

----SUPPORTING INFORMATION----

**Population-based analysis of DNA damage and epigenetic effects
of 1,3-butadiene in the mouse**

Lauren Lewis¹, Barbara Borowa-Mazgaj², Aline de Conti², Grace A. Chappell¹,
Yu-Syuan Luo¹, Wanda Bodnar³, Kranti Konganti⁴, Fred A. Wright⁵, David W. Threadgill⁴,
Weihsueh A. Chiu¹, Igor P. Pogribny², and Ivan Rusyn^{1,*}

¹Department of Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX

³Division of Biochemical Toxicology, National Center for Toxicological Research, US Food and Drug Administration, Jefferson, AR

²Department of Environmental Sciences and Engineering, University of North Carolina, Chapel Hill, NC

⁴Bioinformatics Research Center, North Carolina State University, Raleigh, NC

⁵Department of Molecular and Cellular Medicine, College of Medicine, Texas A&M University, College Station, TX

***Corresponding author:**

Ivan Rusyn, MD, PhD, Texas A&M University, 979-458-9866, e-mail: irusyn@tamu.edu

Disclaimer: The views expressed in this manuscript do not necessarily represent those of the U.S. Food and Drug Administration

Supporting Information Table of Contents:

Figure S1. Strain variability in genotoxicity of 1,3-butadiene across mouse tissues.

Table S1. Primers used for methylated DNA immunoprecipitation qPCR analysis.

Table S2. Primary antibodies used for western blotting.

Table S3. Phenotype data used for genome-wide quantitative trait loci (QTL) mapping

Table S4. P-values for correlation among the phenotypes.

Figure S1. Strain variability in genotoxicity of 1,3-butadiene across mouse tissues. Inter-strain differences in levels of THB-Gua adducts in lung, liver, and kidney of mice exposed to 625 ppm of 1,3-butadiene for 2 weeks. Each red circle represents DNA adduct levels for a Collaborative Cross strain.

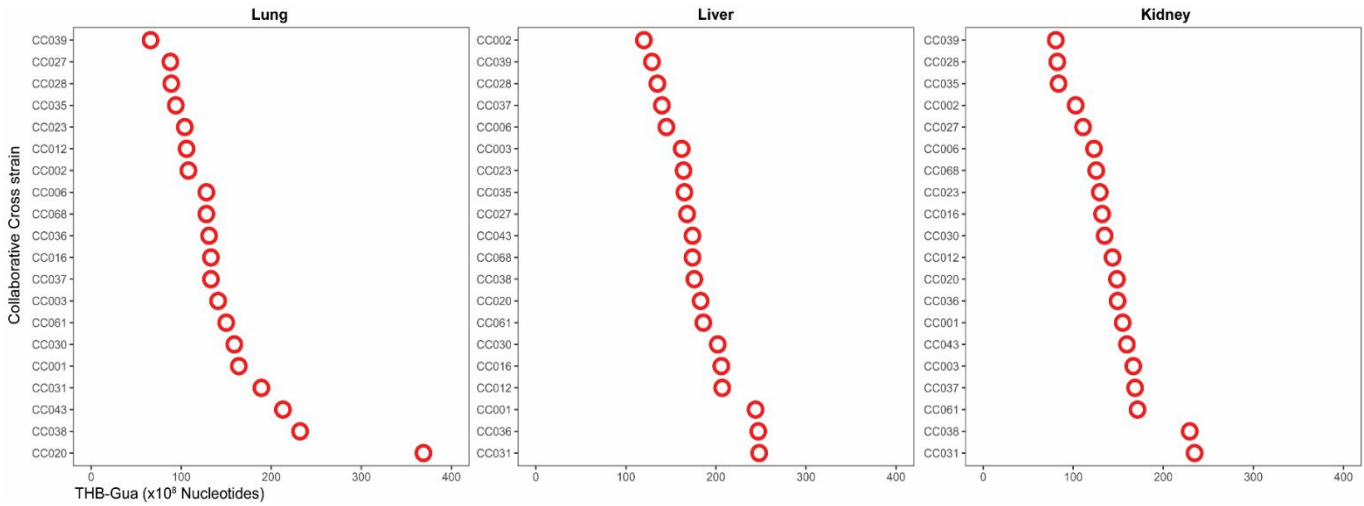


Table S1. Primers used for methylated DNA immunoprecipitation qPCR analysis.

Gene Name	Primer	Sequence
SINEB1	Forward	5'GTGGCGCACGCCTTTAATC3'
	Reverse	5'GACAGGGTTTCTCTGTGTAG3'
LINE1	Forward	5'TTGGGACACAATGAAAGCA3'
	Reverse	5'CTGCCGTCTACTCCTCTTGG3'

Table S2. Primary antibodies used for western blotting.

Target modification	Dilution	Catalog Number	Supplier
H3K9me3	1:1000	ab8898	Abcam
H3K27me3	1:1000	ab6002	Abcam
H4K20me3	1:1000	ab9053	Abcam
H3K9ac	1:1000	ab10812	Abcam
H3K27ac	1:1000	ab4729	Abcam
H4K16ac	1:1000	ab109463	Abcam

Table S3. Phenotype data used for genome-wide quantitative trait loci (QTL) mapping. Data are expressed as the number of adducts per 10⁸ nucleotides (for DNA adduct data) or fold change relative to control (for other data).

Strain	CC001	CC002	CC003	CC006	CC012	CC016	CC020	CC023	CC027	CC028	CC030	CC031	CC035	CC036	CC037	CC038	CC039	CC043	CC061	CC068
Lung DNA adducts	163.95	107.71	141.22	127.57	105.70	133.19	369.28	103.82	87.68	89.48	158.85	188.51	93.67	131.12	133.35	231.88	66.42	212.59	149.67	128.17
Liver DNA adducts	243.65	120.17	162.30	145.48	206.62	206.35	183.20	163.74	167.97	135.24	202.14	247.59	164.99	247.01	139.79	176.21	129.42	173.69	186.48	173.91
Kidney DNA adducts	154.90	102.68	166.66	123.04	143.60	132.03	148.52	129.46	110.89	82.28	134.85	234.75	83.65	149.19	168.62	229.33	80.60	159.56	171.37	125.50
H3K9me3 Lung	1.47	0.72	1.07	0.71	0.80	0.80	0.91	1.20	0.60	1.37	0.88	0.79	0.74	0.89	0.76	0.71	0.68	0.92	0.72	1.51
H3K9me3 Liver	1.17	0.96	1.08	2.11	0.71	0.68	0.85	1.74	0.85	0.91	1.52	1.31	0.89	0.74	1.45	0.77	0.78	0.86	0.75	1.50
H3K9me3 Kidney	1.13	1.02	1.23	1.07	1.23	0.98	1.06	1.33	1.28	1.33	1.10	1.28	0.77	0.62	1.11	1.22	1.23	1.88	1.10	0.90
H3K27me3 Lung	1.31	1.01	1.12	0.51	1.26	1.45	1.10	1.08	0.76	1.52	0.82	0.96	1.09	0.78	0.81	0.75	0.82	1.23	0.71	1.41
H3K27me3 Liver	1.58	1.30	1.06	1.87	0.89	1.34	0.92	1.21	1.04	0.83	0.98	1.40	1.22	0.78	1.35	0.92	1.50	0.66	0.52	1.13
H3K27me3 Kidney	1.36	1.58	1.30	0.85	0.64	2.28	1.64	0.68	1.10	0.67	1.14	0.50	0.73	0.83	1.70	1.58	7.41	0.89	2.06	1.56
H4K20me3 Lung	1.29	1.07	1.17	0.71	1.33	0.87	1.31	0.88	0.52	1.38	0.50	0.83	1.30	0.88	0.91	0.76	1.04	0.99	0.76	1.50
H4K20me3 Liver	1.57	1.57	1.24	1.71	1.21	2.15	0.88	1.20	1.06	1.08	0.98	1.12	1.13	2.11	1.54	0.93	1.28	1.09	0.82	1.43
H4K20me3 Kidney	1.76	1.05	0.62	0.89	1.13	0.71	0.44	1.24	0.73	1.05	0.76	0.83	1.10	0.80	1.00	1.09	1.31	1.34	0.87	1.14
H3K9ac Lung	0.57	0.64	1.17	0.79	1.06	0.83	2.82	1.61	1.58	1.99	1.17	0.58	2.41	0.80	0.69	0.57	0.91	0.91	1.17	0.77
H3K9ac Liver	0.97	0.67	0.87	1.43	1.54	0.89	0.73	1.30	0.76	1.47	0.84	1.24	0.97	0.82	0.76	0.80	0.85	0.92	0.73	0.93
H3K9ac Kidney	1.16	0.93	1.00	0.78	1.13	0.99	0.96	1.05	0.93	1.34	0.95	1.06	1.18	1.21	0.94	1.28	1.09	1.11	1.10	0.81
H3K27ac Lung	1.06	1.00	1.09	0.47	1.15	0.50	0.88	1.27	0.44	1.70	0.60	0.68	1.04	0.69	0.62	0.61	0.62	0.92	0.75	2.16
H3K27ac Liver	1.13	0.76	0.74	1.74	1.42	1.36	0.73	1.57	0.90	1.27	1.21	1.72	1.44	0.87	0.78	0.76	0.96	0.81	0.58	0.83
H3K27ac Kidney	0.95	0.94	1.05	1.14	1.12	0.97	0.74	1.21	0.90	1.21	0.97	1.06	0.95	0.80	0.89	0.90	0.92	1.33	0.77	1.51
H4K16ac Lung	1.24	0.93	1.19	0.62	2.16	0.82	1.14	1.38	0.61	2.44	0.79	0.88	1.55	0.96	0.69	0.70	0.66	1.56	0.90	1.19
H4K16ac Liver	0.99	0.80	0.74	1.09	1.45	1.70	0.72	1.43	0.71	1.27	0.89	1.20	1.26	0.39	0.51	0.73	0.95	0.76	0.77	0.49
H4K16ac Kidney	2.45	0.90	1.50	0.48	1.01	0.85	1.02	1.69	1.01	1.08	1.35	1.00	1.47	1.37	1.15	1.36	1.56	1.21	1.16	0.96
SINEB1 Lung	1.03	3.93	0.84	0.61	1.02	0.57	1.40	0.52	0.91	0.43			0.90	2.08	1.18	2.47		0.64	0.41	0.95
SINEB1 Liver	0.24	1.81	0.57	1.04	0.43	0.98	0.33	1.63	1.34	1.21			1.01	0.69	0.44	0.61		0.50	0.52	1.17
SINEB1 Kidney	1.77	0.24	0.46	0.39	2.99	1.90	0.45	0.49	3.57	0.41	1.93	0.71	0.23	2.15	7.09		0.84	4.77	0.27	0.48
LINE1 Lung	1.79	0.60	0.64	1.72	3.18	0.64	1.42	0.50	0.80	0.16			0.81	0.81	1.19	12.14		0.48	0.18	0.98
LINE1 Liver	0.49	1.17	1.56	0.94	2.44	0.69	0.58	3.05	1.75	0.52			1.40	0.32	0.31	0.83		0.34	1.43	3.32
LINE1 Kidney	8.74	0.87	0.37	0.39	3.38	7.61	0.65	1.38	3.43	0.75	0.30	0.65	0.54	32.50	0.31		0.15	3.12	1.56	0.57

Table S4. P-values for Spearman correlation among phenotypes collected from all tissues.

	DNA adducts Lung	DNA adducts Liver	DNA adducts Kidney	H3K27me3 Kidney	H4K16ac Kidney	H3K9me3 Kidney	H4K20me3 Kidney	H3K9ac Kidney	H3K27ac Kidney	SINEB1 Kidney	LINE1 Kidney	LINE1 Liver	SINEB1 Liver	SINEB1 Lung	LINE1 Lung	H4k20me3 Lung	H3K27me3 Lung	H3K9me3 Lung	H4K16ac Lung	H3K27ac Lung	H3K9ac Lung	H4K20me3 Liver	H3K27me3 Liver	H3K9me3 Liver	H4K16ac Liver	H3K27ac Liver	H3K9ac Liver
DNA adducts Lung	1.00	0.01	0.00	0.38	0.89	0.81	0.33	0.76	0.48	0.56	0.75	0.95	0.00	0.32	0.30	0.43	0.83	0.36	0.92	0.51	0.69	0.26	0.45	0.96	0.24	0.09	0.26
DNA adducts Liver	0.01	1.00	0.01	0.43	0.96	0.54	0.46	0.23	0.67	0.15	0.02	0.95	0.02	0.57	0.14	0.43	0.78	0.32	0.64	0.67	0.36	0.77	0.33	0.17	0.88	0.58	0.64
DNA adducts Kidney	0.00	0.01	1.00	0.74	0.59	0.57	0.42	0.46	0.37	0.18	0.49	0.66	0.00	0.49	0.35	0.26	0.38	0.63	0.82	0.62	0.74	0.34	0.34	0.73	0.21	0.13	0.37
H3K27me3 Kidney	0.38	0.43	0.74	1.00	0.99	0.13	0.57	0.24	0.02	0.97	0.43	0.39	0.32	0.46	0.80	0.67	0.56	0.23	0.03	0.15	0.25	0.80	0.54	0.26	0.13	0.00	0.00
H4K16ac Kidney	0.89	0.96	0.59	0.99	1.00	0.39	0.11	0.01	0.49	0.67	0.79	0.92	0.22	0.99	0.82	0.68	0.97	0.31	0.27	0.25	0.83	0.57	0.68	0.98	0.86	0.66	0.93
H3K9me3 Kidney	0.81	0.54	0.57	0.13	0.39	1.00	0.24	0.35	0.11	0.18	0.81	0.16	0.84	0.17	0.31	0.87	0.63	0.71	0.45	0.54	0.95	0.08	0.48	0.68	0.31	0.58	0.14
H4K20me3 Kidney	0.33	0.46	0.42	0.57	0.11	0.24	1.00	0.13	0.07	0.84	0.81	0.28	0.98	0.94	0.76	0.10	0.30	0.43	0.08	0.04	0.51	0.57	0.58	0.52	0.34	0.35	0.06
H3K9ac Kidney	0.76	0.23	0.46	0.24	0.01	0.35	0.13	1.00	0.85	0.98	0.12	0.21	0.32	0.96	0.84	0.31	0.41	0.46	0.02	0.17	0.15	0.39	0.06	0.03	0.31	0.82	0.27
H3K27ac Kidney	0.48	0.67	0.37	0.02	0.49	0.11	0.07	0.85	1.00	1.00	0.89	0.24	0.24	0.08	0.44	0.22	0.01	0.02	0.03	0.04	0.09	0.43	0.67	0.05	0.04	0.02	0.00
SINEB1 Kidney	0.56	0.15	0.18	0.97	0.67	0.18	0.84	0.98	1.00	1.00	0.28	0.29	0.20	0.46	0.39	0.30	0.93	0.80	0.50	0.18	0.94	0.65	0.67	0.50	0.37	0.99	0.93
LINE1 Kidney	0.75	0.02	0.49	0.43	0.79	0.81	0.81	0.12	0.89	0.28	1.00	0.47	0.69	0.81	0.95	0.87	0.40	0.46	0.24	0.72	0.38	0.50	0.19	0.03	0.69	0.94	0.78
LINE1 Liver	0.95	0.95	0.66	0.39	0.92	0.16	0.28	0.21	0.24	0.29	0.47	1.00	0.52	0.25	0.71	0.52	0.08	0.33	0.11	0.74	0.36	0.81	0.91	0.67	0.01	0.07	0.06
SINEB1 Liver	0.00	0.02	0.00	0.32	0.22	0.84	0.98	0.32	0.24	0.20	0.69	0.52	1.00	0.42	0.07	0.48	0.63	0.47	0.63	0.84	0.22	0.72	0.57	0.25	0.62	0.21	0.83
SINEB1 Lung	0.32	0.57	0.49	0.46	0.99	0.17	0.94	0.96	0.08	0.46	0.81	0.25	0.42	1.00	0.01	0.60	0.51	0.47	0.40	0.57	0.54	0.52	0.63	0.69	0.03	0.18	0.10
LINE1 Lung	0.30	0.14	0.35	0.80	0.82	0.31	0.76	0.84	0.44	0.39	0.95	0.71	0.07	0.01	1.00	0.87	0.56	0.51	0.34	0.38	0.74	0.42	0.18	0.93	0.47	0.61	0.64
H4k20me3 Lung	0.43	0.43	0.26	0.67	0.68	0.87	0.10	0.31	0.22	0.30	0.87	0.52	0.48	0.60	0.87	1.00	0.00	0.01	0.00	0.00	0.00	0.54	0.86	0.83	0.74	0.67	0.20
H3K27me3 Lung	0.83	0.78	0.38	0.56	0.97	0.63	0.30	0.41	0.01	0.93	0.40	0.08	0.63	0.51	0.56	0.00	1.00	0.00	0.00	0.00	0.00	0.42	0.95	0.81	0.11	0.58	0.04
H3K9me3 Lung	0.36	0.32	0.63	0.23	0.31	0.71	0.43	0.46	0.02	0.80	0.46	0.33	0.47	0.47	0.51	0.01	0.00	1.00	0.00	0.00	0.00	0.66	0.41	0.24	0.87	0.94	0.07
H4K16ac Lung	0.92	0.64	0.82	0.03	0.27	0.45	0.08	0.02	0.03	0.50	0.24	0.11	0.63	0.40	0.34	0.00	0.00	0.00	1.00	0.00	0.00	0.78	0.09	0.85	0.19	0.74	0.03
H3K27ac Lung	0.51	0.67	0.62	0.15	0.25	0.54	0.04	0.17	0.04	0.18	0.72	0.74	0.84	0.57	0.38	0.00	0.00	0.00	0.00	1.00	0.00	0.99	0.35	0.56	0.51	0.85	0.08
H3K9ac Lung	0.69	0.36	0.74	0.25	0.83	0.95	0.51	0.15	0.09	0.94	0.38	0.36	0.22	0.54	0.74	0.00	0.00	0.00	0.00	0.00	1.00	0.89	0.07	0.58	0.86	0.80	0.10
H4K20me3 Liver	0.26	0.77	0.34	0.80	0.57	0.08	0.57	0.39	0.43	0.65	0.50	0.81	0.72	0.52	0.42	0.54	0.42	0.66	0.78	0.99	0.89	1.00	0.01	0.66	0.65	0.22	0.35
H3K27me3 Liver	0.45	0.33	0.34	0.54	0.68	0.48	0.58	0.06	0.67	0.67	0.19	0.91	0.57	0.63	0.18	0.86	0.95	0.41	0.09	0.35	0.07	0.01	1.00	0.03	0.24	0.05	0.39
H3K9me3 Liver	0.96	0.17	0.73	0.26	0.98	0.68	0.52	0.03	0.05	0.50	0.03	0.67	0.25	0.69	0.93	0.83	0.81	0.24	0.85	0.56	0.58	0.66	0.03	1.00	1.00	0.21	0.25
H4K16ac Liver	0.24	0.88	0.21	0.13	0.86	0.31	0.34	0.31	0.04	0.37	0.69	0.01	0.62	0.03	0.47	0.74	0.11	0.87	0.19	0.51	0.86	0.65	0.24	1.00	1.00	0.00	0.00
H3K27ac Liver	0.09	0.58	0.13	0.00	0.66	0.58	0.35	0.82	0.02	0.99	0.94	0.07	0.21	0.18	0.61	0.67	0.58	0.94	0.74	0.85	0.80	0.22	0.05	0.21	0.00	1.00	0.00
H3K9ac Liver	0.26	0.64	0.37	0.00	0.93	0.14	0.06	0.27	0.00	0.93	0.78	0.06	0.83	0.10	0.64	0.20	0.04	0.07	0.03	0.08	0.10	0.35	0.39	0.25	0.00	0.00	1.00