Supplementary Data

Metallothionein Family

Gene	Gene Name	logFC	P. Value	False Discovery Rate
MT1G	Metallothionein 1G	2.62	1.19E-10	4.66E-08
MT1H	Metallothionein 1H	2.58	4.87E-08	7.12E-06
MT1M	Metallothionein 1M	2.23	1.18E-07	1.44E-05
MT1X	Metallothionein 1X	2.21	2.64E-11	1.25E-08
MT2A	Metallothionein 2A	1.82	1.38E-12	1.26E-09
MT1E	Metallothionein 1E	1.51	2.41E-11	1.18E-08
MT1F	Metallothionein 1F	1.47	1.85E-09	4.09E-07

Unfolded Protein Response

Gene	Gene Name	logFC	P. Value	False Discovery Rate
AMFR	autocrine motility factor receptor	-0.20	9.94E-01	1.00
ASK1	mitogen-activated protein kinase kinase kinase 5	0.27	8.11E-01	1.00
ATF4	activating transcription factor 4	0.22	9.67E-01	1.00
ATF6	activating transcription factor 6	0.01	1.00	1.00
BCL2	BCL2, apoptosis regulator	-0.43	4.80E-02	4.24E-01
BIP	heat shock protein family A (Hsp70) member 5	0.13	1.00	1.00
CALR	calreticulin	0.12	1.00	1.00
CANX	calnexin	0.12	1.00	1.00
CHOP	DNA damage inducible transcript 3	0.25	7.99E-01	1.00
EDEM	ER degradation enhancing alpha-mannosidase like protein 1	0.37	1.88E-01	1.00
EIFA	eukaryotic translation initiation factor 2A	0.06	1.00	1.00
ERO1LB	endoplasmic reticulum oxidoreductase 1 beta	-0.29	5.69E-01	1.00
GADD34	protein phosphatase 1 regulatory subunit 15A	1.18	3.66E-11	1.62E-08
GRP94	heat shock protein 90 beta family member 1	0.16	9.98E-01	1.00
HSPH1	heat shock protein family H (Hsp110) member 1	0.62	9.70E-06	5.12E-04
INSIG1	insulin induced gene 1	1.69	8.47E-18	3.88E-14
IRE1	endoplasmic reticulum to nucleus signaling 1	0.26	8.13E-01	1.00
JNK1	mitogen-activated protein kinase 8	-0.08	1.00	1.00
KAI1	CD82 molecule	0.60	8.87E-04	1.90E-02
MKK7	mitogen-activated protein kinase kinase 7	-0.08	1.00	1.00
NRF2	nuclear factor, erythroid 2 like 2	-0.03	1.00	1.00
OS9	OS9, endoplasmic reticulum lectin	-0.08	1.00	1.00
P58IPK	DnaJ heat shock protein family (Hsp40) member C3	0.05	1.00	1.00
PERK	eukaryotic translation initiation factor 2 alpha kinase 3	0.11	1.00	1.00
PPARY	peroxisome proliferator activated receptor gamma	0.19	9.57E-01	1.00
SCAP	SREBF chaperone	-0.04	1.00	1.00
SEL1L	SEL1L ERAD E3 ligase adaptor subunit	-0.12	1.00	1.00
SYVN1	synoviolin 1	0.07	1.00	1.00
TRAF2	TNF receptor associated factor 2	0.26	7.99E-01	1.00
UBX	UBX domain protein 4	-0.12	1.00	1.00

VCP	valosin containing protein	0.22	9.97E-01	1.00
XBP1	X-box binding protein 1	0.26	9.19E-01	1.00

NRF2-mediated Oxidative Stress Response

Gene	Gene Name	logFC	P. Value	False Discovery Rate
AKR	aldo-keto reductase family 1 member A1	0.09	1.00	1.0
AKT	AKT serine/threonine kinase 1	0.23	9.91E-01	1.0
AOX1	aldehyde oxidase 1	0.32	5.17E-01	1.0
ASK1	mitogen-activated protein kinase kinase kinase 5	0.27	8.11E-01	1.0
ATF4	activating transcription factor 4	0.22	9.67E-01	1.0
BACH1	BTB domain and CNC homolog 1	0.05	1.00	1.0
cFos	Fos proto-oncogene, AP-1 transcription factor subunit	1.12	2.10E-04	6.04E-03
cMAF	MAF bZIP transcription factor	-0.61	1.42E-02	1.68E-01
cRaf	Raf-1 proto-oncogene, serine/threonine kinase	0.04	1.00	1.0
CAT	catalase	-0.38	2.13E-01	1.0
CBR1	carbonyl reductase 1	-0.08	1.00	1.0
CCT7	chaperonin containing TCP1 subunit 7	0.30	6.54E-01	1.0
CLPP	caseinolytic mitochondrial matrix peptidase proteolytic subunit	0.15	9.90E-01	1.0
CUL3	cullin 3	-0.04	1.00	1.0
EPHX1	epoxide hydrolase 1	-0.29	6.84E-01	1.0
ERK5	mitogen-activated protein kinase 7	0.03	1.00	1.0
ERP29	endoplasmic reticulum protein 29	0.02	1.00	1.0
FKBP5	FK506 binding protein 5	-0.06	9.96E-01	1.0
FRA1	FOS like 1, AP-1 transcription factor subunit	0.90	3.16E-05	1.35E-03
FTH1	ferritin heavy chain 1	0.32	5.06E-01	1.0
FTL	ferritin light chain	-0.25	8.51E-01	1.0
GCLC	glutamate-cysteine ligase catalytic subunit	0.13	1.00	1.0
GCLM	glutamate-cysteine ligase modifier subunit	0.21	9.59E-01	1.0
GSK3B	glycogen synthase kinase 3 beta	0.24	9.78E-01	1.0
GSR	glutathione-disulfide reductase	0.07	1.00	1.0
HERPUD1	homocysteine inducible ER protein with ubiquitin like domain 1	0.02	1.00	1.0
HIP2	ubiquitin conjugating enzyme E2 K	0.03	1.00	1.0
HMOX1	heme oxygenase 1	1.31	1.81E-18	1.82E-14
Jun	Jun proto-oncogene, AP-1 transcription factor subunit	0.71	4.12E-08	6.21E-06
KEAP1	kelch like ECH associated protein 1	0.09	1.00	1.0
MEK5	mitogen-activated protein kinase kinase 5	-0.33	4.80E-01	1.0
MEKK	mitogen-activated protein kinase kinase kinase 1	-0.25	9.52E-01	1.0
MRP1	ATP binding cassette subfamily C member 1	-0.18	1.00	1.0
MRP2	ATP binding cassette subfamily C member 2	0.25	6.32E-01	1.0
MRP4	ATP binding cassette subfamily C member 4	-0.27	8.92E-01	1.0
NRF2	nuclear factor, erythroid 2 like 2	-0.03	1.00	1.0
NRPB	ectodermal-neural cortex 1	0.42	1.32E-01	8.70E-01
p38MAPK	mitogen-activated protein kinase 14	0.08	1.00	1.0
PERK	eukaryotic translation initiation factor 2 alpha kinase 3	0.11	1.00	1.0

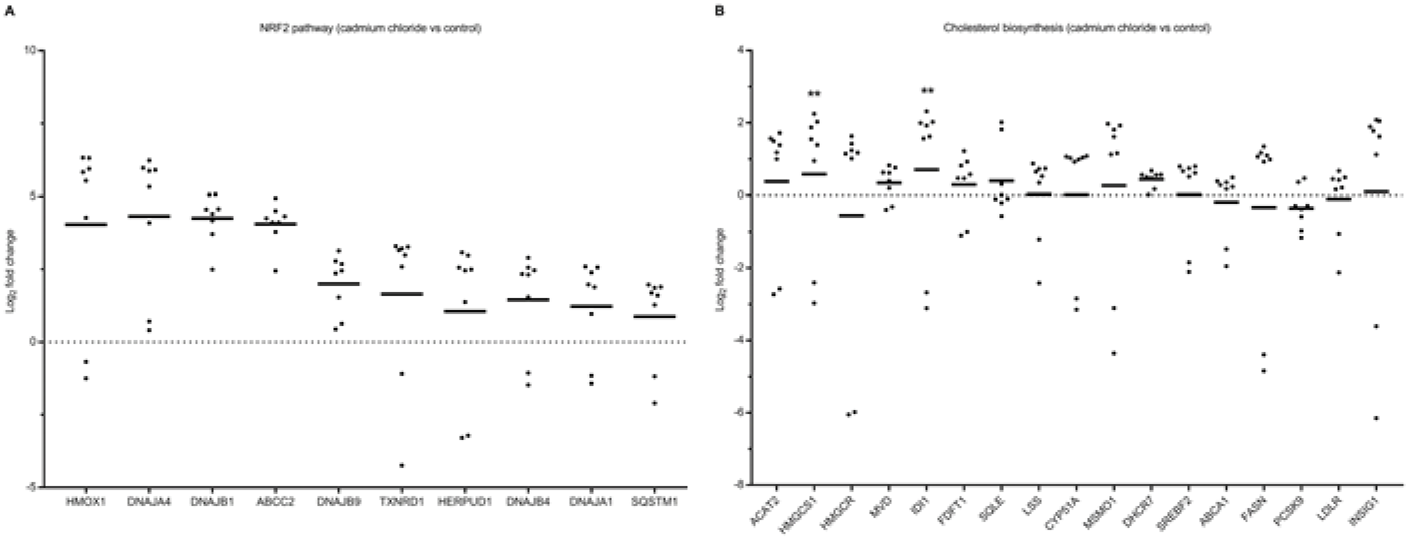
PMF1	polyamine modulated factor 1	-0.46	2.92E-01	1.0
PPIB	peptidylprolyl isomerase B	0.22	9.73E-01	1.0
PRDX1	peroxiredoxin 1	0.51	6.38E-04	1.46E-02
PTPLAD1	3-hydroxyacyl-CoA dehydratase 3	0.00	1.00	1.0
Roc1	ring-box 1	0.09	9.96E-01	1.0
SQSTM1	sequestosome 1	0.51	3.77E-04	9.77E-03
SRBI	scavenger receptor class B member 1	0.23	8.23E-01	1.0
STIP1	stress induced phosphoprotein 1	0.40	7.80E-02	6.08E-01
TAK1	mitogen-activated protein kinase kinase kinase 7	-0.11	1.00	1.0
TRXR1	thioredoxin reductase 1	0.73	2.90E-09	5.94E-07
TXN	thioredoxin	0.54	1.16E-03	2.37E-02
UB2R1	cell division cycle 34	0.11	1.00	1.0
UBB	ubiquitin B	0.25	9.51E-01	1.0
UbcM2	ubiquitin conjugating enzyme E2 E3	-0.09	1.00	1.0
UGT	solute carrier family 35 member A2	0.19	9.58E-01	1.0
USP14	ubiquitin specific peptidase 14	0.30	6.39E-01	1.0
VCP	valosin containing protein	0.22	9.97E-01	1.0

Superpathway of Cholesterol Biosynthesis

Gene	Gene Name	logFC	P. Value	False Discovery Rate
ABCA1	ATP binding cassette subfamily A member 1	-0.71	1.92E-04	5.7E-03
ACAT1	acetyl-CoA acetyltransferase 1	-0.265	8.04E-01	1.0
ACAT2	acetyl-CoA acetyltransferase 2	1.08	3.06E-11	1E-08
CYP51A1	cytochrome P450 family 51 subfamily A member 1	0.86	2.92E-12	2E-09
DHCR7	7-dehydrocholesterol reductase	0.94	6.29E-10	2E-07
DHCR24	24-dehydrocholesterol reductase	0.456	1.00E-02	1E-01
EBP	emopamil binding protein (sterol isomerase)	0.96	1.92E-09	4E-07
FDFT1	farnesyl-diphosphate farnesyltransferase 1	0.93	9.9E-13	1E-09
FDPS	farnesyl diphosphate synthase	1.14	2.16E-13	2E-10
GGPS1	geranylgeranyl diphosphate synthase 1	-0.021	1.0	1.0
HADHA	hydroxyacyl-CoA dehydrogenase trifunctional multienzyme complex subunit alpha	-0.019	1.0	1.0
HADHB	hydroxyacyl-CoA dehydrogenase trifunctional multienzyme complex subunit beta	-0.203	9.89E-01	1.0
HMGCR	3-hydroxy-3-methylglutaryl-CoA reductase	0.88	6.6E-12	4E-09
HMGCS1	3-hydroxy-3-methylglutaryl-CoA synthase 1	1.48	2.65E-18	2E-14
HSD17B7	hydroxysteroid 17-beta dehydrogenase 7	0.62	0.000279	8E-03
IDI1	isopentenyl-diphosphate delta isomerase 1	1.07	1.65E-12	1E-09
LBR	lamin B receptor	-0.154	9.96E-01	1.0
LSS	lanosterol synthase	0.60	8.02E-06	4E-04
MSMO1	methylsterol monooxygenase 1	1.24	2.39E-15	5E-12
MVD	mevalonate diphosphate decarboxylase	1.18	7.85E-11	3E-08
MVK	mevalonate kinase	0.252	8.18E-01	1.0
NSDHL	NAD(P) dependent steroid dehydrogenase-like	0.79	3.03E-06	2E-04
PMVK	phosphomevalonate kinase	0.291	6.52E-01	1.0
SC5D	sterol-C5-desaturase	0.50	0.00187	3E-02

SQLE	squalene epoxidase	0.93	2.07E-11	1E-08
TM7SF2	transmembrane 7 superfamily member 2	0.175	9.75E-01	1.0

Supplemental Table I. Global transcriptional response to PMB exposure, relative to control, results in significant induction of injury response genes. The following genes (blue shaded) were significantly different when cells were exposed to 50 μM PMB, relative to control, as indicated by log$_2$-Fold Change (logFC) between the two treatment groups being compared, *P* value, and False Discovery Rate (FDR) which was the p-value adjusted for multiple testing (Benjamini & Hochberg's method). Specific pathways of interest included the metallothionein family, unfolded protein response, NRF2-mediated Oxidative Stress Response, and Superpathway of Cholesterol Biosynthesis. The following genes (yellow shaded) are recognized genes that are associated with the NRF2 Antioxidant Response.



Supplemental Figure 1. RNAseq analysis of cadmium-treated MPS. Cadmium chloride exposure (25 µM/48 hours) resulted in mRNA induction of genes in the NRF2 pathway (A) but no changes in genes associated with cholesterol biosynthesis (B) (*no significant change relative to control MPS).