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Supplemental Material

Effect of Epidermal Growth Factor Treatment and Polychlorinated Biphenyl Exposure in a Dietary-Exposure Mouse Model of Steatohepatitis

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Table S1. PCB Congener Composition of Aroclor1260 (Adapted from ATSDR CDC)

PCB Congener	% of Aroclor1260	PCB Congener	% of Aroclor1260	PCB Congener	% of Aroclor1260	PCB Congener	% of Aroclor1260
181	11.38	196	0.84	192	0.17	16	0.02
154	9.39	179	0.83	130	0.14	54	0.02
150	8.75	191	0.82	209	0.13	58	0.02
139	6.54	173	0.7	86	0.11	68	0.02
188	5.4	165	0.69	174	0.1	138	0.02
175	4.96	145	0.61	190	0.1	158	0.02
171	4.11	177	0.59	199	0.1	5	0.01
102	3.13	159	0.58	206	0.1	14	0.01
152	3.04	186	0.55	98	0.09	15	0.01
133	2.9	129	0.53	132	0.07	21	0.01
142	2.62	194	0.53	134	0.07	31	0.01
178	2.57	207	0.53	198	0.07	36	0.01
97	2.45	157	0.52	17	0.05	40	0.01
164	2.42	119	0.48	76	0.05	47	0.01
184	2.41	89	0.41	208	0.05	66	0.01
195	2.07	135	0.34	7	0.04	73	0.01
180	2.03	203	0.33	30	0.04	85	0.01
200	1.78	94	0.3	62	0.04	87	0.01
137	1.46	201	0.25	72	0.04	93	0.01
204	1.4	50	0.24	100	0.04	110	0.01
111	1.33	202	0.24	27	0.03	125	0.01
147	1.15	106	0.22	32	0.03	182	0.01
172	1.11	131	0.22	42	0.03	16	0.02
197	1.09	168	0.19	0	0.02		
136	1.08	176	0.17	3	0.02		

Table S2: Taqman Probes

Taqman Probe ID	Gene
Mm00445168_m1	*Abcb11*
Mm01545150_m1	*Apob*
Mm01307193_g1	*Apoe*
Mm00478932_m1	*Ahr*
Mm01283978_m1	*Car*
Mm03047343_m1	*Cd68*
Mm01231183_m1	*Cpt1*α
Mm00487218_m1	*Cyp1a1*
Mm00487224_m1	*Cyp1a2*
Mm01972453_s1	*Cyp2b10*
Mm00731567_m1	*Cyp3a11*
Mm02601690_gH	*Cyp4a10*
Mm00484150_m1	*Cyp7a1*
Mm00444340_m1	*Fabp1*
Mm00662319_m1	*Fasn*
Mm00436425_m1	*Fxr*
Mm00839363_m1	*G6pc*
Mm99999915_g1	*G6pdh*
Mm00802655_m1	*Gclc*
Mm00439154_m1	*Gsr*

Mm01247712_m1	*Hnf4α*
Mm00446190_m1	*Il6*
Mm00443451_m1	*Lxrα*
Mm00459644_m1	*Ly6gd*
Mm00782380_s1	*Me1*
Mm01340842_m1	*Mef2c*
Mm01253561_m1	*Nqo1*
Mm00477784_m1	*Nrf2*
Mm00443090_m1	*Pklr*
Mm00440939_m1	*Pparα*
Mm00772290_m1	*Scd1*
Mm00442278_m1	*Shp*
Mm00550338_m1	*Srebf1*
Mm01178820_m1	*Tgfβ*
Mm00445273_m1	*Tlr4*
Mm00443258_m1	*Tnfα*

Table S3: Antibodies

Antibody	Supplier	Catalog #
p-EGFR Y1173	Abcam	Ab5652
EGFR	Santa Cruz	SC-03
p-ERK 1/2	Cell Signaling Technology	9101
ERK 1/2	Cell Signaling Technology	4695
β-actin	Cell Signaling Technology	8457
CAR	Abcam	Ab186869
LXRα	Abcam	Ab176323
NRF2	Abcam	Ab156883
p62	Cell Signaling Technology	23214
HNF4α	Abcam	Ab201460
PPARα	Abcam	Ab126285
FXR	Abcam	Ab129089
S96 KAP2	Abcam	Ab32390
KAP2	Cell Signaling Technology	3927
CDK2	Cell Signaling Technology	18048
Y15-CDK2	Abcam	Ab133463
ACLY	Cell Signaling Technology	13390
S455-ACLY	Cell Signaling Technology	4331
P-CDK Substrate	Cell Signaling Technology	9477
2° HRP Antibody (Goat anti Rabbit)	Cell Signaling Technology	7074

Table S4: Outliers for each measure and figure.

			# of Outliers			
Tissue	Figure	Measure	CS	CE	AS	AE
Liver	Fig 1Bii	% Sirius Red Area	0	0	0	0
Plasma	Fig 1Ci	TNFα	0	1	0	1
Plasma	Fig 1Cii	PAI-1	0	0	0	0
Plasma	Fig 1Ciii	Resistin	2	2	0	2
Liver	Fig 1D	*Tnfα*	5	1	2	2
Liver	Fig 1D	*Il-6*	0	2	0	0
Liver	Fig 1D	*Ly6g6d*	0	0	0	0
Liver	Fig 1D	*Cd68*	1	2	3	2
Liver	Fig 1D	*Tlr4*	1	2	3	3
Liver	Fig 1E	*Tgfβ*	0	0	0	0
Liver	Fig 1E	*Mef2c*	0	0	0	0
Liver	Fig 2A	Steatosis	0	0	0	0
Liver	Fig 2Bi	FFAs	1	2	0	4
Liver	Fig 2Bii	Triglycerides	0	0	0	0
Liver	Fig 2Biii	Cholesterol	2	2	1	0
Plasma	Fig 2Ci	FFAs	2	3	0	2
Plasma	Fig 2Cii	Triglycerides	0	0	0	0
Plasma	Fig 2Ciii	Cholesterol	0	0	0	0
Plasma	Fig 2Di	HDL	0	0	0	0
Plasma	Fig 2Dii	LDL	0	0	0	0
Plasma	Fig 2Diii	VLDL	0	0	0	0
Liver	Fig 2Ev	*Apob*	0	0	0	0
WAT	Fig 2Ei	WAT wt	0	0	0	0
Plasma	Fig 2Eii	Adiponectin	0	5	0	0
Plasma	Fig 3Bi	Glucose	0	0	0	0
Plasma	Fig 3Bii	Pyruvate	2	3	1	1
Plasma	Fig 3Cii	GTT	0	0	0	0
Plasma	Fig 3Dii	ITT	0	0	0	0
Liver	Fig 4Ai	CAR	0	0	0	0
Liver	Fig 4Aii	*Car*	1	0	0	0
Liver	Fig 4Aii	*Cyp2b10*	8	8	4	7
Liver	Fig 4Aii	*Cyp3a11*	1	2	1	0
Liver	Fig 4Bi	LXRα	0	0	0	0
Liver	Fig 4Bii	*Lxrα*	0	0	0	0
Liver	Fig 4Bii	*Fasn*	0	0	0	0
Liver	Fig 4Bii	*Srebf1*	1	0	2	0
Liver	Fig 4Bii	*Apoe*	2	2	0	2
Liver	Fig 4Ci	HNF4α	0	0	0	0
Liver	Fig 4Cii	*Hnf4α*	0	0	0	0
Liver	Fig 4Cii	*Pklr*	0	0	1	0
Liver	Fig 4Cii	*G6pc*	0	0	0	0
Liver	Fig 4Di	NRF2	0	0	0	0
Liver	Fig 4Di	P62	0	0	0	0
Liver	Fig 4Dii	*Nrf2*	2	3	2	2
Liver	Fig 4Dii	*Nqo1*	1	2	1	2
Liver	Fig 4Dii	*Me1*	0	0	0	0
Liver	Fig 4Dii	*Gclc*	0	0	0	0
Liver	Fig 4Dii	*Gsr*	0	0	0	0
Liver	Fig 4Dii	*G6pdh*	0	0	2	2
Liver	Fig S1A	P-Y1173-EGFR	0	0	0	0
Liver	Fig S1A	P-ERK1/2	0	0	0	0
Liver	Fig S1C	P-Y1173-EGFR	0	0	0	0
Blood	Fig S2B	Glucose 6hr	0	0	0	0
Blood	FigS2C	Glucose 12hr	0	0	0	0
Liver	FigS3A	FXR	0	0	0	0
Liver	FigS3A	*Fxr*	0	0	0	1
Liver	FigS3A	*Cyp7a1*	0	2	0	1
Liver	FigS3A	*Abcb11*	0	0	0	0
Liver	FigS3A	*Shp*	1	0	1	1
Liver	FigS3B	*Ahr*	1	0	0	0
Liver	FigS3B	*Cyp1a1*	0	0	0	0
Liver	FigS3B	*Cyp1a2*	0	0	0	0

Liver	FigS4A	S455-ACLY	0	0	0	0
Liver	FigS4B	S96-KAP2	0	0	0	0
Liver	FigS4C	Y15-CDK2	1	0	0	1
Liver	FigS4C	P-CDK Substrate	0	0	0	0

CS: Control+saline; CE: Control+EGF; AS: Aroclor1260+saline; AE: Aroclor1260+EGF

Table S5: p-values

			Two-Way ANOVA			Sidak's multiple comparison test			
Tissue	Figure	Measure	EGF	Aroclor	Interaction	CSvsCE	CSvsAS	CEvsAE	AS vsAE
Liver	Fig 1Bii	% Sirius Red Area	0.06	0.1	0.03	0.8	0.02	0.6	0.005
Plasma	Fig 1Ci	TNFα	0.02	0.5	0.3	0.3	0.2	0.8	0.02
Plasma	Fig 1Cii	PAI-1	0.03	0.4	0.3	0.9	0.04	0.9	0.02
Plasma	Fig 1Ciii	Resistin	0.03	0.7	0.6	0.05	0.5	0.9	0.2
Liver	Fig 1D	*Tnfα*	0.5	0.2	0.03	0.2	0.02	0.3	0.04
Liver	Fig 1D	*Il-6*	<0.0001	0.8	0.4	0.04	0.1	0.8	0.0002
Liver	Fig 1D	*Ly6g6d*	0.001	0.2	0.2	0.2	0.9	0.04	0.002
Liver	Fig 1D	*Cd68*	0.001	0.2	0.2	0.1	0.9	0.06	0.002
Liver	Fig 1D	*Tlr4*	0.05	0.4	0.5	0.2	0.9	0.02	0.002
Liver	Fig 1E	*Tgfβ*	0.01	0.8	0.9	0.05	0.6	0.8	0.1
Liver	Fig 1E	*Mef2c*	0.7	0.8	0.003	0.3	0.01	0.2	0.008
Liver	Fig 2A	Steatosis	0.5	0.9	0.07	0.07	0.3	0.1	0.4
Liver	Fig 2Bi	FFAs	0.01	0.02	0.1	0.4	0.008	0.6	0.007
Liver	Fig 2Bii	Triglycerides	0.8	0.03	0.006	0.02	0.7	0.004	0.3
Liver	Fig 2Biii	Cholesterol	0.009	0.4	0.6	0.05	0.9	0.8	0.04
Plasma	Fig 2Ci	FFAs	0.3	0.9	0.7	0.4	0.8	0.8	0.3
Plasma	Fig 2Cii	Triglycerides	0.0003	0.0003	0.0005	0.9	0.9	<0.0001	<0.0001
Plasma	Fig 2Ciii	Cholesterol	0.3	0.5	0.0002	0.03	0.02	0.002	0.001
Plasma	Fig 2Di	HDL	0.7	0.2	0.0002	0.002	0.04	0.0007	0.01
Plasma	Fig 2Dii	LDL	0.9	0.7	0.003	0.02	0.05	0.02	0.05
Plasma	Fig 2Diii	VLDL	0.001	0.002	0.003	0.8	0.9	<0.0001	<0.0001
Liver	Fig 2Ev	*Apob*	0.0006	<0.0001	<0.0001	0.5	0.6	<0.0001	<0.0001
WAT	Fig 2Ei	WAT wt	0.9	0.9	0.02	0.1	0.1	0.9	0.08
Plasma	Fig 2Eii	Adiponectin	0.9	0.0009	0.007	0.06	0.6	<0.0001	0.05
Plasma	Fig 3Bi	Glucose	0.007	0.8	0.4	0.2	0.4	0.7	0.01
Plasma	Fig 3Bii	Pyruvate	0.3	<0.0001	0.3	0.9	0.0001	0.008	0.2
Plasma	Fig 3Cii	GTT	0.3	0.3	0.08	0.6	0.6	0.06	0.06
Plasma	Fig 3Dii	ITT	0.9	0.008	0.2	0.3	0.4	0.3	0.006
Liver	Fig 4Ai	CAR	0.9	0.8	0.4	0.3	0.6	0.4	0.5
Liver	Fig 4Aii	*Car*	0.04	<0.0001	0.5	0.3	0.02	0.0007	0.05
Liver	Fig 4Aii	*Cyp2b10*	0.7	0.1	0.008	0.9	0.003	0.3	0.05
Liver	Fig 4Aii	*Cyp3a11*	0.2	0.04	0.3	0.9	0.03	0.5	0.09
Liver	Fig 4Bi	LXRα	0.1	0.06	0.04	0.7	0.8	0.007	0.01
Liver	Fig 4Bii	*Lxrα*	0.03	0.7	0.04	0.9	0.09	0.3	0.004
Liver	Fig 4Bii	*Fasn*	0.03	0.6	0.1	0.6	0.5	0.1	0.01
Liver	Fig 4Bii	*Srebf1*	0.003	0.03	0.02	0.6	0.003	0.8	0.0003
Liver	Fig 4Bii	*Apoe*	0.05	0.3	0.9	0.1	0.5	0.4	0.2
Liver	Fig 4Ci	HNF4α	0.04	0.6	0.6	0.2	0.9	0.5	0.06
Liver	Fig 4Cii	*Hnf4α*	0.7	0.0007	0.6	0.6	0.003	0.01	0.9
Liver	Fig 4Cii	*Pklr*	0.01	0.8	0.05	0.4	0.4	0.1	0.003
Liver	Fig 4Cii	*G6pc*	0.3	0.02	0.9	0.5	0.06	0.02	0.3
Liver	Fig 4Di	NRF2	0.5	0.05	0.1	0.4	0.02	0.3	0.5
Liver	Fig 4Di	P62	0.9	0.04	0.7	0.7	0.2	0.08	0.9
Liver	Fig 4Dii	*Nrf2*	0.02	0.4	0.8	0.1	0.4	0.7	0.05
Liver	Fig 4Dii	*Nqo1*	0.007	0.007	0.5	0.09	0.06	0.03	0.06
Liver	Fig 4Dii	*Me1*	0.06	0.04	0.4	0.4	0.4	0.04	0.06
Liver	Fig 4Dii	*Gclc*	0.2	0.002	0.9	0.3	0.02	0.03	0.4

Liver	Fig 4Dii	*Gsr*	0.02	0.01	0.0001	0.2	0.3	<0.0001	<0.0001
Liver	Fig 4Dii	*G6pd*	0.9	0.004	0.9	0.9	0.04	0.03	0.9
Liver	Fig S1C	P-Y1173-EGFR	0.04	0.5	0.9	0.1	0.6	0.6	0.2
Blood	Fig S2B	Glucose 6hr	0.009	0.6	0.2	0.3	0.6	0.2	0.006
Blood	FigS2C	Glucose 12hr	<0.0001	0.2	0.6	0.006	0.6	0.2	0.0007
Liver	FigS3A	FXR	0.8	0.04	0.3	0.4	0.04	0.4	0.6
Liver	FigS3A	*Fxr*	0.5	0.02	0.07	0.4	0.005	0.7	0.09
Liver	FigS3A	*Cyp7a1*	0.03	<0.0001	0.8	0.08	0.0005	0.002	0.2
Liver	FigS3A	*Abcb11*	0.6	0.03	0.7	0.6	0.2	0.07	0.9
Liver	FigS3A	*Shp*	0.4	0.04	0.3	0.8	0.03	0.5	0.2
Liver	FigS3B	*Ahr*	0.1	0.4	0.6	0.2	0.8	0.4	0.5
Liver	FigS3B	*Cyp1a1*	0.03	0.4	0.4	0.3	0.9	0.2	0.04
Liver	FigS3B	*Cyp1a2*	0.08	0.8	0.7	0.3	0.6	0.9	0.1
Liver	FigS4A	S455-ACLY	0.3	0.05	0.4	0.5	0.2	0.8	0.9
Liver	FigS4B	S96-KAP2	0.8	0.2	0.6	0.9	0.8	0.9	0.9
Liver	FigS4C	Y15-CDK2	0.3	0.9	0.002	0.2	0.06	0.08	0.02
Liver	FigS4C	P-CDK Substrate	0.2	0.2	0.9	0.7	0.8	0.7	0.9

CS: Control+saline; CE: Control+EGF; AS: Aroclor1260+saline; AE: Aroclor1260+EGF

Table S6: Numerical Data

			Numerical Data (mean ± SD)			
Tissue	Figure	Measure	CS	CE	AS	AE
Liver	Fig 1Bii	% Sirius Red Area	0.47 ± 0.38	0.59 ± 0.49	2.09 ± 2.37	0.26 ± 0.24
Plasma	Fig 1Ci	TNFα	3.72 ± 1.50	3.17 ± 1.24	4.42 ± 2.05	3.01 ± 1.38
Plasma	Fig 1Cii	PAI-1	1848 ± 798.6	1794 ± 901.5	2665 ± 1611	1726 ± 834.1
Plasma	Fig 1Ciii	Resistin	2147 ± 700.5	1598 ± 796.2	1981 ± 957.8	1632 ± 483.5
Liver	Fig 1D	*Tnfα*	1 ± 0.67	1.78 ± 1.5	2.62 ± 2.97	1.26 ± 0.99
Liver	Fig 1D	*Il-6*	1 ± 0.34	0.47 ± 0.21	1.41 ± 1.39	0.41 ± 0.15
Liver	Fig 1D	*Ly6g6d*	1 ± 0.30	0.82 ± 0.39	1.02 ± 0.49	0.60 ± 0.21
Liver	Fig 1D	*Cd68*	1 ± 0.32	0.85 ± 0.30	1.01 ± 0.25	0.65 ± 0.23
Liver	Fig 1D	*Tlr4*	1 ± 0.32	0.85 ± 0.30	1.01 ± 0.25	0.61 ± 0.16
Liver	Fig 1E	*Tgfβ*	1 ± 0.35	0.81 ± 0.22	0.94 ± 0.29	0.78 ± 0.27
Liver	Fig 1E	*Mef2c*	1 ± 0.20	1.11 ± 0.29	1.27 ± 0.36	0.98 ± 0.31
Liver	Fig 2A	Steatosis	2.94 ± 1.0	2.18 ± 1.33	2.42 ± 1.17	2.80 ± 1.21
Liver	Fig 2Bi	FFAs	1.78 ± 1.65	1.22 ± 1.14	3.74 ± 3.26	1.64 ± 0.78
Liver	Fig 2Bii	Triglycerides	0.68 ± 0.58	0.43 ± 0.32	0.64 ± 0.47	0.74 ± 0.60
Liver	Fig 2Biii	Cholesterol	0.14 ± 0.03	0.19 ± 0.11	0.15 ± 0.06	0.22 ± 0.11
Plasma	Fig 2Ci	FFAs	3.02 ± 0.06	2.85 ± 1.02	3.12 ± 1.05	2.78 ± 0.8
Plasma	Fig 2Cii	Triglycerides	57.1 ± 9.2	57.6 ± 14.2	57.7 ± 12.7	82.5 ± 16.4
Plasma	Fig 2Ciii	Cholesterol	130.1 ± 21.1	106.8 ± 45.2	104.5 ± 31.9	142.5 ± 20.7
Plasma	Fig 2Di	HDL	90.5 ±11.2	65.4 ± 26.1	74.0 ± 22.6	94.9 ± 7.4
Plasma	Fig 2Dii	LDL	16.6 ± 5.9	10.6 ± 5.9	11.6 ± 4.8	17.0 ± 3.3
Plasma	Fig 2Diii	VLDL	11.4 ± 1.9	11.6 ± 2.7	11.5 ± 2.5	15.9 ± 3.3
Liver	Fig 2Ev	*Apob*	1 ± 0.16	0.97 ± 0.13	1.03 ± 0.12	1.31 ± 0.12
WAT	Fig 2Ei	WAT wt	48.79 ± 11.37	39.98 ± 18.27	39.39 ± 17.51	49.54 ± 14.98
Plasma	Fig 2Eii	Adiponectin	124599 ± 76047	166482 ± 12862	114621 ± 53966	73290 ± 56614

Plasma	Fig 3Bi	Glucose	247.5 ± 78.9	296.6 ± 104.8	216.6 ± 87.7	311.6 ± 131.5
Plasma	Fig 3Bii	Pyruvate	264 ± 184.5	263.5 ± 71.45	668.7 ± 414.8	535.4 ± 264
Plasma	Fig 3Cii	GTT	31368 ± 3695	30632 ± 4933	30610 ± 3498	33444 ± 4074
Plasma	Fig 3Dii	ITT	16030 ± 2259	17392 ± 4186	14870 ± 4461	18906 ± 4752
Liver	Fig 4Ai	CAR	0.69 ± 0.27	0.62 ± 0.16	0.63 ± 0.16	0.72 ± 0.24
Liver	Fig 4Aii	*Car*	1 ± 0.38	1.14 ± 0.47	1.34 ± 0.33	1.62 ± 0.37
Liver	Fig 4Aii	*Cyp2b10*	1 ± 1.09	1.50 ± 2.47	130.9 ± 148.9	23.89 ± 36.69
Liver	Fig 4Aii	*Cyp3a11*	1 ± 0.50	0.98 ± 0.29	1.46 ± 0.90	1.11 ± 0.46
Liver	Fig 4Bi	LXRα	0.29 ± 0.20	0.24 ± 0.12	0.26 ± 0.07	0.64 ± 0.30
Liver	Fig 4Bii	*Lxrα*	1 ± 0.20	1.01 ± 0.19	0.89 ± 0.11	1.08 ± 0.17
Liver	Fig 4Bii	*Fasn*	1 ± 0.23	1.04 ± 0.16	0.95 ± 0.23	1.16 ± 0.27
Liver	Fig 4Bii	*Srebf1*	1 ± 0.44	1.08 ± 0.50	0.48 ± 0.14	1.11 ± 0.52
Liver	Fig 4Bii	*Apoe*	1 ± 0.,09	1.08 ± 0.17	0.97 ± 0.12	1.04 ± 0.15
Liver	Fig 4Ci	HNF4α	0.41 ± 0.20	0.61 ± 0.24	0.40 ± 0.12	0.73 ± 0.30
Liver	Fig 4Cii	*Hnf4α*	1 ± 0.44	0.94 ± 0.39	0.61 ± 0.38	0.60 ± 0.25
Liver	Fig 4Cii	*Pklr*	0.94 ± 0.41	1.08 ± 0.37	0.8 ± 0.30	1.34 ± 0.70
Liver	Fig 4Cii	*G6pc*	1 ± 0.48	0.91 ± 0.38	0.73 ± 0.39	0.58 ± 0.29
Liver	Fig 4Di	NRF2	0.80 ± 0.17	0.67 ± 0.32	0.37 ± 0.14	0.48 ± 0.22
Liver	Fig 4Di	P62	0.56 ± 0.20	0.50 ± 0.15	0.75 ± 0.30	0.78 ± 0.25
Liver	Fig 4Dii	*Nrf2*	1 ± 0.20	1.13 ± 0.25	0.93 ± 0.17	1.09 ± 0.24
Liver	Fig 4Dii	*Nqo1*	1 ± 0.57	1.52 ± 0.83	1.61 ± 0.93	2.24 ± 1.04
Liver	Fig 4Dii	*Me1*	1 ± 0.28	0.91 ± 0.43	0.90 ± 0.30	0.67 ± 0.25
Liver	Fig 4Dii	*Gclc*	1 ± 0.19	0.91 ± 0.27	0.80 ± 0.19	0.73 ± 0.29
Liver	Fig 4Dii	*Gsr*	1 ± 0.17	1.13 ± 0.42	1.11 ± 0.26	0.64 ± 0.28
Liver	Fig 4Dii	*G6pdh*	1 ± 0.91	1.02 ± 0.82	0.38 ± 0.33	0.34 ± 0.28
Liver	Fig S1C	P-Y1173-EGFR	0.28 ± 0.12	0.52 ± 0.40	0.20 ± 0.09	0.44 ± 0.20
Blood	Fig S2B	Glucose 6hr	175.4 ± 15.6	184.5 ± 29.1	169.6 ± 37.8	197.8 ± 27.0
Blood	FigS2C	Glucose 18hr	161.1 ± 31.5	190.8 ± 25.7	167.2 ± 29.8	205.1 ± 32.9
Liver	FigS3A	FXR	0.50 ± 0.17	0.60 ± 0.22	0.75 ± 0.22	0.69 ± 0.28
Liver	FigS3A	*Fxr*	1 ± 0.24	1.09 ± 0.41	1.33 ± 0.35	1.13 ± 0.24
Liver	FigS3A	*Cyp7a1*	1 ± 0.69	2.28 ± 1.18	3.67 ± 2.06	4.68 ± 3.24
Liver	FigS3A	*Abcb11*	1.02 ± 0.13	1.05 ± 0.20	0.93 ± 0.21	0.93 ± 0.16
Liver	FigS3A	*Shp*	1 ± 0.60	1.08 ± 0.66	1.73 ± 1.34	1.30 ± 0.82
Liver	FigS3B	*Ahr*	0.92 ± 0.32	0.81 ± 0.21	0.94 ± 0.22	0.88 ± 0.17
Liver	FigS3B	*Cyp1a1*	1 ± 0.37	1.15 ± 0.48	0.99 ± 0.37	1.34 ± 0.50
Liver	FigS3B	*Cyp1a2*	1 ± 0.29	0.92 ± 0.24	1.05 ± 0.29	0.91 ± 0.17
Liver	FigS4A	S455-ACLY	1 ± 0.82	0.56 ± 0.40	0.35 ± 0.26	0.30 ± 0.10
Liver	FigS4B	S96-KAP2	1 ± 0.48	0.88 ± 0.34	0.72 ± 0.28	0.75 ± 0.26
Liver	FigS4C	Y15-CDK2	0.84 ± 0.05	1.05 ± 0.20	1.13 ± 0.20	0.77 ± 0.06
Liver	FigS4C	P-CDK Substrate	1 ± 0.27	1.41 ± 1.05	0.66 ± 0.40	0.96 ± 0.44

CS: Control+saline; CE: Control+EGF; AS: Aroclor1260+saline; AE: Aroclor1260+EGF

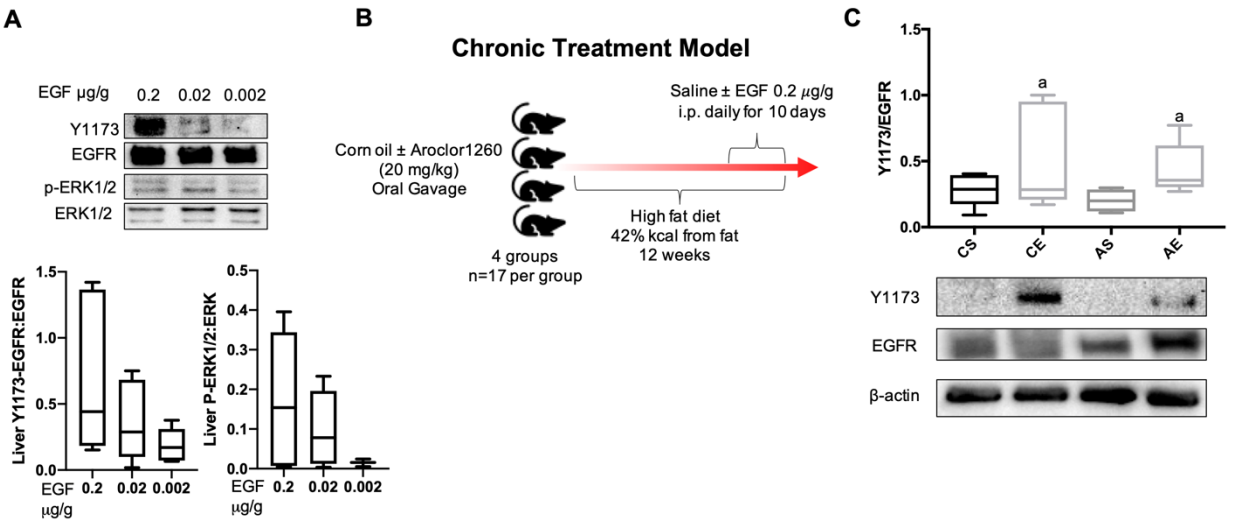

Figure S1: Effects of acute EGF and chronic EGF and Aroclor1260 exposure on hepatic EGFR signaling.

Male WT C57Bl/6 mice fed a control diet were treated with either saline or EGF at multiple doses (0.002, 0.02, 0.2 μg/g) followed by euthanasia at 30 minutes post i.p. injection and tissue harvest for downstream analysis. Male WT C57Bl/6 mice were fed a HFD (12 weeks) and exposed to either vehicle or Aroclor1260 (20mg/kg) by a one-time oral gavage at week 1. Aroclor1260 exposed or vehicle mice were treated (via i.p. injection) with saline or EGF (0.2 μg/g) daily for 10 days starting at week 10. Mice were fasted for 12 hours and euthanized and tissues harvested for downstream analyses. Figure S1: **A.** Western blot analysis of liver EGFR phosphorylation and ERK1/2 after i.p. of EGF at 0.002, 0.02, and 0.2 μg/g. Phosphorylated proteins are normalized to total proteins. A representative western blot image is pictured. **B.** Diagram of chronic treatment animal model. **C.** Hepatic EGFR phosphorylation was evaluated in mice exposed to corn oil and injected with either saline (CS) or EGF (0.2 µg/g) (CE) or gavaged with Aroclor1260 (20 mg/kg) and injected with saline (AS) or EGF (AE) (chronic). Phosphorylated

EGFR was normalized to total EGFR. A representative western blot image is pictured. An n=5 was used for this figure. A two-way ANOVA was used to statistically compare datasets followed by a one-way ANOVA with a Sidak correction for intergroup comparisons. A $p<0.05$ was considered significant. Significance due to EGF is denoted by (a), due to Aroclor1260 denoted by (b), and due to interaction denoted by (c) for the two-way ANOVA. Data are presented as box and whisker plots for figure S1B which illustrate the median (midline), upper and lower quartiles (box) and the upper and lower limits (whiskers). All numerical data are presented in supplemental materials Table S6 as mean ± SD and p-values can be found in Table S5. **Abbreviations**: CS: Control+saline; CE: Control+EGF; AS: Aroclor1260+Saline; AE: Aroclor1260+EGF; EGF: epidermal growth factor; EGFR: Epidermal growth factor receptor.

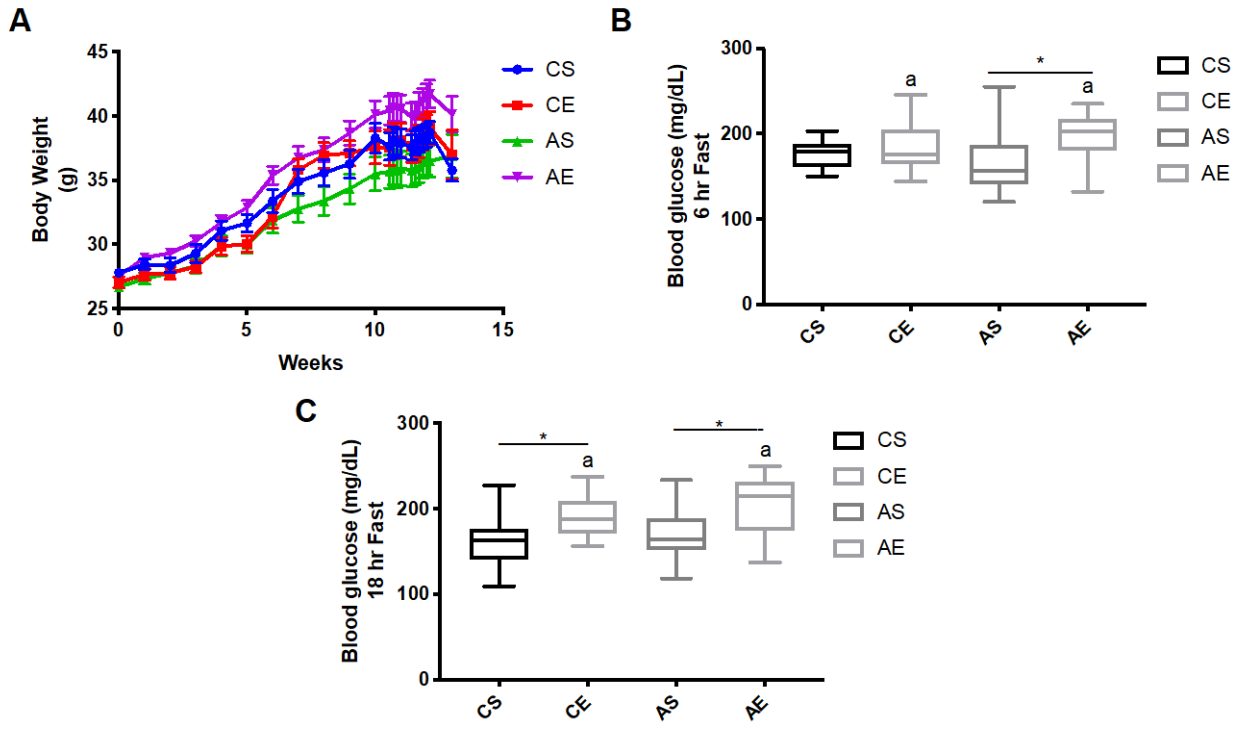

Figure S2: Effects of chronic EGF and Aroclor 1260 exposure on fasted glucose levels at 6 and 12 hours.

Male WT C57Bl/6 mice were fed a HFD (12 weeks) and exposed to either vehicle or Aroclor1260 (20mg/kg) by a one-time oral gavage at week 1. Aroclor1260 exposed or vehicle mice were treated (via i.p. injection) with saline or EGF (0.2 μg/g) daily for 10 days starting at week 10. Mice were fasted for 6 and 18 hours and blood was sampled for measuring blood glucose levels. Figure S2: **A.** Body weight of mice during the course of the study. **B.** Blood glucose after 6 hour fast. **C.** Blood glucose after 12 hour fast. An n=17 was used for this figure. A two-way ANOVA was used to statistically compare datasets followed by a Sidak correction for intergroup comparisons. A $p<0.05$ was considered significant. Significance due to EGF is denoted by (a), due to Aroclor1260 denoted by (b), and due to interaction denoted by (c) for the two-way ANOVA. A $p<0.05$ was denoted by * for the Sidak multiple comparison test. Data are presented as mean ± SEM for Fig S2A. Data are presented as box and whisker plots for figure S2B-C which illustrate the median (midline), upper and lower quartiles (box) and the upper and lower limits (whiskers). All numerical data are presented in supplemental materials Table S6 as mean ± SD and p-values can be found in Table S5. **Abbreviations**: CS: Control+saline; CE: Control+EGF; AS: Aroclor1260+Saline; AE: Aroclor1260+EGF; EGF: epidermal growth factor.

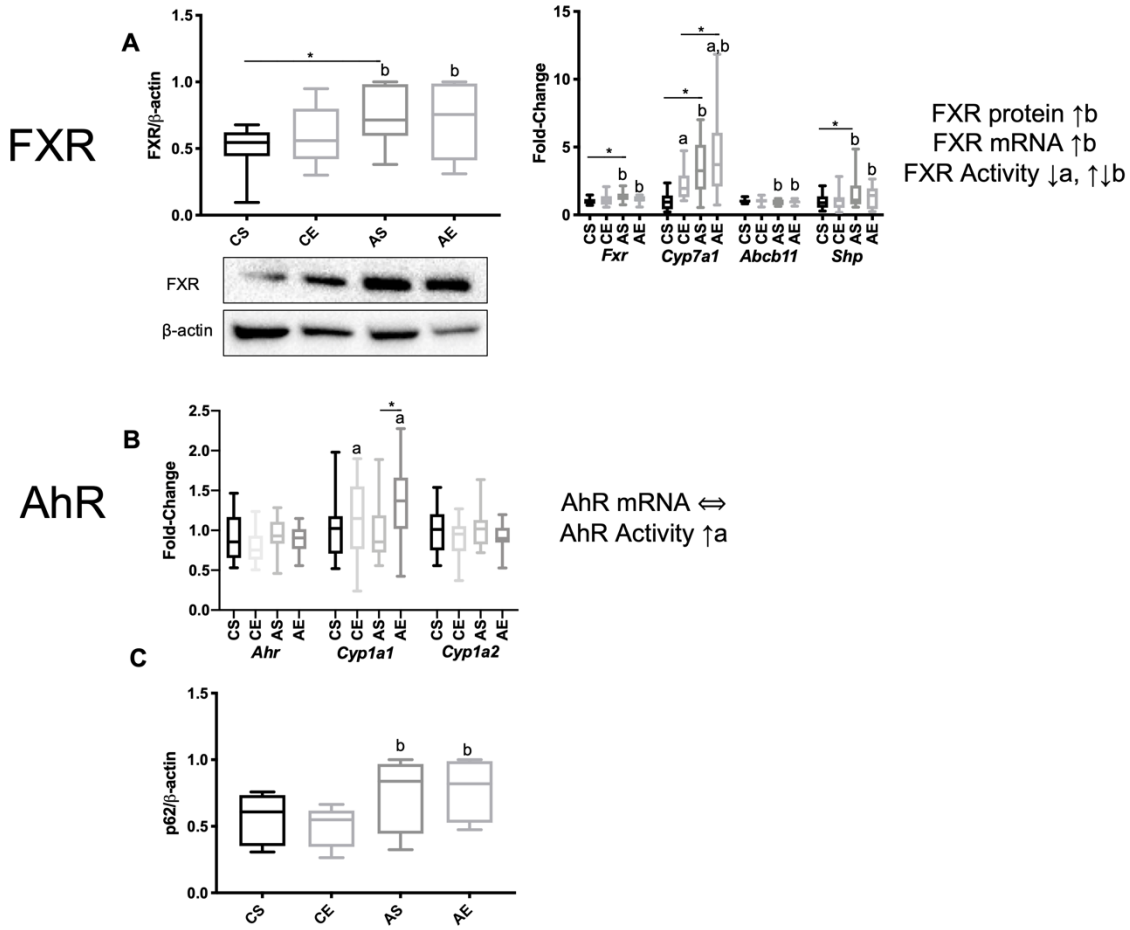

Figure S3: Effects of chronic EGF and Aroclor 1260 exposure on hepatic FXR and AhR expression and target genes.

Male WT C57Bl/6 mice were fed a HFD (12 weeks) and exposed to either vehicle or Aroclor1260 (20mg/kg) by a one-time oral gavage at week 1. Aroclor1260 exposed or vehicle mice were treated (via i.p. injection) with saline or EGF (0.2 μg/g) daily for 10 days starting at week 10. Mice were fasted for 12 hours and euthanized and tissues harvested for downstream analyses. Figure S3. **A.** Hepatic expression of farnesoid x receptor (FXR) and target genes *Cyp7a1*, *Abcb11*, and *Shp*. **B.** Hepatic expression of *Ahr* and target genes *Cyp1a1* and *Cyp1a2*. **C.** Quantification of hepatic p62 protein expression. A n=5 was used for the western blot analysis data and a n=17 was used for all the qPCR data. A two-way ANOVA was used to statistically compare datasets followed by a Sidak correction for intergroup comparisons. A $p<0.05$ was

considered significant. A $p<0.05$ is denoted by * for the Sidak multiple comparison test. Significance due to EGF is denoted by (a), due to Aroclor1260 denoted by (b), and due to interaction denoted by (c) for the two-way ANOVA. Data are presented as box and whisker plots for figure S3 which illustrate the median (midline), upper and lower quartiles (box) and the upper and lower limits (whiskers). All numerical data are presented in supplemental materials Table S6 as mean ± SD and p-values can be found in Table S5. Numeric outliers were identified by ROUT method and removed. The number of outliers are reported in Table S4. **Abbreviations**: CS: Control+saline; CE: Control+EGF; AS: Aroclor1260+Saline; AE: Aroclor1260+EGF; EGF: epidermal growth factor; FXR: Farnesoid X receptor; Cyp7a1: Cytochrome P450 7A1; Abcb11: ATP binding cassette B11; Shp: Small heterodimer partner; Ahr: Aryl hydrocarbon receptor; Cyp1a1: Cytochrome P450 1A1; Cyp1a2: Cytochrome P450 1A2; p62: Sequestosome 1.

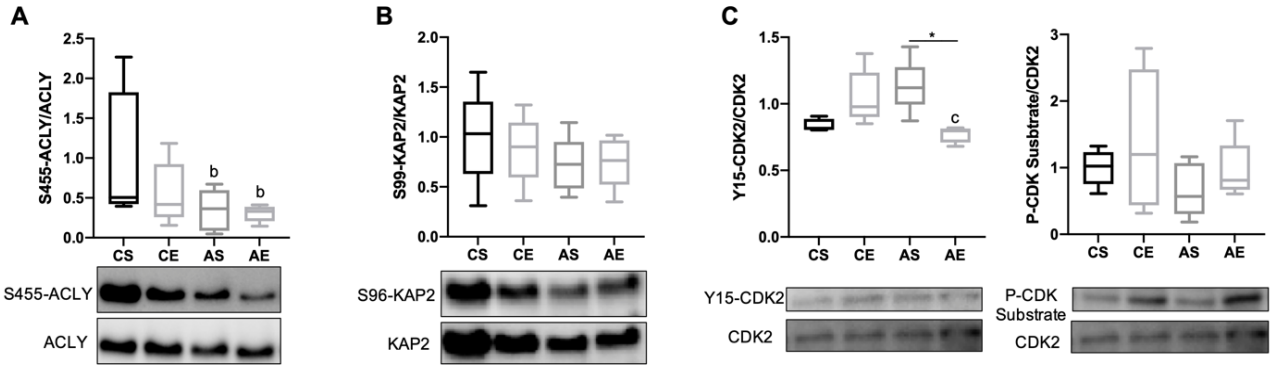

Figure S4: Effect of chronic EGF and A1260 exposure on hepatic phosphoproteomic targets.

Male WT C57Bl/6 mice were fed a HFD (12 weeks) and exposed to either vehicle or Aroclor1260 (20mg/kg) by a one-time oral gavage at week 1. Aroclor1260 exposed or vehicle mice were treated (via i.p. injection) with saline or EGF (0.2 μg/g) daily for 10 days starting at week 10. Mice were fasted for 12 hours and euthanized and tissues harvested for downstream

analyses. Figure S4. **A.** Western blot analysis measuring hepatic S455-ACLY normalized to total ACLY, **B.** S96-KAP2 normalized to KAP2, and **C.** Y15-CDK2 and P-CDK substrate normalized to CDK2. A n=5 was used for the western blot analysis data. A two-way ANOVA was used to statistically compare datasets followed by a Sidak correction for intergroup comparisons. A $p<0.05$ was considered significant. A $p<0.05$ is denoted by *. Significance due to EGF is denoted by (a), due to Aroclor1260 denoted by (b), and due to interaction denoted by (c) for the two-way ANOVA. Data are presented as box and whisker plots for figure S4 which illustrate the median (midline), upper and lower quartiles (box) and the upper and lower limits (whiskers). All numerical data are presented in supplemental materials Table S6 as mean ± SD and p-values can be found in Table S5. Numeric outliers were identified by ROUT method and removed. The number of outliers are reported in Table S4. **Abbreviations**: CS: Control+saline; CE: Control+EGF; AS: Aroclor1260+Saline; AE: Aroclor1260+EGF; EGF: epidermal growth factor; ACLY: ATP citrate synthase; KAP2: Protein kinase CAMP-dependent type II regulatory subunit; CDK2: Cyclin dependent kinase 2; CDK: Cyclin dependent kinase.