time to Analysis:** 24 h post-exposure (single exposure)	UFPM exposure double the size of myocardial infarction attendant to an episode of ischemia and reperfusion while increasing post ischemic oxidant stress. UFPM alters endothelium-dependent/independent regulation of systemic vascular tone; increases platelet number, plasma fibrinogen, and soluble P-selectin levels; reduces bleeding time.
Reference: Chang et al. (2007) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 60 days	UfCB: Ultra fine carbon black: n = 4/group Ferric sulfate $Fe_2(SO_4)_3$: n = 3-5/group Nickel sulfate $NiSO_4$: n = 3-5/group	**Route:** Intratracheal Instillation **Dose/Concentration:** UfCB: 415 and 830 μg Ferric Sulfate: 105 and 210 μg Nickel Sulfate: 263 and 526 μg Combined UfCB and ferric sulfate: 830 μg UfCB + 105 μg Ferric Sulfate Combined UfCB with Nickel Sulfate: 830 μg UfCB + 263 μg Nickel Sulfate **Particle Size (Distribution):** UfCB **Time to Analysis:** Single dose, radiotelemetry readings recorded for 72-h post exposure.	Both high/low-dose UfCB decreased ANN (normal-to-normal intervals) slightly around the 30th hour, concurrent increases of LnSDNN. LnRMSSD returned to baseline levels after small initial increases. Minor effects observed after low-dose Fe and Ni instilllation; biphasic changes occurred after high-dose instillations. Combined exposures of UfCB and either Fe or Ni resulted in HRV trends different from values estimated from individual-component effects.
Reference: Chang et al. (2007) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 10 weeks	CAPs: collected during a dust storm from Chung-Li, Taipei n = 2	**Route:** Inhalation (nose-only exposure system) **Dose/Concentration:** 315.55 μg/m^3 **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 6 h	A linear mixed-effects model revealed sigmoid increases in HR and a sigmoid decrease of QAI during exposure, after an initial incubation period.
Reference: Chang et al. (2004) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 60 days	CAPs collected in Chung-Li, Taipei (spring and summer periods) n = 2	**Route:** Inhalation (nose-only exposure system) **Dose/Concentration:** Spring exposure: 202.0 ± 68.8 μg/m^3; Mean number concentration: 2.30 x 10^5 particles/cm^3 (range: 7.12 x 10^3 - 8.26 x 10^5) summer exposure: 141.0 ± 54.9 μg/m^3; Mean number concentration: 2.78 x 10^5 particles/cm^3 (range: 7.76 x 10^3 - 8.87 x 10^5) **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** Animals were repeatedly exposed to concentrated $PM_{2.5}$ during spring and summer for 5 h/exposure.	During spring exposures, the maximum increase of heart rate (HR) and blood pressure (BP) were 51.6 bpm and 8.5 mmHg respectively. The maximum decrease of QAI (measures cardiac contractility) noted at the same time was 1.6 ms. Similar pattern was observed during summer exposure, however., the responses were less prominent.
Reference: Chang, et al. (2005b) **Species:** Rat **Gender:** Male **Strain:** SH **Weight**: 200 grams	CAPs collected in Chung-Li, Taipei n = 2	**Route:** Inhalation (nose-only exposure system) **Dose/Concentration:** 202.0 ± 68.8 μg/m^3 **Particle Size (Distribution):** $PM_{2.5}$ (0.1-2.5um) **Time to Analysis:** 5h/day for 4 days	During the inhalation stage, crude effects of both LnSDNN and LnRMSSD for exposure and control groups decreased from the baseline values. Immediately after the experiments, both LnSDNN and LNRMSSD decreased due to stresses produced by release from the exposure system, then returned to the baseline values.

Study	Pollutant	Exposure	Effects
Reference: Chauhan et al. (2005) **Tumor Cell Line:** A549 derived from alveolar type II epithelial cells	SRM-1879 (SiO_2) and SRM-154b (TiO_2) from the NIST; EHC-93 from Ontario, Canada (EHCsol, EHCinsol)	**Route:** Cell culture: seeding density of 150,000 cells/flask grown to 75-85% confluence **Dose/Concentration:** 0, 1, 4, and 8 mg EHCtotal equivalent per 5 mL **Particle Size (Distribution):** EHC-93 median physical diameter: 0.4 μm; TiO_2 and SiO_2 particle size distribution: 0.3-0.6 μm **Time to Analysis:** Culture medium was removed from flasks and replaced w/ 5 mL of the particle suspension media. Plates were incubated for 24 h. After 24 h cell culture supernatants were collected and analyzed.	The decreased expression of preproET-1 in A549 cells suggests that epithelial cells may not be the source of higher pulmonary ET-1 spillover in the circulation measured in vivo in response to inhaled urban particles. However, higher levels ECE-1 in A549 post-exposure to particles, suggests an increased ability to process bigET-1 into mature ET-1 peptide, while increased receptor expression implies responsiveness. The increased release of Il-8 and VEGF by epithelial cells in response to particles, could possibly up regulate ET-1 production in the adjacent pulmonary capillary endothelial cells, w/ concomitant increased ET-1 spillover in the systemic circulation.
Reference: Chen et al. (2005) **Species:** Mouse **Strain:** Normal (C57) and $ApoE^{-/-}$	CAPs (NYU, NY)	**Route:** Whole Body Inhalation **Dose/Concentration:** 10 x ambient concentrations 19.7 $\mu g/m^3$ average concentration over 5 months (daily average exposure concentration was 110 $\mu g/m^3$) **Particle Size (Distribution):** Lippmann et al.; 2005 **Time to Analysis:** 6h/day, 5 days/week, for 5 months. Exposure Group: n = 9, Control Group: n = 10	Significant decreasing patterns of HR, body temp., and physical activity for $ApoE^{-/-}$ mice, w/ nonsignificant changes for C57 mice. SDNN and RMSSD in the late afternoon and overnight for $ApoE^{-/-}$ mice showed a gradual increase for the first 6 weeks, a decline for about 12 more weeks, and a slight turn upward at the end of the study period. For C57 mice, there were no chronic effect changes in SDNN or RNSSD in the late afternoon, and a slight increase after 6 weeks for the overnight period.
Reference: Chen et al. (2005) **Species:** Mouse **Strain:** Normal (C57), $ApoE^{-/-}$, **Age:** 26-28 weeks (C57), 39-41 weeks ($ApoE^{-/-}$), and 18-20 weeks ($LDLr^{-/-}$ [DK]) **Use:** Ex-vivo: cross sections of aorta were examined	CAPs (NYU, NY)	**Route:** Whole Body Inhalation **Dose/Concentration:** Mean exposure concentration: 110 $\mu g/m^3$ **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 6h/day, 5days/week for up to 5 months	All DK mice developed extensive lesions in the aortic sinus regions. In male DK mice, the lesion areas appeared to be enhanced by CAPs exposure. Plaque cellularity was increased, but there were no CAPs-associated changes in the lipid content. $ApoE^{-/-}$ and DK mice showed prominent areas of severe atherosclerosis. Quantitative measurements showed that CAPs increased the percentage of aortic intimal surface covered by grossly discernible atherosclerotic lesion.
Reference: Corey et al. (2006) **Species:** Mouse **Gender:** Male **Strain:** $ApoE^{-/-}$ **Age:** 11-12 months **Weight**: 32.84 g (avg)	PM collected November – March (Seattle, WA), Silica	**Route:** Nasal Instillation; PM (1.5 mg/kg), saline (50ul), or silica (Min-u-Sil 5, in 50 ul saline) **Dose/Concentration:** $PM_{2.5}$ **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** Mice were monitored for a 1 day baseline prior to and for 4 days following exposure.	After an initial increase in both HR and activity in all groups, there was delayed bradycardia with no change in activity of the animals in the PM and silica exposed groups. In addition, with PM and silica exposure, there was a decrease in HRV parameters.
Reference: Cozzi et al. (2006) **Species:** Mouse **Strain:** ICR **Age:** 6-10 weeks Aortas from the same mice were also studied	Ultrafine PM (collected continuously over 7 day periods in Oct 2002 in Chapel Hill, NC)	**Route:** Intratracheal Instillation **Dose/Concentration:** 100ug of PM in vehicle **Particle Size (Distribution):** <150nm **Time to Analysis:** 24 h post-exposure	**Ischemia-Reperfusion:** PM exposure doubled the relative size of myocardial infarction compared w/ the vehicle control. No difference was observed in the percentage of the vehicle at the risk of ischemia. PM exposure increased the level of oxidative stress in the myocardium after I-R. The density of neutrophils in the reperfused myocardium was increased by PM exposure, but differences in the numbers of blood leukocytes, expression of adhesion molecules on circulating neutrophils, and activation state of circulating neutrophils, 24 h after PM exposure, could not be correlated to the increase I-R injury observed. **Isolated Aortas:** Aortas isolated from PM-exposed animals exhibited a reduced endothelium-dependent relaxation response to ACh.
Reference: Dvonch et al. (2004) **Species:** Rat **Gender:** Male **Strain:** Brown Norway **n:** 7 (FA), 7 (CAPs)	CAPs, Detroit, MI	**Route:** Whole Body Inhalation Chamber **Dose/Concentration:** Average concentration: 354 $\mu g/m^3$ **Particle Size (Distribution):** $PM_{2.5}$, 0.1-2.5 μm **Time to Analysis:** 8h/day for 3 consecutive days; plasma samples collected 24 h post-exposure.	Plasma concentrations of asymmetric dimethylarginine (ADMA) were significantly elevated in rats exposed to CAPs versus filtered air.

Study	Pollutant	Exposure	Effects
Reference: Elder et al. 2004b **Species:** Rat **Gender:** Male **Strain:** Fischer 344 and SH **Age:** 23 months, Fischer 344; 11-14 months, SH **Weight:** NR	UFP - Ultrafine carbon particles, LPS	**Route:** intraperitoneally (ip) for saline and LPS whole body exposure for inhaled particles **Dose/Concentration:** Particles: 150 mg/m^3 LPS: 2mg/kg body weight **Particle Size (Distribution):** median size 36nm **Time to Analysis:** 6 hours exposure to particles 24 h after exposure to ip LPS to analysis	**BAL fluid cells:** Neither inhaled UFP nor ip LPS cause a significant increase in BAL fluid total cells or the percentage of neutorphils in either rat strain. No significant exposure-related alteration in total protein concentration or the activites of LDH and b-glucuronidase. **Peripheral blood:** In both rat strains ip LPS induced significant increase in the # and % of circulating PMNs.When combined with inhaled UFP, PMNs decreased, significantly for F-344 rats. Plasma fibrinogen increased with ip LPS in both rat strains, magnitude of change greater in SH rats. UFP alone decreased plasma fibrinogen in SH rats. Combined UFP and LPS response was blunted, but significantly higher than controls. Hematocrit was not altered in either rat strain by any treatment. **TAT complexes:** With all exposure groups averaged, plasma TAT complexes in SH rats were 6.5 times higher than in F-344 rats. LPS caused an overall increase in TAT complexes for F-344 rats further augmented by inhaled UFP. UFP alone decreased response. In SH rats UFP alone significant increased respones and LPS decreased response. **ROS in BAL cells:** In F-344 rats both UFP and LPS has independent and significant effects on DCFD oxidation. Effects were in opposite direction- particles decreased ROS, LPS increased ROS.
Reference: Elder et al. (2004) **Species:** Rat **Gender:** Male **Strain:** Fischer 344 and SH **Age:** 23 months (F344), 11-14 months (SH)	UFP (St. Paul, MN); LPS	**Route:** Whole Body Inhalation Chamber **Dose/Concentration:** UFP: 150μg/m^3 LPS: 2mg/kg bw **Particle Size (Distribution):** UFP Count Median Diameter = 36nm **Time to Analysis:** 6h exposure to UFP (ip LPS injection was administered right before exposure to UFP); sample collection time (BALF and blood) was 24 h after ip LPS injection. (1) ip-injected saline, inhaled air (n = 5), (2) ip-injected saline, inhaled particles (n = 5), (3)ip-injected LPS, inhaled air (n = 5), and (4) ip-injected LPS, inhaled particles (n = 5)	In both strains ip LPS induced significant increases in both number and % of circulating PMNs. However, when UFP was combined w/ ip LPS, the PMNs decreased (significant for F-344 strain only). Plasma fibrinogen concentration was also increased by ip LPS in both strains (change was greater for SH rats). UFP alone decreased plasma fibrinogen in SHRs. UFP+LPS caused a decrease in fibrinogen for the F-344 strain. Hematocrit not altered in either treatment or their combination in either strain. Inhaled UFP increased thrombin-anti-thrombin complexes (TAT) in both strains, either through a main effect (SH) or upon interaction w/ LPS (F-344).
Reference: Finnerty et al. (2007) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6 **Age:** 9 weeks **Weight**: 22-27 g	Coal Fly Ash (U.S. EPA), Analysis: ($PM_{2.5}$ samples) low unburned carbon (0.53 wt%), moderate levels of transition metals, including Fe (30, 400 μg/g), Mg (31, 200 μg/g), Ti (6, 180 μg/g), Mn (907 μg/g), and V (108 μg/g).	**Route:** Intratracheal Instillation **Dose/Concentration:** sterile saline (n = 8), 200ug PM (n = 8), 200ug PM+10ug LPS (n = 9), 200ug PM+100ug LPS (n = 8) **Particle Size (Distribution):** $PM_{1.8}$ and 2.5 μm **Time to Analysis:** 18h after Intratracheal Instillation	**Plasma:** TNF-α significantly increased in both PM+LPS10 and PM+LPS100 treatments. For plasma IL-6, all groups tended to rise with a significant increase in the PM+LPS100 group.
Reference: Folkmann et al. (2007) **Species:** Mouse **Gender:** Female **Strain:** wild type and ApoE$^{-/-}$ **Age:** 11-13 weeks **Weight**: 21 g (avg) **n:** 109	DEP SRM2975 particulate fraction of exhaust from a filtering system designed for diesel-powered forklifts).	**Route:** Intraperitoneal Injection **Dose/Concentration:** 0, 50, 500, 5000ug DEP/kg of bw **Particle Size (Distribution):** DEP: NR **Time to Analysis:** 6 or 24 h post-ip injection	The expression of inducible nitric oxide synthase (iNOS) mRNA was increased in the liver 6h post-ip injection. The level of oxidized purine bases, determined by formamidopyrimidine DNA glycosylase sites increased significantly in the liver after 24 h in in mice injected w/ 50μg/kg of bw. There was no indication of systemic inflammation determined as the serum concentration of nitric oxide and iNOS expression, and DNA damage was not increased in the aorta.
Reference: Furuyama et al. (2006) **Species:** Rat **Cell Type:** Heart Micro vessel Endothelial (RHMVE) Cells	OE-DEP, OE-UFP (from Urawa, Saitama, Japan) OE = Organic Extracts	**Route:** 4.0 x 10^5 cells **Dose/Concentration:** 0, 5, 10, 25 μg/mL of OE-DEP or OE-UFP **Particle Size (Distribution):** NR **Time to Analysis:** Incubation	The cell monolayer exposed to 10 μg/mL OE-UFP produced a larger amt. of HO-1 than cells exposed to 10 μg/mL OE-UFP. OE-DEP and OE-UFP exposure reduced PAI-1 production by the cells but did not affect the production of thrombomodulin, tissue-type PA, or urokinase-type PA. Increased PAI-1 synthesis in response to treatment w/ 1ng/mL TNF-α or 0.5ng/mL TGF-β1 was reduced by OE-DEP exposure. Suppression of PAI-1 production by OE-DEP exposure was mediated through oxidative stress and was independent of HO-1 activity.

Study	Pollutant	Exposure	Effects
Reference: Ghelfi et al. (2008) **Species:** Rat **Strain:** Sprague-Dawley **Age:** Adult	CAPs	**Route:** Inhalation **Dose/Concentration:** Mean $PM_{2.5}$ mass concentration: 218 ± 23 μg/m^3 **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis: Experiment 1 (n = 48):** each exposure day rats were pre-treated w/ either saline control (control and CAPS groups) or CPZ (CPZ and CPZ/CAPs groups 10 mg/kg) immediately prior to exposure. Rats were subject to single exposure for 5h to either CAPs or FA. Cardiac oxidative stress was assed immediately post-exposure with in situ chemiluminescence (CL), lipid peroxidation w/ thiobarbituric acid reactive substances (TBARS), and tissue edema in each animal. **Experiment 2 (n = 16):** rats were exposed for 5h to either CAPs or FA repeatedly over 4 months. Radioltelemetry was used during each exposure to record the ECG and assed cardiac function	CPZ (ip or aerosol) decreased CAPs-induced CL, lipid TBARS, and edema in the heart, indicating that blocking TRP receptors, systemically or locally, decreases heart CL. CAPs exposure led to significant decreases in HR and in the length of QT, RT, Pdur and Tpe intervals. These changes were observed immediately upon exposure, and were maintained throughout the 5h period of CAPs inhalation. Changes in cardiac rhythm and ECG morphology were prevented by CPZ.
Reference: Gilmour et al. (2004c) **Species:** Rat **Gender:** Male **Strain:** Wistar (Crl: WI) BR **Use:** 12 weeks acclimatization period: 2 weeks prior to exposure	ufCB or CB	**Route:** Inhalation using whole body exposure chambers. **Dose/Concentration:** ufCB 1.66 mg/m^3, fCB 1.40 mg/m^3 **Particle Size (Distribution):** Average median aerodynamic diameter: 114nm for ufCB, 268 nm for fCB. **Time to Analysis:** 7h exposure period. Animals were sacrificed and samples were taken at 0, 16, and 48h post-exposure.	Exposure to ultrafine, but not fine, CB particles was also associated w/ significant increases in the total number of blood leukocytes. Plasma fibrinogen factor VIII and vWF were unaffected by particle treatments as was plasma Trolox equivalent antioxidant status (TEAC).
Reference: Gilmour et al. (2005) **Species:** Human **Cell Types:** Primary Human Monocyte Derived Macrophages (MP), Human Umbilical Vein Endothelial Cells (HUVEC), Human Alveolar Type II Epithelial Cells (A549), Human Bronchial Epithelial Cells (16HBE)	PM_{10} (Carbon Black), H_2O_2, LPS	**Route:** Density; 0.15 x 10^6 cells/well in 24 wells plate (grown to 80% confluency) **Dose/Concentration:** PM_{10} (50 and 100μg/mL), H_2O_2 (100um), LPS 1μg/mL) **Particle Size (Distribution):** PM_{10} **Time to Analysis:** 6 and 20h	The culture media from MPs and 16HBE cells but not A549 cells, exposed to PM_{10} had an enhanced ability to cause clotting. H_2O_2 also increased clotting activity. Apoptosis was significantly increased in MPs exposed to PM_{10} and LPS as shown by annexin V binding. TF gene expression was enhanced in MPs exposed to PM_{10} and HUVEC tissue factor. tPA gene and protein expression were inhibited.
Reference: Gilmour et al. (2006) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 12-14 weeks **Weight:** 280–340 g	Zinc Sulfate ($ZnSO_4$) in saline solution	**Route:** Intratracheal Instillation **Dose/Concentration:** 131 μg/kg of bw (2 μmol/kg) **Particle Size (Distribution):** NR **Time to Analysis:** 1, 4, 24, 48h	At 1-24 h post-exposure, zinc plasma levels increased to nearly 20% above baseline. Cardiac tissues demonstrated similar temporal increases in expressions of TF, PAI-1 and thrombomodulin mRNA, following pulmonary instillation of Zn. Mild and focal acute, myocardial lesions developed in a few Zn exposed rats. No changes in fibrin deposition or troponin disappearance were observed. At 24 and 48h PE to Zn, increases occurred in levels of systemic fibrinogen an the activated partial thromboplastin time.

Study	Pollutant	Exposure	Effects
Reference: Gong et al. (2007) **Species:** Human and Mouse **Cell Type:** Human Aortic Endothelial Cells (HAEC) **Strain:** ApoE$^{-/-}$ (Mouse)	DEP ox-PAPC In vivo validation: UFPs, $PM_{2.5}$, FA	**Route:** Cell culture exposure in triplicate wells In vivo validation: liver tissue homogenates exposure **Dose/Concentration:** ox-PAPC: 10, 10, and 40 μg/mL DEP: 5, 15, and 25 μg/mL DEP (5 μg/mL)+ox-PAPC: 10 or 20 μg/mL In vivo validation: NR **Particle Size (Distribution):** UFPs: <0.18 μm; $PM_{2.5}$ **Time to Analysis:** 4h	Gene-expression profiling showed that both DEP extract and ox-PAPC co-regulated a large number of genes. U sinfg network analysis to identify co-expressed gene modules, led to the discovery of three modules that were highly enriched in genes that were differentially regulated by the stimuli. These modules were also enriched in synergistically co-regulated genes and pathways relevant to vascular inflammation. In vivo validation: results were validated in vivo by demonstrating that hypercholesterolemic mice exposed to ambient ultrafine particles inhibited significant upregulation of the module genes in the liver.
Reference: Goto et al. 2004 **Species:** Rabbit **Gender:** Female **Strains:** WHHL atherosclerotic and New Zealand White (NZW) non-atherosclerotic **Age:** NR **Weight:** 2.9 kg, WHHL; 2.5 kg, NZW	PM_{10} = EHC-93 (Canada	**Route:** intrapharyngeal instillation **Dose/Concentration:** EHC-93 median mean particle size 0.8 ± 0.4 μm (99 % <3 μm) **Particle Size (Distribution):** 5mg PM as 1 mL of a 5mg/mL solution **Time to Analysis:** twice a week for 4 weeks bone marrow labeling 24-h pre 6th instillation	**Lung Distribution of PM_{10}:** PM-containing AM were distributed diffusely. **Atherosclerosis:** Am positive for particles and volume fraction of vessels (measure of atherosclerosis) positively correlated. **Leukocytes in circulation:** PMN increased from 3rd wk of exposure. **Bone marrow labeling:** PM-exposed animals labeling peaked at 16 h as compared to 24-h for controls. The overall pool of bone marrow monocytes did not change, except for bone marrow mitotic pool of PMN-G1 cells. **Transit time of monocytes through the marrow:** Atherosclerotic rabbit have shorter transit times compared to nonsclerotic rabbits. PM exposure further decreased transit time.
Reference: Goto et al. 2004 **Species:** Rabbit **Gender:** Female **Strains:** NZW **Age:** NR **Weight:** 2.3 kg	PM_{10} = EHC-93 (Canada	**Route:** intrabronchial instillation **Dose/Concentration:** EHC-93 median mean particle size 0.8 ± 0.4 μm (99 % <3 μm) **Particle Size (Distribution):** 500 μg PM as 1 mL of a 500μg/mL solution **Time to Analysis:** BrdU iv at 0 h, single PM at 4 h, blood samples at 4 to 168 h	**Lung distribution of PM_{10}:** PM-containing AM were distributed diffusely. PM-containing AM were more prevalent in PM exposed animals. **Monocyte release from Bone Marrow:** PM exposure increased WBC and Band cell counts from 12-h after exposure. Monocuyte count was not affected. Labeled monocytes peaked quicker after DEP exposure (12h vs 16 h for control). No change in BM monocyte pool.
Reference: Goto et al. 2004 **Species:** Human and Mouse **Cell Type:** Human, alveolar macrophages from 2 females, 60.9 years avg (41-71 years) **Species:** Mouse **Gender:** Male **Strains:** BALF **n:**4	PM_{10} = EHC-93 (Canada	**Route:** 1.0 x 10^7 cells **Dose/Concentration:** EHC-93 median mean particle size 0.8 ± 0.4 μm (99 % <3 μm) **Particle Size (Distribution):** 100 μg PM/mL **Time to Analysis:** AM incubated for 24-h and then instilled as in 3091.1 at 0.6 mL/kg into rabbits	**Cytokine release:** PM increased release of GM-CSF, IL-6, IL-1β, TNF-α, IL-8 and MCP-1. No effect on m-CSF and MIP-1β. **Supernatant instillation:** DP exposed Am supernatant increased circulating WBC and Band cell counts. Circulating monocyted were unaffected. A major increase in fraction and amount of monocyte released --as well as faster clearance. Monocyte pool again was unaffected.
Reference: Graff et al. (2004) **Species:** Rat **Cell Type:** Ventricular Myocytes (Isolated from 1-day-old Sprague-Dawley Rats)	Zinc (Zn) and Vanadium (V)	**Route:** Approx. Density: 250,000 cells/cm^2. **Dose/Concentration:** 0, 6.25, 12.5, 25, or 50μM **Particle Size (Distribution):** NR **Time to Analysis:** Toxicity: 24 h **Beat Rate:** 0.5, 1, 2, 4, and 24 h **PCR:** 6 and 24 h	**BR:** There were statically significant reductions in spontaneous beat rate 4 and 24 h post-exposure (greater reductions were observed with Zn). **Inflammation:** Exposure to Zn or V (6.25-50 μM) for 6h produced significant increases in IL-6, IL-α, heat shock protein 70, and connexin 43 (Cx43). **Impulse Conduction:** 24 h post-exposure, Zn induced significant changes in the gene expression of Kv4.2 and KvQLt, α-1 subunit of L-type Ca channel, Cx43, IL-6, and IL-1α. V produced a greater effect on Cx43 and affected only KvLQT1.
Reference: Gunnison and Chen (2005) **Species:** Mouse **Gender:** Male **Strain:** F2 generation DK (ApoE$^{-/-}$, LDLr$^{-/-}$) **Age:** 18-20 weeks	CAPs (Tuxedo, NY), n = 3 Copollutants measured: O_3 and NO_2. Control: FA, n = 3	**Route:** Whole Body Inhalation **Dose/Concentration:** CAPs: 131 ± 99 μg/m^3 (range 13 - 441 μg/m^3) O_3: 10 ppb NO_2: 4.4 ppb **Particle Size (Distribution):** 389 ± 2 nm **Time to Analysis:** 6h/day, 5days/week for approximately 4 months. Tissue collection was performed 3-4 days after the last day of exposure.	In CAPs-exposed heart tissue, the expression of Limd1 and Rex3 were the most consistently affected genes among the exposed mice. Limd1 was down regulated by 1.5-fold or greater from moderate baseline expression. Rex3 showed a relatively small increase in absolute expression.

Study	Pollutant	Exposure	Effects
Reference: Gurgueira et al. (2002) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley (Pathogen-free) **Weight:** 250-300 g	CAPs; Carbon Black (CB): C (85.9 ± 0.2%), O (13 ± 0.2%), S (1.17 ± 0.02%); ROFA	**Route:** Whole Body Exposure Chamber **Dose/Concentration:** CAPs: average mass concentration: 300 ± 60 μg/m^3; ROFA: 1.7 mg/m^3; CB: 170 μg/m^3 **Particle Size (Distribution):** CAPs size range: 0.1-2.5 μm; CB and ROFA ($PM_{2.5}$) **Time to Analysis:** CAPs: 1, 3, and 5h; ROFA: 30 min; CB: 5h	**CAPs exposure:** Rats breathing CAPs aerosols for 5 h showed significant oxidative stress, determined as in situ chemiluminescence (CL) in the lung, heart, but not in the liver. ROFA also triggered increases in oxidant levels but not particle-free air or CB. Increases in CL showed strong associations w/ the CAPs content of Fe, Al, Si and Ti in the heart. The oxidant stress imposed by 5h exposure to CAPs was associated w/ slight, but significant increases in the lung and heart water content, with increased serum levels of lactate dehydrogenase, indicating mild damage to tissues. CAPs inhalation also led to tissue-specific increases in the activities of SOD and catalase.
Reference: Gursinsky et al. (2006) **Species:** Rat **Cell Type:** fibroblasts isolated from adult male Wistar rats hearts	Fly ash (TAF98)	**Route:** In vitro 7500 cells/cm^2 **Dose/Concentration:** TAF98: 0, 1, 2 3, 10, 25, 50, 100, 200 μg/mL **Particle Size (Distribution):** NR **Time to Analysis:** 0, 5, 10, 30, 60, 120 min	Brief treatment of fibroblasts w/ fly ash triggered the immediate formation of ROS. Using phosphospecific antibodies the activation of p38 MAP kinase, p44/42 MAP kinase (ERK1/2) and p70S6 kinase. Prolonged incubation w/ fly ash increased the expression of collagen 1 and TGF-β1, but decreased mRNA levels of MMP9 and TNF-α. Cell proliferation was inhibited at high concentrations of fly ash. An increase in the level of advanced glycation end product (AGE) modification of various cellular proteins was observed.
Reference: Hansen et al. (2007) **Species:** Mouse **Gender:** Female **Strain:** ApoE$^{-/-}$ and C57BL/6J ApoE$^{+/+}$ **Age:** 11-13 weeks (acclimatized for at least 1 week prior to experiments) **Use:** Aorta rings were used for in-vitro studies	DEP (DEP) SRM-2975 (NIST)	**Route:** Intraperitoneal Injection **Dose/Concentration:** ip injections of DEP suspended in saline: 0, 0.5 and 5 mg/kg of bw. n = 8 Aorta segments from unexposed mice were incubated with 0, 10 and 100 μg DEP/mL before measurement of vasomotor functions. **Particle Size (Distribution):** Aerosols with a geometric mean diameter of 215 nm generated from DEP. **Time to Analysis:** Exposed mice were sacrificed 1h after ip DEP injection.	**In-vivo:** Exposure to 0.5 mg/kg DEP caused a decrease in the endothelium-dependent Ach elicited vasorelaxation in ApoE$^{-/-}$ mice, whereas the response was enhanced in ApoE+/+ mice. No significant changes were observed after administration of 5 mg/kg DEP. K+ or phenylephrine induced constriction was not affected. In-vitro: Exposure to 100 μg DEP/mL enhanced ACh-induced relaxation and attenuated phenylephrine-induced constriction. Vasodilatation induced by sodium nitroprusside was not affected by any DEP exposure.
Reference: Harder et al. (2005) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 12-15 weeks (acclimatized for 14 days prior to exposure) **n:** 12, Telemetry; 24, BALF; 8, Cardiac Histology	Carbon UFPs; Karg et al. (1998)	**Route:** Whole-Body Exposure Chamber; Karg et al. (1998) **Dose/Concentration:** 180 μg/m^3 **Particle Size (Distribution):** Mean Particle Size: 37.6 ± 0.7nm **Time to Analysis:** Days 1-3: baseline reading, Day 4: exposure to UFPs or filtered air for 24 h, Days 5-7: recovery period (PE data collection)	**Cardiovascular Performance:** Mild but consistent increase in heart rate (HR), which was associated w/ a significant decrease in HR variability during exposure (particle-induced alteration of cardiac autonomic balance, mediated by a pulmonary receptor activation). Lung Inflammation and Acute-Phase Response: BALF revealed significant but low-grade pulmonary inflammation. Effects on Blood: There was no evidence of an inflamemation-mediated increase in blood coagulability; no changes in plasma fibrinogen or factor VIIa. Pulmonary and Cardiac Histopathology: Sporadic accumulation of particle-laden macrophages found in the alveolar region. No signs of cardiac inflammation or cardiomyopathy. mRNA Expression Levels: no significant changes in the lung and heart.
Reference: Hirano et al. (2003) **Species:** Rat **Cell Types:** Heart Microvessel Endothelial Cells (RHMVE)	Organic Extracts of DEP (OE-DEP) and Organic Extracts of Ultra Fine Particles (OE-UFP). Urawa City, Saitama, Japan in summer 2001.	**Route:** Cells exposed to OE-DEP and OE-UFP solutions in DMSO. **Dose/Concentration:** OE-DEP and OE-UFP: 40 μg/m^3 during sampling period. Final Concentrations in DMSO: 300 mg/mL (OE-DEP) and 500 mg/mL (OE-UFP). **Particle Size (Distribution):** OE-DEP and OE-UFP: <2.0 μm **Time to Analysis:** 24 h. The cell monolayer was exposed to 0, 1, 3, and 10 μg/mL OE-DEP for 6h.	**Cytotoxicity and Oxidative Stress:** LC50 values were 17 and 34 μg/mL for OE-DEP and OE-UFP respectively. The viability of OE-DEP and OE-UFP exposed cells was ameliorated by N-acetyl-L-cysteine (NAC). mRNA levels increased dose-dependently w/ OE-DEP and HO-1 mRNA showed the most marked response to OE-DEP. mRNA levels of antioxidant enzymes and heat shock protein 72 (HSP72) In OE-DEP-exposed cells were higher than OE-UFP exposed cells at the same concentration. The transcription levels of HO-1 and HSP72 in OE-DEP and OE-UFP-exposed cells, were also reduced by NAC.

Study	Pollutant	Exposure	Effects
Reference: Hwang et al. (2005) **Species:** Mouse **Strain:** Normal (C57) and ApoE$^{-/-}$	CAPs (Tuxedo, NY)	**Route:** Whole Body Inhalation **Dose/Concentration:** CAPs Range: 5-627 μg/m^3. Mean CAPs Concentration: 133μg/m^3. Mean Concentrations of Ozone and Nitrogen in CAPs: 10 and 4.4 ppb respectively. **Particle Size (Distribution):** 389 ± 2 nm **Time to Analysis:** 6h 5days/week, for 5 months.	**Long-term Analysis:** Significant decreasing patterns of heart rate (HR), body temperature (T), and physical activity (PA) in ApoE$^{-/-}$ mice. Nonsignificant changes for C57 mice. The chronic effect changes for HR, T, and PA for ApoE$^{-/-}$ mice were maximal in the last three weeks. **Short-term Analysis:** Dose-dependent relationship for HR variations in ApoE$^{-/-}$ mice. **Heart Rate Fluctuation:** HR fluctuations in Apo E$^{-/-}$ mice during the period of 3-6 h increased by 1.35 fold at the end of the exposure and during a 15 min period increases by 0.7 fold at the end of the exposure.
Reference: Inoue et al. (2006b) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7 weeks **n:** 29-33 g	DEP (DEP): Washed DEP (carbonaceous nuclei of DEP after extraction) and DEP-OC (organic chemicals in DEP extracted with CH2Cl2); Washed DEP+LPS and DEP-OC+LPS	**Route:** Intratracheal Instillation **Dose/Concentration:** Washed DEP: 4 mg/kg bw. DEP-OC: 4mg/kg bw. LPS: 2.5 mg/kg. Washed DEP+LPS and DEP-OC+LPS: respective additions of LPS to each component prior-experimentation. **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** Single dose. Animals sacrificed 24 h post instillation.	Both DEP components exacerbated vascular permeability. The increased fibrinogen and E-selectin levels induced by LPS. This exacerbation was more prominent w/ washed DEP than w/ DEP-OC. Washed DEP+LPS significantly decreased protein C and antithrombin-III and elevated circulatory levels of IL-6, KC and LPs w/o significance.
Reference: Ito et al. (2008) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto (Specific pathogen-free) **Age:** 12 weeks (13-14 weeks old at start of experiment) **Use:** Ex-vivo	CAPs (f-PM) from Inhalation Facility in Yokohama City, Japan. 5-6 rats/group	**Route:** Whole Body Inhalation **Dose/Concentration:** 0.6-1.5 mg/m^3 **Particle Size (Distribution):** 0.1-2.5 μm **Time to Analysis:** This study consisted of three exposure studies (May 2004, November 2004, September 2005). There were three time points for each season. Each exposure study lasted 4 consecutive days. Three groups of rats were exposed to either: (1) filtered air for 4 days, (2) filtered air for 3 days and CAPs for 1 day or (3) CAPs for 4 days. Animals were separated into the three groups evenly according to their mean blood pressure (MBP) the day prior to exposure, and were exposed for a maximum of 4.5h/day.	Messenger RNA expression and cardiovascular function were measured after a 4 day exposure. In samples of heart tissue, the mRNA of cytochrome P450 (CYP) 1B1; heme oxygenase-1 (HO-1); and endothelin A (ET_A) receptor, were up-regulated by CAPs; their levels were significantly correlated w/ the cumulative weight of CAPs in the exposure chamber. The up-regulation of ET_A receptor mRNA was significantly correlated w/ the increase in HO-1 mRNA and weakly w/ the increase in MBP.
Reference: Khandoga et al. (2004) **Species:** Mouse **Gender:** Female **Strain:** C57B1/6 **Age:** 5-7 weeks	UFPs: Ultra fine carbon black particles (Printex 90)	**Route:** Aortic Infusion **Dose/Concentration:** 1 x 10^7 and 5 x 10^7 total particles infused **Particle Size (Distribution):** 14 nm diameter, 60 % <100nm 300 m^2/g surface area **Time to Analysis:** Single exposure, analysis 2-h post exposure	Application of UFPs caused significantly enhanced platelet accumulation on endothelium of postsinusodal venules and sinusoids in healthy mice. UFP-induced platelet adhesion was not preceded by platelet rolling but was strongly associated w/ fibrin deposition and an increase in vWF expression on the endothelial surface. In contrast, inflammatory parameters such as the number of rolling/adherent leukocytes, P-selectin expression/translocation, and the number of apoptotic cells were not elevated. UFPs did not affect sinusoidal perfusion and Kupffer cell function.
Reference: Knuckles et al. (2007) **Species:** Rat **Gender:** Female (Pregnant, purchased at gestation day 19) **Strain** Sprague-Dawley**:** **Age:** 60-90 days **Weight:** 300 g **Use:** 1-day-old neonatal pups were harvested from these animals and RMCs were obtained using the neonatal rat cardiomyocyte isolation kit	ROFA-L: Leachate	**Route:** Cell count: 170, 000 cells/cm^2 **Dose/Concentration:** 3.5 μg/mL **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 1 hour	38 genes were suppressed and 44 genes were induced PE. Genomic alterations in pathways related to IGF-1, VEGF, IL-2, PI3/AKT, CVD, and free radical scavenging were detected. Global gene expression was altered in a manner consistent w/ cardiac myocyte electrophysiological remodeling, cellular oxidative stress and apoptosis. ROFA-L altered the transcription factor proteome by suppressing activity of 24 and activating 40 transcription factors out of 149.

Study	Pollutant	Exposure	Effects
Reference: Kodavanti et al. (2008) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto (WKY) **Age:** 12-14 weeks n = 8/group	G1: saline (control); G2: Mount Saint Helen's ash (SH); G3: whole suspension of oil combustion PM at high concentration (PM-HD); G4: whole suspension of oil combustion PM at low concentration (PM-LD); G5: saline-leachable fraction of PM high-concentration suspension; G6: ZnS 7H20	**Route:** Intratracheal Instillation **Dose/Concentration:** Doses (mg/kg/week) are for 8 and 16 weeks (PM-solid and soluble Zn) respectively. G1: 0.00-0.00 and 0.00-0.00; G2: 4.60-0.00 and 2.30-0.00; G3: 4.60-66.8 and 2.30-33.4; G4: 2.30-33.4 and 1.15-16.7; G5: 0.00-66.8 and 0.00-33.4; G6: 0.00-66.8 and 0.00-33.4 **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 1x/week for 8 or 16 weeks; 48 h after last instillation.	**DNA damage (left ventricular tissue):** all groups except MSH caused varying degrees of damage relative to control. Total cardiac aconitase activity was inhibited in rats receiving soluble Zn. Analysis of heart tissue revealed modest changes in mRNA for genes involved in signaling, ion channels function, oxidative stress, mitochondrial fatty acid metabolism, and cell cycle regulation in Zn, but not MSH-exposed rats.
Reference: Kyoso et al. (2005) **Species:** Rat **Gender:** **Strain:** **Age:** 15 months **n:**40	DE PM and NO_X exposures	**Route:** Whole Body **Dose/Concentration:** PM (mg/m^3): 0.01, 0.109, 0.54, 1.09, 0.01 (from 1.09 concentration w/o PM) NO_X (ppm): 0.19, 0.59, 2.60, 5.53, 5.47 **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 7 months, daily (between 5pm and 9am)	All of the resting R-R intervals before exposure were lower at night than during the day, but few changes were found after exposure.
Reference: Lei et al. (2005) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Weight:** 200-250g (upon arrival) **n:** 16 **Use:** ip STZ (60 mg/kg bw) dissolved in citric acid buffer administered to 8 rats to induce diabetes; ip citric acid buffer administered to 8 non-diabetic rats	CAPs: Hsin-Chuang, Taipei	**Route:** Intratracheal Instillation **Dose/Concentration:** $PM_{2.5}$: 200 µg. Components ($\mu g/m^3$): Organic Carbon (9.8-SD 2.4)), Elemental Carbon (3.6-SD 3.2), Sulfate (4.8-SD 1.2), Nitrate (6.3-SD 3.4) **Particle Size (Distribution):** PM: 0.01 - 2.5 µm **Time to Analysis:** Single dose. Animals sacrificed 24 h post instillation.	**Effects of Diabetes:** BW of diabetic (D) rats (397.5g) was lower than non-diabetic (ND) rats (483.1g). Mean plasma glucose level was 163 mg/dL in ND rats and 448.2 mg/dL in D rats. D rats had significant greater levels of 8-OHdG in plasma compared to ND rats. D rats had significantly increased levels of plasma [nitrate+nitrite]. No observable changes in TNF-α for D and ND rats. **Effects of PM Exposure ND Rats:** Increase in plasma levels of 8-OHdG and plasma IL-6, TNF-α, and serum CRP. Significant reduction of plasma [nitrate+nitrite]. No significant effect on plasma ET-1. **Effects of PM Exposure STZ-D Rats**: Significant elevation of plasma ET-1. Decrease in plasma [nitrate+nitrite] Plasma 8-OHdG and TNF-α significantly increased. No significant alterations in IL-6 and CRP.

Study	Pollutant	Exposure	Effects
Reference: Lemos et al. (2006) **Species:** Mouse **Gender:** **Strain:** BALB/c **Age:** 1 day (neonatal) **n:** 10 **Weight:** 4-6g **Use:** Neonates were randomly placed w/ their mothers into ambient air (non-filtered/n = 20) or clean air (filtered/n = 20) chambers. After weaning the animals were separated and only males continued in the exposure chambers. After completing exposure the weight for control animals was 26.33 ± 2.82g and for exposed animals was 26.14 ± 1.98g.	PM_{10}, CO, NO_2, and SO_2 from Universidade de Sao Paulo, Brazil.	**Route:** Inhalation using whole body exposure chambers. **Dose/Concentration:** Mean (± SD) concentrations were: CO_2: 2.06 ± 0.08 ppm (8-h mean); NO_2: 104.75 ± 42.62 μg/m^3 (24-h mean); SO_2: 11.07 ± 5.32 μg/m^3 (24-h mean); PM_{10}: 35.52 ± 12.84 μg/m^3 (24-h mean) **Particle Size (Distribution):** PM_{10} **Time to Analysis:** 24 h/day; 7 days/week; 4 months	Morphometric measurements of the ratio between the lumen and the wall (L/W) areas were performed on transverse sections of renal, pulmonary and coronary arteries. A significant decrease of L/W w/ exposure to air pollution was detected in pulmonary, and coronary arteries, whereas no effects of air pollution were observed in renal vessels.
Reference: Li et al. (2005) **Species:** Rat **Tissues/Cell Types:** Pulmonary Artery Rings (PARs) from Sprague Dawley Rats, 200-350g. Cultured HPAECs	Urban Particles (UPs [SRM 1648]) Major Constituents (mass fraction): Al (3.4), Fe (3.9), K (1.1). Minor Constituents (mass fraction): Na (0.43), Pb (0.66), Zn (0.48). Trace Constituents (ng/mg): As (115), Cd (75), Cr (403), Cu (609), Mg (786), Ni (82), Se (27), U (5.5), V (127).	**Route:** PARs: In-vitro organ model HPAECs: grown to 80% confluence **Dose/Concentration:** Dose Concentrations: from 1 to 100 μg/mL for PARs and HPAECs. Losartan treatment: 0.2 μmol Captopril treatment: 100 μmol **Particle Size (Distribution):** NR **Time to Analysis:** PARs were exposed to increasing doses of UPs from 1 to 100 μg/mL. Maximum tension was recorded within 5 min after each UPs dose. HPAECs: exposed to UPs from 1 to 100 μg/mL for up to 20 min	Effects of UPs on the constriction of isolated rat pulmonary PARs and the activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2) and p38 mitogen-activated protein kinases (MAPKs) in HPAECs w/ or w/o Losartan at 1-100 μg/mL induced acute vasoconstriction. UPs also produced a time- and dose-dependent increase in phosphorylation of ERK1/2 and p38 MAPK. Losartan pre-treatment inhibited both vasoconstriction and activation of ERK1/2 and p38. The water soluble fraction of UPs was sufficient for inducing ERK1/2 and p38 phosphorylation, which was also inhibited by Losartan. Cu ($CuSO_4$) and V ($VOSO_4$), induced pulmonary vasoconstriction and phosphorylation of ERK1/2 and p38, but only phosphorylation of p38 was inhibited by Losartan. UPs induced activation of ERK1/2 and p38 was attenuated by Captopril.

Study	Pollutant	Exposure	Effects
Reference: Li et al. (2006) **Species:** Rat and Rabbit **Tissues/Cell Types:** Pulmonary Artery Rings (PARs) from Sprague Dawley Rats, 200-350g. Cultured HPAECs	Urban Particles (UPs [SRM 1648]). Major Constituents (mass fraction): Al (3.4), Fe (3.9), K (1.1). Minor Constituents (mass fraction): Na (0.43), Pb (0.66), Zn (0.48). Trace Constituents (ng/mg): As (115), Cd (76), Cr (403), Cu (609), Mg (786), Ni (82), Se (27), U (5.5), V (127).	**Route:** In-vitro **Dose/Concentration:** Dose Concentrations: from 1 to 100 μg/mL for PARs and HPAECs. Treatment was given 15 min prior exposure for PARs **Particle Size (Distribution):** NR **Time to Analysis:** PARs were exposed to increasing doses of UPs from 1 to 100 μg/mL. Maximum tension was recorded within 5 min after each UPs dose. HPAECs: exposed to UPs from 1 to 100 μg/mL for 20 and 120 min.	Within minutes after UPs treatment, HPAEC increased H_2O_2 production that could be inhibited by DPI, APO, and NaN_3. The water soluble fraction of UPs as well as its two transition metal components Cu and V, also stimulated H_2O_2 production. NaN_3 inhibited H_2O_2 production stimulated by Cu and V, whereas DPI and APO inhibited only Cu-stimulated H_2O_2 production. Inhibitors of other H_2O_2-producing enzymes, including N-methyl-L-arginine, indomethacin, allopurinol, cimetidine, rotenone, and antimycin, had no effects. DPI but not NaN_3 attenuated UPs-induced pulmonary vasoconstriction and phosphorylation of ERK1/2 and p38 MAPKs. Knockdown of p47phox gene expression by small interfering RNA attenuated UPs-induced H_2O_2 production and phosphorylation of ERK1/2 and p38 MAPKs.
Reference: Lippmann et al. (2005) **Species:** Mouse **Strain:** C57 and ApoE$^{-/-}$	(March-September 2003). Chemical Composition: regional secondary sulfate (SS) characterized by high S, Si, and organic C; resuspended soil (RS) characterized by high concentrations of Ca, Fe, Al, and Si; RO-fired powered emissions of the Eastern U.S. identified by the presence of V, Ni, and Se; and motor vehicle (MV) traffic and other sources. Contributors to Average Mass: SS (56.1%), RS (11.7%), RO combustion (1.4%), MV traffic and other sources (30.9%)	**Route:** Whole Body Inhalation **Dose/Concentration:** $PM_{2.5}$ concentrated ten-fold, producing an average of 113 μg/m^3 **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 5 months study. 6h/day, 5d/week exposures. Daily time periods: during exposure, the afternoon after exposure, and late at night	**Associations b/w sources and short-term HR changes**: There were no significant associations b/w SS, RS, RO, and MV factors and HR in C57 mice at any of the three intervals. There were significant associations b/w $PM_{2.5}$ and the RS source factor and decreases in HR for the ApoE$^{-/-}$ mice during the daily CAPs exposures but no associations w/ the other factors. There was no residual association of HR with $PM_{2.5}$ or the RS factor later in the afternoon or late at night. In the afternoon, there was a significant association b/w decreases in HR and the SS factor for the ApoE$^{-/-}$ mice that had not been present during exposure and did not persist into the night time period. MV traffic and others were not significantly associated w/ HR during any of these three time periods. For the C57 mice, there were no significant associations of HR w/ $PM_{2.5}$ or any of its components during any of the three daily time periods. **Associations b/w sources and short-term HRV changes:** There was too much signal noise during the exposures to permit reliable analyses of HRV changes during the hours of CAP exposure.
Reference: Lippmann et al. (2006) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 6 weeks	CAPs from Tuxedo, NY. Component of interest: Ni.	**Route:** Whole Body Inhalation **Dose/Concentration:** Average daily CAPs: 85.6 μg/m^3 Average daily Ni: 43 ng/m^3 **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 6h/day, 5d/week, for 6 months (July 2004-January 2005). Ten-second ECG, HR, activity, and body temperature data were sampled every 5 min for the duration of the experiment.	For the CAPs-exposed mice, on 14 days there were Ni peaks at approximately 175 ng/m^3 and usually low CAPs and V. For those days back-trajectory analysis identified a remote Ni point source. ECG measurements on CAPs-exposed and sham-exposed mice showed Ni to be significantly associated with acute changes in HR and HRV.

Study	Pollutant	Exposure	Effects
Reference: Lund et al. (2007) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 10 weeks **Use:** Mice were placed on a high fat at the beginning of the exposure. In-vivo exposure, and ex-vivo collection of aortas and plasma.	Gasoline emissions. Engines fueled with conventional unleaded, non-oxygenated gasoline. PM, NO_X, CO, and HC. Control: Filtered Air (FA)	**Route:** Whole Body Inhalation **Dose/Concentration:** FA: PM (2 μg/m^3), NO_X (0 ppm), CO (0.1 ppm), HC (0.1 ppm); Low (1: 90): PM (8 μg/m^3), NO_X (2 ppm), CO (9 ppm), HC (0.9 ppm); Mid (1: 20): PM (39 μg/m^3), NO_X (12 ppm), CO (50 ppm), HC (8.4 ppm); High (1: 12): PM (61 μg/m^3), NO_X (19 ppm), CO (80 ppm), HC (12 ppm); High-filtered: PM (2 μg/m^3), NO_X (18 ppm), CO (80 ppm), HC (12.7 ppm). **Particle Size (Distribution):** NR **Time to Analysis:** 6h/day, 7d/week for 7 weeks. Mice were sacrificed within 16h PE. During the study period all animals were concurrently exposed to the following: FA: 8 μg/m^3 (n = 8) and 40 μg/m^3 (n = 8); PM Whole Exhaust: 60 μg/m^3 (n = 16); or Filtered Exhaust w/ gases matching the 60 μg/m^3 concentration (n = 16)	Inhalation exposure to gasoline engine emissions resulted in increased aortic mRNA expression of matrix metalloproteinase-3 (MMP-3), MMP-7, and MMP-9, tissue inhibitor of MMP-2, ET-1 and HO-1 in ApoE$^{-/-}$ mice; increased aortic MMP-9 protein levels were confirmed through immunochemistry. Elevated ROS were also observed in arteries from exposed animals, despite absence of plasma markers. Similar findings were also observed in the aortas ApoE$^{-/-}$ mice exposed to particle filtered atmosphere, implicating the gaseous components of the whole exhaust in mediating the expression of markers associated w/ vasculopathy.
Reference: Montiel-Davalos et al. (2007) **Species:** Human **Cell Types:** HUVEC (from primary human endothelial cells) and U937 (human leukemia pro-monocytic) cell cultures.	$PM_{2.5}$ and PM_{10} from Mexico City	**Route:** In-vitro exposure. **Dose/Concentration:** HUVEC cell cultures exposed to TNF-α (10 ng/mL), and to a range of PM that comprised 5, 10, 20, and 40 μg/cm^2 concentrations. **Particle Size (Distribution):** $PM_{2.5}$ PM_1 **Time to Analysis:** 6 or 24 h (early and late adhesion molecules respectively)	Results showed that both $PM_{2.5}$ and PM_{10} induced the adhesion of U937 cells to HUVEC, and their maximal effect was observed at 20 μg/cm^2. This adhesion was associated w/ an increase in the expression of all adhesion molecules evaluated for PM_{10}, and E-selectin, P-selectin, and ICAM-1 for $PM_{2.5}$. In general the maximum expression of adhesion molecules induced by $PM_{2.5}$ and PM_{10} was obtained w/ 20 μg/cm^2; however PM_{10}-induced expression was observed from 5 μg/cm^2. E-selectin and ICAM-1 had the strongest expression in response to particles.
Reference: Moyer et al. (2002) **Species:** Mouse **Gender:** Male and Female **Strain:** B6C3F1	In phosphide, Co sulfate heptahydrate, V pentoxide, Ga arsenide, Ni oxide, Ni subsulfide, Ni sulfate hexahydrate, talc, and Mo trioxide	**Route:** Inhalation **Dose/Concentration:** High-Dose Concentration in Chronic Studies, Male (μg/m^3): In phosphide: 0.3 (n = 60), Co sulfate heptahydrate: 3.0 (n = 50), V pentoxide: 4.0 (n = 50), Ga arsenide: 1.0 (n = 50) High-Dose Concentration in Sub-Chronic Studies, Male or Female (μg/m^3): In phosphide: 100 (n = 10), Co sulfate heptahydrate: 30 (n = 10), V pentoxide: 16 (n = 10), Ga arsenide: 75 (n = 10) **Particle Size (Distribution):** MMAD particle size (μm): In phosphide (1.1-1.3), Co sulfate heptahydrate: (1.5-1.8), V pentoxide: (1.0), Ga arsenide: (1.0) **Time to Analysis:** Phase One: Evaluation of heart, kidney and lung tissues from all control and high dose male B6C3F1 mice exposed by inhalation to 9 particulate compounds for a 2 year period. Phase Two: evaluated heart, lung, kidney and mesentery tissues of control and high dose male and female B6C3F1 mice from the 90-day studies of the 4-compounds demonstrating arteritis after a 2-year period.	Phase One: High-dose males developed significantly increased incidences of arteritis over controls in 2 of the 9 studies (In phosphide and Co sulfate heptahydrate), while marginal increases of arteritis were detected in 2 additional studies (Va pentoxide and Ga arsenide). In contrast, arteritis of the muscular arteries of the lung was not observed. Morphological features of arteritis in these studies included an influx of mixed inflammatory cells including neutrophils, lymphocytes, and macrophages. partial and complete effacement of the normal vascular wall architecture, often w/ the extension of the inflammatory process into the periarterial connective tissue, was observed. Phase Two: Results showed that arteritis did not develop in the 90-day studies, suggesting that long-term chronic exposure to lower-dose metallic PM may be necessary to induce or exacerbate arteritis.
Reference: Mutlu et al. (2007) **Species:** Mouse **Gender:** Male **Strain:** 57BL/6 (IL6$^{+/+}$ and IL6$^{-/-}$) **Age:** 6-8 weeks **Weight:** 20-25 g	PM_{10} from ambient air in Düsseldorf, Germany	**Route:** Intratracheal Instillation **Dose/Concentration:** 10 μg PM_{10}. For alveolar macrophage depletion, 120 mg clodronate was instilled into the mice lungs following endotracheal intubation 48h prior to instillation of PM. **Particle Size (Distribution):** PM_{10} **Time to Analysis:** 24 h post-exposure.	Mice treated w/ PM_{10} exhibited a shortened bleeding time, decreased prothrombin and partial thromboplastin times (decreased plasma clothing times), increased levels of fibrinogen, and increased activity of factors II, VIII, and X. This prothrombotic tendency was associated w/ increased generation of intravascular thrombin, an acceleration of arterial thrombosis, and an increase in BALF concentration of prothrombotic IL-6. IL-6$^{-/-}$ mice were protected against PM-induced intravascular thrombin formation and the acceleration of arterial thrombosis. Depletion of macrophages by the intratracheal administration of liposomal clodronate attenuated PM-induced IL-6 production and the resultant prothrombotic tendency.

Study	Pollutant	Exposure	Effects
Reference: Nadziejko et al. (2002) **Species:** Rat **Gender:** Male **Strain:** SH Wistar Kyoto **Age:** 16 weeks	CAPs ($PM_{2.5}$) from Tuxedo, NY. SO_2, NO_2 O_3 and NH_3 were removed prior to exposure. H_2SO_4 (fine and ultrafine)	**Route:** Nose-Only Inhalation **Dose/Concentration:** CAPs (02-05/2001): 80 and 66 μg/m³ (avg 73); Fine H_2SO_4 (06-07/2001): 299, 280, 119, and 203 μg/m³ (avg 225); Ultrafine H_2SO_4 (07-08/2001): 140, 565, 416, 750 μg/m³ (avg 468) **Particle Size (Distribution):** Ultrafine H_2SO_4 mass median diameter: 50-75 nm **Time to Analysis:** 4 h/exposure	Exposure to CAPs caused a striking decrease in respiratory rate that was apparent soon after the start of exposure and stopped when exposure to CAPs ceased. The decrease in respiratory rate was accompanied by a decrease in HR. Exposure of the same animals to fine-particle-size sulfuric acid aerosol also caused a significant decrease in respiratory rate similar to the effect of CAPs. Ultrafine acid had the opposite effect on respiratory rate compared to CAPs.
Reference: Nadziejko et al. (2004) **Species:** Rat **Gender:** Male **Strain:** F344 **Age:** 18 months old at the start of the experiment **n:** 12	PM/CAPs (Tuxedo, NY) UFC (lab generated), SO_2	**Route:** Nose-Only Inhalation **Dose/Concentration:** PM (μg/m³): 161-200, avg. 180; UFC (μg/m³): 500-1280, avg. 890; SO_2 (ppm): 1.2, 1.2, 1.2, 1.2, avg. 1.2 **Particle Size (Distribution):** PM (Size Range): 0.5-2.5um; UFC (MMAD): 30-50nm **Time to Analysis:** A total of 8 exposures were performed: 2 exposures to CAPs, 2 exposures to UFC, 4 exposures to SO_2. All three pollutants were tested w/ a crossover design so that each group alternated exposure to air and to pollutant. Exposures lasted 4h and were performed at least 1 week apart.	Old F344 rats had many spontaneous arrhythmias. There was a significant increase in the frequency of irregular and delayed beats after exposure to CAPs. The same rats were subsequently exposed to UFC, SO_2 or air w/repeated crossover design. In these experiments there was no significant change in the frequency of any category of spontaneous arrhythmia following exposure to UFC or SO_2.
Reference: Nemmar et al. (2008) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Weight:** 440 ± 14 g **n:** 5-6/group	DEP (SRM 2975)	**Route:** Intravenous via the tail vein **Dose/Concentration:** DEP: 0.02 mg or 0.1 mg DEP/kg (corresponding to about 8 μg or 44 μg DEP/rat **Particle Size (Distribution):** <1 μm **Time to Analysis:** 48h following systemic administration of saline or DEP	Intravenous administration of DEP (0.1 mg/kg) triggered systemic inflammation characterized by an increase in monocyte an granulocyte numbers. Both doses of DEP caused a reduction of RBC numbers and hemoglobin concentration. TEM analysis of RBC safter in vitro incubation (5 μg/mL) or in vivo administration of DEP, revealed the presence of ultrafine-sized aggregates of DEP within the RBC. Larger aggregates were also taken up by the RBC. The myocardial morphology and capillary bed were not affected by DEP exposure.
Reference: Nemmar et al. (2007) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 16 weeks **Weight:** 424 ± 8 g	DEP (SRM 2975)	**Route:** Tail Vein Injection **Dose/Concentration:** 150ul of vehicle or doses of 0.02, 0.1, or 0.5 mg/kg bw corresponding to approximately 8, 42, or 212 μg DEP/rat **Particle Size (Distribution):** NR **Time to Analysis:** 24 h	**Effect of DEP on Blood Pressure:** Significant decrease on BP in DEP-exposed rats at doses of 0.02 mg/kg bw, compared w/ mean BP observed in controls. **Effect of DEP onHR**: Doses of 0.02, 0.1, and 0.5 mg/kg bw in rats, resulted in significant reduction oh HR compared to controls. **Effect of DEP on Tail Bleeding Time:** Shortening of tail bleeding time in rats exposed to 0.02, 0.1, and 0.5 mg/kg bw. The shortening was significant at the dose of 0.02 and 0.5 mg/kg compared w/ controls. Platelet counts in blood did not significantly increased post-DEP administration. **Effect of DEP on WBC and RBC numbers:** No significant effect of DEP at doses of 0.02, 0.1 and 0.5 mg/kg on the numbers of granulocytes, monocytes, or lymphocytes compared w/ control.
Reference: Nemmar et al. (2003c) **Species:** Hamster **Gender:** Male and Female **Weight:** 100-110 g	DEP (SRM 1650)	**Route:** Intratracheal Instillation **Dose/Concentration:** 120 ul of vehicle or DEPs (5, 50, or 500 μg/animal) **Particle Size (Distribution):** NR **Time to Analysis:** In-vivo: formation and embolization of thrombus were continuously monitored for 40 min. Ex-vivo: animals were intratracheally instilled w/ DEPs (0 or 50 μg per animal), and blood was collected 5, 15, 30, and 60 min post-instillation. In-vitro: Saline or saline-containing DEPs (0.1, 0.5, 1, and 5 μg/mL) was added to venous blood from untreated hamsters, and closure time was measured in the PFA-100 after 5 min/animal.	Doses of 5 – 500 μg enhanced experimental arterial and venous platelet-rich thrombus formation in-vivo. Blood samples taken from hamsters 30 and 60 min after instillation of 50 μg of DEPs yielded accelerated aperture closure (platelet activation) ex-vivo, when analyzed in the PFA-100. The direct addition of as little as 0.5 μg/mL DEPs to untreated hamster blood significantly shortened closure time in vitro.

Study	Pollutant	Exposure	Effects
Reference: Nemmar et al. (2004) **Species:** Hamster **Gender:** Male and Female **Weight:** 100-110 g	DEP (SRM 1650); Positively Charged Polystyrene Particles (PCPSP)	**Route:** Intratracheal Instillation **Dose/Concentration:** Vehicle: 120 ul, DEP: 50 μg/animal, or PCPSP: 500 μg/animal **Particle Size (Distribution):** SRM 1650 PCPSP: 400 nm **Time to Analysis:** Pretreatment Phase: Hamsters were pretreated w/ Dexametasone IP (5 mg/kg) or IT (0.1 or 0.5 mg/kg) or Sodium Cromoglycate given IP (40 mg/kg), 1h before DEP or vehicle instillation. Thrombosis: In-vivo thrombogenesis assessed 24 h post-instillation of DEP or vehicle.	DEP increased thrombosis w/o elevating plasma vWF. The IT instillation of PCPSP equally produced histamine release and enhanced thrombosis. Histamine in plasma resulted from basophil activation. IP pretreatment w/ Dexametasone abolished the DEP-induced histamine increase in BALF and plasma and abrogated airway inflammation and thrombogenicity. The IT pretreatment with Dexametasone showed a partial but parallel inhibition of all these parameters. Pretreatment w/ Sodium Cromoglycate strongly inhibited thrombogenicity, and histamine release.
Reference: Nemmar et al. (2003b) **Species:** Hamster **Gender:** Male and Female **Weight:** 100-110 g	Ultrafine Particles: Unmodified Polystyrene Particles (UPSPs); Negatively Charged Carboxylate-Modified Polystyrene Particles (NCC-MPSPs); Positively-Charged Amine Modified Polystyrene Particles (PCA-MPSPs)	**Route:** Intratracheal Instillation **Dose/Concentration:** 5, 50, and 500 μg/animal in 120ul saline **Particle Size (Distribution):** UPSPs: 60nm; NCC-MPSPs: 60nm; PCA-MPSPs: 60 or 400 nm **Time to Analysis:** 1h PI	Unmodified and negative UFPs did not modify thrombosis. Positive UFPs increased thrombosis at 500 μg/animal and at 50 μg/animal, but not at 5 μg/animal. Positive 400 nm particles (500 μg/animal) did not affect thrombosis. PFA-100 analysis showed that platelets were activated by the in-vitro addition of positive UFPs and 400 nm particles to blood.
Reference: Nemmar et al. (2003a) **Species:** Hamster **Weight:** 100-110 g	DEP (SRM 1650)	**Route:** Intratracheal Instillation **Dose/Concentration:** 50 μg/animal in 120 ul saline **Particle Size (Distribution):** NR **Time to Analysis:** 1, 3, 6, and 24 h	At 1, 6, and 24 h after instillation of 50 μg DEPs per hamster, the mean size of in-vivo induced and quantified venous thrombosis was increased by 480, 770, and 460%, respectively. Platelets activation in blood was confirmed by a shortened closure time in the PFA-100 analyzer. In plasma, histamine was increased only at 6 and 24 h. Pre-treatment w/ a H1 receptor antagonist (diphenhydramine, 30 mg/kg intraperitoneally) didn't affect DEP-induced thrombosis or platelet activation at 1 h, however both were markedly reduced at 6 and 24 h.
Reference: Niwa et al. (2007) **Species:** Mouse **Gender:** Male **Strain:** LDLR/KO **Age (n), Use:** 6 weeks (n = 20), used in the intratracheal CB dispersion investigation 10-14 weeks (n = 10), used in acute effect of CB dispersion on circulating CRP study	Carbon Black	**Route:** Intratracheal Dispersion **Dose/Concentration:** Intratracheal CB Dispersion Study: 1 mg per animal/week; Acute Effect of CB Dispersion on Circulating CRP Study: 1mg/animal (single administration) **Particle Size (Distribution):** 23-470nm (mean size 120.7nm) **Time to Analysis:** **Intratracheal CB Dispersion Study:** 1 time/week for 10 weeks; **Acute Effect of CB Dispersion on Circulating CRP Study:** single CB administration, blood samples collected 24 h post-administration	**Intratracheal CB Dispersion Study:** Although no difference in bw between the four groups was observed at baseline, and all mice experienced an increase in bw w/ advancing age, the mice treated w/ CB tended to be smaller than those treated w/ vehicle (air). No significant differences were observed in cholesterol and TG levels among the for groups. Development of aortic lipid-rich lesions occurred in mice under a 0.51% cholesterol diet w/ or w/o CB infusion, but not in the mice fed a 0% cholesterol diet. **Acute Effect of CB Dispersion on Circulating CRP Study:** Circulating levels of CRP were significantly higher in mice exposed to CB versus those exposed to air, indicating an acute inflammatory response. Although the presence of CB in pulmonary macrophage-like cells in CB treated mice under 0.51% cholesterol diet was confirmed, CB was not detected in aortas, livers, kidneys, or spleens.
Reference: Niwa et al. (2007) **Species:** Mouse **Cell Types:** Macrophages Cell Lines (RAW264.7)	Carbon Black (CB); Water-Soluble Fullerene (C60(OH)24); Fluoresbrite Carboxylate Microspheres; Ox-LDL; Acetylated-LDL	**Route:** In vitro **Dose/Concentration:** CB: 1, 10, 100 μg/mL; $C_{60}(OH)_{24}$: 20, 100 ng/mL **Particle Size (Distribution):** Carbon Black and $C_{60}(OH)_{24}$: Fluoresbrite Carboxylate Microspheres: 6 nm **Time to Analysis:** RAW264.7+CB (0, 1, 10, 100 μg/mL) for 24 h, 13d, and 50d; RAW264.7+C60(OH)24 (0 and 20 ng/mL) for 24 h or 10d; RAW264.7+C60(OH)24m (0, 20, and 100 ng/mL) for 8d, then co-treated w/ Ox-LDL (100 ng/mL) for an additional 48h; RAW264.7+Ox-LDL (100 ng/mL) for 5d, and then co-cultured w/ C60(OH)24 (0, 20, and 100 ng/mL) for an additional 48h; RAW264.7+ 6nm beads: 3d, the Ox-LDL or acetylated-LDL added for 24 h	CB alone had no significant effects on RAW264.7 cell growth. C60(OH)24 alone or CB and C60(OH)24 together w/ Ox-LDL induced cytotoxic morphological changes, such as Ox-LDL uptake-induced foam cell-like formation and decreased cell growth, in a dose-dependent manner. C60(OH)24 induced LOX-1 protein expression, pro-matrix metalloprotease-9 protein secretion, and tissue factor mRNA expression in lipid-laden macrophages. Although CB or C60(OH)24 alone did not induce platelet aggregation, C60(OH)24 facilitated ADP-induced platelet aggregation. C60(OH)24 also acted as a competitive inhibitor of ADP receptor antagonists in ADP-mediated platelet aggregation.

Study	Pollutant	Exposure	Effects
Reference: Niwa et al. (2008) **Species:** Rat **Strain:** Sprague-Dawley **Age:** 6 weeks **n:** 25, CB treated group; 25, FA treated group	CB from Kyoto, Japan	**Route:** Inhalation **Dose/Concentration:** 15.6 ± 3.5 mg/m^3 **Particle Size (Distribution):** Mean size (nm) ± SD determined at 1, 8, 15, 22, and 29 days post-exposure was 118.1 ± 2.4, 119.1 ± 2.7, 122.2 ± 2.0, 122.4 ± 2.5 and 121.0 ± 3.6 respectively **Time to Analysis:** 6h/day, 5days/week, for a total of 4 weeks. BP and HR were measured by tail-cuff plethysmography at 1, 14, and 28 days post -exposure. At 1, 7, 14, 28, and 30 days post-exposure, 5 rats from each groups were killed. Blood was collected directly from the abdominal aorta; liver lungs, aorta and spleen were removed.	Although the presence of CB was confirmed in pulmonary macrophages, electron microscopic survey did not detect CB in other tissues including, liver, spleen and aorta. CB exposure raised blood pressure levels in a exposure-time dependent manner. Levels of circulating inflammatory marker proteins, including monocyte chemo attractant protein-1, IL-6, andCRP, were higher in the CB treated groups than in control groups.
Reference: Nurkiewicz et al. (2004) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Age:** 7-8 weeks	ROFA from Everett, MA The major metal contaminants were Fe, Al, V, Ni, Ca, and Z. The main soluble metals were Al, Ni, and Ca.	**Route:** Intratacheal instillation **Dose/Concentration:** ROFA group: 0.1, 0.25, 1, or 2 mg/rat. Vehicle control group: 300 ul saline. Particle control group: TiO_2 0.25 mg/rat. **Particle Size (Distribution):** ROFA mean count diameter: 2.2 µm **Time to Analysis:** After single IT instillation of a particular dose, all rats recovered for 24 h.	**Saline Treated Rats:** A23187 dilated arterioles up to 72 ± 7% max. **ROFA and TiO_2 Exposed Rats:** A23187-induced dilation was significantly attenuated. **Sensitivity of Arteriolar Smooth Muscle to NO:** similar in saline treated and ROFA exposed rats. **Other:** significant increase in venular leukocyte-adhesion and rolling observed in ROFA exposed rats.
Reference: Nurkiewicz et al. (2006) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Age:** 7-8 weeks	ROFA from Everett, MA	**Route:** Intratracheal Instillation **Dose/Concentration:** ROFA group: 0.1 or 0.25 mg/rat. Vehicle control group: 300 ul saline. Particle control group: TiO_2 0.1 or 0.25 mg/rat. **Particle Size (Distribution):** ROFA mean count diameter: 2.2 µm; TiO_2 mean diameter: 1.0 µm **Time to Analysis:** After single IT instillation of a particular dose, all rats recovered for 24 h.	**ROFA or TiO_2 Exposure and Arteriolar Dilation:** exposure caused a dose-dependent impairment of endothelium-dependent arteriolar dilation. **ROFA or TiO_2 Exposure and Arteriolar Constriction:** exposure did not affect microvascular constriction in response to PHE. **ROFA and TiO_2 and Leukocyte Rolling and Adhesion:** exposure significantly increased leukocyte rolling and adhesion in aired venules, and these cells were identified as PMN leukocytes. **ROFA and TiO_2 and MPO:** MPO was found in PMN leukocytes, adhering to the systemic microvascular wall. Evidence suggests that some of this MPO had been deposited in the microvascular wall. There was also evidence of oxidative stress in the microvascular wall.
Reference: Okayama et al. (2006) **Species:** Rat **Cell Type:** Ventricular Cardiac Myocytes from Wistar Rats, approximately 3 days old	DEP (Tsukuba, Japan) DEPE: 5g of DEP in 5 mL PBS containing 0.05% Tween 80. Others: Catalase, LDH, MPG and SOD.	**Route:** In vitro **Dose/ Concentration:** DEPE: 0-100 µg/mL; MPG: 0-1 mM; SOD: 800 U/mL; Catalase: 500 U/mL **Particle Size (Distribution):** DEP mass median diameter: 0.34 µm. **Time to Analysis:** **Long-Term Exposure to DEPE:** cells were incubated for 24 or 48h. **Short-Term Exposure to DEPE:** 1, 2, 4, or 8 h and then medium containing DEPE was replaced by serum-free medium, and incubated for an additional 24 h. **LDH Activity of Supernatant:** 24 h post-DEPE exposure. **SOD and Catalase on DEPE-induced Toxicity**: SOD and catalase activity were added to cells w/ or w/o DEPE (50 µg/mL) and incubated in cell culture medium for 4 h, then medium was replaced w/ serum-free, and cells incubated for another 24 h. **MPG on DEPE-induced Toxicity:** MPG was added to cells w/ or w/o DEPE (50 µg/mL) and incubated for 4 or 24 h, then medium was replaced w/ serum-free, and cells incubated for another 24 h to analysis:	**Cytotoxic Effects of DEPE on Cardiac Myocytes:** DEPE above 20 µg/mL damaged cardiac myocytes in a time and concentration-dependent manner in both long- and short-term exposure conditions. However damage was greater after long-term exposure. LDH activity showed a concentration-dependent increase at higher levels of exposure (greater than 20 µg/mL). **Effects of ROS Scavenging Enzymes and Antioxidant on DEPE-induced Cell Damage:** SOD or catalase attenuated 50 µg/mL DEPE-induced cell damage compared w/ DEPE-treated groups lacking antioxidant enzymes. Co-incubation w/ SOD and catalase showed more protective effects towards DEPE-induced cell damage, although these effects were not statistically significant from cells treated w/ SOD only. MPG attenuated 50 µg/mL DEPE-induced cell damage in a concentration-dependent manner in both long and short-term exposure conditions. Especially in long-term exposure MPG showed strong protective effects against DEPE-induced cell damage. Cell viability was not affected by SOD, catalase, or MPG.

Study	Pollutant	Exposure	Effects
Reference: Proctor et al. (2006) **Species:** Rat **Gender:** Male **Age:** 12 weeks **Use:** Thoracic Aorta from cp/cp and +/? Male Rats cp/cp = homozygous for cp gene. Prone to obesity and insulin resistant. +/? = heterozygous for either +/cp or +/+. Lean and metabolically normal.	ROFA from Birmingham, AL	**Route:** Protocol 1: Used two aorta rings per each experimental treatment group (4 groups total). Protocol 2: Used four rings. **Dose/Concentration:** Protocol 1: cells exposed to 12.5μg/mL ROFA. Protocol 2: cells exposed to 1.56, 3.25, 6.26, 12.5 μg/mL ROFA. ROFA was suspended in saline at a concentration of 10 mg/mL (ROFA-L) **Particle Size (Distribution):** 1.95 ± 0.18um aerodynamic diameter of ROFA **Time to Analysis:** Protocol 1: Cells exposed to 12.5μg/mL ROFA and 104mol/L L-NAME for 20 min. Protocol 2: Cells exposed to 1.56, 3.25, 6.26, 12.5 μg/mol ROFA. (2 times one before a wash and one after PE was washed out) Contractile response to phenylephrine (PE) was measured	ROFA-L (12.5 μg/mL) increased PE-mediated contraction in obese, but not in lean rat aortae. Effect was exacerbated by L-NAME, and it reduced ACh-mediated relaxation in obese and lean aortae. Initial exposure of aortae to ROFA-L caused a small contractile response, which was markedly greater on second exposure in the obese aortae but marginal in lean.
Reference: Radomski et al. (2005) **Species:** Rat and Human **Strain:** Wistar-Kyoto (rats) **Cell Types:** Human Platelets **Use:** Rats: In-vivo Study (Vascular Thrombosis) Human platelets: In-vitro Study (Platelet Aggregation): Human Platelets	Carbon Nano Particles (CNPs): * Multiplewall Nanotubes (MWNT) * Singlewall Nanotubes (SWNT) * C60 Fullerenes (C60CS) * Mixed Carbon Nanoparticles (MCN) PM (SRM1648)	**Route:** In-vivo study: Single injection of PM into the femoral vein, simultaneously as $FeCl_3$ was injected to induce carotid thrombosis. In-vitro Study: $2.5X10^8$ platelets/mL. Prostacyclin (PGI2), S-nitroso-glutathione (GSNO), aspirin, 2-methylthio-AMP, phenanthroline, EDTA and Go6976 were pre-incubated w/ platelets for 1 min before particle addition. **Dose/Concentration:** In-vivo Study: 0.5 mL suspension of 50 μg/mL of PM in 0.9% NaCl solution. In-vitro Study: MWNT, SWNT, C60CS, MCN: 0.2-300 μg/mL concentration range was studied. **Particle Size (Distribution):** Nanoparticles (C60CS, SWNT, MWNT)**:** NR SRM1648: 1.4 μm average size **Time to Analysis:** In-vivo Study: Blood flow was continuously monitored for 900 seconds. In-vitro Study: Particles were added to platelets and platelet aggregation was studied for 8 minutes.	Vascular Thrombosis: $FeCl_3$ induced carotid artery thrombosis and MCN had an amplifying effect in the development of thrombosis. Infusions of MCN, SWNT, and MWNT significantly accelerated the time and rate of development of carotid artery thrombosis in rats. SRM1648 was less effective than CNPs in inducing thrombosis, while C60CS exerted no significant effect on the development of vascular thrombosis. Platelet Aggregation: CNPs except C60CS, stimulated platelet aggregation (MCN ≥ SWNT>MWNT>SRM1648). All particles resulted in upregulation of GPIIb/IIIa in platelets. In contrast particles differentially affected the release of platelet granules, as well as the activity of thromboxane-, ADP, matrix metalloproteinase- and protein kinase C-dependent pathways of aggregation. Particle-induced aggregation was inhibited by prostacyclin and GSNO, but not by aspirin.
Reference: Rhoden et al. (2005) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Age:**Adult **Weight:** 300 g	Urban Ambient Particles (UAPs): SRM-1649; CAPs from Boston, MA	**Route:** UAPs: Intratracheal Instillation; CAPs: Inhalation **Dose/Concentration:** UAPs: 750 μg suspended in 300 ul saline; CAPs: 700 ± 180 $\mu g/m^3$ **Particle Size (Distribution):** NR **Time to Analysis:** UAPs: 30 min post-instillation. CAPs: immediately after 5h exposure period	**Oxidative Stress and HR Function:** UAPs instillation led to significant increases in heart oxidants. HRincreased immediately after exposure and returned to basal levels over the next 30 min. SDNN was unchanged immediately after exposure, but significantly increased during the recovery phase. **Role of ROS in Cardiac malfunction:** rats were treated w/ 50 mg/kg NAC 1h prior to UAPs instillation or CAPs inhalation. NAC prevented changes in heart rate and SDNN in UAPs-exposed rats. **Role of the Autonomic Nervous System in PM-induced Oxidative Stress**: rats were given 5 mg/kg atenolol, 0.30 mg/kg glycopyrrolate, or saline immediately before CAPs exposure. Both atenolol and glycopyrrolate effectively prevented CAPS-induced cardiac oxidative stress.
Reference: Rivero et al. (2005a) **Species:** Rat **Gender:** Male **Strain:** Wistar **Age:** 3 months **Weight:** ~250 g **n:** 38	$PM_{2.5}$, collected from heavy traffic area in Sao Paulo, Brazil. $PM_{2.5}$ Composition (%): S (3.05), As (0.30), Br (0.21), Cl (2.09), Co (2.65), Fe (2.67), La (5.42), Mn (0.64), Sb (0.21), Sc (3.25), Th (8.14)	**Route:** Intratracheal Instillation **Dose/Concentration:** 100 and 500 μg of $PM_{2.5}$. **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 24 h post-instillation	**Blood:** Total reticulocytes significantly increased at both $PM_{2.5}$ doses, while hematocrit levels increased in the 500 μg group. Quantification of segmented neutrophils and fibrinogen levels showed a significant decrease, while lymphocytes counting increased w/ 100 μg of $PM_{2.5}$. **Pulmonary vasculature:** significant dose-dependent decrease of intra-acinar pulmonary arteriole lumen/wall ratio was observed in both $PM_{2.5}$ groups. **Wet-to Dry Weight Ratio:** significant increase in heart wet-to-dry weight ratio was observed in the 500 μg group.

Study	Pollutant	Exposure	Effects
Reference: Rodriguez Ferreira Rivero et al. (2005b) **Species:** Rat **Gender:** Male **Strain:** Wistar **Age:** 3 months **Weight:** ~250 g **n:**47	$PM_{2.5}$, collected from heavy traffic area in Sao Paulo, Brazil. $PM_{2.5}$ Composition (%): S (3.05), As (0.30), Br (0.21), Cl (2.09), Co (2.65), Fe (2.67), La (5.42), Mn (0.64), Sb (0.21), Sc (3.25), Th (8.14)	**Route:** Intratracheal Instillation **Dose/Concentration:** 50 and 100 µg of $PM_{2.5}$. **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** HR and SDNN were assessed immediately before instillation, 30 and 60 min post-instillation.	HR decreased significantly w/ time, but no significant effect of treatment or interaction b/w time and treatment was observed. In contrast, there was a significant SDNN interaction b/w time and treatment. The SDNN decreased 60 min after instillation w/ $PM_{2.5}$ concentration of 50 and 100 µg.
Reference: Simkhovich et al. (2007) **Species:** Rat **Gender:** Female **Strain:** Fischer 344 x Brown Norway hybrid **Use:** Study was performed in isolated Langendorff-perfused rat hearts from young adult (4 months) and old aged (26 months).	Ultra Fine Particles (UFPs) isolated from industrial diesel reference PM 2975	**Route:** Heart Perfusion (ex-vivo). Two treatment groups (control and UFPs-treated) were studied. Young and old were studied within each group. Control hearts were perfused w/ buffer only, UFP-treated hearts were perfused w/ buffer containing UFPs. **Dose/Concentration:** Young adult and old UFPs-treated groups were perfused w/ UFPs 12.5, 25, and 37.5 mg. **Particle Size (Distribution):** UFPs contained particles of sizes equal to and less than 0.1 µm **Time to Analysis:** Hearts were perfused w/ UFPs for 30 minutes and analysis was conducted every 10 minutes.	Young adult and old hearts demonstrated equal functional deterioration in response to direct infusion of UFPs. Developed pressure in young adult UFPs-treated hearts fell from 101 ± 4 to 68 ± 8 mmHg. In the old UFPs-treated hearts developed pressure fell by 35%. Positive dP/dt was equally affected in the young adult and old UFPs-treated hearts and was decreased by 28% in both groups.
Reference: Sun et al. (2005) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 6 weeks old upon arrival **n:** 12, High-Fat Chow Diet (HFCD); 16, Normal Chow Diet (NCD) **Use:** Study diets fed for at least 10 weeks prior to exposure to $PM_{2.5}$ or FA.	CAPs: $PM_{2.5}$ from Tuxedo, NY.	**Route:** Whole Body Inhalation **Dose/Concentration:** $PM_{2.5}$: 85 µg/m^3.; Mean (SD) daily $PM_{2.5}$ concentration at the study site was 10.6 (3.4) µg/m^3 (approximately 8-fold concentration from ambient Tuxedo levels). Because of the length of exposure the normalized concentration value over the 6 mo period was 15.2 µg/m^3. **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 6 h x 5 days/wk x 6 mo (July 2004 to Jan 2005). Animals were sacrificed 15-47 days after exposure.	**Vasomotor Function:** Mice fed HFCD and exposed to $PM_{2.5}$ demonstrated an increase in the half-maximal dose for dilation to ACh with no changes in peak relaxation compared to the mice exposed to FA and fed HFCD and NCD. **Atherosclerosis Burden with $PM_{2.5}$:** In vivo MRI imaging of atherosclerosis burden in the abdominal aorta revealed significantly increased plaque burden in the mice fed HFCD compared with the mice fed NCD. Mean (SD) plaque areas in the mice exposed to $PM_{2.5}$ and fed HFCD vs. mice exposed to FA and fed HFCD were 33 (10) vs. 27 (13) units, respectively. **$PM_{2.5}$ and Vascular Inflammation:** A 2.6-fold higher inducible NOS content was apparent in the mice exposed to $PM_{2.5}$ and fed HFCD compared with the mice exposed to FA and fed HFCD chow and a 4-fold increase in the mice exposed to $PM_{2.5}$ and fed NCD compared with the mice exposed to FA and fed NCD.
Reference: Sun et al. (2008a) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 6 weeks	CAPs $PM_{2.5}$ Collected from Sterling Forest State Park, Tuxedo NY (40 miles NW of Manhattan)	**Route:** Inhalation Chamber **Dose/Concentration:** Average Concentration of: 85µg/m^3 CAPs in chamber. Average exposure over 6 months = 15.2 µg/m^3. **Particle Size (Distribution):** CAPs Composition: NR **Time to Analysis:** 6 hours per day, 5 days per week for ~ 6 months Mice received two different diets, high-fat chow and normal-chow.	**Macrophage and TF Expression in Aortic Segments**: Tissue Factor expression was noted predominantly in the extracellular matrix surrounding macrophages, foam cell-rich areas and around smooth muscle cells. **1. High-Fat Diet:** Increased TF and increased macrophage infiltration was noticed in the palques of the high-fat chow mice exposed to PM compared to mice exposed to air and high fat diet. **2. Normal Diet:** Normal diet mice had an increase in CD68 expression in mice exposed to PM compared to mice exposed to air. However TF expression was not significantly different in PM exposed normal diet mice compared to control normal diet mice.

Study	Pollutant	Exposure	Effects
Reference: Sun et al. (2008a) **Species:** Human **Cell Lines:** 1. Human Bronchial Epithelial Cells (BEAS-2B), 2.Vascular Smooth Muscle Cells (hSMCs) and 3.Monocytes (THP-1)	Ambient Particles collected from Sterling Forest, 24 h/day for 4 weeks.	**Route:** In vitro. Particle Concentration Varied **Dose/Concentration:** SRM- 1649a and BC were used as reference **Particle Size (Distribution):** Particle size ranges: 1. <0.18 μm 2. 1.8 - 2.5 μm 3. 2.5 - 10 μm **Time to Analysis:** Doses were tested for durations up to 24 h.	Dose durations tested for up to 24-h did not indicate detectable effects on cell viability. Effect of PM on TF Expression and Activity: 1. hSMCs: In the PM size range of 1-3um, significant increases in TF expression was observed at doses of 100 and 300 μg/mL. In the <0.18 μm size range, significant increase in TF expression was observed at all doses. The particles with sizes 0.18 - 1.0 μm did not induce significant change in TF expression. 2. Monocyte Cells: TF protein expression increased with <0.18 μm and the 1- 3 μm range particles. Expression was increased in the 0.18-1.0 μm particle range but it was limited compared to the other PM size ranges. In general TF expression was higher in monocytes than in hSMCs cells, but not significantly. 3. Human Bronchial Epithelial Cells: 100 μg/mL of the 1-3 μm and <0.18 μm particles significantly increased TF expression. TF mRNA Expression: TF mRNA was increased rapidly within the first hour in response to SRM-1694a PM. The lowest dose of SRM PM_{10} μg/mL induced highest levels of mRNA in hSMCs, no further increase was observed at higher concentrations.
Reference: Sun et al. (2008b) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Age:** 500-650 g **Use:** In-vivo Exposure, then Cell Culture: Primary Rat Aortic Smooth Muscle Cells (RASMCs), passages 4 to 8 were used for the experiment.	$PM_{2.5}$, UFP or FA	**Route:** Inhalation (in-vivo) and cell culture exposure to $PM_{2.5}$, UFP or FA **Dose/Concentration:** Mean concentration of $PM_{2.5}$ inside the chamber was 79.1 ±7.4 μg/m^3. Because of the exposure period the equivalent $PM_{2.5}$ concentration in the chamber "normalized" over the 10 week period was 14.1 μg/m^3. **Particle Size (Distribution):** $PM_{2.5}$; UFP: <0.1 μm **Time to Analysis:** 6h x 5d/week random exposure to $PM_{2.5}$, UFP, or FA for a total of 10 weeks. At the end of week 9 exposure, rats were infused w/ 0.75 mg/kg/d of AII for 7 days. $PM_{2.5}$, UFP, or FA, continued during AII infusion period. AII = angiotensin II	**Mean Arterial Pressure (MAP):** after AII infusion, MAP was significantly higher in $PM_{2.5}$ -AII vs. FA-AII group. Aortic Vasoconstriction to PE was potentiated w/ exaggerated relaxation to the Rho-kinase (ROCK) inhibitor Y-27632 and increase in ROCK-1 mRNA levels in the $PM_{2.5}$ -AII group. Superoxide production in the aorta was increased in the $PM_{2.5}$. AII group compared to FA-AII group, inhabitable by apocynin and L-NAME w/ coordinate upregulation of NAD(P)HR oxidase subunits p22phox and p47phox and depletion of tetrahydrobipterin. In-vitro exposure to UFPs and $PM_{2.5}$ was associated w/ an increase in ROCK activity, phosphorylation of myosin light chain, and MYPT1. Pretreatment w/ N-Acetylcysteine and the Rho kinase inhibitors (Fasudil and Y-27632) prevented MLC and MYPT-1 phosphorylation by UFPs suggesting a Superoxide-mediated mechanism for $PM_{2.5}$ and UFPs effects.
Reference: Tankersley et al. (2007) **Species:** Mouse **Gender:** Male **Strain:**C3 and B6 **Age:**10 weeks **Weight:** 22-26 g **n:**12, C3; 11 B6	Carbon Black (CB) and Filtered Air (FA)	**Route:** Whole Body Inhalation Chamber **Dose/Concentration:** CB average: 159 ± 12 μg/m^3 **Particle Size (Distribution):** CB average mass median aerodynamic diameter: 2.4 μm (GSD 2.75 μm). **Time to Analysis: Successive 3h CB and FA Exposures:** conducted from 9 a.m. to 1 p.m., or at least 3 h after dark-to-light transition (exposure period selected based on the nadir in circadian pattern in HR responses). **Additional Exposures:** a subgroup of C3 and B6 mice (n = 5 mice per strain) were assigned to the subsequent studies involving acute exposures to CB and FA following: administration of saline or parasympathetic (PS) (atropine, 0.5 mg/kg ip) and sympathetic (S) (propanolol, 1 mg/kg ip) blockade	**FA Exposure w/ Saline:** significantly greater 3 h average response occurred in C3 compared w/ B6 mice. **PS Blockade:** the strain difference b/w C3 and B6 mice was not evident. **S Blockade:** 3 h average HR responses for C3 mice were significantly reduced compared w/ saline. **CB Exposure:** HR responses were significantly elevated in C3 compared w/ B6 mice, but these HR responses were not different relative to FA exposure. **S Blockade:** HR was significantly elevated in B6 mice during CB relative to FA, but was not changed in C3 mice.
Reference: Tankersley et al. (2004) **Species:** Mice **Strain:**AKR/J **Age:** ~180 days **n:** 5, Healthy; 3, terminally senescent **Use:** Age matched animals	Carbon Black (CB) and Filtered Air (FA)	**Route:** Whole Body Inhalation **Dose/Concentration:** CB average concentration: 160 ± 22 μg/m^3 **Particle Size (Distribution):** The majority of CB particle sizes were in the respirable range (fine mode): 0.1 to 1um. **Time to Analysis:** Following a control day of FA exposure (day 1), CB exposure period was initiated and maintained for 3h/day for 3 consecutive days (days 2-4).	On day 1, HR was significantly depressed during FA in terminally senescent mice. By day 4, HR had significantly slowed due to the effects of 3 days CB exposure. The combined effects of terminal senescence and CB exposure acted to depress HR to an average (± SEM) 445 ± 40 bpm, ~ 80 bpm lower compared to healthy HR responses. The change in rMSSD was significantly greater on day 1 and day 4 in terminally senescent mice, compared to healthy mice. LF/HF ratio was significantly depressed in terminally senescent mice on day 1. By day 4, significant increases in LF/HF were evident in healthy mice during CB exposure. Terminally senescent mice modulated a lower HR w/o change in the LH/HF ratio during CB exposure.

Study	Pollutant	Exposure	Effects
Reference: Thomson et al. (2005) **Species:** Rat **Gender:** Male **Strain:** Fischer-344 **Weight:** 200-250 g	Urban Ambient Particles (EHC-93) from Ottawa, Canada; Ozone	**Route:** Nose-only Inhalation **Dose/Concentration:** EHC-93: 0, 5, 50 mg/m^3; Ozone: 0, 0.4, 0.8 ppm **Particle Size (Distribution):** Respirable Modes (aerodynamic diameter): 1.3 and 3.6 μm. Non-respirable Mode (aerodynamic diameter): 15 μm **Time to Analysis:** 4h to particles, ozone, or combination of particles and ozone.	Both pollutants individually increased preproET-1, ET-1 and endothelia NOS mRNA levels in the lungs shortly after exposure, consistent w/ the concomitant increase in plasma of ET-1[1-21]. Prepro-ET1 mRNA remained elevated 24 h post-exposure to particles but no after ozone. Both pollutants transiently increased ET-B receptor mRNA expression, while ozone decreased ET-A receptor mRNA levels. Coexposure to particles plus ozone increased lung preproET-1 mRNA but not plasma ET-1[1-21], suggesting alternative processing or degradations of endothelins. This coincided w/ an increase of MMP-2 in the lungs (this enzyme cleaves bigET-1 to ET-1[1-32]).
Reference: Thomson et al. (2005) **Species:** Rat **Gender:** Male **Strain:** Fischer-344 **Weight:** 200-250 g	Urban Ambient Particles (EHC-93) from Ottawa, Canada; Ozone	**Route:** Nose-only Inhalation **Dose/Concentration:** EHC-93: 0, 50 mg/m^3; Ozone: 0, 0.8 ppm **Particle Size (Distribution):** NR **Time to Analysis:** 4h to particles, ozone, or combination of particles and ozone.	Circulating levels of both ET-1[1-21] and ET-3[1-21] were increased immediately after exposure to PM and ozone. While expression of preproET-1 mRNA in the lungs increased, expression of preproET-3 mRNA decreased immediately after exposure. PreproET-2 mRNA was not detected in the lungs, and exposure to either pollutant did not affect plasma ET-2 levels. Coexposure to ozone and particles, while altering lung preproET-1 and preproET-3 mRNA levels in a fashion similar to ozone alone, did not cause changes in the circulating levels of the two corresponding peptides.
Reference: Totlandsdal et al. (2008) **Species:** Rat **Gender:** Male **Strain:** WKY/NCrl and Crl: WI (Han) **Age:** Adult **Weight:** 220-300 g, WKY/NCrl; 250-300 g, Crl: WI (Han) **Use:** Isolation of Primary Rat Epithelial Lung Cells (PRELCs): from WKY/NCrl rats. Isolation of Rat Ventricular Cardiomyocytes and Cardiofibroblasts (RVCMs and RVCFBs) from Crl: WI (Han) rats.	Pigment Black Printex 90 (Frankfurt, Germany); Standard Reference Material of Urban PM: SRM 1648	**Route:** Culture of PRELCs: 4 x 10^6 cells/well; Culture of RVCMs: 1.2 x 10^5 cells/well; Culture of RVCFBs: 2.4 x 10^5 cells/well **Dose/Concentration:** Printex 90: 0, 50, 100, 200 or 400 μg/mL; SRM 1648: 0, 200 μg/mL **Particle Size (Distribution):** Printex 90: 12-17 nm **Time to Analysis:** 20 h	**Lung cell cultures:** both particles induced release of IL-6 and Il-1 β, whereas TNF α was only detected upon exposure to SRM 1648. **Cardiac Cell Cultures**: IL-6 release was strongly enhanced upon exposure to conditioned media, and markedly exceeded the response to direct particle exposure. IL-1, but not TNF-α, seemed necessary, but not sufficient, for this enhanced IL-6 release. The role of IL-1 was demonstrated by use the use of an IL-1 receptor antagonist that partially reduced the effect of the conditioned media, and by a stimulating effect on the cardiac cell release of IL-6 by exogenous addition of IL-1 α and IL-1 β.
Reference: Tzeng et al. (2007) **Species:** Rat **Strain:** Wistar **Cell Type:** Primary Vascular Smooth Muscle Cell Culture (VSMCs): isolated from thoracic aortas from 200-250g rats.	Motorcycle Exhaust Particulate Extract (MEPE).	**Route:** In vitro **Dose/Concentration:** 10-100 μg/mL **Particle Size (Distribution):** PM_1, $PM_{2.5}$, PM_{10} **Time to Analysis:** 3 days.	Exposure of VSMCs to MEPE (10-100 μg/mL), enhanced serum-induced VSMC proliferation. The expression of proliferating cell antinuclear antigen was also enhanced in the presence of MEPE. VSCMs treated w/ MEPE induced increase COX-2 mRNA, protein expression, and PGE2 production, whereas the level of COX-1 protein was unchanged. MEPE increased the production of ROS in VSMCs, in a dose-dependent manner. MEPE triggered time-dependent ERK1/2 phosphorylation in VSMCs which was attenuate by antioxidants (NAC, PDTC). The level of translocation of NF-kappaB-p65 in the nuclei of VSMCs was also increased during MEPE exposure. The potentiating effect of MEPE in serum-induced VSMC proliferation was abolished by COX-2 selective inhibitor NS-398, specific ERK inhibitor PD98059, and antioxidants (NAC, PTDC).

Study	Pollutant	Exposure	Effects
Reference: Tzeng et al. (2003) **Species:** Rat **Strain:** Wistar **Cell Type:** Primary Vascular Smooth Muscle Cell Culture (VSMCs): isolated from thoracic aortas from 200-250g rats.	Motorcycle Exhaust Particulate Extract (MEPE).	**Route:** In vitro **Dose/Concentration:** MEPE: 10 µg/mL; Nifedipine: 10 µmol; Manganese Acetate: 100 µmol; Staurosporine: 1-2 nM; Chelerythrine: 1µM **Particle Size (Distribution):** NR **Time to Analysis:** 18 hours	MEPE induced a concentration-dependent enhancement of vasoconstriction elicited by phenylephrine in the organ cultures of intact and endothelium-denuded aortas for 18h. Nifedipine, manganese acetate, and staurosporine, but not chelerythrine, inhibited the enhancement of vasoconstriction by MEPE. ML-9 inhibited the enhancement of vasoconstriction by MEPE. MEPE enhanced the phosphorylation of 20k-D_a in rat vascular smooth muscle cells. N-acetylcysteine significantly inhibited the enhancement of vasoconstriction by MEPE. A time-dependent increase in ROS production by MEPE was also detected in primary cultures of VSMCs.
Reference: Wellenius et al. (2004) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Age:** Adult **Weight:** ~250 g **Use:** Rat Model for Acute Myocardial Infarction (AMI): Left-ventricular MI induced by thermocoagulation. Animals allowed to recover for at least 12 h after surgery.	CAPs CO FA	**Route:** Whole Body Inhalation Chambers (animals were sedated w/ Diazepam during exposure) **Dose/Concentration:** FA: (n = 40); CO: 35 ppm (n = 19); CAPs (median concentration): 350.5 µg.m^3 (n = 53); CAPs+CO: (CAPs median concentration): 318.2 µg/m^3 (n = 23) **Particle Size (Distribution):** CAPs: $PM_{2.5}$ **Time to Analysis:** 1-h exposure to CAPs or CAPs+CO for 1h. Exposure to pollutants was preceded and followed by 1h exposure to FA. Exposure experiments were performed during the period of 07/2000 and 01/2003	CO exposure reduced the ventricular premature beat (VPB) frequency by 60.4% during the exposure time compared to controls. This effect was modified by both infarct type and the number of pre-exposure VPBs, and was mediated through changes in hear rate (HR). Overall, CAPs exposure increased VPB frequency during the exposure period, but this did not reach statistical significance. This effect was modified by the number of pre-exposure VPBs. In rats w/ a high number of pre-exposure VPB, CAPS exposure significantly decreased VPB frequency (67.1%). Overall, neither CAPs nor CO had any effect on HR, but CAPs increased HR in specific subgroups. No significant interactions were observed between the effects of CO and CAPs.
Reference: Wellenius et al. (2006) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Age:** Adult **Weight:** ~250 g **Use:** Rat Model for Acute Myocardial Infarction (AMI): Left-ventricular MI induced by thermocoagulation. Animals allowed to recover for at least 12 h after surgery.	CAPs: (Boston, MA)	**Route:** Whole Body Inhalation Chambers (animals were sedated w/ Diazepam during exposure) **Dose/Concentration:** FA: (n = 16); CO: 35 ppm (n = 19); CAPs (median concentration): 645.7 µg.m^3 (n = 23); CAPs+CO: (n = 24) **Particle Size (Distribution):** CAPs: $PM_{2.5}$ **Time to Analysis:** 1-h exposure to CAPs or CAPs+CO for 1h. Exposure to pollutants was preceded an followed by 1h exposure to FA.	Among rats in the CAPs group, the probability of observing supraventricular arrhythmias (SVA) decreased from the baseline to exposure and post-exposure periods. The pattern was significantly different than that observed for the FA group during the exposure period. In the subset with one or more SVA during the baseline period, the change in SVA rate from baseline to exposure period was significantly lower in the CAPs and CO groups only, when compared to the FA group. No significant effects were observed in the group simultaneously exposed to CAPs and CO.

Study	Pollutant	Exposure	Effects
Reference: Wichers et al. (2004) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 75 days	HP-12 from inside wall of a stack at a Boston power plant burning residual oil (number 6). Water-leachable constituents (μg/mg): SO_4 (217.3); Zn (11.4); Ni (6.9); Fe (0.0); V (1.3); Cu (0.2); Pb (0.0) 1M HCl-leachable constituents (μg/mg): SO_4 (220.6); Zn (15.5); Ni (14.8); Fe (15.6); V (32.9); Cu (1.1); Pb (1.7)	**Route:** Intratracheal Instillation **Dose/Concentration:** HP-12 (mg/kg): 0.00 (saline control), 0.83 (low), 3.33 (mid), 8.33 (high) **Particle Size (Distribution):** Mass median aerodynamic diameter: 3.76 μm (GSD 2.16) **Time to Analysis:** Single-dose Animals were sacrificed 96 h or 192 h post-IT.	Exposures to mid and high-dose HP-12 induced large decreases in HR, BP, and body temperature. The decreases in HR and BP were most pronounced at night and did not return to pre-IT values until 72h (HR) and 48h (BP) after dosing. ECG abnormalities (rhythm disturbances, bundle branch block) were observed primarily in the high dose group.
Reference: Wold et al. (2006) **Species:** Rat **Gender:** Female **Strain:** Sprague-Dawley **Use:** In vivo Experiment: L jugular vein and R carotid artery were canulated. In vitro Experiment: heart Langendorff-perfusion apparatus	UFPs from either ambient air (UFAAs) or diesel engine exhaust (UFDGs); UFIDs from industrial forklift exhaust and soluble fraction UFID suspension, particle free (SF-UFID)	**Route:** IV Infusion (in vivo study) and Langendorff heart perfusion (in vitro study) **Dose/Concentration:** In vivo: UFDG (50μg/m) In vitro: UFDG (100 μg /2ml); UFID (12.5 μg/l in perfusate); SF-UFID (12.5 μg/l) **Particle Size (Distribution):** UFAAs diameter; equal to or less than 150 nm; UFDGs diameter: equal to or less than 100 nm **Time to Analysis:** In vivo Experiment: After anesthesia, animals were divided into three groups: control (n = 3); UFAA (n = 4);UFDG (n = 3). Animals were IV infused w/ 1ml of each UFAA preparation. After 1-h of continuous monitoring the animals were euthanized. In vitro Experiment: Lagendorff 1: UFDGs-treated (n = 3); control (n = 5). Heart monitored for 60 min after injection. Langendorff 2: control (n = 8); UFID (n = 6); SF-UFID (n = 5)	**In vivo:** Infusion of UFDGs caused ventricular premature beats (VPBs) in 2 out of 3 rats. Ejection fraction increased slightly in rats receiving UFAA and was unchanged in the UFDG and saline groups. **In vitro:** UFDGs caused a marked increase in left-ventricular and end-diastolic pressure (LVEDP) after 30 min of exposure. UFIDs caused a significant decrease in left-ventricular systolic pressure (LVSP) at 30min after the start of infusion. This effect was absent when SF-UFID was studied.
Reference: Yatera et al. (2008) **Species:** Rabbit **Gender:** Female **Strain:** WHHL **Age:** 42 weeks old at the start of experimental protocol **Weight:** 3.2 ± 0.1 kg (avg) **n:** 15, Experimental; 16 control	EHC-93 from Ottawa, Canada	**Route:** Intratracheal Instillation **Dose/Concentration:** PM_{10} suspension: 5 mg EHC-93 **Particle Size (Distribution):** PM_{10} **Time to Analysis:** Exposure to PM_{10}: Animals or instilled w/ PM_{10} or saline control 2X/week for a total of 4 weeks. 1mm of blood was collected from the central ear artery 2X before instillation for baseline measurements, and at 0.5, 1, 2, 4, 8, 12, and 24 h after the initial instillation to observe acute effects, then once weekly to determine the chronic effects on monocyte adhesion molecule expression.	Exposure to PM_{10} caused progression of atherosclerotic lesions in thoracic and abdominal aorta. It also decreased circulating monocytes expressing high levels of CD31 and CD49d, and increased expression of CD54 (ICAM-1) and CD106 (VCAM-1) in plaques. Exposure to PM_{10} increased the number of BrdU-labeled (*) monocytes into plaques and into smooth muscle underneath plaques. (*)Monocytes labeled w/ BrdU in donor rabbits were transfused to recipient rabbits as whole blood, and the recruitment of BrdU-labeled cells into vessel walls and plaques in recipients was measured by quantitative histological methodology.
Reference: Yokota et al. (2004) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley (IGS) **Weight:** 345-498.2 g	DEP from Japan	**Route:** Intratracheal Instillation **Dose/Concentration:** 10, 12.5 and 25 mg/mL **Particle Size (Distribution):** NR **Time to Analysis:** 24-72 h, Ishemia reperfusion 24 – 48 h post-exposure	An increased mortality was observed in the DEP group compared to the vehicle-treated group. 46% of the animals in DEP died during the first 3 min reperfusion period. The animals of other groups were intratracheally instilled w/ DEP at the beginning of ischemia/reperfusion experiment, or were pretreated w/ polyethylene glycol-conjugated SOD (1000 IU/kg, iv). In these animals, incidences of both arrhythmia and mortality were similar to those in the animals treated w/ the vehicle. **Effects of DEP on the biochemical and hematological parameters:** neutrophil count was elevated by a higher dose (5 mg) of DEP at 24 h after the intratracheal instillation, and oxygen radical production, which was induced by 12-O-tetradecanoylphorbol 13-acetate, was enhanced at 72h.

Study	Pollutant	Exposure	Effects
Reference: Yokota et al. (2005) **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley (IGS) **Weight:** 303-472.2 g **Use:** Rats were used after a 7-day acclimation period	DEP from Japan	**Route:** Intratracheal Instillation **Dose/Concentration:** Vehicle: 0.2 mL/animal DEP: 5 mg/animal **Particle Size (Distribution):** NR **Time to Analysis:** Single exposure 0.5, 1, 2, 3, 6, 12, 24, 48 h	At 12 and 24 h post-instillation, circulatory neutrophil counts in the 5 mg DEP group were significantly elevated, and were 2.1-fold (12h) and 2.3 fold (24 h) in vehicle treated animals. 1 mg DEP caused an increase of approximately 0.4-fold in CNC at 6h. 12-O-tetradecanoylphorbol 13-acetate induced oxyradical production (ORP) in the isolated neutrophil was enhanced at 12 and 24 h after instillation w/ 5 mg DEP. In Serum, a marked elevation of CINC-1 and a slight elevation of MIP-2 were also observed, while TNF α was not detected. GM-CSF was not detected in serum 24 h post-instillation.

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Table D-2. Respiratory effects: in vitro studies.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Aam and Fonnum (2007)	Human, Neutrophil Granulocytes (NG) Rat, Alveolar Macrophages (AM) 10^6 cells/mL	DEP = SRM 1975 Vitamin E (positive control) NR	NG: 8.8 - 280 μg/mL AM: 140, 280 μg/mL Cells PMA-stimulated Vitamin E = 5μM	1 h	ROS of NG: Formation of ROS in NG decreased with increased doses of DEP. Lucigenin chemiluminescence of ROS formation diminished 25% at 8.8 μg/mL DEP and luminol chemiluminescence 32% with 17.5 μg/mL DEP. DCF fluorescence required much higher doses of DEP. Controls without PMA stimulation had highly reduced lucigenin and luminol with DEP dose of 140 μg/mL while DCF increased 116%. ROS of AM: 280 μg/mL of DEP decreased ROS level by 19% with DCF. DEP with PMA-unstimulated cells increased 24% with DCF. Necrosis: NG cell death dose-dependent on DEP. At 280 μg/mL, cell death increased 5.4% vs control. LDH concentration increased 1.6% with 70 μg/mL DEP and 3.9% with 280 μg/mL after 1h.
Agopyan et al. (2003)	Human, BEAS-2B Human, NHBE Human, SAEC $1x10^5$ cells/mL BEAS-2B NR NHBE and SAEC	PC = synthetic carboxylate-modified particles 2, 10um	PC10 = 0.8 g/mL or $3x10^6$ particles/mL PC2 = 0.83 g/mL or $3.4x10^9$ particles/mL	PC10 = 2, 6, 12, 24 h PC2 = 12, 24, 8 h	Calcium Imaging: PC10 induced increase of Ca2+ concentration in all capsaicin-sensitive cells 100%. Similar reaction observed in cells exposed to PC2. However, more than 3-PC2s required to induce Ca increase unlike PC10. CPZ (10um) and amiloride could fully block PC-induced response. cAMP: Post 6h, dose-dependent increase in cAMP observed. Again, CPZ blocked increase 70-90% depending on cell type: SAEC >NHBE ~ BEAS-2B. Apoptosis: PC10 and PC2 induced apoptosis time-dependently. PC2 slower in induction than PC10. Post 48h, 80-95% cells apoptotic in all cell types. Noncapaisin-sensitive cells (which did not bind to particles) did not exhibit apoptosis. CPZ reduced apoptosis by 97% BEAS-2B, 96% NHBE and 98% SAEC. Amiloride did not block apoptosis. Necrosis: Induction of necrosis by PC2 and PC 10 negligible. Slight increase from 1% to 2% observed at 24-48h in NHBE and SAEC. BEAS-2B showed slight decrease from 3% to 4% in same time period.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Agopyan et al. (2004)	Human, NHBE Human, SAEC Mice, Wildtype and TRPV1(-/-) Terminal Ganglion Neurons (TG) NR NHBE and SAEC ~257 Wildtype Neurons ~ 187 TRPV (-/-) Neurons	ROFA MSHA = Mt St Helen Ash NR	100 μg/mL ROFA or MSHA	ROFA/MSHA in NHBE and SAEC = 2, 6, 24, 48 h ROFA/ MSHA in TG = 24 h cAMP measurements with NHBE and SAEC exposed to ROFA/MSHA = 6 h	Calcium Imaging in NHBE and SAEC: In 100% of reactive cells, ROFA/MSHA induced increase in Ca2+. Remained elevated as long as PM bound to plasma membrane. Washing and disjoining PM from membrane caused Ca2+ to slowly declined to baseline. CPZ (or CPZ and amiloride) reversibly inhibited PM induced rises in Ca2+. Calcium Imaging in TRPV1(+/+) and (-/-) mice sensory neurons: All sensitive neurons in TRPV1(+/+) increased Ca2+ in response to ROFA. No effect of ROFA in TRPV1(-/-). cAMP: ROFA and MSHA induced increase in Ca2+ in NHBE and SAEC cells, which was completely blocked by cAMP. Apoptosis: ROFA or MSHA induced time-dependent apoptosis, peaking at 24 h. CPZ again inhibited this response. Neurons bound to PM (<25um) induced apoptosis in TRPV1(+/+). Cells without bound PM or bound with PM (>25 μm) showed no effect. No apoptosis occurred in absence of Ca2+. Necrosis: Necrosis for any of the cell types negligible. PKA: Inhibition of PKA resulted in 90+% apoptosis in NHBE and SAEC. Again no apoptosis in Ca2+ free environment.
Ahn et al. (2008)	Human, A549 $2x10^5$ cells/well	DEP (6 cyl, 11L, turbo-charged, heavy-duty diesel engine, South Korea) NR	0, 1, 5, 10, 50 and 100 μg/mL of DEP Some cells pre-treated with 10, 20, 40, 50 pg/mL of Dex.	24 h	COX-2 Expression: Cells expressed dose-dependent increase in COX-2 expression after treatment with 10-100 μg/mL of DEP. Treatment of 50 μg/mL for 24 h induced statistically significant COX-2 expression in both mRNA and protein levels. Pre-treatment with Dex significantly reduced expression of COX-2 mRNA and protein. Dex treatment induced dose-dependent (10, 20, 40 and 50 pg/mL of Dex) suppression of DEP-induced protein levels. PGE2 Levels: Levels of inflammatory mediator, PGE2, increased when cells exposed to 50 μg/mL of DEP. Pre-treatment with 50 pg/mL Dex completely inhibited DEP-induced release of PGE2.
Ahsan (2005)	Human, Trx-1-transfected Clone of Murine L-929 cells Human, Control Clone (L-929-Neo1) Human, A549 NR	DEP NR	50 μg/mL A549 40 μg/mL hTrx-1- or L-929-Neo1 some pre-treated 1h with rhTrx-1 (10 μg/mL) or DM-rhTrx-1 (NR)	3h	ROS: DEP induced significant increase of ROS in L929-Neo1 cells. hTRx-1 cells showed no affect. RT-PCR revealed hTrx-1 mRNA expression in transfected cells but not control L929-Neo1 cells. Endogenous murine Trx-1 mRNA expression increased in control cells, not in hTrx-1 cells. A549 cells had increased ROS but suppressed with rhTrx-1 pretreatment. Pre-treatment with DM-rhTrx-1 increased ROS level more. Akt (antiapoptotic molecule): Phosphorylated Akt prevents apoptosis. DEP-induced phosphorylation of Akt in control cells after 3h and dephosphorylation after 5h. In hTrx-1 cells, Akt remained phosphorylated after 5h. In A549 cells, Akt phosphorylated at 3h and slowly turned off by 12-24 h. Pre-treatment with rhTrx-1 blocked dephosphorylation. Suggests Trx-1 preserves active form of Akt thus protecting against cytotoxicity from DEP.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Alfaro-Moreno et al. (2002)	Human, A549 Mouse, J774A.1 Mouse, Fibroblasts, BALB-c Rat, Lung Fibroblasts (RLF) Human, Umbilical Vein Endothelial Cells (HUVEC) 15000 cells/cm^2 except: Cytotoxicity: Confluent Cultures 180,000 cells/cm^2. DNA Breakage: 20,000 cells/well. Cytokine Assays: 180,000 cells/cm^2	PM_{10} Collected from 3 zones in Mexico City: North (industrial), Center (business) and South (residential) NR	Cytotoxicity: 10, 20, 40, 80, 160 $\mu g/cm^2$ Apoptosis: 160 $\mu g/cm^2$ f DNA Breakage: 2.5, 5, 10, 20, 40 $\mu g/cm^2$ Cytokine Assays: 10, 20, 40, 80 $\mu g/cm^2$ E-Selectin Expression: 40 $\mu g/cm^2$	Cytotoxicity: 24, 48, 72h Apoptosis: 24 h DNA Breakage: 72h Cytokine Assays: 24 h E-Selectin Expression: 40 $\mu g/cm^2$ PM	Cytotoxicity: Cytotoxic effect dose-dependent after 72h in proliferating cells of J774A.1, BALB-c and RLF cell lines. Proliferating Cells: Particles from north induced statistically larger effect than central or southern particles. J774A.1 more susceptible. BALB-c less susceptible. A549 most resistant to decreased viability during exposure. No significant variation in viability observed when compared to control. Particles not cytotoxic among confluent cells growth for any cell lines when exposed to 20-160 $\mu g/cm^2$. Apoptosis: Overall particles induced low rates of cell death via apoptosis. J774A.1 depicted similar levels of apoptosis when exposed to three PM zones, ~15% apoptotic cells measured. BALB-c not reported. A549 measured apoptotic cells: South- 4%, Central- 11% and North- 15%. HUVEC cells indicated increase in apoptosis with North particles. DNA Breakage: PM_{10} from all zones induced DNA breakage. Dose-dependent relationship established between concentrations of $PM_{2.5}$ - 10 $\mu g/cm^2$. Southern zone required higher dose of PM (10$\mu g/cm^2$) to produced same effect as other zones (2.5$\mu g/cm^2$). Cytokines: Particles induced TNF-α and IL-6 secretion in J774A.1 cells dose-dependently. IL-6 increased significantly with central particles. PGE2 secretion in RLF cells induced by exposure to PM dose-dependently. Observed that PM from the central zone induced most PGE2 secretion. Max secretion observed at dose of 40 $\mu g/cm^2$ from all three PM zones. E-Selectin Expression: HUVEC cells showed 25% increase in E-selectin expression after exposure to 40 $\mu g/cm^2$ PM.
Amakawa et al. (2003)	Mouse, Alveolar Macrophages, Male, ICR, 25-35 g, 6-7wks Human, Alveolar Macrophages, Male, 20-24y Mouse: $5X10^5$ cells/mL Human: $3X10^5$ cells/mL	DEP (4JB1, Isuzu, 1500 rpm, 4cyl diesel engine) DEPE = DEP Extract (methanol) CB = Charcoal (Sigma, 250-350 mesh ~ 40-70 μm) DEP = 0.4um CB = 0.7um	DEP = 1 or 10 $\mu g/mL$ DEPE = 1 or 10 $\mu g/mL$ CB = 1, 10, 100 $\mu g/mL$ Human cells pre-treated with LPS 1 $\mu g/mL$ Murine cells pre-treated with SOD 300 IU/mL	24 h	Cells: For mice, >90% macrophages, >90% viable. For humans, 96% macrophage, 3% lymphocyte, 1% neutrophils, >95% viable. DEP Cytotoxicity: None observed Cytokines: DEP (10$\mu g/mL$) suppressed release of TNF-α and IL-6 for both mice and humans dose-dependently. Murine cells pre-treated with LPS or IFN-y released even less TNF-α and IL-6. IL-10 unaffected. Human macrophages pre-treated with LPS also released lower levels of TNF-α, IL-6 and IL-8. ROS: Pre-treatment of SOD on murine cells lowered effect of DEP so formation of ROS limited. Carbon: No suppression of TNF-α or IL-6 release, 100 $\mu g/mL$ CB induced release of TNF-α. Methanol: No cytotoxicity nor cytokine release effects DEPE: Suppressed TNF-α and IL-6 release similar to DEP.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Amara et al. (2007)	Human, A549 Human, NCI-H292 NR	DEP = SRM 2975 CSC = cigarette smoke condensates DC = DEP + CSC CB CB = 95nm	DEP = 5-10 μg/cm^2 CB = 10 μg/cm^2 = 50 μg/mL CSC = 10 μg/cm^2 = 50μg/mL	6 or 24 h	Inflammatory Markers: LDH of A549 unaffected at either time point with DEP or CB. LDH increased with CSC dose >10μg/mL at both time points. DC had no effect. Proteases: Dose-dependent increase of MMP-1 mRNA expression in A549 cells with DEP. DEP also increased MMP-1 in NCI-H292 cells. CB and CSC had no effect. MMP-1 mRNA expressions inhibited by N-acetylcysteine antioxidant. Similar inhibition with NO_X4 oxidase. DC induced similar effect to DEP. MMP-1 protein expression increased post 24 h with DEP. MMP-2, TIMP-1, TIMP-2 mRNA expression unaffected. TGF: TGF-β mRNA expression unaffected. ROS: DEP and DC increased ROS formation after 1h. DEP effect inhibited by N-acetylcysteine antioxidant pre-treatment. MAP-Kinase: DEP induced effect after 10 min, peaked at 30 and returned to normal after 60 min. CB induced similar effect. Only inhibitors of ERK1/2 reduced DEP induced MMP-1 activity. P38 and JNK inhibitors had no effect.
Anseth et al. (2005)	Human, A549 Human, A549-p0, lacking mitochondria 3X10^5 cells/mL	s-ROFA = soluble portion 1.95 ± 0.18 μm	100 μg/mL	16h	Experimental process: Experiments conducted by spreading monolayer of Infasurf (calf lung surfactant extract (20 ul in 1.5 mL of chloroform/methanol solution)) on PBS, PBS+ROFA or conditioned media from A549 AEC. Lung Surfactant Gelation: ROFA alone and A549 conditioned media alone did not significantly alter Infasurf rheology. However, conditioned media from A549 AEC at 16h induced significant increase in elastic storage and viscous loss moduli. Inhibiting ROS production lowered effect, indicating s-ROFA gelation mediated through ROS. ROS: ROS mediated through mitochondria as evidenced by effect of ROFA-AES on surfactant gelation in presence of mitochondria ROS inhibitors as well as A549-p0 cells.
Auger et al. (2006)	Human, Nasal Epithelial Cells 2-3.5x10^4 cells/cm^2	DEP = SRM1650 $PM_{2.5}$ = Highway, Paris, France DEP = 400nm	10-80 μg/cm^2	24 h	Cytotoxicity (LDH): No cytotoxicity for DEP or $PM_{2.5}$ (80 μg/cm^2). Cytokines: Both DEP and $PM_{2.5}$ deposited on apical surface dose-dependently induced IL-8 and amphiregulin release through basolateral surface, but not apical surface. $PM_{2.5}$ stimulated IL-6 and GM-CSF release through apical surface but not basolateral surface. IL-8 >>GM-CSF = amphiregulin = IL-6. No effect for DEP (no data). ICAM-1 expression: No effect from DEP or $PM_{2.5}$. ROS: DEP and $PM_{2.5}$ both dose-dependently increased ROS production.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Bachoual et al. (2007)	Mouse, RAW 264.7 40,000 cells/mL	PM_{10} from two Paris, France subway sites: RER and Metro CB TiO_2 DEP PM_{10} RER = 79% <0.5 µm 20% 0.5-1 µm Metro = 88% <0.5 µm 11% 0.5-1 µm CB = 95nm TiO_2 = 150um DEP = SRM 1650	0.01, 0.1, 1, 10 µg/cm²	3, 8, 24 h	Cell Viability: No effects from any particulate at concentrations up to 10 µg/cm² for 24 h. Inflammatory Effect: Exposure of cells to 10µg/cm² of RER or Metro induced time-dependent increase in TNF-α and MIP-2 protein release. The effect similar to both locations. No effect observed at low concentrations of PM_{10}. No effect of CB, TiO_2 or DEP observed. GM-CSF or KC production: RER and Metro PM_{10} did not induce any effect at any concentration. Effect on Protease mRNA Expression: Exposure of cells to 10 µg/cm² RER or Metro PM_{10} did not modify mRNA expression of MMP-2 or -9 or their inhibitors TIMP-1 and -2. MMP-12 expression significantly increased after exposure to RER or Metro PM_{10} for 8h. Effects on HO-1 Protein Expression: Exposure to 10 µg/cm² of RER or Metro PM_{10} for 24 h induced positive cytoplasmic staining for HO-1.
Baulig et al. (2007)	Human, 16-HBE14o- 20,000 cells/cm²	WUB = Winter Urban Background Particles (Vitry-sur-Seine, suburb of Paris, France) SUB = summer Urban Background Particles Vitry-sur-Seine) WC = Winter Curbside Particles (Porte-d'Auteuil, ring road of Paris, France) SC = summer Curbside Particles (Porte-d'Auteuil) DEP DPL (control) WUB, SUB = $PM_{2.5}$ WC, SC = SRM 1648 DEP = SRM 1650a	10 µg/cm²	18 or 24 h	EGF: Upregulation of Amphiregulin gene increased significantly with WC >WUB >SC >SUB >DEP >DPL. βcellulin increased with SC>WUB >WC. No data on SUB or DEP. Interleukins: IL-1α increased significantly with WUB >WC >SC >DEP >DPL. No data with SUB. Exposure to WUB caused IL-1β to increase to induction factor of over 2. IL-11 R α decreased significantly with SUB. Cytokines: Exposure to WUB caused G-CSF to increase with an induction factor of over 2. TNF-R1 also increased, but not statistically significant. Proteases: TIMP-2 decreased with WUB but significantly increased with SUB. Overall, SUB downregulated integrins and interleukins seen with other particles while upregulating neurotrophic factors, chemokine receptors and adhesion molecules. MMPs not measured. Chemokines: CCR-3 significantly increased with SUB. GRO-gamma and GRO-α increased with WC at both 18 and 24 h. DEP had no effect with GRO-α. Removal of metal from particles lowered response of GRO-α.
Bayram et al. (2006)	Human, A549 NR	DEP (4JB1-type, light-duty, 4 cyl, 2.74-L Isuzu diesel engine) -FCS = DEP + FCS -NAC = DEP + N-acetylcystine, antioxidant -A = DEP + AEOL10113, catalytic antioxidant -S = DEP + SP600125, inhibitor of JNK -N = DEP + SN50, inhibitor of NF-kB 10% FCS (positive control) 0.4um	0, 5, 10, 50, 100, 200 µg/mL	24, 48, 72h	Cell Growth: With 10% FCS, time dependent growth. With mix of FCS and DEP, cell growth unaffected upto 48h. With DEP alone, cell growth was prevented from reduction due to removal of serum at 48 and 72h. Dose of 10µg/mL induced max effect. Cell Cycle: Increased percentage of serum-starved cells in S phase with DEP at 10µg/mL at 48h. Decreased percentage in G0/1 phase and G2/M phase with DEP. Apoptosis: Prevention of increase in apoptotic, serum-starved cells with DEP. Protein Expression: p21CIP1/WAF1 expression increased at 48h. DEP dose-dependently decreased this expression. NAC: NAC alone induced cell increased with 33mM. DEP-NAC inhibited cell numbers at 48h. DEP-NAC inhibited cell numbers in S phase, thus cells in G0/1 phase increased. DEP-NAC induced further decrease of cells in G2/M phase. AEOL10113: Dose-dependent decrease in cell number with DEP-A. SP600125: Alone, SP600125 increased cell numbers at 33mM. DEP-S decreased cell numbers.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Becher et al. (2007)	Rat, Alveolar Type II, Male, Crl/Wky, 200g Rat, Alveolar Macrophages, Male, Crl/Wky, 200g 1.5x10^6 cells/well AM 6x10^6 cells/well Type II	SPM = suspended PM SRM-1648 6-8um	200μg/mL = 20 μg/cm^2	20h	Cytokines in Macrophages: SPM increased TNF-α and MIP-2. NADPH inhibitor DPI reduced MIP-2 response, whereas iNOS inhibitor 1400W did not affect either. Cytokines in Type 2 Cells: SPM increased IL-6 and MIP-2 significantly. DPI reduced both effects, whereas 1400W reduced IL-6 response significantly. ROS in Type 2 Cells: SPM increased ROS significantly. DPI largely blocked SPM effect. ROS in Macrophages: No significant increases observed.
Becker et al. (2005b)	Human, NHBE, Male and Female, 18-35y Human, Alveolar Macrophages, Male and Female, 20-35y 0.5-1 x 10^5 cells/well NHBE 2-3 x 10^5/mL AM	PM (EPA, Chapel Hill, NC, Chem Vol Cascade) -C = Coarse -F = Fine -UF = Ultrafine LPS (control) Coarse = $PM_{2.5}$ Fine = PM0.1 Ultrafine <0.1um	25, 50, 100, 250 μg/mL for NHBE 50 μg/mL AM 10 ng/mL LPS (AMs only)	18 h for NHBE Overnight for AMs	Cytokines: All 3 fractions induced IL-8 increase dose-dependently with PM-C >PM-F >PM-UF. TLR-2 antibody blocked effects on IL-8. Inhibitors of Endotoxin effects and TLR-4 activation: No effects in NHBE, but repression of IL-6 release in AMs for all 3 fractions. TLR mRNA Expression: PM did not affect TLR-2 mRNA in NHBEs. PM-C and PM-F induced slight increase in TLR-4 mRNA in NHBEs while PM-UF induced substantial increase. PM-C increased TLR-2 mRNA in AMs and decreased TLR-4 mRNA in AMs. Induction of Hsp70: PM-C and PM-F induced Hsp70 in NHBE dose-dependently. AMs unaffected.
Becker et al. (2005a)	Human, NHBE, Male, 18-35y Human, Alveolar Macrophages, Male, 18-35y 3-5 x 10^5 cells/well NHBE 2-3X10^5 cells/mL AM	PM (EPA, Chapel Hill, NC, Chem Vol Cascade) -C = Coarse -F = Fine -UF = Ultrafine ROFA Fe, Si, Cr Components Coarse = $PM_{2.5}$ Fine = PM0.1 Ultrafine = <0.1 μm Oct 2001, Jan 2002, April 2002, July 2002	11 μg/mL NHBE 50 μg/mL AM	18-24 h NHBE 18 h AM	IL-8 Release in NHBE: PM-C and PM-UF induced effects. No effects from PM-F (all 4 dates). IL-6 Release in AM: All 3 fractions induced increase with later dates having generally lower effects. ROS (DCF): NHBE (lower exposure) more responsive than AM - highly variable results over time. ROS (DHR): NHBE more responsive than AM. AM responsive increased over 4 time periods not so for NHBE. Seasonal Variability: IL induction in NHBE and AM highly variable - AM 6 fold, NHBE 3 fold. Metal Correlation to IL-6/8 induction: FE and IL-6 in AM for coarse and fine. Si and IL-6 in AM for coarse, Cr and IL-8 in NHBE for fine and ultrafine.
Beck-Speier et al. (2005)	Canine, Alveolar Macrophages, Beagle Human, Alveolar Macrophages, 18-25y 1X10^6 cells/mL AM	DEP = SRM 1650a EC = Ultrafine Elemental Carbon (spark discharge) P90 = Printex 90 (Carbon Black, Degussa) PG = Printex G (Carbon Black, Degussa) DEP = 20-40nm EC = 5-10nm P90 = 14nm PG = 51nm	1, 3.2, 10, 32, 100 μg/mL	60 min	Phagocytosis: Particles incorporated into CAM within 60 min. Oxidative Potential: EC showed very high effect. DEP, P90 and PG had no effect Formation of Lipid Mediators: DEP, EC P90 and PG increased arachidonic acid and PGE2/TXB2 in CAM dose-dependently. Only EC increased LTB4 and 8-isoprostane. ROS Activation: All particles increased activity in canine macrophages - EC, P90 and PG dose-dependently. DEP increased activity in canine macrophages. Results similar in human alveolar macrophages but only EC and P90 tested. Particle Mass vs Particle Surface Area: PGE2/TXB2 effects highly correlated with particle surface area.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Bitterle et al. (2006)	Human, A549 3 x 10^7 cells	C-UFP = ultrafine carbonaceous particles (spark discharge aerosol generator GFG 1000, Palas, Karlsruhe, Germany) 90nm	44 ± 4 ng/cm^2 87 ± 23 ng/cm^2 230 ± 70 ng/cm^2 ng/cm^2 = total mass of deposited particles per cm^2 cell monolayer after 6h exposure	6h	Cell Viability: 93.7 ± 9.1% viability with clean air. 94.9 ± 9.5% viability with low, mid and high doses of C-UFP. Thus C-UFP had no effect. Interleukins: Clean air controls induced 2-3 fold increase in IL-6 and IL-8 vs submersed control. U-CFP exposures induced similar effect on IL-8 and IL-6. Antioxidant enzyme HO-1: Increased transcription of HO-1 by 2.7 fold at mid dose level. No effect at high dose level, indicating possible cytotoxicity.
Blanchet et al. (2004)	Human, 16HBE 45,000 cells/cm^2	$PM_{2.5}$ (Vitry-sur-Seine, Paris, France) DEP = SRM 1650a CB = Carbon Black (Degussa) TiO_2 (Huntsman) CB = 95 nm TiO_2 = 150 nm	0.1, 1, 10, 30 μg/cm^2	6, 18, 24, 30h	Amphiregulin Expression: DEP and $PM_{2.5}$ both increased AR mRNA expression from 6 to 30h. $PM_{2.5}$ >DEP. Both DEP and $PM_{2.5}$ increased AR protein secretion. No effect for CB and TiO_2. $PM_{2.5}$ induce protein secretion dose-dependently. Signal Pathways in AR Secretion: MAP kinase and tyrosine kinase inhibitors reduced effects of DEP and $PM_{2.5}$ but p38MAP kinase inhibitor did not. Role of Oxidative Stress: N-Acetylcysteine blocked AR secretion following $PM_{2.5}$. Antioxidant enzyme catalase had no effect. Cytokines: DEP induced significantly high release of GM-CSF, higher than $PM_{2.5}$. EGFR antibody reduced GM-CSF release at 0.25 μg/mL dose.
Bonvallot et al. (2001)	Human, 16HBE14o- 3 x 10^6 cells	DEP = SRM 1650 OE-DEP = dichloromethane extract (2x) of DEP nDEP = native DEP sDEP = nDEP - OE-DEP CB = Carbon Black FR103 (Degussa) BaP = Benzo[a]pyrene CB = 95 nm NR	DEP, sDEP, nDEP and CB = 10 μg/cm^2 OE-DEP = 15 μg/mL BaP = 0.25, 50 and 250 μg/mL CB = 95nm	24 h	Proinflammatory Response: At 10μg/cm^2, nDEP induced GM-CSF release of 4.7 fold. OE-DEP increased GM-CSF by 3.7 fold. BaP and sDEP also induced increase of CN-CSF but smaller effect. CB had no effect. nDEP>OE-DEP~ BaP250>BaP50>sDEP>BaP0.25>CB = control. NF-κB Activation: nDEP and OE-DEP induced enhanced degradation of IκB at 2-4h and 1h respectively. NF-κB DNA binding enhanced by OE-DEP (15 μg/mL, peak <1h) and nDEP (10 μg/cm^2, peak at 2-h with plateau till 4 h). Both higher than BaP at 250 μg/mL. CYP1A1 mRNA: nDEP and OE-DEP increased mRNA as did BaP, which may be metabolized by CYP1A1. Radical Scavengers (decreased ROS in situ): Increases of GM-CSF and NF-κB DNA binding by nDEP and OE-DEP attenuated by radical scavengers. MAPK Activation: Increases by nDEP and OE-DEP of GM-CSF inhibited by Erk1/2 inhibitor but not by p38 inhibitors. Both nDEP and OE-DEP triggered Erk1/2 and p38 phosphorylation. sDEP affected p38 phosphorylation only.
Brown et al. (2007)	Mouse, J774A.1 Human, Peripheral Blood Mononuclear Cells (PBMC) Human, A549 1 x 10^6 cells/mL J774A.1 5X10^6 cells/mL PBMC 5X10^5 cells/well A549	PM_{10} (London, England) CM from PM_{10}-treated human monocytes NR	10 μg/mL PM_{10} NR UfCB NR CM	4, 18h	Cytokines: PM_{10} induced release TNF-α protein from PBMCs at 10μg/mL for 4h. Further inhibited by verapamil and BAPTA-AM. Calmodulin inhibitor W-7 had no effect. CM increased IL-8 from A549 cells 3 fold. Verapamil, BAPTA-AM and W-7 significantly inhibited IL-8 release induced by CM. ICAM-1: A549 cells treated with TNF-α showed dose-dependently effect of TNF-α on ICAM-1 upregulation at 18h. CM also induced upregulation. Verapamil, BAPTA-AM and W-7 fully inhibited CM-induced upregulation.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Calcabrini et al. (2004)	Human, A549 5 x 10^4 cells/well	$PM_{2.5}$ (Rome, Italy) NR	30, 60 μg/cm^2 (aliquot of 0.1 μg/ul)	5, 24, 48, 72h	Particle Characterization: Components measured include C-rich particles, Ca sulfates, silica, silicates, Fe-rich particles, metals. Carbonaceous particles made up majority of PM. Cell Surface Changes: PM deposited on cell surface showed dose and time-dependent increase in microvilli rearrangement and cell shape alterations without affecting apoptotic markers for up to 72 h. PM internalization: At 24 h with low dose, aggregates of PM in cytoplasm or surrounded by membrane observed. With high dose, large particle aggregates often close to nuclear envelopes observed. Cytoskeleton: At 72h PM induced dose-dependent alterations from rearrangement/interweaving of microtubules to bundling of microtubules with some shortening/disruption. Cell Growth: PM decreased cell growth dose and time -dependently. ROS: PM increased ROS at high dose for 5h but not at 24 h or at low dose. Cytokines: PM induced TNF-α peaked at 5h at high dose and 48h at low dose, both ND at 72h. PM induced IL-6 starting at 24 h thru 72h in time and dose dependent manner.
Cao et al. (2007)	Human, Airway Epithelial Cells (HAEC), obtained in vivo from adult volunteers 5 x 10^5 cells	NIST-DEP = SRM 2975 C-DEP = U.S. EPA (40 hp 4 cyl diesel engine) NR Organic extract fraction of particles NIST- DEP 2% C-DEP 20 %	0-200 μg/mL	1, 4h	Cell Viability: DEP had no effect. Stat3: Both DEPs induced time-dependent phosphorylization of Stat3 in cytoplasm. NIST-DEP induced phosphorylization dose-dependently from 12.5 to 50 μg/mL but stayed level at 100 and 200 μg/mL. p-Stat3 induction inhibited by antioxidant BHA though reactivated with exposure to H_2O_2. Reaction induced by H_2O_2 similar to that of DEP. pStat3 Nuclear Transport: NIST-DEP induced cytoplasmic pStat3 to move from cytoplasm into nucleus. pEGFR Dephosphorylation: After 4h of NIST-DEP exposure, dephosphorylation inhibited for up to 90 min.
Chang et al. (2005a)	Human, THP-1 (monocyte) Human, A549 7 x 10^5 cells	UfCB (Printex 90, Degussa) 14nm	100 μg/mL	4h	ROS in THP-1 and A549: UFCB increased ROS. NAC blocked most of UFCB-induced ROS production. VEGF in THP-1: UFCB increased VEG. NAC decreased UFCB effects below control. VEGF in A549: Produced same results as for THP-1 but less markedly.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Chauhan et al. (2004)	Mouse, RAW 264.7, leukemia virus transformed macrophages in male BALB/c mice Mouse, J774A.1, from a tumor in female BALB/c mice Mouse, WR19M.1, leukemia virus transformed macrophages from female BALB/c mice 15000 cells/well	EHC - T = total EHC-93 (Env Health Ctr, Ottawa, Canada) - I = insoluble EHC - S = soluble EHC SRM1648 = urban particulate St.Louis SRM1649 = urban dust/organics Washington VERP = fine $PM_{2.5}$ (Vermillion, Ohio) Cristobalite = SRM 1879 TiO_2 = SRM 154b Post-treatment with LPS or IFN-y 0.5um EHC NR LPS, IFN-y	0-100μg/well 0-5 μg/mL LPS 0-1000 U/mL IFN-y	2 h for particulates, then 22 h afterwards for LPS and IFN-y	Stimulation with LPS/IFN-y: LPS and IFN-y each induced NO release. Combination of LPS and IFN-y produced larger effect in all cell lines. L-NMMA, NOS inhibitor, suppressed most of NO production with 100nmol/L. Cellular Viability and Cytotoxicity: Exposure of cells to particulates did not result in overt cytotoxicity or excessive loss of cellular material. No correlation between cytotoxicity of the particles in the surviving cells and the loss of protein mass in monolayers. Nitrite Production: EHC-T, EH-93-I, SRM1648 and SRM 1649 produced dose-dependent decrease. Cristobalite only decreased at higher doses. No effect from EHC-93 soluble, VERP or TiO_2. iNOS: EHC-I, EHC-T, Crisobalite and SRM1648 inhibited iNOs expression. TiO_2 had no effect. EHC sol, SRM 1649 and VERP not tested.
Chauhan et al. (2005)	Human, A549 150000 cells/flask	EHC - T = total EHC-93 - I = insoluble EHC - S = soluble EHC Cristobalite = SRM-1879 TiO_2 = SRM-154b 0.4um EHC	0, 1, 4, 8 mg/5ml	24 h	Cellular Viability: Decreased after exposure to EHC-T, EHC-I and cristobalite. Rate of reduction not consistent across dosage range. EHC-S and TiO_2 had no effect. ET-1: Release of ET-1 peptide decreased dose-dependently for EHC-T, -S and -I. Fractions of EHC-S and EHC-I more potent than EHC-T. TiO_2 and Cristobalite also reduced ET-1 secretion although not consistent across dose range. Cytokines: Results showed no detectable amounts of GM-CSF, IL-1β or TNF-α in cell culture supernatants. IL-8 dose-dependently increased with EHC-T, EHC-I and cristobalite. VEGF: VEGF significantly increased dose-dependently with EHC-T, EHC-S and cristobalite. EHC-S induced significant decrease in VEGF. Gene Expression: mRNA levels for preproET-1 reduced at 24 h for all particle types. EHC-S induced significant decrease in ET-1 expression at high dose. ECE-1 mRNA expression increased with EHC-T and EHC-I. Other particles had no effect. ETaR mRNA increased with EHC-T, EHC-S. and TiO_2 in biphasic manner where highest expression of mRNA seen at middle dose levels. EHC-S had no effect. ETbR mRNA increased with low dose EHC-T and decreased with high dose EHC-T. EHC-S, EHC-I and cristobalite induced increase of ETbR. TiO_2 induced significant decrease. Proteases: mRNA levels for MMP-2 reacted similarly to preproET-1. mRNA levels for TIMP-2 significantly induced with EHC-I. EHC-T and EHC-S induced small effect.
Cheng et al. (2003)	Human, A549 $8x10^5$ cells/mL	DEP -h = DEP with high sulfur -LS = DEP with low sulfur GEP = gasoline engine exhaust particles Primed cells pretreated with TNF-α DEP-h = 15.9nm DEP-LS = 17.7nm GEP = 8.3nm	NR Exhaust flow-through cell culture with air-cell-interface, exhaust diluted 10-15x	60-360 min	IL-8: DEP-h induced 3 fold increase in IL-8 than control. DEP-LS also induced increases. Primed cell cases had higher levels (10x) than unprimed when exposed to DEP-LS. DEP-h induced higher levels of IL-8 than DEP-LS. Response lasted for up to 6h. GEP induced statistically insignificant increase of IL-8 in unprimed cells. WIth primed cells, GEP induced level of IL-8 that exceeded that of DEP-h and DEP-LS. Response lasted for 1-2 h.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Chin, B.Y. Trush, M.A. Choi, A.M.K. 2002	Murine, RAW 264.7 Human, A549 Human, MHS, Alveolar Macrophage Cell Line NR	CB = N339, benzo[a]pyrene absorbed on surface some cells co-exposed or only exposed to BaP BP-1,6-Q 0.1um	1, 2, 4μg/mL 2μg/mL BaP 1μM BP-1,6-Q	1-24 h	HO-1 mRNA Expression: In RAW264.7, HO-1 mRNA increased with 2 and 4 μg/mL at 2h. Increase continued to 8h, declined by 24 h. BaP had no effect. BP-1,6-Q increased Ho-1 mRNA after 1h, maintained until 8h. In A549 and MHS, HO-1 mRNA increased after 1h with peak at 8h in A549 and 4h in MHS. HO-1 Protein Expression: Increase of protein at 4-8h in RAW264.7. AP-1: Increases in binding activity observed in RAW 264.7 cells at 2h.
Churg et al. (2005)	Rat, Epithelial Cells of Tracheal Explants, Sprague-Dawley, 250g NR	EHC93 (Ottawa Urban Air Particles) TiO_2 TiFe = Iron-loaded fine TiO_2 (previously published) 3-4um EHC93 0.12 ± 1.4 μm TiO_2	500 μg/cm^2	1 h and 2 h Some experiments (referred to as 2h) explants transferred to different dish and incubated for additional hour. Pre-treated with Inhibitors/Chelators for 2 h	Activation of NF-κB: Both particle types increased nuclear translocation of NF-κB. TiFe and EHC93-increased NF-κB 1.5 fold at 1h. TiFe- increased NF-κB 3.5 fold at 2h. EHC93- increased NF-κB more than 2 fold. TiO_2 by itself did not increase NF-κB at any exposure duration. Activation of NF-κB through entry of particles into tracheal epithelial cells: No evidence of dust particles (EHC93 or TiO_2) in epithelial cell cytoplasm at 2 h or evidence of morphologic cell damage from particles. Colchicine: Did not prevent NF-kB activation. Inhibitors/Activators: Tetramethylthiourea (TMTU) (membrane-permeable active oxygen scavenger), Deferoxamine (redox-inactive metal chelator), PPS (Src inhibitor) AG1478 (epidermal growth factor receptor inhibitor) prevented NF-κB activation in both EHC93 and TiFe exposed-cells. Iron-containing citrate extract of both dusts increased NF-κB activation in both EHC93 and TiFe exposed-cells.
Dagher, A. Garcon, G. Billet, S. 2007	Human, L132, Normal Lung Epithelial Cells 3 x 10^6 cells/20mL 1.5 x 10^6 cells/20mL 0.75 x 10^6 cells/20mL	LC10, LC50 = $PM_{2.5}$ (collected Jan-Sept in Dunkerque, France) Particle size - cumulative frequency: 0.5 μm; 34 % 1 μm; 64 % 1.5 μm; 79 % 2 μm; 87 % 2.5 μm; 92 % 5 μm; 98 % 10 μm; 100 %	LC10 = 19 μg/mL LC50 = 75 μg/mL	24, 48 or 72h	p65 Protein: Phosphorylation of p65 increased in PM-exposed L132 cells in dose-dependent manner. IkBα Protein: Phosphorylated IkBα protein concentrations increased in cytoplasm with both particle types at all time points. p65 and p50 DNA: p65 DNA binding increased at 24 h with LC10 and LC50, at 48 h with LC10, and at 72 h with LC10 and LC50. p50 DNA binding increased at all time points with LC10 and LC50.
Dai, J. Xie, C. Vincent, R. 2003	Rat, Tracheal Explants, Sprague-Dawley, 250g 2x2 mm each explant	EHC93 DEP = SRM 1650a 3-4um MMAD, 0.5-0.6um CMD EHC93 1.55 ± 0.04um CMD DEP	500 μg/cm^2	1h, 7d post-exposure	Hydroxyproline: EHC93 induced almost 3 fold increase in explant hydroxyproline. DEP increased tissue hydroxyproline 2.5 fold. Procollagen: EHC-93 doubled gene expression of procollagen. Could be fully inhibited by SN50, TMTU or treatment of the PM with DFX. Treatment of explants with p38 or ERK (inhibitors) had no effect on procollagen expression. DEP induced increase in procollagen gene expression but completely prevented by SN50 and MAP kinase inhibitors (SB203580 and PD98059). Neither TMTU or DFX has any effect. TGFβ1: Treatment of explant with EHC93 approximately doubled gene expression for TGFβ1. Treatment with SN50, TMTU and fetuin (TGFβ antagonist) blocked increase. DFX, MAP kinase inhibitors (SB203580 and PD98059) had no effect. DEP roughly doubled TGFβ1 expression.SN50 and MAP kinase inhibitors (SB203580 and PD98059) fully blocked effect. TMTU and DFX had no effect.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Doherty, S.P. Prophete, C. Maciejczyk, P. 2007	Rat, NR8383, Alveolar Macrophages 2X10^5 cells/mL	V: Fe Al: Fe Mn: Fe V = sodium vanadate ($NaVO_3$) Al = aluminum chloride hexahydrate ($AlCl_3$) Mn = manganese chloride tetrahydrate ($MnCl_2$) Fe = ferric chloride hexahydrate ($FeCl_3$) NR	Fe = 16 µmol (equivalent to urban NYC 500 µg $PM_{2.5}$) V and Mn tested in molar rations of 0.02 to 0.4 relative to Fe Al tested in molar rations of 0.125 to 8 relative to Fe. Ratios based on $PM_{2.5}$ measurements from NYC, LA and Seattle	20h	IRP: Addition of V increased IRP activity 5 to 9 fold (due to high variability dose-response unclear). Addition of Mn only resulted in effect at 0.1 molar ratio (two-fold), not at higher or lower ratios. Al resulted in peak increases of 5 fold at molar ratios while declining to 2 fold at molar ratios 4 and 8. Cytoxicity Al cytotoxic at molar ratios of 4 and 8. All other Al, V, Mn ratios without effect. Mixtures: Combination of metals also tested at NYC PM ratio and V drove all Fe transport activity. Combinations of V+Mn and V+Al increased activity more than V: Fe alone.
Doornaert, B. Leblond, V. Galiacy, S. 2003	Human, 16HBE14o- Human, Primary HBE (P-HBE) cells, obtained by fibroscopy from several lung cancer patients, biopsies from tumor confirmed presence of normal bronchial mucosa. NR	DEP = SRM 1650 CB DPC = Dipalmitoyl phosphatidylcholine (positive control) 0.1- 0.5um	1- 100 µg/mL	24 h 24, 48, 72 h post-exposure analysis 1-HBE Cell Deadhesion Capacity: 24 h, evaluation of detachment performed every 5min for 40min after Cell Wound Repair Capacity: 24 h, repair evaluated 3.5, 7, 24 h after	Cytotoxicity: DEP cytotoxic at 100 µg/mL at all time points in time-dependent manner. CB and DPC cytotoxicity substantially lower but significant at 72h. Phagocytosis: 1-HBE cell levels increased in phagocytosis dose-dependently with DEP >CB >control. F-actin: Only DEPs engulfed by F-actin stained cell fragments. Actin CSK Stiffness: DEP (5, 20, 100 µg/mL) induced net dose-dependent decrease in cytoskeleton stiffness and dose-dependent decrease in actin cytoskeleton stiffness. CB produced no significant decrease. Adhesion Molecules: DEP induced concomitant reduction of both CD49 (α3) and CD29 (β1) integrin subunits, and decrease in level of CD44 (HBE cell-cell and cell-matrix adhesion molecule) at both 20 and 100µg/mL. Proteases: DEP also induced isolated decrease in MMP-1 expression without change in tissue inhibitor of TIMP-1 or TIMP-2 at 100 µg/mL. CB produced no change or insignificant results. 1-HBE Cell Deadhesion Capacity: DEP exposure induced dose-dependent amplification of cell detachment at 5min of incubation and onward. Cell Wound Repair Capacity: DEP inhibited wound repair/wound closure in dose-dependent manner.
Dostert et al. (2008)	Human, THP1, Macrophages Human, Monocyte-derived Macropahes (MM) NR	Asbestos Silica DEP CSE = cigarette smoke extract MSU = monosodium urate crystals NR	0.1, 0.2 mg/mL Asbestos 0.1, 0.2, 0.25, 0.5 mg/mL Silica 0.2, 0.25, 0.5 mg/mL DEP 5%, 10% in solution mg/mL CSE 0.1, 0.2 mg/mL MSU	1, 3, 6h	IL-1β: Increased levels of IL-1β with asbestos and silica observed in THP1 at 6h. CSE and DEP had no effect. MM also had increased levels with asbestos, silica and MSU at high dose levels only. Caspase-1: Caspase-1 is enzyme for activating maturation of IL-1β. Asbestos increased caspase-1 activity. ROS: Formation increased with asbestos doses in THP1.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Doyle, M. Sexton, K.G. Jeffries, HR. 2004	Human, A549 Human, Bronchial Epithelial Cells, Nonsmoking Adults NR	BD = 1,3-butadiene, known carcinogen Acrolein = photochemical and NO product of BD in atmosphere Acetaldehyde = photochemical and NO product of BD in atmosphere Formaldehyde = photochemical and NO product of BD and ISO in atmosphere ISO = isoprene, 2-methyl analog of BD Methacrolein = photochemical and NO product of ISO in atmosphere Methyl vinyl ketone = photochemical and NO product of ISO in atmosphere Clean air (control) with A549 cells NR	50 ppb NO 200 ppbV ISO, BD Environmental irradiation (smog) chambers used	5h 9 h post-exposure analysis	Cytotoxicity: ISO+NO and BD+NO induced small increases of LDH in A549. However, ISO+NO+light and BD+NO+light increased LDH levels 4-6 fold indicating photochemical products of ISO and BD highly cytotoxic. LDH levels of each combination equivocal. IL-8 Protein: Methacrolein, methyl vinyl ketone and formaldehyde (products of ISO) increased IL-8 protein levels significantly. ISO+NO had no effect. BD photochemical products (acrolein, acetaldehyde and formaldehyde) also increased IL-8 protein, more than double what ISO photochemical products induced. BD+NO had no effect. IL-8 mRNA: IL-8 mRNA expression also increased with photochemical products of ISO and BD but did not reach statistically significant level.
Duvall, R.M. Norris, G.A. Dailey, L.A. 2008	Human, Airway Epithelial Cells, obtained by brush biopsies from volunteers 100,000 cells/cm^2	PM -UF = ultrafine -F = fine -C = coarse -S = Seattle, WA -SL = Salt Lake City, UT -P = Phoenix, AZ -SB = South Bronx, NY -HR = Hunter College, NY -SF = Sterling Forest, NY. Coarse (>2.5um) Fine (<2.5um) Ultrafine (<0.1um)	NR	2, 24 h	Particle Characterization: PM-HR, PM-SL and PM-S contained highest UF, F, C concentrations. PM-SB and PM-HR had similar F and C concentrations. Sulfate highest in PM-F for all sites except PM-SB and PM-HR. Wood combustion highest in PM-SL, PM-S, PM-P. Soil dust highest in PM-SL and PM-S. IL-8: PM-UF induced greater increase in IL-8 than other types of PM. Exception is PM-P. PM-UF associated with vanadium, lead, copper, sulfate. PM-F-HR caused greatest increase and PM-SB being second. PM-F-SF and PM-F-P least effective. PM-C also caused increase and associated with vanadium and elemental carbon. COX-2: PM-F-S induced greatest increase in COX-2 expression. Other site PM-F induced similar increases. Ultrafine PM had no effect. PM-C induced increase, associated with elemental carbon. HO-1: PM-F-SF induced greatest increase in HO-1. PM-F-SL least effective. Ultrafine PM had no effect. PM-C caused increase, associated with copper, barium, elemental carbon.
Dybdahl, N. Risom, L. Bornholdt, J. 2004	Human, A549 10^5 cells/mL	DEP = SRM 1650 NR	0, 10, 50, 100, 500 µg/mL	2, 5 or 24 h	Cytokines: DEP induced dose-dependent increase of IL-1α, IL-6, IL-8 and TNF-α at 24 h. Cytokines increased between 4 and 18 fold at highest DEP dose compared to controlled cells. DEP also increased IL-6 mRNA expression dose and time-dependently. At 24 h, increased 14 fold. At 5h, increased 8 fold. At 2h, increased 2 fold. Cell Viability: DEP exposure did not decrease cell viability at any dose tested.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Fritsch, S. Diabate, S. Krug, HR. 2006	Mouse, RAW264.7 1 x 10^6 cells/well	MAFO2 = incinerator fly ash NR	6.3-188 μg/cm^2 for Toxicity 2.6, 6.5, 13.2 μg/cm^2 for Arachidonic Acid 13.2 μg/cm^2 for MAPK Pathway Other doses noted in Effect of Particles	1, 2.5, 5, 24 h	Toxicity: Viability decreased from 99% to 18% at 62.5-188 μg/cm^2. Lower doses had no effect. Arachidonic Acid: At 2.5h, AA level increased 2 fold for 6.5 μg/cm^2 and 6 fold for 13.2 μg/cm^2. No increase post 5h. MAPKs: Cells pretreated with PD98059, inhibitor of MEK-1, inhibited AA liberation due to MAFO2 treatment of 13.2 μg/cm^2 COX-2: Time-dependent increase of COX-2 protein expression at 2.5 and 5h. ROS: Increased formation of ROS post 3 h dose-dependently over 31.3 μg/cm^2. GSH: Increased production at 20h. Doses >60 μg/cm^2 reduced total glutathione. HO-1: Increased expression at 4 h dose-dependently.
Fujii, T. Hayashi, S. Hogg, J.C. 2002	Human, HBEC, obtained from current smokers, 48-70y Human, Alveolar Macrophages Coculture = AM + HBEC 2.5-3 x 10^6 HBEC 1.0 x 10^7 AM	PM_{10} NR	100, 500 μg/mL	2, 8, 24 h	Viability: HBECs >90% viable post 24 h of 500 μg/mL. AMs viable with 100 μg/mL post 24 h. Cytokine mRNA: TNF-α, GM-CSF, IL-1β, IL-6, LIF, OSM and IL-8 mRNA expression increased in co-culture with 100 μg/mL at 2 and 8h. In AMs, TNF-α, IL-1β, IL-6 mRNA expression increased with 100 μg/mL at 2h. IN HBECs, IL-1β and LIF increased with 100 μg/mL at 2h. HBECs added to AMs exposed to PM_{10}, further increase in mRNA of IL-1β, LIF and IL-8. Cytokine Protein: In co-culture and AMs, significant increase in protein production of GM-CSF, IL-8, IL-1β, IL-6 and TNF-α in dose-dependent manner. GM-CSF and IL-6 production significantly higher in co-culture then AM or HBEC alone. Bone Marrow: Co-culture instillation of supernatants increased circulating band cell counts at 6 and 24 h with 100 μg/mL.
Fujii, T. Hayashi, S. Hogg J.C. 2001	Human, HBEC, obtained from current smokers, 48-70y 2.5-3 x 10^6 cells/dish	EHC93 99% <3.0um	10, 100, 500 μg/mL	2, 8, 24 h	Phagocytosis: 18.6% of cell engulfed particles when exposed to 100 μg/mL. Over 90% viable. Cytokine mRNA: LIF mRNA increased dose-dependently at 2h. Declined at 8 and 24 h. GM-CSF increased dose-dependently at 8h, peaked at 24 h. IL-1α increased at 2h, dose-dependently increase at 8 h and peaked at 24 h. M-CSF, MCP-1, IL-8 unaffected. Cytokine Protein: LIF, GM-CSF, IL-1β and IL-8 increased dose-dependently. Soluble fraction of 100 μg/mL PM_{10} did not effect cytokine production.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Garcon, G. Dagher, Z. Zerimech, F. 2006	Human, L132, Embryonic Lung Epithelium 3 x 10^6 cells/20ml (24 h) 1.5 x 10^6 cells/20ml (48h) 0.75 x 10^6 cells/20ml (72h)	$PM_{2.5}$ (collected in Dunkerque, France for 9mo, Jan-Sept) 0-0.5um (33.63%) 0.5-1.0um (30.61%) 1.0-1.5um (14.33%) 1.5-2.0um (8.69%) 2.0-2.5um (4.89%) >2.5um (7.87 %)	18.84, 37.68, 56.52, 75.36, 150.72 μg/mL LC10 = 18.84 μg/mL LC50 = 75.36 μg/mL	24, 48 or 72h	Cytotoxicity: PM induced dose-dependent (R^2 =.9907) cytotoxic effect in proliferating L132 cells. LDH: Increase at 72 h with 56.52 and 75.36 μg/mL. MDH: Decreased activity at all exposure levels at 24, 48, and 72 h (72-h <5 % of control). MDA: Increased concentration after 72h, both LC10 and LC50. SOD: Increased activity seen at 24 h at LC10, LC50 and decreases after 48 and 72 h at LC50. 8-OHdG: Increased formation seen at all time points at LC10 and LC50. PARP Activities: Increase at all time points exposure at LC10 or LC50. Inflammatory Response: Increases of TNF-α concentration 24 h at LC50, at 48 h and 72 h at LC10 and LC50. iNOS: Increase in iNOS activity at all time points at LC10 and LC50. NO: Increase in NO concentration at time points after exposure to LC10 and LC50.
Geng, HR. Meng, Z. Zhang, Q. 2005	Rats, Lung Macrophages, Male, Wistar, 230g 2.4x10E6 cells	BPM = Blowing $PM_{2.5}$ NPM = Non Blowing Normal $PM_{2.5}$ Wuwei City, China (Blowing days = desert storm days) NR	0, 33, 100, 300 μg/mL	4h	NOTE: Unless otherwise noted results are identical for BPM and NPM Cytotoxicity: Dosages of 150 μg/mL and up decreased cell viability for both. Plasma Membrane Fluidity: Dose-dependent decrease while no effect on membrane lipid hydrophilic region. Plasma Membrane Permeability: LDH enzyme activity and extracellular AP activity increased dose-dependently, indicating increased membrane permeability. Only statistically significant at 300 μg/mL dose. NPM may effect some parameters at 100μg/mL. Overall NPM induced slightly higher increase than BPM. Intracellular Ca2+: Dose-dependent increase. BPM >NPM >>control. Lipid Peroxidation (TBA): Increase only at 300 μg/mL. Antioxidant (GSH): Decrease only at 300 μg/mL.
Geng, HR. Meng, Z. Zhang, Q. 2006	Rats, Alveolar Macrophages, Male, Wistar, 230g 2.4x10E6 cells/bottle	$PM_{2.5}$ DPM = dust storm samples NPM = normal PM (collected from Baotou city March 1-31, 2004) NR	Particle suspensions: 0, 33, 100, 300 μg/mL Water soluble fractions: 0, 75, 150, 300 μg/mL	4h	NOTE: Unless otherwise noted results are identical for BPM and NPM Cytotoxicity: MTT reduction assay revealed significantly decreased cell viability at 150 μg/mL and 300 μg/mL. LDH enzyme activity significantly increased at 150 and 300 μg/mL. GSH levels: Significant decreases were seen in cellular GSH levels and increases in TBARS levels in both groups with a 300 μg/mL dose. Plasma Membrane Activity: In plasma membrane, Na,K-ATPase significantly inhibited. Ca2+Mg2+ -ATPase unaffected. Plasma Membrane Lipid Fluidity: Results indicate that DPM could increase surface fluidity of membrane lipid. Intracellular Ca2+: Dose-dependent increase in free intracellular Ca2+ levels.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Ghio, A.J. Piantadosi, C.A. Wang, X. 2005	Human, BEAS-2B, Bronchial Epithelial Cells NR	FAC = ferric ammonium citrate (component of ROFA) $VOSO_4$ = vanadyl sulfate (component of ROFA) NR	100μM FAC - preexposed before metal compounds or oil fly ash 50μM $VOSO_4$ - preexposed before metal compounds or oil fly ash 100μg/mL ROFA	0-1h, 4h	IRE DMT1: FAC increased mRNA and protein expression for –IRE DMT1. $VOSO_4$ decreased mRNA and protein expression for –IRE DMT1. +IRE DMT1 unaffected by any treatment. Metal transport: Uptake of iron increased after pre-exposure to FAC and decreased after pre-exposure to $VOSO_4$. Pre-exposure to FAC again increase the uptake of both iron and vandium. $VOSO_4$ induced opposite effect, decreasing Fe uptake. ROS: Increased acetaldehyde, indicating increased oxidative stress. ROS decreased with FAC pretreatment. ROS increased with $VOSO_4$ pretreatment.
Gilmour et al. (2004a)	Rat, Alveolar Macrophages, Sprague-Dawley, 250g $2X10^5$ cells/mL	Coal Fly Ash MU = Montana Ultrafine MF = Montana Fine MC = Montana Coarse KF = West Kentucky Fine KC = West Kentucky Coarse Coal combustion using a laboratory-scale down-fired furnace rated at 50kW. Montana subbituminous coal and western Kentucky bituminous coal Coarse (>2.5um) Fine (<2.5um) Ultrafine (<0.2um)	125 μg/mL or 250 μg/mL	4 or 24 h	LDH: Mid and high doses of Montana ultrafine particles showed significant increase after 4 h exposure vs control. Other particle types had no effect. After 24 h, LDH level not statistically significant between particles tested and control. Cytokines: IL-6, TNF-α and MIP-2 increased with Montana ultrafine particles although highly variable and statistically insignificant.
Gilmour et al. (2005)	Human, A549 Human, 16HBE Human, Peripheral Blood Monocyte-derived Macrophages (PBMM) Human, HUVEC, Umbilical Vein Endothelial Cells $0.15X10^6$ cells/well	PM_{10} NR	50 μg/mL	4, 6, 20h	IL-8: PM_{10} at 50μg/mL induced significant increase in IL-8mRNA and protein expression in PMM and 16HBE at 6 and 20h. A549 also had increase though less substantial. Procoagulant Activity: PM_{10} induced significant decrease in macrophage mediated clotting time in 16HBE. Other cell types unaffected. Annexin V Binding: At 100 μg/mL, PM_{10} induced significant increase in binding in macrophages at 4 and 20h. No effect at 50 μg/mL. Tissue Factor mRNA Expression: Increased expression in macrophages at 6 h only. tPA Expression: Decreased mRNA expression at 6h. Decreased protein expression at 4 h and 20 h in dose-dependent manner. TF Expression: Increased TF mRNA expression in dose-dependent manner at 6 h in HUVECs. Protein levels also increased at 4 h but declined to basal levels by 20h.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Gilmour et al. (2003)	Human, A549 0.15x10E6 cells/well	PM_{10} TSA H_2O_2 NAC Mannitol NR	100 μg/mL PM_{10} 100 ng/mL TSA 200μM H_2O_2 5mM NAC 5mM Mannitol	24 h	IL-8: PM_{10}, TSA, H_2O_2 treatment induced increase of IL-8. Concomitant exposure of TSA with PM_{10} or H_2O_2 significantly increased IL-8 release compared to PM_{10} or H_2O_2 alone. Significant increase of IL-8 mRNA expression with PM_{10} or H_2O_2 exposure and TSA coincubation caused significant increases. Silver staining of PCR products indicates that IL-8 gene promoter associated with acetylated H4 following TSA, PM_{10} and TNF treatment. H4: PM_{10} exposure significantly increased acetylation levels of H4 over controls. Increased acetylated H4 mediated by PM_{10} in dose-dependent manner. Treatment with PM_{10} and H_2O_2 increased HAT activity associated with H4 by 245% and 166% respectively. Significant increase in acetylation of H4 following treatment of cells with TSA, PM_{10} and H_2O_2 for 24 h. PM_{10}-induced HAT activity significantly decreased in presence of NAC (thiol antioxidant) and mannitol (radical scavenger). Nuclear presence of HDAC2 protein significantly reduced by exposure to both HDAC inhibitor and PM_{10}. Trend toward decrease in HDAC2 gene expression following TSA and PM_{10} treatment. NF-kB: NF-kB activity increased following inhibition of HDAC with TSA by treatment with PM_{10}.
Graff et al. (2007)	Human, HAEC, obtained from three healthy volunteers NR	PM -UF = ultrafine -F = fine -C = coarse -S = Seattle, WA -SL = Salt Lake City, UT -P = Phoenix, AZ -SB = South Bronx, NY -HR = Hunter College, NY -SF = Sterling Forest, NY. Coarse (>2.5um) Fine (<2.5um) Ultrafine (<0.1um)	250 μg/mL	6, 24 h	Gene Expression: PM-UF, PM-F, and PM-C both upregulated and downregulated genes in HAECs. Downregulation occurred majority of time with PM-F inducing highest number. IL-8: mRNA expression increased with PM-F-S having greatest impact. PM-S >>PM-SL >>PM-SB ~ PM-P >PM-HR >PM-SF. Aluminum, strontium, manganese and potassium highly associated with expression. Wood combustion moderately associated. HOX-1: mRNA expression increased with PM-F-SF having greatest impact. PM-SF >>PM-HR ~ PM-SB >PM-P >PM-S >PM-SL. Potassium, manganese, strontium and wood combustion highly associated with expression. Aluminum and vanadium moderately associated.
Gualtieri et al. (2005)	Human, A549 1x10E4 cells	TD = Tire debris extracted in methanol, constituent of PM_{10} (generated by spinning a new automotive tire against abrasive surface) 10-80um	10, 50, 60, 75 μg/mL	24, 48, 72 h	Cytotoxic Effect: Treated cells presented inhibitory effect on reduction of MTT which appeared to be dose and time-dependent. Statistically significant reduction observed at 48 and 72 h. Trypan blue showed significant PM lethality well as dose-dependent increase in mortality. DNA Damage: At 24 and 72 h, dose-dependent increase of damaged and ghost cells. Cell Cycle Analysis: At 24 h, TD extract-treated cells presented significant increase in percentage of cells in G1 phase when compared with control. Increase associated with decrease in percentage of cells in S phase. At 48 and 72 h, increase in percentage of cells in G1 associated with decrease in percentage of cells in both S and G2/M phases. Cells exposed to TD extracts presented changed morphology. Modifications most obvious at 72 h. High dose produced increased vacuolization in cytoplasm as well as apoptotic nuclear images.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Hetland et al. (2005)	Rat, Alveolar Macrophages, Male, Crl/Wky 1.5x10E6 cells/well	PMC = Coarse PMF = Fine -A = Amsterdam -L = Lodz -R = Rome -O = Oslo Coexposures PAH, Fe, Al, Zn, Cu, V 2.5 <PMC <10um 0.2 <PMF <2.5um	50, 100 μg/mL PM NR	20 h	IL-6: PMC from all cities increased IL-6 release with spring = summer >winter. During spring and summer, PMC-L >>PMC-R ~ PMC-O >>PMC-A. In winter, PMC-R ~ PMC-A >>PMC-L ~ PMC-O. Dose-dependency not observed mostly as result of apparent cytotoxicity. PMF had no effect. TNF-α: PMC from all cities increased release with 50μg/mL inducing slightly higher increase than 100 μg/mL generally. Constituent Correlation: Levels of Fe, Al, Zn, Cu and V as well as PAH (total and fractions) showed no correlation with IL-6 release. Endotoxin Correlation with IL-6 release: Possible but confirmatory test revealed no correlation.
Hetland et al. (2004)	Rat, Alveolar Type 2 Cells, Male, Wky/NHsd, 180-230g Human, A549 1 x 10E6 cells/well	AMC = Ambient Coarse AMF = Ambient Fine AMUF = Ambient Ultrafine (AM samples from Utrecht, Netherlands) Road = PM_{10}, road tunnel, Trondheim, Norway DEP = SRM 1846 2.5 <AMC <10 μm AMUF <0.1 μm	0, 100, 200, 400, 600, 800, 1000 μg/mL	20 h (Type 2 cells) 40 h (A549 cells)	IL-8: All 3 AM fractions showed dose-dependent increase in A549 cells until 600 μg/mL when levels declined. AMC showed most pronounced decline, correlating with decreased viability. Road showed near linear response until 1000 μg/mL, whereas DEP plateaued at 600 μg/mL in A549. MIP-2: AMC and AMUF had no effect in Type 2 cells. DEP induced increase at 200 μg/mL, whereas Road induced strongest increase, peaking at 600 μg/mL in Type 2. IL-6: AMC induced increase at 100μg/mL in Type 2, declined to below normal at 200 μg/mL. AMUF induced decline of IL-6. Road induced significant increase in Type 2. DEP had slight effect. AM fractions induced increase in A549 cells with peak at 600 μg/mL with AMF. DEP and Road induced in A549 dose-dependent increase. Cell Survival: AMC showed major effect at 200 μg/mL in Type 2. AMUF showed effect 400 μg/mL. Road and DEP slowed gradual decline from 75 to 50% at 800 μg/mL in Type 2. AM fractions all induced decreased viability after 600μg/mL in A549 with AMC>AMUF = AMF. Road and DEP had no effect on A549. Apoptosis: AMC showed major effect at 200 μg/mL in Type 2 cells. AMF showed dose-dependent increase in A549. Others showed some slight increases in both cell types.
Holder et al. (2008)	Human, 16HBE14o Suspension: 1x10E5 cells/cm^2 ALI (Air Liquid Interface) 1x10E5 cells/cm^2	DEP (single cylinder, commercial certified #2, diesel engine) Copollutants: NO_X 7 ppm, CO_2 0.1% DEP in air = 122nm DEP ALI = 223nm	Suspension 0.13, 0.25,1.88, 2.5 and 12.5 μg/cm^2 ALI 2.3 x 10E7 particles/cm^2, 1.0 x 10-4 μg/cm^2	Suspension NR ALI: 6h, 20 h post-exposure	ALI vs Tracheal Bronchial (TB) Deposition: TB region deposition is 1.5 nominally x ALI, but particle diameter is 62 vs 260 nm. Inflammatory Response: Viability decreased in suspension at DEP >/ = 2.5 μg/cm^2. IL-8 release (corrected for viability) increased at DEP >/ = 1.88 μg/cm^2 dose-dependently. No statistically significant results in ALI. Viability near 100% (75% uncorrected). IL-8 intermediate between in vitro levels of 0.25 and 1.88 μg/m2. Comparison of ALI vs Suspension: ALI results 10,000 fold plus more sensitive based on IL-8 data and ALI calculated deposition of 1x10E4 μg/cm^2 deposition rate.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Huang (2003)	Human, BEAS-2B Mouse, RAW 264.7 5X10^5 cells/mL	PMC = PM coarse PMF = PM fine PMSM = PM submicron 4 ambient monitoring stations in Taiwan that represented background, urban, traffic, and industrial sites Collection between September and December 2000 2.5 <PMC >10 µm 1 <PMF <2.5 µm PMSM <1 µm	50, 70, 100 µg/mL	8 h (BEAS-2B) 16 h (RAW264.7)	Viability: Not affected IL-8: Only PMSM induced IL-8 increase significantly in BEAS-2B. IL-8 response associated with combination of Mn and Cr (R^2 = 0.28). Response also correlated with nitrate, although significance disappeared when 1 extreme nitrate value was removed. Lipid Peroxidation: Only PMSM enhanced lipid peroxidation in BEAS-2B, correlating with both elemental and organic carbon. TNF-α: In RAW264.7, PMSM increased TNF production. Polymixin pretreatment significantly reduced TNF for all 3 PMs indicating role of endotoxin in macrophage response. TNF production (after polymixin pretreatment only) associated with Cr and Fe content.
Hutchison et al. (2005)	Mouse, J774.1A NR	PM_{10} samples collected before (-B), during closure (-C) and reopening of steel plant (-R) PMT = PM total (aqueous sonicate) PMS = PM aqueous supernatant PMI = PM insoluble pellet NR	112-180 µg	4h	Particle Characterization: Significant increase in total and acid extractable metal content of PM post reopening of plant. Aqueous extractable metal content did not change. Soluble zinc, copper and manganese increased significantly post reopening. Iron most abundant in acid extractable metals and increased greatly at reopening of plant. TNF-α: PMT-R and PMT-C induced statistically significant increase. Treatment with chelation agent reduced effect to control levels.
Imrich et al. (2007)	Rat, Alveolar Macrophage, Female, CD, 12-14wks 2 X10^5 cells/well	SRM 1649 TiO_2 CAPs (Boston, MA) All cells primed with LPS UAP (positive control) Coexposure with NAC, dimethylthiourea (DMTU), H_2O_2 or catalase CAPs <2.5um NR	Caps 100µg/mL LPS 250 ng/mL NAC 2-20mM DMTU 2-20mM Catalase 1-10mM H_2O_2 0-10um	18-20h	TNF: DMTU at 20mM reduced TNF in LPS-primed cells in control and UAP-treated groups. NAC at 20mM reduced TNF release but not statistically significant. Catalase significantly inhibited TNF in control and UAP-treated groups. CAPs (especially insoluble portion) significantly increased TNF unless co-exposed with NAC, DMTU or catalase. All three reduced levels back to around basal levels. DMTU particularly effective. H_2O_2 increased TNF in CAPs-exposed cells. TiO_2 had no increased ability to induced cytokine release when mixed with H_2O_2. Cell Death: Viability decreased substantially when exposed to H_2O_2 + CAPs. Soluble fraction of CAPs showed to be more effective with H_2O_2 then insoluble portion. TiO_2 had no significant effect. NO: Some CAPs induced slight increase when mixed with H_2O_2. No difference found between soluble and insoluble portions of CAPs. DFO: DFO at 0.05mM completely inhibited oxidation induced with soluble CAPs + H_2O_2. Insoluble CAPs + H_2O_2 also DFO-sensitive. DFO uneffective against insoluble CAPs' induction of TNF and MIP-2.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Ishii et al. (2004)	Human, A549, collected from 6 lobectomy or pneumonectomy smokers Human, HBEC 1x10E7 cells	EHC-93 = PM_{10} NR	100 μg/mL	3, 6, 24 h	Cytokines: TNF-α, IL-1β, GM-CSF, IL-6, and IL-8 significantly increased in A549 cells. mRNA Expression: MCP-1, ICAM-1 and IL-8 mRNA expression increased by untreated AM supernatants at 3h. Only MCP-1 level statistically significant. Levels declined by 6h. PM_{10}-exposed AM significantly increased levels of RANTES, TNF-α, ICAM-1, IL-1β, MCP-1, IL-8, and LIF mRNA at 3h. VEGF increased, but not statistically significant. RANTES mRNA maintained level at 6h, others declined. TNF-α and IL-1β-neutralizing Antibodies: IL-1β antibody alone or combination of TNF-α and IL-1β antibodies significantly reduced expression of all eight mRNAs. Combination for some mRNAs reduced expression by near 1/2. Transcription Factor Binding Activity: Binding of AP-1 and Sp1 increased when A549 treated with supernatants from PM_{10}-exposed AM, but not from control AM.
Ishii et al. (2005)	Human, HEBC Human, Alveolar Macrophages, obtained from 10 smokers who stopped smoking 6wks prior 2.5-3.0x10E6 cells HEBC 1x10E7 cells AM 5x10E6 cells AM/HEBC co-culture	EHC-93 = PM_{10} NR	100 μg/mL	2, 24 h	PM and mRNA Expression - 2h: AM or HEBC alone had no effect. Co-culture in contrast increased MIP-1β, GM-CSF, M-CSF, IL-6, MCP-1 and ICAM-1-mRNA expression. PM and mRNA Expression - 24 h: AM had no effect. HBEC increased GM-CSf, LIF and ICAM-1. Co-culture in contrast increased MIP-1β, GM-CSF, M-CSF and ICAM-1-mRNA. Protein Levels: AM and HBEC both increased GM-CSF, IL-6 and MIP-1β release into supernatant. Co-culture effect not additive but synergistic i.e., higher than expected. MCP-1 levels not significantly increased but co-culture appeared to decrease both control and PM values. M-CSF increased for co-culture only. Surface Expression of ICAM-1: HBEC showed increase (CD54). AM (CD11b) not affected by PM exposure. ICAM-1 Inhibitors: IgG or anti-CD11b antibody unaffected in co-culture.
Jalava et al. (2005)	Mouse, RAW 264.7 5 $X10^5$ cells/mL	I) UPM = SRM1649a II) DEP = SRM1650 III) EHC-93 = Ottawa dust, Ottawa, Canada IV) HFP-00 = Pooled ambient air $PM_{2.5}$ sample (HFP-00) from Helsinki, Finland M-UPM = methanol extract of UPM, etc $PM_{2.5}$, NR	150 μg/mL	1) 24 h 2) 2, 4, 8, 16, 24 h	NOTE: Study looking at effects of sample preparation and then being exposed to PM. 2 studies: 1) evaluation of modification of PM induced cytotoxicity and inflammatory potential by methanol treatment of PM samples 2) time course study screening for optimal time points for measurement of cytokine responses to ambient air PM samples. TNF-α: All the PM samples increased TNF-α in cell culture medium. Cell Viability: SRM1649a most cytotoxic sample, followed by HFP-00 and EHC-93. Methanol only significantly affected cytotoxicity of EHC-93 sample. Cytokines: TNF-α concentrations in cell culture medium significantly increased at all studied time points between 2 and 24 h, highest increase seen in EHC-93 sample. IL-6 production also increased at different levels, highest seen in EHC-93. IL-10 no response. Cell Viability: Exposure duration had no significant effects on samples. 2 h sufficient to induce typical reduction in cell viability.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Jalava et al. (2006)	Mouse, RAW 264.7 500,000 cells/mL	PM Collected between Aug 23 and Sept 23, 2002 east of Helsinki, Finland Divided in 12 groups (4 sizes by 3 exposure types): -S = seasonal average -W = wildfire -M = mixed -B = blank LPS and EHC93 (positive controls) $PM_{10-2.5}$ $PM_{2.5}$ -1 $PM_{1-0.2}$ $PM_{0.2}$	PM15, 50, 150 and 300 μg/mL LPS 0.5μg/mL EHC93 150 μg/mL	24 h	Particulate Mass Concentrations in HVCL Size Ranges: Largest increase of PM concentrations observed in $PM_{1-0.2.}$ NO: All 12 samples increased NO production when compared to corresponding unexposed controls, peaking at 150 μg/mL, except $PM_{1-0.2-M}$. Cytokines: All 12 samples increased TNF-α and IL-6 production. $PM_{10-2.5}$ and $PM_{2.5-1}$ samples produced much larger response than $PM_{1-0.2}$ and $PM_{0.2}$ samples. IL-6 $PM_{0.2}$ not measured. MIP-2 production also increased with similar trends. Cytotoxicity: All 12 samples induced dose-dependent decreases in cell viability. $PM_{10-2.5}$ samples least active inducers of apoptosis, while $PM_{0.2}$ samples showed highest activity (4-17% of apoptotic cells).
Jalava et al. (2007)	Mouse, RAW 264.7 5 $X10^5$ cells/mL	Urban background PM PM_{10}, $PM_{2.5}$, and $PM_{0.2}$ collected from 6 European cities during different times of the year: -D = Duisburg (Fall) -P = Prague (Winter) -A = Amsterdam (Winter) -HR = Helsinki (spring), -B = Barcelona (spring) -AT = Athens (summer) 2.5 <PM_{10} <10um 0.2 <$PM_{2.5}$ <2.5um $PM_{0.2}$ <0.2um	15, 50, 150, 300 μg/mL	24 h	PM Characterizations: Highest mass concentrations of PM_{10} and $PM_{0.2}$ from Athens. Prague had highest $PM_{2.5}$ concentrations. NO: All PM fractions induced statistically significant NO production in macrophages. $PM_{2.5}$ -P (4.1 ± 0.3 μmol) and $PM_{2.5}$ -AT (2.7 ± 0.1 μmol) produced significantly larger responses. $PM_{0.2}$-P (5.5 ± 0.5 μmol) and $PM_{0.2}$-HR (3.4 ± 0.5 μmol) produced significantly larger responses. Cytokines: PM_{10} samples showed average cytokine production to be 7.8 fold and 83 fold for TNF-α, and 4.4 fold and 530 fold for MIP-2 when compared to $PM_{2.5}$ and $PM_{0.2}$ respectively. PM_{10} samples induced statistically significant increased in production of TNF-α, MIP-2 and IL-6. $PM_{2.5}$ samples, with exception of Prague, caused significant increases in cytokines. $PM_{0.2}$-A and -AT showed small statistically significant increase in TNF-α. MIP-2 increase seen with -P and -HR. IL-6 increased significantly with PM_{10} and slightly with $PM_{2.5}$. Unaffected with $PM_{0.2}$. Cytotoxicity: $PM_{0.2}$ samples, except for -HR and -AT, significantly decreased cell viability. PM_{10}-HR least cytotoxic.
Jalava et al. (2008)	Mouse, RAW 264.7 NR	PM_{10}, $PM_{2.5}$ Collected from 6 European cities during different times of the year: -D = Duisburg (Fall) -P = Prague (Winter) -A = Amsterdam (Winter) -HR = Helsinki (spring), -B = Barcelona (spring) -AT = Athens (summer) Also tested water-soluble, organic-solvent soluble and insoluble fractions of PM 2.5 <PM_{10} <10um 0.2 <$PM_{2.5}$ <2.5um	150 μg/mL	24 h	PM Characterizations: $PM_{2.5}$ contained largest POM component. $PM_{2.5}$ -P had highest POM concentration. PM-A had highest secondary inorganic ions. PM-AT and PM-B had highest concentration of unidentified matter. NO: All samples induced increase. PM-P, PM-HR, PM-HR, insoluble and water-soluble particles induced statistically significant increase. Cytokines: $PM_{2.5}$ and PM_{10} total suspension and insoluble fractions significantly increased IL-6 and TNF-α with PM_{10} >>$PM_{2.5}$. Water-soluble fractions induced insignificant increase. Cytotoxicity: All $PM_{2.5}$ samples reduced viability except $PM_{2.5}$ -A. Water-soluble fractions of all samples more cytotoxic than total suspensions. All PM_{10} samples reduced viability significantly.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Jimenez et al. (2002)	Human, A549 Human, THP-1 Human, Mono Mac 6 (DSMZ), Monocytic Leukemia Cells 110,625 cells/well	PM_{10} Collected from London and Edinburgh air particulate monitoring stations. TiO_2 $UFTiO_2$ = ultrafine TiO_2 Both fine and ultra fine TiO_2 fractions obtained from Tioxide Europe (London, UK) and Degussa-Huls (Cheshire, UK) TNF-α NR	PM_{10} 100 μg/mL TiO_2 100 μg/mL $UFTiO_2$ 100 μg/mL TNF-α 10ng/mL	4h	NF-kB and AP-1 DNA Binding: NF-kB DNA binding increased in PM_{10} and TNF-α exposed macrophages by 9.5 and 12 fold. NF-kB activity unaltered in TiO_2 and $UFTiO_2$ exposed macrophages. IL-8: Cells treated with PM_{10} conditioned media increased transcription binding to NF-kB to IL-8 promoter sites. Increases seen in gene expression after exposure to TNF-α and PM_{10}. TiO_2 or $UFTiO_2$ had no effect. Increases observed in IL-8 production with PM_{10}. IL-8 Promoter CAT Activity: PM_{10} media increased CAT expression by 65% over control. No differences observed with TiO_2 or $UFTiO_2$ media. Neutrophil Chemotaxis: PM_{10} conditioned media induced a 2.3 fold increase compared to control. TNF-α and IL-1β Production: PM_{10} media increased TNF-α and IL-1β production. No increase seen in TiO_2 and $UFTiO_2$ media.
Jung et al. (2006)	Surrogate Lung Fluid (no cells) NR	Soot Particles Carbon Black $PM_{2.5}$ 185nm Soot NR	0-30mg Soot 5-10mg CB	NR	OH Radical Formation: Formation occurred with linear dependence on soot mass. Average response was 0.89nmol OH produced per mg of soot. Formation also occurred with soot + hydrogen peroxide. Hydrogen peroxide alone did not form OH radicals. Fe: Average Fe concentration in soot particles was 305 ± 172nM. Observed negative correlation between amount of Fe and amount of OH radical formation. DSF inhibited iron-induced increase in OH radical formation. Carbon Black: OH radical generation by carbon black significantly less than soot. Observed to be linearly proportional to PM mass. $PM_{2.5}$: High variability in increase of OH radicals with $PM_{2.5}$. Pretreatment with DSF partially blocked OH radical production, but significant level remained. May be due to $PM_{2.5}$ containing high levels of Fe and Cu.
Kafoury and Madden (2005)	Mouse, RAW 264.7 Human, U937 (control) 3-4x10E5 cells	DEP BAY11-7082, NF-kB inhibitor (coexposure) Campothecin (positive control) on U937 $PM_{2.5}$ -10	DEP 25, 100, or 250 μg/mL BAY11-7082 25um with 1.5 h pre-incubation Campothecin 4μg/mL	4 h DEP/BAY11-7082 3h Campothecin 1.5 h pre-incubation with BAY11-7082	TNF-α: DEP induced significant release of TNF-a at 100 and 250 μg/mL dose-dependently. Exposure at 25 μg/mL had no effect. IL-1β containing PM samples at 100 μg/mL also resulted in significant release of TNF-α. NF-kB Binding Activity: Treatment of RAW 264.7 with BAY11-7082 significantly inhibited IL-1β-induced TNF-α release. Similar effects observed with DEP-induced TNF-α release. Apoptosis: Inhibition of NF-kB binding activity by BAY11-7082 resulted in DEP-induced apoptotic response. Without BAY11-7082, apoptosis not induced even at DEP dose of 250/μg/mL for 4h. U937 cells with campothecin induced into apoptosis.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Karlsson et al. (2006)	Human, A549 Human, Monocytes, isolated from heparinized whole blood NR	PM Total of 9 samples -W1 = wood burning in old-type boiler -W2 = wood burning in modern boiler -P = wood pellets burning in pellets burner -T1 = PM_{10} tire debris with studded tires and ABT pavement -T2a = PM_{10} tire debris with studded tires and ABS pavement -T2b = $PM_{2.5}$ tire debris with studded tires and ABS pavement -T3 = PM_{10} tire debris with friction tires and ABS pavement -St = PM_{10} from busy street in Stockholm, Sweden -Su = PM_{10} from platform of subway station in Stockholm NR PM_{10}	40 $\mu g/cm^2$	4h	PM Characterization: Boiler emitting PM-W1 led to 4 times higher emission of particles vs PM-W2 and 8 times higher emissions vs PM-P. Total organic carbon concentration and CO substantially higher in old-type wood boiler. Effects with Filter Fibers: No increase of DNA damage observed compared to water control. Filter fibers led to induction of cytokines in human macrophages. Genotoxicity: All particulate samples induced DNA damage in A549 cells. PM-Su most genotoxic and induced 4-5 times more DNA damage than others. Cytokines on Glass Fiber Filters: Significant increase in IL-8 with PM-W2. PM-St induced highest increase in IL-6, IL-8, TNF-α. Cytokines on Teflon Filters: PM-2a and PM-2b samples caused significant increase of IL-6, IL-8, TNF-α.
Katterman et al. (2007)	Rat, RLE-6TN, Alveolar Epithelial Cell Line 50,000 cells/well (cytotoxicity) 25,000 (SEM) NR	PM: Oils: OAAF, Oil Q, OII I II, NF2 PM: Coal Germany and Ohio Diesel ZODDA (doped with Zn) ZSDDA (doped with Zn and S) - S: PMs washed in solution - F: Fresh samples - L: Leached Al_2O_3, Fe_2O_3, SiO_2, TiO_2,ZnO also tested NR	Oils 0.2 mg/mL Coals 0.7 mg/mL Diesel 0.01 mg/mL Al203 0.5 mg/mL Fe_2O_3 0.7 mg/mL SiO_2 0.7 mg/mL TiO_2 0.7 mg/mL ZnO 0.05 mg/mL	24 h	Metabolic Activity: For Oils 3/4 Fresh and 1/4 Leached, metabolism decreased. Coals (fresh and leached) had no effect. Diesel PM: ZODDA fresh only slight effect ZSDDA only fresh decrease; leached no effect Cellular Morphology: PM-S had minimal effect. PM-F induced widespread cell damage. Constituent Differences between PM-F and PM-L: In oil samples Cu, Ti and Ca salts were removed upon washing. Fe, Al, Si remained constant. Grinding Effects: Coal toxicity increased upon grinding, whereas diesel PM toxicity decreased upon grinding. Metal Oxide Effects: Only SiO_2, and ZnO (much higher at lower concentration than other metal oxides) decreased metabolic activity. Fresh, washed and sonicated samples similar. Grinding only affected TiO_2 (increase) and ZnO (decrease).

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Kendall et al. (2004)	Human, BALF via bronchoscope, 6 nonsmokers, 3 smokers NR	$PM_{2.5}$ sample sites; 2 schools in Bronx, NY, 6 background urban, 6 urban roadside. 12 day sampling Particle Surface Chemistry: 79-87% carbonaceous material (Ch, COO, C-(O,N)), 10-17% O (O1s), 1.5-4% N (NH_{4+}, N-C, NO_3 2-), 0.6-1% S, and 0.3-2 % Si. Only NO_3 - higher in roadside samples. NH_4 and NO_3 - correlated with NO and NO_X in air but not NO_2. NR	NR	4 h	Saline Washing: Removed particles and decreased NH_4, NO_3,O and S relative to C1. BALF treatment (XPS): $PM_{2.5}$ surfaces interacted strongly with BALF within hours of contact. BALF collected during fiber-optic bronchoscopy. Specific surface components of $PM_{2.5}$ immersed in BALF desorbed while biomolecules from BALF absorbed to particles. N-C on PM surface increased 3 x smokers and 4 x nonsmokers (range 1.4-7.4), most likely related to protein(like) absorption on PM. Slight increase in COO, decrease in NH_4, NO_3, O and S. ToF-SIMS - Organics: Particle loading and surface hydrocarbon showed linear correlation. Loss of hydrocarbon from $PM_{2.5}$ surface averaged 55% (10-75) after saline and BALF washes. In only 3/12 samples BALF removed less hydrocarbon, 9/12 equivocal. BALF treatment increased amino acid content and phospholipid (DPPC) content of $PM_{2.5}$ surface. ToF-SIMS - Inorganic: Saline washing appears to increase Al, Si but with extreme variability, not statistically significant. Both saline and BALF washing decrease NH_4 and Na to similar extent. BALF washing did not affect Al or Si.
Kim, Y.M. Reed, W. Wu, W. 2006	Human, BEAS-2B NR	Zn2+ NR	15, 50, 100 µmol	1-20h	Cell Viability: At 50µM for 20h, no apoptosis induced. IL-8: At 12h, IL-8 increased in dose-dependent manner. At 15 or 50µM, Zn2+ increased protein 1.6 and 4.6 fold respectively. IL-8 mRNA expression increased dose-dependently, reaching statistical significance at 2 h and continuing until 4h. EGFP (adenoviral IL-8 promoter): Increased 2.4 fold with 50µM Zn2+. Proteases: With 50µM Zn2+, increased phosphorylation of MAPKs ERK, JNK and p38 by 15min and continued increasing up to 2h. Pre-exposure of inhibitors of MEK, JNK, p38 before Zn2+ exposure caused inhibition of Zn-induced IL-8 mRNA and protein production except with p38. Inhibitor of p38 had no effect. Dephosphorylation of ERK and JNK partially inhibited with exposure to Zn2+.
Kleinman et al. (2003a)	Rat, Alveolar Macrophages, Wistar, 10wks Rat, Alveolar Macrophages, Fischer 344, 22-24mo, 10wks 10^5 cells/well 10^6 cells/mL	UF1 = Utrecht 1 Fine (urban freeway) UC1 = Utrecht 1 Coarse UF2 = Utrecht 2 Fine (urban, freeway, light industrial) UC2 = Utrecht 2 Coarse SRM 1650 SRM 1648 0.2<UF1<2.5 µm 2.5<UC1<10 µm 0.2<UF2<2.5 µm 2.5<UC2<10 µm	0.12 -120 ng/10E5 cells NR	4h, 18h	Macrophage PMA-stimulated respiratory burst activity: SRM 1648 and 1650 induced dose-dependent decrease approaching 0 at 50 -100 µg/10E5 cells. Large dose-dependent decrease for AM from old rat with fine PM exposure, followed by young rat AM with fine PM exposure. However, no age-related effects statistically significant. Free radical production: All coarse particles depressed free radical production in somewhat dose-dependent manner, with UC2 being more potent than UC1. Both fine particles also showed dose-dependent response but UF1 and UF2 greater than control at 3 µg/10 E6 cells. PM Characterization: Ratios between coarse and fine PM similar for metals tested (Al, Fe, Mn, Zn). Al higher in coarse samples and Zn higher in fine PM, although large variability observed. Fe and Mn results roughly equivalent for all samples.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Kocbach, A. Namork, E. Schwarze, P.E. 2008	Human, THP-1 1,000,000 cells/mL	PMW = Wood smoke particles Collected from conventional Norwegian wood stove burning birch PMT+ = Traffic-derived particles Collected from road tunnel in winter when studded tires were used PMT- = Traffic-derived particles Collected from road tunnel in summer without studded tires DEP = SRM2975 Porphyr = fine grain syenite porphyr LPS (positive control) Polymyxin B Sulphate (endotoxin inhibitor) NR	30-280 μg/mL LPS 1μg/mL	2, 5, 12h	Particle Characterization: PMT+ contained high mineral particle content. PMT- contained carbon aggregates, organic carbon and polycyclic aromatic hydrocarbons (PAH). PMW and DEP contained carbon aggregates. PAH content of PMW >>>DEP. Porphyr not included in analysis. Cytokines: PMT± induced release of TNF-α, IL-1β, IL-8 with 30 or 70 μg/mL. PMW induced TNF-α and IL-8 similarly. DEP induced IL-1β and IL-8. Porphyr induced increase of IL-8. IL-4, IL-6 and IL-10 unaffected. Overall, effective induction of cytokines was PMT± >PMW >DEP >Porphyr. mRNA expression of TNF-α, IL-1β, IL-8, IL-10 increased with 140 μg/mL of PMT± and slightly for PMW. LDH: PMT ± induced small but statistically significant increase at low doses. DEP increased LDH at 280 μg/mL only. Polymyxin B Sulphate: Endotoxin inhibitor significantly inhibited LPS-induced cytokine release by 80-90%. Reduced PMT± induction by 50-60%. Organic Extraction: PMT+ washed and native particles equivocal for induction of cytokine release. PMT+ organic extract had no effect. PMT- and PMW organic extracts significantly increased TNF-α and IL-8. Washed particles induced less signficant increase of IL-8. DEP organic extract had no effect.
Kristovich, R. Knight, D.A. Long, J.F. 2004	Human, hUVEC, umbilical vein endothelial cells Human, hPAEC, pulmonary artery endothelial cells Human, hPMVEC, pulmonary microvascular endothelial cells Human, hPBMC, peripheral blood mononuclear cells 4x10E6 cells/well	CP = carbon particle (carbonaceous negative image of zeolite) CFE = C/Fe particulate (synthesized) CFE+ = C-Fe/F-Al-Si particulate (synthesized) CFA = Coal Fly Ash (Coal-fired power plant, NOS) DEP (exhaust pipe of diesel powered truck) CP, CFE, CFE+ approx 1 μm (resembling zeolite) CFA <2um DEP = 150 nm	CP = 5-50 μg/cm^2 CFE = 2.5-25 μg/cm^2 CFE+ = 2.5-25 μg/cm^2 CFA = 10-100 μg/cm^2 DEP = 2.5-25 μg/cm^2	4, 8 or 24 h	Particle Characterization (Surface chemistry): CP = 88% C, 1% Si, 10% O, 1% N. CFE = 80% C, 2% Fe, 2% Si, 16% O. CFE+ = 20% C, 6% Al, 3% Si, 50% F, 6% O, 11% N, 4% Na. CFA = 25% C, 3% Fe, 13% Al, 17% Si, 41% O, 1 % N. DEP = 70% C, 3% Fe, 24% O, 1% N, 2% S. Cytotoxicity: CP none, CFE 50-70 μg/cm^2, CFE+ >200 μg/cm^2, CFA none, DEP 50-70 μg/cm^2 in hPBMC. Endothelial Activation: ICAM-1, VCAM-1, E-selectin activated dose-dependently by DEP, CFE, and CFE+. No effects observed for CFA or CP. Effects not result of endotoxin release. Individual Variability: Donors (humans) showed variability in responses especially for CFA. 3/9 had medium response negated by ND responses in 6/9.
Kubatova, A. Dronen, L.C. Picklo, M.J. 2006	Murine, RAW 264.7 Human, BEAS-2B 10^6 cells/mL RAW 264.7 10^5 cells/mL BEAS-2B	PMW = Wood Smoke Collected from airtight wood stove burning hardwoods -C = P + MP + NP -P = Polar (fraction extracted from 25-50 C) -MP = Mid Polar (fraction extracted from 100-150 C) -NP = Nonpolar (fraction extracted from 200-300 C) NR	50, 100, 200 μg/mL	12h	GSH: PMW-MP and PMW-NP induced GSH depletion substantially in dose dependent manner starting at 50 μg/mL in both cell types. DMSO had no effect. Cytotoxicity: Increased with PMW-MP and PMW-NP at 200 μg/mL in RAW 264.7. BEAS-2B unaffected. Particle Characterization: PMW-MP contained higher concentrations of oxy-PAHs, disyringyls, syringylguaiacyls and PAHs. oxy-PAHs include 9-fluorenone, 1-phenalenone, 9,10-anthraquinone and hydroxycadalene. PAHs included phenanthrene, fluoranthene and pyrene. Effects of Individual Components of PMW-MP on GSH: 1,8-dihydroxy-9-10anthraquinone and 9,10-phenanthraquinone depleted GSH. 9,10-anthraquione, anthrone, 1-hydroxypyrene increased GSH. Phenanthrene, 1-methylpyrene, 9-fluorenone and xanthone had no effect.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Kubatova, A. Steckler, T.S. Gallagher, J.R. 2004	Monkey, kidney cells COS-1 (CV-1 cells with origin -defective mutants of SV40), African Green E coli PQ 37 (SOS Chromotest) 10,000 cells/180 ul	DEP Obtained from diesel bus PMW = Wood smoke particulates obtained from airtight wood stove burning hardwood HSF = Hot pressure fractionation -C = P + MP + NP -P = Polar -MP = Mid Polar -NP = Nonpolar OE = Organic Extraction -HNP = n-hexane nonpolar -MEP = methanol polar NR	0-300 μg/mL	24 h Cytoxicity 2 h SOS Chromotest	Cytoxicity: PMW induced dose-dependently. PMW-C intermediate between PMW-HNP and PMW-MEP (highest). Levels above 25 μg/mL cytotoxic. DEP-HNP induced but not dose-dependent. Results similar for all 3 fractions (highly variable). Cytotoxic >100 μg/mL. Extraction Water Temperature Effect: PMW cytotoxic at temperatures over 50 C. DEP cytotoxic >200 C. At 250, cytotoxicity similar. At 300 C, PMW cytotoxicity declines and DEP stays high resulting in DEP>WSP. SOS Chromotest: β-Galactosidase formation increased, peaked at 200 C with DEP and declined to control at 300. Individual fractions showed linear dose response from 25-200 μg/mL with 150 and 200 C extracts significantly higher.
Lee, C.C. Cheng, Y.W. Kang, J.J. 2005	Human, A549 1x10E5 cells/well	MEP = Motorcycle Exhaust Particles (Yamaha Cabin engine, 95 octane unleaded gasoline,150 rpm) MEPE = MEP Particle Free MEP 0.5um MEPE<0.2 μm	MEP 0.02, 0.2, 0.2, 2, 20 μg/mL MEPE 20 μg/mL	24 h	IL-8: MEP induced IL-8 >0.2 μg/mL. Increased 2fold at 24 h with 20 μg/mL. MEPE induced similar response at 20 μg/mL. Dose-dependent induction of IL-8 mRNA expression with both MEP and MEPE. Cytotoxicity: Unaffected. NFκB: MEP (20 μg/l) induced time-dependent activation for 2h, continued at same level at 6h. Pretreatment of PDTC (1mM) fully inhibited MEP induction. MAP Kinase: MEP induced time-dependent activation up to 30 min and stayed elevated until at least 60 min. ROI: Time-dependent increase in ROI for up to 1 h and then continued at same level for up to 6h.
Lee, C.C. Kang, J.J. 2002	Mouse, Peritoneal Macrophages Rat, Alveolar Macrophages Mouse, RAW 264.7 5 $X10^5$ cells/mL Cytotoxicity 3 $X10^5$ cells/mL Apoptosis 2 $X10^6$ cells MMP and ROI 1 $X10^7$ cells GSH NR DNA Fragmentation	MEP = Motorcycle Exhaust Particles Obtained from Yamaha two-stroke engine using unleaded gas MEPE = particle-free MEP 0.5um	5, 10, 50, 100, 300, 1000 μg/mL	6, 12, 18, 24 h	Cytotoxicity: Viability decreased dose and time-dependently in all cell types at 24 h. Apoptosis: Increased apoptosis indicated by significant dose-dependent increase in subG1 with 300 μg/mL in all cell types. MEPE induced similar results. Inhibition successful against MEP-induced apoptosis by calcium chelators EGTA, BAPTA-AM, cyclosporin A and antioxidants NAC, GSH, catalase, SOD. Ca2+: MEP and MEPE induced sustained increase of Ca2+ at 300 μg/mL. BAPTA-AM completely inhibited induction. ROI: MEP induced increase of ROI in time-dependent manner. Peaked at 2h, plateaued until 24 h. Calcium chelators and antioxidants substantially attenuated induction. GSH: Significant decreased levels of GSH with MEP exposure. MMP: Mitochondria membrane potential decreased dose-dependently with MEP 100 μg/mL and 300 μg/mL. Calcium chelators and antioxidants partially inhibited reduction.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Li, N. Kim, S. Wang, M. 2002	Mouse, RAW 264.7 Mouse, THP-1 Murine, RAW264.7 2 X10^6 cells/well Mouse RAW264.7 and THP-1 0.67 X10^6 cells/well Murine RAW264.7	VACES - Biosampler PM_{10} in Downey, CA -DEP concentrate in water -F = fine particles -C = coarse particles DEPM = DEP methanol extract DEPME = DEP methylene chloride extracts DEPAL = DEPME aliphatic (hexane) DEPAR = DEPME aromatic (hexane/methlene chloride) DEPPO = DEPME polar (methylene chloride/methanol) NR	10 - 200 μg/mL JNK Activation and IL-8 Production: THP-1 cells 2.5 - 100 μg/mL DEPM THP-1 cells treated with 1 - 200 μg/mL of DEP RAW264.7 cells exposed to DEP at 10 -100 μg/mL Cytotoxicity: 1, 10, 25 (THP-1 cells only), 50, 100 and 200 μg/mL GHS/GSSG: 0, 10, 25, 50, and 100 μg/mL HO-1 Expression: 0, 25, 50, 100, 200 μg/mL	GHS/GSSG: DEPM and whole DEP (RAW264.7only) for 8h HO-1 and MnSOD Expression: RAW264.7 and THP-1 for 7h. RAW264.7 cells exposed to whole DEP for 16 h JNK Activation and IL-8 Production: THP-1 cells 30 min THP-1 cells 16 h RAW264.7 cells for 90 min. Cytotoxicity: RAW264.7 and THP-1 18 h	GSH/GSSG Ratio: DEPM induced dose-dependent decrease in GSH/GSSG ratios in both mouse cell lines. Gradual decline occurred in dosage range 10-50 μg/mL and steep decline occurred at doses >50 μg/m. DEP induced decrease in GSH/GSSG ratios at comparable dose to DEPM. HO-1 Expression: 1 μg/mL elicited HO-1 expression in both mouse cell lines. Cells depicted dose-dependent increase in HO-1 expression. Plateaued at 100 μg/mL. HO-1 Expression in Murine RAW264.7: VACES-F consistently induced HO-1 expression over 9m period, whereas VACES-C effective in inducing HO-1 only during Fall and Winter. HO-1 induction positively correlated to higher organic carbon (OC) and polyaromatic hydrocarbons (PAHs) that represented in VACES-F, but also seen with rise in PAHs in VACES-C during winter months. MnSOD: Doses of 2.5 μg/mL, DEPM elicited increase in MnSOD expression in THP-1 cells. JNK Activation: DEPM elicited dose-dependent increase in JNK phosphorylation beginning at 2.5 μg/mL DEPM and plateaued at 10 μg/mL in THP-1 cells but occurred without change in JNK expression level. Whole DEP used and mouse RAW264.7 cells exposed, which depicted similar results of increase in JNK phosphorylation (plateau at 100μg/mL DEP) but without increase in JNK expression. IL-8: Exposure to DEPM elicited dose-dependent increase in IL-8 levels of THP-1 cells, starting at doses >10 μg/mL and plateaued at 100 μg/mL.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Li, N. Wang, M. Oberley, T.D. 2002	Human, BEAS-2B Human, NHBE Human, THP-1, macrophages Murine, RAW264.7, macrophages 10^6 cells/mL	DEPM = DEP methanol extract DEPME = DEP methylene chloride extracts DEPAL = DEPME aliphatic (hexane) DEPAR = DEPME aromatic (hexane/methlene chloride) DEPPO = DEPME polar (methylene chloride/methanol) 0.05-1 µm	0, 10, 25, 50, 100 µg/mL	30, 60, 120min	ROS: BEAS-2B cells demonstrated increased HE fluorescence, indicating increased ROS formation. THP-1 cells unaffected. GSH/GSSG Ratio: Increasing amounts of DEPM caused THP-1 and BEAS-2B cells to exhibit dose-dependent decrease in GSH/GSSG. Similar changes occurred with NHBE cells. THP-1 cells maintained higher ratio of GSH/GSSG than BEAS-2B and NHBE cells. NAC on GSH/GSSG Ratio: Exposure to DEPM in the presence of NAC did not affect GSH/GSSG ratio in BEAS-2B and NHBE cells. In THP-1 NAC prevented decline in GSH/GSSG ratio. MnSOD and HO-1: THP-1, BEAS-2B and NHBE cells showed constitutive MnSOD expression and dose-dependent expression of HO-1 protein and mRNA. No change in the expression of β-actin. DEPAL, DEPAR, DEPPO, CoPP on HO-1 Expression: DEPPO more potent than DEPAR. DEPAL lacked activity for THP-1 and BEAS-2B cells. Potency of DEPPO sufficient to affect cellular viability and HO-1. CoPP induction of HO-1 failed in THP-1 cells. CoPP effective HO-1 inducer in BEAS-2B cells. Did not protect against the oxidizing effects of DEPM. JNK: THP-1 and BEAS-2B when exposed to DEP had an increase in JNK activation. JNK isoforms observed at doses of ≥ 25µg/mL. In BEAS-2B cells, high rate of cell death diminished this response at 100µg/mL. NHBE also showed increased JNK phosphorylation at doses 50 - 100 µg/mL. NAC on JNK: NAC led to inhibition of JNK activation. IL-8: THP-1 cells showed dose-dependent increase (over the range of 10-100µg/mL DEP) in IL-8. NHBE cells showed incremental increase (over the range of 10-50µg/mL DEP) followed by rapid decline at 100 µg/mL attributed to apoptosis. BEAS-2B cells responded to 10 µg/mL with increased IL-8 but cellular toxicity and cell death led to drop in IL-8 production at higher doses. Cytotoxicity: Comparing cytotoxicity at 25µg/mL DEP, BEAS-2B cells had higher rate of cell death than THP-1 cells. BEAS-2B cells showed significant rise in cell death at doses larger than 10 µg/mL. In THP-1 cells, it took doses of 25 µg/mL or more before significant increase occurred. In BEAS-2B, cell death began at 2h. In THP-1, increase in cell death prolonged for 8 h or longer. NHBE cells also showed increase rates of cytotoxicity compared to macrophages. NAC in THP-1 interfered with generation of cytotoxicity, but NAC did not have any decreasing effect on cell death in BEAS-2B or NHBE cells.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Lindbom, J. Gustafsson, M. Blomqvist, G. 2007	Mouse, RAW 264.7 130000 cells/cm^2	PM_{10}: -ST = Street -S = Subway -G = Granite -Q = Quartzite Bimodal with peaks around 4-5um and 7-8um.	1, 10 or 100 μg/mL Analysis of Arachidonic Release (AA): Cells pre-incubated w/ 1 uCI tritium marked for AA and washed exposed to 10, 50, 100 and 250 μg/mL	18, 24 h	Cellular Viability: Not influenced by any particle types ≥ 90%, except for combination of 100μg/mL of subway particles and NAC where viability dropped to 20%. Cytokines: All particles induced TNF-α secretion in dose-dependent fashion. PM-S most potent at 1 μg/mL. PM-G and PM-ST induced effect at 10μg/mL. PM-Q induced increase of TNF-α at 100μg/mL.PM-ST induced IL-6 release at 10μg/mL. PM-G, PM-Q, PM-S induced IL-6 secretion at 100μg/mL. DFX inhibited TNF-α in cells exposed to PM-S and PM-ST. DFX induced increase of TNF-α with PM-Q. For all PM types (except PM-ST) DFX inhibited induced IL-6 secretion. NO: PM-G and PM-ST caused significant release of NO. PM-ST >>PM-G. NAC: Significantly inhibited both TNF-α and IL-6 secretion with all PM particles. L-NAME: L-NAME caused decrease in NO secretion at 100 μg/mL of PM-ST. L-NAME did not have any effect on granite induced NO secretion at 100μg/mL. Cytokine Gene Expression: TNF-α mRNA unaffected. IL-6 gene expression increased for PM-Q, PM-ST, PM-S but not for PM-Q. AA Release: PM-S induced AA release. Observed after exposure to 100 and 250 μg/mL Lipid Peroxidation: All particle types induced lipid peroxidation. PM-S and PM-ST >>PM-Q and PM-G. ROS: All particle types induced ROS formation. PM-S and PM-ST induced significantly higher formation at 10μg/mL. PM-Q and PM-G induced small but significant decrease in absorption at 100μg/mL. Both PM-ST and PM-S had significant dose response for all concentrations tested. No difference between PM-G and PM-Q. PM-S and PM-ST pretreated with DFX had lower ability to induce ROS formation. Endotoxin Content: Only PM-ST showed positive result for endotoxin content.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Liu, P. L. Chen, Y.L. Chen, Y.HR. 2005	Human, HPAECS, Pulmonary Artery Endothelial Cells NR	SE = Wood Smoke Extract NR	40 μg/mL	0-4h Mitochondrial Membrane Destabilization: 0-60 min. DNA Defragmentation: 0-6h Cytotoxicity: 24 h	Viability: SE exposure reduced cell viability dose-dependently. Reduction reached ~38% of control. Effect on Oxidative Stress/ Antioxidant Enzymes: SE caused increase in levels of ROS, in particular O2- and H_2O_2 in time-dependent manner. Exposure to SE for up to 4 h caused decrease in GSH levels in time-dependent manner. Increased expression of Cu/Zn SOD mRNA and HO-1 mRNA. Catalase or GPx mRNA expression unaffected. Upregulation of Cu/Zn SOD and HO-1 time-dependently. Mitochondrial Translocation/ Capsase-Independent Apoptosis/DNA fragmentation: Exposure for up to 60 min caused increase in percentage of annexin V-FITC-pos cells but not PI-pos cells. At 4h, FDA-pos cells unaffected. SE exposure caused loss of mitochondrial membrane potential (indicated by change in JC-1 fluorescence). Cytosolic bax levels increased after for 1 or 2h. Returned to basal level at 4 h after exposure. Levels of procaspase-3 and caspase-9 unaltered by SE exposure after 4h. Procaspase-3 increased and caspase-9 decreased by H_2O_2 exposure. SE exposure increased levels of AIF and EndoG (exposure up to 4 h). At 6h, increased DNA defragmentation. Pre-treatment with caspase inhibitors (CMK and Z-VAD-FMK) failed to suppress SE-induced apoptosis. NAC: Treatment with NAC prevented increase in ROS in cells exposed to SE for 60 min. NAC addition prevented reduction of GSH by SE. NAC decreased nuclear levels of AIF and EndoG and completely reduced DNA-fragmentation. Alleviated the SE-induced reduced viability. GSH and DNA fragmentation unaffected.
[FROM Table D-4] **Reference:** Long et al. (2005) **Species:** Human **Cell Types:** Human, Peripheral blood mononuclear cells (PBMCs) differentiated into MDMs (90-95 % CD14+) and T lymphocytes		Synthetic C and C/Fe particles (phenol and paraformaldehyde polymers on a zeolite template) C/Fe analysis Al 1.38 %, Si 0.33 %, Fe 0.46% 1 μm	5 x 10 E6 cells (2 mL /well) MDM s (5 $\mu g/cm^2$	2-24 h	ROSs release: Oxidative burst form C/Fe maxes out at 20 min -- no effect from C particles. Cellular particulate actions: C particulates were present within lysosomes with small clumps forming after 24 h outside of lysosomes with no evidence of organelle lysis and/or agglomeration. C/Fe particulates showed similar initial effects progressing at 24-h total organelle lysis extending to outer cell membrane. T cell effects: No effects from C or C/Fe particles Medium Effect: Particle agglomeration appears to be a direct result of serum present within a cellfree medium Hydroxyl radical formation: C/Fe particles showed an order of magnitude higher hydroxyl formation as compared to C particles

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Ma, C. Wang, J. Luo, J. 2004	Mouse, JB6P+, Epidermal Cell Line NR	DEP = SRM 1975 0.5um	5-20 μg/mL 0-160 μg/mL Cytotoxicity	24, 48h NF-κB and AP-1: 12h Phosphorylation of Akt: 5- 120 min. Effect of LY294002 on DEP: Cells pretreated with LY294002 (0 or 10μM) for 30 min and then exposed to DEP for 0-60 min.	Viability: Below 20 μg/mL, DEP had no effect. At concentrations >20 μg/mL, DEP caused apoptosis. NF-κB and AP-1: DEP stimulated NF-κB activity at 5 and 10 μg/mL. At 20 μg/mL, NF-κB activity decreased, but still >control. DEP had no effect on AP-1 activity. PI3K/Akt Signaling Pathway: DEP induced phosphorylation of Akt on both Thr-308 and Ser-473. LY294002 (an inhibitor of P13K) blocked phosphorylation of Akt, p70/p85 s6 kinase and GSK 3b. LY294002 eliminated DEP-mediated phosphorylation of Akt. Inhibition of P13K by expressing p85 also blocked DEP-induced Akt phosphorylation. DEP induced phosphorylation on GSH-3B on Ser-9 without affecting tyrosine phosphorylation and enhanced phosphorylation of p70/p85 S6 kinase on Thr-389. DEP had no effect on phosphorylation of FKHR. SAPK/JNK Pathway: DEP slightly activated pathway. Increased transient activation of MKK4 (a signal component of the SAPK/JNK pathway) and thus enhanced phosphorylation of SAPK/JNK. DEP promoted phosphorylation of c-Jun and ATF-2. DEP did not affect p38 MAPK or ERK phosphorylation. LY294002: Treatment with LY294002 (P13K inhibitor) eliminated DEP-induced NF-κB activity. Similar effect observed with use of another P13K inhibitor, wortmannin. TDZD-8 (GSK-3B inhibitor), D-JNKI(a JNK inhibitor), SB202190 (inhibitor for p38 MAPK) or PD98059 (inhibitor for MEK1) had little effect on DEP-mediated NF-κB activation.
Maciejczyk, P. Chen, L.C. 2005 "Effects of subchronic exposures to concentrated ambient particles (CAPs) in mice. VIII. Source-related daily variations in in vitro responses to CAPs."	Human, BEAS-2B, epithelial cells isolated from normal bronchial epithelium 9x10E4 cells/well	CAPs = $PM_{2.5}$ Ambient Collected via cyclone inlet on side of building in Tuxedo, NY. Weekdays 9-3 March 4 to September 5, 2003 NR	Ambient 13 ±9 $\mu g/m^3$ CAPS 109 ± 178 $\mu g/m^3$	24 h	Particle Characterization: Study found four distinct source categories contributed to mass concentrations of CAPs. Study also able to estimate daily levels of source apportioned PM concentrations for each category. Categories: Regional Sulfate, Soil, Oil- Combustions and Unknown/Other. Mass contributions of these categories to CAPs is: Regional Sulfate- 65%, Soil- 20%, Unknown/Other- 13% and Oil Combustion- 2%. Composition: * Regional Sulfate characterized by high concentrations of S, Si and organic carbon. * Soil characterized by high concentrations of Ca, Fe, Al and Si. * Oil-Combustion characterized by high concentrations of V, Ni and Se. Attributed Source: * Regional Sulfate - Coal-fired power plant emissions. * Soil - dust from local unpaved roads and trails. Also attributed to the landscaping of a local park. * Oil - Combustion- electrical utilities and industrial and large commercial boilers. Oil-fired power plants. NF-κB: NF-κB response most notably correlated with V and Ni - elements associated with oil combustion source category (oil combustion makes up the group that is smallest percentage of CAP mass).

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Madden, M. C. Dailey, L.A. Stonehuerner, J.G. 2003	Human, NHBE NR	DEP Obtained from Caterpillar diesel engine, 4cycl, 4 stroke, model 3304 - LL = Low Load (0% engine load) - HL = High Load (~75% engine load) SRM 2975 NR	0 -500ug DEP-LL: 2.13 mg/mL (125 mL total volume) DEP-HL-1: 2.63 mg/mL (137 mL total volume) DEP-HL-2: 2.88 mg/mL (140 mL total volume)	24 h	Particle Characterization: DEP-LL extract has greater amount of low-molecular-weight carbonyls (2-5 carbons). DEP-HL had more intermediate size carbonyls (6-9 carbons). Largest carbonyls analyzed (11-12 carbons) found in similar ratios in the two types of extract (number of carbons is indicative of differences in boiling points). Cytotoxicity: DEP-LL, DEP-HL and SRM had no effect on LDH release. ^{51}Cr: Incubation of cells with DEP-LL or SRM (10 to 500 μg/well) had no effect. At 500 μg/well of DEP-HL, significant increase in ^{51}Cr release. IL-8: DEP-HL induced 5 fold increase in IL-8 at 500μg/well. Decrease observed at highest dose of DEP-LL extract. SRM did not significantly alter IL-8 production. PGE2: Production of PGE2 (inflammatory/immune mediator) increased in cells treated with HL extract at 500 μg/well. DEP-LL had no effect. Stimulation with melittin caused DEP-LL extract to have inhibitory effect on PGE2 at 500 μg/well. SRM had no effect.
Matsuo, M. Shimada, T. Uenishi, R. 2003	Human, NHBE (normal human bronchial epithelial cells), Human, NHPAE (normal human pulmonary artery endothelial cells) Human, TIG-1 and TIG-7 (normal human lung embryonic fibroblasts) NHBE 5x10E4 cells/cm^2 NHPAE 3x10E3 cells/cm^2 TIG-1 and TIG -7 3x10E3 cells/cm^2 Apoptosis 2x10E5cells/cm^2 ROS/NO 2x10E4 cells/cm^2 Cytoxicity Modulating Agent 3x10E4 cells/cm^2 GSH 3x10E4 cells/cm^2	DEP RDEP = residual DEP (after sequential extraction with hexane (NOS), benzene, dichloromethane, methanol, 1N ammonium hydroxide) 0.4um	25, 50, 100, 200, 300, 400, 500 μg/mL	1h	Cytoxicity in NHBE: Both DEP and RDEP dose-dependently cytotoxic at >50 μg/mL. RDEP<DEP. DEP exposure resulted in necrosis not apoptosis. Comparative Cytotoxicity: NHBE>NHPAE>>TIG with NHBE most sensitive. ROS/NO: DEP dose-dependently increased at 25 and 50 μg/mL. Reduced Glutathione: DEP dose-dependent decrease to 0 by 300 μg/mL. Antioxidant Effects: Decreased or no effect in DEP toxicity. Chelating Agents: Decreased DEP toxicity. Endocytosis inhibitors: Decreased DEP toxicity.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Matsuzaki, T. Amakawa, K. Yamaguchi, K. 2006	Human, Peripheral Neutrophils, Male and Female, 20-40y 5 X10^5 cells/mL	DEP (4JB1-type, 4 cyl Isuzu diesel engine) me-DEP = methanol extract of DEP (40 % of DEP by dry weight) NR	all me-DEP f-actin: 1, 5, 10 μg/mL CD11b: 5, 10, 30 μg/mL IL-8: 5, 10, 30 μg/mL H_2O_2: 5, 10, 30, 60 μg/mL MMP-9, LTB-4: 5, 10, 30, 60 μg/mL	f-Actin: 15 min CD11b: 2h IL-8: 2 or 24 h H_2O_2: 30 min MMP-9, LTB-4: 2 or 24 h	F-Actin: Dose-dependent increase with me-DEP at 5 and 10 μg/mL CD-11b: Increased 2 fold at 30 μg/mL. IL-8: Minimal response after 2h. Significant increase (243%) at 24 h with 30μg/mL. LTB-4: At 2h, increased 115% and 119% with 30 and 60 μg/mL me-DEP respectively. At 24 h with 60 μg/mL me-DEP, increased 153%. H_2O_2: Massive dose-dependent increase of 563% and 1220% with 30 and 60 μg/mL me-DEP respectively. MMP-9: Increased significantly at 2 and 24 h in similar manner. 30mg/mL >60mg/mL.
Molinelli, A.R. Santacana, G.E. Madden, M.C. 2006	Human, NHBE (normal human bronchial epithelial cells), Human, BEAS-2b (transformed bronchoepithelial cells) 3x10E3 cells/well	PMH = PM_{10} extracts in hexane PMA = PM_{10} extracts in acetone of residue after hexane extraction -G = Guaynabo(Urban) and -F = Fajardo (Preservation Area), PR, USA 1999 PM_{10}-G = 39 μg/m^3 PM_{10}-F = 27 μg/m^3 2000 PM_{10}-G = 37 μg/m^3 PM_{10}-F = 24 μg/m^3 1999 $PM_{2.5}$ -G = 10 μg/m^3 $PM_{2.5}$ -F = 7 μg/m^3 2000 $PM_{2.5}$ -G = 9 μg/m^3 $PM_{2.5}$ -F = 5 μg/m^3	NHBE: 6-10 μg/mL BEAS-2B: 10,100, 250 μg/mL	48h	Metal analysis: Hexane extracts Cu, V, Ni all higher in winter than summer. Generally -F >-G. Methanol extracts: Winter >summer especially for Ni, V, Fe (-F only), Pb, except Cd (equivocal) and -G >-F. Cytotoxicity NHBE: PMH: Winter -G = Winter-F >>summer -G >summer-F. Cytotoxicity BEAS-2: PMH Winter-G >Winter-F >summer-G >summer-F. PMA summer-G >summer-F >Winter-F >Winter-G. Effects trend similar to metal levels (no analysis). NHBE sensitivity >>BEAS-2 cells. summer extracts showed linear dose-response curves. Winter ones more equivocal especially for -F. PMA: summer-G >summer -F >Winter-G (no winter-F data). Rat Tracheal Contractivity: No effects.
Moller, W. Hofer, T. Ziensenis, A. 2002	Canine, BD-AM, Beagle Dog Alveolar Macrophages Mouse, J774A.1, Macrophages, BALB/c/NIH 10E6 cells	$fTiO_2$ $ufTiO_2$ = ultrafine TiO_2 ufP-G = carbon black (Printex-G) ufP90 = carbon black (Printex90) ufEC90 = elemental carbon DEP UrbD = Urban Dust $fTiO_2$ = 220nm $ufTiO_2$ = 20nm ufP-G = 51nm ufP90 = 12nm ufEC90 = 90nm DEP = 120nm UrbD = NR	10-320 μg/mL	1-24 h	Cytoskeleton of J774A.1: At dose of 32 μg/mL or less, no effect by any particles. $fTiO_2$and ufP90 had no effect at any dose. $ufTiO_2$ at 320 μg/mL induced retarded relaxation and significant stiffening. ufEC90 induced dose-dependent retardation of relaxation and increased stiffening. DEP and UrbD induced similar results. Cytoskeleton of BD-AM: $ufTiO_2$ and $fTiO_2$ both induced some retarded relaxation and increased stiffening at 100 μg/mL dose. $ufTiO_2$ appears to have dose-dependent increase of stiffening. ufEC90 induced dose-dependent acceleration of relaxation due to carbon content of ufEC90. DEP also induced acceleration of relaxation as well as decrease in stiffness. Phagocytosis: At 24 h, $ufTiO_2$ and $fTiO_2$ significantly reduced phagocytotic ability in J774A.1 but not BD-AM. All carbonaceous particles induced significant impairment in J774A.1. All ultrafine carbon particles inhibited BD-AMs. Cell Proliferation: $ufTiO_2$ significantly inhibited proliferation compared to control and $fTiO_2$ at 100 μg/mL in J774A.1. ufEC90 and ufP90 inhibited slightly with ufEC90 >ufP90. UrbD and DEP also significantly reduced proliferating. Apoptosis: All particles induced decreased viability at 100 μg/mL in both cell types. $ufTiO_2$ >$fTiO_2$. ufEC90 >ufP90. ufEC90 >ufP-G.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Mutlu et al. (2006)	Human, A549 Rat, Primary Alveolar Type II Epithelial Cells NR	PM_{10} Collected by baghouse from Dusseldorf, Germany NR	NR	24 h	Na,K-ATPase Plasma Membrane Protein: PM_{10} induced decrease of protein amount in plasma membrane in A549 cells. Total Na,K-ATPase level unaffected. ROS: Pretreatment with EUK-134, superoxide dismutase and catalase mimetic, inhibited decrease of GSH. Furthermore attenuated decrease of NA,K-ATPase in A549 cells. NA, K-ATPase Activity: PM_{10} induced dose-dependent decrease in ouabain-sensitive liberation of 32P from AT32P in primary rat alveolar type II cells. Effect inhibited with pretreatment with EUK-134.
Nam, HR.Y. Choi, B.HR. Lee, J.Y. 2004	Human, A549 NR	$PM_{2.5}$ Collected from hospital rooftop, Seoul, South Korea NR	0.5 - 50 μg/cm^2	6h, 24 h	NFκB/IκBα: 50 μg/cm^2 DEP induced IκBα degradation, peaked at 2h, recovered after 4h. Treatment with increasing amount of $PM_{2.5}$ resulted in dose-dependent decrease in IκBα. $PM_{2.5}$ increased NFκB in dose-dependent manner up to 10 μg/cm^2. NFκB induction peaks at 12h. IL-8: Increased protein level more than 3 fold with 100 μg/cm^2 $PM_{2.5}$. mRNA level also increased. iNOS Inhibitor: $PM_{2.5}$ induced IL-8 elevation completely blocked by iNOS inhibitor. iNOS inhibitor also negated $PM_{2.5}$ induction of NFκB activity. Antioxidants and iNOS inhibitor reduced PM-induced IκBα degradation.
Nozaki, J. Yamamoto, R. Ma, L. 2007	Mouse, LA-4, Alveolar Epithelial Cells 1.4x10E4 cells/cm^2	PM = PM Rooftop 5story, urban, Japan PME = dichloromethane extract of PM filtered P90 = Printex 90 (carbon black) (Degussa) PM = 0.22um PME = 2.5um P90 = 14nm	1.1 μg/cm^2	24, 48, 72h	Cytotoxicity: P90 no effect. PM and PME cytotoxic at similar levels. Protein Expression: All particles affected protein expression (no specific protein- 2D gel electrophoresis).
Obot, C.J. Morandi, M.T. Beebe, T.P. 2002	Mouse, Alveolar Macrophage, BALB/c 5 X10^5 cells/mL	PM = SRM 1648 PM-100 = PM heated to 100 C PM-500 = PM heated to 500 C PM-PH = PM acid digestion PMAC = Acetone extraction PMCH = Cyclohexane extraction PMH2O = Water extraction All extract fraction used as residual particles NR	PM = 200 μg/mL PM-100 = 188 μg/mL PM-500 = 130 mg/l PM-PH = 94 μg/mL PMAC = 173 μg/mL PMCH = 171 μg/mL PMH2O = 188 μg/mL Fraction doses adjusted for mass loss during fraction treatment	4h	Cytotoxicity: All 7 fractions had cytotoxic effects. PM had highest cytotoxicity. PM-500, PM-PH, PMAC less toxic than PM. Apoptosis: All 7 fractions increased apoptosis. PM and PMH2O highest effect >PM-100, PM-500, PMAC >>PM-PH, PMCH. PM-induced apoptosis (only PM, PM-500 and PMAC tested) blocked by poly I or 2F8 antibody (scavenger receptors). Particle Characterization: Untreated PM and PM-100 did not have measurable amounts of transition metals on its surface. Measured components include carbon, O2, N, S, Si, Ca, Al, P, Cl. PM-PH mostly contained O2 and Si. PM-500 had increased O2, Si compared to PM and measurable amounts of Na, K., Zn, Co, Pb, Fe. Included increased surface density of S, P, Al. PMCH lacked nonpolar organic compounds.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Obot, C.J. Morandi, M.T. Hamilton, R.F. 2004	Mouse, Alveolar Macrophages, BALB/c, 7-9wks Human, Alveolar Macrophages 5 X10^5 cells/mL	PM = SRM 1648 Collected by baghouse in 174-1976 St.Louis, MO PM-100 = PM heated to 100 C PM-500 = PM heated to 500 C PM-PH = PM acid digestion PMAC = Acetone extraction PMCH = Cyclohexane extraction PMH2O = Water extraction $PM_{2.5}$ Collected in Houston, TX PM fractions = SRM 1648	PM = 200 μg/mL PM-100 = 188 μg/mL PM-500 = 130 mg/l PM-PH = 94 μg/mL PMAC = 173 μg/mL PMCH = 171 μg/mL PMH2O = 188 μg/mL Fraction doses adjusted for mass loss during fraction treatment $PM_{2.5}$ = 50, 100, 150, 200 μg/mL	Mouse 4h Human 24 h	Human AM Viability: Only 4 out of 7 decreased viability: PM, PM-100, PMAC, PMH2O. Human AM Apoptosis: PM, PM-100 and PMH2O increased apoptosis. PM >PM-100, PMH2O Regression Analysis Mouse vs Human: Although individual fraction differed somewhat, cell viability and apoptosis of all 7 fractions showed linear regression Human and Mouse AM Viability with $PM_{2.5}$: Nearly identical dose-dependent decrease starting at 50 μg/mL Human and Mouse AM Apoptosis with $PM_{2.5}$: Nearly identical dose-dependent increase with human AM response peaking at 150 μg /mL and declining at 200 μg/mL (no mouse data for 200 μg/mL). Regression Analysis with $PM_{2.5}$: Excellent correlation of mouse and human responses for viability and apoptosis.
Okeson, C.D. Riley, M.R. Fernandez, A. 2003	Rat, RLE-6TN, Type II Alveolar Epithelial Cells NR	CG = Coal ash, Germany CU = Coal ash, USA 5C = PM # 5 Oil fly ash coarse 5F = PM #5 Oil fly ash fine 6MSC = PM #6 Oil med sulfur fly ash coarse 6HSC = PM # 6 Oil high sulfur fly ash coarse 6HSF = PM # 6 Oil high sulfur fly ash fine CG and CU NR 5C, 6MSC, 6HSC >2.5 μm 5F, 6HSF <2.5 μm	Coal Fly Ash 12.5, 25, 50, 125, 250 μg/mL Oil Fly Ash - 100 μg/mL	24 h	Oil PM Characterization: Generally fine fraction had higher metal levels than coarse except Zn. High sulfur >med sulfur. Sulfur content of # 5 inbetween #6 medium and high sulfur. 6HSF >5C >5F = 6HSC >6MSC. Carbon wt% stable across all 5 fractions. Coal Ash Cytotoxicity: CG = CU. Effect at concentrations of 12.5 μg/mL and above. Effect steady at concentrations above 50 μg/mL. Oil Ash Cytotoxicity: Effect induced by all. 5F >6HSF >6HSC >5C >6MSC. Correlation of Metal Content and Cytotoxicity: Fe, V showed reasonable correlation. Zn had no correlation. Cell Metabolism: Inhibitory effect with 100 μg/mL coal ash after 6h. CO>CG. Oil ash less effective than coal ash. 5F>6HSC>5C>6MSC. 6HSF not tested.
Okeson, C.D. Riley, M.R. Riley-Saxton, E. 2004	Rat, RLE-6TN, Type II Alveolar Epithelial Cells 50000 cells/well	Zn, V, Fe chloride as salts (valence state not reported i.e., Fe II or Fe III) NR	0.001, 0.01, 0.1, 1.0, 10 mM	24 h	Cytotoxicity: All metals cytotoxic >0.1 mM. Zn >>V >Fe. At 10 mM, no surviving cells with all three metals. NCS: Incubation with NCS (5 or 10 %) decreased toxicity of Zn, especially at 0.1 mM, but had no effect on Fe or V toxicity. Albumin: BSA decreased Zn toxicity at equivalent concentrations but to a lesser extent than NCS.
Osornio-Vargas, A.R. Bonner, J.C. Alfaro-Moreno, E. 2003	Mouse, J774A.1, Monocytes Mouse, L929, Mesenchymal Cells 15000 cells/cm^2; 30,000 cells/well	PM_{10} $PM_{2.5}$ -N = Northern (industrial) -SE = Southeastern (lake basin dust) sites, both heavy vehicular traffic, Mexico City, Mexico $PM_{2.5}$ -N = 40 μg/m^3 PM_{10}-N = 82 μg/m^3 $PM_{2.5}$ -SE = 54 μg/m^3 PM_{10}-SE = 114 μg/m^3	20, 40, 80 μg/cm^2	24-72h	PM Characterization: Elements similar in particle types with elements in PM_{10} more abundant. Northern particles contained more Co, Zn, Ni, Pb. Endotoxin: All PM samples had detectable amounts of endotoxin. $PM_{2.5}$ -N had 22 EU/mg. PM_{10}-N had 30 EU/mg. $PM_{2.5}$ -SE had 12 EU/mg. PM_{10}-SE had 59 EU/mg. Cytotoxicity (J774A.1): $PM_{2.5}$ -N = PM_{10}-N steady at 40% survival. PM_{10}-SE and $PM_{2.5}$ -SE induced dose-dependent response. Northern >Southeastern. Apoptosis (J774A.1): Northern >>Southeastern. For each PM_{10} = $PM_{2.5}$. TNF-α and IL-6 (J774A.1): TNF-α and IL-6 dose-dependent increases P10-SE>$PM_{2.5}$ -SE = PM_{10}-N = $PM_{2.5}$ -N. J774A.1 Supernatant Toxicity (L929): Conditioned medium from J774A.1 pre-exposed to each PM type reduced cell viability in L929 cells. Correlated with TNF-α level in supernatants.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Pei, X.HR. Nakanishi, Y. Inoue, HR. 2002	Human, A549 NR	B[a]P = benzo[a]pyrene 1-NP = 1-nitropyrene NR	B[a]P = 10µM 1-NP = 5 µmol	4, 8 or 24 h	Apoptosis: <10 % based on earlier research. IL-8: IL-8 mRNA increased by B[a]P and 1-NP in time-dependent manner with 1-NP >B[a]P (at 1/2 molarity). IL-8 stimulation by 1-NP also time-dependent ~ 5 fold at 24 h; B[a]P 3 fold. NF-κB: 1-NP induced NF-κB-DNA binding activity within 4h, maintained for 24 h. B[a]P induced similar response. Binding negated by 50 fold excess of NF-κB consensus probe. IκBα (NF-κB Inhibitor): More than 50 fold increase in IκBα native levels, suppressed 1-NP induced NF-κB activation and reduced IL-8 mRNA induced by 1-NP by 80%.
Penn et al. (2005)	Human, BEAS-2B 1-1.5x10E6 cells	BDS = Butadiene soot -P1 = <2.5um -P2 = 2.5-10um -P3 = >10um BDS-W = solvent washed Graphite <2.5um = 92% 2.5 - 10um = 5% >10um = 3% NR	3mg BDS NR	5min-72h	Particle Characterization: Elemental carbon 94% by weight. Hydrogen 2% by weight. Nitrogen and sulfur 1%. Oxygen <0.1%. PAH Components of BDS: 13 prominent PAHs: acenaphthylene, fluorene, anthracene, cyclopentaphenanthrene, fluoranthene, acephenanthrylene, pyrene, benzofluorenes, acepyrene, chrysene, benzopyrenes, perylene, benzoperylene. BDS Activity: At 60-120min, BDS observed in cells. At 4h, fluorescence observed in cytoplasmic vesicles and increased during first 24 h, plateaued for next 72h. BDS-W appeared in vesicles sooner than BDS.
Pozzi, R. De Berardis, B. Paoletti, L. 2005	Mouse, RAW 264.7 1.3x10E5 cells/well	PM Collected continuously for 15 days, 8-10m from street, Sept 1999, Rome, Italy -F = Fine particulate -C = Coarse particulate CB (Degussa Huber NG90) PM-F = 0.4-2.5um PM-C = 2.5-10um CB = 200-250nm	30 µg/mL; 14 µg/cm^2 120 µg/mL; 54 µg/cm^2	5, 24 h	Cytotoxicity: Lower levels of PM-F, PM-C, and CB for 24 h had no effect on cell viability. Higher levels of PM-C and CB induced significant release of LDH. Arachidonic Acid (AA): Both fractions of PM increased AA release in dose-dependent manner at 5h. CB increased release only at higher concentration, although`magnitude much less than ambient PM-induced AA release. Pretreatment with deferoxamine not effective in decreasing AA release. TNF-α: TNF-α levels increased significantly for both concentrations and time periods for PM. PM-C at 24 h significantly lower than 5h for both concentrations. PM-C at 30 µg/mL induced much greater TNF-α release than PM-F at 5h. IL-6: PM-F significantly increased at 5h for both concentrations. Elevated IL-6 at both PM-C doses at 24 h; only elevated at 5h for high dose. CB devoid of effect on IL-6. LPS-induced IL-6 response similar to coarse PM at high dose, with the response being greater at 24 h than 5h.
Prophete et al. (2006)	Rat, NR8383, Alveolar Macrophages 2 X10^5 cells/mL	Ambient $PM_{2.5}$ NYC = 1st and 26 St, NYC LA = San Gabriel foothills, Claremont, CA SEA = 15th Ave S and S.Charleston, Seattle, WA V, Mn, Al, Fe levels in PM added metals to cells V = Na3VO4 Al = $AlCl_3$.6H2O Mn = $MnCl_2$.4H20 Fe = $FeCl_3$.6H20 NR	Fe(III) 16 µmol V, Mn, and Fe(III) mixtures with V or Mn in molar ratios 0.02, 0.08, 0.2 and 0.4 X Fe(III) Al and Fe(III) mixtures with Al in molar ratios 0.37, 0.75, 2, 7.5 X Fe(III)	20 h	Particle Characterization: Fe and metal to F ratios based on ratios observed in $PM_{2.5}$ from LA, SEA and NYC sites. V: Fe ratios remarkably similar among sites. Fe levels fixed at NYC level of 16 µm (highest). IRP: Coexposure with 3 metals increased IRP binding activity relative to Fe III alone, by up to 3.5 fold for Al (1.5-3 ratio), 2 fold for Mn (0.08-0.2 ratio) and 7 fold for V (0.2 ratio). IRP activity dropped at higher ratios. For Al, may be result of cytotoxicity but not for V and Mn. iNOS: Al induced dose-dependently. No effect for Mn and V. Induction of Hypoxia-inducible Factor (HIF-1α): Only V and Al induced HIF-1α. Activation of ERK1 and -2: V and AL induced pERK1, but only V induced pERK2. Mn had no increasing effects, but data indicated decreasing induction.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Ramage and Guy (2004)	Human, A549 NR	PM_{10} ufCB = Ultrafine Carbon Particles NR	80 μg/mL	0, 30min, 3, 6, 18 h	CRP: Treatment with ufCB or PM_{10} produced increase in CRP expression, similar effects noted after 6h with PM_{10} >ufCB. CRP in both cytoplasm and nucleus. Hsp70: PM_{10} and ufCB induced increased levels at all time points with ufCB >PM_{10}. Hsp70 observed being expressed in cytoplasm and nucleus. Antioxidants of CRP and Hsp70: ufCB coincubated with Nacystelin and Trolox caused small reduction in CRP and Hsp 70.
Reibman et al. (2003)	Huamn, HBEC, Volunteers or BioWhittaker Human, BEAS-2B NR	UFPM = Ultrafine PM FPM = Fine PM IPM = Intermediate PM CPM = Coarse PM CB = Carbon black All PM collected 8th floor, 26th St and 1st Ave, New York City, NY UFPM <0.18um 0.18 <FPM <1.0um 1.0 <IPM <3.2um CPM >3.2um	11 μg/cm²; 100 μg/mL	6 h, 18 h	Cytotoxicity: Cells more than 90% viable, UFPM and FPM caused no gross alterations in cell morphology or adhesion. MIP3α/CCL20 mRNA (6h): Stimulation of mRNA released by HBEC upon exposure to UFPM appeared similar to that provided by TNF-α (5 μg/mL) and IL-1β (10 mg/mL). MIP3β/CCL20 protein in HBEC (18h): TNF-α and IL-1β induced dose-dependent increase in MIP3α/CCL20 protein (0-10 ng/mL), whereas Il-4 and IL-13 induced MIP3α/CCL20 protein release that reached maximum levels at 1 ng/mL. No release of MIP1α/CCL3 nor RANTES/CCL-5 observed upon stimulation with cytokines. Secretion of MIP3α/CCL20 in response to PM (18h): All PM fractions <2.5 μm resulted in release of MIP3α/CCL20 protein in HBEC roughly equivalent amounts. CB sized similar to UF/fine PM did not result in release of MIP3α/CCL20, nor did LPS (0.01-1.0 μg/mL). No release of MIP1α/CCL3 nor RANTES/CCL 5 was observed upon stimulation PM fractions. Activation of MAPK (ERK1/2 and p38): ERK1/2 and p38 activated by TNF-α, IL-1β, IL-4 and IL-13 within 15 min and sustained for at least 60 min. Erk1/2 and p38 inhibitors reduced MIP3α/CCL20 release in BEAS-2B cells in response to cytokines.
Riley et al. (2003)	Rat, RLE-6TN, Type II Alveolar Epithelial Cells NR	Zn = $ZnCl_2$ Cu = $CuCl_2$ Fe = $FeCl_2$ V = VCl_4 Ni = $NiCl_2$ NR	0.01-10 mM	24 h or 2-72 h (time-course)	Cytotoxicity (SDH): All particles cytotoxic in dose-dependent manner. Zn, V at 0.05 mM, Cu at 0.5mM, Ni at 0.8mM and Fe at 2 mM. For Zn, cell death (LDH) had biphasic response: a slow logslope until approx 0.1mM at which point rapid acceleration to a peak at 5mM with small decline at 10mM. Most of Zn cytotoxicity not due to apoptosis. LPS did not affect either Zn or Cu cytotoxicity. Metabolism Inhibition Time Course Response (Cu and Zn only): At high (1 mM) concentrations, Zn toxicity peaked at 36-48h followed by 2 fold recovery by 72h. Cu showed faster, steady decline plateauing after 36h. At low (0.1 mM) Cu showed steady slow decline. Zn decreased faster to max activity at 48h and returned to control by 72h. IL-6 Secretion: Zn and Cu both decreased IL-6 secretion. Decreases very similar for both metals and concentrations when expressed as secretion per viable cell ratio except for Zn at 1.0 mM. Metal Combinations: Zn and Cu gave variable results. Zn protected against V cytotoxicity. Zn and Cu had additive response. Zn did not affect Fe toxicity.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Riley et al. (2005)	Rat, RLE-6TN Human, A549 Rat, NR8383, Macrophages 5 x10E4 cells/well Alveolar Cells 1.2x10E5 cells/well NR8383	Fe = FeCl2 Ni = NiCl2 Cu = CuCl2 V = VCl2 NR	Alveolar Cells: 0.01-10 mM NR8383: 0.01 -10 mM	2-48 h	Relative Sensitivity of Cell Strains to Metal Chloride: NR8383 >>RLE-6TN = A549 except for V where NR8383 = RLE-6TN >>A549. Relative sensitivity of Cell Strains to Metal Chloride vs Sulfate: Generally sulfate more cytotoxic than chloride except Cr. (note V valence state). A549 Cytotoxicity Time Course: Zn cytotoxicity takes 24 h to develop whereas Cu cytotoxicity develops within 2 h. LDH release for Cu however takes 24 h to develop. RLE Cytotoxicity Time Course: Zn starts at 2 h and develops until 24 h. Cu develops within 2 h and continues until 24 h where it is less toxic than Zn. Both release equivalent amounts of LDH after 24 h. NR8383 Cytotoxicity Time Course: Both Zn and Cu time dependent toxicity starting as early as 4h. LDH release max at 12 h and either stays steady or declines.
Ritz, S.A. Wan, J. Diaz-Sanchez, D. 2007	Human, BEAS-2B Human, NHBEC NR	DX = Extract of DEP NR	0, 20, 50, 100 μg/mL	24 h	NQO1 (Sentinel Phase II Enzyme): Cells transfected with NQO1 reduced induction of IL-8 by DX exposure. Sulfurophane: Increased gene expression of phase II enzymes, particularly NQO1, in both cell types with BEAS-2B >NHBEC. Sulfurophane did not upregulated GSTM1 in BEAS-2B but induced 2 fold increase in NHBEC. Pretreatment also inhibited DX-induction of IL-8 in both cell types. Cytokines: DX induced significant increase of IL-8 in both cell types at 10 μg/mL or higher. GM-CSF and IL-8 unaffected in BEAS-2B. Increased in NHBECs, statistically significant at 25 μg/mL.
Rosas Perez et al. (2007)	Murine, J774A.1 1.5x10E4 cells/cm^2	PM_{10} Collected in Mexico City, Mexico North: Iztacala, manufacturing industry; Center: Merced, heavy traffic; South: Ciudad Universitaria, residential NR	20, 40 or 80 μg/cm^2	72h	Principal Component Analysis of Air Pollution Data: Group 1 = S/K/Ca/Ti/Mn/Fe/Zn/Pb (43% of variance); Group 2 = Cl/Cr/Ni/Cu (16%); Group 3 = Endotoxins/OC/EC (14%). For all 3 sites: Group 1 is different, Group 2 is similar, Group 3 North <Center = South Cytotoxicity: Dose-dependent response - no site interaction. IL-6: Only Center site at 40 μg/cm^2 induced increase. TNF-α: Dose-dependent and site-dependent where center and south sites different from north. p53: Only South PM had effect. Statistical Analysis (effect driven by metals): Cytotoxicity = S/K/Ca/Ti/Mn/Fe/Zn/Pb. TNF-α and IL-6 = S/K/Ca/Ti/Mn/Fe/Zn/Pb and endotoxins/OC/EC. p53 = high Cl/Cr/Ni/Cu and low S/K/Ca/Ti/Mn/Fe/Zn/Pb.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Sakamoto, N. Hayashi, S. Gosselink, J. 2007	Human, HBEC, Smokers, 58-82y NR	PM_{10} = EHC-93 NR	100, 300 and 500 μg/mL	Up to 60 min (calcium responses); 6 or 24 h (cytokines)	Intracellular [Ca2+]: [Ca] concentration slowly increased, elevated after 10 and 30 min for 500 and 300 mg/mL respectively. Response plateaued at 35 min for 500 microgram/mL. Extracellular [Ca2+]: Removal of extracellular Ca decreased PM_{10} response significantly starting at 20 min. Calcium channel blocker (10μM or 1mM) LaCl3 and (5mM) NiCl2 significantly blocked PM-induced intracellular Ca. Lacl2 (1mM) inhibited nearly 100%. Mode of Action: Intracellular Ca induced by ATP declined slower in PM_{10} exposed cells - indicating that PM_{10} blocks Ca clearance via calcium pumps. Cytokines: PM_{10} induced dose-dependent increase in cytokine mRNA and cytokines IL-1β, LIF, IL-8 and GM-CSF. Cytokine expression unaffected by reducing extracellular Ca2+. Preincubation with calcium chelator reduced response for IL-1β and IL-8 but not LIF or GM-CSF.
Salnikow, K. Li, X. Lippman, M. 2004	Human, 1HAEo- NR	$FeSO_4$ $FeCl_3$ $NiSO_4$ NR	0.25mM Fe exposures also contained 60 μg/mL apotransferrin	24 h	Cytotoxicity: Both Fe had no effect. NiCL2 caused marginally cytotoxicity (75%). Hypoxic Stress: At 20h, $NiSO_4$ (0.25 or 0.5mM) induced NDRG-1/Cap43 protein production, indicating hypoxic stress. DFX and DMOG induced similar effect. IL-8: $NiSO_4$ induced IL-8 time-dependent for up to 48h where increase was 6+ fold. Coexposure (Ni + Fe) on Fe uptake: Fe III>Fe II uptake. $NiSO_4$ had no effect. Ni uptake >Fe uptake but decreased by coexposure to Fe. Coexposure also did not effect hypoxic stress. Coexposure with Fe did reduce Ni-induced IL-8 production.
Salonen et al. 2004	Mouse, RAW264.7 2x10E6 cells/well	PM_{10} (urban traffic) Finland (filter sonicated in water and methanol, extracted with methanol) Pooled as Winter (W) spring I (SI) or spring II (SII) based on component/time considerations 0.12<PM_{10}<10 nm HVLI slit impactor	15,50, 150,500, 1000 μg/mL	24 h, 0 h	Air quality parameters: Winter and spring I did not differ. SII much lower $PM_{2.5}$ PM_{10} W = 18.6 ± 10.1; SI = 28.0 ± 5.5; SII = 20.3 ± 2.4 μg/m^3 Metal data equivocal as well as highly variable resuspension rates Total PAHs: W = 303; SI = 233; SII = 204 ng/mg PM_{10} (ppb) Inflammation (IL-6, TNF, NO) /Cytotoxicity: Dose dependent increase for TNF, IL-6 and NO except for SI IL-6 effect which decreased at 1000 μg/mL. TNF, IL-6: SI = SII>>W>control. NO production W> = SI> = SII Cell Viability: W = SI = SII toxic at 500 and 1000 μg/mL Watersoluble vs Insoluble**:** TNF and IL-6 were nearly entirely the result of insoluble components of PM_{10} Cytotoxicity was driven by both soluble and insoluble components. Metal Chelation: Addition of metal chelator did not modify IL-6, TNF or cytotoxicity LPS inhibitor: Eliminated IL-6 response and perhaps slightly reduced TNF response but not cytotoxicity Hydroxy radicals: dose dependent induction of hydroxy radicals and induction of hydroxy radical lesions (500 and 1000 μg/m^3) in calf thymus DNA

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Samet, J.M. Dewar, B.J. Wu, W. 2003	Human, A431, Epidermoid Cells NR	As = $NaASO_3$ V = $VOSO_4$ Zn = $ZnSO_4$ NR	500µM	20, 30 or 90 min	EGFR Dimerization: Zn, V or As did not induced EGFR dimerization in cell free system i.e., no direct crosslinking. Zn did not induce dimerization in whole cells either. Phosphorylation of EGFR: Zn induced phosphorylation at 3 sites similar to EGF. As and V had no effect. EGFR Kinase Inhibitor: While EGF action blocked, Zn continued to induce phosphorylation and was independent of EGFR kinase activity. c-Src: Blocking of c-Src tyrosine kinase (transactivator of phosphorylation) negated all Zn-induced phosphorylation but only slight effect on EGF stimulated cells. ERK1/2 Phosphorylation: Zn increased levels of ERK1/2. Pretreatment with EFGR kinase inhibitor reduced both Zn and EGF effect. Effect not blocked by c-Src blocker.
Santini, M.T. Rainaldi, G. Ferrante, A. 2004	Mice, RAW 264.7 2.5 $X10^5$ cells/mL	DEP = $PM_{2.5}$ Collected beside moderate traffic in Rome, Italy NR	0.01, 0.1, 1.0 µg/mL	24 h	500 MHz results (no 1 µg/mL): DEP induced dose-dependent increase in choline compounds, α- and βgamma- glutamine/glutamate (0.01 >0.1 µg/mL), lactate, and CH_2, CH_3 moieties of fatty acids. DEP decreased inositol and (phospho)creatinine. 700 MHz results (no 1 µg/mL): DEP induced similar results, except α-, βgamma-glutamine dose-dependent. Inositol showed no effect. Taurine slightly increased. Results confirmed after perchloric acid digestion to eliminate biological interferences. Growth Curves/Cell Cycle Analyses/Cell Morphology: DEP had no effect. Cytokines: IL-6 levels increased at 0.1 and 1 µg/mL. TNF-α unaffected.
Saxena, Q.B. Saxena, R.K. Siegel, P.D. 2003	Mouse, RAW264.7 2.5 $X10^4$ cells/mL	DEP = SRM 1650 CO = Crude Organic Extract of DEP Fractionated into asphaltene (pentane/hexane), saturated hydrocarbon, less polar (aromatic) hydrocarbon, more polar (aromatic) hydrocarbon, resins, residual (resins) IFNy LPS NR	DEP, CO 5, 10, 15, 20, 25 µg/mL IFNy 10 ng/mL LPS 1 mg/mL	1-3d	Cytotoxicity: None observed. NO: DEP alone dose-dependently induced NO, peaked after 1d and plateaued for 2 and 3d. IFNy + DEP showed dose and time dependency >>DEP alone but only at 1d. LPS + DEP showed no effect at 1d, but dose-dependently reduced NO production on day 2 and 3. Addition of BC G eliminated effect of DEP at 2d but showed dose-dependent decrease at 3d. Effectiveness of Particulate Components: Carbonaceous core of DEP did not affect BC G-stimulated NO production. Crude organic extract of DEP significantly inhibited BC G-stimulated NO production. Study indicated extract of aromatic hydrocarbons and resins particularly caused inhibitory effect in dose-dependent manner.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Seagrave et al. (2007)	Human, differentiated primary lung epithelial cells (3 donors, male, 23,23,16y) NR, proprietary culture method	DE = DE 5500 watt generator #2 certification oil 5000w load diluted to 3 mg/m^3 total particulate NR	Exposure to 3 mg/m^3 in AIR lowing over cell cultures	3h; 1 or 21-h after	Particle Deposition: 140 and 500 nm microspheres demonstrated uniform deposition of approx. 10% Transepithelial Electric Resistance: No effect of DE: more effect from air controls Macromolecular permeability: DE caused increase 1-h after exposure but at 21-h returned to control LDH/Cytotoxicity: DE had highly variable(donor specific) effect at 1-h and returned to control at 21h Mitochondrial activity (WST): DE reduced at 1-h and possibly increased at 21h (high donor-to-donor variability) MucusLike Substance Excretion: high donor to donor variability - no overall effects Alkaline Phosphatase (AP): DE decreased at 1-h and perhaps increased at 21h Glutathione: DE caused large decrease at 1-h but returned to normal at 21h HO-1: DE increased but lower than air exposed controls Cytokines: No differences for IL- 8 or 12, TNFα, GM-GSF, IL-1α, or IFNγ. IL-4 and 6 were decreased upon DE exposure.
Seagrave et al. (2004)	Human, A549 (ATCC), alveolar epithelial cells 1x10E5 cells/well	DPM = SRM2975 (NIST) DPM-O = DPM organic extract (acetone/DCM) CB = Carbon Black (Elftex-12, Cabot) SRM 2975 CB = 37 nm; Stokes diameter 198 nm; surface area 442 m^2/g	0.03 -1,000 μg/cm^2	18,0 h	IL-8 release: DPM increased semi dose-dependently (perhaps steady based on error range) up to 1 μg/cm^2 after which IL-8 declined dose dependently to zero (control = 100%) at 300 and 1000 μg/cm^2. LDH release was steady indicating no cytotoxicity. DPM interaction with IL-8: DPM depletes IL-8 from solution in a dosedependent (cellfree). BSA preincubation reduced the slope of the dose response but not the final result. CB has no effect. DPM-O residuals act identical to DPM. Increasing NaCl concentrations reduced DPMs depletion of IL-8 Neutrophil responses: DPM and bound IL-8 together caused a marked aggregation of cells resulting in spindle shapes. DEM or IL-8 alone did not cause this aggregation although DEP did recruit neutrophils
Seagrave et al. (2003)	Human, A549 Rat, Alveolar Macrophages, Male, F344/Crl BR, 11wks, 250g 1x10E5 cells/well	PM filter collection Collected from diesel or gasoline powered vehicles as follows: BG = Black Smoke Gasoline G30 = Normal Emitter gasoline (30F) G = Normal emitter gasoline (72F) HD = High Emitter Diesel D30 = current technology diesel (30F) D = current technology diesel (72F) WG = White Smoke Gasoline DS = SRM2975 positive control NR	0.03 - 10,000 μg/cm^2	16-18h	Cytotoxicity: LDH activity increased in A549 cells with BG = G30 = G >HD = D30 = D = WG >DS. Also increased in rat macrophages with G = G30 = BG >/ = HD = D30 >/ = D = WG >>DS. Note gasoline more cytotoxic than diesel in both cell types. Cytokines: All particle types except DS increased IL-8 in A549 though not all statistically significant. Also many particle samples produced apparent suppression of IL-8 release at high concentrations. Alkaline Phosphatase: G30 and G more potent than the other particle samples in A549. WG and D30 induced no significant effect. Increased at low concentrations and suppressed at higher concentrations. Macrophage Peroxide Production: Using two different statistical methods D30 >6 others which in turn >DS. Using the second method D30 and D >all other 6. Order of potency between two methods completely different. Authors noted that in vitro potency quite different from in vivo potency (previous paper).

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Seaton, A. et al. 2005	Human Alveolar epithelial cell line A5949 Not Reported	$PM_{2.5}$ from London PM_{10} from Manchester (positive control) PM from Holland Park, Hampstead and Oxford Circus stations (HP, HR and OC) TiO_2 (negative control) $PM_{2.5}$ monitoring Holland Park, Hampstead and Oxford Circus PM had a median diameter of 0.4 µm. 80% of the particles had a diameter less than 1 µm.	Dosages range from 1 - 100 µg/mL	Cytotoxicity: 24 h IL-8: 8 h Generation of hydroxy radicals: 8 h	Cytotoxicity: Dust from all three tunnels (Holland Park, Hampstead and Oxford Circus) were able to cause cell death (LDH). The release of LDH indicated a dose-dependent relationship. At highest dose Holland Park PM induced the ~17% release of LDH, Hampstead triggered ~ 13% and Oxford Circus ~3% (no different than control). PM_{10} from Manchester caused 7% LDH release at the highest dose and the negative control (TiO_2) caused no response (2% release at highest dose). IL-8: Results indicated a dose-dependent release of IL-8 indicated in all three tunnel PM. At highest dose, all three tunnel dusts induced IL-8 stimulation more so than the $PM_{2.5}$ from the control site. HP 3 fold increase. Also at highest concentration TiO_2 caused the least IL-8 stimulation. Hydroxy Radical Generation/ DNA Plasmid assay: The plasmid assay indicated that the tunnel dusts induce more free radical activity than the Manchester PM_{10} and TiO_2. HP near doubled % DNA damage with intermediate results for HR and OC. PM_{10}, TiO_2 and control were identical
Singal et al. 2005	Human, A549Luc1 lung adenocarcinoma epithelial cell line Mouse, MLE15Luc1 and MLE15Luc2, epithelial cells, all cells contain human cytokine IL-8 controlling firefly luciferase 5x10E5 cells/well	AE2 = Aerosil 200, amorphous silica (Degussa) CI: Carbon iron particles (25 % Fe) AE2: 12nm surface area ~200 ± 25 m^2/g CI: ~40 nm	18 µg/mL = 4.7 $\mu g/cm^2$ 36 µg/mL = 9.5 $\mu g/cm^2$ 72 µg/mL = 18.9 $\mu g/cm^2$ all in 1 mL /well	24 h	Luc activity: positive control TNFα stimulus, time and dose dependent activity peaking at 5-8 h (increasing with dose) MLE15Luc2>MLE15Luc1 Aerosil 200: AE2 induced dose and time dependent Luc response peaking at 3 h and decreasing thereafter similar to TNF. Contrary to TNF, AE2 induced massive cytotoxicity starting at 6h Effect of proteasomal inhibitors (MG-132): Inhibitor reduced AE2 Luc activity to near control levels. Similarly LDH-cytotoxicity was halved A549 human cell response: AE2 acted similar to MLE response, CI particles showed slightly less activity without peaks. AE2 increase cytotoxicity after 12 h, CI had no effect Contrary to MLE mouse, MG_132 did not affect Luc activity but PD98059 (selective noncompetitive inhibitor of the MAP pathway) and SN50 (NF- κB inhibitor) reduced AE 2 and CI induced activity.
[FROM Table D-4] **Reference:** Song et al. (2008) **Cell Line:** Alveolar Macrophages, RAW 264.		DEP collected from a 4JB1-type, light-duty (2740 cc), four-cylinder diesel engine operated using standard diesel fuel at speeds of 1500 rpm under a load of 10 torque. DEP Composition: Previously reported in another study. mean diameter of 0.4 µm	Cells were incubated with various concentrations of DEP (50 µg/mL is the only one discussed) Cell Concentration: 5 X 10^5 cells were seeded on a 24-well plate. Cells were to exposed to 50 µg/mL DEP	Nitrate production was measured in response to 50 µg/mL DEP over 72 h.	Nitrite Production In Vitro: 50 µg/mL of DEP induced nitrite when compared to the control. Over the 72-h studied there was not a general trend depicted, but maximal induction of nitrite occurred at 4 h after stimulation.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Steerenberg et al. (2006)	Rat, Crl/WKY, alveolar macrophages and Type 2 alveolar epithelial cell lines Human, A549, alveolar epithelial cell line NA	PMC = PM Coarse PMF = PM fine Ambient air samples European Cities 2.35 <PMC<8.5 µm 0.12 <PMF <2.35 µm	NA	NA	Crustal material (metals and endotoxin but not Ti, As, Cd, Zn, V, Ni, Se)) were positively associated with In vitro rat macrophage IL-6 and TNFα and In vitro Type 2 (rat alveolar) MP-2 and Il-6. Sea spray (Na and Cl) was also correlated with Macrophage IL-6
Tal et al. (2006)	Human, HAEC; volunteers; primary normal human airway epithelial cells NR	100 mM Zn(II) or V(IV) stock solutions (NOS) NA	500 µmol	5 and 20 min	Zn-mediated EGFR phosphorylation: EGFR kinase activity required but not EFGR ligand binding EGFR Kinase inhibition reduced Zn mediated EGFR activation,. (authors NOTE: complete reverse of results in B82L and A431 cells) Src Kinase is not required. Zn inhibits Src kinase nearly total after 20 min. EGFR-specific protein tyrase phosphatase (PTP): Zn inhibited PTPs, similar to V(IV) resulting in decrease of exogenous EGFR dephosphorylation
Tamaoki, 2004	Human, cadaver, bronchial epithelial cells 10E4 cells/well	UFCB = Ultrafine Carbon Black - (Tokai Carbon, Japan) FCB = Fine Carbon Black (Tokai Carbon, Japan) UFCB = 11 ± 0.5 nm surf 457 m^2/g FCB = 250 ± 16 nm surf 7.8 m^2/g	6.1, 12.3, 18.4, 24.5, 30.7 $\mu g/cm^2$	up to 72 h	DNA synthesis/ Protein synthesis: increased by UFCB (30.7) for up to 72 h, flattens after 48 h. FCB no effect UFCB also showed dose dependency starting at 12.3 $\mu g.cm^2$ up to 24.5 whereafter it plateaued Addition of Cu/Zn Super oxide dismutase (SOD) or a NADPH oxidase inhibitor completely inhibited UFCB effects Similarly two different EGFR tyrosine kinase inhibitors, and a Me inhibitor all reduced UFCB response to control ERK activation: UFCB caused phosphorilization of ERK starting at 2 min, peak at 5 and decrease at 10 min. Activation was inhibited by EGFR tyrosine kinase inhibitor Cu/Zn SOD, and neutralizing body for HB-EGF but not by PDGF-R kinase inhibitor. HB (polyclonal heparin binding)-EGF release: UFCB induced rapid cell surface loss with recovery after 20 min to near full recovery at 360 min Metalloproteinase inhibitor and Cu/Zn SOD both prevented HB-EGF release
Tao, F. Kobzik, L. 2002	Rat, RLE-6TN (RLE), Alveolar Type II Epithelial Cells Rat, Fetal Lung Fibroblasts (RFL) Rat, Alveolar Macrophages, Female, CD, 6-12wks 1x10E5 cells AM 1.4x10E5 cells RLE/RFL NR Co-culture	UAP = Urban Air Particles = SRM 1649 TiO_2 = Titanium dioxide SiO_2 ROFA LPS (positive control) UAP = SRM 1649 TiO_2 = ~ 1um SiO_2 = ~ 1um ROFA = NR	1-50 µg/mL	24 h	Cytokines: TNF-α and MIP-2 in RLE unaffected by any particle samples. TNF-α and MIP-2 in AM significantly increased with 25 µg/mL UAP. TNF-α and MIP-2 in co-culture AM + RLE increased with each particle, SiO_2 at 25µg/mL >UAP at 12.5 µg/mL >ROFA at 25 µg/mL >TiO_2 at 50 µg/mL. Except for SiO_2, blocking of effects caused by LPS absorbed on particles did not affect cytokine response. For SiO_2, response reduced but still above control. Co-culture: Physically separating AM and RLE cells and adding PM completely negated response to PMs in co-culture indicating that cell to cell contact is required for co-culture potentiation of PM effects. Inhibitors: Various inhibitors of cell adhesion molecules (heparin, β -1, 2 or 3 integrin) had no effect on UAP-induced cytokine release.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Veranth et al. 2007	Human,(cell line/medium) BEAS-2B/LHC-9 BEAS-2B/KGM A549/DMEM/F12 NHBE/BEGM 35,000 cells/cm^2 BEAS 2500 cells/cm^2 NHBE 20,000 cm^2 A549	Artificial particles and PMs N-Al = nano alumina Al_2O_3 M-Al = Micro Al_2O_3 N-Ce = nano CeO_2 M-Ce = micro CeO_2 N-Fe = nano Fe_2O_3 M-Fe = micro Fe_2O_3 N-Ni = nano NiO M-Ni = micro NiO N-Si = nano SiO_2 M-Si = micro SiO_2 N-Ti = nano TiO_2 M-Ti = micro TiO_2 KLN = kaolin MUS = Min-U-Sil (ground crystalline silica) DD = desert rural soil Utah $PM_{2.5}$ JE = Juarez, urban street $PM_{2.5}$ MNC = Mancos, rural Utah $PM_{2.5}$ LPS = lipopolysaccharide V = $VOSO_4$ (soluble) (19 μg/mL) TNFα (0.01 μg/mL) Surface mean diameter/ surface N-Al = 6 nm (261 m^2/g) M-Al = 210 nm (7.7) N-Ce = 14 nm (71) M-Ce = 1500 nm (0.6) N-Fe = 5 nm (221) M-Fe = 100 nm (12) N-Ni = 6 nm (145) M-Ni = 16 nm (57) N-Si = 19 nm (127) M-Si = 440 nm (5.4) N-Ti = 6 nm (242) M-Ti = 410 nm (3.5) KLN = 100 nm (24.3) MUS (NOS <5 μm) DD = 400 nm (6.2) JE (NOS <3 μm) MNC = 200 nm (13.0)	0.53, 5.3 and 53 μg/cm^2 (= 1, 10, 100 μg/mL)	24 h	Cell Viability: Except for Ni and V no cytotoxicity was observed at highest concentration IL-6 secretion in BEAS-2 B cells: nano and micro of same metal showed no difference in response (high experiment to experiment variability) Actual Dust samples MC = DD = JE = V (pos control) >>N-Fe ~N-Si (LHC-9 media) Very different response pattern in KGM media: V>>JE>DD>N-Si~MC>N-Fe IL-8 secretion in BEAS/LHC vs NHBE in BEGM cells: NHBE>>BEAS-2 B cells (including controls ~ 40 fold) For BEAS-2B N-Si>>M-Si. Ni (both) only other` response. NHBE only Si and Ni >control IL-6 in NHBE: Al, Ce, Fe pair and N-Si (no response for N-Ni, M-Ni and M-Si) BSA/ Bovine serum addition effect: In a fixed solution N-Ni, N-Ti and KLN all reduced the measured IL-6 by 60 +%. Addition of BSA or bovine serum dose dependently reduced the action of the particles till near control. PM effects (without added protein) on IL-6 in solution: Increasing metal concentration did not affect a fixed IL-6 concenbtrtaion until 100 or 316 μg/mL level

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Veranth et al. 2007	Human, mouse,Rat detailed description in study 6203-2 under results 20 - 89 X 10 E3 /cm^2 ` also see 6203-3 effect for details on culture media	S = desert dust ($PM_{2.5}$ enriched) V = vanadium soluble ($VOSO_4$) C = Coal fly ash ($PM_{2.5}$ enriched) D = Diesel PM L = Lipopolysaccharide T = Titanium dioxide K = Kaolin BET surface (m^2/g) S = 6.2 (PM.25 enriched) V = NA C = 5.4 ($PM_{2.5}$ enriched) D = NR L = NA T = 3.5 (1-2 µm) K = 24 (<200 mesh = 74 µm)	maximum concentrations S = 100 µg/cm^2 V = 100 µg/cm^2 C = 100 µg/cm^2 D = 32 µg/cm^2 L = 1000 EU/mL T = 100 µg/cm^2 K = 100 µg/cm^2	most 24 h	Comparative analysis of effects of 7 PMs in a variety of cells, media and other culture conditions. Viability: most except Vanadium (50 %) were more than 75% of control (text only) Cytokine IL-6: BEAS-2B A or U in LHC-9 showed response to S and L. BEAS-2B (U) was in lHC-9 medium with added serum (FBS). This resulted in doubling of response coupled with at least an 8 fold increase in control levels. BEAS-2B (E) showed response for S and V but not L. A549 showed response to S and K. RAW 264.7 and Rat macrophages showed response to S(very low) and L. A 549 = RAW 264.7<<rat macrophages or BEAS Effect of culture media composition (BEAS-2B): varying ratios of LHC-9 and KGM media resulted in near 10 fold increase in control rate once LHC was 33% or more of media. Upon Soil Dust (NOS) exposure IL-6 increased linear with % LHC-9 in culture/exposure media. Addition of calf serum (0.1-10 %) raised control IL-6 at least 40 fold. At a steady PM concentration addition of serum resulted in a log-linear increase in IL-6 release, blocking any PM effect. Reversibility of media effect: Changing media with every passage showed that effect of media do not persist once media are changed. Culture Well Size: Going from a 6 well to 96 well plate (decreasing well size) increased IL-6 control values about ten fold, while the positive control (TNF) response increased 3 fold. Hence the sensitivity of the test (i.e., positive/control response) declined from 11 fold to 3 fold with increasing well number / decreasing well size. (authors note**:** effect of edge effects e.g., meniscus)

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Veranth et al. 2006	Human, BEAS-2B, bronchial epithelial cells 35,000 cells/ cm^2 in KGM media	$PM_{2.5}$ samples from 28 samples from 8 locations in Utah, New Mexico and Texas (rural, industrial, road side, military as well as 2 coal fly ash samples and TiO_2 and kaolin clay $PM_{2.5}$	10,20,40, 80 μg/cm^2 (NR)	24 h	**Components:** actual analyses not provided only used in correlation analysis Cell assays: viability, IL-6 and IL-8 were studied (actual results for viability and IL-8 only for 3 soils). In sample soils viability declined dose dependently while IL-6 increased dose-dependently. IL-8 was highly variable (peak at 20 μg/l, dose-dependent increase or flat response.) IL-6 assays for all soil PMs: Soils ranged across an order of magnitude >>LPS, coal fly ash or TiO_2 or kaolin samples. One soil even exceeded the pos V control at equal concentrations Correlation with cell viability: Strong (P<0.001) for Mn, weak (0.01<p<0.05) EC3, K, Se, Hg IL-6 -10 μg/cm^2**:** Medium (0.001<p<0.01) for OC-1(Organic Carbon) and P IL-6 80 μg/ cm^2**:** Strong for OC3, OP (pyrolized Carbon), OC, EC1, TC; Medium OC2, OC4, Zn; Weak Ca2+, EC2, Si, Ca, Ca: Al IL-8 10 μg/cm^2**:** Weak EU (Endotoxin), CO_3, Si, Br. IL-8 80 μg/cm^2**:** Medium CO_3, Sr; Weak K+, EC3, Mg, Si, IL-8 trend (corr over 10-80 range): Strong EC; Medium OC4, EC1, EC2, EC3, TC, Ni**;** Weak OP, OC, Cr, Sr IL-6 and Il-8 were not correlated nor were IL-6 and Cell viability Authors noted that weak correlations 0.01<p<0.05 contained false positives
Veranth et al. 2004	Human, BEAS-2B, bronchial epithelial cells 20,000/cm^2	$PM_{2.5}$ enriched soil samples DD = desert dust, unpaved road, Utah WM = West Mesa, sandy grazing site, NM R40 = Range 40 gravel soil, TX UN = Uinta, sandy soil, UT Soil samples $PM_{2.5}$ enriched in 0.4<PM<3 μm range (previously published)	10, 20, 40, 80, 160 μg/cm^2	24 h	Elemental Analysis of PM's: Major differences UN generally lower in major minerals but high Fe content and high EC. High Mn. Low Pb and Zn Cytotoxicity: DD 40, WM 10, R40 20, UN 10 μg/cm^2 ~ dose-dependent IL-6 Release: All at 10 μg/cm^2 up. DD (least cytotoxic) and R40 dose dependent; WM peaked at 40 and UN peaked at 10 μg/cm^2 IL- 8 release: DD dose dependent>WM >UN both peaked at 10 μg/cm^2, R40 not tested TNF-α**:** No response DD, Wm and Un at 80 μg.cm^2 LPS: No cytotoxicity and limited IL-6 and IL-8 response at 2000 EU/mL compared with DD at 80 μg/cm^2 Endotoxin: Inverse relation between endotoxin content and IL-6 release Viability vs Physical Modification of Dust Sample (no UN): Only leaching in a variety of water based vehicles increased viability minimally (generally <25 %). Heat treatment (150-, 300, 550F) and methanol extraction had no effect IL-6 release vs Physical Modification of Dust Sample (no UN): 150 F no effect all other treatments reduced IL-6 release (heat 350, 500 and extractions)

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Veronesi, B. de Haar, C. Lee, L. 2002	Human, BEAS-2B NR	Ambient PM - St. Louis = Urban particulates - Ottawa = Urban particulates -MSH = Volcanic dust from Washington state's Mt. St. Helen -Woodstove = Woodstove particles from conventional fireplace burner -CFA = Coal fly ash from western U.S. powerplant -OFA = Oil fly ash from Niagara, NY - A = Total Fractions - B = Soluble Fractions - C = Washed Fractions PM >2.5um 2 <PM >10um PM >10um	50 μg/mL; 30 μg/cm^2 100μg/mL; 60μg/cm^2	4, 16h	Ca: Calcium increased significantly with all particles types: OFA (-A, -B, -C) >>St. Louis >>Ottawa >/ = Woodstove >/ = CFA = MSH (-A >C >B) >control at 60 and 100 μg/mL. IL-6: At 50 and 100 μg/mL, IL-6 increased with all particle types at 4 and 16h. OFA >>>St. Louis >>Woodstove >Ottawa >CFA >MSH = media. Overall fraction -A most potent. Surface charge: Surface charge correlated strongly with increases in both Ca2+ and IL-6 levels. However OFA was unmeasurable due to technical difficulties.
Vogel et al. 2005	Human, U937 (ATCC) monocytes (macrophage differentiation) 2 X10^5 - 2 X10^6 cells/mL	UDP = SRM 1649 (NIST) UDP-OE = DCM extract of SRM-1649, 0.45 μm filter sUDP = stripped particles UDP DEP = SRM 2975 (NIST) DEP-OE = DCM extract of SRM-2975, 0.45 μm filter sDEP = stripped particles DEP CB95 = Carbon Black (Degussa) UDP = SRM 1649 DEP = SRM 2975 CB95 = 95 nm	DEP, UDP = 2.5, 10 or 40 μg/cm^2 (eq to 12.5, 40, 200 μg/mL) DEP-OE, UDP-OE = 10 μg/cm^2 (particle equivalent)	24 h	Effect on mRNA expression (COX-2, TNFα, IL-6, IL-8, C/EBPβ, CRP, CYP1a1): Dose dependent increase for all for DEP and UDP. IL-6 tended to plateau at 10 μg/cm^2. Generally UDP>DEP (COX-2 reverse). Cytotoxicity: Both DEP and UDP were cytotoxic at 40 μg/cm^2 Fractionation and mRNA expression: For COX-2, TNFα, IL-8 mRNA fractions were much more active than parent particles and consequently stripped particles were much less active than parent particles. CB95 had no effect. The reverse effect occurred for IL-6 and CRP mRNA expression: sUDP>UDP>UDP-OE same for DEP Inhibition of mRNA expression: CRP: pretreatment with IgG and wortmannin (Fcγ receptor binding and ingestion dependent inhibitors resp) blocked effects of DEP, UDP and sDEP and sUDP. Luteolin (AhR inhibitor) had no effect. COX-2: Only luteolin inhibited COX-2 expression for DEP, DEP-OE, UDP, and UDP-OE. CYP1a1: luteolin also inhibited OE-DEP and OE-DUP effects (only ones tested) Cholesterol accumulation: DEP, UDP and UDP-OE and DEP-OE at 10 μg/cm^2 all increased cholesterol accumulation by at least 2 fold
Wang et al. (2003)	Rat, Lung Myofibroblasts 1 X10^5 cells/100 mm dish 3.2 X10^4 cells/cm^2	V2O5 NR	400μM	0.5, 1, 4, 24 h	NO PM EFFECTS

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Wilson et al. (2007)	Mouse, J774, macrophage 4 X10^5 cells/mL	CB = Carbon Black, Printex 90 (Degussa) $FeCl_3$ ZnCl2 CB = 14 nm surface area 254 m^2/g	CB 1.9 -31 μg/mL $FeCl_3$, ZnCl2 0.01 - 100 μmol	4h	ROS production in cells: CB alone increased ROS. Coexposure with ZnCl2 did not affect ROS. ROS production - cell free: CB significant increase in ROS, ZnCl2 no effect and no effect of coexposure CB/Zn TNFα production (Fe -Zn 0.01-100 μmol): Coexposure of CB over a range of metals gave no change over CB alone for Fe. For Zn, only at 100 μmol was there a small interaction between Zn and CB. Similar results were seen at metal concentrations 20 -100 μmol similar showed synergism between Zn and CB and no effect of Fe. Macrophage cytoskeleton: CB resulted in black vacuoles. Cotreatment of cells with Zn and CB increased severity of Zn effects. Fe no synergism. Apoptosis /necrosis: No synergism of CB with Fe or Zn Phagocytosis: Only at 31 μmol CB and 50 μmol Zn did a synergistic effect occur with a 4 fold reduction
Wottrich, R. Diabate, S. Krug, HR. 2004	Human, A549 Human, THP-1, Monocytic Leukemia Cells Human, Mono Mac 6, Monocytic Leukemia Cells 2 X10^4 cells/well Co-culture: 2 X10^4 A549 and 2 X10^3 Macrophages	Fe = hematite α-Fe_2O_3 Si60 = silicasol (SiO_2, amorphous silica) Si100 = silicasol Q = crystalline quartz DQ12 Fe = 50 - 90nm Si60 = 60nm Si100 = 80 -110 nm Q <5 μm	A549 light microscopy hematite 100μg/mL (23 μg/cm^2) TEM hematite 50 μg/mL (16 μg/cm^2) Cytotoxicity 10, 50, 100 and 200 μg/mL (6.1, 30, 61 and 121 μg/cm^2) Cytokines 50 and 200 μg/mL	24 h	Particle Uptake: Hematite agglomeration observed in all 3 cell lines. TEM confirmed cytosol aggregates as well as single particles including particle transported intracellularly to basolateral membrane of epithelial cells. Cytotoxicity: LDH increased significantly in A549 with Q >Fe >S60 >S100 = control. THP-1 cells appeared most sensitive with Q >Fe >>S60 >S100 >control. Mono Mac 6 cells least sensitive with Fe >S60 >/ = Q>/ = S100. Cytokines: IL-6 and IL-8 released from A549 cells upon exposure to all particles. No response in Mono Mac 6 or THP-1. Co-cultures: Mix of A549 with either Mono Mac 6 or THP-1 led to massive (ten fold) increase in response to particles. IL-6 when using Mono Mac 6 or IL-6 and IL-8 when using THP-1.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Wu et al. 2002	Human, B82L- par parental fibroblasts B82L-wt, wild type EGFR B82L-K721M, kinase defective EGFR B82L-c'958, COOH-terminally truncated EGFR at Tyr-958 confluent (NOS)	$ZnSO_4$ NA	Zn = 500 µmol EGF = 100ng/mL	20 min	EGFR mutations: EGFR-wt = Tyrosine kinase domain,intact Src phosphorylation (Tyr 845) and 5 tyrosine autophosphorylation sites EGFR-c'958 = EGFR-wt -- less all 5 tyrosine autophosphorylation sites EGFR-K721M = EGFR-wt -- less tyrosine kinase (ATP binding) EGFR-Y845F = EGFR-wt less Src autophosphorylation (Tyr 845) instead has receptor at Tyr 845 that is phosphorylated by nonreceptor Tyrosine kinase Src. Zn Induced Ras (MAPK signaling protein): No effect in B82L-par cells. Zn had effect in -wt, -c'958, and -K721M confirming need for EGFR, indicating neither tyrosine kinase nor autophosphorylation sites were required for Zn effects. No increase for Y845F indicated that EGFR tyrosine 845 (phosphorylated by c-Src) is required for Zn effects. It was however not required for EGF effects. Src Kinase requirement: Using a Src blocker drastically reduced Zn effect but not EGF effect. Src activation occurred independent of existence of EGFR Tyr-845. Zn induced association of EGFR with Src: Zn induced a physical association in all 4 mutants; EGF did not Zn induced phosphorylation of EGFR at Tyr-845: Zn induced phosporylation of EGFR at Tyr-845 in B82L-wt,-c'958 and -K721M. EGF had same effects. Src blockers significantly reduced phosphorylation induced by Zn but not for EGF. Neither Zn or EGF induced phosphorylation in B82L-Y845F cells

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Wu, W. Wang, X. Zhang, W. 2003	Human, BEAS-2B NR	Zinc Ion: Zn2+ NR	10, 25, 50 µmol	0-8h	Cytotoxicity: Exposure to 50 µmol Zn2+ for 8h did not result in significant alterations in cell viability, indicated by no significant change in LDH. PTEN Protein Levels: 50 µmol Zn2+ for 4 and 8h significantly decreased dose-dependently. Exposure to 50µM vanadyl sulfate (tyrosine phosphatase inhibitor) had minimal effects on PTEN. 100 ng/mL of non-specified EGF receptor ligand for 1-8h did not indicate any significant effect on PTEN levels. P13K/Akt: Zinc induced Akt activation in dose- and time- dependent fashion. Active Akt levels highest 1h post exposure to Zn2+, corresponding with time period when there was minimal effect on PTEN protein level. When treated with LY294002 (inhibitor of P13K activity), Akt phosphorylation significantly inhibited. PTEN mRNA Levels: Decreased PTEN mRNA expression observed in cells exposed to 50 µmol Zn2+ for 8h whereas PTEN protein levels declined as early as 4h. Proteasome-mediated PTEN Degradation: Use of MG132 (proteasome inhibitor) had no significant effect on Zn2+ induced PTEN mRNA expression. Therefore mRNA expression may not play critical role in PTEN protein reduction. Instead data suggested that 26 S proteasome played vital role in Zn2+ induced PTEN degradation. PI3K inhibitor blocked Zn-induced PTEN degradation, but failed to prevent significant Zn-induced down-regulation of PTEN mRNA.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Wu, Weidong et al. 2004	Normal Human Bronchial Epithelial Cells (NHBE) Not Reported	Zinc Ion: Zn2+ NA	100 µmol concentration of Zn2+	2 h.	Cell Viability: 50, 100 and 200 µmol concentrations of Zn2+. After 2 h of exposure, Zn2+ induced effects in NHBE cells at 100 and 200 µmol levels (but not 50 µmol). Continuing exposure to 100 µmol Zn2+ for 4 h and also 6 did not significantly alter cell viability, thus in all subsequent studies, NHBE cells were treated with 100 µmol Zn2+. Induced EGFR Phosphorylation: exposure to 100µM Zn2+ for 1-4 h induced phosphorylation of EGFR in NHBE cells. EGFR kinase inhibitor PD153035 (to determine ifphosphorylation of EGFR was the result of autophosphorylation of activated EGFR tyrosine kinase activity) caused Zn2+ -induced phosphorylation to subside. Zn2+ activity requires tyrosine kinase activity. EGFR Phosphorylation Pathway: To test whether Zn exposure results in ligand release, which in turn can activate phosphorylation, NHBE cells were pretreated with LA1 blocking antibody. Results showed significant suppression of Zn2+ induced phosphorylation, therefore Zn2+ phosphorylation might be initiated by the release of EGFR ligands. To examine the involvement of specific ligands (HB-EGF. TGF-α and EGF) in the phosphorylation pathway, cells were exposed to anti-HB-EGF, anti-TGF-α and anti-EGF. Results showed: anti-HB-EGF reduced Zn2+ induced phosphorylation significantly, anti-TGF-α produced partial inhibition and anti-EGF had no inhibitory effect. Exposure with blocking antibody LA1 to determine if caused an increase in soluble HB-EGF. HB-EGF mRNA expression was also elevated in cells exposed to Zn2+. Prev. studies indicate metalloproteinase (MMP) involvement in cleaving ligand precursors. It was found that MMP-3 inhibitor partially blocks Zn2+ induced HB-EGF release. (MMP-2 and MMP-9 did not show similar inhibition patterns) Zn2+ exposure increased the release of MMP-3 from HNBE cells.

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Wu, Weidong et al. 2005	Human, bronchial, BEAS-2B (subclone S6 cell line) Not Reported	Zinc Ion: Zn2+ NA	50 µmol Zn2+	4 or 8 h EGFR phosphorylation: 30, 60, 120, 240 min.	Exposure to 50 µmol Zn2+ for 8 h did not result in significant alterations in cell viability (assessed by LDH release). P13K/Akt signaling pathway: To evaluate P13K's on COX-2 Zn2±induced expression, LY-294002 (a P13 inhibitor) and another unnamed P13 inhibitor were used. Exposed cells indicated suppressed levels of Zn2+ induced COX-2. To determine Akt role, ad-DN-Akt(AAA) was used. Infected cells indicated over-expression of Akt and significant reduction of Zn2+ induced GSK-3α/β phosphorylation. Over expression of DN-Akt(AAA) blocked Zn2+ induced COX-2 expression. PTEN's role in blocking Zn2±induced COX-2 mRNA expression: PTEN is an antagonist of P13/Akt pathway. Overexpression of wildtype PTEN blocked Zn2+ induced mRNA COX-2 expression, suggesting PTEN inhibits PIP3 signal transduction to Akt. Analysis of the Src/EGFR signaling pathway: Zn2+ induced a time-dependent increase in Src and EGFR phosphorylation in cells. Blockage of Src activity via PP2 (Src inhibitor) decreased Zn2+ induced EGFR phosphorylation. The EGFR tyrosine inhibitor completely blocked Zn2+ induced EGFR phosphorylation. EGF (a ligand of EGFR signaling) induced COX-2 expression, suggesting that EGFR regulated Zn2+ -induced COX-2 expression. p-38 and EGFR kinase activity: Use of PD-153035 (EGFR inhibitor) and PP2 (Src inhibitor) and SB-203580 (p38 inhibitor) all blocked Zn2+ induced Akt phosphorylation of Src., EGFR and p38. It is thought that p38 is a critical kinase in regulation of Zn2±induced COX-2 protein expression.
Yacobi et al. (2007)	Rat, L2, lung epithelial cells (plasmids TAK1, TAK1K63W and TAB1) 1.2x10E6 cells/cm^2 all exposures on apical surface i.e., exposed to lumen	PNP = Polystyrene nanoparticles, negatively charged (Molecular Probes, Eugene, OR) PNPA = Amidine modified PNP, positively charged SWCNT = Single-wall carbon nanotubes (Carbon Nanotech, Houston, TX) QDC = Chitosan coated (CdSe/ZnS) Quantum dots, positively charged (made) QDA = Alginate coated QD, negatively charged UAPS = Ultrafine Ambient particulate suspensions (VACES) (48 % organic carbon) PNP20 = 20 nm PNP100 = 100 µm SWCNT 0.8 <d <1.2 nm SWCNT 100<L <1000 nm QD = 30 nm UAPS <150 nm	PNP up to 706 µg/mL QD up to 176 µg/mL SWCNT up to 88 µg/ mL UAPS up to 36 µg/mL	on days 4,5 or 6 by replacing monolayer apical fluid with PM in suspension for up to 1440 min intermediate measurements at 15, 30, 60, 120, 240 and 1440 min	UAPS and Rt (transmonolayer resistance): Rt declined up to 60 % within 1-h at 36 µg/mL. Rt plateaued/ very slight upgradient for up to 24-h (last measurement). No cytotoxicity. Replacement of apical fluid with fresh media after 2-h of exposure restored Rt to near control values within 24 h. UAPS and Ieq (short-circuit current): Peak decline of 30 % after 4 h followed by gradual recovery over 24 h. replacing media after 2-h exposure returned Ieq to control values within 24 h. UAPS and apparent permeability: permeability measured via C14 mannitol and inulin showed no effect of UAPS QD and Rt: QD depressed Rt by nearly 55 % at 4h for positively charged and 30 % for negatively charged QDs. Recovery towards control values started at 4 h and was near complete at 24 h SWCNT and Rt: SWCNT depressed Rt by ~ 40 % at 1h (same for 22,44 and 88 µg/mL) recovery was near complete at 4 h and complete at 24 h PNP and Rt: No stat significant effects

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles
Yun et al. (2005)	Human type II alveolar-like epithelial cell line A549 3x10E4 cells/well (pre-transfection)	DEP (6 cyl 11L, heavy duty (2001 yr) bus engine (S. Korea) NR	1, 10, 100, 250, 500 and 1000 μg/mL from a 1000 mg/mL stock main testing 250 μg/mL	12 h	NF-κB transcription activation: DEP induced dose dependently with peak at 250 μg/mL with decline to below control at 1000 μg/mL (cytotoxicity NR). Activity peaked at 12-h for 250 μg/mL and declined to control at 24 or 48 h. The mechanism of DEP action was the degradation of IκBα which is an intracellular inhibitor of nuclear translocation of NF-κB. TAK1 and NIK required for NF-κB activation by DEP: dominant negative mutants of TAK1 and NIK reduced DEP induced response to basal level. TAK1 was phosphorylated after DEP exposure and was sustained for at least 90 min.
Zhang et al. (2007)	Human, A549 Rat, RLE-6TN, Alveolar Type II Epithelial Cells NR	$PM_{2.5}$ Collected by baghouse from Dusseldorf, Germany NR	100 μg/cm^2	24 h	Particle Characterization: Carbon 20%, Hydrogen 1.4%, Nitrogen <0.5%, Oxygen 14.1%, Sulfur 2.1%, Ash 63.2%. Apoptosis: At 100 μg/mL for 24 h, Pm induced 2.5 fold increase in apoptosis in A549. Mitochondrial Membrane Potential: Significant reduction in AEC mitochondrial membrane potential. Caspase -3 & -9: Increased activity of both enzymes in both cell types. 2-2.5 fold increase in A549. 8 fold increase of caspase-9 and 4 fold increase of caspase-3 in RLE-6TN. BIM: Downregulation of BIM by RNA interference inhibited PM-induced apoptosis. Inhibited decrease in mitochondrial membrane potential and activation of both caspases.
Zhang et al. (2004)	NR	DEP = SRM 1650a	5 or 25 μg/mL	30-360 min	fra expression: DEP induces fra-1 but not fra-2 expression mRNA induction peaks around 180 min DEP affects fra-1 mRNA expression at the transcriptional level ERK/JNK/p38 MAPK signaling pathways: 3 inhibitors (PD-98059, SB-202190 or SP-600125) all reduced DEP stimulated fra-1 induction to near control levels. DEP stimulates phosphorylation of the MAPKs which peaks at 60 min but stays elevated at 180 min MMP-9 promoter activity: fra-1 upregulation may play a role in DEP induced increase in MMP-9 promoter activity as fra-1 appears to bind at the -79 TRE sequence of the MMP-9 promoter. Study 6203 cell lines: BEAS-2B (A) HR. Bronch. Epith ATCC # CRL-9609 passage 44 BEAS-2B (E) HR. bronch. Epith. U.S. EPA passage 76-87 BEAS-2C (U) HR. bronch. Epith U. Utah sample passage 89-97 A 549 HR. alveolar epith U. Utah sample starts at passage 84 RAW 264.7 M. macrophage ATCC # TIB-71 1 macrophages Rat lung lavage primary cells Study 6203 culture media LHC-9 Lechner and Laveck medium Invitrogen KGM Keratinocyte growth medium Lonza DMEM/F12 50 % Dulbecco's modification of Eagle's medium, 50% Ham's F12 medium Gibco FBS Fetal bovine serum (added to media formulations) Invitrogen

Reference	Species, Cell Type, Etc. Cell count	Particle or Constituent Particle Size Distribution	Concentration	Exposure Duration	Effect of Particles

Table D-3. Respiratory effects: in vivo studies.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Adamson et al. (2003) Rats, Male, Sprague-Dawley, 150g	105, 90, 15	PM_{10}: EHC-93W (whole dust) EHC-93S (soluble) EHC-93L (leached) EHC-2KW, -S, -L	Intratracheal Instillation	5 mg/rat; 33.3 mg/kg	NR Measured components Zn, Mg, Pb, Fe, Cu, Al	single; 4h, 1d, 3d, 7d, 14d	BALF Cells: Greatest increase in cell number seen with EHC-93W. Activity peaked at 1d with return to normal by 7d. EHC-93L also induced cell increase, more so than EHC-93S but all induced statistically significant inflammation. Day 1: EHC-93W - 29% AMs, 71% PMNs EHC-93L - 20% AMs, 80% PMNs EHC-93S - 64% AMs, 36% PMNs BALF Inflammatory/Injury Markers: Metallo-proteinase (MMP) 2 and 9 both increased, peaking at 1d and 4h respectively. MMP2 activity appears related to soluble fraction whereas MMP-9 activity appears related to leachable fraction.
Ahn, E.K. Yoon HR.K. Jee, B.K. 2008 Mice, Male, BALB/C1, 6wks, 19-24g	24, 15, 9	DEP DPBS = control	Oropharyngeal Aspiration	1, 10, 25 mg/kg per day Those receiving 25 mg/kg DEP also received pre-treatment of Dex (1, 5 mg/kg) 1-h prior	NR	5 consecutive days; 72h post final exposure	BALF Inflammatory/Injury Markers: Lung injury more severe in mice exposed to 25 mg/kg of DEP when compared to mice exposed to 1 mg/kg DEP. However, lung injury caused by exposure to 25 mg/kg DEP could be completely prevented with pre-treatment of 5mg/kg Dex. Treatment with 1 mg/kg Dex prior to exposure to 25 mg/kg DEP depicted partial reduction in lung injury. BALF Cells: Treatment with DEP over 5d period caused increase in total number of cells (macrophages, neutrophils and lymphocytes) when compared to control. Total Cells: Control - 5.33 ± 0.44 cells 1mg/kg DEP - 6.26±0.87 cells 10mg/kg DEP - 14.40± 1.90 cells 25 mg/kg DEP - 47.20 ±3.40 cells COX-2 Expression: Exposure to DEP lead to a dose-dependent increase in COX-2 levels, specifically treatment with 25 mg/kg significantly increased COX-2 levels. Effect completely reduced by treatment with 5mg/kg of Dex.
Ahsan, M.K. Nakamura, HR Tanito, M. 2005 Mice, Males and Females, hTrx-1-transgenic and C57BL/6 (control), 8-8.5wks	NR	DEP	Intratrachael Instillation	0.1 mg/mouse Lung Damage 0.2 mg/mouse Survival Analysis, 0.05 mg/mouse ESR bw NR	NR	single; 24 h	ESR: hTrx-1 induced 0.05 mg generation of hydroxyl radicals in lungs (mid thorax ESR spectra) compared to control. BALF Inflammatory/Injury Markers: hTrx-1 attenuated cellular damage from 0.1mg DEP. Control mice showed massive edema with neutrophilic infiltration, hemorrhagic alveolar damage and collapsed air spaces. hTrx-1 mice showed mild/moderate edema with clear demarcation of air spaces. Viability: After 4, 12 and 24 h, survival was 32, 24 and 12% respectively as compared to 80, 52 and 40% for hTrx-1 mice.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Andre, E. Stoeger, T. Takenaka, S. 2006 Mice, Female, BALB/cJ, 10-12wks	96, 48, 48	UFCP = Ultra Fine Carbon Particles (electric spark generator, Model GFG 1000; Palas, Karlsruhe, Germany) Measured Component: UFCP>96% elemental carbon	Whole-body Inhalation	380 μg/m^3 bw NR	49nm	4 and 24 h; 0 and 24 h post-exposure	BALF Cells: Small increase in PMN number suggesting minor inflammatory response after 24 h exposure. Number of macrophages did not increase. BALF Inflammatory/Injury Markers: Total protein concentration significantly increased post 24 h inhalation. Post 4h, heat shock proteins were induced. Post 24 h, immunomodulatory proteins (osteopontin, galectin-3 and lipocalin-2) significantly increased in alveolar macrophages and septal cells. 236 (1.9%) genes was increased and 307 (2.5%) genes were decreased with upregulated genes being primarily related to inflammatory process.
Antonini et al. (2004) Rats, Male, Sprague-Dawley, ~250g	NR	ROFA-P = Precipitator ROFA -S = Soluble (0.22 μm filter) - Fe, Al, Ni, Ca, Mg, Zn -I = Insoluble - Fe, Al, Ni, Ca, Mg, Zn, V ROFA-AH = Air Heater ROFA -S = Soluble (0.22 μm filter) - Fe, V, Ni, AL -I = Insoluble - Fe, V, Ni, AL ROFA-P-T = (ROFA-P) Total (Boston Edison, Mystic #4, Everett, MA) Silica = control	Intratracheal Instillation	1 mg/100g bw; 60 mg/kg	diameter <3 μm ROFA-P-S = 0.60 ROFA-P-I ROFA-AH-S = 0.20 ROFA-AH-I	single; 24 h Clearance Experiment: two single exposures day 0 and 3 observed at day 6, 8 and 10	ESR: Only ROFA-P contained free radicals, primarily in ROFA-P-S. BALF Cells: No effects on alveolar macrophages, but all ROFA-P fractions increased lung neutrophils. ROFA-P-S and ROFA-P-I effects combined more or less equaled ROFA-P-T. BALF Inflammatory/Injury Markers: ROFA-AH-T and ROFA-AH-I increased LDH. ROFA-P and AH increase albumin for T and I fractions. Pulmonary Clearance (Listeria Monocytogenes): ROFA-P-T and ROFA-P-S significantly slowed bacteria clearance from lungs. ROFA-AH and ROFA-P-I had no effect.
Arimoto, T. Takano, HR. Inoue, K. 2007 Mice, Male, IRC, 6wks, 29-33g	NR	DEP (4JB1 4-cyl, 2.74L Isuzu diesel engine) DEP-OC = organic chemical extracts LPS DL = DEP + LPS DOL = DEP-OC + LPS	Intratracheal Instillation	4mg/kg DEP or DEP-OC 2.5 mg/kg LPS NR DL or DOL	0.4um	single; 24 h	Cytokines: DEP-OC or DEP alone did not change levels of MIP-1α, MCP-1 or MIP-2. DL induced significant increases in MIP-1, MIP-2 and MCP-1. LPS: LPS and DOL induced increase in MCP-1 though not as much as DL. No effect on MIP-1α or MIP-2.
Bachoual, R. Boczkowski, J. Goven, D. 2007 Mice, Male, C5B17, 7 wks, 22.3 ± 0.73g	NR	RER = PM_{10} Paris, France subway CB TiO_2 DEP	Intratracheal Instillation	5, 50, 100 μg/mouse, 0.22, 2.2, 4.5 mg/kg	RER = 79% <0.5 μm 0.5<20% >1 μm CB = 95nm TiO_2 = 150um DEP = SRM1650	Single; 8 or 24 h	BALF Cells: 100ug RER and 100ug DEP increased total cell count and neutrophil influx after 8h. Normalized by 24 h. Smaller doses of RER and DEP induced no effect. CB induced no effect. BALF Inflammatory/Injury Markers: 100ug RER increased BALF protein after 8h. No effect after 24 h nor with smaller doses of PM. RER increased MMP-12 mRNA level significantly after 8h and HO-1 total lung mRNA content. No effect on MMP-2 or -9 or TIMP-1 or -2 expression. No effects from CB or DEP were observed. Cytokines: 100ug RER increased BAL TNF-α and MIP-2 protein content after 8h.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Becher, R. Bucht, A. Ovrevik, J. 2007 Mice, Male, Crl/Wky (iNOS(-/-)) and C57Bl/6, 8-14wks, 25g	NR	Suspended PM = SRM-1648	Intratracheal Instillation	1.6 μg/lung; 64 mg/kg	NR	Single; 20h	Cytokines: In both wild and KO strains, all particles caused increases of IL-6, MIP-2 and TNF-α levels. NADPH-oxidase KO mice showed significantly lower levels of IL-6 and MIP-2 responses to SPM comparatively to wildtype. iNOS KO mice showed significantly reduced IL-6, TNF-α, MIP-2 responses to SPM comparatively to wildtype. Free Radicals: SPM induced significant increase in free radical formation in alveolar type 2 cells but could be inhibited by DPI.
Bhattacharyy Bhattacharyya a et al. (2004) Rats, NR, Sprague-Dawley, 200-250g	12, 8-9, 3-4	Douglas Fir Wood Smoke	Nose-only Inhalation	25g/mouse bw NR	NR	0, 5, 1 0, 15, 20 min; 24 h post-exposure	Biochemical Parameters: Lipid peroxidation increased after 20 min of woodsmoke inhalation as did Myeloperoxidase at 20 min. No effects were observed at other times or for total antioxidant status, reduced or oxidized glutathione. Antioxidant Enzyme Activities: No effect Histology: Dose-dependent damage progressing from loss of cilia (5 min), degeneration of mucosal epithelium, loss of mucosal epithelium to disrupted mucosal epithelium with submucosal edema and inflammation. Changes persisted for up to 4 days.
Cao, Q. Zhang, S. Dong, C. 2007 Rats, NR, SH and WKY, 12wks	NR	$PM_{2.5}$ (Thermo Anderson G-2.5 sampler, Shanghai, China) Component: As, Cd, Cr, Cu, Fe, Ni, Pb, Zn, V, Ba, Se, Mg, Co, Mn	Intratracheal Instillation	1.6, 8.0 and 40 mg/kg	NR	1/d x 3 d; 24 h	BALF Inflammatory/Injury Markers: LDH activity and TBARs increased in dose-dependent manner. Notably SH>WKY at same dose exposed for each dose level. BALF Cells: PM decreased macrophages, increased neutrophils and lymphocytes, all dose-dependent, all doses and control SH>WKY. Cytokines: PM induced pro-inflammatory cytokine release (IL-1β, TNF-α, CD44, MIP-2, TLR-4, OPN). Again, SH cytokine level >WKY at all dose levels. PM induced anti-inflammatory cytokines CC16 and HO-1 in similar manner but at much lower rate.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Carter, J.M. Corson, N. Driscoll, K.E. 2006 Rats, Female, F-344, 7-10wks Mice, Female, B6C3F1, 7-10wks Hamsters, Female, Syrian Golden (F1B), 7-10wks	NR	CB = Printex 90	Whole-body Inhalation	1, 7, 50 mg/m^3 bw NR	17nm SA = 300 m^2/g	6h/day for 5d/wk for 13 wks; 1d, 3mo, 11mo post-exposure	Superoxide: Levels rose in all species at 50mg dose. Hamsters had no increase at 7mg and 1mg doses. Mice also increased at 7mg. Rats significantly increased at all dose levels. Rats maintained elevation except 50mg dose 11mo postexposure declined - still higher than control. Mice maintained elevation at 50mg dose while 7 mg dose returned to control level by 3mo postexposure. H_2O_2: At 50mg dose, increased levels in all species - rat highest. At 7mg dose, increased levels in rats and mice initially, returned to baseline by 11mo. Hamster level not significant. At 1mg dose, no significant changes. NO: Induced similar reaction as H_2O_2. Rat response continued through study while mice and hamsters returned to baseline by 11mo postexposure. Rats produced significantly higher levels at all times than other species. BALF Cells: CB induced significant increase in neutrophils at 7 and 50mg level for all three species. Rats had highest and most prolonged PMN response. Mice and hamsters had very similar reactions. Cytokines: TNF-α, MIP-2 and IL-10 increased in dose-dependent manner in rats and mice. Hamsters increased for IL-10 only. MIP-2 levels highest in rats. TNF-α level similarly in all three species at 50mg dose, but hamsters started with markedly higher basal level. Glutathione Peroxidase: Hamsters most responsive with significant increases at all levels. Rats and mice increased at 50mg level and continued to increase for up to 11mo. Hamster level declined with time though continued to be higher than control. Glutathione Reductase: Rats increased only at 50mg level and remained elevated for up to 11mo. Mice increased at 7 and 50mg levels and remained elevated for up to 11mo. Hamsters increased at all levels at 11mo, only increased post 1d and 3mo at 50mg level. Superoxide Dismutase: All species dose-dependently reacted. Rats least responsive. Rat SOD activity increased over time while rat and mouse activity decreased at 50mg dose. Data consistent with cytokine data. Summary: Rats appear to produce proinflammatory response while mice and hamsters produce antiinflammatory response.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Cassee, F.R. Boere, A.J.F., Fokkens, P.HR.B. 2005 Rats, Male, SPF HsdCpb: WU Wistar and SH/NHsd, 7 wks and 8-12wks	Wistar: 208, 104, 104 SH: 204, 102, 102	CAPs = $PM_{2.5}$ Netherland suburban, industrial and freeway tunnel site collections Wistar rats pre-exposed to ozone	Nose-only Inhalation	PM 365-3720 μg/m³ (results from 16 different exposures 2000, 2002) bw NR O_3 = 1600 μg/m³ (0.8 ppm) bw NR	$PM_{2.5}$ (0.15<PM<2.5 μm) SO_4, NO_3 and NH_4 ions: 54±4% suburban, 53±7% industrial and 35±5% freeway site conc of total CAPS mass	8h O_3 pre-exposure; 6h CAPS exposure; 48h post-exposure	BALF Cells: BALF collected by cannulation, fluid from right lung. Wistar had increased protein, albumin and NAG. Decreased ALP activity and macrophage numbers. Wistar had increased PMNs due to ozone, did not significantly increase with additional CAPs exposure. SH showed no effect of CAPS except increased PMNs. BALF Inflammatory/Injury Markers: No effect on AL, LDH, Glutathione, GSSG, GSH, Uric Acid. Cytokines: No effect on IL-6, MIP-2 or TNF-α. CAPs induced increase in CC16 plasma of SH rats. Hematology: CAPS induced increase in RBC, HGB and HCT of Wistar rats and fibrinogen of SH rats. Histology: Wistar and SH rats had no obvious lung abnormalities. Small changes include increased macrophages and cellularity of centriacinar septa of ozone-only rats. Both ozone-only and ozone+CAPS showed bronchial epithelium hypertrophy and perivascular influx of PMNs. BrdU Labeling Index of Terminal Bronchiolar Epithelium: No CAPs effects observed.
Chang, C.C. Chiu, HR.F. Wu, Y.S. 2005 Mice, Male, ICR, 5wks, 25-30g	24, NR	UFCB = Ultrafine CarbonBlack - Printex 90 (Degussa)	Intratracheal Instillation	200μg/100ul/mouse bw NR	14nm 253.9 m^2/g = SA	single at 4, 16, 21, 42h NR	BALF Cells: Neutrophil number was at control level at 4h, increased after 16h, peaked at 21h and returned to normal at 42h. No effect on macrophage count. BALF Inflammatory/Injury Markers: UfCB increased total protein with peak at 21h. Cytokines: TNF-α increased at 4h and returned to normal at 16h. VEGF (Vascular Endothelial Growth Factor): Increased at 4h and peaked at 16h but remained elevated at 21 and 42h. VEGF and total protein in BALF were correlated (R^2 = 0.7352). ROS: Pretreatment with NAC (ROS inhibitor) decreased induction of BALF VEGF and total protein by UfCB but did not fully block effect. Histology: Thickened alveolar walls in lungs of UfCB-treated mice 16h post-IT.
Chang, C.C. Chen, S.HR. Ho, S.HR. 2007 Mice, Male, ICR, 5wks, 25-30g	NR	UFCB = Ultrafine Carbon Black - Printex 90 (Degussa)	Intratracheal Instillation	200 μg/mouse; 8 mg/kg Pretreatment with NAC (N-acetylcysteine) ip 320 mg/kg, 2-h before UFCB IT	14 nm diameter 254 m^2/g = SA	single; 24 h	BALF Cells: Increased relative lung weight, total protein (2 fold), total cells (11 fold) and number of neutrophils. BALF AM count not affected. BALF Inflammatory/Injury Markers: 33 identified proteins, 6 confirmed and validated: Cp (ceruluplasmin), albumin, EGFR, LIFR (leukemia inhibitory factor receptor), α2M and β-actin. All increased following UFCB exposure. Also identified: 3 membrane proteins, 3 intracellular proteins, 10 protease inhibitors and 6 antioxidants. UfCB increased LIFR and EGFR in BALF. UfCB significantly reduced EGFR and LIFR in lung homegenate. UfCB did not affect EGFR protein but down-regulated LIFR in A549 cells treated with UfCB. Antioxidant: Pretreatment with NAC reduced the intensity of albumin and α2M bands in BALF as well as most other proteins. Statistical analysis showed positive correlation between VEGF and albumin (R^2 = 0.796) and VEGF and α2M (R^2 = 0.7331) in BALF.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Cho et al. (2005) Mice, Male, Seven Strains: DBA/2J, 129P3/J, C57BL/6J BALB/cJ, A/J, HeJ, OuJ, 6-8wks	NR	ROFA (Power unit 4, Boston, MA) Absent of LPS 4x10-7ng endotoxin/µg ROFA	Intratracheal Instillation	6mg/kg	NR	single; 24 h Additional HeJ and OuJ mice: single: 1.5, 3 and 6h (compare TLR-mediated molecular events)	BALF Cells: Significant genetic effects on number of macrophages and PMNs after ROFA challenge. For PMNs, DBA/2J, 129P3/J, BALB/cJ and C57BL/6J>>C3H/HeJ. For macrophages, A/J>>C57BL/6J. Total protein, PMNs and macrophages all increased with HeOuJ>>HeJ. BALF Inflammatory/Injury Markers: Significant genetic effect on mean total protein concentration. DBA/2J, 129P3/J and C57BL/6J>>C3H/He TLR4 mRNA Expression: Significant decrease in TLR4 transcript level in HeJ- ROFA exposed mice post 1.5h. Post 6h, TLR4 levels greater than the control levels. OuJ expression increased starting 1.5h postexposure. TLR4 Protein Level: Protein level of OuJ mice significantly exceeded (~2-3 fold) HeJ mice at 1.5, 3 and 6h. Activation of Downstream Signal Molecules: Greater activation of MYD88, TRAF6, IRAK-1, NF-KB, MAPK, and AP-1 observed in OuJ mice than HeJ mice before development of ROFA-induced pulmonary injury. Cytokines: IL-1β, LT-β, IL-1α, IL-7, IL-13, IL-16 increased in both strains. Levels of all fore mentioned significantly higher in OuJ compared to HeJ.
Costa, D. Lehmann, J.R. Winsett, D. 2006 Rats, Male, Sprague-Dawley, 60d	80, 40, 40	ROFA FP&L plant #6 oil, 1% sulfur	Intratracheal Instillation (IT) vs Nose-only Inhalation (IH)	IT = 110 µg/rat IH = 12 mg/m^3 bw NR	~1.95 µm	IT = single IH = 6h 24, 48, 96 h (histopath 24 and 48 only)	ROFA distribution: IH and IT resulted in equivocal distribution (µg/g lung tissue) in 5 different lung lobes. Airway Hyperactivity: IT resulted in doubled airway hyperreactivity at 24 h, sustained for 96h. IH hyperreactivity did not reach statistically significance level. BALF Inflammatory/Injury Markers: IH and IT showed very similar responses (R^2 = 0.98). Increases (progressing with time) for protein and LDH. BALF Cells: Neutrophils peaked at 24-h and slowly declined at 48 and 96h. Lung Pathology: IT showed more alveolitis, bronchial inflammatory and fibrinous fluid infiltrate. IH showed relatively more congestion of small airways and alveolar hemorrhage.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Dick, C. Singh, P. Daniels, M. 2003 Mice, Female, CD1, 8-10wks, 20-25g	NR	CO = PM Coarse FI = PM Fine FU = PM ultrafine PM collected in RTP, NC See details under Pulmonary Effects DMTU = dimethyl-thiourea Saline = control	Intratracheal Instillation = PM Intraperitoneal injection = DMTU	10ug, 50ug, 100μg/mouse; 0.5, 2.5, 5.0 mg/kg DMTU 500 mg/kg bw i 30 min pre-exposure for some mice	3.5 <CO <20 μm 1.7<FI <3.5 μm FU <1.7 μm	single, 18h	Particle Characteristics: S increased (CO-33.20μg/mg, FI- 49.44μg/mg FU-122.79μg/mg) with decreasing particle size (mostly in the water-soluble fraction). Fe and Cu higher in coarse and fine fractions (mostly present in the insoluble). CO PM contained more nickel (in both soluble and insoluble) than FI or FU particles. Also, endotoxin levels similar in CO and FI; much lower in FU (0.165 EU/mg). BALF Cells: PMN increased with exposure for all 3 fractions except 100 μg FI. FU>>FI> = CO>>Control BALF Inflammatory/Injury Markers: Albumin increased only at 100ug FI. No differences in NAG or LDH observed. Cytokines: IL-6 increased at 100ug dose for all 3 fractions with similar responses. TNF-α increased a 100ug dose of fine PM vs control. Effect of PM After Pre-treatment w/ DMTU: Systemic administration of DMTU alone depicted twofold increase in total antioxidant capacity. DMTU halved neutrophil response observed with PMs alone: no fractions were increased over DMTU alone which was at least two-fold saline control. IL-6 concentrations drastically reduced in the DMTU group for the mice exposed to coarse particles (all fractions reduced but only coarse had significant response). TNF-α levels were decreased after treatment with particles and DMTU but treatment with particles and saline (control) produced similar results.
Dyhdahl, M. Rísom, L. Bornholdt, J. 2004 Mice, Female, BALB/CJ or trans-genic (MutaMouse), 9-10 wks, ~20 g	NR	DEP = SRM 1650 (NIST) Control: Filtered Clean Air	Nose-only Inhalation	I: 20 & 80 mg/m^3 II: 5 & 20 mg/m^3 bw NR	DEP: NR Control: PM 0.13 μm diameter	I: single 90 min II: 90 min x 4 days I & II: 1, 3, or 22h post exposure	Cytokines: Single 90-min DEP exposure increased IL-6 gene level dose-dependently in the lung. For 80 mg/m^3 DEP, significantly higher IL-6 gene level, both 1 and 22h post exposure. For 20 mg/m^3 DEP, significantly higher IL-6 level at 1-h post exposure but normalized at 3h. BALF Cells: Inhalation of DEP did not decrease viability of BAL cells (see Table1). One h post exposure in BAL fluid there was 3 fold increase in total cell number in mice exposed to 20 mg/m^3 DEP. DNA Damage: Level of 8-oxodG increased post single exposure, 80 mg/m^3 exposure significantly higher than controls. Repeated exposures associated with significantly higher DNA strand breaks.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
[FROM Table D-4] **Reference:** Elder et al. 2004 **Species:** Rat **Gender:** Male **Strain:** Fischer 344 and SH **Age:** 23 months, Fischer 344; 11-14 months, SH **Weight:** NR		UFP - Ultrafine carbon particles (TSI, Inc., St. Paul, MN) LPS (Sigma Chemical, Co., St. Louis, MO; L-9143) median size 36nm	intraperitoneally (ip) for saline and LPS whole body exposure for inhaled particles Particles: 150 mg/m^3 LPS: 2mg/kg body weight			6 hours exposure to particles 24 h after exposure to ip LPS to analysis	BAL fluid cells: Neither inhaled UFP nor ip LPS cause a significant increase in BAL fluid total cells or the percentage of neutorphils in either rat strain. No significant exposure-related alteration in total protein concentration or the activites of LDH and b-glucuronidase. Peripheral blood: In both rat strains ip LPS induced significant increase in the # and % of circulating PMNs.When combined with inhaled UFP, PMNs decreased, significantly for F-344 rats. Plasma fibrinogen increased with ip LPS in both rat strains, magnitude of change greater in SH rats. UFP alone decreased plasma fibrinogen in SH rats. Combine UFP and LPS response was blunted, but significantly higher than controls. Hematocrit was not altered in either rat strain by any treatment. TAT complexes: With all exposure groups averaged, plasma TAT complexes in SH rats were 6.5 times higher than in F-344 rats. LPS caused an overall increase in TAT complexes for F-344 rats further augmented by inhaled UFP. UFP alone decreased response. In SH rats UFP alone significant increased respones and LPS decreased response. ROS in BAL cells: In F-344 rats both UFP and LPS has independent and significant effects on DCFD oxidation. Effects were in opposite direction- particles decreased ROS, LPS increased ROS.
Elder, A.C.P Gelein, R. Azadniv, M. 2004 Rats, Male, Fischer 344, 23mo Rats, Male, SH, 11-14mo	20 Fischer and 20 SH, 30, 10	UFP = argon-filled chamber with electric arc discharge (TSI, Inc., St. Paul, MN) LPS (Sigma Chemical, Co., St. Louis, MO; L-9143)	Whole-body Inhalation Intraperitoneal (ip) for saline and LPS	150 μg/m^3 = UFP bw NR 2 mg/kg = LPS	36nm NR	single for 6h, 18h	BALF Cells: Neither inhaled UFP nor LPS cause significant increase in BAL fluid total cells or percentage of neutrophils in either rat strain. No significant exposure-related alteration in total protein concentration. In both rat strains LPS induced significant increase in amount of circulating PMNs. When combined with inhaled UFP, PMNs decreased, significantly for F-344 rats. BALF Inflammatory/Injury Markers: Plasma fibrinogen increased with LPS in both rat strains, magnitude of change greater in SH rats. UFP alone decreased plasma fibrinogen in SH rats. Combined UFP and LPS response blunted, but significantly higher than controls. Hematocrit was not altered in either rat strain by any treatment. No change in activites of LDH and b-glucuronidase. TAT complexes: With all exposure groups averaged, plasma TAT complexes in SH rats were 6.5 times higher than in F-344 rats. LPS caused overall increase in TAT complexes for F-344 rats further augmented by inhaled UFP. UFP alone decreased response. In SH rats, UFP alone significant increased response and LPS decreased response. ROS in BALF: In F-344 rats, both UFP and LPS has independent and significant effects on DCFD oxidation. Effects were in opposite direction - particles decreased ROS, LPS increased ROS.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Elder, A. Gelein, R. Finkelstein, J. 2004 Rats, Male, F344, 21mo National Institutes of Aging colony	NR	Freshly generated vehicle exhaust emissions from I-90 between Rochester and Buffalo, NY Pre-treatment of endotoxin, human influenza virus	Whole-body inhalation	Vehicle exhaust: 0.95-3.13 x 105 particles/cm^3 bw NR Endotoxin = 84 EU Influenza: 10, 000 EID 50 in 250ul	NR	1 x 6h, 3 x 6h, or both. 18 h postexposure 48 pre-exposure of influenza Immediate pre-exposure of endotoxin EXPERIMENTS 1: LPS + PM 6 h 2: LPS + PM 6h, 3 x 6h 3: IV + PM 6 h 4: IV + PM 6h, 3x 6 h	No departures from normal baseline cellular or biochemical values were observed, suggesting that on-road exposures were well tolerated by the rats. BALF Inflammatory/Injury Markers: Increase in total protein concentration, LDH and B-glucuronidase activities. Specific results according to groups 1-4 are as follows: Experiment 1: No endpoints revealed significant differences between groups of rats exposed to gas phase only versus the gas-phase/particle mixture. Experiment 2: Combination of endotoxin and particles produced greater inflammatory response than those treated with saline and particles post 1d. After 3 days, no statistically significant changes noted. Experiment 3: Influenza virus significantly increased ROS release in BAL cells. Experiment 4: Influenza virus significantly increased both percentage of PMNs in lavage fluid and BAL cell ROS release.
Elder, A. Gelein, R. Finkelstein, J.N. 2005 Rats, Female, F-344, 7wks Mice, Female, B6C3F1, 7wks Syrian Golden Hamsters, Female, FIB, 7wks	320 rats, 670 mice, 276 hamsters, NR	HSCb = Printex-90 high surface area carbon black, Deguss-Huels (Trostberg, Germany). LSCb = Sterling V, low surface area carbon black, Cabot (Boston, MA)	Whole-body Inhalation	0, 1, 7, 50 mg/m^3 HSCb 50 mg/m^3 LSCb (rats only) bw NR	HSCb = 14 nm, 300 m^2/g SA LSCb = 70 nm, 37 m^2/g SA	6 h/d, 5 d/wk, 13wks. Postexposure 1d, 3mo, 11mo	Body Weight: Environmental changes pre and post-exposure affected test subjects' life spans, particularly hamsters. Hamsters also experienced significant loss of bw when exposed to high dose HSCb. Effects of Carbon Black: In rats, lung weight of the high dose HSCb doubled. After 11mo, analysis of all lungs showed no significant difference. Mice had highest relative lung burdens at the end of exposure time but also cleared particles faster at high dose than rats. However, clearance slowed over 11mo recovery period, especially in high dose mice. Hamsters showed significant elevations in lung carbon black burden for all exposures at all time points. Hamsters exposed to high dose HSCb exhibited impaired clearance. BALF Cells: Presence of PMNs limited to mid and high dose groups. Overall maximal response reached in mice and hamsters, but not in rats with increasing mass dose of HSCb.
Evans, S.A. Al-Mosawi, A. Adams, R.A. 2006 Rats, Male, Sprague-Dawley, NR	NR	DEP Cabosil = amorphous silicon dioxide (British Drug Houses, UK)	Intratracheal Instillation Pretreatment with 0.5 unit of bleomycin	1 mg/rat DEP 1 mg/rat Cabosil bw NR	DEP: 30 nm; 10% UF, 90% fine Cabosil: 7 nm; 16% UF, 84% fine	IT 3 or 7d after pretreatment; 1wk post-IT	Lung permeability: In bleomycin-treated group, obvious inflammatory status and edema within the lung, shown by significant increases in acellular protein and free cells. Changes in lung: body weight ratio, lung surface protein content, free cell counts, and apical surface protein of rat type I cells were only altered by bleomycin treatment and not particle exposure.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Finnerty, K. Choi, J.E. Lau, A. 2007 Mice, Male, C57BL/6, 12wks, 24.3±0.3g	NR	Coal Fly Ash (generated at U.S EPA National Risk Management Research Laboratory) Montana subbituminous coal = Fe, Mg, Ti, Mn, V	Intratracheal Instillation	Control: sterile saline PM: 200mg PM/mouse; 9.1 mg/kg PM+LPS10: 200mg PM+10mg LPS PM+LPS100: 200mg PM+100mg LPS LPS: 100ug	>$PM_{2.5}$	single, 18h	BALF Cells: No significant differences in platelet concentration or white blood cell count in any groups. % neutrophils increased significantly with PM+LPS100. PMN rose in PM groups and increased further with LPS treatment. Increases in PM+LPS groups statistically significant. More leukocytes present in the alveolar space in PM+LPS10 compared to PM group. Most severe response was in PM+LPS100 group. Cytokines: Plasma TNF-α and IL-6 significantly increased for the PM+LPS100 group. Additive effect of LPS and PM for IL-6. For saline and PM groups, pulmonary TNF-α was below detection range. Synergistic effect for TNF-α. Less than additive effect for IL-6. Pulmonary TNF-α significantly increased in the PM+LPS100 group. Pulmonary IL-6 significantly increased in both PM+LPS groups.
Fujimaki et al. (2006) Mice, Male, IL-6(-/-) and WT: B6J129Sv (control), 5-6wks	15, 10, 5	DEP (4-cylinder, 2.74 L, Isuzu diesel engine)	Whole-body Inhalation	1.0 mg/m^3 or 3.0 mg/m^3 bw NR	0.4 µm	12 h/d x 4wks, 1d postexposure	BALF Cells: Significantly increase of BAL cells from WT mice at both dose levels. Increase of macrophages and neutrophils dose-dependent. Increased lymphocytes in WT mice with low dose. No significant increase in cells from IL-6 (-/-). Cytokines: TNF-α largely increased in IL-6(-/-) mice with high dose compared to WT mice. IL-6 production increased in WT mice exposed to 3 mg/m^3. CCL3 increased in both WT and IL-6(-/-) at high dose. IL-1β remained at control level.
Gerlofs-Nijland, M.E. Boere, A.J. Leseman, D. 2005 Rats, Male, SH/NHsd, 11-12wks, 250-350g	NR	RTD = road tunnel dust (Motorway tunnel in Hendrik-Ido-Ambacht, Netherlands) EHC-93 (Ottawa, Canada)	Intratracheal Instillation	0.3, 1, 3, 10 mg/kg EHC-93 10 mg/kg	Coarse (2.5-10 µm) and fine (0.1-2.5)	single 4, 24, 48 h postexposure	BALF Cells: PMN significantly increased in RTD (3 and 10 mg/kg dose) and EHC-93 exposed animals at 24 h and decreased by 48h but remained statistically significant. AM numbers decreased for 3 mg/kg RTD group at 4h. BALF Inflammatory/Injury Markers: Myeloperoxidase (measured at 24 h in 1, 3, 10 mg/kg RTD groups) was elevated in dose-dependent manner. RTD induced time-dependent increase in LDH activity at 24 and 48h, although less than EHC-93 values at these time points. Alkaline phosphatase increased dose-dependently for RTD at 48h. GSH decreased at 24 h to approximately the same levels in 0.3, 1, and 3 mg/kg RTD dose groups. Uric acid only decreased in 1 mg/kg RTD group at 24 h. Cytokines: IL-6 elevated only at 10 mg/kg dose for RTD and EHC-93 at 4 and 24 h; remained elevated for EHC-93 at 48h. Dose-dependent increase in TNF-α at 4h for RTD; remained elevated only for 10 mg/kg groups at 24 h and returned to control by 48h. Dose-dependent increase in MIP-2 for all RTD dose groups and remained elevated through 48h for both PM types (although values were returning to control). Hematology: No significant changes in plasma for bigET-1 or von Willebrand factor. Fibrinogen levels significantly increased at 24 and 48h for both PM types only at the highest dose (10 mg/kg). Pulmonary histopathology: Dose-dependent increase in number of inflammatory foci at 24 and 48h for 3 and 10 mg/kg RTD groups. Response was even greater for EHC-93 group at these time points.

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Gerlofs-Nijland, M.E. Dormans, J. Bloemen, HR.J.T 2007 Rats, Male, SH/NHsd, 13wks, 250-350g	NR	PM Locations: 1. MOB high traffic density 2. HIA high traffic density 3. ROM high traffic density 4. DOR moderate traffic density 5 MGH low traffic density 6 LYC low traffic density	Intratracheal Instillation	3mg/kg or 10mg/kg	Coarse: 2.5um - 10um Fine: 0.1um - 2.5um	single, 24 h	BALF Inflammatory/Injury Markers: LDH significantly increased for all doses of coarse PM and for high dose of fine PM. BALF protein concentration observed predominantly at high dose of coarse PM. Location ROM had evidence of attenuated responses with fine PM. Ascorbate concentrations were reduced but only significant for rats exposed to highest dose of coarse PM fractions from locations MOD, HIA, and LYC. BALF Cells: Pulmonary inflammation dose-dependently significant for both dose levels. Includes airway neutrophilia, increased macrophages and mild lymphocytosis. Both coarse and fine PM caused dose-dependent aveolitis. Fine PM from LYC (10mg/kg dose) also caused some bronchiolitis. Cytokines: TNF-α concentrations increased for all coarse samples with exception of DOR and LYC. Fine PM induced similar response for all sites. MIIP-2 concentrations increased only at certain sites for coarse but not fine PM. Hematology: Fibrinogen responses of SH rats increased significantly at high dose of both fractions of all PM samples, except fine PM from DOR. Location-related differences: Coarse PM from MOB, HIA and MGH induced higher LDH response than other locations. Coarse PM from HIA produced BALF protein concentrations higher than LYC and ROM. MGH induced greater amounts of BALF protein than ROM. Coarse PM from LYC lowered fibrinogen values more than PM from location MOB, HIA, and MGH. Fine PM showed less differences among the various sites. Fine PM - significant correlation between zinc content and BALF cytotoxicity markers protein and LDH - mainly from one site, HIA. Also positive correlations with copper and barium. Coarse PM - positive correlation were found with barium and copper, mainly from one site MOB.
Ghio, A.J. Piantadosi, C.A. Wang, X. 2005 Rats, Males or Females, N8 b/b Belgrade rats and N8+ Ib Belgrade controls, NR	NR	Oil Fly Ash (Southern Research Institute, Birmingham, AL)	Intratracheal Instillation	500μg/rat; 2mg/kg 0.5 mL Saline (control)	NR	Single, 24 h	BALF Cells: Homozygous Belgrade with mutation G185R had higher levels of Fe and V 24 h postexposure. May demonstrate less ability to remove Fe and V from lower respiratory tract than heterozygous +Ib littermates. Indicates DMT1 normally responsible for at least some Fe and V uptake and defective DMT1 transports less. BALF Inflammatory/Injury Markers: Increased protein and LDH concentrations in homozygous vs control.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Ghio, A.J. Piantadosi, C.A. Wang, X. 2005 Rats, Male, Sprague-Dawley, 60 days, 250-300g	NR	Ferric ammonium citrate (FAC) Vanadyl sulfate ($VOSO_4$)	Intratracheal Instillation	0.5 mL 100 µM FAC/rat 0.5 mL 10 µM $VOSO_4$/rat bw NR 500 µg oil fly ash; 2 mg/kg 0.5 mL Saline (control)	NR	Single or double with 24 h rest period, Postexposure 15, 30, 60 min, 24 h	DMT1 immunohistochemistry and lung injury: FAC increased and $VOSO_4$ decreased –IRE DMT1 staining. Same exposures had no effect on +IRE DMT1. –IRE DMT1 expression in macrophages, airway and alveolar epithelial cells increased with increased Fe exposure. Vanadium nearly eliminated staining except in alveolar macrophages. Increased metal clearance with pre-exposure to FAC. Less metal clearance with pre-exposure to $VOSO_4$. Pre-exposure to iron diminished lung injury whereas pre-exposure to vandium increased lung injury after oil fly ash instillation. Lung injury measured by concentration of protein and LDH in BAL.
Gilmour et al. (2007) Mice, Female, BALB/c, 10-12wks, 20-22g	144, 138, 6	PM - CO, FI, UF (U.S. Seattle (S), Salt Lake City (SL), South Bronx (SB), Sterling Forest (SF))	Oropharyngeal Aspiration	25ug or 100ug PM; 1.25 or 5 mg/kg 2ug bacterial endotoxin (positive control)	CO (2.5-10um) FI (</ = 2.5um) UF (</ = 0.1um) See Pulmonary Effects for details	Single, 18h	BALF Inflammatory/Injury Markers: Seattle CO fractions showed no dose-dependent effect on protein concentration. Results for other locations distinctly higher with 100ug dose than 25ug and saline doses. SL CO high dose induced most significant increase. LDH response weakly dose-related. Only SB showed statistical significant increase for LDH with high dose UF. BALF Cells: PMN increased with high dose of CO samples from SB, SL, S, not SF. No significant increases from FI, though high dose induced increased PMN. UF from SL caused highly variable response. Cytokines: MIP-2 similar to PMN response. SB CO induced most significant response. SL UF highly variable. Particle Characteristics: LPS higher in S (CO, FI, UF) and SL (CO, FI, UF). Zn highest in SB (CO, FI, UF). Fe higher in all CO and FI samples with SB CO highest. SB also included 35% sulfate, 22% gasoline, diesel and brake wear. SF 48% sulfate. SL 34% wood combustion and 28% sulfate. S 39% wood combustion and 29% sulfate. Residual oil combustion and soil dust less than 5% for all sites.
Gilmour et al. (2004a) Mice, Female, CD1, 8-10 wks, 20-25g	20, 10, 10	Coal Fly Ash MU = Montana Ultrafine MF = Montana Fine MC = Montana Coarse KF = West Kentucky Fine KC = West Kentucky Coarse	Oropharyngeal Aspiration	25ug or 100µg/mouse 10ug LPS (positive control) Saline (negative control) bw NR	Coarse (>2.5 µm) Fine (<2.5 µm) Ultrafine (<0.2 µm) See Pulmonary Effects for details	Single, 18h	BALF Cells: PMN highly increased for MU at both doses. Level comparable to positive control. Also increased with KF at high dose. Coarse particles caused no significant increase in PMN. Number of macrophages did not change, but NAG increased significantly with MU for both dose levels and with KF and MF at high dose level. BALF Inflammatory/Injury Markers: Total protein and LDH not significantly elevated. Albumin concentration increased significantly with high dose of both fine coals. Cytokines: MU particles caused significant increase in TNF-α. MIP-2 increased in all fine and ultrafine PM-instilled animals, highest in the MU and KF at both doses. IL-6 detectable only in BALF of MU and KF at substantial variability - not significant. Particle Characteristics: Montana Sulfur 0.83%, Ash 11.72%. Trace amounts of Ba, P, Sr, V, Nb, Cd, Se, Ga, Cu. Depleted in Si, Al, Fe, Mg, Ti. Kentucky Sulfur 3.11%, Ash 8.07%

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Gilmour et al. (2004b) Rats, Male, SH/NCrlBR and WKY, 12 wks, 280-340g	NR	PM (precipitator unit of an oil burning power plant in Boston)	Intratracheal Instillation	0.0, 0.83, 3.3, and 8.3 mg/kg in SH rats 0.0 or 3.3 mg/kg in WKY and SH rats	Measured Components of PM: S, Zn, Ni, V, Al, Cu, Pb, Fe, Ca, Na, K, Mg, Endotoxin	single, 24 h	BALF Inflammatory/Injury Markers: LDH dose-related increase observed in SH rats after 0.83, 3.33 and 8.3 mg/kg PM exposure. SH rats showed greater lung permeability following PM exposure than WKY rats. SH rats showed acute lung inflammatory response after exposure to PM vs WKY rats. BALF Cells: No increase in macrophage number in either rat strain following saline or PM exposure at 24 h time. Cytokines: MIP2 mRNA expression increased significantly in SH PM exposure group only. No significant difference in TNF-α RNA expression in either WKY, SH rats or control treatment groups. CD14 - Significant increase in lung CD14 protein only in SH rats exposed to PM. TLR4 - Significant increase in TLR4 protein in SH rats exposed to PM. NF-□B - Significant increase in NF-□B binding protein in nuclei of SH rats exposed to PM and not in control or PM-exposed WKY rats.
Gilmour et al. (2004c) Rats, Male, Wistar, 12 wk	NR	ufCB = Ultrafine carbon black (Printex 90 (Degussa) CB (Huber 990, HR. Haeffner and Co)	Whole-body Inhalation	TSP ufCB: 1.66 mg/m^3 fCB: 1.40 mg/m^3 Number concentrations ufCB: 52380 particles/cm^3 fCB: 3800 particles/cm^3 bw NR	14 nm ufCB 260 nm CB	7 h; 0, 16 or 48 h post-exposure	BAL Cells: Total number of cells increased significantly in UfCB-exposed rats at 0 and 16 h. Recruitment of cells did not occur in response to CB exposure. PMN increased significantly difference in the BALF of ufCB-exposed rats at 16 h. May be an effect at 0 h as well, but due to 1 control rat with very high PMN, not significant at this time point. Leukocytes unchanged following CB exposure. Increased significantly at 0 and 48 h post exposure to ufCB. Cytokine mRNA: Significant increase in BALF MIP-2 mRNA expression at 48 h. No differences in MIP-2 mRNA levels in whole lung tissue.
Gunnison and Chen (2005) Mice, Male, DK (ApoE$^{-/-}$, LDLr$^{-/-}$), 18-20wks	6, 3, 3	CAPS (Northeastern regional background) Ambient Air copollutants measured O_3, NO_2 Filtered air (control)	Whole-body Inhalation	CAPS = 131 ± 99 μg/m^3 including O_3 = 10 ppb and NO_2 = 4.4 ppb bw NR	389 ± 2 nm	6h/d, 5d/wk, 4 mo (5/12/03-9/5/03), 3-4 d	Microarray Data: 13 genes in heart tissue and 47 genes in lung tissue identified as possibly affected. Strict standards (1.5 fold response, 10 % false discovery rate) resulted in response by only 1/13 genes (Rex3 - no known heart physiology) in heart tissue and 0/47 genes in lung tissue. Using more liberal response (nonstatistical) standards (1.5 fold only) and comparison of each CAPS animal with all 3 control animals (3x3 array) resulted in possible effects on 7 additional genes in heart tissue and 37 genes in lung tissue.

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Gurgueira et al. (2002) Rats, Male, Sprague-Dawley, 250-300g	36, 18, 18	CAPs (Harvard Ambient Particle Concentrator) CB (C198 Fischer Scientific, Pittsburg, PA USA) ROFA (Boston, MA USA oil-fired power plant) Filtered air (control)	Whole-body Inhalation	300 ± 60 µg/m^3 bw NR	1-2.5 µm CAPs <2.5um CB Composed of 85.9± 0.2% Carbon, 13.0± 0.2% O2, 1.17± 0.2% Sulfur <2.5um ROFA	1, 3, 5h CAPs Exposure, Immediate Post-exposure Analysis 5h CB, Immediate 30min ROFA, Immediate	in situ chemiluminescence(CL): Data show significant increase in lung and heart CL at 5h. Lung CL increased linearly with time of exposure. Oxidants: CAPs-initiated oxidative stress not detectable in those rats allowed to recover in room air after simulated "peak" in particulate air pollution. Rats breathing particle-free filtered air for 3 days had significantly lower levels of oxidants. Exposure to inert CB did not exert oxidant effects on heart and lung. BALF Inflammatory/Injury Markers: Water content of lung and heart increase significantly upon exposure to CAPs but not to filtered air. Increases as a function of length of exposure. Rats breathing CAPs also showed increases in LDH and CPK as a function of length of exposure. Antioxidant enzymes: Data showed increase in SOD and catalase activities in both lung and heart. The pattern of increase was tissue specific.
Hamoir et al. (2003) Rabbits, NR, New Zealand, 12-16wks, 2.8 ± 0.5kg	28, 24, 4	PSC = Polystyrene particles, Carboxylate modified, 3 types PSA = Polystyrene particles, Amine modified, 1 type	Intratracheal Instillation	PSC24 = 0.04 or 4 mg/rabbit PSC110 = 4 mg/rabbit PSC190 = 4mg/rabbit PSA190 = 4mg/rabbit bw NR	PSC = 24, 110 or 190nm (PSC24, PSC110, PSC190) with surface area of 1.81 10E-11, 3.80 x 10E-10, and 1.13 10E-9 cm^2/particle PSA = 190 nm at 1.13 10 E-9cm^2/particle	30, 60, 90, 120 min	Capillary Filtration Coefficient: Time-dependent increase correlating to total number of particles/surface area, not particle size. PSA190>PSC190. PSA induced significant increase in microvascular permeability vs PSC. Suggests number of particles exposed should be considered important parameter for measuring air quality rather than total particle surface area.
Happo et al. (2007) Mice, Male, C57B1/6J, 10-11wks, 19-30g	NR	PMC (Coarse) = $PM_{10-2.5}$ (5.9-29.6 µg/m^3) PMF (Fine) = $PM_{2.5}$ -0.2 (8.3-25.2 µg/m^3) PMUF (Ultrafine) = $PM_{0.2}$ (2.7-6.7 µg/m^3)	Intratracheal Instillation	1, 3, 10 mg/kg	Collected in 6 European cities: Duisburg, Prague, Amsterdam, Helsinki, Barcelona, Athens	single 4, 12, 24 h post-exposure	BALF Cells: At mid and high dose of PMC (6/6cities), total cell number increased dose-dependently at 12h time point. At 24 h, cell number had lowered but still significantly higher than basal level. PMF at all dose levels induced cell number to increase significantly at 12h (3/3). PMUF no effect except with Athens, which did not produce remarkable increase. PMC increased neutrophils (6/6) and lymphoplasmacytic cells (3/6) at 12h high dose and decreased macrophages (1/6). PMF increased neutrophils (5/6) and lymphoplasmacytic cells (1/6). BALF Inflammatory/Injury Markers: Protein increased at high dose PMC (5/6) and PMF (4/6) at 12h; Continued to increase at 24 h in 3 cities and decreased significantly in 1 city. LDH no effects. Cytokines: TNF-α dose-dependent increase PMC (6/6): and PMUF variable slight increase (2/6). At high dose, TNF-α peaked 4h with decrease to basal level at 24 h. IL-6 dose-dependent significant increase only for PMC (6/6); Variable slight increases PMF (1/6), PMUF (5/6). Il-6 peaked at 4h high dose with decline to basal level by 24 h. KC dose-dependent increase only for PMC (6/6); variable slight increases PMF (1/6), PMUF (2/6). KC doses with high dose of PMC peaked at 4h (4/6) and 12h (2/6) and returned to control level by 24 h.

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Hiramatsu et al. (2003) Mice, Female, BALB/c and C57BL/6, 8wks, 17-22g	48, NR	DE = DE	Whole-body Inhalation	DEP = 100μg/m^3 or 3 mg/m^3 SO_2<0.01ppm NO_2 2.2±0.3 or 15 ±1.5 ppm CO 3.5 ± 0.1 or 9.5 ± 0.6 ppm bw NR	NR Measured Components: SO_2, NO_2, CO	7h/d 5d/wk for 4 or 12wks, Immediate	BALF Cells: Alveolar macrophages (AMs) increased dose-dependently at 30 and 90d. High DE exposure resulted in bronchus-associated lymphoid tissue (BALT) around DEP-AMs. AM phagocytosis increased in BALB/c mice at high exposure level - minimal change in C57BL/6. B and T cells both occurred with no difference between strains. Lympohocytes and neutrophils increased with time and dose. Greater increase in BALB/c than C57BL/6. No eosinophils or basophils were observed. Mac-1-positive cells exposed to high DE levels increased in both strains at 1 month (33.8%) and 3 months (20.3%) vs. low dose group (5.3 and 7% respectively). Cytokines: At 30d, TNF-α, IL-12p40, IL-4 and IL-10 mRNA increased, IL1b and iNOS decreased. IFNγ increased in BALB/c but decreased in C57BL/c. IL-6 mRNA no effect. At 90d, similar IL--4 and IL-10 mRNA increased in C57BL/6 mice at low level but decreased at high level.
Hollingsworth et al. (2004) Mice, Male, C57BL/6 TLR4(-/-) and C57BL/6 TLR4 (+/+), 8-9 wks	12, 6, 6	ROFA	Oropharyngeal Aspiration	50 ul of 1μg/mL suspension per mouse bw NR	NR	Single, 6 and 24 h	TLR4-Knockout vs Wild type: No differences. Methacholine sensitivity: No ROFA effect. BALF Cells: ROFA increased total cell number. Total number of neutrophils with lavage fluid increased 24 h post-exposure in both C57BL/6(-/-) and C57BL/6 (+/+).
Hutchison, G.R. Brown, D.M. Hibbs, L.R. 2005 Rats, Male, Wistar, 3 mo, 250-300g	12, 9, 3	PM_{10} United Kingdom samples collected before (-B), during closure (-C) and reopening of steel plant (-R) Saline (control)	Intratracheal Instillation	112 to 180 μg PM in 500 ul; 0.44-0.72 mg/kg	NR PMT = PM total (aqueous sonicate) PMS = PM aqueous supernatant PMI = PM insoluble pellet	Single, 18h	BALF Cells: PMT-R neutrophil cell number and percentage higher than PMT-C or control. PMS-R and PMI-R higher than control. PMI-R >PMI-C. Total cell count unchanged. BALF Inflammatory/Injury Markers: Only albumin increased after PMT-R. Protein, LDH, MIP2 and TNF-α unaffected. Cytokine mRNA expression: Only PMT-R increased IL-1 mRNA expression. No effects on TNF and TGF mRNA.
Inoue et al. (2006a) Mice, Male, C3H/HeJ (TLR-4 point mutant) and C3H/HeN (Control), 6 wk	32-40, NR	DEP (derived from 4 cyl, 2.74l light duty diesel engine) Saline (Control)	Intratracheal Instillation	12 mg/kg	NR	Single, 24 h	Airway Inflammation: DEP induced increased total cells (P<0.01), neutrophils (P<0.01) and mononuclear cells in BALF. TLR4 knockout mice (C3H/HeJ) showed much lower response. BALF harvested from gentle aspiration. Cytokines: DEP induced massive increase in MIP-1x, IL-1β and KC. However, level of MIP-1x significantly less in knockout then wild type while levels of IL-1β and KC significantly higher in knockouts vs wild type. Hematology: DEP increased plasma fibrinogen but more in knockout mice than wild type.
Inoue et al. (2006b) Mice, Male, NC/Nga, 10wks	36, 18, 18	DEP (derived from 4 cyl, 2.74l light duty diesel) Saline (control)	Intratracheal Instillation	100 μg/mouse bw NR	NR	1/wk for 6wks, 24 h	BALF Cells: DEP significantly increased total cells, neutrophils and mononuclear cells but no effect on eosinophils. Cytokines: DEP increased IL-4, KC and MIP-1. Increase in IL-5 not statistically significant.

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Ishihara et al. (2003) Rats, Male, Wistar, 5wks	120, NR	DE (from 2 engines, produced on site) L = low level DE M = medium level DE MG = DE w/o particulates HR = high level DE Filtered Air (control)	Whole-body Inhalation	L = 0.18 - 0.21 mg/m^3 M = 0.92- 1.18 mg/m^3 MG = 0.01 mg/m^3 HR = 2.57 - 2.94 mg/m^3 bw NR	L = 0.33 -0.50 µm M = 0.35 - 0.40 µm HR = 0.42 - 0.45 µm Measured Components: NO_2, SO_4, SO_2, CO, CO_2, NO_x, NO, HTHC, HCHO, O2	16 h/d, 6 d/wk, for 6, 12, 18 & 24 mo Immediate post-exposure	Morbidity and Mortality: Weight gain in HR group less than other groups at 18 and 24 mo, indicating significant difference between HR and C group. Mortality during study frequent. C group 8%, L group 12%, M group 15%, MG group 12% and HR group 23%. BALF Inflammatory/Injury Markers: Significant differences seen among groups with respect to number of total cells and percentages of cell differential, total protein, fucose, sialic acid, phospholipid and prostoglandin E2. Total protein increase in both M and HR dose groups with HR group increasing time-dependently. BALF Cells: HR group showed significant increase in total cell count from 6mo to 18mo. Percentage of PMN increased at 6mo in M, MG and HR group. M group lymphocytes significantly increased at 6, 12, 24mo of exposure. Macrophages decreased at 6mo for M and HR group. Mucus and Surfactant: HR group showed significant increase from 12mo to 18mo.
Jones, HR.A. Hamacher, K. Clark, J.C. 2005 Rabbits, NR, New Zealand, 2.5- 3.5kg	NR	ASP = Amorphous silica particles (Hypersil) MCSP = Microcrystalline silica particles	Intratracheal Instillation	20 mg/kg	ASP = 5 µm MCSP = 5 µm	single, 6h up to 91d	MCSP: At 6h, neutrophils increased. Macrophages increased 3 fold. At 60h, neutrophils pyknotic, thickened interstitium containing silica particles. At 5d, Collagen deposition appeared. AT 8d, fibroblastic activity and necrosis. At 15d, aggregation of silica particles and necrotic debris. AT 8 wks, fibroblasts still present. Progressing to active scarring and raised neutrophil macrophage counts at 13 wk. ASP: At 15h, neurophils increased. Macrophages tripled and remained increased for 3wks. At 4d, macrophages bore particles. At 13d, neutrophils decreased significantly. By 25d, silica spheres removed from lungs. PET Scanning: 18F-fluoroproline showed increased activity starting at 14d and peaking at 41-54d (left lung control vs right lung challenged). Microautoradiography: 3h-proline at 13 weeks showed label localization mostly to fibroblasts.
Kato, A. Kagawa, J. 2003 Rats, Male, Jcl Wistar, 5wks	385, NR	Roadside air (Prefectural Tokyo-Danishi-Yokohama highway, Yokohama-Haneda Airport Metropolitan expressway and Satsukibashi-Mizuecho city road, Japan) Filtered Air (control)	Whole-body Inhalation	Exposed group: 55.7 ppb NO_2, 62.7 µg/m^3 PM Control group: 5.1 ppb NO_2, 14.3 µg/m^3 PM bw NR	NR	24, 48, 60 wks Immediate post-exposure	Respiratory tissue: Post 24wks, light gray surface color with some BC particle deposits. Post 48-60wks, surface light gray with particle deposits all over lung surface. Airway changes: After 60 wks, no remarkable changes seen in epithelium. Structure of airways remained normal. Cells: No proliferation or ectopic growth of goblet cells noted. Mast cells increased in epithelial intercellular space. No mast cell degranulation observed. Lysosomes increased in cilitated cells post 48wks. Clara cells unaffected. Lymph nodes: Deposition of carbon particles noted in trachea and bronchiole-associated lymph nodes post 24wks. Alveolar changes: No changes in morphology of broncho-alveolar junctions noted. Anthracosis observed within alveolar walls and pleura post 24wks. Became progressively marked with increased exposure. No change in number of alveolar holes between exposure and control groups.

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Kato, T. Yashiro, T. Murata, Y. 2003 Rats, Male, Sprague-Dawley, 7wks, 190-220g	NR	Polystyrene latex suspension of latex beads (Japan Synthetic Rubber Co.), uncoated or coated with lecithin	Intratracheal Instillation	5ml of 0.2% suspension administered over 20 min at flow rate of 0.25ml/min bw NR	240 nm	20 min, 30 min	Alveolar Macrophages: Appeared undamaged. Ingested both beads, uncoated>coated. Ingestion of beads differed as coated beads engulfed individually while uncoated beads engulfed individually or in aggregates. Epithelial Cells: Type I cells incorporated coated beads within layer of cytoplasm. Type II cells incorporated beads in lamellar bodies. Uncoated beads not incorporated. Other: Neither type of beads were incorporated into endothelial cells, fibroblasts or interstitium of alveolar wall Monocytes: Only incorporated coated beads -- inside and outside phagosomes and lysosomes. PMNs did not incorporate any beads.
Kleinman et al. (2003b) Rats, NR, F344N-NIA, 22-24mo	88, 66, 22	O_3 CCL = O_3 + Ammonium bisulfate (ABS) + Elemental Carbon (EC) CCH = O_3 + ABS + EC Purified Air (control)	Nose-only Inhalation	O_3 = 0.2 ppm CCL = 50 μg/m^3 EC + 70 μg/m^3 ABS + 0.2 ppm O_3 CCH = 100 μg/m^3 EC + 140 μg/m^3 ABS + 0.2 ppm O_3 bw NR	CCL = 0.30 ± 2.5 μm CCH = 0.29 ± 2.3 μm	4h/d, 3 consecutive d/wk, 4wks NR post-exposure	DNA Replication: O_3 caused slight effect of 20-40% increase. CCL and CCH caused between 250 - 340% increase for interstitial and epithelial cells. Low concentration particle mixture induced greater reaction than high dose. BALF Inflammatory/Injury Markers: Total protein, mucus glycoprotein and albumin somewhat elevated in all exposure groups but only statistically significant for CCL and protein (very high variability). CCL and CCH both depressed Fc receptor side binding, no effect for O_3. BALF Cells: CL and CCH induced macrophage respiratory burst activity, O_3 effect not significant.
Kleinman, M.T. Phalen, R.F. 2006 Rats, Male, Sprague-Dawley, 6wks, 200g	180, 164-168, 12-16	LO_3 = Low O_3 HO_3 = High O_3 LS = Low H_2SO_4 HS = High H_2SO_4 LOLS = Low O_3 + Low H_2SO_4 LOHS = Low O_3 + High H_2SO_4 HOLS = High O_3 + low H_2SO_4 HOHS = High O_3 + high H_2SO_4	Nose-only Inhalation	LO_3 = 0.30 ppm HO_3 = 0.61 ppm LS = 0.48 mg/m^3 HS = 1.00 mg/m^3 LOLS = 0.31 ppm + 0.41 mg/m^3 LOHS = 0.31 ppm +1.04 mg/m^3 HOLS = 0.60 ppm + 0.52 mg/m^3 HOHS = 0.60 ppm + 0.86 mg/m^3 bw NR	LS = 0.23 μm±2.3 HS = 0.28 μm±2.1 LOLS = 0.23 μm ±2.3 LOHS = 0.28 μm ± 2.1 HOLS = 0.23 μm ± 2.3 HOHS = 0.28 μm ± 2.1	4h, 42h	Inflammatory Lesions in Lung Parenchyma: Neither Type 1 or 2 lung lesions affected by sulfuric acid alone. HO_3 doubled Type 1 lesions and 25 fold for Type 2 lesions. Additions of H_2SO_4 to O_3 appeared to have dose-dependent protective effect for both types of lesions. DNA Synthesis in Nasal, Tracheal and Lung Tissue: Increased DNA synthesis observed at all high O_3 exposures but not affected by coexposure to H_2SO_4. Macrophage FcR binding: No effects (no data for LO_3 and HO_3). Macrophage Phagocytosis: At all levels of exposure (no data for LO_3 and HO_3) decreased phagocytosis.
Kodavanti, U.P. Schladweiler, M.C. Ledbetter, A.D. 2005 Rats, Male, WKY and SH/NCrlBR, 11-14 wks	NR	CAPs (EPA, NC) Filtered Air (control)	Whole-body Inhalation	1d study: 1138-1765 μg/m^3 2d study: 144-2758 μg/m^3 bw NR	CAPs 1d: 1.07-1.19 μm CAPs 2d: 1.27-1.48 μm	4hr (SH only) 4hr/day, 2d (WKY and SH) Post-exposure: 1d: 3h except study #4, 18-20h 2d: 18-20h	Particle Characteristics: Measured components included Al, Be, Ba, Co, Cu, Zn, Pb, Mn, Ni, Ag, Ti, As. Breathing Parameters: In paired analysis, SH rats showed increase in expiratory and inspiratory time due to CAPs. Not significantly different in WKY rats. BALF Cells: In 2d study, WKY rats showed decreases in total cells and associated with macrophages. WKY showed while increases in neutrophils. BALF Inflammatory/Injury Markers: Total protein and albumin in WKY rats decreased while SH rats maintained approximately same level. LDH activity lowered slightly in both strains. Cell Membrane Integrity: SH rats showed increased GGT (membrane bound enzyme) activity and plasma fibrinogen for 5/7 exposures but did not appear to be dose-dependent. Cytokines: Levels were undetermined in SH rats. WKY showed slight increase in IL-6, TNF-α, MIP-2 but not statistically significant.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Kooter et al. (2006) Rats, Male, SH, 12-14wks	104, 52, 52	CAP-F = fine (Site I) CAP-UF = fine + ultrafine (Site II) (Netherlands) Filtered Air (control)	Nose-only Inhalation	CAP-F 399- 3613 μg/m^3 CAP-UF 269-556 μg/m^3 bw NR	0.15<CAP-F<2.5 0.65-0.75 μm CAP-UF<2.5 0.58-1.41 μm Some measured **Components:** Ammonium, nitrate, sulphate ions: 56± 16% CAP-F mass, 17 ± 6% CAP-UF mass	6h/d for 2d consecutive, 18h	BALF Inflammatory/Injury Markers: No cytotoxicity noted based on unchanged levels of LDH and ALP. No significant change in levels of total cells. MDA (malondialdehyde) for lipid peroxidation decreased with CAP-UF. Ho-1 for oxidative stress increased with CAP-UFand CAP-F. Cytokines: CC16 decreased at 457μg/m^3 CAP-F and increased at 3613 μg/m^3 CAP-F. Hematology: WBC and lymphocytes decreased with both CAP-F and CAP-UF. MPV and MPC (mean platelet volume and component) increased with CAP-UF. BALF Cells: Decrease in absolute neutrophils as well as % reticulocytes and % neutrophils with CAP-F. Increased % lymphocytes with CAP-F. Pathology. No changes observed.
Kumar et al. (2004) Rats, Male, Wistar, 150±20g	NR	Fly Ash (Obra Thermal power Station, India)	Whole-body Inhalation	14.4±1.77 mg/m^3 (fluid bed generator) bw NR	PM <5 μm (90%)	4h/d for 28d, Immediate	Lung Weight: 25.58% lung body weight increase relative to bw over controls. Total body weight slightly decreased. BALF Inflammatory/Injury Markers: All increased massively: LDH, GGT, ALP and lavagable protein by 140, 450, 160 and 50% BALF Cells: Only eosinophils(%) increased 95% over controls.Congestion and focal infiltration of monocytes in alveolar area. Fly Ash laden macrophages in alveoli combined with hypertrophy of epithelial lining cells.
Lei et al. (2004) Rats, Male, Sprague-Dawley, NR, 318 ± 8g	NR	CAPs (Yaipei, Taiwan) HEPA-filtered air (control)	Nose-only Inhalation	371 ± 208 μg/m^3 bw NR	0.01<PM<2.5 μm	6h/d for 3d, 5h post-exposure pulmonary function, 2d post-exposure for BALF collection Pulmonary hypertension induced 2wks pre-exposure	Respiratory Effects: Decreased respiratory frequency and increased tidal volume for both experimental and control groups, but only experimental group levels statistically significant. Increase in airway responsiveness (Penh/methacholine) for CAPs group vs control. BALF Cells: Massive increase in total cell number and % neutrophils. No changes in % macrophages, lymphocytes and eosinophils. BALF Inflammatory/Injury Markers: Total protein and LDH increased in CAPs group. Cytokines: TNF-α and IL-6 not affected.
Lei et al. (2004) Rats, Male, Sprague-Dawley, NR, 300-350g	12, 8, 4	CAPs from Asian dust storm (Taiwan)	Nose-only Inhalation	LOW = 315.6 μg/m^3 HIGH = 684.5 μg/m^3 bw NR	0.01<PM<2.5 μm Measured **Components:** Si, Al, S, Ca, K, Mg, Fe, As, Ni, W, V, organic carbon, elemental carbon, SO_2, NO_2, nitrate, sulfate	LOW: single 6h, 36h post-exposure HIGH: single 4.5h, 36h post-exposure Pulmonary hypertension induced 2 wk pre-exposure	Hematology: PM dose-dependent increase in WBC s. No change in RBC s. Highly variable platelet results. BALF Cells: PM dose-dependent increase of 4 fold in total cells and % of neutrophils. No change in macrophages, lymphocytes or eosinphils. Basophils highly variable. BALF Inflammatory/Injury Markers: Dose-dependent increase observed for total protein and LDH. Cytokines: IL-6 increased dose-dependently (control: 33.5 ± 7.5, LOW 165.1 ± 117.2, 273.6 ± 62.8 pg/mL)

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Mangum et al. (2004) Rats, Female, CDF (F344)/CrlBR, 7wks	NR	TiO_2 pigment grade (DuPont) Filtered Air (control)	Whole-body Inhalation	10, 50 or 250 mg/m^3 TiO_2 bw NR	NR	6h/d x 5d/wk for 13wks, 0, 4, 13, 26, 52wks post-exposure	OPN (osteopontin) Expression: 0 wks: OPN mRNA expression dose-dependent increase. Low dose induced 2-fold increase. High dose induced almost 100 -fold increase. 4wks: At mid-dose and high-dose, OPN mRNA levels elevated 13wks: At high dose, OPN mRNA levels elevated. No significant elevation with mid dose level. 26wks: Mid and high dose induced elevated OPN mRNA levels. 52wks: Rats in low, mid and high dose groups all indicated elevated levels of OPN mRNA. Low- 3-fold increase, Mid- 7-fold increase and High- 400-fold increase. OPN Protein in BALF: 0 and 4wks: NR 13wks: Protein increased 9-fold (~800 pg/mL OPN) at mid dose and by 100 -fold (~8000 pg/mL OPn) at high dose. 26wks: Mid and high dose groups remained elevated. 52wks: Protein increased by 2.5 fold in low dose, 7-fold in mid dose and 166-fold in high dose group. Histopathology: At 52wks, slight OPN immunoreactivity observed in control and low dose group (immunostaining mostly limited to intraalveolar MACS). Trichrome-stained lung sections from control and low dose groups showed no increase in collagen. Rats exposed to mid or high dose groups showed areas of lesions.
Martin, S. Dawidowski, L. Mandalunis, P. 2007 Mice, Male, BALB/c, 1-2mo	NR	UAP-BA = Urban Air particles (Buenos Airs, Argentina)	Intranasal Installation	0.17 mg/kg bw	<2.5um See Pulmonary Effects	3xday, 3d/wk, 2d apart (1, 4, 7d), 1h post-exposure	Particle Characteristics: 3 types, ultrafines <0.2um (inorganics ND), bunched agglomerates of ultrafines and <40um with aluminum silicates, ions and trace metals. Morphometry: Induced focal inflammatory lesions. Accumulation of refractile material in upper and lower respiratory tract. PM in phagocytes of bronchiolar lumen and alveolar space. No evidence of fibrosis and/or collagen changes. BALF Cells: Increased amount of phagocytes in alveolar area, reducing airspace percentage (control 52.9% ± 1.39, UAP-BA 24.7% ± 2.87). Increased number of PAS positive cells.
McDonald, J.D. Harrod, K.S. Seagrave, J. 2004 Mice, NR, C57Bl/6, 8-10wks	16, 8, 8	DEE = DE (high load, No 2, No cat) (620: 1 dilution) DEE-ER (Control) = DEE (high load, low sulfur ECD1) same dilution (Yanmar diesel generator, 406 cc, 5500 watt load)	Intratracheal Installation	DEE PM = 236 μg/m^3 DEE-ER PM = 7 μg/m^3	DEE: 110 nm DEE-ER: NR	DEE: 6h/d for 7d, 0 DEE-ER: 6h/d for 7d, 0 RSV administered post-exposure for some: single, 4d	Differences in Exposure Conditions: 90-100% decrease: CO, PM, elemental carbon, organic carbon, nitrate, alkyne, c2-c212 alkenes, phenanthrenes, total particle PAHs, total Oxy-PAHs, benzene, pyrene, benzo(a)pyrene, zinc. Most others around 60% reduction. DEE vs. DEE-ER Effects: DEE increased viral retention and lung histopathology. DEE-ER increases were not statistically significant. Cytokines: DEE increased TNF-α, IL-6, IFN-γ and HO-1. DEE-ER responses not statistically significant (significantly higher variability in DEE-ER controls vs. DEE controls).

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
McQueen et al. (2007) Rats, Male, Wistar, 228-500g	NR	DEP SRM 2975 Saline (control)	Intratracheal Instillation	0.5 mL/rat of 1 mg/mL; 1-2.2 mg/kg	NR	single, 6h Pre-exposure: Vagotomy (sectioning of vagus nerve) or Atropine 1mg/kg i.p. administered 30 min prior, 2 and 4h post.	BALF Cells: 9 fold increase in neutrophils with high individual variability in response. Bilateral vagotomy prior to DEP reduced neutrophil increase to 3 fold. Vagotomy with saline instillation had no effect. Atropine reduced neutrophils to level similar to saline response. No differences were observed between DEP response in anesthetized versus conscious animals. Macrophages, eosinophils and lymphocytes unchanged. Respiratory Response: RMV increased post DEP. Vagatomy reduced response by a third. Atropine pre-treatment did not have effect. Cardiovascular Response: Blood pressure and heart rate unaffected. Average arterial O2 increased after DEP, but not when compared for each animal. CO_2 and pH were not affected
Medeiros (2004) Mice, Male, BALBc, 60d, 20-30g	80, 70, 10	CP = Carbon particles PMA = ROFA (solid waste incinerator hospital Sao Paulo, Brazil) PMB = electric precipitator, steel plant, Brazil) Saline (control)	Intranasal Instillation	CP = 10 μg/mouse; 0.5mg/kg PMA, 0.1, 1 or 10 μg/mouse; 0.005, 0.05, 0.5 mg/kg PMB 0.1, 1 or 10 μg/mouse; 0.005, 0.05, 0.5 mg/kg	CP = 1.7 ± 2.5 μm (78%<2.5 μm) PMA = 1.2 ±2.2 μm(98 %<2.5 μm) PMB = 1.2 ± 2.2 μm (98%<2.5 μm) See Pulmonary Effects	single, 24 h	PMA/PMB Characteristics: PMB>PMA: Br (100+x), Cr (3x), Fe (10+x), Mn (2x), Rb (60+x), Se (7x), Zn (4x). PMA>PMB: Ce (3x), Co (10+x), La (100x), Sb (15x), V (50x). Hematology: PMA and PMB decreased leukocyte count (all 3 doses), platelet count (2 high doses). No effect on hemoglobin, erythrocytes and reticulocytes. Fibrinogen levels increased PMB>PMA. None of the effects dose-dependent. Bone Marrow: Erythroblasts increased for PMA at all dose levels and PMB at mid and high dose level (high variability). BALF Cells: No change in BAL cell count. Quantitative cellular counts increased for perivascular area for both groups at all dose levels. Inflammatory cells in alveolar septum area only increased for PMA.
Mutlu et al. (2006) Mice, NR, C57BL/6, 6-8wks, 20-25g	NR	PM_{10} Collected by baghouse from Dusseldorf, Germany	Intratracheal Instillation	100 ng/mouse 1 μg/mouse 10 μg/mouse 100 μg/mouse	NR	1-7d	Alveolar Fluid Clearance: At 100 μg/mouse, decreased clearance peaking at 24 h, recovered at 7d. Histology: Evidence of mild lung injury at doses of 100 μg/mouse or more. BALF Cells: Significant increased in total cell number. Neutrophils increased but not statistically significant. Wet/Dry Ratio: Unaffected. Na, K-ATPase: At 100μg/mouse, decreased activity of Na, K-ATPase in basolateral membranes.
Nadziejko, et al. (2002) Rats, Male, WKY(SH), 16wks	12, NR, NR 5 rats eliminated from study in first 5mo	CAPs FA = Fine Particle Sulfuric Acid Aerosol UFA = Ultra-Fine Particle Sulfuric Acid Aerosol Filtered Air (control)	Nose-only Inhalation implanted blood pressure transmitters	CAPS 80, 66 μg/m^3; avg 73 μg/m^3 FA 299, 280, 119, 203 μg/m^3; avg 225 μg/m^3 UFA 140, 565, 416, 750 μg/m^3; avg 468 μg/m^3 bw NR	CAPs = $PM_{2.5}$ FA = 160nm UFA = 50-75nm	10 exposures of 4h each being 1+ wk apart (2 exposures to CAPs, 4 to FA and 4 to UFA)	Respiratory rate: CAPs decreased respiratory rate as did FA at all dose levels though FA not statistically significant unless data combined. UFA increased rate significantly. Heart Rate: CAPS depressed heart rate significantly in combined data. Normalized post-exposure. FA induced decrease as well with continuation 7h post-exposure. UFA again increased heart rate. Diastolic Blood Pressure: Caps and FA induced decrease but not statistically significant. UFA increased just slightly.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Nemmar et al. (2007) Rats, Male, Wistar Kyoto, 16wks, 424 ± 8g	NR	DEP = SRM 2975	Intravenous Injection	0.02, 0.1 or 0.5 mg/kg	<1um	single, 24 h	Cardiovascular: DEP depressed blood pressure at all doses approximately equally. DEP depressed heart rate at all doses equally. Hematology: No effect on number of platelets, granulocytes, monocytes, lymphocytes or RBC s. Tail bleeding time (associated with platelet activity) decreased at doses of 0.02 and 0.5mg/kg. BALF Cells: Marked cellular influx at all dose levels. Macrophages increased at high dose, but not statistically significant. PMN increased significantly at all dose levels. Wet/Dry Ratio: Increased at all dose levels.
Nemmar et al. (2003b) Hamsters, Male and Female, NR, 100-110g	NR	PS = Polystyrene particles PSC = Polystyrene particles, Carboxylate modified PSA = Polystyrene particles, Amine modified	Intratracheal Instillation	5, 50 or 500 μg/animal; 0.05, 0.5, 5 mg/kg	PS, PSC, PSA-60 = 60nm PSA-400 = 400nm	single, 10 min post-exposure Rose Bengal administered to induce thrombosis, immediate study thereafter	Thrombosis: Only PSA-60 at 50 and 500 levels enhanced thrombus formation but not dose-dependently. At 500 μg, PSA-60 showed evidence of pulmonary thrombosis. No effect with PSA-400. BALF Cells: Both PSA-60 and PSA-400 (PSA-60>PSA-400) induced massive influx of PMNs. PSA-60 effect may exhibit some dose-dependency. BALF Inflammatory/Injury Markers: Small increases in total protein were seen at 500 μg level for both PSA-60 and PSA-400. LDH was increased at all PSA-60 levels but not for 500ug PSA-400. Histamine increased for all PSA-60 levels and PSA-400 but due to high variability only effect at 500 μg PSA-60 statistically significant. Hematology: PSA-60 and PSA-400 had effect on platelet closure time at very low concentrations: 3 and 9 μg/l respectively and plateaued from thereon.
Nemmar et al. (2003c) Hamsters, NR, NR, 100-110g	NR	DEP = SRM 1650	Intratracheal Instillation	50 μg/animal bw NR	NR	single, 1, 3, 6 or 24 h	BALF Cells: DEP led to significant PMN flux at 1-h (13% of total cell number), 6 h (22%) and 24-h (37%). Thrombosis: DEP induced significant increase in cumulative mass of in vivo generated thrombus comparatively to control subjects. Hematology: No decrease in platelet count. Consistent (non time-dependent) decrease in closure time signifying increased platelet activation for DEP-exposed groups. Histamine: Concentrations in BALF were consistently elevated starting at 1 h. Plasma histamine did not increase until 6 h. Pretreatment with histamine receptor antagonist: Major decrease in DEP induced PMN infiltration. Thrombogenicity was decreased after 6 h as was closure time shortening. No effect on histamine in BALF or plasma.
Pereira et al. (2007) Rats, Male, Wistar, 3mo	NR	Ambient Particles (Porto Allegre, Brazil)	Whole-body Inhalation	P-6: 34, 22 or 225 μg/m^3 P-20: 139 or 112 μg/m^3 P-I: 99 μg/m^3 bw NR	<10um	P-6: single for 6h P-20: single for 20h P-I: 5h/d for 4d consecutively 0 or 24 h post-exposure	BALF Inflammatory/Injury Markers: Increase lipid peroxidation p-20 >P-I >P-6 = control. Only P-20 statistically significant. Leukocytes increased at P-20. No change at P-6. Total protein unaffected at all dose levels. Wet to Dry Ratio (0h): No effect.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Pires-Neto, R.C. Lichtenfels, A.J. Soares, S.R. 2006 Mice, Male, Swiss, 6d	40, 20, 20	Ambient Air = $PM_{2.5}$, NO_2 and CB (Sao Paulo, Brazil)	Whole-body Inhalation	$PM_{2.5}$ = 46.49 μg/m^3 Control = 18.62 μg/m^3 NO_2 = 59.52 μg/m^3 Control = 37.08 μg/m^3 CB = 12.52 μg/m^3 Control = 0 μg/m^3 bw NR	NR	5mo (weaned at 21d into exposure - mothers removed)	Nasal Cavity: Increased total mucus and acidic mucus at proximal and medial areas of cavity. Nonsecretory epithelium declined. No significant changes in amount of neutral mucus, volume proportion of neutral mucus, volume proportion of total mucus, thickness of epithelium, volume proportion of nonsecretory epithelium or ratio between neutral and acidic mucus. Types of Acidic Mucus Cells: Proximal and medium cells increased. Effects on distal cells equivocal.
Pourazar, J. Mudway, I.A. Samet, J.M. 2005 Humans, 11 Males and 4 Females, nonatopic and nonsmokers, 21-28y	NR	DEP (from idling Volvo diesel engine) Filtered Air (control)	exposure chamber	DEP 300 μg/m^3 NO_2 1.6ppm NO 4.5ppm CO 7.5ppm Hydrocarbons 4.3ppm Formaldehyde 0.26mg/m^3 Suspended particulates 4.3x10^6/cm^3 bw NR	<10um	single for 1h, 6h	Transcription Factors: Increased cytoplasmic and nuclear immunoreactivity of phosphorylated p38 MAPK in bronchial epithelium. Increased nuclear translocation of phosphorylated p38 and JNK MAPK. Increased nuclear phosphorylated tyrosine immunoreactivity. No change in total or nuclear c-fos immunoreactivity. Increased nuclear translocation of phosphorylated JNK significantly associated with phosphorylation of nuclear c-jun and increase in nuclear p65. Cytokines: Expression of IL-8 positively associated with nuclear phosphorylated p38 post-exposure.
Pradhan, A. Waseem, M. Dogra, A. 2005 Rats, Female, Wistar Albino, 120-180g	25, 12, 13	RSPM = Respirable Suspended PM (Lucknow, India) Quartz dust (positive control) Saline (negative control)	Intratracheal Instillation	2.5, 5.0, or 10.0mg/ 0.05ml; 20, 42, 83 mg/kg	<5um	Single, 15d	Relative Lung Weight: Dose-dependent increase in total lung weight of RSPM-instilled animals. BALF Cells: Increase in total cells dose-dependent with low and mid dose levels. PMNs increased massively at all dose levels with RSPM <Quartz. Exposure at low dose level resulted in influx of inflammatory cells, predominantly macrophages into lumen of alveolar ducts and alveoli. Reaction at high dose more intense than that seen in mid dose-exposed lungs. BALF Inflammatory/Injury Markers: Significant dose-dependent increase in LDH and NO but Quartz >RSPM. Increase in protein significant at mid dose level for RSPM and high dose level for both RSPM and Quartz. Lung biochemistry: Increase in lipid peroxidation dose-dependent. Superoxide dismutase (SOD) enzyme levels showed dose-dependent decrease.
Rao, K.M.K. Ma, J.Y.C. Meighan, T. 2005 Rats, NR, Sprague-Dawley, 175g	24, 16, 8	DEP = SRM 2975	Intratracheal Instillation	5, 35, 50 mg/kg	0.5um	single, 1, 7, 30d	BALF Inflammatory/Injury Markers: Increased albumin at 1 and 30d at all dose levels. Increased LDH except at low dose at 7d. BALF Cells: Macrophages unaffected. Increased PMNs at 1d for all dose levels, sustained elevation at 7d for mid and high dose and at 30d for all dose levels. Cytokines: High dose induced significant increase of mRNA expression for IL-1β, iNOS, MCP-1, and MIP-2 in BAL cells. MCP-1 mRNA sustained high level at 7d for mid and high dose and at 30d for all dose levels. mRNA expression of IL-6, IL-10, TGF-β1, TNF-α unaffected. However, IL-6 and MCP-1 proteins increased significantly in BALF at 1d for mid and high dose, returning to basal levels at 7d. MIP-2 increased for all dose levels at all time points. NO level unaffected.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Reed et al. (2006) Rats, Male and Female, CDF (F344)/CrlBR and SH, 6-12wks Mice, Male and Female, A/J and C57BL/6, 6-12wks	860, 688, 172	HWS (burned mix of hardwood in noncertified wood stove (Pineridge model 27000, Heating and Energy Systems, Inc. Clackamas, OR)	Whole-body Inhalation	Low: 30 μg/m^3 Mid-low: 100 μg/m^3 Mid-high: 300 μg/m^3 High: 1000 μg/m^3 bw NR	~0.25um Measured **Components:** EC, OM, NO_3, SO_4, NH_4, metals	6hr/d, 7d/wk for 1wk or 6mo Immediate post-exposure	Organ weights: Liver declined in rats of both genders at 1 wk and female rats at 6mo. Lung volume increased and lung weight decreased in female rats at 6mo. Spleen weight increased in female mice and rats at 1wk. Thymus weight decreased in male rats at 1wk. Clinical Chemistry: Cholesterol decreased at high dose for male rats at 1wk and 6mo and increased at mid-low and mid-high doses for female rats at 6mo. ALP decreased for rats of both genders at 1wk and 6mo for mid-low, mid-high and high dose levels (14-38%). AST decreased by 24% in male rats at 1wk with high dose. No effect on females. Creatinine serum levels decreased in males at 1wk at mid-high and high dose by 13%. No effect observed at 6mo. BUN/Cre ratio decreased in females at 1wk (25%) and both genders at 6mo at mid-high and high dose (18-19%). Hematology: Hemoglobin and hematocrit increased in 6mo male rats. Bilirubin increased in female rats at 6mo at high dose. Platelets increased for male and female rats at 1wk (21%, 19% respectively). No effect observed at 6mo. WBC increased in males at 1wk. Cells: Eosinphils decreased and lymphocytes increased in males at 6mo. Neutrophils decreased at 6mo in both genders. Minimal increases in alveolar macrophages and sparse brown-appearing macrophages in all species. Bacterial Clearance: Mice instilled with bacteria largely mostly unaffected by exposure, except for decline in histopathology summary score after 6mo. Tumorigenesis: No values for exposed groups differed significantly from controls. No evidence of progressive exposure related trend.
Reed et al. (2004) Rats, Male and Female, CDF (F344)/CrlBR, 12wks Mice, Male and Female, A/J, 12wks	640, 512, 128	DE (two 2000 model 5.9 L Cummins ISM turbo diesel engines) Co-expoure to 8 gas and 8 solid exhaust components measured	Whole-body Inhalation	Low: 30 μg/m^3 Mid-low: 100 μg/m^3 Mid-high: 300 μg/m^3 High: 1000 μg/m^3 bw NR	0.10 - 0.15um	6h/d, 7d/wk for 1wk or 6mo 1d post-exposure	Organ weights: Increased kidney weight after 6 mo for both males and female rats at high dose. Increased kidney and liver for female mice at all dose levels at 6mo. Lung weight increased at high dose at 6mo for female mice and male rats. Spleen weight decreased in male mice at low and mid-high levels. Clinical Chemistry: Massive decrease in cholesterol (24%) for rats of both genders after 1wk and smaller decrease for male rats at 6mo. GGT significantly increased at 6mo for male and female rats at mid-high and high dose. ALP increased in male rats at 1 wk by 10%. AST decreased at mid-high (15%) and high dose in female rats at 6mo. BUN and BUN/Creatine declined (19%, 17%) in female rats at mid-high and high doses after 6 mo. BUN increased by 21% at mid-low, mid-high and high doses in male rats at 1wk. Hematology: WBC decreased in high females after 6 mo. Factor VII (blood clotting) decreased in MH and HR males after 1 wk and male and female HR after 6 mo. Thrombin-antithrombin complex declined massively but only in males after 1 wk. Cells: Minimal increases in alveolar macrophages and PM within the macrophages. Cytokines: Decreases in TNF-α in female rats after 6mo. Tumorigenesis: No significant effect.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Rengasamy et al. (2003) Rats, Male, Sprague-Dawley, ~200g	NR	DEP = SRM1650 CB (Elftex-12 furnace black, Cabot, Boston, MA)	Intratracheal Instillation	5, 15, or 35 μg/kg	NR	single; 1, 3, 5, 7d post exposure	CYP1A1: DEP at all doses significantly increase CYP1A1 protein, maximal at 1d, normalized at 5d. CB had no effect. CYP2B1: DEP and CB at 15 and 35 mg/kg inhibited activity at 1 day. Protein level significantly decreases at 1 day with DEP at 5, 15 and 35 mg/kg doses and CB at 15 and 35 mg/kg doses. Time dependence decrease shown at 35mg/kg dose for both DEP and CB.
Renwick, L.C. Brown, D. Clouter, A. 2004 Rats, Male, Wistar, 370-470g	NR	FCB = Fine Carbon Black (Huber 990) UCB = Ultrafine Carbon Black (Printex 90, Degussa) FTO = Fine Titanium Dioxide (Tioxide) UTO = Ultrafine Titanium dioxide (Degussa)	Intratracheal Instillation	125 or 500 μg/rat bw NR	FCB = 260nm; 7.9 m^2/g UCB = 14nm; 254 m^2/g FTO = 250nm; 6.6 m^2/g UTO = 29nm; 50 m^2/g	single, 24 h	BALF Cells: UTO and UCB induced large dose-dependent increase in % neutrophils (only statistically significant at 500 μg for UTO). BALF Inflammatory/Injury Markers: UTO and UCB also increased total protein content only at 500 μg dose. UCB induced LDH release at 125 and 500 μg, UTO and CB at 500 μg. UTO and UCB induced large dose-dependent increase in GGT activity (only statistically significant at 500 μg for UTO). Phagocytosis: Decrease for all 4 particles but only at 500 μg level. Chemotaxis: Only UTO and UCB at 500 μg/l increased chemotactic migration.
Rhoden et al. (2004) Rats, Male, Sprague-Dawley, 250-300g	NR	CAPs (Boston, MA) Filtered Air (control)	Whole-body Inhalation	1060 ± 300 $\mu g/m^3$ bw NR CAPS-NAC = CAPS with 50mg/kg bw NAS (N-acetylcysteine) pretreatment	0.1<CAPS<2.5 μm See Pulmonary Effects	single 5h, 24 h	Particle Characteristics: Major components did not appear to show any correlation to total particle mass. Included Na, Mg, Al, Si, S, Cl, K, Ca, Ti, V, Cr, Mn, Fe, Ni, Cu, Zn, Br, Ba, Pb. Metals Al, Si and Fe (somewhat less for Pb, Cu, K) correlated with TBARS. Oxidative Stress: CAPS increased TBARS and oxidized protein by over 2 fold. NAS fully prevented increase in TBARS and partially prevented increase in protein carbonyl. Tissue Damage: Wet/dry ratio increased with CAPS but significantly decreased with NAC. BALF Cells: CAPS increased PMN 4 fold. NAS reduced to control levels. BALF Inflammatory/Injury Markers: LDH and total protein not affected. Histology confirms slight inflammation with CAPS and no inflammation with CAPs-NAC.
Rivero, D.HR.R.F. Soares, S.R.C. Lorenzi-Filho, G. 2005 Rats, Male, Wistar, 3mo, 250g	38, NR	Ambient Air (Sao Paulo, Brazil) Distilled H_2O (control)	Intratracheal Instillation	100 or 500 μg/rat; 0.4 or 2 mg/kg	<2.5um	single, 24 h	Hematology: Reticulocytes increased at both doses. At high dose, hematocrit, % segmented, % neutrophils increased and % lymphocytes decreased (relative to control or 100 - very high variability). Fibrinogen decreased at low dose but not at high dose. Histopathology: At both doses, acute alveolar inflammation, apparently more pronounced in 500 μg group. Lung Morphometry: Lumen wall ratio values shows dose-dependent increase in peribronchial as well as intra-acinar pulmonary arterioles. No effect in myocardial arterioles. Tissue Damage: Increase in heart wet/dry ratio at high dose. Lung wet/dry ratios unaffected.
Roberts, E.S. Charboneau, L. Espina, V. 2004 Rats, Male, Sprague-Dawley, 60-90d, 300-350g	NR	ROFA = SRI (cyclone power plant) Saline (control)	Intratracheal Instillation	0.5 mg/rat; 1.67mg/kg	NR	Single, 6 and 24 h	Technology: Laser capture microdissection of airway cells used to analyze results. Protein: pERK1/2: ERK1/2 ratio increased by 60% at 6h and 80% at 24 h. NFkB activity increased at 6h but not statistically significant.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Saber, A.T. Bronholdt, J. Dybdahl, M. 2005 Mice, Female, TNF(-/-) (B6, 129S-Tnftm1Gk1), 9-10wks Mice, Female, C57/BL (control), 9-10wks	NR	DEP = SRM 2975 CB = Carbon Black - Printex 90 (Degussa) Filtered Air (control)	Nose-only Inhalation	DEP = 20 mg/m^3 CB = 20 mg/m^3	DEP = 215nm -surface area 90 m^2/g -pyenometric particle density 2.2 g/cm^3 CB = 90nm -surface area 295 m2/g -pyenometric particle density 2.1 g/cm^3	90min/d for 4d consecutively, 1h	BALF Cells: Neutrophils increased significantly to 15% vs control (4%) with DEP exposure. No response difference between TNF (+/+) and TNF(-/-) observed. CB induced statistically insignificant increase in neutrophils. Cytokines: IL-6 increased 2-3 fold in DEP and CB exposure in both normal and knockout mice. IL-1β unaffected. mRNA: In TNF (+/+) mice, DEP and CB increased expression of TNF mRNA 2 fold. IL-6 mRNA expression high in DEP-exposed knockout mice than normal. DNA: DNA strand breaks increased in both strains. Knockout mice showed higher response to CB and DEP exposure. In normal mice only CB induced statistically significant effect.
Schins, R.P.F. Lightbody, J.HR. Borm, P.J.A. 2004 Rats, Female, Wistar, 350-550g	25, 20, 5	Soluble fractions PMC = $PM_{10-2.5}$ PMF = $PM_{2.5}$ -B = Borken, Germany (rural) -D = Duisburg, Germany (industrialized)	Intratracheal Instillation	0.32 ± 0.01 mg/rat; 0.91± 0.58 mg/kg	See Pulmonary Effects	single, 18h	Particle Characteristics: Measure metal levels: Cu: PMC-B = PMC-D; PMF-B = PMF-D PMF> = PMC Fe: PMC-B>PMC-D; PMF-B<PMF-D; PMF>>PMC V: PMC-B = PMC-D; PMF-B = PMF-D Ni: PMC-B>PMC-D; PMF-B<PMF-D; Cr: PMC-B = PMC-D; PMF-B = PMF-D; PMF>>PMC Al: PMC-B>PMC-D; PMF-B> = PMF-D; PMF>>PMC Radical Formation: Formation of hydroxl radicals increased with exposure. Relative intensity follows: PMC-D>PMF-D>PMC-B> = PMF-B>>control Cytokines: TNF-α and IL-8 increased with PMC from both sites. PMF induced slight increased in IL-8, no increase in TNF-α. BALF cells: Both PMC showed massive increase in neutrophils: PMC-B>PMC-D; PMF no effect BALF Inflammatory/Injury Markers: PMC from both sites induced markedly higher endotoxin concentration vs PMF as follows: PMC-B>PMC-D>>PMF-B>PMF-D> = control. Glutathione decreased only for PMC-B. LDH and total protein unaffected.
Seagrave et al. (2005a) Rats, Male, F344/Crl BR, 11±1 wk	NR	PM from 3 sources: NT = New Technology bus, Detroit Diesel 50G, exhaust oxidation catalyst, 216 miles, 2002 model - in use NE = Normal emitter bus, Detroit Diesel 50G, no catalyst, 134259 miles, 1997 model - in use HE = High Emitter bus, Cummins L10G, no catalyst, >250, 000 miles, 1992, retired SRM2975 (NIST) positive control	Intratracheal Instillation	0.25 - 2.2 mg/rat bw NR	NR Fuel composition very similar for 3 vehicles: methane (96-96.8%), ethane (1.6-1.9%), carbon dioxide (0.9-1.1%), nitrogen (0.6-0.8%), traces of other gases	single, 24 h	Engine Specific Emission data: PMs: HE>>>NT = NE SVOC: HE>>NE>NT Organic mass in PM: HE>NE>NT Total PAH: HE>NT>NE<control Nitro PAH: NE>HE>NT<control Authors note confounding technical issues (mostly technique related) with mostly mild effects. BALF Inflammatory/Injury Markers: LDH dose-dependent increase HE>>NT = NE. Total protein dose-dependent increase HE = NT = SRM2975>NE Emission Volume HE>>>NT = NE or Mass based SRM 2975>HE>NT>NE. Potency Factors Cytotoxicity and Inflammation: HE>>>NT> = NE. Lung Toxicity: Highly variable but NE <NT < = HE< = Normal gasoline <diesels <high gasolines - individual factors may differ greatly.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Seagrave et al. (2006) Rats, Male, F344/Crl BR, 11±1 wk	NR	$PM_{2.5}$ sources: BHM = Birmingham, Alabama; urban JST = Jefferson Street, Atlanta, Georgia; urban PNS = Pensacola, Florida; urban/residential CTR = Centreville, Alabama; rural "smoke" = downwind of forest fires/burns (NR) SRM 2975 positive control	Intratracheal Instillation	0.75, 1.5, 3 mg/rat bw NR	NR	single, 24 h	BALF Total cells and PMN: Winter>summer except for PNS where Winter, summer. Winter: JST>BHM>CTR> = PNS = SMOKE summer BHM> = JST = PNS> = CTR BALF macrophages: Winter: JST = BHM = CTR> = PNS> = smoke summer: JST = BHM = CTR = PNS >control BALF lymphocytes: Winter: JST> = BHM> = CTR = PNS> = smoke summer: BHM> = JST> = CTR = PNS Histopathological Inflammation: Winter: JST> = BHM = CTR = PNS> = smoke summer: BHM = CTR = PNS> = JST Lung weight/body weight ratio: Winter: JST>BHM = CTR = PNS = Smoke summer: BHM = CTR = PNS = JST = control Winter potency JST always highest. summer BHM and CTR are general higher.
Seagrave, J. McDonald, J.D. Reed, M.D. 2005 Rats, Male and Female, CDF(F-344)/CrlBR, 10-12wks	NR	DE (Two 6 cyl Cummins ISB turb0) HWS = hardwood smoke (mixed black/white oak, uncertified conventional wood stove)	Whole-body Inhalation	30, 100, 300, 1000 μg/m³ TPM HWS: EC = 43 OC = 908 μg/m³ NO or NO_2 = 0 ppm CO = 13 ppm THV = 3 ppm DE: EC = 557 OC = 269 μg/m³ NO = 45 ppm NO_2 = 4 ppm CO = 30 PPM THV = 2 ppm bw NR	DE = 0.14 ±1.8 μm HWS = 0.36 ± 2.1 μm (MMAD + GSD See Pulmonary Effects	6h/d, 7d/wk for 6 mo 1d post-exposure	Particle Characteristics: Major differences K: HWS>>DE; Ca DE>>HWS; Zn: DE>>HWS. BALF Inflammatory/Injury Markers: LDH unaffected by DE. HWS increased at 100 and 300 but not at 1000 for males only. Protein unaffected by DE and HWS showed male only effects at 100 and 300 μg/m³ but not at 1000. AP unaffected by DE or HWS except for slight decline for HWS at 1000 for both genders. Other: β-glucose unaffected by DE. HWS females decrease at 100, 300 but not at 1000. BALF GSH to (GSH+GSSG): No effects for DE. HWS decreased ratio in both males and females significantly at 1000 μg/m³. Female effect>male. BALF Cells: No effects except for increase in macrophages at 30 μg/m³ for HWS males. Cytokines: IL-1β unaffected by DE or HWS. MIP-2 decreased for both genders at 1000 HWS. TNF-α decreased in females with DE exposure. No effects for HWS.
Singh, P. DeMarini, D.M. Dick, C.A.J. 2004 Mice, Female, CD-1, 6-8wks	NR	A-DEP (4cyl light duty 2.7l Isuzu diesel at 6 kg/m) DEP = SRM 2975 Endotoxin (positive control) Saline (negative control)	Oropharyngeal Aspiration	25 or 100μg/mouse bw NR 10μg/mouse endotoxin (control)	A-DEP >50 μm See Pulmonary Effects	single, 4h (18h post-exposure measurements taken but NR due to similar results)	Particle Characteristics: SRM 2975 had 60% EC vs 9% in A-DEP. A-DEP had 50% OC vs 5% in SRM 2975. Phenanthrene and Fluoranthene fractions were much more prevalent in PAH from SRM 2975 than A-DEP BALF Inflammatory/Injury Markers: Microalbumin increased for both except SRM 2975 only at 100 μg. Endotoxin increased microalbumin. NAG increased with 100 μg A-DEP. BALF Cells: PMNs significantly increased dose-dependently with SRM 2975 and remained elevated at 18h. Increase greatest with endotoxin. Macrophages increased with A-DEP and unaffected by SRM 2975. Cytokines: Endotoxin massive response for IL-6, MIP-2 and TNF-α. No response from IL-5. A-DEP increased all 4 cytokines but only at 100ug dose level. SRM 2975 only increased IL-6 at 100ug dose level.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Smith, K.R. Kim, S. Recendez, J.J. 2003 Rats, Male, Sprague-Dawley, 11-12wks	NR	CAPs (Fresno, CA)	Whole-body Inhalation	6 exp in 2 sets of 3 Fall1 = 847 μg/m^3 Fall2 = 260 μg/m^3 Fall3 = 369 μg/m^3 Winter1 = 815 μg/m^3 Winter2 = 190 μg/m^3 Winter3 = 371 μg/m^3 bw NR	<2.5um See Pulmonary Effects	4h/d for 3d consecutively, Immediate	Particle Characteristics: Nitrate shows highest variability near 10 fold, followed by Si, S and EC. OC concentration relatively consistent. Metals otherwise appear proportionate to concentrations. BALF Cells: Total cells increased at wk1. % of macrophages reduced in wk2 with CAPs. Number of neutrophils increased with CAPs, only statistically significant during wk1 of fall and winter. Lymphocytes increased but statistically insignificance. BAL cell permeability increased 242% but not related to dose: Fall2>Fall1 = Fall3 = Winter3>Winter1 = Winter2
Smith, K.R. Veranth, J.M. Kodavanti, U.P. 2006 Rats, Male, Sprague-Dawley, 8wks, 260-270g	48	CFA = Coal Fly Ash (400 MW, Wasatch Plateau, Utah) (aerodynamic separation)	Nose-only Inhalation	1400 μg/m^3 $PM_{2.5}$ including 600 μg/m^3 PM_1 bw NR	0.4<CFA<2.5 μm	4h/d for 3d consecutively, 18 or 36h post-exposure	BALF Cells: Percent and total number of neutrophils in BALF and blood increased significantly at both 18 and 36h. Percent of macrophages decreased slightly while number of macrophages increased in bronchiole-alveolar duct regions at both time periods. Cytokines: MIP-2 and transferrin increased at 18h. IL-1β increased at 36h. Hematology: Plasma protein increase at 18h. Lymphocyte and hematocrit percentage decreased at 36h. Other: Gamma glutamyl transferase decreased at 36h. Lung antioxidant increased at 18h.
[FROM Table D-4] **Reference:** Song et al. (2008) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 5-6 weeks		DEP collected from a 4JB1-type, light-duty (2740 cc), four-cylinder diesel engine operated using standard diesel fuel at speeds of 1500 rpm under a load of 10 torque. DEP Composition: Previously reported mean diameter of 0.4 μm	Intranasal Instillation for the first 5 days and Whole-body Exposure Chamber on days 6-8 5 Days of intranasal instillations of: 0.6 mg/mL in 50 mL of saline. 3 Days of 6 mg/m^3 DEP for 1-h in Whole-Body Inhalation Chamber.	0.6 mg/mL DEP were administered intranasally in 50 μL of saline for days 1-5. On days 6-8 mice were exposed to DEP through whole-body inhalation chamber at doses of 6 mg/m^3 for 1 hour. Enhanced Pause (Penh), a marker for airway obstruction, was measured on day 9. BAL and lung tissues were collected on day 10.			Airway Hyper-Responsiveness: (measure of Penh) Intranasal exposure plus aerosolized DEP caused a significant increase in methacholine-induced Penh over the control. BAL Fluid Analysis: There was no significant increase in IFN-γ in BAL fluid following DEP treatment but there was a significant increase in IL-4 levels compared to the control. (IL-4 increase could indicate that DEP modulates Th-2 cytokines in the mouse model). DEP also induced an increase in total neutrophils and lymphocytes in the BAL when compared to the control. Also the nitrite concentration in BAL (indicating NO generation) was significantly greater in the DEP exposed group than the control. Histological Assessment: Peribronchial and perivascular infiltrates were more common in the group exposed to DEP than the control. Ym1 and Ym2 Expression: (see explanation in comments section) Ym1 and Ym2 transcripts were upregulated in response to DEP exposure in mice.
Steerenberg et al. (2006) Rats, NR, Crl/WKY, NR	NR	Ambient air samples PMC = Pm Coarse PMF = PM Fine -I = Rome, Italy -N = Oslo, Norway -PL = Lodz, Poland -NL = Amsterdam, Netherlands	Intratracheal Instillation	1 and 2.5 mg/animal bw NR	2.35 <PMC<8.5um 0.12 <PMF<2.35um Measured **Components:** Li, Be, B, Na, Mg, Al, K, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Sr, Mo, Cd, Sn, Sb, Ba, Ce, Nd, Sm, Au, Hg, Tl, Pb, Bi, U, Si, Endotoxins, Cl, NO-, SO_4	Single, 24 h	Particle Characteristics: Concentrations of metals highest in Rome. Amsterdam noted for high Mg and V. Lodz noted for high Pb, Zn, PAH. PMC composed more of Fe, Mn, Al, Cr, Cu. PMF composed more of Zn, Pb, Ni, V. BALF Inflammatory/Injury Markers: CC16 decreased substantially. Crustal material (endotoxin, Na, Cl and metals but not Ti, As, Cd, Zn, V, Ni, Se) positively associated with short term CC16. Albumin increased. Cytokines: MIP-2 increased dose-dependently. TNF-α also increased. BALF Cells: PMNs increased.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Stinn, W. Teredesai, A. Anskeit, E. 2005 Rats, Male and Female, Crl: (WI)WU BR, 40d	NR, 594, NR	DE (generated from 1.6 L VW diesel under USFTP 72)	Nose-only Inhalation	3 and 10 mg/m^3 CO = 10 and 37 ppm CO_2 = 2170 and 6540 ppm NO = 7.0 and 22.8 ppm NO_X = 8.6 and 28.3 ppm SO_2 = 0.83 and 3.09 ppm NH_4 = ND bw NR	3 mg/m^3: MMAD = 0.19 µm GSD = 1.86 10 mg/m^3: MMAD = 0.21 µm GSD = 1.91 Measured Major **Components:** NO, SO_2, 1-nitropyrene, Zi. 50% by DE weight is elemental carbon.	6h/d, 7d/wk for 24mo; 6 mo post-exposure	**Body Weight:** Mean weight increased substantially during first few wks in all groups. Food consumption decreased in 1-24mo but recovered in 24-30mo, whereas body weight decreased at 23mo in all categories, but recovered except high dose males at 30mo. Organ Weight: Absolute weight of lungs, larynx and trachea increased from 0 to 12 to 24mo and stayed elevated at 30 mo: Low<Hi, male ~ female. Pulmonary Parameters: Respiratory frequency, tidal volume, minute volume unaffected in any group measured between 3 and 24mo. Elemental carbon increased dose-dependently in exposure groups. No male/female difference, but 24 mo>18 mo. BALF Cells: PMNs and lymphocytes showed dose and time-dependent effects at 18 and 24 mo (no data at 30 mo). Lymphocytes increased 50 fold in high dose males at 24mo. Peripheral monocytes and neutrophils increased 3 fold in DE groups at end of study. Particle-filled macrophages in alveolar lumen and interstitium increased at 12, 24, 30mo in both genders at all dose levels. BALF Inflammatory/Injury Markers: LDH increased in dose and time-dependent manner. Hematology: Erythrocytes unaffected (12, 24, 30) except high dose females at 24 and 30. Hemoglobin and hematocrit increased dose-dependently with no gender differences. Leukocytes increased in doe and time-dependent manner. Nasal Cavity Histopathology: all effects resolved at 30 mo. Nasal cavity hyperplasia increased at high dose 12 and 24mo in both genders. Squamous metaplasia of respiratory epithelium increased in high dose females (12, 24mo). Larynx Histopathology: No effects. Lung Histopathology: Alveolar region hyperplasia of alveolar epithelium increased at 12, 24, 30mo in both genders at all dose levels except for 12mo low dose males and females. Above lung histopathology not time-dependent, perhaps some small dose-dependency. Following histopathology findings strongly dose and time-dependent increases and increased from 24-30 mo in both genders: goblet cell hyperplasia of bronchial epithelia, cuboidal/columnar hyperplasia of alveolar epithelium, chronic active inflammation and septal fibrosis. Tumorigenicity: Lung tumors more prevalent in females than males and appeared to be dose-dependent. Major 3 types: bronchio-alveolar adenoma, bronchiolo-alveolar adenoma and benign keratinizing cystic cell tumors. Enhanced effects in female vs males may be result of enhanced metabolism (body volume vs bw) and increased repiratory volume/bw for females.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Sureshkumar et al. (2005) Mice, Male, Swiss, 10-12wks, 20-25g	24, 18, 6	GE = Gasoline Exhaust (Honda generator EBK 1200, four stroke one cyl)	Nose-only Inhalation	0.635 mg PM/m^3 Including: SO_2 = 0.11 mg/m^3 NO_X = 0.49 mg/m^3 CO = 18.7 ppm bw NR	GE >4 µm = 34.1 % 3-4 µm = 15.8 % 2-3 µm = 15.8 % 1.5-2 µm = 10.6 % 0.5-1.5 µm = 5.3 % <0.5 µm = 18.4 %	15 min/d 7, 14 or 21d, less than 1-h post-exposure	Cytokines: GE caused time-dependent increase in TNF-α and IL-6. IL-10 and IL-1β unaffected. BALF Inflammatory/Injury Markers: y-GGT, ALP and LDH increased after 2wks of GE exposure and stayed stable at 21d. Total protein slightly increased on 14 and 21d, statistically insignificant. BALF Cells: Neutrophils (%) increased at 7, 14 and 21d (stable). Total cell count, macrophages and eosinophils unaffected. Leukocytes and lymphocytes increased insignificantly. Histopathology: Time-dependent increase: minor changes at 7d, mild edema in alveolar region at 14d and sloughing of epithelial cell in bronchiolar region and focal accumulation of inflammatory cells in alveolar region at 21d.
Tin-Tin-Win-Shwe Yamamoto, S. Ahmed, S. 2006 Mice, Male, BALB/c, 7wks	NR	CB14 = Printex 90 (Degussa) CB90 = Flammruss 101 (Degussa)	Intratracheal Instillation	25, 125, 625 µg/mouse; approx. 1, 5, 25 mg/kg	CB14 = 14nm CB95 = 95 nm	1/wk for 4wks, 4h (mRNA expression in lungs and mediastinal lymph nodes), 24 h	Body weight, thymus, spleens, splenic cell count: No effects BALF Cells: Increased total cell number for 125, 625ug CB14 (dose-dependent) and 625ug CB95. Count twice as high for CB14 at 125 and 625 µg compared to CB95. Dose-response for AM numbers for both CB14 and CB95 except at 125ug. Lymphocyte numbers increased at 125 and 625ug for CB14 and 625ug for CB95. PMN numbers increased at 125 and 625ug for CB14 and CB95, but response greater with CB14. PMN numbers proportional to dose surface area for both PM sizes. BALF Cytokines: Dose-dependent increase for CB14 and CB95 in IL-1β. TNF-α increased at 125 and 625ug dose in CB14 and 125 dose is slightly greater. CCL-3 increased for CB14 and CB95 at 125 and 625ug doses. Chemokine mRNA in lung and lymph nodes: CCL-3 mRNA increased for CB14 but not CB95 4h following the last exposure. CCL-2 unchanged. Mediastinal lymph nodes: Number of CB-laden phagocytes increased in dose-dependent manner for CB14 and CB95. CB14 had higher numbers at all doses compared to CB95.
Tong, Y. Zhang, G. Li, Y. 2006 Mice, Male, KP600 CD-1, 22-26g	36, 30, 6	$PM_{2.5}$ (Shanghai, China) Fe = $FeSO_4$ Zn = $ZnSO_4$ PMF = $PM_{2.5}$ + $FeSO_4$ PMFZ = $PM_{2.5}$ + $FeSO_4$ + $ZnSO_4$ Saline (control)	Intratracheal Instillation	PM = 25 mg/mL, 1 mg/mouse Fe = 15 mg/mL, 0.6 mg/mouse Zn = 15 mg/mL, 0.6 mg/mouse PMF = PM 25 mg/mL + Fe 15 mg/mL, 1.6 mg/mouse PMFZ = PM 25 mg/mL + Fe 15 mg/mL, 1.6 mg/mouse bw NR	NR Major Measured **Components:** Fe 26 ppm, Zn 9 ppm, S 61 ppm	Twice (24 h apart), 48h in vivo microradiography post-exposure, then dissection	Synchrotron X-ray imaging (in vivo): PMFZ shows greatest increase in alveolar changes; Fe induced more hemorrhagic changes, Zn induced more nonuniformity of lung texture. Suggests Zn induces PBMC in dose-dependently manner which releases IL-1, IL-6, TNF-α, IFN-y. Histopathology: PMFZ induced most severe changes including serious inflammation/pus in bronchia and bronchial epidermal cell hyperplasia. For Fe or PMF hemorrhagic changes predominated but less severe than PMFZ.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Wallenborn, J.G. Schladweiler, M.C. Nyska, A. 2007 Rats, Male, WKY, SHRWKY and stroke-prone SH (SHRSP), 12-15wks	NR	PM = precipator unit power plant residual oil combustion Saline (control)	Intratracheal Instillation	WKY vs SHRSP: 1.11, 3.33, 8.33 mg/kg SH vs SHRSP: 3.33, 8.33 mg/kg	PM = 3.76um (bulk) ± 2.15	WKY vs SHRSP: single, 24 h SH vs SHRSP: single, 24 h Note: 4h post-exposure study done on WKY vs SHRSP but not published.	BALF Cells: Dose-dependent increase in total cells and neutrophils. Equal response for all 3 strains except for SH where both concentrations gave more or less identical results. BALF inflammation/Injury Markers: LDH dose-dependent increase in equal response for all 3 strains. NAG had inconsistent results at 3.33 mg/l between experiments all respond at highest concentration: WKY>SHRSP>SH. GGT had dose-dependent response for all 3 strains with SHRSP>WKY> = SH. Protein induced at high dose level with SHRSP>SH>WKY. Albumin inconsistent between experiments. Oxidative Stress - Lung: (WKY vs SHRSP only): SOD decreased upon exposure SHRSP>WKY. Ferritin only SHRSP declined. Oxidative Stress - Cardiac: SOD increased in SHRSP vs WKY experiment only otherwiseSHR = WKY = SHRSP. GPx**:** No action but SHRSP = SH>WKY Ferritin: Equivocal - Decreased at high level for WKY and SHRSP but increased at medium level for SH and SHRSP. ICDH: Increased for WKY and decreased for SHRSP.
Wichers, L.B. Nolan, J.P. Winsett, D.W. 2004 Rats, Male, SH, 75d	NR	PM (HP-12) = inside wall of stack of Boston, MA power plant burning # 6 oil.	Intratracheal Instillation	0.83, 3.33 or 8.33 mg/kg	PM = 3.76 µm ± 2.15	single, 6h for whole body plethysmographs (WBP) and repeated daily for 4-7d, 96 or 192h post-exposure non-WBP animals: single, 24, 96, 192h post-exposure	Tidal Volume: Dose-dependent decrease in tidal volume (45 % at high dose) sustained for 1d with very slow recovery over 7d. Breathing frequency: Dose-dependent increase (100 % at high dose) with recovery at 7d. Minute ventilation: Small dose-dependent increases returning to normal in 2d. Penh (enhanced pause): Equivocal results in all groups(due to major control variation). BALF Cells: Dose-dependent increase in total cells at 24 h, declined, though still elevated, at 192h. Neutrophils increase significantly at 24 h in mid and high dose groups (10 fold), declined, though still elevated, at 192h. Macrophages slowly increased, dose-dependent response only at 192h. BALF Inflammatory/Injury Markers: Protein and albumin increased at 24 h, returns to relative basal level at 192h at mid and high dose levels. NAG dose-dependent increase at 24 and sustained level through 192h.
Wichers, L.B. Rowan, W.HR. Nolan, J.P. 2006 Rats, Male, SH, 71-73d, 255-278g	NR	PM (HP-12) = inside wall of stack of Boston, MA power plant burning # 6 oil.	Whole-body Inhalation	13 mg/m^3 bw NR	PM = 1.95 µm +/- 3.49	Phase I: 1st day, filtered air, 2nd day, 6h of PM Phase II: 1st D_a, y filtered air, 4 days of 6h PM each Immediate post-exposure	Body/ Lung weight: No effects on Phase I rats. HP-12 exposure increased body weight, left lung, right intercostal, right diaphragmatic in Phase II rats. However, results appeared due to normal growth apptern in juvenile rats over 4d. Lung lobe to Body Weight Ratio: No effects at 1 or 4d. Deposition calculations: V and Co used to estimate deposition rates. Good agreement between two metals R^2 = 0.94. Total HP-12 deposition using Co was 26 and 99ug (for 1 day and 4 day experiments) and using V was 31 and 116ug. Modeling information estimated HP-12 deposition at 43% in conducting airways and 57% in alveolar region. Breathing parameters: No changes for 1 or 4d studies except for possible decrease in frequency for 1d study.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Wegesser, T.C. Last, J.A. 2008 Mice, Male, BALB/c, 8-10wks	NR	Ambient $PM_{2.5}$ - PM_{10} Collected from San Joaquin Valley, CA PBS (control)	Intratracheal Instillation	25-50 μg/mouse	NR	3, 6, 18, 24, 48, 72h NR	BALF Cells: Increased amount of viable cells found in PM-exposed mice with dose-response relationship between dose of PM and number of total cells recovered in BALF. At 6h, increased numbers of macrophages at both 25 and 50 μg/mouse. Increased percentage of neutrophils observed with 50 μg/mouse PM only. Furthermore, both macrophages and neutrophils increased with longer time period from instillation, peaking at 24 h. MIP-2: At 50 μg/mouse, MIP-2 concentrations increased, peaking at 3h, though not statistically significant and returned to basal levels by 6h. Positive correlation observed between MIP-2 concentration and increased neutrophil counts. No correlation found between MIP-2 and macrophages.
Wu, W. Wang, X. Zhang, W. 2003 Rats, Male, Sprague-Dawley, 60d	NR	Zn2+	Intratracheal Instillation	50um/rat bw NR	NA	Single, 24 h	Cells: Decreased number of airway epithelial cells shown with PTEN protein immunostaining. Macrophages unaffected.
Yamamoto, S. Tin-Tin-Win-Shwe Ahmed, S. 2006 Mice, Male, BALB/c, 7wks, 23g	30-48, NR	CB14 = Printex 90 (Degussa) CB95 = Flammruss 101 (Degussa) LTA = Lipoteichoic acid 14CL = CB14 + LTA 95CL = CB95 + LTA	Intratracheal Instillation	CB14 = 0, 25, 125, 625 μg/mouse CB95 = 0, 25, 125, 625 μg/mouse LTA = 10 or 50 μg/mouse 14CL = 125ug CB14 + 10 or 50ug LTA 95CL = 125ug CB95 + 10 or 50ug LTA bw NR	CB14 = 14nm CB95 = 90 nm CB14 measured **Components:** C 96.79%, HR 0.19%, N0.13%, S 0.11%, Ash 0.05%, O 2.74% CB95 measured **Components:** C 97.98%, HR 0.15%, N 0.28%, S 0.46%, Ash 0%, O 1.14%	single, 4 and 24 h	BALF Cells: CB95 induced dose-dependent increase of PMN. CB14 induced increase in PMNs but not dose-dependent. LTA massively increased PMN. LTA induced dose-dependent increase in total cells, especially at high dose 24 h. LTA had massive synergistic effect with CB14 and CB95 for total cells and PMNs. Total cell count and PMN level highest in 14CL with 24 h >4h. Macrophage data inconsistent. Cytokines: CB95 induced dose-dependent increase in IL-6, TNF-α, CCL2 and CCL3. CB14 induced dose-dependent increase in CCL2 and CCL3. Induced increase of IL-6 at high dose only. Slight effect on TNF-α. LTA induced dose-dependent increase of IL-6, TNF-α and CCL3. 14CL massively induced IL-6 and CCL2. No combination of CB and LTA effected TNF-α or CCL3. mRNA Expression: LTA, 14CL and 95CL increased TLR2 mRNA expression. 95CL = 14CL >LTA. No effect on TLR4 mRNA expression.
Yanagisawa, R. Takano, HR. Inoue, K. 2003 Mice, Male, ICR, 6wks, 29-33g	NR	DEP (4JB1 light duty 4cyc 2, 74 liter Isuzu engine) LPS DEP-OC = organic compounds DL = DEP + LPS DOL = DEP-OC + LPS	Intratracheal Instillation	DEP/DEP-OC = 125 μg/mouse LPS = 75 μg/mouse bw NR	0.4um	Single, 24 h	BALF Cells: DEP and DEP-OC increased neutrophils but not statistically significant. LPS increased neutrophils significantly. DL and DOL massively increased neutrophils, more than LPS alone. Macrophages unaffected. Pulmonary Edema: LPS, DEP and DEP-OC increased edema. DL further increased effect. DOL had no effect compared to LPS alone. Histology: DL elevated neutrophil inflammation interstitial edema and alveolar hemorrhages. DOL equivocal except no hemorrhages. Cytokines: LPS increased IL-1β, MIP-1α, MCP-1 and KC. DEP and DEP-OC had no effect. DL induced further increase. DOL decreased cytokines compared to LPS alone. DEP-OC increased IL-1β and MIP-1α mRNA expression slightly. DEP had no effect. LPS significantly increased IL-1β and MIP-1α mRNA expression. DL increased expressions while DOL did not. mRNA Expression of TLRs: DEP-OC, DL, DOL and LPS increased TLR2. DEP had no effect. All particles increased TLR4 mRNA expression.

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Yokohira, M. Takeuchi, HR. Yamakawa, K. 2007 Rats, Male, F344/ DuCrj, 10wks	108, 70, 38	DQ-12 = Quartz dust (Douche Montan) HT = Hydrotalcite (Kyoward 500, PL-1686, KYOWA) POF = Potassium Octatitanate fiber (TISMO, Otsuka) PdO = Palladium Oxide CB = Carbon Black (Mitsubishi Kasei) PG-CMC (control) Saline (control)	Intratracheal Instillation	4 mg/rat bw NR	DQ12 <7um HT = 7.8 ±1.5um POF = <50um length; <2um width PdO = 0.54 ± 1.11um CB = 28nm	single, 1 and 28d	Lung weight/body weight ratio: DQ-12, HT and POF induced increase after 1d; DQ-12, HT, POF, PdO and CB after 28d. BALF Cells: Neutrophils increased significantly in walls and alveolar spaces in all groups on 1d except at HT. AT 28d, increase maintained only in walls - except for DQ-12 which still had severe and moderate elevations. Histopathology: DQ-12 caused pulmonary edema both at 1 and 28d. PdO and CB induced edema at 28d. Fibrosis observed after 28d with most significant increase being DQ-12 >PdO >POF >HT = CB >control. Histiocyte infiltration observed after 1d for DQ-12, POF and PdO and 28d for DQ-12, HT, POF and PdO. Restructuring of alveolar walls & microgranulation observed for all 5 particles but only at 28d with DQ 12 >PdO >HT = POF = CB >control. Immunohistochemistry: BrdU: At 1d all 5 particles elevated in both area and number. Activity declined after 28d but still higher than control. iNOS: At 1d DQ-12, POF and PdO increased. At 28d DQ-12, HT induced increased. MMP-3: DQ-12 induced increased at both 1 and 28d and PdO at 28d. Toxicity scoring: DQ-12>HT = PdO = POF>CB
[FROM Table D-4] **Reference:** Yokohira et al. (2007) **Species:** Rat **Gender:** Male **Strain:** F344/DuCrj **Age:** 8 weeks **Weight:** NR		DQ-12 = Quartz dust (Douche Montan) HT = Hydrotalcite (Kyoward 500, PL-1686, KYOWA) POF = Potassium Octatitanate fiber (TISMO, Otsuka) PdO = Palladium Oxide CB = Carbon Black (Mitsubishi Kasei) DQ12 <7 µm HT = 7.8 ±1.5 µm (avg diam) POF = <50 µm (length; <2um (width) PdO = 0.54 ± 1.11 µm (avg diam) CB = 28 nm (NOS)	Intratracheal instillation 4 mg/rat (mg/kg bw NR) in 0.2 mL			single, day 1 and 28	Lung weight/body weight ratio: DQ-12, HT and POF were increased after day 1; DQ-12, HT, POF, PdO and CB after 28 days Histopathology: Neutrophil Infiltration: All except at HT at 1 day, all 5 at 28 days. On day 1 moderate neutrophils in walls and alveolar spaces, at day 28 only in walls -- except for DQ-12 which still had both (severe and moderate) Pulmonary Edema/ Fibrosis: Only DQ-12 caused edema both at 1 and 28 days. PdO and CB showed edema at 28 d only. Fibrosis was observed after 28 day in alveolins only in DQ-12, POF and PdO Histiocyte infiltration in alveoli: Observed after 1 day for DQ-12, POF and PdO. At 28 days HT, POF and PdO (DQ-12) Restructuring of alveolar walls & microgranulation: For all 5 particles but only on day 28 DQ 12>PdO>HT = POF = CB>control Immunohistochemistry: BrdU: On day 1 all 5 particles were elevated both area and number. Activity dropped off after 28 days but still area and/or number was elevated iNOS: On day 1 DQ-12, POF and PdO increased On day 28 DQ-12, HT increased MMP-3: DQ-12 increased both day 1 and 28 and PdO on day 28 Toxicity scoring: (authors system of weighted effects) DQ-12>HT = PdO = POF>CB

Reference Species, Gender, Strain, Age or Body weight	Number in Group, Experimental, Control	Particle Type	Exposure Technique	Dose or Concentration	Particle Size and Characteristics (Distribution)	Exposure; Post exposure Time to Analysis	Pulmonary Effects
Zhao, HR. Barger, M. Ma, J.K.HR. 2006 Rats, NR, Sprague-Dawley (Hla: SD-CVF), 200g	NR	DEP = SRM 2975 DEPE = SRM 1975	Intratracheal Instillation	35 mg/kg bw DEP and DEPE AG (amino guanidine) group pretreated with 100 mg/kg bw	NR	Single, 1d AG group coexposed 30 pre and 3, 6, 9h post DEP/DEPE	iNOS expression in AMs: Both DEP and DEPE increased 12 and 6 fold respectively. NO and peroxynitrite levels increased accordingly. AG had no effect on iNOS expression but AG attenuated NO for both DEP and DEPE but peroxynitrite only for DEPE. DEP induced much higher levels of oxidants than DEPE. DEP unaffected by AG whereas DEPE was. Role of iNOS in Lung Injury: DEP and DEPE induced inflammation (PMN), cellular toxicity (LDH) and lung injury (protein). AG significantly attenuated DEPE response but no effect on DEP responses. Cytokines: IL-12 DEPE>>DEP both significantly attenuated by AG. IL-10 DEP = DEPE. AG increased DEP effect 3 fold and attenuated DEPE to control. CYP enzymes: CYP1A1 level and activity increased by both DEP and DEPE. AG only attenuated CYP1A1 activity for both DEP and DEPE. CYP2B1 level and activity slightly decreased by DEP and DEPE. AG had no effect. Cytosol phase II enzymes: DEPE had no effect; AG treatment increased catalase activity. DEP reduced catalase and GST activities. AG had no effect. Neither DEP, DEPE nor AG affected QR quinone reductase.
Zhou, Y.M. Zhong, C.Y. Kennedy, I.M. 2003 Rats, Male, Sprague-Dawley, 10-12wks	NR	UFe = Ultrafine Fe particles	Whole-body Inhalation	57 or 90μg/m^3 bw NR	72nm	6h/d for 3d, <2h	BALF Inflammatory/Injury Markers: At high dose, total protein increased. No significant changes observed in LDH. BALF Cells: No significant changes observed in total cell number, cell viability or cell differentials. Intracellular ferritin: Increased with high dose. No significant differences observed between low dose group and control group. Oxidative stress: Antioxidant level by FRAP value decreased at high dose. GST (glutathione-S-tranferase) activity increased at high dose. No effect on intracellular GSH and GSSG (glutathione disulfide). Cytokines: Only a thigh dose was increase in IL-1β observed. No effect on TNF-alph or NFkB-DNA binding activity.

Table D-4. Effects related to immunity and allergy.

Study	Pollutant	Exposure	Particle Effects
Reference: Apicella et al. (2006) **Species:** Mouse **Cell Line:** BALB/c 112D5 hybridoma	Poly OVA (Ovalbumin on polystyrene beads) versus soluble OVA	**Route:** Cell culture **Dose/Concentration:** 2 x 10 4 cells/ 200 µl 0.2,1 or 5 µg/mL **Particle Size (Distribution):** 4.5 µm **Time to Analysis:** 48 h	Both PolyOVA and rm IL-6 increased synthesis of asymmetric IgG i.e. PolyOVA effects results from IL-6 induction

Study	Pollutant	Exposure	Particle Effects
Reference: Archer et al. (2004) **Species:** Mouse **Strain:** BALB/c DO11.10+/+ transgenic - ova specific receptor for OVA peptide 323-339 **Age:** 4 weeks	PM = SRM 1648 (NIST) Control particulate Titanium dioxide avg 0.3 µg (sic)	**Route:** intranasal instillation **Dose/Concentration:** 500 µg PM/30 µl sterile saline (ultrasonic suspension) initial 0-750 µg rangefinding **Particle Size (Distribution):** **Time to Analysis:** Ova challenge at 68 h, Methacholine aerosolization/AR at 72 h	AR(whole body plethysmography) showed AR increased with dose and methacholine challenge Only amounts = >500ug stat sig increased AR ($p<0.05$ 1-way ANOVA) TiO_2/Ova exposure was not significantly different from Saline Ova PM associated endotoxin did not contribute to enhanced AR Alveolar macrophages (by lavage) nor histological alterations were not increased after PM exposure Both TiO_2 and PM increased pulmonary neutrophils ($p<0.05$) indicating particle size alone would be responsible for this increase Increases in pulmonary neutrophils after exposure to PM are not associated with increased AR
Reference: Barrett, E.G. et al. (2006) **Species:** Mouse **Gender:** Male **Strain:** BALB/c (NR,) **Age:** 8-10 weeks **n:** Groups of 14 incl. controls	HWS (black/white oak) CO Total Vapor Hydrocarbon	**Route:** HWS Inhalation whole-body Pretreatment: ip 10 mg OVA and 2mg alum Post-Ova received OVA aerosol challenge on day 14, followed by 3 days of HWS Pre-Ova received aerosol Ova challenge on day 14, followed by 3 days of HWS on days 26-28 **Dose/Concentration:** 34, 107, 313, 1035 µg/m^3 0.7, 1.6, 4.0, 13 ppm 0.3, 0.6, 1.3, 3.1 ppm **Particle Size (Distribution):** 0.25, 0.35, 0.35, 0.36 µm **Time to Analysis:** HWS 6 h/day for 3 days 18 h post-exposure	POST-OVA: Only at 300 µg/m^3 did HWS result in increase in eosinophils as compared to OVA alone. (No changes in macrophages, neurophils and lymphocytes) HWS decreased levels of Il-2, Il-4 and IFNy (dose-dependent) but not on IL-13 and IL-5 HWS increased levels of OVA specific IgE but not stat sig for total IgE, OVA IgG1 or OVA IG2a No histological changes associated with HWS exposure PRE-OVA Except for an increase in serum OVA -IgG1 no other changes attributable to HWS Acute HWS can minimally exacerbate allergic airway inflammation following OVA exposure but does not alter Th1/Th2 cytokinin levels
Reference: Burchiel et al. (2005) **Species:** Mouse **Gender:** Female **Strain:** A/J **Age:** 10-12 weeks	HWS (black/white oak) HWS particle Mass BC Organic Carbon CO Total Vapor Hydrocarbon 29 other minor components PAH and metals	**Route:** Inhalation chambers **Dose/Concentration:** 34,106,313,1035 µg/m^3 3, 12, 25, 43 µg/m^3 40, 107, 281, 908 µg/m^3 1, 2, 4, 13 ppm ND, 1, 1, 3 ppm **Particle Size (Distribution):** 0.3±3, 0.4 ±2, 0.4±2, 0.4 ±2 µm (±GSD) (low to high concentrations) **Time to Analysis:** 6 h/day for 6 mos (details lacking ref to previous studies)	HWS increased splenic T cell proliferation at 100 µg/m^3 with a dose dependent decrease at 300 and 1000 µg/m^3 exposures ($p<0.05$) HWS exposure did not affect T (CD3), helper T cell (Th, CD4), cytotoxic T cell (CTL, CD8), macrophage (Mac-1), natural killer cell (NK, CD16) cell markers.
Reference: Burchiel et al. (2004) **Species:** Mouse **Gender:** NR **Strain:** AJ **Age:** 10-12 weeks	DE (generated from two (alternatively) 2000 Cummins ISB Turbo Diesel 5.9 L engines using no 2 (chevron) oil and 15w/40 oil (Rotella T, Shell) run according to USEPA Dynamometer Schedule for Heavy-Duty Diesel Engines 18 PAHs quantified at exposure levels (text mentions 65)	**Route:** Inhalation chambers **Dose/Concentration:** 30,100,300, 1000 mg/m^3 diesel PM **Particle Size (Distribution):** NR (details referred to paper in press) **Time to Analysis:** 6 h/day 7 days/wk for 6 mos	DE depressed splenic T cell proliferation at all exposure levels but was not dose-dependent and most pronounced at the 30 µg/m^3 level ($p<0.05$ at all levels) Splenic B cell proliferation was increased at the 30 µg/m^3 level but not at the other exposure levels
Reference: Burchiel et al. (2004) **Species:** Mouse **Strain:** AJ **Age:** 10-12 weeks **Cell Type:** spleen cells **Use:** In vitro	Benzo(a)pyrene (BaP) Benzo[a]pyrene-r-7,t-8-dihydrodiol-t-9,10 epoxide(±) ((anti)BPDE) Benzo[a]pyrene-trans-7,8-dihydrodiol (±) (BP-7,8-diol) Benzo[a]pyrene-1,6-dione (1,6-BPQ) Benzo[a]pyrene-3,6-dione (3,6-BPQ) Benzo[a]pyrene-6,12-dione (6,12 BPQ)	**Route:** Cell culture **Dose/Concentration:** 1 x 10 6 cells/mL in 100 µl aliquots 0.01, 0.1 and 1 µM **Particle Size (Distribution):** NA **Time to Analysis:** 72 h	In vitro results are contrary to in vivo results above. BaP at the highest concentration was found to double Splenic T cell proliferation. The BPQs all also increased T cell proliferation at much lower concentrations but not in a dosedependent manner. Splenic B cell was increased by Bp-(7,8)-diol, and inhibited by BPDE and 3,6 BPQ but only at the highest level. Authors concluded that due to low level of PAH in DE and absence of BPQs these compounds are not responsible for immunosuppressive effects of DE.

Study	Pollutant	Exposure	Particle Effects
Reference: Chan et al. (2006) **Species:** (see reviewer comments section) Mouse **Strain:** NR, DO11.10, (NR, NR): CD11+ NR, BALB/c, (NR,NR): BC -1 NR, Nrf2, (NR,NR): Nrf2 **Cell Types:** Bone marrow dendritic cells BMDC of mice: BMDC	DEP: DE particulate, provided by Dr. Marsaru Sagai DEP extract: Preparation described in Supplementary Methods text (not provided)	**Route:** Cell culture, 2 x 10^5 cells in 500 ul of cultured medium **Dose/Concentration:** DEPs 10 μg/mL LPS 5 ng/mL **Particle Size (Distribution):** $PM_{2.5}$ **Time to Analysis:** 24 h, frozen in -20C until analyzed	Organic DEP extracts inhibit the maturation of BMDCs and a DC line during LPS stimulation: No effect on expression of the adhesion molecule CD54. Stimulation of LPS increased expression of maturation markers. DEP extract significantly suppressed the expression of I-Ad, CD86, and CD54, all dose dependently. No significant BC 1 toxicity occurred. Similar effects were seen between BMDCs and BC 1 cells. Treatment with DEP extract induced a significant decrease in I-Ad and CD86 expression in CD11c+ gated cells. Taken together, these data indicate that organic DEP chemicals interfere in the expression of several DC maturation markers. DEP extract inhibits IL-12 secretion in LPS-exposed DCs: DEP extract failed to exert an effect on IL-12p40 production. DEP extract suppressed the LPS-induced production of IL-12p40 in BC 1 cells and BMDCs. Similar effects seen with IL-12p70 levels. Intact particles inhibit CD86 expression and IL-12 production in LPS-exposed DCs: I Intact particles found not as effective as DEP extract. DC exposure to DEP extract affects their ability to induce cytokine production in antigen specific T cells: Co-cultured T cells produce a small quantity of IFN-y in presence of antigen pulsed BC 1 cells. Prior treatment with LPS leads to increased expression of co-stimulatory receptors and IL-12 production. Exposure of BC 1 cells to DEP extract plus LPS induced a statistically significant decrease in IFN-y production. Exposure of BC 1 cells to DEP extract alone, before antigen pulsing, induced a statistically significant increase in IL-10 production. Same treatment has no effect on IL-4 and IL-13. DEP extract alone did not stimulate IL-10 production in DCs. DEP extract interferes in the effect of several TLR agonists: No effect was seen with treatment of TLR5, TLR7, and TLR8 agonists. Similar effects seen on IL-12 production except that TLR9 did not interfere in IL-12 production. DEPs interfere in LPS-induced NF-kB activetion: Addition of DEP extract to LPS-treated cells interfered in IkBb degradation in a dose dependent manner. Less effect on IkBa. DEP extract alone has no effect on IkBb degradation. Effects of the DEP extract are mediated by pro-oxidative DEP chemicals that engage the Nrf2 pathway: IL-12 production could not be suppressed in Nrf2 deficient cells. In contrast, response inhibition in WT BMDCs was intact, this inhibitory effect was dependent on dose of DEP extract. Sulfurophane induced HO-1 expression and inhibited LPS-induced I-Ad and CD54 expression.

Study	Pollutant	Exposure	Particle Effects
Reference: Ciencewicki et al. (2007) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 10-12 weeks **Weight:** 17-20 g	DE: DE generated from a 30-kW (40 hp), 4-cylinder Deutz BF4M1008 diesel engine O_2, CO, NO_2, NO, SO_2 Influeza A/Bangkok/1/79 (H3N2 serotype) from Dr. Melinda Beck of the University of North Carolina, Chapel Hill	**Route:** Inhalation oropharyngeal aspiration of virus **Dose/Concentration:** DE: 0.5 or 2 mg/m^3 (nominal) actual 529 or 2070 μg/m^3 O_2: 20.9- 20.5% (Lo, Hi) CO: 0.9-5.4 ppm NO_2: 0.25-1.13 ppm NO: 2.5-10.8 ppm SO_2: 0.06-0.32 ppm H3N2: NR **Particle Size (Distribution):** NR **Time to Analysis:** 4 h/day for 5 days virus exposure immediately after last exposure analyzed 18 h post last exposure	Effect of DE exposure on susceptibility to Influenza infection: Mice exposed to 0.5 mg/m^3 of DE had significantly greater levels of HA mRNA compared to air-exposed mice. HA levels were not significantly altered in mice exposed to 2.0 mg/m^3. Effect of DE exposure on the Influenza-induced inflammatory response: The levels of IL-6 mRNA were significantly greater in the lungs of mice exposed to 0.5 mg/m^3 of DE prior to infection compared to mice exposed to air. A significantly increased amount of IL-6 protein was seen in BAL fluid of exposed mice. Exposure to DE in the absence of influenza infection had no significant effect on IL-6 mRNA or protein levels. Effect of DE exposure on pulmonary injury: Infection with the influenza virus increases the levels of PMN in the BAL fluid. Exposure to either dose of DE prior to infection showed no significant effect on the levels of BAL fluid PMNs. Exposure to DE alone had no effect on PMNs in BAL fluid. Neither exposure to DE nor infection with influenza significantly increased BAL fluid protein levels. Other markers of injury, NAG and MIA were not statistically affected by either DE or influenza exposure. Effect of DE exposure on the influenza induced interferon response: No significant change in TFN-a mRNA levels at either dose of DE, although mice exposed to 0.5 mg/m^3 of DE prior to infection had significantly greater levels of IFN-B MRNA compared to air controls. The IFN-y mRNA levels were elevated, although not significantly in mice exposed to 0.5 mg/m^3. No effect on any of the IFNs observed in uninfected mice exposed to DE. Effect of DE expousre on surfactant protein expression: Influenza virus infection alone significantly increased the expression of SP-A in the lungs of mice exposed to air. Mice exposed to 0.5 mg/m^3 of DE prior to infection had significant decreases in levels of SP-A mRNA in the lungs, this effect was not observed in mice exposed to 2.0 mg/m^3 DE. Decrease seen in expression of SP-A protein in lungs of mice exposed to 0.5 mg/m^3 DE prior to infection. Levels of SP-D mRNA and protein were significantly decreased in lungs of mice exposed to 0.5 mg/m^3 of DE prior to infection compared with mice exposed to air or 2.0 mg/m^3 DE prior to infection. Exposure to 0.5 mg/m^3 of DE prior to infection with influenza decreased levels of SP-D, especially in airways. Mice exposed to 2.0 mg/m^3 DE prior to infection showed no significant difference.

Study	Pollutant	Exposure	Particle Effects
Reference: De Haar et al. (2005) **Species:** Mouse **Gender:** Female **Strain:** BALB/cANNCr **Age:** 6-8 weeks **Weight:** NR	CBP: Carbon black particles in phosphate buffered saline, 1: 10 & 1: 100 dilutions from Brunschwich Chemicals, Amsterdam, The Netherlands OVA: Ovalbumin prepared in phosphate buffered saline, from Sigma-Aldrich, Zwijndrecht, The Netherlands	**Route:** Intranasal droplet **Dose/Concentration:** CBP± OVA 200, 20, 2 µg CBP and 10 µg OVA per animal (see notes) **Particle Size (Distribution):** CBP: 30-50 nm **Time to Analysis:** Droplet applied on days 0, 1, 2 Sacrificed on day 4 or 8 OR Challenged with OVA droplet on days 25, 26, & 27 Sacrificed on day 28	CBP+OVA Exposure induces concentration dependent acute airway damage and inflammation: Only day 4 had LDH increased in the 200 µg CBP+OVA group. The 200 µg CBP+OVA group induced significantly higher numbers of BAL cells compared to OVA control. Total protein and TNF-a levels were increased only in 200 µg CBP+OVA group. RAS, parameter for phagocytosis, 200 µg and 20 µg CBP+OVA had higher levels than OVA controls. Dose-dependent CPB+OVA adjuvant activity on PBLN: Total lymphocytes in PBLN significantly increased 4-5 fold in the 200 µg CBP+OVA exposed. 20 µg and 2 µg exposures did not increase the number of PBLN cells compared to OVA control. All CBP+OVA concentrations induced higher levels of IL-4, IL-5, IL-10, and IL-13, with 200 µg concentration having 10-200 times higher levels. IFN-y cytokine was increased in the 200 µg dose.CBP+OVA Sensitization Induces Systemic IgE Production: OVA IgE were significantly increased at day 21 in CBP+OVA exposed mice. Day 28 had higher IfE levels. PBLN and Lung Lymphocytes are stimulated after intranasal OVA challenge: Challenge with OVA increased PBLN cell numbers in both OVA and CBP+OVA sensitized mice. CD4 and CD8 populations increased in both groups. PBLN levels in CBP+OVA and challenged with PBS were higher than mice treated with OVA and challenged with PBS, both groups cytokine production was low, only IL-5 levels were significant in the CBP+OVA/PBS group. Higher lung lymphocyte numbers were caused by higher numbers of CD4 and CD19. Production of IL-5 and IL-10 was four to five times higher than in OVA treated mice. Intranasal challenge with OVA induces asthma like airway inflamemation in CBP+OVA sensitized mice: Total number of cells in BAL increased 10 fold in CBP+OVA mice challenged with OVA. Eosinophils were the highest increased in the CBP+ OVA/OVA group at 50 times higher than other groups. Perivascular and peribronchial infiltrates and globlet cell hyperplasia in CBP+OVA/OVA was confirmed by histological examination. Antigen specific inflammation with predominantly eosinophilic influx is induced in only CBP+OVA mice.

Study	Pollutant	Exposure	Particle Effects
Reference: de Haar et al. (2006) **Species:** Mouse **Gender:** Female **Strain:** BALB/cANNCr **Age:** 6-8 weeks **Weight:** NR	CBP: fine and ultrafine carbon black particles TiO_2: fine and ultrafine titanium oxide particles OVA: Ovalbumin *all provided by the group of Ken Donaldson.	**Route:** Intranasal exposure **Dose/Concentration:** CBP: 200 µg OVA: 10 µg CBP+OVA: 200 +10 µg (see note in 3008) **Particle Size (Distribution):** fine CBP: 250.0 nm ultrafine CBP: 29.0 nm fine TiO_2: 250.0 nm ultrafine TiO_2: 29.0 nm **Time to Analysis:** Exposed to OVA or particle + OVA on days 0, 1, 2. Sacrificed on day 8 & analyzed after 2 h, or continued to second group. Second group given OVA challenge on day 25, 26, & 27, killed on day 28, analyzed after 24-h	Ultrafine particles induce lung inflammation: Day 8, both ultrafine TiO_2 and CBP induced a local inflammatory response in the airways, and showed higher levels of LDH and total protein as compared to mice exposed to the fine particles. Cytokine levels were much higher in groups exposed to ultrafine particles. Histologic analysis of the airways showed that exposure to ultrafine TiO_2 or CBP leads to peribronchial and perivascular inflammatory infiltrates (mostly neutrophils). Exposure to OVA alone, or combined with fine TiO_2 and fine CBP had no effects on lung histology. Ultrafine stimulate local immune responses: Both TiO_2 and CBP particles stimulated the local immune response against co administered OVA antigen. Fine TiO_2 particles induced a low but significant increase in PBLN cell number. Both types of ultrafine particles elicited higher levels of Th-2 associated cytokines, with CBP stimulating a greater response. Production of Th-1 associated cytokine IFN-y was low, but significantly higher than OVA exposures. Ultrafine TiO_2 increase ovalbumin-specific IgE and IgG1 levels: Levels of OVA specific IgE were significantly increased in animals exposed to the combined ultrafine TiO_2 + OVA compared to single doses. Average IgE level in mice exposed to ultrafine CBP+OVA was not a significant increase. Ultrafine particles stimulate allergic airway sensitization against ovalbumin: At day 28, the PBLN cell numbers were significantly higher in both ultrafine and combination with OVA. Production of OVA specific IL-4, IL-5, IL-10 and IL-13 by PBLN cells was significantly increased in both ultrafine TiO_2 and CBP. IFN-y levels were significantly increased in ultrafine CBP+OVA treated animals. Fine TiO_2 had low, but significant increases in IL-4 and IFN-y compared to OVA only. Influxes of eosinophils, neutrophils and lymphocytes were only found in both groups exposed to ultrafine particles, as well as allergic airway inflammation. All particle treated groups showed some macrophages containing particles, indicating not all particulates were removed from the airway at day 28.

Study	Pollutant	Exposure	Particle Effects
Reference: Dong et al. (2005a) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 200-225 g	SRM 2975 DEP: DE particulate (NIST) OVA: Ovalbumin from the Sigma Chemical company, St Louis, MO.	**Route:** Inhalation **Dose/Concentration:** DEP: 20.6 ± 2.7 mg/m^3 OVA 40.5 ± 6.3$mg.m^3$ **Particle Size (Distribution):** SRM 2975 **Time to Analysis:** 4 h/day for 5 days + OVA 30 min/day 1 x wk on days 8,15 & 29. Sacrificed on days 9 or 30.	Lung Inflammation/Injury: Both the BAL proteins and inflammatory cell counts for DEP exposure alone, when measured at 9 and 30 days were not different from those of the air exposed control, suggesting that DEP exposure did not cause lung injury at 9 or 30 days post-exposure. Exposure of rats to OVA caused significant increases in neutrophils, lymphocytes, eosinophils, albumin and LDH activity in the rat lung after two exposures. DEP did show a strong effect on OVA-induced inflammatory responses. Alveolar Macrophage function: OVA exposure resulted in an increase in NO levels in the acellular BAL fluid and AM conditioned medium. This increase was significantly attenuated in rats exposed to DEP. DEP exposure had no significant effect on the production of IL-10 or IL-12 by AM recovered from rats 9 and 30 days post exposure. In contrast OVA sensitization elevated both IL-10 and IL-12 secretion by AM at both time points. Lymphocyte population and cytokine production: DEP exposure was found to increase the numbers of total lymphocytes, T cells and their CD4+ and CD8+ subsets in LDLN. OVA exposure significantly increased these cell counts on days 9 and 30. Combined DEP+OVA exposure showed a significant reduction in total lymphocytes, T cells, CD4+ and CD8+ subsets in rat lung on day 30. Levels of IL-4 and IFN-y in lymphocyte conditioned media were below detection limit of the ELISA kits. Intracellular GSH levels in AM and Lymphocytes: DEP exposure alone slightly decrease GSH levels in AM, but markedly reduced GSH concentration in lymphocytes on days 9 and 30. OVA exposure significantly decreased intracellular GSH in both cell types. Combined exposure showed AM and lymphocytes to have depleted intracellular GSH. OVA specific IgE and IgG levels in serum: In all samples collected on day 9, both serum IgG and IgE levels were under the detection limits. On day 30, no measureable IgE levels were found. The OVA exposure, however, resulted in elevated IgE levels, and was enhanced in rats preexposed to DEP. These results indicate that DEP have an adjuvant effect on the production of both IgG and IgE. Effects of DEP and OVA on Lung iNOS expression: AM from various exposure groups did not stain for iNOS. 1 rat at day 9 from the combined DEP+OVA group showed a slightly positive iNOS staining. On day 30, 2 of 5 rats from combined exposure group and 1 from the OVA group showed a positive airway staining.

Study	Pollutant	Exposure	Particle Effects
Reference: Dong et al. (2005b) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 200-225 g	SRM 2975 DEP: DE particulate (NIST) OVA: Ovalbumin, from Sigma Chemical Company, St Louis, MO	**Route:** Inhalation **Dose/Concentration:** DEP 22.7 ± 2.5 mg/m^3 OVA 42.3 ± 5.7mg/m^3 **Particle Size (Distribution):** SRM 2975 **Time to Analysis:** 4 h/day for 5 days + OVA 30 min/day 1 x wk on days 1, 8, 15. Analyzed 24-h post exposure	Effect of DEP on OVA induced allergic responses: DEP exposure had a synergistic effect with OVA on inducing airway hyper-responsiveness (AHR) in rats. DEP alone had no effect on IgG production, indicating that DEP pre-exposure augments the immune response of rats to OVA in the production of allergen specific IgG and IgE. Effect of DEP on OVA induced cell differentiation: Neither DEP, OVA nor the combination induced elevated levels of LDH activity and albumin content, indicating that the exposure protocols did not cause significant lung injury. OVA exposure induced a greater infiltration of neutrophils than DEP, and infiltration of eosinophils and lymphocytes. Total lymphocytes, T cells, and their CD4+ and CD8+ subsets in LDLN from rats sensitized and challenged by OVA were significantly higher than those of air-exposed non sensitized rats. Effect of DEP on OVA-induced oxidant generation and GSH depletion: Exposure to DEP or OVA alone had no effect on CL production by AM. Substantial elevation seen in CL for the DEP+OVA exposed group. Both OVA and DEP exposures resulted in an increased presence of NO in the acellular BAL fluid and in AM conditioned media. The ATII cells from OVA exposed rats exhibited a higher percentage of cells that produce NO and superoxide than air exposed, non sensitized rats. DEP and OVA exposure resulted in a significant increase in the percentage of cells that produce NO and superoxide over the control. No staining of AM in immunohistochemical analysis for iNOS expression was done for any exposure group. Airway epithelium was found to be positive in all 5 rats from the DEP+OVA group and 3 of 5 rats from single exposure of DEP or OVA and 2 of 5 in air only exposed rats. GSH levels were slightly lowered by DEP or OVA exposure, not significant The combined exposure DEP+OVA showed a significant reduction in GSH levels.

Study	Pollutant	Exposure	Particle Effects
Reference: N Drela, et al. 2006 **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 6 weeks **Weight:** NR	ASM: Air suspended PM from Upper Silesia (Poland)	**Route:** Intraperitoneal injection **Dose/Concentration:** 170 mg ASM/kg bw **Particle Size (Distribution):** 0.3-10 µm **Time to Analysis:** One time exposure, sacrificed 72-h post exposure	CD28 expression on thymocytes at different stages of development: The expression of CD28 was not changed on peripheral CD4 and CD8 T cells examined in the population of lymph node lymphocytes isolated from ASM-exposed mice. The expression of CD28 on spleen T cells from ASM animals demonstrated a slight, statistically not significant decrease. The distribution of CD28(low) and CD28(high): Acute exposure to ASM resulted in the increase of CD28(low) and decrease of CD28 (high) thymocyte percentages in the total thymocyte population. The percenttages of CD28 low and high thymocytes did not differ between intact and PBS controls. Acute ASM exposure resulted in the increase of the percentage of CD28(low) and the decrease of CD28(high) thymocytes in the CD3 low subset. The percentage of CD28 low and high positive thymocytes did not differ in CD3 high thymocyte subset. Natural regulatory CD4+ CD25+ T cells in the thymus: The development of thymic natural regulatory cells progresses inparallel with other SP thymocytes and their percentage in the CD4+ CD8- subset did not change in ASM treated mice. Proliferating activity of splenocytes and lymph node lymphocytes: The potential of lymph node lymphocytes from ASM treated mice to proliferate was increased independently of anti-CD3 concentration. The percentage of cells undergoing proliferation in the presence of anti-CD3 and anti-CD28 acgivation was higher in cultures of lymph node lymphocytes isolated from ASM exposed mice. Both CD4+ and CD8+ T cells from ASM treated mice proliferated more vigorously than from controls. Almost all CD8+ T cells from ASM mice were induced to proliferate.
Reference: E Dybing, et al. 2004 **Species:** Mouse **Gender:** NR **Strain:** BALB/c **Age:** NR **Weight:** NR **Assay:** PLN Assay	UP: Urban ambient particles collected in 4 different cities, close to busy streets during staggered 4 week periods from March 2001 until March 2004 for spring summer and winter particles. SRM 1650 DEP: DE particulate, NIST OVA	**Route:** Injection in hind foot pad **Dose/Concentration:** UP: 100 µg- 200 µg DEP: 50 µg OVA: 50 µg **Particle Size (Distribution):** NR **Time to Analysis:** One time exposure, lymph nodes harvested on day 6. Day 21 injection of OVA, analysed on day 26	Allergy screening: The presence of OVA with the particles showed a statistically significant increase, indicative of an adjuvant effect. Particles elicited gernerally weak popliteal responses in the absence of OVA. The antibody response to OVA was usually significantly stronger as compared to the control groups. Except a few coarse samples, all fractions significantly increased the IgE and anti-OVA response. In general, the fine particles have a stronger adjuvant activity than the coarse ones following a pair wise comparison of the coarse and fine particles from the same location.
Reference: E Dybing, et al. 2004 **Species:** Human and Rat **Cell Lines:** Human, A549 cells, primary human small airway epithelial cells Rat, primary rat type 2 Clara cells, Rat alveolar macrophages **Use:** Inflammatory screening	UP: Urban ambient particles collected in 4 different cities, close to busy streets during staggered 4 week periods from March 2001 until March 2004 for spring summer and winter particles. SRM 1650 DEP: DE particulate, NIST OVA	**Route:** Cell culture **Dose/Concentration:** Various concentrations of particle samples **Particle Size (Distribution):** NR **Time to Analysis:** 20 h	Inflammation screening: The coarse fractions were more potent than the fine fraction. Among the samples, the overall effects of the coarse fractions on the cells were dependent on the site of collection. High MIP-2 levels were found in some spring collections, 1 sample in the summer showed the highest potency, and the winter collections proved to be the least potent of all. Only minor responses were found by the fine fractions at urban sites.

Study	Pollutant	Exposure	Particle Effects
Reference: A. K. Farraj, et al. 2006 **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 6 weeks **Weight:** NR	SRM 2975 DEP: Standard reference material 2975 DE particulate, NIST	**Route:** Nose only exposure **Dose/Concentration:** 2.0 mg/m^3 **Particle Size (Distribution):** <2.5 µm **Time to Analysis:** On day 0: ip injection of 20 µg OVA Day 14: intranasal instilation of 50 ul rabbit anti-mouse p75NTR neurotrophin receptor polyclonal antibody Day 14, 1-h after 1st exposure: challenged with 1% OVA for 1-h followed by a 5 h exposure to SRM 2975 DEP	Whole body plethysmography: 1 day following challenge and DEP exposure, no significant differences in avg Pehn (enhanced pause) values. In vehicle sensitized mice, DEP exposure or antibody p75NTR had no effect on Pehn values. In OVA sensitized mice exposed to DEP, an increase of Pehn values was seen. Lung function in ventilated mice: Central airway resistance (Rn) increased 62% in OVA sensitized mice, compared to vehicle sensitized mice, this was not a significant increase. Airway pathology: OVA sensitized mice had small increases in intraepithelial mucus compared to vehicle-sensitized mice. DEP exposure did not enhance severity of OVA induced airway pathology. Cells in Lavage fluid: DEP exposure in vehicle sensitized mice significantly increased the macrophages in fluid by 92%. OVA sensitized mice had a 142% increase in number of macrophages. DEP co exposure significantly decreased number of macrophages in OVA sensitized mice to control levels. p75NTR had no effect on either group. Eosinophils increased 90% in OVA sensitized mice, and a 110% increase in coexposure mice, both these values were not statistically significant. Neutrophils were not significant affected in any group.Cytokines: OVA sensitized mice had no significant IL-4, IL-5 or IL-13 levels. DEP exposed OVA mice had a 5 fold increase in IL-4 levels. No other significant effects seen.Serum IgE: OVA sensitized mice had a 10 fold increase in IgE levels. DEP did not cause significant effects.

Study	Pollutant	Exposure	Particle Effects
Reference: A. K. Farraj, et al. 2006 **Species:** Mouse **Gender:** Male **Strains:** C57 and B16 **Age:** 6 weeks **Weight:** NR	SRM 2975 DEP, collected from a filter from a diesel-powered industrial forklift (NIST) MCH: Methacholine airway smooth muscle antagonist OVA: Ovalbumin (Sigma Chemical, St. Louis, MO) Anti-p75: Rabbit anti-mouse p75 neurotrophin receptor polyclonal antibody (Chemicon, Temecula, CA)	**Route:** Nose only exposure **Dose/Concentration:** DEP: 0.87 mg/m^3 MCH: 0, 16, 32, 64 mg/mL OVA: 20 µg Anti-p75: 50 ul **Particle Size (Distribution):** <2.5 µm **Time to Analysis:** DEP: 1 x 5 h exposure, NR MCH: Given 48 h after DEP exposure	Airway physiology: No significant differences in average Pehn(enhanced pause) values between any groups. No significant differences in treatment groups in OVA sensitized mice at baseline 0, 16, or 32 mg/mL of MCH. At 64 mg/mL MCH, mice had a 22% increase in Pehn compared to vehicle mice, and a 68% increase compared to air-exposed. Instillation of anti-p75 inhibited completely the DEP induced increased Pehn. Airway pathology: Of mice challenged with OVA a small increase in the number of mucous-secreting cells in the epithelium lining the airway lumen was seen. No effects seen with anti p75 administration. OVA and DEP exposure did not result in any lesions in the nasal airway.Cells in Broncholaveolar Lavage fluid: DEP exposure in vehicle-sensitized mice significantly increased lavaged macrophages by 161% compared to air-exposed, vehicle-sensitized mice, while OVA mice had a 69% increase. OVA air exposed mice had a several hundred fold increase in the number of eosinophils. No significant effects of DEP exposure or anti-p75 treatment on eosinophils from OVA exposed mice. Cytokines: OVA exposed mice did not have an increase in IL-4 protein levels, nor in DEP exposed mice. No significant effect of anti-p75 administration on IL-4. OVA air-exposed mice caused a 34% increase in IL-5 protein levels. Anti-p75 and DEP exposure had no significant effect on IL-5 levels. OVA air-exposed mice caused a 148% increase in IL-13 protein levels. No significant effects of DEP or anti-p75 on IL-13 levels. Serum IgE: OVA sensitization in the presence or absence of DEP or anti-p75 caused at least a 3 fold increase in OVA specific serum IgE levels. No significant effects of DEP or anti-p75 treatment on serum IgE levels.
Reference: Finkelman, F. et al. 2004 **Species:** Mouse **Gender:** Female **Strains:** BALB/c and C57BL/6 **Age:** 2-4 months **Cell Types** Spleen Cells	2 mg of DEP suspended in saline	**Route:** Two groups: Group1: Injected with 2 mg of DEP suspended in 0.2mL of saline once. Group 2: Injected with 2mg of DEP suspended in 0.2mL of saline daily for 3 days. **Dose/Concentration:** 2 mg per injection **Particle Size (Distribution):** average particle size: 2 µM in diameter **Time to Analysis:** 2 h -96 h (depending on test)	Mice injected a single time with 2mg of DEP demonstrated an increase in IL-6 production but no increase in IL-4 or IL-2 production. IFN-γ levels were decreased considerably in some experiments, the decrease was by 75% when mice were injected with DEP on 3 successive days. TNF production was not affected. When injected with or before LPS, DEP had little effect on the LPS-induced TNF-α response but partial inhibited the LPS-induced IL1- response. DEP injected w/ or before LPS completely suppressed the LPS-induced IFN-γ response. DEP inhibited the IFN-γ responses to IL-12, IL-12 plus IL-18, IL-2 and poly (I·C) DEP had little or no effect on the percentage of NK or NKT cells in the spleen. DEP inhibited LPS-induced IFN-γ production by NK and NKT spleen cells. DEP failed to inhibit the IFN-γ response by anti-CD3 mAb-activated NKT cells.

Study	Pollutant	Exposure	Particle Effects
Reference: Finkelman, F. et al. 2004 **Species:** Mouse **Gender:** Female **Strains:** BALB/c and C57BL/6 **Age:** 2-4 months **Cell Types** Spleen Cells	DEP was generated by a four-cylinder diesel engine (4JB1 type) using standard diesel fuel. DEP Composition: Not Reported.	**Route:** IP Injection **Dose/Concentration:** Injection(s) of 2mg DEP suspended in 0.2mL saline **Particle Size (Distribution):** average particle size: 2 µm in diameter (reported as 2 µmol) **Time to Analysis:** To measure effects on IL-2, IL-4, IL-6 and IFN-γ: (BALB/c mice) Mice were injected with either: 1. 2 mg of DEP or saline suspended in 0.2mL of saline once 2. 2mg of DEP or saline suspended in 0.2mL of saline daily for 3 consecutive days. To measure effects of DEP plus TLRL and Cytokine Treatment on Responses: (BALB/c mice) Mice were injected with: 1. Saline (control) 2. LPS (100ug) 3. DEP(2mg) +LPS (100ug) 4. LPS (100ug) + activated charcoal (2mg) 5. IL-12 (1ug) 6. DEP + IL-12 7. IL-12 (2ng) + IL-18 (1ug) 8. DEP+ IL-12 + IL-18 9. IL-2 (100,000U) 10. IL-2 + DEP 11. PolyIC (1mg) 12. Poly IC + DEP Effect on LPS-Induced IFN-γ Production in Spleen NK and NKT Cells: (C57BL6 and BALB/c) 1.C57BL6 mice treated with: 1. saline, 2. 2mg DEP suspended in saline or 3. 2mg activated charcoal 2. BALB/c mice treated with 1. saline, 2. LPS (100ug), 3. DEP (2mg) 4. DEP+LPS 3. BALB/c mice treated with saline or DEP and followed 1-h later with 10 µg anti-CD3mAb.	Effects on Cytokines: (in BALB/c mice) 1.Mice injected a single time and in triplicate with 2mg of DEP demonstrated an increase in IL-6 production. Single injection did not increase IL-4 or IL-2 production (results not shown for the mice exposed to 3 consecutive injections of DEP). 2.IFN-γ levels were decreasedby 75 % after three injections of DEP. 3.TNF production was not affected. Effect on Induced Cytokines: (in BALB/c mice) 1.LPS alone increased production of IL-6, IL-10, TNF and IFN-γ. Injection of 2 mg DEP before LPS injection decreased the stimulatory effect of LPS on IFN-γ and had a slight effect on IL-10. IL-6 and TNF were not effected. DEP also suppressed the LPS induced increase in IFN-γ mRNA. 2.Activated charcoal produced no effect on LPS induced increase in IFN-γ secretion. 3.LPS induced a large increase in IL-12 secretion. DEP injected before LPS suppressed the LPS induction of IL-12 (by a factor of ~3) but more completely decreased the IFN-γ responses to IL-12, IL-12 plus IL-18. 4.DEP also suppressed the stimulatory effect of IL-2 and PolyIC on IFN-γ production. Analysis of Dose/Response: (in BALB/c mice) DEP depicted a dose-related suppression of LPS stimulated IFN-γ production. Effect on NK and NKT Cells: NK and NKT cells were chosen because of their rapid production of IFN-γ. 1.C57BL/6 Mice: DEP injection caused a decrease in spleen cells but had little or no effect on the percentage of NK or NKT cells in the spleen. DEP inhibited LPS-induced IFN-γ production by NK and NKT spleen cells. 2.BALB/c Mice: (using DX5 as a marker for NK cells) DEP inhibited LPS-induced IFN-γ production by NK and NKT spleen cells but DEP failed to suppress anti-CD3 mAb-induced production of IFN-γ.
Reference: Fujimaki et al. (2004) **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** 4 weeks **Cell Types** Lymph-node cells	A comparison of exposure to DE particle (composed of SPM, NO_x, NO_2, NO, SO_2 and CO_2)-and-Exposure to Particle-free Diesel Gas (composed of SPM, NO_x, NO_2, NO, SO_2 and CO_2) All mice were injected with SBP, an allergen before exposure to gas or DE and on days 14 and 35	**Route:** Cell culture **Dose/Concentration:** Exposure to: 0, 1.0 mg DEP/m^3 or 1.0mg DEP/m^3 DE gas **Particle Size (Distribution):** Average diameter of DEP 0.4 µm **Time to Analysis:** Exposure for 12 h daily for 5 weeks. Evaluation is 24 and 48 h after final SBP injection	Exposure to DE or gas did not affect lymphocyte subpopulations of CLN. Culture supernatants of CLN cells from DE exposed/SBP immunized mice has significant increase in MCPC-1. Exposure to gas significantly increased the amount of TARC MIP-1α in CLN cells from SBP-immunized mice. Increased production of chemokines by SBP stimulation was more prominent in gas components than in DE inhalation.

Study	Pollutant	Exposure	Particle Effects
Reference: Fujimaki, HR. et al, 2004 **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** 4 weeks **Cell Types** Lymph-node cells	DE particle (composed of SPM, NO_X, NO_2, NO, SO_2 and CO_2) and suspended in saline -and- Particle-free Diesel Gas (composed of SPM, NO_X, NO_2, NO, SO_2 and CO_2) DEP Composition: listed in ppm in the "Effects Section"	**Route:** Whole-body Exposure Chamber **Dose/Concentration:** 0, 1.0 mg DEP/m^3 DEP particle or 1.0mg DEP/m^3 filtered DE gas. (actual 0.01, 1.01 and 0.04 mg/m^3 actual SPM) **Particle Size (Distribution):** Average diameter of DEP 0.4 µm **Time to Analysis:** Exposure for 12 h daily for 5 weeks. All mice were injected with 100 µg SBP, an allergen before exposure to gas or DE and again received 50 µg SBP on days 14 and 35 Evaluation is 24 and 48 h after final SBP injection	Effect on CLN: CLN is a lymph node that plays an important role in mucosal response to antigens. Exposure to DE or gas did not affect CD45R/B220+, CD45R/B220-, CD4 = , CD8+, CD3+TCR-αβ+ and CD3+TCR-δ+) cells in the CLN, similar to control. MCP-1: 24 h- DE/SBP and Gas/SBP both increased MCP-148 h- All groups increased MCP-1. But DE/SBP and Gas/SBP both increased MCP-1 production to a higher degree, DE/SBP exposure induced slightly higher MIP-1 production at 48 h MIP-1α: 24 h- gas/SBP increased MIP-1α production 48hr- All groups increased MIP-1α production. DE/SBP and gas/SBP increased MIP-1α production to a slightly higher degree. TARC/MIP-224 h- No significant differences between the exposure and control groups for TARC and MIP-2 levels after 24 h. 48 h- TARC was significantly enhanced in the gas/SBP group. MIP-2 no changes Composition of DE and DE Gas: DE: 12.09 ± 0.15 NO_X, 1.99±0.02 NO_2, 10.02±0.12 NO, 0.18±0.002SO_2 and 1769.2±13.2 CO_2 (all in ppm) DE gas: 11.93 ± 0.13 NO_X, 2.93±0.06 NO_2, 8.91±0.09 NO, 0.11±0.003SO_2 and 1838.8±15.3 CO_2 (all in ppm)
Reference: Fujimaki et al. (2005) **Species:** Mouse **Gender:** Male **Strains:** C57BL/6 **Age:** 4 weeks **Cell Types** CLN (lymph node) Cells and Plasma Cells	DE generated by 4 cyl 2.74 l Isuzu diesel DE gas = DE filtered to remove particles Composition of Disel Exhaust**:** DE DEP: 1.01 mg/m^3 1796ppm CO_2 12.09ppm NO_X 0.18 ppm SO_2 Composition of filtered DE Gas: DEP: 0.04 mg/m^3 1839ppm CO_2 11.93ppm NO_X 0.11 ppm SO_2	**Route:** Whole-body Exposure Chamber **Dose/Concentration:** Exposure to: 0, 1.0 mg DEP/m^3 or 1.0mg DEP/m^3 DE gas (nominal) **Particle Size (Distribution):** Average diameter of DEP 0.4 µm **Time to Analysis:** Exposure for 12 h daily for 5 weeks. All mice were injected with 100 µg SBP, an allergen before exposure to gas or DE and again received 50 µg SBP on days 14 and 35 Evaluation is 1 day after final SBP-immunization (mice are euthanized and CLN and blood samples are collected)	CLN: 1.Exposure to DE and gas lead to a decrease in total number of CLN cells. DE and gas resulted in lower CD4+ and TCR-β, gas exposed mice presented significantly lower percentages. 2.Cell proliferation response to SBP was higher in gas-exposed mice than in the control group. The production of MCP-1 increased in CLN cells when stimulated with SBP (in vitro) but not significant difference in the production at 24 and 48 h between the DE-exposed and the control. The 3. SBP-stimulated cells of the gas-exposed showed greatly enhanced MIP-1α production at 24 h. At 48 h the production of MIP-1α was more prominent in the gas-exposed group. Exposure to gas increased the amount of TARC in the culture supernatants of CLN cells. 4. Production of IP-10 for DE, gas-exposed and control mice was below L.O.D PLASMA: 1. Exposure to DE or gas significantly decreased the anti-SBP IgG1 antibody titers in the plasma of the mice. 2. Exposure to DE or gas increased the anti-SBP IgG2a antibody titers in the mice plasma. 3. The levels of SBP-specific IgE were below L.O.D.

Study	Pollutant	Exposure	Particle Effects
Reference: Fujimaki et al. (2005) **Species:** Mouse **Gender:** Female (Pregnant- 1st day of pregnancy) **Strains:** Sic: IRC **Cell Types** Fetal Cells/ RNA Spleen Cells	Exposure to DE DEP generated by a 2369-cc diesel engine operated at 1050 rpm and 80% load with commercial light oil Composition of DEP: Not Reported	**Route:** Whole-Body Inhalation Chambers **Dose/Concentration:** 0.3, 1.0 and 3.0 mg DEP/m^3 **Particle Size (Distribution):** Average diameter of DEP = 0.4um **Time to Analysis:** Exposure began at 2 days postcoitum and was continued until 13 days postcoitum. Exposure time was 12 h daily for 7 days/week Group 1: 0.3 mg DEP/m^3 Group 2: 1.0 mg DEP/m^3 Group 3: 3.0 mg DEP/m^3 Group 4: Exposed to clean air Pregnant females were killed 14 days postcoitum.	mRNA Expression in Placentas: In groups that were exposed to DE, during placental absorption the expression of CYP1A1 mRNA decreased to undetectable levels. Levels of CYP1A1 mRNA in normal placentas from DE-exposed mice were unchanged. Expression of TNFα mRNA increased approximately twofold over the control. mRNA levels of inflammatory cytokines IL-2, IL-5, IL-12α, IL-12β and GM-CSF increased as placentas were exposed to DE (O.3 and 3.0 mg DEP/m^3) and IL-6 mRNA expression was increased 10-fold in placentas exposed to 3.0 mg DEP/m^3 DE.

Study	Pollutant	Exposure	Particle Effects
Reference: Gao et al. (2004) **Species:** Human **Cell Line:** Lung Fibroblasts that were infected with *Mycoplasma fermentans*	ROFA ROFA was collected near a power plant in FL that was burning low sulfur # 6 oil. ROFA Composition: Reported in previous study. *PM from Dusseldorf, volcanic ash for Mt. St. Helens, PM from Utah were used to compare against ROFA in one experiment*	**Route:** Cells were incubated with medium containing particles. **Dose/Concentration:** Cell Concentration: Cells were seeded inot 6-well plates (3-4.5X105 cells/3mL/well) or 24-well plates (0.6-1 X105 cells/1.0 mL/well) ROFA concentration varied with experiment (see results) **Particle Size (Distribution):** Not Reported **Time to Analysis:** Exposure methods and exposure time varied with experiment (see results)	IL-6 Production After Exposure to M. fermentans and ROFA: M. fermentans and ROFA synergistically induced the production of IL-6 when compared to either stimulus acting alone. Cells were exposed to M. fermentans alone and with varying concentrations of ROFA (0 - 60 μg/mL) for 24 h. M. fermentans alone produced a 5-fold increase in IL-6 when compared to the control and exposure to the bacteria + ROFA expressed a significant increase in IL-6 release. Uninfected cells also produced a dose-dependent IL-6 response to ROFA, but the coexposure to the bacteria and PM led to a response that was 21-50 times greater than seen in uninfected cells. Cell Viability: The LD50 was found to be 100 μg/mL significantly higher than the synergistic effects of ROFA and M. fermentans. Comparison of ROFA and Other PM: Infected and uninfected cells were exposed to 20 μg/mL of dust collected from Dusseldorf Germany, aqueous extract of PM from Provo Valley (near Salt Lake City Utah) and volcanic ash from Mt. St. Helens and 20 μg/mL ROFA for comparison. 20 μg/mL of ROFA increased IL-6 production by 4-fold in uninfected cells compared to the control and the other sources of PM had little effect on IL-6 compared to the control. In the infected cells, ROFA caused a 20-fold increase in IL-6 compared to control (100-fold compared to the uninfected control) and the other sources of PM again did not produce any significant change in Il-6 levels. MALP-2 Lipopetide + ROFA Synergistic Effect: MALP-2 is a membrane lipoprotein derived from M. fermentans and because many lipoproteins exhibit stimulatory effects on macrophages, the researchers examined MALP-2 to see if it plus ROFA would produce the same IL-6 response as the actual bacteria + ROFA. HLF cells were exposed to varying concentrations of MALP-2 with and without ROFA (40μg/mL) for 24 and 48 h exposure. Exposure to MALP-2 alone caused a moderate dose-dependent increase in IL-6, exposure for 48 h produced a 2-fold higher response than at 24 h. ROFA alone had a minimal effect on IL-6, with an IL-6 release of 11±4 pg/μg DNA at 24-h and 45±21 pg/μg DNA at 48 h exposure. Combination of ROFA + MALP-2 caused a significant increase in IL-6 release. At 24-h the ROFA+MALP-2 release was 3-fold higher than MALP-2 alone induced release and at 48 h, ROFA+MALP-2 induced IL-6 release was 6-fold greater than MALP-2 alone. IL-6 Release Caused By The Water-Soluble Fraction of ROFA: Cells were exposed to 20 or 40 μg/mL ROFA or 20 or 40 μg/mL soluble portion of ROFA for 24 and 48 h in the presence or absence of MAPL-2. Exposure to MALP-2 or ROFA (whole or soluble fraction) alone had minimal effects on IL-6 release. The soluble fraction of ROFA +MALP-2 did not significantly alter IL-6 release at 20μg/mL or 40 μg/mL dose at 24-h or at the 20 μg/mL dose at 48 h but induced IL-6 release was significantly higher in response to the 40 μg/mL dose of the soluble fraction of ROFA at 48 h. In comparison the whole ROFA +MALP2 caused significant increase at 40μg/mL at 24-h and at both 20 μg/mL and 40 μg/mL at 48 h exposure. Therefore the synergy expressed in the soluble fraction of ROFA+ MALP-2 is slightly weaker than whole ROFA. Effect of V, Ni, Fe and Cu on IL-6 Release: Ni +MALP-2 produced the greatest synergistic release of IL-6 and to a lesser degree V did as well. Cu did not synergistically induced IL-6 release.

Study	Pollutant	Exposure	Particle Effects
Reference: Gavett et al. (2003) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 7 weeks **Weight:** 18-21 g	Exposure to $PM_{2.5}$ from the German cities of Hettstedt or Zerbst Composition of PM in the "Effects Section"	**Route:** Oropharyngeal aspirations **Dose/Concentration:** 100ug PM in 50 µL saline **Particle Size (Distribution):** $PM_{2.5}$ - Specific mean diameter: Not Reported **Time to Analysis:** Exposure Group: Mice were exposed to one dose of 100 µg PM in 50 µL saline. Lungs Lavage (BAL) 18 hours after dosage in the exposed group. (used to measure toxicity of dose) Sensitization Phase: Only OVA-allergic mice were examined. Mice were exposed to 50 µg PM by oropharyngeal aspiration 2-h before being sensitized with 10 µg OVA, repeated two days later. Then on day 14- all mice were challenged by aspiration of 20 µg OVA. Challenge Phase: Both allergic and non-allergic mice were examined. Mice were sensitized intraperitoneally with 20 µg OVA. Fourteen days later mice were exposed to 100 µg $PM_{2.5}$ followed 2-h later by 20 µg OVA aspirated. Parameters measured on days 2 and 7 after FINAL exposure to OVA.	PM Composition: PM samples from Hettstedt has several-fold higher levels of zinc, magnesium, lead, copper and cadmium than samples from Zerbst. Exposure Group: Measure of Toxicity Hettstedt PM significantly increased BAL protein and NAG levels (compared to the control). Zerbst PM did not. Mice exposed to Zerbst has lower levels of LDH than the control groups. 2. Hettstedt exposed mice had increased levels of IL-1β, IL-6 and MIP-2 in comparison to control and to mice exposed to Zerbst. $PM_{2.5}$ at a dose of 100 µg was not found to be toxic, therefore used for subsequent studies. Immediate Airway Response (measured by PenH): 1. Challenge Phase: In allergic mice, Hettstedt PM increased PenH 190% compared to baseline, Zerbst increased PenH by 120% and the Control increased by 44%. 2. Sensitization Phase: No differences. Two Days After OVA Challenge Airway Response (McH responsiveness): 1. Challenge Phase: No difference in non-allergic mice from either group. In allergic mice, Hettstedt PM still caused a significant response to Mch responsiveness, Zerbst none.No effects on day 7. 2. Sensitization Phase: No effect. IgE Levels: Serum collected on day 2 showed Antigen-specific IgE was increased by Hettstedt $PM_{2.5}$ in both the sensitization and challenge phases when compared to the control and exposure to Zerbst. Day 7 serum indicated no effect. BAL Analysis: Cell Counts: 1. Challenge Phase: In non-allergic mice both Hettstedt and Zerbst Pm increased BAL neutrophil numbers (3-fold) and in allergic mice only Hettstedt PM significantly increased neutrophil count. Eosinophil numbers were increased only in allergic mice exposed to Hettstedt PM. Lymphocyte numbers were not different among groups. 2. Sensitization Phase: Exposure to PM had no significant effect on BAL cell counts. Lung Injury: 1. Challenge Phase: At 2 days after both Hettstedt and Zerbst PM administered in allergic mice caused significant increases in proteins, LDH and NAG compared to the non-allergic groups. Both PMs caused an increase in LDH in allergic mice compared to the control, but only Hettstedt caused an increase NAG in allergic mice compared to control. At 7 days no effect. 2. Sensitization Phase- No significant differences noted. Cytokines: 1. Challenge Phase: Allergic mice had increased levels of IL-4, IL-5 and IL-13 compared to non-allergic mice (at 2 days after). IL-5 was significantly increased by exposure to either PM in allergic mice compared to non-allergic mice. Exposure to either PM caused an increase in TNF-α and IFN-γ (by 6-8 fold) in allergic mice, there was also an increase in these inflammatory cytokines in the non-allergic group but was not statistically significant. 2. Sensitization Phase- not reported.

Study	Pollutant	Exposure	Particle Effects
Reference: Hamada et al. (2007) **Species:** Mouse **Gender:** Female (Pregnant: 5, 3 and 1 day before partruition) **Strain:** BALB/c **Use:** Pregnant mice were exposed and offspring were analyzed	ROFA ROFA was obtained from a precipitator until of a local power plant. Composition of ROFA: In The "Effects Section"	**Route:** Nebulized ROFA lechate **Dose/Concentration:** ROFA was in a 50mg/mL dilution in PBS **Particle Size (Distribution):** Not Reported **Time to Analysis:** Pregnant mice were exposed to nebulized ROFA leachate for 30 min/day at days 14, 16 and 18 of pregnancy (5, 3, and 1 day before delivery). Newborns received a single injection (ip) of OVA(5ug)+ alum (1mg0 at day 3 (of life) followed by exposure to: 1. aerosolized OVA days 12, 13 and 14 (2-week old protocol) OR 2. aerosolized OVA days 32, 33 and 34 (5-week old protocol) Analysis performed 48 h after final allergen exposure	Susceptibility to Asthma: 1.Exposure only to PBS aerosols during pregnancy did not develop prominent asthma features. 2.The offspring of the ROFA mothers revealed increasing airway hyper responsiveness (enhanced pause to methacholine challenge) and elevated numbers of eosinophils in the BAL fluid. Similar results were seen in both the 2-week and 5-week old groups. IgE Levels: Histopathology revealed prominent inflammation in the lungs of the ROFA neonates and increased allergen-specific IgE and IgG1 levels in the 5-week group. Maternal Influence: Breast milk was not shown to be responsible for the increased susceptibility to allergy seen in offspring. IL-4 and IFN-γ: 1. IL-4 and IFN-γ levels in maternal mice (measured 1day after delivery) showed no difference between PBS exposed or ROFA exposed mice. 2. Cultured spleen cells from mice born of ROFA-exposed mothers showed either increased or similar levels of IL-4 and decreased production of IFN-γ causing an increase in the ratio of IL-4/IFN-γ indicating greater susceptibility to develop Th2- allergic response. Composition of ROFA (in μg/mL): 341.2 Ni, 323.4 V, 232.2 Zn, 18.3 Co, 15.8 Mn, 8.4 Ca, 6.7 Cu, 6.1 Sr, 5.0 mg, 0.9 Sb, and 0.6 Cd.
Reference: Hao et al. (2003) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-7 weeks **Use:** Used mice that exhibit transgenic IL-5 expression in lung epithelium.	DEP DEP collected from a 4-cylinder diesel engine under a 10-torque load. DEP Composition: Not Reported	**Route:** Nebulization of a 10mg/mL DEP solution **Dose/Concentration:** 2 mg/m^3 DEP Number of doses depends on methods **Particle Size (Distribution):** Not Reported **Time to Analysis:** Mild Sensitization-Mice received 20 μg of OVA without alum in 500uL of PBS intraperitoneally on day1. Negative control received 500 μL PBS (group 1) and positive control received 20 μg of OVA plus 2 mg of alum in 500uL PBS (group 2). All mice were exposed on days 14-17 to nebulized saline (group 1), saline for 1-h followed by 1% OVA (group 2), 2mg/m^3 DEPs for an hour followed by 1%OVA (group 3), or saline for 1-h followed by 1%OVA. (see Fig. 1 A) Postchallenge Model- All groups in postchallenge (minus negative control) received 20 μg of OVA plus 2mg of alum intraperitoneally on day 1. Afterwards the animals were challenged with either nebulizer saline or 1% OVA daily for 20 min on days 15-17 and afterwards mice received nebulized saline, 1% OVA or 2mg/m^3 DEPs for 1-h daily on days 18-21. (see Fig. 6 A) Mild- Sensitization Model killed on day 19 Postchallenge Model killed on day 23 Transgenic Mice: Mice exposed to nebulized saline or DEPs (200μg/m^3) for 1-h daily for 3 days. Mice were killed on day 5.	Mild Sensitization Model: BAL Cell Count: Group 2 (ova + alum) - showed strong increase in BAL total cell count and BAL eosinophils. The mildly sensitized groups (groups 3 and 4) showed a smaller increase in BAL eosinophil counts. Cytokines: Group 2- produced a significant increase in OVA-specific IgE and IgG1 and IL-13. Mildly sensitized groups (group 3 and 4) should a small increase in OVA-specific IgE and IgG1 Methocholine-Induced AHR: DEP exposure (group 3) produced a strong increase in methacholine-induced airway hyperreactivity. Histology: DEPs induced foci of inflammation associated with large /intermediary airways, as well as the influx of MBP eosinophils in the mucosa. IL-5 Transgenic Mice (NJ.1726 Mice) Exposure of transgenic mice to DEP daily for 3 days (independent of an allergen) resulted in increased AHR compared with that of animals receiving saline only. These mice did not show changes in BAL cell count or BAL cytokine levels. Postchallenge Model: AHR: Showed no response for mice receiving DEPs without prior OVA challenge. However mice receiving OVA challenge on days 15-17 and DEPs on days 18-21 show a statistically significant increase in AHR compared to those receiving saline or DEPs without OVA challenge. BAL: DEP exposure resulted in a slight increase (not significant) in IgE and IgG1- more so in the group that received OVA days 15-17 and DEP on days 18-21. No significant increase in cytokine levels was observed with DEP exposure but again OVA (group 3) caused a strong increase in IL-13.

Study	Pollutant	Exposure	Particle Effects
Reference: Harrod, K. et al. 2002 **Species:** Mouse **Gender:** NR **Strains:** C57BL/6 **Age:** 8-10 weeks **Use:** Infected with RSV	Diesel Engine Emissions (DEE)- generated from a 5.9-liter turbo diesel engine fueled by Number 2 fuel.	**Route:** Whole-body Inhalation **Dose/Concentration:** Daily mean of**:** 30 μg/m^3 (low level) or 100 μg/m^3 (high level) DEE Composition: Low: (ppm) Nitogen oxides- 2.0 ±0.19. Nitrogen oxide- 1.9±0.15, Nitrogen dioxide- 0.07±0.03, CO- 0.94±0.22, Sulphur Dioxide- 8.3±0.51 High: (ppm) Nitogen oxides- 43.3 ±2.2. Nitrogen oxide- 38.7±1.9, Nitrogen dioxide- 4.7±0.3, CO- 29.0±2.9, Sulphur Dioxide- 364.9±22.3 **Particle Size (Distribution):** 0.05- 10 μm aerodynamic diameter **Time to Analysis:** 6 hours/day for 7 days. After the final 6 hour exposure period mice were infected with RSV (106 pfu). Time to analysis varied with test.	Viral Gene Expression: RNA isolated from lungs 4 days after infection indicated that RSV-F gene expression was not apparent in the lungs of air-exposed infected animals but low-level RSV-G gene expression was detectable. In comparison both RSV-F and RSV-G gene expression was detectable in particle-exposed animals (both low and high level doses) but high-level doses indicated a more significant increase when compared to air- exposed. BALF: Exposure to low-level DEE caused a slight increase in cell numbers (not sig.) and exposure to high-level DEE also increased cell numbers, with macrophages being the most predominantly increased cell in both groups (see Table 3 for a complete comparison of inflammatory cell numbers). Lung Histology: Histological analysis of the lung showed dose-dependent bronchi and bronchioles inflammation. Inflammatory Mediators: TNF-α and IFN-γ were significantly increased in RSV-infected mice exposed to low or high level DEE and not increased in RSV-infected mice exposed to air. Mucous Cell Metaplasia: Mucous metaplasia was increased in epithelium of RSV-infected mice when exposed to DEE in a dose-dependent manner. CCSP Production: CCSP staining was more dense in the terminal airways than in the large airways of the lungs. DEE alone did not have an effect on CCSP production, except the high dose of DEE caused increased staining in the terminal airway. Low DEE + RSV infection did produce a significant increase in CCSP staining in the large airway when compared to air-exposure. Surfactant Protein B: Surfactant protein B levels were decreased when exposed to high-level DEE in RSV infected mice, when compared to air or low-level exposed. SP-A: Prior exposure to low or high level DEE decreased SP-A staining in alveolar type II cells and airways epi cells during RSV infection.
Reference: Hiramatsu, K. (2003) 29: 607 **Species:** Mouse **Gender:** Female **Strains:** BALB/c and C57BL/6 **Age:** 8 weeks **Weight:** 17-22 g	DE -DE (generated by diesel engine and diluted with filtered clean air)	**Route:** Exposure chamber **Dose/Concentration:** Low level group: DE - 100mg/m^3 High level group: DE - 3mg/m^3 **Particle Size (Distribution):** NR **Time to Analysis:** 1 month or 3 months (7 hours per day, 5 days per week)	Lung Histopathology: After 1 month DE exposure, DEP-laden alveolar macrophages (AM) were seen in the alveoli and peribronchial tissues of both BALB/c and C57Bl/6 mice. More DEP carrying AM were recognized in the high DEP exposure group than in the low DEP exposure group. After 3 months of DE exposure, marked accumulation of DEPs was recognized in the alveoli and peribronchial tissues. More DEP deposition in high level group than low level group. Lungs exposed to high DE level showed BALT around the DEP laden AM. The BALT was more conspicuous in BALB/c mice than in C57BL/6 mice. Immunohistochemistry: 3 month exposure to high DE level lungs of both strains showed BALT around the DEP-laden AM. No significant differences were found in the T- and B- cell populations between the BALB/c and C57BL/6 mice.

Study	Pollutant	Exposure	Particle Effects
Reference: Hiramatsu, K. (2003) 29: 607 **Species:** Mouse **Gender:** Female **Strains:** BALB/c and C57BL/6 **Age:** 8 weeks **Weight:** 17-22 g	DE -DE (generated by diesel engine and diluted with filtered clean air)	**Route:** Exposure chamber **Dose/Concentration:** Low level group: DE - 100mg/m^3 High level group: DE - 3mg/m^3 **Particle Size (Distribution):** NR **Time to Analysis:** 1 month or 3 months (7 hours per day, 5 days per week)	BALF: 1 month DE exposure, the percentage of lymphocytes and neutrophils had increased slightly in all groups. 3 months DE exposure this percentage increased further, especially in the high-level exposure group. Lymphocytes and neutrophils showed a greater increase in BALB/c mice than in C57BL/6 mice. AM carried more DEPS and were more swollen after 3 months' exposure than after 1 month. No eosinophils or basophils were observed in any of the groups. MAC-1-positive cells in BALF: 1 month exposure, the percentages of MAC-1-positive cells in both BALB/C and C57BL/6 mice in the high level exposure group were significantly higher (33.8% vs. 5.3%) than those in the corresponding low-level exposure group. 3 months exposure percentages of MAC-1-positive cells were also significantly higher (20.3% vs. 7.0%) in both strains of mice exposed to high DE level compared with the low-level exposure groups and the control group.
Reference: Hiramatsu, K. (2003) **Species:** Mouse **Gender:** Female **Strains:** BALB/c and C57BL/6 **Age:** 8 weeks **Weight:** 17-22 g	DE -DE (generated by diesel engine and diluted with filtered clean air)	**Route:** Exposure chamber **Dose/Concentration:** Low level group: DE - 100mg/m^3 High level group: DE - 3mg/m^3 **Particle Size (Distribution):** NR **Time to Analysis:** 1 month or 3 months (7 hours per day, 5 days per week)	Cytokine and iNOS mRNA expression**:** 1 month DE exposure - expression levels of TNF-a, IL-12p40, IL-4 and IL-10 mRNA in the DE-exposed lung tissue increased in a dose dependent manner. In contrast IL-1b and iNOS showed dose-dependent decreases in the DE-exposed groups.IFNF-g mRNA expression increased in BALB/c mice, but decreased in C57BL/6 mice. Il-6 mRNA expression was very low in both groups. 3 months DE exposure - IL-12 mRNA expression had increased slightly and IL-1b, IL-4, and IFNF-g mRNA expression had decreased slightly in the BALB/c mice. In C57BL/6 mice, IL-12 adn IFNF-g mRNA expression had increased. Expression levels of IL-4 and IL-10 mRNA had increase in the C56BL/6 mice exposed to low level DE, but decreased in the high-level exposure group. No significant differences in levels of TNF-c or iNOS between the 1-month and 3-month DE exposure groups. EMSA: even 1 week of DE exposure increased binding of the nuclear proteins to the labeled oligonucleotide of the NF-kB activation in BALB/c mice was more intense than in C57BL/6 mice.
Reference: Hiramatsu, K. (2003) 31: 405 **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 8 weeks **Weight:** 17-22 g	DE (generated by diesel engine and diluted with filtered clean air.) Mycobacterial Infection -M.tuberculosis (ATCC35812) Kurono strain	**Route:** Exposure chamber **Dose/Concentration:** Inhalation exposure system (1X106 colony forming units) Low level group: DE - 100mg/m^3 High level group: DE - 3mg/m^3 Mycobaterial infection**:** 5mL of a suspension containing 106 colony-forming units **Particle Size (Distribution):** NR **Time to Analysis:** 1 month, 2 months, or 6months (7 hours a day, 5 days a week). On last day of DE exposure, 6 mice from each group were infected. Exposure time 90 minutes. Lungs and spleen were removed to evaluate growth of mycobacterium at 7 weeks after infection. Colonies on the medium were counted after 4 weeks of incubation.	Granulomatous lesions in lungs: The text says there was a statistical difference in number of gross lesions between 6-month DE exposed mice and 6-month control mice. The table referenced in the text doesn't match the text. Mycobacterial CFU in lungs and spleens: Mice exposed to DE for 1 month - slightly but not significantly smaller mycobacterial CFU in the spleen than control. Mice exposed to DE for 2 months - greater mycobacterial CFU in the lungs and spleens, but no significant difference between DE-exposed mice and control mice. For mice exposed to DE for 6 months there was a marked (~4 fold) increase in mycobacterial CFU in the lung tissues.

Study	Pollutant	Exposure	Particle Effects
Reference: Hiramatsu, K. (2003) 31: 405 **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 8 weeks **Weight:** 17-22 g	DE (generated by diesel engine and diluted with filtered clean air.) Mycobacterial Infection -M.tuberculosis (ATCC35812) Kurono strain	**Route:** Exposure chamber **Dose/Concentration:** Inhalation exposure system (1X106 colony forming units) Low level group: DE - 100mg/m^3 High level group: DE - 3mg/m^3 Mycobaterial infection**:** 5mL of a suspension containing 106 colony-forming units **Particle Size (Distribution):** NR **Time to Analysis:** 1 month, 2 months, or 6months (7 hours a day, 5 days a week). On last day of DE exposure, 6 mice from each group were infected. Exposure time 90 minutes. Lungs and spleen were removed to evaluate growth of mycobacterium at 7 weeks after infection. Colonies on the medium were counted after 4 weeks of incubation.	Histopatholgoical observations: Lungs of DE-exposed mice -the number of DEP-laden AM and DEPs observed in the alveoli and peribronchial tissues increased in a time dependent manner. BALT was seen around the DEPs in mice exposed to DE for 2 and 6 months. Both DE and control showed multifocal tuberculous lesions with a massive accumulation of tubercle bacilli in the lungs. In control mice, granulomas consisted of epithelioid cells and lymphocytes were focal and their borders relatively clear. The mycobaterial lesions in DE-exposed mice were disseminated. Tubercle bacilli and DEPs coexisted in the AM. In the mice exposed to DE for 6 months the infiltration of inflammation cells was more prominent than in control mice and in the mice exposed to DE for the 1 or 2 month period.
Reference: Hiramatsu, K. (2003) 31: 405 **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 8 weeks **Weight:** 17-22 g	DE (generated by diesel engine and diluted with filtered clean air.) Mycobacterial Infection -M.tuberculosis (ATCC35812) Kurono strain	**Route:** Exposure chamber **Dose/Concentration:** Inhalation exposure system (1X106 colony forming units) Low level group: DE - 100mg/m^3 High level group: DE - 3mg/m^3 Mycobaterial infection**:** 5mL of a suspension containing 106 colony-forming units **Particle Size (Distribution):** NR **Time to Analysis:** 1 month, 2 months, or 6months (7 hours a day, 5 days a week). On last day of DE exposure, 6 mice from each group were infected. Exposure time 90 minutes. Lungs and spleen were removed to evaluate growth of mycobacterium at 7 weeks after infection. Colonies on the medium were counted after 4 weeks of incubation.	Cytokines and iNOS mRNA Expression: In 6-month DE exposed mice with mycobacterial infection, the expression levels of TNF-a, IL-1b, and IFNg mRNSAs were increased as compared to those of unexposed control mice. As to IL-12 and iNOS mRNAs, the expression levels were unchanged. In infected control mice, the expression levels of TNFa mRNA was slightly increased and IL-1b mRNA level was slightly decreased incomparison with infected negative-control mice. In 1- or 2-month DE-exposed mice with mycobacterial infection the expressions levels of TNFa, IL-1b, IL-12p40, IFNg, and iNOS mRNAs were increased.
Reference: Ichinose, T. et al. (2002) **Species:** Mouse **Gender:** NR **Strains:** BALB/cAnN, ICR, and C3H/HeN **Age:** 5 weeks **Weight:** NR	DE: DE generate by light duty (3059cc) four cylinder diesel engine (4JG2-type, Isuzu Automobile Company Tokyo Japan) Der f: Crude extract of Dermatophagoides farinae - LSL Co. Tokyo Japan	**Route:** exposure chamber intratracheal instillation **Dose/Concentration:** 1. Air 2. DE only: 3.0 mg/m^3 3. Air + Der f**:** 1mg Der f 4. DE 3.0 mg/m^3 + 1mg Der f **Particle Size (Distribution):** DEP - Mass median aerodynamic diameter of 0.4mm **Time to Analysis:** DE: 8 weeks (12 h/day, 7 days per week) Der f: doses of Der f @ 2 week intervals for 6 weeks Analysis three days after last instillation	DE exposure caused the proliferation of nociliated cells and epithelial cell hypertrophy in the airway. DP contained macrophages in the alveolar tissue spaces and the accumulation of lymphocytes in the peribronchiolar lymphoid tissue and the submucosal layer of the airway were observed. Der f treatment induced the proliferation of goblet cells in the airway. Desquamated goblet cells were seen only in the airway of the C3H/He mice. All three strains exposed to DE with Der f showed inflammatory cells and soot-containing macrophages in the submucosal layer and in the interstitium around a vessel. C3H/He mice had higher number of eosinophils than the other strains. Eosinophil infiltration in the airway: DE alone caused a slight infiltration of eosinophils to the submucosal layer of the bronchi and bronchioles in the C3H/He mice. Air +Der f produced from very slight to moderate infiltration of eosinophils in the three strains. DE+ Der f produced slight to moderate infiltration of eosinophils in the three strains. The combination of DE + Der f significantly induced an infiltration of eosinophils in the BALB/c and ICR mice compared with the mice treated with air+Der f. The combination only slightly decreased the number of eosinophils in the C3H/He mice.

Study	Pollutant	Exposure	Particle Effects
Reference: Ichinose, T. et al. (2002) **Species:** Mouse **Gender:** NR **Strains:** BALB/cAnN, ICR, and C3H/HeN **Age:** 5 weeks **Weight:** NR	DE: DE generate by light duty (3059cc) four cylinder diesel engine (4JG2-type, Isuzu Automobile Company Tokyo Japan) Der f: Crude extract of Dermatophagoides farinae - LSL Co. Tokyo Japan	**Route:** exposure chamber intratracheal instillation **Dose/Concentration:** 1. Air 2. DE only: 3.0 mg/m^3 3. Air + Der f**:** 1mg Der f 4. DE 3.0 mg/m^3 + 1mg Der f **Particle Size (Distribution):** DEP - Mass median aerodynamic diameter of 0.4mm **Time to Analysis:** DE: 8 weeks (12 h/day, 7 days per week) Der f: doses of Der f @ 2 week intervals for 6 weeks Analysis three days after last instillation	Lymphocyte accumulation in the airways: DE exposure w/o Der f significantly increased the accumulation of lymphocytes in the submucosal layer of the the three strains compared with air+saline. Air +Der f significantly increased only in the C3H/He mice. DE+Der f caused further increases of lympyocytes in the three strains. Goblet cell proliferation in the airways: DE without Der f caused little proliferation of goblet cells in the airway epithelium in the three strains. Air + Der f induced a slight proliferation of globelt cells in the BALB/c and ICR mice and moderate proliferation in the C3H/He mice. DE+ Der f caused more proliferation of goblet cells in the ICR mice than did Air+Der f - statistically significant. For the C3H/He mice the combination significantly decreased goblet cells proliferation compared to the mice treated with air+ Der f.
Reference: Ichinose, T. et al. (2002) **Species:** Mouse **Gender:** NR **Strains:** BALB/cAnN, ICR, and C3H/HeN **Age:** 5 weeks **Weight:** NR	DE: DE generate by light duty (3059cc) four cylinder diesel engine (4JG2-type, Isuzu Automobile Company Tokyo Japan) Der f: Crude extract of Dermatophagoides farinae - LSL Co. Tokyo Japan	**Route:** exposure chamber intratracheal instillation **Dose/Concentration:** 1. Air 2. DE only: 3.0 mg/m^3 3. Air + Der f**:** 1mg Der f 4. DE 3.0 mg/m^3 + 1mg Der f **Particle Size (Distribution):** DEP - Mass median aerodynamic diameter of 0.4mm **Time to Analysis:** DE: 8 weeks (12 h/day, 7 days per week) Der f: doses of Der f @ 2 week intervals for 6 weeks Analysis three days after last instillation	Local cytokine and chemokine expression in lung tissue supernatant: DE+ saline significantly increased the protein level of MIP-1a in all three strains. MCP-1 increase too, but not significantly. Air + Der f increased the protein levels of IL-5 and eotaxin in the C3H/He mice. DE+Der f considerably increased IL-5, RANTES, eotaxin, MCP-1, and MIP-1a in the three strains compared with Air + saline. or Air +Der f. A synergistic phonomenon was observed in the increase of MCP-1. The protein IL-5 in the C3H/He mice treated with DE + Der f decreased compared with air + Der f. Protein levels of IL-3 in the ICR and C3H/He mice treated with DE + Der f were lower than with air+saline. C3H/He mice significantly. Der f-specific immunoglobulin production in plasma: The increasing order of the antigen-specific IgG1 production in mice treated with DE + Der f was BALB/c<ICR<C3H/He mice. The adjuvant effect of DE on IgG1 production was observed in the ICR and C3H/He mice - the increase statistically significant compared to mice treated with air+Der f. The IgE antibodies were lower than one titer in all mice strains.
Reference: Ichinose, T. et all (2004) **Species:** Mouse **Gender:** NR **Strains:** BALB/c, ICR, and C3H/He **Age:** 5 weeks **Weight:** NR	Dust mites: (D. farinae) LSL, Tokyo Japan DEPs prepared from light duty(2740cc) four-cylinder diesel engine	**Route:** intratracheal instillation **Dose/Concentration:** 1. Dust mites: 1mg dissolved in PBS 2. Mites + DEP: 1mg dissolved in PBS + 50mg DEP **Particle Size (Distribution):** DEP - Mass median aerodynmaic diamter of 0.4mm **Time to Analysis:** 4 times at 2 week intervals. 3 weeks after the last instillation mice were sacrificed	Histological changes: Dust mite treatment produced very slight to moderate recruitment of eosinophils in all three strains of mice. The combination of Dust mite+ DEP induced a significant recruitment of eosinophils in all three strains compared with mice treated with dust mites alone. Similar changes in lymphocytes were observed among all three strains with either treatment. The combination of Dust mite + DEP induced a significant recruitment of lymphocytes in BALB/c and ICR mice compared with mice treated with dust mites alone. Goblet cells: Dust mite treatment induced a slight proliferation of goblet cells in the airway epithelium of BALB/C and ICR mice and a moderate proliferation in C3H/He mice. Dust mite+DEP caused more proliferation of goblet cells in all three strains than dust mites alone. The increased level in ICR mice treated with Dust Mite +DEP was statistically significant compared with that in mice treated with dust mites alone.

Study	Pollutant	Exposure	Particle Effects
Reference: Ichinose, T. et all (2004) **Species:** Mouse **Gender:** NR **Strains:** BALB/c, ICR, and C3H/He **Age:** 5 weeks **Weight:** NR	Dust mites: (D. farinae) LSL, Tokyo Japan DEPs prepared from light duty(2740cc) four-cylinder diesel engine	**Route:** intratracheal instillation **Dose/Concentration:** 1. Dust mites: 1mg dissolved in PBS 2. Mites + DEP: 1mg dissolved in PBS + 50mg DEP **Particle Size (Distribution):** DEP - Mass median aerodynmaic diamter of 0.4mm **Time to Analysis:** 4 times at 2 week intervals. 3 weeks after the last instillation mice were sacrificed	Local cytokine expression: IL-5 was not detected in BALB/c and ICR mice treated with Dust mite alone, where as the mean level of IL-5 in C3H/He mice showed 76.3 ± 1.45pg in lung tissue. Dust mite + DEP induced significant elevation of local IL-5 in ICR and C3H/He mice compare to dust mite alone. Eotaxin levels in C3H/He mice were 3 times and 2.8 times higher than BALB/c and ICR mice respectively. Dust mite + DEP caused significant elevation of eotaxin in all three strains than those treated with dust mite alone. The expression order of RANTES with dust mite alone was ICR<BALB/c<C3H/He mice. These levels were unaffected by DEP. The expression order of IL-4 with dust mite alone was C3H/He<ICR<BALB/c mice. The changes of levels by DEP were not significant. The production levels of IL-4 and RANTES in lung tissue did not correlate with the manifestations of allergic airway inflammation induced by dust mite treatment with or without DEP.
Reference: Ichinose, T. et all (2004) **Species:** Mouse **Gender:** NR **Strains:** BALB/c, ICR, and C3H/He **Age:** 5 weeks **Weight:** NR	Dust mites: (D. farinae) LSL, Tokyo Japan DEPs prepared from light duty(2740cc) four-cylinder diesel engine	**Route:** intratracheal instillation **Dose/Concentration:** 1. Dust mites: 1mg dissolved in PBS 2. Mites + DEP: 1mg dissolved in PBS + 50mg DEP **Particle Size (Distribution):** DEP - Mass median aerodynmaic diamter of 0.4mm **Time to Analysis:** 4 times at 2 week intervals. 3 weeks after the last instillation mice were sacrificed	Cytokine expression in plasma: IL-5 in plasma of ICR mice in dust mite or dust mite+DEP groups were below detection limits. BALB/c and C3H/He mice were slightly higher than detection limits. The level of IL-5 in C3H/He mice in dust mite+DEP group was significantly higher than dust mite alone groups. RANTES was unaffected by DEP. Dust mite-specific immunoglogulin production: The production order of antigen-specific IgG1 antibody in mice treated with dust mite alone or dust mite+DEP was BALB/c<ICR<C3H/He mice. The adjuvant effect of DEP on increased IgG1 production was observed in all three strains. Increased dustmite-specific-IgG1 production in C3H/He mice was statistically significant compared with dust mite alone. The production levels of dust -specific-IgG1 in plasma correlated with the manifestations of eosinophilic airway inflammation by dust mite alone or dust mite+DEP. IgE levels were low in all strains and DEP did not increase IgE production.

Study	Pollutant	Exposure	Particle Effects
Reference: Inoue, K (2006) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 weeks **Weight:** 29-33 g	PM-OC: Urban PM, collected for 1 month during early summer, 2001 by Andersen high volume samplers (AH-600, Tokyo-Dylec,Tokyo) in Urawa city Saitama, Japan Extracts were filtered and evaporated. Residues weighed, dissolved in 1100% dimethyl sulfoxide and prepared as PM-OC. 12% of the PM was OC when recoveries were based on the weight of the residue. Bacterial endotoxin (LPS) - (E. Coli B55: 05, Difco Lab, Detroit, MI,USA)	**Route:** intratracheal instillation **Dose/Concentration:** Vehicle group: PBS PM-OC group: 4mg/kg of PM-OC in vehicle LPS group: 2.5mg/kg of LPS in vehicle PM-OC+LPS group: combined adminstration of PM-OC +LPS in vehicle **Particle Size (Distribution):** average concentration of particles less than 2.0 mm was 40 mg/m^3. **Time to Analysis:** single, mice were evaluated 24-h after intratracheal administration	Effects of PM-OC on LPS related lung inflammation: PM-OC alone did not significantly increase the infiltration of neutrophils, but LPS challenge showed a marked increase in the number of neutrophils compared with vehicle. Administration of LPS combined with PM-OC significantly increased the infiltration of neutrophils compared with LPS administration alone. Effects of PM-OC on histological changes in the lung: Combined treatment with PM-OC and LPS resulted in enhanced neutrophilic inflammation. Effects of PM-OC on pulmonary edema related to LPS: LPS group compared with vehicle group had a significant increase in lung water. The combined administration of PM-OC and LPS resulted in further increase in the lung water compared with LPS administration alone however it was not statistically significant. Effects of PM-OC on protein expression of proinflammatory molecules related to LPS: The concentrations of these molecules were below the detection limits in the PM-OC group. LPS treatment significantly increased the protein levels of these molecules compared with the vehicle treatment. In the PM-OC + LPS group KC was smaller than in the LPS group.
Reference: Inoue et al. (2006c) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 weeks **Weight:** 29-33 g	Carbon black (14 nm PrinteX 90; 56nm PrinteX 25; Degussa, Dusseldorf, Germany)	**Route:** intratracheal instillation **Dose/Concentration:** Vehicle group: PBS at pH7.4 LPS group: 2.5mg/kg of LPS in vehicle Nanoparticle groups: 4 mg/kg carbon black nanoparticles (14nm or 56 nm) in vehicle LPS + nanoparticle group: combined adminstration of carbon black and LPS in vehicle **Particle Size (Distribution):** 14 nm - 300 m2/g 56nm - 45 m2/g **Time to Analysis:** single, mice were evaluated 24-h after intratracheal administration	Effects of nanoparticles: Nanoparticles alone increased the # of total cells and neutrophils, but not statistically significant. LPS exposure significantly increased numbers for both groups. Exposure and/or LPS enhance pulmonary edema. Histological changes: Treatment with LPS+14 nm nanoparticles marketly enhanced neutrophil sequestration into the lung parenchyma compared to LPS alone. LPS+56 nm nanoparticles did not. Proinflammatory cytokine proteins: IL-1b level significantly greater for both LPS+ nanoparticles groups. TNF-a was not significantly altered among the experimental groups. Chemokine proteins: Challenge with 14nm nanoparticles alone elevated the levels of all chemokines without significance except for KC. LPS alone caused significant increases in all chemokines and when combined with both nanoparticle groups. Formations of 8-OHdG in lung: LPS plus nanparticles resulted in intensive expression 8-OHdG, strongest in LPS-14nm nanoparticle Plasma coagulatory changes: PT - no change for any group, APTT - some change with LPS and LPS +nanoparticle groups, fibrinogen level significantly elevated after LPS and for LPS+14nm nanoparticle, APC decrease with LPS (significant) and LPS + nanoparticle groups, vWF increase with LPS (significant) and LPS+14 nm (significant).

Study	Pollutant	Exposure	Particle Effects
Reference: Inoue et al. (2004) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 weeks **Weight:** 29-33 g	DEPs [4JB-1 type light-duty, four-cylinder, 2.74 litre Isuzu diesel engine (Isuzu Automobile Co., Tokyo Japan)] Washed DEP and DEP-OC - extracted with dichloromethane,. Suspended in dichloromethane and sonicated, the centrifuged and residue then washed with dichloromethane -this was repeated three times. Residual particle prepared as washed DEP. Extracts combined, evaporated and dissolved in 100% dimethylsuphoxide prepared as DEP-OC	**Route:** intratracheal instillation **Dose/Concentration:** Vehicle group: PBS Washed DEPgroup: 4mg/kg of DEP in vehicle DEP-OC group: 4mg/kg of DEP-OC in vehicle LPS group: 2.5mg/kg of LPS in vehicle Washed DEP+LPS group: combined adminstration of washed DEP +LPS in vehicle DEP-OC+ LPS group: combined admininstration of DEP-OC + LPS in vehicle **Particle Size (Distribution):** **Time to Analysis:** single, evaluated 4 hours after	COX-1mRNA was slightly elevated in both the washed DEP and DEP-OC groups, but slightly decreased in the other groups compared to vehicle group. COX-2mRNA was slightly increased with DEP-OC alone compared to vehicle. The LPS showed a more intense expression of Cox-2 than the vehicle group. The washed DEP+LPS group demonstrated the most intense expression of COX-2. DEP-OC+LPS group showed a decrease in COX-2 compared with the LPS group.
Reference: Inoue et al. (2006a) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7weeks **Weight:** 29-33 g	Carbon black (14 nm PrinteX 90; 56nm PrinteX 25; Degussa, Dusseldorf, Germany)	**Route:** intratracheal instillation **Dose/Concentration:** Vehicle group: PBS Ovalbumin (OVA) group: 1mg OVA in vehicle Nanoparticle groups: 50mg carbon black nanoparticles (14nm or 56 nm) in vehicle OVA + nanoparticle group: combined adminstration of nanoparticles and OVA in vehicle **Particle Size (Distribution):** 14 nm - 300 m2/g 56nm - 45 m2/g **Time to Analysis:** Vehicle group - 1x per week for 6 weeks OVA group - every 2 weeks for 6 weeks (4 administrations) Nanoparticle groups - every week for 6 weeks (7 administrations) OVA+Nanoparticle group (same protocol as for OVA and Nanoparticle) studied 24-h after last administration	TARC: Nanoparticles significantly elevated the level of TARC in the absence of allergen as compared to vehicle. The level of significantly greater in the OVA+nanoparticle groups MIP-1c: Nanoparticles significantly elevated the level of MIP-1c in the absence of allergen as compared to vehicle. The level of significantly greater in the OVA+nanoparticle groups. OVA+14nm nanoparticle significantly greater than 14nm nanoparticle group. GM-CSF: Nanoparticles significantly elevated the level of GM-CSF in the absence of allergen as compared to vehicle. The level was signifcantly greater in the OVA+14 nm nanoparticle group than in OVA group. IL-2: Significantly greater in the OVA+14 nm group than in the vehicle, OVA, or 14nm group. No significant differences between the OVA, OVA+56nm or 56 nm groups IL-10: Significantly great in the OVA+14nm group than in the OVA group. No significant differences between the OVA, OVA+56nm or 56 nm groups
Reference: Inoue, K., et al. 2005 **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7weeks **Weight:** 29-33 g	Carbon black (14 nm PrinteX 90; 56nm PrinteX 25; Degussa, Dusseldorf, Germany)	**Route:** intratracheal instillation **Dose/Concentration:** Vehicle group: PBS Ovalbumin (OVA) group: 1mg OVA in vehicle Nanoparticle groups: 50mg carbon black nanoparticles (14nm or 56 nm) in vehicle OVA + nanoparticle group: combined adminstration of nanoparticles and OVA in vehicle **Particle Size (Distribution):** 14 nm - 300 m2/g 56nm - 45 m2/g **Time to Analysis:** Vehicle group - 1x per week for 6 weeks OVA group - every 2 weeks for 6 weeks Nanoparticle groups - every week for 6 weeks OVA+Nanoparticle group (same protocol as for OVA and Nanoparticle) studied 24-h after last adminstration	Cellular profile in BAL: Numbers of total cells and macrophages were significantly greater in the nanoparticle, OVA and OVA+nanoparticle groups than in vehicle. OVA+14 nm group significantly greater than 14nm group or OVA group. OVA+56 nm group greater but not signficant. Eosinophils: greater in the OVA+nanoparticle groups than in vehicle. OVA+14 nm group significantly greater than 14nm group or OVA group.OVA+56 nm group greater but not significant. Neutrophils: OVA+14 nm group significantly greater than 14nm group. Mononuclear cells: OVA+14 nm group significantly greater than vehicle or OVA group. OVA+56 nm group greater but not significant. Goblet cells: OVA+14nm group significant increase vs. vehicle, OVA or 14nm groups. OVA+56 nm increased, but not significant.

Study	Pollutant	Exposure	Particle Effects
Reference: Inoue, K., et al. 2005 **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7weeks **Weight:** 29-33 g	Carbon black (14 nm PrinteX 90; 56nm PrinteX 25; Degussa, Dusseldorf, Germany)	**Route:** intratracheal instillation **Dose/Concentration:** Vehicle group: PBS Ovalbumin (OVA) group: 1mg OVA in vehicle Nanoparticle groups: 50mg carbon black nanoparticles (14nm or 56 nm) in vehicle OVA + nanoparticle group: combined adminstration of nanoparticles and OVA in vehicle **Particle Size (Distribution):** 14 nm - 300 m2/g 56nm - 45 m2/g **Time to Analysis:** Vehicle group - 1x per week for 6 weeks OVA group - every 2 weeks for 6 weeks Nanoparticle groups - every week for 6 weeks OVA+Nanoparticle group (same protocol as for OVA and Nanoparticle) studied 24-h after last adminstration	Th2 cytokines: OVA+nanoparticles significantly elevated levels of IL-5 vs. vehicle. IL-13: OVA+14nm significantly elevated vs OVA or 14nm groups. OVA+56 nm significantly greater that 56 nm group. IL-4: significantly lower in the OVA+56nm group than OVA group. Eotaxin: OVA+nanoparticle groups significantly greater than other groups. MCP-1: 14nm group significantly higher than vehicle, 56 nm group higher not significant. OVA+ 14nm signifcantly higher. RANTES: OVA+nanoparticle groups significantly higher than other groups. IL-6: OVA+14nm group and OVA+56nm groups significantly higher than other groups. 8-OHdG formations: OVA + nanoparticles resulted in intense immunoreactive 8-OHdG staining as compared to OVA or nanoparticles alone. OVA+14nm more intense than OVA+56nm. IgE: significantly greater in both OVA+nanoparticles groups. IgG1: significantly greater in OVA+14nm group than in other groups. IgG2a: not significantly different among experimental groups.
Reference: Inoue, K, et al. 2006 - Basic and clinical pharm and tox **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 weeks **Weight:** 29-33 g	whole DE (generated by 4-cylinder, 3.059l, Isuzu diesel engine, Isuzu automobile, Tokyo, Japan) LPS DEP = soot (undefined)	**Route:** whole body exposure chamber (air or DE) intratracheal instillation (LPS) **Dose/Concentration:** 0.3mgsoot/m^3 1.0mgsoot/m^3 3.0mg soot/m^3 LPS: 125 mg/kg **Particle Size (Distribution):** peak particle size 110nm **Time to Analysis:** LPS instillation prior to exhaust exposure 12hr exposure to exhaust	DE on LPS related lung inflammation - BAL fluid: Total cells no different between air and exhaust groups w/o LPS. With LPS total cells increase compared to vehicle, LPS+exhaust the number was smaller. Neutrophils - no difference between groups w/o LPS. LPS total cells increase compared to vehicle, LPS+exhaust the number was smaller. Histological changes: Infiltration of neutrophils was moderate in the LPS groups. No significant differences between exhaust and clean air groups with LPS. Protein and Gene levels: MCP-1 and KC: The protein and gene levels were negligible in the vehicle groups. LPS alone significantly increased the protein level and gene level compared to vehicle. With LPS the protein and gene levels were significantly lower in the exhaust groups than clean air group.
Reference: Inoue et al. (2007) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 weeks **Weight:** 29-33 g **Cell Type** splenocytes	DEPs [4JB-1 type light-duty, four-cylinder, 2.74 litre Isuzu diesel engine (Isuzu Automobile Co., Tokyo Japan)] LPS - escherichia coli B55: 05, Difco Lab, Detroit, MI	**Route:** cell culture **Dose/Concentration:** Splenocytes resuspended to cell density of 1X106 mL-1 and 1000 mL applied into each of 12-well plate DEP: 100 mg mL-1 LPS: 1 mg mL-1 LPS(1mg mL-1) + DEP (1, 10 or 100 mg mL-1) **Particle Size (Distribution):** NR ($PM_{2.5}$) **Time to Analysis:** Supernatants collected after 72 h	Cell viability: No effect Mononuclear cell response: Incubation with DEP alone did not induce any cytokine production. LPS significantly increased protein levels of IFN-g, IL-2, and IL-10 compared to control. DEP suppressed the LPS-enhanced protein levels of IFN-g and IL-10 dose dependently with statistical significance at 10 and 100 mg mL-1. DEP at 100 mg mL-1 completely abolished production of IFN-g, IL-2 and IL-10. IL-13 was higher at LPS+DEP (1 and 10 mg mL-1) groups than control or LPS alone.
Reference: Inoue et. al 2007 **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7 weeks **Weight:** 20-30 g	Carbon nanoparticles (Dusseldorf, Germany) OVA (Sigma Chemical, St. Louis, MO)	**Route:** intratracheal instillation **Dose/Concentration:** 50ug and/or 1ug OVA in PBS **Particle Size (Distribution):** CB14 (PrinteX 90) = 14nm CB56 (PrinteX 25) = 56nm **Time to Analysis:** 1X/week for 6 weeks; sacrifice 24 h after last exposure	Lung responsiveness (total respiratory resistance, Newtonian resistance, elastance, tissue damping, and tissue elastance): CB14/CB56 were significantly higher than vehicle. (Compliance): CB14/CB56 was significantly lower than in vehicle. Lung mRNA level for Muc5ac: levels were significantly higher in CB14/CB56 groups versus vehicle.

Study	Pollutant	Exposure	Particle Effects
Reference: Inoue et. al 2007 **Species:** Mouse **Gender:** Male **Strain:** ICR (Japan Clen Co, Tokyo, Japan) **Age:** 6-7 weeks **Weight:** 29-34 g	DEP-OC = carbonaceous nuclei of DEP (DEP collected from Isuzu diesel engine, Isuzu Automobile Company, Tokoyo, Japan) OVA = ovalbumin (Sigma Chemical Co, St. Louis, MO)	**Route:** intratracheal instillation **Dose/Concentration:** 50ug and/or 1ug OVA in PBS **Particle Size (Distribution):** DEP = 0.4 µm **Time to Analysis:** DEP or DEP-OC w/ or w/o OVA initially; OVA or vehicle every 2wk for 6wks; DEP components or vehicle 1X/wk for 6wks; sacrifice 24 h after last instillation	Total respiratory system resistance, elastance, Newtonian resistance, tissue damping, tissue elastance: higher in OVA or DEP-OC+OVA (compliance was lower in these groups).
Reference: Ito et al. (2006) **Species:** Rat **Cell Line:** L2 cells from adult rat lung and of alveolar epithelial cell type II origin	DEP - generated from 2982-cc common rail direct injection diesel engine with oxidation catalyst and exahust gas recirculation system.	**Route:** Cell culture **Dose/Concentration:** 1X106 1,10 or 30 mg/mL **Particle Size (Distribution):** NR ($PM_{2.5}$) **Time to Analysis:** 3 hours	ICAM-1 mRNA: up-regulation in a dose-dependent manner. Statistically significant at 30 mg/mL compared to control. LDL receptor mRNA: up-regulation in a dose-dependent manner. Statistically significant at 30 mg/mL compared to control. PAF receptor mRNA: up regulation in dose-dependent manner and statistically significant at all doses compared to control. HO-1 mRNA: up regulation in dose-dependent manner and statistically significant at all doses compared to control. Correlation between HO-1 and ICAM-1, LDL, and PAF: There was a significant correlation between HO-1 and each of these.
Reference: Jang, A, et al. 2005 **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 5-6 weeks **Weight:** NR	DEP -generated from 4JB1 type, light duty, four-cylinder diesel engine (Isuzu Automobile, Co,Tokyo Japan) Ozone - (generated with Sander Model 50 ozonizers,Sander, Eltze Germany) OVA -ovalbumin (Grade V OVA, Signma Chemical St. Louis)	**Route:** whole body exposure chamber intra-peritoneal injection and ultrasonic nebulizer (OVA) **Dose/Concentration:** DEP: 2,000 µg/µL (sic) Ozone: 2 ppm (ave 1.98 ± 0.08 ppm) OVA sensitization: 10 mg OVA challenge: 1%wt/vol OVA in saline **Particle Size (Distribution):** NR - previously described **Time to Analysis:** OVA sensitized days 1 and day 14 DEP, Ozone and OVA Challenge on days 21 to 23 After OVA challenge on days 21-23 - Exposed to ozone for 3 h and DEP for 1-h Airway responsiveness measured 1 day after last challenge BAL after last airwway responsiveness measure	Airway responsiveness: OVA +ozone+ DEP exposure group had significantly higher methacholine-induce Ptnh than sham group or OVA group. Total cells, proportion of eosinophils and neutrophils: the OVA +ozone+DEP group increased significantly than OVA group and OVA+Ozone group (Eosinophils: OVA+Ozone+DEP 8.9 ± 1.12% vs. OVA 2.9 ± 0.09% and OVA+Ozone 7.2 ± 1.15%) (Neutrophils: OVA+Ozone+DEP 10.1 ± 1.18% vs. OVA 2.3 ± 0.17% and OVA+ozone 8.3 ± 1.26%) IL-4: OVA+ozone, OVA+DEP and OVA+ozone+DEP IL-4 level increased compare to OVA group. IFN-g: levels significantly decreased in OVA+DEP and OVA+ozone+DEP compared to OVA+ozone
Reference: Jaspers, I., et al, 2005 **Species:** Human **Cell Lines:** A549 cells, primary human bronchial cells and primary human nasal cells	DEas**:** aqueous-trapped solution of DE (previously described from Caterpiller diesel engine, model 3304) Influenza: A/Bangkok/1/79	**Route:** Cell culture, DEas: added to apical side of cells **Dose/Concentration:** Influenza: 3 x 105 cells infected with 320 hemagglutination units (HAU) DEas**:** For A549 cells: 6.25, 12.5, 25 mg/cm^2. For bronicial and nasal cells: 22 or 44 mg/cm^2. **Particle Size (Distribution):** NR **Time to Analysis:** 2-h incubation with DEas then influenza virus added. Analysis 24-h after infection.	A549 cells increased suscesptibility: DEas enhances HA RNA levels in A549 cells in a dose-dependent manner. 25 mg/cm^2 significantly enhanced levels in A549 cells compared to the influenza-infected controls. Viral protein levels were increased in A549 cells. Exposure to DEas increased the number of influenza-infected epithelial cells in A549 cells. Human nasal and bronchial cells suscesptibility: Exposure to DEas increased HA RNA levels in the nasal and bronchial cells. Statistically significant at 22mg/cm^2 for nasal cells and approaching significance at 44 mg/cm^2 for bronchial cells. Exposure of both types to 44 mg/cm^2 enhanced viral protein levels.

Study	Pollutant	Exposure	Particle Effects
Reference: Jaspers, I., et al, 2005 **Species:** Human **Cell Lines:** A549 cells, primary human bronchial cells and primary human nasal cells	DEas**:** aqueous-trapped solution of DE (previously described from Caterpiller diesel engine, model 3304) Influenza: A/Bangkok/1/79	**Route:** Cell culture, DEas added to apical side of cells **Dose/Concentration:** Influenza: 3 x 105 cells infected with 320 hemagglutination units (HAU) DEas**:** For A549 cells: 6.25, 12.5, 25 mg/cm^2. For bronicial and nasal cells: 22 or 44 mg/cm^2. **Particle Size (Distribution):** NR **Time to Analysis:** 2-h incubation with DEas then influenza virus added. Analysis 24-h after infection.	Influenza induced IFN response in A549: Exposure to DEas does not suppress IFNb mRNA levels. Treatment enhanced influenza-induced nuclear levels of both phospho-STAT-1 and ISFG3g. ISRE-promoter activity was enhanced, but not significantly. Treatment enhanced MxA mRNA levels. This data suggest that DEas exposure enhances influenza virus replication without suppressing production of IFNb or IFNb-inducible genes. Influenza induced IFN response in human nasal and bronchial cells: The results were analogous to the effects seen in A549 cells. Oxidative stress in A549: DEas exposure dose-dependently increases oxidative stress in A549 cells within 2-h post-exposure. Add the antioxidant GSH-ET and it reverses the effect. Pretreated with GSH-ET A549 cells exposed to DEas and then infected with influenza - showed pretreatment reversed the effects of DEas on the number of influenza-infected cells, and reduced HA RNA levels. Oxidative stress in Human bronchial cells: The results were the same as A549 cells pretreated with GSH-ET.
Reference: Jaspers, I., et al, 2005 **Species:** Human **Cell Lines:** A549 cells, primary human bronchial cells and primary human nasal cells	DEas**:** aqueous-trapped solution of DE (previously described from Caterpiller diesel engine, model 3304) Influenza: A/Bangkok/1/79	**Route:** Cell culture, DEas added to apical side of cells **Dose/Concentration:** Influenza: 3 x 105 cells infected with 320 hemagglutination units (HAU) DEas**:** For A549 cells: 6.25, 12.5, 25 mg/cm^2. For bronicial and nasal cells: 22 or 44 mg/cm^2. **Particle Size (Distribution):** NR **Time to Analysis:** 2-h incubation with DEas then influenza virus added. Analysis 24-h after infection.	Influenza virus attachment A549 cells: DEas exposed A549 cells were infected with influenza and immediately or 15, 30, 60 and 120 minutes after virus, the nonattached virus was removed by rinsing the cells. It was found that exposure to DEas significantly increases attachment of inlfuenza virus to A549 cells wihin 2-h post infection. Influenza virus attachment human nasal cells: The same experiment was conducted with human nasal cells and similar results to the A549 cells were seen.
Reference: Kaan, P.M., et al. 2002 **Species:** Guinea pig **Gender:** Female **Strain:** Cam Hartley **Age:** 22-29 days **Weight:** 250-300 g **Cell Types** Alveolar macrophages (AM) obtained by bronchoalveolar lavage	PM_{10} - urban air dust preparation obtained from Environmental Health Canada, Ottawa (EHC-93) RSV - Human RSV (long strain/lot18D) from American Tissue Culture Collection, Bethesda, MD	**Route:** Cell culture **Dose/Concentration:** PM_{10} added to AM in 6 well plates ~2x106 cells/well RSV exposure: AM in 6-well plates 2x106 cells/well PM_{10} - 500 mL added to each well RSV - multiplicity of infection of 3 - 1 mL of RSV stock applied to each well Groups: PM_{10}+RSV RSV+PM_{10} RSV only PM_{10} only negative control **Particle Size (Distribution):** PM_{10} **Time to Analysis:** PM_{10} - 60 minutes RSV - 90 minutes	Interaction on phagocytic ability of AM: More than 95% of AM exposed to PM_{10} engulfed PM. AM exposed to PM_{10} showed significant increase in mean side scatter in comparison to negative control and RSV-infected AM. No significant difference between AM exposed only to PM_{10} and AM exposed to both agents. Interaction on RSV Immunopositivity: All RSV-treated groups showed significantly greater proportion of RSV-immunopositive cells comparte with negative control. PM_{10}+RSV showed significantly smaller proportion of RSV-immunopositive cells compared with RSV group. RSV+PM_{10} group similar to RSV group. Proportion of RSV-immunopositive AM was influenced by the sequence of exposure to RSV and PM_{10}. Interaction on RSV Replication: AM exposed to both agents produced 3 to 9 fold less RSV progency compared with RSV alone group. Quantity of RSV progency was not significantly affected by the sequence of exposure RSV and PM_{10}. Interaction of RSV Yield: RSV alone group produced the highest RSV yield, those exposed to both agents showed a 5-fold decrease.

Study	Pollutant	Exposure	Particle Effects
Reference: Kaan, P.M., et al. 2002 **Species:** Guinea pig **Gender:** Female **Strain:** Cam Hartley **Age:** 22-29 days **Weight:** 250-300 g **Cell Types** Alveolar macrophages (AM) obtained by bronchoalveolar lavage	PM_{10} - urban air dust preparation obtained from Environmental Health Canada, Ottawa (EHC-93) RSV - Human RSV (long strain/lot18D) from American Tissue Culture Collection, Bethesda, MD	**Route:** Cell culture **Dose/Concentration:** PM_{10} added to AM in 6 well plates ~2x106 cells/well RSV exposure: AM in 6-well plates 2x106 cells/well PM_{10} - 500 mL added to each well RSV - multiplicity of infection of 3 - 1 mL of RSV stock applied to each well Groups: PM_{10}+RSV RSV+PM_{10} RSV only PM_{10} only negative control **Particle Size (Distribution):** PM_{10} **Time to Analysis:** PM_{10} - 60 minutes RSV - 90 minutes	Cytokine production: RSV infection stimulated all three cytokines measure (IL-6, IL-8 and TNF-a) compared to negative control. IL-6: PM_{10} significantly reduced RSV-induced IL-6. IL-6 was affected by the sequence of exposure to PM_{10} and RSV (PM_{10}+RSV vs. RSV+ PM_{10}, p<3x10-6). IL-8: PM_{10} significantly decreases RSV-induced IL-8 production as well as that of baseline. No affect on sequence of exposure. TNF-a: production was increased when exposed to RSV, PM_{10} or a combination of both agents. No differences among treatments.
Reference: Kleinman et al. (2005) **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** NR **Weight:** NR	CAPS - concentrated fine (F) and ultrafine (UF) using VACES system - performed a 2 sites in Los Angeles, CA, on 50-m downwind and another 150-m downwind from a complex of three roadways, State Road CA60, Interstate 10, and Interstate 5. F CAPS in 2001 and 2002, UF CAPS in 2002 only OVA - Sigma Chemical	**Route:** CAPS: whole body chamber OVA sensitization: nasal instillation **Dose/Concentration:** 50m- UF: June 02 433 mg/m^3 150m - UF: August 02 283 mg/m^3 50m or 150 m F: 17 X ambient (although diluted with air when necessary to achieve an ~400 mg/m^3 average exposure) OVA - 50 mg in 5 mL saline **Particle Size (Distribution):** UF: ≤ 150 nm F: ≤ 2.5 mm **Time to Analysis:** CAPS: 4 h/day, 5 days/week for 2 weeks OVA: On the morning of each exposure	There were significantly higher concentrations of IL-5, IgE, IgG1 and eosinophils in mice exposed to either CAPS compared to air. Mice exposed to CAPS at 50-m downwind showed higher levels of IL-5, IgG1, and eosinophils than those exposed to CAPS 150-m downwind.
Reference: Kleinman et al. (2007) **Species:** Mouse **Gender:** NR **Strains:** BALB/c **Age:** 6-8weeks **Weight:** NR	CAPS - concentrated fine (F) and ultrafine (UF) using VACES system - performed a 2 sites in Los Angeles, CA, on 50-m downwind and another 150-m downwind from State Road CA60 and Interstate 5. Fall 2001-summer 2004 OVA - Sigma Chemical	**Route:** CAPS: whole body chamber OVA sensitization: nasal instillation **Dose/Concentration:** 50m - F: 394 ± 94 mg/m^3 50m - UF: 297 ± 189 mg/m^3 150m - F: 387 ± 68 mg/m^3 150m - UF: 213 ± 95 mg/m^3 OVA - 50 mg in 5 mL saline **Particle Size (Distribution):** UF: ≤ 150 nm F: ≤ 2.5 mm **Time to Analysis:** CAPS: Performed over 4 years. Three 2 week exposures - 4 hours days/5 consecutive days/week for 2 consecutive weeks. OVA: On the morning of each exposure	IL-5: showed significant effects of exposure and location in mice exposed 50 m downwind compared to those at 150m downwind and levels were greater than air control. IgG1: showed significant effects of exposure and location in mice exposed 50 m downwind compared to those at 150m downwind and levels were greater than air control. 150m: in no cases were responses in exposed mice greate thatn those in control mice in the groups exposed at 150m downwind site. Regression for IL-5 and IgG1: for all of the components the slopes of the concentration curves are numerically greater for the exposure at 50m than at 150m - For IL-5 as function of EC and OC the slopes were significantly greater for 50m than 150m. For IgG1 as function of both EC and OC the slopes approached signficance.

Study	Pollutant	Exposure	Particle Effects
Reference: Klein-Patel et al. (2006) **Species:** Ox and Human **Cell Types** Bovine tracheal epithelial cells (BTE) and Human A549 cells	ROFA (U.S. EPA NHEERL, Research Triangle Park, NC) Vanadium pentoxide (V2O5), vanadium sulfate ($VOSO_4$), (SiO_2), titanium dioxide (TiO_2), ferric sulfate ($Fe2(SO_4)3$) nickel sulfate ($NiSO_4$) (Sigma-Aldrich Corp, St. Louis, MO) Pseudo-mona aeruginsoa LPS (Sigma-Aldrich Corp, St. Louis, MO) Recombinant human TNF-a and IL-1b (R&D Systems, Minneapolis, MN)	**Route:** Cell culture **Dose/Concentration:** $2x10^6$ Mentioned in a foot note for the mass spectrometry, otherwise NR ROFA: 0, 2.5, 5, 10, 15, 20 mg/cm^2 LPS: 100ng/mL V2O5: 0, 0.15, 0.3, 0.61, 1.25, 2.5, 5, 10, 20 mg/cm^2 $NiSO_4$, $Fe2(SO_4)3$, TiO_2, SiO_2: 0, 1.23, 2.5, 5, 10, 20 mg/cm^2 $VOSO_4$: 0, 0.145, 0.29, 0.58, 1.16, 2.32 mg/cm^2 **Particle Size (Distribution):** ROFA MMAD = 1.95 mm **Time to Analysis:** LPS: 0, 6, or 18 hours ROFA: 0, 2,4,6 h V2O5: 0, 0.25, 0.5, 1, 2, 4, 6, 8 h $NiSO_4$, $Fe2(SO_4)3$, TiO_2, SiO_2: 6 h $VOSO_4$: 6 h	ROFA inhibition of TAP is time-dependent and dose-dependent: ROFA inhibited the induction of TAP gene expression by LPS after 2-h exposure increasing inhibition with longer duration of exposure. LPS-induced expression of TAP gene inhibited by increasing doses of ROFA at 6 hours. (BTE cells) ROFA leacate and washed particles: ROFA-leachate singificantly inhibited the induction of TAP expression in response to LPS. Washed particles of ROFA significantly increased the inducible expression of TAP at doses of 2.5 to 10 mg/cm^2. (BTE cells) V2O5 inhibition of inducible TAP is dose-dependent and time-dependent: a reproducible trend, although not statistically significant, of decreased inducible TAP gene expression was observed with increating durations of pre-exposure to V2O5. Increasing concentrations of V2O5 at 6 hours the same dose-dependent inhibition of LPS-stimulated TAP was seen as with ROFA. (BTE cells).
Reference: Klein-Patel et al. (2006) **Species:** Ox and Human **Cell Types** Bovine tracheal epithelial cells (BTE) and Human A549 cells	ROFA (U.S. EPA NHEERL, Research Triangle Park, NC) Vanadium pentoxide (V2O5), vanadium sulfate ($VOSO_4$), SiO_2, titanium dioxide (TiO_2), ferric sulfate ($Fe2(SO_4)3$) nickel sulfate ($NiSO_4$) (Sigma-Aldrich Corp, St. Louis, MO) Pseudo-mona aeruginsoa LPS (Sigma-Aldrich Corp, St. Louis, MO) Recombinant human TNF-a and IL-1b (R&D Systems, Minneapolis, MN)	**Route:** Cell culture **Dose/Concentration:** $2x10^6$ Mentioned in a foot note for the mass spectrometry, otherwise NR ROFA: 0, 2.5, 5, 10, 15, 20 mg/cm^2 LPS: 100ng/mL V2O5: 0, 0.15, 0.3, 0.61, 1.25, 2.5, 5, 10, 20 mg/cm^2 $NiSO_4$, $Fe2(SO_4)3$, TiO_2, SiO_2: 0, 1.23, 2.5, 5, 10, 20 mg/cm^2 $VOSO_4$: 0, 0.145, 0.29, 0.58, 1.16, 2.32 mg/cm^2 **Particle Size (Distribution):** ROFA MMAD = 1.95 mm **Time to Analysis:** LPS: 0, 6, or 18 hours ROFA: 0, 2,4,6 h V2O5: 0, 0.25, 0.5, 1, 2, 4, 6, 8 h $NiSO_4$, $Fe2(SO_4)3$, TiO_2, SiO_2: 6 h $VOSO_4$: 6 h	TAP gene expression in response to IL-1b is inhibited by V2O5: pretreatment of BTE cells with V2O5 significantly inhibited TAP induction in response to the inflammatory cytokine IL-1b. A similar inhibition of induction by TNF-a was also observed. (BTE cells) Other soluble metal Components: Increasing doses of the other metal components ($NiSO_4$, $Fe2(SO_4)3$, TiO_2, SiO_2) - Interaction between stimulus and dose for $NiSO_4$ is not significantly different, a trend towards decreased TAP expression with increased dose of $NiSO_4$ similar to that observed with V2O5. $Fe2(SO_4)3$, TiO_2 and SiO_2 had no effect on inducible TAPgene expression. (BTE cells) TAP in BTE cells: mass spectrophotometric analysis if TAP performed on BTE cells treated with 10 mg/cm^2 V2O5 for 6 h, followed by induction of TAP by LPS for 18 h then the cytoplasmic extreacts analyzed for TAP peptide - TAP detected in LPS-stimulated cells but not in unstimulated cells. As predicted by the gene expression data, TAP was not observed cultures treated with V2O5.
Reference: Klein-Patel et al. (2006) **Species:** Human **Cell Types** Human A549 cells	ROFA (U.S. EPA NHEERL, Research Triangle Park, NC) Vanadium pentoxide (V2O5), vanadium sulfate ($VOSO_4$), SiO_2, titanium dioxide (TiO_2), ferric sulfate ($Fe2(SO_4)3$) nickel sulfate ($NiSO_4$) (Sigma-Aldrich Corp, St. Louis, MO) Pseudo-mona aeruginsoa LPS (Sigma-Aldrich Corp, St. Louis, MO) Recombinant human TNF-a and IL-1b (R&D Systems, Minneapolis, MN)	**Route:** Cell culture **Dose/Concentration:** $2x10^6$ Mentioned in a foot note for the mass spectrometry, otherwise NR ROFA: 0, 2.5, 5, 10, 15, 20 mg/cm^2 LPS: 100ng/mL V2O5: 0, 0.15, 0.3, 0.61, 1.25, 2.5, 5, 10, 20 mg/cm^2 $NiSO_4$, $Fe2(SO_4)3$, TiO_2, SiO_2: 0, 1.23, 2.5, 5, 10, 20 mg/cm^2 $VOSO_4$: 0, 0.145, 0.29, 0.58, 1.16, 2.32 mg/cm^2 **Particle Size (Distribution):** ROFA MMAD = 1.95 mm **Time to Analysis:** LPS: 0, 6, or 18 hours ROFA: 0, 2,4,6 h V2O5: 0, 0.25, 0.5, 1, 2, 4, 6, 8 h $NiSO_4$, $Fe2(SO_4)3$, TiO_2, SiO_2: 6 h $VOSO_4$: 6 h	A549 cells: cells stimulated with LPS, TNF-a (50ng/mL), IL-1b (100ng/mL), and TLR2 ligand, PAm^3CSK4 (300 ng/mL)**:** Il-1b induced the highest amount of hBD-2 in A549 cells. When preincubated with ROFA for 6 h and then stimulated with IL-1b a significant inhibition of hBD-2 induction was observed. Molar equivalent doses of V2O5 demonstrated the same dose-dependent inhibition of Il-1b -induced hBD-2 mRNA levels. Experiment was repeated with $VOSO_4$ which produced a similar dose-dependent inhibition of hBD-2 expression. There was no significant effect on cell viability of either salt at concentrations of up to 2.5 mg/cm^2.

Study	Pollutant	Exposure	Particle Effects
Reference: Koike, E., et al. 2005 **Species:** Rat **Gender:** Male **Strains:** Wistar **Age:** 8-10 weeks **Weight:** 280-350g **Cell Types** AM - aveolar macrophages PBM - peripheral blood monocytes T-cells: antigen sensitized	DEP (collected in the dilution tunnel of a diesel inhalation facility (previously reported). The ratio of organic extract to residual particles in the whole DEP was 3: 1 Organic extract of DEP (DCM) Residual particles of DEP Ovalbumin (OVA)	**Route:** Cell culture **Dose/Concentration:** Exposure to DEP: $1X10^6$ cells/mL AM or PBM (peripheral blood monocytes) PBM and OVA-sensitized T cells: 1.25X104 to 2 X 105 - in 96 well flatbottom plates HO-1 measurement: PBM 5x106 Whole DEP: 10, 30, 100 mg/mL Organic extract of DEP: 7.5, 22.5, 75 mg/mL Residual particles: 2.5, 7.5, 25 mg/mL **Particle Size (Distribution):** NR **Time to Analysis:** 24-h	Ia antigen and costimulatory molecules: Most control AM did not express these cell-surface molecules and whole DEP did not cause any increase in expression level. PBM - 20% of control expressed Ia and 10% B7; expression of these molecules significantly increased by whole DEP. Organic extract significantly increased the expression of Ia and B7 molecules on PBM similar to whole DEP. Residuals caused no effect. 100/75/25 mg/mL exposure of DEP/organic extract/residual particles: results showed that the DEP-incrased expresion of Iq and B7 in PBM by DEP was caused by the organic extract fraction. Organic extract-induced expression of Ia antigen in PBM was reduced by treatment with NAC AP activity of PBM: assessed in terms of OVA-specific T cell proliferation; after exposure to organic extract T cell proliferation was significantly increased by the addition of control PBM in a cell number-dependent manner.The AP activity of PBM was increased over control by 3 mg/mL organic extract, although higher concentrations suppressed the activity of PBM.
Reference: Koike, E., et al. 2005 **Species:** Rat **Gender:** Male **Strains:** Wistar **Age:** 8-10 weeks **Weight:** 280-350g **Cell Types** AM - aveolar macrophages PBM - peripheral blood monocytes T-cells: antigen sensitized	DEP (collected in the dilution tunnel of a diesel inhalation facility (previously reported). The ratio of organic extract to residual particles in the whole DEP was 3: 1 Organic extract of DEP (DCM) Residual particles of DEP Ovalbumin (OVA)	**Route:** Cell culture **Dose/Concentration:** Exposure to DEP: 1X106 cells/mL AM or PBM (peripheral blood monocytes) PBM and OVA-sensitized T cells: 1.25X104 to 2 X 105 - in 96 well flatbottom plates HO-1 measurement: PBM 5x106 Whole DEP: 10, 30, 100 mg/mL Organic extract of DEP: 7.5, 22.5, 75 mg/mL Residual particles: 2.5, 7.5, 25 mg/mL **Particle Size (Distribution):** NR **Time to Analysis:** 24-h	IFN-g content in the presence of PBM (50% of T-cell number) exposed to 0, 3, 10, 30, and 100 mg/mL organic extract the INF-g contect was 94.3 ± 11.1, 46.9 ± 14.2, 10.9 ± 4.3, 2.4 ± 0.1, and 2.5 ± 0.1 pg/mL, respectively. Organic extract treatment decreased IFN-g production. IL-4 content in the presence of PBM (50% of T cell number) exposed to the same amounts of organic extract as above was 5.0 ± 0.5, 5.8 ± 0.4, 4.6 ± 0.3, 7.9 ± 1.3, and 6.2 ± 0.3 pg/mL, respectively - no significant effect on IL-4 production observed. HO-1**:** Level of HO-1 protein in PBM was significantly increased by exposure to whole DEP or organic extract. HO-1 protein induced by organic extract was diminished by NAC treatment.
Reference: Last et al. (2004) **Species:** Mouse **Gender:** NR **Strains:** BALB/c **Age:** NR **Weight:** 16-20 g	PM - aerosol of soot and iron oxide OVA (ovalbumin, grade V, 98% pure, Sigma, St. Louis, MO)	**Route:** PM - exposure chamber OVA - intraperitoneal injections and aerosol exposure in chamber **Dose/Concentration:** PM - 250 mg/m^3 OVA - 10 mg/0.1 mL OVA for ip, 10ml of a 10mg/nl solution for aerosol **Particle Size (Distribution):** $PM_{2.5}$ - PM0.1 **Time to Analysis:** PM: 4h/day, 3 days/wk OVA: sensitized to OVA by 2 ip injections on days 1 and 15. OVA aerosol begun on day 28 after first ip for 60 min 3x per week 1. 2 week PM exposure followed by a 4 week OVA aerosol exposure 2. 4 week OVA aerosol exposure followed by a 2 week PM exposure (2 week cessation in OVA exposure and sacrifice for analysis) 3. 6 weeks simultaneos OVA and PM exposure	Experiment 1: Total Cells: After 2 wk PM exposure total cells were 309,000 ± 76,800. After 4 week OVA (12 exposures) 237,200 ± 31,700, of these cells 38 ± 1% lymphocytes, 52 ± 2% macrophages, 6.2 ± 2% neutrophils, and 4 ± 2% eosinophils. No significant difference between total cell counts or cell differential counts from OVA alone mice and PM exposed followed by OVA. Airway Collagen content: OVA alone significant increase in airway collagen than air or pm alone groups. No signficant difference between OVA alone and OVA+PM group. Histology showed significantly greate amount of collagen in OVA or PM+OVA as compared to air. Goblet cells: no apparent goblet cells in air or pm alone groups. About 23% of total epithelial cells in OVA alone group and 35% of cells in PM followed by OVA group stained as goblet cells. The combined exposure group had significantly more goblet cells than OVA alone. Airway reactivity: No significant differences in Penh values between any of the groups

Study	Pollutant	Exposure	Particle Effects
Reference: Last et al. (2004) **Species:** Mouse **Gender:** NR **Strains:** BALB/c **Age:** NR **Weight:** 16-20 g	PM - aerosol of soot and iron oxide OVA (ovalbumin, grade V, 98% pure, Sigma, St. Louis, MO)	**Route:** PM - exposure chamber OVA - intraperitoneal injections and aerosol exposure in chamber **Dose/Concentration:** PM - 250 mg/m^3 OVA - 10 mg/0.1 mL OVA for ip, 10ml of a 10mg/nl solution for aerosol **Particle Size (Distribution):** $PM_{2.5}$ - PM0.1 **Time to Analysis:** PM: 4h/day, 3 days/wk OVA: sensitized to OVA by 2 ip injections on days 1 and 15. OVA aerosol begun on day 28 after first ip for 60 min 3x per week 1. 2 week PM exposure followed by a 4 week OVA aerosol exposure 2. 4 week OVA aerosol exposure followed by a 2 week PM exposure (2 week cessation in OVA exposure and sacrifice for analysis) 3. 6 weeks simultaneos OVA and PM exposure	Experiment 2: Total cells: No significant differences in total cells in air, PM alone and OVA alone groups. Difference between OVA (297,000 ± 68,300) and OVA+PM (461,000 ± 86,000) was not significant. None of the differentials were significant either. In OVA+PM group 36 ± 4% lymphocytes, 54 ± 4% macrophages. 4 ± 1% neutrophils, 6 ± 1% eosinophils. Airway Collagen content: no signficant increased in collagen between air and OVA and no significant differences between OVA alone, to PM alone, to aire alone, or to OVA +PM. Histology showed significant differences between air and OVA and OVA+PM groups. Goblet cells: No apparent goblet cells in air or PM alone group. 22% of epithelial cell in OVA and 34% in OVA+PM - significantly different. Airway reactivity: No significant difference in Penh values between any of the groups.
Reference: Last et al. (2004) **Species:** Mouse **Gender:** NR **Strains:** BALB/c **Age:** NR **Weight:** 16-20 g	PM - aerosol of soot and iron oxide OVA (ovalbumin, grade V, 98% pure, Sigma, St. Louis, MO)	**Route:** PM - exposure chamber OVA - intraperitoneal injections and aerosol exposure in chamber **Dose/Concentration:** PM - 250 mg/m^3 OVA - 10 mg/0.1 mL OVA for ip, 10ml of a 10mg/nl solution for aerosol **Particle Size (Distribution):** $PM_{2.5}$ - PM0.1 **Time to Analysis:** PM: 4h/day, 3 days/wk OVA: sensitized to OVA by 2 ip injections on days 1 and 15. OVA aerosol begun on day 28 after first ip for 60 min 3x per week 1. 2 week PM exposure followed by a 4 week OVA aerosol exposure 2. 4 week OVA aerosol exposure followed by a 2 week PM exposure (2 week cessation in OVA exposure and sacrifice for analysis) 3. 6 weeks simultaneos OVA and PM exposure	Experiment 3: Total cells: Significantly more cells in OVA for 6 weeks alone group vs the simultaneous six week OVA/PM exposure group. Cell differentials were similar between the groups. In OVA/PM group - 46 ± 2% were lymphocytes and 50 ± 2% were macrophages. Simultaneous exposure showed significantly higher percentage of lymphocytes and significantly lower percent of macrophages than groups exposed to PM before or after OVA. Airway collagen content: No significant differences as previously noted. Histology showed significant more collagen in OVA and OVA/PM than air or PM alone groups. Goblet cells: OVA alone 51% goblet cells, Simultaneous OVA/PM group was significantly higher at 61% goblet cells Airway reactivity: No significant differences in Penh values between any of the groups

Study	Pollutant	Exposure	Particle Effects
Reference: Liu et al. 2007 **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 11 weeks	DEP DEP collected from a 5500-watt single-cylinder diesel engine. The engine was operated using Number 2 Diesel Certification Fuel and 40 weight motor oil. DEP Composition: Previously reported in another study.	**Route:** Inhalation (Intranasal) Exposure **Dose/Concentration:** Average particle concentration 1.28 mg/m^3. **Particle Size (Distribution):** Not Reported **Time to Analysis:** Study had four groups (each with 5 mice): 1. Aerosol vehicle (saline) + air 2. Aerosol vehicle (saline) + DEP 3. *A. fumigatus* + air 4. *A. fumigatus* + DEP *A. fumigatus* sensitization was induced according to a previously published method, intranasal exposure to 62.5 µg aerosolized A. fumigatus protein extract in 50 µL PBS every 4 days for a total of six doses. DEP exposure occurred for 5 h per day for 3 weeks at the same times as *A. fumigatus* treatment.	IgE Production: IgE production was increased by treatment with *A.fumigatus* and increased further in the group exposed to *A.fumigatus* and DEP. Histopathology: Both *A.fumigatus* alone and *A. fumigatus* in combo with DEP caused an increase in goblet cell hyperplasia and infiltrate of eosinophil and mononuclear cells around the airways and blood vessels of the mice exposed compared to the control and DEP alone- treated mice. Gene Methylation: 1. IFN-γ promoter At the CpG-53 site of the IFN-γ promoter, there was increased methylation after exposure to *A. fumigatus* + DEP than compared with *A. fumigatus* alone or DEP alone. The methylation was correlated with increase in IgE production. At CpG-45 and CpG-205 there was also an increase in methylation after exposure to A. fumigatus + DEP but it did not reach a significant level to be considered different from the other groups. DEP alone did not alter any methylation patterns at the IFN-γ promoter region. 2. IL-4 promoter Hypomethylation occurred at the IL-4 promoter at CpG-408 after exposure to *A. fumigatus* + DEP when compared to saline, *A. fumigatus* alone or DEP alone. Altered methylation was not detected at any other sites on the IL-4 promoter. Hypomethylation was associated with decreased IgE.
Reference: Matsumoto et al. (2006) **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 6 weeks **Weight:** 15-20 g	DE DE collected from a 2369 cm^3 diesel engine operated at 1050 rpm and 80% load with commercial light oil. Engine exhaust passed through a particulate air filter and charcoal filer. Diluted DE introduced into the exposure chamber. Composition of the DE: 3.5±0.1ppm CO, 2.2±0.3ppm NO_2, <0.01ppm SO_2 and 103.1 ±9.2µg/m^3 DEP.	**Route:** Whole-body exposure chambers after prior sensitization with OVA through ip injection **Dose/Concentration:** 100 µg/m^3 DE **Particle Size (Distribution):** Not Reported **Time to Analysis:** Mice were initially sensitized w/ OVA (20ug absorbed to 2 mg alum diluted with 0.5 mL saline) via ip injection on day 0, 6 and 7. Two weeks later the mice were challenged with OVA (0.1mg in 0.1mL saline) intranasally on day 21. DE for 1day or 1,2, 3, 4 or 8 weeks (at 7 hours a day for 5 days a week).	Airway Hyper-Responsiveness: Airway Reactivity (evaluated by an increase in PenH)- Exposure to DE significantly increased airway reactivity to methacholine after 1 week in both 24 and 48 mg/mL Mch and after 4 weeks in the 48 mg/mL. Airway Sensitivity (evaluated by PC200)- DE exposure caused an increase in airway sensitivity after 1 week of exposure, 4 weeks and 8 weeks of exposure did not result in a significant increase. BAL Cell Counts: The total cell count was increased after 1 week of DE exposure. This increase was mostly due to an increase in eosinophils. After 1 week the total cell count dropped drastically even after continuous exposure to DE. DE did not effect the number of CD3, CD4, CD8 or NK1 cells at any point in time. Cytokine/Chemokine mRNA Levels: DE exposure on day 1 caused an increase in mRNA levels of IL-4, IL-5 and IL-13 when compared to the control mice but longer periods of DE exposure failed to cause an increase. Protein levels of IL-4 were significantly elevated at compared to control at day 1, but did not persist with time. mRNA levels of MDC were increased at 1 week of exposure (compared to control) but also decreased at time periods after. mRNA levels of RANTES were increased at 2 and 3 weeks after exposure and remained elevated at 4 weeks but not significantly. The level of RANTES protein increased as the weeks went along, but increased significantly only at 8 weeks. Lung Histopathology: OVA sensitization caused an increase peribronchial and perivascular infiltration of inflammatory cells which peaked at 1 week after exposure and decreased afterward. DE exposure did not cause/show any additional signs of inflammation.

Study	Pollutant	Exposure	Particle Effects
Reference: Morishita, A. et al. 2004 **Species:** Rat **Gender:** Male **Strain:** Brown-Norway **Age:** 10-12 weeks	Concentrated Air Particles (CAPs) CAPs were generated from ambient air in an urban Detriot community. The sampling site was chosen because it has a high percentage of pediatric asthma and is located near a lot of industry.	**Route:** Whole-body Inhalation Chambers **Dose/Concentration:** Air chamber received CAPs at a flow rate of 50 L/min and at a pressure of 0.94-0.95 atm. July 676 μg/m^3 September 313 μg/m^3 **Particle Size (Distribution):** 0.1-2.5 μm **Time to Analysis:** First rats were sensitized (days 1-3) and challenged (days 14-16) with saline (control) or ovalbumin by intranasal instillation (5% in saline, 150 μL/nasal passage). 4 days after the last intranasal challenge, rats began exposure in the chambers. Exposures were 10 h long. There were two separate exposure periods in July and September. The July exposure was for 4 consecutive days. The September exposure was for 5 consecutive days.	Recovery of Trace Elements in Animal Lung Tissues: July Exposure- Anthropogenic trace elements were below limit of detection in pulmonary tissue of animals exposed to July CAPs. September Exposure- Several elements were recovered from pulmonary tissue during the Sept. exposure. La concentrations were increased in both control/CAPs exposure and in the Ova/CAPs exposure groups. V concentration was increased in Ova/CAPs exposed animals but not in rats exposed to just CAPs. S content was only significant in animals exposed to Ova/CAPs compared to the non-exposed control. Particle Characterization: July PM had an average mass concentration twice as high as the September mass concentration. S concentration was four-folds higher in July PM. In the September PM- the concentration of La was 12.5 fold higher than in July PM, V was 2.7 fold higher than in July PM and Mn was 1.5 fold higher than in July PM. BALF Analysis: Eosinophil concentration was not significantly different when comparing rats exposed to CAPs only in either July or September (this was explained by the elapsed time between exposure and BALF collection). However OVA and CAP exposure in the September group led to elevated eosinophil levels. Similarly, the protein content was only significantly increased in the September OVA/CAP exposed rats, compared to the control group.
Reference: Nygaard et al. 2005 **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-7 weeks	Coarse and Fine ambient air particles collected from Rome, Oslo, Lodz, and Amsterdam during the spring and summer. Rome, Oslo, Lodz and Amsterdam represent areas with high population and dominance of traffic.	**Route:** Subcutaneous Injection into both mouse footpads. **Dose/Concentration:** 100ug of particle suspended in 20uL of Hank's Balanced Salt Solution (HBSS) per injection. (one injection per footpad) **Particle Size (Distribution):** Fine PM- defined as: 0.1 - 2.5 μm and Coarse PM- defined as: 2.5 - 10 μm **Time to Analysis:** The particles tested were: fine and coarse particle fractions from Amsterdam (spring), Lodz (summer) and Oslo (spring). Animals were in eight groups: 1. HBSS-control 2. OVA- 50ug in 20uL HBSS 3. OVA (50ug)+ Amsterdam Coarse PM (100ug) in 20uL HBSS 4. OVA (50ug)+ Amsterdam Fine PM (100ug) in 20uL HBSS 5. OVA (50ug)+ Lodz Coarse PM (100ug) in 20uL HBSS 6. OVA (50ug)+ Lodz Fine PM (100ug) in 20uL HBSS 7. 5. OVA (50ug)+ Oslo Coarse PM (100ug) in 20uL HBSS 8. OVA (50ug)+ Oslo Fine PM (100ug) in 20uL HBSS Mice were killed and analyzed 5 days after injection	Cell Numbers and Cell Phenotypes in the Lymph Node: The overall number of B lymphocytes and expression of MHC class II, CD86 and CD23 on B lymphocytes were increased by coexposure of OVA+ the particles compared to the OVA group alone. There were no differences observed between coarse and fine PM fractions. Cytokine Production by Lymph Node (ex vivo culture of popliteal lymph node cells): All coarse and fine particle fractions co-exposed with OVA significantly increased IL-4 and IL-10 compared to OVA alone. There was no significant difference between coarse and fine particles. IFN-γ levels were not significantly effected by any of the groups, but the fine fractions of PM did tend to produce higher levels of IFN-γ.

Study	Pollutant	Exposure	Particle Effects
Reference: Nygaard et al. 2005 **Species:** Mouse **Gender:** Female **Strains:** BALB/cA **Age:** 6-8 weeks	Polysterene Particles (PSP)- which is a model for the insoluble particle core. PSP were purchased from Polybead Polystyrene Microspheres: Polysciences Europe	**Route:** Subcutaneous Injection into both mouse footpads. **Dose/Concentration:** 40 µg PSP (5.94 X 1010 particles) per injection suspended in HBSS. One injection per footpad, therefore 80 µg PSP per animal. **Particle Size (Distribution):** PSP has a diameter = 0.1 µm **Time to Analysis:** Four groups were tested: 1. HBSS 2. OVA (10 µg per injection) 3. PSP (40 µg per injection) 4. OVA (10 µg per injection) + PSP (40 µg per injection). In the antibody experiments, mice were reinjected with 10 µg OVA on day 21 and killed on Day 26. In the popliteal lymph node cell experiments, animals were injected and then killed 1 to 21 days after the injection.	The Adjuvant Effect of PSP on OVA-specific IgE, IgG1 and IgG2a Antibodies: Analysis at day 26 indicated IgE, IgG1 levels were significantly higher in mice exposed to OVA+PSP compared to mice injected with HBSS, OVA or PSP. No significant difference was observed for IgG2a levels. Number of Particle Containing Cells: There was no significant difference between PSP alone and OVA+PSP. Throughout days 0 -21 the number of particle-containing cells in the PSP or OVA+ PSP was significantly greater than HBSS. Total Cell Numbers, B and T Lymphocytes and MHC class II Expression: Total cell number- was significantly increased by coexposure to OVA+ PSP when compared to the other groups. Total cell levels reached a maximum on Day 5 declining thereafter. B Lymphocytes- significantly increased by coexposure to OVA+ PSP when compared to the other groups. Total cell levels reached a maximum on Day 5 after injection with OVA+PSP after day 5 there was a steady decline. T Lymphocytes: Both OVA and OVA+PSP induced an increased in T lymphocytes on Days 1, 3 and 5- after which there was a steady decline. MCH class II expression- was significantly higher in the OVA+PSP group on days 5, 7 and 21 than other groups. Cell Types and Surface Markers on Day 5: CD4+ and CD8+ T lymphocytes and the amount of CD4+ and CD8+ molecules per cell was not significantly different among groups. The number of CD40+ B Lymphocytes showed a slight but significant decrease with OVA+PSP and OVA compared to HBSS and PSP. The expression of CD40+ molecules did not change among groups. CD80+ lymphocytes were not detected. CD86+, CD23+ and CD69+ B lymphocytes were significantly higher in OVA+PSP group than other groups. PSP alone did not effect CD86+ or CD23+ levels. In some cases OVA had an increasing effect on CD23+ levels. Cytokine Production- Day 5: IL-4 and IL-10 production was significantly higher in cells exposed to OVA+PSP when compared to the other groups. OVA alone caused a slight increase compared to HBSS and PSP. Neither HBSS or PSP altered IL-4 or IL-10 levels. IFN-γ levels did not differ among groups. Cellular Response to CpG-DNA and OVA+ CpG-DNA: In contrast to PSP, both CpG-DNA alone and OVA+ CpG-DNA increased total cell number, number of B lymphocytes, expression of MHC class II and CD86. CpG-DNA alone and OVA+ CpG-DNA significantly decreased number of CD23+ B lymphocytes.

Study	Pollutant	Exposure	Particle Effects
Reference: Nygaard et al. (2004) **Species:** Mouse **Gender:** Female **Strain:** BALB/cA **Age:** 6-7 weeks **Weight:** NR	PSP = polystyrene particles (CB = carbon black/DEP = SRM 2975 DEPs as references)	**Route:** single sc injection into footpad **Dose/Concentration:** 10 µg OVA (ovalbumin) + 40 µg (low dose) or 200 µg (high dose) of particles **Particle Size (Distribution):** (in nm) PSP59, PSP202, PSP1050, PSP460, PSP11000 **Time to Analysis:** Antibody study: Day 0-high/low dose particles with OVA or OVA alone injection into footpad; Day 21-OVA injection (booster); Day 26-sacrifice. Lymph Node study: single injection of HBSS, OVA, or OVA with high or low dose PSP202, PSP1050, or PSP11000; analysis 5 days after injection	Allergen-specific IgE serum: PSP59 and PSP200 as well as CB and DEP elicited a stat. greater response than PSP1050, PSP4600, PSP11000; Popliteal Lymph Node (PLN) cell numbers; expression of CD19, MHC class II, CD86, CD23; ex vivoIL-4 and IL-10 production: PSP202 with OVA elicited a greater response than PSP11000 Regression analysis: Particle mass did not predict any cellular parameters or IgE/IgG2a levels with stat. significance. Total particle area, number, and diameter explained 60-80% of the variation in PLN cellular parameters (except CD23 expression) and 36-64% of variation in IgE/IgG2a levels
Reference: Roberts et al. 2007 **Species:** Rat **Gender:** Male **Strain:** Sprague-Dawley **Age:** 10 weeks **Weight:** 250-300 g	R-Total = ROFA (Residual oily fish ash) Sample R-Soluble = Soluble fraction of ROFA R-Chelex = R-Soluble+Chelex (insoluble resin)	**Route:** Intratracheal instillation **Dose/Concentration:** 10 mg/kg of body weight (2.5-3mg) **Particle Size (Distribution):** 2.2 µm **Time to Analysis:** pre-exposure to ROFA samples on Day 0; Inoculation with 5 x 10^4 L. monocytogenes or saline on day 3; Sacrifice on days 6, 8, and 10	Lung injury parameters in uninfected/infected groups (LDH and albumin): R-Soluble significantly increased these levels by day 6 BAL cell numbers and types in uninfected/infected groups (total number, PMNs, lymphocytes): R-Soluble significantly increased these cell populations at day 3 and increased AM number by day 6. ROS, RNS, Cytokine levels in infected groups (TNF-a, IL-6, IL-10, IL-12): R-soluble significantly increased these levels by day 6
Reference: Saxena et al. 2003 **Species:** Mouse **Gender:** Female **Strain:** C57B1/6J **Age:** 18-30 weeks **Weight:** NR	DEPs	**Route:** intrapulmonary instillation **Dose/Concentration:** 100 µg/mouse **Particle Size (Distribution):** NR **Time to Analysis:** Pre-exposure to 2.5 x 10^4 bacillus Calmette-Guerin bacteria (BC G) with or without coadministration of DEP; Sacrifice 5 weeks later	BC G load: BC G+DEP had a 4-fold higher BC G lung load than BC G alone. Increased in liver and lymph node as well. Recovery of lymphocytes from lungs: DEP + BC G increased lymphocyte, T, B and NK cells over BC G alone. IFNγ gene transcrription in lung lymphocytes: DEP + BC G no different from BC G alone except for an increase in CD T8 cells (no stats)
Reference: Schneider et al. 2005 **Species:** Mouse **Cell Line:** RAW 264.7 macrophage cells derived from BALB/c mice	SRM 1648 (NIST) Titanium dioxide (Fisher Chemical, Fair Lawn, NJ, catalog #T315-500)	**Route:** Cell culture, 625,000 cells/cm^2 in 96 well plate **Dose/Concentration:** 62.5µg/cm^2 **Particle Size (Distribution):** TiO_2 = 0.3um SRM 1648 = 0.4um **Time to Analysis:** particulate introduction at 0, 7.8, 15.6, 31.2, and 62.5 µg/cm^2. Measurements made at 1, 3, 6, and 12-h after particulate introduction	SRM 1648 demonstrated no significant toxicity Oxidative Stress (rate of redox-sensitive dye oxidation, reduced glutathione): SRM 1648 significantly increased rate of dye oxidation; SRM 1648 significantly increased levels of reduced glutathione at 12 h PGE2 release: SRM 1648 significantly elevated PGE2 production at 3hrs
Reference: Schober et al. 2006 **Species:** Human **Gender:** Male and Female **Age:** 21-39 yrs, treatment group; 23-32 yrs, control group **Tissue Type:** Whole blood samples	AERex1d = urban aerosol 1 day sample AERex5d = urban aerosol 5 day sample rBet v 1 (birch pollen allergen 1a, Biomay, Vienna, Austria) rBet v 1 = 100ul AERex1d/5d = 0.007 to 0.755 m^3 air equiv	**Route:** Cell culture **Dose/Concentration:** 100 µL heparinized whole blood **Particle Size (Distribution):** NR **Time to Analysis:** blood was stimulated with PBS/IL-3 for 10 min, incubated with rBet v 1 alone or with AERex1d/5d	Total air volume: AERex1d = 1270 m^3 AERex5d = 6230 m^3 Basophil activation: AERex1d/5d increased these levels up to 90%, enhanced CD63 up regulation of rBet v 1 levels in sensitized basophils
Reference: Shwe et al. 2005 **Species:** Mouse **Gender:** Male **Strains:** BALB/c (Charles River Japan, Inc, Tokoyo, Japan) **Age:** 8 weeks **Weight:** NR	CB = carbon black (Degussa, Germany)	**Route:** Intratracheal instillation **Dose/Concentration:** 25, 125, or 625ug in 1 mL saline solution **Particle Size (Distribution):** CB14 = 14nm CB95 = 95nm **Time to Analysis:** CB14 or CB95 instillation once a week for 4 weeks; sacrifice 24 h after last instillation	total cell count and differential cell count (macrophages, lymphocytes, neutrophils in BAL fluid) IL-1B, IL-6, TNF-a, Macrophage inflammatory protein 1 a/CCL-3 protein: CB14 significantly incrased mRNA (or protein) expression in dose-dependent manner.

Study	Pollutant	Exposure	Particle Effects
Reference: Sigaud, S. et al. 2007 **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** 8-10 weeks **Weight:** NR	Concentrated Ambient Particles (CAPs) collected from ambient Boston air on Teflon filters. CAPs Composition: Not Reported TiO_2	**Route:** Intranasal Instillation **Dose/Concentration:** 50 µg of CAPs or TiO_2 suspended in 50 µL PBS introduced into both nostrils **Particle Size (Distribution):** CAPs: <2.5 µm **Time to Analysis:** Measuring Inflammation: Mice exposed to PBS or IFN-γ (priming) and then 50 µg CAPs or TiO_2. 24-h later BAL conducted. Cytokine Levels: Mice exposed as above. RNA analyzed at 3, 6 and 24 h Measuring Inflammation+ S. pneumo: Mice exposed as above. 24-h later mice infected with 105 CFU S. pneumo. 24 h after infection BAL conducted. Bacterial Load: Mice exposed as above. 24-h later mice infected with 105 CFU S. pneumo. 24 hr after infection lung homogenates were plated on SBA and incubated overnight. Bacterial Uptake AM and PMN Cells: Mice exposed as above. 24-h later mice infected with 105 CFU S. pneumo labeled with SYTO 9. BAL was performed 3 h after infection. Measuring ROS in AM and PMN Cells: Mice exposed as above. BAL was performed 24-h later. Lavaged cells were incubated for 30 min with anti-Gr-1 antibody and DCFH-D_a.	Inflammation: 1. PBS+ TiO_2- only produced a moderate increase in PMN numbers (not significantly different) 2. PBS + CAPs- produced a significant increase in PMNs in the lung (100% more than in mice exposed to TiO_2) 3. IFN+ PBS and IFN+TiO_2- only produced a small increase in PMNs, not statistically significant. 4. IFN+ CAPs- produced a strong inflammatory response, 2.5 increase in PMNs when compared to the increase caused by PBS+ CAPs exposure. Cytokine Levels: Exposure to CAPs and IFN-γ primer both stimulated cytokines levels- see Table 1 Inflammation+ S. pneumo Infection: The lungs of mice infected with s. pneumo displayed inflammation (increased PMNs) in all 6 groups: 1. PBS+ TiO_2 + S.pneumo- no significant change in PMNs when compared mice infected with just S.pneumo alone 2. PBS + CAPs+S.pneumo- produced a significant increase in PMNs (2-fold more than control) 3. IFN+ PBS+ S. pneumo and IFN+TiO_2 + S.pneumo- did not produce a significant change. 4. IFN+ CAPs+ S.pneumo- produced a 3.5 fold increase compared to control and a 1.6-fold increase compared to PBS+CAPs+ S.pneumo. Bacterial Load: 1. In the control groups, PBS+TiO_2, INF+ PBS, IFN+ TiO_2- 50% of the bacteria were alive after 24 h. 2. PBS+ CAPs- Bacterial count did not decrease or increase 3. IFN+CAPs- Bacterial count displayed a 2.5 fold increase compared to control. Histopathology: Indicated moderate pneumonia in PBS+CAPs exposed cells and severe pneumonia in IFN+CAPs exposed cells. The other groups did not indicate areas of pneumonia. Bacterial Uptake AM and PMN Cells: 1. AM Cells- NONE of the groups had a statistically significant decrease. 2. PMN Cells- All groups had a decrease in bacterial content in, but PBS+ CAPs and IFN+CAPs produced a sig. decrease. ROS Levels in AM and PMN Cells: 1. AM Cells- There was an increase in intracellular ROS for with PBS, PBS+CAPs, IFN, IFN+CAPs but only IFN+CAPs produced a significant increase. 2. PMN Cells- There was an increase in intracellular ROS for with PBS, PBS+CAPs, IFN, IFN+CAPs but only IFN+CAPs produced a significant increase.
Reference: Sigaud, S. et al. 2007 **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Cell Type:** AM and PMN Cells from BAL fluid	CAPs (collected from Boston ambient air) CAPs Composition: Not Reported and TiO_2	**Route:** Cell culture**,** 1: 50 ratio of cells to viral load **Dose/Concentration:** 50 µg of CAPs or TiO_2 suspended in 50 µL PBS **Particle Size (Distribution):** CAPs: <2.5 µm TiO_2: NR **Time to Analysis:** Mice exposed to PBS or IFN-γ (priming) and then 50 µg CAPs or TiO_2. 24-h later BAL was performed. Lavaged cells were incubated with FITC-labeled S. pneumo for 90 min. After cells were stained and analyzed via flow cytometry.	Bacterial Content of AM and PMN Cells: 1. AM cells that were exposed to CAPs (CAPs+PBs and CAPS+IFN) showed a trend that indicated reduced uptake of bacteria when compared to the control, PBS or IFN exposed cells. Not statistically different decrease. 2. PMN cells showed a statistically significant decrease in uptake in cells exposed to CAPs (CAPs+PBs and CAPS+IFN). PBS and IFN alone did not display significant decreases.

Study	Pollutant	Exposure	Particle Effects
Reference: Steerenberg, et al. 2004 **Species:** Rat **Gender:** Male **Strain:** Wistar **Age:** 6-8 weeks	Ozone (positive control) DEP (SRM1650a) EHC-93	**Route:** Ozone- was administered via whole-body inhalation chamber. DEP/EHC-93 were suspended in saline and administered into the nostrils. **Dose/Concentration:** Ozone: Exposed to 2mg/m^3 DEP/EHC-93: Exposed to 50μg/rat suspended in saline **Particle Size (Distribution):** Ozone: NA DEP: SRM1650a EHC-93: standard urban PM collected in Canada. **Time to Analysis:** Ozone: Exposed to 2mg/m^3 for 24 h/day for 7 days. DEP/EHC-93: Exposed to 50μg/rat suspended in saline for 7 days. All rats were infected with 0.2mL L. monocytogenes (strain L242/73 type B) intratracheally (5 X 106 PFU/mL) on the day after the last exposure. Rats from each group were sacrificed 2, 4, and 5 days after bacterial infection and the lungs and spleen were analyzed for bacterial load.	Bacterial Count in The Lung: At 3 Days: The number of bacteria in the lung of those rats exposed to ozone was significantly greater than those in the negative control group (exposed to 50 μL saline). The bacterial count for the lungs of rats exposed to DEP or EHC-93 was not significantly different than those exposed to the control. At 4 and 5 Days: The bacterial count in the lungs of rats exposed to ozone continued to remain significantly greater than those exposed to saline. In the control animal lungs and those exposed to DEP and EHC-93 the bacterial count gradually decreased from days 3 to 4 to 5, indicating a host defense system response. There was also a slight (but statistically insignificant) decrease in bacterial count in the lungs exposed to ozone. Bacterial Count in The Spleen: At 3 Days: None of the groups expressed bacterial counts statistically greater than the control group. However the bacterial count in the spleen of rats exposed to ozone was higher than those exposed to DEP or EHC-93. At 4 and 5 Days: The bacterial load decreased from day 3 in the spleen of those exposed to ozone but it remained statistically greater than those exposed to the control. The bacterial count in the spleens of rats exposed to DEP and EHC-93 were still similar to the control. At day 5 the bacteria count in the spleens of the rats exposed to control, DEP and EHC-93 decreased substantially while those exposed to ozone remained fairly steady (slight decrease in bacterial count). DEP and EHC-93 did not appear to effect the host defense system in regards to clearing/fighting Listeria Monocytogenes.

Study	Pollutant	Exposure	Particle Effects
Reference: Steerenberg, et al. (2005) **Species:** Mouse **Gender:** Male **Strain:** BALB/cByJ.ico **Age:** 6-8 weeks	Concentrations of: Coarse PM and Fine PM collected from Rome, Oslo, Lodz, Amsterdam and De Zilk during the spring, summer and winter. Rome, Oslo, Lodz and Amsterdam represent areas with high population and dominance of traffic. De Zilk was an area 800m from the sea surrounded with sand dunes and fields, not a lot of traffic. EHC-93 was used as a standard reference.	**Route:** Intranasal Exposure to PM **Dose/Concentration:** Particle Exposure: Total dose of 20 µg ovalbumin and 450 µg PM per mouse in 50 ul For intranasal sensitization: 20 µg ovalbumin in 50 µL saline administered in both nostrils on days 0 and 14. For challenge: ovalbumin administered intranasally at 20 µg in 50 µL saline at day 35, 38 and 41. EHC-93 was administered at 0 - 900 µg to evaluate any dose-response relationship. **Particle Size (Distribution):** Coarse PM: defined as: 2.5 - 10.0 µm. (no exact measure reported) Fine PM: defined as: 0.1 - 2.5 µm. (no exact measure reported) EHC-93- has a standard reference diameter. **Time to Analysis:** Particle Exposure: 3 mg/mL PM was mixed with 0.4mg/mL ovalbumin. For intranasal sensitization Groups: 0.4mg/mL ovalbumin in 50 µL saline was administered in both nostrils on days 0 and 14. For challenge Groups: ovalbumin was administered intranasally at 0.4mg/mL in 50 µL saline at day 35, 38 and 41. Animals were sacrificed on Day 42.	**Dose Response to EHC-93:** Antibodies: All three antibodies of ovalbumin (IgE, IgG1 and IgG2a) showed a dose-dependent increase in response to EHC-93. **Histopathology:** At doses of 50 µg there was significant increase in peribronchiolar and prevascular infiltrates. At concentrations equal to or greater than 3 mg/mL induced an increase in eosinophils and hypertrophy of mucous cells. Alveolar Macrophage (AM) clusters were observed and had varying quantities of phagocytized PM. **Bronchoalveolar Cells:** At 150 and 450 µg eosinophils, neutrophils and monocytes were significantly increased. At 900 µg only neutrophils were increased. **Cytokine Production:** 150 µg induced a minimal amount of IL-4 the BAL fluid. IFN-γ was already present in high concentrations in mice just exposed to saline, exposure to EHC-93+ovalbumin at a dose of 15 µg caused a slight increase but increased doses of EHC-93 caused a steady but not significant decrease in IFN-γ. TNF-α did not change after exposure. IL-5 showed a significant increase after exposure to 50 µg but it did not reflect a dose-dependent relationship. **Effects of Coarse and Fine Particles:** Immunoglobulins: 6/13 of the coarse and 9/13 fine PM samples induced an increase in IgE and IgG1when compared to the control. IgG2a levels were increased in 3/13 of the coarse and 5/13 of the fine PM. Interestingly particles from De Zilk induced all three immunoglobulins, accept the fine PM did not induce IgG2a. De Zilk was intended as a negative control (see Table 3). Analysis amount the sites comparing the subclasses of antibodies indicated a rank as follows: Lodz >Rome ≥ Oslo. Histopathology: 9/13 of the samples of coarse PM and 5/13 samples of fine PM induced an inflammatory response. **Bronchoalveolar Cells:** Of the samples, Lodz (spring/ summer) had the most prominent effect. Lodz (spring/summer) coarse and fine PM induced an increase in eosinophils, neutrophils and monocytes. The coarse and fine PM from Rome (spring) induced an increase in neutrophils and the coarse PM induced an increase in eosinophils. Also both Lodz and Rome from the coarse PM from the spring induced an increase in macrophages. Other PM samples did not have an effect on BAL cell counts. (see Table 6) **Cytokine Production:** None of the samples produced a significant effect on IL-4 levels. IFN-γ levels were de-creased in mice exposed to the fine PM fraction (in 8/13 of the samples) when compared to control. Coarse particle exposure did not appear to effect IFN-γ levels. TNF-α levels were increased by 2 of the 13 samples exposed to coarse PM, fine PM did not appear to have an effect. IL-5 was increased in 4/13 of the coarse and 4/13 of the fine PM samples. Analysis of PM **Components:** Samples from Lodz, Oslo and Rome (all spring) were evaluated and the water-soluble coarse PM fraction showed increased immunoglobulin and pathological responses and the water-insoluble fine PM fraction from Lodz (Spring) showed increased reactivity.

Study	Pollutant	Exposure	Particle Effects
Reference: Steerenberg, et al. (2004) **Species:** Mouse **Gender:** Male **Strain:** BALB/cByJ.ico **Age:** 6-8 weeks **Treatment:** 1. C.D2-Vil6: NrampS and NrampR deficient 2. C57B1/6 and B6.129P2-Nos2tmLau: iNOS deficient 3. BALB/clL4(tm2Nnt): deficient in IL-4 4. BALB/c pretreated with NAC	Coexposure to EHC-93 and ovalbumin	**Route:** Intranasally **Dose/Concentration:** 150 µg EHC-93 and 20 µg OVA **Particle Size (Distribution):** EHC-93- has a standard reference size. **Time to Analysis:** Mice were exposed to intranasal sensitization on days 0 and 14. 20 µg ovalbumin in 50 µL saline was administered in both nostrils. The challenge on days 35, 38 and 41 consisted of exposing the mice to ovalbumin (at same concentration). Animals were sacrificed on day 42 * To study the effects of NAC- mice received a 320mg/kg intraperitoneal injection before intranasal exposure to ovalbumin and/or the particles on days 0 and 14.	Natural-Resistance-Associated Macrophage Protein 1 (Nramp1): C.D2-Vil6 strain Antibody Reaction: When exposed to only ovalbumin, NrampS evoked less of an antibody responses (IgE, IgG1 and IgG2a) compared to NrampR. However when coexposed to ovalbumin and EHC-93, the level of increased production of antibodies was similar in both groups. Histopathology: The wild-type mice showed increased histopathological lesions, whereas the macrophage-stimulation-deficient types showed only a slight increase (not significant). BAL Cell Counts: IL-4, IFN-γ, TNF-α and IL-5 levels were similar in wild-type and the Nramp strains. Pretreatment with N-Acetylcysteine (NAC): Antibody Reaction: BALB/c mice (wild type) exposed to ovalbumin and EHC-93 showed strong adjuvant activity for IgE, IgG1 and IgG2a. IgG2a concentration was increased further in the group pretreated with NAC. The IgE and IgG1 concentrations were similar. Histopathology: The wild-type mice and the pretreated with NAC mice showed similar histopathological lesion patterns. BAL Cell Counts: IL-4 levels were similar in wild-type and the pretreated mice. (IFN-γ, TNF-α and IL-5 levels not reported) Inducible Nitric Oxide Synthase (iNOS): C57B1/6 and B6.129P2-Nos2tmLau strains Antibody Reaction: The wild-type mice and the iNOS-deficient mice had similar levels of increased IgE antibody production. The IgG1 and IgG2a antibody response was twice as great in the iNOS-deficient mice compared to the wild type. Histopathology: The wild-type mice and the iNOS-deficient mice showed similar histopathological lesions. BAL Cell Counts: No difference between BAL cell counts when comparing the wild-type and iNOS-deficient mice. Interleukin-4 (IL-4): BALB/clL4(tm2Nnt) strain Antibody Reaction: The IL-4-deficient mice did not produce an increase in IgE or IgG1 antibodies, as was seen in the wild-type mice. The IgG2a antibody response in the IL-4-deficient mice was similar when compared to the wild type (Increased IgG2a antibodies). Histopathology: Overall the histological response of the wild-type mice was greater compared to the IL-4 deficient mice. BAL Cell Counts: There was no real difference between the two strains observed in the BAL cells, except IL-5 was significantly lower in the IL-4-deficient mice.

Study	Pollutant	Exposure	Particle Effects
Reference: Takizawa et al. (2003) **Species:** Human **Cell Lines:** Normal Small Airway Epithelial Cells and Bronchial Epithelial Cells (BET-1A)	Suspended or Gaseous DEP DEP was collected using a standard diesel fuel at 1,050 rpm under a load of 6 torque. The composition of the gaseous material was exhaust FPM (1 mg/m^3), CO (10.6 ppm), NO_2 (7.3 ppm) and S02 (3.3ppm).	**Route:** Cell culture **Dose/Concentration:** Normal Small Airway Epithelial Cells: seeded at a density of 2 x 104 cells/well Bronchial epithelial cells (BET-1A): seeded at a density of 5 X 104 cells/well. Cells were exposed to DEP by conventional suspended method (DEP suspended in solution) and by in vitro cell exposure to DE. Cell culture 0.1 - 50 μg/mL Air exposure (flow-over) 100 μg/m^3 **Particle Size (Distribution):** NR **Time to Analysis:** Cells were exposed to varying concentrations of DEP (0-50 μg/mL) for up to 24 h. Air exposure 2, 4, 8 or 14 h	Preliminary experiments indicated that DEP at 0.1- 50 μg/mL had no significant cytotoxicity to BET-1A cells and human bronchial epithelial cells (as analyzed by LDH levels). **Eotaxin Production:** (Eotaxin is a cc chemokine that plays a role in eosinophil accumulation in a variety of allergic disorders) In cells treated with DEP (0-50 μg/mL) for 24-h, DEP showed a dose-dependent stimulatory effect on eotaxin production by normal human bronchial epithelial cells and BET-1A cells. Human re-combinant IL-13 also showed a dose-dependent stimulatory effect on eotaxin production in both cell types. Simultaneous exposure to 25ng/mL IL-13 and DEP(varying 0-50μg/mL) depicted an additive effect. **Eotaxin mRNA:** Cellular RNA was extracted from human bronchial epithelial and BET-1A cells over varying time period (0-24 h) after exposure to 25 μg/mL DEP. At 25 μg/mL DEP showed a time-dependent effect on eotaxin mRNA levels up to 12 h. Extracted RNA from human bronchial epithelial cells exposed to varying doses of DEP (1-50μg/mL) showed a dose-dependent effect (up to 25 μg/mL DEP) on eotaxin mRNA levels after 12 h of exposure. IL-13 also induced a dose-dependent increase on eotaxin mRNA levels in cells. Combination of IL-13 (25ng/mL) and DEP showed an additive effect on mRNA levels. **NF-κB / STAT6 Activation:** (it has been suggested that NF-κB plays a role in the transcriptional regulation of eotaxin gene expression) Cells exposed to 1-25 μg/mL DEP for 6 h activated NF-κB in BET-1A cells. IL-13 failed to activate NF-κB. Whereas BET-1A cells treated with 0-100μg/mL DEP failed to activate STAT6 and treatment with 10 ng/mL IL-13 for 30 min induced the phosphorylation of STAT6. Effect of NAC and PDTC on Eotaxin mRNA **Levels:** (NAC and PDTC are antioxidant reagents with inhibitory effects on NF-κB activation) in BET-1A cells both NAC and PDTC showed a dose-dependent inhibitory effect on DEP-induced eotaxin production after 24-h of DEP treatment of 25 μg/mL. Both reagents also blocked DEP-induced eotaxin mRNA levels in BET-1A cells. NAC and PDTC did not suppress eotaxin production or eotaxin mRNA levels in IL-13 stimulated BET-1A cells. In addition pre-treatment with NAC attenuated NF-κB activation induced by DEP but had no effect on STAT6 induction by IL-13.

Study	Pollutant	Exposure	Particle Effects
Reference: Tesfaigzi et al. (2005) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway **Age:** 6 weeks	Wood Smoke Wood smoke was generated from an conventional wood stove that has a 0.5m^3 firebox and a sliding gate air intake damper. The stove was operated over a 3-phase burn cycle that spanned 6 h. Fire was started (initiated exposure) with unprinted / unbleached newspaper and a mix of black and white oak. The components of wood smoke are: organic material, small amounts of elemental carbon and metals and associated analytes.	**Route:** Whole-body Inhalation for 6 hours/day for 7 days/week for 70 days. **Dose/Concentration:** Rats were exposed to a concentration of 1 mg PM/m^3 or to filtered air. More specifically wood smoke was passed through the chamber that was 2 m^3 in size at ~ 500 l/min yielding a material residence time in the chamber of ~ 4 min. **Particle Size (Distribution):** PM of the wood smoke had a mean aerodynamic diameter of ~ 0.3um. **Time to Analysis:** After the first day of exposure, both air and PM rat groups were injected (ip) with a mix of 10 µg ovalbumin in 0.5 mL PBS. This process was repeated 7 days later. On Day 67-70 rats were first exposed to normal daily PM or air and then exposed for 2 h per day to OVA aerosols at 2mg/m^3 for four consecutive days.	**Body Weight and Respiratory Function:** No difference in clinical signs or body weight was observed when comparing the two rat groups. The rats who were exposed to wood smoke did have 45% lower dynamic lung compliance (0.35 ±0.05 mL) when compared to those exposed to filtered air (0.64 ± 0.29mL) before the methacholine challenge. Challenging the rats with methacholine caused a decrease in dynamic lung compliance in both groups, but the decrease was greater in the air-exposed group. (The authors offered up a possible explanation for this result being that the PM-exposed group already had such a low baseline). The only other factor that was significantly different was that the wood smoke exposed rats (5.3±0.3 mL) had a slightly higher functional residual capacity than the air-exposed (4.5 ± 0.5 mL). **BAL Cell Counts and Cytokines:** There was no difference in lymphocyte, eosinophil or neutrophils in the BAL of either group. There was an increase in macrophages in rats exposed to wood smoke compared to filtered air. The were significant differences in cytokine levels in the BALF compared to the plasma in both groups. IFN-γ levels were decreased and IL-4 levels were increased in rats exposed to wood smoke compared to filtered air. Serum IgE levels experienced a reduction trend but it did not reach significance. Histopathology: Both groups showed mild signs of inflammation. The average eosinophils present in stained tissue was 21% higher in the wood smoke exposed group compared to the air exposed.
Reference: Tomita et al. (2006) **Species:** Mouse **Gender:** Female **Strain:** C57BL/6J, AHR deficient, mEH deficient ARNT floxed (loxP sequences inserted in Arnt gene) Tcell-specific ARNT-deficient **Age:** ~ 7 weeks **Weight:** 20 g	DEP = two different types (not further distinguished in study- supposedly similar in results) both derived fromn 4 cylinder light duty diesel engines DEP was fractionated into 13 different fractions based on acidic and basic functionality Individual PAH tested: BbF = benzo[b]fluoranthene BeP = Benzo[e]pyrene IDP = Indeno[1,2,3-cd]pyrene BpPe = Benzo[ghi]perylene BaP = Benzo[a]pyrene BkF = Benzo[k]fluoranthene Per = Perylene DBA = Dibenzo[a,h]anthracene	**Route:** intraperitoneal injection **Dose/Concentration:** 0.5 µg - 10 mg/kg bw in 50 ul of olive oil **Particle Size (Distribution):** NR **Time to Analysis:** single ip, euthanasia after 3 days	Effect on thymus: DEP (10 mg/kg) reduced size of thym,us as well as caused severe atrophy of thymus with normal appearing spleen and lymph nodes. Total number of thymocytes (flow cytometry) was reduced by more than 70 % mostly due to a massive reduction in DP cells (CD4+CD8+ double positive). Cell reduction in organs were only observed in thymus not spleen or lymph node. DEP Extracts**:** Most of the DEP extrcats 10 out of 12 showed thymocytic reduction similar to crude extract or DEP. Only BE-weak basic fraction and WAC (Water phase carbonic acid fraction) did not. PAH effects: All PAHs except BpPe (NO effect) showed activity similar to DEP. AHR/ARNT and mEH deficient mice (BaP and DEP only): DEP caused loss of immature thymocytes in all 3 mouse strains. BaP showed no effect in AHR- strains and only a partial effect in ARNT deficient strains. DEP and Bap similar effects in mEH strain.
Reference: Verstraelen et al. (2005) **Species:** Human **Tissue/Cell Types:** Monocyte-derived dendritic cells (Mo-DC) Cord blood samples of seven women were collected from umbilical vessels of placentas of normal, full-term infants.	DEP- SRM 2975 DEP- SRM 2975	**Route:** Cell culture, cells were cultured in 24 wells plated at a density of 10^6 cells/mL **Dose/Concentration:** Varying concentrations of DEP: 0.2, 2, 20, 200, 2000 ng/mL DEP LPS was administered or co-administered at 100 ng/mL **Particle Size (Distribution):** **Time to Analysis:** Cells were incubated for 24 h and analyzed the following day via flow cytometry.	Biological Markers: Exposure to DEP alone did not alter expression levels of HLA-DR, CD86 or CD83. Treatment with LPS alone did cause a slight increase in all three markers, but not significantly when compared to the control. Co-treatment with DEP+LPS caused a significant increase in the expression of CD83 and increased expression of HLA-DR and CD86 (but not significant). DEP+ LPS induced a bell-shape dose-response curve on the expression of all three markers, with a dose of 20 ng/mL DEP + 100 ng/mL LPS being the max dose to cause the largest increase in upregulation.

Study	Pollutant	Exposure	Particle Effects
Reference: Walczak-Drzewiecka et al. (2003) **Species:** Mouse **Cell Line:** C1.MC/C57.1 (C57) Mast Cells	Metal and Transition Metal Ions: Sr^{2+}, Ni^{2+}, Cd^{2+}, Al^{3+}, Pb^{2+}	**Route:** Cell culture, Mast Cells were incubated with metals. Cell Concentration: varies with assay **Dose/Concentration:** Metal Concentration varies with assay 0.1- 5 µmol **Particle Size (Distribution):** NR **Time to Analysis: β-Hex Mediator Release in Mast Cells:** 10-7 M of 1. SrCl2, 2. $NiSO_4$, 3. CdCl2, 4. $AlCl_3$ or 5. a 10-7 mix of Sr, Ni, Cd and Al was incubated with 4 X 104 mast cells for 10 min. **Cell Viability:** Concentrations (0, 10-7, 10-6, 5 X 10-6) of 1. $AlCl_3$, 2.CdCl2 3. $NiSO_4$, 4. SrCl2 or 5. $Pb(NO_3)2$ were incubated with mast cells (106 cells/mL) for 4 h. **Antigen-Mediated Mediator Release in Mast Cells:** Mast cells were sensitized with IgE and incubated for 10 min with antigen (DNP-hA 1, 10 or 100 ng/mL) or antigen combined with concentrations (0, 10-7, 10-6, 5 X 10-6) of 1. $AlCl_3$, 2.CdCl2 3. $NiSO_4$, 4. SrCl2 or 5. $Pb(NO_3)2$. **Antigen-Induced Protein Phosphorylation:** mast cells were sensitized with IgE and incubated with media alone (control) or antigen (50ng/mL DNP-hA) or a combination of antigen and 1. 10-7M $NiSO_4$, 2. 10-7M $Pb(NO_3)2$ or 3. 10-6 M $AlCl_3$. **Antigen-Mediated Cytokine Secretion (IL-4):** Mast cells at 106 cells/mL were sensitized with IgE and incubated for 4 h with antigen (DNP-hA) or antigen combined with concentrations (0, 10-7, 10-6, 5 X 10-6) of 1. $AlCl_3$, 2.CdCl2 3. $NiSO_4$, 4. SrCl2 or 5. $Pb(NO_3)2$.	β-Hex Mediator Release in Mast Cells: Incubation with SrCl2, $NiSO_4$, CdCl2 or $AlCl_3$ resulted in a 2-5% release of β-hexoaminidase in mast cells. Incubation with a mixture of all these compounds induced a greater (11%) release in β-hexoaminidase. Indicating there might be a additive effect. Cell Viability: Incubation of cells in concentrations of 10-7 - 5 X 10-6 did not result in decrease in cell viability. Antigen-Mediated Mediator Release in Mast Cells: Al3+ and Ni2+ enhanced antigen-mediated release. 10-7 M $AlCl_3$ released 23% of β-hexoaminidase compared to antigen alone which induced 11% release of β-hexoaminidase. Cd2+, Sr2+ and Pb2+ also enhanced antigen-mediated release but to a lesser extent. Ni2+, Al3+, Sr2+ and Cd2+ all depicted a dose-dependent relationship with antigen-mediated β-hexoaminidase release. Antigen-Induced Protein Phosphorylation: Addition of the antigen induced phosphorylation of multiple proteins in C57 mast cells (this was anticipated). The addition of metals changed this response. The presence of Ni2+ and Pb2+ mediated an increase in phosphorylation of several of the proteins and Al3+ mediated a decrease in phosphorylation of multiple proteins (specifically the 56 and 37 kD bands). Antigen-Mediated Cytokine Secretion (IL-4): At certain concentrations all tested metal and transition metal ions were able to either induce IL-4 secretion or enhance antigen-induced IL-4 secretion in mast cells, but there was no dose-dependent relationship established.
Reference: Wan et al. (2006) **Species:** Human **Cell Lines:** Human, B cell lymphocytes PMBC (>98.5% B cells-CD19+CD20+; <1 % Tcells (CD3+)) Human lymphocyte cell lines -- DG75 NQO1 wild type	DEP = DEP from 4 cyl Isuzu diesel methanol extracts (Previously published)	**Route:** Cell culture, PMBC = 1 x 10^6 cell DG 75 = 3 x 10^6 cells IgE PMBC 1 x 10^6/mL B-cells 0.5x 10^6/mL **Dose /Concentration:** 2.5, 5, 10, 20 µg DEPX/ plate (text refers to 20 µg/mL) IgE DEPX 100 ng/mL sulfurophane at 0 - 30 µmol **Particle Size (Distribution):** NR **Time to Analysis:** 6h mRNA; 16 h protein assay IgE 14 days	Induction of NQO1 by DEPX: In PBMCs DEPX dose-dependently inudced NQO1 mRNA expression more than order of magnitude at 20 µg/mL. Similar dose-response in DG 75 cell line (increase only 4 fold). NQO1 ARE was increased 5 fold by 20 µg/mL DEPX. NAC inhibited NQO1 gene expression. p38 MAPK and P13K inhibition partially blocked NQO1 mRNA and ARE induction by DEPX. Induction of phase II enzymes: DEPX induced IgE potentiattion was reduced dosedpeendently by induced phase II enzymes.

Study	Pollutant	Exposure	Particle Effects
Reference: Yanagisawa et al. (2006) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 5 weeks **Weight:** 25-28 g	Washed DEP (carbonaceous core), DEP-OC(extracted organic chemicals) and Whole DEP Particles collected from: 4JB1-Type, four-cylinder, 2.74 L, Isuzu diesel engine, while operated on standard diesel fuel at 200g under a load of 10 torques. DEP were extracted in benzene-ethanol. The residue particles of DEP were prepared as washed DEP. THe extracted were evaporated and dissolved in DMXO and prepared as DEP-OC.	**Route:** Intratracheally Administered **Dose/Concentration:** DEP exposure was multiple 50μg/0.1L intratracheal inoculations. Inoculations were once a week for 6 weeks. **Particle Size (Distribution):** Median aerodynamic diameter = 0.4um **Time to Analysis:** Mice divided into eight groups: 1. Control (PBS 0.1mL) 2. DEP-OC (50 μg) dissolved in PBS (0.1mL) 3. Washed DEP (50ug) dissolved in PBS (0.1mL) 4. Whole DEP (50ug DEP-OC + 50ug Washed DEP) dissolved in PBS (0.1mL) 5. OVA (1ug) dissolved in PBS (0.1mL) 6. DEP-OC(1ug) + OVA (1ug) dissolved in PBS (0.1mL) 7. Washed DEP (50ug) + OVA (1ug) dissolved in PBS (0.1mL) 8. Whole DEP (50ug DEP-OC + 50ug Washed DEP) + OVA (1ug) dissolved in PBS (0.1mL) All groups received OVA or PBS every 2 weeks for 6 weeks and the PM component or PBS once a week for 6 weeks.	BAL Analysis: 1. PMNs: DEP-OC + OVA caused a significant increase (20.43 ± 10.9 X 104 PMN) in PMN infiltration in the BAL compared to the control (0.56±0.25 X 104 PMN). Exposure to Whole DEP+ OVA had a greater effect and caused PMN count to rise to 43.58±11.3 X 104 PMN. 2. Macrophages: OVA alone (54.3± 6.6 X 104 MACs), DEP-OC +OVA (65.0± 7.8 X 104 MACs), Washed DEP + OVA (57.9± 3.4 X 104 MACs) and Whole DEP + OVA(69.1± 10 X 104 MACs) all caused a significant increase in macrophages compared to the control (35.2± 6.6 X 104 MACs). 3. Mononuclear Cells: The number of mononuclear cells was not significantly different among the experimental groups. Lung Histology: Exposure to OVA, Washed DEP, DEP-OC and Whole DEP caused a slight increase in PMNs, mononuclear cells and goblet cell proliferation. Treatment with all three DEP groups + OVA had even more of an effect on mononuclear cells, PMNs and goblet cell proliferation. Whole DEP + OVA had the greatest impact. Th1 and Th2 Cytokine Expression: 1. IFN-γ: Washed DEP+OVA caused a significant increase (696± 74 pg/lung) in IFN-γ compared to control (561± 37 pg/lung), whereas Whole DEP+OVA caused a significant decrease (455±75 pg/lung) compared to control. 2. IL-2: No significant differences among groups. 3. IL-4: No significant differences among groups. 4. IL-5: DEP-OC+ OVA (75.3± 18) and Whole DEP+ OVA (184.2±23.1) caused significant increases in IL-5 compared to control (12.3± 0.3) and compared to OVA (33.5±13). 5. IL-13: Whole DEP+OVA caused significant increase (165.03±36.3) in IL-13 compared to control (1.29±1.29). Eotaxin and MIP-1α Expression: OVA increased eotaxin levels and DEP-OC+OVA caused a more significant increase in eotaxin. Whereas Whole DEP alone caused a significant increase in MIP-1α and Whole DEP+OVA caused an even greater increase in MIP-1α. IgG1 Levels: Exposure to DEP-OC+OVA caused an increase in IgG1 and exposure to Whole DEP+OVA caused greater elevation in IgG1 levels.

Study	Pollutant	Exposure	Particle Effects
Reference: Yang, HR.M. et al. 2003 **Species:** Mouse **Gender:** Female **Strain:** B6C3F1 **Age:** 6-8 weeks	DEP- SRM 1650 DEP- SRM 1650	**Route:** Intratracheal Aspiration **Dose/Concentration:** 1, 5, or 15 mg DEP/kg body weight **Particle Size (Distribution):** **Time to Analysis:** Mice were exposed to 1, 5, or 15 mg DEP/kg of body weight for: 1. 3 times in a period of two weeks (ex. Monday, Friday week 1 and Wed- week2) or 2. 6 times in a period of four weeks In sterile saline volume of 25uL/10g body weight.	Toxicity of DEP Exposure: DEP did not have a significant effect on body, liver or spleen weight in exposed mice. Mice exposed to the highest dose for 2 weeks have an increase in lung weight and in lung weight relative to body weight, a similar results occurred in the mice exposed for 4 weeks. None of the hematological parameters were significantly different in the 2 week exposed mice, in the 4 week exposed mice there was a significant decrease in platelet counts in mice exposed to 15mg/kg. DEP Exposure on Spleen IgM AFC: DEP exposure for 2-weeks induced a dose-dependent decrease in spleen AFC in response to sRBC immunization. 1 mg/kg resulted in a 33% decrease, 5 μg/kg resulted in a 37% decrease and 15μg/kg resulted in a 42% decrease. Mice exposed to 15 μg/kg depicted a 35% reduction in total spleen activity. In the group exposed to DEP for 4 weeks, the decrease in AFC was no longer significantly different than the control. DEP Exposure on Spleen Cell Number/Lymphocyte Counts: Exposure for 2 or 4 weeks did not effect total number of nucleated splenocytes. DEP did have a 30% reduction in total T cells. The number of B cells was not significantly affected. DEP Exposure on Spleen T-Cell Function: (evaluated in 2 week exposure group only) DEP induced a dose-dependent decrease in spleen cell proliferation to ConA. 1 mg/kg DEP decreased response by 8%, 5μg/kg decreased by 25% and 15mg/kg decreased response by 34%. DEP did not affect spleen cell proliferation in response to anti-CD3 mAb. Production of IL-2 in response to ConA was also reduced in a dose-dependent manner by DEP exposure. IFN-γ production was also decreased by exposure to DEP. IL-4 production was not measured.
Reference: Yin et al. 2005 **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) (Charles River Laboratories, Wilmington, MA) **Age:** NR **Weight:** 200-250 g	DEP = SRM 2975 (NIST) Listeria (Difco Laboratories, Detroit, MI)	**Route:** Nose-only inhalation (DEP), lintratracheal instillation (Listeria) **Dose/Concentration:** 100,000 CFU bacteria per 500 μL sterile saline (Listeria) 21.2 + 2.3 mg/m^3 (DEP) **Particle Size (Distribution):** DEP = SRM 2975 **Time to Analysis:** DEP exposure for 4 h/day for 5 days; infection with Listeria 7 days postexposure; sacrifice 3 and 7 days postinfection	Estimated mean lung deposit of DEP = 406 + 29 μg/rat DEP prolonged growth of bacteria in lung IL-1B, TNF-a, IL-12, IL-10: DEP significantly increased these pulmonary responses to bacteria CD4/CD8: DEP significantly increased the presence of T-lymphocytes and subsets in lung draining lymph nodes Listeria-induced production of IL-1B, TNF-a, IL-2, IL-10, IFN-gamma: DEP significantly reduced these levels
Reference: Yin et al. 2004 **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) (Charles River Laboratories, Wilmington, MA) **Age:** NR **Weight:** 200-250 g	DEP = SRM 2975 (NIST) Listeria (Difco Laboratories, Detroit, MI)	**Route:** inhalation exposure (DEP) intratracheal instillation (Listeria) **Dose/Concentration:** 20.62 + 1.31 mg/m^3 (DEP). 100,000 CFU Listeria in 500uL saline **Particle Size (Distribution):** DEP = SRM 2975 **Time to Analysis:** DEP exposure for 4 h/day for 5 days; inoculation with bacteria 2hr postexposure; sacrifice 3, 7, 10 days postinfection	Estimated mean lung deposit of DEP = 389 + 25 μg/rat Innate and T-cell mediated responses: DEP represses these responses to Listeria IL-1B, TNF-a, IL-12, IL-2 (day 7), IFN-gamma (days 3-10): DEP inhibited production but enhanced IL-10 (day 3 and 7) production. CD4/CD8: DEP suppressed development of bacteria-specific lymphocytes

Study	Pollutant	Exposure	Particle Effects
Reference: Yin et al. 2007 **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) (Charles River Laboratories, Wilmington, MA) **Age:** NR **Weight:** 225-250 g	DEP = SRM 2975 (NIST) eDEP = organic extract (DCM)of DEPs wDEP = washed DEP (DEP purchased from National Institute of Standards and Technology, Gaithersburg, MD) CB = carbon black (Cabot Co, Boston, MA)	**Route:** intratracheal instillation of Listeria. treatment after AM cell isolation **Dose/Concentration:** 10, 50, 100 μg/mL (DEP/CB) 100,000 cells/500uL saline (Listeria) **Particle Size (Distribution):** SRM 2975 (DEP) 0-1-0.6 μm (CB) **Time to Analysis:** Treatment/no treatment with bacteria; sacrifice and isolation of AM; DEP or CB treatments for 1, 4, 16, 24 h	Phagocytosis and killing of bacteria: DEP or eDEP significantly decreased these levels in uninfected rats' TNF-a, IL-1B, IL-12 (AM), IL-2, interferon-gamma (lymphocytes): DEP or eDEP dependently suppressed bacteria-induced secretion of these levels, but augmented secretion of IL-12
Reference: Yin et al. 2004 **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) (Charles River Laboratories, Wilmington, MA) **Age:** NR **Weight:** 225-250 g	DEP = SRM2975 (NIST) eDEP = organic extract (DCM)of DEPs wDEP = washed DEP (DEP purchased from National Institute of Standards and Technology, Gaithersburg, MD) CB = carbon black (Cabot Co, Boston, MA)	**Route:** intratracheal instillation of Listeria. treatment after AM cell isolation **Dose/Concentration:** 50μg/mL (DEP) 100,000 cells/500uL saline (Listeria) **Particle Size (Distribution):** DEP = SRM 2975 0.1-0.6 μm (CB) **Time to Analysis:** treatment/no treatment with bacteria; sacrifice 7 days postinfection; isolation of AM; DEP treatments for up to 24 h at 37 degrees	Intracellular ROS and HO-1 expression: DEP or eDEP significantly increased expression of these levels in AM LPS-stimulated secretion of TNF-a and IL-12: eDEP significantly inhibited these levels but augmented production of IL-10 by AM
Reference: Yin et al. 2003 **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) (Harlan Laboratories, Indianapolis, IN **Age:** NR **Weight:** 200-250 g	DEP = SRM 1650a Listeria	**Route:** nose-only inhalation (DEP). intratracheal instillation (Listeria) **Dose/Concentration:** 100,000 bacteria per 500uL sterile saline (Listeria) 50 or 100 mg/m^3 (DEP) **Particle Size (Distribution):** SRM 1650a **Time to Analysis:** DEP exposure for 4 h and inoculated with bacteria. Sacrifice 3 and 7 days postexposure	CD4 and CD8: Listeria-infected rats showed significantly increased cell counts and increased production of IFN-gamma and IL-2 receptor at 7 days postinfection Pulmonary bacterial count: 100mg/m^3 DEP and Listeria produced a 10-fold increase at 3 days postinfection compared to Listeria-olnly exposure
Reference: Zelikoff et al. (2003) **Species:** Rat **Gender:** Male **Strain:** Fischer 344 (Harlan Sprague Dawley, Indianapolis, IN) **Age:** 7-8 months **Weight:** NR	CAPS = concentrated ambient $PM_{2.5}$ from New York City *S.pneumoniae*	**Route:** nose only inhalation (CAPS) intratracheal instillation (*S.pneumoniae*) **Dose/Concentration:** (*S.pneumoniae* 2-4 x 10^7) 345 μg/m^3 (CAPS) **Particle Size (Distribution):** MMAD = 0.4um **Time to Analysis:** Study 1: uninfected rats exposed to air or CAPS for 3 h; sacrifice 3, 24, or 72-h postecposure or IT instilled 4, 24, 72, 120 h postexposure with S.pneumoniae and sacrificed 4, 24, 72-h postinfection Study 2: infection with bacteria and exposed 48 h later to CAPS or filtered air for 5 h. Sacrifice 9, 18, 24, 72, 120 h postexposure	Bacterial burdens/immune response: CAPS significantly increased bacterial burden and decreased percentages of lavageable neutrophils and proinflammatory cytokine levels in previously infected rats
Reference: Zelikoff et al. (2002) **Species:** Rat **Gender:** Male **Strain:** Fischer 344 (Harlan Sprague Dawley, Indianapolis, IN) **Age:** 7-9 months **Weight:** NR	Ambient NYC PM = NYC PM25 Chloride salts of Fe, Mn, Ni *S.pneumoniae*	**Route:** nose only inhalation (chloride salts) intratracheal instillation (*S.pneumoniae*) **Dose/Concentration:** 15-20 x 10^6 (*S.pneumoniae*) 65-90μg/m^3 (chloride salts/NYC PM25) **Particle Size (Distribution):** MMAD = 0.4um **Time to Analysis:** infection/no infection followed by 5 h exposure to ambient NYC PM25 or single transition metal. Sacrifice 4, 5, 9, 18, 24, and 120 h after exposure	Innate and adaptive immunity (B- and T-lymphocytes, splenic lymphocytes): Fe significantly decreased these levels in uninfected rats Bacterial clearance: Fe and Ni significantly reduced clearance in infected previously rats

Study	Pollutant	Exposure	Particle Effects
Reference: Zhou et al. 2006 **Species:** Mouse **Gender:** Male **Strain:** BALB/c (Charles River Laboratories, Wilmington, MA) **Age:** 6-8 weeks **Weight:** NR **Cell Line:** J774A.1 (American Tyoe Culture Collection, Manassas, VA)	Urban air particles (UAP) (Washington, DC) Titanium Oxide (TiO_2) (Baker Chemicals, Phillipsburg, NJ) Carbon Black (CB) (Sigma, St. Louis, MO) COLLECTIVELY KNOWN AS CAPS	**Route:** Cell culture, 1 x 10^6 cells/mL in a 6-well plate **Dose/Concentration:** 100 μg/mL **Particle Size (Distribution):** UAP = SRM 1649 TiO_2/CB = 0.1-2.5 μmol **Time to Analysis:** Sacrifice and AM isolation 3 h after IFN-gamma pretreatment J774A.1: particle exposure for 1-h at 37 degrees, exposure to S.pneumoniae for 1-h at 37 degrees	Binding of bacteria: CAPS significantly increased binding of bacteria by AMs and J774A.1. Internalization: CAPS decreased internalization and absolute number of bacteria killed by macrophages
Reference: Stevens et al. (2008) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 10-13 weeks **Weight:** 17-20 g	DE was generated using a 30 kW 4-cylinder Deutz BF4M1008 diesel engine connected to a 22.3 kW Saylor Bell air compressor. The engine was operated on diesel fuel purchased from a service station in Research Triangle Park, NC. The engine was operated at a steady-state, approx. 20% of engine's full load.	**Route:** Whole-body Inhalation Chambers (flow rate = 142 L/min) **Dose/Concentration:** 1. High = 2000μg/m^3 2. Low = 500μg/m^3 **Particle Size (Distribution):** NR **Time to Analysis:** Mice received either 500 or 2000 μg/m^3 DE for 4 h per day for 5 consecutive days (days 0-4). On day 0-2 100 μg OVA intranasal 40 min after DE Mice were challenged on days 18 and 28. On day 18 mice received 100ug OVA in 20 μL saline or 20 μL saline alone. On day 28 Mice received 100 μg OVA in 20 μL saline. Mice were killed on either day 4 (4 h after the final exposure) or 18, 48 or 96 hours after the day 28 OVA challenge.	Composition Analysis of DE: Concentrations in the high dose (200μg/m^3) chamber: 4.3ppm CO, 9.2 ppm NO, 1.1ppm NO_2 and 0.2ppm SO_2. Concentrations in the low dose (500 μg/m^3)chamber were below limit of detection. IgE Antibody Production: In the absence OVA, IgE antibodies were not detected. 18, 48 and 96 hours following OVA, mice exposed to low and high doses of DE had an increase in antibodies over time. Mice exposed to high dose had an increase (non-significant) to the OVA exposed control at the 48 h time mark. Both the low and high dose showed an increase in IgE response when compared to the OVA control (not significant increase though). BAL Cell Counts: Cell counts at 18 and 96 hours after OVA treatment did not differ among treatment groups. At 48 hours the number of eosinophils, neutrophils and lymphocytes were significantly increased in mice exposed to both high and low concentrations of DE. BAL Cytokine Production: IL-6: IL-6 production appeared to show a dose-dependent and time-dependent increase. But IL-6 production was significantly increased in mice exposed to the high dose at the 96 hour mark. IL-10: IL-10 production did not reflect a pattern. The greatest increase in IL-10 was exposure to the low-dose DE at 18 hours after OVA stimulation and with the high dose at 96 hours after.

Table D-5. Effects of the central nervous system.

Reference	Species, Strain, Gender, Age, Body Weight	PM and Particle Size	Exposure Technique and Exposure Concentration or Dose	Exposure Duration	Results
Campbell et al. (2005)	Mice, BALB/c, male, 7 weeks, Sensitized to OVA	CAPs from Los Angeles, lacking reactive organic and H_2O soluble gases, O_3, NO_X, SO_X F+UF = <2.5 μm UF = <0.18 μm	Whole body exposure 20-fold concentration of near highway ambient air, avg UF conc. = 282.5 μg/m^3, avg F conc. = 441.7 μg/m^3	4 h/day, 5 days/week for 2 weeks	Mice were challenged with OVA prior to exposure and 1 and 2 weeks following exposure, and then brains were assayed. F+UF and UF exposure increased NFκB DNA binding in brain. TNFα: increased with F+UF IL-1α: increased with UF and F+UF Suggests possible link between PM exposure and neurodegenerative disease processes.

Reference	Species, Strain, Gender, Age, Body Weight	PM and Particle Size	Exposure Technique and Exposure Concentration or Dose	Exposure Duration	Results
Che et al. (2007)	Rat, Sprague-Dawley, male and female, 9 weeks, 190-220 g	Gasoline exhaust Not provided	Intratracheal instillation 5.6, 16.7, or 50.0 L/kg, final volume 0.3 mL/rat	Once per week for 4 weeks	Dose-dependent increase in brain DNA damage starting at 5.6 L/kg. Increase in lipid peroxidation and carbonyl protein at 50 L/kg. Decrease in brain SOD at all exposures. GPx activity was unchanged with exposure. Suggests association between gasoline exhaust and oxidative damage to brain.
Liu et al. (2005)	Rat, Wistar, male, 8 weeks	CAPs from Taiyuan, China <2.5 µm	Intratracheal instillation 0, 1.5, 7.5, or 37.5 mg/kg, final volume 0.2 mL/rat	Assayed 24-h following instillation	In brain, SOD and CAT activity was significantly decreased at 2 highest doses; GSH levels were significant decreased at highest dose. Suggests association between PM exposure and oxidative damage mediated by prooxidant/antioxidant imbalance or high levels of free radicals
Veronesi et al. (2001)	Mouse, ApoE$^{-/-}$ or C57Bl/6, young adults	CAPs from Tuxedo, NY <2.5 µm	Whole-body exposure Varied daily, $PM_{2.5}$ concentrated 10-fold, producing an average of 113 µg/m^3.	6 h/day, 5 day/week for 4 months	CAPs-exposed ApoE$^{-/-}$ mice had a 29% reduction in TH-stained neurons and a 8% increase in GFAP staining compared to air-exposed ApoE$^{-/-}$. No differences see in C57 mice. Suggests that ApoE$^{-/-}$ mice, characterized by increased brain oxidative stress, are susceptible to PM-induced neurodegeneration.
Sirivelu et al. (2006)	Rat, Brown Norway, male, 12-13 weeks, with or without OVA sensitization and challenge	CAPs from Grand Rapids, MI <2.5 µm	Whole body exposure 500 µg/m^3	8h, assayed at 24-h PE	PVN: CAPs alone or with OVA increased NE MPA: CAPs increased D_a when treated with OVA, no changes in NE, 5-HIAA and DOPAC Arcuate nucleus: OVA sensitization increased NE levels OB: CAPs and OVA increased NE levels, but no changes in D_a, DOPAC, or 5-HIAA Other areas: no differences in other areas of hypothalamus, substantia nigra, or cortex CAPs alone or with OVA increased serum corticosterone Suggests CAPs can cause region-specific modulation of neurotransmitters in brain and that the stress axis may be activated causing aggravation of allergic airway disease.
Calderón-Garcidueñas et al. (2003)	Mongrel dogs, 15 male and 25 female, 7 days to 10 years, Controls from Tlaxcala, Exposed from Southwest Metropolitan Mexico City (MC)	Mexico City ambient exposures; Ni and V present Not provided	Ambient MC: PM_{10} – 78 µg/m^3; $PM_{2.5}$ – 21.6 µg/m^3; O_3 - 4 ± 1 h/day over 0.08 ppm. Control**:** "below current U.S. standard"	Continuous lifetime exposure in MC or Tlaxcala	MC dogs: deposition gradient of Ni and V in olfactory epithelium>OB>frontal cortex; A/P sites increased in OB and hippocampus; histological changes in sensory olfactory and sustentacular cells and neuroepithelium; increased immunostaining of NFκB, iNOS, COX2 (glial and endothelial), GFAP, ApoE, APP, β-amyloid plaques, and vascular β-amyloid. Suggests air pollution exposure increases brain DNA damage, brain deposition of metals, inflammatory and stress protein responses, and acceleration of Alzheimer's type pathology. Caveat – exposure conditions and diets not standardized; dog were mixed breeds; ages variable.
Zanchi, et al. (2008)	Rat, Wistar; male, 45 days	ROFA from Universidade de São Paulo, Brazil Mean aerodynamic diameter = 1.2 ± 2.24 µm	Intranasal instillation 20 µg	30 days	Exposed rats had increased lipid peroxidation in striatum and cerebellum. This could be reversed with N-acetylcysteine treatment. ROFA treatment altered motor activity shown by decreased general exploration and peripheral walking, not prevented by NAC. Suggests chronic ROFA induces behavioral changes and brain oxidative stress.

Table D-6. Reproductive and developmental effects.

Reference	Species, Strain, Gender, Age, Body Weight	Particle or Constituent and Particle Characteristics Size (µm)	Exposure Technique and Mass Conc	Exposure Duration	Reproductive Toxicological Outcomes
Yoshida et al. (2006b)	ICR, C57Bl/6J or DDY pregnant mice	DE	inhalation 0.1 mg DEP/m^3	GD 2-13 dams saced GD14 and male pups Collected	Strain-dep. Most sens ICR, C57Bl/6J, ddY Male gonadal RNAs-decreased MIS (ICR, C57Bl/6J) Ad4BP/SF-1 (ICR).
Watanbe 2005	F344/DuCrj rats Pregnant dams	DE	0.17 or 1.71 mg DEP/m^3 or filtered air PM filtration only GD7- parturition 6h/day		Adult male offspring decreased DSP & sertioli cell # at PND 96. Filtered & DE air produced similar outcomes. Conclude effects Not PM dependent.
Yoshida et al. (2006b)	ICR female mice Pregnant dams Effects in male offspring	DE	0.3, 1.0 or 3.0 mg DEP/m^3	2dpc to 16dpc continuous	NOAEL 0.3 mg DEP/m^3 DE exposure induced increased repro gland weight (two higher doses) male mice. mRNA decreases aromatase & 3 µ-hD (3.0 mg DEP/m^3)
Ueng et al. (2004)	BALB/c Female Mice 21 days old. MCF-7 Cell line.	ME	intraperiotenially 1 or 10 mg MEP/kg	3 days 24 h/day ± E2 ± PAH	10 mg/kg +E2 induced anti-estrogenic Uterine effects & Antiestrogenic With in vitro (MCF-7 cells) E2 screen.
Ono et al. (2007)	ICR male mice 6 weeks old	DE	0.3, 1.0 or 3.0 mg DEP/m^3	12 h/day 6 months or 6 mo+ 1 mo recovery	Dose-dep increase seminif. Tubule degeneration & decreased DSP. 1 mo recovery, DSP recovered at lowest dose.
Huang et al. (2008)	Adult male Wistar rats 8 weeks old	Motorcycle Exhaust (ME)	1: 10 ME 1: 50 ME	2 or 4 weeks 5 days/wk 2h/day ± 1 wk recovery (clean air)	Decreased body wt after exposure. Decreased testicular spermatid #. 1: 10 ME exposure for 4 weeks (no recovery) decreased testicular wt, increased inflammatory cytokine mRNA. Glutathione system Not affected. LipidPeroxidation unaffected.
Mori 2007	Male Mice Adults 6 week old C57/BL mice	ME	Subcutaneous injection		cDNA library screen after Sub-cut. Injection Found identified activated Clones related to Prostanoids & Arachadonic Acid (Platg2c2c, Acsl6) & sperm Production (Stk35). Route of exposure. Unconventional.
Yoshida et al. (2006a)	ICR mice Pregnant dams PND 28 Male offspring	DEP	0.3, 1.0 or 3.0 mg DEP/m^3	2dpc to 6dpc	Sex ratio no change. 2 higher doses induced sig increased repro organ wt. Male pup wt Increased at PND 28. 1.0mg DEP/m^3 pup increased serum T. Serum T positively correlated with DSP, testis wt, steroid enzyme mRNA.
Lichtenfels et al. (2007)	Male Swiss Mice PND 10 mice After exposure Bred to non-expoxed Females. Females Saced at GD19 and Pups collected. Exposed males Saced after breeding.	ambient air	inhalation	4 months 24-h/day 7 days/wk	Decreased testicular & Epididymal sperm counts, decreased # germ cells, decreased elongated Spermatids. Decreased SSR, Sex ratio shift (fewer Males).
Fujimoto et al. (2005)	Slc: ICR mice Pregnant dams Placental hanges Offspring collected 14dpc	DE or clean air	inhalation 0.3, 1.0 or 3.0 mg DEP/m^3	2dpc to 13dpc	Significant increase in absorbed placentas (0.3, 3.0). Decrease in absorbed placentas (1.0). Increased Inflammatory cytokine mRNA in placentas from exposed offspring. Increased # of Absorbed placentas In DE-exposed Offspring.

Reference	Species, Strain, Gender, Age, Body Weight	Particle or Constituent and Particle Characteristics Size (µm)	Exposure Technique and Mass Conc	Exposure Duration	Reproductive Toxicological Outcomes
Silva et al. (2008)	Swiss Mice Pregnant dams Windows of Exposure 1st, 2nd or 3rd week of preg Fetuses collected GD 19 (near term)	Ambient air Sao Paulo		1st week 2nd week 3rd week or combo of exposure during preg.	Decreased fetal wt with exposure in 1st week of preg. Decreased placental Wt with exposure in any of 3 weeks.
Sugamata et al. (2006)	ICR female mice Pregnant dams Pup brain cerebullar Tissue collected 11 week old pups	DE	inhalation 0.3 mg DEP/m^3	2dpc to 13dpc	Exposed pups increased caspase 3 positive cells & decreased purkinjie cell # (cerebellum). Similar to human Autism brain phenotype.
Hougard 2008	C57Bl/6 females Pregnant dams Effects in pups Body wt Behavioral	DEP reference Material (PM only)	inhalation	GD7 to 19	Body wt of exposed Unchanged at birth. Body wt decreased At weaning. T4 Unchanged dams & Pups @ weaning. At 2 months, exposed Female pups required Less time to locate Platform in spatial Reversal task of Morris Water maze.
Tozuka et al. (2004)	Fischer 344 rats Pregnant dams Milk, pup, dam Air PAHS	DE	inhalation 1.73 mg/m^3	GD 7 to 20 6h/day	Gest & lactational Exposure to DE's And PAHs. 7 milk PAHs increased in DE exposed dams. DE exposure Can lead to PAH Pup exposure through Breast milk.
Somers et al. (2002)	Swiss Webster Mice Male and Females 6-8 weeks old Mice bred to unaffected partners. ESTR germ Line mutations Followed.	Ambient air at 2 sites Canada (rural & urban)	inhalation	10 weeks exposure+ 6 weeks clean air Allows for sperm maturation so exposed sperm used in fertilization.	Heritable mutation rate increased 1.5 to 2 fold in urban vs. rural site. Increased freq is paternal line dependent.
Yauk 2007	C57BlxCBA F1 Hybrid mice Mature male mice Germ line Mutations	Ambient air or Hepa-Filtered air (PM removed) @ 2 sites (rural and urban) TSP 9.4+17 µg/m^3	inhalation	3, 10, or 10+6 wk recovery clean air	10+6 weeks exposure induced increased ESTR mutations in sperm DNA of exposed v filtered. No testicular DNA adducts seen in exposed males. @ 3wks DNA increased adducts seen in lungs of exposed males, not in filtered males. Mutations PM dependent Gas phase independent.
Tsukue et al. (2004)	Slc: ICR mice Pregnant dams Female fetuses GD14	DE	inhalation 0.1 mg DEP/m^3	GD 2-13 8h/day	SF-1 & MIS mRNA no change. Other steroidogenic Genes unchanged. BMP-15, oocyte Differentiation mRNA decreased.
Mohallem et al. (2005)	BALB/c female Mice PND10 Newborn or Adult 10wk old Exposures Then bred.	Ambient air or filtered air (PM & chemicals removed)	inhalation	24 h/7days/wk	No effects in adult exposed animals. Increased implantation Failure of neonatal Exposed-dams. Sex ratio, # of Pregnancies, Resorbtions, Fetal deaths, And fetal placenta Weights unchanged After neonatal Ambient air exposure.

Reference	Species, Strain, Gender, Age, Body Weight	Particle or Constituent and Particle Characteristics Size (µm)	Exposure Technique and Mass Conc	Exposure Duration	Reproductive Toxicological Outcomes
Tsukue et al. (2002)	Female mice 6 weeks old @ 4 months age collected or females bred & offspring collected as adults. C57/BL mice	DE or filtered air	inhalation 0.3, 1.0 or 3.0 mg DEP/m^3	4 months ± breeding	DE-exposed females had Decreased uterine wt at 4 months. Offspring decreased Body weight @ 6 & 8 weeks of age. Decreased rate Of good nest Construction (3 mg/m^3). AGD decreased In males (30 & 70 days old). Organ weight Decreased in Females. Female Crown to rump Length decreased. Relative weights Not taken.
Ono et al. (2007)	ICR mice Pregnant dams	DE	inhalation mg DEP/m^3 Or filtered air	2dpc-16dpc pups collected At 8, 16, 21, 35, & 84 days of age	PND 8 and 16 male repro accessory gl weight decreased. PND 21decreased serum T; PND 84 increased serum T. FSHr, sTAR mRNA Decreased PND 35 & 84. Rel. testis and epididymal wt unchanged. Sertoli cell degeneration

Carcinogenisis, Mutagenesis, Genotoxicity

Table D-7. Mutagenic / genotoxic effects.

Reference	Species, Gender, Strain, Age	Particle or Constituent	Concentration Dose (µg/mL)	Test Response	Exposure Duration	Endpoint
BACTERIAL MUTATION						
De Kok et al. (2005)	*Salmonella* TA98	Ambient PM_{10} and $PM_{2.5}$ [DCM extract] six urban locations (Maastricht, The Netherlands)	2.5, 9, or 18 m^3 air per 100 µL DMSO	+	1 h	Reverse mutation
Erdinger et al. (2005)	*Salmonella* TA98. TA100, and TA98NR	Ambient PM [organic extract] eight urban areas (Germany)	0.25, 2.5, 5, 12.5, and 25 m^3/plate	+	NG	
Sharma et al. (2007)	*Salmonella* TA98, YG1041 YG5161	Ambient PM	0.25 mg/mL	++ + (+)	24 h	Reverse mutation (microsuspension) polar and crude fractions moderately polar fractions non-polar fractions
Löfroth et al. (1986)	*Salmonella*	Wood stove PM [organic extract] (birch, pine, and spruce)	32-100 µg/m^3 PM 2.6-200 µg organics	(+) +	48 h	Reverse mutation
Houk et al. (1991)	*Salmonella*: TA98 TA100	Wood, diesel, and coal emissions	200 µg/plate Wood smoke, 500 µg/plate DE and 200 µg/plate coal	(+) + +	72-h	Reverse mutation

Reference	Species, Gender, Strain, Age	Particle or Constituent	Concentration Dose (µg/mL)	Test Response	Exposure Duration	Endpoint
Heussen et al. (1994)	*Salmonella*: TA98	Fireplace emission [methanol extract]	Not given	+	1 week	Reverse mutation
Putnam et al. (1999)	*Salmonella*: TA98 TA100	Wood smoke condensate (Sigma)	0, 125, 250, 500, 750 and 100 µg/plate	-	48 h	Reverse mutation
Kim Oanh et al. (2002)	*Salmonella*: TA98 TA100	Wood smoke PM and gas phase	Not given	+ +	48 h	Reverse mutation
Vinitketkumnuen et al. (2002)	*Salmonella*: TA100	Field burning PM $PM_{2.5}$ & PM_{10}	units µg/m^3 130 & 170 (winter) 15 & 37 (summer)	+ (+)	48 h	Reverse mutation
Munford and Lewtas (1982)	*Salmonella*: TA98 TA100 TA1538 TA1535 TA1537	Coal fly-ash FBC and CC plants	mean diameter 0.54 µm 1.05 µm	 + -	72-h	Reverse mutation
Granville et al. (2003)	*Salmonella*: TA98 TA100 TA104	Smoky coal Extracts (China)	≥10 µg/plate	+		Reverse mutation
Löfroth (1981)	*Salmonella*	DEP	Not given	+	48 h	Reverse mutation
Rannug et al. (1983)	*Salmonella*: TA98 TA100	DEP	Not given	++	48 h	Reverse mutation
Strandell et al. (1994)	*Salmonella*: TA98 TA98NR	DEP [organic fraction]	emission values 0.021 g/km and 0.23 g/km	+	48 h	Reverse mutation
Bunger (2000)	*Salmonella*: TA98 TA100	DEP Low sulfur DEP High sulfur DEP Rapeseed oil methyl ester (RME) [DCM extracts]	Not given	+ ++ +	48 h	Reverse mutation Cytotoxicity in fibroblast cells higher for RME DEP.
Seagrave et al. (2002)	*Salmonella*: TA98 TA100	DEP high emitter (HE) normal emitter (NE)	25-500 µg/plate	 + ++	Not given	Reverse mutation
Pohjola et al. (2003)	*Salmonella*: TA98	DEP	30-500 µg/pl (-S9) 10-1000 µg/pl (+S9)	+	Not given	Reverse mutation
DeMarini et al. (2004)	*Salmonella*: TA98 TA98NR, TA98/1,8-DNP6, YG1021, and YG1024) TA100	DEP and DEP (SRM 2975) [organic extracts]	0.5, 1.0, and 2.0 µg/plate	++ +	72 h	Reverse mutation
Liu, 2005	*Salmonella*: YG1024 YG1029	DEP [organic extract]	1.48, 4.44, 13.3, 40, 120, 360, or 1080 µg/plate	+	30-min. preinc., 48 h (YG1029) 66 h (YG1024)	Reverse mutation

Reference	Species, Gender, Strain, Age	Particle or Constituent	Concentration Dose (µg/mL)	Test Response	Exposure Duration	Endpoint
Bunger et al. (2006)	*Salmonella*: TA98 TA 100	DEP: low-sulfur rapeseed oil methyl ester (RME), and soybean oil methyl ester (SME)	Not given	+	48 h	Reverse mutation
Bunger et al. (2007)	*Salmonella*: TA98 TA 100	DEP: rapeseed oil (RSO) and RME), natural gas derived synthetic fuel (GTL), and diesel fuel (DF)	Not given	+	Not given	Reverse mutation Compared to DF, RSO significantly increased mutagenic effects of particle extracts.
Song et al. (2007)	*Salmonella*: TA98 TA100	DEP E0 - base diesel fuel E5 - 5% E10 - 10% E15 - 15% E20 - 20%	0.025, 0.05, or 0.1 mg/plate	+	Not given	Reverse mutation
Löfroth (1981)	*Salmonella*	GEP	Not given	+	48 h	Reverse mutation
Rannug et al. (1983)	*Salmonella*: TA98 TA100	GEP Gasoline + alcohol Liquified petroleum	Not given	+ + (+)	48 h	Reverse mutation
Strandell et al. (1994)	*Salmonella*: TA98 TA98NR	GEP [organic fraction]	emission values 0.021 g/km and 0.23 g/km	+	48 h	Reverse mutation
Seagrave et al. (2002)	*Salmonella*: TA98 TA100	GEP high emitter (HE) normal emitter (NE)	25-500 µg/plate	++ +	Not given	Reverse mutation
Pohjola et al. (2003)	*Salmonella*: TA98	GEP	30-500 µg/pl (-S9) 10-1000 µg/pl (+S9)	+	Not given	Reverse mutation
Liu, 2005	*Salmonella*: YG1024 YG1029	GEP [organic extract]	1.48, 4.44, 13.3, 40, 120, 360, or 1080 µg/plate	+	30-min. preinc., 48 h (YG1029) 66 h (YG1024)	Reverse mutation
Zhang (2007)	*Salmonella*: TA98 TA100	Gasoline engine exhaust or MEE	0.3125, 0.625, 1.25, 2.5, 5.0, 10, or 20 L/plate	+ (TA98) -	72 h	Reverse mutation
Seagrave et al. (2005b)	*Salmonella*: TA98 TA100	Compressed natural gas (CNG) PM	Not given	+	Not given	Reverse mutation

Table D-8. Mutagenicity and genotoxicity data summary: in vitro studies.

Reference	Species, gender, strain, age	Particle or constituent	Concentration Dose (µg/mL)	Test Response	Exposure Duration	Endpoint
DNA DAMAGE						
Oh and Chung (2006)	Human lung epithelial A549 cells	DEP extract and extract fractions	100	+	6 or 24-h (Comet)	DNA damage (Comet)
Landvik et al. (2007)	Mouse hepatoma Hepa1c1c7 cells	DEP (DEPE extracts in the paper)	10, 20, 30, 50, or 70	+	24 h	DNA fragmentation

Reference	Species, gender, strain, age	Particle or constituent	Concentration Dose (µg/mL)	Test Response	Exposure Duration	Endpoint
Song et al. (2007)	Rat fibrocytes L-929 cells	DEP: E0 - base diesel fuel E5 - 5% E10 - 10% E15 - 15% E20 - 20%	0.125, 0.25, 0.5, or 1.0 mg/mL	+	24 h	DNA Damage (Comet) (E0 and E20 caused most damage)
Liu, 2005	CHL V79 cells	DEP GEP [organic extract]	Not given	+ +	overnight preinc., 20 h	DNA damage (Comet)
Zhang (2007)	Human lung epithelial A549 cells	Gasoline engine exhaust or MEE	0.025, 0.05, 0.1, 0.2, or 0.4 L/mL	+ –	2-h	DNA damage (Comet)
GENE MUTATION						
Hannigan et al. (1997)	Human h1A1v2	Ambient PM Los Angeles, San Nicolas Island, Long Beach, Azusa, and Rubidoux, CA	120 µg EOC per 12 mL 300 - 1200 µg (composite PM)	+	72h	Mutation
Jacobsen et al. (2008)	Mouse, FE1-Muta™ lung epithelial cellls	DEP	35 75	- +	72-h x 8	Mutation
SCE, MN, OR CA						
Hornberg et al. (1998)	Human BEAS-2B bronchioepithelial cells	Ambient PM: [DCM extract] $PM_{2.5}$ & 10 Urban, Industrial and Rural (Germany)	6.6-26.5 1.7- 6.9 10.8-43.2 5.8-23.1 7.8-34.1 3.7-14.4	+	72 h.	SCE
Hornberg and Seemayer (1996)	Syrian Hamster tracheal epithelial cells Rat tracheal epithelial cells	Ambient PM: [DCM extract] industrial and high traffic area (Germany)	Not given	.+	48 h.	SCE . LOEL - 0.11 m^3 air/mL medium LOEL - 0.16 m^3air/mL medium
Poma et al. (2006)	Mouse RAW 264.7 macrophages	Ambient $PM_{2.5}$ [extract] urban winter air	2.2, 6.6, and 22	+	44 h	MN
Roubicek et al. (2007)	Human lung adenocarcinoma A549 cells	Ambient PM [aqueous or organic extract]; urban (Mexico City)	1.25, 1.63, and 2.5 m^3/mL PM_{10} equivalents	+	24	MN
Liu, 2005	CHL V79 cells	DEP GEP [organic extract]	Not given	+ ++	overnight preinc., 20 h	MN
Oh and Chung (2006)	CHO-K1 (CBMN)	DEP extract and extract fractions	100 µg/mL	+	4 h (CBMN)	MN
Zhang (2007)	Human lung epithelial A549 cells	Gasoline engine exhaust MEE	0.025, 0.05, 0.1, or 0.2 L/mL	+ -	24-h	MN
OTHER						
Abou Chakra et al. (2007)	HeLa S3 cells	Ambient PM from [organic extract] Urban $PM_{2.5}$ and PM_{10} (France)	200 µL	+	24 h	Genotoxic

Reference	Species, gender, strain, age	Particle or constituent	Concentration Dose (µg/mL)	Test Response	Exposure Duration	Endpoint
Hamers (2000)	Hepatoma cells	Ambient PM [Acetone/DCM extraction] (Netherlands)	Not given	+	6 or 48 h	Genotoxic
Seemayer and Hornberg (1998)	Syrian Hamster kidney cells	Ambient PM [DCM extract] urban and industrial areas (Germany)	Not given	+	18 h followed by infection with SV-40.	Transformation (SV-40-Induced)
Alink (1998)	Human liver tumor cells (HEPA1c1c7)	Ambient PM (urban	6-12 µg	-	4 h	GJIC (aqueous extract positive; organic extract negative)
		DEP	17-37 µg	+		
		Rubber industries	36-47 µg	+		
		Metal industries	32-175 µg	-		
		Poultry/swine farm	81-137 µg	+		
		Compost	42 µg			

Table D-9. Mutagenicity and genotoxicity data summary: in vivo studies.

Reference	Species, gender, strain, age	Particle or constituent	Concentration Dose (µg/mL)	Test Response	Exposure Duration	Endpoint
DNA DAMAGE						
Yauk et al. (2008)	Mice, Male, C57BL/CBA Germ cells	Ambient PM near major highway and two steel mills (Hamilton, Ontario, Canada)	TSP 50-150 µg/m^3	+ + -	3 and 10wk 3, 10, & 10 wks, with 6-wk recov. 3, 10, & 10 wks, with 6-wk recov.	DNA strand breaks DNA methylation DNA adduct
GENE MUTATION						
Yauk et al. (2008)	Mice, Male, C57BL/CBA	Ambient PM near major highway and two steel mills (Hamilton, Ontario, Canada)	TSP 50-150 µg/m^3	+	10 wks, with 6-wk recov.	Mutation: ESTR *Ms6-hm* locus
Hashimoto et al. (2007)	Mice, *gpt* delta, 7-wk-old 9-wk-old	DEP inhalation DEP extract i.t. instillation	1 or 3 mg/m^3 0.125, 0.25, 0.5 mg DEP 0.05, 0.1, 0.2 mg extract	+ +	12 h/d x 7 d/wk 4, 12, or 24 wk; sac 3 days later 1x; sac 14 days later	Mutation
SCE, MN, OR CA						
Soares et al. (2003)	Mice, Male, BALB/c, 8–10 weeks old	Ambient PM_{10} downtown Sao Paulo, (urban) and countryside of Atibaia, (rural) Brazil;	Monthly mean 31 - 47 µg/m^3	++ +	120 days; blood taken after 15, 30, 60, 90, and 120 days	MN

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