

## **Appendix**

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**Appendix Table S1.** List of antibodies used in this study.

<b>Antibody</b>	<b>Source</b>	<b>Reference</b>	<b>Dilution</b>
8-oxo-dG	Abcam	62623	1:1000
AKT	Cell Signaling	4685	1:1000
Aldolase A	Novus Biologicals	600-915	1:5000
APP	AbD Serotec	AHP538	1:100
Cytochrome C	BD Biosciences Pharmigen	55643	1:500
GFAP	Dako	Z0334	1:500
GSK-3 $\beta$	Cell Signaling	9315	1:1000
IBA1	Wako	019-19741	1:1000
Lamin B1	Abcam	16048	1:10000
Neurofilament H non-phosphorylated (SMI32)	Covance Antibody-Biolegend	801701	1:3000
NRF2	Abcam	31163	1:500
pSer473 AKT	Cell Signaling	4060	1:1000
pSer9/21 GSK-3 $\beta$	Cell Signaling	9331	1:1000
pThr308 AKT	Cell Signaling	13038	1:1000
pTyr216/279 GSK-3 $\beta$	EMD Millipore	05-413	1:1000
Synaptophysin	Leica Biosystems	299-L-CE	1:500
$\gamma$ -Tubulin	Sigma-Aldrich	T6557	1:20000
<b>Antibody (secondary)</b>	<b>Source</b>	<b>Reference</b>	<b>Dilution</b>
Goat anti-rabbit HRP	Dako	P0448	1:10000
Goat anti-mouse HRP	Dako	P0447	1:15000
Rabbit anti-goat HRP	Dako	P0449	1:15000

**Appendix Table S2.** List of Q-PCR probes used in this study.

<b>Gene</b>	<b>Taqman ref.</b>
<i>Cebpa</i>	Mm00514283
<i>Ccl5</i>	Mm01302427
<i>Ccr6</i>	Mm99999114
<i>Chil3</i>	Mm00657889
<i>Cxcl9</i>	Mm00434946
<i>Cxcl10</i>	Mm00445235
<i>Cxcl12</i>	Mm00457276
<i>Gsta3</i>	Mm01233706
<i>Hmox1</i>	Mm00516005
<i>Igf1</i>	Mm00439560
<i>Il10</i>	Mm00439614
<i>Il1<math>\beta</math></i>	Mm01336189
<i>Il6</i>	Mm00446190
<i>Mif</i>	Mm01611157
<i>Nfkb2</i>	Mm00479807
<i>Nqo1</i>	Mm01253561
<i>Nrf1</i>	Mm00447996
<i>Pgc-1<math>\alpha</math></i>	Mm00447183
<i>Retnla</i>	Mm00445109
<i>Rplp0</i>	Mm01974474
<i>Sirt1</i>	Mm00490758
<i>Tfam</i>	Mm00447485
<i>Tgf<math>\beta</math>1</i>	Mm01178820
<i>Tnfa</i>	Mm00443258
<i>Tnfrsf1a</i>	Mm01182929
<i>GCLC</i>	Hs00155249
<i>HMOX1</i>	Hs01110250
<i>NQO1</i>	Hs00168547
<i>RPLP0</i>	Hs99999902

**Appendix Table S3.** List of exact p values reported in this article

Figures	Parameter	Comparisons	P value
Figure 1A	NRF2	WT vs <i>Abcd1</i> <sup>-</sup>	0.031
Figure 1B	<i>Hmox1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.022
Figure 1B	<i>Nqo1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.028
Figure 1B	<i>Gstα3</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.033
Figure 1D	pThr308 AKT	WT vs <i>Abcd1</i> <sup>-</sup>	0.020
Figure 1D	pSer9 GSK-3β	WT vs <i>Abcd1</i> <sup>-</sup>	0.014
Figure 2B	Nucleus NRF2	CTL veh vs CTL + C26:0	0.043
Figure 2B	Nucleus NRF2	CTL veh vs CTL + oligomycin	<0.0001
Figure 2B	Cytoplasm NRF2	CTL veh vs CTL + C26:0	0.034
Figure 2C	<i>HMOX1</i>	CTL veh vs CTL + C26:0	0.002
Figure 2C	<i>HMOX1</i>	CTL veh vs CTL + oligomycin	0.011
Figure 2C	<i>NQO1</i>	CTL veh vs CTL + C26:0	0.004
Figure 2C	<i>NQO1</i>	CTL veh vs CTL + oligomycin	0.002
Figure 2C	<i>GCLC</i>	CTL veh vs CTL + C26:0	<0.0001
Figure 2C	<i>GCLC</i>	CTL veh vs CTL + oligomycin	0.029
Figure 2E	pSer473 AKT	CTL veh vs CTL + C26:0	0.046
Figure 2E	pSer473 AKT	CTL veh vs CTL + oligomycin	0.034
Figure 2E	pThr308 AKT	CTL veh vs CTL + C26:0	0.029
Figure 2E	pThr308 AKT	CTL veh vs CTL + oligomycin	0.008
Figure 2E	pSer9 GSK-3β	CTL veh vs CTL + C26:0	0.002
Figure 2E	pSer9 GSK-3β	CTL veh vs CTL + oligomycin	0.036
Figure 2F	<i>HMOX1</i>	CTL veh vs CTL + C26:0	0.003
Figure 2F	<i>HMOX1</i>	CTL + C26:0 vs CTL + C26:0 + SB216763	0.008
Figure 2F	<i>HMOX1</i>	CTL + C26:0 + SB216763 vs CTL + SB216763	0.025
Figure 2F	<i>NQO1</i>	CTL veh vs CTL + C26:0	0.006
Figure 2F	<i>GCLC</i>	CTL veh vs CTL + C26:0	0.0007
Figure 2F	<i>GCLC</i>	CTL + C26:0 vs CTL + C26:0 + C99021	0.007
Figure 2F	<i>GCLC</i>	CTL + C26:0 vs CTL + C26:0 + SB216763	0.0009
Figure 2F	<i>GCLC</i>	CTL veh vs CTL + SB216763	0.029
Figure 2F	<i>HMOX1</i>	X-ALD + C26:0 vs X-ALD + C26:0 + C99021	0.0003
Figure 2F	<i>HMOX1</i>	X-ALD + C26:0 vs X-ALD + C26:0 + SB216763	<0.0001
Figure 2F	<i>HMOX1</i>	X-ALD + C26:0 + C99021 vs X-ALD + C99021	0.028
Figure 2F	<i>HMOX1</i>	X-ALD + C26:0 + SB216763 vs X-ALD + SB216763	0.0008
Figure 2F	<i>NQO1</i>	X-ALD + C26:0 vs X-ALD + C26:0 + C99021	0.0007
Figure 2F	<i>NQO1</i>	X-ALD + C26:0 vs X-ALD + C26:0 + SB216763	0.0007
Figure 2F	<i>NQO1</i>	X-ALD + C26:0 + SB216763 vs X-ALD + SB216763	0.038
Figure 2F	<i>GCLC</i>	X-ALD + C26:0 vs X-ALD + C26:0 + C99021	0.02
Figure 2F	<i>GCLC</i>	X-ALD + C26:0 vs X-ALD + C26:0 + SB216763	0.002
Figure 3A	NRF2	WT vs <i>Abcd1</i> <sup>-</sup>	0.043
Figure 3A	NRF2	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.031
Figure 3B	<i>Hmox1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.041
Figure 3B	<i>Hmox1</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.032
Figure 3B	<i>Nqo1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.0005
Figure 3B	<i>Nqo1</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.013
Figure 3B	<i>Gstα3</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.009

Figure 3B	<i>Gsta3</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.041
Figure 3C	AASA	WT vs <i>Abcd1</i> <sup>-</sup>	0.048
Figure 3C	AASA	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.011
Figure 3C	CEL	WT vs <i>Abcd1</i> <sup>-</sup>	0.009
Figure 3C	CEL	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.002
Figure 3C	CML	WT vs <i>Abcd1</i> <sup>-</sup>	0.0097
Figure 3C	CML	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.0014
Figure 3C	MDAL	WT vs <i>Abcd1</i> <sup>-</sup>	0.0013
Figure 3C	MDAL	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.002
Figure 3D	mtDNA	WT vs <i>Abcd1</i> <sup>-</sup>	<0.0001
Figure 3D	mtDNA	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.011
Figure 3E	<i>Sirt1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.005
Figure 3E	<i>Sirt1</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.015
Figure 3E	<i>Pgc-1α</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.037
Figure 3E	<i>Pgc-1α</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.015
Figure 3E	<i>Nrf1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	<0.0001
Figure 3E	<i>Nrf1</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.007
Figure 3E	<i>Tfam</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.001
Figure 3E	<i>Tfam</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.012
Figure 3F	ATP	WT vs <i>Abcd1</i> <sup>-</sup>	0.013
Figure 3F	ATP	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.023
Figure 4A	<i>Nfκb2</i>	WT vs <i>Abcd1</i> <sup>-</sup>	<0.0001
Figure 4A	<i>Nfκb2</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.004
Figure 4A	<i>Il1β</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.008
Figure 4A	<i>Il1β</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.007
Figure 4A	<i>Il6</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.028
Figure 4A	<i>Il6</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.022
Figure 4A	<i>Tnfα</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.031
Figure 4A	<i>Tnfα</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.035
Figure 4A	<i>Tnfrs1a</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.016
Figure 4A	<i>Ccl5</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.010
Figure 4A	<i>Ccl5</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.049
Figure 4A	<i>Cxcl9</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.0001
Figure 4A	<i>Cxcl10</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.005
Figure 4A	<i>Cxcl10</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.028
Figure 4A	<i>Ccr6</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.013
Figure 4A	<i>Ccr6</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.047
Figure 4B	<i>Chil3</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.033
Figure 4B	<i>Chil3</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.009
Figure 4B	<i>Fizz1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.006
Figure 4B	<i>Cxcl12</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.0006
Figure 4B	<i>Cxcl12</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.043
Figure 4B	<i>Il10</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.0005
Figure 4B	<i>Igfl</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.0011
Figure 4B	<i>Igfl</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.046
Figure 4B	<i>Mif</i>	WT vs <i>Abcd1</i> <sup>-</sup>	<0.0001
Figure 4B	<i>Mif</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.005
Figure 4B	<i>Tgfb1</i>	WT vs <i>Abcd1</i> <sup>-</sup>	0.0006
Figure 4B	<i>Tgfb1</i>	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.030
Figure 5Y	Iba1 <sup>+</sup> cells/mm <sup>2</sup>	WT vs DKO	0.0004
Figure 5Y	Iba1 <sup>+</sup> cells/mm <sup>2</sup>	DKO vs DKO + DMF	0.003
Figure 5Y	GFAP <sup>+</sup> cells/mm <sup>2</sup>	WT vs DKO	0.003
Figure 5Y	GFAP <sup>+</sup> cells/mm <sup>2</sup>	DKO vs DKO + DMF	0.004
Figure 5Y	Synaptophysin	WT vs DKO	<0.001
Figure 5Y	Synaptophysin	DKO vs DKO + DMF	<0.001
Figure 5Y	APP	WT vs DKO	0.0082

Figure 5Y	APP	DKO vs DKO + DMF	0.019
Figure 5Z	Number of slips	WT vs DKO	< 0.0001
Figure 5Z	Number of slips	DKO vs DKO + DMF	0.036
Figure 5Z	Time to cross (s)	WT vs DKO	0.003
Figure 5Z	Time to cross (s)	DKO vs DKO + DMF	0.027
Figure 5Z	Number of shocks	WT vs DKO	0.004
Figure 5Z	Number of shocks	DKO vs DKO + DMF	0.006
Figure 5Z	Time of shocks (s)	WT vs DKO	0.013
Figure 5Z	Time of shocks (s)	DKO vs DKO + DMF	0.013
Figure EV2	C26:0	WT vs <i>Abcd1</i> <sup>-</sup>	< 0.001
Figure EV2	C26:0	<i>Abcd1</i> <sup>-</sup> vs <i>Abcd1</i> <sup>-</sup> + DMF	0.037
Figure EV2	C24:0/C22:0	WT vs <i>Abcd1</i> <sup>-</sup>	0.0016
Figure EV2	C26:0/C22:0	WT vs <i>Abcd1</i> <sup>-</sup>	< 0.001
Figure EV3	<i>HMOX1</i>	CTL veh vs CTL C26:0	0.003
Figure EV3	<i>HMOX1</i>	CTL veh vs CTL DMF	0.006
Figure EV3	<i>NQO1</i>	CTL veh vs CTL C26:0	0.005
Figure EV3	<i>NQO1</i>	CTL veh vs CTL DMF	0.025
Figure EV3	<i>GCLC</i>	CTL veh vs CTL C26:0	0.0007
Figure EV3	<i>GCLC</i>	CTL C26:0 vs CTL C26:0 + DMF	0.016
Figure EV3	<i>HMOX1</i>	X- ALD C26:0 vs X-ALD C26:0 + DMF	<0.0001
Figure EV3	<i>HMOX1</i>	X-ALD veh vs X-ALD DMF	<0.0001
Figure EV3	<i>NQO1</i>	X- ALD C26:0 vs X-ALD C26:0 + DMF	<0.0001
Figure EV3	<i>NQO1</i>	X- ALD C26:0 + DMF vs X-ALD DMF	0.031
Figure EV3	<i>GCLC</i>	X- ALD C26:0 vs X-ALD C26:0 + DMF	0.0004
Figure EV3	<i>GCLC</i>	X- ALD C26:0 + DMF vs X-ALD DMF	0.018