

## SUPPLEMENTARY TABLES

**Table S1: LC-MS/MS conditions used to determine the AA-, EPA- and DHA-derived metabolites.**

Compound Name	ISTD	Precursor Ion [m/z]	Product Ion [m/z]	Fragmentor Voltage [V]	Collision Energy [V]	Cell Accelerator Voltage [V]	Retention Time [min]
d17-6-keto-PGF1 $\alpha$	1	367,0	163,0	120	20	1	4,87
6-keto-PGF1 $\alpha$	1	369,2	163,0	130	24	8	4,90
TXB3	1	367,2	169,1	100	10	1	5,12
TXB2	1	369,2	195,0	100	9	1	5,25
PGE3	1	349,2	269,2	130	7	6	5,32
11-dehydro TXB3	1	365,2	303,0	120	9	4	5,40
PGE2-d4	ISTD-1	355,3	319,0	110	4	5	5,59
PGE2	1	351,3	315,0	110	4	5	5,61
11-dehydro TXB2	1	367,2	305,0	140	8	4	5,67
Resolvin D1	2	375,2	141,1	110	9	1	5,96
LTB5	3	333,2	195,1	130	8	1	6,50
17,18-DHEQ	2	335,2	247,1	120	10	1	7,10
LTB4-d4	ISTD-2	339,2	197,1	130	7	1	7,32
LTB4	3	335,2	195,1	130	7	1	7,42
14,15-DHEQ	3	335,2	207,1	140	11	3	7,45
11,12-DHEQ	3	335,2	167,1	160	7	1	7,54
8,9-DHEQ	3	335,2	127,1	140	15	1	7,70
5,6-DHEQ	3	335,2	145,1	120	11	3	8,09
14,15-DHET-d11	ISTD-3	348,3	207,1	120	10	1	8,15
19,20-DHDP	3	361,0	273,0	130	11	3	8,18
14,15-DHET	3	337,2	207,1	120	10	1	8,21
16,17-DHDP	3	361,0	233,0	140	10	2	8,53
11,12-DHET	3	337,2	167,1	120	12	1	8,59
13,14-DHDP	3	361,0	193,0	140	10	1	8,65
10,11-DHDP	3	361,0	153,0	140	11	1	8,85
8,9-DHET	3	337,2	127,1	140	15	1	8,91
18-HEPE	5	317,2	259,1	140	3	5	9,11
20-HEPE	4	317,2	287,1	130	8	1	9,11
7,8-DHDP	3	361,0	113,0	140	15	8	9,35

5,6-DHET	5	337,2	145,1	130	11	1	9,40
20-HETE-d6	ISTD-4	325,2	295,1	130	11	2	9,59
15-HEPE	5	317,2	219,1	120	5	1	9,63
20-HETE	4	319,2	289,1	150	11	3	9,67
12-HEPE	5	317,2	179,1	120	5	1	9,84
9-HEPE	5	317,2	167,1	110	5	1	10,17
5-HEPE	5	317,2	115,1	110	6	1	10,43
22-HDHA	4	343,0	313,0	150	8	1	10,45
15-HETE-d8	ISTD-5	327,2	226,1	140	4	1	10,99
15-HETE	5	319,2	219,1	140	4	8	11,13
17,18-EEQ	6	317,2	259,1	120	3	1	11,32
17-HDHA	5	343,2	201,1	110	6	6	11,33
14-HDHA	5	343,2	205,1	110	6	2	11,59
12-HETE	5	319,2	179,1	110	5	1	11,84
14,15-EEQ	6	317,2	207,1	110	3	4	11,95
9-HETE	5	319,2	151,1	130	5	2	12,14
5-HETE	5	319,2	115,1	110	10	1	12,27
11,12-EEQ	6	317,2	167,1	130	4	1	12,41
8,9-EEQ	6	317,2	255,1	110	2	1	12,44
5,6-EEQ	6	317,2	189,1	110	2	1	12,69
4-HDHA	5	343,2	101,1	130	7	2	12,86
19,20-EDP	6	343,0	241,0	160	8	2	13,47
14,15-EET-d8	ISTD-6	327,2	226,1	120	3	8	13,80
14,15-EET	6	319,2	219,1	120	3	1	13,88
16,17-EDP	6	343,0	233,0	110	4	2	14,24
13,14-EDP	6	343,0	234,0	120	3	2	14,44
10,11-EDP	6	343,0	153,0	120	4	1	14,55
11,12-EET	6	319,2	167,1	120	2	1	14,70
4,5-EDP	6	343,0	281,0	130	6	4	14,73
7,8-EDP	6	343,0	109,0	130	9	1	14,82
8,9-EET	6	319,2	155,1	120	3	1	14,90
5,6-EET	6	319,2	191,1	120	4	1	15,08

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*Legend: ISTD- internal standard*

**Table S2: Effect of EPA/DHA supplementation on the fatty acid composition in RBCs.** Individual fatty acids are given as percentage of total fatty acids (mean  $\pm$  SEM, n=19). A general linear model for repeated measurements was used for analysis. p<0.05 was considered statistical significant. ns = not significant. Week 0 = basal = W0 and week 8 = maximum treatment = W8.

	Basal (week 0)		2g OM-3 (week 8)			Follow up (week 16)			
	Mean	SEM	Mean	SEM	p (vs W0)	Mean	SEM	p (vs W0)	p (vs W8)
<b>C14:0</b>	<b>0.43</b>	0.03	<b>0.38</b>	0.03	ns	<b>0.37</b>	0.04	ns	ns
<b>C16:0</b>	<b>20.97</b>	0.23	<b>20.77</b>	0.31	ns	<b>21.38</b>	0.25	ns	ns
<b>C16:1 n-7</b>	<b>0.67</b>	0.16	<b>0.32</b>	0.04	ns	<b>0.47</b>	0.06	ns	ns
<b>C18:0</b>	<b>15.18</b>	0.30	<b>15.15</b>	0.25	ns	<b>15.29</b>	0.33	ns	ns
<b>C18:1 n-9</b>	<b>15.70</b>	0.27	<b>14.77</b>	0.39	= 0.048	<b>15.71</b>	0.18	ns	ns
<b>C18:2 n-6</b>	<b>12.74</b>	0.45	<b>11.95</b>	0.44	= 0.007	<b>12.61</b>	0.39	ns	ns
<b>C18:3 n-6</b>	<b>0.10</b>	0.02	<b>0.11</b>	0.04	ns	<b>0.11</b>	0.01	ns	ns
<b>C20:1 n-9</b>	<b>0.20</b>	0.01	<b>0.24</b>	0.09	ns	<b>0.20</b>	0.01	ns	ns
<b>C18:3 n-3</b>	<b>0.21</b>	0.02	<b>0.17</b>	0.02	ns	<b>0.18</b>	0.02	ns	ns
<b>C20:2 n-6</b>	<b>0.22</b>	0.01	<b>0.28</b>	0.08	ns	<b>0.22</b>	0.01	ns	ns
<b>C20:3 n-6</b>	<b>1.76</b>	0.08	<b>1.52</b>	0.12	ns	<b>1.77</b>	0.09	ns	ns
<b>C20:4 n-6 (AA)</b>	<b>16.88</b>	0.30	<b>15.96</b>	0.25	= 0.038	<b>15.65</b>	0.29	= 0.012	ns
<b>C24:0</b>	<b>1.28</b>	0.09	<b>1.19</b>	0.10	ns	<b>1.40</b>	0.10	ns	ns
<b>C20:5 n-3 (EPA)</b>	<b>0.69</b>	0.04	<b>2.32</b>	0.11	< 0.001	<b>1.06</b>	0.06	< 0.001	< 0.001
<b>C24:1 n-9</b>	<b>1.45</b>	0.10	<b>1.38</b>	0.08	ns	<b>1.40</b>	0.05	ns	ns
<b>C22:4 n-6</b>	<b>3.00</b>	0.10	<b>2.68</b>	0.11	= 0.038	<b>2.47</b>	0.10	< 0.001	ns
<b>C22:5 n-6</b>	<b>0.69</b>	0.04	<b>0.64</b>	0.09	ns	<b>0.56</b>	0.04	= 0.006	ns
<b>C22:5 n-3</b>	<b>2.65</b>	0.09	<b>3.04</b>	0.07	< 0.001	<b>2.84</b>	0.07	= 0.015	= 0.020
<b>C22:6 n-3 (DHA)</b>	<b>4.25</b>	0.18	<b>6.10</b>	0.18	< 0.001	<b>5.56</b>	0.18	< 0.001	< 0.001

**Table S3: Effect of EPA/DHA supplementation on the CYP-eicosanoid profile in plasma.** The concentration of the metabolites is given in ng/ml as mean  $\pm$  SEM, n=19. A general linear model for repeated measurements was used for analysis. p<0.05 was considered significant with \* vs week 0 and # vs week 8. Week 0 = basal, week 8 = maximum treatment and week 16 = follow-up.

		<i>Epoxymetabolite</i>			<i>Diol</i>			<i>Ratio Diol/Epoxymetabolite</i>		
		<i>Week 0</i>	<i>Week 8</i>	<i>Week 16</i>	<i>Week 0</i>	<i>Week 8</i>	<i>Week 16</i>	<i>Week 0</i>	<i>Week 8</i>	<i>Week 16</i>
<b>AA</b>			<b>EET</b>		<b>DHET</b>		<b>DHET/EET</b>			
<b>14,15-</b>	Mean	<b>2.64</b>	<b>2.40</b>	<b>2.37</b>	<b>0.60</b>	<b>0.57</b>	<b>0.60</b>	0.23	0.24	0.25
	SEM	0.24	0.22	0.21	0.03	0.03	0.03			
<b>11,12-</b>	Mean	<b>1.72</b>	<b>1.44 *</b>	<b>1.42 *</b>	<b>0.64</b>	<b>0.57 *</b>	<b>0.60</b>	0.37	0.40	0.42
	SEM	0.13	0.13	0.12	0.04	0.03	0.03			
<b>8,9-</b>	Mean	<b>3.28</b>	<b>2.90</b>	<b>2.96</b>	<b>1.94</b>	<b>1.70</b>	<b>1.87</b>	0.59	0.59	0.63
	SEM	0.29	0.25	0.26	0.11	0.10	0.13			
<b>5,6-</b>	Mean	<b>1.26</b>	<b>1.00 *</b>	<b>1.07 *</b>	<b>5.36</b>	<b>4.85</b>	<b>5.26</b>	4.24	4.87	4.91
	SEM	0.13	0.07	0.12	0.41	0.49	0.47			
<b>EPA</b>			<b>EEQ</b>		<b>DHEQ</b>		<b>DHEQ/EEQ</b>			
<b>17,18-</b>	Mean	<b>0.27</b>	<b>1.34 *</b>	<b>0.30 #</b>	<b>1.61</b>	<b>4.81 *</b>	<b>1.78 #</b>	6.07	3.58	6.00
	SEM	0.07	0.12	0.06	0.20	0.39	0.23			
<b>14,15-</b>	Mean	<b>0.09</b>	<b>0.55 *</b>	<b>0.10 #</b>	<b>0.30</b>	<b>1.63 *</b>	<b>0.39 #</b>	3.33	2.95	3.89
	SEM	0.02	0.05	0.02	0.07	0.23	0.06			
<b>11,12-</b>	Mean	<b>0.07</b>	<b>0.61 *</b>	<b>0.16 * #</b>	<b>0.01</b>	<b>0.04 *</b>	<b>0.01 #</b>	0.18	0.06	0.08
	SEM	0.02	0.07	0.02	0.00	0.00	0.00			
<b>8,9-</b>	Mean	<b>0.08</b>	<b>0.49 *</b>	<b>0.08 #</b>	<b>0.02</b>	<b>0.07 *</b>	<b>0.02 #</b>	0.23	0.15	0.27
	SEM	0.04	0.09	0.03	0.00	0.01	0.00			
<b>5,6-</b>	Mean	<b>0.91</b>	<b>3.61 *</b>	<b>1.12 #</b>	<b>1.56</b>	<b>6.04 *</b>	<b>1.97 #</b>	1.71	1.67	1.77
	SEM	0.18	0.34	0.19	0.20	0.76	0.25			
<b>DHA</b>			<b>EDP</b>		<b>DHDP</b>		<b>DHDP/EDP</b>			
<b>19,20-</b>	Mean	<b>0.74</b>	<b>1.60 *</b>	<b>0.83 #</b>	<b>0.49</b>	<b>0.92 *</b>	<b>0.60 * #</b>	0.67	0.57	0.72
	SEM	0.08	0.14	0.13	0.05	0.06	0.07			
<b>16,17-</b>	Mean	<b>1.71</b>	<b>3.39 *</b>	<b>1.48 #</b>	<b>0.13</b>	<b>0.28 *</b>	<b>0.17 * #</b>	0.08	0.08	0.12
	SEM	0.29	0.39	0.30	0.02	0.03	0.02			
<b>13,14-</b>	Mean	<b>0.36</b>	<b>0.92 *</b>	<b>0.47 #</b>	<b>nd</b>	<b>nd</b>	<b>nd</b>	nd	nd	nd
	SEM	0.07	0.09	0.07	nd	nd	nd			
<b>10,11-</b>	Mean	<b>0.39</b>	<b>0.83 *</b>	<b>0.41 #</b>	<b>0.17</b>	<b>0.31 *</b>	<b>0.20 #</b>	0.44	0.37	0.48
	SEM	0.03	0.08	0.03	0.02	0.02	0.02			
<b>7,8-</b>	Mean	<b>0.77</b>	<b>1.67 *</b>	<b>1.03 * #</b>	<b>0.65</b>	<b>1.34 *</b>	<b>0.77 * #</b>	0.84	0.80	0.75
	SEM	0.08	0.16	0.11	0.07	0.10	0.07			

**Table S4: Effect of EPA/DHA supplementation on the eicosanoid profile in urine.** The concentration of the metabolites is given in ng/ml as mean  $\pm$  SEM, n=19. A general linear model for repeated measurements was used for analysis.  $p < 0.05$  was considered significant with \* week 0 and # vs week 8. Week 0 = basal, week 8 = maximum treatment and week 16 = follow-up.

		Week 0	Week 8	Week 16	Week 0	Week 8	Week 16
<b>AA</b>		<b>EET</b>			<b>DHET</b>		
<b>14,15-</b>	Mean	nd	nd	nd	<b>0.25</b>	<b>0.29</b>	<b>0.26</b>
	SEM				0.02	0.05	0.03
<b>11,12-</b>	Mean	nd	nd	nd	<b>0.05</b>	<b>0.05</b>	<b>0.05</b>
	SEM				0.01	0.01	0.01
<b>8,9-</b>	Mean	<b>0.01</b>	<b>0.02</b>	<b>0.03</b>	<b>0.84</b>	<b>0.84</b>	<b>0.75</b>
	SEM	0.01	0.01	0.02	0.11	0.15	0.12
<b>5,6-</b>	Mean	nd	nd	nd	<b>0.10</b>	<b>0.08</b>	<b>0.08</b>
	SEM				0.02	0.02	0.01
<b>20-</b>		<b>HETE</b>					
	Mean	<b>0.09</b>	<b>0.11</b>	<b>0.09</b>			
	SEM	0.02	0.02	0.02			
<b>PGI2</b>		<b>6-keto-PGF1<math>\alpha</math></b>					
	Mean	<b>0.42</b>	<b>0.45</b>	<b>0.32</b>			
	SEM	0.14	0.19	0.12			
<b>EPA</b>		<b>EEQ</b>			<b>DHEQ</b>		
<b>17,18-</b>	Mean	nd	nd	nd	<b>0.31</b>	<b>1.24 *</b>	<b>0.32 #</b>
	SEM				0.05	0.23	0.07
<b>14,15-</b>	Mean	nd	nd	nd	<b>0.04</b>	<b>0.24 *</b>	<b>0.05 #</b>
	SEM				0.02	0.06	0.01
<b>11,12-</b>	Mean	nd	nd	nd	nd	<b>0.02</b>	nd
	SEM					0.00	
<b>8,9-</b>	Mean	nd	<b>0.01</b>	<b>0.01</b>	<b>0.04</b>	<b>0.22 *</b>	<b>0.04 #</b>
	SEM		0.00	0.01	0.00	0.04	0.01
<b>5,6-</b>	Mean	nd	nd	nd	<b>0.17</b>	<b>1.00 *</b>	<b>0.17 #</b>
	SEM				0.05	0.21	0.04
<b>20-</b>		<b>HEPE</b>					
	Mean	<b>0.07</b>	<b>0.24 *</b>	<b>0.08 #</b>			
	SEM	0.02	0.05	0.02			
<b>PGI3</b>		<b><math>\Delta</math>17-6-keto-PGF1<math>\alpha</math></b>					
	Mean	<b>0.74</b>	<b>1.14</b>	<b>0.78</b>			
	SEM	0.40	0.40	0.35			
<b>DHA</b>		<b>EDP</b>			<b>DHDP</b>		
<b>19,20-</b>	Mean	nd	nd	nd	<b>0.06</b>	<b>0.12 *</b>	<b>0.08</b>
	SEM				0.02	0.02	0.01
<b>16,17-</b>	Mean	nd	nd	nd	<b>0.02</b>	<b>0.03</b>	<b>0.03</b>
	SEM				0.00	0.01	0.01
<b>13,14-</b>	Mean	nd	nd	nd	<b>0.15</b>	<b>0.16</b>	<b>0.19</b>
	SEM				0.07	0.07	0.08
<b>10,11-</b>	Mean	nd	nd	nd	<b>0.10</b>	<b>0.43 *</b>	<b>0.14 #</b>
	SEM				0.01	0.08	0.03
<b>7,8-</b>	Mean	<b>0.01</b>	<b>0.01</b>	<b>0.01</b>	<b>0.39</b>	<b>0.52 *</b>	<b>0.25 #</b>
	SEM	0.01	0.01	0.01	0.22	0.30	0.12
<b>22-</b>		<b>HDHA</b>					
	Mean	<b>0.04</b>	<b>0.11</b>	<b>0.03</b>			
	SEM	0.03	0.04	0.01			