

| Supplementary Table 4: Ingenuity Canonical Pathways: Anakinra Vehicle Contrast | | | |
|---------------------------------------------------------------------------------------|----------------|--------------|---------------------|
| Canonical Pathways | p-value | Ratio | Genes |
| 24 h post-TBI | | | |
| Salvage Pathways of Pyrimidine Ribonucleotides | 0.04 | 9.8E-03 | UPP2 |
| Role of NFAT in Regulation of the Immune Response | 0.07 | 5.08E-03 | AKAP5 |
| Calcium Signaling | 0.07 | 4.74E-03 | AKAP5 |
| cAMP-mediated signaling | 0.09 | 4.52E-03 | AKAP5 |
| Protein Kinase A Signaling | 0.16 | 2.44E-03 | |
| 72 h post-TBI | | | |
| PXR/RXR Activation | 0.0002 | 3.45E-02 | NR1I3,IGFBP1,CYP2B6 |
| GADD45 Signaling | 0.0005 | 9.09E-02 | GADD45A,GADD45G |
| Retinol Biosynthesis | 0.0026 | 3.28E-02 | AADAC,Ces2g |
| Guanine and Guanosine Salvage I | 0.0041 | 1.11E-01 | HPRT1 |
| ATM Signaling | 0.0055 | 3.28E-02 | GADD45A,GADD45G |
| Growth Hormone Signaling | 0.0076 | 2.63E-02 | SOCS2,ONECUT1 |
| Adenine and Adenosine Salvage III | 0.0081 | 6.67E-02 | HPRT1 |
| Prolactin Signaling | 0.0091 | 2.5E-02 | MYC,SOCS2 |
| VDR/RXR Activation | 0.0098 | 2.47E-02 | GADD45A,IGFBP1 |
| Xenobiotic Metabolism Signaling | 0.0117 | 1.01E-02 | Ces2g,NR1I3,CYP2B6 |
| IGF-1 Signaling | 0.0145 | 1.9E-02 | SOCS2,IGFBP1 |
| p38 MAPK Signaling | 0.0200 | 1.71E-02 | MYC,IL1RN |
| Ubiquinol-10 Biosynthesis (Eukaryotic) | 0.0219 | 3.45E-02 | ECHDC1 |
| Aryl Hydrocarbon Receptor Signaling | 0.0257 | 1.24E-02 | MYC,Rarb |
| Fatty Acid Activation | 0.0257 | 5.26E-02 | ACSL3 |
| Oxidative Ethanol Degradation III | 0.0257 | 2.5E-02 | ACSL3 |
| Ethanol Degradation IV | 0.0302 | 3.45E-02 | ACSL3 |
| Mitochondrial L-carnitine Shuttle Pathway | 0.0339 | 4.55E-02 | ACSL3 |
| γ -linolenate Biosynthesis II (Animals) | 0.0355 | 4E-02 | ACSL3 |
| Acute Phase Response Signaling | 0.0389 | 1.12E-02 | IL1RN,SOCS2 |
| Estrogen-mediated S-phase Entry | 0.0417 | 3.57E-02 | MYC |
| Triacylglycerol Degradation | 0.0490 | 3.03E-02 | AADAC |
| Ethanol Degradation II | 0.0490 | 2.33E-02 | ACSL3 |
| Fatty Acid β -oxidation I | 0.0550 | 2.22E-02 | ACSL3 |
| Role of JAK2 in Hormone-like Cytokine Signaling | 0.0603 | 2.78E-02 | SOCS2 |
| IL-9 Signaling | 0.0631 | 2.5E-02 | SOCS2 |
| Stearate Biosynthesis I (Animals) | 0.0661 | 2E-02 | ACSL3 |
| Role of Cytokines in Mediating Communication between Immune Cells | 0.0708 | 1.82E-02 | IL1RN |

| | | | |
|------------------------------------------------------------|--------|----------|---------------------|
| Transcriptional Regulatory Network in Embryonic Stem Cells | 0.0741 | 2.5E-02 | ONECUT1 |
| Cell Cycle: G2/M DNA Damage Checkpoint Regulation | 0.0741 | 2.08E-02 | GADD45A |
| Retinoic acid Mediated Apoptosis Signaling | 0.0776 | 1.45E-02 | Rarb |
| Bupropion Degradation | 0.0776 | 1.92E-02 | CYP2B6 |
| Acetone Degradation I (to Methylglyoxal) | 0.0794 | 1.82E-02 | CYP2B6 |
| Heparan Sulfate Biosynthesis (Late Stages) | 0.0813 | 1.64E-02 | AADAC |
| Estrogen Biosynthesis | 0.1000 | 1.47E-02 | CYP2B6 |
| Cell Cycle: G1/S Checkpoint Regulation | 0.1000 | 1.52E-02 | MYC |
| Thrombopoietin Signaling | 0.1038 | 1.59E-02 | MYC |
| ErbB2-ErbB3 Signaling | 0.1038 | 1.67E-02 | MYC |
| Myc Mediated Apoptosis Signaling | 0.1074 | 1.67E-02 | MYC |
| Nicotine Degradation III | 0.1074 | 1.1E-02 | CYP2B6 |
| Melatonin Degradation I | 0.1074 | 1.2E-02 | CYP2B6 |
| ERK5 Signaling | 0.1109 | 1.54E-02 | MYC |
| T Helper Cell Differentiation | 0.1146 | 1.39E-02 | BCL6 |
| Communication between Innate and Adaptive Immune Cells | 0.1164 | 9.17E-03 | IL1RN |
| Nicotine Degradation II | 0.1199 | 9.71E-03 | CYP2B6 |
| IL-10 Signaling | 0.1253 | 1.28E-02 | IL1RN |
| JAK/Stat Signaling | 0.1253 | 1.43E-02 | SOCS2 |
| FXR/RXR Activation | 0.1393 | 9.9E-03 | IL1RN |
| PDGF Signaling | 0.1413 | 1.18E-02 | MYC |
| Neuregulin Signaling | 0.1535 | 9.8E-03 | MYC |
| Apoptosis Signaling | 0.1549 | 1.05E-02 | BCL2L11 |
| SAPK/JNK Signaling | 0.1603 | 9.8E-03 | GADD45A |
| Mouse Embryonic Stem Cell Pluripotency | 0.1652 | 1.01E-02 | MYC |
| PPAR Signaling | 0.1671 | 9.52E-03 | IL1RN |
| Cholecystinin/Gastrin-mediated Signaling | 0.1738 | 9.43E-03 | IL1RN |
| LXR/RXR Activation | 0.1871 | 7.35E-03 | IL1RN |
| Estrogen Receptor Signaling | 0.2037 | 7.35E-03 | IGFBP1 |
| IL-6 Signaling | 0.2037 | 8.06E-03 | IL1RN |
| NF-κB Signaling | 0.2541 | 5.71E-03 | IL1RN |
| B Cell Receptor Signaling | 0.2553 | 6.06E-03 | BCL6 |
| RAR Activation | 0.2793 | 5.29E-03 | Rarb |
| ILK Signaling | 0.2825 | 5.21E-03 | MYC |
| Glucocorticoid Receptor Signaling | 0.3846 | 3.4E-03 | IL1RN |
| | | | |
| 7 days post-TBI | | | |
| T Helper Cell Differentiation | 0.0005 | 4.17E-02 | HLA-DMA,FCER1G,BCL6 |
| Isoleucine Degradation I | 0.0005 | 6.67E-02 | ACAT2,SDS |

| | | | |
|------------------------------------------------------------|--------|----------|----------------|
| Acetyl-CoA Biosynthesis III (from Citrate) | 0.0026 | 1.25E-01 | ACLY |
| Epoxy-squalene Biosynthesis | 0.0051 | 1.11E-01 | SQLE |
| Nur77 Signaling in T Lymphocytes | 0.0055 | 3.17E-02 | HLA-DMA,FCER1G |
| Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells | 0.0065 | 2.35E-02 | HLA-DMA,FCER1G |
| Calcium-induced T Lymphocyte Apoptosis | 0.0076 | 2.86E-02 | HLA-DMA,FCER1G |
| OX40 Signaling Pathway | 0.0076 | 2.13E-02 | HLA-DMA,FCER1G |
| Glutamate Degradation II | 0.0078 | 1E-01 | GOT1 |
| L-cysteine Degradation I | 0.0102 | 9.09E-02 | GOT1 |
| Growth Hormone Signaling | 0.0123 | 2.63E-02 | SOCS2,ONECUT1 |
| CTLA4 Signaling in Cytotoxic T Lymphocytes | 0.0170 | 2.04E-02 | HLA-DMA,FCER1G |
| Aspartate Degradation II | 0.0178 | 7.14E-02 | GOT1 |
| Ketolysis | 0.0204 | 5.56E-02 | ACAT2 |
| iCOS-iCOSL Signaling in T Helper Cells | 0.0240 | 1.63E-02 | HLA-DMA,FCER1G |
| Glutaryl-CoA Degradation | 0.0257 | 4.17E-02 | ACAT2 |
| Ketogenesis | 0.0257 | 4.76E-02 | ACAT2 |
| Mevalonate Pathway I | 0.0257 | 3.57E-02 | ACAT2 |
| Glycine Betaine Degradation | 0.0257 | 4.35E-02 | SDS |
| CD28 Signaling in T Helper Cells | 0.0295 | 1.52E-02 | HLA-DMA,FCER1G |
| PKC θ Signaling in T Lymphocytes | 0.0295 | 1.4E-02 | HLA-DMA,FCER1G |
| Lipid Antigen Presentation by CD1 | 0.0309 | 4.35E-02 | FCER1G |
| Bile Acid Biosynthesis, Neutral Pathway | 0.0309 | 1.72E-02 | CYP7A1 |
| Cholesterol Biosynthesis I | 0.0331 | 2.5E-02 | SQLE |
| Phenylalanine Degradation IV (Mammalian, via Side Chain) | 0.0331 | 2.56E-02 | GOT1 |
| Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol) | 0.0331 | 2.5E-02 | SQLE |
| Cholesterol Biosynthesis III (via Desmosterol) | 0.0331 | 2.5E-02 | SQLE |
| Cdc42 Signaling | 0.0363 | 1.13E-02 | HLA-DMA,FCER1G |
| Valine Degradation I | 0.0407 | 2.86E-02 | SDS |
| Insulin Receptor Signaling | 0.0407 | 1.41E-02 | SGK1,ACLY |
| B Cell Development | 0.0501 | 3.03E-02 | HLA-DMA |
| Pyrimidine Ribonucleotides Interconversion | 0.0501 | 2.78E-02 | CTPS1 |
| Role of NFAT in Regulation of the Immune Response | 0.0562 | 1.02E-02 | HLA-DMA,FCER1G |
| Hematopoiesis from Pluripotent Stem Cells | 0.0646 | 1.59E-02 | FCER1G |
| Antigen Presentation Pathway | 0.0676 | 2.5E-02 | HLA-DMA |
| Fatty Acid β -oxidation I | 0.0708 | 2.22E-02 | SDS |
| Role of JAK2 in Hormone-like Cytokine Signaling | 0.0776 | 2.78E-02 | SOCS2 |
| IL-9 Signaling | 0.0794 | 2.5E-02 | SOCS2 |
| Netrin Signaling | 0.0891 | 1.75E-02 | ABLIM3 |
| cAMP-mediated signaling | 0.0891 | 9.05E-03 | DUSP1,DUSP6 |
| Transcriptional Regulatory Network in Embryonic Stem Cells | 0.0933 | 2.5E-02 | ONECUT1 |

| | | | |
|--------------------------------------------------------|--------|----------|-------------------|
| Retinol Biosynthesis | 0.0933 | 1.64E-02 | Ces2g |
| G-Protein Coupled Receptor Signaling | 0.1135 | 5.69E-03 | DUSP1,DUSP6,RGS16 |
| Glucocorticoid Receptor Signaling | 0.1256 | 6.8E-03 | DUSP1,SGK1 |
| PXR/RXR Activation | 0.1330 | 1.15E-02 | CYP7A1 |
| ERK5 Signaling | 0.1396 | 1.54E-02 | SGK1 |
| Pyridoxal 5'-phosphate Salvage Pathway | 0.1396 | 1.39E-02 | SGK1 |
| CCR5 Signaling in Macrophages | 0.1419 | 1.06E-02 | FCER1G |
| Communication between Innate and Adaptive Immune Cells | 0.1466 | 9.17E-03 | FCER1G |
| JAK/Stat Signaling | 0.1574 | 1.43E-02 | SOCS2 |
| IL-4 Signaling | 0.1574 | 1.27E-02 | HLA-DMA |
| Prolactin Signaling | 0.1706 | 1.25E-02 | SOCS2 |
| FXR/RXR Activation | 0.1750 | 9.9E-03 | CYP7A1 |
| Salvage Pathways of Pyrimidine Ribonucleotides | 0.1750 | 9.8E-03 | SGK1 |
| TR/RXR Activation | 0.1791 | 1.04E-02 | CYP7A1 |
| SAPK/JNK Signaling | 0.2004 | 9.8E-03 | FCER1G |
| IGF-1 Signaling | 0.2109 | 9.52E-03 | SOCS2 |
| Natural Killer Cell Signaling | 0.2128 | 8.62E-03 | FCER1G |
| Fc Epsilon RI Signaling | 0.2312 | 8.55E-03 | FCER1G |
| Protein Kinase A Signaling | 0.2328 | 4.89E-03 | DUSP1,DUSP6 |
| LXR/RXR Activation | 0.2328 | 7.35E-03 | CYP7A1 |
| p38 MAPK Signaling | 0.2449 | 8.55E-03 | DUSP1 |
| NF-κB Signaling | 0.3126 | 5.71E-03 | FCER1G |
| B Cell Receptor Signaling | 0.3148 | 6.06E-03 | BCL6 |
| EIF2 Signaling | 0.3236 | 4.95E-03 | RPL32 |
| Acute Phase Response Signaling | 0.3342 | 5.62E-03 | SOCS2 |
| RAR Activation | 0.3428 | 5.29E-03 | DUSP1 |
| Phospholipase C Signaling | 0.4102 | 3.85E-03 | FCER1G |
| Xenobiotic Metabolism Signaling | 0.4634 | 3.36E-03 | Ces2g |
| Axonal Guidance Signaling | 0.6138 | 2.27E-03 | ABLIM3 |