APPENDIX A.

SUPPORTING TABLES FOR CHAPTER 5

Appendix A contains additional tables that support the work shown in Chapter 5.

Table A-1. Weight of evidence (WOE) for statistically significant gene expression changes after in utero exposure to dibutyl phthalate (DBP) from the whole rat testis microarray studies[a] as reported in Thompson et al. (2005)[b], Shultz et al. (2001)[b], Liu et al. (2005)[c,d], and Plummer et al. (2007)[e]

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Aacs	Acetoacetyl-CoA synthetase	GDs 12−19	Down	−0.37 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Aadat	Aminoadipate aminotransferase	GDs 12−19	Down	−0.38 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Abcg1	ATP-binding cassette, sub-family G (WHITE), member 1	GDs 12−19	Up	0.38 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Acaa1	Acetyl-Coenzyme A acyltransferase 1	GDs 12−19	Down	−0.37 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Acaca	Acetyl-Coenzyme A carboxylase alpha	GDs 12−19	Down at GD 19	≥ 2	2-fold	Shultz et al., 2001
Acadl	Acetyl-Coenzyme A dehydrogenase, long-chain	GDs 12−19	Down at GD 19	≥ 2	2-fold	Shultz et al., 2001
Acads	Acyl-Coenzyme A dehydrogenase, short chain	GDs 12.5−15.5	Up	1.50	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Acsl4	Acyl-CoA synthetase long-chain family member 4	GDs 12−19	Down	−0.60 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Adam15	A disintegrin and metallopeptidase domain 15 (metargidin)	GDs 12.5−17.5	Up	1.20	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Adamts1	A disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 1	GDs 12.5−19.5	Down	−1.35	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Admr	Adrenomedullin receptor	GDs 12−19	Down	−0.90 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Adra1b	Adrenergic receptor, alpha 1b	GDs 12−19	Down	−0.30 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Akt2	Thymoma viral proto-oncogene 2	GDs 12−21	Down at GD 21	≥ 2	2-fold	Shultz et al., 2001
Alas1	Aminolevulinic acid synthase 1	GDs 12−19	Down	−1.01 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Alas1	Aminolevulinic acid synthase 1	GDs 12.5−17.5	Down	−1.33	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Alas1	Aminolevulinic acid synthase 1	GDs 12.5−19.5	Down	−1.44	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Aldh1a3	Aldehyde dehydrogenase family 1, subfamily A3	GDs 12−19	Down	−0.43 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Aldh2	Aldehyde dehydrogenase 2	GDs 12−19	Down	−0.82 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Aldh2	Aldehyde dehydrogenase 2	GDs 12.5−17.5	Down	−1.50	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Aldh2	Aldehyde dehydrogenase 2	GDs 12.5−19.5	Down	−1.91	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Aldoa	Aldolase A, fructose-bisphosphate	GDs 12.5−19.5	Down	−1.24	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Aldoc	Aldolase C	GDs 12−19	Down	−0.44 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Anxa5	Annexin A5	GDs 12.5−19.5	Down	−1.20	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Aox1	Aldehyde oxidase 1	GDs 12−19	Down	−0.50 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Aqp1	Aquaporin 1	GDs 12.5−15.5	Down	−1.29	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Arf3	ADP-ribosylation factor 3	GDs 12.5−17.5	Down	−1.23	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Arrb2	Arrestin, beta 2	GDs 12−21	Down at GD 21	≥ 2	2-fold	Shultz et al., 2001
Asns	Asparagine synthetase	GDs 12−19	Down	−0.24 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ass	Argininosuccinate synthetase	GDs 12−19	Down	−0.82 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Atf2	Activating transcription factor 2	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Atf4	Activating transcription factor 4	GD 19 for 3 hr	Up after 3 hr	0.67	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Atp1b1	ATPase, $Na^{+/}K^{+}$ transporting, beta 1 polypeptide	GDs 12−19	Down	−0.24 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Atp4b	ATPase, H^{+}/K^{+} exchanging, beta polypeptide	GDs 12−19	Down	−0.60 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Atp5f1	ATP synthase, H^{+} transporting, mitochondrial F0 complex, subunit B1	GDs 12.5−15.5	Up	1.22	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Baiap2	Brain-specific angiogenesis inhibitor 1-associated protein 2	GDs 12−19	Down	−0.22 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Bhlhb2	Bhlhb2 basic helix-loop-helix domain containing, class B2	GD 19 for 3 hr	Up after 3 hr	0.88	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Bhmt	Betaine-homocysteine methyltransferase	GDs 12−19	Down	−0.24 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Birc5	Baculoviral IAP repeat-containing 5	GDs 12.5−15.5	Up	1.68	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Btg2	B-cell translocation gene 2, anti-proliferative	GD 19 for 1 hr	Up after1 hr	1.30	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Btg2	B-cell translocation gene 2, anti-proliferative	GD 19 for 3 hr	Up after 3 hr	1.88	$p < 0.05$ (ANOVA)	Thompson et al., 2005
C4a	Complement component 4a	GD 19 for 6 hr	Down after 6 hr	−0.77	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cadps	Ca^{2+}-dependent secretion activator	GDs 12−19	Up	0.31 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Calb2	Calbindin 2	GDs 12−19	Down	−0.77 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Cd63	CD63 antigen	GDs 12.5−19.5	Down	−1.36	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cdkn1c	Cyclin-dependent kinase inhibitor 1C (P57)	GDs 12−19	Down	−0.81 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Cdkn1c	Cyclin-dependent kinase inhibitor 1C (P57)	GD 19 for 6 hr	Down after 6 hr	−1.08	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cdkn1c	Cyclin-dependent kinase inhibitor 1C (P57)	GDs 18−19 for 18 hr	Down after 18 hr	1.63	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cebpb	CCAAT/enhancer binding protein (C/EBP), beta	GDs 12−19	Down	−0.6 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Cebpd	CCAAT/enhancer binding protein (C/EBP), delta	GD 19 for 3 hr	Up after 3 hr	1.62	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Clu	Clusterin	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Clu	Clusterin	GD 18 for 18 hr	Up after 18 hr	1.03	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cmklr1	Chemokine-like receptor 1	GDs 12.5−19.5	Down	−1.17	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cnr1	Cannabinoid receptor 1 (brain)	GD 19 for 3 hr	Up after 3 hr	0.99	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cnbp	Cellular nucleic acid binding protein	GDs 12.5−19.5	Down	−1.29	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cpa1	Carboxypeptidase A1	GDs 12.5−17.5	Down	−1.73	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cpa1	Carboxypeptidase A1	GDs 12.5−19.5	Down	−2.33	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cpd	Carboxypeptidase D	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Cpe	Carboxypeptidase E	GDs 12−19	Up	0.59 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Cpt1a	Carnitine palmitoyltransferase 1a, liver	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Cpt1a	Carnitine palmitoyltransferase 1a, liver	GDs 12−21	Down at GD 21	−≥ 2	2-fold	Shultz et al., 2001
Cpt1b	Cpt1b carnitine palmitoyltrans-ferase1b, muscle	GDs 12−19	Up	0.23 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Cpz	Carboxypeptidase Z	GDs 12−19	Up	0.21 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Crabp2	Cellular retinoic acid binding protein 2	GDs 12−19	Down	−0.31 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Crabp2	Cellular retinoic acid binding protein 2	GD 19 for 6 hr	Down after 6 hr	−1.24	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Crem	cAMP responsive element modulator	GD 19 for 3 hr	Up after 3 hr	0.58	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Crispld2	Cysteine-rich secretory protein LCCL domain containing 2	GDs 12−19	Down	−0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Cryab	Crystallin, alpha B	GDs 12−19	Up	0.22 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ctgf	Connective tissue growth factor	GD 19 for 3 hr	Up after 3 hr	2.10	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Ctgf	Connective tissue growth factor	GD 19 for 6 hr	Up after 6 hr	2.37	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Ctsb	Cathepsin B	GDs 12.5−15.5	Up	1.53	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Ctsd	Cathepsin D	GDs 12.5−19.5	Down	−1.22	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cxcl10	Chemokine (C-X-C motif) ligand 10	GD 19 for 3 hr	Up after 3 hr	2.07	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cyb5	Cytochrome b-5	GDs 12−19	Down	−0.30 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	GDs 12−19	Down	−1.07 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	GDs 12−19	Down at GD 19	−≥ 2	2-fold	Shultz et al., 2001
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	GD 18 for 18 hr	Down after 18 hr	−1.93	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	GDs 12.5−17.5	Down	−1.71	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	GDs 12.5−19.5	Down	−2.85	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cyp11b1	Cytochrome P450, subfamily 11B, polypeptide 1	GD 18 for 18 hr	Down after 18 hr	−1.63	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	GDs 12−19	Down	−1.76 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	GD 18 for 18 hr	Down after 18 hr	−2.1	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	GDs 12.5−17.5	Down	−2.15	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	GDs 12.5−19.5	Down	−3.08	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cyp51	Cytochrome P450, subfamily 51	GD 18 for 18 hr	Down after 18 hr	−1.06	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Cyp51	Cytochrome P450, subfamily 51	GDs 12.5−17.5	Down	−1.59	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Cyp51	Cytochrome P450, subfamily 51	GDs 12.5−19.5	Down	−1.81	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Dab2	Disabled homolog 2 (Drosophila)	GDs 12−19	Up	0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Daf1	Decay accelerating factor 1	GDs 12−19	Up	0.19 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Dbi	Diazepam binding inhibitor	GDs 12−19	Down	−0.38 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Dbi	Diazepam binding inhibitor	GDs 12.5−19.5	Down	−1.28	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Dcc	Deleted in colorectal carcinoma	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Ddc	Dopa decarboxylase	GDs 12−19	Down	−1.14 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ddc	Dopa decarboxylase	GD 18 for 18 hr	Down after 18 hr	−1.38	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Ddc	Dopa decarboxylase	GDs 12.5−19.5	Down	−1.44	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Ddit4	DNA-damage-inducible transcript 4	GDs 12−19	Down	−1.02 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ddit4	DNA-damage-inducible transcript 4	GD 18 for 18 hr	Down after 18 hr	−1.57	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Ddt	D-dopachrome tautomerase	GDs 12.5−19.5	Down	−1.22	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Decr1	2,4-dienoyl CoA reductase 1, mitochondrial	GDs 12−19	Down	−0.21 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Dhcr7	7-dehydrocholesterol reductase	GDs 12−19	Down	−0.73 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Dhcr7	7-dehydrocholesterol reductase	GD 19 for 6 hr	Down after 6 hr	−1.34	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Dhcr7	7-dehydrocholesterol reductase	GDs 18−19 for 18 hr	Down after 18 hr	−1.18	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Dnm3	Dynamin 3	GDs 12−19	Down	−0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Dusp1	Dual specificity phosphatase 1	GD 19 for 3 hr	Up after 3 hr	0.91	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Dusp6	Dual specificity phosphatase 6	GDs 12−19	Up	0.39 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Dusp6	Dual specificity phosphatase 6	GD 19 for 3 hr	Up after 3 hr	1.28	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Ebp	Phenylalkylamine Ca^{2+} antagonist (emopamil) binding protein	GDs 12−19	Down	−0.64 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Echs1	Enoyl Coenzyme A hydratase, short chain 1, mitochondrial	GDs 12−19	Down	−0.18 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Egr1	Early growth response 1	GDs 12−19	Up	0.77 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Egr2	Early growth response 2	GD 19 for 1 hr	Up after 1 hr	1.93	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Egr2	Early growth response 2	GD 19 for 3 hr	Up after 3 hr	1.53	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Elovl5	ELOVL family member 5, elongation of long chain fatty acids (yeast)	GDs 12−19	Down	−0.17 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Elovl6	ELOVL family member 6, elongation of long chain fatty acids (yeast)	GDs 12−19	Down	−0.40 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Emp3	Epithelial membrane protein 3	GDs 12.5−19.5	Down	−1.24	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Eno1	Enolase 1, alpha non-neuron	GDs 12.5−19.5	Down	−1.63	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Enpep	Glutamyl aminopeptidase	GDs 12−19	Up	0.48 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Entpd5	Ectonucleoside triphosphate diphosphohydrolase 5	GDs 12−19	Down	−0.52 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Epas1	Endothelial PAS domain protein 1	GDs 12−19	Down	−0.21 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ephx1	Epoxide hydrolase 1, microsomal	GDs 12−19	Down	−0.57 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Erbb2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian)	GDs 12.5−17.5	Up	1.26	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Etfdh	Electron-transferring-flavoprotein dehydrogenase	GDs 12−19	Down	−0.39 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ezr	Ezrin	GDs 12−19	Up	0.20 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ezr	Ezrin	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
F10	Coagulation factor X	GDs 12−19	Down	−0.51 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fabp3	Fatty acid binding protein 3	GDs 12−19	Down	−0.49 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fabp3	Fatty acid binding protein 3	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Fabp3	Fatty acid binding protein 3	GD 19 for 3 hr	Down after 3 hr	−0.78	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fabp3	Fatty acid binding protein 3	GD 19 for 6 hr	Down after 6 hr	−1.68	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fabp3	Fatty acid binding protein 3	GDs 18−19 for 18 hr	Down after 18 hr	−1.09	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fabp5	Fatty acid binding protein 5, epidermal	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Fabp6	Fatty acid binding protein 6, ileal (gastrotropin)	GDs 12−19	Down	−0.23 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fads1	Fatty acid desaturase 1	GDs 12−19	Down	−0.80 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fads1	Fatty acid desaturase 1	GDs 12.5−15.5	Up	1.42	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fads1	Fatty acid desaturase 1	GDs 12.5−19.5	Down	1.47	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fads2	Fatty acid desaturase 2	GDs 12−19	Down	−0.42 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fat1	FAT tumor suppressor homolog 1 (Drosophila)	GDs 12.5−15.5	Down	−1.32	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Fbp2	Fructose-1,6-bisphosphatase 2	GDs 12−19	Up	0.28 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fdft1	Farnesyl diphosphate farnesyl transferase 1	GDs 12−19	Down	−0.58 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fdft1	Farnesyl diphosphate farnesyl transferase 1	GDs 12.5−19.5	Down	−1.40	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fdps	Farensyl diphosphate synthase	GDs 12−19	Down	−0.73 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fdps	Farensyl diphosphate synthase	GDs 12.5−17.5	Down	−1.49	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fdps	Farensyl diphosphate synthase	GDs 12.5−19.5	Down	−1.41	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fdx1	Ferredoxin 1	GDs 12−19	Down	−1.65 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fdx1	Ferredoxin 1	GD 18 for 18 hr	Down after 18 hr	−2.53	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fdx1	Ferredoxin 1	GDs 12.5−17.5	Down	−2.06	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fdx1	Ferredoxin 1	GDs 12.5−19.5	Down	−2.97	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fdxr	Ferredoxin reductase	GDs 12−19	Down	−0.37 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fdxr	Ferredoxin reductase	GDs 12.5−17.5	Down	−1.41	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Fgfr4	Fibroblast growth factor receptor 4	GDs 12−19	Down	−0.19 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Folr1	Folate receptor 1 (adult)	GDs 12−19	Down	−0.48 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fos	FBJ murine osteosarcoma viral oncogene homolog	GD 19 for 1 hr	Up after 1 hr	3.28	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fos	FBJ murine osteosarcoma viral oncogene homolog	GD 19 for 3 hr	Up after 3 hr	2.70	$p < 0.05$ (ANOVA)	Thompson et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Frag1	FGF receptor activating protein 1	GDs 12−19	Down	−0.48 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Frag1	FGF receptor activating protein 1	GD 18 for 18 hr	Down after 18 hr	−0.65	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fthfd	Formyltetrahydro-folate dehydrogenase	GDs 12−19	Down	−1.03 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Fthfd	Formyltetrahydro-folate dehydrogenase	GD 19 for 6 hr	Down after 6 hr	−0.98	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fthfd	Formyltetrahydro-folate dehydrogenase	GDs 18−19 for 18 hr	Down after 18 hr	−0.83	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Fzd2	Frizzled homolog 2 (Drosophila)	GD 19 for 3 hr	Down after 3 hr	−0.7	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Gaa	Glucosidase, alpha, acid	GDs 12−19	Down	−0.30 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ggtl3	Gamma-glutamyltransferase-like 3	GDs 12−19	Down	−0.32 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Gja1	Gap junction membrane channel protein alpha 1	GDs 12−19	Down	−0.36 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Glrx1	Glutaredoxin 1 (thioltransferase)	GDs 12−19	Down	−0.20 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Gnrhr	Gonadotropin releasing hormone receptor	GD 19 for 3 hr	Up after 3 hr	1.38	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Gnrhr	Gonadotropin releasing hormone receptor	GD 19 for 6 hr	Up after 6 hr	2.03	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Gpsn2	Glycoprotein, synaptic 2	GDs 12−19	Down	−0.42 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Grb14	Growth factor receptor bound protein 14	GDs 12−19	Up	0.68 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Grb14	Growth factor receptor bound protein 14	GD 19 for 6 hr	Up after 6 hr	1.78	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Grb14	Growth factor receptor bound protein 14	GDs 18−19 for 18 hr	Up after 18 hr	0.93	$p < 0.05$ (ANOVA)	Thompson et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Grina	Glutamate receptor, ionotropic, N-methyl D-aspartate-associated protein 1 (glutamate binding)	GDs 12.5−15.5	Up	1.59	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Gsta2	Glutathione-S-transferase, alpha type2	GDs 12.5−17.5	Down	−1.48	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Gsta2	Glutathione-S-transferase, alpha type2	GDs 12.5−19.5	Down	−2.23	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Gsta3	Glutathione S-transferase A3	GDs 12−19	Down	−0.96 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Gsta3	Glutathione S-transferase A3	GDs 12.5−17.5	Down	−1.75	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Gsta3	Glutathione S-transferase A3	GDs 12.5−19.5	Down	−2.63	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Gstm2	Glutathione S-transferase, mu 2	GDs 12−19	Down	−0.42 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Gstm2	Glutathione S-transferase, mu 2	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Gstm2	Glutathione S-transferase, mu 2	GDs 18−19 for 18 hr	Down after 18 hr	−0.47	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Gsto1	Glutathione S-transferase omega 1	GDs 12−19	Down	−0.42 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Gstp1	Glutathione-S-transferase, pi 1	GDs 12.5−15.5	Up	1.34	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Hao2	Hydroxyacid oxidase 2 (long chain)	GDs 12−19	Down	−0.58 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hmgcr	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	GDs 12−19	Down	−0.47 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hmgcr	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	GDs 12.5−19.5	Down	−1.83	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Hmgcs1	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1	GDs 12−19	Down	−1.03 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Hmgcs1	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1	GDs 12.5−17.5	Down	−1.72	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Hmgcs1	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1	GDs 12.5−19.5	Down	−1.87	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Hmox1	Heme oxygenase (decycling) 1	GDs 12−19	Down	−0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hpgd	Hydroxyprostaglandin dehydrogenase 15 (NAD)	GDs 12−19	Down	−0.46 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hprt	Hypoxanthine guanine phosphoribosyl transferase	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Hrasls3	HRAS like suppressor 3	GDs 12−19	Down	−0.45 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hsd11b2	Hydroxysteroid (11-beta) dehydrogenase 2	GD 19 for 6 hr	Down after 6 hr	−1.16	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Hsd17b3	Hydroxysteroid (17-beta) dehydrogenase 3	GDs 12−19	Up	0.28 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hsd17b7	Hydroxysteroid (17-beta) dehydrogenase 7	GDs 12−19	Down	−0.32 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hsd3b1_predicted	Hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted)	GDs 12−19	Down	−0.50 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Hsd3b1_predicted	Hsd3b1_predicted hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted)	GD 18 for 18 hr	Down after 18 hr	−0.7	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Hspb7	Heat shock 27kD protein family, member 7 (cardiovascular)	GDs 12−19	Up	0.41 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Idh1	Isocitrate dehydrogenase 1 (NADP+), soluble	GDs 12−19	Down	−0.52 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Idh1	Isocitrate dehydrogenase 1 (NADP+), soluble	GD 18 for 18 hr	Down after 18 hr	−0.67	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Idi1	Isopentenyl-diphosphate delta isomerase	GDs 12−19	Down	−0.85 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Idi1	Isopentenyl-diphosphate delta isomerase	GDs 12.5−17.5	Down	−1.57	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Igfbp2	Insulin-like growth factor binding protein 2	GDs 12−19	Down	−0.39 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Igfbp3	Insulin-like growth factor binding protein 3	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Il6st	Interleukin 6 signal transducer	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Ifitm2	Interferon induced transmembrane protein 2	GDs 12.5−17.5	Down	−1.11	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Inha	Inhibin alpha	GDs 12−19	Down	−1.00 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Inha	Inhibin alpha	GDs 12.5−19.5	Down	−1.64	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Insig1	Insulin induced gene 1	GDs 12−19	Down	−0.77 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Insl3	Insulin-like 3	GDs 12−19	Down	−1.56 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
interim symbol: *Loc314323*	Interim full name: transporter	GDs 12−19	Down	−0.35 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
interim symbol: *Ratsg2*	Interim name: *Ratsg2*	GDs 12−19	Down	−0.13 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Kcnj8	Potassium inwardly-rectifying channel, subfamily J, member 8	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Khk	Ketohexokinase	GDs 12.5−17.5	Up	1.30	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Kit	V-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Krt2-8	Keratin complex 2, basic, gene 8	GDs 12−19	Up	0.28 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Ldha	Lactate dehydro-genase A	GDs 12.5−19.5	Down	−1.30	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Ldlr	Low density lipoprotein receptor	GDs 12−19	Down	−0.79 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ldlr	Low density lipoprotein receptor	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Lhcgr	Luteinizing hormone/choriogonadotropin receptor	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Lhcgr	Luteinizing hormone/choriogonadotropin receptor	GD 19 for 6 hr	Down after 6 hr	−1.00	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Lhcgr	Luteinizing hormone/choriogonadotropin receptor	GDs 18−19 for 18 hr	Down after 18 hr	−1.51	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Lhcgr	Luteinizing hormone/choriogonadotropin receptor	GDs 12−19	Down	−1.39 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Limk1	LIM motif-containing protein kinase 1	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Lnk	Linker of T-cell receptor pathways	GD 19 for 3 hr	Up after 3 hr	1.17	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Lr8	LR8 protein	GDs 12−19	Down	−0.45 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Lss	Lanosterol synthase	GDs 12−19	Down	−0.48 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Mapk1	Mitogen activated protein kinase 1	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Marcks	Myristoylated alanine rich protein kinase C substrate	GDs 12−19	Up at GD 19	≥ 2	2-fold	Shultz et al., 2001
Mdk	Midkine	GDs 12−19	Up	0.20 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Me1	Malic enzyme 1, NADP($^+$)-dependent, cytosolic	GDs 12−19	Down	−0.67 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Me1	Malic enzyme 1, NADP(+)-dependent, cytosolic	GDs 12.5−17.5	Down	−1.36	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Men1	Multiple endocrine neoplasia 1	GDs 12.5−15.5	Down	−1.17	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Mgat1	Mannoside acetylglucosaminyltransferase 1	GDs 12−19	Up	0.28 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Mgp	Matrix Gla protein	GD 19 for 6 hr	Up after 6 hr	1.66	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Mgst1	Microsomal glutathione S-transferase 1	GDs 12−19	Down	−0.36 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Mgst1	Microsomal glutathione S-transferase 1	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Mir16	Membrane interacting protein of RGS16	GDs 12−19	Down	−0.56 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Mlxipl	MLX interacting protein-like	GDs 12−19	Down	−0.31 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Mmp2	Matrix metallopeptidase 2	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Mtus1	Mitochondrial tumor suppressor 1	GD 19 for 3 hr	Up after 3 hr	0.67	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Mtus1	Mitochondrial tumor suppressor 1	GD 19 for 6 hr	Up after 6 hr	0.55	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Mvd	Mevalonate (diphospho) decarboxylase	GDs 12−19	Down	−0.41 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Myd116	Myeloid differentiation primary response gene 116	GD 19 for 3 hr	Up after 3 hr	0.58	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Myh6	Myosin, heavy polypeptide 6, cardiac muscle, alpha	GDs 12−19	Down	−0.72 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Myh6	Myosin, heavy polypeptide 6, cardiac muscle, alpha	GDs 18−19 for 18 hr	Down after 18 hr	−1.52	$p < 0.05$ (ANOVA)	Thompson et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Myh6	Myosin, heavy polypeptide 6, cardiac muscle, alpha	GDs 12.5−19.5	Down	−1.64	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Myom2	Myomesin 2	GDs 12−19	Up	0.64 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Myrip	Myosin VIIA and Rab interacting protein	GDs 12−19	Down	−0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nalp6	NACHT, leucine rich repeat and PYD containing 6	GDs 12−19	Up	0.45 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nexn	Nexilin	GDs 12−19	Up	0.26 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nf1	Neurofibromatosis 1	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Nfil3	Nuclear factor, interleukin 3 regulated	GDs 12−19	Up	0.31 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nfkbia	Nuclear factor of kappa light chain gene enhancer in B-cells inhibitor, alpha	GD 19 for 3 hr	Up after 3 hr	0.79	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Npc2	Niemann pick type C2	GDs 12−19	Down	−0.26 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nppc	Natriuretic peptide precursor type C	GDs 12−19	Down	−0.56 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nr0b1	Nuclear receptor subfamily 0, group B, member 1	GDs 12−19	Down	−0.37 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nr0b1	Nuclear receptor subfamily 0, group B, member 1	GDs 12.5−19.5	Down	−1.15	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Nr4a1	Nuclear receptor subfamily 4, group A, member 1	GDs 12−19	Up	0.3 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Nr4a1	Nuclear receptor subfamily 4, group A, member 1	GD 19 for 3 hr	Up after 3 hr	1.83	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Nr4a3	Nuclear receptor subfamily 4, group A, member 3	GD 19 for 3 hr	Up after 3 hr	2.25	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Nr5a1	Nr5a1 nuclear receptor subfamily 5, group A, member 1	GDs 12.5−19.5	Down	−1.18	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Ntf3	Neurotrophin 3	GDs 12.5−17.5	Up	1.34	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Okl38	Pregnancy-induced growth inhibitor	GDs 12−19	Down	−0.33 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Olfm1	Olfactomedin 1	GDs 12−19	Down	−0.14 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
P2ry14	Purinergic receptor P2Y, G-protein coupled, 14	GDs 12−19	Down	−0.37 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Park7	Parkinson disease (autosomal recessive, early onset) 7	GDs 12.5−17.5	Down	−1.32	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Pawr	PRKC, apoptosis, WT1, regulator	GD 19 for 3 hr	Up after 3 hr	1.02	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Pcna	Proliferating cell nuclear antigen	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Pcyt2	Phosphate cytidylyltransferase 2, ethanolamine	GDs 12−19	Down	−0.20 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Pdap1	PDGFA associated protein 1	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
Pdyn	Prodynorphin	GDs 12−19	Down	−1.06 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Pebp1	Phosphatidylethanolamine binding protein 1	GDs 12−19	Down	−0.36 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Pebp1	Phosphatidylethanolamine binding protein 1	GDs 12.5−19.5	Down	−1.67	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Penk1	Proenkephalin 1	GDs 12.5−17.5	Down	−1.41	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Penk1	Proenkephalin 1	GDs 12.5−19.5	Down	−1.86	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Pfkp	Phosphofructokinase, platelet	GDs 12.5−19.5	Down	−1.41	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Pgam1	Phosphoglycerate mutase 1	GDs 12.5−19.5	Down	−1.26	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Pgk1	Phosphoglycerate kinase 1	GDs 12.5−19.5	Down	−1.25	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Phb	Prohibitin	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Phb	Prohibitin	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Phyh	Phytanoyl-CoA hydroxylase	GD 19 for 6 hr	Down after 6 hr	−1.02	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Plat	Plasminogen activator, tissue	GDs 12−19	Up at GD 19	≥ 2	2-fold	Shultz et al., 2001
Plaur	Plasminogen activator, urokinase receptor	GD 19 for 3 hr	Up after 3 hr	0.86	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Pmp22	Peripheral myelin protein 22	GDs 12−19	Up at GD 19	≥ 2	2-fold	Shultz et al., 2001
Pmp22	Peripheral myelin protein 22	GD 19 for 3 hr	Down after 3 hr	−0.75	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Pmp22	Peripheral myelin protein 22	GD 19 for 6 hr	Down after 6 hr	−0.59	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Pnliprp2	Pancreatic lipase-related protein 2	GDs 12−19	Down	−0.28 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Por	P450 (cytochrome) oxidoreductase	GDs 12−19	Down	−0.64 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Por	P450 (cytochrome) oxidoreductase	GDs 12.5−19.5	Down	−1.39	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Ppib	Peptidylprolyl isomerase B	GDs 12.5−17.5	Down	−1.21	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Ppp1cb	Protein phosphatase 1, catalytic subunit, beta isoform	GDs 12.5−17.5	Down	−1.37	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Prdx3	Peroxiredoxin 3	GDs 12−19	Down	−0.53 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Prdx3	Peroxiredoxin 3	GDs 18−19 for 18 hr	Down after 18 hr	−0.86	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Prdx3	Peroxiredoxin 3	GDs 12.5−19.5	Down	−1.63	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Prg1	Plasticity related gene 1	GDs 12−19	Down	−0.97 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Prkar2b	Protein kinase, cAMP dependent regulatory, type II beta	GDs 12−19	Down	−0.33 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Prkcbp1	Protein kinase C binding protein 1	GDs 12−19	Up	0.32 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Prlr	Prolactin receptor	GDs 12−19	Down	−1.02 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ptma	Prothymosin alpha	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Ptp4a1	Protein tyrosine phosphatase 4a1	GDs 12−21	Up at GD 21	≥ 2	2-fold	Shultz et al., 2001
PVR	Poliovirus receptor	GD 19 for 3 hr	Up after 3 hr	1.26	$p < 0.05$ (ANOVA)	Thompson et al., 2005
PVR	Poliovirus receptor	GD 19 for 6 hr	Up after 6 hr	0.92	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Rabep2	Rabaptin, RAB GTPase binding effector protein 2	GD 19 for 3 hr	Down after 3 hr	−0.48	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Rasd1	RAS, dexamethasone-induced 1	GDs 12−19	Down	−0.52 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Rln1	Relaxin 1	GDs 12−19	Down	−0.36 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Rnh1	Ribonuclease/angiogenin inhibitor 1	GDs 12.5−17.5	Down	−1.20	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rpa2	Replication protein A2	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Rpl13	Ribosomal protein L13	GDs 12.5−15.5	Up	1.17	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rpl32	Ribosomal protein L32	GDs 12.5−19.5	Up	1.13	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rpl37	Ribosomal protein L37	GDs 12.5−19.5	Up	1.13	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rpl36a	Large subunit ribosomal protein L36a	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Rpl36a	Large subunit ribosomal protein L36a	GDs 12.5−15.5	Up	1.22	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rpn2	Ribophorin II	GDs 12.5−19.5	Down	−1.19	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rps13	Ribosomal protein S13	GDs 12.5−15.5	Up	1.30	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rps17	Ribosomal protein S17	GDs 12.5−19.5	Up	1.25	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rps19	Ribosomal protein S19	GDs 12.5−17.5	Up	1.25	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Rps29	Ribosomal protein S29	GDs 12.5−19.5	Down	−1.13	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Sc4mol	Sterol-C4-methyl oxidase-like	GDs 12−19	Down	−1.02 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Sc4mol	Sterol-C4-methyl oxidase-like	GDs 12.5−17.5	Down	−1.82	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Sc4mol	Sterol-C4-methyl oxidase-like	GDs 12.5−19.5	Down	−2.36	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Sc5d	Sterol-C5-desaturase (fungal ERG3, delta-5-desaturase) homolog (*S. cerevisae*)	GDs 12−19	Down	−0.32 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Scarb1	Scavenger receptor class B, member 1	GDs 12−19	Down	−1.91 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Scarb1	Scavenger receptor class B, member 1	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Scarb1	Scavenger receptor class B, member 1	GD 19 for 6 hr	Down after 6 hr	−1.60	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Scarb1	Scavenger receptor class B, member 1	GDs 18−19 for 18 hr	Down after 18 hr	−2.72	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Scarb1	Scavenger receptor class B, member 1	GDs 12.5−17.5	Down	−2.23	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Scarb1	Scavenger receptor class B, member 1	GDs 12.5−19.5	Down	−2.85	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Scd1	Stearoyl-Coenzyme A desaturase 1	GDs 12−19	Down	−0.58 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Scn3b	Sodium channel, voltage-gated, type III, beta	GD 19 for 6 hr	Up after 6 hr	1.49	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Scp2	Sterol carrier protein 2	GDs 12−19	Down	−0.17 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Scp2	Sterol carrier protein 2	GDs 12.5−19.5	Down	−1.24	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Sdf4	Stromal cell derived factor 4	GDs 12−19	Down	−0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Sepp1	Selenoprotein P, plasma, 1	GDs 12−19	Down	−0.45 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Serpine1	Serine (or cysteine) peptidase inhibitor, clade E, member 1	GD 19 for 3 hr	Up after 3 hr	1.56	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Serpinh1	Serine (or cysteine) peptidase inhibitor, clade H, member 1	GDs 12.5−15.5	Down	−1.32	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Sgk	Serum/glucocorticoid regulated kinase	GDs 12−19	Down	−0.45 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Slc3a2	Solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	GDs 12−19	Down	−0.48 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Slc12a2	Solute carrier family 12 (sodium/potassium/chloride transporters), member 2	GDs 12.5−17.5	Down	−1.39	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Slc16a6	Solute carrier family 16 (monocarboxylic acid transporters), member 6	GDs 12−19	Down	−0.38 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Slc25a1	Solute carrier family 25, member 1	GDs 12−19	Down	−0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Slc25a20	Solute carrier family 25 (mitochondrial carnitine/acylcarnitine translocase), member 20	GDs 12−19	Down	−0.23 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Slc7a8	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 8	GDs 12.5−17.5	Down	−1.82	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Slc7a8	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 8	GDs 12.5−19.5	Down	−2.18	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Smpx	Small muscle protein, X-linked	GDs 12−19	Up	0.21 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Sod2	Superoxide dismutase 2, mitochondrial	GDs 12−19	Down	−0.51 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Sod3	Superoxide dismutase 3, extracellular	GDs 12−19	Down	−0.33 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Sqle	Squalene epoxidase	GDs 12−19	Down	−0.59 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Sqle	Squalene epoxidase	GD 18 for 18 hr	Down after 18 hr	−1.26	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Ssr4	Signal sequence receptor 4	GDs 12−19	Down	−0.23 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Ssrp1	Structure specific recognition protein 1	GDs 12−19	Down at GD 19	−≥ 2	2-fold	Shultz et al., 2001
Star	Steroidogenic acute regulatory protein	GDs 12−19	Down	−2.45 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Star	Steroidogenic acute regulatory protein	GDs 18−19 for 18 hr	Down after 18 hr	−2.33	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Star	Steroidogenic acute regulatory protein	GDs 12.5−17.5	Down	−2.19	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Star	Steroidogenic acute regulatory protein	GDs 12.5−19.5	Down	−2.53	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Stc1	Stanniocalcin 1	GDs 12−19	Up	0.98 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Stc1	Stanniocalcin 1	GD 19 for 6 hr	Up after 6 hr	1.61	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Stc2	Stanniocalcin 2	GDs 12−19	Down	−1.18 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Stc2	Stanniocalcin 2	GDs 12.5−19.5	Down	−1.59	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Sts	Steroid sulfatase	GDs 12−19	Down at GD 19	−≥ 2	2-fold	Shultz et al., 2001
Suclg1	Succinate-CoA ligase, GDP-forming, alpha subunit	GDs 12.5−19.5	Down	−1.21	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Svs5	Seminal vesicle secretion 5	GDs 12−19	Down	−3.75 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Svs5	Seminal vesicle secretion 5	GDs 18−19 for 18 hr	Down after 18 hr	−3.36	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Svs5	Seminal vesicle secretion 5	GDs 12.5−17.5	Down	−5.89	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Svs5	Seminal vesicle secretion 5	GDs 12.5−19.5	Down	−3.75	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Syngr1	Synaptogyrin 1	GDs 12−19	Down	−0.16 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tcf1	Transcription factor 1	GDs 12−19	Down	−0.14 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tcf21	Transcription factor 21	GDs 12−19	Up	0.17 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tec	Tec protein tyrosine kinase	GD 19 for 3 hr	Up after 3 hr	0.69	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Testin	Testin gene	GDs 12−19	Up	0.59 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tfrc	Transferrin receptor	GDs 12−19	Down	−0.23 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tgfb3	Transforming growth factor, beta 3	GDs 12−19	Down at GD 19	$-\geq 2$	2-fold	Shultz et al., 2001
Timp1	Tissue inhibitor of metallopeptidase 1	GD 19 for 6 hr	Up after 6 hr	1.04	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Timp3	Tissue inhibitor of metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory)	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Tkt	Transketolase	GDs 12.5−17.5	Down	−1.19	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Tkt	Transketolase	GDs 12.5−19.5	Down	−1.28	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Tmed10	Transmembrane emp24-like trafficking protein 10 (yeast)	GDs 12.5−19.5	Down	−1.20	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Tnfrsf12a	Tumor necrosis factor receptor superfamily, member 12a	GD 19 for 6 hr	Up after 6 hr	1.34	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Tnni1	Troponin I, skeletal, slow 1	GDs 12−19	Up	0.33 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tnni3	Troponin I type 3 (cardiac)	GDs 12−19	Up	0.26 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tnnt2	Troponin T2, cardiac	GDs 12−19	Up	0.77 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Tpi1	Triosephosphate isomerase 1	GDs 12−19	Down	−0.24 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tpm1	Tropomyosin 1, alpha	GDs 12−19	Up	0.36 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tpm1	Tropomyosin 1, alpha	GD 19 for 6 hr	Up after 6 hr	1.04	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Tsc22d1	TSC22 domain family, member 1	GDs 12.5−19.5	Down	−1.34	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Tsn	Translin	GDs 12.5−17.5	Up	1.54	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Tst	Thiosulfate sulfurtransferase	GDs 12−19	Down	−0.33 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Tuba1	Tubulin, alpha 1	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Tuba1	Tubulin, alpha 1	GDs 12.5−19.5	Down	−1.26	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Txn1	Thioredoxin 1	GD 18 for 18 hr	Down after 18 hr	−0.62	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Txnl1	Thioredoxin-like 1	GDs 12.5−15.5	Up	1.20	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Uba52	Ubiquitin A-52 residue ribosomal protein fusion product 1	GDs 12.5−19.5	Up	1.10	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Unc5b	Unc-5 homolog B (*C. elegans*)	GDs 12−21	Down at GD 21	$-\geq 2$	2-fold	Shultz et al., 2001
Vapa	VAMP (vesicle-associated membrane protein)-associated protein A	GDs 12.5−19.5	Down	−1.37	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Vcam1	Vascular cell adhesion molecule 1	GDs 12−19	Down	−0.63 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Vdac1	Voltage-dependent anion channel 1	GDs 12.5−19.5	Down	−1.13	$p < 0.01$ (ANOVA)	Plummer et al., 2007

Table A-1 (continued)

Official gene symbol	Official gene name[f]	Exposure window	Up or down	Fold change	Cutoff used (method)	Reference
Vim	Vimentin	GDs 12.5−19.5	Down	−1.60	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Vnn11	Vanin 1	GDs 12−19	Down	−0.32 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Vsnl1	Visinin-like 1	GDs 12−19	Down	−0.62 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Ywhae	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide	GDs 12.5−19.5	Down	−1.37	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Zfp36	Zinc finger protein 36	GD 19 for 1 hr	Up after 1 hr	1.79	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Zyx	Zyxin	GD 19 for 3 hr	Up after 3 hr	1.03	$p < 0.05$ (ANOVA)	Thompson et al., 2005
Not found	Listed as "Tppc" and 289920_Rn in article, and Genbank #BF400584 (Plummer, personal communication) does not match a gene name.	GDs 12.5−17.5	Down	−1.39	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Not found	Listed as "Similar to mouse IAP-binding protein" and 205510_Rn in article, and Genbank #:BG378907 (Plummer, personal communication) does not match a gene name.	GDs 12.5−15.5	Up	1.26	$p < 0.01$ (ANOVA)	Plummer et al., 2007
Not found	LOC499942 similar to WAP four-disulfide core domain protein 8 precursor (Putative protease inhibitor WAP8) (*Rattus norvegicus*).	GDs 12−19	Down	−0.25 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005
Not found	LOC497726 hypothetical gene supported by NM_138518 (*Rattus norvegicus*). This record was discontinued.	GDs 12−19	Down	−0.27 log2	$p < 0.05$ (ANOVA)	Liu et al., 2005

[a]The four studies dosed at 500 mg/kg-d DBP in the Sprague-Dawley (SD) rat.
[b]Thompson et al. (2005) and Shultz et al. (2001) dosed with DBP alone; gene expression changes for DBP were relative to vehicle control expression.

Table A-1. (continued)

[c]Liu et al. (2005) presented microarray data for all five developmental phthalates, including DBP, since they did not find any differences in statistical significance among the five phthalates. Thus, we present the data for all five phthalates, which should be the same as for DBP.

[d]The Affy ID 1387057_at was found to be significantly down-regulated by Liu et al. (2005). This Affy ID was listed as the gene *Slc7a8* (solute carrier family 7 [cationic amino acid transporter, y+ system], member 8) at the time of their publication. As of January 2007, Affy now lists both *Slc7a8* and *Syngap1*. This probeset is apparently capable of hybridizing with two different genes. Thus, this Affy ID was not incorporated in the case study evaluation since it is not clear which gene was altered after DBP in utero exposure.

[e]The Plummer et al. (2007) data from the whole testis are included in this table. The data from microdissection of testicular regions are not presented since no other studies were comparable. Plummer et al. (2007) performed their study in the Wistar rat whereas the other three microarray studies were performed in the SD rat.

[f]Gene function and pathway information was gathered from GeneGo (www.genego.com).

ANOVA, analysis of variance; GD, gestation day; hr, hour.

Table A-2. WOE for statistically significant gene expression changes after in utero exposure to DBP from whole-rat testis reverse transcription-polymerase chain reaction (RT-PCR) studies

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Ar	Androgen receptor	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005
Bmp4	Bone morphogenetic protein 4	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005
Btg2	B-cell translocation gene 2, anti-proliferative	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−6 hr (peak ~2 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Bzrp	Benzodiazepine receptor, peripheral	500 mg/kg-d	GDs 12−19	Up	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Cebpb	CCAAT/enhancer binding protein (C/EBP), beta	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA; $p < 0.05$	Liu et al., 2005
Cebpd	CCAAT/enhancer binding protein (C/EBP), delta	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−6 hr (peak ~3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Clu	Clusterin	500 mg/kg-d	GDs 12−19	Up	ANOVA, nested design, $p < 0.05$	Barlow et al., 2003
Clu	Clusterin	500 mg/kg-d	GDs 12−19	Up	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Clu	Clusterin	500 mg/kg-d	GDs 12−16, 12−19, or 12−21	Up	$p < 0.05$	Shultz et al., 2001
Cxcl1	Chemokine (C-X-C motif) ligand 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−12 hr (peak at ~3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−19	Down	ANOVA, nested design, $p < 0.05$	Barlow et al., 2003
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	50 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	100 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−16, 12−19, or 12−21	Down	$p < 0.05$	Shultz et al., 2001
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−17 and 12−18	Down at GD 18	t-test, ANOVA (one-way) with Tukey post hoc analysis; $p < 0.05$	Thompson et al., 2004
Cyp11a1	Cytochrome P450, family 11, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12.5−19.5	Down	One-way ANOVA followed by Bonferroni post test using GraphPad Prism; $p < 0.05$	Plummer et al., 2007
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−19	Down	Repeated measure ANOVA, nested design, $p < 0.05$	Barlow et al., 2003
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−16, 12−19, or 12−21	Down at GD 19	$p < 0.05$	Shultz et al., 2001
Cyp17a1	Cytochrome P450, family 17, subfamily a, polypeptide 1	500 mg/kg-d	GDs 12−17 and 12−18	Down at GD 17 and 18	t-test, ANOVA (one-way) with Tukey post hoc analysis; $p < 0.05$	Thompson et al., 2004
Daf1	Decay accelerating factor 1	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Ddc	Dopa decarboxylase	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Dusp6	Dual specificity phosphatase 6	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−12 hr (peak at ~3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Edg3	Endothelial differentiation sphingolipid G-protein-coupled receptor 3	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−6 and 18 hr (peak ~3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Egfr	Epidermal growth factor receptor	500 mg/kg-d	GDs 12−19 and 12−21	Un-changed	t-test, $p < 0.05$	Bowman et al., 2005
Egr1	Early growth response 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−7 hr (peak ~2 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Egr1	Early growth response 1	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA; $p < 0.05$	Liu et al., 2005

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Egr2	Early growth response 2	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−12 hr (peak ~2 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Fgf10	Fibroblast growth factor 10	500 mg/kg-d	GDs 12−21	Up	t-test, $p < 0.05$	Bowman et al., 2005
Fgfr2	Fibroblast growth factor receptor 2	500 mg/kg-d	GDs 12−19 and 12−21	No stat. change	t-test, $p < 0.05$	Bowman et al., 2005
Fos	FBJ murine osteosarcoma viral oncogene homolog	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after 30 min and 6 hr (peak at 1 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Grb14	Growth factor receptor bound protein 14	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Hes6	Hairy and enhancer of split 6 (Drosophila)	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Down after 1−3 hr (peak at 3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Hsd17b3	Hydroxysteroid (17-beta) dehydrogenase 3	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Hsd17b7	Hydroxysteroid (17-beta) dehydrogenase 7	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Hsd3b1_predicted	Hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted)	500 mg/kg-d	GDs 12−19	Down	ANOVA, nested design, $p < 0.05$	Barlow et al., 2003

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Hsd3b1_ predicted	Hsd3b1_predicted hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted) or Hsd3b1 hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1	0.1 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Hsd3b1_ predicted	Hsd3b1_predicted hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted) or Hsd3b1 hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1	1 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Hsd3b1_ predicted	Hsd3b1_predicted hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted) or Hsd3b1 hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1	10 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Hsd3b1_ predicted	Hsd3b1_predicted hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted) or Hsd3b1 hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1	50 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Hsd3b1_predicted	Hsd3b1_predicted hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted) or Hsd3b1 hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1	100 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Hsd3b1_predicted	Hsd3b1_predicted hydroxysteroid dehydrogenase-1, delta< 5 >-3-beta (predicted) or Hsd3b1 hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1	500 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Ier3	Immediate early response 3	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after 1−12 hr (peak ~2 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Ifrd1	Interferon-related developmental regulator 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−6 and 18 hr (peak ~3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Igf1	Insulin-like growth factor 1	500 mg/kg-d	GDs 12−21	Up	t-test, $p < 0.05$	Bowman et al., 2005
Igf1	Insulin-like growth factor 1	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005
Igf1r	Insulin-like growth factor 1 receptor	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Igf2	Insulin-like growth factor 2	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005
Igfbp5	Insulin-like growth factor binding protein 5	500 mg/kg-d	GDs 12−21	Up	t-test, $p < 0.05$	Bowman et al., 2005
Insig1	Insulin induced gene 1	500 mg/kg-d	GDs 12−19	Down	One way; and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Insl3	Insulin-like 3	500 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Insl3	Insulin-like 3	1000 mg/kg-d	GDs 13−17 (GDs 14−18 in Wilson et al., 2004 was changed to GDs 13−17 to make the GD comparable to the other 7 studies)	Down	ANOVA followed by LSMEANS, $p < 0.01$ or less	Wilson et al., 2004
Insl3	Insulin-like 3	500 mg/kg-d	GDs 12.5−19.5	Down	One-way ANOVA followed by Bonferroni post test using GraphPad Prism; $p < 0.05$	Plummer et al., 2007
Itgav	Integrin alpha V	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005
Junb	Jun-B oncogene	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	UP after ~1−12 hr (peak ~2−3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Kit	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	500 mg/kg-d	GDs 12−19	Down	ANOVA, nested design, $p < 0.05$	Barlow et al., 2003
Kit	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	0.1 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Kit	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	1 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Kit	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	50 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Kit	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	100 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Kit	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	500 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Kit	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	500 mg/kg-d	GDs 12-19	Down at GD 19	$p < 0.05$	Shultz et al., 2001
Kitl	Kit ligand	500 mg/kg-d	GDs 12−19	Down	ANOVA, nested design, $p < 0.05$	Barlow et al., 2003
Ldlr	Low density lipoprotein receptor	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Lhcgr	Luteinizing hormone/choriogonadotropin receptor	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Map3k12	Mitogen activated protein kinase kinase kinase 12	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005
Marcks	Myristoylated alanine rich protein kinase C substrate	500 mg/kg-d	GDs 12−16, 12−19, or 12−21	No stat. Change	$p < 0.05$	Shultz et al., 2001
Mgp	Matrix Gla protein	500 mg/kg-d	GDs 12−21	Up	t-test, $p < 0.05$	Bowman et al., 2005

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Mmp2	Matrix metallopeptidase 2	500 mg/kg-d	GDs 12−19	Up	t-test, $p < 0.05$	Bowman et al., 2005
Mmp2	Matrix metallopeptidase 2	500 mg/kg-d	GDs 12−21	Up	t-test, $p < 0.05$	Bowman et al., 2005
Nfil3	Nuclear factor, interleukin 3 regulated	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Nfil3	Nuclear factor, interleukin 3 regulated	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~2−24 hr (peak ~6 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Notch2	Notch gene homolog 2 (Drosophila)	500 mg/kg-d	GDs 12−21	Up	t-test, $p < 0.05$	Bowman et al., 2005
Npc2	Niemann Pick type C2	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Nr0b1	Nuclear receptor subfamily 0, group B, member 1	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Nr0b1	Nuclear receptor subfamily 0, group B, member 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Down at 2 hr, Up 12 hr (peak at 12 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Nr4a1	Nuclear receptor subfamily 4, group A, member 1	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Nr4a1	Nuclear receptor subfamily 4, group A, member 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~6 and 18 hr (peak at 12 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Nr4a3	Nuclear receptor subfamily 4, group A, member 3	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−12 hr (peak at ~3−6 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Pawr	PRKC, apoptosis, WT1, regulator	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~2−24 hr (peak ~6 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Pcna	Proliferating cell nuclear antigen	500 mg/kg-d	GDs 12−16, 12−19, or 12−21	No stat. change	$p < 0.05$	Shultz et al., 2001
Prkcbp1	Protein kinase C binding protein 1	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Scarb1	Scavenger receptor class B, member 1	500 mg/kg-d	GDs 12−19	Down	ANOVA, nested design, $p < 0.05$	Barlow et al., 2003
Scarb1	Scavenger receptor class B, member 1	1 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Scarb1	Scavenger receptor class B, member 1	50 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Scarb1	Scavenger receptor class B, member 1	100 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Scarb1	Scavenger receptor class B, member 1	500 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Scarb1	Scavenger receptor class B, member 1	500 mg/kg-d	GDs 12−16, 12−19, or 12−21	Down	$p < 0.05$	Shultz et al., 2001
Scarb1	Scavenger receptor class B, member 1	500 mg/kg-d	GDs 12−17 and 12−18	Down at GDs 17 and 18	t-test, ANOVA (one-way) with Tukey post hoc analysis, $p < 0.05$	Thompson et al., 2004

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Sgk	Serum/glucocorticoid regulated kinase	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Down and Up; Down after 2 hr; Up after 4 and 10 hr (peak at 6 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Sostdc1	Sclerostin domain containing 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Down after 2−6 hr; Up at 18 hr (peak)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Star	Steroidogenic acute regulatory protein	500 mg/kg-d	GDs 12−19	Down	Repeated measure ANOVA, nested design, $p < 0.05$	Barlow et al., 2003
Star	Steroidogenic acute regulatory protein	50 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Star	Steroidogenic acute regulatory protein	100 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Star	Steroidogenic acute regulatory protein	500 mg/kg-d	GDs 12−19	Down	Dunnett's test, ANOVA (one way), $p < 0.05$	Lehmann et al., 2004
Star	Steroidogenic acute regulatory protein	500 mg/kg-d	GDs 12−16, 12−19, or 12−21	Down at GDs 16, 19, and 21	$p < 0.05$	Shultz et al., 2001
Star	Steroidogenic acute regulatory protein	500 mg/kg-d	GDs 12−17 and 12−18	Down at GDs 17 and 18	t-test, ANOVA (one-way) with Tukey post hoc analysis; $p < 0.05$	Thompson et al., 2004
Star	Steroidogenic acute regulatory protein	500 mg/kg-d	GDs 12.5−19.5	Down	One-way ANOVA followed by Bonferroni post test using GraphPad Prism; $p < 0.05$	Plummer et al., 2007

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Stc1	Stanniocalcin 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~3−24 hr (peak ~6 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Svs5	Seminal vesicle secretion 5	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Tcf1	Transcription factor 1	500 mg/kg-d	GDs 12−19	Down	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Tcf1	Transcription factor 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Down after 1−3 hr (peak at 1 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Testin	Testin gene	500 mg/kg-d	GDs 12−19	Up	One way and two-way nested ANOVA, $p < 0.05$	Liu et al., 2005
Thbs1	Thrombospondin 1	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after 2−4 hr (peak ~3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Timp1	Tissue inhibitor of metalloproteinase 1	500 mg/kg-d	GDs 12−21	Up	t-test, $p < 0.05$	Bowman et al., 2005
Tnfrsf12a	Tumor necrosis factor receptor superfamily, member 12a	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~1−12 hr (peak at ~3 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005
Wnt4	Wingless-related MMTV integration site 4	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after ~12 and 18 hr (peak 12 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005

Table A-2. (continued)

Official gene symbol	Official gene name*	Dose	Exposure window	Up or down	Statistical analysis method	Reference
Zfp36	Zinc finger protein 36	500 mg/kg-d	GD 19 for 30 min to 6 hr timepoints and GD 18 for 12, 18, and 24 hr time points	Up after 30 min and 6 hr and 15 and 20 hr (peak at 1 hr)	Relative expression determined using mean Ct; triplicate samples; GADPH control; SE; but *p* value not calculated	Thompson et al., 2005

*Gene function and pathway information was gathered from GeneGo (www.genego.com).

Table A-3. Genes identified using the Rosetta Error Model statistical filter and mapping to the five most significant biochemical functions and /or pathways using Ingenuity

Gene symbol	Gene name
Genes mapped to integrin pathway	
F2r	Coagulation factor II (thrombin) receptor
Src	Rous sarcoma oncogene
Gng5	Guanine nucleotide binding protein (G protein), gamma 5 subunit
Gnai3	Guanine nucleotide binding protein, alpha inhibiting 3
Gng7	Guanine nucleotide binding protein, gamma 7
Mapk3	Mitogen activated protein kinase 3
Gnao1	Guanine nucleotide binding protein, alpha o
Actc1	Actin alpha cardiac 1
Camk2d	Calcium/calmodulin-dependent protein kinase II, delta
Gnaq	Guanine nucleotide binding protein
Cxcl12	Chemokine (C-X-C motif) ligand 12
Prkce	Protein kinase C, epsilon
Genes mapped to cholesterol biosynthesis/metabolism	
Hmgcs1	3-Hydroxy-3-methylglutaryl-Coenzyme A synthase 1
Hsd3b1	Hydroxyl-delta-5-steroid dehydrogenase
Dhcr7	7-Dehydrocholesterol reductase
Sqle	Squalene epoxidase
Soat1	Sterol O-acyltransferase 1
Cyp51a1	Cytochrome P450, family 51, subfamily a, polypeptide 1
Cyp27a1	Cytochrome P450, family 27, subfamily a, polypeptide 1
Hsd11b1	Hydroxysteroid 11-beta dehydrogenase 1
Hmgcr	3-Hydroxy-3-methylglutaryl-Coenzyme A reductase
Idi1	Osopentenyl-diphosphate delta isomerase
Sc4mol	Sterol-C4-methyl oxidase-like
Cyp7b1	Cytochrome P450, family 7, subfamily b, polypeptide 1

Table A-3. (continued)

Gene symbol	Gene name
Genes mapped to chemokine mediated signaling	
Src	Rous sarcoma oncogene
Gng5	Guanine nucleotide binding protein (G protein), gamma 5 subunit
Hmgcs1	3-Hydroxy-3-methylglutaryl-Coenzyme A synthase 1
Serpine2	Serine (or cysteine) proteinase inhibitor, clade E, member 2
Itgb5	Integrin, beta 5
Dhcr7	7-Dehydrocholesterol reductase
Gnai3	Guanine nucleotide binding protein, alpha inhibiting 3
Gng7	Guanine nucleotide binding protein, gamma 7
Sqle	Squalene epoxidase
Mapk3	Mitogen activated protein kinase 3
Gnao1	Guanine nucleotide binding protein, alpha o
Actn1	Actinin, alpha 1
Actc1	Actin alpha cardiac 1
Cav2	Caveolin 2
Cyp51a1	Cytochrome P450, family 51, subfamily a, polypeptide 1
Genes mapped to chemokine mediated signaling	
Col1a2	Procollagen, type I, alpha 2
Cfl1	Cofilin 1, non-muscle
Cav1	Caveolin 2
Hmgcr	3-Hydroxy-3-methylglutaryl-Coenzyme A reductase
Mmp2	Matrix metallopeptidase 2
Msn	Moesin
Gsk3b	Glycogen synthase kinase 3 beta
Idi1	Isopentenyl-diphosphate delta isomerase
Plat	Plasminogen activator, tissue
Sdc2	Syndecan 2
Sc4mol	Sterol-C4-methyl oxidase-like
Lef1	Lymphoid enhancer binding factor 1

Table A-3. (continued)

Gene symbol	Gene name
Vegf	Vascular endothelial growth factor
Genes mapped to glycolysis/gluconeogenesis	
Pgk1	Phosphoglycerate kinase 1
Hmgcs1	3-Hydroxy-3-methylglutaryl-Coenzyme A synthase 1
Tpi1	Triosephosphate isomerase 1
Fbp2	Fructose-1,6-bisphosphatase 2
Dhcr7	7-Dehydrocholesterol reductase
Pfkm	Phosphofructokinase, muscle
Pfkp	Phosphofructokinase, platelet
Mdh1	Malate dehydrogenase 1, NAD (soluble)
Sqle	Squalene epoxidase
Pgam1	Phosphoglycerate mutase 1
Aldoa	Aldolase A
Cyp51a1	Cytochrome P450, family 51, subfamily a, polypeptide 1
Hmgcr	3-Hydroxy-3-methylglutaryl-Coenzyme A reductase
Hk1	Hexokinase 1
Gpi	Glucose phosphate isomerase
Gapdh	Glyceraldehyde-3-phosphate dehydrogenase
Idi1	Isopentenyl-diphosphate delta isomerase
Sc4mol	Sterol-C4-methyl oxidase-like
Pfkl	Phosphofructokinase, liver

Table A-4. Differentially expressed genes that mapped to statistically significant pathways identified using the Signal to Noise Ratio (SNR) statistical filter

Gene symbol	Entrez gene ID	Gene name
Aadat	29416	Aminoadipate aminotransferase
Acadm	24158	Acetyl-Coenzyme A dehydrogenase, medium chain
Acads	64304	Acyl-Coenzyme A dehydrogenase, short chain
Acat1	25014	Acetyl-Coenzyme A acetyltransferase 1
Aco2	79250	Aconitase 2, mitochondrial
Acsl4	113976	Acyl-CoA synthetase long-chain family member 4
Akr1b4	24192	Aldo-keto reductase family 1, member B4 (aldose reductase)
Alas1	65155	Aminolevulinic acid synthase 1
Aldh1a4	29651	Aldehyde dehydrogenase family 1, subfamily A4
Aldh2	29539	Aldehyde dehydrogenase 2
Aldh6a1	81708	Aldehyde dehydrogenase family 6, subfamily A1
Aldoa	24189	Aldolase A
Aldoc	24191	Aldolase C, fructose-biphosphate
Ass	25698	Arginosuccinate synthetase
Bhmt	81508	Betaine-homocysteine methyltransferase
Chkb	29367	Choline kinase beta
Cyp11a1	29680	Cytochrome P450, family 11, subfamily a, polypeptide 1
Cyp17a1	25146	Cytochrome P450, family 17, subfamily a, polypeptide 1
Dcxr	171408	Dicarbonyl L-xylulose reductase
Ddc	24311	Dopa decarboxylase
Dhcr7	64191	7-dehydrocholesterol reductase
Ebp	117278	Phenylalkylamine Ca^{2+} antagonist (emopamil) binding protein
Ephx1	25315	Epoxide hydrolase 1
Fbp2	114508	Fructose-1,6-bisphosphatase 2
Fdft1	29580	Farnesyl diphosphate farnesyl transferase 1
Fdps	83791	Farnesyl diphosphate synthase
Fh1	24368	Fumarate hydratase 1

Table A-4. (continued)

Gene symbol	Entrez gene ID	Gene name
G6pdx	24377	Glucose-6-phosphate dehydrogenase
Gad2	24380	Glutamate decarboxylase 2
Gapdh	24383	Glyceraldehyde-3-phosphate dehydrogenase
Gatm	81660	Glycine amidinotransferase (L-arginine:glycine amidinotransferase)
Ggtl3	156275	Gamma-glutamyltransferase-like 3
Gsta2	24422	Glutathione-S-transferase, alpha type2
Gsta3	24421	Glutathione S-transferase A5
Gstm2	24424	Glutathione S-transferase, mu 2
Gstm3	81869	Glutathione S-transferase, mu type 3
Hmgcr	25675	3-hydroxy-3-methylglutaryl-Coenzyme A reductase
Hmgcs1	29637	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1
Idh1	24479	Isocitrate dehydrogenase 1 ($NADP^+$), soluble
Me1	24552	Malic enzyme 1
Mgst1	171341	Microsomal glutathione S-transferase 1
Mif	81683	Macrophage migration inhibitory factor
Mvd	81726	Mevalonate (diphospho) decarboxylase
Nos1	24598	Nitric oxide synthase 1, neuronal
Pycr2	364064	Pyrroline-5-carboxylate reductase family, member 2 (predicted)
Sqle	29230	Squalene epoxidase
Suclg1	114597	Succinate-CoA ligase, GDP-forming, alpha subunit
Tpi1	24849	Tpi1 protein

Table A-5. GeneGo pathway analysis of significant genes identified by REM

Pathway	Biological process	p-Value[a]	No. of genes[b,c]
NF-AT signaling in cardiac hypertrophy	Disease	2.23E−04	19/90
MIF—the neuroendocrine-macrophage connector	Immune response	3.00E−04	19/92
Lysine metabolism	Amino acid metabolism	3.05E−04	9/27
Cholesterol metabolism	Steroid metabolism	6.95E−04	6/14
Glycolysis and gluconeogenesis (short map)	Carbohydrates metabolism	7.40E−04	10/36
Integrin-mediated cell adhesion	Cell adhesion	8.44E−04	18/92
Tryptophan metabolism	Amino acid metabolism	9.56E−04	9/31
Cholesterol biosynthesis	Steroid metabolism	1.44E−03	7/21
ECM remodeling	Cell adhesion	1.64E−03	13/60
Regulation of lipid metabolism via PPAR, RXR, and VDR	Transcription	1.96E−03	7/22
Propionate metabolism p.2	Carbohydrates metabolism	1.96E−03	7/22
PPAR regulation of lipid metabolism	Regulation of lipid metabolism	2.04E−03	8/28
Mitochondrial long chain fatty acid beta-oxidation	Lipid metabolism	2.28E−03	6/17
Role of VDR in regulation of genes involved in osteoporosis	Transcription	3.16E−03	12/57
ChREBP regulation pathway	G-protein coupled receptor signaling	3.82E−03	10/44
Androstenedione and testosterone biosynthesis and metabolism p.1	Steroid metabolism	4.30E−03	6/19
Arginine metabolism	Amino acid metabolism	4.45E−03	9/38
Regulation of fatty acid synthesis: NLTP and EHHADH	Regulation of lipid metabolism	5.02E−03	4/9
Angiotensin signaling via STATs	Growth and differentiation	5.18E−03	11/53
Cytoskeleton remodeling	Cell adhesion	5.19E−03	26/176
dGTP metabolism	Nucleotide metabolism	5.34E−03	9/39
TCA	Amino acid metabolism	5.70E−03	6/20
Glycolysis and gluconeogenesis p. 1	Carbohydrates metabolism	5.70E−03	6/20
Peroxisomal branched chain fatty acid oxidation	Lipid metabolism	5.70E−03	6/20

Table A-5. (continued)

Pathway	Biological process	p-value[a]	No. of genes[bc]
Gamma-aminobutyrate (GABA) biosynthesis and metabolism	Metabolism of mediators	5.70E−03	6/20
Ligand-dependent activation of the ESR1/SP pathway	Response to hormone stimulus	6.38E−03	9/40
Integrin inside-out signaling	Cell adhesion	6.85E−03	14/78
Reverse signaling by ephrin B	Cell adhesion	6.86E−03	15/86
G-protein beta/gamma signaling cascades	G-protein coupled receptor protein signaling pathway	6.94E−03	11/55
Activation of PKC via G-Protein coupled receptor	G-protein coupled receptor protein signaling pathway	7.65E−03	15/87
Gap junctions	Cell adhesion	8.51E−03	10/49
WNT signaling pathway	Proteolysis	8.59E−03	7/28
Angiotensin activation of ERK	G-protein coupled receptor protein signaling pathway	9.12E−03	11/57
Role of Akt in hypoxia induced HIF1 activation	Proteolysis	9.83E−03	10/50
Regulation of actin cytoskeleton by Rho GTPases	Small GTPase mediated signal transduction	1.18E−02	11/59
CCR3 signaling in eosinophils	Immune response	1.22E−02	18/117
MAG-dependent inhibition of neurite outgrowth	Response to extracellular stimulus	1.47E−02	10/53
Endothelial cell contacts by junctional mechanisms	Cell adhesion	1.80E−02	7/32
Fructose metabolism	Carbohydrates metabolism	1.80E−02	7/32
Regulation of lipid metabolism via LXR, NF-Y and SREBP	Transcription	1.80E−02	7/32
CXCR4 signaling pathway	Cytokine and chemokine mediated signaling pathway	1.89E−02	10/55
Serotonin-melatonin biosynthesis and metabolism	Metabolism of mediators	2.04E−02	5/19
Glycolysis and gluconeogenesis p. 2	Carbohydrates metabolism	2.15E−02	4/13
Oxidative phosphorylation	Energy metabolism	2.37E−02	15/99
Urea cycle	Amino acid metabolism	2.58E−02	6/27
G-proteins mediated regulation p.38 and JNK signaling	G-protein coupled receptor protein signaling pathway	2.60E−02	11/66

Table A-5. (continued)

Pathway	Biological process	p-value[a]	No. of genes[bc]
Transcription factor tubby signaling pathways	Transcription	2.63E−02	8/42
Role PKA in cytoskeleton reorganization	Protein kinase cascade	2.64E−02	13/83
Ephrins signaling	Cell adhesion	2.66E−02	10/58
Propionate metabolism p.1	Carbohydrates metabolism	2.81E−02	4/14
Estrone metabolism	Steroid metabolism	2.81E−02	4/14
Regulation of acetyl-CoA carboxylase 2 activity in muscle	Response to extracellular stimulus	2.81E−02	4/14
Chemokines and adhesion	Cytokine and chemokine mediated signaling pathway	2.82E−02	23/174
Arachidonic acid production	Lipid metabolism	2.87E−02	7/35
dCTP/dUTP metabolism	Nucleotide metabolism	2.99E−02	8/43
Regulation of lipid metabolism by niacin and isoprenaline	Regulation of lipid metabolism	3.01E−02	9/51
Ubiquinone metabolism	Vitamin and cofactor metabolism	3.01E−02	9/51
Phenylalanine metabolism	Amino acid metabolism	3.05E−02	6/28
Leptin signaling via JAK/STAT and MAPK cascades	Response to hormone stimulus	3.57E−02	6/29
IMP biosynthesis	Nucleotide metabolism	3.70E−02	3/9
EPO-induced Jak-STAT pathway	Response to extracellular stimulus	3.78E−02	7/37
Integrin outside-in signaling	Cell adhesion	3.95E−02	12/79
Brca1 as transcription regulator	Cell cycle	4.15E−02	6/30
P53 signaling pathway	Transcription regulation	4.28E−02	8/46
Bile acid biosynthesis	Steroid metabolism	4.43E−02	5/23
Histidine-glutamate-glutamine and proline metabolism	Amino acid metabolism	4.79E−02	8/47
NTS activation of IL-8 in colonocytes	Immune response	4.85E−02	10/64

[a]Ordered from most significant (lowest *p*-value) to less significant.
[b]Number of genes from the DBP-exposed gene list mapping to the GeneGo pathway.
[c]Total number of genes in the GeneGo pathway.

Table A-6. Significant biological pathways corresponding to differentially expressed genes (DEGs) obtained from SNR analysis input into GeneGo

Pathway	Biological Process	p-Value[a]	No. of genes[bc]
Cholesterol Biosynthesis	Steroid metabolism	1.81E−09	15/21
Propionate metabolism p.2	Carbohydrates metabolism	5.54E−06	12/22
MIF—the neuroendocrine-macrophage connector	Immune response	3.22E−04	25/92
Tryptophan metabolism	Amino acid metabolism	3.78E−04	12/31
Lysine metabolism	Amino acid metabolism	3.93E−04	11/27
Cholesterol metabolism	Steroid metabolism	1.09E−03	7/14
NF-AT signaling in cardiac hypertrophy	Disease	1.38E−03	23/90
Glycolysis and gluconeogenesis (short map)	Carbohydrates metabolism	1.77E−03	12/36
G-alpha(q) regulation of lipid metabolism	Regulation of lipid metabolism	1.93E−03	13/41
Activation of PKC via G-protein coupled receptor	G-proteins/GPCR	2.00E−03	22/87
Fructose metabolism	Carbohydrates metabolism	2.06E−03	11/32
Regulation of lipid metabolism by niacin and isoprenaline	Regulation of lipid metabolism	2.08E−03	15/51
ATP metabolism	Nucleotide metabolism	2.09E−03	16/56
Angiotensin activation of ERK	Growth and differentiation	2.55E−03	16/57
NTS activation of IL-8 in colonocytes	Immune response	3.60E−03	17/64
Leucine, isoleucine, and valine metabolism.p.2	Amino acid metabolism	3.64E−03	9/25

Table A-6. (continued)

Pathway	Biological Process	p-Value[a]	No. of genes[bc]
Reverse signaling by ephrin B	Cell adhesion	3.92E−03	21/86
Cortisone biosynthesis and metabolism	Steroid metabolism	4.31E−03	7/17
CXCR4 signaling pathway	Immune response	4.63E−03	15/55
G-Protein beta/gamma signaling cascades	G-proteins/GPCR	4.63E−03	15/55
Glutathione metabolism	Vitamin and cofactor metabolism	5.77E−03	11/36
Mitochondrial ketone bodies biosynthesis and metabolism	Lipid metabolism	5.96E−03	5/10
Integrin inside-out signaling	Cell adhesion	6.07E−03	19/78
Propionate metabolism p.1	Carbohydrates metabolism	6.51E−03	6/14
Role of VDR in regulation of genes involved in osteoporosis	Transcription factors	6.63E−03	15/57
Endothelial cell contacts by junctional mechanisms	Cell adhesion	7.02E−03	10/32
EPO-induced Jak-STAT pathway	Cell survival	7.24E−03	11/37
A3 receptor signaling	G-proteins/GPCR	8.08E−03	19/80
Angiotensin signaling via STATs	Growth and differentiation	8.28E−03	14/53
MAG-dependent inhibition of neurite outgrowth	Growth and differentiation	8.28E−03	14/53
Phenylalanine metabolism	Amino acid metabolism	8.48E−03	9/28
Androstenedione and testosterone biosynthesis and metabolism p.1	Steroid metabolism	8.76E−03	7/19
Cytoskeleton remodeling	Cell adhesion	9.69E−03	35/176

Table A-6. (continued)

Pathway	Biological Process	p-Value[a]	No. of genes[bc]
ChREBP regulation pathway	Regulation of transcription	1.08E−02	12/44
Leptin signaling via JAK/STAT and MAPK cascades	Growth and differentiation	1.09E−02	9/29
dGTP metabolism	Nucleotide metabolism	1.10E−02	11/39
TCA	Amino acid metabolism	1.20E−02	7/20
Glycolysis and gluconeogenesis p. 1	Carbohydrates metabolism	1.20E−02	7/20
Gamma-aminobutyrate (GABA) biosynthesis and metabolism	Metabolism of mediators	1.20E−02	7/20
BAD phosphorylation	Apoptosis	1.21E−02	19/83
Ligand-dependent activation of the ESR1/SP pathway	Hormones	1.34E−02	11/40
RAB5A regulation pathway	G-proteins/RAS-group	1.49E−02	5/12
Integrin outside-in signaling	Cell adhesion	1.50E−02	18/79
Hedgehog and PTH signaling pathways participation in bone and cartilage development	Growth and differentiation	1.62E−02	11/41
G-Proteins mediated regulation MARK-ERK signaling	G-proteins/GPCR	1.64E−02	17/74
Integrin-mediated cell adhesion	Cell adhesion	1.78E−02	20/92
Mitochondrial long chain fatty acid beta-oxidation	Lipid metabolism	1.88E−02	6/17
CCR3 signaling in eosinophils	Immune response	2.02E−02	24/117
Regulation of lipid metabolism via PPAR, RXR, and VDR	Transcription factors	2.07E−02	7/22

Table A-6. (continued)

Pathway	Biological Process	p-Value[a]	No. of genes[bc]
Glycolysis and gluconeogenesis p. 2	Carbohydrates metabolism	2.16E−02	5/13
Regulation of fatty acid synthesis: NLTP and EHHADH	Regulation of lipid metabolism	2.30E−02	4/9
Role PKA in cytoskeleton reorganization	Kinases	2.43E−02	18/83
Arginine metabolism	Amino acid metabolism	2.44E−02	10/38
ECM remodeling	Cell adhesion	2.45E−02	14/60
Ca ($^{2+}$)-dependent NF-AT signaling in cardiac hypertrophy	Disease	2.55E−02	15/66
WNT signaling pathway	Growth and differentiation	2.64E−02	8/28
PPAR regulation of lipid metabolism	Regulation of lipid metabolism	2.64E−02	8/28
Insulin regulation of the protein synthesis	Translation regulation	2.67E−02	13/55
CXCR4 signaling via second messenger	Immune response	2.67E−02	13/55
Angiotensin signaling via beta-Arrestin	Growth and differentiation	2.71E−02	11/44
Estrone metabolism	Steroid metabolism	2.99E−02	5/14
Regulation of acetyl-CoA carboxylase 2 activity in muscle	Growth and differentiation	2.99E−02	5/14
Prolactin receptor signaling	Growth factors	3.19E−02	14/62
Triacylglycerol metabolism p.1	Lipid metabolism	3.23E−02	8/29
Serotonin-melatonin biosynthesis and metabolism	Metabolism of mediators	3.27E−02	6/19
Angiotensin signaling via PYK2	Growth and differentiation	3.32E−02	16/74

Table A-6. (continued)

Pathway	Biological Process	p-Value[a]	No. of genes[bc]
G-Protein alpha-i signaling cascades	G-proteins/GPCR	3.36E−02	12/51
dATP/dITP metabolism	Nucleotide metabolism	3.86E−02	12/52
Brca1 as transcription regulator	Cell-cycle control	3.90E−02	8/30
Ephrins signaling	Cell adhesion	3.99E−02	13/58
Mitochondrial unsaturated fatty acid beta-oxidation	Lipid metabolism	4.01E−02	5/15
GDNF signaling	Growth and differentiation	4.08E−02	7/25
Aspartate and asparagine metabolism	Amino acid metabolism	4.15E−02	6/20
Peroxisomal branched chain fatty acid oxidation	Lipid metabolism	4.15E−02	6/20
Histidine-glutamate-glutamine and proline metabolism	Amino acid metabolism	4.24E−02	11/47
TGF-beta receptor signaling	Growth and differentiation	4.51E−02	13/59
Regulation of actin cytoskeleton by Rho GTPases	G-proteins/RAS-group	4.51E−02	13/59
G-Protein alpha-s signaling cascades	G-proteins/GPCR	4.51E−02	13/59
A1 receptor signaling	G-proteins/GPCR	4.61E−02	16/77
Membrane-bound ESR1: interaction with growth factors signaling	Growth and differentiation	4.64E−02	10/42
Transcription factor Tubby signaling pathways	Regulation of transcription	4.64E−02	10/42
Histamine metabolism	Metabolism of mediators	4.83E−02	4/11
PPAR pathway	Transcription factors	4.86E−02	11/48

Table A-6. (continued)

Pathway	Biological Process	p-Value[a]	No. of genes[bc]
Cross-talk VEGF and angiopoietin 1 signaling	Growth and differentiation	5.08E−02	9/37
EPO-induced MAPK pathway	Growth and differentiation	5.08E−02	13/60

[a]Ordered from most significant (lowest *p*-value) to less significant.
[b]Number of genes from the DBP exposed gene list mapping to the GeneGo pathway.
[c]Total number of genes in the GeneGo pathway.

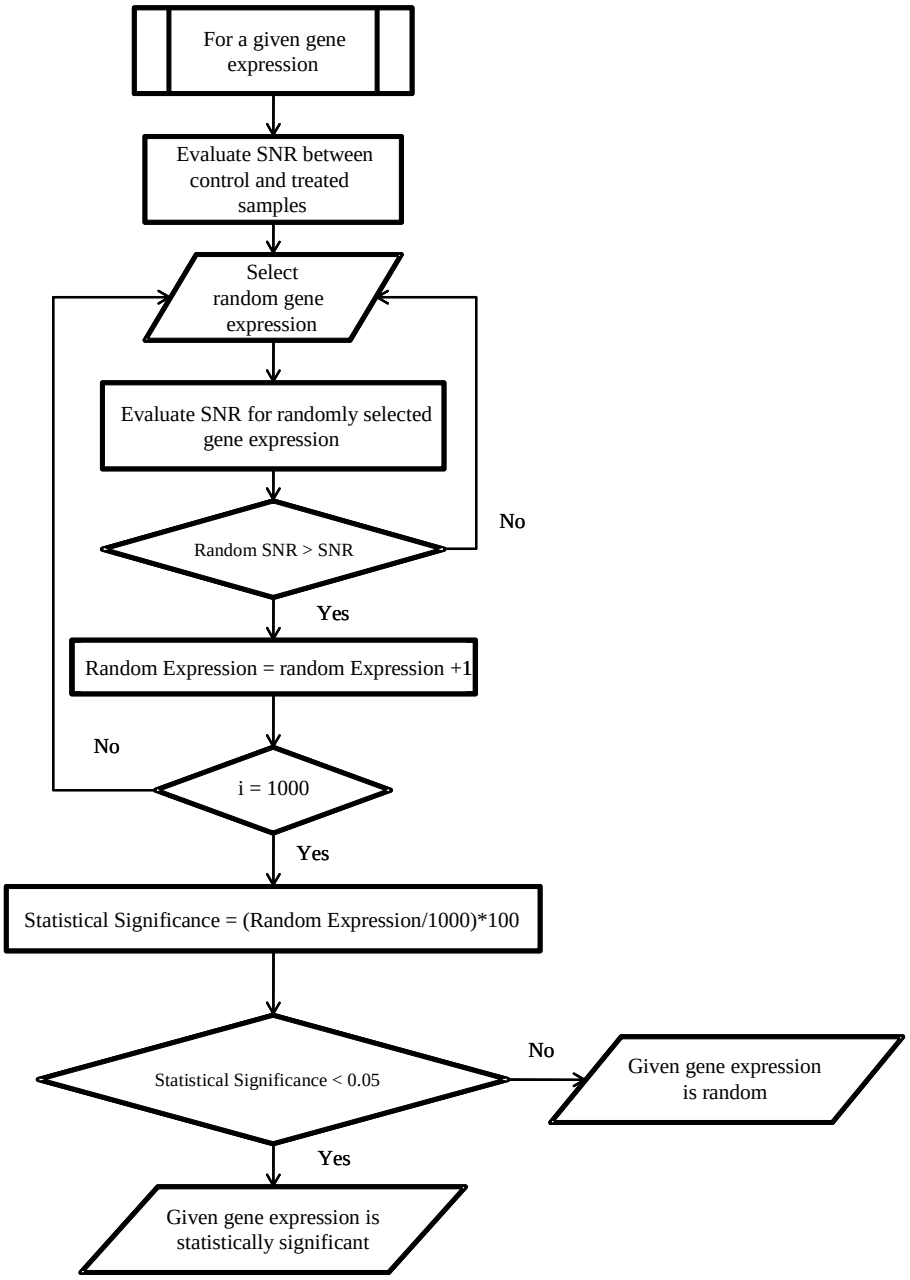

Figure A-1. Algorithm for selecting differentially expressed genes (DEGs) using signal-to-noise ration (SNR). 1,000 random gene expressions were generated for each probe set, and then, SNRs were calculated. The ratio of the randomly generated SNR that was higher than the actual SNR determined whether individual probe set's expression was discriminating or not.

APPENDIX B.

SUPPORTING TABLES AND FIGURES FOR CHAPTER 6

Appendix B contains additional tables and figures supportive of the work described in Chapter 6.

Table B-1. Nodes added by using Ingenuity® Pathway Analysis (IPA) software in developing the gene network model for DBP

Gene symbol	Gene name
Aco1	Aconitase 1, soluble
Esrra	Estrogen-related receptor alpha
Fgf4	Fibroblast growth factor 4
Insig1	Insulin induced gene 1
Kcnj11	Potassium inwardly-rectifying channel, subfamily J, member 11
Lep	Leptin
Lnpep	Leucyl/cystinyl aminopeptidase
Nfic	Nuclear factor I/C (CCAAT-binding transcription factor)
Nme1	Non-metastatic cells 1, protein (NM23A) expressed in
Nr2f1	Nuclear receptor subfamily 2, group F, member 1
Nr5a1	Nuclear receptor subfamily 5, group A, member 1
Pld2	Phospholipase D2
Ppargc1b	Peroxisome proliferative activated receptor, gamma, coactivator 1, beta
Srebf1	Sterol regulatory element binding transcription factor 1
Srebf2	Sterol regulatory element binding transcription factor 2
Zdhhc23	Zinc finger, DHHC-type containing 23

Figure B-1. Algorithm for selecting significant pathways using the pathway activity method. 1,000 random sets of gene expressions were generated for each pathway, then pathway activity, *PAp*, was evaluated. The *p*-value of each *PAp* is computed as the fraction of the randomized *PAp* that exceeded the actual *PAp*.

APPENDIX C.

QUALITY CONTROL AND ASSURANCE

Appendix C contains quality assurance/quality control (QA/QC) information for the work described in Chapters 5 and 6. The work described in this Appendix (C) is secondary data analysis. The studies include exploratory studies using new methods for analyzing genomic data for risk assessment purposes as well as some preliminary analyses using well-established of the raw data from two published studies.

Three projects were performed:

(1) A qualitative analysis and presentation of the 9 toxicogenomic DBP studies. No statistical analyses were performed by members of our team.

(2) In-house analysis of the raw data from Liu et al. (2005) study performed at both NHEERL, US EPA by Drs. Susan Hester and Banalata Sen, and by by collaborators, Dr. Ioannis Androulakis and Meric Ovacik, STAR Grantees at the STAR Bioinformatics Center at Rutgers/UMDNJ.

(3) New analyses of Thompson et al. (2005) data performed by collaborators, Dr. Ioannis Androulakis and Meric Ovacik, STAR Grantees at the STAR Bioinformatics Center at Rutgers/UMDNJ.

C.1. PROJECT 1

The data presented in 9 published toxicogenomic studies for DBP were compared. No additional analyses were performed. Data were entered directly into an excel spreadsheet from the published literature. Study descriptions in tables and figures were developed. The data entry process included team members entering in the data from the published articles into tables for differentially expressed genes and pathways affected. One person entered the data for a subset of genes. A second person checked the results in the table against the articles.

C.2. PROJECT 2

The data source was the DBP treatment only data from the Liu et al. (2005) study. The Liu et al. (2005) data were kindly provided by Dr. Kevin Gaido, a collaborator on this project. The study was performed in his laboratory at The Hamner Institutes for Health Sciences (formerly CIIT). His QA statement for the collection and analysis of the data is provided below.

C.3. PROJECT 3

The data source was the Thompson et al. (2005) study. The Thompson et al. (2005) data were kindly provided by Dr. Kevin Gaido, a collaborator on this project. The study was performed in his laboratory at The Hamner Institutes for Health Sciences (formerly CIIT). His QA statement for the collection and analysis of the data is provided below.

C.4. PROJECTS 2 AND 3: DATA SOURCES

The sources of the data used in the secondary analyses were the Liu et al. (2005) and Thompson et al. (2005) studies. Both of these studies were performed in the laboratory of Dr. Kevin Gaido. The QA details for the two studies are presented below. The Hamner Institute's Quality Assurance Director is Patricia O. Pomerleau, M.S., RQAP (pomerleau@thehamner.org).

C.4.1. Sample Handling Procedures

Virgin female SD outbred CD rats, 8 weeks old, were time mated. Dams were assigned to a treatment group by randomization using Provantis NT 2000 and subsequently be identified by an ear tag and cage card. Dams were kept in the Association for Assessment and Accreditation of Laboratory Animal Care International accredited animal facility at The Hamner Institute (at the time of the two studies, The Hmaner was named CIIT) in a humidity- and temperature-controlled, high-efficiency particulate-air-filtered, mass air-displacement room.

Dams were treated by gavage daily from gestation day (GD) 12−19 with corn oil (vehicle control) and dibutyl phthalate. Body weights were recorded daily before dosing (GDs 12−19). The oral treatments were administered on a mg/kg-body weight basis and adjusted daily for weight changes. Animal doses were calculated through Provantis NT 2000. All calculations were checked by a second individual and recorded in the investigators' The Hamner Institute notebooks. Analytical support staff confirmed appropriate dose solutions at the beginning of the dosing period. Body weights and doses administered were recorded each day in Provantis NT 2000. Pups and dams were euthanized by carbon dioxide asphyxiation.

Fetal tissues for RIA's and RNA isolation were snap frozen in liquid nitrogen and stored at −80°C. The remaining tissues were either be embedded in optical coherence tomography and frozen or fixed in formalin for 6 to 24 hours followed by 70% ethanol and then processed and embedded in paraffin for histological examination within 48 hours. The embedded tissues were

sectioned at approximately 5 microns and stained with hematoxylin and eosin. The study pathologist in consultation with the histology staff determined the gross trim, orientation, and embedding procedure for each tissue. RNA were isolated from the frozen male reproductive tract, and changes in gene expression were identified by real-time reverse transcription-polymerase chain reaction (RT-PCR) analysis (following manufacturer's protocols P/N 402876 and P/N 4304965, Applied Biosystems, Foster City, CA) and in some cases, by complementary DNA (cDNA) microarray (following manufacturers protocol PT3140, Clontech, Palo Alto, CA).

Total RNA were treated with DNase I at 37°C for 30 minutes in the presence of RNasin to remove DNA contamination before cDNA synthesis, followed by heat inactivation at 75°C for 5 minutes. Primer pairs were selected using the program Primer Express and optimized for use prior to quantification. cDNA were synthesized using random hexamers and TaqMan Reverse Transcription Reagents according to the manufacturer's suggested protocol. Real-time PCR (TaqMan) were performed on a Perkin-Elmer/Applied Biosystems 7500 Prism using TaqMan probe chemistry according to the manufacturer's instructions for quantification of relative gene expression. Relative differences among treatment groups were determined using the CT method as outlined in the Applied Biosystems protocol for reverse transcriptase(RT)-PCR. A CT value was calculated for each sample using the CT value for glyceraldehyde-3-phosphate dehydrogenase (or an appropriate housekeeping gene) to account for loading differences in the RT-PCRs.

C.4.2. Microarray Hybridization

Testes from individual fetuses were homogenized in RNA Stat 60 reagent (Tel-Test, Inc., Friendswood, TX) and RNA was isolated using the RNeasy Mini Kit (Qiagen, Valencia, CA) following manufacturer's protocol. RNA integrity was assessed using the Agilent 2100 Bioanalyzer (Agilent Technologies, Palo Alto, CA), and optical density was measured on a NanoDrop ND 1000 (NanoDrop Technologies, Wilmington, DE). cDNA was synthesized from 2.5 or 3 µg total RNA and purified using the Affymetrix® One-Cycle Target Labeling and control reagents kit (Affymetrix, Santa Clara, CA) according to manufacturer's protocol. Equal amounts of purified cDNA per sample were used as the template for subsequent in vitro transcription reactions for complementary RNA (cRNA) amplification and biotin labeling using

the Affymetrix GeneChip® IVT labeling kit (Affymetrix) included in the One-Cycle Target Labeling kit (Affymetrix). cRNA was purified and fragmented according to the protocol provided with the GeneChip® Sample Cleanup module (Affymetrix). All GeneChip® arrays were hybridized, washed, stained, and scanned using the Complete GeneChip® Instrument System according to the Affymetrix Technical Manual.

For immunocytochemistry, tissues were rapidly removed, immersed in 10% (v/v) neutral-buffered formalin for 24−48 hours, and then stored in ethanol 70% (v/v) until processed. The reproductive tissues were embedded in paraffin, sectioned at 5 μ, and processed for immunohistochemistry or stained with hematoxylin and eosin.

Experimental notes and data were entered into uniquely numbered Hamner Institute laboratory notebooks and three-ring binders along with descriptions of procedures used, according to SOP# QUA-007. Specimens (RNA and frozen tissue) were retained until analysis or discarded after a maximum of 1 year after collection. Formalin-fixed tissues, blocks, and slides were archived at the end of the study. Retention of these materials will be reassessed after 5 years.

C.4.3. Quality Assurance

Both QA and QC procedures are integral parts of our research program. The research was conducted under the The Hamner Institute Research Quality Standards program. These standards include (1) scientifically reviewed protocols that are administratively approved for meeting requirements in data quality, animal care, and safety regulations; (2) standardized laboratory notebooks and data recording procedures; (3) documented methods or standard operating procedures for all experimental procedures—including calibration of instruments; (4) a central managed archive for specimens and documentation; and (5) internal peer review for scientific quality of abstracts and manuscripts. The Hamner Institute QA and QC processes assessing overall study performance and records ensure that conduct of the proposed research satisfies the intended project objectives.

C.4.4. Statistical Analysis

RT-PCR data were analyzed using JMP statistical analysis software (SAS Institute, Cary, NC). RNA were isolated from at least 3 pups from 3 different dams for each treatment group.

PCR reactions, radioimmunoassays, and protein analysis were repeated 3−5 times for each sample. Based on our experience, the number of animal replicates has the statistical power to detect a significant change in gene expression ≥20% at $p < 0.05$. The effect of treatment was analyzed using a general-linear model regression analysis. Posthoc tests were conducted when the overall analysis of variance is significant at the $p < 0.05$ level using the LS-means procedure and adjusted for multiple comparisons by Dunnett's method.

Microarray data were analyzed by a linear mixed model with SAS Microarray Solution software. Perfect-match only data were normalized to a common mean on a log2 scale, and a linear mixed model was then applied for each probe set. Restricted maximum likelihood was used for estimating the parameters for both the fixed and random effects. Significance was determined using mixed-model based F-tests ($p < 0.05$).

C.4.5. Procedures used to Evaluate Success

Uniquely numbered written protocols were prepared and reviewed internally prior to the start of this study. The content of a protocol includes study design, materials, laboratory methods, sample collection, handling and custody, record keeping, data analysis and statistical procedures, animal care requirements, and safety measures. Numbered standardized laboratory notebooks and guidelines for date recording ensures completeness of data and the ability to reconstruct the study. An independent QA department manages the overall research data quality. Manuscripts describing the results of our study were prepared at the completion of each stage of this study. All manuscripts undergo a rigorous internal peer review that includes review by all authors, at least two additional PhD- level scientists, the science editor, the division manager, and the vice president for research.

C.5. PROJECT 2: DATA REVIEW, VERIFICATION, AND VALIDATION

Banalata Sen received the Liu et al. (2005) raw data files from Dr. Kevin Gaido. Two team members, Dr. Banalata Sen (National Center for Environmental Assessment, Research Triangle Park [NCEA-RTP]) and Dr. Susan Hester (National Health and Environmental Effects Research Laboratory [NHEERL]) performed the data analysis at NHEERL, RTP. Barbara Collins (collins.barbara@epa.gov) at NHEERL-RTP has agreed to serve as the Quality Assurance Manager (QAM) for the project. Dr. Hester and Sen performed analyses of the “DBP

only" data that is a subset of the data presented in Liu et al. (2005). The analyses at NHEERL included statistical filtering to identify of differentially expressed genes and pathway analysis.

C.5.1. Verification of Data upon Receipt

Upon receiving data from Kevin Gaido at the Hamner Institute, EPA NHEERL scientisits conducted a QA review of the data by gross inspection of the cel files to confirm that the data had been transmitted successfully. The scientists at the STAR Bioinformatics Center/Rutgers received the data files from Susan Euling at EPA NCEA who had received the data from Kevin Gaido at the Hamner Institute. Kevin Gaido gave permission to Susan Euling to provide the data for these analyses. A review of the data was performed by inspection of the txt files and the published data to confirm that the data had been transmitted successfully.

C.5.2. Verification of Data Analysis Calculations

EPA NHEERL used a principal component analysis (PCA) to evaluate the within-group and across-group variance of the six samples. PCA elucidates the separation of different treatment groups and provides information about whether the data contain significant information. This was conducted using the raw data cel files in Rosetta Resolver Software. The analyses were in silico without functional validation (RT-PCR of individual genes).

The Star Bioinformatics Center also performed a principal component analysis (PCA) and displayed a 3-D plot to evaluate the within-group and across-group variance of the samples. This was conducted using the txt files in MATLAB® Software. This was an in silico analysis. The data were normalized to a zero mean and a unity standard deviation over samples. They assessed the degree of separation for Liu et al. (2005) data. A regular regular t-test and ANOVA analyses of the data were performed. The filtered data were visualized in a heatmap to determine the statistically significant subset of genes to provide a differentially expressed gene (DEG) list.

Drs. Susan Hester and Banalata Sen also performed some comparative analyses between the two outpus (above). The two independent analyses of the same dataset were contrasted with one another. Correlation plots comparing the Log10 average intensities of control samples vs. DBP treated samples was performed in order to determine the noise in both groups. Average background signal and scaling factors will be applied based on the vendor recommendations. QC plots will be made to determine the relationship between light intensity and each genechip.

C.6. PROJECT 3: DATA REVIEW, VERIFICATION, AND VALIDATION

This project analyzed the time-course data from Thompson et al. (2005) dataset to then build a regulatory network model. The STAR Center's internal QA/QC procedures are implemented and monitored by a QA official, Clifford Weisel (weisel@eohsi.rutgers.edu), at Rutgers University that reports to the National Center for Environmental Research (NCER), the granting organization for the STAR program.

C.6.1. Verification of Data upon Receipt

Data were received from Susan Euling at EPA who had received the data from Kevin Gaido at the Hamner Institute. Kevin Gaido gave permission to Susan Euling to provide the data for these analyses. A review of the data was performed by inspection of the txt files and the published data to confirm that the data had been transmitted successfully.

C.6.2. Verification of Data Analysis Calculations

A principal component analysis (PCA) was performed and a 3-D plot was displayed to evaluate the within-group and across-group variance of the samples. This was conducted using the txt files in MATLAB® Software. This was an in silico analysis. The data were normalized to a zero mean and a unity standard deviation over samples. They assessed the degree of separation for the Thompson et al. (2005) data. A regular regular t-test and ANOVA analyses of the data were performed. The filtered data will be visualized in a heatmap to determine the statistically significant subset of genes to provide a differentially expressed gene (DEG) list.