Electronic Supplementary Material (ESI) for Food & Function.

Supplementary information

Effect of dietary EPA and DHA on murine blood and liver fatty acid profile and liver oxylipin pattern depending on high and low dietary n6-PUFA

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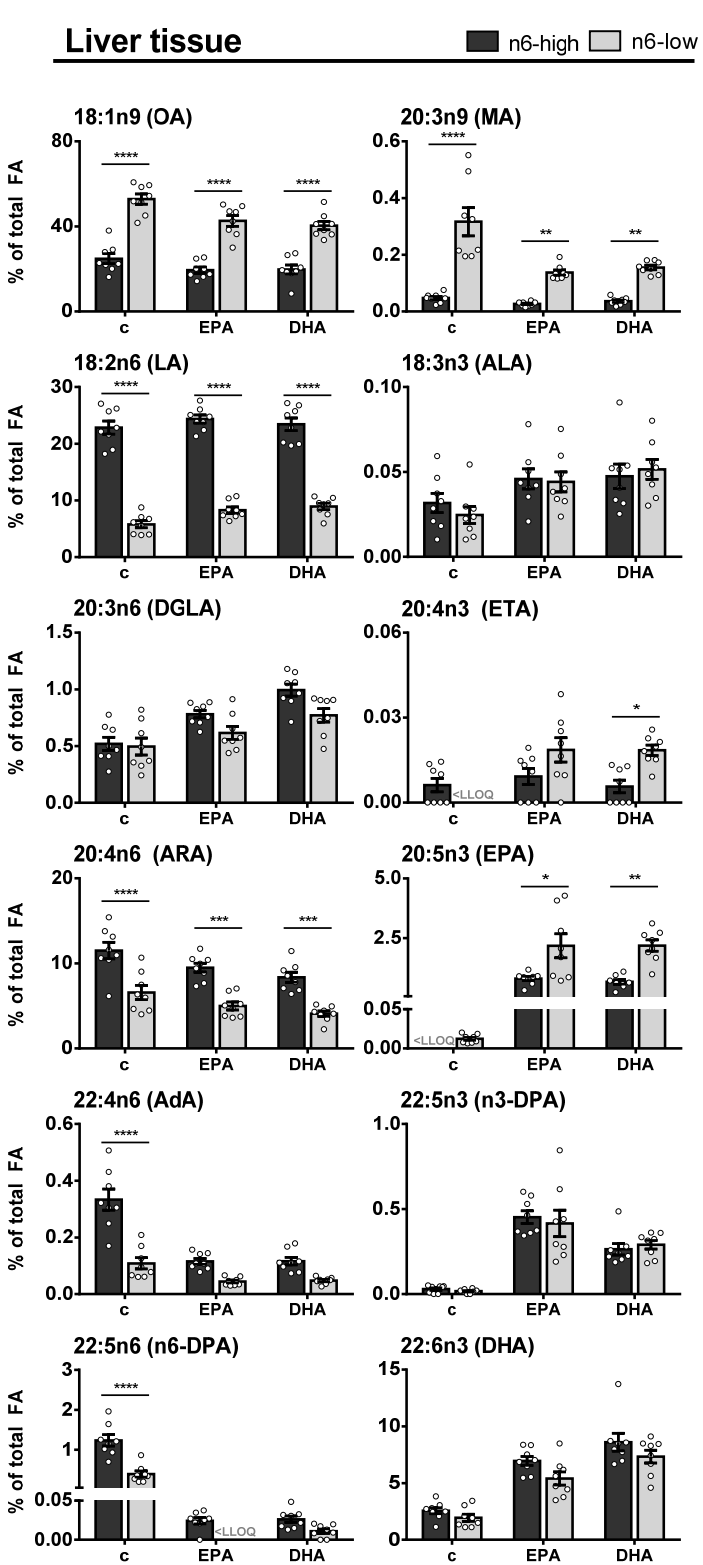

Fig. S1: Relative FA concentrations in mouse liver tissue.
Relative fatty acid concentrations (% of total FA) of n9-MUFA and -PUFA as well as n3- and n6-PUFA in liver tissue of NMRI mice after 28 days of feeding an n6-PUFA-rich diet (dark grey) or an n6-PUFA-low diet (light grey) without (c) or with n3-PUFA supplementation (EPA, DHA). Shown are mean ± SEM as well as individual values (n=8). If >50% of the samples within one group were <LLOQ (lower limit of quantification), no mean was calculated and "<LLOQ" is indicated. Statistically significant differences (* $p<0.05$; ** $p<0.01$; *** $p<0.001$; **** $p<0.0001$) were determined by two-way ANOVA with Tukey's post-test and are indicated for n6-high vs. n6-low groups (results for comparisons of all groups are summarized in Table S8).

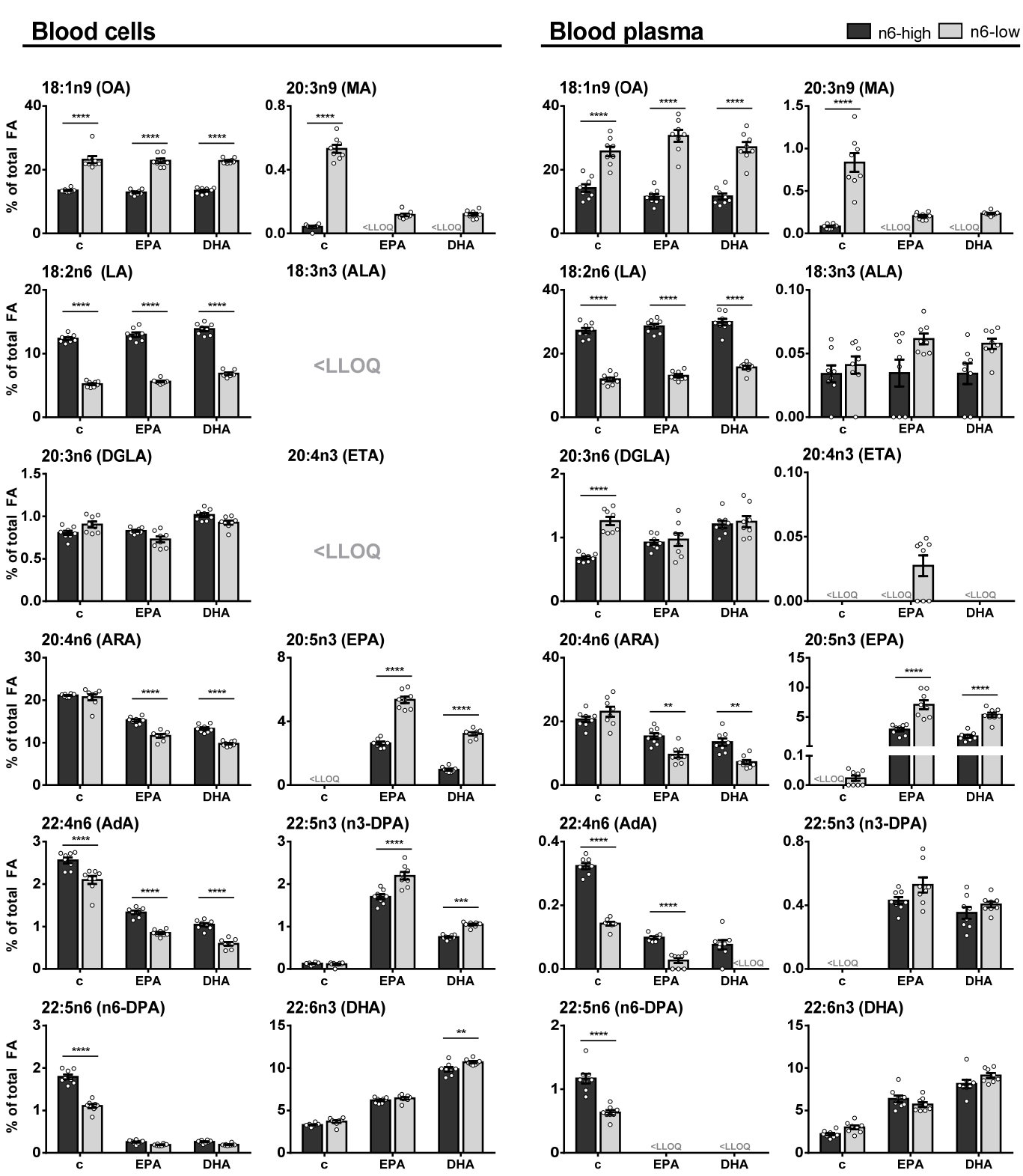

Fig. S2: Relative FA concentrations in mouse blood cells and blood plasma.
Relative fatty acid concentrations (% of total FA) of n9-MUFA and -PUFA as well as n3- and n6-PUFA in blood cells and plasma of NMRI mice after 28 days of feeding an n6-PUFA-rich diet (dark grey) or an n6-PUFA-low diet (light grey) without (c) or with n3-PUFA supplementation (EPA, DHA). Shown are mean ± SEM as well as individual values (n=8). If >50% of the samples within one group were <LLOQ (lower limit of quantification), no mean was calculated and "<LLOQ" is indicated. Statistically significant differences (** $p<0.01$; *** $p<0.001$; **** $p<0.0001$) were determined by two-way ANOVA with Tukey's post-test and are indicated for n6-high vs. n6-low groups (results for comparisons of all groups are summarized in Table S8).

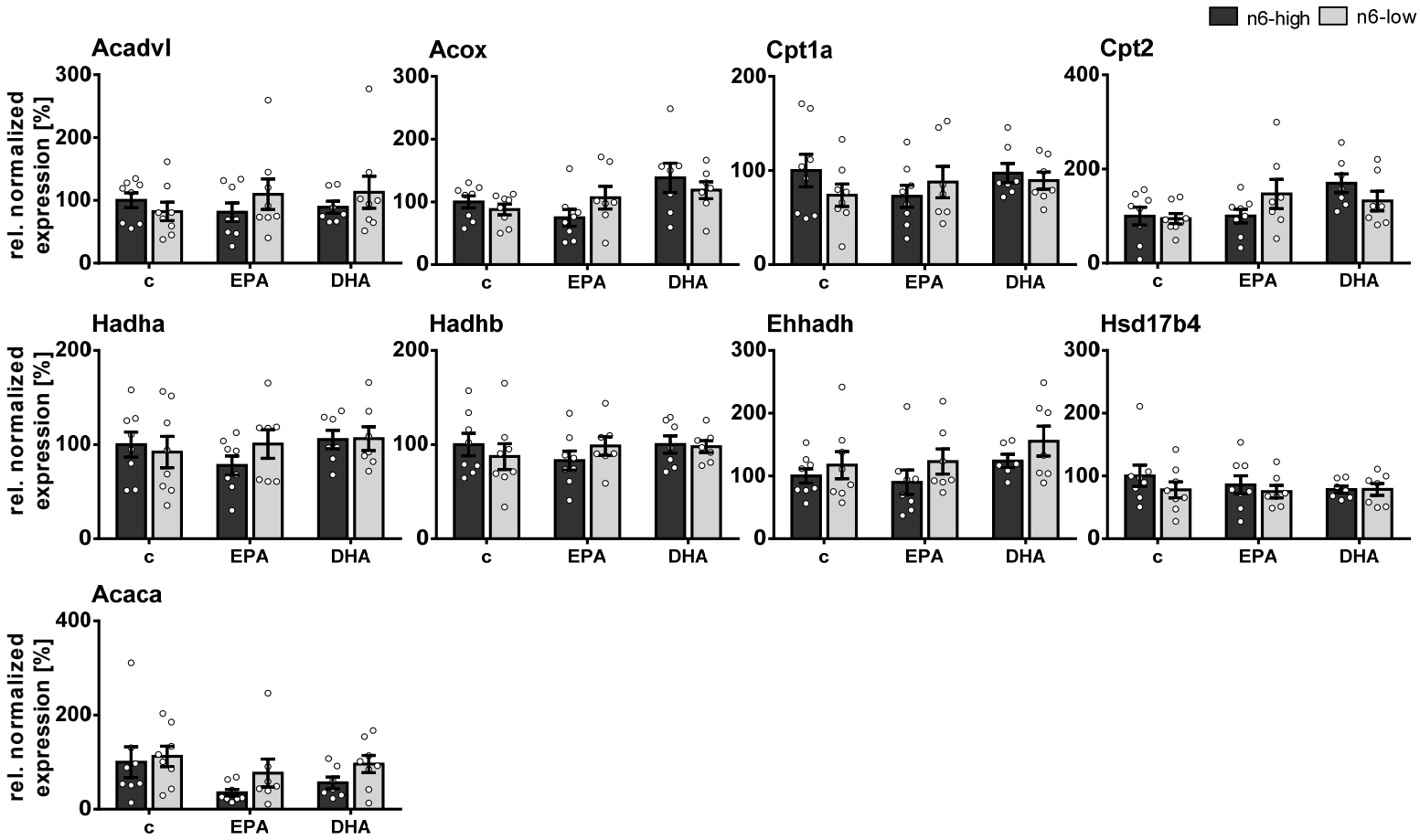

Figure S3: Gene expression of enzymes involved in fatty acid β-oxidation.
Normalized gene expression relative to the c/n6-high group of enzymes involved in fatty acid β-oxidation in liver tissue of NMRI mice after 28 days of feeding an n6-PUFA-rich diet (dark grey) or an n6-PUFA-low diet (light grey) without (c) or with n3-PUFA supplementation (EPA, DHA). Shown are mean ± SEM (n=6-8) as well as individual values for β-oxidation enzymes very long-chain acyl-CoA dehydrogenase (Acadvl), acyl-CoA oxidase 1 (Acox), carnitine palmitoyltransferase 1a and 2 (Cpt1a, Cpt2), α- and β-subunit of mitochondrial multifunctional protein (Hadha, Hadhb), peroxisomal multifunctional protein (Ehhadh, Hsd17b4) and acetyl-CoA carboxylase α (Acaca), which is involved in fatty acid synthesis. Data outliers were removed based on ROUT outlier test (Q=1%). Statistically significant differences were determined by two-way ANOVA with Tukey's post-test and no significant differences were detected for n6-high vs. n6-low groups (results for comparisons of all groups are summarized in Table S8).

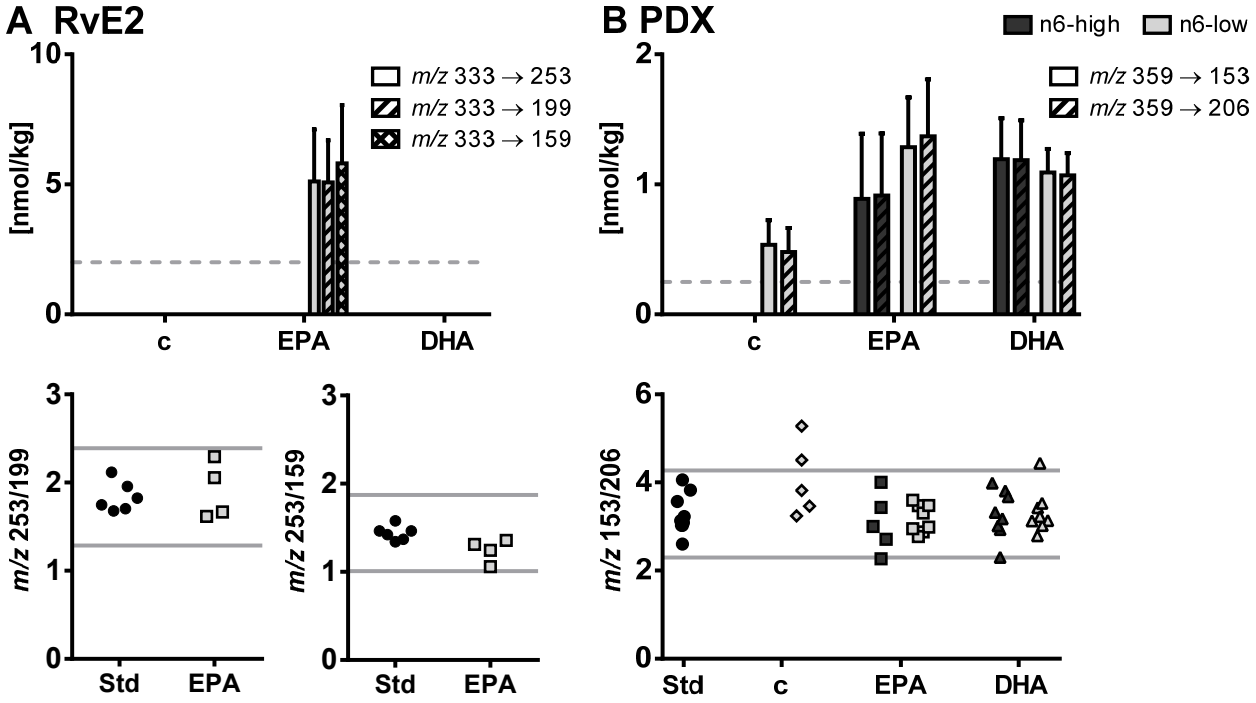

Figure S4: SPM concentrations in mouse liver tissue.
Concentration of SPMs (**A**) RvE2 and (**B**) PDX (10(*S*),17(*S*)-DiHDHA) derived from EPA and DHA, respectively, in liver tissue of NMRI mice after 28 days of feeding an n6-PUFA-rich diet (dark grey) or an n6-PUFA-low diet (light grey) without (c) or with n3-PUFA supplementation (EPA, DHA). **Top**: Shown are concentrations (mean ± SEM) quantified using 2-3 MRM transitions for each compound. If >50% of the samples within one group were <LLOQ (lower limit of quantification), no mean was calculated and the LLOQ is indicated as dotted line. **Bottom**: Shown are area ratios of 2-3 MRM transitions for every sample >LLOQ in comparison to area ratios of calibration standards (RvE2: 1-100 nM, PDX: 0.25-500 nM). Deviation of ±30% from mean area ratio of calibration standards are indicated as grey line.

Tab. S1: Composition of feed/feeding oil.
Composition of the experimental diets and fatty acid profile of the oils (as %FA of total FA) used for production of the diets. Shown are specifications by the manufacturer (sniff Spezialitäten GmbH) for the diets and own analysis of the feeding oils (mean ± deviation from the mean (n=2)).

Feed composition	**c/n6-high**	**EPA/n6-high**	**DHA/n6-high**	**c/n6-low**	**EPA/n6-low**	**DHA/n6-low**
Crude protein [%]		17.6			17.6	
Crude fat [%]		10.1			10.1	
Crude fiber [%]		5.0			5.0	
Crude ash [%]		5.3			5.3	
Starch [%]		31.4			31.4	
Sugar [%]		11.0			11.0	
Vitamin A [IU·kg^{-1}]		15000			15000	
Vitamin D3 [IU·kg^{-1}]		1500			1500	
Vitamin E [mg·kg^{-1}]		150			150	
Vitamin K3 [mg·kg^{-1}]		20			20	
Vitamin C [mg·kg^{-1}]		30			30	
Copper [mg·kg^{-1}]		14			14	
Energy [MJ]		16.5			16.5	
Feeding oil [%FA of total FA]	**c/n6-high**	**EPA/n6-high**	**DHA/n6-high**	**c/n6-low**	**EPA/n6-low**	**DHA/n6-low**
C14:0	0.08 ± 0.08	0.10 ± 0.01	<0.05	<LLOQ	<LLOQ	<LLOQ
C15:0	<0.05	<0.05	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C16:0	6.59 ± 0.02	6.17 ± 0.05	6.11 ± 0.03	4.00 ± 0.01	3.738 ± 0.008	3.708 ± 0.003
C17:0	<0.05	0.060 ± 0.001	<0.05	<0.05	<0.05	<0.05
C18:0	3.376 ± 0.007	3.130 ± 0.003	3.13 ± 0.01	2.913 ± 0.001	2.714 ± 0.005	2.706 ± 0.006
C20:0	0.24 ± 0.01	0.227 ± 0.007	0.224 ± 0.003	0.276 ± 0.003	0.261 ± 0.001	0.255 ± 0.001
C22:0	0.84 ± 0.07	1.03 ± 0.01	0.76 ± 0.04	0.84 ± 0.02	0.94 ± 0.01	0.8029 ± 0.0001
C24:0	0.236 ± 0.007	0.23 ± 0.01	0.17 ± 0.01	0.30 ± 0.02	0.260 ± 0.003	0.21 ± 0.01
C16:1n7	0.07 ± 0.01	0.065 ± 0.003	0.052 ± 0.004	<0.05	<0.05	<0.05
C18:1n9	27.14 ± 0.06	25.417 ± 0.002	25.21 ± 0.02	79.97 ± 0.05	75.14 ± 0.02	74.32 ± 0.05
C18:1n7	0.910 ± 0.004	0.82 ± 0.02	0.866 ± 0.007	1.250 ± 0.002	1.21 ± 0.02	1.25 ± 0.02
C20:1n9	0.178 ± 0.006	0.16 ± 0.02	0.154 ± 0.003	0.265 ± 0.007	0.251 ± 0.002	0.258 ± 0.001
C22:1n9	<LLOQ	<0.05	<0.05	<0.05	<0.05	<0.05
C24:1n9	<LLOQ	<LLOQ	0.12 ± 0.02	<LLOQ	<LLOQ	0.116 ± 0.006
C18:3n3	0.080 ± 0.002	0.065 ± 0.003	0.065 ± 0.008	0.167 ± 0.001	0.155 ± 0.001	0.161 ± 0.004
C18:4n3	<LLOQ	0.067 ± 0.004	<LLOQ	<LLOQ	0.052 ± 0.004	<LLOQ
C20:4n3	<LLOQ	0.131 ± 0.002	<LLOQ	<LLOQ	0.129 ± 0.007	<0.05
C20:5n3	<LLOQ	5.735 ± 0.005	0.80 ± 0.02	<LLOQ	5.46 ± 0.02	0.751 ± 0.003
C22:5n3	0.15 ± 0.15	<LLOQ	0.712 ± 0.006	<LLOQ	<LLOQ	0.666 ± 0.005
C22:6n3	<LLOQ	<LLOQ	5.72 ± 0.04	<LLOQ	<LLOQ	5.42 ± 0.03
C18:2n6	60.0 ± 0.3	56.278 ± 0.001	55.79 ± 0.09	9.92 ± 0.01	9.335 ± 0.004	9.2178 ± 0.0002
C20:4n6	<LLOQ	0.264 ± 0.005	<0.05	<LLOQ	0.241 ± 0.005	<0.05
SFA	11.4 ± 0.2	10.97 ± 0.03	10.45 ± 0.02	8.36 ± 0.05	7.95 ± 0.02	7.72 ± 0.01
MUFA	28.30 ± 0.05	26.49 ± 0.04	26.42 ± 0.02	81.55 ± 0.05	76.676 ± 0.003	76.01 ± 0.03
PUFA	60.3 ± 0.1	62.541 ± 0.001	63.133 ± 0.005	10.083 ± 0.008	15.37 ± 0.02	16.28 ± 0.04
n3-PUFA	0.23 ± 0.15	5.998 ± 0.003	7.30 ± 0.08	0.167 ± 0.001	5.79 ± 0.02	7.03 ± 0.03
n6-PUFA	60.0 ± 0.3	56.543 ± 0.004	55.84 ± 0.08	9.92 ± 0.01	9.575 ± 0.009	9.247 ± 0.009
n6/n3-PUFA ratio	260 : 1	9.4 : 1	7.7 : 1	59 : 1	1.7 : 1	1.3 : 1

Tab. S2: Feed consumption.
Mean feed consumption across the whole feeding period and feed consumed on day one after diet change. Displayed are mean ± SEM. A t-test was performed to determine statistical significance with **** $p < 0.0001$.

Group	Feed consumed 4 weeks	Feed consumed day 1	t-Test
c/n6-high	25.1 ± 2.0	35	
EPA/n6-high	28.2 ± 1.7	36	
DHA/n6-high	25.5 ± 1.1	30	
c/n6-low	27.3 ± 1.7	33	
EPA/n6-low	26.1 ± 1.7	36	
DHA/n6-low	26.1 ± 1.5	34	
Mean	26.4 ± 0.5	34 ± 0.9	****

Tab.S3: Body weight.
Mean mice's body weight before and after the feeding period of 28 days. Displayed are mean ± SEM. A t-test was performed to determine statistical significance with ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Group	Body weight before feeding [g]	Body weight after feeding [g]	t-Test
c/n6-high	27.0 ± 0.5	30.9 ± 0.7	****
EPA/n6-high	27.5 ± 0.4	30.9 ± 1.1	**
DHA/n6-high	26.8 ± 0.8	32.2 ± 1.2	***
c/n6-low	27.4 ± 0.4	33.0 ± 0.8	***
EPA/n6-low	27.2 ± 0.4	32.5 ± 1.2	***
DHA/n6-low	26.8 ± 0.6	32.2 ± 0.6	****
Mean	27.1 ± 0.1	32.0 ± 0.4	****

Tab. S4: Fatty acid profile in mouse tissue and blood.
Concentrations of individual FA and total FA in g/kg wet liver tissue (**A-1**), as well as relative FA profile (%FA of total FA) in liver tissue (**A-2**), blood cells (**B**) and blood plasma (**C**) of NMRI mice after 28 days of feeding an n6-PUFA-rich diet (n6-high) or an n6-PUFA-low diet (n6-low) without (c) or with n3-PUFA supplementation (EPA, DHA). Shown are mean ± SEM (n=8). Individual FA that were <LLOQ in all feeding groups were not taken into account for calculation of sum of total FA; for FA that were <LLOQ in >50% of the samples within a feeding group, for the whole group the LLOQ (0.0017 g/kg) was used for calculation of total FA and n3-PUFA status (i.e. %EPA+DHA, %n3 in HUFA, %n6 in HUFA); for FA that were <LLOQ in ≤50% within a feeding group for these FA 1/2 LLOQ was used for calculation of mean ± SEM, total FA and n3-PUFA status. For calculation of relative FA distribution only areas of FA >LLOQ were taken into account, FA <LLOQ were set to zero; if >50% of the samples within a feeding group were <LLOQ, the whole group was set to zero.

Tab. S4: ***Continued.*** Fatty acid profile in mouse blood and tissue.

(A-1) Liver tissue

g FA/kg wet tissue	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
C10:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C11:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C12:0	0.005 ± 0.001	0.005 ± 0.000	0.005 ± 0.000	0.012 ± 0.002	0.008 ± 0.001	0.008 ± 0.001
C13:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C14:0	0.185 ± 0.042	0.139 ± 0.019	0.145 ± 0.021	0.355 ± 0.065	0.257 ± 0.040	0.225 ± 0.031
C14:1n5	0.006 ± 0.001	0.004 ± 0.001	0.005 ± 0.001	0.014 ± 0.002	0.009 ± 0.002	0.009 ± 0.001
C15:0	0.035 ± 0.003	0.032 ± 0.002	0.034 ± 0.003	0.045 ± 0.005	0.043 ± 0.004	0.038 ± 0.003
C15:1n5	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C16:0	11.979 ± 1.521	11.471 ± 0.725	11.977 ± 0.561	17.252 ± 2.305	15.434 ± 1.823	14.415 ± 1.187
C16:1n7	1.088 ± 0.230	0.816 ± 0.100	0.720 ± 0.075	2.257 ± 0.408	1.531 ± 0.290	1.329 ± 0.139
C17:0	0.081 ± 0.005	0.071 ± 0.003	0.076 ± 0.004	0.088 ± 0.010	0.080 ± 0.007	0.073 ± 0.005
C17:1n7	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C18:0	5.727 ± 0.236	6.084 ± 0.233	6.023 ± 0.171	5.558 ± 0.530	5.659 ± 0.367	5.709 ± 0.372
C18:1n9	15.884 ± 3.540	10.957 ± 1.366	11.325 ± 1.445	53.189 ± 9.758	33.003 ± 5.620	28.362 ± 4.212
C18:1n7	1.457 ± 0.228	1.009 ± 0.121	1.016 ± 0.102	2.971 ± 0.496	1.733 ± 0.256	1.466 ± 0.105
C18:2n6	13.411 ± 1.097	13.348 ± 0.822	13.144 ± 1.054	5.173 ± 0.584	5.981 ± 0.694	5.936 ± 0.371
C18:3n6	0.262 ± 0.039	0.164 ± 0.021	0.139 ± 0.019	0.101 ± 0.016	0.062 ± 0.014	0.047 ± 0.008
C19:0	0.017 ± 0.002	0.018 ± 0.001	0.023 ± 0.002	0.012 ± 0.001	0.014 ± 0.001	0.012 ± 0.001
C18:3n3	0.018 ± 0.003	0.025 ± 0.003	0.027 ± 0.005	0.022 ± 0.004	0.035 ± 0.008	0.034 ± 0.003
C18:4n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:0	0.029 ± 0.001	0.029 ± 0.001	0.027 ± 0.002	0.027 ± 0.002	0.027 ± 0.001	0.026 ± 0.001
C20:1n9	0.178 ± 0.021	0.137 ± 0.014	0.154 ± 0.022	0.575 ± 0.097	0.347 ± 0.050	0.304 ± 0.035
C20:2n6	0.146 ± 0.020	0.148 ± 0.011	0.163 ± 0.013	0.042 ± 0.004	0.049 ± 0.004	0.054 ± 0.002
C20:3n9	0.029 ± 0.005	0.015 ± 0.002	0.020 ± 0.003	0.272 ± 0.031	0.098 ± 0.009	0.104 ± 0.006
C20:3n6	0.291 ± 0.018	0.423 ± 0.016	0.549 ± 0.034	0.413 ± 0.027	0.428 ± 0.034	0.506 ± 0.026
C21:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n6	6.477 ± 0.160	5.101 ± 0.159	4.584 ± 0.250	5.590 ± 0.272	3.459 ± 0.258	2.683 ± 0.156
C20:3n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n3	0.004 ± 0.001	0.005 ± 0.001	0.004 ± 0.001	<LLOQ	0.012 ± 0.002	0.012 ± 0.001
C20:5n3	<LLOQ	0.431 ± 0.048	0.358 ± 0.050	0.010 ± 0.001	1.326 ± 0.188	1.431 ± 0.138
C22:0	0.122 ± 0.005	0.132 ± 0.004	0.116 ± 0.003	0.128 ± 0.007	0.119 ± 0.003	0.120 ± 0.003
C22:1n9	0.017 ± 0.001	0.017 ± 0.003	0.015 ± 0.002	0.028 ± 0.005	0.027 ± 0.003	0.030 ± 0.005
C22:2n6	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C22:4n6	0.185 ± 0.007	0.062 ± 0.004	0.063 ± 0.007	0.088 ± 0.005	0.030 ± 0.001	0.031 ± 0.001
C22:5n6	0.687 ± 0.032	0.014 ± 0.002	0.014 ± 0.002	0.313 ± 0.015	<LLOQ	0.008 ± 0.002
C22:5n3	0.016 ± 0.004	0.243 ± 0.016	0.142 ± 0.011	0.016 ± 0.004	0.264 ± 0.020	0.188 ± 0.008
C24:0	0.097 ± 0.005	0.097 ± 0.004	0.076 ± 0.003	0.091 ± 0.003	0.078 ± 0.003	0.083 ± 0.003
C22:6n3	1.427 ± 0.063	3.731 ± 0.100	4.669 ± 0.198	1.622 ± 0.120	3.662 ± 0.197	4.790 ± 0.159
C24:1n9	0.103 ± 0.004	0.114 ± 0.003	0.159 ± 0.006	0.128 ± 0.008	0.148 ± 0.011	0.170 ± 0.006
Total FA	59.965 ± 6.622	54.841 ± 3.194	55.770 ± 2.900	96.394 ± 14.250	73.924 ± 9.217	68.201 ± 6.177
SFA	18.277 ± 1.783	18.078 ± 0.883	18.501 ± 0.591	23.568 ± 2.903	21.719 ± 2.205	20.709 ± 1.509
MUFA	18.734 ± 4.008	13.053 ± 1.588	13.392 ± 1.619	59.162 ± 10.722	36.798 ± 6.200	31.668 ± 4.469
PUFA	22.954 ± 1.101	23.710 ± 0.999	23.877 ± 1.228	13.664 ± 0.974	15.407 ± 0.998	15.824 ± 0.532
n3-PUFA	1.466 ± 0.066	4.435 ± 0.123	5.200 ± 0.194	1.673 ± 0.126	5.298 ± 0.207	6.456 ± 0.217
n6-PUFA	21.459 ± 1.111	19.260 ± 0.930	18.657 ± 1.187	11.719 ± 0.872	10.011 ± 0.979	9.265 ± 0.538
n9-PUFA	0.029 ± 0.005	0.015 ± 0.002	0.020 ± 0.003	0.272 ± 0.031	0.098 ± 0.009	0.104 ± 0.006
%EPA+DHA	2.573 ± 0.273	7.751 ± 0.434	9.265 ± 0.804	1.959 ± 0.312	7.575 ± 1.027	9.521 ± 0.720
%n3 in HUFA	15.874 ± 0.726	43.990 ± 0.584	49.829 ± 1.144	19.679 ± 0.825	56.897 ± 2.185	65.829 ± 1.526
%n6 in HUFA	83.806 ± 0.701	55.860 ± 0.590	49.975 ± 1.133	76.997 ± 0.476	42.049 ± 2.120	33.108 ± 1.509
D5D index	22.704 ± 1.145	12.105 ± 0.245	8.422 ± 0.351	13.890 ± 1.054	8.134 ± 0.220	5.311 ± 0.157
D6D index	0.019 ± 0.002	0.012 ± 0.001	0.010 ± 0.001	0.019 ± 0.002	0.010 ± 0.001	0.008 ± 0.001
Elongase index	0.029 ± 0.001	0.012 ± 0.001	0.014 ± 0.001	0.016 ± 0.001	0.009 ± 0.000	0.012 ± 0.001

Tab. S4: ***Continued.*** Fatty acid profile in mouse blood and tissue.

(A-2) Liver tissue

% of total FA	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
C10:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C11:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C12:0	0.009 ± 0.000	0.009 ± 0.000	0.009 ± 0.001	0.012 ± 0.001	0.010 ± 0.001	0.011 ± 0.001
C13:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C14:0	0.289 ± 0.030	0.246 ± 0.021	0.255 ± 0.031	0.357 ± 0.026	0.340 ± 0.026	0.324 ± 0.019
C14:1n5	0.010 ± 0.001	0.007 ± 0.001	0.008 ± 0.001	0.015 ± 0.001	0.011 ± 0.001	0.013 ± 0.001
C15:0	0.059 ± 0.002	0.058 ± 0.002	0.060 ± 0.003	0.049 ± 0.003	0.060 ± 0.003	0.056 ± 0.002
C15:1n5	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C16:0	19.821 ± 0.418	20.901 ± 0.388	21.560 ± 0.390	18.173 ± 0.404	21.037 ± 0.507	21.233 ± 0.237
C16:1n7	1.713 ± 0.142	1.456 ± 0.114	1.266 ± 0.089	2.252 ± 0.149	1.968 ± 0.175	1.944 ± 0.101
C17:0	0.140 ± 0.007	0.131 ± 0.005	0.136 ± 0.004	0.096 ± 0.007	0.114 ± 0.007	0.109 ± 0.003
C17:1n7	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C18:0	9.960 ± 0.556	11.255 ± 0.498	11.030 ± 0.710	6.149 ± 0.428	8.137 ± 0.595	8.541 ± 0.495
C18:1n9	24.819 ± 2.380	19.482 ± 1.414	19.759 ± 2.069	52.901 ± 2.424	42.630 ± 2.530	40.422 ± 2.013
C18:1n7	2.370 ± 0.130	1.808 ± 0.127	1.797 ± 0.118	3.049 ± 0.173	2.298 ± 0.124	2.181 ± 0.096
C18:2n6	22.844 ± 1.165	24.371 ± 0.705	23.429 ± 1.119	5.787 ± 0.620	8.300 ± 0.544	8.936 ± 0.556
C18:3n6	0.432 ± 0.037	0.298 ± 0.032	0.244 ± 0.026	0.108 ± 0.014	0.080 ± 0.011	0.070 ± 0.009
C19:0	0.031 ± 0.005	0.032 ± 0.002	0.041 ± 0.005	0.015 ± 0.004	0.021 ± 0.004	0.018 ± 0.002
C18:3n3	0.032 ± 0.006	0.046 ± 0.006	0.047 ± 0.007	0.025 ± 0.005	0.044 ± 0.006	0.052 ± 0.006
C18:4n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:0	0.051 ± 0.004	0.054 ± 0.002	0.049 ± 0.003	0.032 ± 0.004	0.040 ± 0.004	0.040 ± 0.003
C20:1n9	0.298 ± 0.022	0.246 ± 0.013	0.269 ± 0.031	0.605 ± 0.056	0.463 ± 0.023	0.445 ± 0.033
C20:2n6	0.263 ± 0.045	0.274 ± 0.018	0.294 ± 0.021	0.051 ± 0.010	0.071 ± 0.007	0.083 ± 0.006
C20:3n9	0.048 ± 0.006	0.027 ± 0.003	0.037 ± 0.005	0.317 ± 0.050	0.137 ± 0.009	0.155 ± 0.008
C20:3n6	0.520 ± 0.058	0.782 ± 0.033	0.994 ± 0.054	0.496 ± 0.074	0.616 ± 0.057	0.771 ± 0.059
C21:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n6	11.513 ± 0.983	9.492 ± 0.525	8.367 ± 0.594	6.584 ± 0.834	5.006 ± 0.470	4.092 ± 0.322
C20:3n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n3	0.006 ± 0.002	0.009 ± 0.003	0.006 ± 0.002	<LLOQ	0.019 ± 0.004	0.018 ± 0.002
C20:5n3	<LLOQ	0.797 ± 0.090	0.655 ± 0.095	0.012 ± 0.002	2.174 ± 0.503	2.185 ± 0.240
C22:0	0.218 ± 0.021	0.246 ± 0.013	0.212 ± 0.013	0.150 ± 0.019	0.179 ± 0.023	0.183 ± 0.012
C22:1n9	0.030 ± 0.003	0.031 ± 0.005	0.027 ± 0.003	0.035 ± 0.009	0.040 ± 0.006	0.043 ± 0.007
C22:2n6	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C22:4n6	0.334 ± 0.037	0.116 ± 0.010	0.116 ± 0.014	0.108 ± 0.020	0.044 ± 0.005	0.048 ± 0.004
C22:5n6	1.233 ± 0.142	0.024 ± 0.004	0.026 ± 0.004	0.391 ± 0.077	<LLOQ	0.011 ± 0.003
C22:5n3	0.030 ± 0.008	0.453 ± 0.037	0.264 ± 0.034	0.017 ± 0.004	0.416 ± 0.078	0.290 ± 0.026
C24:0	0.172 ± 0.016	0.181 ± 0.012	0.141 ± 0.013	0.110 ± 0.016	0.121 ± 0.019	0.128 ± 0.011
C22:6n3	2.570 ± 0.273	6.954 ± 0.395	8.610 ± 0.779	1.947 ± 0.311	5.402 ± 0.582	7.336 ± 0.558
C24:1n9	0.185 ± 0.018	0.213 ± 0.016	0.292 ± 0.024	0.157 ± 0.027	0.220 ± 0.027	0.260 ± 0.020
SFA	30.751 ± 0.621	33.113 ± 0.487	33.493 ± 0.938	25.144 ± 0.801	30.060 ± 0.899	30.645 ± 0.568
MUFA	29.424 ± 2.598	23.244 ± 1.612	23.418 ± 2.231	59.012 ± 2.583	47.632 ± 2.717	45.308 ± 2.014
PUFA	39.825 ± 2.222	43.643 ± 1.324	43.089 ± 1.590	15.843 ± 1.875	22.308 ± 1.948	24.047 ± 1.489
n3-PUFA	2.638 ± 0.281	8.259 ± 0.466	9.582 ± 0.836	2.000 ± 0.316	8.054 ± 1.106	9.881 ± 0.749
n6-PUFA	37.139 ± 1.975	35.357 ± 0.995	33.471 ± 1.209	13.526 ± 1.542	14.117 ± 1.042	14.011 ± 0.930
n9-PUFA	0.048 ± 0.006	0.027 ± 0.003	0.037 ± 0.005	0.317 ± 0.050	0.137 ± 0.009	0.155 ± 0.008
%EPA+DHA	2.570 ± 0.273	7.751 ± 0.434	9.265 ± 0.804	1.959 ± 0.312	7.575 ± 1.027	9.521 ± 0.720
%n3 in HUFA	15.857 ± 0.726	43.991 ± 0.585	49.829 ± 1.144	19.677 ± 0.825	56.908 ± 2.186	65.831 ± 1.526
%n6 in HUFA	83.824 ± 0.702	55.859 ± 0.590	49.975 ± 1.133	76.999 ± 0.476	42.038 ± 2.120	33.107 ± 1.509
D5D index	22.704 ± 1.145	12.105 ± 0.245	8.422 ± 0.351	13.890 ± 1.054	8.134 ± 0.220	5.311 ± 0.157
D6D index	0.019 ± 0.002	0.012 ± 0.001	0.010 ± 0.001	0.019 ± 0.002	0.010 ± 0.001	0.008 ± 0.001
Elongase index	0.029 ± 0.001	0.012 ± 0.001	0.014 ± 0.001	0.016 ± 0.001	0.009 ± 0.000	0.012 ± 0.001

Tab. S4: ***Continued.*** Fatty acid profile in mouse blood and tissue.

(B) Blood cells

% of total FA	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
C10:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C11:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C12:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C13:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C14:0	0.158 ± 0.011	0.166 ± 0.019	0.183 ± 0.023	0.195 ± 0.041	0.232 ± 0.025	0.190 ± 0.018
C14:1n5	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C15:0	0.077 ± 0.003	0.075 ± 0.002	0.085 ± 0.005	0.073 ± 0.006	0.101 ± 0.008	0.084 ± 0.005
C15:1n5	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C16:0	24.386 ± 0.247	26.008 ± 0.209	26.107 ± 0.238	23.244 ± 0.338	25.605 ± 0.295	25.568 ± 0.261
C16:1n7	0.522 ± 0.046	0.524 ± 0.056	0.484 ± 0.053	0.658 ± 0.175	0.606 ± 0.070	0.559 ± 0.071
C17:0	0.219 ± 0.009	0.209 ± 0.004	0.212 ± 0.005	0.173 ± 0.008	0.192 ± 0.009	0.189 ± 0.006
C17:1n7	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C18:0	13.096 ± 0.149	13.227 ± 0.165	12.475 ± 0.202	11.253 ± 0.353	11.024 ± 0.193	10.904 ± 0.180
C18:1n9	13.484 ± 0.209	12.882 ± 0.288	13.436 ± 0.336	23.158 ± 1.100	22.797 ± 0.684	22.754 ± 0.281
C18:1n7	1.512 ± 0.039	1.285 ± 0.042	1.312 ± 0.038	1.817 ± 0.050	1.403 ± 0.056	1.343 ± 0.039
C18:2n6	12.350 ± 0.217	12.991 ± 0.346	13.857 ± 0.317	5.210 ± 0.166	5.600 ± 0.132	6.859 ± 0.177
C18:3n6	0.082 ± 0.011	0.053 ± 0.004	0.041 ± 0.006	0.025 ± 0.007	0.018 ± 0.006	0.011 ± 0.004
C19:0	0.079 ± 0.004	0.069 ± 0.003	0.086 ± 0.005	0.055 ± 0.005	0.068 ± 0.004	0.053 ± 0.005
C18:3n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C18:4n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:0	0.207 ± 0.008	0.210 ± 0.010	0.211 ± 0.012	0.193 ± 0.010	0.215 ± 0.008	0.204 ± 0.006
C20:1n9	0.281 ± 0.007	0.246 ± 0.008	0.265 ± 0.009	0.469 ± 0.021	0.380 ± 0.012	0.364 ± 0.015
C20:2n6	0.267 ± 0.015	0.254 ± 0.007	0.258 ± 0.008	0.116 ± 0.008	0.119 ± 0.006	0.134 ± 0.004
C20:3n9	0.041 ± 0.006	<LLOQ	<LLOQ	0.531 ± 0.025	0.116 ± 0.008	0.121 ± 0.009
C20:3n6	0.805 ± 0.025	0.828 ± 0.012	1.015 ± 0.024	0.903 ± 0.035	0.728 ± 0.034	0.926 ± 0.024
C21:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n6	21.134 ± 0.123	15.268 ± 0.283	13.290 ± 0.328	20.717 ± 0.719	11.602 ± 0.398	9.749 ± 0.211
C20:3n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:5n3	<LLOQ	2.626 ± 0.095	0.967 ± 0.063	<LLOQ	5.353 ± 0.199	3.223 ± 0.101
C22:0	0.765 ± 0.023	0.747 ± 0.028	0.766 ± 0.022	0.722 ± 0.028	0.760 ± 0.023	0.733 ± 0.012
C22:1n9	0.103 ± 0.019	0.160 ± 0.037	0.269 ± 0.083	0.181 ± 0.023	0.173 ± 0.035	0.221 ± 0.025
C22:2n6	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C22:4n6	2.560 ± 0.069	1.333 ± 0.039	1.042 ± 0.039	2.098 ± 0.094	0.849 ± 0.026	0.592 ± 0.041
C22:5n6	1.792 ± 0.057	0.255 ± 0.016	0.261 ± 0.013	1.105 ± 0.046	0.188 ± 0.009	0.192 ± 0.009
C22:5n3	0.125 ± 0.010	1.697 ± 0.060	0.753 ± 0.018	0.113 ± 0.017	2.195 ± 0.091	1.050 ± 0.021
C24:0	1.659 ± 0.051	1.709 ± 0.062	1.670 ± 0.053	1.413 ± 0.032	1.491 ± 0.044	1.527 ± 0.037
C22:6n3	3.284 ± 0.070	6.190 ± 0.112	9.855 ± 0.257	3.692 ± 0.156	6.430 ± 0.142	10.674 ± 0.125
C24:1n9	1.013 ± 0.029	0.988 ± 0.033	1.101 ± 0.035	1.885 ± 0.087	1.753 ± 0.048	1.777 ± 0.045
SFA	40.645 ± 0.198	42.420 ± 0.136	41.795 ± 0.261	37.321 ± 0.392	39.689 ± 0.178	39.451 ± 0.180
MUFA	16.915 ± 0.246	16.084 ± 0.337	16.866 ± 0.394	28.168 ± 1.280	27.112 ± 0.747	27.019 ± 0.379
PUFA	42.440 ± 0.187	41.496 ± 0.280	41.339 ± 0.306	34.511 ± 0.973	33.199 ± 0.650	33.530 ± 0.282
n3-PUFA	3.409 ± 0.076	10.514 ± 0.206	11.575 ± 0.284	3.806 ± 0.158	13.978 ± 0.304	14.947 ± 0.188
n6-PUFA	38.990 ± 0.215	30.982 ± 0.283	29.764 ± 0.124	30.174 ± 0.829	19.105 ± 0.520	18.462 ± 0.280
n9-PUFA	0.041 ± 0.006	<LLOQ	<LLOQ	0.531 ± 0.025	0.116 ± 0.008	0.121 ± 0.009
%EPA+DHA	3.284 ± 0.070	8.817 ± 0.170	10.823 ± 0.279	3.692 ± 0.156	11.783 ± 0.266	13.897 ± 0.190
%n3 in HUFA	11.467 ± 0.273	37.302 ± 0.700	42.589 ± 0.703	13.039 ± 0.254	50.951 ± 0.883	56.370 ± 0.742
%n6 in HUFA	88.395 ± 0.272	62.698 ± 0.700	57.411 ± 0.703	85.128 ± 0.183	48.626 ± 0.869	43.174 ± 0.730

Tab. S4: ***Continued.*** Fatty acid profile in mouse blood and tissue.

(C) Blood plasma

% of total FA	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
C10:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C11:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C12:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C13:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C14:0	0.262 ± 0.018	0.300 ± 0.013	0.280 ± 0.021	0.267 ± 0.019	0.292 ± 0.022	0.301 ± 0.019
C14:1n5	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C15:0	0.101 ± 0.008	0.123 ± 0.005	0.126 ± 0.006	0.093 ± 0.006	0.101 ± 0.003	0.100 ± 0.002
C15:1n5	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C16:0	16.558 ± 0.487	17.029 ± 0.255	16.832 ± 0.327	15.542 ± 0.504	17.009 ± 0.265	17.712 ± 0.234
C16:1n7	1.042 ± 0.082	1.019 ± 0.087	0.866 ± 0.084	1.307 ± 0.098	1.368 ± 0.092	1.510 ± 0.066
C17:0	0.177 ± 0.010	0.171 ± 0.004	0.173 ± 0.006	0.139 ± 0.007	0.150 ± 0.007	0.140 ± 0.006
C17:1n7	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C18:0	11.772 ± 0.330	12.244 ± 0.507	12.129 ± 0.400	12.051 ± 0.654	9.968 ± 0.371	10.451 ± 0.468
C18:1n9	14.230 ± 1.228	11.497 ± 0.852	11.620 ± 0.908	25.758 ± 1.529	30.653 ± 1.832	27.088 ± 1.609
C18:1n7	1.450 ± 0.100	1.082 ± 0.086	1.050 ± 0.059	1.916 ± 0.144	1.528 ± 0.093	1.457 ± 0.060
C18:2n6	27.206 ± 0.846	28.601 ± 0.754	29.883 ± 1.071	11.925 ± 0.605	13.055 ± 0.527	15.696 ± 0.577
C18:3n6	0.316 ± 0.022	0.214 ± 0.013	0.202 ± 0.009	0.163 ± 0.008	0.103 ± 0.013	0.104 ± 0.011
C19:0	0.110 ± 0.012	0.111 ± 0.007	0.134 ± 0.015	0.082 ± 0.009	0.104 ± 0.009	0.088 ± 0.009
C18:3n3	0.034 ± 0.007	0.035 ± 0.011	0.034 ± 0.008	0.041 ± 0.007	0.061 ± 0.004	0.058 ± 0.004
C18:4n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:0	0.127 ± 0.006	0.138 ± 0.008	0.135 ± 0.009	0.104 ± 0.007	0.114 ± 0.006	0.099 ± 0.006
C20:1n9	0.296 ± 0.020	0.255 ± 0.015	0.270 ± 0.011	0.424 ± 0.035	0.428 ± 0.025	0.383 ± 0.026
C20:2n6	0.231 ± 0.027	0.208 ± 0.011	0.212 ± 0.013	0.106 ± 0.010	0.102 ± 0.003	0.124 ± 0.003
C20:3n9	0.082 ± 0.009	<LLOQ	<LLOQ	0.835 ± 0.111	0.203 ± 0.014	0.234 ± 0.009
C20:3n6	0.684 ± 0.023	0.922 ± 0.040	1.208 ± 0.058	1.260 ± 0.065	0.968 ± 0.098	1.249 ± 0.089
C21:0	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n6	20.660 ± 0.901	15.308 ± 0.927	13.490 ± 1.153	23.059 ± 1.556	9.565 ± 0.951	7.242 ± 0.661
C20:3n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C20:4n3	<LLOQ	<LLOQ	<LLOQ	<LLOQ	0.027 ± 0.008	<LLOQ
C20:5n3	<LLOQ	2.889 ± 0.304	1.749 ± 0.254	0.023 ± 0.009	7.094 ± 0.747	5.351 ± 0.386
C22:0	0.209 ± 0.009	0.241 ± 0.015	0.222 ± 0.013	0.220 ± 0.007	0.196 ± 0.011	0.208 ± 0.016
C22:1n9	0.282 ± 0.091	0.169 ± 0.028	0.250 ± 0.084	0.266 ± 0.079	0.103 ± 0.050	0.191 ± 0.082
C22:2n6	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ	<LLOQ
C22:4n6	0.324 ± 0.009	0.098 ± 0.004	0.076 ± 0.015	0.143 ± 0.006	0.026 ± 0.008	<LLOQ
C22:5n6	1.168 ± 0.076	<LLOQ	<LLOQ	0.634 ± 0.037	<LLOQ	<LLOQ
C22:5n3	<LLOQ	0.430 ± 0.022	0.352 ± 0.037	<LLOQ	0.528 ± 0.047	0.406 ± 0.018
C24:0	0.169 ± 0.013	0.190 ± 0.012	0.166 ± 0.015	0.186 ± 0.007	0.140 ± 0.009	0.154 ± 0.012
C22:6n3	2.214 ± 0.146	6.361 ± 0.406	8.129 ± 0.488	2.999 ± 0.230	5.691 ± 0.283	9.111 ± 0.289
C24:1n9	0.294 ± 0.028	0.364 ± 0.027	0.412 ± 0.037	0.456 ± 0.034	0.422 ± 0.051	0.546 ± 0.047
SFA	29.486 ± 0.630	30.548 ± 0.508	30.197 ± 0.354	28.686 ± 0.479	28.073 ± 0.384	29.252 ± 0.422
MUFA	17.595 ± 1.364	14.387 ± 0.979	14.467 ± 0.907	30.128 ± 1.648	34.502 ± 1.890	31.173 ± 1.675
PUFA	52.919 ± 1.013	55.065 ± 0.690	55.336 ± 0.835	41.187 ± 1.326	37.425 ± 1.597	39.574 ± 1.335
n3-PUFA	2.248 ± 0.146	9.714 ± 0.273	10.265 ± 0.495	3.064 ± 0.226	13.403 ± 0.751	14.926 ± 0.453
n6-PUFA	50.589 ± 0.942	45.351 ± 0.661	45.072 ± 0.973	37.288 ± 1.152	23.819 ± 1.519	24.415 ± 1.238
n9-PUFA	0.082 ± 0.009	<LLOQ	<LLOQ	0.835 ± 0.111	0.203 ± 0.014	0.234 ± 0.009
%EPA+DHA	2.214 ± 0.146	9.250 ± 0.284	9.878 ± 0.472	3.023 ± 0.229	12.785 ± 0.702	14.462 ± 0.439
%n3 in HUFA	8.802 ± 0.410	37.500 ± 1.416	41.366 ± 2.237	10.437 ± 0.481	55.667 ± 2.999	63.345 ± 2.073
%n6 in HUFA	90.859 ± 0.393	62.500 ± 1.416	58.634 ± 2.237	86.592 ± 0.255	43.477 ± 2.963	35.660 ± 2.070

Tab. S5: Primer sequences for qPCR.
Oligonucleotide primer sequences, product sizes and primer concentrations for quantitative real-time PCR; bp: base pairs, conc: concentration.

Primer	Sequence	Manufacturer	Size [bp]	Conc. [µM]	Annealing Temp. (time), (cycle no.)
Acaca	5'-CTGGTGAAGCTGGACCTAGA-'3 5'-ACTTTATTTCCCCCAAAACG-3'	Biomol Hamburg, Germany	242	0.1	58 °C (45 s), (50x)
Acadvl	5'-TATCTCTGCCCAGCGACTTT-3' 5'-TGGGTATGGGAACACCTGAT-3'	Biomol Hamburg, Germany	175	0.1	58 °C (45 s), (45x)
Acox1	5'-AGACAGAGATGGGTCATGGA-3' 5'-ACAAAGGCATGTAACCCGTA-3'	Biomol Hamburg, Germany	205	0.2	62.8 °C (45 s), (45x)
B2M	5'-GGCCTGTATGCTATCCAGAA-3' 5'-GAAAGACCAGTCCTTGCTGA-3'	Biomol Hamburg, Germany	198	0.4	58 °C (45 s), (45x)
Cpt1a	5'-TCGACTCACCTTTCCTGAAG-3' 5'-GAAACACCATAGCCGTCATC-3'	Biomol Hamburg, Germany	163	0.2	58 °C (30 s), (45x)
Cpt2	5'-TCCTCGATCAAGATGGGAAC-3' 5'-GATCCTTCATCGGGAAGTCA-3'	Biomol Hamburg, Germany	237	0.1	56 °C (30 s), (45x)
Decr1	5'-ACCGTGGTCTTCCACTTGTC-3' 5'-TGCCCCTTTTTGTTTTTCAC-3'	Biomol Hamburg, Germany	248	0.1	58 °C (45 s), (45x)
Decr2	5'-GCCAGTTCGAAATTAAAGCA-3' 5'-GAATGTCATCCAGCTTCCAC-3'	Biomol Hamburg, Germany	153	0.2	56 °C (30 s), (45x)
Eci1	5'-GGATCAGGTACACAGCAAGG-3' 5'-TGTAGGGACTTCTGGATGGA-3'	Biomol Hamburg, Germany	186	0.2	53 °C (30 s), (40x)
Eci2	5'-CTGTACAAGCAGGCCACAGA-3' 5'-GGCTTTCTCATCAGCTCCAC-3'	Biomol Hamburg, Germany	248	0.4	58 °C (30 s), (50x)
Ehhadh	5'-TTGGCTCCCTATTACAACCA-3' 5'-GTACCTGGTATTGCCCCTCT-3'	Biomol Hamburg, Germany	222	0.2	58 °C (30 s), (45x)
Elovl2	5'-GCCAGTGAGAGGCGTTTAAG-3' 5'-TTTCGTAGCTCTGCATGGTG-3'	Biomol Hamburg, Germany	220	0.4	58 °C (30 s), (50x)
Elovl5	5'-CCCCCGAGATACAAGAGTCA-3' 5'-TGTATTTGCCTTCCCACACA-3'	Biomol Hamburg, Germany	227	0.1	58 °C (45 s), (45x)
Fads1	5'-AAGCACATGCCATACAACCA-3' 5'-CAGCGGCATGTAAGTGAAGA-3'	Biomol Hamburg, Germany	177	0.2	58 °C (30 s), (45x)
Fads2	5'-AAAGAGCCTGCATGTGTTTG-3' 5'-GATGCCGTAGAAAGGGATGT-3'	Biomol Hamburg, Germany	250	0.1	58 °C (45 s), (45x)
Hadha	5'-GTGTTTGAGGACCTCGGTGT-3' 5'-CGTTGTGTCCTTGGAGGTTT-3'	Biomol Hamburg, Germany	225	0.2	62.8 °C (45 s), (45x)
Hadhb	5'-GAGCTGTTCTTCCCAACTGC-3' 5'-ACCCCGAAAGTGCAGCTCTA-3'	Biomol Hamburg, Germany	182	0.2	62.8 °C (45 s), (45x)
Hsd17B4	5'-AAGCCCTGAAGCCAGAGTAT-3' 5'-AATAGGCCACCATTTTCCTC-3'	Biomol Hamburg, Germany	79	0.2	62.8 °C (45 s), (45x)
PGK1	5'-GCAGATTGTTTGGAATGGTC-3' 5'-TGCTCACATGGCTGACTTTA-3'	Biomol Hamburg, Germany	185	0.4	58 °C (45 s), (45x)

Tab. S6: Normalized enzyme expression relative to c/n6-high.
Gene expression of enzymes involved in fatty acid β-oxidation, synthesis, elongation and desaturation in liver tissue of NMRI mice after 28 days of feeding an n6-PUFA-rich diet (n6-high) or an n6-PUFA-low diet (n6-low) without (c) or with n3-PUFA supplementation (EPA, DHA). Shown are mean ± SEM (n=6-8). Outliers were removed according to ROUT outlier test (Q=1%).

Gene		c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
acetyl-CoA carboxylase α	Acaca	100 ± 33	35 ± 7	56 ± 12	112 ± 22	77 ± 30	96 ± 18
acyl-CoA dehydrogenase very long chain	Acadvl	100 ± 12	81 ± 15	89 ± 10	82 ± 15	110 ± 24	113 ± 26
acyl-CoA oxidase 1	Acox1	100 ± 10	75 ± 13	138 ± 23	88 ± 9	107 ± 18	119 ± 14
carnitine palmitoyltransferase 1a	Cpt1a	100 ± 17	73 ± 12	97 ± 10	74 ± 12	88 ± 17	89 ± 9
carnitine palmitoyltransferase 2	Cpt2	100 ± 19	100 ± 14	170 ± 20	95 ± 11	147 ± 31	132 ± 21
mitochondrial multifunctional protein α-subunit	Hadha	100 ± 13	78 ± 10	105 ± 10	92 ± 17	100 ± 15	106 ± 13
mitochondrial multifunctional protein β-subunit	Hadhb	100 ± 12	83 ± 10	100 ± 9	87 ± 14	98 ± 10	98 ± 6
peroxisomal multifunctional protein MFE-1 (L-bifunctional protein, LBP)	Ehhadh	100 ± 11	90 ± 19	124 ± 11	117 ± 22	123 ± 20	155 ± 24
peroxisomal multifunctional protein MFE-2 (D-bifunctional protein, LBP)	Hsd17B4	100 ± 17	86 ± 14	78 ± 6	78 ± 13	75 ± 10	79 ± 10
2,4-dienoyl-CoA reductase 1	Decr1	100 ± 9	128 ± 10	142 ± 23	111 ± 17	121 ± 9	153 ± 20
2,4-dienoyl-CoA reductase 2	Decr2	100 ± 13	85 ± 12	104 ± 6	78 ± 9	90 ± 6	114 ± 10
cis-Δ^3-enoyl-CoA isomerase 1	Eci1	100 ± 10	108 ± 8	134 ± 11	85 ± 6	119 ± 6	139 ± 15
cis-Δ^3-enoyl-CoA isomerase 2	Eci2	100 ± 11	103 ± 11	129 ± 13	97 ± 15	119 ± 8	172 ± 33
fatty acid desaturase 1 (Δ5-desaturase)	Fads1	100 ± 11	64 ± 8	64 ± 8	79 ± 14	74 ± 8	77 ± 9
fatty acid desaturase 2 (Δ6-desaturase)	Fads2	100 ± 13	60 ± 8	89 ± 16	88 ± 19	92 ± 13	113 ± 22
very long chain elongase 2	Elovl2	100 ± 13	71 ± 7	89 ± 8	91 ± 12	97 ± 15	95 ± 9
very long chain elongase 5	Elovl5	100 ± 12	63 ± 8	71 ± 7	89 ± 15	71 ± 6	76 ± 14

Tab. S7: Oxylipin concentrations in mouse liver tissue.
Concentrations of free oxylipins in nmol/kg wet liver tissue of NMRI mice after 28 days of feeding an n6-PUFA-rich diet (n6-high) or an n6-PUFA-low diet (n6-low) without (c) or with n3-PUFA supplementation (EPA, DHA). Shown are mean ± SEM (n=8). For oxylipins that were <LLOQ in >50% of the samples within a feeding group, mean value was set to LLOQ; for oxylipins that were <LLOQ in ≤50% within a feeding group 1/2 LLOQ was used for calculation of mean ± SEM.
[1)] analyte not quantified in liver tissue due to matrix interference

Tab. S7: ***Continued.*** Oxylipin concentrations in mouse liver tissue.

	nmol/kg wet tissue	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
Prostanoids and isoprostanoids							
ARA	PGB2	<0.40	<0.40	<0.40	<0.40	<0.40	<0.40
	PGD2	2.77 ± 0.78	1.47 ± 0.31	<1.00	5.61 ± 2.26	<1.00	<1.00
	PGE2	0.83 ± 0.37	0.49 ± 0.19	<0.25	1.57 ± 0.96	<0.25	<0.25
	13,14-dihydro-15-keto-tetranor-PGE2	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	20-OH-PGE2	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	6-keto-PGF1a	16.30 ± 4.35	15.87 ± 5.79	8.66 ± 2.81	30.14 ± 10.36	14.57 ± 5.47	<1.81
	PGF2a[1)]	-	-	-	-	-	-
	11b-PGF2a	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	13,14-dihydro-15-keto-PGF2a	2.46 ± 0.67	1.93 ± 0.32	1.49 ± 0.36	4.88 ± 1.27	2.40 ± 0.42	1.78 ± 0.26
	PGJ2	<1.60	<1.60	<1.60	<1.60	<1.60	<1.60
	15-deoxy-PGJ2	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	D-12-PGJ2	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	TXB2	1.86 ± 0.39	<1.25	<1.25	3.18 ± 1.20	1.37 ± 0.34	<1.25
	2,3-dinor-TxB2	1.01 ± 0.19	0.94 ± 0.18	<1.00	2.25 ± 0.74	1.14 ± 0.16	<1.00
	11-dehydro-TxB2	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	12-HHTrE	12.13 ± 4.03	4.10 ± 0.97	2.86 ± 0.68	27.73 ± 18.75	3.83 ± 0.94	1.70 ± 0.20
	15(S)-F2t-IsoP (8i-PGF2a)	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	5(R,S)-F2t-IsoP	<0.50	<0.50	<0.50	0.96 ± 0.13	<0.50	<0.50
EPA	PGD3	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	PGE3	<0.30	<0.30	<0.30	<0.30	<0.30	<0.30
	d17-6-keto-PGF1a	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	TxB3	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	11-dehydro-TxB3	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
DGLA	PGD1	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	PGE1	<0.33	<0.33	<0.33	<0.33	<0.33	<0.33
	13,14-dihydro-15-keto-PGE1	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	PGF1a	0.69 ± 0.23	<0.25	<0.25	<0.25	<0.25	<0.25
	15-keto-PGF1a	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	TxB1	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	2,3-dinor-TxB1	<5.01	<5.01	<5.01	<5.01	<5.01	<5.01
AdA	dihomo-PGF2a	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10

Tab. S7: ***Continued.*** Oxylipin concentrations in mouse liver tissue.

	nmol/kg wet tissue	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
Multiple hydroxylated FA							
ARA	LTB4	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	6-trans-LTB4	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	20-COOH-LTB4	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	20-OH-LTB4	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	5(S),6(R),15(S)-LXA4	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	5(S),6(R),15(R) LxA4	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	5(S),6(S),15(S)-LxA4	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	LxB4	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	8,15-DiHETE	1.70 ± 0.47	<0.80	<0.80	2.36 ± 0.88	<0.80	<0.80
	5,15-DiHETE	0.44 ± 0.16	<0.25	<0.25	0.49 ± 0.17	<0.25	<0.25
EPA	LTB5	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
	LxA5	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	Rv E1	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	18(R)-RvE2 (333 → 253)	<2.00	<2.00	<2.00	<2.00	5.11 ± 1.99	<2.00
	18(R)-RvE2 (333 → 199)	<2.00	<2.00	<2.00	<2.00	5.08 ± 1.61	<2.00
	18(R)-RvE2 (333 → 159)	<2.00	<2.00	<2.00	<2.00	5.80 ± 2.25	<2.00
	18(S)-RvE3	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	18(R)-RvE3	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
DHA	RvD1	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
	17(R) RvD1	<0.75	<0.75	<0.75	<0.75	<0.75	<0.75
	Rv D2	<0.75	<0.75	<0.75	<0.75	<0.75	<0.75
	RvD3	<0.38	<0.38	<0.38	<0.38	<0.38	<0.38
	Rv D5	<0.75	<0.75	<0.75	<0.75	<0.75	<0.75
	MaR1	<2.00	<2.00	<2.00	<2.00	<2.00	<2.00
	7epi MaR1	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	PDX (359 → 153)	<0.25	0.89 ± 0.50	1.19 ± 0.31	0.54 ± 0.19	1.29 ± 0.38	1.09 ± 0.18
	PDX (359 → 206)	<0.25	0.91 ± 0.48	1.19 ± 0.31	0.48 ± 0.19	1.37 ± 0.44	1.07 ± 0.17
n3-DPA	7(S),17(S)-DiHDPA	<0.75	<0.75	<0.75	<0.75	<0.75	<0.75
DGLA	LTB3	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50

Tab. S7: ***Continued.*** Oxylipin concentrations in mouse liver tissue.

	nmol/kg wet tissue	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
Hydroxy FA							
ARA	5-HETE	25.04 ± 4.59	20.35 ± 6.83	12.91 ± 1.64	22.76 ± 6.25	12.53 ± 2.10	6.53 ± 0.61
	8-HETE	47.64 ± 10.72	35.72 ± 11.22	26.86 ± 4.80	40.92 ± 13.06	23.61 ± 4.86	12.13 ± 1.38
	9-HETE	14.58 ± 3.35	11.54 ± 4.11	7.19 ± 0.88	13.48 ± 3.69	7.57 ± 1.30	3.91 ± 0.35
	11-HETE	31.39 ± 5.99	21.14 ± 5.63	16.30 ± 1.92	34.40 ± 10.18	15.35 ± 1.85	9.51 ± 1.17
	12-HETE	109.27 ± 25.48	121.86 ± 65.20	51.79 ± 12.46	146.24 ± 46.52	54.21 ± 13.06	30.06 ± 6.24
	15-HETE	71.22 ± 13.95	51.24 ± 17.48	38.36 ± 4.47	94.93 ± 26.81	37.12 ± 5.00	26.28 ± 4.87
	19-HETE	9.97 ± 1.18	8.12 ± 1.21	<10.01	11.18 ± 2.21	<10.01	<10.01
	20-HETE	2.11 ± 0.65	1.42 ± 0.36	<1.00	3.21 ± 0.69	1.78 ± 0.29	<1.00
EPA	5-HEPE	<0.50	20.40 ± 4.26	10.66 ± 1.57	0.63 ± 0.14	39.86 ± 8.26	15.49 ± 1.31
	8-HEPE	<0.63	47.61 ± 11.16	27.23 ± 6.61	<0.63	115.95 ± 34.44	34.83 ± 3.24
	9-HEPE	<0.50	21.38 ± 5.06	10.01 ± 1.98	<0.50	45.38 ± 10.71	14.28 ± 1.17
	11-HEPE	<0.50	31.63 ± 6.40	16.92 ± 3.41	0.78 ± 0.21	71.89 ± 17.13	26.32 ± 2.00
	12-HEPE	<0.63	57.58 ± 13.60	28.85 ± 5.54	2.33 ± 0.62	145.32 ± 36.23	52.06 ± 5.52
	15-HEPE	<1.25	37.20 ± 10.37	17.25 ± 3.27	<1.25	81.09 ± 21.44	30.84 ± 2.76
	18-HEPE	<1.00	36.08 ± 7.64	19.23 ± 3.04	1.10 ± 0.19	87.75 ± 18.87	46.69 ± 9.17
	19-HEPE	<0.71	13.01 ± 1.40	10.95 ± 0.77	<0.71	34.09 ± 5.36	25.65 ± 2.22
	20-HEPE	8.54 ± 0.52	37.08 ± 4.40	22.55 ± 1.79	9.23 ± 1.65	59.38 ± 12.02	30.17 ± 1.61
DHA	4-HDHA	6.53 ± 1.64	25.66 ± 8.67	35.91 ± 4.88	10.32 ± 2.09	31.84 ± 4.14	36.37 ± 1.97
	7-HDHA	3.79 ± 1.23	13.18 ± 3.86	24.10 ± 3.42	5.76 ± 1.31	20.60 ± 3.73	23.50 ± 1.47
	8-HDHA	10.18 ± 2.58	40.94 ± 12.70	61.14 ± 6.89	17.42 ± 3.52	56.17 ± 6.66	67.34 ± 3.12
	10-HDHA	20.02 ± 8.02	57.53 ± 16.36	118.06 ± 23.09	25.88 ± 7.28	100.82 ± 25.01	99.14 ± 7.27
	11-HDHA	5.93 ± 1.81	20.16 ± 5.94	36.87 ± 5.85	9.76 ± 2.50	32.90 ± 6.40	34.82 ± 1.94
	13-HDHA	12.20 ± 3.48	37.22 ± 9.51	67.34 ± 10.31	20.30 ± 5.38	56.71 ± 9.53	65.28 ± 3.49
	14-HDHA	30.25 ± 10.06	102.16 ± 37.35	149.34 ± 27.16	58.82 ± 18.20	134.87 ± 30.05	150.64 ± 14.79
	16-HDHA	11.41 ± 2.55	33.22 ± 7.27	56.08 ± 5.84	20.16 ± 4.62	49.37 ± 6.08	61.83 ± 4.09
	17-HDHA	29.57 ± 8.51	96.90 ± 27.15	171.46 ± 26.78	56.34 ± 14.90	143.13 ± 26.43	165.70 ± 6.59
	20-HDHA	14.49 ± 3.49	47.69 ± 10.65	76.84 ± 8.76	24.68 ± 5.50	67.78 ± 9.12	81.72 ± 3.07
	21-HDHA	23.13 ± 2.38	77.83 ± 7.15	90.90 ± 6.34	32.39 ± 5.46	105.53 ± 7.08	123.21 ± 8.84
	22-HDHA	3.08 ± 0.79	7.68 ± 1.03	29.69 ± 2.51	4.04 ± 0.82	14.59 ± 1.72	34.53 ± 6.00
ALA	9-HOTrE	1.00 ± 0.26	1.14 ± 0.27	1.18 ± 0.20	1.01 ± 0.25	1.91 ± 0.43	1.28 ± 0.15
	13-HOTrE	2.34 ± 0.60	2.34 ± 0.63	2.06 ± 0.53	4.71 ± 1.40	3.10 ± 0.65	3.21 ± 0.99
LA	9-HODE	233.55 ± 51.33	215.65 ± 56.29	168.11 ± 13.57	107.62 ± 23.79	116.71 ± 16.79	97.63 ± 15.20
	13-HODE	313.25 ± 66.75	417.35 ± 207.65	205.99 ± 21.79	218.50 ± 58.34	168.19 ± 35.23	183.96 ± 52.01
DGLA	5(S) HETrE	0.50 ± 0.10	<0.20	<0.20	2.23 ± 0.42	0.72 ± 0.06	0.38 ± 0.05
	15(S)-HETrE	13.53 ± 2.10	11.42 ± 2.58	11.04 ± 1.03	21.33 ± 5.00	11.79 ± 1.27	12.77 ± 2.46

Tab. S7: ***Continued.*** Oxylipin concentrations in mouse liver tissue.

	nmol/kg wet tissue	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
Epoxy FA							
ARA	5(6)-EpETrE	23.60 ± 2.82	14.40 ± 1.80	10.84 ± 1.14	21.99 ± 4.52	11.24 ± 0.96	6.39 ± 0.71
	8(9)-EpETrE	3.30 ± 0.41	2.21 ± 0.45	1.63 ± 0.16	3.64 ± 0.56	1.80 ± 0.15	<1.00
	11(12)-EpETrE	2.80 ± 0.26	2.03 ± 0.29	1.32 ± 0.14	2.67 ± 0.50	1.36 ± 0.07	0.84 ± 0.07
	14(15)-EpETrE	4.72 ± 0.36	3.19 ± 0.38	2.45 ± 0.21	4.40 ± 0.72	2.17 ± 0.14	1.42 ± 0.12
EPA	8(9)-EpETE	<1.00	1.53 ± 0.20	<1.00	<1.00	3.47 ± 0.56	1.70 ± 0.10
	11(12)-EpETE	<0.50	1.81 ± 0.23	0.84 ± 0.06	<0.50	3.96 ± 0.60	1.76 ± 0.16
	14(15)-EpETE	<0.50	2.60 ± 0.26	1.31 ± 0.08	<0.50	5.11 ± 0.78	2.54 ± 0.14
	17(18)-EpETE	<1.00	7.90 ± 0.98	4.56 ± 0.39	<1.00	18.72 ± 2.36	9.27 ± 0.78
DHA	10(11)-EpDPE	0.79 ± 0.14	2.82 ± 0.35	4.62 ± 0.22	1.50 ± 0.20	4.23 ± 0.36	5.76 ± 0.24
	13(14)-EpDPE	0.63 ± 0.10	2.17 ± 0.27	3.24 ± 0.22	1.05 ± 0.13	3.06 ± 0.28	4.21 ± 0.22
	16(17)-EpDPE	0.69 ± 0.12	2.61 ± 0.26	3.99 ± 0.28	1.26 ± 0.14	3.33 ± 0.24	4.79 ± 0.21
	19(20)-EpDPE	4.95 ± 0.59	17.37 ± 1.97	25.64 ± 2.07	8.57 ± 0.67	21.65 ± 1.38	28.26 ± 2.05
ALA	9(10)-EpODE	<0.40	<0.40	<0.40	<0.40	<0.40	<0.40
	12(13)-EpODE	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
	15(16)-EpODE	0.72 ± 0.12	0.88 ± 0.12	1.04 ± 0.29	0.87 ± 0.17	1.34 ± 0.12	1.20 ± 0.16
LA	9(10)-EpOME	18.57 ± 2.20	20.12 ± 3.12	16.08 ± 1.20	7.43 ± 0.90	8.92 ± 0.60	8.60 ± 0.66
	12(13)-EpOME	22.61 ± 2.46	23.68 ± 3.37	18.54 ± 1.37	8.97 ± 1.19	10.29 ± 0.74	9.64 ± 0.72
OA	9(10)-Ep-stearic acid	111.19 ± 7.01	111.07 ± 9.35	97.89 ± 7.77	139.07 ± 11.18	135.44 ± 9.97	126.47 ± 8.93
Dihydroxy FA							
ARA	5,6-DiHETrE	1.45 ± 0.19	0.91 ± 0.18	0.65 ± 0.11	1.59 ± 0.31	0.74 ± 0.06	<0.50
	8,9-DiHETrE	9.53 ± 0.90	6.30 ± 0.70	5.31 ± 0.67	8.74 ± 1.41	5.22 ± 0.45	3.67 ± 0.43
	11,12-DiHETrE	19.85 ± 1.51	13.18 ± 1.26	11.96 ± 1.23	16.87 ± 2.21	9.88 ± 0.90	7.25 ± 0.66
	14,15-DiHETrE	59.03 ± 3.90	43.11 ± 3.76	37.25 ± 3.70	50.12 ± 5.40	30.61 ± 2.21	22.35 ± 1.76
EPA	8,9-DiHETE	<0.50	3.10 ± 0.33	2.74 ± 0.20	0.56 ± 0.10	9.25 ± 1.36	6.82 ± 0.57
	11,12-DiHETE	0.85 ± 0.10	4.23 ± 0.32	4.16 ± 0.27	0.96 ± 0.15	10.17 ± 1.29	8.59 ± 0.58
	14,15-DiHETE	2.40 ± 0.32	15.18 ± 1.74	14.01 ± 0.80	2.73 ± 0.47	36.59 ± 4.72	29.12 ± 1.83
	17,18-DiHETE	7.10 ± 0.89	30.95 ± 2.45	34.47 ± 2.21	7.41 ± 1.17	65.82 ± 6.20	68.46 ± 5.44
DHA	4,5-DiHDPE	2.24 ± 0.51	5.21 ± 1.08	8.23 ± 0.96	6.64 ± 1.67	11.67 ± 1.64	18.51 ± 3.83
	7,8-DiHDPE	1.22 ± 0.19	2.82 ± 0.35	3.48 ± 0.31	2.10 ± 0.37	4.23 ± 0.35	5.50 ± 0.36
	10,11-DiHDPE	4.72 ± 0.47	10.56 ± 1.05	12.89 ± 1.53	7.46 ± 1.30	14.30 ± 0.93	17.77 ± 1.14
	13,14-DiHDPE	6.58 ± 0.60	16.79 ± 1.79	19.22 ± 1.90	9.01 ± 1.26	21.03 ± 1.79	25.98 ± 1.83
	16,17-DiHDPE	18.06 ± 1.75	49.18 ± 4.11	53.71 ± 3.83	22.09 ± 2.27	62.26 ± 5.72	72.47 ± 5.10
	19,20-DiHDPE	49.40 ± 4.43	137.24 ± 10.55	153.98 ± 10.12	63.24 ± 9.94	184.82 ± 16.04	222.54 ± 14.61
ALA	9,10-DiHODE	0.23 ± 0.04	0.21 ± 0.03	0.22 ± 0.04	0.19 ± 0.04	0.31 ± 0.02	0.30 ± 0.02
	12,13-DiHODE	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	15,16-DiHODE	1.04 ± 0.18	1.26 ± 0.25	0.96 ± 0.15	1.20 ± 0.20	2.17 ± 0.22	1.82 ± 0.16
LA	9,10-DiHOME	34.78 ± 4.18	26.27 ± 2.23	23.55 ± 2.55	11.66 ± 1.39	14.74 ± 0.78	13.97 ± 1.64
	12,13-DiHOME	89.25 ± 9.38	80.64 ± 8.27	58.64 ± 5.08	29.70 ± 3.90	37.20 ± 1.40	37.44 ± 3.40
OA	9,10-DiH-stearic acid	17.31 ± 4.10	10.22 ± 0.74	17.09 ± 4.09	18.77 ± 2.34	15.64 ± 1.99	20.13 ± 4.50

Tab. S7: ***Continued.*** Oxylipin concentrations in mouse liver tissue.

	nmol/kg wet tissue	c/n6-high	EPA/n6-high	DHA/n6-high	c/n6-low	EPA/n6-low	DHA/n6-low
Miscellaneous							
ARA	11,12-,15-TriHETrE[1)]	-	-	-	-	-	-
	5-oxo-ETE	<2.00	<2.00	<2.00	<2.00	<2.00	<2.00
	15-oxo-ETE	2.17 ± 0.41	2.67 ± 1.33	1.48 ± 0.21	2.50 ± 0.62	1.50 ± 0.23	0.75 ± 0.14
	THF diol	<0.25	<0.25	<0.25	<0.25	<0.25	<0.25
EPA	12-OH-17(18)-EpETE	<0.50	<0.50	<0.50	<0.50	<0.50	<0.50
LA	13-oxo-ODE	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
	9-oxo-ODE	14.66 ± 2.06	23.54 ± 9.68	18.64 ± 3.84	7.06 ± 0.79	9.20 ± 1.00	8.05 ± 0.85

Tab. S8: Results for two-way ANOVA with Tukey's post-test for multiple comparisons.
Shown are significant differences and multiplicity adjusted p-values (ns p>0.05; * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001) for group comparisons. Two-way ANOVA was performed with GraphPad Prism Software (factor 1: background diet (n6-high, n6-low); factor 2: n3-PUFA feeding (c, EPA, DHA)) and Tukey's post-test to corret for multiple comparisons (each mean with every other mean). If one group was <LLOQ, only 4 groups were analyzed with two-way ANOVA and (if applicable) additional analyses were performed with one-way ANOVA or a t-Test. Statistical analysis was carried out for a subset of FA in liver (**A-1**, **A-2**), blood cells (**B**), blood plasma (**C**), for qPCR analysis (**D**) and a subset of free oxylipins in liver (**E**).
[a)] One-way ANOVA with Tukey's post-test for comparison of three groups with the same background diet.
[b)] t-Test for comparison of two groups.

Tab. S8: ***Continued.*** Results for two-way ANOVA with Tukey's post test for multiple comparisons.

(A-1) ANOVA of liver tissue FA concentrations (g/kg liver tissue)

FA	Tukey's multiple comparisons test	c:n6-high vs. EPA:n6-high	c:n6-high vs. DHA:n6-high	EPA:n6-high vs. DHA:n6-high	c:n6-low vs. EPA:n6-low	c:n6-low vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-low	c:n6-high vs. c:n6-low	EPA:n6-high vs. EPA:n6-low	DHA:n6-high vs. DHA:n6-low	EPA:n6-high vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-high
C18:1n9	Summary	ns	ns	ns	ns	*	ns	***	*	ns	ns	ns
	Adjusted P Value	0.9840	0.9887	> 0.9999	0.0854	0.0179	0.9878	0.0001	0.0472	0.2069	0.1882	0.0533
C20:3n9	Summary	ns	ns	ns	****	****	ns	****	**	**	***	**
	Adjusted P Value	0.9791	0.9978	0.9998	< 0.0001	< 0.0001	0.9997	< 0.0001	0.0013	0.0012	0.0005	0.0029
C18:2n6	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	> 0.9999	0.9999	> 0.9999	0.9803	0.9848	> 0.9999	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C18:3n6	Summary	*	**	ns	ns	ns	ns	****	*	*	**	ns
	Adjusted P Value	0.0305	0.0031	0.9595	0.7916	0.4964	0.9965	< 0.0001	0.0203	0.0491	0.0053	0.1447
C20:2n6	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	> 0.9999	0.8999	0.9420	0.9961	0.9631	0.9995	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C20:3n6	Summary	*	****	*	ns	ns	ns	*	ns	ns	ns	*
	Adjusted P Value	0.0127	< 0.0001	0.0186	0.9986	0.1550	0.3191	0.0253	> 0.9999	0.8528	0.2527	0.0267
C20:4n6	Summary	***	****	ns	****	****	ns	ns	****	****	****	**
	Adjusted P Value	0.0007	< 0.0001	0.5412	< 0.0001	< 0.0001	0.1338	0.0593	< 0.0001	< 0.0001	< 0.0001	0.0077
C22:4n6	Summary	****	****	ns	****	****	ns	****	***	***	***	***
	Adjusted P Value	< 0.0001	< 0.0001	> 0.9999	< 0.0001	< 0.0001	> 0.9999	< 0.0001	0.0005	0.0004	0.0008	0.0002
C22:5n6	Summary	**** a)	****	ns a)	-	****	-	****	-	ns	-	-
	Adjusted P Value	< 0.0001	< 0.0001	> 0.9999	-	< 0.0001	-	< 0.0001	-	0.9943	-	-
C18:3n3	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9281	0.8252	0.9998	0.5240	0.5738	> 0.9999	0.9911	0.7523	0.9093	0.7953	0.8801
C20:4n3	Summary	ns a)	ns a)	ns	-	-	ns	-	*	**	**	**
	Adjusted P Value	0.6152	0.9902	0.8907	-	-	0.9976	-	0.0116	0.0011	0.0072	0.0019
C20:5n3	Summary	-	-	ns	**** a)	**** a)	ns	-	****	****	****	****
	Adjusted P Value	-	-	0.9742	< 0.0001	< 0.0001	0.9276	-	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C22:5n3	Summary	****	****	****	****	****	***	ns	ns	ns	*	****
	Adjusted P Value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.0009	> 0.9999	0.8217	0.0919	0.0285	< 0.0001
C22:6n3	Summary	****	****	***	****	****	****	ns	ns	ns	***	***
	Adjusted P Value	< 0.0001	< 0.0001	0.0008	< 0.0001	< 0.0001	< 0.0001	0.9354	0.9994	0.9920	0.0001	0.0003
total FA	Summary	ns	ns	ns	ns	ns	ns	*	ns	ns	ns	ns
	Adjusted P Value	0.9975	0.999	> 0.9999	0.3738	0.1543	0.9958	0.0293	0.5543	0.8818	0.8466	0.6063
SFA	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	> 0.9999	> 0.9999	> 0.9999	0.9786	0.8742	0.9987	0.3297	0.7180	0.9543	0.9078	0.8095
MUFA	Summary	ns	ns	ns	ns	*	ns	***	ns	ns	ns	ns
	Adjusted P Value	0.9803	0.9850	> 0.9999	0.0813	0.0168	0.9875	0.0001	0.0546	0.2294	0.2124	0.0604
n3-PUFA	Summary	****	****	*	****	****	***	ns	**	****	****	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.0236	< 0.0001	< 0.0001	0.0002	0.9478	0.0076	< 0.0001	< 0.0001	0.9982
n6-PUFA	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.5893	0.3240	0.9976	0.8045	0.4706	0.9936	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n9-PUFA	Summary	ns	ns	ns	****	****	ns	****	**	**	***	**
	Adjusted P Value	0.9791	0.9978	0.9998	< 0.0001	< 0.0001	0.9997	< 0.0001	0.0013	0.0012	0.0005	0.0029
%EPA+DHA	Summary	****	****	ns	****	****	ns	ns	ns	ns	ns	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.5826	< 0.0001	< 0.0001	0.3080	0.9851	> 0.9999	0.9998	0.4117	0.4631
%n3 HUFA	Summary	****	****	*	****	****	***	ns	****	****	****	**
	Adjusted P Value	< 0.0001	< 0.0001	0.0290	< 0.0001	< 0.0001	0.0002	0.3130	< 0.0001	< 0.0001	< 0.0001	0.0046
%n6 HUFA	Summary	****	****	*	****	****	****	**	****	****	****	***
	Adjusted P Value	< 0.0001	< 0.0001	0.0186	< 0.0001	< 0.0001	< 0.0001	0.0043	< 0.0001	< 0.0001	< 0.0001	0.0006

Tab. S8: ***Continued.*** Results for two-way ANOVA with Tukey's post test for multiple comparisons.

(A-2) ANOVA of liver tissue FA profile (% of total FA)

FA	Tukey's multiple comparisons test	c:n6-high vs. EPA:n6-high	c:n6-high vs. DHA:n6-high	EPA:n6-high vs. DHA:n6-high	c:n6-low vs. EPA:n6-low	c:n6-low vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-low	c:n6-high vs. c:n6-low	EPA:n6-high vs. EPA:n6-low	DHA:n6-high vs. DHA:n6-low	EPA:n6-high vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-high
C18:1n9	Summary	ns	ns	ns	*	**	ns	****	****	****	****	****
	Adjusted P Value	0.5152	0.5724	> 0.9999	0.0201	0.0027	0.9785	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C20:3n9	Summary	ns	ns	ns	****	****	ns	****	**	**	**	*
	Adjusted P Value	0.9809	0.9989	0.9995	< 0.0001	< 0.0001	0.9901	< 0.0001	0.0075	0.0033	0.0013	0.0181
C18:2n6	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.7798	0.9959	0.9649	0.2821	0.0976	0.9939	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C18:3n6	Summary	**	****	ns	ns	ns	ns	****	****	***	****	***
	Adjusted P Value	0.004	< 0.0001	0.6076	0.9595	0.8636	0.9996	< 0.0001	< 0.0001	0.0001	< 0.0001	0.0003
C20:2n6	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.9995	0.9232	0.9861	0.9878	0.9093	0.9988	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C20:3n6	Summary	*	****	ns	ns	*	ns	ns	ns	ns	ns	***
	Adjusted P Value	0.0276	< 0.0001	0.1158	0.6781	0.0179	0.4106	0.9997	0.3371	0.0868	> 0.9999	0.0004
C20:4n6	Summary	ns	*	ns	ns	ns	ns	****	***	***	****	*
	Adjusted P Value	0.2759	0.0189	0.8316	0.5453	0.1032	0.9222	< 0.0001	0.0003	0.0006	< 0.0001	0.0101
C22:4n6	Summary	****	****	ns	ns	ns	ns	****	ns	ns	ns	ns
	Adjusted P Value	< 0.0001	< 0.0001	> 0.9999	0.1694	0.2163	> 0.9999	< 0.0001	0.0966	0.1199	0.1271	0.0908
C22:5n6	Summary	**** a)	****	ns a)	-	*	-	****	-	ns	-	-
	Adjusted P Value	< 0.0001	< 0.0001	0.9998	-	0.0123	-	< 0.0001	-	0.9991	-	-
C18:3n3	Summary	ns	ns	ns	ns	*	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.5518	0.4380	> 0.9999	0.2113	0.0294	0.9481	0.9575	> 0.9999	0.9962	0.9837	0.9987
C20:4n3	Summary	ns a)	ns a)	ns	-	-	ns	-	ns	*	ns	*
	Adjusted P Value	0.6682	0.9884	0.8288	-	-	> 0.9999	-	0.1334	0.0225	0.1404	0.0211
C20:5n3	Summary	-	-	ns	*** a)	*** a)	ns	-	*	**	**	**
	Adjusted P Value	-	-	0.9849	0.0003	0.0003	> 0.9999	-	0.0104	0.0040	0.0097	0.0043
C22:5n3	Summary	****	**	*	****	***	ns	ns	ns	ns	ns	ns
	Adjusted P Value	< 0.0001	0.0019	0.0184	< 0.0001	0.0002	0.2403	> 0.9999	0.9852	0.9968	0.0605	0.0930
C22:6n3	Summary	****	****	ns	***	****	ns	ns	ns	ns	ns	***
	Adjusted P Value	< 0.0001	< 0.0001	0.2261	0.0003	< 0.0001	0.1052	0.9543	0.2895	0.5066	0.9948	0.0009
SFA	Summary	ns	ns	ns	***	****	ns	****	ns	ns	ns	*
	Adjusted P Value	0.2329	0.1137	0.9991	0.0004	< 0.0001	0.9930	< 0.0001	0.0581	0.0913	0.1933	0.0235
MUFA	Summary	ns	ns	ns	*	**	ns	****	****	****	****	****
	Adjusted P Value	0.4283	0.4603	> 0.9999	0.0148	0.0020	0.9801	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n3-PUFA	Summary	****	****	ns	****	****	ns	ns	ns	ns	ns	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.7559	< 0.0001	< 0.0001	0.4375	0.9862	> 0.9999	0.9996	0.5682	0.6290
n6-PUFA	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.9324	0.3908	0.9155	0.9996	0.9998	> 0.9999	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n9-PUFA	Summary	ns	ns	ns	****	****	ns	****	**	**	**	*
	Adjusted P Value	0.9809	0.9989	0.9995	< 0.0001	< 0.0001	0.9901	< 0.0001	0.0075	0.0033	0.0013	0.0181
%EPA+DHA	Summary	****	****	ns	****	****	ns	ns	ns	ns	ns	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.5826	< 0.0001	< 0.0001	0.3082	0.9854	> 0.9999	0.9998	0.4117	0.4632
%n3 HUFA	Summary	****	****	*	****	****	***	ns	****	****	****	**
	Adjusted P Value	< 0.0001	< 0.0001	0.0291	< 0.0001	< 0.0001	0.0002	0.3089	< 0.0001	< 0.0001	< 0.0001	0.0045
%n6 HUFA	Summary	****	****	*	****	****	***	**	****	****	****	***
	Adjusted P Value	< 0.0001	< 0.0001	0.0187	< 0.0001	< 0.0001	0.0001	0.0042	< 0.0001	< 0.0001	< 0.0001	0.0006

Tab. S8: ***Continued.*** Results for two-way ANOVA with Tukey's post test for multiple comparisons.

(B) ANOVA of blood cell FA profile (% of total FA)

FA	Tukey's multiple comparisons test	c:n6-high vs. EPA:n6-high	c:n6-high vs. DHA:n6-high	EPA:n6-high vs. DHA:n6-high	c:n6-low vs. EPA:n6-low	c:n6-low vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-low	c:n6-high vs. c:n6-low	EPA:n6-high vs. EPA:n6-low	DHA:n6-high vs. DHA:n6-low	EPA:n6-high vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-high
C18:1n9	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.9759	> 0.9999	0.9834	0.9977	0.9961	> 0.9999	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C20:3n9	Summary	-	-	-	**** a)	**** a)	ns a)	**** b)	-	-	-	-
	Adjusted P Value	-	-	-	< 0.0001	< 0.0001	0.9742	< 0.0001	-	-	-	-
C18:2n6	Summary	ns	***	ns	ns	***	**	****	****	****	****	****
	Adjusted P Value	0.4213	0.0008	0.1302	0.8568	0.0002	0.0072	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C18:3n6	Summary	*	**	ns	ns	ns	ns	****	*	*	**	ns
	Adjusted P Value	0.0409	0.0012	0.8062	0.9846	0.7154	0.9739	< 0.0001	0.0104	0.0391	0.0012	0.2037
C20:2n6	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.8866	0.9754	0.9994	0.9997	0.6629	0.8280	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C20:3n6	Summary	ns	****	***	***	ns	****	ns	ns	ns	ns	****
	Adjusted P Value	0.9890	< 0.0001	0.0002	0.0005	0.9906	< 0.0001	0.1180	0.1117	0.1936	0.1231	< 0.0001
C20:4n6	Summary	****	****	*	****	****	*	ns	****	****	****	*
	Adjusted P Value	< 0.0001	< 0.0001	0.0111	< 0.0001	< 0.0001	0.0203	0.9740	< 0.0001	< 0.0001	< 0.0001	0.0435
C22:4n6	Summary	****	****	**	****	****	*	****	****	****	****	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.0083	< 0.0001	< 0.0001	0.0276	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.1709
C22:5n6	Summary	****	****	ns	****	****	ns	****	ns	ns	ns	ns
	Adjusted P Value	< 0.0001	< 0.0001	> 0.9999	< 0.0001	< 0.0001	> 0.9999	< 0.0001	0.6630	0.6221	0.7076	0.5758
C20:5n3	Summary	-	-	****	-	-	****	-	****	****	*	****
	Adjusted P Value	-	-	< 0.0001	-	-	< 0.0001	-	< 0.0001	< 0.0001	0.0111	< 0.0001
C22:5n3	Summary	****	****	****	****	****	****	ns	****	***	****	****
	Adjusted P Value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	> 0.9999	< 0.0001	0.0007	< 0.0001	< 0.0001
C22:6n3	Summary	****	****	****	****	****	****	ns	ns	**	****	****
	Adjusted P Value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.4365	0.8805	0.0067	< 0.0001	< 0.0001
SFA	Summary	****	*	ns	****	****	ns	****	****	****	****	****
	Adjusted P Value	< 0.0001	0.0175	0.4492	< 0.0001	< 0.0001	0.9806	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
MUFA	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.9493	> 0.9999	0.9606	0.8709	0.8257	> 0.9999	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n3-PUFA	Summary	****	****	*	****	****	*	ns	****	****	****	****
	Adjusted P Value	< 0.0001	< 0.0001	0.0146	< 0.0001	< 0.0001	0.0322	0.7861	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n6-PUFA	Summary	****	****	ns	****	****	ns	****	****	****	****	****
	Adjusted P Value	< 0.0001	< 0.0001	0.3905	< 0.0001	< 0.0001	0.9066	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n9-PUFA	Summary	-	-	-	**** a)	**** a)	ns a)	**** b)	-	-	-	-
	Adjusted P Value	-	-	-	< 0.0001	< 0.0001	0.9742	< 0.0001	-	-	-	-
%EPA+DHA	Summary	****	****	****	****	****	****	ns	****	****	****	*
	Adjusted P Value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.7060	< 0.0001	< 0.0001	< 0.0001	0.0185
%n3 HUFA	Summary	****	****	****	****	****	****	ns	****	****	****	****
	Adjusted P Value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.5161	< 0.0001	< 0.0001	< 0.0001	< 0.0001
%n6 HUFA	Summary	****	****	****	****	****	****	**	****	****	****	****
	Adjusted P Value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.0084	< 0.0001	< 0.0001	< 0.0001	< 0.0001

Tab. S8: ***Continued.*** Results for two-way ANOVA with Tukey's post test for multiple comparisons.

(C) ANOVA of blood plasma FA profile (% of total FA)

FA	Tukey's multiple comparisons test	c:n6-high vs. EPA:n6-high	c:n6-high vs. DHA:n6-high	EPA:n6-high vs. DHA:n6-high	c:n6-low vs. EPA:n6-low	c:n6-low vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-low	c:n6-high vs. c:n6-low	EPA:n6-high vs. EPA:n6-low	DHA:n6-high vs. DHA:n6-low	EPA:n6-high vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-high
C18:1n9	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.7236	0.7600	> 0.9999	0.1422	0.9828	0.4561	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C20:3n9	Summary	-	-	-	**** a)	**** a)	ns a)	**** b)	-	-	-	-
	Adjusted P Value	-	-	-	< 0.0001	< 0.0001	0.9417	< 0.0001	-	-	-	-
C18:2n6	Summary	ns	ns	ns	ns	*	ns	****	****	****	****	****
	Adjusted P Value	0.7789	0.1439	0.8328	0.8941	0.0120	0.1539	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
C18:3n6	Summary	****	****	ns	*	*	ns	****	****	***	****	****
	Adjusted P Value	< 0.0001	< 0.0001	0.9900	0.0379	0.0431	> 0.9999	< 0.0001	< 0.0001	0.0001	< 0.0001	< 0.0001
C20:2n6	Summary	ns	ns	ns	ns	ns	ns	****	****	***	**	****
	Adjusted P Value	0.8334	0.9150	> 0.9999	> 0.9999	0.9330	0.8646	< 0.0001	< 0.0001	0.0006	0.0011	< 0.0001
C20:3n6	Summary	ns	****	*	*	ns	ns	****	ns	ns	*	ns
	Adjusted P Value	0.1480	< 0.0001	0.0475	0.0416	> 0.9999	0.0548	< 0.0001	0.9964	0.9981	0.0159	0.1415
C20:4n6	Summary	*	***	ns	****	****	ns	ns	**	**	****	ns
	Adjusted P Value	0.0112	0.0003	0.8293	< 0.0001	< 0.0001	0.637	0.6046	0.0054	0.0020	< 0.0001	0.1162
C22:4n6	Summary	****	**** a)	ns a)	****	-	-	****	****	-	-	-
	Adjusted P Value	< 0.0001	< 0.0001	0.2910	< 0.0001	-	-	< 0.0001	< 0.0001	-	-	-
C22:5n6	Summary	-	-	-	-	-	-	**** b)	-	-	-	-
	Adjusted P Value	-	-	-	-	-	-	< 0.0001	-	-	-	-
C18:3n3	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	> 0.9999	> 0.9999	> 0.9999	0.3388	0.5598	0.9990	0.9818	0.1040	0.1993	0.2186	0.0932
C20:5n3	Summary	-	-	ns	**** a)	**** a)	ns	-	****	****	**	****
	Adjusted P Value	-	-	0.3260	< 0.0001	< 0.0001	0.0592	-	< 0.0001	< 0.0001	0.0043	< 0.0001
C22:5n3	Summary	-	-	ns	-	-	ns	-	ns	ns	ns	**
	Adjusted P Value	-	-	0.3746	-	-	0.0659	-	0.1800	0.6754	0.9561	0.0045
C22:6n3	Summary	****	****	**	****	****	****	ns	ns	ns	****	****
	Adjusted P Value	< 0.0001	< 0.0001	0.0054	< 0.0001	< 0.0001	< 0.0001	0.5405	0.6969	0.2942	< 0.0001	< 0.0001
SFA	Summary	ns	ns	ns	ns	ns	ns	ns	**	ns	ns	*
	Adjusted P Value	0.6076	0.8921	0.9947	0.9398	0.9561	0.4971	0.8348	0.0074	0.7179	0.3918	0.0307
MUFA	Summary	ns	ns	ns	ns	ns	ns	****	****	****	****	****
	Adjusted P Value	0.6302	0.6548	> 0.9999	0.2955	0.9956	0.5932	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n3-PUFA	Summary	****	****	ns	****	****	ns	ns	****	****	****	***
	Adjusted P Value	< 0.0001	< 0.0001	0.9481	< 0.0001	< 0.0001	0.1632	0.7773	< 0.0001	< 0.0001	< 0.0001	0.0001
n6-PUFA	Summary	*	*	ns	****	****	ns	****	****	****	****	****
	Adjusted P Value	0.0211	0.0132	> 0.9999	< 0.0001	< 0.0001	0.9989	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
n9-PUFA	Summary	-	-	-	**** a)	**** a)	ns a)	**** b)	-	-	-	-
	Adjusted P Value	-	-	-	< 0.0001	< 0.0001	0.9417	< 0.0001	-	-	-	-
%EPA+DHA	Summary	****	****	ns	****	****	ns	ns	****	****	****	***
	Adjusted P Value	< 0.0001	< 0.0001	0.8961	< 0.0001	< 0.0001	0.0743	0.7511	< 0.0001	< 0.0001	< 0.0001	0.0002
%n3 HUFA	Summary	****	****	ns	****	****	ns	ns	****	****	****	****
	Adjusted P Value	< 0.0001	< 0.0001	0.6835	< 0.0001	< 0.0001	0.0580	0.9887	< 0.0001	< 0.0001	< 0.0001	< 0.0001
%n6 HUFA	Summary	****	****	ns	****	****	*	ns	****	****	****	****
	Adjusted P Value	< 0.0001	< 0.0001	0.6745	< 0.0001	< 0.0001	0.0476	0.5771	< 0.0001	< 0.0001	< 0.0001	< 0.0001

Tab. S8: ***Continued.*** Results for two-way ANOVA with Tukey's post test for multiple comparisons.

(D) ANOVA of liver tissue qPCR data (rel. normalized expression)

Enzyme/ enzyme index	Tukey's multiple comparisons test	c:n6-high vs. EPA:n6-high	c:n6-high vs. DHA:n6-high	EPA:n6-high vs. DHA:n6-high	c:n6-low vs. EPA:n6-low	c:n6-low vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-low	c:n6-high vs. c:n6-low	EPA:n6-high vs. EPA:n6-low	DHA:n6-high vs. DHA:n6-low	EPA:n6-high vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-high
Decr1	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.7877	0.4127	0.9894	0.9977	0.4231	0.6986	0.9956	0.9993	0.9963	0.8767	0.9288
Decr2	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.8853	0.9998	0.7709	0.9581	0.1405	0.5807	0.6035	0.9994	0.9827	0.3449	0.9302
Eci1	Summary	ns	ns	ns	ns	**	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9905	0.1802	0.4459	0.1568	0.0052	0.7260	0.8691	0.9536	0.9993	0.2170	0.9154
Eci2	Summary	ns	ns	ns	ns	*	ns	ns	ns	ns	ns	ns
	Adjusted P Value	> 0.9999	0.8619	0.9041	0.9455	0.0385	0.3081	> 0.9999	0.9856	0.5247	0.0693	0.9991
Fads1	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.1340	0.1436	> 0.9999	0.9995	> 0.9999	> 0.9999	0.6691	0.9816	0.9464	0.9519	0.9779
Fads2	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.4708	0.9958	0.8106	> 0.9999	0.8649	0.9351	0.9945	0.7303	0.8862	0.1772	> 0.9999
Elovl2	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.4137	0.9807	0.8614	0.9994	0.9999	> 0.9999	0.9919	0.5914	0.9989	0.6477	0.9971
Elovl5	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.1746	0.4043	0.9961	0.8533	0.9466	0.9998	0.9795	0.9939	0.9995	0.9638	> 0.9999
Acaca	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.3029	0.7349	0.9860	0.8733	0.9949	0.9900	0.9986	0.7776	0.8024	0.3694	0.9874
Acadvl	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9747	0.9982	0.9996	0.8855	0.8277	> 0.9999	0.9808	0.8670	0.9406	0.8050	0.9681
Acox	Summary	ns	ns	*	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.8104	0.4633	0.0462	0.9420	0.6836	0.9938	0.9903	0.6452	0.9436	0.3099	0.6983
Cpt1a	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.6677	> 0.9999	0.7834	0.9755	0.9614	> 0.9999	0.7026	0.9667	0.9984	0.9495	0.9963
Cpt2	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	> 0.9999	0.1484	0.1513	0.4249	0.7563	0.9950	> 0.9999	0.5521	0.7794	0.8605	0.9684
Hadha	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.8227	0.9997	0.6823	0.9975	0.9730	0.9997	0.9978	0.8302	> 0.9999	0.6571	0.9998
Hadhb	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.8520	> 0.9999	0.8665	0.9755	0.9810	> 0.9999	0.9499	0.9098	> 0.9999	0.9233	> 0.9999
Ehhadh	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9986	0.9504	0.8127	> 0.9999	0.6948	0.8358	0.9834	0.8052	0.8731	0.1515	> 0.9999
Hsd17b4	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9614	0.8309	0.9984	> 0.9999	> 0.9999	> 0.9999	0.7934	0.9907	> 0.9999	0.9985	> 0.9999
D6D index	Summary	**	****	ns	****	****	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.0022	< 0.0001	0.8779	< 0.0001	< 0.0001	0.8560	> 0.9999	0.6763	0.6443	0.1108	0.9989
D5D index	Summary	****	****	**	****	****	*	****	**	*	****	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.0043	< 0.0001	< 0.0001	0.0496	< 0.0001	0.0018	0.0231	< 0.0001	0.9996
Elongase index	Summary	****	****	ns	****	**	ns	****	*	ns	ns	***
	Adjusted P Value	< 0.0001	< 0.0001	0.7140	< 0.0001	0.0087	0.0949	< 0.0001	0.0456	0.5158	0.9995	0.0008

Tab. S8: ***Continued.*** Results for two-way ANOVA with Tukey's post test for multiple comparisons.

(E) ANOVA of liver tissue oxylipin concentrations (nmol/kg liver tissue)

Oxylipin	Tukey's multiple comparisons test	c:n6-high vs. EPA:n6-high	c:n6-high vs. DHA:n6-high	EPA:n6-high vs. DHA:n6-high	c:n6-low vs. EPA:n6-low	c:n6-low vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-low	c:n6-high vs. c:n6-low	EPA:n6-high vs. EPA:n6-low	DHA:n6-high vs. DHA:n6-low	EPA:n6-high vs. DHA:n6-low	EPA:n6-low vs. DHA:n6-high
5-HETE	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9726	0.3788	0.8319	0.5661	0.1125	0.9244	0.9990	0.8007	0.9039	0.2423	> 0.9999
5-HEPE	Summary	-	-	ns	**** a)	ns a)	**	-	*	ns	ns	***
	Adjusted P Value	-	-	0.4810	< 0.0001	0.0991	0.0060	-	0.0349	0.8892	0.8840	0.0009
4-HDHA	Summary	ns	***	ns	*	**	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.0558	0.0007	0.6192	0.0223	0.0032	0.9813	0.9916	0.9310	> 0.9999	0.5735	0.9885
7-HDHA	Summary	ns	****	ns	**	***	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.1797	< 0.0001	0.0786	0.0059	0.0006	0.9756	0.9958	0.4182	> 0.9999	0.1107	0.9455
12-HETE	Summary	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9998	0.8552	0.7220	0.4466	0.2034	0.9964	0.9752	0.7502	0.9978	0.4493	> 0.9999
12-HEPE	Summary	-	-	ns	*** a)	ns a)	*	-	*	ns	ns	**
	Adjusted P Value	-	-	0.7339	0.0003	0.2431	0.0120	-	0.0194	0.8391	0.9972	0.0014
14-HDHA	Summary	ns	*	ns	ns	ns	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.3320	0.0175	0.7580	0.2735	0.1150	0.9975	0.9631	0.9356	> 0.9999	0.7367	0.9984
15-HETE	Summary	ns	ns	ns	ns	*	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.9266	0.6121	0.9888	0.0790	0.0219	0.9949	0.8599	0.9831	0.9917	0.8322	> 0.9999
15-HEPE	Summary	-	-	ns	-	-	*	-	ns	ns	ns	**
	Adjusted P Value	-	-	0.6529	-	-	0.0314	-	0.0714	0.8566	0.9821	0.0045
17-HDHA	Summary	ns	***	ns	*	**	ns	ns	ns	ns	ns	ns
	Adjusted P Value	0.2025	0.0002	0.1229	0.0469	0.0058	0.9688	0.9366	0.6002	> 0.9999	0.1838	0.9207
18-HEPE	Summary	-	-	ns	*** a)	* a)	ns	-	*	ns	ns	**
	Adjusted P Value	-	-	0.7172	0.0001	0.0373	0.0696	-	0.0153	0.3309	0.9092	0.0010
PDX	Summary	-	-	ns	ns a)	ns a)	ns	-	ns	ns	ns	ns
(*m/z* 359 → 153)	Adjusted P Value	-	-	0.9348	0.1408	0.3254	0.9811	-	0.8660	0.9973	0.9789	0.9977
PDX	Summary	-	-	ns	ns a)	ns a)	ns	-	ns	ns	ns	ns
(*m/z* 359 → 206)	Adjusted P Value	-	-	0.9539	0.1032	0.3478	0.9377	-	0.8182	0.9960	0.9908	0.9843
14(15)-EpETrE	Summary	ns	**	ns	**	****	ns	ns	ns	ns	*	ns
	Adjusted P Value	0.069	0.0017	0.7436	0.0021	< 0.0001	0.7369	0.9906	0.4177	0.4109	0.0238	0.9948
17(18)-EpETE	Summary	-	-	ns	-	-	***	-	****	ns	ns	****
	Adjusted P Value	-	-	0.3208	-	-	0.0002	-	< 0.0001	0.0890	0.8903	< 0.0001
19(20)-EpDPE	Summary	****	****	**	****	****	ns	ns	ns	ns	***	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.0078	< 0.0001	< 0.0001	0.0540	0.5918	0.4110	0.8487	0.0002	0.4866
14,15-DiHETrE	Summary	*	**	ns	**	****	ns	ns	ns	ns	**	ns
	Adjusted P Value	0.0398	0.0017	0.8647	0.0062	< 0.0001	0.6040	0.5246	0.1735	0.0637	0.0031	0.7916
17,18-DiHETE	Summary	***	****	ns	****	****	ns	ns	****	****	****	****
	Adjusted P Value	0.0005	< 0.0001	0.9834	< 0.0001	< 0.0001	0.9956	> 0.9999	< 0.0001	< 0.0001	< 0.0001	< 0.0001
19,20-DiHDPE	Summary	****	****	ns	****	****	ns	ns	ns	**	****	ns
	Adjusted P Value	< 0.0001	< 0.0001	0.9073	< 0.0001	< 0.0001	0.2145	0.9569	0.0600	0.0018	< 0.0001	0.4250
20-HETE	Summary	ns	-	-	ns	-	-	ns	ns	-	-	-
	Adjusted P Value	0.7945	-	-	0.2366	-	-	0.4592	0.9650	-	-	-
20-HEPE	Summary	**	ns	ns	****	ns	**	ns	ns	ns	ns	***
	Adjusted P Value	0.0064	0.4485	0.4067	< 0.0001	0.0844	0.0050	> 0.9999	0.0559	0.9135	0.9415	0.0002
22-HDHA	Summary	ns	****	****	ns	****	***	ns	ns	ns	****	**
	Adjusted P Value	0.8556	< 0.0001	< 0.0001	0.1076	< 0.0001	0.0001	0.9999	0.5168	0.8264	< 0.0001	0.0060