**Supplementary Information**

**Pearl farming micro-nanoplastics affect both oyster physiology**

**and pearl quality**

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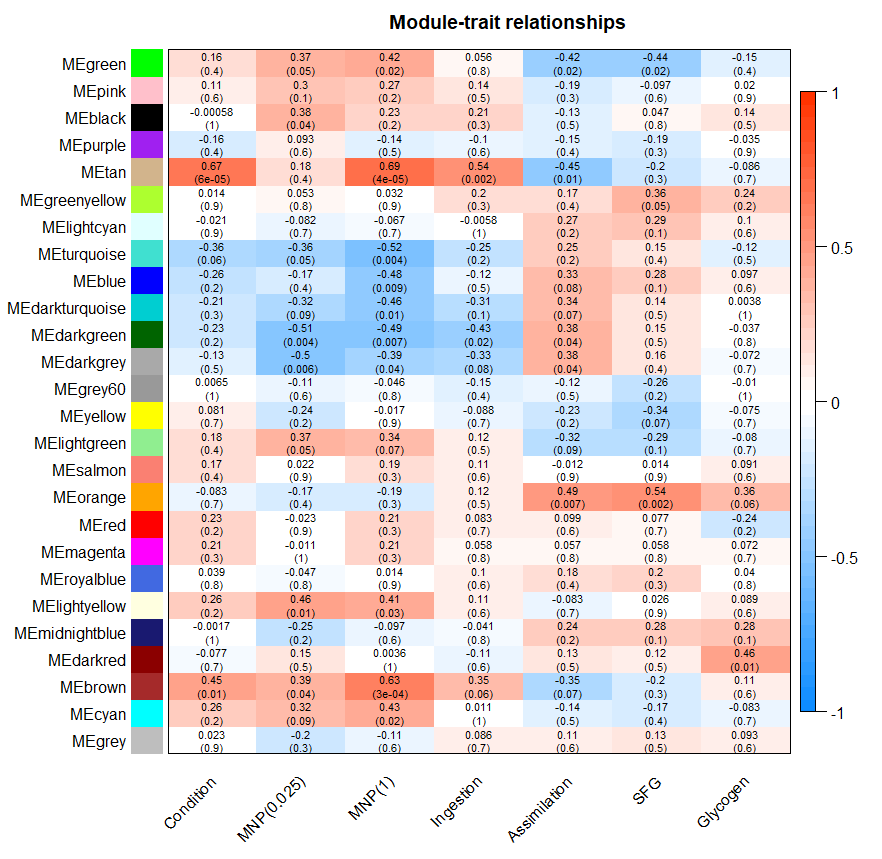
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**Supplementary Table 1.** Sequencing results and reads survival after trimming and mapping.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Sample** | **Individual** | **Condition (µg L–1)** | **Input read pairs** | **Reads survival** | **Reads mapped** |
| Mantle | 1 | 0 (control) | 2.97 × 107 | 2.81 × 107 | 1.35 × 107 |
| Mantle | 2 | 0 (control) | 7.84 × 107 | 7.45 × 107 | 3.91 × 107 |
| Mantle | 3 | 0 (control) | 3.60 × 107 | 3.42 × 107 | 1.43 × 107 |
| Mantle | 4 | 0 (control) | 2.82 × 107 | 2.68 × 107 | 1.40 × 107 |
| Mantle | 5 | 0 (control) | 3.37 × 107 | 3.19 × 107 | 1.42 × 107 |
| Mantle | 6 | 0 (control) | 5.24 × 107 | 5.01 × 107 | 2.20 × 107 |
| Mantle | 7 | 0 (control) | 5.19 × 107 | 4.96 × 107 | 2.46 × 107 |
| Mantle | 8 | 0 (control) | 3.10 × 107 | 2.92 × 107 | 1.46 × 107 |
| Mantle | 9 | 0 (control) | 2.50 × 107 | 2.39 × 107 | 1.15 × 107 |
| Mantle | 10 | 0.025 | 2.69 × 107 | 2.55 × 107 | 1.26 × 107 |
| Mantle | 11 | 0.025 | 2.96 × 107 | 2.81 × 107 | 1.20 × 107 |
| Mantle | 12 | 0.025 | 3.79 × 107 | 3.60 × 107 | 1.73 × 107 |
| Mantle | 13 | 0.025 | 2.89 × 107 | 2.76 × 107 | 1.40 × 107 |
| Mantle | 14 | 0.025 | 2.71 × 107 | 2.59 × 107 | 1.14 × 107 |
| Mantle | 15 | 0.025 | 2.87 × 107 | 2.73 × 107 | 1.34 × 107 |
| Mantle | 16 | 0.025 | 4.22 × 107 | 4.02 × 107 | 1.93 × 107 |
| Mantle | 17 | 0.025 | 3.34 × 107 | 3.18 × 107 | 1.56 × 107 |
| Mantle | 18 | 0.025 | 4.62 × 107 | 4.40 × 107 | 2.07 × 107 |
| Mantle | 19 | 0.025 | 4.21 × 107 | 4.00 × 107 | 2.12 × 107 |
| Mantle | 20 | 1 | 2.77 × 107 | 2.65 × 107 | 1.29 × 107 |
| Mantle | 21 | 1 | 3.74 × 107 | 3.56 × 107 | 1.80 × 107 |
| Mantle | 22 | 1 | 5.87 × 107 | 5.58 × 107 | 2.48 × 107 |
| Mantle | 23 | 1 | 2.78 × 107 | 2.65 × 107 | 1.39 × 107 |
| Mantle | 24 | 1 | 3.95 × 107 | 3.76 × 107 | 1.97 × 107 |
| Mantle | 25 | 1 | 4.03 × 107 | 3.82 × 107 | 1.76 × 107 |
| Mantle | 26 | 1 | 4.52 × 107 | 4.31 × 107 | 2.28 × 107 |
| Mantle | 27 | 1 | 1.69 × 107 | 1.60 × 107 | 7.18 × 106 |
| Mantle | 28 | 1 | 2.75 × 107 | 2.62 × 107 | 1.32 × 107 |
| Mantle | 29 | 1 | 2.99 × 107 | 2.85 × 107 | 1.40 × 107 |
| Hemocytes | 1 | 0 (control) | 2.72 × 107 | 2.59 × 107 | 1.01 × 107 |
| Hemocytes | 2 | 0 (control) | 4.22 × 107 | 3.94 × 107 | 1.38 × 107 |
| Hemocytes | 3 | 0 (control) | 8.63 × 106 | 8.24 × 106 | 2.75 × 106 |
| Hemocytes | 4 | 0 (control) | 1.71 × 107 | 1.64 × 107 | 6.41 × 106 |
| Hemocytes | 5 | 0 (control) | 3.21 × 107 | 3.06 × 107 | 1.15 × 107 |
| Hemocytes | 6 | 0 (control) | 3.21 × 107 | 3.00 × 107 | 1.13 × 107 |
| Hemocytes | 7 | 0 (control) | 3.05 × 107 | 2.88 × 107 | 1.19 × 107 |
| Hemocytes | 8 | 0.025 | 3.50 × 107 | 3.31 × 107 | 1.24 × 107 |
| Hemocytes | 9 | 0.025 | 3.12 × 107 | 2.99 × 107 | 1.17 × 107 |
| Hemocytes | 10 | 0.025 | 4.08 × 107 | 3.89 × 107 | 1.53 × 107 |
| Hemocytes | 11 | 0.025 | 3.86 × 107 | 3.67 × 107 | 1.51 × 107 |
| Hemocytes | 12 | 0.025 | 3.11 × 107 | 2.97 × 107 | 1.23 × 107 |
| Hemocytes | 13 | 0.025 | 3.69 × 107 | 3.53 × 107 | 1.29 × 107 |
| Hemocytes | 14 | 0.025 | 3.58 × 107 | 3.42 × 107 | 1.13 × 107 |
| Hemocytes | 15 | 0.025 | 3.44 × 107 | 3.29 × 107 | 1.35 × 107 |
| Hemocytes | 16 | 0.025 | 2.08 × 107 | 1.99 × 107 | 8.11 × 106 |
|  |  |  |  |  |  |
| **Supplementary Table 1** (*continued*) | |  |  |  |  |
| Hemocytes | 17 | 0.025 | 2.41 × 107 | 2.30 × 107 | 9.38 × 106 |
| Hemocytes | 18 | 0.025 | 4.22 × 107 | 4.02 × 107 | 1.47 × 107 |
| Hemocytes | 19 | 1 | 4.02 × 107 | 3.84 × 107 | 1.48 × 107 |
| Hemocytes | 20 | 1 | 3.55 × 107 | 3.37 × 107 | 1.32 × 107 |
| Hemocytes | 21 | 1 | 2.76 × 107 | 2.63 × 107 | 9.54 × 106 |
| Hemocytes | 22 | 1 | 5.31 × 107 | 5.06 × 107 | 1.93 × 107 |
| Hemocytes | 23 | 1 | 3.06 × 107 | 2.90 × 107 | 1.07 × 107 |
| Hemocytes | 24 | 1 | 4.29 × 107 | 4.10 × 107 | 1.65 × 107 |
| Hemocytes | 25 | 1 | 3.33 × 107 | 3.17 × 107 | 1.13 × 107 |
| Hemocytes | 26 | 1 | 4.33 × 107 | 4.14 × 107 | 1.53 × 107 |
| Hemocytes | 27 | 1 | 4.02 × 107 | 3.83 × 107 | 1.36 × 107 |
| Hemocytes | 28 | 1 | 3.27 × 107 | 3.12 × 107 | 1.12 × 107 |
| Hemocytes | 29 | 1 | 2.41 × 107 | 2.28 × 107 | 8.51 × 106 |
| Pearl sac | 1 | 0 (control) | 2.68 × 107 | 2.56 × 107 | 1.11 × 107 |
| Pearl sac | 2 | 0 (control) | 3.14 × 107 | 2.99 × 107 | 1.34 × 107 |
| Pearl sac | 3 | 0 (control) | 3.34 × 107 | 3.18 × 107 | 1.56 × 107 |
| Pearl sac | 4 | 0 (control) | 3.80 × 107 | 3.63 × 107 | 1.61 × 107 |
| Pearl sac | 5 | 0 (control) | 3.40 × 107 | 3.24 × 107 | 1.41 × 107 |
| Pearl sac | 6 | 0 (control) | 3.13 × 107 | 2.98 × 107 | 1.36 × 107 |
| Pearl sac | 7 | 0 (control) | 3.66 × 107 | 3.49 × 107 | 1.63 × 107 |
| Pearl sac | 8 | 0 (control) | 2.42 × 107 | 2.30 × 107 | 9.55 × 106 |
| Pearl sac | 9 | 0 (control) | 3.89 × 107 | 3.72 × 107 | 1.66 × 107 |
| Pearl sac | 10 | 0 (control) | 4.55 × 107 | 4.34 × 107 | 1.89 × 107 |
| Pearl sac | 11 | 0.025 | 3.47 × 107 | 3.31 × 107 | 1.62 × 107 |
| Pearl sac | 12 | 0.025 | 3.22 × 107 | 3.07 × 107 | 1.31 × 107 |
| Pearl sac | 13 | 0.025 | 4.47 × 107 | 4.25 × 107 | 1.88 × 107 |
| Pearl sac | 14 | 0.025 | 3.22 × 107 | 3.05 × 107 | 1.34 × 107 |
| Pearl sac | 15 | 0.025 | 3.05 × 107 | 2.92 × 107 | 1.23 × 107 |
| Pearl sac | 16 | 0.025 | 5.59 × 107 | 5.35 × 107 | 2.61 × 107 |
| Pearl sac | 17 | 0.025 | 3.20 × 107 | 3.05 × 107 | 1.44 × 107 |
| Pearl sac | 18 | 0.025 | 3.36 × 107 | 3.21 × 107 | 1.32 × 107 |
| Pearl sac | 19 | 0.025 | 3.06 × 107 | 2.90 × 107 | 1.25 × 107 |
| Pearl sac | 20 | 0.025 | 3.59 × 107 | 3.43 × 107 | 1.67 × 107 |
| Pearl sac | 21 | 1 | 3.43 × 107 | 3.24 × 107 | 1.29 × 107 |
| Pearl sac | 22 | 1 | 3.29 × 107 | 3.13 × 107 | 1.32 × 107 |
| Pearl sac | 23 | 1 | 3.83 × 107 | 3.62 × 107 | 1.49 × 107 |
| Pearl sac | 24 | 1 | 3.92 × 107 | 3.73 × 107 | 1.59 × 107 |
| Pearl sac | 25 | 1 | 3.35 × 107 | 3.18 × 107 | 1.46 × 107 |
| Pearl sac | 26 | 1 | 3.25 × 107 | 3.10 × 107 | 1.31 × 107 |
| Pearl sac | 27 | 1 | 2.83 × 107 | 2.70 × 107 | 1.11 × 107 |
| Pearl sac | 28 | 1 | 2.95 × 107 | 2.81 × 107 | 1.38 × 107 |
| Pearl sac | 29 | 1 | 2.65 × 107 | 2.53 × 107 | 1.09 × 107 |

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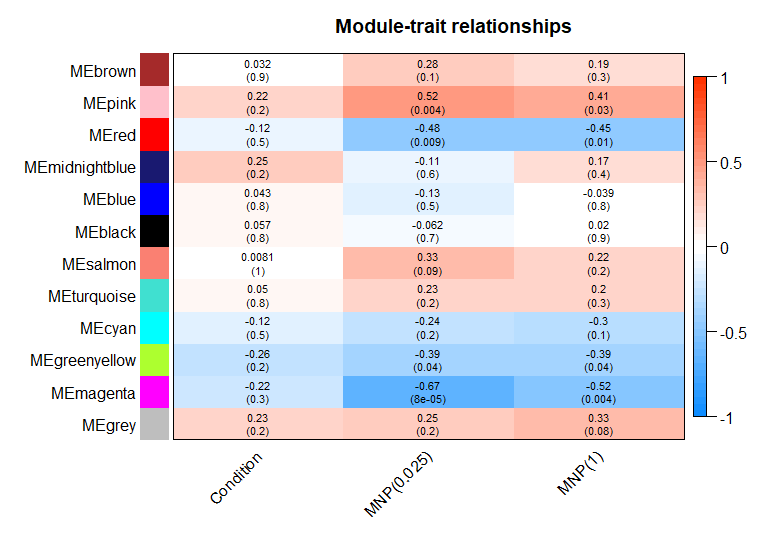
**Supplementary Figure 1. Correlations of eukaryotic orthologous group (KOG) expressions between tissues sampled in *P. margaritifera* after a 5-month exposure to 0.025 and 1 µg L–1 micro-nanoplastics.** Pearson’s correlations of KOG delta rank values between mantle and hemocytes (**a**–**b**), mantle and pearl sac (**c**–**d**), and hemocytes and pearl sac (**e**–**f**) in 0.025 and 1 µg MNPs L–1, respectively.



**Supplementary Figure 2. WGCNA module identification on mantle samples sequencing dataset.** Correlation analysis of the identified modules according to conditions (control and MNP conditions), single MNP condition (0.025 or 1 µg L–1) and to physiological traits of individuals showing significant effects in response to MNP exposure (*i.e.*, ingestion, assimilation efficiency, scope for growth and glycogen stores).



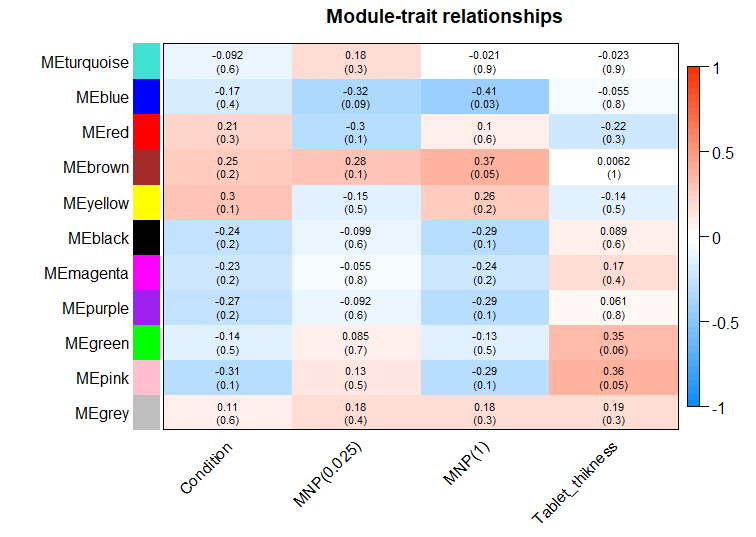
**Supplementary Figure 3.** **Gene significance for MNP conditions showing the best correlation *vs.* module membership in modules of interest illustrating module-trait associations from WGCNA on mantle samples sequencing dataset.** Scatterplots of module genes in (**a**) turquoise, (**b**) blue, (**c**) darkturquoise, (**d**) darkgreen, (**e**) darkgrey, (**f**) lightyellow and (**g**) brown modules. Gray genes represent module genes; blue and red genes represent DEGs specific to 0.025 µg MNPs L–1 and 1 MNPs µg L–1, respectively, and black genes represent common DEGs to both MNP conditions. DEGs identified in each module genes are detailed in Supplementary Table 4.



**Supplementary Figure 4.** **WGCNA module identification on hemocyte samples sequencing dataset.** Correlation analysis of the identified modules according to conditions (control and MNP conditions) and single MNP condition (0.025 or 1 µg L–1).



**Supplementary Figure 5. Transcriptomic responses in the hemocytes of *P. margaritifera* after a 5-month exposure to micro-nanoplastics.** (**a**) Heatmap of identified modules (*y*-axis) and functionally enriched pathways in relation to experimental traits (|*r*| ≥ 0.45, *P* ≤ 0.01; *x*-axis) from WGCNA. The clustering tree of module eigengenes (MEs) on the left is based on a merging threshold of 100% dissimilarity initially established at 25% for network construction. The numbers on the right of the heatmap represent the number of genes identified in each module. (**b**) Eigengene expression for selected WGCNA modules significantly correlated with experimental conditions and/or physiological traits in response to MNP exposure (“\*”, *P* < 0.05; “\*\*”, *P* < 0.01). Data are expressed as the mean with the 95% confidence interval (*N* = 7–12). (**c**) Representative functional enrichment analysis of module genes identified in the magenta module based on an adjusted *P* value cutoff (*P* < 0.01) and cut-height (0.8) of the GO terms tree to obtain “independent groups”. The dendrograms depict the sharing of genes between categories; the fractions correspond to genes with *P* < 0.05 relative to the total number of genes within the category. (**d**) Venn diagram of differentially expressed genes (DEGs) in both MNP conditions compared to the control (|log2FC| > 2; FDR < 0.01). (**e**) Scatterplots of gene significance for condition *vs.* module membership in the in magenta, pink and red modules illustrating module-trait associations. Gray genes represent module genes; blue and red genes represent DEGs specific to 0.025 and 1 µg L–1 MNPs, respectively. DEGs identified in each module genes are detailed in Supplementary Table 5.



**Supplementary Figure 6. WGCNA module identification on pearl sac samples sequencing dataset.** Correlation analysis of the identified modules according to conditions (control and MNP conditions), single MNP condition (0.025 or 1 µg L–1), and pearl quality traits of individuals showing significant effects in response to MNP exposure (*i.e.*, aragonite platelet thickness).

**Supplementary Table 2.** Gene Ontology (GO) enrichments in molecular function (MF) and biological process (BP) of module genes of interest (turquoise, darkgrey, brown and tan modules) identified in mantle samples from WGCNA.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **GO ID** | **GO term** | **Level** | **Nseqs** | ***P*adj** |
| * **Turquoise module** | |  |  |  |
| **MF** |  |  |  |  |
| GO:0045505 | dynein intermediate chain binding | 2 | 47 | < 0.001 |
| GO:0003774 | motor activity | 2 | 149 | < 0.001 |
| GO:0003777 | microtubule motor activity | 2 | 84 | < 0.001 |
| GO:0015631 | tubulin binding | 4 | 288 | < 0.001 |
| GO:0008017 | microtubule binding | 2 | 205 | < 0.001 |
| GO:0008092 | cytoskeletal protein binding | 3 | 859 | < 0.001 |
| GO:0030371 | translation repressor activity | 2 | 43 | < 0.001 |
| GO:0045504 | dynein heavy chain binding | 2 | 19 | < 0.001 |
| GO:0005509 | calcium ion binding | 5 | 845 | < 0.001 |
| GO:0030234 | enzyme regulator activity | 2 | 775 | 0.0015 |
| GO:0004550 | nucleoside diphosphate kinase activity | 5 | 17 | 0.0017 |
| GO:0003735 | structural constituent of ribosome | 2 | 134 | 0.0020 |
| GO:0001103 | RNA polymerase II repressing transcription factor binding | 2 | 20 | 0.0025 |
| GO:0045503 | dynein light chain binding | 3 | 13 | 0.0027 |
| GO:0004826 | phenylalanine-tRNA ligase activity | 2 | 8 | 0.0028 |
| GO:0004096 | catalase activity | 2 | 10 | 0.0033 |
| GO:0003723 | RNA binding | 3 | 1325 | 0.0043 |
| GO:0032027 | myosin light chain binding | 2 | 7 | 0.0053 |
| GO:0015038 | glutathione disulfide oxidoreductase activity | 2 | 10 | 0.0060 |
| GO:0070410 | co-SMAD binding | 2 | 25 | 0.0074 |
| GO:0004708 | MAP kinase kinase activity | 5 | 11 | 0.0097 |
| GO:0043015 | gamma-tubulin binding | 2 | 24 | 0.0118 |
| GO:0098772 | molecular function regulator | 1 | 1264 | 0.0119 |
| GO:0003810 | protein-glutamine gamma-glutamyltransferase activity | 2 | 22 | 0.0123 |
| GO:0005272 | sodium channel activity | 2 | 44 | 0.0134 |
| GO:0004198 | calcium-dependent cysteine-type endopeptidase activity | 6 | 22 | 0.0164 |
| GO:0016881 | acid-amino acid ligase activity | 4 | 22 | 0.0221 |
| GO:0017022 | myosin binding | 4 | 75 | 0.0232 |
| GO:0032036 | myosin heavy chain binding | 2 | 5 | 0.0241 |
| GO:0050145 | nucleoside monophosphate kinase activity | 2 | 23 | 0.0268 |
| GO:0070739 | protein-glutamic acid ligase activity | 2 | 10 | 0.0285 |
| GO:0016887 | ATPase activity | 2 | 549 | 0.0300 |
| GO:0005248 | voltage-gated sodium channel activity | 3 | 11 | 0.0335 |
| GO:0097371 | MDM2/MDM4 family protein binding | 2 | 6 | 0.0362 |
| GO:0004653 | polypeptide N-acetylgalactosaminyltransferase activity | 2 | 16 | 0.0449 |
| **BP** |  |  |  |  |
| GO:0000226 | microtubule cytoskeleton organization | 4 | 362 | < 0.001 |
| GO:0003006 | developmental process involved in reproduction | 2 | 686 | < 0.001 |
| GO:0003341 | cilium movement | 2 | 141 | < 0.001 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0003352 | regulation of cilium movement | 2 | 23 | < 0.001 |
| GO:0003356 | regulation of cilium beat frequency | 4 | 12 | < 0.001 |
| GO:0006928 | movement of cell or subcellular component | 2 | 1001 | < 0.001 |
| GO:0007010 | cytoskeleton organization | 4 | 725 | < 0.001 |
| GO:0007017 | microtubule-based process | 2 | 680 | < 0.001 |
| GO:0007018 | microtubule-based movement | 3 | 343 | < 0.001 |
| GO:0007224 | smoothened signaling pathway | 3 | 59 | < 0.001 |
| GO:0007288 | sperm axoneme assembly | 3 | 22 | < 0.001 |
| GO:0007389 | pattern specification process | 2 | 368 | < 0.001 |
| GO:0008543 | fibroblast growth factor receptor signaling pathway | 7 | 70 | < 0.001 |
| GO:0008589 | regulation of smoothened signaling pathway | 3 | 73 | < 0.001 |
| GO:0010457 | centriole-centriole cohesion | 2 | 11 | < 0.001 |
| GO:0010586 | miRNA metabolic process | 3 | 48 | < 0.001 |
| GO:0018095 | protein polyglutamylation | 3 | 22 | < 0.001 |
| GO:0018149 | peptide cross-linking | 2 | 28 | < 0.001 |
| GO:0018200 | peptidyl-glutamic acid modification | 2 | 37 | < 0.001 |
| GO:0019722 | calcium-mediated signaling | 2 | 119 | < 0.001 |
| GO:0021532 | neural tube patterning | 3 | 6 | < 0.001 |
| GO:0021591 | ventricular system development | 3 | 32 | < 0.001 |
| GO:0021915 | neural tube development | 4 | 58 | < 0.001 |
| GO:0022402 | cell cycle process | 2 | 750 | < 0.001 |
| GO:0022412 | cellular process involved in reproduction in multicellular organism | 2 | 294 | < 0.001 |
| GO:0022414 | reproductive process | 1 | 1077 | < 0.001 |
| GO:0030030 | cell projection organization | 3 | 814 | < 0.001 |
| GO:0030902 | hindbrain development | 2 | 15 | < 0.001 |
| GO:0031023 | microtubule organizing center organization | 3 | 63 | < 0.001 |
| GO:0031503 | protein-containing complex localization | 2 | 150 | < 0.001 |
| GO:0032886 | regulation of microtubule-based process | 4 | 192 | < 0.001 |
| GO:0035295 | tube development | 2 | 213 | < 0.001 |
| GO:0035721 | intraciliary retrograde transport | 6 | 19 | < 0.001 |
| GO:0035735 | intraciliary transport involved in cilium assembly | 2 | 18 | < 0.001 |
| GO:0035845 | photoreceptor cell outer segment organization | 3 | 11 | < 0.001 |
| GO:0036158 | outer dynein arm assembly | 4 | 30 | < 0.001 |
| GO:0036159 | inner dynein arm assembly | 8 | 22 | < 0.001 |
| GO:0040011 | locomotion | 1 | 674 | < 0.001 |
| GO:0044458 | motile cilium assembly | 2 | 19 | < 0.001 |
| GO:0045494 | photoreceptor cell maintenance | 2 | 51 | < 0.001 |
| GO:0045724 | positive regulation of cilium assembly | 2 | 22 | < 0.001 |
| GO:0046599 | regulation of centriole replication | 6 | 23 | < 0.001 |
| GO:0048598 | embryonic morphogenesis | 2 | 326 | < 0.001 |
| GO:0048609 | multicellular organismal reproductive process | 2 | 443 | < 0.001 |
| GO:0048793 | pronephros development | 5 | 20 | < 0.001 |
| GO:0050678 | regulation of epithelial cell proliferation | 3 | 176 | < 0.001 |
| GO:0060287 | epithelial cilium movement involved in determination of left/right asymmetry | 3 | 11 | < 0.001 |
| GO:0060429 | epithelium development | 4 | 168 | < 0.001 |
| GO:0060438 | trachea development | 2 | 9 | < 0.001 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0060562 | epithelial tube morphogenesis | 2 | 96 | < 0.001 |
| GO:0060632 | regulation of microtubule-based movement | 2 | 41 | < 0.001 |
| GO:0061512 | protein localization to cilium | 5 | 39 | < 0.001 |
| GO:0070286 | axonemal dynein complex assembly | 2 | 51 | < 0.001 |
| GO:0070925 | organelle assembly | 2 | 481 | < 0.001 |
| GO:0072089 | stem cell proliferation | 2 | 45 | < 0.001 |
| GO:0097499 | protein localization to non-motile cilium | 6 | 11 | < 0.001 |
| GO:0097711 | ciliary basal body-plasma membrane docking | 3 | 38 | < 0.001 |
| GO:0120036 | plasma membrane bounded cell projection organization | 2 | 590 | < 0.001 |
| GO:1902017 | regulation of cilium assembly | 6 | 46 | < 0.001 |
| GO:1902115 | regulation of organelle assembly | 2 | 137 | < 0.001 |
| GO:1902117 | positive regulation of organelle assembly | 2 | 51 | < 0.001 |
| GO:1904158 | axonemal central apparatus assembly | 4 | 9 | < 0.001 |
| GO:1904491 | protein localization to ciliary transition zone | 6 | 9 | < 0.001 |
| GO:1905515 | non-motile cilium assembly | 2 | 56 | < 0.001 |
| GO:0009653 | anatomical structure morphogenesis | 2 | 1184 | 0.0012 |
| GO:0007051 | spindle organization | 2 | 117 | 0.0017 |
| GO:1903047 | mitotic cell cycle process | 3 | 502 | 0.0017 |
| GO:0051865 | protein autoubiquitination | 9 | 98 | 0.0018 |
| GO:0030154 | cell differentiation | 2 | 1247 | 0.0022 |
| GO:0051302 | regulation of cell division | 2 | 102 | 0.0032 |
| GO:0007166 | cell surface receptor signaling pathway | 2 | 1153 | 0.0033 |
| GO:0021756 | striatum development | 2 | 16 | 0.0033 |
| GO:0003002 | regionalization | 2 | 236 | 0.0034 |
| GO:0010838 | positive regulation of keratinocyte proliferation | 2 | 14 | 0.0035 |
| GO:1902855 | regulation of non-motile cilium assembly | 2 | 11 | 0.0035 |
| GO:0001822 | kidney development | 2 | 125 | 0.0036 |
| GO:0060296 | regulation of cilium beat frequency involved in ciliary motility | 2 | 8 | 0.0036 |
| GO:0060830 | ciliary receptor clustering involved in smoothened signaling pathway | 3 | 5 | 0.0037 |
| GO:0035148 | tube formation | 3 | 115 | 0.0037 |
| GO:0050680 | negative regulation of epithelial cell proliferation | 2 | 84 | 0.0039 |
| GO:1902116 | negative regulation of organelle assembly | 3 | 31 | 0.0043 |
| GO:0035239 | tube morphogenesis | 3 | 252 | 0.0043 |
| GO:0010564 | regulation of cell cycle process | 5 | 438 | 0.0047 |
| GO:0090394 | negative regulation of excitatory postsynaptic potential | 3 | 9 | 0.0047 |
| GO:1903441 | protein localization to ciliary membrane | 5 | 9 | 0.0050 |
| GO:0051262 | protein tetramerization | 2 | 85 | 0.0051 |
| GO:1902412 | regulation of mitotic cytokinesis | 2 | 5 | 0.0059 |
| GO:0071599 | otic vesicle development | 2 | 7 | 0.0059 |
| GO:0060041 | retina development in camera-type eye | 2 | 42 | 0.0061 |
| GO:0009888 | tissue development | 2 | 459 | 0.0061 |
| GO:0072178 | nephric duct morphogenesis | 2 | 5 | 0.0062 |
| GO:0046602 | regulation of mitotic centrosome separation | 2 | 7 | 0.0079 |
| GO:0051640 | organelle localization | 2 | 363 | 0.0079 |
| GO:0021670 | lateral ventricle development | 2 | 8 | 0.0080 |
| GO:0030916 | otic vesicle formation | 5 | 6 | 0.0082 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0030216 | keratinocyte differentiation | 3 | 32 | 0.0088 |
| GO:0007507 | heart development | 4 | 175 | 0.0089 |
| GO:0045880 | positive regulation of smoothened signaling pathway | 2 | 37 | 0.0089 |
| GO:0048646 | anatomical structure formation involved in morphogenesis | 2 | 648 | 0.0091 |
| GO:0008283 | cell population proliferation | 2 | 370 | 0.0108 |
| GO:1902857 | positive regulation of non-motile cilium assembly | 3 | 8 | 0.0109 |
| GO:0034453 | microtubule anchoring | 2 | 26 | 0.0109 |
| GO:0019236 | response to pheromone | 4 | 7 | 0.0114 |
| GO:0009953 | dorsal/ventral pattern formation | 2 | 73 | 0.0120 |
| GO:2000177 | regulation of neural precursor cell proliferation | 5 | 90 | 0.0122 |
| GO:0006432 | phenylalanyl-tRNA aminoacylation | 3 | 7 | 0.0129 |
| GO:0070986 | left/right axis specification | 2 | 21 | 0.0131 |
| GO:0048839 | inner ear development | 3 | 34 | 0.0133 |
| GO:0031122 | cytoplasmic microtubule organization | 2 | 47 | 0.0134 |
| GO:0008544 | epidermis development | 3 | 42 | 0.0136 |
| GO:0048731 | system development | 2 | 457 | 0.0163 |
| GO:0032465 | regulation of cytokinesis | 2 | 65 | 0.0168 |
| GO:0032053 | ciliary basal body organization | 4 | 7 | 0.0169 |
| GO:0018243 | protein O-linked glycosylation via threonine | 3 | 12 | 0.0211 |
| GO:2000574 | regulation of microtubule motor activity | 2 | 10 | 0.0215 |
| GO:0009141 | nucleoside triphosphate metabolic process | 2 | 75 | 0.0217 |
| GO:0035610 | protein side chain deglutamylation | 2 | 5 | 0.0248 |
| GO:1901068 | guanosine-containing compound metabolic process | 3 | 40 | 0.0276 |
| GO:0031424 | keratinization | 2 | 11 | 0.0277 |
| GO:0007281 | germ cell development | 3 | 121 | 0.0279 |
| GO:2000027 | regulation of animal organ morphogenesis | 5 | 72 | 0.0280 |
| GO:0009887 | animal organ morphogenesis | 3 | 439 | 0.0297 |
| GO:0120034 | positive regulation of plasma membrane bounded cell projection assembly | 2 | 91 | 0.0318 |
| GO:0046548 | retinal rod cell development | 7 | 10 | 0.0327 |
| GO:0042733 | embryonic digit morphogenesis | 4 | 42 | 0.0338 |
| GO:0007286 | spermatid development | 2 | 42 | 0.0350 |
| GO:0045185 | maintenance of protein location | 2 | 107 | 0.0351 |
| GO:0070121 | Kupffer's vesicle development | 3 | 11 | 0.0352 |
| GO:0030856 | regulation of epithelial cell differentiation | 5 | 84 | 0.0354 |
| GO:0046039 | GTP metabolic process | 4 | 28 | 0.0356 |
| GO:0002467 | germinal center formation | 4 | 11 | 0.0363 |
| GO:0060831 | smoothened signaling pathway involved in dorsal/ventral neural tube patterning | 2 | 5 | 0.0364 |
| GO:0007160 | cell-matrix adhesion | 4 | 73 | 0.0365 |
| GO:0048666 | neuron development | 2 | 120 | 0.0372 |
| GO:0003170 | heart valve development | 2 | 11 | 0.0381 |
| GO:0010837 | regulation of keratinocyte proliferation | 4 | 37 | 0.0408 |
| GO:0003254 | regulation of membrane depolarization | 3 | 35 | 0.0410 |
| GO:0048562 | embryonic organ morphogenesis | 4 | 79 | 0.0444 |
| GO:1903546 | protein localization to photoreceptor outer segment | 2 | 6 | 0.0453 |
| GO:0031589 | cell-substrate adhesion | 2 | 115 | 0.0484 |
| GO:0051457 | maintenance of protein location in nucleus | 3 | 27 | 0.0495 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0002250 | adaptive immune response | 2 | 49 | 0.0497 |
| * **Darkgrey module** | |  |  |  |
| **MF** |  |  |  |  |
| GO:0030492 | hemoglobin binding | 3 | 15 | < 0.001 |
| GO:0017075 | syntaxin-1 binding | 2 | 18 | < 0.001 |
| GO:0000182 | rDNA binding | 7 | 5 | < 0.001 |
| GO:0098695 | inositol 1,4,5-trisphosphate receptor activity involved in regulation of postsynaptic cytosolic calcium levels | 2 | 5 | < 0.001 |
| GO:0015086 | cadmium ion transmembrane transporter activity | 3 | 6 | < 0.001 |
| GO:1905394 | retromer complex binding | 3 | 6 | < 0.001 |
| GO:0019238 | cyclohydrolase activity | 2 | 6 | < 0.001 |
| GO:0005544 | calcium-dependent phospholipid binding | 3 | 53 | < 0.001 |
| GO:0005375 | copper ion transmembrane transporter activity | 3 | 7 | < 0.001 |
| GO:0015093 | ferrous iron transmembrane transporter activity | 2 | 7 | < 0.001 |
| GO:1990226 | histone methyltransferase binding | 4 | 7 | < 0.001 |
| GO:0004040 | amidase activity | 4 | 7 | < 0.001 |
| GO:0015926 | glucosidase activity | 2 | 33 | < 0.001 |
| GO:0004096 | catalase activity | 3 | 10 | < 0.001 |
| GO:0005220 | inositol 1,4,5-trisphosphate-sensitive calcium-release channel activity | 5 | 10 | < 0.001 |
| GO:0005381 | iron ion transmembrane transporter activity | 3 | 10 | < 0.001 |
| GO:0008422 | beta-glucosidase activity | 2 | 10 | < 0.001 |
| GO:0031994 | insulin-like growth factor I binding | 2 | 10 | < 0.001 |
| GO:0001968 | fibronectin binding | 3 | 11 | < 0.001 |
| GO:0005384 | manganese ion transmembrane transporter activity | 3 | 11 | < 0.001 |
| GO:0016857 | racemase and epimerase activity, acting on carbohydrates and derivatives | 4 | 11 | < 0.001 |
| GO:0019855 | calcium channel inhibitor activity | 2 | 11 | < 0.001 |
| GO:0050662 | obsolete coenzyme binding | -1 | 11 | < 0.001 |
| GO:0001786 | phosphatidylserine binding | 2 | 45 | < 0.001 |
| GO:0004622 | lysophospholipase activity | 2 | 13 | 0.0012 |
| GO:0042301 | phosphate ion binding | 2 | 13 | 0.0012 |
| GO:0000149 | SNARE binding | 2 | 103 | 0.0017 |
| GO:0035251 | UDP-glucosyltransferase activity | 2 | 14 | 0.0023 |
| GO:0030276 | clathrin binding | 2 | 53 | 0.0032 |
| GO:0046982 | protein heterodimerization activity | 3 | 189 | 0.0053 |
| GO:0005509 | calcium ion binding | 2 | 845 | 0.0054 |
| GO:0001085 | RNA polymerase II transcription factor binding | 3 | 16 | 0.0067 |
| GO:0003951 | NAD+ kinase activity | 2 | 16 | 0.0067 |
| GO:0090599 | alpha-glucosidase activity | 2 | 16 | 0.0067 |
| GO:0016854 | racemase and epimerase activity | 2 | 17 | 0.0104 |
| GO:0005520 | insulin-like growth factor binding | 4 | 19 | 0.0236 |
| GO:0019905 | syntaxin binding | 4 | 69 | 0.0275 |
| GO:0001103 | RNA polymerase II repressing transcription factor binding | 3 | 20 | 0.0312 |
| GO:0043023 | ribosomal large subunit binding | 4 | 20 | 0.0314 |
| GO:0008131 | primary amine oxidase activity | 3 | 21 | 0.0393 |
| **BP** |  |  |  |  |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0017158 | regulation of calcium ion-dependent exocytosis | 2 | 33 | < 0.001 |
| GO:0045920 | negative regulation of exocytosis | 2 | 22 | < 0.001 |
| GO:0045955 | negative regulation of calcium ion-dependent exocytosis | 2 | 11 | < 0.001 |
| GO:1903306 | negative regulation of regulated secretory pathway | 3 | 15 | < 0.001 |
| GO:2000301 | negative regulation of synaptic vesicle exocytosis | 3 | 7 | 0.0143 |
| GO:0023061 | signal release | 2 | 104 | 0.0200 |
| GO:0061792 | secretory granule maturation | 2 | 8 | 0.0227 |
| GO:1903233 | regulation of calcium ion-dependent exocytosis of neurotransmitter | 5 | 8 | 0.0227 |
| GO:0014049 | positive regulation of glutamate secretion | 4 | 9 | 0.0308 |
| GO:0031339 | negative regulation of vesicle fusion | 2 | 9 | 0.0308 |
| GO:1903305 | regulation of regulated secretory pathway | 4 | 101 | 0.0357 |
| GO:0045956 | positive regulation of calcium ion-dependent exocytosis | 2 | 14 | 0.0375 |
| GO:0099550 | trans-synaptic signaling, modulating synaptic transmission | 2 | 14 | 0.0375 |
| GO:0014048 | regulation of glutamate secretion | 3 | 13 | 0.0382 |
| GO:0032252 | secretory granule localization | 5 | 12 | 0.0406 |
| GO:0048172 | regulation of short-term neuronal synaptic plasticity | 2 | 19 | 0.0460 |
| * **Brown module** | |  |  |  |
| **MF** |  |  |  |  |
| GO:0140318 | protein transporter activity | 2 | 25 | < 0.001 |
| GO:0001517 | N-acetylglucosamine 6-O-sulfotransferase activity | 5 | 6 | < 0.001 |
| GO:0008273 | calcium, potassium:sodium antiporter activity | 4 | 7 | < 0.001 |
| GO:0031994 | insulin-like growth factor I binding | 2 | 10 | < 0.001 |
| GO:0005452 | inorganic anion exchanger activity | 2 | 11 | < 0.001 |
| GO:0070012 | oligopeptidase activity | 3 | 7 | < 0.001 |
| GO:0016843 | amine-lyase activity | 2 | 5 | < 0.001 |
| GO:0015297 | antiporter activity | 5 | 72 | < 0.001 |
| GO:0005534 | galactose binding | 2 | 5 | < 0.001 |
| GO:0004567 | beta-mannosidase activity | 2 | 5 | < 0.001 |
| GO:0004104 | cholinesterase activity | 2 | 5 | < 0.001 |
| GO:0048037 | obsolete cofactor binding | -1 | 13 | < 0.001 |
| GO:0005520 | insulin-like growth factor binding | 4 | 19 | 0.0010 |
| GO:0008447 | L-ascorbate oxidase activity | 2 | 6 | 0.0012 |
| GO:0008061 | chitin binding | 2 | 46 | 0.0015 |
| GO:0030492 | hemoglobin binding | 3 | 15 | 0.0023 |
| GO:0015347 | sodium-independent organic anion transmembrane transporter activity | 2 | 11 | 0.0051 |
| GO:0030165 | PDZ domain binding | 2 | 71 | 0.0057 |
| GO:0022821 | potassium ion antiporter activity | 4 | 17 | 0.0101 |
| GO:0004089 | carbonate dehydratase activity | 3 | 30 | 0.0120 |
| GO:0008191 | metalloendopeptidase inhibitor activity | 4 | 30 | 0.0121 |
| GO:1905172 | RISC complex binding | 2 | 7 | 0.0121 |
| GO:0016840 | carbon-nitrogen lyase activity | 3 | 25 | 0.0246 |
| GO:0005125 | cytokine activity | 5 | 52 | 0.0274 |
| GO:0016742 | hydroxymethyl-, formyl- and related transferase activity | 2 | 13 | 0.0274 |
| GO:0047631 | ADP-ribose diphosphatase activity | 3 | 8 | 0.0364 |
| GO:0070883 | pre-miRNA binding | 3 | 8 | 0.0388 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0070008 | serine-type exopeptidase activity | 2 | 14 | 0.0469 |
| GO:0004553 | hydrolase activity, hydrolyzing O-glycosyl compounds | 2 | 179 | 0.0486 |
| **BP** |  |  |  |  |
| GO:0000272 | polysaccharide catabolic process | 3 | 55 | < 0.001 |
| GO:0005975 | carbohydrate metabolic process | 2 | 484 | < 0.001 |
| GO:0006022 | aminoglycan metabolic process | 2 | 151 | < 0.001 |
| GO:0006030 | chitin metabolic process | 3 | 42 | < 0.001 |
| GO:0006814 | sodium ion transport | 2 | 101 | < 0.001 |
| GO:0015672 | monovalent inorganic cation transport | 6 | 221 | < 0.001 |
| GO:0032526 | response to retinoic acid | 2 | 44 | < 0.001 |
| GO:0033280 | response to vitamin D | 2 | 15 | < 0.001 |
| GO:0048806 | genitalia development | 3 | 25 | < 0.001 |
| GO:0048878 | chemical homeostasis | 4 | 756 | < 0.001 |
| GO:0097242 | amyloid-beta clearance | 2 | 41 | < 0.001 |
| GO:1901135 | carbohydrate derivative metabolic process | 2 | 773 | < 0.001 |
| GO:0042592 | homeostatic process | 2 | 1074 | 0.0024 |
| GO:0006812 | cation transport | 2 | 569 | 0.0025 |
| GO:0006044 | N-acetylglucosamine metabolic process | 2 | 11 | 0.0042 |
| GO:0015701 | bicarbonate transport | 8 | 16 | 0.0043 |
| GO:0042454 | ribonucleoside catabolic process | 7 | 12 | 0.0056 |
| GO:0035277 | spiracle morphogenesis, open tracheal system | 2 | 8 | 0.0058 |
| GO:0044321 | response to leptin | 2 | 16 | 0.0067 |
| GO:0014015 | positive regulation of gliogenesis | 4 | 40 | 0.0069 |
| GO:0003002 | regionalization | 3 | 236 | 0.0100 |
| GO:0061642 | chemoattraction of axon | 3 | 13 | 0.0103 |
| GO:0045056 | transcytosis | 4 | 22 | 0.0105 |
| GO:0030001 | metal ion transport | 6 | 416 | 0.0108 |
| GO:0097186 | amelogenesis | 3 | 5 | 0.0113 |
| GO:0030206 | chondroitin sulfate biosynthetic process | 5 | 17 | 0.0115 |
| GO:0070445 | regulation of oligodendrocyte progenitor proliferation | 4 | 14 | 0.0150 |
| GO:1903510 | mucopolysaccharide metabolic process | 2 | 67 | 0.0191 |
| GO:0007600 | sensory perception | 3 | 315 | 0.0196 |
| GO:0050918 | positive chemotaxis | 2 | 24 | 0.0200 |
| GO:0007389 | pattern specification process | 2 | 368 | 0.0205 |
| GO:0098609 | cell-cell adhesion | 2 | 354 | 0.0206 |
| GO:0002532 | production of molecular mediator involved in inflammatory response | 2 | 7 | 0.0207 |
| GO:0046621 | negative regulation of organ growth | 3 | 33 | 0.0208 |
| GO:0035461 | vitamin transmembrane transport | 2 | 31 | 0.0210 |
| GO:0043174 | nucleoside salvage | 2 | 8 | 0.0212 |
| GO:0010817 | regulation of hormone levels | 2 | 380 | 0.0217 |
| GO:1901136 | carbohydrate derivative catabolic process | 2 | 188 | 0.0306 |
| GO:0009256 | 10-formyltetrahydrofolate metabolic process | 2 | 5 | 0.0307 |
| GO:0007435 | salivary gland morphogenesis | 3 | 17 | 0.0328 |
| GO:0009653 | anatomical structure morphogenesis | 2 | 1184 | 0.0331 |
| GO:0014013 | regulation of gliogenesis | 2 | 58 | 0.0333 |
| GO:0048608 | reproductive structure development | 2 | 142 | 0.0336 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0034404 | nucleobase-containing small molecule biosynthetic process | 2 | 71 | 0.0379 |
| GO:0035725 | sodium ion transmembrane transport | 2 | 37 | 0.0391 |
| GO:0044282 | small molecule catabolic process | 2 | 415 | 0.0397 |
| GO:0032729 | positive regulation of interferon-gamma production | 3 | 10 | 0.0439 |
| GO:0061052 | negative regulation of cell growth involved in cardiac muscle cell development | 2 | 14 | 0.0453 |
| GO:0006826 | iron ion transport | 2 | 50 | 0.0453 |
| GO:0055072 | iron ion homeostasis | 4 | 67 | 0.0463 |
| GO:1901077 | regulation of relaxation of muscle | 4 | 5 | 0.0465 |
| GO:0001568 | blood vessel development | 2 | 78 | 0.0478 |
| GO:0043652 | engulfment of apoptotic cell | 2 | 21 | 0.0494 |
| GO:0043649 | dicarboxylic acid catabolic process | 3 | 23 | 0.0494 |
| GO:0033273 | response to vitamin | 2 | 53 | 0.0494 |
| * **Tan module** | |  |  |  |
| **MF** |  |  |  |  |
| GO:0015106 | bicarbonate transmembrane transporter activity | 3 | 17 | < 0.001 |
| GO:0005310 | dicarboxylic acid transmembrane transporter activity | 2 | 20 | < 0.001 |
| GO:0003700 | DNA-binding transcription factor activity | 2 | 497 | < 0.001 |
| GO:0016725 | oxidoreductase activity, acting on CH or CH2 groups | 2 | 25 | < 0.001 |
| GO:0140030 | modification-dependent protein binding | 2 | 150 | < 0.001 |
| GO:0036435 | K48-linked polyubiquitin modification-dependent protein binding | 3 | 5 | < 0.001 |
| GO:0008401 | retinoic acid 4-hydroxylase activity | 3 | 18 | < 0.001 |
| GO:1990405 | protein antigen binding | 2 | 5 | < 0.001 |
| GO:0003858 | 3-hydroxybutyrate dehydrogenase activity | 2 | 12 | < 0.001 |
| GO:0016880 | acid-ammonia (or amide) ligase activity | 2 | 6 | 0.0012 |
| GO:0015349 | thyroid hormone transmembrane transporter activity | 5 | 6 | 0.0016 |
| GO:0140110 | transcription regulator activity | 1 | 804 | 0.0016 |
| GO:0098770 | FBXO family protein binding | 3 | 6 | 0.0018 |
| GO:0008391 | arachidonic acid monooxygenase activity | 3 | 43 | 0.0019 |
| GO:0008392 | arachidonic acid epoxygenase activity | 5 | 32 | 0.0019 |
| GO:0034185 | apolipoprotein binding | 2 | 41 | 0.0021 |
| GO:1901682 | sulfur compound transmembrane transporter activity | 2 | 43 | 0.0021 |
| GO:0031593 | polyubiquitin modification-dependent protein binding | 2 | 43 | 0.0022 |
| GO:0070530 | K63-linked polyubiquitin modification-dependent protein binding | 3 | 14 | 0.0036 |
| GO:0000981 | DNA-binding transcription factor activity, RNA polymerase II-specific | 3 | 328 | 0.0053 |
| GO:0047485 | protein N-terminus binding | 2 | 75 | 0.0078 |
| GO:0061578 | Lys63-specific deubiquitinase activity | 2 | 8 | 0.0118 |
| GO:0005436 | sodium:phosphate symporter activity | 2 | 8 | 0.0146 |
| GO:0016964 | alpha-2 macroglobulin receptor activity | 2 | 8 | 0.0214 |
| GO:0032451 | demethylase activity | 2 | 40 | 0.0250 |
| GO:0016500 | protein-hormone receptor activity | 3 | 18 | 0.0374 |
| GO:0015297 | antiporter activity | 5 | 72 | 0.0378 |
| GO:0022853 | active ion transmembrane transporter activity | 2 | 282 | 0.0378 |
| GO:0070491 | repressing transcription factor binding | 5 | 43 | 0.0378 |
| GO:0101020 | estrogen 16-alpha-hydroxylase activity | 2 | 30 | 0.0378 |
| GO:0030226 | apolipoprotein receptor activity | 2 | 9 | 0.0407 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0001046 | core promoter sequence-specific DNA binding | 3 | 19 | 0.0444 |
| **BP** |  |  |  |  |
| GO:0000185 | activation of MAPKKK activity | 2 | 16 | < 0.001 |
| GO:0035864 | response to potassium ion | 2 | 11 | < 0.001 |
| GO:1900744 | regulation of p38MAPK cascade | 4 | 28 | < 0.001 |
| GO:0009612 | response to mechanical stimulus | 3 | 156 | 0.0050 |
| GO:1900745 | positive regulation of p38MAPK cascade | 2 | 20 | 0.0056 |
| GO:0015698 | inorganic anion transport | 3 | 80 | 0.0063 |
| GO:0071850 | mitotic cell cycle arrest | 2 | 14 | 0.0071 |
| GO:0097267 | omega-hydroxylase P450 pathway | 2 | 12 | 0.0083 |
| GO:0031399 | regulation of protein modification process | 3 | 962 | 0.0100 |
| GO:0044092 | negative regulation of molecular function | 2 | 586 | 0.0125 |
| GO:0071260 | cellular response to mechanical stimulus | 3 | 51 | 0.0125 |
| GO:0002931 | response to ischemia | 3 | 33 | 0.0136 |
| GO:0031400 | negative regulation of protein modification process | 4 | 333 | 0.0143 |
| GO:1901700 | response to oxygen-containing compound | 2 | 828 | 0.0154 |
| GO:0008645 | hexose transmembrane transport | 2 | 13 | 0.0175 |
| GO:0043086 | negative regulation of catalytic activity | 3 | 406 | 0.0176 |
| GO:0009751 | response to salicylic acid | 2 | 7 | 0.0182 |
| GO:0019369 | arachidonic acid metabolic process | 2 | 59 | 0.0184 |
| GO:0019373 | epoxygenase P450 pathway | 2 | 30 | 0.0190 |
| GO:0071479 | cellular response to ionizing radiation | 2 | 56 | 0.0194 |
| GO:0042573 | retinoic acid metabolic process | 7 | 22 | 0.0217 |
| GO:0046328 | regulation of JNK cascade | 4 | 82 | 0.0313 |
| GO:0006805 | xenobiotic metabolic process | 2 | 108 | 0.0343 |
| GO:0009719 | response to endogenous stimulus | 2 | 638 | 0.0351 |
| GO:0002933 | lipid hydroxylation | 4 | 14 | 0.0352 |
| GO:0042759 | long-chain fatty acid biosynthetic process | 3 | 14 | 0.0352 |
| GO:0070988 | demethylation | 2 | 51 | 0.0353 |
| GO:0002683 | negative regulation of immune system process | 2 | 171 | 0.0355 |
| GO:0043405 | regulation of MAP kinase activity | 2 | 155 | 0.0357 |
| GO:2000515 | negative regulation of CD4-positive, alpha-beta T cell activation | 2 | 5 | 0.0364 |
| GO:0070371 | ERK1 and ERK2 cascade | 2 | 11 | 0.0366 |
| GO:0000122 | negative regulation of transcription by RNA polymerase II | 2 | 448 | 0.0372 |
| GO:0060216 | definitive hemopoiesis | 4 | 12 | 0.0375 |
| GO:0045582 | positive regulation of T cell differentiation | 4 | 21 | 0.0379 |
| GO:0046330 | positive regulation of JNK cascade | 2 | 50 | 0.0383 |
| GO:0010996 | response to auditory stimulus | 2 | 9 | 0.0387 |
| GO:0042126 | nitrate metabolic process | 4 | 6 | 0.0388 |
| GO:0045621 | positive regulation of lymphocyte differentiation | 2 | 29 | 0.0404 |
| GO:1905939 | regulation of gonad development | 2 | 5 | 0.0407 |
| GO:0060349 | bone morphogenesis | 2 | 25 | 0.0410 |
| GO:1902916 | positive regulation of protein polyubiquitination | 3 | 17 | 0.0413 |
| GO:0006357 | regulation of transcription by RNA polymerase II | 2 | 1086 | 0.0415 |
| GO:0031401 | positive regulation of protein modification process | 2 | 608 | 0.0420 |
| GO:0001676 | long-chain fatty acid metabolic process | 6 | 85 | 0.0422 |
|  |  |  |  |  |
| **Supplementary Table 2** (*continued*) | |  |  |  |
| GO:0120254 | olefinic compound metabolic process | 3 | 91 | 0.0431 |
| GO:0021895 | cerebral cortex neuron differentiation | 3 | 6 | 0.0435 |
| GO:0007098 | centrosome cycle | 3 | 32 | 0.0438 |
| GO:0046636 | negative regulation of alpha-beta T cell activation | 5 | 8 | 0.0445 |
| GO:0051172 | negative regulation of nitrogen compound metabolic process | 5 | 1344 | 0.0450 |
| GO:0017144 | drug metabolic process | 3 | 73 | 0.0456 |
| GO:1901537 | positive regulation of DNA demethylation | 2 | 6 | 0.0458 |

**Supplementary Table 3.** Gene Ontology (GO) enrichments in molecular function (MF) and biological process (BP) of module genes of interest (magenta, pink and red modules) identified in hemocyte samples from WGCNA.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **GO ID** | **GO term** | **Level** | **Nseqs** | ***P*adj** |
| * **Magenta module** | |  |  |  |
| **MF** |  |  |  |  |
| GO:0003735 | structural constituent of ribosome | 2 | 166 | < 0.001 |
| GO:0005198 | structural molecule activity | 1 | 499 | < 0.001 |
| GO:0019843 | rRNA binding | 2 | 73 | < 0.001 |
| GO:0070180 | large ribosomal subunit rRNA binding | 3 | 6 | < 0.001 |
| GO:0003746 | translation elongation factor activity | 2 | 30 | < 0.001 |
| GO:0016427 | tRNA (cytosine) methyltransferase activity | 2 | 10 | < 0.001 |
| GO:0008186 | RNA-dependent ATPase activity | 3 | 6 | < 0.001 |
| GO:0140098 | catalytic activity, acting on RNA | 2 | 561 | < 0.001 |
| GO:0004549 | tRNA-specific ribonuclease activity | 3 | 14 | < 0.001 |
| GO:0001091 | RNA polymerase II general transcription initiation factor binding | 2 | 10 | < 0.001 |
| GO:0017176 | phosphatidylinositol N-acetylglucosaminyltransferase activity | 2 | 5 | < 0.001 |
| GO:0008173 | RNA methyltransferase activity | 3 | 81 | < 0.001 |
| GO:0140101 | catalytic activity, acting on a tRNA | 2 | 168 | < 0.001 |
| GO:0045182 | translation regulator activity | 1 | 180 | 0.0013 |
| GO:0008097 | 5S rRNA binding | 4 | 12 | 0.0015 |
| GO:0016428 | tRNA (cytosine-5-)-methyltransferase activity | 6 | 6 | 0.0025 |
| GO:0106029 | tRNA pseudouridine synthase activity | 2 | 6 | 0.0026 |
| GO:0000049 | tRNA binding | 3 | 106 | 0.0027 |
| GO:0030621 | U4 snRNA binding | 2 | 6 | 0.0027 |
| GO:0008172 | S-methyltransferase activity | 5 | 14 | 0.0077 |
| GO:0001094 | TFIID-class transcription factor complex binding | 4 | 7 | 0.0093 |
| GO:0016635 | oxidoreductase activity, acting on the CH-CH group of donors, quinone or related compound as acceptor | 2 | 7 | 0.0097 |
| GO:0001968 | fibronectin binding | 2 | 7 | 0.0115 |
| GO:0015450 | P-P-bond-hydrolysis-driven protein transmembrane transporter activity | 2 | 8 | 0.0212 |
| GO:0016892 | endoribonuclease activity, producing 3'-phosphomonoesters | 5 | 8 | 0.0290 |
| GO:0004888 | transmembrane signaling receptor activity | 3 | 530 | 0.0381 |
| GO:0030515 | snoRNA binding | 2 | 40 | 0.0381 |
| GO:0003743 | translation initiation factor activity | 2 | 69 | 0.0411 |
| GO:0004745 | retinol dehydrogenase activity | 4 | 17 | 0.0424 |
| GO:0008175 | tRNA methyltransferase activity | 2 | 40 | 0.0425 |
| **BP** |  |  |  |  |
| GO:0000027 | ribosomal large subunit assembly | 3 | 31 | < 0.001 |
| GO:0000028 | ribosomal small subunit assembly | 3 | 11 | < 0.001 |
| GO:0000463 | maturation of LSU-rRNA from tricistronic rRNA transcript (SSU-rRNA, 5.8S rRNA, LSU-rRNA) | 4 | 20 | < 0.001 |
| GO:0000470 | maturation of LSU-rRNA | 3 | 35 | < 0.001 |
| GO:0002181 | cytoplasmic translation | 4 | 33 | < 0.001 |
|  |  |  |  |  |
| **Supplementary Table 3** (*continued*) | |  |  |  |
| GO:0006396 | RNA processing | 2 | 949 | < 0.001 |
| GO:0006518 | peptide metabolic process | 4 | 356 | < 0.001 |
| GO:0034470 | ncRNA processing | 2 | 460 | < 0.001 |
| GO:0034660 | ncRNA metabolic process | 5 | 615 | < 0.001 |
| GO:0043603 | cellular amide metabolic process | 4 | 575 | < 0.001 |
| GO:0043604 | amide biosynthetic process | 2 | 320 | < 0.001 |
| GO:0043628 | ncRNA 3'-end processing | 3 | 54 | < 0.001 |
| GO:0044271 | cellular nitrogen compound biosynthetic process | 2 | 1186 | < 0.001 |
| GO:1901566 | organonitrogen compound biosynthetic process | 2 | 813 | < 0.001 |
| GO:0031123 | RNA 3'-end processing | 2 | 113 | 0.0026 |
| GO:0016071 | mRNA metabolic process | 2 | 618 | 0.0050 |
| GO:0006399 | tRNA metabolic process | 2 | 245 | 0.0058 |
| GO:0006414 | translational elongation | 3 | 51 | 0.0060 |
| GO:0034472 | snRNA 3'-end processing | 2 | 33 | 0.0065 |
| GO:0034622 | cellular protein-containing complex assembly | 6 | 670 | 0.0068 |
| GO:0070972 | protein localization to endoplasmic reticulum | 2 | 49 | 0.0200 |
| GO:0001732 | formation of cytoplasmic translation initiation complex | 7 | 25 | 0.0203 |
| GO:0071025 | RNA surveillance | 2 | 21 | 0.0210 |
| GO:0071051 | polyadenylation-dependent snoRNA 3'-end processing | 2 | 7 | 0.0235 |
| GO:0006413 | translational initiation | 3 | 52 | 0.0286 |
| GO:0006401 | RNA catabolic process | 2 | 191 | 0.0458 |
| * **Pink module** | | | | |
| **MF** |  |  |  |  |
| GO:0002151 | G-quadruplex RNA binding | 2 | 8 | < 0.001 |
| GO:0051010 | microtubule plus-end binding | 2 | 20 | < 0.001 |
| GO:0004534 | 5'-3' exoribonuclease activity | 3 | 7 | < 0.001 |
| GO:0106018 | phosphatidylinositol-3,5-bisphosphate phosphatase activity | 7 | 7 | < 0.001 |
| GO:0034593 | phosphatidylinositol bisphosphate phosphatase activity | 2 | 23 | < 0.001 |
| GO:0016308 | 1-phosphatidylinositol-4-phosphate 5-kinase activity | 2 | 5 | < 0.001 |
| GO:0015924 | mannosyl-oligosaccharide mannosidase activity | 2 | 15 | < 0.001 |
| GO:0034595 | phosphatidylinositol phosphate 5-phosphatase activity | 6 | 15 | < 0.001 |
| GO:0003700 | DNA-binding transcription factor activity | 2 | 532 | < 0.001 |
| GO:0035197 | siRNA binding | 2 | 7 | < 0.001 |
| GO:0052866 | phosphatidylinositol phosphate phosphatase activity | 2 | 31 | < 0.001 |
| GO:0050291 | sphingosine N-acyltransferase activity | 2 | 7 | < 0.001 |
| GO:0005096 | GTPase activator activity | 4 | 218 | < 0.001 |
| GO:0016964 | alpha-2 macroglobulin receptor activity | 2 | 8 | < 0.001 |
| GO:0004572 | mannosyl-oligosaccharide 1,3-1,6-alpha-mannosidase activity | 4 | 8 | < 0.001 |
| GO:0008392 | arachidonic acid epoxygenase activity | 2 | 19 | 0.0011 |
| GO:0140110 | transcription regulator activity | 1 | 887 | 0.0011 |
| GO:0003831 | beta-N-acetylglucosaminylglycopeptide beta-1,4-galactosyltransferase activity | 2 | 9 | 0.0014 |
| GO:0016491 | oxidoreductase activity | 2 | 1073 | 0.0018 |
| GO:0032051 | clathrin light chain binding | 3 | 9 | 0.0028 |
| GO:0015026 | coreceptor activity | 2 | 23 | 0.0036 |
| GO:0035091 | phosphatidylinositol binding | 4 | 227 | 0.0036 |
|  |  |  |  |  |
| **Supplementary Table 3** (*continued*) | |  |  |  |
| GO:1990380 | Lys48-specific deubiquitinase activity | 4 | 16 | 0.0042 |
| GO:0015183 | L-aspartate transmembrane transporter activity | 2 | 5 | 0.0071 |
| GO:0070728 | leucine binding | 2 | 5 | 0.0071 |
| GO:0005543 | phospholipid binding | 2 | 352 | 0.0072 |
| GO:0043515 | kinetochore binding | 2 | 10 | 0.0072 |
| GO:0008289 | lipid binding | 2 | 590 | 0.0075 |
| GO:0008047 | enzyme activator activity | 3 | 355 | 0.0097 |
| GO:0016404 | 15-hydroxyprostaglandin dehydrogenase (NAD+) activity | 3 | 5 | 0.0106 |
| GO:0030276 | clathrin binding | 2 | 43 | 0.0108 |
| GO:0015095 | magnesium ion transmembrane transporter activity | 2 | 11 | 0.0146 |
| GO:0043422 | protein kinase B binding | 5 | 11 | 0.0151 |
| GO:0003707 | steroid hormone receptor activity | 2 | 45 | 0.0158 |
| GO:0043325 | phosphatidylinositol-3,4-bisphosphate binding | 2 | 18 | 0.0180 |
| GO:0004652 | polynucleotide adenylyltransferase activity | 5 | 6 | 0.0198 |
| GO:0016884 | carbon-nitrogen ligase activity, with glutamine as amido-N-donor | 3 | 18 | 0.0209 |
| GO:0005522 | profilin binding | 3 | 12 | 0.0237 |
| GO:0051721 | protein phosphatase 2A binding | 2 | 37 | 0.0264 |
| GO:0046966 | thyroid hormone receptor binding | 2 | 20 | 0.0284 |
| GO:1901981 | phosphatidylinositol phosphate binding | 5 | 130 | 0.0284 |
| GO:0004715 | non-membrane spanning protein tyrosine kinase activity | 5 | 48 | 0.0301 |
| GO:0008391 | arachidonic acid monooxygenase activity | 2 | 27 | 0.0301 |
| GO:0015296 | anion:cation symporter activity | 5 | 13 | 0.0388 |
| GO:0071889 | 14-3-3 protein binding | 2 | 20 | 0.0388 |
| GO:0034452 | dynactin binding | 3 | 13 | 0.0391 |
| GO:0000340 | RNA 7-methylguanosine cap binding | 2 | 13 | 0.0400 |
| GO:0005545 | 1-phosphatidylinositol binding | 5 | 14 | 0.0482 |
| GO:0005159 | insulin-like growth factor receptor binding | 3 | 7 | 0.0490 |
| **BP** |  |  |  |  |
| GO:0030509 | BMP signaling pathway | 2 | 29 | < 0.001 |
| GO:0035304 | regulation of protein dephosphorylation | 3 | 71 | < 0.001 |
| GO:0070647 | protein modification by small protein conjugation or removal | 2 | 1017 | < 0.001 |
| GO:1903146 | regulation of autophagy of mitochondrion | 2 | 52 | < 0.001 |
| GO:0035303 | regulation of dephosphorylation | 2 | 137 | 0.0038 |
| GO:0008286 | insulin receptor signaling pathway | 6 | 67 | 0.0063 |
| GO:0016241 | regulation of macroautophagy | 5 | 125 | 0.0071 |
| GO:1902667 | regulation of axon guidance | 3 | 19 | 0.0088 |
| GO:0061912 | selective autophagy | 5 | 38 | 0.0119 |
| GO:1901524 | regulation of mitophagy | 2 | 32 | 0.0125 |
| GO:0045732 | positive regulation of protein catabolic process | 2 | 154 | 0.0130 |
| GO:1904562 | phosphatidylinositol 5-phosphate metabolic process | 5 | 5 | 0.0139 |
| GO:0048584 | positive regulation of response to stimulus | 2 | 1298 | 0.0143 |
| GO:0016458 | gene silencing | 3 | 118 | 0.0146 |
| GO:0006508 | proteolysis | 3 | 1101 | 0.0148 |
| GO:0099003 | vesicle-mediated transport in synapse | 4 | 69 | 0.0154 |
| GO:0048609 | multicellular organismal reproductive process | 2 | 490 | 0.0217 |
| GO:0022603 | regulation of anatomical structure morphogenesis | 3 | 640 | 0.0226 |
|  |  |  |  |  |
| **Supplementary Table 3** (*continued*) | |  |  |  |
| GO:0010628 | positive regulation of gene expression | 4 | 1376 | 0.0258 |
| GO:0031047 | gene silencing by RNA | 2 | 75 | 0.0386 |
| GO:0060341 | regulation of cellular localization | 2 | 686 | 0.0408 |
| GO:0022604 | regulation of cell morphogenesis | 5 | 232 | 0.0419 |
| GO:1903599 | positive regulation of autophagy of mitochondrion | 4 | 32 | 0.0431 |
| * **Red module** | | | | |
| **MF** |  |  |  |  |
| GO:0004497 | monooxygenase activity | 2 | 167 | < 0.001 |
| GO:0005506 | iron ion binding | 4 | 231 | < 0.001 |
| GO:0003964 | RNA-directed DNA polymerase activity | 3 | 94 | < 0.001 |
| GO:0015293 | symporter activity | 5 | 220 | < 0.001 |
| GO:0005343 | organic acid:sodium symporter activity | 4 | 56 | < 0.001 |
| GO:0008395 | steroid hydroxylase activity | 3 | 69 | < 0.001 |
| GO:0008028 | monocarboxylic acid transmembrane transporter activity | 2 | 84 | < 0.001 |
| GO:0016705 | oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen | 3 | 240 | < 0.001 |
| GO:0004930 | G protein-coupled receptor activity | 2 | 276 | < 0.001 |
| GO:0033781 | cholesterol 24-hydroxylase activity | 5 | 5 | < 0.001 |
| GO:0016491 | oxidoreductase activity | 2 | 1073 | < 0.001 |
| GO:0004062 | aryl sulfotransferase activity | 2 | 21 | < 0.001 |
| GO:0101021 | estrogen 2-hydroxylase activity | 4 | 14 | < 0.001 |
| GO:0016709 | oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, NAD(P)H as one donor, and incorporation of one atom of oxygen | 2 | 52 | < 0.001 |
| GO:0008146 | sulfotransferase activity | 2 | 53 | < 0.001 |
| GO:0016798 | hydrolase activity, acting on glycosyl bonds | 2 | 269 | < 0.001 |
| GO:0004132 | dCMP deaminase activity | 2 | 7 | < 0.001 |
| GO:0004888 | transmembrane signaling receptor activity | 2 | 530 | < 0.001 |
| GO:0015081 | sodium ion transmembrane transporter activity | 2 | 166 | < 0.001 |
| GO:0004499 | N,N-dimethylaniline monooxygenase activity | 2 | 10 | < 0.001 |
| GO:0015171 | amino acid transmembrane transporter activity | 2 | 90 | < 0.001 |
| GO:0101020 | estrogen 16-alpha-hydroxylase activity | 2 | 23 | < 0.001 |
| GO:0001758 | retinal dehydrogenase activity | 5 | 11 | < 0.001 |
| GO:0016887 | ATPase activity | 3 | 688 | < 0.001 |
| GO:0034061 | DNA polymerase activity | 2 | 136 | < 0.001 |
| GO:1990935 | splicing factor binding | 2 | 5 | < 0.001 |
| GO:0046914 | transition metal ion binding | 3 | 1373 | < 0.001 |
| GO:0031628 | opioid receptor binding | 4 | 8 | < 0.001 |
| GO:0003943 | N-acetylgalactosamine-4-sulfatase activity | 4 | 8 | < 0.001 |
| GO:0008453 | alanine-glyoxylate transaminase activity | 2 | 5 | < 0.001 |
| GO:0042165 | neurotransmitter binding | 2 | 13 | 0.0010 |
| GO:0015291 | secondary active transmembrane transporter activity | 4 | 295 | 0.0013 |
| GO:0050649 | testosterone 6-beta-hydroxylase activity | 4 | 12 | 0.0013 |
| GO:0050051 | leukotriene-B4 20-monooxygenase activity | 2 | 8 | 0.0014 |
| GO:0030274 | LIM domain binding | 3 | 9 | 0.0022 |
|  |  |  |  |  |
| **Supplementary Table 3** (*continued*) | |  |  |  |
| GO:0016782 | transferase activity, transferring sulfur-containing groups | 3 | 84 | 0.0028 |
| GO:0043237 | laminin-1 binding | 2 | 6 | 0.0029 |
| GO:0008391 | arachidonic acid monooxygenase activity | 2 | 27 | 0.0030 |
| GO:0008532 | N-acetyllactosaminide beta-1,3-N-acetylglucosaminyltransferase activity | 2 | 6 | 0.0030 |
| GO:0004553 | hydrolase activity, hydrolyzing O-glycosyl compounds | 4 | 183 | 0.0034 |
| GO:0015631 | tubulin binding | 2 | 361 | 0.0039 |
| GO:0003774 | motor activity | 4 | 200 | 0.0046 |
| GO:0046920 | alpha-(1->3)-fucosyltransferase activity | 2 | 14 | 0.0046 |
| GO:0015926 | glucosidase activity | 2 | 36 | 0.0053 |
| GO:0030246 | carbohydrate binding | 2 | 276 | 0.0066 |
| GO:0070410 | co-SMAD binding | 3 | 25 | 0.0077 |
| GO:0008422 | beta-glucosidase activity | 3 | 10 | 0.0078 |
| GO:0050840 | extracellular matrix binding | 2 | 39 | 0.0100 |
| GO:0008227 | G protein-coupled amine receptor activity | 2 | 16 | 0.0108 |
| GO:0046974 | histone methyltransferase activity (H3-K9 specific) | 6 | 12 | 0.0108 |
| GO:0017017 | MAP kinase tyrosine/serine/threonine phosphatase activity | 4 | 7 | 0.0112 |
| GO:0018685 | alkane 1-monooxygenase activity | 2 | 6 | 0.0122 |
| GO:0008417 | fucosyltransferase activity | 4 | 33 | 0.0137 |
| GO:0008195 | phosphatidate phosphatase activity | 2 | 7 | 0.0145 |
| GO:0043236 | laminin binding | 2 | 17 | 0.0163 |
| GO:0003777 | microtubule motor activity | 2 | 125 | 0.0163 |
| GO:0004065 | arylsulfatase activity | 5 | 16 | 0.0175 |
| GO:0015245 | fatty acid transmembrane transporter activity | 3 | 34 | 0.0175 |
| GO:0008484 | sulfuric ester hydrolase activity | 3 | 22 | 0.0218 |
| GO:0005540 | hyaluronic acid binding | 4 | 24 | 0.0249 |
| GO:0070412 | R-SMAD binding | 3 | 34 | 0.0251 |
| GO:0005096 | GTPase activator activity | 2 | 218 | 0.0290 |
| GO:0030234 | enzyme regulator activity | 2 | 838 | 0.0334 |
| GO:0003682 | chromatin binding | 2 | 481 | 0.0338 |
| GO:0005328 | neurotransmitter:sodium symporter activity | 4 | 17 | 0.0338 |
| GO:0098772 | molecular function regulator | 1 | 1334 | 0.0338 |
| GO:0008047 | enzyme activator activity | 2 | 355 | 0.0349 |
| GO:0008017 | microtubule binding | 2 | 263 | 0.0368 |
| GO:0008514 | organic anion transmembrane transporter activity | 2 | 175 | 0.0387 |
| **BP** |  |  |  |  |
| GO:0007186 | G protein-coupled receptor signaling pathway | 2 | 347 | < 0.001 |
| GO:0007530 | sex determination | 2 | 11 | < 0.001 |
| GO:0008202 | steroid metabolic process | 2 | 258 | < 0.001 |
| GO:0015074 | DNA integration | 5 | 89 | < 0.001 |
| GO:0030238 | male sex determination | 2 | 7 | < 0.001 |
| GO:0034308 | primary alcohol metabolic process | 2 | 80 | < 0.001 |
| GO:0042445 | hormone metabolic process | 3 | 162 | < 0.001 |
| GO:0006720 | isoprenoid metabolic process | 3 | 112 | 0.0019 |
| GO:0060134 | prepulse inhibition | 6 | 13 | 0.0020 |
| GO:0110053 | regulation of actin filament organization | 2 | 199 | 0.0021 |
| GO:0032102 | negative regulation of response to external stimulus | 2 | 230 | 0.0022 |
|  |  |  |  |  |
| **Supplementary Table 3** (*continued*) | |  |  |  |
| GO:0042572 | retinol metabolic process | 3 | 34 | 0.0023 |
| GO:0030855 | epithelial cell differentiation | 4 | 196 | 0.0024 |
| GO:0006805 | xenobiotic metabolic process | 3 | 79 | 0.0026 |
| GO:0006066 | alcohol metabolic process | 2 | 335 | 0.0028 |
| GO:0044282 | small molecule catabolic process | 3 | 412 | 0.0033 |
| GO:0034035 | purine ribonucleoside bisphosphate metabolic process | 2 | 26 | 0.0036 |
| GO:0110110 | positive regulation of animal organ morphogenesis | 5 | 7 | 0.0038 |
| GO:1901615 | organic hydroxy compound metabolic process | 3 | 478 | 0.0042 |
| GO:0034754 | cellular hormone metabolic process | 2 | 85 | 0.0045 |
| GO:0030155 | regulation of cell adhesion | 2 | 407 | 0.0047 |
| GO:0050878 | regulation of body fluid levels | 3 | 146 | 0.0048 |
| GO:0050807 | regulation of synapse organization | 3 | 207 | 0.0052 |
| GO:0031333 | negative regulation of protein-containing complex assembly | 2 | 114 | 0.0054 |
| GO:0019935 | cyclic-nucleotide-mediated signaling | 5 | 108 | 0.0056 |
| GO:0120254 | olefinic compound metabolic process | 2 | 75 | 0.0108 |
| GO:0015800 | acidic amino acid transport | 6 | 41 | 0.0114 |
| GO:0010817 | regulation of hormone levels | 3 | 383 | 0.0118 |
| GO:0050907 | detection of chemical stimulus involved in sensory perception | 2 | 16 | 0.0132 |
| GO:0060049 | regulation of protein glycosylation | 4 | 20 | 0.0134 |
| GO:0071425 | hematopoietic stem cell proliferation | 2 | 7 | 0.0137 |
| GO:0042472 | inner ear morphogenesis | 4 | 28 | 0.0140 |
| GO:0019932 | second-messenger-mediated signaling | 2 | 210 | 0.0141 |
| GO:0045058 | T cell selection | 2 | 7 | 0.0144 |
| GO:0007218 | neuropeptide signaling pathway | 2 | 64 | 0.0146 |
| GO:0048935 | peripheral nervous system neuron development | 2 | 10 | 0.0148 |
| GO:0021537 | telencephalon development | 2 | 21 | 0.0149 |
| GO:1902903 | regulation of supramolecular fiber organization | 2 | 304 | 0.0151 |
| GO:0031532 | actin cytoskeleton reorganization | 2 | 49 | 0.0158 |
| GO:0045216 | cell-cell junction organization | 3 | 126 | 0.0192 |
| GO:0022407 | regulation of cell-cell adhesion | 2 | 189 | 0.0195 |
| GO:0009653 | anatomical structure morphogenesis | 2 | 1205 | 0.0210 |
| GO:0060070 | canonical Wnt signaling pathway | 6 | 33 | 0.0222 |
| GO:0030834 | regulation of actin filament depolymerization | 3 | 36 | 0.0262 |
| GO:0034110 | regulation of homotypic cell-cell adhesion | 3 | 30 | 0.0269 |
| GO:1900016 | negative regulation of cytokine production involved in inflammatory response | 2 | 7 | 0.0272 |
| GO:0009247 | glycolipid biosynthetic process | 2 | 63 | 0.0273 |
| GO:0007160 | cell-matrix adhesion | 3 | 78 | 0.0307 |
| GO:0060124 | positive regulation of growth hormone secretion | 2 | 6 | 0.0312 |
| GO:0090183 | regulation of kidney development | 4 | 8 | 0.0317 |
| GO:0070371 | ERK1 and ERK2 cascade | 6 | 10 | 0.0322 |
| GO:0060485 | mesenchyme development | 4 | 22 | 0.0349 |
| GO:0007162 | negative regulation of cell adhesion | 2 | 167 | 0.0353 |
| GO:0060563 | neuroepithelial cell differentiation | 6 | 6 | 0.0370 |
| GO:1905332 | positive regulation of morphogenesis of an epithelium | 2 | 9 | 0.0450 |
| GO:0015849 | organic acid transport | 7 | 202 | 0.0457 |
| GO:0007610 | behavior | 1 | 504 | 0.0470 |
|  |  |  |  |  |
| **Supplementary Table 3** (*continued*) | |  |  |  |
| GO:0051241 | negative regulation of multicellular organismal process | 4 | 526 | 0.0488 |
| GO:0006694 | steroid biosynthetic process | 2 | 123 | 0.0489 |
| GO:0034330 | cell junction organization | 2 | 331 | 0.0494 |
| GO:0022408 | negative regulation of cell-cell adhesion | 2 | 76 | 0.0494 |

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**Supplementary Figure 7. Differentially expressed genes between MNP conditions and the control in mantle, hemocytes and pearl sac of *P. margaritifera* after a 5-month exposure to micro-nanoplastics.** Volcano plot showing expression of differentially expressed genes between MNP conditions (0.025 and 1 µg L–1) compared to the control (|log2FC| > 2; FDR < 0.01) with a *P*adj < 0.05 used as the threshold to judge the significance of the difference in gene expression in (**a**) mantle (**b**) hemocytes and (**c**) pearl sac. Blue plots represent downregulated genes; red plots represent upregulated genes and gray plots represent genes with no significant difference.

**Supplementary Table 4.** Differentially expressed genes (DEGs) across MNP conditions (0.025 and 1 µg L–1) compared with the control condition identified in modules of interest from WGCNA performed on mantle samples sequencing dataset.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **MNP condition** | **Sharing DEG** | **Sequencing gene ID** | **Log2FC** | ***P*adj** | **Uniprot *sp.*** | **Uniprot ID** |
| * **Turquoise module** | | | | | | |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2282size117561.2 | -3.47 | 2.63E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7792size68911.4 | -3.42 | 2.84E-03 | MOUSE | *NCAM2* |
| 0.025 / Ctrl | Common | evm.TU.scaffold460size299527.3 | -3.06 | 4.13E-02 | ACRMI | *CADN* |
| 0.025 / Ctrl | Common | evm.TU.scaffold1472size116207.6 | -2.89 | 3.70E-03 | METSE | *CALM* |
| 0.025 / Ctrl | Common | evm.TU.scaffold10887size56046.3 | -2.82 | 3.70E-03 | RAT | *LR74A* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold556size242659.10 | -2.81 | 1.18E-02 | MYTGA | *PLCL* |
| 0.025 / Ctrl | Common | evm.TU.scaffold10132size55633.1 | -2.53 | 1.26E-02 | XENLA | *ZMY10* |
| 0.025 / Ctrl | Common | evm.TU.scaffold5130size104591.3 | -2.52 | 1.34E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold7826size43469.2 | -2.43 | 1.10E-03 | BLAGE | *GST1* |
| 0.025 / Ctrl | Common | evm.TU.scaffold1520size200124.4 | -2.39 | 7.76E-03 | XENLA | *CRHBP* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold670size250180.11 | -2.37 | 2.20E-02 | NEMVE | *CIAO1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold13117size21283.1 | -2.30 | 2.15E-02 | PINMG | *PLSP* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3650size121286.1 | -2.27 | 4.13E-02 | MOUSE | *SO4C1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold538size272809.12 | -2.14 | 4.88E-02 | HUMAN | *CHIT1* |
| 0.025 / Ctrl | Common | evm.TU.scaffold2782size126472.5 | -2.08 | 1.07E-02 | HUMAN | *ANR50* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2782size126472.1 | -1.90 | 3.49E-02 | HUMAN | *LR74A* |
| 0.025 / Ctrl | Common | evm.TU.scaffold274size189192.2 | -1.87 | 4.41E-02 | PIG | *GGLO* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1550size128617.3 | -1.62 | 3.57E-02 | CAEEL | *PDE5* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1520size200124.2 | -1.57 | 2.53E-03 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold813size224748.4 | -1.51 | 2.74E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold1174size268520.11 | -1.47 | 1.86E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold486size164273.5 | -1.44 | 9.80E-05 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold410size171622.1 | -1.39 | 2.01E-02 | DROME | *GC76C* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold6926size48685.2 | -1.35 | 4.63E-02 | HUMAN | *CBPC2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold392size205118.3 | -1.34 | 6.85E-03 | DROME | *CPO* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold13755size19307.2 | -1.30 | 3.38E-02 | HUMAN | *MRM1* |
| 0.025 / Ctrl | Common | evm.TU.scaffold1280size446155.31 | -1.28 | 3.49E-02 | XENLA | *CE152* |
| 0.025 / Ctrl | Common | evm.TU.scaffold1523size134303.2 | -1.27 | 1.79E-02 | MOUSE | *RSPO2* |
| 0.025 / Ctrl | Common | evm.TU.scaffold2120size147150.8 | -1.22 | 3.61E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7149size67001.1 | -1.18 | 4.15E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold4715size154169.2 | -1.17 | 3.32E-02 | MOUSE | *NIM1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8450size40129.2 | -1.11 | 3.97E-02 | CAEEL | *CEX2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5824size123299.3 | -1.03 | 2.52E-02 | HUMAN | *HERC1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3605size77135.2 | -4.68 | 2.86E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold11951size25182.10 | -3.68 | 4.66E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5027size97772.4 | -3.42 | 4.63E-02 | ACRMI | *MLRP2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5957size328954.4 | -3.40 | 1.75E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7195size65380.3 | -3.32 | 8.34E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1500size115322.2 | -3.29 | 4.11E-02 | BOVIN | *CD63* |
| 1 / Ctrl | Common | evm.TU.scaffold460size299527.3 | -3.12 | 1.47E-02 | ACRMI | *CADN* |
|  | | | | | | |
| **Supplementary Table 4** (*continued*) | | | | | | |
| 1 / Ctrl | Non-common | evm.TU.scaffold3500size108302.6 | -3.08 | 2.23E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8287size40987.2 | -3.06 | 2.09E-02 | EPHMU | *CAS4* |
| 1 / Ctrl | Common | evm.TU.scaffold1472size116207.6 | -3.02 | 7.02E-04 | METSE | *CALM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5009size125620.3 | -3.01 | 4.14E-02 | HUMAN | *PFD2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2994size85130.2 | -2.95 | 4.32E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold12753size22481.4 | -2.87 | 1.98E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3542size77893.2 | -2.80 | 1.98E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1634size311462.7 | -2.79 | 3.65E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold5130size104591.3 | -2.78 | 1.17E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7224size46994.4 | -2.77 | 9.15E-08 | HUMAN | *HEBP2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6290size68442.3 | -2.73 | 2.18E-02 | BRAFL | *FUCO* |
| 1 / Ctrl | Common | evm.TU.scaffold10887size56046.3 | -2.71 | 2.30E-03 | RAT | *LR74A* |
| 1 / Ctrl | Common | evm.TU.scaffold10132size55633.1 | -2.71 | 1.69E-03 | XENLA | *ZMY10* |
| 1 / Ctrl | Common | evm.TU.scaffold1520size200124.4 | -2.63 | 7.28E-04 | XENLA | *CRHBP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9515size85861.3 | -2.62 | 3.94E-02 | CAEEL | *ARF12* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4607size257860.4 | -2.58 | 1.57E-03 | NEOPA | *XYNB* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1007size132311.14 | -2.52 | 4.14E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1320size225772.10 | -2.49 | 6.86E-03 | CHICK | *MOXD1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3098size175394.6 | -2.47 | 6.07E-03 | BOVIN | *SE6L2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold646size212683.7 | -2.42 | 4.49E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3856size74363.3 | -2.41 | 2.07E-03 | BOVIN | *TEKT3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10440size30953.1 | -2.40 | 5.19E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1323size145704.4 | -2.39 | 2.18E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3246size246367.21 | -2.39 | 2.30E-03 | MOUSE | *LMX1B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4870size90196.3 | -2.38 | 4.27E-02 | DROME | *HIL* |
| 1 / Ctrl | Non-common | evm.TU.scaffold76size343677.22 | -2.36 | 1.00E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1680size293446.12 | -2.32 | 4.32E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3930size73502.1 | -2.27 | 1.01E-02 | XENTR | *ANKR1* |
| 1 / Ctrl | Common | evm.TU.scaffold274size189192.2 | -2.27 | 1.57E-03 | PIG | *GGLO* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4646size66185.1 | -2.27 | 4.86E-03 | HUMAN | *DTHD1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1203size265927.9 | -2.25 | 1.23E-02 | MOUSE | *STMN2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2679size89875.3 | -2.13 | 3.66E-02 | DROME | *PERC* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5224size119327.1 | -2.13 | 2.21E-02 | HUMAN | *CG031* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2440size155032.13 | -2.10 | 1.04E-02 | THACU | *LAC3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11153size28117.2 | -2.05 | 1.47E-02 | RAT | *TGM1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold628size555846.12 | -2.00 | 4.45E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold213size200314.6 | -1.99 | 4.22E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2654size138451.1 | -1.99 | 4.74E-03 | CAEEL | *CPLX1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3765size102138.2 | -1.99 | 1.64E-02 | MOUSE | *ASB16* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4017size72682.1 | -1.98 | 1.34E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3979size95817.2 | -1.97 | 3.00E-02 | HUMAN | *MOT12* |
| 1 / Ctrl | Non-common | evm.TU.scaffold12597size42776.3 | -1.96 | 4.35E-03 | MOUSE | *RSPH1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7734size44023.2 | -1.95 | 1.57E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1538size192633.5 | -1.94 | 1.44E-02 | CAEEL | *UNC22* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9079size64000.2 | -1.92 | 4.27E-02 | HUMAN | *DYH7* |
| 1 / Ctrl | Non-common | evm.TU.scaffold188size206906.5 | -1.90 | 3.11E-02 | LYMST | *MYOM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7991size81123.4 | -1.89 | 3.49E-02 | NA | NA |
|  | | | | | | |
| **Supplementary Table 4** (*continued*) | | | | | | |
| 1 / Ctrl | Non-common | evm.TU.scaffold695size399694.13 | -1.89 | 1.64E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold14873size16104.1 | -1.88 | 2.00E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7907size43009.11 | -1.87 | 1.03E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1198size224948.9 | -1.86 | 3.29E-02 | VILV2 | *POL* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2908size86298.2 | -1.85 | 3.69E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3889size73985.2 | -1.84 | 4.23E-02 | MACFA | *DZAN1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold336size211905.15 | -1.82 | 3.10E-02 | HUMAN | *FCN1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1906size173792.7 | -1.82 | 2.21E-03 | HUMAN | *WSB1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2120size147150.9 | -1.78 | 5.93E-04 | DROYA | *PER* |
| 1 / Ctrl | Common | evm.TU.scaffold7826size43469.2 | -1.78 | 2.31E-02 | BLAGE | *GST1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2158size160354.12 | -1.75 | 3.89E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1026size247016.2 | -1.75 | 4.16E-02 | BOVIN | *LEG9* |
| 1 / Ctrl | Common | evm.TU.scaffold2782size126472.5 | -1.75 | 2.61E-02 | HUMAN | *ANR50* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5090size62038.6 | -1.75 | 3.51E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1027size182162.1 | -1.74 | 9.15E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3256size155363.1 | -1.73 | 2.34E-02 | SCHAM | *ANNU* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11396size27145.2 | -1.73 | 3.29E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5050size86062.2 | -1.72 | 4.31E-02 | MOUSE | *PXDN* |
| 1 / Ctrl | Non-common | evm.TU.scaffold637size177620.6 | -1.71 | 7.44E-03 | STRPU | *FBP1* |
| 1 / Ctrl | Common | evm.TU.scaffold813size224748.4 | -1.70 | 1.82E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold31size304358.11 | -1.70 | 2.23E-02 | HUMAN | *NWD2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2120size147150.7 | -1.68 | 1.04E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2148size296962.7 | -1.66 | 3.78E-02 | XENLA | *TEKT4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6434size52003.1 | -1.65 | 4.16E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5707size57206.1 | -1.65 | 2.84E-02 | CHICK | *EMC1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1121size199104.8 | -1.65 | 4.30E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5009size125620.1 | -1.64 | 2.23E-02 | HUMAN | *SSNA1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold850size206783.7 | -1.63 | 2.35E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold12690size49544.1 | -1.62 | 3.99E-02 | HUMAN | *HELZ2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6209size89422.1 | -1.61 | 4.91E-03 | HUMAN | *ZMY12* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2802size169182.3 | -1.61 | 1.85E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2026size102104.8 | -1.60 | 2.79E-02 | HUMAN | *ANR63* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11744size25915.3 | -1.60 | 1.59E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1471size234825.3 | -1.59 | 3.38E-02 | RAT | *TBA1A* |
| 1 / Ctrl | Common | evm.TU.scaffold486size164273.5 | -1.59 | 5.00E-06 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1444size196405.7 | -1.59 | 4.66E-02 | BOMMO | *EXD1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7924size79650.2 | -1.56 | 3.19E-02 | RAT | *TBA1A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold112size675390.27 | -1.55 | 3.78E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6949size137242.7 | -1.54 | 4.84E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold1174size268520.11 | -1.52 | 5.19E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4367size111109.1 | -1.52 | 3.67E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1866size105213.8 | -1.52 | 3.00E-02 | MOUSE | *FHAD1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9784size33764.1 | -1.51 | 9.67E-03 | HUMAN | *ANR66* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4626size149477.4 | -1.51 | 9.07E-03 | MOUSE | *STPG3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2627size90695.3 | -1.50 | 3.00E-02 | DROME | *CANB* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1802size107121.5 | -1.50 | 1.47E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7961size42695.1 | -1.49 | 2.10E-02 | MACFA | *AXDN1* |
|  | | | | | | |
| **Supplementary Table 4** (*continued*) | | | | | | |
| 1 / Ctrl | Non-common | evm.TU.scaffold12729size22574.1 | -1.49 | 4.79E-02 | MOUSE | *KITH* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5921size55650.4 | -1.48 | 4.22E-02 | DANRE | *CF161* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1298size186980.4 | -1.47 | 2.56E-02 | HUMAN | *M21D2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11369size27302.2 | -1.46 | 1.74E-02 | HUMAN | *ACHA3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10308size55656.6 | -1.44 | 3.99E-02 | HUMAN | *ENKUR* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8267size41080.3 | -1.43 | 1.44E-02 | MOUSE | *PTPRM* |
| 1 / Ctrl | Common | evm.TU.scaffold410size171622.1 | -1.43 | 5.00E-03 | DROME | *GC76C* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1430size117431.3 | -1.43 | 3.78E-03 | HUMAN | *ABCA1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold46size318859.15 | -1.43 | 4.32E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5634size57725.1 | -1.43 | 2.57E-02 | HUMAN | *SACS* |
| 1 / Ctrl | Non-common | evm.TU.scaffold789size245146.23 | -1.42 | 4.04E-02 | XENTR | *ODF3A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4384size136806.1 | -1.42 | 2.76E-02 | STRPU | *TBB* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1472size116207.2 | -1.41 | 4.27E-02 | LUMRU | *CALM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2326size392610.8 | -1.41 | 4.46E-02 | DANRE | *CP135* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6655size50433.2 | -1.41 | 1.77E-02 | HUMAN | *CI135* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5563size58257.2 | -1.40 | 3.19E-02 | HUMAN | *EFHC1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4431size68472.3 | -1.40 | 4.11E-02 | DANRE | *EFHC2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5171size61321.2 | -1.40 | 4.46E-02 | HUMAN | *CC173* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1089size185187.1 | -1.39 | 1.41E-02 | PIG | *SUCB2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10980size28775.1 | -1.39 | 2.56E-02 | HUMAN | *STKL1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10710size29754.5 | -1.39 | 3.69E-02 | RAT | *F13A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4384size136806.2 | -1.38 | 3.29E-02 | LYTPI | *TBB* |
| 1 / Ctrl | Common | evm.TU.scaffold1523size134303.2 | -1.38 | 1.93E-03 | MOUSE | *RSPO2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold815size266289.1 | -1.38 | 4.91E-03 | MOUSE | *ZAN* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2578size177840.3 | -1.38 | 1.36E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold518size431291.5 | -1.37 | 3.99E-02 | RICFE | *Y580* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1319size120382.1 | -1.37 | 4.61E-02 | MOUSE | *KIF9* |
| 1 / Ctrl | Common | evm.TU.scaffold2120size147150.8 | -1.36 | 4.86E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold637size177620.4 | -1.36 | 8.74E-04 | STRPU | *FBP3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold432size238846.15 | -1.36 | 4.05E-02 | MOUSE | *GPV* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2743size200640.4 | -1.34 | 4.05E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold11133size58585.6 | -1.34 | 3.33E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold304size184890.1 | -1.33 | 3.70E-02 | SCHAM | *ANNU* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2300size96173.4 | -1.33 | 9.31E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5659size115446.3 | -1.32 | 4.57E-02 | HUMAN | *TEKT1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold125size413603.34 | -1.32 | 9.07E-03 | CVHN1 | *R1A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8336size101972.4 | -1.31 | 4.48E-02 | RAT | *K895L* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11274size27659.1 | -1.31 | 4.78E-02 | HUMAN | *PTPRT* |
| 1 / Ctrl | Non-common | evm.TU.scaffold17134size9437.1 | -1.31 | 3.98E-02 | HUMAN | *IQCG* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5701size57243.3 | -1.29 | 4.51E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6382size52386.1 | -1.29 | 5.58E-03 | RAT | *LEXM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold682size148060.6 | -1.28 | 3.48E-02 | DANRE | *C2512* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2202size278870.8 | -1.28 | 4.31E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2610size137834.5 | -1.27 | 4.44E-02 | MACFA | *IQUB* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3189size104933.3 | -1.27 | 4.38E-02 | HUMAN | *SPAS1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold720size228729.12 | -1.26 | 1.68E-02 | MOUSE | *GRAN* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4710size123841.1 | -1.25 | 4.84E-02 | NA | NA |
|  | | | | | | |
| **Supplementary Table 4** (*continued*) | | | | | | |
| 1 / Ctrl | Non-common | evm.TU.scaffold4505size150176.5 | -1.25 | 4.05E-02 | MOUSE | *RSH3B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold14275size36645.2 | -1.25 | 2.34E-02 | MOUSE | *CFA58* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1617size112222.5 | -1.25 | 1.44E-02 | HUMAN | *VWA3B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2605size181081.8 | -1.24 | 2.62E-02 | HUMAN | *ARMC3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1147size838866.2 | -1.23 | 2.41E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold198size204315.2 | -1.23 | 4.06E-02 | MOUSE | *TEX26* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1031size131350.6 | -1.21 | 3.99E-02 | RAT | *LR74A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold175size299376.1 | -1.21 | 5.00E-03 | HUMAN | *WSB1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7783size43717.1 | -1.21 | 3.43E-02 | HUMAN | *GRAN* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2756size88728.1 | -1.20 | 4.16E-02 | HUMAN | *LRC72* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6780size235009.14 | -1.20 | 5.12E-04 | HUMAN | *PGFS* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1437size117226.3 | -1.20 | 4.76E-02 | CHLRE | *DYH1B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1205size150501.3 | -1.19 | 3.59E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8352size63603.2 | -1.18 | 3.78E-02 | HUMAN | *MYO3A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1131size175864.3 | -1.18 | 3.78E-02 | HUMAN | *KAD9* |
| 1 / Ctrl | Non-common | evm.TU.scaffold796size284195.5 | -1.18 | 4.04E-02 | DANRE | *LARG2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1718size205308.5 | -1.17 | 3.53E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold1280size446155.31 | -1.16 | 3.29E-02 | XENLA | *CE152* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3867size409801.10 | -1.16 | 2.75E-02 | XENLA | *CCNF* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1184size197641.11 | -1.16 | 4.04E-02 | BOVIN | *TPMT* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1794size145318.5 | -1.16 | 4.73E-02 | MACFA | *CCD96* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1704size161865.4 | -1.15 | 2.40E-02 | HUMAN | *FA47E* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1617size112222.6 | -1.15 | 2.76E-02 | HUMAN | *VWA3B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6730size147307.1 | -1.13 | 3.89E-02 | SAGLB | *ASPM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold46size318859.11 | -1.10 | 6.35E-03 | MOUSE | *CO6A6* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11086size92184.1 | -1.09 | 3.03E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2157size244387.4 | -1.08 | 3.97E-02 | DROME | *DLL* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2400size294214.10 | -1.08 | 4.46E-02 | BOVIN | *ANXA6* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3834size181686.2 | -1.07 | 3.99E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1947size217951.13 | -1.06 | 4.27E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6051size132328.4 | -1.06 | 4.11E-02 | XENLA | *NOCT* |
| 1 / Ctrl | Non-common | evm.TU.scaffold13839size19094.1 | -1.06 | 4.05E-02 | MOUSE | *DCLK1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1303size315076.16 | -1.05 | 3.26E-02 | XENLA | *PGS1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold14823size27136.1 | -1.05 | 4.91E-02 | HUMAN | *IQCA1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4133size128356.1 | -1.02 | 4.85E-02 | HUMAN | *PNKP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8881size78301.3 | -1.02 | 1.51E-03 | CHICK | *5NTC* |
| 1 / Ctrl | Common | evm.TU.scaffold4715size154169.2 | -1.00 | 4.30E-02 | MOUSE | *NIM1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7948size42762.3 | -1.00 | 5.24E-04 | MOUSE | *TRIM2* |
| * **Blue module** | | | | | | |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7986size42548.1 | 2.04 | 4.73E-02 | ARATH | *USPAL* |
| 0.025 / Ctrl | Common | evm.TU.scaffold211size252336.1 | 1.41 | 4.13E-02 | RAT | *MRC2* |
| 1 / Ctrl | Common | evm.TU.scaffold211size252336.1 | 1.28 | 3.99E-02 | RAT | *MRC2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2212size97855.2 | -1.03 | 4.04E-02 | HUMAN | *FAT4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11857size74220.2 | -1.06 | 4.05E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6770size108272.1 | -1.23 | 4.19E-02 | DICDI | *MKCD* |
|  | | | | | | |
| **Supplementary Table 4** (*continued*) | | | | | | |
| 1 / Ctrl | Non-common | evm.TU.scaffold2313size96057.1 | -1.32 | 4.31E-02 | DROME | *DUOX* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1577size270204.4 | -1.46 | 4.63E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold15032size15714.1 | -1.58 | 1.21E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold908size168178.1 | -1.69 | 2.46E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8527size135830.4 | -1.90 | 1.03E-03 | MOUSE | *GCH1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold264size320753.24 | -1.96 | 1.10E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold9119size116109.8 | -1.97 | 4.78E-02 | MOUSE | *LGR6* |
| 1 / Ctrl | Non-common | evm.TU.scaffold264size320753.25 | -1.98 | 4.31E-02 | CRIGR | *TLR2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold815size266289.2 | -2.15 | 4.27E-02 | MOUSE | *KCP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2082size139968.2 | -2.27 | 3.19E-02 | HUMAN | *ANGL7* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1068size322763.10 | -2.33 | 4.67E-02 | HUMAN | *FCGBP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5648size169074.4 | -4.27 | 1.98E-04 | DROME | *TBH1* |
| * **Darkturquoise module** | | | | | | |
| 1 / Ctrl | Non-common | evm.TU.scaffold258size299806.9 | -1.07 | 3.49E-02 | NA | NA |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | * **Darkgreen module** | | | | | | | | 0.025 / Ctrl | Common | evm.TU.scaffold2612size116661.2 | -4.06 | 1.83E-05 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold2383size182244.4 | -3.51 | 1.79E-02 | HUMAN | *CELR2* | | 0.025 / Ctrl | Common | evm.TU.scaffold2108size145499.4 | -3.06 | 7.98E-03 | HUMAN | *FAT1* | | 0.025 / Ctrl | Common | evm.TU.scaffold5595size58030.2 | -3.05 | 1.37E-02 | NA | NA | | 0.025 / Ctrl | Non-common | evm.TU.scaffold5793size56674.1 | -3.04 | 3.57E-02 | HUMAN | *VWDE* | | 0.025 / Ctrl | Common | evm.TU.scaffold10747size58510.3 | -2.99 | 1.09E-03 | DANRE | *ODF3B* | | 0.025 / Ctrl | Non-common | evm.TU.scaffold240size211441.8 | -2.97 | 3.19E-02 | RAT | *WFD18* | | 0.025 / Ctrl | Common | evm.TU.scaffold16833size10418.1 | -2.77 | 3.51E-02 | DANRE | *CDHR1* | | 0.025 / Ctrl | Non-common | evm.TU.scaffold240size211441.7 | -2.75 | 1.36E-02 | HUMAN | *VWDE* | | 0.025 / Ctrl | Common | evm.TU.scaffold69size251715.7 | -2.62 | 5.62E-03 | DROME | *RYAR* | | 0.025 / Ctrl | Common | evm.TU.scaffold2944size186744.16 | -2.45 | 9.73E-03 | HUMAN | *PCDH9* | | 0.025 / Ctrl | Common | evm.TU.scaffold1047size340248.4 | -1.90 | 3.49E-02 | NA | NA | | 0.025 / Ctrl | Non-common | evm.TU.scaffold8293size79692.4 | -1.75 | 4.53E-02 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold7160size101947.5 | -1.66 | 3.20E-02 | DANRE | *CDHR1* | | 0.025 / Ctrl | Non-common | evm.TU.scaffold3375size152648.8 | -1.60 | 3.06E-02 | DICDI | *CALM* | | 1 / Ctrl | Non-common | evm.TU.scaffold2108size145499.3 | -4.70 | 1.98E-02 | HUMAN | *FAT4* | | 1 / Ctrl | Common | evm.TU.scaffold2108size145499.4 | -3.79 | 5.14E-05 | HUMAN | *FAT1* | | 1 / Ctrl | Common | evm.TU.scaffold2612size116661.2 | -3.68 | 9.85E-05 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold16833size10418.1 | -3.61 | 3.09E-04 | DANRE | *CDHR1* | | 1 / Ctrl | Non-common | evm.TU.scaffold1067size129500.1 | -3.41 | 5.77E-03 | NA | NA | | 1 / Ctrl | Non-common | evm.TU.scaffold984size332810.1 | -3.39 | 4.80E-03 | NA | NA | | 1 / Ctrl | Non-common | evm.TU.scaffold4421size170941.6 | -3.30 | 7.85E-03 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold10747size58510.3 | -3.30 | 5.14E-05 | DANRE | *ODF3B* | | 1 / Ctrl | Non-common | evm.TU.scaffold10319size85128.6 | -3.27 | 2.73E-02 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold2383size182244.4 | -3.27 | 1.43E-02 | HUMAN | *CELR2* | | 1 / Ctrl | Common | evm.TU.scaffold5595size58030.2 | -3.13 | 3.39E-03 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold2944size186744.16 | -2.98 | 1.03E-04 | HUMAN | *PCDH9* | | 1 / Ctrl | Non-common | evm.TU.scaffold5775size102228.5 | -2.49 | 2.23E-02 | DROME | *GSC* | | 1 / Ctrl | Non-common | evm.TU.scaffold11346size27402.1 | -2.49 | 2.12E-02 | ORYSJ | *CALM2* | |  |  |  |  |  |  |  | | **Supplementary Table 4** (*continued*) | | |  |  |  |  | | 1 / Ctrl | Non-common | evm.TU.scaffold7164size47312.3 | -2.38 | 3.33E-02 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold1047size340248.4 | -2.07 | 5.19E-03 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold69size251715.7 | -2.04 | 3.26E-02 | DROME | *RYAR* | | 1 / Ctrl | Non-common | evm.TU.scaffold12250size24140.1 | -1.80 | 1.08E-02 | DROME | *ACH1* | | 1 / Ctrl | Non-common | evm.TU.scaffold2069size138995.8 | -1.78 | 1.43E-02 | NA | NA | | 1 / Ctrl | Non-common | evm.TU.scaffold8670size39024.1 | -1.76 | 1.65E-02 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold7160size101947.5 | -1.61 | 1.65E-02 | DANRE | *CDHR1* | | 1 / Ctrl | Non-common | evm.TU.scaffold1190size145671.3 | -1.60 | 4.90E-02 | NA | NA | | 1 / Ctrl | Non-common | evm.TU.scaffold521size160855.1 | -1.29 | 2.56E-02 | MOUSE | *WNT6* | | 1 / Ctrl | Non-common | evm.TU.scaffold2625size211361.5 | -1.09 | 9.50E-03 | RAT | *LHX5* | | * **Darkgrey module** | | | | | | | | 0.025 / Ctrl | Common | evm.TU.scaffold5737size147992.4 | -10.22 | 1.19E-13 | PLAYO | *CSP* | | 0.025 / Ctrl | Common | evm.TU.scaffold2059size101583.8 | -9.83 | 2.75E-12 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold3140size111674.1 | -8.82 | 1.05E-08 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold1765size248259.2 | -7.66 | 9.60E-06 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold12797size22360.1 | -7.52 | 9.65E-07 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold200size231477.1 | -6.87 | 6.89E-06 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold6483size290382.9 | -6.17 | 3.25E-04 | HUMAN | *LOXH1* | | 0.025 / Ctrl | Non-common | evm.TU.scaffold3140size111674.2 | -5.23 | 2.52E-02 | PINMA | *GRP3* | | 0.025 / Ctrl | Common | evm.TU.scaffold2106size257207.9 | -5.19 | 3.96E-05 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold821size195697.10 | -5.14 | 3.15E-04 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold50size263963.6 | -5.10 | 2.53E-05 | PINMG | *PLSP* | | 0.025 / Ctrl | Non-common | evm.TU.scaffold2330size266946.11 | -3.60 | 3.70E-03 | PINMG | *KCP2* | | 0.025 / Ctrl | Non-common | evm.TU.scaffold1181size313700.16 | -2.24 | 1.84E-02 | NA | NA | | 0.025 / Ctrl | Common | evm.TU.scaffold269size275974.15 | -1.84 | 4.63E-02 | HUMAN | *SNED1* | | 1 / Ctrl | Common | evm.TU.scaffold5737size147992.4 | -9.92 | 3.31E-13 | PLAYO | *CSP* | | 1 / Ctrl | Common | evm.TU.scaffold2059size101583.8 | -9.19 | 5.61E-11 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold6483size290382.9 | -6.44 | 5.14E-05 | HUMAN | *LOXH1* | | 1 / Ctrl | Common | evm.TU.scaffold1765size248259.2 | -6.13 | 7.28E-04 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold12797size22360.1 | -5.51 | 8.64E-04 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold3140size111674.1 | -4.73 | 1.64E-02 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold2106size257207.9 | -4.54 | 3.86E-04 | NA | NA | | 1 / Ctrl | Non-common | evm.TU.scaffold1310size120650.5 | -4.39 | 4.86E-03 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold50size263963.6 | -4.30 | 5.59E-04 | PINMG | *PLSP* | | 1 / Ctrl | Common | evm.TU.scaffold200size231477.1 | -3.97 | 3.49E-02 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold821size195697.10 | -3.84 | 9.91E-03 | NA | NA | | 1 / Ctrl | Non-common | evm.TU.scaffold8841size45349.2 | -2.41 | 3.00E-02 | HUMAN | *HIPL2* | | 1 / Ctrl | Non-common | evm.TU.scaffold602size184052.6 | -2.37 | 2.91E-02 | NA | NA | | 1 / Ctrl | Common | evm.TU.scaffold269size275974.15 | -1.87 | 1.85E-02 | HUMAN | *SNED1* | | 1 / Ctrl | Non-common | evm.TU.scaffold5152size61452.2 | -1.79 | 3.09E-02 | NA | NA |  * **Brown module** | | | | | | |
| 0.025 / Ctrl | Common | evm.TU.scaffold43size421361.3 | 2.61 | 3.61E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold7152size47383.1 | 2.32 | 3.38E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1886size104796.7 | 1.70 | 4.53E-03 | MOUSE | *TIMP3* |
|  |  |  |  |  |  |  |
| **Supplementary Table 4** (*continued*) | | |  |  |  |  |
| 0.025 / Ctrl | Common | evm.TU.scaffold2796size88200.2 | 1.39 | 4.18E-02 | RAT | *SQSTM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3135size191244.13 | 3.39 | 2.48E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4691size150772.6 | 3.26 | 3.00E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2520size198016.9 | 3.23 | 9.44E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold195size421668.4 | 3.05 | 3.59E-02 | DROME | *ORCT* |
| 1 / Ctrl | Non-common | evm.TU.scaffold589size246915.7 | 2.88 | 3.99E-02 | PINMG | *USP11* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4038size138132.1 | 2.68 | 4.05E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7389size103885.2 | 2.67 | 4.22E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold9793size46053.1 | 2.61 | 4.32E-02 | RENRE | *CALM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4719size195833.2 | 2.39 | 4.78E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold7152size47383.1 | 2.39 | 9.07E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold43size421361.3 | 2.28 | 4.31E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold15973size12996.1 | 2.13 | 3.69E-02 | RAT | *S22A1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold954size354069.4 | 2.12 | 4.11E-02 | DANRE | *CHSTB* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10557size30422.4 | 1.92 | 4.04E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold14275size36645.1 | 1.91 | 4.46E-02 | DANRE | *PPR3B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9061size109501.3 | 1.89 | 5.92E-03 | ARATH | *CNIF3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1051size221401.11 | 1.88 | 9.44E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2334size95770.5 | 1.84 | 2.21E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold17038size9778.1 | 1.79 | 2.10E-02 | HUMAN | *CHK2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7295size46532.3 | 1.77 | 5.24E-04 | CRIGR | *ASNS* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1347size133901.9 | 1.77 | 4.39E-02 | HUMAN | *TYSY* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2293size159229.6 | 1.65 | 3.69E-02 | MOUSE | *ANPRA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10540size30515.2 | 1.57 | 9.21E-06 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold331size210939.5 | 1.52 | 6.07E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold2796size88200.2 | 1.49 | 9.07E-03 | RAT | *SQSTM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold669size217235.14 | 1.48 | 3.35E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2289size96356.2 | 1.44 | 2.48E-03 | RAT | *ACOX1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold331size210939.6 | 1.43 | 9.39E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold331size210939.7 | 1.42 | 3.13E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold804size228196.3 | 1.39 | 3.69E-02 | DANRE | *CHST1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10998size55334.1 | 1.33 | 3.78E-02 | CHICK | *HENMT* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2763size110907.3 | 1.31 | 4.31E-02 | PONAB | *GUAD* |
| 1 / Ctrl | Non-common | evm.TU.scaffold20size301897.8 | 1.29 | 3.59E-02 | MOUSE | *PTPRK* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3153size131015.3 | 1.27 | 3.25E-02 | HUMAN | *NCKX4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6202size53514.4 | 1.19 | 1.44E-02 | HUMAN | *NCKX4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5648size169074.2 | 1.15 | 4.78E-02 | MOUSE | *CO6A4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6645size79183.4 | 1.10 | 2.10E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5864size56104.1 | 1.07 | 4.05E-02 | XENTR | *RN126* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6245size92827.2 | 1.06 | 3.53E-02 | NA | NA |
| * **Tan module** | | | | | | |
| 0.025 / Ctrl | Common | evm.TU.scaffold7405size45879.10 | 5.12 | 3.19E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold4668size197402.2 | 4.16 | 3.54E-02 | HUMAN | *HDHD5* |
| 0.025 / Ctrl | Common | evm.TU.scaffold547size159297.1 | 4.07 | 1.34E-02 | PONAB | *CRYAB* |
| 0.025 / Ctrl | Common | evm.TU.scaffold8768size38583.2 | 3.44 | 4.13E-02 | HUMAN | *HDHD5* |
|  |  |  |  |  |  |  |
| **Supplementary Table 4** (*continued*) | | |  |  |  |  |
| 0.025 / Ctrl | Common | evm.TU.scaffold3144size225807.5 | 2.74 | 3.06E-02 | METMA | *Y045* |
| 0.025 / Ctrl | Common | evm.TU.scaffold4142size191490.2 | 2.28 | 3.49E-02 | DROVI | *TIM* |
| 0.025 / Ctrl | Common | evm.TU.scaffold156size437243.7 | 1.80 | 2.77E-03 | DROME | *RIM2* |
| 1 / Ctrl | Common | evm.TU.scaffold7405size45879.10 | 5.98 | 1.32E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold516size244129.2 | 5.54 | 1.03E-04 | BIOOB | *ACTC* |
| 1 / Ctrl | Non-common | evm.TU.scaffold423size170276.3 | 5.50 | 2.23E-06 | ANOAL | *HSP74* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7405size45879.11 | 5.25 | 1.35E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold4668size197402.2 | 5.18 | 7.02E-04 | HUMAN | *HDHD5* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7304size63610.2 | 5.07 | 8.63E-04 | ANOAL | *HSP71* |
| 1 / Ctrl | Common | evm.TU.scaffold4142size191490.2 | 4.72 | 9.93E-13 | DROVI | *TIM* |
| 1 / Ctrl | Common | evm.TU.scaffold547size159297.1 | 4.55 | 8.63E-04 | PONAB | *CRYAB* |
| 1 / Ctrl | Common | evm.TU.scaffold8768size38583.2 | 4.36 | 7.02E-04 | HUMAN | *HDHD5* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10008size45161.1 | 4.30 | 2.30E-03 | MOUSE | *XIAP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4507size80223.1 | 4.19 | 9.57E-08 | HUMAN | *ST1B1* |
| 1 / Ctrl | Common | evm.TU.scaffold156size437243.7 | 4.09 | 9.60E-23 | DROME | *RIM2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4142size191490.1 | 4.03 | 7.21E-13 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold15236size35086.2 | 3.99 | 1.02E-05 | HUMAN | *CP2J2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1977size112688.7 | 3.96 | 3.33E-06 | HUMAN | *CP2C8* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4424size135461.1 | 3.86 | 1.39E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2381size136822.10 | 3.86 | 5.59E-04 | STRPU | *SUREJ* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4914size63546.4 | 3.80 | 1.51E-02 | MOUSE | *XIAP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3992size72970.1 | 3.55 | 2.98E-05 | LYTVA | *ERG* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3340size152636.6 | 3.29 | 6.20E-06 | HUMAN | *BAG4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8613size59507.2 | 3.22 | 1.28E-03 | HUMAN | *CP2C8* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8613size59507.1 | 3.19 | 6.87E-06 | HUMAN | *CP2C8* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6111size64662.2 | 3.17 | 2.18E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold10769size29507.1 | 3.16 | 2.19E-04 | XENTR | *CRBL2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1859size193902.2 | 3.16 | 3.59E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1306size120932.1 | 3.08 | 5.96E-03 | RAT | *TANC1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold923size253024.9 | 3.00 | 3.31E-13 | MOUSE | *GLNA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1402size289848.5 | 2.93 | 1.31E-03 | CUPNH | *BDHA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1232size123727.3 | 2.92 | 8.94E-06 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2263size96786.2 | 2.91 | 1.42E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold16572size11220.1 | 2.88 | 1.32E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6147size107483.2 | 2.79 | 1.32E-03 | MOUSE | *DNJB4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold14314size34631.2 | 2.77 | 8.34E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4007size117063.6 | 2.75 | 2.64E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold3144size225807.5 | 2.71 | 1.23E-02 | METMA | *Y045* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4421size170941.3 | 2.65 | 7.46E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6705size50169.3 | 2.61 | 7.21E-13 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold911size301844.6 | 2.56 | 3.27E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1569size194665.2 | 2.50 | 1.23E-02 | HUMAN | *S26A5* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8459size104388.2 | 2.48 | 4.54E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4500size109838.9 | 2.41 | 2.30E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6782size89013.6 | 2.37 | 1.44E-02 | EMENI | *AOX* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2268size120505.4 | 2.35 | 2.42E-02 | HUMAN | *PERT* |
|  |  |  |  |  |  |  |
| **Supplementary Table 4** (*continued*) | | |  |  |  |  |
| 1 / Ctrl | Non-common | evm.TU.scaffold1569size194665.3 | 2.25 | 2.31E-02 | MOUSE | *S26A5* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4354size153558.3 | 2.17 | 9.35E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4799size148529.5 | 2.15 | 4.05E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2268size120505.3 | 2.15 | 3.34E-02 | AEDAE | *PERC* |
| 1 / Ctrl | Non-common | evm.TU.scaffold52size326587.11 | 2.11 | 5.29E-03 | DROME | *CRERF* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2920size86078.3 | 2.10 | 6.87E-06 | RAT | *RUNX1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2571size175983.3 | 2.08 | 5.17E-03 | BOVIN | *GA45G* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3054size84299.8 | 2.05 | 1.54E-03 | RAT | *GA45G* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10893size29080.1 | 2.03 | 2.30E-03 | HUMAN | *SC6A5* |
| 1 / Ctrl | Non-common | evm.TU.scaffold566size390051.15 | 1.99 | 5.61E-06 | DROME | *HR4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3108size104591.9 | 1.98 | 9.07E-03 | DROME | *TOLL8* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9443size112071.3 | 1.89 | 6.65E-06 | MOUSE | *GLNA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2size410065.8 | 1.87 | 1.03E-03 | URECA | *PAPSS* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1232size123727.5 | 1.78 | 2.01E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3850size100891.3 | 1.77 | 3.99E-02 | MOUSE | *PHKG2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11014size28661.1 | 1.76 | 3.49E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2595size215894.2 | 1.75 | 2.30E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold91size419679.12 | 1.74 | 2.18E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold10028size32743.1 | 1.72 | 1.75E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3469size173103.3 | 1.71 | 1.20E-02 | DROME | *GBS76* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1217size124397.2 | 1.67 | 1.08E-02 | RAT | *RAD* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1975size160888.6 | 1.61 | 2.18E-02 | MOUSE | *OTUD4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2754size425210.25 | 1.61 | 3.89E-02 | DROME | *GBS76* |
| 1 / Ctrl | Non-common | evm.TU.scaffold284size239466.4 | 1.56 | 5.24E-04 | CANLF | *CREM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2243size120663.1 | 1.55 | 9.07E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2230size106613.2 | 1.52 | 1.65E-02 | MOUSE | *LICH* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8726size38766.3 | 1.50 | 9.29E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1073size243907.6 | 1.50 | 4.06E-02 | HUMAN | *ZF64A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4865size132635.2 | 1.44 | 1.83E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6537size128148.3 | 1.43 | 4.57E-02 | PONAB | *KCNJ6* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2595size215894.3 | 1.39 | 9.30E-03 | HUMAN | *S12A2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4865size132635.8 | 1.38 | 3.62E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4355size182761.1 | 1.23 | 3.15E-03 | DROME | *TIPT* |
| 1 / Ctrl | Non-common | evm.TU.scaffold988size360591.6 | 1.16 | 4.94E-02 | HUMAN | *MOT9* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9548size76407.1 | 1.15 | 4.78E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1657size298101.24 | 1.09 | 4.02E-02 | MOUSE | *SOX9* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2138size251389.4 | 1.07 | 2.76E-02 | RAT | *FAXC* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2375size239988.1 | 1.05 | 6.30E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold487size301406.5 | 1.01 | 2.40E-02 | HUMAN | *BMX* |
| * **Other modules** | | | | | | |
| 0.025 / Ctrl | Common | evm.TU.scaffold1962size430023.11 | 4.97 | 2.34E-03 | FOAMV | *POL* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold311size184142.4 | 2.75 | 4.18E-02 | HUMAN | *MRC1* |
| 0.025 / Ctrl | Common | evm.TU.scaffold5998size98449.3 | 2.31 | 2.34E-03 | RAT | *T53I1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold363size555997.8 | 2.04 | 2.87E-02 | XENLA | *LSM11* |
| 0.025 / Ctrl | Common | evm.TU.scaffold9632size86143.8 | 1.67 | 5.67E-03 | HUMAN | *C1QT6* |
|  |  |  |  |  |  |  |
| **Supplementary Table 4** (*continued*) | | |  |  |  |  |
| 0.025 / Ctrl | Common | evm.TU.scaffold821size195697.6 | 1.67 | 4.55E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold2074size101205.4 | 1.34 | 3.51E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4780size84937.2 | 1.24 | 2.90E-02 | HUMAN | *NALD2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3988size84221.2 | 1.11 | 3.61E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7882size77958.3 | 1.11 | 8.30E-03 | HUMAN | *ZN704* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1879size416184.6 | 1.06 | 3.97E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold8273size41043.2 | -1.83 | 3.49E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7920size91439.1 | -2.78 | 3.49E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1001size193257.4 | 4.21 | 2.56E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4248size70342.2 | 4.10 | 2.05E-03 | RAT | *SVEP1* |
| 1 / Ctrl | Common | evm.TU.scaffold1962size430023.11 | 3.47 | 4.44E-02 | FOAMV | *POL* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2659size90145.1 | 3.20 | 4.04E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1865size145351.3 | 2.99 | 1.65E-02 | MYCUA | *PHMT1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold530size229996.12 | 2.83 | 3.99E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8832size38300.1 | 2.80 | 3.49E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7495size74862.7 | 2.73 | 4.90E-02 | CRAGI | *GIGA3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5528size58456.2 | 2.47 | 3.13E-02 | HUMAN | *MMEL1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11073size57721.2 | 2.43 | 2.35E-02 | BOVIN | *PPBT* |
| 1 / Ctrl | Non-common | evm.TU.scaffold538size272809.1 | 2.39 | 4.46E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold11862size25470.1 | 2.34 | 2.91E-02 | CHICK | *PCKGC* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4199size70737.3 | 2.17 | 4.61E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold6329size140121.4 | 2.06 | 4.62E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1672size179538.1 | 2.04 | 3.78E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold9910size82706.2 | 1.88 | 1.18E-02 | RAT | *ATPD* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4679size173293.8 | 1.87 | 5.31E-03 | CHICK | *CP2H2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2355size147709.9 | 1.85 | 3.25E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold5998size98449.3 | 1.67 | 4.05E-02 | RAT | *T53I1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2431size306300.17 | 1.64 | 4.23E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold9632size86143.8 | 1.64 | 2.42E-03 | HUMAN | *C1QT6* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8802size110191.3 | 1.62 | 3.59E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2431size306300.16 | 1.60 | 1.64E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2939size141835.1 | 1.59 | 9.44E-03 | RAT | *RAD* |
| 1 / Ctrl | Common | evm.TU.scaffold821size195697.6 | 1.53 | 3.99E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8size399332.9 | 1.53 | 7.85E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1860size168990.7 | 1.51 | 4.31E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold12246size24154.1 | 1.44 | 4.04E-02 | CHICK | *TSN* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4614size66670.1 | 1.43 | 4.19E-02 | HUMAN | *NAA25* |
| 1 / Ctrl | Common | evm.TU.scaffold2074size101205.4 | 1.39 | 9.28E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold13683size19512.2 | 1.36 | 3.49E-02 | MOUSE | *AP2A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2259size212231.7 | 1.35 | 2.53E-02 | CHICK | *SSPO* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9364size86438.2 | 1.19 | 2.31E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold9293size58634.2 | 1.15 | 4.05E-02 | SHEEP | *LYAM3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1567size137386.7 | 1.13 | 3.96E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2112size310749.7 | 1.04 | 7.00E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3440size326921.3 | 1.02 | 3.25E-02 | XENLA | *SESN1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1933size142028.6 | -1.03 | 2.14E-02 | NA | NA |
|  |  |  |  |  |  |  |
| **Supplementary Table 4** (*continued*) | | |  |  |  |  |
| 1 / Ctrl | Non-common | evm.TU.scaffold1695size255123.7 | -1.06 | 4.06E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold276size362962.24 | -1.52 | 3.63E-02 | HUMAN | *PC11X* |
| 1 / Ctrl | Common | evm.TU.scaffold8273size41043.2 | -1.59 | 4.16E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2434size116401.5 | -2.12 | 3.96E-02 | MOUSE | *ST1B1* |

**Supplementary Table 5.** Differentially expressed genes (DEGs) across MNP conditions (0.025 and 1 µg L–1) compared with the control condition identified in modules of interest from WGCNA performed on hemocyte samples sequencing dataset.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **MNP condition** | **Sharing DEG** | **Sequencing gene ID** | **Log2FC** | ***P*adj** | **Uniprot *sp.*** | **Uniprot ID** |
| * **Magenta module** | | | | | | |
| 0.025 / Ctrl | Common | evm.TU.scaffold7393size256918.12 | -5.24 | 1.60E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2333size276275.9 | -3.96 | 3.95E-03 | CAEEL | *TYR1* |
| 0.025 / Ctrl | Common | evm.TU.scaffold7711size59887.2 | -3.55 | 3.45E-03 | ARATH | *ARI4* |
| 0.025 / Ctrl | Common | evm.TU.scaffold3049size175038.8 | -3.31 | 2.41E-03 | HUMAN | *KLH35* |
| 0.025 / Ctrl | Common | evm.TU.scaffold4074size126334.5 | -3.17 | 1.12E-02 | HUMAN | *KLH35* |
| 0.025 / Ctrl | Common | evm.TU.scaffold5110size61824.5 | -3.08 | 3.99E-02 | RAT | *RAB1A* |
| 0.025 / Ctrl | Common | evm.TU.scaffold16265size12078.1 | -2.78 | 4.89E-03 | PONAB | *NUDT4* |
| 0.025 / Ctrl | Common | evm.TU.scaffold2538size306768.10 | -2.46 | 3.41E-02 | XENLA | *UBC12* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold13744size19329.1 | -2.39 | 3.69E-02 | MACFA | *GRIK3* |
| 0.025 / Ctrl | Common | evm.TU.scaffold5948size109308.5 | -2.38 | 1.45E-03 | MOUSE | *LENG9* |
| 0.025 / Ctrl | Common | evm.TU.scaffold361size559435.11 | -2.26 | 3.52E-02 | TETFL | *FOS* |
| 0.025 / Ctrl | Common | evm.TU.scaffold1983size149908.5 | -2.11 | 6.64E-03 | MOUSE | *RASM* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold13157size21177.1 | -1.89 | 3.71E-02 | CAEEL | *LACT2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3050size175475.11 | -1.85 | 1.90E-02 | HUMAN | *PAR12* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8752size38646.1 | -1.75 | 1.12E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold2938size139678.6 | -1.63 | 1.42E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3884size204650.3 | -1.44 | 1.12E-02 | PONAB | *T2EA* |
| 0.025 / Ctrl | Common | evm.TU.scaffold12639size22886.1 | -1.22 | 4.55E-02 | HUMAN | *STX16* |
| 0.025 / Ctrl | Common | evm.TU.scaffold297size379208.5 | -1.18 | 8.80E-03 | BOVIN | *WDR55* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7115size64842.1 | -1.17 | 1.12E-02 | BACSU | *YDAC* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5111size79043.2 | -1.10 | 1.58E-02 | HUMAN | *TBCD4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9515size85861.4 | -5.12 | 4.66E-06 | ASHGO | *ARF* |
| 1 / Ctrl | Common | evm.TU.scaffold5110size61824.5 | -5.05 | 5.06E-06 | RAT | *RAB1A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6666size83753.9 | -4.82 | 2.70E-03 | DROME | *RHO1* |
| 1 / Ctrl | Common | evm.TU.scaffold4074size126334.5 | -4.57 | 5.06E-06 | HUMAN | *KLH35* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3375size152648.1 | -4.26 | 5.63E-03 | RAT | *BATF3* |
| 1 / Ctrl | Common | evm.TU.scaffold7393size256918.12 | -4.07 | 2.80E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold3049size175038.8 | -3.94 | 1.62E-05 | HUMAN | *KLH35* |
| 1 / Ctrl | Common | evm.TU.scaffold7711size59887.2 | -3.91 | 1.42E-04 | ARATH | *ARI4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold950size134745.6 | -3.61 | 2.93E-02 | DIPOM | *RAB1* |
| 1 / Ctrl | Common | evm.TU.scaffold2538size306768.10 | -3.29 | 4.04E-04 | XENLA | *UBC12* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4572size145658.10 | -3.19 | 3.26E-02 | RHIFE | *MET* |
| 1 / Ctrl | Common | evm.TU.scaffold16265size12078.1 | -2.83 | 1.44E-03 | PONAB | *NUDT4* |
| 1 / Ctrl | Common | evm.TU.scaffold1983size149908.5 | -2.81 | 5.06E-06 | MOUSE | *RASM* |
| 1 / Ctrl | Common | evm.TU.scaffold5948size109308.5 | -2.38 | 4.04E-04 | MOUSE | *LENG9* |
| 1 / Ctrl | Common | evm.TU.scaffold361size559435.11 | -2.35 | 2.81E-02 | TETFL | *FOS* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4254size144808.2 | -2.27 | 1.27E-04 | HUMAN | *GRHPR* |
| 1 / Ctrl | Common | evm.TU.scaffold2938size139678.6 | -1.84 | 2.43E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold12639size22886.1 | -1.47 | 5.64E-03 | HUMAN | *STX16* |
| 1 / Ctrl | Non-common | evm.TU.scaffold950size134745.10 | -1.24 | 4.44E-02 | XENLA | *RNF8B* |
|  |  |  |  |  |  |  |
| **Supplementary Table 5** (*continued*) | | |  |  |  |  |
| 1 / Ctrl | Common | evm.TU.scaffold297size379208.5 | -1.15 | 8.05E-03 | BOVIN | *WDR55* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7344size46251.4 | -1.00 | 2.80E-02 | HUMAN | *AAMP* |
| * **Pink module** | | | | | | |
| 1 / Ctrl | Non-common | evm.TU.scaffold15236size35086.2 | 5.63 | 4.34E-05 | HUMAN | *CP2J2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8613size59507.1 | 4.99 | 4.35E-05 | HUMAN | *CP2C8* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4507size80223.1 | 3.90 | 1.27E-04 | HUMAN | *ST1B1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7855size43288.1 | 3.72 | 4.02E-02 | RAT | *APJ* |
| 1 / Ctrl | Non-common | evm.TU.scaffold208size201665.19 | 2.97 | 2.81E-02 | HUMAN | *FEM1B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3917size111660.3 | 1.89 | 2.70E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8043size64624.1 | 1.36 | 4.04E-04 | MOUSE | *ZNT1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1363size181262.6 | 1.36 | 3.89E-02 | MOUSE | *ZNT10* |
| * **Red module** | | | | | | |
| 0.025 / Ctrl | Common | evm.TU.scaffold16787size10633.1 | -2.97 | 1.12E-02 | ARATH | *ARI4* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold309size232637.11 | -2.83 | 3.34E-02 | CAEEL | *YRD6* |
| 0.025 / Ctrl | Common | evm.TU.scaffold919size193053.2 | -2.78 | 5.06E-05 | HUMAN | *RN126* |
| 0.025 / Ctrl | Common | evm.TU.scaffold13945size18790.1 | -2.60 | 4.17E-02 | ARATH | *ARI1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12218size40870.3 | -2.34 | 9.55E-03 | MOUSE | *SIAE* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7564size139168.1 | -2.15 | 4.17E-02 | DANRE | *JAG1A* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7356size111678.5 | -2.01 | 4.99E-02 | XENLA | *RO60* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7549size111641.1 | -1.99 | 1.29E-02 | BOVIN | *OXDD* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold15230size15130.1 | -1.96 | 3.62E-02 | DICDI | *VWKA* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3615size291024.22 | -1.88 | 1.88E-02 | XENLA | *BECN1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2076size120888.4 | -1.66 | 1.12E-02 | HUMAN | *CEBPG* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2571size175983.7 | -1.48 | 1.51E-02 | RAT | *GA45A* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold320size404118.4 | -1.06 | 3.62E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold9515size85861.2 | -5.14 | 1.38E-04 | ASHGO | *ARF* |
| 1 / Ctrl | Non-common | evm.TU.scaffold950size134745.7 | -4.33 | 4.04E-04 | DIPOM | *RAB1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5110size61824.6 | -3.81 | 1.60E-03 | DIPOM | *RAB1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1131size175864.5 | -3.39 | 2.84E-04 | DICDI | *AAC4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5902size97825.3 | -3.28 | 2.00E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4897size63734.4 | -3.15 | 7.82E-05 | DROME | *RHO1* |
| 1 / Ctrl | Common | evm.TU.scaffold13945size18790.1 | -3.12 | 5.52E-03 | ARATH | *ARI1* |
| 1 / Ctrl | Common | evm.TU.scaffold16787size10633.1 | -3.10 | 5.52E-03 | ARATH | *ARI4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold13307size20673.1 | -2.59 | 1.81E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold14583size16930.1 | -2.49 | 2.49E-03 | HUMAN | *GRHPR* |
| 1 / Ctrl | Common | evm.TU.scaffold919size193053.2 | -2.43 | 2.16E-04 | HUMAN | *RN126* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2007size114573.3 | -2.38 | 4.45E-02 | MOUSE | *COCA1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4760size205847.8 | -2.35 | 2.97E-02 | MOUSE | *EAA2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold11219size78477.2 | -2.29 | 3.93E-03 | MIMIV | *YR811* |
| 1 / Ctrl | Non-common | evm.TU.scaffold812size140740.3 | -2.04 | 3.32E-02 | XENLA | *EGR1B* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2964size95999.5 | -1.21 | 2.88E-02 | CHICK | *PGGHG* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8467size62171.3 | -1.11 | 1.73E-03 | HUMAN | *PIR* |
| * **Other modules** | | | | | | |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| **Supplementary Table 5** (*continued*) | | |  |  |  |  |
| 0.025 / Ctrl | Common | evm.TU.scaffold11837size49671.2 | 7.90 | 7.58E-03 | MOUSE | *RSP14* |
| 0.025 / Ctrl | Common | evm.TU.scaffold221size240150.25 | 6.47 | 2.05E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold222size381503.2 | 6.12 | 1.29E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold2404size94544.2 | 6.02 | 9.72E-03 | DROME | *Y3556* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4647size66183.6 | 5.99 | 1.12E-02 | DANRE | *CFA53* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold681size258651.11 | 5.94 | 3.92E-02 | MOUSE | *BAI1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12294size23998.1 | 5.91 | 7.52E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold463size180809.1 | 5.86 | 4.34E-03 | HUMAN | *IF* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7393size256918.3 | 5.78 | 2.90E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2610size137834.4 | 5.76 | 1.12E-02 | MACFA | *IQUB* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold850size206783.3 | 5.75 | 3.03E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5921size55650.4 | 5.72 | 1.12E-02 | DANRE | *CF161* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold6456size51796.1 | 5.71 | 4.55E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3546size132595.3 | 5.68 | 7.52E-03 | HUMAN | *ANK3* |
| 0.025 / Ctrl | Common | evm.TU.scaffold8940size68868.3 | 5.56 | 1.12E-02 | XENTR | *CF157* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3321size121371.3 | 5.51 | 1.12E-02 | DANRE | *PKD2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12592size23029.1 | 5.50 | 6.64E-03 | HUMAN | *DYH8* |
| 0.025 / Ctrl | Common | evm.TU.scaffold4459size79009.8 | 5.26 | 6.64E-03 | BOVIN | *PPR32* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold806size231242.2 | 5.14 | 2.88E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4672size195439.9 | 5.05 | 1.55E-02 | HUMAN | *CC113* |
| 0.025 / Ctrl | Common | evm.TU.scaffold3517size464559.25 | 5.03 | 1.27E-02 | MOUSE | *RSP14* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2197size98154.8 | 4.93 | 3.45E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3241size249433.15 | 4.91 | 1.12E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold563size157350.3 | 4.88 | 1.12E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5174size81425.5 | 4.87 | 3.68E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold992size143308.6 | 4.86 | 1.87E-02 | XENTR | *MORN5* |
| 0.025 / Ctrl | Common | evm.TU.scaffold146size219328.4 | 4.86 | 2.87E-02 | DROME | *DCHS* |
| 0.025 / Ctrl | Common | evm.TU.scaffold226size262146.9 | 4.86 | 1.51E-02 | MOUSE | *CJ107* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4142size191490.3 | 4.80 | 1.12E-02 | HUMAN | *IQCG* |
| 0.025 / Ctrl | Common | evm.TU.scaffold4681size152784.13 | 4.77 | 1.12E-02 | DANRE | *CA194* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3836size146814.7 | 4.73 | 1.88E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold463size180809.4 | 4.63 | 2.08E-02 | HUMAN | *IF* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold9143size36786.1 | 4.59 | 4.24E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2529size92329.8 | 4.53 | 4.99E-02 | MOUSE | *TTLL3* |
| 0.025 / Ctrl | Common | evm.TU.scaffold1897size104575.3 | 4.46 | 1.90E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1829size129277.8 | 4.39 | 1.55E-02 | DANRE | *RSPH9* |
| 0.025 / Ctrl | Common | evm.TU.scaffold5577size58180.9 | 4.23 | 4.93E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold9510size88084.1 | 4.02 | 1.28E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2595size215894.1 | 4.02 | 3.03E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4133size128356.4 | 4.02 | 1.75E-02 | BOVIN | *CA228* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5653size69837.1 | 3.91 | 2.51E-02 | XENLA | *STPG1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold221size240150.23 | 3.90 | 4.22E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1719size162498.5 | 3.76 | 4.01E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1436size266347.2 | 3.75 | 3.67E-02 | HUMAN | *PPE2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4185size140911.1 | 3.71 | 1.14E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4372size109182.3 | 3.61 | 3.41E-02 | RAT | *ATS7* |
|  |  |  |  |  |  |  |
| **Supplementary Table 5** (*continued*) | | |  |  |  |  |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7961size42695.2 | 3.46 | 2.36E-02 | HUMAN | *AXDN1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5998size98449.3 | 3.46 | 3.52E-02 | RAT | *T53I1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3088size183400.8 | 3.38 | 7.59E-03 | CAEEL | *NU301* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5484size173863.14 | 3.37 | 1.12E-02 | ANOGA | *ACT5C* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1685size218742.7 | 3.36 | 1.12E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold533size312678.16 | 3.34 | 1.12E-02 | MOUSE | *FRS1L* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8115size110444.6 | 3.22 | 4.99E-02 | XENLA | *DRC1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold91size419679.4 | 3.09 | 4.99E-02 | HUMAN | *DCST1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1359size119114.5 | 3.07 | 4.75E-02 | DROME | *ORCT* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4725size212881.2 | 3.06 | 2.45E-02 | RAT | *PA216* |
| 0.025 / Ctrl | Common | evm.TU.scaffold4142size191490.2 | 3.00 | 7.58E-03 | DROVI | *TIM* |
| 0.025 / Ctrl | Common | evm.TU.scaffold779size161378.9 | 2.93 | 3.00E-02 | MOUSE | *ASGR1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold827size139563.7 | 2.83 | 4.55E-02 | MOUSE | *THSD4* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8864size38164.3 | 2.83 | 1.12E-02 | CAEEL | *SAR1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4943size115742.4 | 2.58 | 1.81E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3170size128794.5 | 2.39 | 4.97E-02 | PONAB | *DERL2* |
| 0.025 / Ctrl | Common | evm.TU.scaffold4142size191490.1 | 2.35 | 1.12E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold11862size25470.1 | 2.33 | 2.90E-02 | CHICK | *PCKGC* |
| 0.025 / Ctrl | Common | evm.TU.scaffold11383size52394.5 | 2.32 | 4.71E-02 | RAT | *EXOC5* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold630size420493.13 | 2.24 | 2.45E-02 | ECOK1 | *NEUO* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold9302size36091.2 | 2.22 | 1.25E-02 | MOUSE | *I23O2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold42size538778.13 | 1.90 | 3.77E-02 | HUMAN | *PLMN* |
| 0.025 / Ctrl | Common | evm.TU.scaffold156size437243.7 | 1.59 | 1.55E-02 | DROME | *RIM2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2559size260802.11 | 1.48 | 2.45E-02 | CAEEL | *UNC9* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12791size22372.1 | 1.35 | 3.62E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4076size181903.4 | 1.24 | 1.55E-02 | HUMAN | *ANK1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12116size42260.2 | 1.17 | 3.52E-02 | SAIBB | *FUT1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold731size258772.7 | -1.06 | 2.45E-02 | MOUSE | *F10C1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8669size39025.1 | -1.22 | 4.93E-02 | HUMAN | *TAF4* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold68size278367.11 | -1.34 | 9.72E-03 | RAT | *ANM3* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold11975size49011.2 | -1.35 | 3.28E-02 | MOUSE | *TMPS2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2857size108847.1 | -1.83 | 3.41E-02 | MOUSE | *SIK2* |
| 0.025 / Ctrl | Common | evm.TU.scaffold5172size117595.4 | -1.98 | 4.90E-02 | ORYSJ | *KNOS3* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold10size363274.2 | -2.18 | 4.55E-02 | HUMAN | *FUT7* |
| 0.025 / Ctrl | Common | evm.TU.scaffold957size414861.12 | -2.21 | 2.64E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold3726size140820.4 | -2.26 | 9.49E-03 | DIPOM | *RB11B* |
| 0.025 / Ctrl | Common | evm.TU.scaffold5948size109308.4 | -2.33 | 1.45E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold17170size9325.1 | -2.36 | 2.05E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold787size141661.9 | -2.58 | 4.84E-02 | CAEEL | *NPR15* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3680size154855.9 | -2.65 | 1.12E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8681size70456.2 | -2.83 | 2.79E-02 | DANRE | *WSCD2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold11219size78477.3 | -3.06 | 1.17E-02 | HUMAN | *BIRC2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3164size130232.2 | -3.13 | 2.48E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold107size612490.55 | -3.32 | 1.12E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold9246size95691.2 | -3.44 | 1.88E-02 | HUMAN | *MET27* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3500size108302.4 | -3.48 | 3.28E-02 | NA | NA |
|  |  |  |  |  |  |  |
| **Supplementary Table 5** (*continued*) | | |  |  |  |  |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1926size250250.4 | -3.81 | 4.63E-04 | XENLA | *BIR7A* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold720size228729.1 | -4.17 | 3.14E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8216size41291.3 | -4.19 | 1.83E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold2723size101665.4 | -4.38 | 1.84E-04 | HUMAN | *CO6A5* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5577size58180.7 | -5.08 | 1.87E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5176size75793.4 | -5.44 | 6.64E-03 | HUMAN | *ZN862* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10457size30855.2 | 6.69 | 3.37E-06 | STRPU | *FBP3* |
| 1 / Ctrl | Common | evm.TU.scaffold11837size49671.2 | 6.48 | 4.80E-02 | MOUSE | *RSP14* |
| 1 / Ctrl | Common | evm.TU.scaffold221size240150.25 | 6.48 | 2.39E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold5577size58180.8 | 6.36 | 2.52E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold2404size94544.2 | 6.27 | 3.17E-03 | DROME | *Y3556* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4341size142224.5 | 5.58 | 4.06E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold463size180809.4 | 4.98 | 9.08E-03 | HUMAN | *IF* |
| 1 / Ctrl | Common | evm.TU.scaffold5577size58180.9 | 4.98 | 9.38E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold8940size68868.3 | 4.88 | 4.08E-02 | XENTR | *CF157* |
| 1 / Ctrl | Common | evm.TU.scaffold146size219328.4 | 4.85 | 3.22E-02 | DROME | *DCHS* |
| 1 / Ctrl | Common | evm.TU.scaffold3517size464559.25 | 4.78 | 2.52E-02 | MOUSE | *RSP14* |
| 1 / Ctrl | Common | evm.TU.scaffold4681size152784.13 | 4.69 | 1.33E-02 | DANRE | *CA194* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2628size90693.2 | 4.56 | 1.71E-02 | HUMAN | *HYDIN* |
| 1 / Ctrl | Common | evm.TU.scaffold226size262146.9 | 4.33 | 4.99E-02 | MOUSE | *CJ107* |
| 1 / Ctrl | Common | evm.TU.scaffold4459size79009.8 | 4.29 | 4.24E-02 | BOVIN | *PPR32* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6774size130978.2 | 4.27 | 4.34E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2445size93778.1 | 4.25 | 3.90E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold1897size104575.3 | 4.13 | 4.50E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold9130size57754.1 | 3.83 | 2.09E-02 | RAT | *CRFR1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold13701size19462.1 | 3.82 | 4.08E-02 | XENLA | *LR2BP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8613size59507.2 | 3.52 | 7.51E-03 | HUMAN | *CP2C8* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8085size55599.1 | 3.50 | 4.08E-02 | HUMAN | *BMX* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8043size64624.2 | 3.46 | 7.51E-03 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold4142size191490.2 | 3.37 | 4.04E-04 | DROVI | *TIM* |
| 1 / Ctrl | Common | evm.TU.scaffold779size161378.9 | 3.30 | 7.63E-03 | MOUSE | *ASGR1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2404size94544.3 | 3.17 | 9.38E-03 | MOUSE | *IF* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3865size74240.7 | 2.88 | 2.85E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1977size112688.7 | 2.86 | 4.76E-02 | HUMAN | *CP2C8* |
| 1 / Ctrl | Common | evm.TU.scaffold156size437243.7 | 2.76 | 1.92E-08 | DROME | *RIM2* |
| 1 / Ctrl | Common | evm.TU.scaffold4142size191490.1 | 2.74 | 5.96E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3232size114449.5 | 2.70 | 3.35E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4865size132635.8 | 2.68 | 1.09E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold566size390051.15 | 2.67 | 3.06E-05 | DROME | *HR4* |
| 1 / Ctrl | Common | evm.TU.scaffold11383size52394.5 | 2.48 | 2.81E-02 | RAT | *EXOC5* |
| 1 / Ctrl | Non-common | evm.TU.scaffold38size466805.16 | 2.45 | 2.52E-02 | HUMAN | *FBX41* |
| 1 / Ctrl | Non-common | evm.TU.scaffold1113size334742.4 | 2.39 | 4.08E-02 | MOUSE | *ALK* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6370size96622.1 | 2.14 | 4.24E-02 | DICDI | *DRKC* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5716size144689.4 | 2.11 | 2.80E-02 | MOUSE | *KCNJ1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6202size53514.4 | 1.96 | 3.73E-02 | HUMAN | *NCKX4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3957size93592.6 | 1.94 | 1.71E-02 | HUMAN | *KNTC1* |
|  |  |  |  |  |  |  |
| **Supplementary Table 5** (*continued*) | | |  |  |  |  |
| 1 / Ctrl | Non-common | evm.TU.scaffold8417size54106.2 | 1.65 | 4.08E-02 | PONAB | *KCNK1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2697size303698.3 | 1.63 | 7.80E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold11491size26846.2 | 1.50 | 4.08E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold331size210939.7 | 1.47 | 4.44E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold9157size73761.1 | 1.36 | 4.23E-02 | BOMMO | *AGO3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold331size210939.6 | 1.30 | 4.02E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2452size260681.5 | 1.05 | 2.26E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8874size38082.3 | -1.00 | 2.20E-02 | MOUSE | *TRXR2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6654size66187.1 | -1.11 | 3.90E-02 | SYLBO | *CRY1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold154size320920.13 | -1.22 | 3.67E-02 | DROME | *POL3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9826size33606.1 | -1.33 | 2.26E-02 | CAEEL | *UNC9* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2120size147150.7 | -1.43 | 1.33E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold102size233204.2 | -1.45 | 1.33E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2726size89241.1 | -1.90 | 8.05E-04 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold5172size117595.4 | -2.05 | 3.90E-02 | ORYSJ | *KNOS3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9183size36649.2 | -2.31 | 2.34E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold957size414861.12 | -2.40 | 1.07E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold5948size109308.4 | -2.44 | 1.27E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2938size139678.12 | -2.55 | 4.06E-03 | MIMIV | *YR811* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8767size92048.1 | -2.69 | 3.40E-02 | RAT | *PRAX* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6397size112829.3 | -2.91 | 2.09E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold3726size140820.4 | -3.04 | 8.40E-06 | DIPOM | *RB11B* |
| 1 / Ctrl | Common | evm.TU.scaffold2723size101665.4 | -3.58 | 2.49E-03 | HUMAN | *CO6A5* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7359size46131.3 | -4.52 | 2.89E-02 | NA | NA |

**Supplementary Table 6.** Differentially expressed genes (DEGs) across MNP conditions (0.025 and 1 µg L–1) compared with the control condition in pearl sac samples.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **MNP condition** | **Sharing DEG** | **Sequencing gene ID** | **Log2FC** | ***P*adj** | **Uniprot *sp.*** | **Uniprot ID** |
| 0.025 / Ctrl | Common | evm.TU.scaffold7405size45879.10 | 4.74 | 8.66E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold9393size35692.1 | 3.97 | 4.73E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4903size63670.1 | 3.93 | 6.60E-04 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2435size262771.5 | 3.40 | 4.02E-03 | BOVIN | *PHLD* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12241size24179.1 | 3.11 | 8.66E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold547size159297.1 | 2.90 | 2.97E-02 | PONAB | *CRYAB* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4162size71203.4 | 2.87 | 2.97E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3145size187703.3 | 2.68 | 2.31E-02 | MOUSE | *XLRS1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1275size122086.11 | 2.67 | 1.11E-04 | HUMAN | *FGL2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold311size184142.4 | 2.58 | 2.08E-02 | HUMAN | *MRC1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold645size150701.3 | 2.44 | 1.15E-02 | RAT | *MRP1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold104size934493.2 | 2.19 | 2.97E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2052size135315.9 | 2.09 | 2.08E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2436size218809.4 | 2.05 | 1.16E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1034size318021.7 | 2.02 | 1.15E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2388size190213.3 | 1.93 | 3.51E-02 | CELJU | *MANA* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2074size101205.4 | 1.62 | 4.10E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold10097size32462.1 | 1.52 | 4.98E-02 | MOUSE | *RU2A* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold6718size110288.2 | 1.41 | 3.51E-02 | CAEEL | *YT66* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold363size555997.8 | 1.28 | 2.63E-02 | XENLA | *LSM11* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8574size39536.1 | 1.26 | 2.63E-02 | MOUSE | *SLD5* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4177size70991.1 | 1.25 | 4.02E-03 | HUMAN | *DAPLE* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold580size251751.7 | -1.11 | 8.66E-03 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold7564size139168.1 | -1.30 | 1.52E-02 | DANRE | *JAG1A* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12667size22784.1 | -1.43 | 4.10E-02 | THEMA | *FABG* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold9784size33764.1 | -1.44 | 4.73E-02 | HUMAN | *ANR66* |
| 0.025 / Ctrl | Common | evm.TU.scaffold4314size145107.7 | -1.45 | 2.63E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5446size199412.6 | -1.58 | 4.21E-02 | XENLA | *TM145* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8273size41043.2 | -1.62 | 3.51E-02 | NA | *NA* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8309size80043.3 | -1.76 | 3.51E-02 | DANRE | *AOF* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5027size97772.4 | -1.78 | 4.73E-02 | ACRMI | *MLRP2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold6385size101604.2 | -1.82 | 3.58E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold6157size72139.1 | -1.83 | 2.93E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold164size248782.21 | -1.85 | 1.84E-02 | MOUSE | *NID1* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold812size140740.3 | -1.87 | 2.97E-02 | XENLA | *EGR1B* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1408size188276.17 | -1.92 | 8.66E-03 | MOUSE | *MARK2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3260size138505.1 | -2.09 | 3.88E-02 | NA | NA |
| 0.025 / Ctrl | Common | evm.TU.scaffold1544size237200.6 | -2.11 | 4.10E-02 | BOVIN | *AMPN* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12018size52989.2 | -2.16 | 2.97E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2778size160406.2 | -2.51 | 8.66E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold13284size59462.3 | -2.74 | 2.41E-02 | XENLA | *ADA10* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7276size46712.1 | -2.75 | 4.87E-02 | MOUSE | *TIF1B* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold538size272809.1 | -2.83 | 2.63E-02 | NA | NA |
|  |  |  |  |  |  |  |
| **Supplementary Table 6** (*continued*) | | |  |  |  |  |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2106size257207.8 | -2.90 | 3.88E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold6071size54414.2 | -2.94 | 2.97E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold740size376897.13 | -2.97 | 8.66E-03 | MOUSE | *C1QL4* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3198size82302.8 | -2.99 | 3.55E-02 | MOUSE | *MFAP4* |
| 0.025 / Ctrl | Common | evm.TU.scaffold1323size145704.4 | -3.03 | 2.97E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold14903size16010.2 | -3.12 | 1.22E-02 | MOUSE | *C1QL3* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1107size194094.9 | -3.19 | 4.98E-02 | MOUSE | *ST1C2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold16800size10565.1 | -3.24 | 3.28E-02 | XENLA | *S15A4* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold11359size27355.1 | -3.35 | 9.68E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7354size99212.1 | -3.37 | 4.02E-03 | HUMAN | *NOS1* |
| 0.025 / Ctrl | Common | evm.TU.scaffold3440size326921.10 | -3.42 | 4.73E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold831size317030.14 | -3.46 | 8.66E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2454size124454.1 | -3.50 | 2.93E-02 | PINMG | *KCP2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2454size124454.3 | -3.54 | 4.67E-03 | PINMG | *KCP2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold113size299110.2 | -3.56 | 4.05E-03 | HUMAN | *QRIC2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2095size529737.6 | -3.57 | 8.66E-03 | RHILO | *BETA* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7792size68911.4 | -3.66 | 3.11E-06 | MOUSE | *NCAM2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold11357size27364.3 | -3.69 | 9.15E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold9616size78232.4 | -3.78 | 1.15E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1224size307968.2 | -3.80 | 8.66E-03 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold3739size110585.1 | -3.80 | 4.73E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold7423size132347.6 | -3.89 | 8.66E-03 | MOUSE | *ANR17* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold634size277710.2 | -3.89 | 4.73E-02 | MOUSE | *NQO2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold12851size36164.1 | -3.91 | 1.84E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold14337size55465.1 | -3.97 | 8.66E-03 | DROME | *CAD99* |
| 0.025 / Ctrl | Common | evm.TU.scaffold6274size151240.1 | -4.05 | 6.46E-04 | PINMG | *PMN14* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold8832size38300.1 | -4.19 | 2.63E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold5124size61716.4 | -4.26 | 2.87E-02 | MOUSE | *MOT9* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1748size108773.7 | -4.32 | 2.97E-02 | PINMA | *SLP2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold26size344546.7 | -4.38 | 2.90E-02 | STRPU | *SPAN* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1263size221832.6 | -4.43 | 2.08E-02 | STRPU | *SPAN* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2454size124454.2 | -4.56 | 2.63E-02 | PINMG | *KCP2* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold15685size13759.1 | -4.57 | 4.67E-03 | PINMG | *NCP* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold2099size100549.2 | -4.70 | 3.73E-02 | NA | NA |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold10285size61330.4 | -4.71 | 4.02E-03 | PINMA | *SLP3* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold1748size108773.5 | -5.61 | 3.51E-02 | PINMA | *SLP3* |
| 0.025 / Ctrl | Non-common | evm.TU.scaffold4288size69999.1 | -5.98 | 2.66E-02 | PINMA | *KCP1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7304size63610.2 | 4.24 | 1.03E-02 | ANOAL | *HSP71* |
| 1 / Ctrl | Common | evm.TU.scaffold7405size45879.10 | 4.22 | 3.55E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold15236size35086.2 | 4.08 | 1.36E-04 | HUMAN | *CP2J2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold423size170276.3 | 4.07 | 8.75E-03 | ANOAL | *HSP74* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7405size45879.11 | 4.06 | 1.41E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4914size63546.4 | 3.56 | 3.08E-02 | MOUSE | *XIAP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4424size135461.1 | 3.47 | 8.17E-05 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold10008size45161.1 | 3.28 | 4.59E-02 | MOUSE | *XIAP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8613size59507.1 | 3.21 | 2.02E-04 | HUMAN | *CP2C8* |
|  |  |  |  |  |  |  |
| **Supplementary Table 6** (*continued*) | | |  |  |  |  |
| 1 / Ctrl | Non-common | evm.TU.scaffold2995size85125.1 | 3.08 | 3.08E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4500size109838.9 | 2.87 | 1.03E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4507size80223.1 | 2.87 | 6.18E-04 | HUMAN | *ST1B1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4142size191490.2 | 2.65 | 1.24E-04 | DROVI | *TIM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold156size437243.7 | 2.55 | 1.66E-10 | DROME | *RIM2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5544size66712.3 | 2.47 | 3.66E-02 | SCYTO | *TIMP3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold4917size106096.5 | 2.46 | 4.71E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1402size289848.5 | 2.40 | 4.04E-02 | CUPNH | *BDHA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6207size71120.2 | 2.36 | 1.19E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4142size191490.1 | 2.25 | 2.41E-05 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold4679size173293.8 | 2.06 | 1.11E-02 | CHICK | *CP2H2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3385size80003.5 | 2.03 | 3.66E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2967size360768.11 | 1.88 | 9.79E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1232size123727.3 | 1.87 | 7.84E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2192size98314.3 | 1.86 | 4.59E-02 | ARATH | *GAMT2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold463size180809.9 | 1.85 | 8.75E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold334size341206.3 | 1.83 | 4.24E-02 | XENLA | *UBIQP* |
| 1 / Ctrl | Non-common | evm.TU.scaffold3340size152636.6 | 1.78 | 1.19E-02 | HUMAN | *BAG4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9271size36218.1 | 1.77 | 2.92E-02 | MOUSE | *V1BR* |
| 1 / Ctrl | Non-common | evm.TU.scaffold91size419679.12 | 1.75 | 3.08E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2263size96786.2 | 1.74 | 3.55E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3230size151995.1 | 1.73 | 2.92E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7032size48018.1 | 1.55 | 4.22E-03 | STRPU | *BMPH* |
| 1 / Ctrl | Non-common | evm.TU.scaffold923size253024.9 | 1.52 | 9.79E-03 | MOUSE | *GLNA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold14782size16399.1 | 1.39 | 3.08E-02 | MIMIV | *COLL7* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2796size88200.2 | 1.37 | 3.08E-02 | RAT | *SQSTM* |
| 1 / Ctrl | Non-common | evm.TU.scaffold9443size112071.3 | 1.36 | 4.59E-02 | MOUSE | *GLNA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold566size390051.15 | 1.33 | 2.74E-04 | DROME | *HR4* |
| 1 / Ctrl | Non-common | evm.TU.scaffold7880size108515.1 | 1.31 | 3.53E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold1962size430023.13 | 1.26 | 3.85E-02 | XENLA | *TLL1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6705size50169.3 | 1.22 | 7.84E-04 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold303size331505.6 | 1.16 | 4.24E-02 | HUMAN | *MMP16* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10028size32743.1 | 1.08 | 2.29E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7554size95047.2 | 1.04 | 2.11E-02 | MOUSE | *ATRX* |
| 1 / Ctrl | Non-common | evm.TU.scaffold936size300356.3 | 1.02 | 3.53E-02 | DANRE | *SBK1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold14668size16684.2 | -1.08 | 4.59E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2120size147150.8 | -1.21 | 1.19E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold7564size139168.1 | -1.25 | 3.08E-02 | DANRE | *JAG1A* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2120size147150.9 | -1.39 | 7.50E-03 | DROYA | *PER* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2120size147150.7 | -1.39 | 2.86E-04 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold4314size145107.7 | -1.40 | 4.71E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7224size46994.4 | -1.61 | 6.69E-05 | HUMAN | *HEBP2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold8809size38378.3 | -1.65 | 4.71E-02 | APIME | *TREA* |
| 1 / Ctrl | Non-common | evm.TU.scaffold10833size58035.4 | -1.65 | 3.08E-02 | CHICK | *ST1B1* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2627size90695.4 | -1.93 | 1.19E-02 | CHICK | *CAN3* |
| 1 / Ctrl | Non-common | evm.TU.scaffold2328size202496.4 | -1.94 | 3.47E-02 | NA | NA |
|  |  |  |  |  |  |  |
| **Supplementary Table 6** (*continued*) | | |  |  |  |  |
| 1 / Ctrl | Non-common | evm.TU.scaffold5381size147161.1 | -2.10 | 3.08E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold3392size79886.2 | -2.34 | 8.75E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold264size320753.24 | -2.42 | 1.01E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold1544size237200.6 | -2.49 | 9.60E-03 | BOVIN | *AMPN* |
| 1 / Ctrl | Non-common | evm.TU.scaffold5957size328954.4 | -2.55 | 3.02E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold1323size145704.4 | -2.72 | 1.00E-02 | NA | NA |
| 1 / Ctrl | Common | evm.TU.scaffold6274size151240.1 | -3.04 | 3.62E-02 | PINMG | *PMN14* |
| 1 / Ctrl | Non-common | evm.TU.scaffold13924size18829.1 | -3.18 | 1.07E-02 | HUMAN | *CD109* |
| 1 / Ctrl | Non-common | evm.TU.scaffold6363size103460.4 | -3.18 | 4.53E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold16332size27114.1 | -3.30 | 4.40E-03 | CAEEL | *BAT38* |
| 1 / Ctrl | Non-common | evm.TU.scaffold891size137303.3 | -3.36 | 3.83E-03 | PIG | *PNMT* |
| 1 / Ctrl | Common | evm.TU.scaffold3440size326921.10 | -4.00 | 1.11E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold7216size47029.4 | -4.25 | 5.45E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold8499size142240.4 | -4.34 | 3.46E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold2109size100372.3 | -5.03 | 6.19E-03 | MOUSE | *SRPX2* |
| 1 / Ctrl | Non-common | evm.TU.scaffold14848size34703.1 | -6.70 | 3.76E-02 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold12174size24356.2 | -7.29 | 2.65E-03 | NA | NA |
| 1 / Ctrl | Non-common | evm.TU.scaffold12174size24356.1 | -8.74 | 1.93E-02 | HUMAN | *FBLN7* |



**Supplementary Figure 8. Polymer identification by FT-IR and Py-GC-MS in both plastic pearl farming gear used for micro-nanoplastic production.** (**a**) FT-IR identification of polyethylene (PE) for the synthetic rope and (**b**) polypropylene (PP) for the spat collector. (**c**) Synthetic rope analyzed by Py-GC-MS with the specific pattern of PE including the 1,13 tetradecadiene specific marker in red and (**d**) the pyrogram of spat collector with the specific detection of 2,4 dimethyl-1-heptene in red.



**Supplementary Figure 9.** **Particle size distribution of micro-nanoplastics by laser diffraction analysis.** Bar plots show the differences in volume and number of particle sizes made from (**a**–**b**) rope and (**c**–**d**) spat collector.

**Supplementary Methods 1. Shell nacre deposition**

At the end of the experiment, the shells of dissected oysters were sawn with a “Swap Top” Trim Saw machine, which included a diamond Trim Saw Blade (Thin Cut) IC-40961. The shell edges were then polished for 5 s with various grades of water sandpaper sheets. The shell sections were examined under a Leitz Dialux 22 compound fluorescence microscope equipped with an I3-filter block and an optical micrometer. Shell growth was measured by evaluating the thickness of deposits on the ventral side of the shell, from the surface to the calcein mark, with an optical micrometer1. The shell deposit rate (SDR) was calculated by dividing the thickness of the deposits by the time that had elapsed since marking. SDR is expressed in µm d–1.

**Supplementary Methods 2. Pearl rotation**

Pearl rotation was conducted in receiver oysters transplanted with a magnetized nucleus. The magnetized nucleus was produced by piercing the bead and including a bar magnet inside (length 0.5 mm; Ø 0.15 mm) before filling the holes with dental resin. Pearl rotation was then monitored in the pearl pouch of pearl oysters with a magnetometer placed in the derivation of the studied treatment tank as described in Le Moullac et al.2. The magnetometer was made of a half-sphere in acrylic glass (Ø 20 cm) on which were set 25 magnetic sensors spread across the convex surface at different angles (0°, 30°, 60° and 90°) to the base (where the grafted oyster was located). The human–machine interface (HMI), called “magneto” (VEGA Industrie, Avrainville, France), was composed of a microcontroller that uses internal software to collect, process and transfer data to the software (magneto-magnetometer interface 1.0) that produces visualized data from a real-time sensor. Data were processed with a MATLAB® system and converted into 3D coordinates for calculation of pearl movement kinetics. The mean angular speed of rotation (min–1) was recorded for 48 h.

**Supplementary Methods 3. Gametogenesis**

For histological analysis, the fixed gonads were dehydrated through a graded series of ethanol, embedded in paraffin, sectioned into 3 µm slices on a rotary microtome, stained using hematoxylin and eosin and finally mounted on glass microscope slides. Gametogenesis was evaluated for each individual through the identification of regression signs (*i.e.*, epithelial detachment or advanced regression stage).

**Supplementary Methods 4. Glycogen content**

Glycogen levels in muscle were measured in triplicate with a Glycogen Colorimetric/Fluorometric Assay Kit (BioVision©, Milpitas, CA, USA) following the manufacturer’s instructions. Briefly, 10 mg of thawed muscle was diluted with 200 µl of distilled water, then boiled at 100 °C for 10 min and centrifuged at 13,000 rpm for 5 min. The supernatants were hydrolyzed by incubation with a hydrolysis enzyme mixture for 30 min at room temperature. To avoid glucose background readings, a glucose control without the addition of a hydrolysis enzyme mixture was used to determine the level of glucose present in the samples, and thus, the glucose background was subtracted from the glycogen readings. Subsequently, the samples were incubated with a reaction mixture for the oxidation reaction, and the resulting-colored product was evaluated for optical density (OD) at 570 nm.

**Supplementary References**

1. Linard, C. et al. Calcein staining of calcified structures in pearl oyster *Pinctada margaritifera* and the effect of food resource level on shell growth. *Aquaculture* **313,** 149-155 (2011).

2. Le Moullac, G. et al. Influence of temperature and pearl rotation on biomineralization in the pearl oyster, *Pinctada margaritifera*. *J. Exp. Biol.* **221,** jeb186858 (2018).