**Supplementary Table 1: Upstream regulators of CD4+ IFNγ+ T-cells in CPI colitis vs CD4+ IFNγ+ T-cells in control mice**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Master Regulator | Molecule Type | Predicted Activation | Activation z-score | p-value of overlap |
| parathyroid hormone-related protein | biologic drug | Activated | 4.003 | 3.55E-17 |
| prosaptide d1 | biologic drug | Activated | 3.25 | 5.93E-21 |
| afamelanotide | biologic drug | Activated | 3.048 | 8.83E-20 |
| lypressin | biologic drug | Activated | 2.828 | 4.44E-23 |
| filgrastim | biologic drug | Activated | 2.777 | 1.03E-10 |
| GLP-1 (7-36) amide | biologic drug | Activated | 2.683 | 3.19E-27 |
| filgrastim | biologic drug | Activated | 2.682 | 1.55E-26 |
| blinatumomab | biologic drug | Activated | 2.236 | 0.00000139 |
| enterotoxin B | biologic drug | Activated | 2.183 | 8.23E-13 |
| amino acids | chemical - endogenous mammalian | Activated | 4.841 | 1.14E-39 |
| 2'-fucosyllactose | chemical - endogenous mammalian | Activated | 3.719 | 2.61E-29 |
| leukotriene D4 | chemical - endogenous mammalian | Activated | 3.181 | 3.23E-26 |
| 1-octanol | chemical - endogenous mammalian | Activated | 2.955 | 5.03E-72 |
| copper | chemical - endogenous mammalian | Activated | 2.573 | 1.23E-39 |
| heparan sulfate | chemical - endogenous mammalian | Activated | 2.55 | 1.06E-26 |
| histamine | chemical - endogenous mammalian | Activated | 2.496 | 1.33E-09 |
| diadenosine triphosphate | chemical - endogenous mammalian | Activated | 2.449 | 1.55E-15 |
| 24R,25-dihydroxyvitamin D3 | chemical - endogenous mammalian | Activated | 2.321 | 1.69E-19 |
| leukotriene D4 | chemical - endogenous mammalian | Activated | 2.111 | 0.00000071 |
| phosphate | chemical - endogenous mammalian | Activated | 2.086 | 1.9E-22 |
| leukotriene E4 | chemical - endogenous mammalian | Activated | 2 | 0.0000245 |
| E. coli B5 lipopolysaccharide | chemical - endogenous non-mammalian | Activated | 2.897 | 6.35E-21 |
| archazolid B | chemical - endogenous non-mammalian | Activated | 2.885 | 1.89E-18 |
| proteoglycan | chemical - other | Activated | 4.885 | 3.68E-27 |
| cardiotoxin | chemical - other | Activated | 2 | 3.94E-09 |
| lobeline | chemical drug | Activated | 6.557 | 2.15E-56 |
| SGI 1776 | chemical drug | Activated | 5.425 | 2.65E-57 |
| CB-5083 | chemical drug | Activated | 5.248 | 5.88E-57 |
| 5-fluorouracil | chemical drug | Activated | 4.636 | 1.38E-27 |
| ST1926 | chemical drug | Activated | 4.271 | 1.19E-12 |
| beta-hydroxy simvastatin acid | chemical drug | Activated | 4.243 | 7.8E-62 |
| CD 437 | chemical drug | Activated | 3.773 | 2.96E-13 |
| sirolimus | chemical drug | Activated | 3.545 | 1.08E-44 |
| nomifensine | chemical drug | Activated | 3.415 | 4.64E-58 |
| verteporfin | chemical drug | Activated | 3.179 | 1.11E-57 |
| cysteamine | chemical drug | Activated | 2.994 | 1.35E-23 |
| highly active antiretroviral therapy | chemical drug | Activated | 2.985 | 9.4E-14 |
| (-)-isoproterenol | chemical drug | Activated | 2.907 | 1.47E-21 |
| amrinone | chemical drug | Activated | 2.889 | 2.04E-23 |
| levocabastine | chemical drug | Activated | 2.689 | 3.6E-19 |
| dobutamine | chemical drug | Activated | 2.546 | 9.32E-18 |
| xylometazoline | chemical drug | Activated | 2.54 | 3.64E-31 |
| SN-38 | chemical drug | Activated | 2.331 | 4.17E-27 |
| ciprofloxacin | chemical drug | Activated | 2.263 | 1.98E-16 |
| AGN194204 | chemical drug | Activated | 2.16 | 1.44E-22 |
| PLX5622 | chemical drug | Activated | 2.065 | 1.73E-13 |
| benzo[1,3]dioxol-5-yl-[2-(4-fluoro-phenylamino)-4-methyl-thiazol-5-yl]-methanone | chemical reagent | Activated | 6.557 | 1.84E-56 |
| 4OH-GTS-21 | chemical reagent | Activated | 6.557 | 1.84E-56 |
| epibatidine | chemical reagent | Activated | 6.123 | 1.77E-57 |
| CGP 57380 | chemical reagent | Activated | 5.343 | 3.45E-61 |
| D-Pen-2,5-enkephalin | chemical reagent | Activated | 3.487 | 4.77E-26 |
| SC144 | chemical reagent | Activated | 3.252 | 4.28E-57 |
| dioctanoylphosphatidic acid | chemical reagent | Activated | 2.964 | 4.02E-25 |
| N6-cyclohexyladenosine | chemical reagent | Activated | 2.61 | 4.81E-20 |
| alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid | chemical reagent | Activated | 2.562 | 2.67E-19 |
| ionomycin | chemical reagent | Activated | 2.53 | 7.66E-22 |
| MALP-2s | chemical reagent | Activated | 2.449 | 0.0000392 |
| galactosylceramide-alpha | chemical reagent | Activated | 2.324 | 4.26E-11 |
| trinitrobenzenesulfonic acid | chemical reagent | Activated | 2.324 | 6.73E-11 |
| compound 48/80 | chemical reagent | Activated | 2.321 | 1.95E-22 |
| silver | chemical reagent | Activated | 2.287 | 3.33E-14 |
| CpG ODN D-19 | chemical reagent | Activated | 2.101 | 3.17E-22 |
| NSC-295642 | chemical reagent | Activated | 2.023 | 1.2E-17 |
| NSC-150117 | chemical reagent | Activated | 2.023 | 1.2E-17 |
| Ige | complex | Activated | 4.749 | 1.3E-32 |
| Ige | complex | Activated | 4.715 | 5.34E-23 |
| Stat1 dimer | complex | Activated | 4.372 | 1.79E-71 |
| HLA-DQ | complex | Activated | 3.775 | 1.39E-24 |
| IL6 receptor | complex | Activated | 3.442 | 1.69E-26 |
| Fcer1 | complex | Activated | 3.153 | 9.53E-14 |
| IL23 | complex | Activated | 2.887 | 6.28E-10 |
| MHC Class I (complex) | complex | Activated | 2.673 | 1.35E-21 |
| IL17a dimer | complex | Activated | 2.646 | 1.77E-08 |
| IL23 | complex | Activated | 2.578 | 6.75E-30 |
| IL-17f dimer | complex | Activated | 2.449 | 1.13E-08 |
| Gm-Csf Receptor | complex | Activated | 2.325 | 3.35E-24 |
| E2f-Dp1 | complex | Activated | 2.309 | 1E-10 |
| NFAT (complex) | complex | Activated | 2.021 | 1.42E-22 |
| Glycoprotein 1B | complex | Activated | 2.021 | 4.55E-16 |
| IL12 (complex) | complex | Activated | 2 | 2.8E-20 |
| IL2 | cytokine | Activated | 5.047 | 1.65E-31 |
| IL15 | cytokine | Activated | 3.775 | 1.16E-30 |
| IL33 | cytokine | Activated | 3.656 | 4.51E-13 |
| IL15 | cytokine | Activated | 3.382 | 5.18E-34 |
| IL5 | cytokine | Activated | 2.949 | 4.15E-17 |
| IFNL3 | cytokine | Activated | 2.714 | 7.4E-26 |
| IL7 | cytokine | Activated | 2.667 | 3.94E-23 |
| IL23A | cytokine | Activated | 2.578 | 2.02E-31 |
| IL4 | cytokine | Activated | 2.429 | 1.24E-20 |
| IL20 | cytokine | Activated | 2.405 | 1.12E-21 |
| IL25 | cytokine | Activated | 2.333 | 0.000000808 |
| CCL11 | cytokine | Activated | 2.278 | 6.26E-25 |
| MYDGF | cytokine | Activated | 2.121 | 2.16E-10 |
| IL18 | cytokine | Activated | 2 | 3.94E-23 |
| IFNL1 | cytokine | Activated | 2 | 1.97E-25 |
| FBXL14 | enzyme | Activated | 5.167 | 8.36E-56 |
| NDST1 | enzyme | Activated | 3.732 | 1.01E-23 |
| GNG3 | enzyme | Activated | 3.333 | 1.12E-15 |
| PLA2G5 | enzyme | Activated | 3.255 | 9.88E-24 |
| GPNMB | enzyme | Activated | 3.201 | 4.55E-21 |
| ATE1 | enzyme | Activated | 3.201 | 6.98E-18 |
| ANXA1 | enzyme | Activated | 2.969 | 2.09E-24 |
| CD38 | enzyme | Activated | 2.785 | 1.8E-12 |
| CCS | enzyme | Activated | 2.777 | 2.48E-15 |
| PLCG2 | enzyme | Activated | 2.753 | 1.22E-26 |
| PPIF | enzyme | Activated | 2.673 | 1.52E-08 |
| TKT | enzyme | Activated | 2.673 | 7.59E-22 |
| RC3H1 | enzyme | Activated | 2.425 | 1.31E-25 |
| RNASE2 | enzyme | Activated | 2.333 | 1.9E-09 |
| PDE6G | enzyme | Activated | 2.287 | 3.88E-14 |
| PLCD4 | enzyme | Activated | 2.252 | 3.18E-21 |
| GNAI3 | enzyme | Activated | 2.251 | 5.45E-23 |
| LTC4S | enzyme | Activated | 2.236 | 0.00000024 |
| RAP1B | enzyme | Activated | 2.236 | 0.00000024 |
| OTUD5 | enzyme | Activated | 2.138 | 0.000000028 |
| GNAI3 | enzyme | Activated | 2.121 | 1.04E-09 |
| FAAH | enzyme | Activated | 2.121 | 0.000000718 |
| UBE3C | enzyme | Activated | 2.121 | 1.14E-13 |
| METTL3 | enzyme | Activated | 2.065 | 1.56E-10 |
| CRHR1 | G-protein coupled receptor | Activated | 3.58 | 3.43E-26 |
| OPRM1 | G-protein coupled receptor | Activated | 3.392 | 1.81E-30 |
| ADRA2C | G-protein coupled receptor | Activated | 3.25 | 5.93E-21 |
| GNRHR | G-protein coupled receptor | Activated | 3.15 | 5.36E-19 |
| CCR2 | G-protein coupled receptor | Activated | 3.087 | 7.69E-30 |
| ADRA1A | G-protein coupled receptor | Activated | 3 | 9.13E-29 |
| ADRA2B | G-protein coupled receptor | Activated | 2.954 | 2.13E-21 |
| TRHR | G-protein coupled receptor | Activated | 2.944 | 1.19E-24 |
| ADRA1B | G-protein coupled receptor | Activated | 2.626 | 1.2E-32 |
| ADORA3 | G-protein coupled receptor | Activated | 2.6 | 3.84E-28 |
| LTB4R2 | G-protein coupled receptor | Activated | 2.502 | 1.18E-27 |
| ADORA3 | G-protein coupled receptor | Activated | 2.333 | 1.18E-12 |
| HRH1 | G-protein coupled receptor | Activated | 2 | 0.0000706 |
| Ap2 | group | Activated | 6.158 | 4.98E-69 |
| TLR7/8 | group | Activated | 3.989 | 1.88E-28 |
| Eotaxin | group | Activated | 3.713 | 8.54E-29 |
| apyrase | group | Activated | 3.615 | 3.65E-56 |
| Presenilin | group | Activated | 3.111 | 7.62E-16 |
| G protein alpha | group | Activated | 3.109 | 1.77E-24 |
| MIR124 | group | Activated | 3.073 | 1.19E-59 |
| STAT5a/b | group | Activated | 2.828 | 1.7E-10 |
| PI3Kγ | group | Activated | 2.708 | 5.31E-21 |
| BET | group | Activated | 2.619 | 1.13E-25 |
| Profilin | group | Activated | 2.4 | 1.38E-12 |
| Fcer | group | Activated | 2.309 | 5.01E-11 |
| Nfatc | group | Activated | 2.197 | 8E-16 |
| STAT | group | Activated | 2.117 | 2.92E-26 |
| antigen | group | Activated | 2 | 0.0000245 |
| TGFB1 | growth factor | Activated | 4.619 | 4.68E-27 |
| EDN2 | growth factor | Activated | 2.287 | 3.33E-14 |
| KCND2 | ion channel | Activated | 3.536 | 1.82E-26 |
| ILK | kinase | Activated | 6.596 | 9.04E-34 |
| BRAF | kinase | Activated | 3.967 | 1.79E-23 |
| PINK1 | kinase | Activated | 3.447 | 1.73E-20 |
| TEK | kinase | Activated | 3.317 | 1.19E-28 |
| BTK | kinase | Activated | 3.153 | 3.25E-10 |
| AGK | kinase | Activated | 2.964 | 9.66E-24 |
| MOS | kinase | Activated | 2.8 | 4.79E-24 |
| NTRK2 | kinase | Activated | 2.762 | 1.27E-26 |
| FGR | kinase | Activated | 2.373 | 1.2E-24 |
| CARD11 | kinase | Activated | 2.333 | 5.94E-11 |
| STYK1 | kinase | Activated | 2.25 | 1.97E-22 |
| NEK6 | kinase | Activated | 2.177 | 9.9E-23 |
| SKAP1 | kinase | Activated | 2.064 | 8.73E-16 |
| miR-125b-5p (and other miRNAs w/seed CCCUGAG) | mature microRNA | Activated | 2.889 | 1.8E-57 |
| miR-542-3p (miRNAs w/seed GUGACAG) | mature microRNA | Activated | 2 | 0.000159 |
| mir-24 | microRNA | Activated | 3.507 | 6.31E-19 |
| mir-191 | microRNA | Activated | 2.524 | 6.42E-11 |
| RICTOR | other | Activated | 6.719 | 2.21E-33 |
| AMBRA1 | other | Activated | 5.879 | 1.04E-60 |
| CUL4B | other | Activated | 5.691 | 5.12E-59 |
| CDR2 | other | Activated | 5.683 | 2.34E-55 |
| Ifi202b | other | Activated | 5.06 | 1.08E-58 |
| IGHE | other | Activated | 3.983 | 1.44E-22 |
| SDC2 | other | Activated | 3.637 | 5.61E-24 |
| MFGE8 | other | Activated | 3.578 | 5.05E-23 |
| C5 | other | Activated | 3.53 | 4.45E-30 |
| UCN2 | other | Activated | 3.255 | 5.8E-21 |
| RBM8A | other | Activated | 3.17 | 1.19E-25 |
| ANK2 | other | Activated | 3.15 | 4.55E-20 |
| RICTOR | other | Activated | 3.103 | 6.21E-41 |
| Prl3d1 (includes others) | other | Activated | 3 | 5.92E-23 |
| TRG | other | Activated | 2.714 | 2.67E-15 |
| IAPP | other | Activated | 2.712 | 5.63E-22 |
| SH2D5 | other | Activated | 2.673 | 7.59E-22 |
| ICOSLG/LOC102723996 | other | Activated | 2.646 | 0.000000149 |
| IFNL2 | other | Activated | 2.574 | 2.31E-27 |
| MSLN | other | Activated | 2.462 | 9.47E-24 |
| MUC16 | other | Activated | 2.405 | 1.97E-21 |
| PTGFRN | other | Activated | 2.287 | 3.33E-14 |
| CNN3 | other | Activated | 2.287 | 3.33E-14 |
| COL5A3 | other | Activated | 2.287 | 3.33E-14 |
| NMU | other | Activated | 2.236 | 0.0000496 |
| RASSF5 | other | Activated | 2.236 | 0.00205 |
| NPHP1 | other | Activated | 2.188 | 2.41E-16 |
| MS4A1 | other | Activated | 2.183 | 1.19E-10 |
| TNFAIP8 | other | Activated | 2.111 | 6.15E-08 |
| GP9 | other | Activated | 2.021 | 4.55E-16 |
| MOG | other | Activated | 2 | 3.19E-17 |
| RTKN | other | Activated | 2 | 0.000159 |
| METRNL | other | Activated | 2 | 0.000159 |
| USP10 | peptidase | Activated | 4.566 | 1.09E-55 |
| KLK5 | peptidase | Activated | 4.15 | 1.48E-32 |
| MMP14 | peptidase | Activated | 3.817 | 9.34E-29 |
| MMP2 | peptidase | Activated | 2.858 | 4.7E-25 |
| MMP17 | peptidase | Activated | 2.828 | 1.32E-25 |
| FAP | peptidase | Activated | 2.066 | 3.89E-22 |
| CTDSP1 | phosphatase | Activated | 5.539 | 2.6E-55 |
| PTPRD | phosphatase | Activated | 3.238 | 4.91E-57 |
| PTP4A1 | phosphatase | Activated | 2.654 | 1.19E-16 |
| PTPN22 | phosphatase | Activated | 2.449 | 0.0000146 |
| SP3 | transcription regulator | Activated | 4.383 | 4.61E-28 |
| HIF3A | transcription regulator | Activated | 4.111 | 5.41E-29 |
| LMO2 | transcription regulator | Activated | 4.062 | 1.1E-58 |
| TRIM24 | transcription regulator | Activated | 4.041 | 2.13E-16 |
| ETV6 | transcription regulator | Activated | 3.709 | 1.11E-57 |
| BHLHE40 | transcription regulator | Activated | 3.578 | 1.33E-10 |
| IRF6 | transcription regulator | Activated | 3.077 | 4.98E-23 |
| ZHX2 | transcription regulator | Activated | 3.048 | 5.61E-20 |
| STAT6 | transcription regulator | Activated | 3 | 7.06E-19 |
| IRF9 | transcription regulator | Activated | 3 | 3.29E-24 |
| NKX2-3 | transcription regulator | Activated | 2.858 | 2.21E-08 |
| ARNT | transcription regulator | Activated | 2.828 | 5.06E-14 |
| ELF4 | transcription regulator | Activated | 2.828 | 0.0000132 |
| ETV5 | transcription regulator | Activated | 2.828 | 2.41E-25 |
| TWIST2 | transcription regulator | Activated | 2.782 | 1.05E-21 |
| HES5 | transcription regulator | Activated | 2.734 | 5.99E-24 |
| ISL1 | transcription regulator | Activated | 2.689 | 8.54E-24 |
| STAT3 | transcription regulator | Activated | 2.562 | 3.69E-21 |
| TCF4 | transcription regulator | Activated | 2.557 | 1.01E-21 |
| BCL3 | transcription regulator | Activated | 2.496 | 3.14E-09 |
| WT1 | transcription regulator | Activated | 2.425 | 3.53E-22 |
| GATA3 | transcription regulator | Activated | 2.302 | 9.54E-37 |
| PRDM1 | transcription regulator | Activated | 2.263 | 3.24E-16 |
| MTPN | transcription regulator | Activated | 2.224 | 4.94E-22 |
| TBX21 | transcription regulator | Activated | 2.132 | 4.53E-17 |
| NFATC2 | transcription regulator | Activated | 2.121 | 1.89E-15 |
| SMAD1 | transcription regulator | Activated | 2.121 | 0.000000718 |
| LARP1 | translation regulator | Activated | 7.488 | 1.41E-68 |
| IGF2BP2 | translation regulator | Activated | 2.287 | 4.51E-14 |
| IGF2R | transmembrane receptor | Activated | 4.156 | 3.82E-32 |
| HMMR | transmembrane receptor | Activated | 3.579 | 1.16E-25 |
| CD69 | transmembrane receptor | Activated | 3.501 | 1.24E-18 |
| IL10RA | transmembrane receptor | Activated | 3.286 | 5.83E-12 |
| MPL | transmembrane receptor | Activated | 3.273 | 1.67E-27 |
| IL10RA | transmembrane receptor | Activated | 3.222 | 1.9E-27 |
| Klrk1 | transmembrane receptor | Activated | 3.13 | 4.19E-18 |
| CLEC6A | transmembrane receptor | Activated | 2.835 | 3.45E-27 |
| CNTFR | transmembrane receptor | Activated | 2.734 | 5.13E-22 |
| Klra7 (includes others) | transmembrane receptor | Activated | 2.646 | 0.000000712 |
| CD3E | transmembrane receptor | Activated | 2.496 | 8.6E-12 |
| ICOS | transmembrane receptor | Activated | 2.496 | 8.6E-12 |
| CD244 | transmembrane receptor | Activated | 2.449 | 0.000000292 |
| CD86 | transmembrane receptor | Activated | 2.324 | 1.51E-15 |
| IL13RA1 | transmembrane receptor | Activated | 2.294 | 1.53E-23 |
| CD46 | transmembrane receptor | Activated | 2.25 | 8.8E-20 |
| CD247 | transmembrane receptor | Activated | 2.138 | 1.27E-23 |
| FCER1G | transmembrane receptor | Activated | 2.121 | 0.00000012 |
| TLR4 | transmembrane receptor | Activated | 2.058 | 8.23E-15 |
| EDNRA | transmembrane receptor | Activated | 2.047 | 5.18E-24 |
| CD79B | transmembrane receptor | Activated | 2.018 | 1.62E-24 |
| CD19 | transmembrane receptor | Activated | 2 | 0.0000245 |
| ULBP2 | transmembrane receptor | Activated | 2 | 0.0000706 |
| CRLF2 | transmembrane receptor | Activated | 2 | 0.000159 |
| TRPC4AP | transporter | Activated | 5.66 | 3.5E-62 |
| TNNI3 | transporter | Activated | 2.646 | 5.34E-10 |
| RBP3 | transporter | Activated | 2.183 | 1.11E-09 |
| FLVCR1 | transporter | Activated | 2 | 0.0000245 |
| TRPC4AP | transporter | Activated | 2 | 0.0000245 |