Science Question 7: In vivo Mutagenicity

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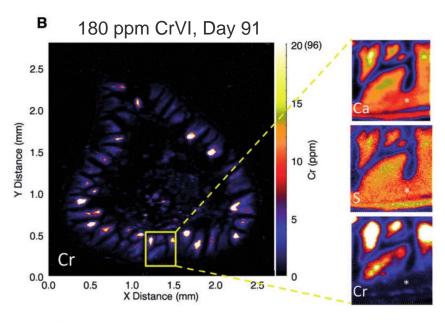
ToxStrategies, Inc.

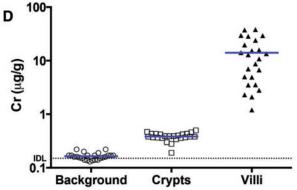
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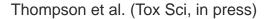
Oct 30, 2014

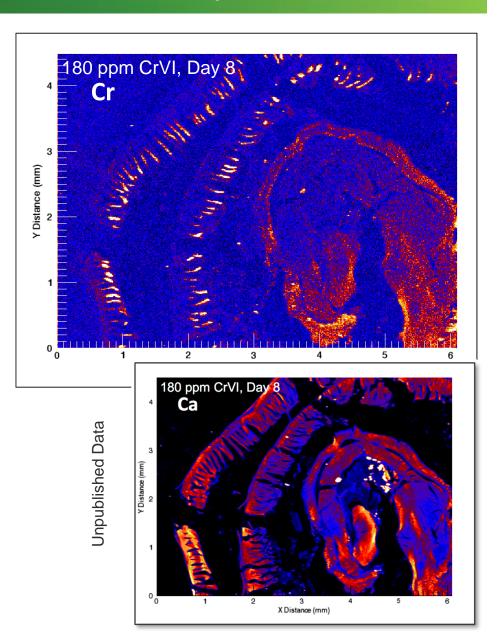
Tox Strategies

Cr Not Localized in Stem Cell Compartment









In vivo Genotoxicity & Mutagenicity Endpoints in Duodenum

γ-H2AX Immunostaining, Day 91 (Transverse):

	0,	•	,
Animal	Crypt Epithel.	Villus Epithel.	Lamina propria, villus tip
6	2	0	0
7	2	0	0
8	2	0	0
9	2	0	0
10	2	0	0
482	2	1	2
483	2	0	2
484	2	1	2
485	2	1	2
486	2	2	2
	6 7 8 9 10 482 483 484 485	Animal Crypt Epithel. 6 2 7 2 8 2 9 2 10 2 482 2 483 2 484 2 485 2	Animal Crypt Epithel. Villus Epithel. 6 2 0 7 2 0 8 2 0 9 2 0 10 2 0 482 2 1 483 2 0 484 2 1 485 2 1

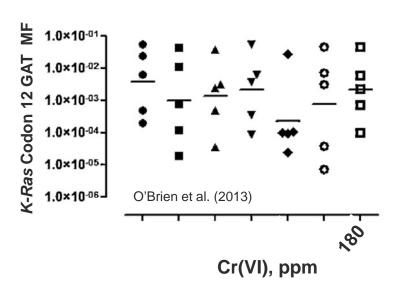
Thompson et al. (Tox Sci, in press)

Micronuclei, Day 91 (Transverse):

Dose (ppm)	Enterocytes	Micronuclei
0	1921	0
0.1	1707	0
1.4	1825	0
5	1420	0
20	2386	0
60	2746	0
180	3194	0

O'Brien et al. (2013)

Kras Codon 12 Mutant Frequency After 90 Days of Exposure:



Micronuclei, Day 8 (Swiss Roll):

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Treatment	Enterocytes	Micronuclei			
0	3210	4			
0	3484	0			
1.4 ppm Cr6	3159	1			
20 ppm Cr6	3876	1			
180 ppm Cr6	5103	0			
CP _{po} (50 mg/kg)	3400	30			
	0 0 1.4 ppm Cr6 20 ppm Cr6 180 ppm Cr6	0 3210 0 3484 1.4 ppm Cr6 3159 20 ppm Cr6 3876 180 ppm Cr6 5103			