

Supplemental Table 1. Adipose metabolomics of C57BL/6J mice consuming a high fat diet in the absence or presence of EPA.

Full Metabolite Name	Shortened Metabolite Name	MetaboliteGroup	Type	EPA_containing	Log2FC	GreaterDiet	BH.adjust	EPA 122	EPA 123	EPA 125	EPA 129	EPA 130	HF60 101
Arg Lys Pro	Arg.Lys.Pro	Amino Acids	Amino Acids	NO	2.391435934	EPA	0.004137	41894.47	38245.23	56102.32	58578.34	43989.35	8663.335
Bouillonamide A	Bouillonamide.A	Macrolide	Macrolide	NO	1.711871457	EPA	0.007652	2001.916	3728.059	2887.93	3233.896	4153.081	1078.604
C-12 NBD-dihydro-Ceramide	C-12.NBD.dihydro.Ceramide	NBD.dihydro.Ceramide	Ceramide	NO	4.485092	EPA	0.016708	672955	542882.1	654727.6	730481.1	478854.4	27675.25
DG(20:5(5Z,8Z,11Z,14Z,17Z),	DG(40:10)	Diacylglycerols	DG	YES	4.559313244	EPA	0.016708	1547479	1255585	1513081	1675377	1083498	57893.07
DG(20:5(5Z,8Z,11Z,14Z,17Z),	DG(42:10)	Diacylglycerols	DG	YES	1.738211816	EPA	0.005847	292851.9	226247.3	289155.9	329190.8	190577.6	75241.01
DG(20:5(5Z,8Z,11Z,14Z,17Z),	DG(42:11)	Diacylglycerols	DG	YES	2.118246586	EPA	0.004137	324616.8	266936.5	309371.6	359380.9	207733.8	62216.59
DG(18:3(9Z,12Z,15Z)/20:4(5Z,8Z,11Z,14Z,17Z))	DG(38:7)	Diacylglycerols	DG	NO	5.106853826	EPA	0.016708	591422.6	422151.2	628096	655187.3	360216.1	13433.45
GalCer(d18:1/24:0)	GalCer(d42:1)	Ceramide	Ceramide	NO	1.529804365	EPA	0.023611	8047.386	7886.809	12235.32	11425.62	8383.121	3561.868
Gln His Thr	Gln.His.Thr	Amino Acids	Amino Acids	NO	2.576216408	EPA	0.016708	4723.736	2775.599	7812.237	7943.821	16620.54	701.1674
Gln Pro Pro	Gln.Pro.Pro	Amino Acids	Amino Acids	NO	5.075716094	EPA	0.010623	19884.19	15018.81	15175.21	25062.05	34061.88	601.2257
LysoPE(22:5(7Z,10Z,13Z,16Z))	LysoPE(22:5)	Phosphoethanolamines	LysoPE	NO	1.764144874	EPA	0.007334	1982.953	2203.75	3399.473	2836.308	2298.321	898.3778
MGDG(18:2(9Z,12Z)/18:2(9Z,12Z))	MGDG(36:4)	Galactolipid	Galactolipid	NO	1.687142212	EPA	0.004137	22238.4	19629.72	28516.85	32115.17	26479.77	8665.813
PA(12:0/17:0)	PA(29:0)	Phosphatidic Acids	PA	NO	2.937431556	EPA	0.007652	15879.7	14858.32	19699.08	25203.4	11927.55	2266.021
PA(18:3(9Z,12Z,15Z)/17:0)	PA(35:3)	Phosphatidic Acids	PA	NO	3.255724591	EPA	0.016708	42002.08	28932.78	34168.86	41965.23	22321.74	3606.446
PA(17:0/22:6(4Z,7Z,10Z,13Z,16Z))	PA(39:6)	Phosphatidic Acids	PA	NO	3.785281402	EPA	0.016708	7638.216	5490.414	7429.427	7544.938	4383.755	208.382
PA(20:0/22:6(4Z,7Z,10Z,13Z,16Z))	PA(42:6)	Phosphatidic Acids	PA	NO	2.420649931	EPA	0.016708	74219.69	63436.55	99286.06	98334.77	75512.99	15055.03
PC(18:3(6Z,9Z,12Z)/20:5(5Z,8Z,11Z,14Z,17Z))	PC(38:8)	Phosphocholines	PC	YES	2.722774527	EPA	0.002979	4101.255	5884.606	4602.603	5707.123	6459.831	930.0704
PC(16:1(9Z)/20:4(5Z,8Z,11Z,14Z,17Z))	PC(36:5)	Phosphocholines	PC	NO	2.472924133	EPA	0.016708	10474.66	15040.6	11436.22	15269.43	17119.56	2475.902
PC(22:4(7Z,10Z,13Z,16Z)/15:0)	PC(37:5)	Phosphocholines	PC	NO	-2.900490407	HF	0.016708	2977.967	1935.826	3053.077	2062.363	2362.217	20396.75
PC(17:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z))	PC(39:8)	Phosphocholines	PC	NO	-2.282567229	HF	0.016708	2802.963	2917.057	3138.978	4667.757	2869.894	17602.83
PE(20:5(5Z,8Z,11Z,14Z,17Z)/18:2(9Z,12Z))	PE(36:5)	Phosphoethanolamines	PE	NO	4.467561729	EPA	0.009449	50903.57	71080.22	58075.29	92887.58	115453.3	3197.142

Full metabolite names, shortened metabolite names, the metabolite group and type, EPA (22:5) containing metabolites (labeled as YES/NO), Log 2 fold changes (EPA/HF), the diet with the higher abundance of the metabolite (GreaterDiet), Benjamini-Hochberg adjusted p-values, and the raw metabolomic data are listed for all adipose metabolites below a BH p-value of 0.05 and Log2FC +/- 1.5. Each metabolite was tested for normality, followed by a T-test or Wilcoxon Rank-Sum Test and a BH-post hoc correction.

Supplemental Table 2. Liver metabolomics of C57BL/6J mice consuming a high fat diet in the absence or presence of EPA.

Full Metabolite Name	Shortened Metabolite Name	MetaboliteGroup	Type	EPA_containing	Log2FC	GreaterDiet	BH.adjust	EPA 122	EPA 123	EPA 125	EPA 129	EPA 130	HF60 101	HF60 106	HF60 108	HF60 110
Anandamide (20:5, n-3)	AEA(20:5, n-3)	Anandamide (AEA)	Anandamide	YES	1.77397947	EPA	0.013388	5544.752	9706.924	11790.29	7592.302	9388.817	2357.634	2535.948	1960.771	3443.565
Arg Asp Lys	Arg.Asp.Lys	Amino Acids	Amino Acids	NO	1.690842337	EPA	0.03356	4620.197	19906.6	9057.827	11523.84	13019.46	1677.761	5617.889	2838.67	4269.591
C-12 NBD-dihydro-Ceramide	C.12.NBD.dihydro.Ceramide	Ceramide	Ceramide	NO	2.451081568	EPA	0.007747	10463.06	16019.61	9227.833	13892.19	13687.45	3279.367	2155.511	2348.021	1476.377
Cer(d18:1/16:0)	Cer(d34:1)	Ceramide	Ceramide	NO	2.806386276	EPA	0.019909	258567.7	24724.76	18302.2	46148.13	25671.25	11874.42	12609.47	7067.425	11153.23
Chivosazole A	Chivosazole.A	Macrolide	Macrolide	NO	2.230318498	EPA	0.019909	5544.418	23564.94	15462.14	19384.21	25806.14	4561.172	3281.618	4022.359	3438.289
DG(20:5(5Z,8Z,11Z,14Z,17Z)/	DG(40:10)	Diacylglycerols	DG	YES	2.46414865	EPA	0.007747	23530.11	35746.75	19845.19	29930.08	28854.08	7229.963	4803.678	4693.606	3266.36
DG(20:5(5Z,8Z,11Z,14Z,17Z)/	DG(42:11)	Diacylglycerols	DG	YES	2.039717555	EPA	0.019909	11097.93	3923.338	2991.482	2748.868	3084.674	1937.356	970.5071	1147.446	584.4419
DG(18:3(9Z,12Z,15Z)/20:4(5Z	DG(38:7)	Diacylglycerols	DG	NO	-1.454841989	HF	0.045162	124.2307	2269.188	2845.917	1539.615	1970.302	6350.403	2968.094	6651.087	3217.633
DG(20:1(11Z)/20:3(8Z,11Z,14	DG(40:4)	Diacylglycerols	DG	NO	-1.857840044	HF	0.035631	414.5454	1591.887	3075.688	432.7505	977.9517	6765.352	3022.686	6120.513	2918.794
Docosahexaenoic Acid	DHA	DHA	DHA	NO	2.093197428	EPA	0.012841	6307.439	11071.47	14491.03	8609.298	10978.73	2129.609	2069.175	1364.805	4084.19
3b,16a-Dihydroxyandrostenc	Dihydroxyandrostene.sulfate	Sulfated steroids	Sulfated Steroids	NO	1.96847808	EPA	0.013388	11954.14	27967.65	27321.35	18912.04	22915.02	3666.087	6275.025	3135.668	9219.126
5,7-Dihydroxy-4'-methoxy-8-	flavanone	Flavanone	Flavanone	NO	1.773772164	EPA	0.019909	18642.88	6532.969	21835.32	13081.24	19067.81	4479.47	3854.67	2387.179	7798.568
alNAcbeta1-4(NeuGcalpha2-3	Galactosylceramide(40:1)	Ceramide	Ceramide	NO	-2.478892208	HF	0.019909	63.55114	8998.725	6000.511	3711.413	8571.961	35945.59	22819.03	41036.7	22155.83
alNAcbeta1-4(NeuGcalpha2-3	Galactosylceramide(42:2)	Ceramide	Ceramide	NO	-2.648712069	HF	0.019909	51.88366	2932.832	2233.087	1409.415	2700.981	11711.04	7210.651	15555.01	12321.55
GalCer(d18:1/23:0)	GalCer(d41:1)	Ceramide	Ceramide	NO	-2.269075549	HF	0.007747	1373.163	15020.28	12032.07	12290.28	12843.27	55005.07	38233.4	58684.57	54606.76
GalCer(d18:1/24:0)	GalCer(d42:1)	Ceramide	Ceramide	NO	-2.51113696	HF	0.012681	1244.782	19636.7	13633.65	10585.63	10700.94	70605.63	53197.37	79620.25	51063.36
Gln His Thr	Gln.His.Thr	Amino Acids	Amino Acids	NO	3.198828512	EPA	0.019909	14619.02	56504.84	40374.21	31303.57	39140.37	2275.044	4568.387	2306.273	6702.135
Gln Pro Pro	Gln.Pro.Pro	Amino Acids	Amino Acids	NO	5.488421468	EPA	0.01494	39666.98	74021.31	33478.31	46037.73	36157.77	1011.432	871.2841	802.8488	1401.694
Ivermectin B1b	Ivermectin.B1b	Lactone	Lactone	NO	1.602176418	EPA	0.024292	1305.993	4252.53	4142.477	5564.524	5344.6	1.00E-05	1951.182	1296.642	2183.021
LysoPE(20:5(5Z,8Z,11Z,14Z,1	LysoPE(20:5)	Phosphoethanolamines	LysoPE	YES	3.279364063	EPA	0.019909	4486.95	26065.36	13399.95	14635.8	17630.4	2847.858	389.3203	2752	290.8725
Macaf flavone II	Macaf flavone.II	Flavonoids	Flavanone	NO	1.487277655	EPA	0.000994	7015.207	7118.376	8670.256	6795.163	7589.154	3165.605	2474.736	1896.907	3074.318
Methylsyringin	Methylsyringin	Glucoside	Glucoside	NO	1.510848086	EPA	0.019909	3731.94	5056.865	3272.364	4056.697	4533.18	860.1353	1523.693	304.9037	3108.51
(2R,6x)-7-Methyl-3-methylen	octanetetrol.2.glucoside.	Glucoside	Glucoside	NO	1.983520777	EPA	0.012681	54919.93	89409.12	110605.6	71151.7	84976.09	18161.23	19857.25	16118.41	29020.05
Oxo-Ergotamine	Oxo.Ergotamine	Ergopeptines	Ergopeptines	NO	4.437344148	EPA	0.019909	519.9044	5112.722	3086.143	2678.54	3973.033	62.25989	177.7969	71.35096	256.1367

Full metabolite names, shortened metabolite names, the metabolite group and type, EPA (22:5) containing metabolites (labeled as YES/NO), Log 2 fold changes (EPA/HF), the diet with the higher abundance of the metabolite (GreaterDiet), Benjamini-Hochberg adjusted p-values, and the raw metabolomic data are listed for all liver metabolites below a BH p-value of 0.05 and Log2FC +/- 1.5. Each metabolite was tested for normality, followed by a T-test or Wilcoxon Rank-Sum Test and a BH-post hoc correction.

Supplemental Table 3. Single Nucleotide Polymorphisms in EPA/RvE1 metabolizing genes.

Variant name	chr	chr.start	chr.end	Minor allele	Global minor allele frequency	Gene
rs1046587	14	24316854	24316854	A	0.2716	BLT1
rs1046584	14	24316578	24316578	T	0.2358	BLT1
rs2224123	14	24313752	24313752	T	0.1567	BLT1
rs4981503	14	24317087	24317087	T	0.155	BLT1
rs3181384	14	24317770	24317770	T	0.1532	BLT1
rs2224122	14	24314208	24314208	C	0.111	BLT1
rs3742510	14	24314475	24314475	C	0.07188	BLT1
rs3742511	14	24315705	24315705	C	0.07169	BLT1
rs551001577	10	45407402	45407402	C	0.05092	5LOX
rs17157756	10	45385220	45385220	G	0.05112	5LOX
rs115074014	10	45385210	45385210	A	0.05112	5LOX
rs12266963	10	45433456	45433456	G	0.05471	5LOX
rs71494783	10	45432341	45432341	G	0.05471	5LOX
rs115200794	10	45427617	45427617	C	0.05671	5LOX
rs72796464	10	45410446	45410446	C	0.05851	5LOX
rs55661611	10	45424378	45424378	T	0.0607	5LOX
rs7080977	10	45421868	45421868	C	0.0615	5LOX
rs12783037	10	45434517	45434517	C	0.0617	5LOX
rs11239501	10	45383352	45383352	A	0.0619	5LOX
rs7077173	10	45421751	45421751	G	0.0621	5LOX
rs17444064	10	45396252	45396252	C	0.0625	5LOX
rs41526545	10	45395767	45395767	G	0.0637	5LOX
rs55700434	10	45391508	45391508	T	0.0637	5LOX

SNPs in genes of the EPA/RvE1 pathway are listed by reference SNP (RS) number, chromosome number, chromosome locations (chr.start and chr.end), minor allele, global minor allele frequency, and the gene the SNP is contained within.