**Table S4.** Gene Ontology pathways (biological processes) that were significantly enriched (*P*<0.05 after permutation) among the transcripts up-regulated after sleep restriction. *Total no. of genes in pathway* represents the number of genes that are annotated to the pathway. *Top no. of genes in pathway* represents the number of genes that were found in the study setting and contributed to the significance of the pathway.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Gene Ontology ID** | **Pathway** | **Opt. *P* value** | **Permuted *P* value** | **Total no. of genes in pathway** | **Gene rank** | **Top no. of genes in pathway** |
| GO:0042113 | B cell activation | 3.62E-06 | 0.001 | 90 | 1868 | 43 |
| GO:0032637 | interleukin-8 production | 6.49E-06 | 0.001 | 9 | 1282 | 8 |
| GO:0001530 | lipopolysaccharide binding | 6.49E-06 | 0.001 | 9 | 1282 | 8 |
| GO:0006805 | xenobiotic metabolic process | 1.23E-05 | 0.001 | 8 | 352 | 5 |
| GO:0050817 | coagulation | 1.40E-05 | 0.001 | 75 | 821 | 22 |
| GO:0045321 | leukocyte activation | 1.77E-05 | 0.001 | 208 | 1499 | 68 |
| GO:0001775 | cell activation | 2.20E-05 | 0.002 | 217 | 1499 | 70 |
| GO:0002460 | adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | 2.41E-05 | 0.002 | 83 | 2853 | 51 |
| GO:0005543 | phospholipid binding | 2.63E-05 | 0.003 | 91 | 1083 | 29 |
| GO:0046649 | lymphocyte activation | 2.96E-05 | 0.002 | 184 | 1499 | 61 |
| GO:0045416 | positive regulation of interleukin-8 biosynthetic process | 3.32E-05 | 0.001 | 8 | 1282 | 7 |
| GO:0042228 | interleukin-8 biosynthetic process | 3.32E-05 | 0.001 | 8 | 1282 | 7 |
| GO:0045414 | regulation of interleukin-8 biosynthetic process | 3.32E-05 | 0.001 | 8 | 1282 | 7 |
| GO:0015671 | oxygen transport | 3.61E-05 | 0.001 | 10 | 1329 | 8 |
| GO:0005833 | hemoglobin complex | 3.61E-05 | 0.001 | 10 | 1329 | 8 |
| GO:0002250 | adaptive immune response | 3.74E-05 | 0.001 | 88 | 2853 | 53 |
| GO:0002521 | leukocyte differentiation | 3.89E-05 | 0.002 | 110 | 2624 | 60 |
| GO:0009410 | response to xenobiotic stimulus | 5.10E-05 | 0.003 | 10 | 352 | 5 |
| GO:0005885 | Arp2/3 protein complex | 6.33E-05 | 0.001 | 15 | 3855 | 15 |
| GO:0030098 | lymphocyte differentiation | 7.09E-05 | 0.005 | 93 | 1482 | 35 |
| GO:0007249 | I-kappaB kinase/NF-kappaB cascade | 8.34E-05 | 0.003 | 107 | 1499 | 39 |
| GO:0042108 | positive regulation of cytokine biosynthetic process | 9.67E-05 | 0.003 | 26 | 2593 | 19 |
| GO:0015669 | gas transport | 1.11E-04 | 0.001 | 11 | 1329 | 8 |
| GO:0007596 | blood coagulation | 1.44E-04 | 0.006 | 65 | 588 | 15 |
| GO:0009620 | response to fungus | 1.51E-04 | 0.001 | 17 | 1282 | 10 |
| GO:0002695 | negative regulation of leukocyte activation | 1.88E-04 | 0.001 | 19 | 907 | 9 |
| GO:0050866 | negative regulation of cell activation | 1.88E-04 | 0.002 | 19 | 907 | 9 |
| GO:0042094 | interleukin-2 biosynthetic process | 1.95E-04 | 0.001 | 9 | 2843 | 9 |
| GO:0002449 | lymphocyte mediated immunity | 2.08E-04 | 0.007 | 76 | 3212 | 49 |
| GO:0045086 | positive regulation of interleukin-2 biosynthetic process | 2.41E-04 | 0.002 | 8 | 2593 | 8 |
| GO:0045076 | regulation of interleukin-2 biosynthetic process | 2.41E-04 | 0.002 | 8 | 2593 | 8 |
| GO:0050792 | regulation of viral reproduction | 2.41E-04 | 0.003 | 8 | 2593 | 8 |
| GO:0030097 | hemopoiesis | 2.45E-04 | 0.011 | 160 | 2624 | 79 |
| GO:0050819 | negative regulation of coagulation | 2.47E-04 | 0.001 | 10 | 807 | 6 |
| GO:0004859 | phospholipase inhibitor activity | 2.47E-04 | 0.002 | 10 | 807 | 6 |
| GO:0055102 | lipase inhibitor activity | 2.47E-04 | 0.005 | 10 | 807 | 6 |
| GO:0002520 | immune system development | 2.59E-04 | 0.013 | 176 | 2718 | 88 |
| GO:0030856 | regulation of epithelial cell differentiation | 2.76E-04 | 0.003 | 9 | 2954 | 9 |
| GO:0045884 | regulation of survival gene product expression | 2.93E-04 | 0.002 | 13 | 2528 | 11 |
| GO:0006916 | anti-apoptosis | 2.99E-04 | 0.006 | 153 | 1933 | 60 |
| GO:0002443 | leukocyte mediated immunity | 3.00E-04 | 0.012 | 85 | 2599 | 46 |
| GO:0001848 | complement binding | 3.11E-04 | 0.002 | 8 | 1152 | 6 |
| GO:0050850 | positive regulation of calcium-mediated signaling | 3.37E-04 | 0.002 | 12 | 2954 | 11 |
| GO:0050848 | regulation of calcium-mediated signaling | 3.37E-04 | 0.005 | 12 | 2954 | 11 |
| GO:0009595 | detection of biotic stimulus | 3.59E-04 | 0.005 | 13 | 2579 | 11 |
| GO:0045620 | negative regulation of lymphocyte differentiation | 3.67E-04 | 0.003 | 8 | 367 | 4 |
| GO:0045581 | negative regulation of T cell differentiation | 3.67E-04 | 0.004 | 8 | 367 | 4 |
| GO:0045637 | regulation of myeloid cell differentiation | 3.76E-04 | 0.004 | 25 | 2706 | 18 |
| GO:0006954 | inflammatory response | 3.79E-04 | 0.007 | 169 | 1160 | 44 |
| GO:0033764 | steroid dehydrogenase activity. acting on the CH-OH group of donors. NAD or NADP as acceptor | 3.85E-04 | 0.003 | 9 | 3066 | 9 |
| GO:0001816 | cytokine production | 4.04E-04 | 0.015 | 89 | 1160 | 27 |
| GO:0050868 | negative regulation of T cell activation | 4.43E-04 | 0.005 | 18 | 439 | 6 |
| GO:0051250 | negative regulation of lymphocyte activation | 4.43E-04 | 0.007 | 18 | 439 | 6 |
| GO:0048546 | digestive tract morphogenesis | 4.47E-04 | 0.003 | 8 | 2800 | 8 |
| GO:0048547 | gut morphogenesis | 4.47E-04 | 0.005 | 8 | 2800 | 8 |
| GO:0050776 | regulation of immune response | 4.66E-04 | 0.015 | 91 | 3215 | 56 |
| GO:0007599 | hemostasis | 4.73E-04 | 0.013 | 72 | 588 | 15 |
| GO:0009952 | anterior/posterior pattern formation | 4.93E-04 | 0.01 | 34 | 34 | 3 |
| GO:0030183 | B cell differentiation | 4.99E-04 | 0.011 | 53 | 1868 | 25 |
| GO:0045619 | regulation of lymphocyte differentiation | 5.18E-04 | 0.01 | 45 | 1339 | 18 |
| GO:0002682 | regulation of immune system process | 5.35E-04 | 0.015 | 158 | 3215 | 90 |
| GO:0004499 | flavin-containing monooxygenase activity | 5.57E-04 | 0.005 | 16 | 748 | 7 |
| GO:0050878 | regulation of body fluid levels | 6.43E-04 | 0.016 | 74 | 588 | 15 |
| GO:0006891 | intra-Golgi vesicle-mediated transport | 6.51E-04 | 0.004 | 15 | 1435 | 9 |
| GO:0048534 | hemopoietic or lymphoid organ development | 6.72E-04 | 0.017 | 166 | 2718 | 82 |
| GO:0006690 | icosanoid metabolic process | 6.80E-04 | 0.01 | 26 | 2948 | 19 |
| GO:0003002 | regionalization | 7.41E-04 | 0.014 | 39 | 34 | 3 |
| GO:0016064 | immunoglobulin mediated immune response | 7.59E-04 | 0.015 | 50 | 2853 | 31 |
| GO:0019724 | B cell mediated immunity | 7.59E-04 | 0.022 | 50 | 2853 | 31 |
| GO:0045580 | regulation of T cell differentiation | 7.73E-04 | 0.008 | 36 | 527 | 9 |
| GO:0042060 | wound healing | 8.02E-04 | 0.016 | 92 | 478 | 15 |
| GO:0046696 | lipopolysaccharide receptor complex | 8.29E-04 | 0.005 | 6 | 1282 | 5 |
| GO:0031201 | SNARE complex | 8.61E-04 | 0.007 | 6 | 1292 | 5 |
| GO:0050818 | regulation of coagulation | 8.94E-04 | 0.01 | 12 | 807 | 6 |
| GO:0032680 | regulation of tumor necrosis factor production | 9.41E-04 | 0.005 | 14 | 1282 | 8 |
| GO:0045087 | innate immune response | 9.68E-04 | 0.017 | 77 | 2599 | 41 |
| GO:0045444 | fat cell differentiation | 9.84E-04 | 0.012 | 17 | 3133 | 14 |
| GO:0003727 | single-stranded RNA binding | 1.00E-03 | 0.007 | 16 | 1094 | 8 |
| GO:0042805 | actinin binding | 1.01E-03 | 0.006 | 7 | 565 | 4 |
| GO:0002683 | negative regulation of immune system process | 1.06E-03 | 0.017 | 32 | 907 | 11 |
| GO:0016229 | steroid dehydrogenase activity | 1.10E-03 | 0.007 | 11 | 3066 | 10 |
| GO:0045638 | negative regulation of myeloid cell differentiation | 1.10E-03 | 0.009 | 11 | 1339 | 7 |
| GO:0019825 | oxygen binding | 1.21E-03 | 0.011 | 14 | 1329 | 8 |
| GO:0043123 | positive regulation of I-kappaB kinase/NF-kappaB cascade | 1.23E-03 | 0.03 | 75 | 1499 | 27 |
| GO:0016046 | detection of fungus | 1.31E-03 | 0.008 | 8 | 2208 | 7 |
| GO:0048562 | embryonic organ morphogenesis | 1.33E-03 | 0.011 | 11 | 1865 | 8 |
| GO:0007389 | pattern specification process | 1.33E-03 | 0.037 | 63 | 448 | 11 |
| GO:0001818 | negative regulation of cytokine production | 1.34E-03 | 0.01 | 8 | 3212 | 8 |
| GO:0030217 | T cell differentiation | 1.36E-03 | 0.031 | 57 | 1210 | 19 |
| GO:0042093 | T-helper cell differentiation | 1.37E-03 | 0.006 | 8 | 222 | 3 |
| GO:0045628 | regulation of T-helper 2 cell differentiation | 1.37E-03 | 0.009 | 8 | 222 | 3 |
| GO:0002294 | CD4-positive. alpha-beta T cell differentiation during immune response | 1.37E-03 | 0.01 | 8 | 222 | 3 |
| GO:0002292 | T cell differentiation during immune response | 1.37E-03 | 0.011 | 8 | 222 | 3 |
| GO:0045622 | regulation of T-helper cell differentiation | 1.37E-03 | 0.011 | 8 | 222 | 3 |
| GO:0002293 | alpha-beta T cell differentiation during immune response | 1.37E-03 | 0.011 | 8 | 222 | 3 |
| GO:0002285 | lymphocyte activation during immune response | 1.37E-03 | 0.013 | 8 | 222 | 3 |
| GO:0045064 | T-helper 2 cell differentiation | 1.37E-03 | 0.013 | 8 | 222 | 3 |
| GO:0002286 | T cell activation during immune response | 1.37E-03 | 0.014 | 8 | 222 | 3 |
| GO:0051241 | negative regulation of multicellular organismal process | 1.42E-03 | 0.019 | 33 | 907 | 11 |
| GO:0005544 | calcium-dependent phospholipid binding | 1.42E-03 | 0.02 | 15 | 942 | 7 |
| GO:0002684 | positive regulation of immune system process | 1.60E-03 | 0.037 | 126 | 3212 | 72 |
| GO:0050778 | positive regulation of immune response | 1.71E-03 | 0.034 | 79 | 2853 | 44 |
| GO:0051606 | detection of stimulus | 1.72E-03 | 0.026 | 32 | 1282 | 13 |
| GO:0046006 | regulation of activated T cell proliferation | 1.76E-03 | 0.009 | 10 | 2954 | 9 |
| GO:0042104 | positive regulation of activated T cell proliferation | 1.76E-03 | 0.018 | 10 | 2954 | 9 |
| GO:0005344 | oxygen transporter activity | 1.78E-03 | 0.006 | 9 | 1329 | 6 |
| GO:0050864 | regulation of B cell activation | 1.78E-03 | 0.019 | 31 | 2954 | 21 |
| GO:0045646 | regulation of erythrocyte differentiation | 1.80E-03 | 0.016 | 14 | 2706 | 11 |
| GO:0045066 | regulatory T cell differentiation | 1.94E-03 | 0.008 | 6 | 2593 | 6 |
| GO:0045069 | regulation of viral genome replication | 1.94E-03 | 0.016 | 6 | 2593 | 6 |
| GO:0016628 | oxidoreductase activity. acting on the CH-CH group of donors. NAD or NADP as acceptor | 1.99E-03 | 0.015 | 23 | 299 | 5 |
| GO:0034101 | erythrocyte homeostasis | 2.00E-03 | 0.029 | 33 | 3891 | 26 |
| GO:0002263 | cell activation during immune response | 2.00E-03 | 0.009 | 9 | 222 | 3 |
| GO:0043370 | regulation of CD4-positive. alpha beta T cell differentiation | 2.00E-03 | 0.013 | 9 | 222 | 3 |
| GO:0043367 | CD4-positive. alpha beta T cell differentiation | 2.00E-03 | 0.016 | 9 | 222 | 3 |
| GO:0002366 | leukocyte activation during immune response | 2.00E-03 | 0.019 | 9 | 222 | 3 |
| GO:0043029 | T cell homeostasis | 2.04E-03 | 0.015 | 15 | 2954 | 12 |
| GO:0043627 | response to estrogen stimulus | 2.29E-03 | 0.029 | 23 | 3122 | 17 |
| GO:0006693 | prostaglandin metabolic process | 2.30E-03 | 0.016 | 14 | 3325 | 12 |
| GO:0006692 | prostanoid metabolic process | 2.30E-03 | 0.023 | 14 | 3325 | 12 |
| GO:0008081 | phosphoric diester hydrolase activity | 2.38E-03 | 0.027 | 23 | 185 | 4 |
| GO:0050863 | regulation of T cell activation | 2.38E-03 | 0.041 | 75 | 527 | 13 |
| GO:0019864 | IgG binding | 2.38E-03 | 0.012 | 7 | 709 | 4 |
| GO:0043122 | regulation of I-kappaB kinase/NF-kappaB cascade | 2.39E-03 | 0.045 | 78 | 1499 | 27 |
| GO:0035091 | phosphoinositide binding | 2.42E-03 | 0.036 | 66 | 2393 | 33 |
| GO:0008637 | apoptotic mitochondrial changes | 2.44E-03 | 0.021 | 20 | 2348 | 13 |
| GO:0007156 | homophilic cell adhesion | 2.52E-03 | 0.025 | 16 | 961 | 7 |
| GO:0002694 | regulation of leukocyte activation | 2.60E-03 | 0.033 | 88 | 3212 | 52 |
| GO:0016709 | oxidoreductase activity. acting on paired donors. with incorporation or reduction of molecular oxygen. NADH or NADPH as one donor. and incorporation of one atom of oxygen | 2.62E-03 | 0.025 | 20 | 748 | 7 |
| GO:0048565 | gut development | 2.66E-03 | 0.019 | 9 | 2800 | 8 |
| GO:0045596 | negative regulation of cell differentiation | 2.66E-03 | 0.043 | 67 | 991 | 18 |
| GO:0009395 | phospholipid catabolic process | 2.76E-03 | 0.019 | 7 | 1311 | 5 |
| GO:0048584 | positive regulation of response to stimulus | 2.82E-03 | 0.045 | 92 | 3140 | 53 |
| GO:0032640 | tumor necrosis factor production | 2.90E-03 | 0.022 | 16 | 1282 | 8 |
| GO:0002764 | immune response-regulating signal transduction | 2.95E-03 | 0.043 | 43 | 527 | 9 |
| GO:0001974 | blood vessel remodeling | 3.05E-03 | 0.008 | 6 | 1681 | 5 |
| GO:0050869 | negative regulation of B cell activation | 3.07E-03 | 0.009 | 7 | 3212 | 7 |
| GO:0032760 | positive regulation of tumor necrosis factor production | 3.15E-03 | 0.024 | 13 | 1282 | 7 |
| GO:0007406 | negative regulation of neuroblast proliferation | 3.15E-03 | 0.026 | 12 | 3669 | 11 |
| GO:0045885 | positive regulation of survival gene product expression | 3.20E-03 | 0.018 | 8 | 2528 | 7 |
| GO:0009897 | external side of plasma membrane | 3.23E-03 | 0.049 | 72 | 1169 | 21 |
| GO:0045577 | regulation of B cell differentiation | 3.26E-03 | 0.024 | 19 | 2954 | 14 |
| GO:0016627 | oxidoreductase activity. acting on the CH-CH group of donors | 3.52E-03 | 0.043 | 44 | 528 | 9 |
| GO:0008060 | ARF GTPase activator activity | 3.59E-03 | 0.037 | 19 | 1936 | 11 |
| GO:0032312 | regulation of ARF GTPase activity | 3.59E-03 | 0.038 | 19 | 1936 | 11 |
| GO:0007405 | neuroblast proliferation | 3.66E-03 | 0.034 | 15 | 3669 | 13 |
| GO:0001889 | liver development | 3.78E-03 | 0.031 | 14 | 358 | 4 |
| GO:0034329 | cell junction assembly | 3.88E-03 | 0.025 | 11 | 472 | 4 |
| GO:0002347 | response to tumor cell | 3.89E-03 | 0.021 | 8 | 3669 | 8 |
| GO:0042035 | regulation of cytokine biosynthetic process | 3.96E-03 | 0.035 | 34 | 1475 | 14 |
| GO:0033180 | proton-transporting V-type ATPase. V1 domain | 4.00E-03 | 0.029 | 8 | 2615 | 7 |
| GO:0045088 | regulation of innate immune response | 4.14E-03 | 0.041 | 15 | 1129 | 7 |
| GO:0002833 | positive regulation of response to biotic stimulus | 4.24E-03 | 0.018 | 6 | 2954 | 6 |
| GO:0002836 | positive regulation of response to tumor cell | 4.24E-03 | 0.02 | 6 | 2954 | 6 |
| GO:0002837 | regulation of immune response to tumor cell | 4.24E-03 | 0.022 | 6 | 2954 | 6 |
| GO:0002834 | regulation of response to tumor cell | 4.24E-03 | 0.022 | 6 | 2954 | 6 |
| GO:0002418 | immune response to tumor cell | 4.24E-03 | 0.025 | 6 | 2954 | 6 |
| GO:0002839 | positive regulation of immune response to tumor cell | 4.24E-03 | 0.025 | 6 | 2954 | 6 |
| GO:0032623 | interleukin-2 production | 4.30E-03 | 0.037 | 12 | 3082 | 10 |
| GO:0008329 | pattern recognition receptor activity | 4.35E-03 | 0.03 | 9 | 2208 | 7 |
| GO:0006014 | D-ribose metabolic process | 4.36E-03 | 0.022 | 6 | 2967 | 6 |
| GO:0022409 | positive regulation of cell-cell adhesion | 4.36E-03 | 0.036 | 11 | 3555 | 10 |
| GO:0046626 | regulation of insulin receptor signaling pathway | 4.62E-03 | 0.025 | 6 | 474 | 3 |
| GO:0046627 | negative regulation of insulin receptor signaling pathway | 4.62E-03 | 0.028 | 6 | 474 | 3 |
| GO:0042100 | B cell proliferation | 4.63E-03 | 0.038 | 20 | 3212 | 15 |
| GO:0043020 | NADPH oxidase complex | 4.64E-03 | 0.026 | 6 | 1034 | 4 |
| GO:0040018 | positive regulation of multicellular organism growth | 4.66E-03 | 0.026 | 7 | 1468 | 5 |
| GO:0048566 | embryonic gut development | 5.00E-03 | 0.025 | 6 | 1865 | 5 |
| GO:0006997 | nucleus organization | 5.17E-03 | 0.04 | 16 | 2954 | 12 |
| GO:0043648 | dicarboxylic acid metabolic process | 5.26E-03 | 0.042 | 17 | 2725 | 12 |
| GO:0002863 | positive regulation of inflammatory response to antigenic stimulus | 6.20E-03 | 0.047 | 11 | 2954 | 9 |
| GO:0050798 | activated T cell proliferation | 6.20E-03 | 0.047 | 11 | 2954 | 9 |
| GO:0042092 | T-helper 2 type immune response | 6.24E-03 | 0.045 | 13 | 222 | 3 |
| GO:0032606 | type I interferon production | 6.80E-03 | 0.034 | 7 | 940 | 4 |
| GO:0045351 | type I interferon biosynthetic process | 6.80E-03 | 0.037 | 7 | 940 | 4 |
| GO:0030865 | cortical cytoskeleton organization | 6.91E-03 | 0.036 | 10 | 1015 | 5 |
| GO:0030018 | Z disc | 7.18E-03 | 0.048 | 12 | 826 | 5 |
| GO:0033081 | regulation of T cell differentiation in the thymus | 7.34E-03 | 0.039 | 6 | 1169 | 4 |
| GO:0006573 | valine metabolic process | 8.22E-03 | 0.039 | 7 | 2528 | 6 |
| GO:0032615 | interleukin-12 production | 8.27E-03 | 0.036 | 6 | 2075 | 5 |
| GO:0055088 | lipid homeostasis | 8.85E-03 | 0.043 | 8 | 2954 | 7 |
| GO:0055092 | sterol homeostasis | 8.85E-03 | 0.046 | 8 | 2954 | 7 |
| GO:0042632 | cholesterol homeostasis | 8.85E-03 | 0.047 | 8 | 2954 | 7 |
| GO:0016500 | protein-hormone receptor activity | 9.12E-03 | 0.042 | 6 | 2119 | 5 |
| GO:0042535 | positive regulation of tumor necrosis factor biosynthetic process | 1.03E-02 | 0.039 | 6 | 1282 | 4 |
| GO:0042533 | tumor necrosis factor biosynthetic process | 1.03E-02 | 0.045 | 6 | 1282 | 4 |
| GO:0002762 | negative regulation of myeloid leukocyte differentiation | 1.03E-02 | 0.047 | 6 | 1282 | 4 |