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**Supplementary File**

**Table S1.** Forward and reverse primers for real-time PCR.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Acronym | Gene Bank ID | Eff1 | AT2 | Product lenght3 | Forward primer sequence | Reverse primer sequence |
| *40s* | HE978789.1 | 92.96 | 55 | 79 | TGATTGTGACAGACCCTCGTG | CACAGAGCAATGGTGGGGAT |
| *il1β* | AJ311925 | 96.70 | 57 | 105 | AGCGACATGGTGCGATTTCT | CTCCTCTGCTGTGCTGATGT |
| *il8* | AM490063.1 | 102.87 | 55 | 140 | CGCTGCATCCAAACAGAGAGCAAAC | TCGGGGTCCAGGCAAACCTCTT |
| *il6* | AM490062.1 | 134.62 | 55 | 81 | AGGCACAGAGAACACGTCAAA | AAAAGGGTCAGGGCTGTCG |
| *tgfβ* | AM421619.1 | 105.56 | 55 | 143 | ACCTACATCTGGAACGCTGA | TGTTGCCTGCCCACATAGTAG |
| *tnfα* | DQ070246.1 | 108.81 | 55 | 112 | AGCCACAGGATCTGGAGCTA | GTCCGCTTCTGTAGCTGTCC |
| *cox 2* | AJ630649.1 | 81.30 | 61 | 160 | CATTCTTTGCCCAGCACTTCACC | AGCTTGCCATCCTTGAAGAGTC |
| *il10* | [AM268529.1](https://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=nucleotide&id=148472689) | 116.00 | 55 | 164 | ACCCCGTTCGCTTGCCA | CATCTGGTGACATCACTC |
| *ccr3* | DLAgn\_00000190 | 117.69 | 55 | 381 | GCACTGTATGTGACCCGGAA | AGCAGATGTTTTGTTATCAGGACT |
| *cxcr4* | FN687464.1 | 93.43 | 57 | 171 | ACC AGA CCT TGT GTT TGC CA | ATG AAG CCC ACC AGG ATG TG |
| *sod* | CX660893.1 | 103.03 | 55 | 71 | GGAGAGTGATTCAGCCCCTG | GGAAACCATGCTCACCAGGA |
| *gpx* | DT044993 | 94.17 | 57 | 176 | GTTTGGACATCAGGAGAACTGC | CATCGCTGGGGTATGGAAGC |
| *hep* | DQ131605.1 | 94.17 | 57 | 152 | CTGGAGGAGCCAATGAGCAA | TGGAGAGAGCATCAGAGCAC |
| *noxin* | KM225775 | 106.97 | 62 | 72 | AGAGGTTGGTGGAGAACTTGGATGGA | CGACAGCCTTCATCAACAATGTGGATCT |
| *mhc II* | AM113468.1 | 98.15 | 55 | 81 | ATCCCTCCATGTTGGTCTGC | CTTCCTGTCCGTCTCTGAGC |
| *c3zeta* | DLAgn\_00052540 | 131.01 | 55 | 819 | GCCACCAAAGACACCTACGA | GTGTTGAACGCAGGAGGGTA |
| *cd8 β* | DLAgn\_00090370 | 113.81 | 55 | 651 | CGGAACCCAAAAGGCCAAAG | TAGGCTGTAGATGCAGTGCT |
| *tlr 9* | KX399289 | 115.17 | 55 | 100 | TCTTGGTTTGCCGACTTCTTGCGT | TACTGTTGCCCTGTTGGGACTCTGG |
| *tlr 2* | DLAgn\_00214290 | 118.84 | 55 | 615 | GGCTCCACCACCTACCTAGA | AGGTGGATCTTCTGTCAAAAATGG |
| *mcsf1r1* | DLAgn\_00109630 | 125.93 | 55 | 807 | TTGACCGTGGAGAAGGCAAA | AGAATGGACCTCAGCCAGTC |
| *mmp 9* | FN908863.1 | 98.44 | 57 | 166 | TGT GCC ACC ACA GAC AAC TT | TTC CAT CTC CAC GTC CCT CA |
| *c3* | HM563078.1 | 111.48 | 57 | 165 | CAGTGGGAATCTGTGGGCTT | GGCAAACACCTTGGCAAC |
| *mtor* | DLAgn\_00134190 | 127.25 | 55 | 848 | CAGAACCAAGGACGTGACGA | TGGTAGTAGAGGTCCCAGGC |
| *casp 3* | DQ345773.1 | 130.10 | 55 | 235 | CTGATTTGGATCCAGGCATT | CGGTCGTAGTGTTCCTCCAT |
| *casp 1* | DQ198377.1 | 124.32 | 55 | 190 | GTGTTTCAGATGCGGGAGGA | ATTTAAGTTAACTCACCGGGGG |
| *stat 3* | DLAgn\_00192560 | 110.68 | 55 | 275 | GACATCAGCGGAAAGACCCA | GGGGTGACGCAGATGAACTT |
| *mc2r* | FR870225.1 | 108.68 | 55 | 676 | GGAACAGGAACCTCCACTCG | ACCACGTGTAGCTGGAACAG |
| *hsp 70* | AY423555.2 | 134.14 | 55 | 88 | ACAAAGCAGACCCAGACCTTCACCA | TGGTCATAGCACGTTCGCCCTCA |
| *hsp 90* | AY395632.1 | 105.63 | 55 | 112 | GCTGACAAGAACGACAAGGCTGTGA | AGATGCGGTTGGAGTGGGTCTGT |
| *sat 1* | KM225772 | 97.55 | 63 | 55 | GCATCATCGCTGAAATCCAAGGAGAGAACA | CCAACCACCTTCAGGCCGTCACT |
| *amd 1* | KM225770 | 118.64 | 57.2 | 63 | CTGACGGAACTTACTGGACCATC | CGAAGCTGACGTAGGAGAACTC |

1 Efficiency of PCR reactions were calculated from serial dilutions of tissue RT reactions in the validation procedure.

2 Annealing temperature (°C)

3 Amplicon (nt)

**Table S2.** Quantitative expression of immune-related genes in the head-kidney of European seabass fed the dietary treatments during 2 and 4 weeks.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Parameters | |  | Dietary treatments | | | | | | | |
|  | CTRL | |  | MET 0.5 | |  | MET 1 | |
|  | 2 weeks | 4 weeks |  | 2 weeks | 4 weeks |  | 2 weeks | 4 weeks |
| *il1β* | Normalized mRNA expression |  | 0.114 ± 0.090 | 0.021 ± 0.029 |  | 0.054±0.043 | 0.028 ± 0.041 |  | 0.020 ± 0.020 | 0.028 ± 0.041 |
| *il8* |  | 0.094 ± 0.103 | 0.048 ± 0.086 |  | 0.020 ± 0.028 | 0.046 ± 0.060 |  | 0.029 ± 0.038 | 0.051 ± 0.074 |
| *il6* |  | 0.008 ± 0.008 | 0.003 ± 0.004 |  | 0.004 ± 0.004 | 0.003 ± 0.006 |  | 0.001 ± 0.002 | 0.003 ± 0.005 |
| *tgfβ* |  | 0.003 ± 0.001 | 0.003 ± 0.001 |  | 0.004 ± 0.002 | 0.003 ± 0.001 |  | 0.003 ± 0.002 | 0.004 ± 0.003 |
| *tnfα* |  | 0.079 ± 0.084 | 0.079 ± 0.114 |  | 0.031 ± 0.030 | 0.098 ± 0.215 |  | 0.017 ± 0.018 | 0.033 ± 0.051 |
| *cox 2* |  | 0.055 ± 0.058 | 0.134 ± 0.178 |  | 0.071 ± 0.080 | 0.243 ± 0.415 |  | 0.024 ± 0.025 | 0.065 ± 0.094 |
| *il10* |  | 0.051 ± 0.059 | 0.017 ± 0.028 |  | 0.020 ± 0.018 | 0.010 ± 0.014 |  | 0.011 ± 0.014 | 0.008 ± 0.011 |
| *ccr3* |  | 0.008 ± 0.008 | 0.021 ± 0.038 |  | 0.005 ± 0.005 | 0.005 ± 0.007 |  | 0.003 ± 0.003 | 0.004 ± 0.008 |
| *cxcr4* |  | 0.121 ± 0.197 | 0.016 ± 0.023 |  | 0.101 ± 0.185 | 0.061 ± 0.112 |  | 0.052 ± 0.074 | 0.150 ± 0.302 |
| *sod* |  | 0.157 ± 0.176 | 0.194 ± 0.249 |  | 0.129 ± 0.090 | 0.095 ± 0.065 |  | 0.054 ± 0.015 | 0.074 ± 0.070 |
| *gpx* |  | 0.276 ± 0.147 | 0.405 ± 0.250 |  | 0.288 ± 0.099 | 0.212 ± 0.059 |  | 0.230 ± 0.093 | 0.244 ± 0.096 |
| *hep* |  | 0.074 ± 0.377 | 0.726 ± 1.128 |  | 0.523 ± 0.888 | 0.591 ± 0.995 |  | 0.080 ± 0.086 | 1.612 ± 3.026 |
| *noxin* |  | 0.024 ± 0.025 | 0.023 ± 0.037 |  | 0.009 ± 0.008 | 0.012 ± 0.013 |  | 0.003 ± 0.005 | 0.008 ± 0.011 |
| *mhc II* |  | 0.688 ± 0.508 | 0.410 ± 0.354 |  | 0.469 ± 0.489 | 1.205 ± 1.304 |  | 0.220 ± 0.177 | 0.709 ± 0.509 |
| *c3zeta* |  | 0.000 ± 0.000 | 0.021 ± 0.037 |  | 0.005 ± 0.005 | 0.005 ± 0.007 |  | 0.003 ± 0.003 | 0.004 ± 0.008 |
| *cd8 β* |  | 0.032 ± 0.028 | 0.093 ± 0.132 |  | 0.013 ± 0.019 | 0.018 ± 0.029 |  | 0.010 ± 0.012 | 0.016 ± 0.024 |
| *tlr 9* |  | 0.020 ± 0.021 | 0.054 ± 0.074 |  | 0.011 ± 0.011 | 0.015 ± 0.021 |  | 0.007 ± 0.008 | 0.012 ± 0.018 |
| *tlr 2* |  | 0.005 ± 0.005 | 0.007 ± 0.016 |  | 0.002 ± 0.001 | 0.003 ± 0.005 |  | 0.003 ± 0.002 | 0.003 ± 0.005 |
| *mcsf1r1* |  | 0.004 ± 0.004 | 0.020 ± 0.031 |  | 0.002 ± 0.002 | 0.002 ± 0.003 |  | 0.001 ± 0.001 | 0.003 ± 0.004 |
| *mmp 9* |  | 0.095 ± 0.087 | 0.057 ± 0.065 |  | 0.055 ± 0.040 | 0.040 ± 0.029 |  | 0.045 ± 0.031 | 0.061 ± 0.074 |
| *c3* |  | 0.091 ± 0.131 | 0.055 ± 0.123 |  | 0.084 ± 0.106 | 0.044 ± 0.077 |  | 0.010 ± 0.013 | 0.096 ± 0.142 |
| *mtor* |  | 0.001 ± 0.001 | 0.001 ± 0.001 |  | 0.000 ± 0.001 | 0.000 ± 0.001 |  | 0.000 ± 0.000 | 0.001 ± 0.002 |
| *casp 3* |  | 0.065 ± 0.079 | 0.208 ± 0.304 |  | 0.081 ± 0.129 | 0.021 ± 0.024 |  | 0.027 ± 0.038 | 0.019 ± 0.030 |
| *casp 1* |  | 0.039 ± 0.046 | 0.025 ± 0.036 |  | 0.031 ± 0.050 | 0.006 ± 0.009 |  | 0.006 ± 0.011 | 0.019 ± 0.030 |
| *stat 3* |  | 0.405 ± 0.393 | 0.488 ± 0.693 |  | 0.410 ± 0.503 | 0.584 ± 0.737 |  | 0.150 ± 0.145 | 0.199 ± 0.250 |
| *mc2r* |  | 0.004 ± 0.003a | 0.002 ± 0.002 |  | 0.001 ± 0.001b | 0.003 ± 0.003 |  | 0.001 ± 0.001b | 0.001 ± 0.001 |
| *hsp 70* |  | 0.026 ± 0.019 | 0.045 ± 0.069 |  | 0.014 ± 0.010 | 0.011 ± 0.008 |  | 0.013 ± 0.009 | 0.014 ± 0.017 |
| *hsp 90* |  | 0.872 ± 0.628 | 1.190 ± 1.661 |  | 0.533 ± 0.375 | 0.424 ± 0.357 |  | 0.373 ± 0.211 | 0.478 ± 0.555 |
| *sat 1* |  | 0.044 ± 0.019 | 0.025 ± 0.013 |  | 0.030 ± 0.012 | 0.021±0.009 |  | 0.023 ± 0.009 | 0.021 ± 0.011 |
| *amd 1* |  | 0.006 ± 0.011 | 0.004 ±0.007 |  | 0.007 ± 0.006 | 0.002±0.002 |  | 0.002 ± 0.002 | 0.002 ± 0.004 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Two-way ANOVA | | | | | | | |
|  |  |  |  |  |  | Diet | | |
| Parameters |  | Time | Diet | Time × Diet |  | CTRL | MET 0.5 | MET 1 |
| *il1β* |  | - | 0.028 | - |  | A | AB | B |
| *il8* |  | - | - | - |  | - | - | - |
| *il6* |  | - | - | - |  | - | - | - |
| *tgfβ* |  | - | - | - |  | - | - | - |
| *tnfα* |  | - | - | - |  | - | - | - |
| *cox 2* |  | - | - | - |  | - | - | - |
| *il10* |  | - | - | - |  | - | - | - |
| *ccr3* |  | - | - | - |  | - | - | - |
| *cxcr4* |  | - | - | - |  | - | - | - |
| *sod* |  | - | - | - |  | - | - | - |
| *gpx* |  | - | - | - |  | - | - | - |
| *hep* |  | - | - | - |  | - | - | - |
| *noxin* |  | - | 0.047 | - |  | A | AB | B |
| *mhc II* |  | - | - | - |  | - | - | - |
| *c3zeta* |  | - | - | - |  | - | - | - |
| *cd8 β* |  | - | 0.038 | - |  | A | B | B |
| *tlr 9* |  | - | - | - |  | - | - | - |
| *tlr 2* |  | - | - | - |  | - | - | - |
| *mcsf1r1* |  | - | - | - |  | - | - | - |
| *mmp 9* |  | - | - | - |  | - | - | - |
| *c3* |  | - | - | - |  | - | - | - |
| *mtor* |  | - | - | - |  | - | - | - |
| *casp 3* |  | - | 0.039 | - |  | A | AB | B |
| *casp 1* |  | - | - | - |  | - | - | - |
| *stat 3* |  | - | - | - |  | - | - | - |
| *mc2r* |  | - | - | 0.019 |  | - | - | - |
| *hsp 70* |  | - | - | - |  | - | - | - |
| *hsp 90* |  | - | - | - |  | - | - | - |
| *sat 1* |  | 0.008 | 0.020 | - |  | A | AB | B |
| *amd 1* |  | - | - | - |  | - | - | - |

Values are presented as means ± SD (n=9). P-values from two-way ANOVA (p ≤0.05). If interaction was significant, Tukey post hoc test was used to identify differences in the experimental treatments. Different lowercase letters stand for significant differences among dietary treatments for the same time while different symbols stands for significant differences between times for the same diet. Different capital letters indicate differences among times regardless diets and among diets regardless time.

**Table S3.** Quantitative expression of immune-related genes in the head-kidney of European seabass fed the dietary treatments at 4 weeks (0 h), 4, 24 and 48 h after infection

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Parameters | |  | Dietary treatments | | | | | | | | | | | | | |
|  | CTRL | | | |  | MET 0.5 | | | |  | MET 1 | | | |
|  | 0h | 4h | 24h | 48h |  | 0h | 4h | 24h | 48h |  | 0h | 4h | 24h | 48h |
| *il1β* | Normalized mRNA expression |  | 0.021 ± 0.029 | 0.178 ± 0.160 | 0.243 ± 0.107 | 0.219 ± 0.088 |  | 0.028 ± 0.041 | 0.085 ± 0.077 | 0.222 ± 0.124 | 0.118 ± 0.100 |  | 0.028 ± 0.041 | 0.236 ± 0.284 | 0.186 ± 0.154 | 0.133 ± 0.122 |
| *il8* |  | 0.048 ± 0.086 | 0.430 ± 0.651 | 0.199 ± 0.087 | 0.254 ± 0.099 |  | 0.046 ± 0.060 | 0.128 ± 0.070 | 0.352 ± 0.243 | 0.079 ± 0.030 |  | 0.051 ± 0.074 | 0.073 ± 0.046 | 0.614 ± 0.738 | 0.226 ± 0.267 |
| *il6* |  | 0.003 ± 0.004 | 0.000 ± 0.000 | 0.015 ± 0.007 | 0.007 ± 0.005 |  | 0.003 ± 0.006 | 0.012 ± 0.009 | 0.009 ± 0.009 | 0.001 ± 0.001 |  | 0.003 ± 0.005 | 0.004 ± 0.006 | 0.021 ± 0.026 | 0.002 ± 0.003 |
| *tgfβ* |  | 0.003 ± 0.001 | 0.002 ± 0.001 | 0.001 ± 0.000 | 0.004 ± 0.002b |  | 0.003 ± 0.001 | 0.003 ± 0.001 | 0.002 ± 0.002 | 0.003 ± 0.007b |  | 0.004 ± 0.003\* | 0.003 ± 0.001\* | 0.007 ± 0.008\*£ | 0.013 ± 0.010a£ |
| *tnfα* |  | 0.079 ± 0.114 | 0.129 ± 0.099 | 0.156 ± 0.129 | 0.186 ± 0.124 |  | 0.098 ± 0.215 | 0.125 ± 0.089 | 0.131 ± 0.082 | 0.023 ± 0.009 |  | 0.033 ± 0.051\* | 0.017 ± 0.030\* | 0.355 ± 0.225£ | 0.093 ± 0.097£\* |
| *cox 2* |  | 0.134 ± 0.178 | 0.732 ± 0.439 | 0.974 ± 0.537 | 0.567 ± 0.703 |  | 0.243 ± 0.415 | 0.632 ± 0.370 | 0.842 ± 0.649 | 0.034 ± 0.025 |  | 0.065 ± 0.094 | 0.237 ± 0.250 | 1.324 ± 0.766 | 0.146 ± 0.116 |
| *il10* |  | 0.017 ± 0.028 | 0.097 ± 0.072 | 0.050 ± 0.058 | 0.099 ± 0.078 |  | 0.010 ± 0.014 | 0.010 ± 0.014 | 0.080 ± 0.067 | 0.100 ± 0.103 |  | 0.008 ± 0.011 | 0.021 ± 0.019 | 0.060 ± 0.076 | 0.135 ± 0.136 |
| *ccr3* |  | 0.021 ± 0.038 | 0.036 ± 0.033 | 0.036 ± 0.026b | 0.049 ± 0.038 |  | 0.005 ± 0.007 | 0.032 ± 0.025 | 0.054 ± 0.043ab | 0.013 ± 0.009 |  | 0.004 ± 0.008\* | 0.002 ± 0.003\* | 0.155 ± 0.163a£ | 0.025 ± 0.030\* |
| *cxcr4* |  | 0.016 ± 0.023 | 0.470 ± 0.541 | 3.520 ± 2.830 | 2.479 ± 1.912 |  | 0.061 ± 0.112 | 0.137 ± 0.100 | 4.217 ± 3.044 | 0.382 ± 0.229 |  | 0.150 ± 0.302 | 0.038 ± 0.023 | 4.123 ± 2.974 | 0.763 ± 0.926 |
| *hep* |  | 0.726 ± 1.128 | 1.600 ± 2.825 | 2.809 ± 1.124 | 2.599 ± 1.118 |  | 0.591 ± 0.995 | 3.117 ± 2.568 | 3.476 ± 2.873 | 0.385 ± 0.297 |  | 1.612 ± 3.026 | 0.822 ± 0.479 | 3.099 ± 1.751 | 2.321 ± 2.198 |
| *noxin* |  | 0.023 ± 0.037 | 0.034 ± 0.022 | 0.069 ± 0.045 | 0.070 ± 0.025 |  | 0.012 ± 0.013 | 0.038 ± 0.028 | 0.060 ± 0.037 | 0.014 ± 0.010 |  | 0.008 ± 0.011 | 0.012 ± 0.013 | 0.069 ± 0.038 | 0.034 ± 0.029 |
| *mhc II* |  | 0.410 ± 0.354 | 0.231 ± 0.481 | 2.192 ± 1.276 | 2.847 ± 1.425 |  | 1.205 ± 1.304 | 1.545 ± 1.397 | 2.224 ± 1.328 | 1.014 ± 0.935 |  | 0.709 ± 0.509 | 0.352 ± 0.349 | 2.310 ± 1.560 | 1.636 ± 1.521 |
| *tlr9* |  | 0.054 ± 0.074 | 0.071 ± 0.057 | 0.098 ± 0.099 | 0.119 ± 0.080 |  | 0.015 ± 0.021 | 0.061 ± 0.036 | 0.114 ± 0.084 | 0.016 ± 0.011 |  | 0.012 ± 0.018 | 0.014 ± 0.020 | 0.146 ± 0.111 | 0.059 ± 0.064 |
| *tlr2* |  | 0.007 ± 0.016 | 0.032 ± 0.033 | 0.022 ± 0.012 | 0.000 ± 0.000 |  | 0.003 ± 0.005 | 0.015 ± 0.012 | 0.049 ± 0.058 | 0.002 ± 0.001 |  | 0.003 ± 0.005 | 0.004 ± 0.003 | 0.094 ± 0.131 | 0.001 ± 0.002 |
| *mcsf1r1* |  | 0.020 ± 0.031 | 0.022 ± 0.023 | 0.013 ± 0.012 | 0.019 ± 0.019 |  | 0.002 ± 0.003 | 0.010 ± 0.009 | 0.017 ± 0.015 | 0.016 ± 0.011 |  | 0.003 ± 0.004 | 0.002 ± 0.002 | 0.036 ± 0.031 | 0.008 ± 0.009 |
| *mmp9* |  | 0.057 ± 0.065 | 1.498 ± 2.087 | 0.354 ± 0.155 | 0.434 ± 0.377 |  | 0.040 ± 0.029 | 0.271 ± 0.208 | 0.401 ± 0.245 | 0.179 ± 0.116 |  | 0.061 ± 0.074 | 0.613 ± 0.790 | 0.401 ± 0.245 | 0.187 ± 0.151 |
| *c3* |  | 0.055 ± 0.123 | 0.389 ± 0.385 | 0.286 ± 0.137 | 0.319 ± 0.216 |  | 0.044 ± 0.077 | 0.236 ± 0.121 | 0.329 ± 0.187 | 0.293 ± 0.283 |  | 0.096 ± 0.142 | 0.049 ± 0.054 | 0.350 ± 0.192 | 0.174 ± 0.188 |
| *mtor* |  | 0.001 ± 0.001 | 0.007 ± 0.006 | 0.005 ± 0.002 | 0.005 ± 0.003 |  | 0.000 ± 0.001 | 0.003 ± 0.002 | 0.005 ± 0.004 | 0.001 ± 0.001 |  | 0.001 ± 0.002 | 0.001 ± 0.001 | 0.004 ± 0.002 | 0.001 ± 0.000 |
| *casp 3* |  | 0.208 ± 0.304 | 0.331 ± 0.191 | 0.200 ± 0.087 | 0.296 ± 0.175 |  | 0.021 ± 0.024 | 0.134 ± 0.095 | 0.337 ± 0.272 | 0.092 ± 0.083 |  | 0.019 ± 0.030 | 0.048 ± 0.053 | 0.175 ± 0.111 | 0.148 ± 0.166 |
| *casp 1* |  | 0.025 ± 0.036 | 0.061 ± 0.051 | 0.041 ± 0.024 | 0.074 ± 0.039 |  | 0.006 ± 0.009 | 0.037 ± 0.028 | 0.053 ± 0.041 | 0.019 ± 0.015 |  | 0.019 ± 0.030 | 0.010 ± 0.011 | 0.075 ± 0.062 | 0.031 ± 0.031 |
| *stat 3* |  | 0.488 ± 0.693 | 1.466 ± 0.987 | 1.147 ± 0.547 | 1.863 ± 0.965 |  | 0.584 ± 0.737 | 0.959 ± 0.659 | 1.780 ± 1.190 | 0.732 ± 0.586 |  | 0.199 ± 0.250 | 0.554 ± 0.240 | 2.121 ± 1.584 | 1.145 ± 1.116 |
| *m2cr* |  | 0.002 ± 0.002 | 0.002 ± 0.001 | 0.024 ± 0.029 | 0.011± 0.009 |  | 0.003 ± 0.003 | 0.006 ± 0.006 | 0.000 ± 0.000 | 0.019 ± 0.016 |  | 0.001 ± 0.001 | 0.006 ± 0.0010 | 0.012 ± 0.018 | 0.024 ± 0.041 |
| *hsp70* |  | 0.045 ± 0.069 | 0.061 ± 0.057 | 0.054 ± 0.041 | 0.052 ± 0.038 |  | 0.011 ± 0.008 | 0.035 ± 0.030 | 0.054 ± 0.035 | 0.007 ± 0.003 |  | 0.014 ± 0.017 | 0.010 ± 0.009 | 0.127 ± 0.122 | 0.034 ± 0.038 |
| *hsp90* |  | 1.190 ± 1.661 | 1.656 ± 1.327 | 2.007 ± 1.612 | 2.648 ± 2.219 |  | 0.424 ± 0.357 | 1.225 ± 0.793 | 2.360 ± 1.803 | 0.346 ± 0.159 |  | 0.478 ± 0.555 | 0.296 ± 0.293 | 3.999 ± 3.368 | 1.099 ± 1.020 |
| *sat 1* |  | 0.025 ± 0.013 | 0.004 ± 0.002 | 0.023 ± 0.012 | 0.023 ± 0.026ab |  | 0.021±0.009 | 0.021 ± 0.013 | 0.034 ± 0.029 | 0.004 ± 0.003b |  | 0.021 ± 0.011 | 0.023 ± 0.018 | 0.034 ± 0.015 | 0.040 ± 0.020a |
| *amd 1* |  | 0.004 ±0.007 | 0.113 ± 0.064b | 0.054 ± 0.012 | 0.216 ± 0.196 |  | 0.002±0.002\* | 0.417 ± 0.327ab£ | 0.031 ± 0.017£ | 0.046 ± 0.040£ |  | 0.002 ± 0.004 | 0.753 ± 0.468a£ | 0.081 ± 0.046 | 0.256 ± 0.180 |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Two-way ANOVA | | | | | | | | | | | |
|  |  |  |  |  |  | Time | | | |  | Diet | | |
| Parameters |  | Time | Diet | Time × Diet |  | 0h | 4h | 24h | 48h |  | CTRL | MET 0.5 | MET 1 |
| *il1β* |  | 0.003 | - | - |  | B | A | A | AB |  | - | - | - |
| *il8* |  | 0.001 | - | - |  | B | A | AB | AB |  | - | - | - |
| *il6* |  | < 0.001 | - | - |  | B | B | A | B |  | - | - | - |
| *tgfβ* |  | 0.012 | < 0.001 | 0.195 |  | B | B | AB | A |  | B | B | A |
| *tnfα* |  | 0.033 | - | 0.032 |  | B | AB | A | AB |  | - | - | - |
| *cox 2* |  | < 0.001 | - | - |  | C | B | A | CB |  | - | - | - |
| *il10* |  | 0.013 | - | - |  | B | AB | AB | A |  | - | - | - |
| *ccr3* |  | 0.001 | - | 0.021 |  | B | B | A | AB |  | - | - | - |
| *cxcr4* |  | < 0.001 | - | - |  | BC | C | A | B |  | - | - | - |
| *hep* |  | 0.019 | - | - |  | B | AB | A | AB |  | - | - | - |
| *noxin* |  | < 0.001 | - | - |  | B | BC | A | C |  | - | - | - |
| *mhc II* |  | < 0.001 | - | - |  | B | B | A | A |  | - | - | - |
| *tlr9* |  | < 0.001 | - | - |  | B | B | A | AB |  | - | - | - |
| *tlr2* |  | 0.008 | - | - |  | B | AB | A | B |  | - | - | - |
| *mcsf1r1* |  | - | - | - |  | - | - | - | - |  | - | - | - |
| *mmp9* |  | 0.019 | - | - |  | B | A | AB | AB |  | - | - | - |
| *c3* |  | 0.002 | - | - |  | B | AB | A | A |  | - | - | - |
| *mtor* |  | < 0.001 | 0.005 | - |  | B | A | A | AB |  | A | AB | B |
| *casp 3* |  | - | 0.024 | - |  | - | - | - | - |  | A | AB | B |
| *casp 1* |  | 0.008 | - | - |  | B | AB | A | AB |  | - | - | - |
| *stat 3* |  | < 0.001 | - | - |  | B | AB | A | A |  | - | - | - |
| *m2cr* |  | 0.014 | - | - |  | B | AB | AB | A |  | - | - | - |
| *hsp70* |  | 0.012 | - | - |  | B | AB | A | AB |  | - | - | - |
| *hsp90* |  | 0.001 | - | - |  | B | B | A | AB |  | - | - | - |
| *sat 1* |  | - | - | 0.041 |  | - | - | - | - |  | - | - | - |
| *amd 1* |  | < 0.001 | 0.006 | 0.003 |  | C | A | BC | B |  | B | AB | A |

Values are presented as means ± SD (n=6). P-values from two-way ANOVA (p ≤0.05). If interaction was significant, Tukey post hoc test was used to identify differences in the experimental treatments. Different lowercase letters stand for significant differences among dietary treatments for the same time while different symbols stands for significant differences between times for the same diet. Different capital letters indicate differences among times regardless diets and among diets regardless time.