**S15 Table. Predicted upstream regulators in the endometrium of pregnant cows compared to non-pregnant cows using all studies. Predicted activation state was either activated (+) or inhibited (-).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| ACKR2 | --3.161.21E-16 | DDX58, DHX58, EIF2AK2, IFI16, IFI44, OAS1, OAS2, RSAD2, STAT1, USP18 | --3.749.28E-26 | ADAR, CXCL10, DDX58, DHX58, EIF2AK2, IFI16, IFI44, IRF7, ISG15, ISG20, OAS1, RSAD2, STAT1, USP18 | --3.873.53E-20 | ADAR, CCL11, CXCL10, EIF2AK2, IFI16, IFIT2, IFIT3, ISG15, ISG20, OAS1, OAS2, RSAD2, STAT1, STAT2, USP18 | --4.002.30E-22 | ADAR, CXCL10, DDX58, DHX58, EIF2AK2, IFI16, IFI44, IFIT2, IRF7, ISG15, ISG20, OAS1, RSAD2, STAT1, STAT2, USP18 |
| APP | +3.785.41E-08 | CMPK2, DDX58, DKK1, GBP2, HERC6, IFI16, IFIH1, LBP, PARP14, PAX5, RNF213, RSAD2, RTP4, TNFSF10, USP18, XAF1 | +3.903.35E-11 | C4A/C4B, CRYM, CXCL10, DDX58, DKK1, FABP3, GBP4, HERC6, IFI16, IFIH1, IRF7, ISG20, PARP14, RNF213, RSAD2, RTP4, TNFSF10, USP18, XAF1 | +3.907.10E-12 | C1S, C4A/C4B, CCL11, CCND1, CD40, CMPK2, COL13A1, CXCL10, DKK1, FCGR1A, GBP2, GBP4, GBP6, HERC6, IDO1, IFI16, IFI35, IFIH1, IFIT2, IRF3, IRF4, ISG20, KYNU, MAPT, NAMPT, PARP14, RNASEL, RNF213, RNF24, RSAD2, RTP4, TNFSF10, TRIM21, USP18, XAF1 | +3.496.42E-10 | CD40, CD69, CD86, CRYM, CXCL10, DDX58, DKK1, EPAS1, FABP3, FAP, FCGR1A, GBP4, H19, IDO1, IFI16, IFI35, IFIH1, IFIT2, IRF7, ISG20, MCM10, NCDN, PARP14, PYCARD, RNF213, RSAD2, RTP4, SHISA3, SOCS1, USP18, XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| BTK | --2.452.13E-06 | IFIT1, IRF9, MX1, MX2, OAS2, STAT1 | --3.162.03E-12 | CXCL10, IFI44L, IFIT1, IFITM1, IRF9, ISG15, ISG20, MX1, MX2, STAT1 | --3.863.49E-13 | CD274, CD40, CXCL10, IFI35, IFI44L, IFIT1, IFIT3, IRF4, IRF9, ISG15, ISG20, MX1, MX2, OAS2, STAT1 | --3.422.76E-12 | CCR7, CD40, CD69, CD86, CXCL10, IFI35, IFI44L, IFITM1, IRF9, ISG15, ISG20, MX1, MX2, STAT1 |
| CD3 | +2.551.08E-03 | BST2, GBP1, IFIT1, IRF9, PSMF1, STAT1, TNFSF10, XAF1 | +2.524.25E-07 | BST2, CXCL10, EIF4E, GBP1, IFIT1, IFITM1, IRF9, PPA1, SP100, STAT1, TNFSF10, XAF1 | +3.205.24E-08 | ANXA1, C2, CASP8, CCND1, CD274, CD53, COX7A1, CXCL10, GBP1, IFI35, IFIT1, IRF4, IRF9, MAP3K8, NAMPT, PPA1, PSMF1, STAT1, SYT7, TNFSF10, TRIM25, UBE2L6, XAF1 | +3.182.16E-05 | ALAS1, C2, CD69, CD86, CREM, CXCL10, GBP1, H19, IFI35, IFITM1, IRF9, PPA1, PSMF1, SMPDL3B, SOCS1, STAT1, UBE2L6, XAF1 |
| CGAS | +2.201.59E-08 | IFI44, IFIT1, OAS1, RSAD2, USP18 | +2.972.40E-17 | CXCL10, IFI44, IFI44L, IFIT1, IRF7, ISG15, OAS1, RSAD2, USP18 | +2.959.80E-13 | CXCL10, IFI44L, IFIT1, IFIT2, IFIT3, ISG15, OAS1, RSAD2, USP18 | +2.976.04E-13 | CXCL10, IFI44, IFI44L, IFIT2, IRF7, ISG15, OAS1, RSAD2, USP18 |
| DDX58 | +2.382.70E-14 | DDX58, EIF2AK2, IFI27, IFI44, IFIH1, IFIT1, OAS1, RSAD2, STAT1, TNFSF10 | +3.042.68E-22 | CXCL10, DDX58, EIF2AK2, IFI27, IFI44, IFIH1, IFIT1, IRF7, ISG15, ISG20, OAS1, RSAD2, STAT1, TNFSF10 | +3.631.52E-19 | CASP4, CXCL10, EIF2AK2, IFI27, IFI35, IFIH1, IFIT1, IFIT2, IFIT3, IRF3, ISG15, ISG20, OAS1, RSAD2, STAT1, STAT2, TNFSF10 | +3.171.51E-21 | CASP4, CXCL10, DDX58, EIF2AK2, IFI27, IFI35, IFI44, IFIH1, IFIT2, IRF7, ISG15, ISG20, NMI, OAS1, RSAD2, SOCS1, STAT1, STAT2 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| EIF2AK2 | +3.433.46E-16 | DDX58, EIF2AK2, IFI27, IFI6, IFIT1, IFIT5, OAS1, PARP12, PARP9, SP140, STAT1, USP18 | +3.824.61E-22 | DDX58, EIF2AK2, IFI27, IFI6, IFIT1, IFIT5, IFITM1, ISG15, ISG20, OAS1, PARP12, PARP9, SP140, STAT1, USP18 | +3.821.25E-15 | CCND1, EIF2AK2, IFI27, IFI35, IFI6, IFIT1, IFIT5, ISG15, ISG20, LGALS3BP, OAS1, PARP12, PARP9, STAT1, UBE2L6, USP18 | +4.282.84E-20 | ATF3, DDX58, EIF2AK2, IFI27, IFI35, IFI6, IFIT5, IFITM1, ISG15, ISG20, LGALS3BP, NMI, OAS1, PARP12, PARP9, SP140, STAT1, UBE2L6, USP18 |
| Ifn | +3.531.07E-16 | DDX58, DHX58, EIF2AK2, IFI16, IFIH1, IFIT1, IFITM3, MX1, OAS2, PML, RSAD2, STAT1, ZBP1 | +3.922.90E-24 | CXCL10, DDX58, DHX58, EIF2AK2, IFI16, IFIH1, IFIT1, IFITM1, IRF7, ISG15, ISG20, MX1, PML, RSAD2, SP100, STAT1, ZBP1 | +4.571.44E-23 | B2M, CASP8, CD40, CXCL10, EIF2AK2, IDO1, IFI16, IFIH1, IFIT1, IL23A, IRF3, ISG15, ISG20, MX1, OAS2, PML, RNASEL, RSAD2, STAT1, TAP1, TNFSF13B, TRIM21, ZBP1 | +4.153.16E-21 | CD40, CD58, CD69, CD86, CXCL10, DDX58, DHX58, EIF2AK2, IDO1, IFI16, IFIH1, IFITM1, IRF7, ISG15, ISG20, MX1, RSAD2, SOCS1, STAT1, TAP1, TNFSF13B |
| IFN Beta | +4.592.71E-31 | BST2, CMPK2, DDX58, EIF2AK2, HERC5, IFI16, IFI27, IFI44, IFI6, IFIH1, IFIT1, IRF9, MX1, MX2, OAS1, OAS2, RSAD2, STAT1, TNFSF10, USP18, XAF1, ZBP1 | +4.704.87E-36 | BST2, CXCL10, DDX58, EIF2AK2, IFI16, IFI27, IFI44, IFI6, IFIH1, IFIT1, IFITM1, IRF7, IRF9, ISG15, MX1, MX2, OAS1, PNPT1, RSAD2, STAT1, TNFSF10, USP18, XAF1, ZBP1 | +5.451.32E-34 | C3AR1, CASP4, CD274, CD40, CMPK2,CXCL10,EIF2AK2,HERC5,IDO1, IFI16,IFI27, IFI35,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IRF9,ISG15,MX1,MX2,OAS1,OAS2,PNPT1,RSAD2,STAT1,STAT2,TNFSF10, USP18, USP25, XAF1, ZBP1 | +5.017.85E-34 | ATF3, CASP4, CCR7, CD40, CD69, CD86, CXCL10, DDX58, EIF2AK2, IDO1,IFI16,IFI27,IFI35,IFI44,IFI6,IFIH1,IFIT2,IFITM1,IRF7,IRF9,ISG15,MX1,MX2,OAS1,PNPT1,RSAD2,SOCS1,STAT1,STAT2,USP18,XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| Ifn gamma | +2.428.41E-07 | EIF2AK2, GBP1, PML, STAT1, TNFSF10, XAF1 | +2.951.70E-11 | ADAR,CXCL10,EIF2AK2,GBP1,IFI44L,PML,STAT1,TNFSF10,XAF1 | +3.262.75E-09 | ADAR,CXCL10,EIF2AK2,GBP1,IFI44L,LGALS9,PML,PSME2,STAT1,TNFSF10,XAF1 | +2.482.24E-08 | ADAR,CD86,CXCL10,EIF2AK2,GBP1,IFI44L,LGALS9,SOCS1,STAT1,XAF1 |
| IFN type 1 | +3.118.25E-18 | BST2, DDX58, DHX58, EIF2AK2, IFI16, IFIH1, IFIT1, PML, STAT1, TNFSF10, UBA7 | +3.372.26E-22 | BST2,CXCL10,DDX58,DHX58,EIF2AK2,IFI16,IFIH1,IFIT1,ISG15,PML,STAT1,TNFSF10,UBA7 | +3.386.95E-19 | CGAS,CXCL10,EIF2AK2,IDO1,IFI16,IFIH1,IFIT1,IFIT2,ISG15,PML,STAT1,STAT2,TNFSF10,TNFSF13B,UBA7 | +3.381.47E-17 | CD69,CXCL10,DDX58,DHX58,EIF2AK2,IDO1,IFI16,IFIH1,IFIT2,ISG15,STAT1,STAT2,TNFSF13B,UBA7 |
| IFNA1/ IFNA13 | +3.663.47E-23 | CCL8, DHX58, EIF2AK2, IFI27, IFI6, IFIH1, IFIT1, MX1, OAS1, OAS2, RSAD2, SIGLEC1, STAT1, ZBP1 | +4.012.97E-30 | CCL8,CXCL10,DHX58,EIF2AK2,IFI27,IFI6,IFIH1,IFIT1,IFITM1,IRF7,ISG15,MX1,OAS1,RSAD2,SIGLEC1,STAT1,ZBP1 | +4.271.21E-24 | CD274,CD40,CXCL10,EIF2AK2,IFI27,IFI6,IFIH1,IFIT1,IFIT2,ISG15,MX1,OAS1,OAS2,RSAD2,SIGLEC1,STAT1,STAT2,UBE2L6,ZBP1 | +4.571.39E-30 | CCL8,CD40,CD69,CD86,CXCL10,DHX58,EIF2AK2,IFI27,IFI6,IFIH1,IFIT2,IFITM1,IRF7,ISG15,MX1,OAS1,RSAD2,SIGLEC1,SOCS1,STAT1,STAT2,UBE2L6 |
| IFNA10 | +2.206.16E-10 | CCL8, IFIH1 ,IFIT1, MX1, ZBP1 | +2.595.69E-15 | CCL8,CXCL10,IFIH1,IFIT1,ISG15,MX1,ZBP1 | +2.401.97E-09 | CXCL10,IFIH1,IFIT1,ISG15,MX1,ZBP1 | +2.191.07E-07 | CCL8,CXCL10,IFIH1,ISG15,MX1 |
| IFNA14 | +2.206.16E-10 | CCL8, IFIH1 ,IFIT1, MX1, ZBP1 | +2.595.69E-15 | CCL8,CXCL10,IFIH1,IFIT1,ISG15,MX1,ZBP1 | +2.401.97E-09 | CXCL10,IFIH1,IFIT1,ISG15,MX1,ZBP1 | +2.191.07E-07 | CCL8,CXCL10,IFIH1,ISG15,MX1 |
| IFNA16 | +2.209.21E-10 | CCL8, IFIH1 ,IFIT1, MX1, ZBP1 | +2.591.06E-14 | CCL8,CXCL10,IFIH1,IFIT1,ISG15,MX1,ZBP1 | +2.403.26E-09 | CXCL10,IFIH1,IFIT1,ISG15,MX1,ZBP1 | +2.191.60E-07 | CCL8,CXCL10,IFIH1,ISG15,MX1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IFNA2 | +5.715.88E-48 | BST2, CCL8, CMPK2, DDX58, EIF2AK2, GBP1, GBP2, HERC5, HERC6, IFI16, IFI27, IFI44, IFI6, IFIH1, IFIT1, IFIT5, IFITM3, IRF9, MX1, MX2, OAS1, OAS2, PARP12, PARP9, PML, RSAD2, SAMD9, SP110, STAT1, TNFSF10, UBA7, USP18, XAF1, ZBP1 | +5.901.73E-53 | BST2, CCL8, CXCL10,DDX58, EIF2AK2,GBP1, GBP4,HERC6, IFI16,IFI27,IFI44, IFI44L,IFI6,IFIH1, IFIT1,IFIT5,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,OAS1,PARP12, PARP9,PML, RSAD2,SAMD9, SP100,STAT1, TNFSF10,UBA7, USP18,XAF1, ZBP1 | +7.029.08E-56 | ANXA1,B2M,C1S,CD274,CMPK2, CXCL10,EIF2AK2,GBP1,GBP2,GBP4,HERC5,HERC6, HSH2D,IDO1,IFI16,IFI27,IFI35,IFI44L,IFI6,IFIH1,IFIT1, IFIT2,IFIT3,IFIT5, IRF9,ISG15,ISG20,LAMP3,LGALS3BP,LY6E,MX1,MX2, OAS1,OAS2,PARP12,PARP9,PML, RSAD2,SHFL, SLC15A3,SP110, STAT1,TAP1, TDRD7,TNFSF10,TREX1,TRIM21, UBA7,UBE2L6,USP18,XAF1,ZBP1 | +6.453.03E-43 | BCL2L14,CCL8,CD69,CD86,CNP,CXCL10,DDX58,EIF2AK2,GBP1,GBP4,IDO1,IFI16,IFI27,IFI35,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IFIT5,IFITM1,IRF7,IRF9,ISG15,ISG20,LGALS3BP,LY6E,MX1,MX2,OAS1,PARP12,PARP9,RSAD2,SAMD9,SOCS1,STAT1,TAP1,TDRD7,TREX1,UBA7,UBE2L6,USP18,XAF1 |
| IFNA21 | +2.206.16E-10 | CCL8, IFIH1, IFIT1, MX1, ZBP1 | +2.595.69E-15 | CCL8, CXCL10, IFIH1, IFIT1, ISG15,MX1,ZBP1 | +2.401.97E-09 | CXCL10,IFIH1, IFIT1,ISG15,MX1, ZBP1 | +2.181.07E-07 | CCL8,CXCL10, IFIH1,ISG15,MX1 |
| IFNA4 | +2.762.37E-12 | CCL8, GBP2, IFIH1, IFIT1, MX1, RSAD2, USP18, ZBP1 | +3.061.52E-16 | CCL8, CXCL10, GBP5, IFIH1, IFIT1,ISG15,MX1,RSAD2,USP18, ZBP1 | +3.178.57E-18 | CD274,CXCL10, GBP2, H2-T24, IFIH1,IFIT1,IFIT2,ISG15,MAP3K8,MX1,PMEPA1,RSAD2, USP18,ZBP1 | +3.378.41E-15 | CCL8,CD69,CD86,CXCL10,GBP5, H2-T24, IFIH1,IFIT2,ISG15,MX1,RSAD2, USP18 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IFNA5 | +2.206.16E-10 | CCL8, IFIH1, IFIT1, MX1, ZBP1 | +2.595.69E-15 | CCL8,CXCL10, IFIH1,IFIT1,ISG15, MX1,ZBP1 | +2.401.97E-09 | CXCL10,IFIH1, IFIT1,ISG15,MX1, ZBP1 | +2.191.07E-07 | CCL8,CXCL10, IFIH1,ISG15,MX1 |
| IFNA6 | +2.206.16E-10 | CCL8, IFIH1, IFIT1, MX1, ZBP1 | +2.595.69E-15 | CCL8, CXCL10, IFIH1, IFIT1, ISG15, MX1, ZBP1 | +2.401.97E-09 | CXCL10, IFIH1, IFIT1, ISG15, MX1, ZBP1 | +2.191.07E-07 | CCL8, CXCL10, IFIH1, ISG15, MX1 |
| IFNA7 | +2.206.16E-10 | CCL8, IFIH1, IFIT1, MX1, ZBP1 | +2.595.69E-15 | CCL8, CXCL10, IFIH1, IFIT1, ISG15, MX1, ZBP1 | +2.401.97E-09 | CXCL10, IFIH1, IFIT1, ISG15, MX1, ZBP1 | +2.191.07E-07 | CCL8, CXCL10, IFIH1, ISG15, MX1 |
| IFNA8 | +2.209.21E-10 | CCL8, IFIH1, IFIT1, MX1, ZBP1 | +2.601.06E-14 | CCL8, CXCL10, IFIH1, IFIT1, ISG15, MX1, ZBP1 | +2.413.26E-09 | CXCL10, IFIH1, IFIT1, ISG15, MX1, ZBP1 | +2.201.60E-07 | CCL8, CXCL10, IFIH1, ISG15, MX1 |
| Ifnar | +3.921.41E-23 | DDX58, EIF2AK2, GBP2, IFI16, IFIH1, IFITM3, IRF9, OAS1, OAS2, RNF213, RSAD2, STAT1, TNFSF10, USP18, XAF1, ZBP1 | +4.134.31E-28 | CXCL10, DDX58, EIF2AK2, IFI16, IFIH1, IRF7, IRF9, ISG15, ISG20, OAS1, PNPT1, RNF213, RSAD2, STAT1, TNFSF10, USP18, XAF1, ZBP1 | +5.286.08E-36 | B2M, CD274, CD40, CXCL10, EIF2AK2, GBP2, IDO1, IFI16, IFI35, IFIH1, IFIT2, IFIT3, IRF9, ISG15, ISG20, OAS1, OAS2, PNPT1, RNF213, RSAD2, STAT1, STAT2, TAP1, TNFSF10, TRIM21, UBE2L6, USP18, XAF1, ZBP1 | +4.897.33E-30 | CD40, CD86, CXCL10, DDX58, EIF2AK2, IDO1, IFI16, IFI35, IFIH1, IFIT2, IRF7, IRF9, ISG15, ISG20, NLRC5, OAS1, PNPT1, RNF213, RSAD2, STAT1, STAT2, TAP1, UBE2L6, USP18, XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IFNAR1 | +2.805.42E-20 | CMPK2, EIF2AK2, IFI16, IFI44, IFI6, IFIH1, MX2, OAS1, OAS2, PARP12, RSAD2, RTP4, STAT1, TNFSF10, USP18, XAF1 | +2.968.61E-26 | CXCL10, EIF2AK2, GBP4, IFI16, IFI44, IFI6, IFIH1, IFITM1, IRF7, ISG15, MX2, OAS1, PARP12, RSAD2, RTP4, STAT1, TNFSF10, USP18, XAF1 | +3.471.48E-30 | B2M, CD274, CD40, CGAS, CMPK2, CXCL10, EIF2AK2, F2, GBP4, HSH2D, IDO1, IFI16, IFI6, IFIH1, IFIT2, IFIT3, ISG15, LAMP3, MX2, OAS1, OAS2, PARP12, RSAD2, RTP4, STAT1, TNFSF10, TNFSF13B, USP18, USP25, XAF1 | +3.551.68E-25 | ATF3, BCL2L14, CD40, CD86, CXCL10, EIF2AK2, GBP4, IDO1, IFI16, IFI44, IFI6, IFIH1, IFIT2, IFITM1, IRF7, ISG15, MX2, OAS1, PARP12, RSAD2, RTP4, SOCS1, STAT1, TNFSF13B, USP18, XAF1 |
| IFNAR2 | +2.241.89E-20 | DDX58, HERC5, IFI44, IFI6, IFIH1, MX2, OAS1, OAS2, TNFSF10, UBA7, USP18, XAF1 | +2.242.82E-25 | CXCL10, DDX58, GBP4, IFI44, IFI6, IFIH1, IFITM1, ISG15, MX2, OAS1, TNFSF10, UBA7, USP18, XAF1 | +2.654.51E-25 | CXCL10, GBP4, HERC5, HSH2D, IDO1, IFI6, IFIH1, ISG15, LAMP3, MX2, OAS1, OAS2, PSME2, TNFSF10, UBA7, UBE2L6, USP18, XAF1 | +2.458.39E-22 | BCL2L14, CXCL10, DDX58, GBP4, IDO1, IFI44, IFI6, IFIH1, IFITM1, ISG15, MX2, OAS1, UBA7, UBE2L6, USP18, XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IFNB1 | +4.708.18E-31 | BST2, CMPK2, DDX58, DHX58, EIF2AK2, GBP2, HERC5, IFI16, IFI27, IFI6, IFIH1, IFIT1, IRF9, MX1, OAS1, OAS2, PARP12, PARP14, PML, RSAD2, STAT1, TNFSF10, UBA7, USP18, XAF1, ZBP1 | +5.064.65E-37 | BST2, CXCL10, DDX58, DHX58, EIF2AK2, GBP4, GBP5, IFI16, IFI27, IFI6, IFIH1, IFIT1, IFITM1, IRF7, IRF9, ISG15, ISG20, MX1, OAS1, PARP12, PARP14, PML, RSAD2, STAT1, TNFSF10, UBA7, USP18, XAF1, ZBP1 | +5.676.60E-32 | CASP8, CD274, CD40, CMPK2, CXCL10, EIF2AK2, GBP2, GBP4, GBP6, HERC5, IDO1, IFI16, IFI27, IFI6, IFIH1, IFIT1, IFIT2, IFIT3, IRF3, IRF9, ISG15, ISG20, MX1, OAS1, OAS2, PARP12, PARP14, PML, RNASEL, RSAD2, STAT1, STAT2, TNFSF10, TRIM21, UBA7, USP18, XAF1, ZBP1 | +5.355.44E-29 | CD40, CD86, CREM, CRYAB, CXCL10, DDX58, DHX58, EIF2AK2, GBP4, GBP5, IDO1, IFI16, IFI27, IFI6, IFIH1, IFIT2, IFITM1, IRF7, IRF9, ISG15, ISG20, MCM10, MX1, NMI, NT5C3A, OAS1, PARP12, PARP14, RSAD2, SOCS1, STAT1, STAT2,UBA7, USP18,XAF1 |
| IFNE | +2.801.10E-12 | BST2, HERC5, IFIH1, IFITM3, MX2, STAT1, USP18, ZBP1 | +3.134.39E-19 | BST2, CXCL10, EIF4E, IFIH1, ISG15, ISG20, MX2, SLC7A2, STAT1, USP18, ZBP1 | +3.132.00E-13 | CD40, CXCL10, HERC5, IFIH1, IFIT2, ISG15, ISG20, MX2, STAT1, USP18, ZBP1 | +2.974.28E-12 | CD40, CD86, CXCL10, IFIH1, IFIT2, ISG15, ISG20, MX2, STAT1, USP18 |

S15 Table. Continued.

|  |  |  |  |  |
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|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IFNG | +6.131.93E-27 | BATF2, BST2, CCL8, CMPK2, DDX58, DKK1, DTX3L, EIF2AK2, GBP1, GBP2, HERC6, IFI16, IFI27, IFI44, IFI6, IFIH1, IFIT1, IFIT5, IFITM3, IRF9, MLKL, MX1, MX2, OAS1, OAS2,PARP14, PARP9,PLAAT3, PML,PSMF1, PTX3,RSAD2, RTP4, SAMD9,SP110, STAT1,TNFSF10, USP18,XAF1 | +6.164.54E-29 | BST2, C4A/C4B, CCL8,CXCL10,DDX58,DKK1,DTX3L,EIF2AK2,GBP1, GBP4,GBP5, HERC6,IFI16, IFI27,IFI44,IFI44L, IFI6,IFIH1,IFIT1, IFIT5,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,OAS1, PARP14,PARP9, PML,RSAD2,RTP4,SAMD9,SP100, STAT1,TNFSF10,USP18,XAF1 | +7.693.22E-46 | AGRN,B2M,BATF2,C1QB,C1QC,C2,C4A/C4B,CASP4,CASP8,CCL11,CCND1,CD274,CD40,CGAS,CMPK2,CXCL10,DKK1,DTX3L,EDNRB,EIF2AK2,ESM1,FCGR1A,GBP1,GBP2,GBP4,GBP6,HERC6,IDO1,IFI16,IFI27,IFI35,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IFIT5,IL23A,IRF3,IRF4,IRF9,ISG15,ISG20,KRT17,KYNU,LAMP3,LGALS3BP,LGALS9,LY6E,MAP3K8,MLKL,MST1R,MX1,MX2,NAMPT,OAS1,OAS2,OPTN,P2RY14,PARP14,PARP9,PLAUR,PML,PSMA2,PSME2,PSMF1,RNF114,RSAD2,RTP4,SCLY,SLC15A3,SLC40A1,SOAT1,SP110,STAT1,STAT2,SYT7,TAP1,TNFSF10,TNFSF13B,TREM2,TRIM21,UBE2L6, USP18,XAF1 | +7.428.60E-33 | ABLIM3,ALOX12, ALOX5AP,ARG2, ATF3,C1QB,C1QC,C2,CALHM6, CASP4,CCL8, CD40,CD86,CFB, CREM,CXCL10, DDX58,DKK1, EIF2AK2,FBP1, FCGR1A,GBP1, GBP4,GBP5,IDO1, IFI16,IFI27,IFI35, IFI44,IFI44L,IFI6, IFIH1,IFIT2,IFIT5, IFITM1,IRF7,IRF9, ISG15,ISG20, KRT17,LGALS3BP,LGALS9,LY6E, MLKL,MST1R,MX1,MX2,NCF2,NLRC5,NMI,OAS1, PARP14,PARP9, PIGR,PSMF1, PTX3,RSAD2, RTP4,SAMD9, SCNN1A,SLC12A2,SOCS1,STAT1,STAT2,TAP1,TNFSF13B,UBE2L6,USP18,WARS1,XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
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|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IFNK | +2.459.20E-11 | EIF2AK2,IFIH1,MX1,OAS1,STAT1,ZBP1 | +2.453.98E-13 | CXCL10,EIF2AK2,IFIH1,MX1,OAS1,STAT1,ZBP1 | +2.652.59E-11 | CD40,CXCL10,EIF2AK2,IFIH1,MX1,OAS1,STAT1,ZBP1 | +2.651.69E-11 | CD40,CD86,CXCL10,EIF2AK2,IFIH1,MX1,OAS1,STAT1 |
| IFNL1 | +5.083.49E-48 | BST2,CMPK2,DDX58,EIF2AK2,GBP1,HERC5,HERC6,IFI27,IFI44,IFI6,IFIH1,IFIT1,IFIT5,IFITM3,IRF9,MLKL,MX1,OAS1,OAS2,PML,RSAD2,RTP4,SAMD9,SP110,STAT1,USP18,XAF1 | +5.191.21E-51 | BST2,CXCL10,DDX58,EIF2AK2,GBP1,GBP5,HERC6,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IFIT5,IFITM1,IRF9,ISG15,ISG20,MX1,OAS1,PML,RSAD2,RTP4,SAMD9,SP100,STAT1,USP18,XAF1 | +6.041.24E-54 | CD40,CMPK2,CXCL10,EIF2AK2,GBP1,HERC5,HERC6,IFI27,IFI35,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IFIT5,IRF9,ISG15,ISG20,LAMP3,LGALS3BP,MLKL,MX1,OAS1,OAS2,PML,RSAD2,RTP4,SHFL,SLC15A3,SP110,STAT1,STAT2,TDRD7,TMEM140,UBE2L6,USP18,XAF1 | +5.711.16E-47 | ATF3,CCR7,CD40,CXCL10,DDX58,EIF2AK2,GBP1,GBP5,IFI27,IFI35,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IFIT5,IFITM1,IRF9,ISG15,ISG20,LGALS3BP,MLKL,MX1,OAS1,RSAD2,RTP4,SAMD9,STAT1,STAT2,TDRD7,TMEM140,UBE2L6,USP18,XAF1 |
| IFNL3 | +2.426.57E-10 | DDX58,IFIH1,MX1,RSAD2,STAT1,USP18 | +2.604.19E-12 | DDX58,IFIH1,ISG20,MX1,RSAD2,STAT1,USP18 | +2.763.90E-10 | IFIH1,IL23A,ISG20,MX1,RNASEL,RSAD2,STAT1,USP18 | +2.008.17E-06 | CXCL10,IRF7,MX1,RSAD2 |
| IFNL4 | +2.804.08E-18 | DDX58,DHX58,IFIH1,IFIT1,MX1,OAS1,OAS2,STAT1 | +2.972.66E-21 | CXCL10,DDX58,DHX58,IFIH1,IFIT1,ISG15,MX1,OAS1,STAT1 | +2.802.86E-14 | CXCL10,IFIH1,IFIT1,ISG15,MX1,OAS1,OAS2,STAT1 | +2.792.55E-10 | DDX58,IFIH1,ISG20,MX1,RSAD2,SOCS1,STAT1,USP18 |
| IKBKG | +2.001.07E-03 | GBP2,IFI16,PTX3,TNFSF10 | +2.206.20E-05 | CXCL10,IFI16,IRF7,ISG15,TNFSF10 | +2.211.05E-02 | CXCL10,GBP2,IFI16,ISG15,TNFSF10 | +2.801.85E-14 | CXCL10,DDX58,DHX58,IFIH1,ISG15,MX1,OAS1,STAT1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IKZF1 | --2.755.43E-10 | CYP2J2,DKK1,DTX3L,EPSTI1,IFI16,IFI27,IFI6,IFIT5,PAX5,RNF213,RTP4 | --2.956.70E-08 | DKK1,DTX3L,EPSTI1,IFI16,IFI27,IFI6,IFIT5,RNF213,RTP4 | --3.099.75E-07 | B2M,DIPK1A,DKK1,DTX3L,EPSTI1,IFI16,IFI27,IFI6,IFIT3,IFIT5,IRF4,RNF213,RTP4 | --2.618.16E-03 | DKK1,IFI16,IFI27,IFI6,IFIT5,RNF213,RTP4 |
| IKZF3 | --2.653.20E-09 | DDX58,DKK1,IFI27,IFI6,IFIT5,RNF213,RTP4 | --2.834.19E-11 | DDX58,DKK1,IFI27,IFI6,IFIT5,IRF7,RNF213,RTP4 | --2.635.13E-06 | DKK1,IFI27,IFI6,IFIT3,IFIT5,RNF213,RTP4 | --2.832.52E-07 | DDX58,DKK1,IFI27,IFI6,IFIT5,IRF7,RNF213,RTP4 |
| IL10RA | --3.007.59E-07 | BATF2,GBP2,IFI16,MLKL,PLAAT3,RNF213,RSAD2,STAT1,ZBP1 | --2.654.36E-05 | GBP5,IFI16,IRF7,RNF213,RSAD2,STAT1,ZBP1 | --3.761.30E-09 | BATF2,CD40,CLEC12A,DRAM1,EDNRB,GBP2,GBP6,GDA,IFI16,IL23A,MLKL,NAMPT,RIPK3,RNF213,RSAD2,STAT1,TAP1,ZBP1 | --4.123.98E-09 | ARG2,CALHM6,CCR7,CD40,CD69,CFB,COL14A1,DRAM1,GBP5,IFI16,IRF7,MLKL,NLRC5,RNF213,RSAD2,STAT1,TAP1 |
| IL1B | +3.206.99E-08 | CCL8,CMPK2,GBP1,GBP2,HERC5,IFI16,IFIT1,LBP,MEF2B,MX1,OAS2,PTX3,RSAD2,STAT1,TNFSF10,USP18 | +3.321.00E-06 | CCL8,CXCL10,EIF4E,GBP1,IFI16,IFIT1,IRF7,ISG15,ISG20,MX1,RSAD2,STAT1,TNFSF10,USP18 | +5.395.10E-13 | ANXA1,B2M,CASP4,CCL11,CD274,CD40,CMPK2,CXCL10,GBP1,GBP2,GBP6,HERC5,IDO1,IFI16,IFIT1,IFIT3,IL23A,IRF4,ISG15,ISG20,LGALS9,MAP3K8,MAPT,MX1,NAMPT,OAS2,OXTR,PSME2,RSAD2,SCLY,STAT1,TCIM,TNFSF10,TNFSF13B,TREM2,UBE2L6,USP18 | +4.661.10E-11 | ATF3,CASP4,CCL8,CCR7,CD40,CD69,CD86,CFB,CREM,CRYAB,CXCL10,EPAS1,GBP1,H19,IDO1,IFI16,IRF7,ISG15,ISG20,LGALS9,MX1,NMI,OSMR,OXTR,PIGR,PTX3,RGS16,RSAD2,SCNN1A,SOCS1,STAT1,TNFSF13B,UBE2L6,USP18 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IL1RN | --4.369.22E-27 | DDX58,GBP1,HERC6,IFI27,IFI44,IFI6,IFIH1,IFIT5,IRF9,MX1,MX2,OAS1,OAS2,PML,RSAD2,RTP4,SAMD9,TNFSF10,USP18 | --4.692.77E-33 | DDX58,GBP1,HERC6,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT5,IRF7,IRF9,ISG20,MX1,MX2,OAS1,PML,RSAD2,RTP4,SAMD9,SP100,TNFSF10,USP18 | --4.803.15E-24 | GBP1,HERC6,IFI27,IFI44L,IFI6,IFIH1,IFIT3,IFIT5,IL23A,IRF9,ISG20,LAMP3,LGALS9,MX1,MX2,OAS1,OAS2,PML,RSAD2,RTP4,SLC15A3,STAT2,TNFSF10,USP18 | --4.581.52E-20 | ATF3,DDX58,GBP1,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT5,IRF7,IRF9,ISG20,LGALS9,MX1,MX2,OAS1,RSAD2,RTP4,SAMD9,STAT2,USP18 |
| IL21 | +2.335.97E-09 | CMPK2,EIF2AK2,HERC6,IFI16,IFIT1,OAS2,PAX5,RSAD2,USP18 | +2.531.39E-10 | CXCL10,EIF2AK2,GBP5,HERC6,IFI16,IFIT1,IRF7,ISG15,RSAD2,USP18 | +2.935.12E-16 | CCL11,CMPK2,CXCL10,EIF2AK2,GBP6,HERC6,HSH2D,IDO1,IFI16,IFIT1,IFIT2,IFIT3,IL23A,IRF4,ISG15,OAS2,RSAD2,STAT2,TAP1,USP18 | +3.293.94E-14 | ARG2,CALHM6,CCR7,CD69,CD86,CXCL10,EIF2AK2,GBP5,IDO1,IFI16,IFIT2,IRF7,ISG15,RSAD2,SOCS1,STAT2,TAP1,USP18 |
| IL27 | +2.614.81E-07 | BST2,EIF2AK2,GBP2,MX1,OAS1,STAT1,TNFSF10 | +2.612.94E-07 | BST2,CXCL10,EIF2AK2,MX1,OAS1,STAT1,TNFSF10 | +3.411.65E-08 | B2M,CD274,CXCL10,EIF2AK2,GBP2,MX1,OAS1,STAT1,STAT2,TAP1,TNFSF10,TNFSF13B | +3.119.41E-08 | CD69,CD86,CXCL10,EIF2AK2,MX1,OAS1,SOCS1,STAT1,STAT2,TAP1,TNFSF13B |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| Interferon alpha | +5.051.09E- 41 | BST2,DDX58,DHX58,EIF2AK2,EPSTI1,GBP1,GBP2,HERC5,HERC6,IFI16,IFI27,IFI44,IFI6,IFIH1,IFIT1,IFITM3,IRF9,MX1,MX2,OAS1,OAS2,PARP12,PARP14,PARP9,PML,RNF213,RSAD2,RTP4,SAMD9,SIGLEC1,SP110,STAT1,TNFSF10,UBA7,USP18,ZBP1 | +5.512.38E-54 | ADAR,BST2,CXCL10,DDX58,DHX58,EIF2AK2,EPSTI1,GBP1,GBP5,HERC6,IFI16,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,OAS1,PARP12,PARP14,PARP9,PML,PNPT1,RNF213,RSAD2,RTP4,SAMD9,SIGLEC1,SP100,STAT1,TNFSF10,TRANK1,UBA7,USP18,ZBP1 | +6.571.62E-59 | ADAR,B2M,C3AR1,CASP8,CCND1,CD274,CD40,CGAS,CMTR1,COX7A1,CXCL10,EIF2AK2,EPSTI1,FCGR1A,GBP1,GBP2,GBP6,HERC5,HERC6,IDO1,IFI16,IFI27,IFI35,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IRF4,IRF9,ISG15,ISG20,LAMP3,LGALS9,MX1,MX2,OAS1,OAS2,PARP10,PARP12,PARP14,PARP9,PML,PNPT1,RNASEL,RNF213,RSAD2,RTP4,SHFL,SIGLEC1,SP110,STAT1,STAT2,TAP1,TDRD7,TMEM140,TNFSF10,TNFSF13B,TRANK1,TRIM21,UBA7,UBE2L6,USP18,USP25,ZBP1 | +6.283.71E-46 | ADAR,ATF3,CCR7,CD40,CD69,CD86,CXCL10,DDX58,DHX58,EIF2AK2,FCGR1A,GBP1,GBP5,IDO1,IFI16,IFI27,IFI35,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IFITM1,IRF7,IRF9,ISG15,ISG20,LGALS9,MX1,MX2,NMI,NT5C3A,OAS1,PARP12,PARP14,PARP9,PNPT1,RNF213,RSAD2,RTP4,SAMD9,SIGLEC1,SLC5A1,SOCS1,STAT1,STAT2,TAP1,TDRD7,TMEM140,TNFSF13B,TRANK1,UBA7,UBE2L6,USP18,WARS1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IRF1 | +4.509.49E-29 | CMPK2,DDX58,EIF2AK2,GBP2,IFI27,IFI44,IFI6,IFIH1,IFIT1,IFIT5,IFITM3,IRF9,MX1,OAS1,OAS2,PLAAT3,PML,RSAD2,SP110,STAT1,TNFSF10,XAF1 | +4.489.54E-28 | CXCL10,DDX58,EIF2AK2,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IFIT5,IFITM1,IRF7,IRF9,ISG15,MX1,OAS1,PML,RSAD2,STAT1,TNFSF10,XAF1 | +5.471.31E-36 | B2M,CASP8,CCND1,CD274,CD40,CMPK2,CXCL10,EIF2AK2,GBP2,IDO1,IFI27,IFI35,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IFIT5,IRF4,IRF9,ISG15,MX1,OAS1,OAS2,PML,PSME2,RSAD2,SP110,STAT1,STAT2,TAP1,TNFSF10,TNFSF13B,TRIM21,XAF1 | +4.534.58E-26 | CD40,CFB,CXCL10,DDX58,EIF2AK2,IDO1,IFI27,IFI35,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IFIT5,IFITM1,IRF7,IRF9,ISG15,MX1,OAS1,PIGR,RSAD2,SOCS1,STAT1,STAT2,TAP1,TNFSF13B,XAF1 |
| IRF3 | +4.679.84E-30 | CMPK2,DDX58,DHX58,EIF2AK2,GBP1,IFI16,IFI27,IFI44,IFI6,IFIH1,IFIT1,IFITM3,OAS1,OAS2,PARP12,PARP14,PLAC8,PML,RSAD2,STAT1,TNFSF10,USP18,ZBP1 | +5.034.21E-38 | ADAR,CXCL10,DDX58,DHX58,EIF2AK2,GBP1,GBP5,IFI16,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IRF7,ISG15,ISG20,OAS1,PARP12,PARP14,PLAC8,PML,RSAD2,STAT1,TNFSF10,USP18,ZBP1 | +5.737.33E-37 | ADAR,B2M,CD274,CD40,CMPK2,CXCL10,EIF2AK2,FCGR1A,GBP1,IFI16,IFI27,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IL23A,IRF3,ISG15,ISG20,OAS1,OAS2,PARP12,PARP14,PLAC8,PML,RSAD2,STAT1,STAT2,TAP1,TDRD7,TNFSF10,TREX1,UBE2L6,USP18,ZBP1 | +5.892.92E-39 | ADAR,ARG2,CALHM6,CD40,CD58,CD69,CD86,CXCL10,DDX58,DHX58,EIF2AK2,FCGR1A,GBP1,GBP5,IFI16,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IRF7,ISG15,ISG20,NLRC5,NT5C3A,OAS1,PARP12,PARP14,PLAC8,RSAD2,STAT1,STAT2,TAP1,TDRD7,TREX1,UBE2L6,USP18 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| IRF4 | --2.622.53E-06 | GBP1,IRF9,OAS1,PAX5,SPIB,STAT1,TNFSF10 | --2.425.07E-09 | CXCL10,GBP1,IRF7,IRF9,ISG15,ISG20,OAS1,STAT1,TNFSF10 | --3.103.60E-10 | B2M,CXCL10,GBP1,IRF4,IRF9,ISG15,ISG20,OAS1,PLAUR,PSMA2,STAT1,STAT2,TNFSF10,TNFSF13B,TRIM21 | --2.638.18E-06 | CXCL10,GBP1,IRF7,IRF9,ISG15,ISG20,OAS1,STAT1,STAT2,TNFSF13B |
| IRF5 | +3.532.04E-20 | CMPK2,DDX58,DHX58,IFI44,IFIH1,IFIT1,IFITM3,OAS1,OAS2,PARP12,RSAD2,SP110,STAT1,TNFSF10 | +3.526.89E-21 | CXCL10,DDX58,DHX58,IFI44,IFIH1,IFIT1,IRF7,ISG15,ISG20,OAS1,PARP12,RSAD2,STAT1,TNFSF10 | +4.148.85E-21 | CMPK2,CXCL10,IFIH1,IFIT1,IFIT2,IFIT3,IL23A,ISG15,ISG20,NAMPT,OAS1,OAS2,PARP12,RSAD2,SP110,STAT1,STAT2,TNFSF10,UBE2L6 | +3.918.81E-17 | CXCL10,DDX58,DHX58,IFI44,IFIH1,IFIT2,IRF7,ISG15,ISG20,NT5C3A,OAS1,PARP12,RSAD2,STAT1,STAT2,UBE2L6 |
| IRF7 | +5.164.75E-41 | CCL8,CMPK2,DDX58,DHX58,GBP1,HERC5,IFI16,IFI44,IFI6,IFIH1,IFIT1,IFITM3,IRF9,MX1,MX2,OAS1,OAS2,PARP12,PARP14,PLAC8,RSAD2,RTP4,STAT1,TNFSF10,UBA7,USP18,XAF1,ZBP1 | +5.598.71E-53 | ADAR,CCL8,CXCL10,DDX58,DHX58,GBP1,GBP4,GBP5,IFI16,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,OAS1,PARP12,PARP14,PLAC8,RSAD2,RTP4,STAT1,TNFSF10,UBA7,USP18,XAF1,ZBP1 | +6.605.54E-56 | ADAR,CASP4,CD40,CMPK2,CXCL10,FCGR1A,GBP1,GBP4,HERC5,IDO1,IFI16,IFI35,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IRF9,ISG15,ISG20,MAP3K8,MX1,MX2,NAMPT,OAS1,OAS2,PARP12,PARP14,PLAC8,PSME2,RSAD2,RTP4,STAT1,STAT2,TAP1,TDRD7,TNFSF10,TNFSF13B,TREX1,TRIM21,UBA7,UBE2L6,USP18,USP25,XAF1,ZBP1 | +6.683.41E-57 | ADAR,CALHM6,CASP4,CCL8,CD40,CD69,CXCL10,DDX58,DHX58,FCGR1A,GBP1,GBP4,GBP5,IDO1,IFI16,IFI35,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,NMI,NT5C3A,OAS1,PARP12,PARP14,PLAC8,RSAD2,RTP4,SOCS1,STAT1,STAT2,TAP1,TDRD7,TNFSF13B,TREX1,UBA7,UBE2L6,USP18,XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| Irgm1 | --2.001.38E-05 | IFI16,OAS2,RSAD2,USP18 | --2.242.43E-07 | CXCL10,IFI16,IRF7,RSAD2,USP18 | --2.652.16E-07 | CXCL10,IFI16,IFIT2,IFIT3,OAS2,RSAD2,USP18 | --2.453.07E-06 | CXCL10,IFI16,IFIT2,IRF7,RSAD2,USP18 |
| JAK | +2.831.10E-12 | DDX58,EIF2AK2,IFI6,IFIH1,IFIT1,IFITM3,RSAD2,STAT1 | +3.006.34E-15 | CXCL10,DDX58,EIF2AK2,IFI6,IFIH1,IFIT1,ISG15,RSAD2,STAT1 | +3.162.00E-13 | CD40,CXCL10,EIF2AK2,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,ISG15,RSAD2,STAT1 | +3.001.11E-13 | CD40,CXCL10,DDX58,EIF2AK2,IFI6,IFIH1,IFIT2,ISG15,RSAD2,SOCS1,STAT1 |
| JAK1 | +2.243.23E-06 | EIF2AK2,IRF9,MX1,STAT1,USP18 | +2.246.89E-08 | EIF2AK2,IRF7,IRF9,MX1,STAT1,USP18 | +2.991.21E-09 | CD40,EIF2AK2,IFIT2,IRF9,MAP3K8,MX1,STAT1,STAT2,TAP1,USP18 | +2.993.38E-11 | CD40,EIF2AK2,IFIT2,IRF7,IRF9,MX1,OSMR,STAT1,STAT2,TAP1,USP18 |
| JAK1/2 | +2.223.47E-06 | EIF2AK2,GBP2,MX1,PLAC8,RSAD2 | +2.631.92E-09 | EIF2AK2,GBP5,IRF7,ISG15,MX1,PLAC8,RSAD2 | +2.635.13E-06 | EIF2AK2,GBP2,GDA,ISG15,MX1,PLAC8,RSAD2 | +2.812.52E-07 | CD69,EIF2AK2,GBP5,IRF7,ISG15,MX1,PLAC8,RSAD2 |
| KRAS | --3.157.65E-06 | CPM,CYP2J2,EIF2AK2,IFI6,IFIT1,IFITM3,IRF9,MX1,MX2,OAS1,STAT1,TNFSF10 | --3.301.72E-09 | ADAR,CXCL10,EIF2AK2,EIF4E,IFI6,IFIT1,IFITM1,IRF9,ISG15,MX1,MX2,OAS1,SP100,STAT1,TNFSF10 | --2.865.59E-10 | ADAR,AGRN,B2M,BTC,BZW2,CCND1,CD274,CXCL10,EIF2AK2,IDO1,IFI6,IFIT1,IRF9,ISG15,LAMP3,MX1,MX2,OAS1,P2RY14,PGAM2,SLC34A2,SOAT1,STAT1,STAT2,TAP1,TNFSF10,XRN2 | --3.051.31E-06 | ADAR,ATF3,BCL2L14,BZW2,CRYAB,CXCL10,EIF2AK2,H1-2,IDO1,IFI6,IFITM1,IRF9,ISG15,MX1,MX2,NCF2,OAS1,PYCARD,STAT1,STAT2,TAP1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| MAPK1 | --4.771.18E-24 | BST2,DDX58,EIF2AK2,GBP1,GBP2,HERC5,IFI16,IFI27,IFI44,IFI6,IFIH1,IFIT1,IFIT5,IFITM3,IRF9,MX2,OAS1,OAS2,PARP12,PML,SP110,STAT1,TNFSF10,USP18 | --5.073.11E-30 | ADAR,BST2,DDX58,EIF2AK2,GBP1,GBP5,IFI16,IFI27,IFI44,IFI6,IFIH1,IFIT1,IFIT5,IFITM1,IRF7,IRF9,ISG15,ISG20,MX2,OAS1,PARP12,PML,SP100,STAT1,TNFSF10,TRANK1,USP18 | --6.286.80E-31 | ADAR,C1S,CCND1,EIF2AK2,GBP1,GBP2,GRAMD1B,HERC5,IFI16,IFI27,IFI35,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IFIT5,IRF9,ISG15,ISG20,KRT17,LAMP3,LGALS3BP,MX2,OAS1,OAS2,PARP12,PML,PSME2,SP110,STAT1,STAT2,TAP1,TDRD7,TNFSF10,TRANK1,TRIM21,TRIM25,TRIM34,UBE2L6,USP18 | --4.582.59E-28 | ADAR,ARG2,ATF3,CD69,CFB,DDX58,EIF2AK2,GBP1,GBP5,IFI16,IFI27,IFI35,IFI44,IFI6,IFIH1,IFIT2,IFIT5,IFITM1,IRF7,IRF9,ISG15,ISG20,KRT17,LGALS3BP,MX2,NMI,OAS1,PARP12,RGS16,SCNN1A,STAT1,STAT2,TAP1,TDRD7,TRANK1,TRIM34,UBE2L6,USP18 |
| MAVS | +3.273.57E-16 | CMPK2,DDX58,DHX58,IFIT1,IFITM3,OAS1,OAS2,PARP12,RSAD2,STAT1,USP18 | +3.392.16E-20 | ADAR,CXCL10,DDX58,DHX58,IFIT1,IRF7,ISG15,ISG20,OAS1,PARP12,RSAD2,STAT1,USP18 | +3.921.17E-19 | ADAR,CGAS,CMPK2,CXCL10,IFIT1,IFIT2,IFIT3,ISG15,ISG20,OAS1,OAS2,PARP12,RSAD2,STAT1,STAT2,UBE2L6,USP18 | +3.914.63E-20 | ADAR,CXCL10,DDX58,DHX58,IFIT2,IRF7,ISG15,ISG20,NT5C3A,OAS1,PARP12,RSAD2,SOCS1,STAT1,STAT2,UBE2L6,USP18 |
| mir-21 | --2.603.99E-05 | DHX58,GBP2,IFI16,OAS2,SIGLEC1,STAT1,UBA7 | --2.782.37E-06 | CXCL10,DHX58,GBP5,IFI16,PPA1,SIGLEC1,STAT1,UBA7 | --4.304.01E-11 | CASP4,CCND1,CD274,CXCL10,FCGR1A,GBP2,GBP6,IDO1,IFI16,OAS2,PPA1,PSME2,SIGLEC1,STAT1,STAT2,TAP1,TREM2,UBA7,UBE2L6 | --3.835.58E-08 | CASP4,CXCL10,DHX58,FCGR1A,GBP5,IDO1,IFI16,NLRC5,PPA1,SIGLEC1,STAT1,STAT2,TAP1,UBA7,UBE2L6 |
| MSC | +2.453.03E-08 | EPSTI1,IFI27,IFI44,IFIT1,PAX5,XAF1 | +2.653.96E-10 | EPSTI1,IFI27,IFI44,IFI44L,IFIT1,IRF7,XAF1 | +2.242.10E-04 | EPSTI1,IFI27,IFI44L,IFIT1,XAF1 | +2.241.64E-04 | IFI27,IFI44,IFI44L,IRF7,XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| NFATC2 | +2.004.72E-03 | CMPK2,PML,RSAD2,STAT1 | +2.652.15E-07 | CXCL10,GBP4,IRF7,ISG15,ISG20,PML,RSAD2,STAT1 | +2.701.72E-11 | CASP4,CD274,CD40,CMPK2,CXCL10,GBP4,IFIT2,IFIT3,IRF4,ISG15,ISG20,PML,RSAD2,STAT1,STAT2,TNFSF13B,USP25 | +2.507.29E-12 | CASP4,CCR7,CD40,CD86,CRYAB,CXCL10,GBP4,IFIT2,IRF7,ISG15,ISG20,NMI,RSAD2,SOCS1,STAT1,STAT2,TNFSF13B |
| NFkB (complex) | +2.405.00E-03 | CCL8,GBP2,HERC5,PTX3,RSAD2,SPIB,TNFSF10 | +2.161.35E-02 | CCL8,CXCL10,IRF7,ISG15,RSAD2,TNFSF10 | +3.923.21E-09 | CASP4,CASP8,CCL11,CCND1,CD274,CD40,CXCL10,EDNRB,FCGR1A,GBP2,HERC5,IDO1,IL23A,IRF3,IRF4,ISG15,KRT17,KYNU,MAP3K8,NAMPT,RSAD2,SCLY,SOAT1,TAP1,TNFSF10 | +4.012.41E-08 | ATF3,CASP4,CCL8,CCR7,CD40,CD69,CD86,CFB,CREM,CXCL10,EPAS1,FCGR1A,IDO1,IRF7,ISG15,KRT17,MSTN,NCF2,PTX3,RGS16,RSAD2,SOCS1,TAP1 |
| NGLY1 | --2.391.43E-09 | IFI27,IFI44,IFIT1,OAS1,RSAD2,USP18 | --2.761.01E-13 | CXCL10,IFI27,IFI44,IFI44L,IFIT1,OAS1,RSAD2,USP18 | --2.913.12E-11 | CXCL10,IFI27,IFI44L,IFIT1,IFIT2,IFIT3,OAS1,RSAD2,USP18 | --2.767.37E-10 | CXCL10,IFI27,IFI44,IFI44L,IFIT2,OAS1,RSAD2,USP18 |
| NKX2-3 | --4.363.22E-22 | BATF2,CMPK2,DDX58,DHX58,EIF2AK2,GBP1,GBP2,PARP12,PARP14,PARP9,RNF213,RTP4,SAMD9,SP110,STAT1,UBA7,USP18,XAF1,ZNFX1 | --4.004.04E-18 | DDX58,DHX58,EIF2AK2,GBP1,PARP12,PARP14,PARP9,PNPT1,RNF213,RTP4,SAMD9,STAT1,UBA7,USP18,XAF1,ZNFX1 | --4.756.23E-26 | BATF2,CMPK2,EIF2AK2,GBP1,GBP2,IDO1,LY6E,MFNG,PARP10,PARP12,PARP14,PARP9,PNPT1,PTPRE,RNF213,RTP4,SHFL,SLC40A1,SP110,STAT1,STAT2,TAP1,TCIM,TIPARP,TRIM21,UBA7,UBE2L6,USP18,XAF1,ZNFX1 | --4.602.39E-20 | C2CD4B,CRYAB,DDX58,DHX58,EIF2AK2,GBP1,IDO1,LY6E,NT5C3A,PARP12,PARP14,PARP9,PLEKHA4,PNPT1,RNF213,RTP4,SAMD9,STAT1,STAT2,TAP1,UBA7,UBE2L6,USP18,XAF1,ZNFX1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| NRAS | --2.622.80E-07 | GBP2,IFI16,IFIH1,IFIT1,LBP,PTX3,STAT1,USP18 | --2.213.19E-05 | IFI16,IFIH1,IFIT1,ISG15,STAT1,USP18 | --2.748.25E-09 | AGRN,B2M,CCND1,GBP2,IFI16,IFI35,IFIH1,IFIT1,ISG15,RNASE6,SLC66A3,STAT1,TAP1,USP18 | --2.182.95E-07 | CD86,EPAS1,IFI16,IFI35,IFIH1,ISG15,NCF2,PTX3,RNASE6,STAT1,TAP1,USP18 |
| P38 MAPK | +2.401.40E-03 | BATF2,CCL8,GBP1,PML,STAT1,TNFSF10 | +2.601.40E-04 | CCL8,CXCL10,GBP1,IRF7,PML,STAT1,TNFSF10 | +2.877.01E-05 | BATF2,CCL11,CCND1,CD40,CXCL10,EDNRB,GBP1,IL23A,PLAUR,PML,SLC6A12,STAT1,TNFSF10 | +2.778.90E-06 | ARG2,ATF3,CCL8,CCR7,CD40,CD69,CD86,CXCL10,DDC,GBP1,IRF7,S100A12,SCNN1A,STAT1 |
| PAF1 | +2.451.19E-08 | DDX58,HERC5,IFI44,IFITM3,OAS2,ZNFX1 | +2.457.72E-09 | DDX58,IFI44,IFI44L,ISG15,ISG20,ZNFX1 | +3.162.97E-11 | HERC5,IDO1,IFI44L,IFIT3,ISG15,ISG20,OAS2,PLAUR,SERTAD1,ZNFX1 | +2.831.27E-08 | DDX58,IDO1,IFI44,IFI44L,ISG15,ISG20,SERTAD1,ZNFX1 |
| PARP9 | +2.222.61E-09 | IFI44,IFIT1,OAS2,SP110,STAT1 | +2.211.81E-09 | IFI44,IFIT1,IRF7,ISG15,STAT1 | +2.631.88E-10 | IFIT1,IFIT2,IFIT3,ISG15,OAS2,SP110,STAT1 | +2.214.46E-07 | IFI44,IFIT2,IRF7,ISG15,STAT1 |
| PIK3CG | --2.242.47E-05 | GBP2,OAS2,STAT1,TNFSF10,ZBP1 | --2.458.23E-07 | CXCL10,GBP4,GBP5,STAT1,TNFSF10,ZBP1 | --3.295.73E-09 | B2M,C2,CXCL10,GBP2,GBP4,GBP6,OAS2,STAT1,TAP1,TNFSF10,ZBP1 | --2.655.07E-05 | C2,CXCL10,GBP4,GBP5,NLRC5,STAT1,TAP1 |
| PML | +3.442.03E-13 | BST2,EPSTI1,HERC6,IFI27,IFI44,IFIH1,IFIT1,MX1,OAS1,OAS2,PML,STAT1 | +3.993.50E-20 | BST2,EPSTI1,HERC6,IFI27,IFI44,IFI44L,IFIH1,IFIT1,IFITM1,IRF7,ISG15,ISG20,MX1,OAS1,PML,STAT1 | +4.084.00E-13 | CCND1,EPSTI1,HERC6,IFI27,IFI35,IFI44L,IFIH1,IFIT1,IFIT3,ISG15,ISG20,MX1,OAS1,OAS2,PML,STAT1,TAP1 | +3.593.61E-09 | IFI27,IFI35,IFI44,IFI44L,IFIH1,IFITM1,IRF7,ISG15,ISG20,MX1,OAS1,STAT1,TAP1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| PNPT1 | --3.971.17E-28 | CMPK2,DDX58,EIF2AK2,GBP2,IFI16,IFI44,IFIH1,OAS1,PARP12,PARP14,PARP9,RNF213,RTP4,STAT1,USP18,XAF1 | --4.226.26E-34 | CXCL10,DDX58,EIF2AK2,GBP4,IFI16,IFI44,IFIH1,IRF7,ISG15,OAS1,PARP12,PARP14,PARP9,RNF213,RTP4,STAT1,USP18,XAF1 | --4.778.39E-34 | AGRN,CMPK2,CXCL10,EIF2AK2,GBP2,GBP4,GBP6,IFI16,IFIH1,IFIT3,ISG15,LGALS3BP,OAS1,PARP12,PARP14,PARP9,RNF213,RTP4,STAT1,STAT2,UBE2L6,USP18,XAF1 | --4.562.17E-30 | CXCL10,DDX58,EIF2AK2,GBP4,IFI16,IFI44,IFIH1,IRF7,ISG15,LGALS3BP,OAS1,PARP12,PARP14,PARP9,RNF213,RTP4,STAT1,STAT2,UBE2L6,USP18,XAF1 |
| PRL | +5.205.94E-33 | BST2,CMPK2,DDX58,DHX58,DTX3L,EIF2AK2,EPSTI1,HERC5,HERC6,IFI44,IFI6,IFIH1,IFIT1,IFIT5,IRF9,MLKL,MX2,OAS1,OAS2,PARP12,PARP14,RSAD2,SAMD9,SP110,STAT1,USP18,XAF1 | +5.452.18E-39 | ADAR,BST2,CXCL10,DDX58,DHX58,DTX3L,EIF2AK2,EPSTI1,HERC6,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IFIT5,IFITM1,IRF7,IRF9,ISG15,MX2,OAS1,PARP12,PARP14,PNPT1,RSAD2,SAMD9,SP100,STAT1,USP18,XAF1 | +5.681.43E-40 | ADAR,B2M,CCND1,CD40,CMPK2,CXCL10,DTX3L,EIF2AK2,EPSTI1,HERC5,HERC6,IFI35,IFI44L,IFI6,IFIH1,IFIT1,IFIT3,IFIT5,IRF9,ISG15,LAMP3,LY6E,MLKL,MX2,OAS1,OAS2,PARM1,PARP10,PARP12,PARP14,PNPT1,PSME2,RSAD2,SHFL,SHISA5,SP110,STAT1,STAT2,TDRD7,TMEM140,TNFSF13B,TRIM25,USP18,XAF1 | +5.461.42E-29 | ADAR,CD40,CD69,CXCL10,DDX58,DHX58,EIF2AK2,IFI35,IFI44,IFI44L,IFI6,IFIH1,IFIT5,IFITM1,IRF7,IRF9,ISG15,LY6E,MLKL,MX2,OAS1,PARP12,PARP14,PNPT1,RSAD2,SAMD9,SHISA5,SOCS1,STAT1,STAT2,TDRD7,TMEM140,TNFSF13B,USP18,XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| PTGER4 | --3.572.42E-15 | CMPK2,DDX58,GBP2,HERC6,IFI16,IFIH1,PARP14,RNF213,RSAD2,RTP4,TNFSF10,USP18,XAF1 | --3.844.47E-19 | CXCL10,DDX58,GBP4,HERC6,IFI16,IFIH1,IRF7,ISG20,PARP14,RNF213,RSAD2,RTP4,TNFSF10,USP18,XAF1 | --3.593.43E-21 | CD40,CMPK2,CXCL10,GBP2,GBP4,GBP6,HERC6,IFI16,IFI35,IFIH1,IFIT2,IL23A,ISG20,PARP14,RNASEL,RNF213,RNF24,RSAD2,RTP4,TNFSF10,TRIM21,USP18,XAF1 | --4.328.56E-18 | CCR7,CD40,CD69,CXCL10,DDX58,GBP4,IFI16,IFI35,IFIH1,IFIT2,IRF7,ISG20,NCF2,PARP14,RNF213,RSAD2,RTP4,SHISA3,USP18,XAF1 |
| RC3H1 | --3.871.00E-23 | BST2,DDX58,IFI16,IFI27,IFI44,IFI6,IFIT1,IFITM3,IRF9,MX1,OAS1,OAS2,PARP9,RSAD2,STAT1 | --4.002.59E-26 | BST2,DDX58,IFI16,IFI27,IFI44,IFI44L,IFI6,IFIT1,IFITM1,IRF9,ISG15,MX1,OAS1,PARP9,RSAD2,STAT1 | --4.473.10E-24 | IFI16,IFI27,IFI44L,IFI6,IFIT1,IFIT2,IFIT3,IRF9,ISG15,MX1,OAS1,OAS2,PARP9,RSAD2,SHFL,STAT1,STAT2,TRIM21,TRIM25,TRIM56 | --4.007.85E-20 | CCR7,DDX58,IFI16,IFI27,IFI44,IFI44L,IFI6,IFIT2,IFITM1,IRF9,ISG15,MX1,OAS1,PARP9,RSAD2,STAT1,STAT2 |
| RNY3 | +3.612.77E-26 | BATF2,EPSTI1,HERC5,IFI44,IFIT1,IFITM3,MX1,OAS1,OAS2,RSAD2,RTP4,SIGLEC1,XAF1 | +3.463.50E-24 | CXCL10,EPSTI1,IFI44,IFI44L,IFIT1,ISG15,MX1,OAS1,RSAD2,RTP4,SIGLEC1,XAF1 | +4.248.77E-31 | BATF2,CXCL10,EPSTI1,HERC5,HES4,IFI44L,IFIT1,IFIT3,ISG15,LAMP3,LY6E,MX1,OAS1,OAS2,RSAD2,RTP4,SIGLEC1,XAF1 | +3.322.85E-16 | CXCL10,IFI44,IFI44L,ISG15,LY6E,MX1,OAS1,RSAD2,RTP4,SIGLEC1,XAF1 |
| SAMSN1 | +2.002.21E-04 | CMPK2,PML,RSAD2,STAT1 | +2.651.12E-08 | CXCL10,IRF7,ISG15,ISG20,PML,RSAD2,STAT1 | +3.741.86E-13 | CD40,CMPK2,CXCL10,IFIT2,IFIT3,IL23A,ISG15,ISG20,PML,RSAD2,STAT1,STAT2,TRIM21,USP25 | +3.326.27E-10 | CD40,CXCL10,IFIT2,IRF7,ISG15,ISG20,NMI,RSAD2,SOCS1,STAT1,STAT2 |
| SASH1 | +2.008.45E-05 | CMPK2,PML,RSAD2,STAT1 | +2.651.92E-09 | CXCL10,IRF7,ISG15,ISG20,PML,RSAD2,STAT1 | +3.611.32E-13 | CD40,CMPK2,CXCL10,IFIT2,IFIT3,ISG15,ISG20,PML,RSAD2,STAT1,STAT2,TRIM21,USP25 | +3.323.97E-11 | CD40,CXCL10,IFIT2,IRF7,ISG15,ISG20,NMI,RSAD2,SOCS1,STAT1,STAT2 |

S15 Table. Continued.

|  |  |  |  |  |
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|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| SIRT1 | --3.629.97E-16 | CMPK2,DDX58,DHX58,DKK1,IFI44,IFITM3,OAS1,OAS2,PARP12,PARP14,PML,RNF213,RSAD2,RTP4,SP110,STAT1,UBA7,USP18 | --3.348.21E-14 | ADAR,DDX58,DHX58,DKK1,IFI44,IRF7,OAS1,PARP12,PARP14,PML,RNF213,RSAD2,RTP4,STAT1,UBA7,USP18 | --3.841.31E-11 | ADAR,CCND1,CMPK2,DKK1,GBP6,IFIT3,LGALS3BP,LY6E,MAPT,OAS1,OAS2,PARP12,PARP14,PML,PRDM16,RNF213,RSAD2,RTP4,SP110,STAT1,TAP1,UBA7,USP18 | --4.037.30E-14 | ADAR,DDX58,DHX58,DKK1,EPAS1,IFI44,IRF7,LGALS3BP,LY6E,NEDD4L,NLRC5,OAS1,PARP12,PARP14,PCK2,RGS16,RNF213,RSAD2,RTP4,SCNN1A,STAT1,TACSTD2,TAP1,UBA7,USP18 |
| SOCS1 | --3.423.04E-14 | DDX58,IFI16,IFI27,IFI44,IFIH1,IFIT1,MX1,OAS1,OAS2,RSAD2,STAT1,USP18 | --3.822.61E-21 | CXCL10,DDX58,GBP5,IFI16,IFI27,IFI44,IFIH1,IFIT1,IRF7,ISG15,ISG20,MX1,OAS1,RSAD2,STAT1,USP18 | --3.761.01E-16 | CCND1,CD40,CXCL10,GBP6,H2-T24,IFI16,IFI27,IFIH1,IFIT1,IFIT2,IFIT3,ISG15,ISG20,MX1,OAS1,OAS2,RSAD2,STAT1,USP18 | --3.983.94E-21 | CCR7,CD40,CD69,CD86,CXCL10,DDX58,GBP5,H2-T24,IFI16,IFI27,IFI44,IFIH1,IFIT2,IRF7,ISG15,ISG20,MX1,OAS1,RSAD2,SOCS1,STAT1,USP18 |
| SP110 | --3.163.02E-11 | BST2,IFI27,IFI6,IFIH1,IFIT1,IFITM3,IRF9,MX1,OAS1,STAT1 | --3.324.47E-13 | BST2,CXCL10,IFI27,IFI6,IFIH1,IFIT1,IFITM1,IRF9,MX1,OAS1,STAT1 | --2.711.13E-07 | BCL2L12,CXCL10,IFI27,IFI6,IFIH1,IFIT1,IFIT3,IRF9,MX1,OAS1,STAT1 | --2.716.58E-08 | ATF3,BCL2L12,CXCL10,IFI27,IFI6,IFIH1,IFITM1,IRF9,MX1,OAS1,STAT1 |
| SPI1 | +3.562.97E-13 | CMPK2,IFI27,IFI44,IFI6,IFIT1,IFITM3,IRF9,MX1,PARP12,PML,RSAD2,SP110,TNFSF10,USP18 | +3.956.39E-18 | CXCL10,IFI27,IFI44,IFI44L,IFI6,IFIT1,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,PARP12,PML,RSAD2,TNFSF10,USP18 | +4.533.20E-16 | C1QC,C3AR1,CCND1,CMPK2,CXCL10,IFI27,IFI44L,IFI6,IFIT1,IFIT2,IFIT3,IRF4,IRF9,ISG15,ISG20,LAMP3,LY6E,MX1,PARP12,PML,RSAD2,SP110,TNFSF10,USP18 | +3.871.09E-11 | C1QC,CCR7,CXCL10,IFI27,IFI44,IFI44L,IFI6,IFIT2,IFITM1,IRF7,IRF9,ISG15,ISG20,LY6E,MX1,NCF2,PARP12,RSAD2,USP18 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| STAT1 | +4.564.49E-33 | BATF2,BST2,CMPK2,EIF2AK2,EPSTI1,GBP1,GBP2,HERC6,IFI16,IFI27,IFI44,IFI6,IFIH1,IFIT1,IFITM3,IRF9,MX1,OAS1,OAS2,PARP9,RNF213,RSAD2,RTP4,SP110,STAT1,TNFSF10,USP18,XAF1,ZBP1 | +4.751.24E-37 | BST2,C4A/C4B,CXCL10,EIF2AK2,EPSTI1,GBP1,GBP4,GBP5,HERC6,IFI16,IFI27,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IFITM1,IRF7,IRF9,ISG15,MX1,OAS1,PARP9,RNF213,RSAD2,RTP4,STAT1,TNFSF10,USP18,XAF1,ZBP1 | +5.756.21E-46 | B2M,BATF2,C1S,C4A/C4B,CASP4,CASP8,CCND1,CD274,CD40,CMPK2,CXCL10,EIF2AK2,EPSTI1,FCGR1A,GBP1,GBP2,GBP4,GBP6,HERC6,IDO1,IFI16,IFI27,IFI35,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IL23A,IRF9,ISG15,LY6E,MX1,OAS1,OAS2,PARP9,PSME2,RNF213,RSAD2,RTP4,SOAT1,SP110,STAT1,STAT2,TAP1,TNFSF10,TNFSF13B,TRIM21,USP18,XAF1,ZBP1 | +5.544.63E-34 | CALHM6,CASP4,CCR7,CD40,CD86,CFB,CREM,CXCL10,EIF2AK2,FCGR1A,GBP1,GBP4,GBP5,IDO1,IFI16,IFI27,IFI35,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IFITM1,IRF7,IRF9,ISG15,LY6E,MX1,NLRC5,OAS1,PARP9,RNF213,RSAD2,RTP4,SOCS1,STAT1,STAT2,TAP1,TNFSF13B,USP18,WARS1,XAF1 |
| STAT4 | +2.228.32E-04 | DDX58,IFIH1,PLAC8,STAT1,STC2 | +2.635.29E-06 | CXCL10,DDX58,IFIH1,ISG15,ISG20,PLAC8,STAT1 | +2.351.12E-05 | CXCL10,IFIH1,IFIT2,IRF4,ISG15,ISG20,MAP3K8,PLAC8,PRDM16,SERTAD1,STAT1 | +3.296.77E-06 | ARHGAP15,CXCL10,DDX58,IFIH1,IFIT2,ISG15,ISG20,PLAC8,RGS16,SERTAD1,STAT1 |
| STING1 | +2.203.37E-08 | IFI16,IFI44,IFITM3,OAS1,RSAD2,USP18 | +2.939.79E-14 | CXCL10,GBP5,IFI16,IFI44,IRF7,ISG15,OAS1,RSAD2,USP18 | +2.933.32E-09 | CGAS,CXCL10,IFI16,IFIT2,IFIT3,ISG15,OAS1,RSAD2,USP18 | +3.523.12E-15 | CD86,CXCL10,GBP5,IFI16,IFI44,IFIT2,IRF7,ISG15,OAS1,PLEKHA4,RGS16,RSAD2,USP18 |
| TAB1 | --2.438.07E-10 | GBP1,GBP2,IFIH1,IFIT1,TNFSF10,XAF1 | --2.635.34E-12 | CXCL10,GBP1,IFIH1,IFIT1,IRF7,TNFSF10, XAF1 | --2.815.16E-10 | CXCL10,GBP1,GBP2,IFIH1,IFIT1,TNFSF10,TNFSF13B,XAF1 | --2.651.23E-08 | CFB,CXCL10,GBP1,IFIH1,IRF7,TNFSF13B,XAF1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| TGM2 | +3.594.52E-13 | IFI6,IFIT1,IFIT5,IRF9,OAS1,OAS2,PARP14,PARP9,RNF213,SP110,STAT1,UBA7,XAF1 | +3.051.71E-13 | CXCL10,IFI6,IFIT1,IFIT5,IRF9,OAS1,PARP14,PARP9,RNF213,SLC7A2,STAT1,UBA7,XAF1 | +3.564.17E-17 | CCND1,CD93,CXCL10,IFI35,IFI6,IFIT1,IFIT2,IFIT3,IFIT5,IRF9,LGALS9,LY6E,OAS1,OAS2,PARP14,PARP9,PPP1R16B,RNF213,SP110,STAT1,TAP1,UBA7,XAF1 | +3.292.20E-15 | CD86,CD93,CXCL10,IFI35,IFI6,IFIT2,IFIT5,IRF9,LGALS9,LY6E,NCF2,OAS1,PARP14,PARP9,PPP1R16B,RNF213,SLC16A1,STAT1,TAP1,UBA7,XAF1 |
| TICAM1 | +2.417.46E-06 | CMPK2,DDX58,IFI16,IFIT1,RSAD2,TNFSF10 | +3.091.79E-11 | CXCL10,DDX58,IFI16,IFIT1,IRF7,ISG15,ISG20,RSAD2,SLC7A2,TNFSF10 | +3.778.56E-12 | CASP4,CD40,CMPK2,CXCL10,EDNRB,IFI16,IFIT1,IFIT2,IFIT3,IL23A,IRF3,ISG15,ISG20,RSAD2,TNFSF10 | +3.516.75E-10 | CASP4,CD40,CD86,CFB,CXCL10,DDX58,IFI16,IFIT2,IRF7,ISG15,ISG20,RSAD2,SOCS1 |
| TLR3 | +3.267.37E-24 | CMPK2,CPM,DDX58,DHX58,EIF2AK2,GBP2,HERC5,IFI16,IFI44,IFI6,IFIH1,IFIT1,MX1,MX2,OAS1,PTX3,RSAD2,STAT1,TNFSF10,USP18,ZNFX1 | +3.093.08E-26 | CXCL10,DDX58,DHX58,EIF2AK2,GBP4,IFI16,IFI44,IFI44L,IFI6,IFIH1,IFIT1,IRF7,ISG15,ISG20,MX1,MX2,OAS1,RSAD2,STAT1,TNFSF10,USP18,ZNFX1 | +4.151.16E-23 | CD274,CD40,CMPK2,CXCL10,EIF2AK2,GBP2,GBP4,HERC5,IFI16,IFI44L,IFI6,IFIH1,IFIT1,IFIT2,IFIT3,IL23A,IRF3,ISG15,ISG20,LIPA,MAP3K8,MX1,MX2,OAS1,RSAD2,STAT1,TNFSF10,TNFSF13B,USP18,ZNFX1 | +4.141.35E-25 | ARG2,ATF3,CD40,CD69,CD86,CFB,CXCL10,DDX58,DHX58,EIF2AK2,GBP4,IFI16,IFI44,IFI44L,IFI6,IFIH1,IFIT2,IRF7,ISG15,ISG20,MX1,MX2,NMI,OAS1,PTX3,RSAD2,SOCS1,STAT1,TNFSF13B,USP18,ZNFX1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| TLR4 | +2.754.32E-09 | BPI,CCL8,CMPK2,GBP2,IFI16,IFITM3,MX1,PML,PTX3,RSAD2,STAT1,TNFSF10 | +2.562.28E-08 | CCL8,CXCL10,IFI16,IRF7,ISG15,ISG20,MX1,PML,RSAD2,STAT1,TNFSF10 | +3.505.86E-14 | BPI,CASP8,CD274,CD40,CMPK2,CXCL10,GBP2,IFI16,IFIT2,IFIT3,IL23A,IRF3,ISG15,ISG20,MX1,OXTR,PML,RSAD2,SLC6A12,STAT1,STAT2,TNFSF10,TREM2,TRIM21,USP25 | +3.511.42E-13 | ATF3,CCL8,CCR7,CD40,CD86,CFB,CXCL10,IFI16,IFIT2,IRF7,ISG15,ISG20,MX1,NMI,OXTR,PTX3,RGS16,RSAD2,SMPDL3B,SOCS1,SPTLC2,STAT1,STAT2,TNFRSF13B |
| TLR7 | +2.812.09E-09 | DKK1,IFI44,IFIT1,IRF9,MX1,MX2,OAS2,PTX3,RSAD2,STAT1 | +3.413.07E-15 | CXCL10,DKK1,IFI44,IFI44L,IFIT1,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,RSAD2,STAT1 | +4.142.19E-15 | CCND1,CD274,CD40,CXCL10,DKK1,ESM1,IDO1,IFI35,IFI44L,IFIT1,IFIT3,IL23A,IRF9,ISG15,ISG20,MX1,MX2,OAS2,RSAD2,STAT1,STAT2 | +4.463.73E-18 | ATF3,CCR7,CD40,CD69,CD86,CXCL10,DKK1,IDO1,IFI35,IFI44,IFI44L,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,PTX3,RSAD2,SOCS1,STAT1,STAT2 |
| TLR9 | +3.153.86E-10 | CPM,IFI16,IFIT1,IRF9,MX1,MX2,OAS2,RSAD2,STAT1,TNFSF10,USP18 | +3.655.81E-16 | CXCL10,IFI16,IFI44L,IFIT1,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,RSAD2,STAT1,TNFSF10,USP18 | +4.307.35E-20 | CCND1,CD274,CD40,CXCL10,IDO1,IFI16,IFI35,IFI44L,IFIT1,IFIT2,IFIT3,IL23A,IRF4,IRF9,ISG15,ISG20,MX1,MX2,NAMPT,OAS2,RSAD2,STAT1,STAT2,TNFSF10,TNFSF13B,USP18 | +4.984.32E-24 | ARG2,ATF3,CCR7,CD40,CD69,CD86,CXCL10,IDO1,IFI16,IFI35,IFI44L,IFIT2,IFITM1,IRF7,IRF9,ISG15,ISG20,MX1,MX2,PYCARD,RSAD2,SMPDL3B,SOCS1,SPTLC2,STAT1,STAT2,TNFRSF13B,TNFSF13B,USP18 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| TNF | +4.044.42E-10 | BST2,DDX58,DKK1,EIF2AK2,GBP1,GBP2,HERC5,IFI16,IFI27,IFI6,IFIH1,IFIT1,IFIT5,LBP,MX1,OAS1,OAS2,PARP14,PLAAT3,PML,PTX3,SAMD9,STAT1,TIFA,TNFSF10 | +4.501.05E-11 | BST2,C4A/C4B,CXCL10,DDX58,DKK1,EIF2AK2,GBP1,GBP4,IFI16,IFI27,IFI6,IFIH1,IFIT1,IFIT5,IFITM1,IRF7,ISG15,MX1,OAS1,PARP14,PML,SAMD9,SLC7A2,STAT1,TIFA,TNFSF10 | +5.359.79E-19 | ANXA1,B2M,C3AR1,C4A/C4B,CASP4,CASP8,CCL11,CCND1,CD274,CD40,CXCL10,DKK1,EDNRB,EIF2AK2,ESM1,FRMD4A,GBP1,GBP2,GBP4,GBP6,HERC5,IDO1,IFI16,IFI27,IFI6,IFIH1,IFIT1,IFIT3,IFIT5,IL23A,IRF4,ISG15,ITGA10,KYNU,LAMP3,LGALS9,MAP3K8,MST1R,MX1,NAMPT,OAS1,OAS2,OPTN,PARP14,PLAUR,PLVAP,PML,PSMA2,PSME2,SLC15A3,SLC40A1,SOAT1,STAT1,TAP1,TCIM,TDRD7,TIFA,TM4SF1,TNFSF10,TNFSF13B,TREM2,TRIM56 | +4.753.67E-14 | AATK,ALOX5AP,ATF3,CASP4,CCR7,CD40,CD69,CD86,CFB,CNP,CREM,CRYAB,CXCL10,DDX58,DKK1,EIF2AK2,GBP1,GBP4,H19,IDO1,IFI16,IFI27,IFI6,IFIH1,IFIT5,IFITM1,IRF7,ISG15,LGALS9,MST1R,MSTN,MX1,NCF2,OAS1,OSMR,PARP14,PCK2,PIGR,PLVAP,PTX3,PYCARD,RGS16,S100A12,SAMD9,SCNN1A,SLC16A2,SOCS1,STAT1,TAP1,TDRD7,TIFA,TMEM40,TNFSF13B |
| TNFSF10 | +2.781.32E-09 | EIF2AK2,IFI16,IFI27,IFI6,IFIT1,IRF9,STAT1,TNFSF10 | +3.271.06E-14 | EIF2AK2,IFI16,IFI27,IFI6,IFIT1,IFITM1,IRF9,ISG15,SP100,STAT1,TNFSF10 | +3.233.42E-09 | CASP8,EIF2AK2,IFI16,IFI27,IFI6,IFIT1,IRF9,ISG15,PSME2,STAT1,TNFSF10 | +2.133.42E-07 | CD69,EIF2AK2,IFI16,IFI27,IFI6,IFITM1,IRF9,ISG15,STAT1 |
| TNK1 | +2.002.36E-07 | IFI16,IFIH1,OAS2,TNFSF10 | +2.241.31E-09 | IFI16,IFIH1,IRF7,ISG20,TNFSF10 | +2.457.92E-09 | IFI16,IFIH1,IFIT2,ISG20,OAS2,TNFSF10 | +2.243.25E-07 | IFI16,IFIH1,IFIT2,IRF7,ISG20 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| TP53 | +2.192.16E-02 | DKK1,GBP1,HERC5,IFI16,IRF9,MX1,OAS1,PLAAT3,PML,STAT1,TNFSF10,XAF1 | +2.281.70E-03 | CXCL10,DKK1,FABP3,GBP1,IFI16,IRF7,IRF9,ISG15,MX1,OAS1,PML,STAT1,TNFSF10,XAF1 | +2.665.92E-06 | ANXA1,C1QC,C2,CASP4,CASP8,CCND1,COL13A1,COX7A1,CXCL10,DKK1,DRAM1,FAM83D,FRMD4A,GBP1,GDA,HERC5,IFI16,IFI35,IRF9,ISG15,LAMP3,MAP3K8,MX1,NAMPT,OAS1,P2RY14,PGAM2,PLAUR,PMEPA1,PML,POLK,PSMA2,PTPRE,SHISA5,SLC66A3,STAT1,TAP1,TNFSF10,XAF1 | +3.011.25E-03 | ATF3,C1QC,C2,CASP4,COL14A1,CRYAB,CXCL10,DKK1,DRAM1,EPAS1,FABP3,FGFBP1,GBP1,H19,IFI16,IFI35,IRF7,IRF9,ISG15,MX1,OAS1,PYCARD,RGS16,SCNN1A,SHISA5,SLC16A1,SPHK2,SPTLC2,STAT1,TAP1,XAF1 |
| TREX1 | --2.414.97E-11 | IFI16,IFI44,IFIT1,MX1,OAS1,USP18 | --3.091.10E-20 | CXCL10,IFI16,IFI44,IFI44L,IFIT1,ISG15,ISG20,MX1,OAS1,USP18 | --3.081.61E-15 | CXCL10,IFI16,IFI44L,IFIT1,IFIT2,ISG15,ISG20,MX1,OAS1,USP18 | --3.078.10E-18 | CD86,CXCL10,IFI16,IFI44,IFI44L,IFIT2,ISG15,ISG20,MX1,OAS1,USP18 |
| TRIM24 | --3.942.26E-22 | CMPK2,DDX58,DHX58,EPSTI1,GBP2,HERC6,IFI44,IFIH1,IRF9,OAS1,PARP12,PLAC8,RTP4,STAT1,UBA7,USP18 | --4.191.02E-26 | CXCL10,DDX58,DHX58,EPSTI1,GBP4,HERC6,IFI44,IFIH1,IRF7,IRF9,ISG15,OAS1,PARP12,PLAC8,RTP4,STAT1,UBA7,USP18 | --4.952.64E-27 | AGRN,CMPK2,CXCL10,EPSTI1,GBP2,GBP4,HERC6,IFI35,IFIH1,IFIT2,IFIT3,IRF9,ISG15,LGALS3BP,MOV10,OAS1,PARP12,PLAC8,RTP4,SHISA5,STAT1,STAT2,TAP1,UBA7,USP18 | --4.956.64E-28 | CALHM6,CXCL10,DDX58,DHX58,GBP4,IFI35,IFI44,IFIH1,IFIT2,IRF7,IRF9,ISG15,LGALS3BP,NMI,OAS1,PARP12,PLAC8,RTP4,SHISA5,SOCS1,STAT1,STAT2,TAP1,UBA7,USP18 |
| USP18 | --2.597.01E-12 | IFI6,IFIH1,IFITM3,IRF9,MX1,OAS1,TNFSF10 | --2.942.33E-16 | CXCL10,IFI6,IFIH1,IRF7,IRF9,ISG15,MX1,OAS1,TNFSF10 | --2.773.90E-10 | CXCL10,IFI6,IFIH1,IRF9,ISG15,MX1,OAS1,TNFSF10 | --2.965.69E-12 | CXCL10,IFI6,IFIH1,IRF7,IRF9,ISG15,MX1,OAS1,SOCS1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| VCAN | +2.531.27E-10 | IFI44,IFI6,IFIT1,LBP,MX1,MX2,OAS2,PARP14,STAT1,XAF1 | +2.712.21E-12 | C4A/C4B,IFI44,IFI44L,IFI6,IFIT1,IFITM1,MX1,MX2,PARP14,STAT1,XAF1 | +2.515.95E-09 | AGRN,C1S,C4A/C4B,IFI44L,IFI6,IFIT1,IFIT2,MX1,MX2,OAS2,PARP14,STAT1,XAF1 | +2.893.13E-08 | IFI44,IFI44L,IFI6,IFIT2,IFITM1,MX1,MX2,PARP14,PRELP,SMPDL3B,STAT1,XAF1 |
| ISG15 | --2.226.58E-12 | DDX58,IFI6,IFITM3,MX1,OAS1 |     |   |     |   |     |   |
| AIRE | --2.246.66E-06 | EIF2AK2,HERC6,IFI44,PARP14,TNFSF10 |     |   |     |   |     |   |
| PF4 | +2.225.19E-09 | CMPK2,CPM,DDX58,EPSTI1,RSAD2,STAT1,USP18 |     |   |     |   |     |   |
| DUSP1 | +2.005.58E-04 | CMPK2,DKK1,IFIT1,MX1 |     |   |     |   |     |   |
| NFKBIA | +2.181.45E-02 | GBP2,IFI16,IFI6,PTX3,TNFSF10 |     |   |     |   |     |   |
| CNOT7 |     |   | --2.216.65E-21 | BST2,HERC6,IFI27,IFI44L,IFI6,IFIT5,IFITM1,ISG15,OAS1,PARP12,STAT1 | --2.225.43E-27 | B2M,CMPK2,HERC6,IFI27,IFI35,IFI44L,IFI6,IFIT5,ISG15,LGALS3BP,OAS1,OAS2,PARP12,SP110,STAT1,TAP1,UBE2L6 | --2.213.23E-19 | IFI27,IFI35,IFI44L,IFI6,IFIT5,IFITM1,ISG15,LGALS3BP,OAS1,PARP12,STAT1,TAP1,UBE2L6 |
| DNASE2 |     |   | --2.603.96E-18 | CXCL10,DHX58,IRF7,ISG15,OAS1,RSAD2,RTP4,TNFSF10,USP18,ZBP1 | --2.405.37E-13 | ACKR4,CXCL10,IFIT3,ISG15,OAS1,RSAD2,RTP4,TNFSF10,USP18,ZBP1 | --2.205.73E-10 | CXCL10,DHX58,IRF7,ISG15,OAS1,RSAD2,RTP4,USP18 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| DOCK8 |     |   | +2.456.31E-08 | CXCL10,IRF7,ISG15,ISG20,RSAD2,STAT1 | +3.462.25E-12 | CD40,CMPK2,CXCL10,IFIT2,IFIT3,ISG15,ISG20,RSAD2,STAT1,STAT2,TRIM21,USP25 | +3.322.87E-11 | CD40,CXCL10,IFIT2,IRF7,ISG15,ISG20,NMI,RSAD2,SOCS1,STAT1,STAT2 |
| IFI16 |     |   | +2.213.88E-06 | CXCL10,DDX58,IFI16,ISG15,OAS1 | +2.201.01E-04 | CCND1,CXCL10,IFI16,ISG15,OAS1,STAT2 | +2.427.55E-05 | CXCL10,DDX58,IFI16,ISG15,OAS1,STAT2 |
| IFIH1 |     |   | +2.401.91E-16 | CXCL10,IFI27,IFI44L,IFIT1,IRF7,ISG15,OAS1,RSAD2,SIGLEC1,USP18 | +2.402.39E-11 | CXCL10,IFI27,IFI44L,IFIT1,ISG15,OAS1,OAS2,RSAD2,SIGLEC1,USP18 | +2.204.14E-10 | CXCL10,IFI27,IFI44L,IRF7,ISG15,OAS1,RSAD2,SIGLEC1,USP18 |
| IFN alpha/ beta |     |   | +2.391.66E-07 | CXCL10,IFI16,IRF7,RSAD2,STAT1,TNFSF10 | +3.527.86E-13 | CD40,CXCL10,IDO1,IFI16,IFIT2,IFIT3,LY6E,RSAD2,STAT1,STAT2,TNFSF10,TNFSF13B,TRIM21 | +3.796.20E-16 | CCR7,CD40,CD69,CD86,CXCL10,IDO1,IFI16,IFIT2,IRF7,LY6E,RSAD2,SOCS1,STAT1,STAT2,TNFSF13B |
| IFNL2 |     |   | +2.246.40E-10 | CXCL10,IFIT1,IRF7,MX1,RSAD2 | +2.001.01E-05 | CXCL10,IFIT1,MX1,RSAD2 | +2.008.17E-06 | CXCL10,IRF7,MX1,RSAD2 |
| MAP2K3 |     |   | +2.621.92E-09 | CCL8,CXCL10,IRF9,ISG15,PPA1,STAT1,TNFSF10 | +2.435.97E-05 | CXCL10,IRF9,ISG15,PPA1,STAT1,TNFSF10 | +2.623.61E-06 | ARG2,CCL8,CXCL10,IRF9,ISG15,PPA1,STAT1 |
| mir-155 |     |   | --2.213.18E-05 | CXCL10,IRF7,IRF9,MX1,STAT1 | --2.001.55E-04 | CCND1,CXCL10,IFIT3,IRF4,IRF9,MX1,STAT1 | --2.591.11E-04 | CD69,CXCL10,IRF7,IRF9,MX1,SOCS1,STAT1 |

S15 Table. Continued.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bacteria infused day 16 | Healthy day 15 | Healthy day 16 | Healthy day 17 |
| Predicted upstream regulator | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules | +/-z-score*P* value | Molecules |
| MYD88 |     |   | +2.321.77E-04 | CXCL10,IRF7,ISG15,RSAD2,SLC7A2,USP18 | +3.391.31E-05 | CASP4,CD274,CD40,CMPK2,CXCL10,EDNRB,IFIT2,IL23A,ISG15,RSAD2,TNFSF13B,USP18 | +3.327.62E-06 | CASP4,CD40,CD86,CXCL10,IFIT2,IRF7,ISG15,RSAD2,SOCS1,TNFRSF13B,TNFSF13B,USP18 |
| OSM |     |   | +2.712.94E-04 | CXCL10,GBP1,IRF7,IRF9,ISG20,MX1,OAS1,STAT1 | +4.101.18E-07 | ANXA1,B2M,BTC,C1S,CASP4,CCL11,CCND1,CXCL10,GBP1,GBP2,IFI35,IRF9,ISG20,KRT17,MX1,NAMPT,OAS1,STAT1,TAP1,TM4SF1,UBE2L6 | +3.509.54E-09 | ATF3,CASP4,CXCL10,GBP1,IFI35,IRF7,IRF9,ISG20,KRT17,LY6G6C,MX1,NEDD4L,OAS1,OSMR,PIGR,S100A12,SLC15A1,SLC16A1,SOCS1,STAT1,TAP1,UBE2L6 |
| PRDM16 |     |   | --2.181.11E-09 | CXCL10,GBP4,IFI44,IRF7,MX2,STAT1 | --2.404.27E-08 | CXCL10,GBP4,IFIT2,MX2,OAS2,STAT1,STAT2 | --2.589.41E-10 | CXCL10,GBP4,IFI44,IFIT2,IRF7,MX2,STAT1,STAT2 |
| SOCS3 |     |   | --2.219.23E-06 | CXCL10,IFIT1,ISG20,MX1,OAS1 | --2.891.40E-09 | CCND1,CD40,CXCL10,FCGR1A,IFIT1,IFIT2,IL23A,ISG20,MX1,OAS1,OAS2 | --2.371.22E-08 | ATF3,CD40,CD86,CXCL10,FCGR1A,IFIT2,ISG20,MX1,OAS1,SOCS1 |
| STAT2 |     |   | +2.015.80E-30 | CXCL10,GBP1,IFI27,IFI6,IFIT1,IFITM1,IRF7,IRF9,ISG15,MX1,OAS1,RSAD2,RTP4,STAT1,TNFSF10,USP18,ZBP1 | +2.397.64E-28 | CD40,CXCL10,GBP1,GBP6,IFI27,IFI35,IFI6,IFIT1,IFIT2,IFIT3,IRF9,ISG15,MX1,OAS1,OAS2,RSAD2,RTP4,STAT1,TNFSF10,USP18,ZBP1 | +2.801.52E-26 | CD40,CD86,CXCL10,GBP1,IFI27,IFI35,IFI6,IFIT2,IFITM1,IRF7,IRF9,ISG15,MX1,OAS1,RSAD2,RTP4,SOCS1,STAT1,USP18,WARS1 |