**Supplemental Table 1.** Plasma oxylipins from 8- and 16-week old WT and *Dsg2mut/mut* mice. Free plasma oxylipins are shown in pg/ml as mean +/- SEM. BD indicates that >50% of samples were below detection. n=5-6, \*p<0.05 vs. WT using Mann-Whitney with 5% false discovery rate.

|  |  |  |
| --- | --- | --- |
|  | 8 weeks | 16 weeks |
|   | WT | *Dsg2mut/mut* | WT | *Dsg2mut/mut* |
| 14,15-EET | 187 ± 19 | 120 ± 15\* | 281 ± 26 | 133 ± 25\* |
| 11,12-EET | 106 ± 14 | 73 ± 12 | BD | BD |
| 8,9-EET | 65 ± 14 | 40 ± 11 | 60 ± 7 | 56 ± 7 |
| 17,18-EpETE | 840 ± 81 | 863 ± 100 | 1236 ± 149 | 819 ± 113 |
| 12,13-EpOME | 2741 ± 258 | 3917 ± 662 | 4978 ± 658 | 1805 ± 354\* |
| 9,10-EpOME | 2555 ± 334 | 1654 ± 167\* | 2148 ± 99 | 1091 ± 107\* |
| 19,20-EpDPE | 9974 ± 2950 | 4319 ± 855 | 5260 ± 340 | 3956 ± 216\* |
| 16,17-EpDPA | 151 ± 16 | 101 ± 9 | 89 ± 20 | 53 ± 27 |
| 13,14-EpDPA | 382 ± 52 | 187 ± 29\* | 135 ± 24 | 56 ± 13 |
| 10,11-EpDPA | 557 ± 64 | 274 ± 37\* | 176 ± 35 | 102 ± 22 |
| 7,8-EpDPA | 382 ± 54 | 190 ± 27\* | BD | BD |
| 14,15-DHET | 260 ± 75 | 137 ± 19 | 206 ± 23 | 238 ± 17 |
| 11,12-DHET | 148 ± 40 | 85 ± 12 | 123 ± 16 | 126 ± 8 |
| 8,9-DHET | 259 ± 44 | 164 ± 19 | 304 ± 40 | 236 ± 19 |
| 5,6-DHET | 125 ± 13 | 96 ± 10 | 190 ± 20 | 125 ± 7\* |
| 17,18-DiHETE | 6596 ± 1649 | 6523 ± 694 | 9392 ± 1092 | 8313 ± 1006 |
| 14,15-DiHETE | 723 ± 152 | 993 ± 144 | 1726 ± 266 | 1007 ± 57\* |
| 9,10-DHOME | 6383 ± 1684 | 3395 ± 597 | 3028 ± 378 | 3126 ± 511 |
| 12,13-DHOME | 20354 ± 5057 | 11537 ± 2213 | 9181 ± 1139 | 8634 ± 2214 |
| 19,20-DiHDPA | 2370 ± 642 | 1459 ± 187 | 2338 ± 288 | 2396 ± 163 |
| 16,17-DiHDPA | 438 ± 100 | 400 ± 31 | 574 ± 66 | 396 ± 16\* |
| 13,14-DiHDPA | 157 ± 28 | 121 ± 8 | 192 ± 21 | 141 ± 18 |
| 10,11-DiHDPA | 58 ± 12 | 45 ± 3 | 70 ± 7 | 54 ± 2 |
| 7,8-DiHDPA | 219 ± 30 | 160 ± 9 | 332 ± 16 | 268 ± 17\* |
| 20-HETE | 122 ± 29 | 84 ± 13 | BD | BD |
| 15-HETE | 272 ± 77 | 303 ± 103 | 455 ± 170 | 684 ± 208 |
| 12-HETE | 8402 ± 3999 | 3103 ± 1078 | 14753 ± 4160 | 55029 ± 31115 |
| 11-HETE | 349 ± 102 | 363 ± 147 | 692 ± 254 | 975 ± 357 |
| 5-HETE | 419 ± 81 | 334 ± 60 | 708 ± 154 | 515 ± 67 |
| 13-HODE | 14451 ± 2493 | 12711 ± 1563 | 14840 ± 3547 | 9899 ± 1495 |
| 9-HODE | 8586 ± 2007 | 5283 ± 661 | 6595 ± 1531 | 3544 ± 397 |
| 17-HDHA | 2085 ± 412 | 2848 ± 855 | 2318 ± 692 | 3671 ± 966 |
| 18-HEPE | 768 ± 74 | 894 ± 102 | 1672 ± 401 | 870 ± 113 |
| PGE2 | 441 ± 68 | 78 ± 22\* | 135 ± 21 | 217 ± 76 |
| PGD2 | 317 ± 132 | 99 ± 47 | 2787 ± 481 | 399 ± 85\* |
| TXB2 | 570 ± 339 | 809 ± 694 | 1919 ± 632 | 3961 ± 1340 |
| 6-keto-PGF1a | 49 ± 11 | 245 ± 84\* | 80 ± 7 | 434 ± 188 |
| AA | 30533 ± 1071 | 28324 ± 233 | 17140 ± 8555 | 15310 ± 8057 |
| EPA | 47090 ± 1144 | 44529 ± 306 | 21435 ± 9996 | 14239 ± 6105 |
| LA | 34456 ± 1361 | 29630 ± 512\* | 34132 ± 14409 | 34769 ± 9799 |
| DHA | 64814 ± 4624 | 49720 ± 2458\* | 70076 ± 22396 | 63658 ± 18071 |
| 14,15-EET:DHET | 0.91 ± 0.19 | 0.91 ± 0.08 | 1.42 ± 0.14 | 0.57 ± 0.11\* |
| 12,13-EpOME:DiHOME | 0.19 ± 0.06 | 0.43 ± 0.11\* | 0.61 ± 0.25 | 0.25 ± 0.07\* |

**Supplemental Table 2.** Heart oxylipins from 8- and 16-week old WT and *Dsg2mut/mut-* mice. Free plasma oxylipins are shown in pg/ml as mean +/- SEM. BD indicates that >50% of samples were below detection. n=5-9, \*p<0.05 vs WT using Mann-Whitney with 5% false discovery rate.

|  |  |  |
| --- | --- | --- |
|  | 8 weeks | 16 weeks |
|   | WT | *Dsg2mut/mut* | WT | *Dsg2mut/mut* |
| 14,15-EET | 1309 ± 214 | 2236 ± 247\* | 3945 ± 774 | 3544 ± 537 |
| 11,12-EET | 1089 ± 164 | 1752 ± 208\* | 2691 ± 697 | 2699 ± 378 |
| 8,9-EET | 5922 ± 2486 | 10303 ± 2158 | 8923 ± 2486 | 15670 ± 2362 |
| 17,18-EpETE | 816 ± 148 | 1206 ± 156\* | 1444 ± 297 | 1175 ± 210 |
| 14,15-EpETE | 154 ± 32 | 260 ± 30\* | 633 ± 122 | 606 ± 113 |
| 12,13-EpOME | 8132 ± 1598 | 13931 ± 1349\* | 17785 ± 5128 | 14445 ± 2406 |
| 9,10-EpOME | 20804 ± 4911 | 33134 ± 3606 | 48798 ± 13678 | 37013 ± 4781 |
| 19,20-EpDPE | 38874 ± 8162 | 50628 ± 6216 | 121279 ± 35901 | 83228 ± 14273 |
| 16,17-EpDPA | 1511 ± 275 | 2249 ± 357 | 5163 ± 1252 | 3862 ± 577 |
| 13,14-EpDPA | 4564 ± 710 | 6155 ± 1053 | 6743 ± 1706 | 4641 ± 546 |
| 10,11-EpDPA | 7616 ± 1495 | 10984 ± 2472 | 8726 ± 2207 | 6598 ± 1147 |
| 7,8-EpDPA | 4611 ± 1001 | 5776 ± 747 | 13413 ± 3306 | 10601 ± 1687 |
| 14,15-DHET | 313 ± 39 | 355 ± 35 | 347 ± 31 | 307 ± 28 |
| 11,12-DHET | 337 ± 45 | 424 ± 52 | 412 ± 80 | 433 ± 34 |
| 8,9-DHET | 347 ± 44 | 443 ± 55 | 532 ± 74 | 606 ± 59 |
| 5,6-DHET | 406 ± 56 | 551 ± 74 | 1291 ± 302 | 842 ± 74 |
| 17,18-DiHETE | 9978 ± 1744 | 13191 ± 3123 | 16998 ± 1545 | 11629 ± 1752 |
| 14,15-DiHETE | 943 ± 265 | 1500 ± 279 | 2634 ± 216 | 1147 ± 185\* |
| 11,12-DiHETE | 15 ± 3 | 24 ± 4 | 30 ± 8 | 17 ± 2 |
| 9,10-DHOME | 6953 ± 1239 | 11926 ± 1766\* | 11333 ± 1505 | 5033 ± 918\* |
| 12,13-DHOME | 11139 ± 2721 | 20672 ± 3606\* | 20248 ± 2420 | 7612 ± 1413\* |
| 19,20-DiHDPA | 2255 ± 187 | 2480 ± 329 | 3576 ± 307 | 2933 ± 305 |
| 16,17-DiHDPA | 476 ± 78 | 701 ± 70\* | 990 ± 88 | 675 ± 88\* |
| 13,14-DiHDPA | 398 ± 86 | 499 ± 60 | 722 ± 169 | 596 ± 43 |
| 10,11-DiHDPA | 228 ± 44 | 284 ± 37 | 433 ± 90 | 314 ± 44 |
| 20-HETE | 179 ± 16 | 176 ± 19 | 252 ± 128 | 201 ± 91 |
| 15-HETE | 7678 ± 1259 | 13341 ± 1696\* | 29507 ± 5175 | 25669 ± 2988 |
| 12-HETE | 102634 ± 18212 | 130064 ± 21265 | 79454 ± 7961 | 405410 ± 65425\* |
| 11-HETE | 4064 ± 602 | 6973 ± 674\* | 14035 ± 2263 | 13353 ± 1143 |
| 5-HETE | 7187 ± 1215 | 10049 ± 1242 | 47936 ± 6231 | 32638 ± 2372\* |
| 13-HODE | 215252 ± 50836 | 309206 ± 27472 | 492206 ± 98070 | 338588 ± 49364 |
| 9-HODE | 166293 ± 39852 | 237030 ± 22132 | 416218 ± 82363 | 266083 ± 37482 |
| 22-HDoHE | 358 ± 50 | 586 ± 76\* | BD | BD |
| 17-HDHA | 24596 ± 5378 | 33276 ± 4519 | 128951 ± 23709 | 89128 ± 12489 |
| 18-HEPE | 6297 ± 1845 | 10066 ± 1197 | 41125 ± 7577 | 26395 ± 3117 |
| LTB4 | 203 ± 51 | 286 ± 39 | 468 ± 55 | 308 ± 54 |
| PGE2 | 2806 ± 560 | 8485 ± 1672\* | 5745 ± 922 | 4586 ± 794 |
| PGD2 | 4931 ± 639 | 9963 ± 1666\* | 12207 ± 1894 | 9032 ± 2568 |
| TXB2 | 964 ± 173 | 1571 ± 136\* | 1189 ± 153 | 2431 ± 274\* |
| 6-keto-PGF1a | 1086 ± 218 | 2892 ± 475\* | 2529 ± 611 | 2148 ± 510 |
| PGF2a | 1809 ± 397 | 5413 ± 1373\* | 5620 ± 1111 | 4365 ± 920 |
| AA | 52822 ± 10965 | 35107 ± 10407 | 394390 ± 115680 | 247343 ± 22470 |
| EPA | 68363 ± 9608 | 51789 ± 6949 | 380212 ± 75986 | 262754 ± 36074 |
| LA | 80813 ± 19982 | 70077 ± 15831 | 854591 ± 168776 | 517743 ± 47337 |
| DHA | 331610 ± 46572 | 278680 ± 64901 | 2057999 ± 523972 | 1235263 ± 87437 |
| 14,15-EET:DHET | 4.17 ± 0.40 | 6.31 ± 1.37 | 11.13 ± 1.64 | 11.59 ± 1.62 |
| 12,13-EpOME:DiHOME | 0.80 ± 0.11 | 0.77 ± 0.15 | 0.83 ± 0.16 | 2.09 ± 0.30\* |