**Supplementary file 1a. Summary of differently expressed genes of comparison between ds *GFP* and ds *ISARL* injection after 96h feeding on clean mice.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **Annotation** | **Gene Name** | **Log2FoldChange** | **P-value** |
| ISCW003049-RA | Soluble maltase-glucoamylase, putative (Fragment) | MGA | 6.956779911 | 3.80E-06 |
| ISCW007360-RA | Gamma glutamyl transpeptidase, putative | GGT | 6.22827548 | 5.26E-07 |
| ISCW024014-RA | Gamma glutamyl transpeptidase, putative (Fragment) | GGT | 6.190152254 | 5.27E-06 |
| ISCW024661-RA | Gamma glutamyl transpeptidase, putative (Fragment) | GGT | 6.190152254 | 5.27E-06 |
| ISCW012872-RA | Gamma-glutamyltransferase, putative (Fragment) | GGT | 6.012757202 | 2.94E-11 |
| ISCW009571-RA | Uncharacterized protein (Fragment) | ISCW009571 | 3.298128524 | 2.41E-05 |
| ISCW024915-RA | REX4, RNA exonuclease 4 (S. cerevisiae) family protein (Fragment) | REX4 | -0.549991457 | 2.24E-05 |
| ISCW024422-RA | Superoxide dismutase, putative | SOD | -1.11031654 | 5.27E-05 |
| ISCW012336-RA | Superoxide dismutase [cu-zn], putative  | CuZnSOD | -1.117657247 | 3.62E-05 |
| ISCW005879-RA | Uncharacterized protein | ISCW005879 | -1.608105744 | 1.35E-05 |
| ISCW012069-RA | Uncharacterized protein | ISCW012069 | -1.810228584 | 2.52E-06 |
| ISCW009622-RA | Uncharacterized protein | ISCW009622 | -2.535341888 | 1.26E-06 |
| ISCW018477-RA | Adiponectin receptor, putative (Fragment) | ISARL | -2.75905145 | 3.57E-22 |
| ISCW003837-RA | G2/mitotic-specific cyclin A, putative (Fragment) | cyclinA | -3.145555868 | 1.43E-06 |
| ISCW002566-RA | Acyl-CoA synthetase, putative (Fragment) | ACS | -3.53392918 | 5.23E-05 |
| ISCW008490-RA | Gamma glutamyl transpeptidase, putative | GGT | -5.476120094 | 5.66E-08 |
| ISCW013319-RA | Uncharacterized protein | ISCW013319 | -7.608882724 | 2.05E-07 |
| ISCW009608-RA | Glutathione S-transferase, putative | GST | -7.655953275 | 1.37E-05 |

“-” indicates downregulation of genes in the guts of ds *ISARL*-injected ticks when compared to that in control ds *GFP*-injected tick guts.

**Supplementary file 1b. Summary of differently expressed genes of comparison between ds *GFP* and ds *ISARL* injection after 96h feeding on *B. burgdorferi*-infected mice.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **Annotation** | **Gene Name** | **Log2FoldChange** | **P-value** |
| ISCW003218-RA | FADdependent oxidoreductase domain-containing protein 2, putative | FOXRED2 | -2.879056472 | 0.000239 |
| ISCW005667-RA | Secreted protein, putative | Reeler | -2.678543731 | 0.000119 |
| ISCW003629-RA | Secreted protein, putative | ISCW003629 | -2.426582135 | 0.0001 |
| ISCW018477-RA | Adiponectin receptor, putative (Fragment) | ISARL | -1.912092255 | 1.72E-11 |
| ISCW011292-RA | Cyclic nucleotidebinding domain-containing protein | CNBD | -1.620397316 | 0.00021 |
| ISCW003135-RA | Cytochrome p450, putative | CYP | -1.427275425 | 7.35E-05 |
| ISCW001955-RA | AMP dependent CoA ligase, putative  | AMP | -1.427082757 | 0.00027 |
| ISCW002185-RA | Uncharacterized protein | ISCW002185 | -1.251407193 | 3.40E-05 |
| ISCW024631-RA | 3-hydroxyacyl-CoA dehydrogenase, putative (Secreted salivary gland peptide, putative) | 3HADH | -1.089854316 | 2.66E-05 |
| ISCW013566-RA | Alpha-actinin, putative  | ACTN | -1.051823169 | 4.99E-05 |
| ISCW020505-RA | Uncharacterized protein | ISCW020505 | -1.038498406 | 4.11E-05 |
| ISCW019656-RA | Secreted salivary gland peptide, putative (Fragment) | ISCW019656 | -1.000151879 | 5.89E-05 |
| ISCW016391-RA | Cytochrome P450, putative  | CYP | -0.983747879 | 0.000348 |
| ISCW006151-RA | Transport protein, putative (Fragment) | ISCW006151 | -0.869973215 | 1.75E-05 |
| ISCW021203-RA | Uncharacterized protein | ISCW021203 | -0.826491344 | 9.19E-05 |
| ISCW024161-RA | Uncharacterized protein | ISCW024161 | -0.753881171 | 4.99E-05 |
| ISCW018609-RA | Hemomucin, putative (Fragment) | Hmu | -0.730567529 | 0.000361 |
| ISCW017282-RA | Oxodicarboxylate carrier protein, putative | ODC | -0.701243498 | 4.69E-05 |
| ISCW009471-RA | Phospholipase B-like (Fragment) | PLB | -0.694463465 | 8.01E-05 |
| ISCW006150-RA | Sugar transporter, putative | ISCW006150 | -0.666272429 | 6.70E-05 |
| ISCW012299-RA | Adenylosuccinate synthetase (Fragment) | ADSS | -0.649923076 | 0.00038 |
| ISCW022913-RA | cAMP and cAMP-inhibited cGMP 3,5-cyclic phosphodiesterase, putative | PDE | -0.612276289 | 3.11E-06 |
| ISCW000885-RA | Alpha-1,4 glucan phosphorylase | GP | -0.588614232 | 0.000254 |
| ISCW019117-RA | Pyridoxine kinase, putative (Fragment) | PDXK | -0.535676385 | 0.000478 |
| ISCW018543-RA | GMP synthase, putative (Fragment) | GMPS | -0.53194689 | 0.000465 |
| ISCW004028-RA | Phosphatidylserine synthase I, putative | PTDSS1 | -0.529598437 | 3.12E-05 |
| ISCW012521-RA | Uncharacterized protein | ISCW012521 | -0.517853294 | 2.92E-05 |
| ISCW009548-RA | Uncharacterized protein | ISCW009548 | -0.504914087 | 0.000199 |
| ISCW015732-RA | RNA polymerase II transcription elongation factor, putative | Elongin-C | -0.48942716 | 4.89E-05 |
| ISCW022144-RA | N-CAM Ig domain-containing protein, putative | Ncam | -0.437192969 | 0.000289 |
| ISCW009549-RA | Selenoprotein P precursor, putative | Selenop | -0.436460074 | 0.000423 |
| ISCW013692-RA | V-type proton ATPase subunit G | V-ATPase | -0.414399839 | 0.000311 |
| ISCW010157-RA | Receptor expression-enhancing protein | REEP | -0.405156446 | 0.000104 |
| ISCW023312-RA | Sidoreflexin | SFXN | -0.3999554 | 0.000229 |
| ISCW006433-RA | AP complex subunit sigma (Fragment) | APS | -0.395796427 | 0.000508 |

“-” indicates downregulation of genes in the guts of ds *ISARL*-injected ticks when compared to that in control ds *GFP*-injected tick guts.

**Supplementary file 1c. Summary of differently expressed genes of comparison between recombinant *GFP* and adiponectin proteins injection after 8h.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene** | **Annotation** | **Log2FoldChange** | ***P*-value** |
| ISCW004553-RA | Cuticle protein, putative | 18.51302808 | 2.05E-12 |
| ISCW002039-RA | Cuticle protein, putative | 17.49563794 | 2.29E-07 |
| ISCW001782-RA | Uncharacterized protein | 17.27754175 | 7.09E-10 |
| ISCW013798-RA | Cuticle protein, putative | 17.20315541 | 7.96E-05 |
| ISCW015495-RA | Secreted protein, putative (Fragment) | 17.15463748 | 0.00016026 |
| ISCW005191-RA | Secreted glycine rich protein, putative (Fragment) | 17.11093994 | 2.95E-08 |
| ISCW003789-RA | Uncharacterized protein | 16.81877212 | 2.70E-06 |
| ISCW016297-RA | Uncharacterized protein | 16.74612219 | 1.13E-06 |
| ISCW008562-RA | Cuticle protein, putative | 15.3237752 | 1.02E-06 |
| ISCW002925-RA | Uncharacterized protein | 2.857394251 | 1.82E-05 |
| ISCW024478-RA | Secreted cysteine rich protein, putative (Fragment) | 2.851254132 | 1.38E-05 |
| ISCW021558-RA | Secreted salivary gland peptide, putative | 2.689268024 | 3.51E-05 |
| ISCW021555-RA | Uncharacterized protein | 2.656702948 | 4.30E-05 |
| ISCW023547-RA | Secreted salivary gland peptide, putative | 2.589439049 | 0.0001213 |
| ISCW023623-RA | Serpin-4 precursor, putative (Serpin-4, putative) | 2.173997552 | 5.42E-05 |
| ISCW008209-RA | Hebreain, putative | 2.158930697 | 1.20E-06 |
| ISCW024733-RA | Beat protein, putative (Fragment) | 2.105356324 | 1.12E-05 |
| ISCW024387-RA | Serpin-2 precursor, putative (Fragment) | 2.00955178 | 5.56E-05 |
| ISCW002113-RA | Antimicrobial peptide microplusin | 1.940836315 | 0.00014064 |
| ISCW011893-RA | ANK\_REP\_REGION domain-containing protein | 1.808330643 | 1.28E-08 |
| ISCW015113-RA | Uncharacterized protein | 1.783621042 | 6.95E-05 |
| ISCW012685-RA | Myosin light chain 1, putative | 1.61605594 | 9.51E-05 |
| ISCW005837-RA | Uncharacterized protein | 1.582477028 | 3.43E-05 |
| ISCW024686-RA | Ixoderin, putative (Fragment) | 1.545371762 | 3.67E-06 |
| ISCW014652-RA | Serpin-8 precursor, putative  | 1.431124914 | 1.89E-06 |
| ISCW009063-RA | Tropomyosin, putative | 1.358977546 | 0.00014404 |
| ISCW023442-RA | Uncharacterized protein | 1.288696108 | 0.00015793 |
| ISCW023441-RA | Troponin, putative (Fragment) | 1.2703018 | 0.00010777 |
| ISCW016762-RA | LIM domain-containing protein, putative | 1.268776381 | 6.91E-06 |
| ISCW002637-RA | Reductase, putative | 1.195839092 | 5.26E-05 |
| ISCW017459-RA | Glucose-6-phosphatase | -1.182920138 | 0.00012321 |
| ISCW015064-RA | Cytochrome P450, putative | -1.276584666 | 5.75E-06 |
| ISCW015956-RA | Serine/threonine protein kinase, putative | -1.438675023 | 1.25E-05 |
| ISCW016390-RA | Cytochrome P450, putative | -1.643963635 | 3.32E-06 |
| ISCW016391-RA | Cytochrome P450, putative | -1.678990788 | 6.27E-05 |
| ISCW006560-RA | Cytochrome P450, putative | -2.209859052 | 1.42E-06 |
| ISCW024348-RA | Salivary HBP family protein, putative (Fragment) | -3.822772331 | 2.76E-05 |
| ISCW008563-RA | Cuticle protein, putative | -14.56782308 | 1.01E-06 |
| ISCW005940-RA | Elongation of very long chain fatty acids protein | -15.77527062 | 7.81E-08 |
| ISCW012372-RA | Cysteine rich secreted peptide, putative | -17.69968417 | 3.20E-09 |

“-” indicates downregulation of genes in the guts of adiponectin-injected ticks when compared to that in control GFP-injected tick guts.

**Supplementary file 1d. The primers used in this study.**

|  |  |
| --- | --- |
| **Gene name** | **Primer sequence** |
| Tick *actin* | F: GGCGACGTAGCAGR: GGTATCGTGCTCGACTC |
| Mouse *β-actin* | F: AGCGGGAAATCGTGCGTG R: CAGGGTACATGGTGGTGCC |
| *Borrelia* *flaB* | F: TTCAATCAGGTAACGGCACA R: GACGCRRGAGACCCTGAAAG |
| ds *GFP* | F: *TAATACGACTCACTATAGGGAGA*GCGACGTAAACGGCCACAAGTT R: *TAATACGACTCACTATAGGGAGA*CGGGTCTTGTAGTTGCCGTC |
| ds *ISARL* | F: *TAATACGACTCACTATAGGGAGA*GACGATGACGAGGATGAGCR: *TAATACGACTCACTATAGGGAGA*CGTGTGGAAGGTGAAGGAC |
| *ISARL* qPCR | F: TGCAGGACAACGACTACCTG R: ACCAGATGTTCCCGGTCTC |
| *ISARL*\_pEZT\_Dlux | F: AGGCGTTCAGTCTAGAATGGAGGTCCGCGAGCGACG R: AGACCGGCGGCCGCTCAAGCGTAATCTGGAACATCGTATGGGTAGTCGAATGGTGGACCCTCCT |
| 3HADH qPCR | F: GACCCCCTGATTGTTATTCG R: GCCATCCACTTCTTTCTTGA |
| ADSS qPCR | F: CACCGAGCAGAAGAACGAG R: GAGTAGCGGAGAACCACCAG |
| GMPS qPCR | F: CACCTTCATCACCCAGGACT R: TCTCGCTCACCATCTTCTTG |
| FOXRED2 qPCR | F: CCATCAACAACGACCTCTT R: GGCGTCCTAACTATCTTCAGT |
| Reeler qPCR | F: CCTGGAGGAACCTGAAGAAG R: AATGGCGTGGACGAAGTAAT |
| AMP qPCR | F: TACCACAACAAGCCACAAGC R: CGATGTAGAACTGCCCACTC |
| ODC qPCR | F: GTCTCACGGAGGCTGTCTTC R: TACGTGCTACGGCAAAGGTA |
| PDE qPCR | F: GACGGTGCGAAAGAACTACC R: TTGAATGCTCCTGTGGAATG |
| GP qPCR | F: GTGGAGATGCGAGAGGAGAT R: GTAGTCCCAGGCGTTGTAGC |
| PTDSS1 qPCR | F: ATGGCTTCGGCATCTTCTT R: TCGTGGTCTGAATGTCCTTG |
| Ncam qPCR | F: GCTGCGGGAGAACTATGTG R: CTTGTTGAGGTGTTGCTGCT |
| VATPase qPCR | F: ATGGCTAGTCAAAGCCAAGG R: CATCGGCGACTTTTTCAGAC |
| ACTN qPCR | F: ACCGCTACACCCAGTACACC R: TCTCGACCTCGTTGATGTTG |
| HMU qPCR | F: TCGACGCTTACTACGGTGTC R: GTCGTCCAGAAAGAGGATGC |
| PLB qPCR | F: GAATTTTCTCTGGCGACGAC R: AAGAGTTGCCGTTCCCTGT |
| PDXK qPCR | F: CTGAAAGAGGACAACCCTTCA R: GCTCCCTGTAGATGCTCACC |
| Selenop qPCR | F: CAGTGCAAGAAACTCCACCA R: AAAGTCTGGACGCCTTCGTA |
| SFXN qPCR | F: TCTCTGCGGTCTTCTGCTC R: CGAACCACCTCCTGAATCTC |
| ds *3HADH* | F: *TAATACGACTCACTATAGGGAGA*GTTGCACTCTTTGACGTGGA R: *TAATACGACTCACTATAGGGAGA*AGTGGGACGTAGTATGGTGGA |
| ds *PTDSS1* | F: *TAATACGACTCACTATAGGGAGA*CTAGTCAAAAGCCCGACCAC R: *TAATACGACTCACTATAGGGAGA*TGACCGCATACTCCTTCTCA |
| ds *ADSS* | F: *TAATACGACTCACTATAGGGAGA*CAGTGGTGAACAGCGTGAA R: *TAATACGACTCACTATAGGGAGA*TTGGTGGAAGTCAAAAACGA |
| ds *GMPS* | F: *TAATACGACTCACTATAGGGAGA*AAGGACTTCCACAAGGACGA R: *TAATACGACTCACTATAGGGAGA*ACACGTACACCACCCTGTTG |
| ds *NCAM* | F: *TAATACGACTCACTATAGGGAGA*ACTTTGGAGGTGCTGGACA R: *TAATACGACTCACTATAGGGAGA*AGAGAGTGGCAGACGGAGAC |
| ds *ACTN* | F: *TAATACGACTCACTATAGGGAGA*ATCTGCTGGACTACGGGAAG R: *TAATACGACTCACTATAGGGAGA*GGGTGTTGAAGTTGGTCTCC |
| ds *SFXN* | F: *TAATACGACTCACTATAGGGAGA*TTGGGACCAGAGCACCTACT R: *TAATACGACTCACTATAGGGAGA*GAAGCGTCCTACCAGAGGAG |
| ds *V-ATPase* | F: *TAATACGACTCACTATAGGGAGA*GAAGCAGGCAAAGGATGAAG R: *TAATACGACTCACTATAGGGAGA*AACGTCAGGAGCTGCTCAAT |
| ds *PSD* | F: *TAATACGACTCACTATAGGGAGA*GACTACCACCGCTTCCACTC R: *TAATACGACTCACTATAGGGAGA*CCTCGAAGATGAGCACCAC |
| PSD qPCR | F: GAAGGGCATCACCTACTCC R: CTTCTGCTGGTACTCCTCCTC |
| G6P1 qPCR | F: AGCCTGTCCCGAATCTACA R: CGTTGTCCGTGTCCATCTT |
| G6P2 qPCR | F: TCCATCTATTTCGGGCTGAT R: GTTCACGTAGGTCGGGTCAT |
| PEPCK1 qPCR | F: CAACACCATTTTCACCAACG R: AGTTTGCCTCCCTTTTCCA |
| PEPCK2 qPCR | F: TTCCACTGCCCAAGTATCG R: GCTCCGTGCTGATGAATGT |
| PEPCK3 qPCR | F: GAGCACAAAGGCAAGGTGA R: TTCCCAGACTCAGCCAATG |
| ds *G6P1* | F: *TAATACGACTCACTATAGGGAGA*GCCAGTGCTATGTCCACCT R: *TAATACGACTCACTATAGGGAGA*GAGACGCCCCGATAAAGAC |
| ds *G6P2* | F: *TAATACGACTCACTATAGGGAGA*AGCACCGACCCTTCTGGTA R: *TAATACGACTCACTATAGGGAGA*GATGACCCCACTGACTACGG |
| ds *C1QL3* | F: *TAATACGACTCACTATAGGGAGA*GAACATGCAGGCAGAAATCAR: *TAATACGACTCACTATAGGGAGA*ACGAGAAAGCCCGAGAAAG |
| C1QL3 qPCR | F: ACGAGAGCCATCACCTCCT R: TCCCCTTTCTGCGAATAAGA |
| C1QL3\_pMT | F: CTCGCTCGGGAGATCTATGCAGACCTGGGTTGTTCTTG R: GCCCTCTAGACTCGAGTACCGTCCCCTTTCTGCGAAT |

The underlines indicate restriction enzymes sites. The italicized letters indicate T7 promoter sequence.