ADDITIONAL MATERIALS AVAILABLE ON THE HEI WEBSITE

Research Report 198

Understanding the Early Biological Effects of Isoprene-Derived Particulate Matter Enhanced by Anthropogenic Pollutants

Surratt et al.

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Appendix A

Quality assurance and calibrations for DTT Assay

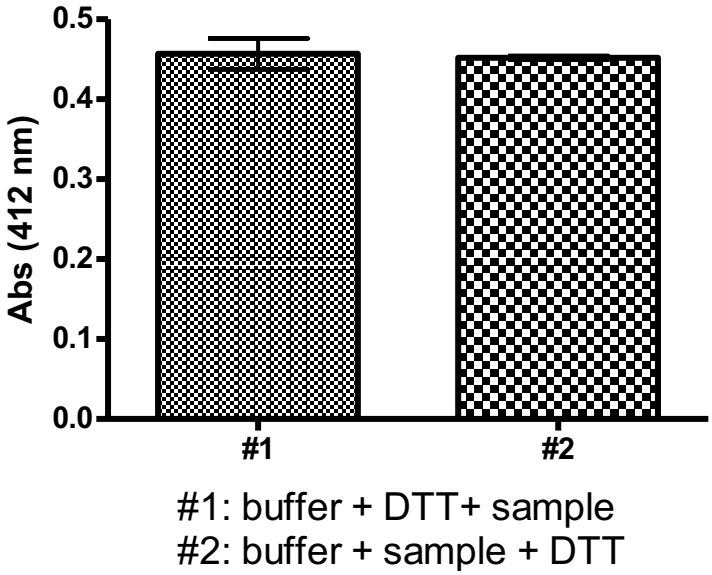

Figure A.1. To test if there are significant differences regarding the order of solution additions under our experimental conditions, we used 1,4-NQ standards to test this order when using the DTT assay. We tested this with the 1,4-NQ standards when adding buffer, then DTT, and then samples versus when adding buffer, then sample, then DTT. No significant difference was observed likely due to agents (solutions) made fresh each time the DTT assay was conducted and also because agents were added within a few minutes in order to prevent DTT from being oxidized in air.

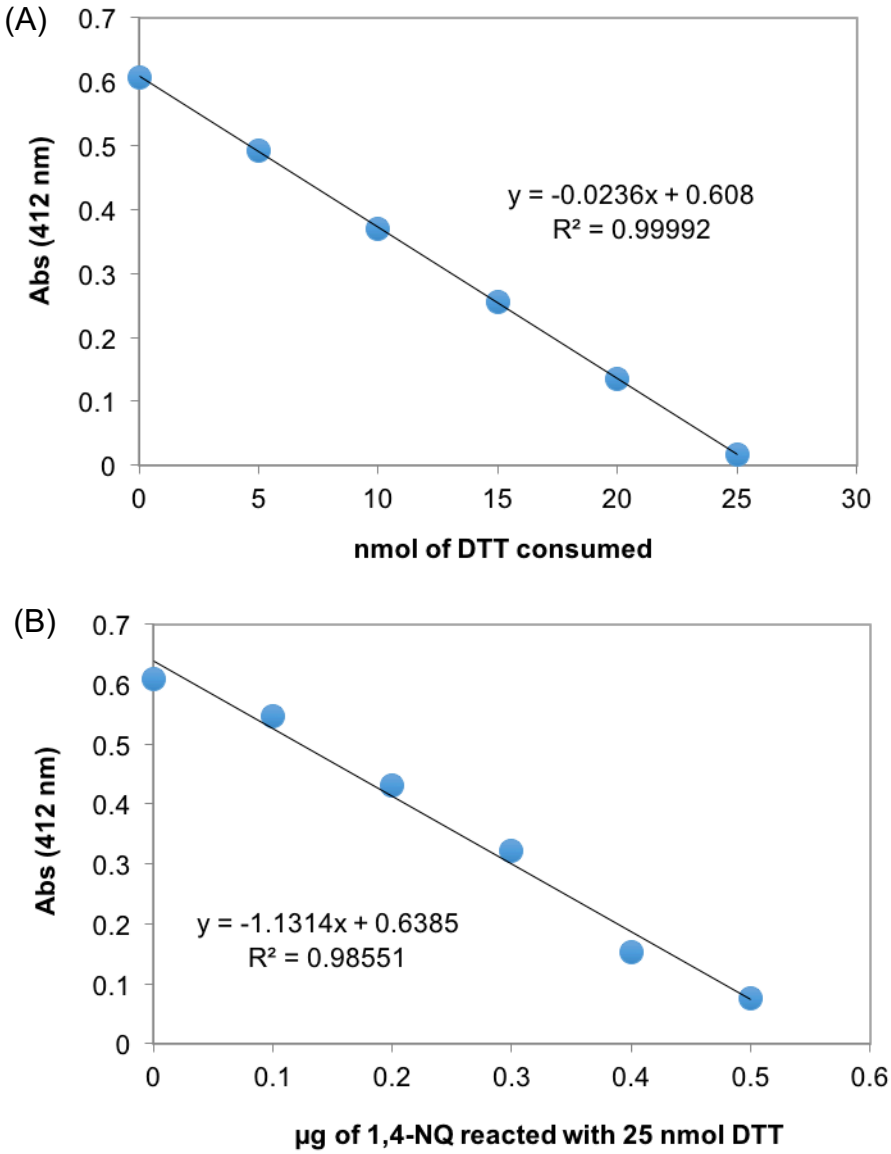

Figure A.2. Calibration curves for the measured absorbance versus (A) nmol of DTT consumed and (B) various amount of 1,4-NQ reacted with 25 nmol DTT.

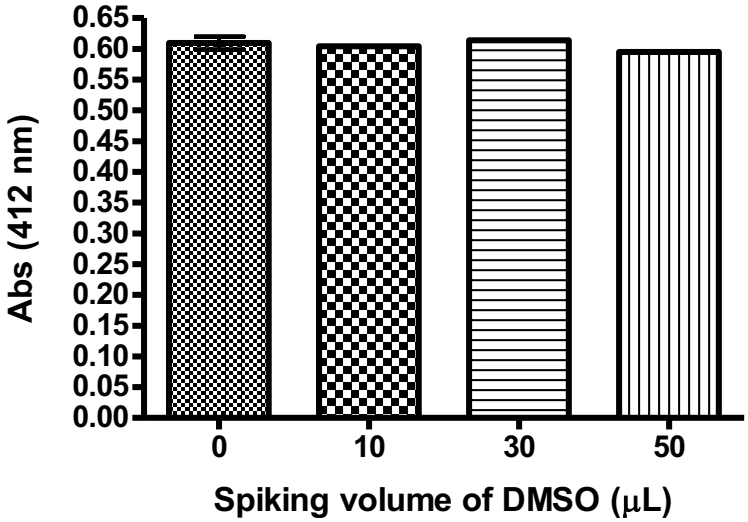

Figure A.3. DMSO consuming DTT was negligible up to a spiking volume of 30 μL. However, with a larger spiking volume (i.e., 50 μL), a slightly decreasing absorbance at 412 nm (by 2%) was observed.

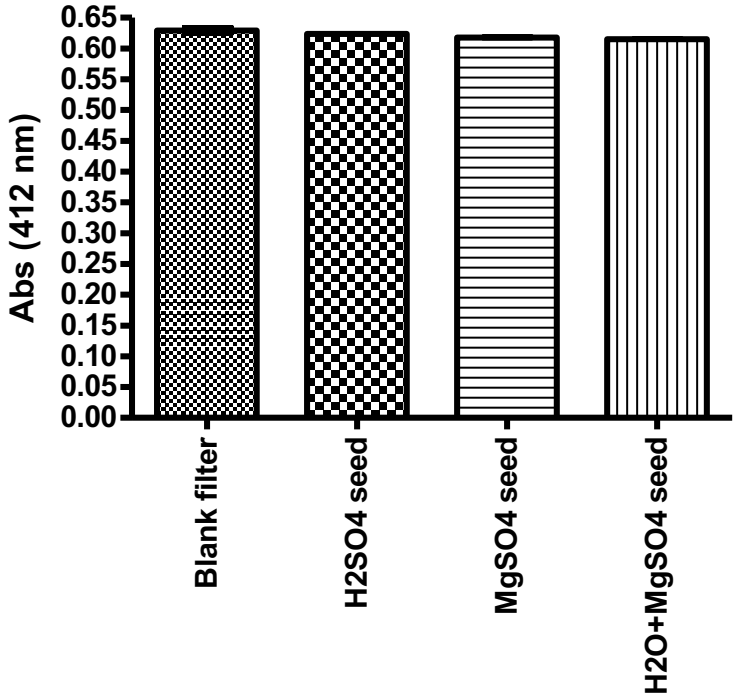

Figure A.4. To examine the effects of aerosol acidity and the presence of Mg^{2+} on DTT responses, H_2SO_4 and $MgSO_4$ aerosols were atomized separately into the chamber and collected filter samples (n=3) to compare with the responses from acidified sulfate aerosols (1:1 $MgSO_4$:H_2SO_4). No significant difference was observed compared to the blank filter samples.

APPENDIX B

Additional Characterization Results of Exposure Conditions

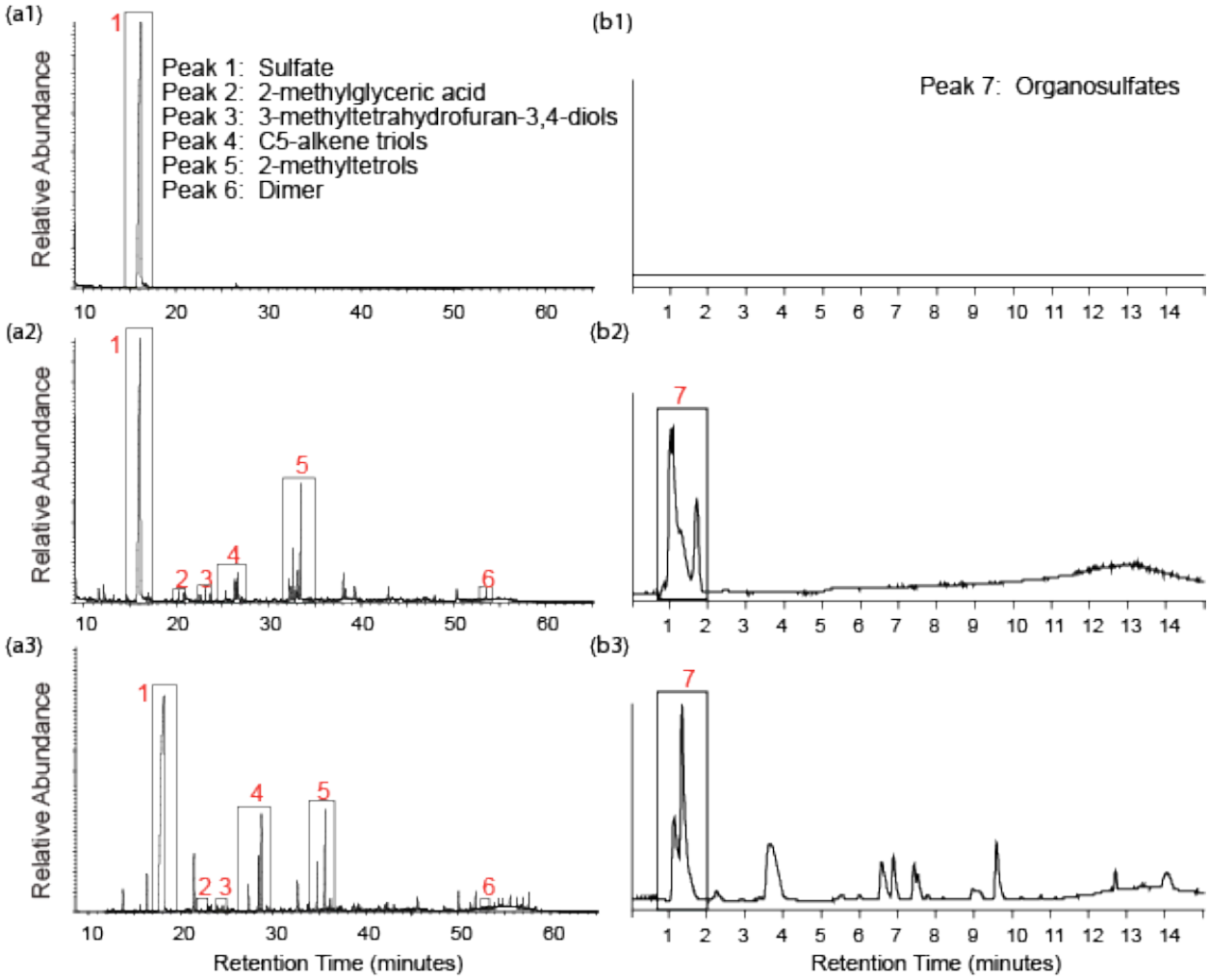

Figure B.1. (a) GC/EI-MS total ion chromatograms (TICs) and (b) UPLC/ESI-HR-QTOFMS base peak chromatograms (BPCs) from a (1) dark control chamber experiment, (2) isoprene-derived SOA exposure chamber experiment, and (3) $PM_{2.5}$ sample collected from Yorkville, GA during summer 2010.

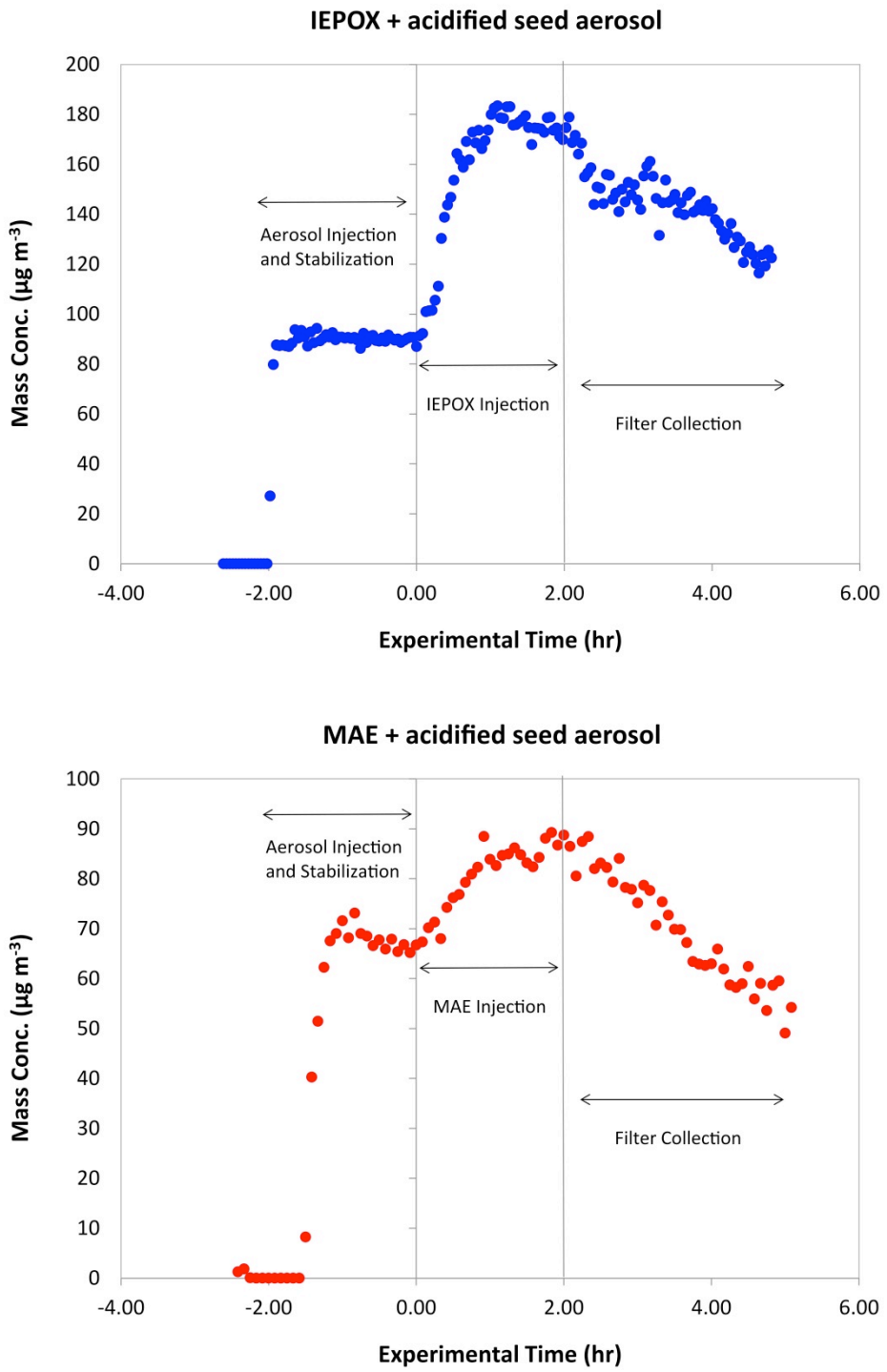

Figure B.2. Time profiles of measured aerosol mass concentrations during the reactive uptake of 166 (A) *trans*-β-IEPOX, and (B) MAE by acidified sulfate aerosols in chamber experiments.

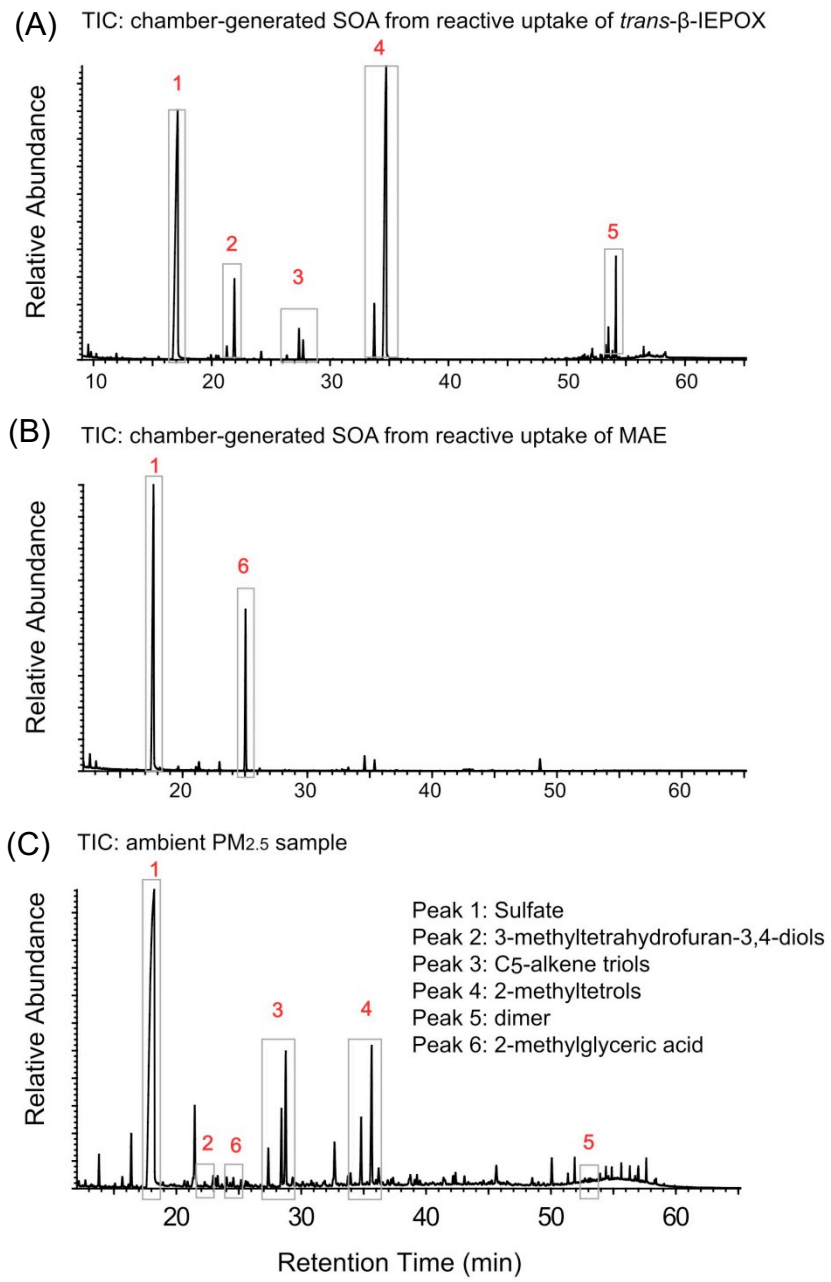

Figure B.3. GC/MS total ion current chromatograms (TICs) of TMS-derivatized particle-phase reaction products from reactive uptake of (A) *trans*-β-IEPOX and (B) MAE onto acidified sulfate seed aerosol in chamber experiments, and (C) $PM_{2.5}$ field sample from Yorkville, GA. Mixtures of isomeric SOA products are grouped as one peak.

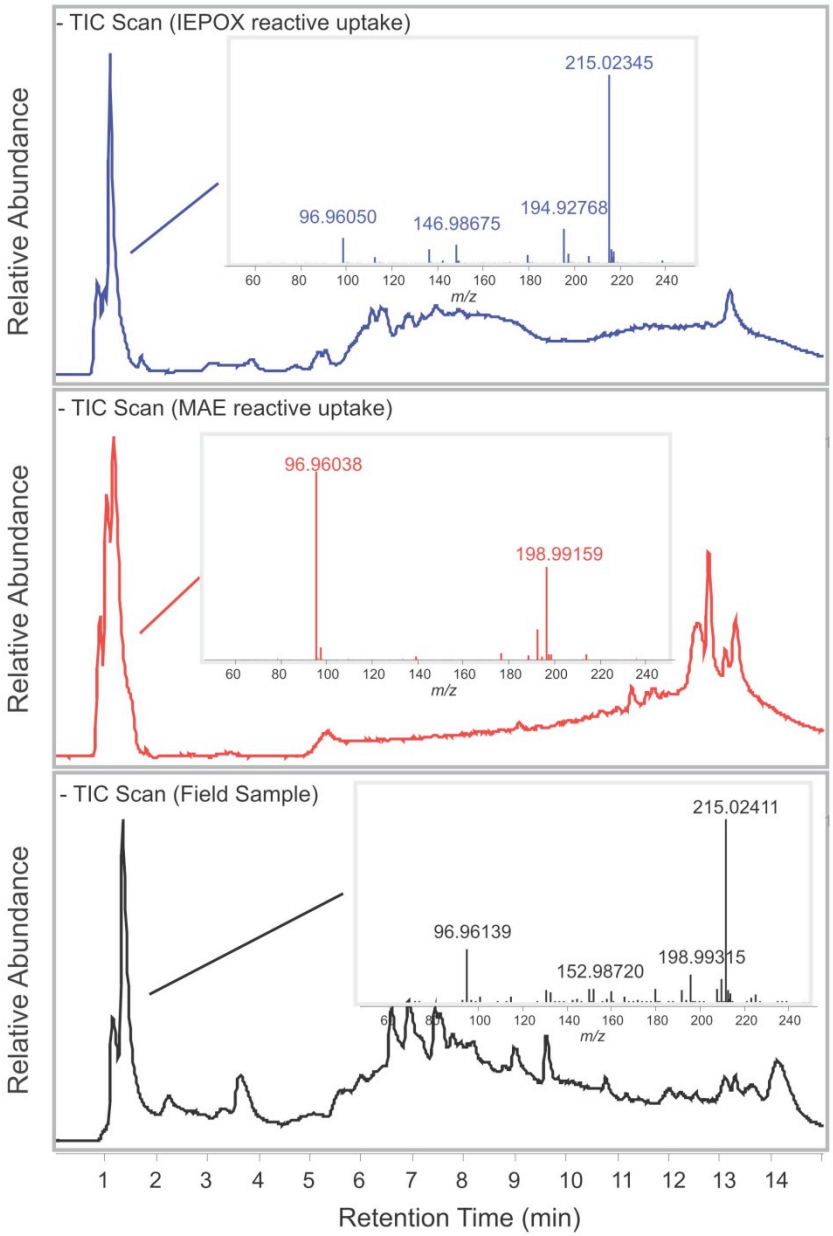

Figure B.4. UPLC/ESI-HR-QTOFMS total ion current chromatograms (TICs) of particle-phase 176 reaction products from reactive uptake of (A) *trans*-β-IEPOX and (B) MAE onto acidified 177 sulfate seed aerosol in chamber experiments, and (C) a $PM_{2.5}$ field sample from Yorkville, GA. 178

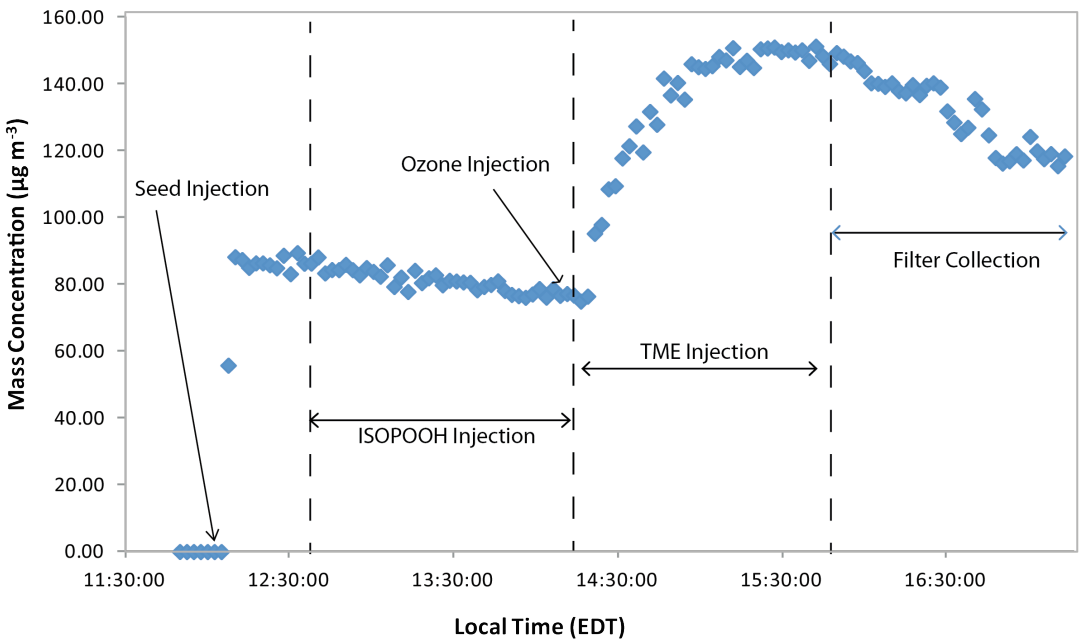

Figure B.5. Experimental time profile of measured aerosol mass concentrations during ISOPOOH oxidation experiments.

Appendix C

Additional Results from the DTT Assay

Table C.1. DTT activity of PM constituents measured in this study. Results in this study are expressed as mean ± standard error of the mean (SEM), n=3 for each sample.

Sample	DTT activity (nmol of DTT consumed/min/µg sample)
Pure Compounds	
IEPOX	$7.00 \pm 1.39 \times 10^{-5}$
2-MT	$4.44 \pm 0.92 \times 10^{-5}$
2-MT_OS	$5.77 \pm 2.07 \times 10^{-5}$
MAE	$9.84 \pm 0.97 \times 10^{-5}$
2-MG	$2.51 \pm 0.37 \times 10^{-4}$
2-MG_OS	$7.58 \pm 1.14 \times 10^{-5}$
ISOPOOH	$4.90 \pm 2.20 \times 10^{-1}$
Outdoor Chamber Samples	
Isoprene SOA	$2.10 \pm 0.22 \times 10^{-3}$
MACR SOA	$2.30 \pm 0.27 \times 10^{-3}$
Indoor Chamber Samples	
IEPOX-derived SOA	$1.79 \pm 0.16 \times 10^{-3}$
MAE-derived SOA	$3.13 \pm 0.30 \times 10^{-3}$

Table C.2. Means Comparison (Fisher Test) of Isoprene SOA Types

Comparisons of Aerosol Type	MeanDiff	SEM	t Value	Prob	Alpha	Sig	LCL	UCL
MACR SOA vs. isoprene SOA	1.64E-04	2.58E-04	0.6381	0.5413	0.05	0	-4.30E-04	7.59E-04
IEPOX SOA vs. isoprene SOA	-4.93E-04	2.58E-04	-1.9133	0.0921	0.05	0	-1.09E-03	1.01E-04
IEPOX SOA vs. MACR SOA	-6.58E-04	2.58E-04	-2.5514	0.0341	0.05	1	-1.25E-03	-6.32E-05
MAE SOA vs. isoprene SOA	4.30E-04	2.58E-04	1.6694	0.1336	0.05	0	-1.64E-04	1.02E-03
MAE SOA vs. MACR SOA	2.66E-04	2.58E-04	1.0313	0.3326	0.05	0	-3.29E-04	8.60E-04
MAE SOA vs. IEPOX SOA	9.23E-04	2.58E-04	3.5827	0.0072	0.05	1	3.29E-04	1.52E-03

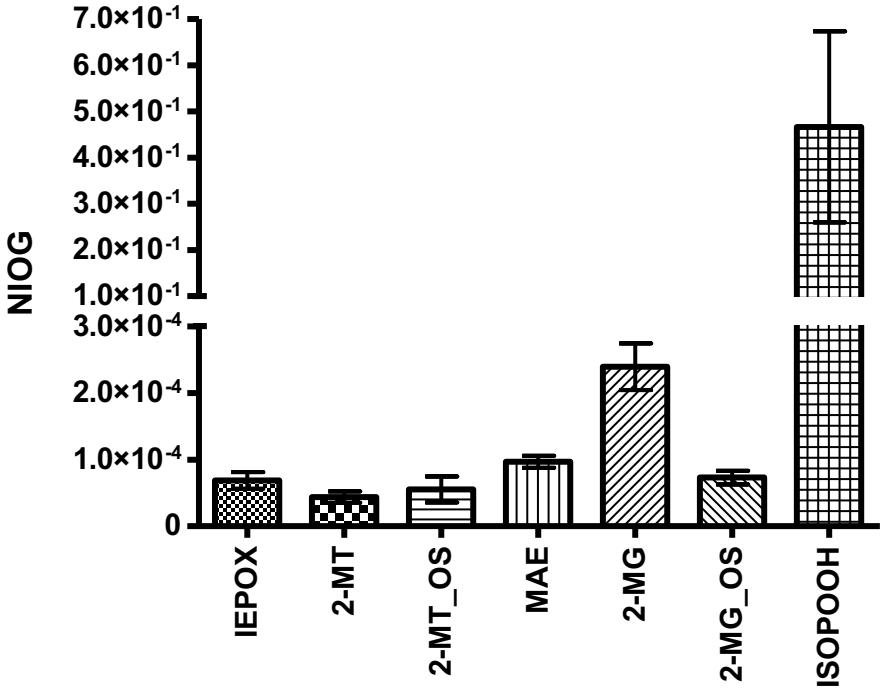

Figure C.1 NIOG of isoprene-derived epoxides (IEPOX and MAE), their hydrolysis products (2-MT and 2-MG), their organosulfate derivatives (2-MT_OS and 2-MG_OS), and the isoprene-derived hydroxyhydroperoxide (ISOPOOH) that are known to contribute to ambient SOA.

APPENDIX D

Cytotoxicity Measurements of Exposure Conditions

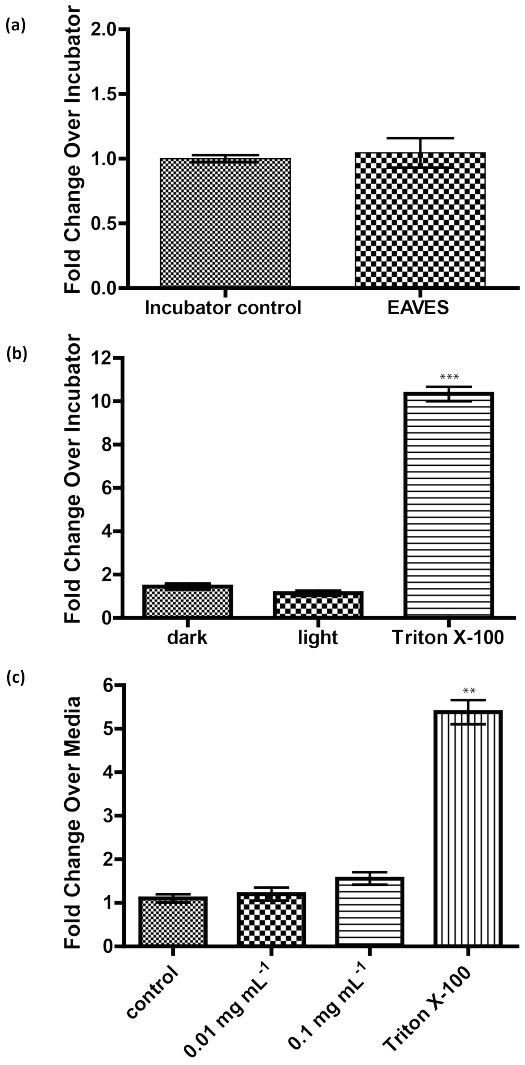

Figure D.1. LDH release for (a) clean air controls, (b) EAVES exposures, normalized to incubator control, and (c) resuspension exposures, normalized to KBM only control. **$p<0.005$ and ***$p<0.0005$.

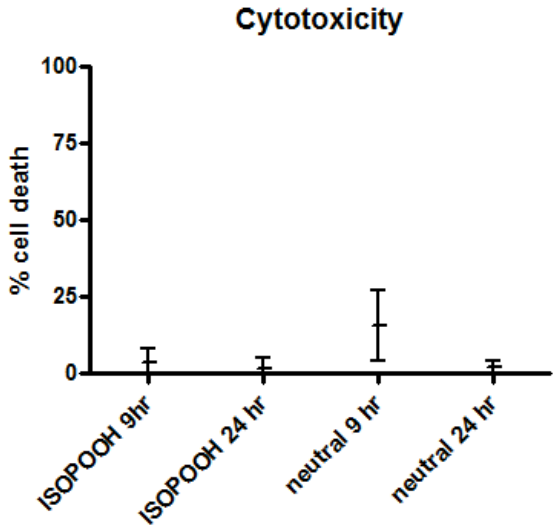

Figure D.2. Cytotoxicity for each exposure type for the ISOPOOH-derived SOA system represented as % cell death determined by LDH assay.

Appendix E

Full Lists of Genes Analyzed and Additional Gene Expression Data of Exposures

Table E.1. Gene symbols and full names of 84 oxidative stress-associated genes and housekeeping genes included in RT² Profiler™ PCR Array Human Oxidative Stress Pathway Plus (PAHS-065Y).

#	Gene Symbol	Full Name
1	*ALB*	Albumin
2	*ALOX12*	Arachidonate 12-lipoxygenase
3	*AOX1*	Aldehyde oxidase 1
4	*APOE*	Apolipoprotein E
5	*ATOX1*	ATX1 antioxidant protein 1 homolog (yeast)
6	*BNIP3*	BCL2/adenovirus E1B 19kDa interacting protein 3
7	*CAT*	Catalase
8	*CCL5*	Chemokine (C-C motif) ligand 5
9	*CCS*	Copper chaperone for superoxide dismutase
10	*CYBB*	Cytochrome b-245, beta polypeptide
11	*CYGB*	Cytoglobin
12	*DHCR24*	24-dehydrocholesterol reductase
13	*DUOX1*	Dual oxidase 1
14	*DUOX2*	Dual oxidase 2
15	*DUSP1*	Dual specificity phosphatase 1
16	*EPHX2*	Epoxide hydrolase 2, cytoplasmic
17	*EPX*	Eosinophil peroxidase
18	*FOXM1*	Forkhead box M1
19	*FTH1*	Ferritin, heavy polypeptide 1
20	*GCLC*	Glutamate-cysteine ligase, catalytic subunit
21	*GPX1*	Glutathione peroxidase 1
22	*GPX2*	Glutathione peroxidase 2 (gastrointestinal)
23	*GPX3*	Glutathione peroxidase 3 (plasma)
24	*GPX4*	Glutathione peroxidase 4 (phospholipid hydroperoxidase)
25	*GPX5*	Glutathione peroxidase 5 (epididymal androgen-related protein)
26	*GSR*	Glutathione reductase
27	*GSS*	Glutathione synthetase
28	*GSTP1*	Glutathione S-transferase pi 1
29	*GSTZ1*	Glutathione transferase zeta 1
30	*HSPA1A*	Heat shock 70kDa protein 1A
31	*KRT1*	Keratin 1

32	*LPO*	Lactoperoxidase
33	*MB*	Myoglobin
34	*MBL2*	Mannose-binding lectin (protein C) 2, soluble
35	*MPO*	Myeloperoxidase
36	*MPV17*	MpV17 mitochondrial inner membrane protein
37	*MSRA*	Methionine sulfoxide reductase A
38	*MT3*	Metallothionein 3
39	*NCF1*	Neutrophil cytosolic factor 1
40	*NCF2*	Neutrophil cytosolic factor 2
41	*NOS2*	Nitric oxide synthase 2, inducible
42	*NOX4*	NADPH oxidase 4
43	*NOX5*	NADPH oxidase, EF-hand calcium binding domain 5
44	*NUDT1*	Nudix (nucleoside diphosphate linked moiety X)-type motif 1
45	*PDLIM1*	PDZ and LIM domain 1
46	*PRDX1*	Peroxiredoxin 1
47	*PRDX2*	Peroxiredoxin 2
48	*PRDX3*	Peroxiredoxin 3
49	*PRDX4*	Peroxiredoxin 4
50	*PRDX5*	Peroxiredoxin 5
51	*PRDX6*	Peroxiredoxin 6
52	*PRNP*	Prion protein
53	*PTGS1*	Prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)
54	*PTGS2*	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)
55	*RNF7*	Ring finger protein 7
56	*VIMP*	Selenoprotein S
57	*SEPP1*	Selenoprotein P, plasma, 1
58	*SFTPD*	Surfactant protein D
59	*SIRT2*	Sirtuin 2
60	*SOD1*	Superoxide dismutase 1, soluble
61	*SOD2*	Superoxide dismutase 2, mitochondrial
62	*SOD3*	Superoxide dismutase 3, extracellular
63	*SQSTM1*	Sequestosome 1
64	*SRXN1*	Sulfiredoxin 1
65	*TPO*	Thyroid peroxidase
66	*TTN*	Titin
67	*TXNRD2*	Thioredoxin reductase 2
68	*UCP2*	Uncoupling protein 2 (mitochondrial, proton carrier)
69	*AKR1C2*	Aldo-keto reductase family 1, member C2 (dihydrodiol dehydrogenase 2; bile acid binding protein; 3-alpha hydroxysteroid dehydrogenase, type III)
70	*BAG2*	BCL2-associated athanogene 2
71	*FHL2*	Four and a half LIM domains 2

72	*GCLM*	Glutamate-cysteine ligase, modifier subunit
73	*GLA*	Galactosidase, alpha
74	*HMOX1*	Heme oxygenase (decycling) 1
75	*HSP90AA1*	Heat shock protein 90kDa alpha (cytosolic), class A member 1
76	*LHPP*	Phospholysine phosphohistidine inorganic pyrophosphate phosphatase
77	*NCOA7*	Nuclear receptor coactivator 7
78	*NQO1*	NAD(P)H dehydrogenase, quinone 1
79	*PTGR1*	Prostaglandin reductase 1
80	*SLC7A11*	Solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11
81	*SPINK1*	Serine peptidase inhibitor, Kazal type 1
82	*TRAPPC6A*	Trafficking protein particle complex 6A
83	*TXN*	Thioredoxin
84	*TXNRD1*	Thioredoxin reductase 1
Housekeeping Genes	*ACTB*	Actin, beta
	B2M	Beta-2-microglobulin
	GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
	HPRT1	Hypoxanthine phosphoribosyltransferase 1
	RPLP0	Ribosomal protein, large, P0

Table E.2. Gene symbols and full names of 249 Inflammation-associated genes and housekeeping genes included in nCounter® GX Human Inflammation Kit.

#	Gene Symbol	Full Name
1	*AGER*	advanced glycosylation end product-specific receptor
2	*ALOX12*	arachidonate 12-lipoxygenase
3	*ALOX15*	arachidonate 15-lipoxygenase
4	*ALOX5*	arachidonate 5-lipoxygenase
5	*AREG*	amphiregulin
6	*ARG1*	arginase, liver
7	*ATF2*	activating transcription factor 2
8	*BCL2L1*	BCL2-like 1
9	*BCL6*	B-cell CLL/lymphoma 6
10	*BIRC2*	baculoviral IAP repeat containing 2
11	*C1QA*	complement component 1, q subcomponent, A chain
12	*C1QB*	complement component 1, q subcomponent, B chain
13	*C1R*	complement component 1, r subcomponent
14	*C1S*	complement component 1, s subcomponent
15	*C2*	complement component 2
16	*C3*	complement component 3
17	*C3AR1*	complement component 3a receptor 1
18	*C4A*	complement component 4A (Rodgers blood group)
19	*C5*	complement component 5
20	*C6*	complement component 6
21	*C7*	complement component 7
22	*C8A*	complement component 8, alpha polypeptide
23	*C8B*	complement component 8, beta polypeptide
24	*C9*	complement component 9
25	*CCL11*	chemokine (C-C motif) ligand 11
26	*CCL13*	chemokine (C-C motif) ligand 13
27	*CCL16*	chemokine (C-C motif) ligand 16
28	*CCL17*	chemokine (C-C motif) ligand 17
29	*CCL19*	chemokine (C-C motif) ligand 19
30	*CCL2*	chemokine (C-C motif) ligand 2
31	*CCL20*	chemokine (C-C motif) ligand 20
32	*CCL21*	chemokine (C-C motif) ligand 21
33	*CCL22*	chemokine (C-C motif) ligand 22
34	*CCL23*	chemokine (C-C motif) ligand 23
35	*CCL24*	chemokine (C-C motif) ligand 24
36	*CCL3*	chemokine (C-C motif) ligand 3

37	*CCL4*	chemokine (C-C motif) ligand 4
38	*CCL5*	chemokine (C-C motif) ligand 5
39	*CCL7*	chemokine (C-C motif) ligand 7
40	*CCL8*	chemokine (C-C motif) ligand 8
41	*CCR1*	chemokine (C-C motif) receptor 1
42	*CCR2*	chemokine (C-C motif) receptor 2
43	*CCR3*	chemokine (C-C motif) receptor 3
44	*CCR4*	chemokine (C-C motif) receptor 4
45	*CCR7*	chemokine (C-C motif) receptor 7
46	*CD163*	CD163 molecule
47	*CD4*	CD4 molecule
48	*CD40*	CD40 molecule, TNF receptor superfamily member 5
49	*CD40LG*	CD40 ligand
50	*CD55*	CD55 molecule, decay accelerating factor for complement (Cromer blood group)
51	*CD86*	CD86 molecule
52	*CDC42*	cell division cycle 42 (GTP binding protein, 25kDa)
53	*CEBPB*	CCAAT/enhancer binding protein (C/EBP), beta
54	*CFB*	complement factor B
55	*CFD*	complement factor D (adipsin)
56	*CFL1*	cofilin 1 (non-muscle)
57	*CREB1*	cAMP responsive element binding protein 1
58	*CRP*	C-reactive protein, pentraxin-related
59	*CSF1*	colony stimulating factor 1 (macrophage)
60	*CSF2*	colony stimulating factor 2 (granulocyte-macrophage)
61	*CSF3*	colony stimulating factor 3 (granulocyte)
62	*CXCL1*	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)
63	*CXCL10*	chemokine (C-X-C motif) ligand 10
64	*CXCL2*	chemokine (C-X-C motif) ligand 2
65	*CXCL3*	chemokine (C-X-C motif) ligand 3
66	*CXCL5*	chemokine (C-X-C motif) ligand 5
67	*CXCL6*	chemokine (C-X-C motif) ligand 6 (granulocyte chemotactic protein 2)
68	*CXCL9*	chemokine (C-X-C motif) ligand 9
69	*CXCR1*	chemokine (C-X-C motif) receptor 1
70	*CXCR2*	chemokine (C-X-C motif) receptor 2
71	*CXCR4*	chemokine (C-X-C motif) receptor 4
72	*CYSLTR1*	cysteinyl leukotriene receptor 1
73	*CYSLTR2*	cysteinyl leukotriene receptor 2

74	*DAXX*	death-domain associated protein
75	*DDIT3*	DNA-damage-inducible transcript 3
76	*DEFA1*	defensin, alpha 1
77	*ELK1*	ELK1, member of ETS oncogene family
78	*FASLG*	Fas ligand (TNF superfamily, member 6)
79	*FLT1*	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)
80	*FOS*	FBJ murine osteosarcoma viral oncogene homolog
81	*FXYD2*	FXYD domain containing ion transport regulator 2
82	*GNAQ*	guanine nucleotide binding protein (G protein), q polypeptide
83	*GNAS*	GNAS complex locus
84	*GNB1*	guanine nucleotide binding protein (G protein), beta polypeptide 1
85	*GNGT1*	guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 1
86	*GRB2*	growth factor receptor-bound protein 2
87	*HDAC4*	histone deacetylase 4
88	*HIF1A*	hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)
89	*HLA-DRA*	major histocompatibility complex, class II, DR alpha
90	*HLA-DRB1*	major histocompatibility complex, class II, DR beta 1
91	*HMGB1*	high mobility group box 1
92	*HMGB2*	high mobility group box 2
93	*HMGN1*	high mobility group nucleosome binding domain 1
94	*HRAS*	v-Ha-ras Harvey rat sarcoma viral oncogene homolog
95	*HSH2D*	hematopoietic SH2 domain containing
96	*HSPB1*	heat shock 27kDa protein 1
97	*HSPB2*	heat shock 27kDa protein 2
98	*IFI44*	interferon-induced protein 44
99	*IFIT1*	interferon-induced protein with tetratricopeptide repeats 1
100	*IFIT2*	interferon-induced protein with tetratricopeptide repeats 2
101	*IFIT3*	interferon-induced protein with tetratricopeptide repeats 3
102	*IFNA1*	interferon, alpha 1
103	*IFNB1*	interferon, beta 1, fibroblast
104	*IFNG*	interferon, gamma
105	*IL10*	interleukin 10
106	*IL10RB*	interleukin 10 receptor, beta
107	*IL11*	interleukin 11
108	*IL12A*	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)
109	*IL12B*	interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic

		lymphocyte maturation factor 2, p40)
110	*IL13*	interleukin 13
111	*IL15*	interleukin 15
112	*IL17A*	interleukin 17A
113	*IL18*	interleukin 18 (interferon-gamma-inducing factor)
114	*IL18RAP*	interleukin 18 receptor accessory protein
115	*IL1A*	interleukin 1, alpha
116	*IL1B*	interleukin 1, beta
117	*IL1R1*	interleukin 1 receptor, type I
118	*IL1RAP*	interleukin 1 receptor accessory protein
119	*IL1RN*	interleukin 1 receptor antagonist
120	*IL2*	interleukin 2
121	*IL21*	interleukin 21
122	*IL22*	interleukin 22
123	*IL22RA2*	interleukin 22 receptor, alpha 2
124	*IL23A*	interleukin 23, alpha subunit p19
125	*IL23R*	interleukin 23 receptor
126	*IL3*	interleukin 3 (colony-stimulating factor, multiple)
127	*IL4*	interleukin 4
128	*IL5*	interleukin 5 (colony-stimulating factor, eosinophil)
129	*IL6*	interleukin 6 (interferon, beta 2)
130	*IL6R*	interleukin 6 receptor
131	*IL7*	interleukin 7
132	*IL8*	interleukin 8
133	*IL9*	interleukin 9
134	*IRF1*	interferon regulatory factor 1
135	*IRF3*	interferon regulatory factor 3
136	*IRF5*	interferon regulatory factor 5
137	*IRF7*	interferon regulatory factor 7
138	*ITGB2*	integrin, beta 2 (complement component 3 receptor 3 and 4 subunit)
139	*JUN*	jun proto-oncogene
140	*KEAP1*	kelch-like ECH-associated protein 1
141	*KNG1*	kininogen 1
142	*LIMK1*	LIM domain kinase 1
143	*LTA*	lymphotoxin alpha (TNF superfamily, member 1)
144	*LTB*	lymphotoxin beta (TNF superfamily, member 3)
145	*LTB4R*	leukotriene B4 receptor
146	*LTB4R2*	leukotriene B4 receptor 2
147	*LY96*	lymphocyte antigen 96

148	*MAFF*	v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)
149	*MAFG*	v-maf musculoaponeurotic fibrosarcoma oncogene homolog G (avian)
150	*MAFK*	v-maf musculoaponeurotic fibrosarcoma oncogene homolog K (avian)
151	*MAP2K1*	mitogen-activated protein kinase kinase 1
152	*MAP2K4*	mitogen-activated protein kinase kinase 4
153	*MAP2K6*	mitogen-activated protein kinase kinase 6
154	*MAP3K1*	mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase
155	*MAP3K5*	mitogen-activated protein kinase kinase kinase 5
156	*MAP3K7*	mitogen-activated protein kinase kinase kinase 7
157	*MAP3K9*	mitogen-activated protein kinase kinase kinase 9
158	*MAPK1*	mitogen-activated protein kinase 1
159	*MAPK14*	mitogen-activated protein kinase 14
160	*MAPK3*	mitogen-activated protein kinase 3
161	*MAPK8*	mitogen-activated protein kinase 8
162	*MAPKAPK2*	mitogen-activated protein kinase-activated protein kinase 2
163	*MAPKAPK5*	mitogen-activated protein kinase-activated protein kinase 5
164	*MASP1*	mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Ra-reactive factor)
165	*MASP2*	mannan-binding lectin serine peptidase 2
166	*MAX*	MYC associated factor X
167	*MBL2*	mannose-binding lectin (protein C) 2, soluble
168	*MEF2A*	myocyte enhancer factor 2A
169	*MEF2BNB-MEF2B*	MEF2BNB-MEF2B readthrough
170	*MEF2C*	myocyte enhancer factor 2C
171	*MEF2D*	myocyte enhancer factor 2D
172	*MKNK1*	MAP kinase interacting serine/threonine kinase 1
173	*MMP3*	matrix metallopeptidase 3 (stromelysin 1, progelatinase)
174	*MMP9*	matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)
175	*MRC1*	mannose receptor, C type 1
176	*MX1*	myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse)
177	*MX2*	myxovirus (influenza virus) resistance 2 (mouse)
178	*MYC*	v-myc myelocytomatosis viral oncogene homolog (avian)
179	*MYD88*	myeloid differentiation primary response gene (88)
180	*MYL2*	myosin, light chain 2, regulatory, cardiac, slow

181	*NFATC3*	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 3
182	*NFE2L2*	nuclear factor (erythroid-derived 2)-like 2
183	*NFKB1*	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1
184	*NLRP3*	NLR family, pyrin domain containing 3
185	*NOD1*	nucleotide-binding oligomerization domain containing 1
186	*NOD2*	nucleotide-binding oligomerization domain containing 2
187	*NOS2*	nitric oxide synthase 2, inducible
188	*NOX1*	NADPH oxidase 1
189	*NR3C1*	nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)
190	*OAS2*	2'-5'-oligoadenylate synthetase 2, 69/71kDa
191	*OASL*	2'-5'-oligoadenylate synthetase-like
192	*OXER1*	oxoeicosanoid (OXE) receptor 1
193	*PDGFA*	platelet-derived growth factor alpha polypeptide
194	*PIK3C2G*	phosphatidylinositol-4-phosphate 3-kinase, catalytic subunit type 2 gamma
195	*PLA2G4A*	phospholipase A2, group IVA (cytosolic, calcium-dependent)
196	*PLCB1*	phospholipase C, beta 1 (phosphoinositide-specific)
197	*PPP1R12B*	protein phosphatase 1, regulatory subunit 12B
198	*PRKCA*	protein kinase C, alpha
199	*PRKCB*	protein kinase C, beta
200	*PTGDR2*	prostaglandin D2 receptor 2
201	*PTGER1*	prostaglandin E receptor 1 (subtype EP1), 42kDa
202	*PTGER2*	prostaglandin E receptor 2 (subtype EP2), 53kDa
203	*PTGER3*	prostaglandin E receptor 3 (subtype EP3)
204	*PTGER4*	prostaglandin E receptor 4 (subtype EP4)
205	*PTGFR*	prostaglandin F receptor (FP)
206	*PTGIR*	prostaglandin I2 (prostacyclin) receptor (IP)
207	*PTGS1*	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)
208	*PTGS2*	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)
209	*PTK2*	PTK2 protein tyrosine kinase 2
210	*RAC1*	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
211	*RAF1*	v-raf-1 murine leukemia viral oncogene homolog 1
212	*RAPGEF2*	Rap guanine nucleotide exchange factor (GEF) 2
213	*RELA*	v-rel reticuloendotheliosis viral oncogene homolog A (avian)
214	*RELB*	v-rel reticuloendotheliosis viral oncogene homolog B

215	*RHOA*	ras homolog family member A
216	*RIPK1*	receptor (TNFRSF)-interacting serine-threonine kinase 1
217	*RIPK2*	receptor-interacting serine-threonine kinase 2
218	*ROCK2*	Rho-associated, coiled-coil containing protein kinase 2
219	*RPS6KA5*	ribosomal protein S6 kinase, 90kDa, polypeptide 5
220	*SHC1*	SHC (Src homology 2 domain containing) transforming protein 1
221	*SMAD7*	SMAD family member 7
222	*STAT1*	signal transducer and activator of transcription 1, 91kDa
223	*STAT2*	signal transducer and activator of transcription 2, 113kDa
224	*STAT3*	signal transducer and activator of transcription 3 (acute-phase response factor)
225	*TBXA2R*	thromboxane A2 receptor
226	*TCF4*	transcription factor 4
227	*TGFB1*	transforming growth factor, beta 1
228	*TGFB2*	transforming growth factor, beta 2
229	*TGFB3*	transforming growth factor, beta 3
230	*TGFBR1*	transforming growth factor, beta receptor 1
231	*TLR1*	toll-like receptor 1
232	*TLR2*	toll-like receptor 2
233	*TLR3*	toll-like receptor 3
234	*TLR4*	toll-like receptor 4
235	*TLR5*	toll-like receptor 5
236	*TLR6*	toll-like receptor 6
237	*TLR7*	toll-like receptor 7
238	*TLR8*	toll-like receptor 8
239	*TLR9*	toll-like receptor 9
240	*TNF*	tumor necrosis factor
241	*TNFAIP3*	tumor necrosis factor, alpha-induced protein 3
242	*TNFSF14*	tumor necrosis factor (ligand) superfamily, member 14
243	*TOLLIP*	toll interacting protein
244	*TRADD*	TNFRSF1A-associated via death domain
245	*TRAF2*	TNF receptor-associated factor 2
246	*TREM2*	triggering receptor expressed on myeloid cells 2
247	*TSLP*	thymic stromal lymphopoietin
248	*TWIST2*	twist homolog 2 (Drosophila)
249	*TYROBP*	TYRO protein tyrosine kinase binding protein
Internal Reference Genes	*CLTC*	clathrin, heavy chain (Hc)
	GAPDH	glyceraldehyde-3-phosphate dehydrogenase
	GUSB	glucuronidase, beta
	HPRT1	hypoxanthine phosphoribosyltransferase 1

	PGK1	phosphoglycerate kinase 1
	TUBB	tubulin, beta class I

Table E.3. Pathways associated with isoprene SOA exposure.

#	pathway name	set size	candidates contained	members_input_overlap	p-value	q-value	pathway source
1	Photodynamic therapy-induced NFE2L2 (NRF2) survival signaling	23	6 (26.1%)	*GCLM; FOS; HMOX1; JUN; GCLC; SRXN1*	1.30E-12	2.96E-10	Wikipathways
2	Oxidative Stress	30	6 (20.0%)	*FOS; HMOX1; GCLC; CAT; NOX4; TXNRD1*	7.58E-12	8.64E-10	Wikipathways
3	NRF2 pathway	142	8 (5.6%)	*SQSTM1; GCLM; HMOX1; GCLC; HSPA1A; MAFG; MAFF; TXNRD1*	5.77E-11	4.39E-09	Wikipathways
4	oxidative stress induced gene expression via nrf2	19	5 (26.3%)	*JUN; FOS; HMOX1; MAFF; MAFG*	1.12E-10	6.36E-09	BioCarta
5	Nuclear Receptors Meta-Pathway	316	9 (2.8%)	*SQSTM1; GCLM; JUN; HMOX1; GCLC; HSPA1A; TXNRD1; MAFF; MAFG*	1.26E-09	5.74E-08	Wikipathways
6	Tacrolimus/Cyclosporine Pathway, Pharmacodynamics	44	4 (9.1%)	*FOS; JUN; MAFF; MAFG*	8.88E-07	3.38E-05	PharmGKB
7	Transcriptional activation by NRF2	15	3 (20.0%)	*GCLM; HMOX1; GCLC*	2.05E-06	5.83E-05	Wikipathways
8	Quercetin and Nf-kB-AP-1 Induced Cell Apoptosis	15	3 (20.0%)	*FOS; JUN; MAFG*	2.05E-06	5.83E-05	Wikipathways
9	Cellular responses to stress	393	7 (1.8%)	*BAG2; FOS; JUN; CAT; HSPA1A; NOX4; TXNRD1*	2.91E-06	7.37E-05	Reactome
10	glutathione biosynthesis	3	2 (66.7%)	*GCLM; GCLC*	8.65E-06	1.97E-04	HumanCyc
11	MAPK targets/ Nuclear events mediated by MAP kinases	31	3 (9.7%)	*MEF2C; JUN; FOS*	1.99E-05	4.12E-04	Reactome
12	Detoxification of Reactive Oxygen Species	36	3 (8.6%)	*TXNRD1; NOX4; CAT*	2.88E-05	5.05E-04	Reactome
13	angiotensin ii mediated activation of jnk pathway via pyk2 dependent signaling	35	3 (8.6%)	*MEF2C; JUN; FOS*	2.88E-05	5.05E-04	BioCarta
14	Selenium Metabolism and Selenoproteins	38	3 (7.9%)	*FOS; JUN; TXNRD1*	3.70E-05	6.02E-04	Wikipathways
15	Glutathione conjugation	40	3 (7.7%)	*GCLM; GSTZ1; GCLC*	4.00E-05	6.08E-04	Reactome
16	γ-glutamyl cycle	6	2 (33.3%)	*GCLM; GCLC*	4.31E-05	6.14E-04	HumanCyc
17	tsp-1 induced apoptosis in microvascular	7	2 (28.6%)	*JUN; FOS*	6.03E-05	7.63E-04	BioCarta

	endothelial cell						
18	Oxidative Stress Regulatory Pathway (Erythrocyte)	7	2 (28.6%)	*CAT; TXNRD1*	6.03E-05	7.63E-04	PharmGKB
19	IL6-mediated signaling events	48	3 (6.2%)	*IL6R; JUN; FOS*	7.50E-05	9.00E-04	PID
20	Brain-Derived Neurotrophic Factor (BDNF) signaling pathway	144	4 (2.8%)	*MEF2C; SQSTM1; JUN; FOS*	1.00E-04	1.02E-03	Wikipathways
21	Beta-mercaptolactate-cysteine disulfiduria	9	2 (22.2%)	*GCLM; GCLC*	1.03E-04	1.02E-03	SMPDB
22	Cysteine Metabolism	9	2 (22.2%)	*GCLM; GCLC*	1.03E-04	1.02E-03	SMPDB
23	Cystinosis, ocular nonnephropathic	9	2 (22.2%)	*GCLM; GCLC*	1.03E-04	1.02E-03	SMPDB
24	RANKL-RANK (Receptor activator of NFKB (ligand)) Signaling Pathway	55	3 (5.5%)	*SQSTM1; JUN; FOS*	1.13E-04	1.07E-03	Wikipathways
25	mapkinase signaling pathway	57	3 (5.3%)	*MEF2C; JUN; FOS*	1.26E-04	1.08E-03	BioCarta
26	Activation of the AP-1 family of transcription factors	10	2 (20.0%)	*JUN; FOS*	1.29E-04	1.08E-03	Reactome
27	Gamma-glutamyl-transpeptidase deficiency	11	2 (18.2%)	*GCLM; GCLC*	1.57E-04	1.08E-03	SMPDB
28	5-oxoprolinase deficiency	11	2 (18.2%)	*GCLM; GCLC*	1.57E-04	1.08E-03	SMPDB
29	Gamma-Glutamyltransferase Deficiency	11	2 (18.2%)	*GCLM; GCLC*	1.57E-04	1.08E-03	SMPDB
30	Glutathione Metabolism	11	2 (18.2%)	*GCLM; GCLC*	1.57E-04	1.08E-03	SMPDB
31	Glutathione Synthetase Deficiency	11	2 (18.2%)	*GCLM; GCLC*	1.57E-04	1.08E-03	SMPDB
32	5-Oxoprolinuria	11	2 (18.2%)	*GCLM; GCLC*	1.57E-04	1.08E-03	SMPDB
33	pertussis toxin-insensitive ccr5 signaling in macrophage	11	2 (18.2%)	*JUN; FOS*	1.57E-04	1.08E-03	BioCarta
34	MAP kinase activation in TLR cascade	62	3 (4.8%)	*MEF2C; JUN; FOS*	1.61E-04	1.08E-03	Reactome
35	MAPK Signaling Pathway	168	4 (2.4%)	*MEF2C; HSPA1A; JUN; FOS*	1.82E-04	1.18E-03	Wikipathways

36	HIF-1-alpha transcription factor network	67	3 (4.5%)	*HMOX1; JUN; FOS*	2.03E-04	1.29E-03	PID
37	AP-1 transcription factor network	71	3 (4.2%)	*MAFG; JUN; FOS*	2.41E-04	1.49E-03	PID
38	Prostate Cancer	72	3 (4.2%)	*JUN; SPINK1; FOS*	2.52E-04	1.51E-03	Wikipathways
39	TRAF6 Mediated Induction of proinflammatory cytokines	74	3 (4.1%)	*MEF2C; JUN; FOS*	2.73E-04	1.60E-03	Reactome
40	Glutathione synthesis and recycling	16	2 (13.3%)	*GCLM; GCLC*	2.99E-04	1.66E-03	Reactome
41	repression of pain sensation by the transcriptional regulator dream	15	2 (13.3%)	*JUN; FOS*	2.99E-04	1.66E-03	BioCarta
42	IL6	77	3 (3.9%)	*IL6R; JUN; FOS*	3.07E-04	1.67E-03	NetPath
43	Regulation of nuclear SMAD2/3 signaling	79	3 (3.8%)	*MEF2C; JUN; FOS*	3.19E-04	1.69E-03	PID
44	cadmium induces dna synthesis and proliferation in macrophages	16	2 (12.5%)	*JUN; FOS*	3.41E-04	1.73E-03	BioCarta
45	calcium signaling by hbx of hepatitis b virus	16	2 (12.5%)	*JUN; FOS*	3.41E-04	1.73E-03	BioCarta
46	MyD88 cascade initiated on plasma membrane	82	3 (3.7%)	*MEF2C; JUN; FOS*	3.69E-04	1.75E-03	Reactome
47	Toll Like Receptor 10 (TLR10) Cascade	82	3 (3.7%)	*MEF2C; JUN; FOS*	3.69E-04	1.75E-03	Reactome
48	Toll Like Receptor 5 (TLR5) Cascade	82	3 (3.7%)	*MEF2C; JUN; FOS*	3.69E-04	1.75E-03	Reactome
49	TRAF6 mediated induction of NFkB and MAP kinases upon TLR7/8 or 9 activation	83	3 (3.6%)	*MEF2C; JUN; FOS*	3.83E-04	1.78E-03	Reactome
50	MyD88 dependent cascade initiated on endosome	85	3 (3.5%)	*MEF2C; JUN; FOS*	4.11E-04	1.84E-03	Reactome
51	Toll Like Receptor 7/8 (TLR7/8) Cascade	85	3 (3.5%)	*MEF2C; JUN; FOS*	4.11E-04	1.84E-03	Reactome
52	nerve growth factor pathway (ngf)	18	2 (11.1%)	*JUN; FOS*	4.34E-04	1.87E-03	BioCarta
53	mets affect on macrophage differentiation	18	2 (11.1%)	*JUN; FOS*	4.34E-04	1.87E-03	BioCarta
54	Toll Like Receptor 9	89	3 (3.4%)	*MEF2C; JUN; FOS*	4.70E-	1.98E-	Reactome

	(TLR9) Cascade				04	03	
55	Apoptosis Modulation and Signaling	92	3 (3.3%)	*HSPA1A; JUN; FOS*	5.18E-04	1.98E-03	Wikipathways
56	Apoptosis Modulation and Signaling	92	3 (3.3%)	*HSPA1A; JUN; FOS*	5.18E-04	1.98E-03	Wikipathways
57	Apoptosis Modulation and Signaling	92	3 (3.3%)	*HSPA1A; JUN; FOS*	5.18E-04	1.98E-03	Wikipathways
58	MyD88:Mal cascade initiated on plasma membrane	93	3 (3.2%)	*MEF2C; JUN; FOS*	5.35E-04	1.98E-03	Reactome
59	Toll Like Receptor TLR1:TLR2 Cascade	93	3 (3.2%)	*MEF2C; JUN; FOS*	5.35E-04	1.98E-03	Reactome
60	Toll Like Receptor TLR6:TLR2 Cascade	93	3 (3.2%)	*MEF2C; JUN; FOS*	5.35E-04	1.98E-03	Reactome
61	Toll Like Receptor 2 (TLR2) Cascade	93	3 (3.2%)	*MEF2C; JUN; FOS*	5.35E-04	1.98E-03	Reactome
62	Glutathione metabolism	20	2 (10.0%)	*GCLM; GCLC*	5.38E-04	1.98E-03	Wikipathways
63	igf-1 signaling pathway	21	2 (9.5%)	*JUN; FOS*	5.94E-04	2.14E-03	BioCarta
64	inhibition of cellular proliferation by gleevec	22	2 (9.1%)	*JUN; FOS*	6.53E-04	2.14E-03	BioCarta
65	PDGFR-alpha signaling pathway	22	2 (9.1%)	*JUN; FOS*	6.53E-04	2.14E-03	PID
66	Estrogen signaling pathway - Homo sapiens (human)	100	3 (3.0%)	*HSPA1A; JUN; FOS*	6.61E-04	2.14E-03	KEGG
67	TRIF-mediated TLR3/TLR4 signaling	101	3 (3.0%)	*MEF2C; JUN; FOS*	6.81E-04	2.14E-03	Reactome
68	MyD88-independent TLR3/TLR4 cascade	101	3 (3.0%)	*MEF2C; JUN; FOS*	6.81E-04	2.14E-03	Reactome
69	Toll Like Receptor 3 (TLR3) Cascade	101	3 (3.0%)	*MEF2C; JUN; FOS*	6.81E-04	2.14E-03	Reactome
70	2-Hydroxyglutric Aciduria (D And L Form)	23	2 (8.7%)	*GCLM; GCLC*	7.14E-04	2.14E-03	SMPDB
71	Homocarnosinosis	23	2 (8.7%)	*GCLM; GCLC*	7.14E-04	2.14E-03	SMPDB
72	Hyperinsulinism-Hyperammonemia Syndrome	23	2 (8.7%)	*GCLM; GCLC*	7.14E-04	2.14E-03	SMPDB
73	Succinic semialdehyde dehydrogenase deficiency	23	2 (8.7%)	*GCLM; GCLC*	7.14E-04	2.14E-03	SMPDB
74	4-Hydroxybutyric Aciduria/Succinic Semialdehyde Dehydrogenase Deficiency	23	2 (8.7%)	*GCLM; GCLC*	7.14E-04	2.14E-03	SMPDB

75	Glutamate Metabolism	23	2 (8.7%)	*GCLM; GCLC*	7.14E-04	2.14E-03	SMPDB
76	Estrogen signaling pathway	23	2 (8.7%)	*JUN; FOS*	7.14E-04	2.14E-03	Wikipathways
77	Urea cycle and metabolism of arginine, proline, glutamate, aspartate and asparagine	105	3 (2.9%)	*GCLM; GSTZ1; GCLC*	7.41E-04	2.19E-03	EHMN
78	EGF-Core	105	3 (2.9%)	*MEF2C; JUN; FOS*	7.62E-04	2.20E-03	Signalink
79	Senescence and Autophagy in Cancer	105	3 (2.9%)	*SQSTM1; JUN; IL6R*	7.62E-04	2.20E-03	Wikipathways
80	Physiological and Pathological Hypertrophy of the Heart	24	2 (8.3%)	*JUN; FOS*	7.78E-04	2.21E-03	Wikipathways
81	ErbB1 downstream signaling	107	3 (2.8%)	*MEF2C; JUN; FOS*	7.83E-04	2.21E-03	PID
82	Th17 cell differentiation - Homo sapiens (human)	107	3 (2.8%)	*IL6R; JUN; FOS*	8.05E-04	2.24E-03	KEGG
83	Phase II conjugation	112	3 (2.8%)	*GCLM; GSTZ1; GCLC*	8.27E-04	2.27E-03	Reactome
84	Disulfiram Action Pathway	25	2 (8.0%)	*GSTZ1; CAT*	8.45E-04	2.27E-03	SMPDB
85	tpo signaling pathway	25	2 (8.0%)	*JUN; FOS*	8.45E-04	2.27E-03	BioCarta
86	MAPK signaling pathway - Homo sapiens (human)	255	4 (1.6%)	*MEF2C; HSPA1A; JUN; FOS*	8.85E-04	2.35E-03	KEGG
87	Sulfur amino acid metabolism	27	2 (7.7%)	*GCLM; GCLC*	9.14E-04	2.40E-03	Reactome
88	S1P2 pathway	27	2 (7.4%)	*JUN; FOS*	9.86E-04	2.53E-03	PID
89	pdgf signaling pathway	27	2 (7.4%)	*JUN; FOS*	9.86E-04	2.53E-03	BioCarta
90	Activated TLR4 signalling	117	3 (2.6%)	*MEF2C; JUN; FOS*	1.04E-03	2.64E-03	Reactome
91	Glutamate Glutamine metabolism	28	2 (7.1%)	*GCLM; GCLC*	1.06E-03	2.66E-03	INOH
92	fc epsilon receptor i signaling in mast cells	29	2 (6.9%)	*JUN; FOS*	1.14E-03	2.82E-03	BioCarta
93	Calcium signaling in the CD4+ TCR pathway	30	2 (6.7%)	*JUN; FOS*	1.22E-03	2.99E-03	PID
94	Trans-sulfuration and one carbon metabolism	31	2 (6.5%)	*GCLM; GCLC*	1.30E-03	3.16E-03	Wikipathways
95	Toll Like Receptor 4 (TLR4) Cascade	128	3 (2.3%)	*MEF2C; JUN; FOS*	1.35E-03	3.23E-03	Reactome

96	IL12 signaling mediated by STAT4	32	2 (6.2%)	*JUN; FOS*	1.39E-03	3.23E-03	PID
97	Osteopontin-mediated events	32	2 (6.2%)	*JUN; FOS*	1.39E-03	3.23E-03	PID
98	bcr signaling pathway	32	2 (6.2%)	*JUN; FOS*	1.39E-03	3.23E-03	BioCarta
99	Osteoclast differentiation - Homo sapiens (human)	132	3 (2.3%)	*SQSTM1; JUN; FOS*	1.45E-03	3.30E-03	KEGG
100	role of egf receptor transactivation by gpcrs in cardiac hypertrophy	33	2 (6.1%)	*JUN; FOS*	1.47E-03	3.30E-03	BioCarta
101	Trk receptor signaling mediated by the MAPK pathway	33	2 (6.1%)	*MEF2C; FOS*	1.47E-03	3.30E-03	PID
102	TGF-beta Signaling Pathway	132	3 (2.3%)	*MEF2C; JUN; FOS*	1.48E-03	3.30E-03	Wikipathways
103	Signaling of Hepatocyte Growth Factor Receptor	34	2 (5.9%)	*JUN; FOS*	1.56E-03	3.46E-03	Wikipathways
104	Signaling mediated by p38-alpha and p38-beta	35	2 (5.7%)	*MEF2C; JUN*	1.66E-03	3.63E-03	PID
105	toll-like receptor pathway	36	2 (5.6%)	*JUN; FOS*	1.75E-03	3.81E-03	BioCarta
106	Regulation of toll-like receptor signaling pathway	143	3 (2.1%)	*SQSTM1; JUN; FOS*	1.86E-03	4.00E-03	Wikipathways
107	Validated transcriptional targets of AP1 family members Fra1 and Fra2	38	2 (5.3%)	*HMOX1; JUN*	1.95E-03	4.12E-03	PID
108	IL1-mediated signaling events	38	2 (5.3%)	*SQSTM1; JUN*	1.95E-03	4.12E-03	PID
109	signal transduction through il1r	39	2 (5.1%)	*JUN; FOS*	2.06E-03	4.30E-03	BioCarta
110	ErbB2/ErbB3 signaling events	40	2 (5.0%)	*JUN; FOS*	2.16E-03	4.37E-03	PID
111	Integrated Lung Cancer Pathway	40	2 (5.0%)	*JUN; FOS*	2.16E-03	4.37E-03	Wikipathways
112	IL-5 Signaling Pathway	40	2 (5.0%)	*JUN; FOS*	2.16E-03	4.37E-03	Wikipathways
113	Metabolism of amino acids and derivatives	328	4 (1.2%)	*GCLM; GSTZ1; GCLC; TXNRD1*	2.17E-03	4.37E-03	Reactome
114	Toll-Like Receptors Cascades	155	3 (1.9%)	*MEF2C; JUN; FOS*	2.34E-03	4.64E-03	Reactome
115	Myometrial Relaxation and Contraction Pathways	155	3 (1.9%)	*JUN; MAFF; FOS*	2.34E-03	4.64E-03	Wikipathways
116	IL-2 Signaling Pathway	42	2 (4.8%)	*JUN; FOS*	2.38E-	4.68E-	Wikipathways

					03	03	
117	Oxytocin signaling pathway - Homo sapiens (human)	159	3 (1.9%)	*MEF2C; JUN; FOS*	2.47E-03	4.81E-03	KEGG
118	FOXM1 transcription factor network	43	2 (4.7%)	*HSPA1A; FOS*	2.50E-03	4.82E-03	PID
119	Sudden Infant Death Syndrome (SIDS) Susceptibility Pathways	159	3 (1.9%)	*MEF2C; JUN; IL6R*	2.51E-03	4.82E-03	Wikipathways
120	EGF-EGFR Signaling Pathway	162	3 (1.9%)	*MEF2C; JUN; FOS*	2.65E-03	5.04E-03	Wikipathways
121	Cysteine and methionine metabolism - Homo sapiens (human)	45	2 (4.4%)	*GCLM; GCLC*	2.73E-03	5.14E-03	KEGG
122	FOXA1 transcription factor network	46	2 (4.3%)	*JUN; FOS*	2.85E-03	5.33E-03	PID
123	RhoA signaling pathway	47	2 (4.3%)	*JUN; FOS*	2.97E-03	5.47E-03	PID
124	Presenilin action in Notch and Wnt signaling	47	2 (4.3%)	*JUN; FOS*	2.97E-03	5.47E-03	PID
125	One carbon metabolism and related pathways	49	2 (4.1%)	*GCLM; GCLC*	3.23E-03	5.80E-03	Wikipathways
126	IL-3 Signaling Pathway	49	2 (4.1%)	*JUN; FOS*	3.23E-03	5.80E-03	Wikipathways
127	Calcineurin-regulated NFAT-dependent transcription in lymphocytes	49	2 (4.1%)	*JUN; FOS*	3.23E-03	5.80E-03	PID
128	TGF_beta_Receptor	176	3 (1.7%)	*MEF2C; JUN; FOS*	3.30E-03	5.87E-03	NetPath
129	Photodynamic therapy-induced AP-1 survival signaling.	50	2 (4.0%)	*JUN; FOS*	3.36E-03	5.87E-03	Wikipathways
130	Hepatitis C and Hepatocellular Carcinoma	50	2 (4.0%)	*JUN; IL6R*	3.36E-03	5.87E-03	Wikipathways
131	Immune System	1950	9 (0.5%)	*SQSTM1; EPX; FOS; GLA; JUN; CAT; MEF2C; HSPA1A; IL6R*	3.37E-03	5.87E-03	Reactome
132	Apoptosis-related network due to altered Notch3 in ovarian cancer	53	2 (3.8%)	*SQSTM1; GCLC*	3.77E-03	6.36E-03	Wikipathways
133	keratinocyte differentiation	53	2 (3.8%)	*JUN; FOS*	3.77E-03	6.36E-03	BioCarta
134	CD4 T cell receptor signaling-JNK cascade	53	2 (3.8%)	*JUN; FOS*	3.77E-03	6.36E-03	INOH

135	mechanism of gene regulation by peroxisome proliferators via ppara	53	2 (3.8%)	*HSPA1A; JUN*	3.77E-03	6.36E-03	BioCarta
136	Glutathione metabolism - Homo sapiens (human)	54	2 (3.7%)	*GCLM; GCLC*	3.91E-03	6.50E-03	KEGG
137	IL2-mediated signaling events	54	2 (3.7%)	*JUN; FOS*	3.91E-03	6.50E-03	PID
138	Arginine Proline metabolism	55	2 (3.6%)	*GCLM; GCLC*	4.05E-03	6.55E-03	INOH
139	t cell receptor signaling pathway	55	2 (3.6%)	*JUN; FOS*	4.05E-03	6.55E-03	BioCarta
140	TGF-beta Receptor Signaling	55	2 (3.6%)	*JUN; FOS*	4.05E-03	6.55E-03	Wikipathways
141	IL-1 signaling pathway	55	2 (3.6%)	*SQSTM1; JUN*	4.05E-03	6.55E-03	Wikipathways
142	FGF signaling pathway	56	2 (3.6%)	*JUN; FOS*	4.20E-03	6.69E-03	PID
143	IL1	56	2 (3.6%)	*SQSTM1; JUN*	4.20E-03	6.69E-03	NetPath
144	ATF-2 transcription factor network	61	2 (3.3%)	*JUN; FOS*	4.96E-03	7.85E-03	PID
145	Innate Immune System	1309	7 (0.5%)	*EPX; FOS; GLA; JUN; CAT; MEF2C; HSPA1A*	4.99E-03	7.85E-03	Reactome
146	Fc-epsilon receptor I signaling in mast cells	62	2 (3.2%)	*JUN; FOS*	5.12E-03	7.94E-03	PID
147	Colorectal cancer - Homo sapiens (human)	62	2 (3.2%)	*JUN; FOS*	5.12E-03	7.94E-03	KEGG
148	T-Cell antigen Receptor (TCR) pathway during Staphylococcus aureus infection	63	2 (3.2%)	*JUN; FOS*	5.28E-03	8.14E-03	Wikipathways
149	Longevity regulating pathway - multiple species - Homo sapiens (human)	64	2 (3.1%)	*HSPA1A; CAT*	5.45E-03	8.28E-03	KEGG
150	LPA receptor mediated events	65	2 (3.1%)	*JUN; FOS*	5.45E-03	8.28E-03	PID
151	Regulation of retinoblastoma protein	65	2 (3.1%)	*MEF2C; JUN*	5.62E-03	8.48E-03	PID
152	Endothelins	66	2 (3.0%)	*JUN; FOS*	5.79E-03	8.62E-03	PID
153	Human Thyroid Stimulating Hormone (TSH) signaling pathway	66	2 (3.0%)	*JUN; FOS*	5.79E-03	8.62E-03	Wikipathways
154	EGFR Inhibitor Pathway, Pharmacodynamics	67	2 (3.0%)	*JUN; FOS*	5.96E-03	8.82E-03	PharmGKB

155	Amphetamine addiction - Homo sapiens (human)	68	2 (2.9%)	*JUN; FOS*	6.13E-03	8.96E-03	KEGG
156	Downstream signaling in naïve CD8+ T cells	68	2 (2.9%)	*JUN; FOS*	6.13E-03	8.96E-03	PID
157	BCR signaling pathway	69	2 (2.9%)	*JUN; FOS*	6.31E-03	9.10E-03	PID
158	Regulation of Telomerase	69	2 (2.9%)	*JUN; FOS*	6.31E-03	9.10E-03	PID
159	Prolactin	70	2 (2.9%)	*JUN; FOS*	6.49E-03	9.19E-03	NetPath
160	TP53 Regulates Transcription of DNA Repair Genes	72	2 (2.9%)	*JUN; FOS*	6.49E-03	9.19E-03	Reactome
161	Biological oxidations	229	3 (1.3%)	*GCLM; GSTZ1; GCLC*	6.49E-03	9.19E-03	Reactome
162	Leishmaniasis - Homo sapiens (human)	73	2 (2.8%)	*JUN; FOS*	6.85E-03	9.58E-03	KEGG
163	B cell receptor signaling pathway - Homo sapiens (human)	73	2 (2.8%)	*JUN; FOS*	6.85E-03	9.58E-03	KEGG
164	Alpha6Beta4Integrin	74	2 (2.7%)	*JUN; FOS*	7.22E-03	1.00E-02	NetPath
165	VEGFA-VEGFR2 Signaling Pathway	236	3 (1.3%)	*MEF2C; HSPA1A; JUN*	7.59E-03	1.04E-02	Wikipathways
166	Prolactin Signaling Pathway	76	2 (2.6%)	*JUN; FOS*	7.61E-03	1.04E-02	Wikipathways
167	Pertussis - Homo sapiens (human)	76	2 (2.6%)	*JUN; FOS*	7.61E-03	1.04E-02	KEGG
168	Regulation of HSF1-mediated heat shock response	81	2 (2.5%)	*BAG2; HSPA1A*	8.60E-03	1.16E-02	Reactome
169	Glucocorticoid receptor regulatory network	81	2 (2.5%)	*JUN; FOS*	8.60E-03	1.16E-02	PID
170	Selenium Micronutrient Network	83	2 (2.4%)	*CAT; TXNRD1*	9.02E-03	1.21E-02	Wikipathways
171	Neutrophil degranulation	497	4 (0.8%)	*GLA; HSPA1A; EPX; CAT*	9.46E-03	1.26E-02	Reactome
172	Salmonella infection - Homo sapiens (human)	86	2 (2.3%)	*JUN; FOS*	9.65E-03	1.28E-02	KEGG

Table E.4. List of genes identified with significant expression fold-changes ($p<0.05$) upon exposure to IEPOX or MAE-derived SOA constituents. False Discovery Rate (FDR) adjusted p-value: 0.05/84=0.0005. Full names of gene symbols can be found in Appendix E, Table E.1.

SOA Precursor	Gene Name	Fold Change	p-value	NRF2-associated Genes	<FDR
IEPOX	*ALOX12*	1.75	0.019612		
	CYGB	1.55	0.000313		*
	DUOX2	1.80	0.012251		
	LHPP	1.63	0.004871		
	NQO1	1.59	0.002976	+	
	PTGS2	2.85	0.000080		*
MAE	*AKR1C2*	13.61	0.002067		
	ALB	1.60	0.008062		
	ALOX12	1.97	0.024048		
	APOE	2.07	0.004920		
	ATOX1	2.08	0.000666		*
	B2M	1.93	0.005968		
	BNIP3	2.68	0.000278		*
	CCL5	23.64	0.000160		*
	CYGB	1.91	0.000004		*
	FTH1	2.56	0.000144	+	*
	GCLC	1.84	0.006009	+	
	GCLM	1.64	0.009746	+	
	GLA	2.10	0.002010		
	GPX2	3.47	0.019059	+	
	GSTP1	1.71	0.001398	+	
	HMOX1	6.03	0.001071	+	
	HSPA1A	1.69	0.015415		
	MB	1.70	0.039873		
	NCF1	1.64	0.005790		
	NCF2	9.94	0.000523		
	NCOA7	2.36	0.000064		*
	NOX5	1.56	0.002049		
	NQO1	2.36	0.001263	+	
	PRDX1	1.67	0.001969	+	
	PRDX4	1.59	0.000644		*
	PRDX5	1.57	0.007514		
	PRNP	2.35	0.003207		
	PTGR1	1.99	0.001422	+	
	PTGS2	5.04	0.000355		*
	SEPP1	1.50	0.000177		*

SOD2	5.98	0.000230	+	*
SPINK1	1.87	0.038476		
SQSTM1	4.57	0.000017	+	*
TXN	2.11	0.000451	+	*
TXNRD1	2.98	0.000169	+	*
VIMP	2.04	0.000516		

Table E.5. List of genes identified with significant expression fold-changes ($p<0.05$) upon exposure to ISOPOOH-derived SOA constituents. False Discovery Rate (FDR) adjusted p-value: 0.05/84=0.0005. Full names of gene symbols can be found in Table E.1.

Gene Name	Fold Regulation	p-value	NRF2-associated Genes	<FDR
AKR1C2	2.2038	0.013377		
ATOX1	1.5619	0.024189		
BAG2	2	0.00763		
CAT	1.5801	0.006833	+	
DHCR24	1.5837	0.001557		
FTH1	2.2763	0.008796	+	
GCLC	2.5907	0.003719	+	
GCLM	2.8945	0.001271	+	
GLA	1.7371	0.034903		
GPX1	1.544	0.014517		
GPX2	5.9518	0.000725	+	
GPX3	1.8747	0.000538		
GSR	1.6857	0.027743	+	
GSTP1	1.6283	0.041316	+	
HMOX1	2	0.016293	+	
HSP90AA1	2.0946	0.000988		
HSPA1A	1.5948	0.001239		
NQO1	4.9588	0.003367	+	
PRDX1	2.1886	0.007017	+	
PRDX3	1.6133	0.047334		
PRDX6	1.5018	0.023451		
PTGS1	2.0186	0.025923		
RNF7	1.7818	0.040105		
SIRT2	1.6396	0.000194		*
SLC7A11	3.4343	0.000005		*
SQSTM1	2.3565	0.000085	+	*
SRXN1	2.7195	0.000015		*
TXN	2.2294	0.016836	+	
TXNRD1	4.8793	0.003985	+	
TXNRD2	1.7859	0.000992		
VIMP	1.5619	0.001192		
DUOX1	-2.0139	0.011647		

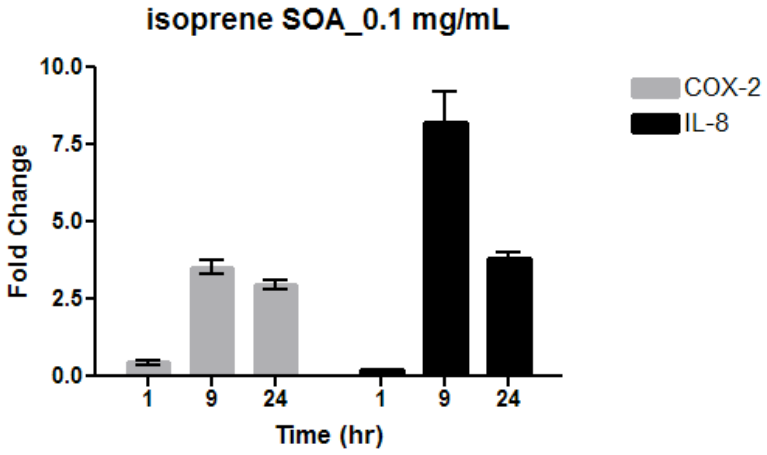

Figure E.1. Time course analysis conducted using filter resuspension to show that COX-2 and IL-8 were maximized at 9 hours. In addition to be consistent with prior studies at UNC-Chapel Hill (Lichtveld et al., 2012), this data further guided us in selecting 9-hour post exposure conditions for our genomic analyses.

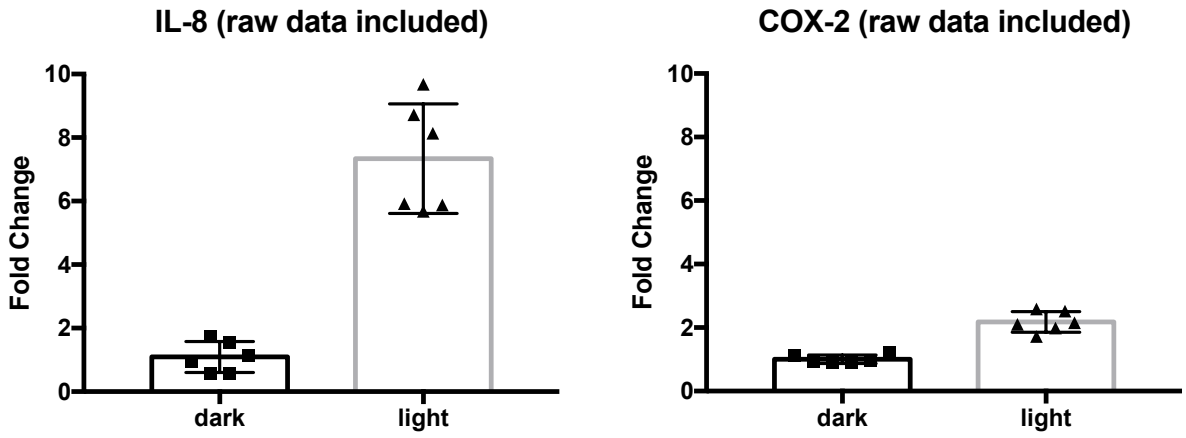

Figure E.2. Raw data corresponding to Figure 5 in the main text. The means of the fold changes are as follows: 1.01 and 1.09 for the EAVES COX-2 dark and EAVES IL-8 dark, respectively, where as 2.18 and 7.34 for EAVES COX-2 light and EAVES IL-8 light, respectively. N=6 (3 experiemntal replicates, 2 PCR replicates) for these data.

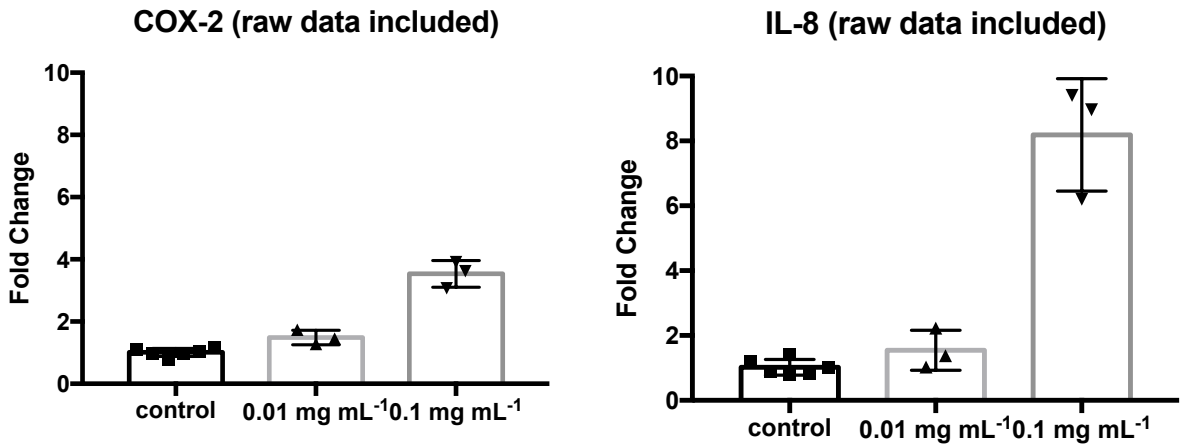

Figure E.3. Raw data corresponding to Figure 6 in the main text. The means of the fold changes are as follows: 1.01, 1.49, 3.54 for the COX-2 control, COX-2 0.01 mg/ml, and COX-2 0.1 mg/ml resuspension exposures, respectively, where as 1.02, 1.54, and 8.19 for the IL-8 control, IL-8 0.01 mg/ml, and IL-8 0.1 mg/ml resuspension exposures, respectively. N=3 (3 well replicates) for these data.

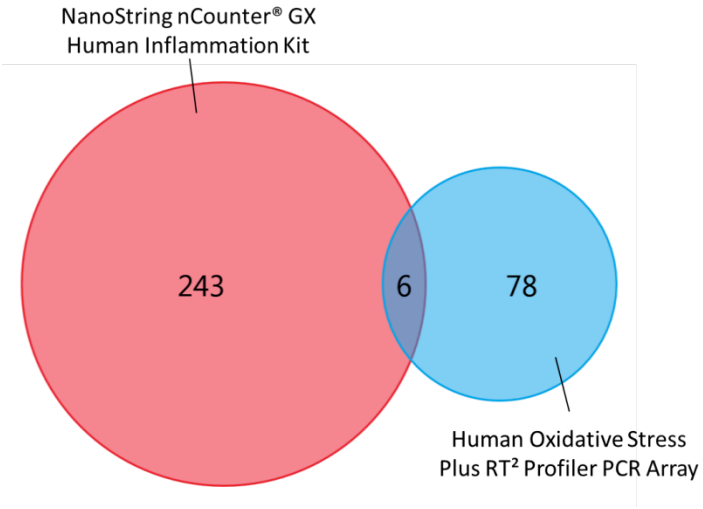

Figure E.4. Venn diagram of two gene expression platforms profiled in this study. There are 6 genes overlapping in two platforms (*ALOX12*, *MBL2*, *PTGS1*, *PTGS2*, *NOS2*, *CCL5*), but none of these genes was found significant with the threshold of FC ≥ |1.5| and $p < 0.05$. Complete lists of genes included in each platform are provided in Appendix E, Table E.1 and E.2.

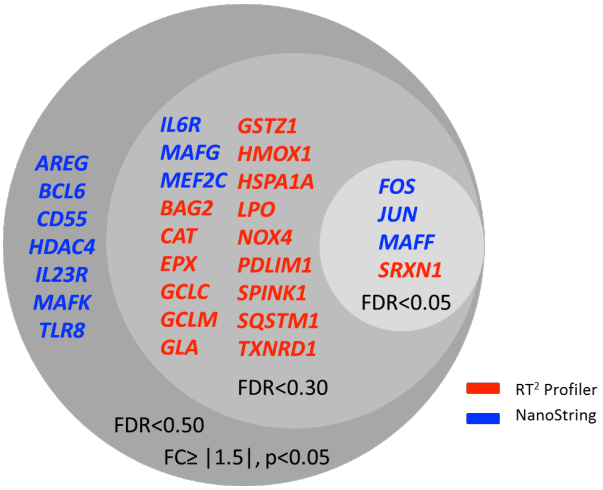

Figure E.5. Total 29 genes were found differentially expressed (FC ≥ |1.5|, $p < 0.05$), with 22 genes passing a FDR threshold of 0.3, and 4 genes passing a stringent FDR threshold of 0.05.

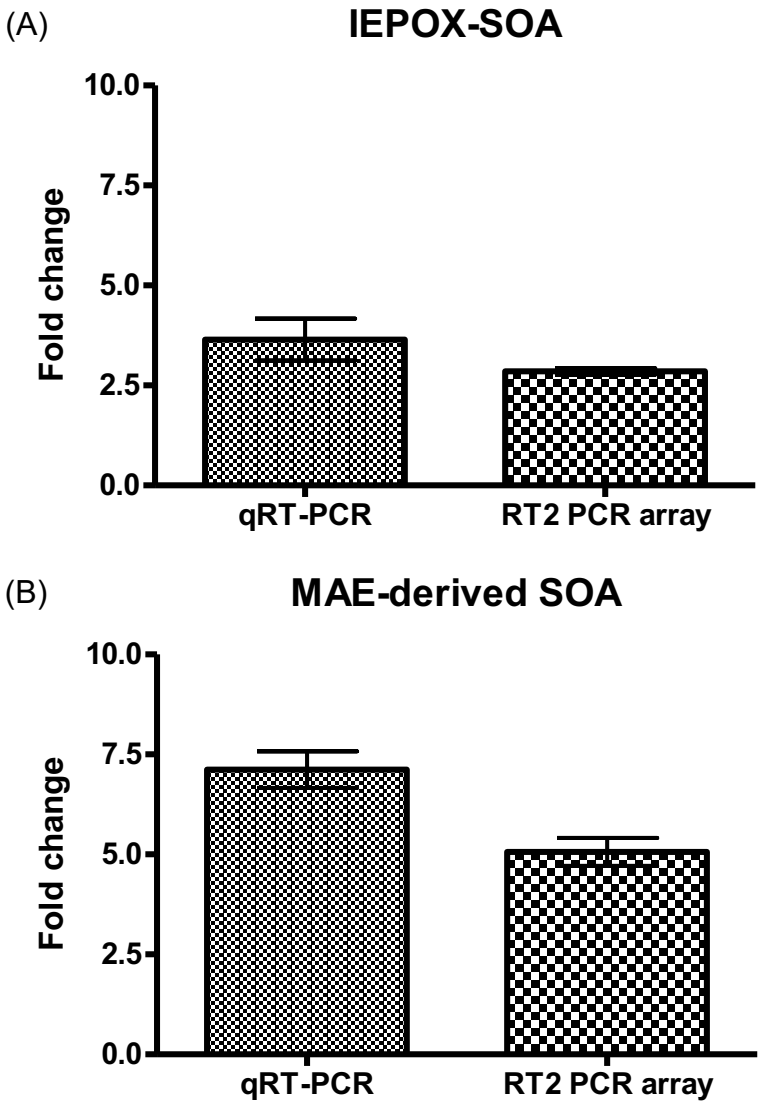

Figure E.6. Quality check of *PTGS2* gene expression changes induced by (a) IEPOX- and (b) MAE-derived SOA through qRT-PCR.

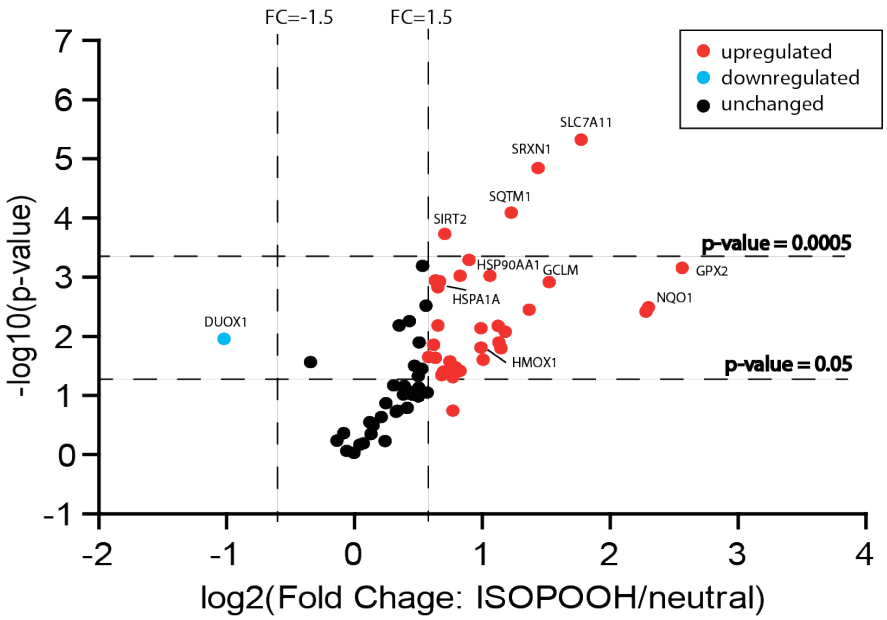

Figure E.7. Volcano plot of differentially expressed genes in BEAS-2B cells upon exposure to ISOPOOH-derived SOA for 24 hours. A full list of differentially expressed genes can be found in Table 3.2.

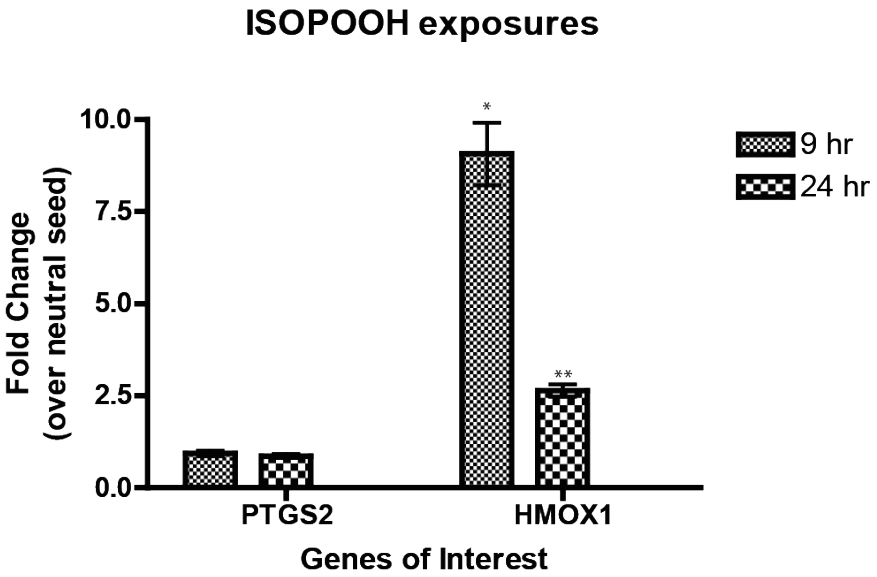

Figure E.8. *PTGS2 and HMOX1* mRNA expression induced by exposure to 0.1 mg/mL ISOPOOH-derived SOA all normalized to non-acidified $(NH_4)_2SO_4$ seed and against housekeeping gene, β-actin. *p<0.05 and **p<0.005