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# Supplementary Materials for

## Neutrophilic inflammation in the respiratory mucosa predisposes to RSV infection

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**Other Supplementary Material for this manuscript includes the following:**
(available at science.sciencemag.org/content/370/6513/eaax9301/suppl/DC1)

MDAR Reproducibility Checklist (PDF)

## Materials and Methods

Flow cytometry reagents for murine studies

| Target | Clone or order number | Fluorochrome | Vendor | Final concentration and dilution |
|---|---|---|---|---|
| Live cells | L34957 | Aqua | Invitrogen | 1:500 |
| CD3 | 17A2 | AF700 | eBioscience | 2 mg/ml |
| CD3 | 145-2C11 | FITC | Biolegend | 2.5 mg/ml |
| CD4 | GK1.5 | PE | eBioscience | 0.5 mg/ml |
| CD8 | 53-6.7 | eFluor780 | eBioscience | 0.5 mg/ml |
| CD11b | M1/70 | AF700 | eBioscience | 0.5 mg/ml |
| CD11c | HL3 | PE-CF594 | BD Horizon | 1 mg/ml |
| CD19 | 6D5 | FITC | Biolegend | 5 mg/ml |
| CD44 | IM7 | PE-Cy7 | Biolegend | 2 mg/ml |
| CD45 | 30-F11 | BV605 | Biolegend | 0.25 mg/ml |
| CD62L | MEL-14 | BV421 | Biolegend | 1 mg/ml |
| CD64 | X54-5/7 | APC | Biolegend | 1 mg/ml |
| CD69 | H1.2F3 | BUV737 | BD Horizon | 1 mg/ml |
| CD103 | 2E7 | PerCP-Cy5.5 | Biolegend | 1 mg/ml |
| Fc block (CD16/32) | 93 | | Biolegend | 2.5 mg/ml |
| Granzyme B | GB11 | PECF594 | BD Horizon | 1:200 |
| IFN-γ | XMG1.2 | BV711 | BD Horizon | 1 mg/ml |
| Ly6C | HK1.4 | BV421 | Biolegend | 0.125 mg/ml |
| Ly6C | HK1.4 | eFluor450 | eBioscience | 0.25 mg/ml |
| Ly6G | 1A8 | FITC | Biolegend | 5 mg/ml |
| Ly6G | 1A8 | APC-Cy7 | Biolegend | 0.5 mg/ml |
| Ly6G | 1A8 | BV785 | Biolegend | 1 mg/ml |
| MHC-II | M5/114.15.2 | APC-eF780 | eBiosciences | 1 mg/ml |
| Siglec-F | E50-2440 | PE | BD Pharmingen | 1 mg/ml |
| Tetramer | RSV $M_{187-195}$ | Alexa647 | NIH Tetramer facility | 15 mg/ml |

qPCR reagents for murine studies

| Gene | Primer/Probe | Assay ID or order number | Vendor |
|---|---|---|---|
| *Ccl2* | TaqMan® Gene Expression Assay | Mm00441242_m1<br>FAM | Thermo Fisher (ABI) |
| *Cxcl2* | TaqMan® Gene Expression Assay | Mm00436450_m1<br>FAM | Thermo Fisher (ABI) |
| *Cxcl10* | TaqMan® Gene Expression Assay | Mm00445235_m1<br>FAM | Thermo Fisher (ABI) |
| *Gapdh* | TaqMan® Gene Expression Assay | 4351309<br>VIC | Thermo Fisher (ABI) |
| *Il1b* | TaqMan® Gene Expression Assay | Mm00434228_m1<br>FAM | Thermo Fisher (ABI) |
| L gene | Fwd: 5'-gaactcagtgtaggtagaatgtttgca-3'<br>Rev: 5'-ttcagctatcattttctctgccaat-3'<br>Probe: 5'-(FAM)tttgaacctgtct gaacattcccggtt(TAM)-3' | Previously reported *(65)* | Invitrogen<br>Invitrogen<br>Eurofin |
| *Tnfa* | Fwd: 5'-catcttctcaaaattcgagtgacaa-3'<br>Rev: 5'-tgggagtagacaaggtacaaccc-3'<br>Probe:5'-(FAM)cacgtcgtagcaaac (TAM)-3' | Previously reported *(64)* | Invitrogen<br>Invitrogen<br>Eurofin |

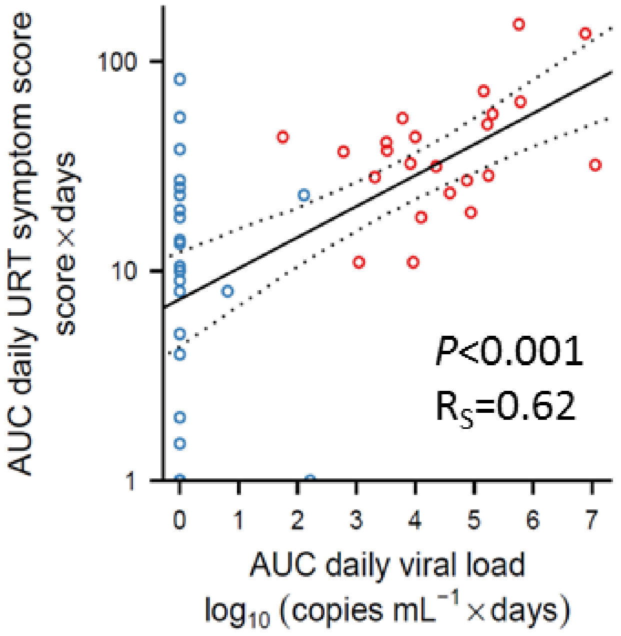


**Fig. S1: Correlation between total upper respiratory tract symptom scores and viral load.**

Correlation between area under the curve (AUC) of upper respiratory tract (URT) symptoms and AUC of daily viral load within the "Cold" (red, n=23) and "No Cold" (blue, n=25) groups was assessed using Spearman's test.

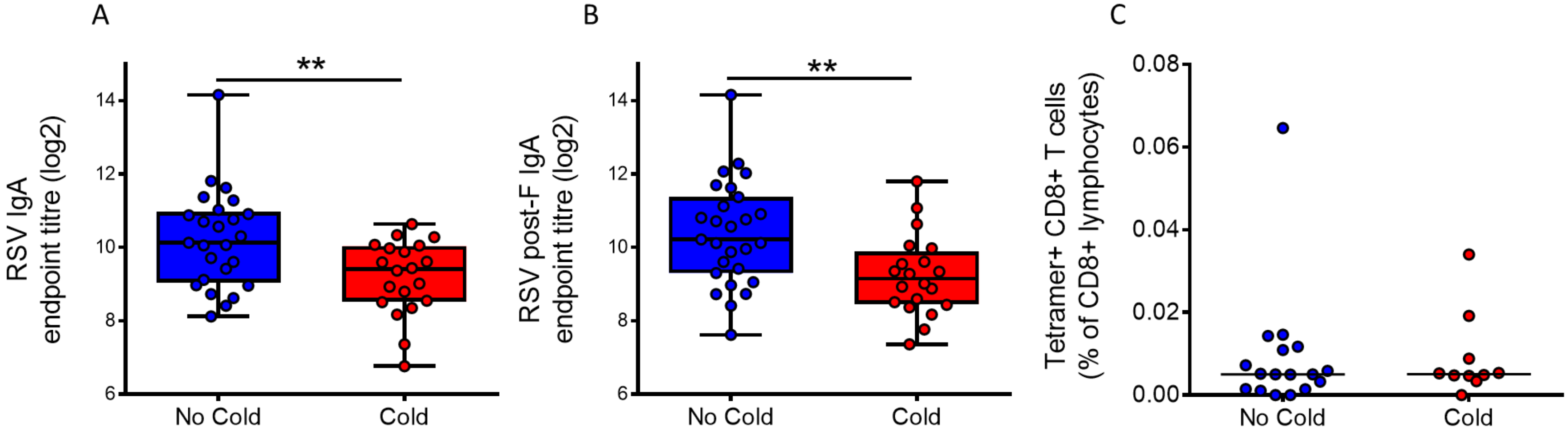


**Fig. S2: Pre-inoculation nasal anti-RSV antibody levels, but not anti-RSV CD8$^+$ T cell proportions, are associated with protection from infection.**

Baseline levels of **(A)** total anti-RSV IgA and **(B)** post-F specific IgA in nasal lavage from “No Cold” (n=25, blue) and “Cold” (n=20, red) groups were measured by ELISA. **(C)** Frequencies of RSV-specific tetramer positive CD8$^+$T cells in the lung from “No Cold” (n=17) and “Cold” (n=10) groups were quantified by flow cytometry. Data in panels A and B are represented as medians with interquartile ranges and minimum and maximum values. Data in panel C are represented as medians. Significance was tested by Mann Whitney *U* test. **$P$<0.01.

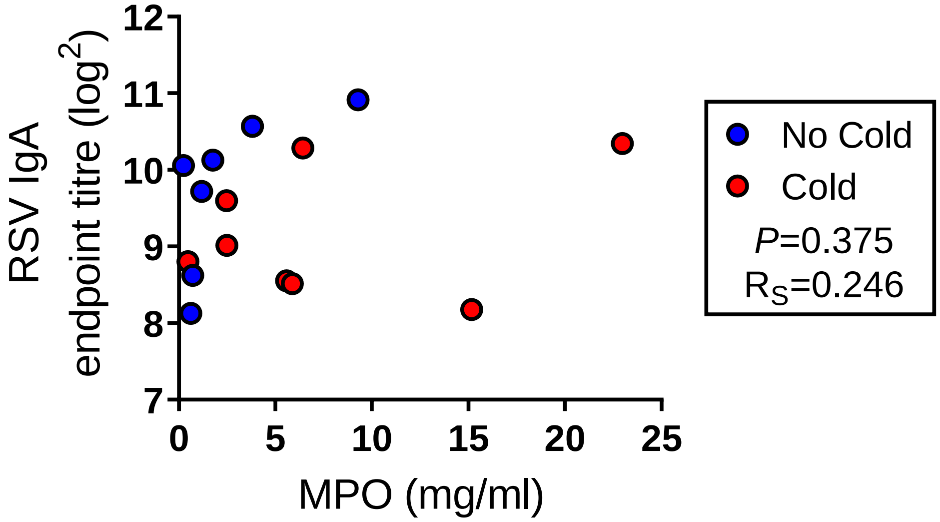


**Fig. S3: Pre-inoculation nasal anti-RSV antibody levels are not associated with measures of neutrophilic inflammation.**

Levels of total anti-RSV IgA and myeloperoxidase (MPO) were measured by ELISA and correlation determined in baseline samples from “No Cold” (n=7) and “Cold” (n=8) groups. Significance was tested in the combined group by Spearman’s test.

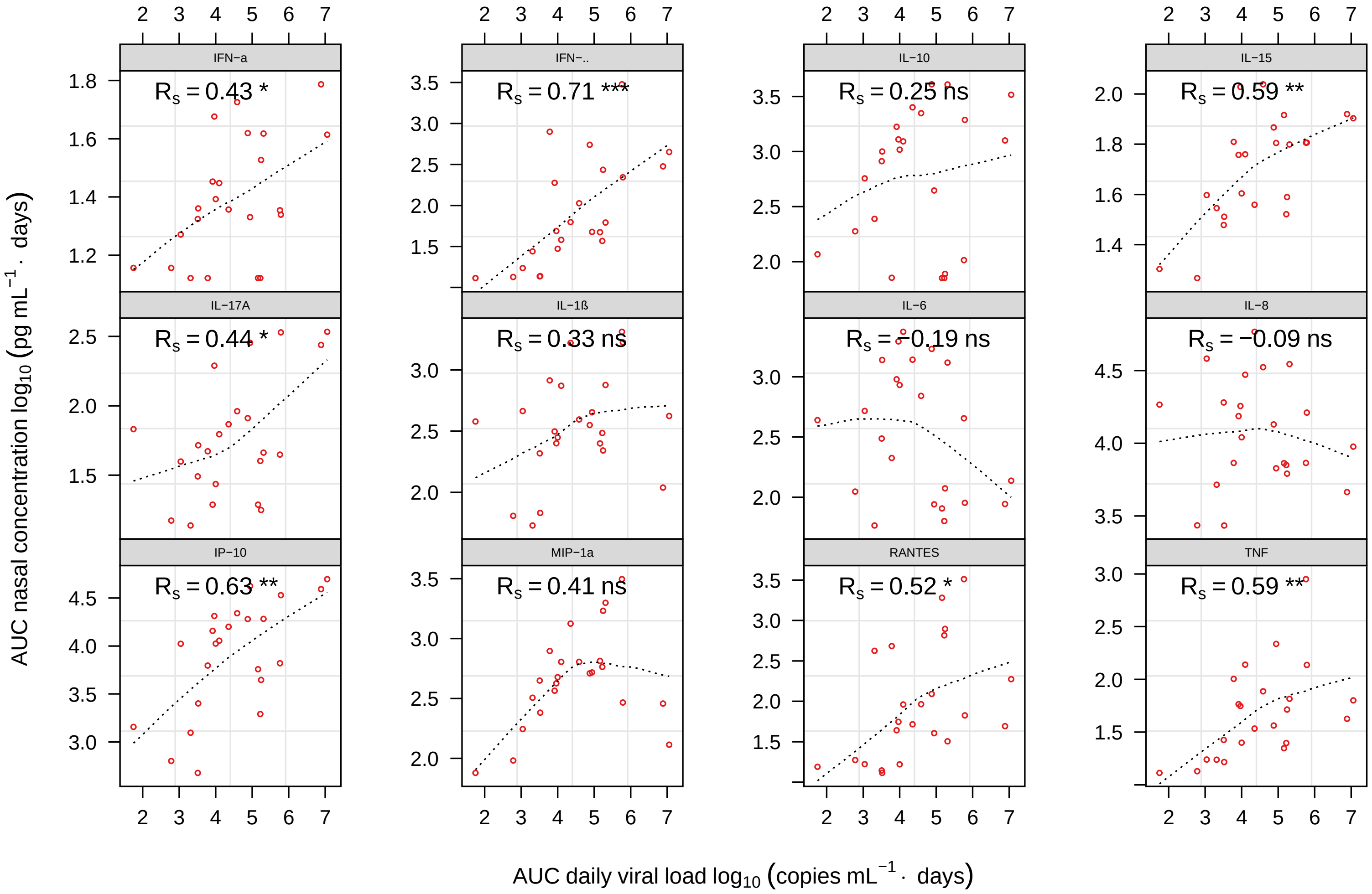


**Fig. S4: Cumulative viral load correlates with the levels of several inflammatory mediators.**

Within the Cold group (n=23), correlations between area under the curve (AUC) levels of daily viral load and cytokine/chemokine mediator levels for **(A)** IFN-α, **(B)** IL-17A, **(C)** CXCL10/IP-10, **(D)** IFN-γ, **(E)** IL-1β, **(F)** CCL3/MIP-1α, **(G)** IL-10, **(H)** IL-6, **(I)** CCL5/RANTES, **(J)** IL-15, **(K)** CXCL8/IL-8 and **(L)** TNF-α. Correlations were assessed using Spearman's test. **P*<0.05, ***P*<0.01, ****P*<0.001, ns=not significant.

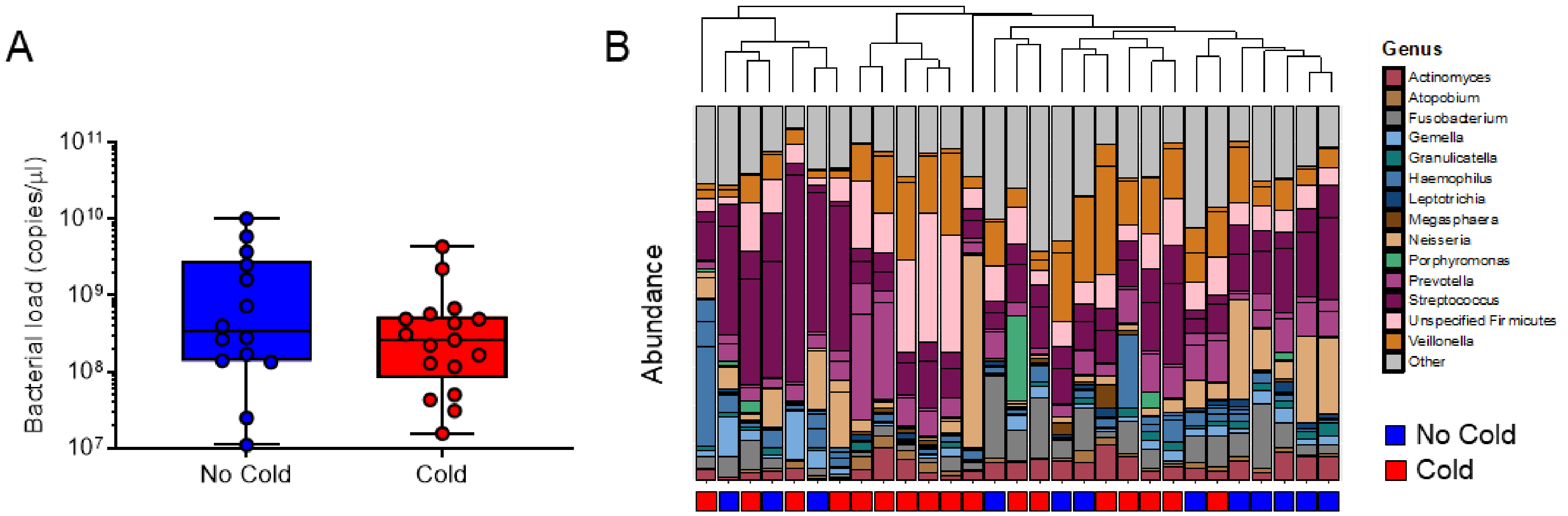
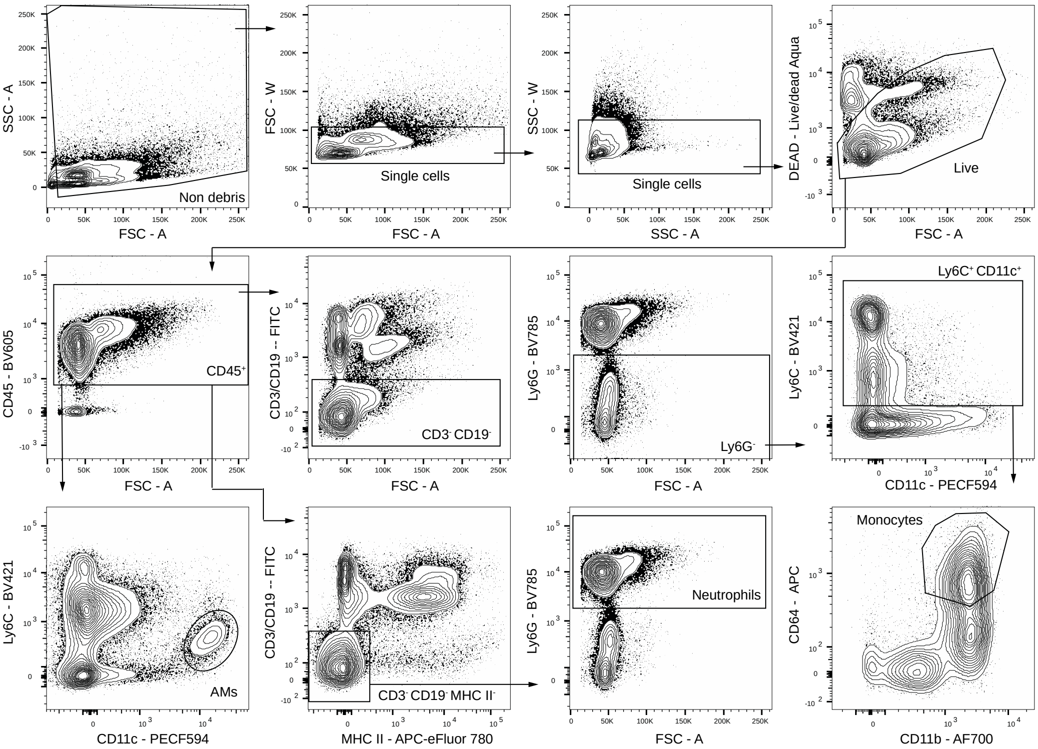


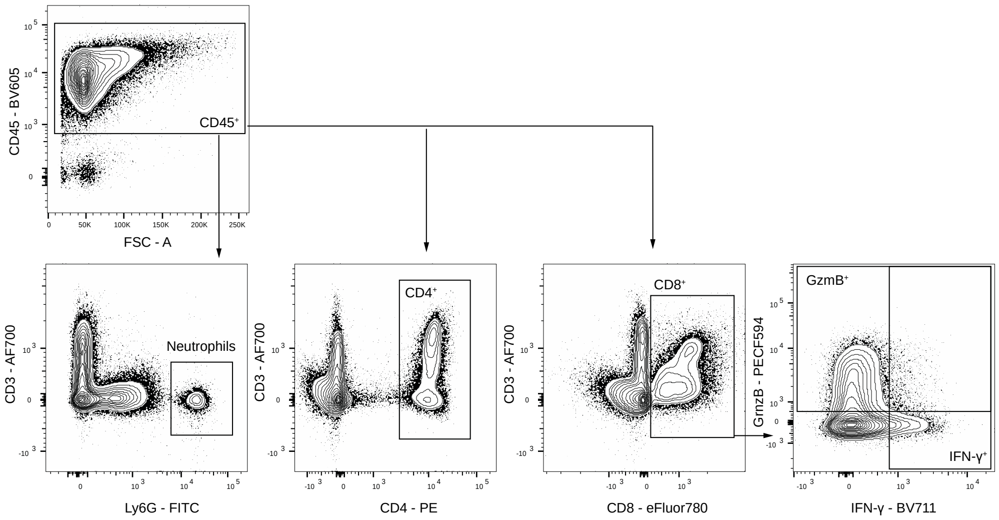
**Fig. S5: The airway microbiome at point of virus exposure is not associated with susceptibility to infection.**

**(A)** Bacterial load, measured by 16S qPCR, from baseline nasopharyngeal swabs of No Cold (n=12) and Cold (n=17) participants. **(B)** Baseline bacterial community ordered by Bray-Curtis hierarchical clustering where the top 20 OTUs are shown. Data in part A are represented as median and interquartiles with minimum and maximum values.

**A** Alveolar macrophages, monocytes and neutrophils



**B** T cell staining panel - Intracellular cytokine stain (gated to live cells as above)



**C** T cell staining panel - CD8⁺ tetramer stain (gated to live cells as above)

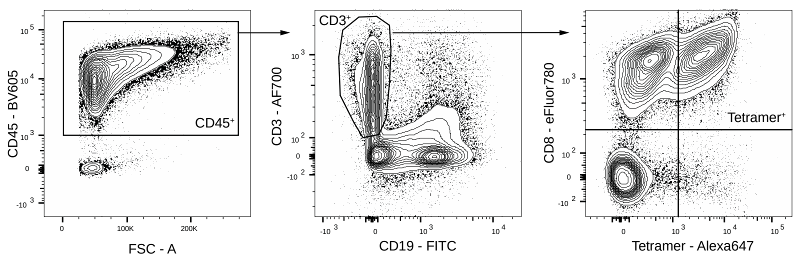


**Fig. S6: Gating strategies for identifying murine lung cells.**

**(A)** Mice were treated with mock (PBS) or 5-10 µg rCXCL1 i.n.. **(A)** At 12 hours or 18 hours post-RSV infection airway and lung innate immune cells were obtained by collagenase digestion and stained for the indicated cell surface molecules. After excluding debris and gating on single, live, CD45$^{+}$ cells, the depicted gates were used to identify AMs, monocytes, and neutrophils. **(B)** Mice were treated with mock (PBS) or 10 µg rCXCL1 i.n. and after 12 hours infected with mock (PBS) or 7.5×10$^{5}$ FFU RSV i.n.. After 8 days, lung cells were obtained by collagenase digestion and stained for the indicated cell surface molecules. After excluding debris and gating on single, live, CD45$^{+}$ cells, the depicted gates were used to identify neutrophils, CD4$^{+}$ and CD8$^{+}$ T cells as well as GzmB$^{+}$ and IFN-γ$^{+}$ CD8$^{+}$ T cells. **(C)** After excluding debris and gating on single, live, CD45$^{+}$ cells, the depicted gates were used to identify RSV tetramer$^{+}$ CD8$^{+}$ T cells.

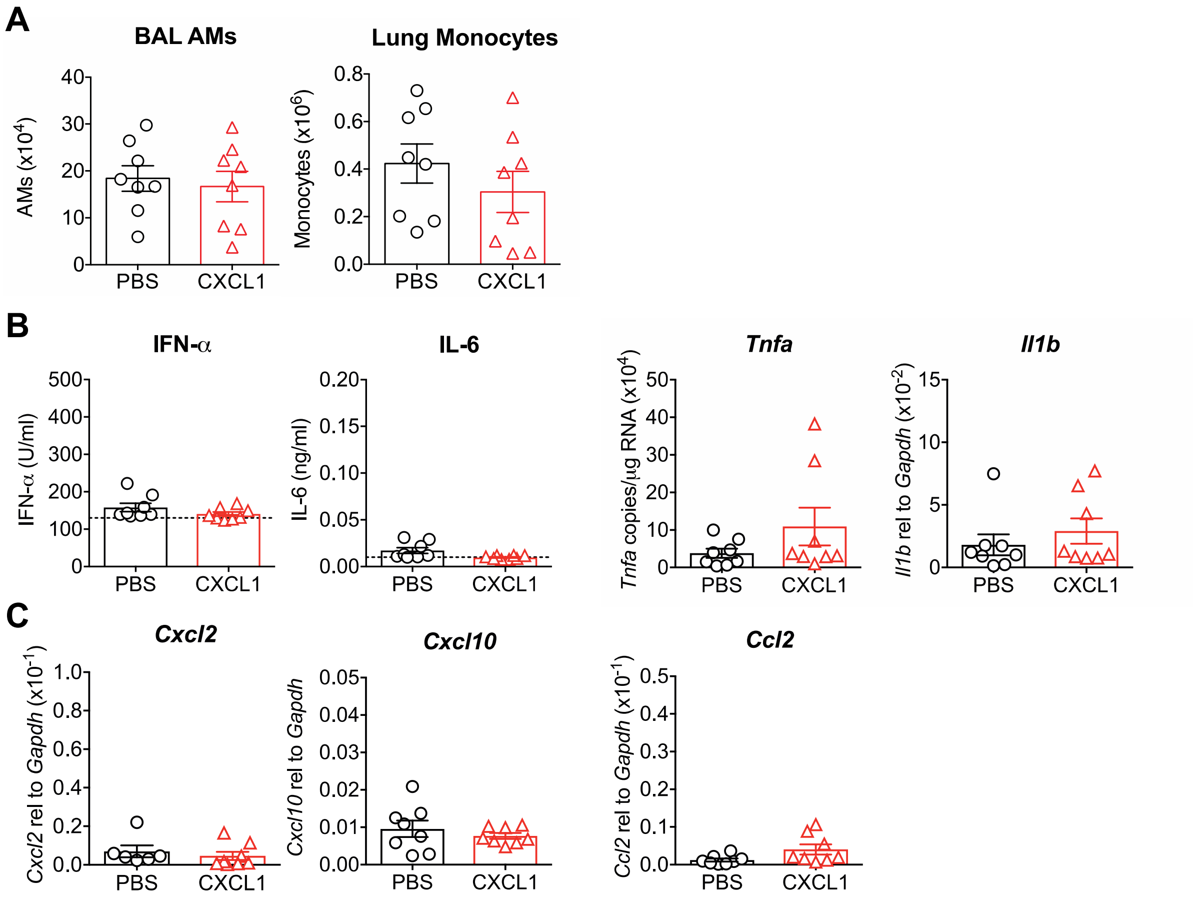


**Fig. S7: Treatment with rCXCL1 alone causes no change in alveolar macrophages, monocytes or inflammatory mediators in the lung.**

Mice were treated with mock (PBS) or 10 µg rCXCL1 i.n. and after 12 hours, cells and mediators were quantified in the lung. **(A)** BAL AMs and lung monocytes were quantified 12 hours post CXCL1 treatment by flow cytometry. **(B)** IFN-α and IL-6 was quantified in BAL using ELISA and levels of *Il1b* and *Tnfa* were determined in lung tissue using qPCR. **(C)** *Cxcl2, Cxcl10,* and *Ccl2* were determined in lung tissue using qPCR. Data are presented as mean±SEM of eight individual mice per group, pooled from two independent experiments. The dotted line represents the limit of detection of the assay. Statistical significance was analyzed using unpaired, two-tailed Student's *t* test.

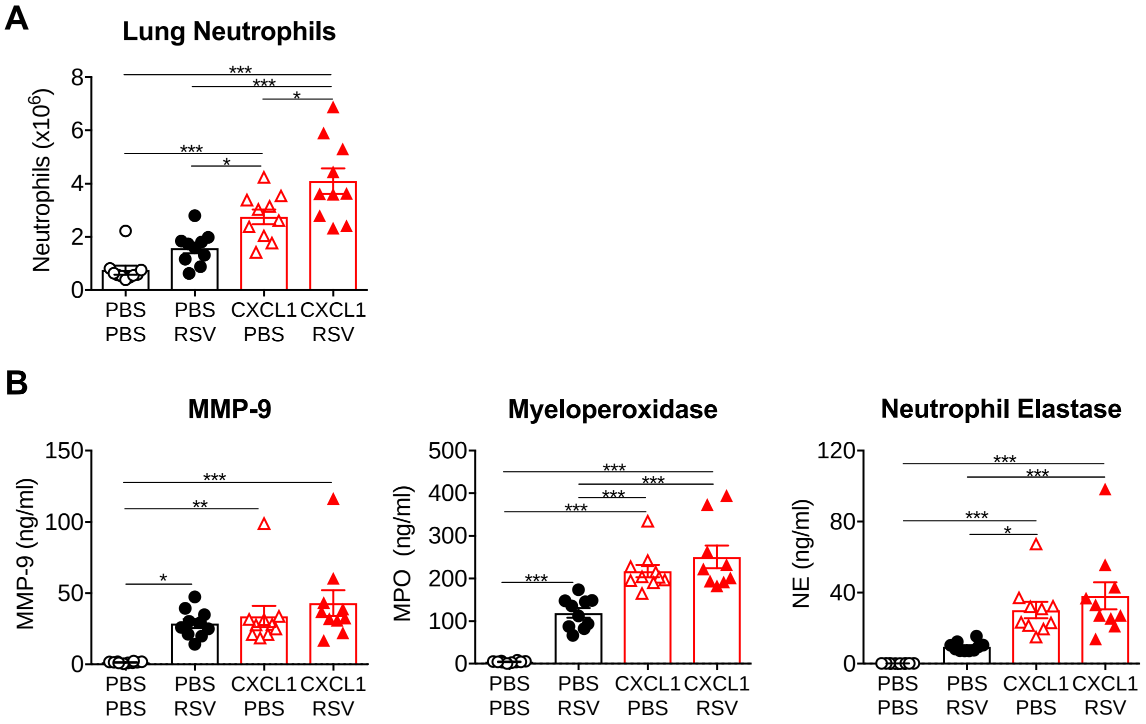


**Fig. S8: RSV infection of rCXCL1 pre-treated mice enhances the early production of neutrophil markers.**

Mice were treated with mock (PBS) or 5 µg rCXCL1 i.n. and after 9 hours infected with mock (PBS) or 7.5×$10^5$ FFU RSV i.n. for 18 hours. **(A)** The total number of lung neutrophils was quantified by flow cytometry as previously described in *(65)*. **(B)** MMP-9, MPO and NE was quantified in BAL using ELISA. The data are presented as mean±SEM of 10 individual mice per group, pooled from two independent experiments. Statistical significance of differences was analyzed by one-way ANOVA with Tukey's post hoc test.**P*<0.05, ***P*<0.01, ****P*<0.001.

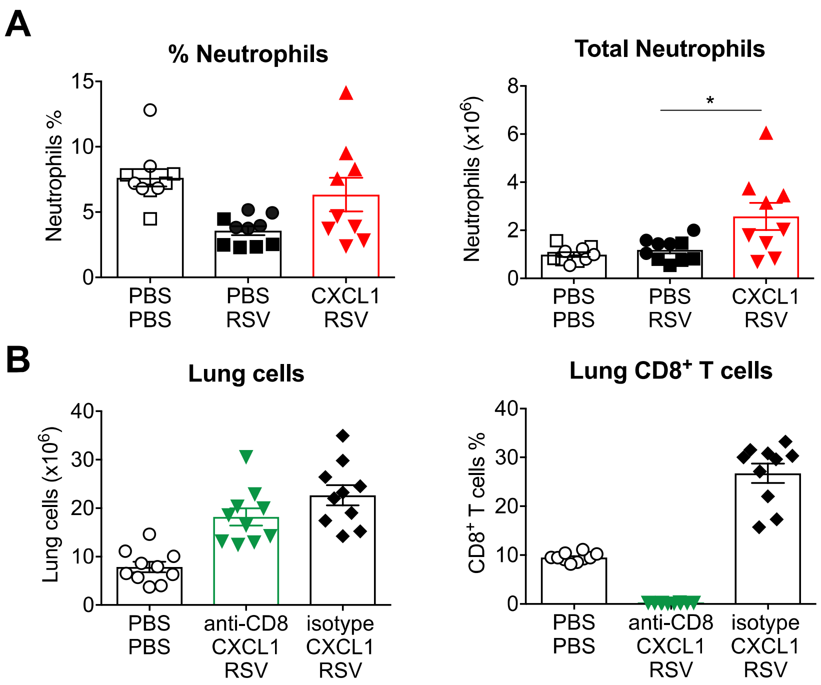


**Fig. S9: Treatment with rCXCL1 pre-RSV infection does not result in an increase in neutrophil frequency on day 8 p.i. and treatment with anti-CD8 antibodies is sufficient to remove CD8$^+$ T cells during RSV infection.**

Mice were treated with mock (PBS) or 8 µg or 10 µg rCXCL1 i.n. and after 12 hours infected with mock (PBS) or 7.5×10$^5$ FFU RSV i.n.. **(A)** The frequency and total number of lung neutrophils was quantified by flow cytometry. **(B)** To deplete CD8$^+$ T cells, mice were treated with 250 µg anti-CD8 or isotype control i.p. on day -1, day 2 and day 5 p.i. and lung were analyzed on day 8 p.i.. Total number of lung cells and frequency of CD8$^+$ T cells as quantified by flow cytometry. Data from (A) are presented as mean±SEM of 10 (PBS/PBS, PBS/RSV) or 9 (CXCL1/RSV) mice, pooled from two independent experiments - repeat 1 (10 µg CXCL1; circles) and repeat 2 (8 µg CXCL1; squares). Data from (B) are presented as mean±SEM of 10 mice, pooled from two independent experiments. Data in (A and B) were analyzed using one-way ANOVA with Tukey's post hoc test. **P*<0.05

Table S1

| | Cold (n=23) | No Cold (n=25) | *P*-value |
|---|---|---|---|
| Age in years, mean (range) | 23.3 (18-50) | 23.6 (18-39) | 0.84 |
| Sex (M:F) | 12:11 | 15:10 | 0.77 |
| Ethnicity (n=) | | | |
| White | 17 (74%) | 19 (76%) | >0.99 |
| Black | 1 (4%) | 4 (16%) | 0.37 |
| Asian | 2 (9%) | 0 | 0.22 |
| Mixed | 1 (4%) | 2 (8%) | >0.99 |
| Other | 2 (9%) | 0 | 0.22 |

**Table S1: Demographics**

Volunteer demographics were collected at study enrolment and categorized on subsequent development of a symptomatic infection following RSV inoculation (Cold, n=23) or not (No Cold, n=25). A two-tailed *t*-test was used to assess significance in volunteer age. Fisher's exact tests were used to assess significance in sex and ethnicity data.

Table S2: Baseline DEGs between “Cold” and “No Cold” groups (*P*adj<0.1, LFC>0.5)

| | GeneName | baseMean | log$^2$FoldChange | lfcSE | stat | *P*value | *P*adj |
|---|---|---|---|---|---|---|---|
| ENSG00000129455 | *KLK8* | 64.04073471 | 4.50463631 | 0.725538 | 6.208681 | 0.0000000005 | 0.0000078 |
| ENSG00000140519 | *RHCG* | 327.2661994 | 3.899687376 | 0.687333 | 5.673651 | 0.0000000140 | 0.0001025 |
| ENSG00000143536 | *CRNN* | 717.7315072 | 3.961919136 | 0.710893 | 5.573155 | 0.0000000250 | 0.0001124 |
| ENSG00000136688 | *IL36G* | 119.3575404 | 3.485458598 | 0.629406 | 5.537698 | 0.0000000306 | 0.0001124 |
| ENSG00000203785 | *SPRR2E* | 549.5597617 | 3.759191643 | 0.694542 | 5.412479 | 0.0000000622 | 0.0001823 |
| ENSG00000244617 | *ASPRV1* | 201.6683348 | 2.541982486 | 0.473897 | 5.363995 | 0.0000000814 | 0.0001990 |
| ENSG00000163216 | *SPRR2D* | 493.240127 | 3.489918519 | 0.673736 | 5.179946 | 0.0000002219 | 0.0004651 |
| ENSG00000172137 | *CALB2* | 7.432513115 | 3.827424619 | 0.744758 | 5.139154 | 0.0000002760 | 0.0005060 |
| ENSG00000102837 | *OLFM4* | 9.018542922 | 2.379694573 | 0.485505 | 4.901481 | 0.0000009512 | 0.0015502 |
| ENSG00000164867 | *NOS3* | 39.06236907 | 2.172068356 | 0.455328 | 4.770338 | 0.0000018392 | 0.0024524 |
| ENSG00000104327 | *CALB1* | 97.2215325 | 3.213472664 | 0.672135 | 4.780991 | 0.0000017443 | 0.0024524 |
| ENSG00000145879 | *SPINK7* | 214.5721968 | 3.777459369 | 0.795095 | 4.750953 | 0.0000020246 | 0.0024747 |
| ENSG00000167755 | *KLK6* | 219.7775905 | 3.749018528 | 0.793685 | 4.723561 | 0.0000023175 | 0.0026149 |
| ENSG00000143369 | *ECM1* | 368.3426926 | 2.548748229 | 0.543078 | 4.693155 | 0.0000026902 | 0.0028186 |
| ENSG00000088386 | *SLC15A1* | 58.06521529 | 1.444700757 | 0.309249 | 4.671646 | 0.0000029880 | 0.0029218 |
| ENSG00000167754 | *KLK5* | 58.04069283 | 4.183165833 | 0.901151 | 4.642025 | 0.0000034501 | 0.0031629 |
| ENSG00000244094 | *SPRR2F* | 174.9314565 | 3.559094351 | 0.769266 | 4.62661 | 0.0000037170 | 0.0032071 |
| ENSG00000197948 | *FCHSD1* | 433.0477186 | 0.555918016 | 0.122298 | 4.545597 | 0.0000054780 | 0.0044639 |
| ENSG00000188508 | *KRTDAP* | 56.82226766 | 4.12052942 | 0.913535 | 4.510532 | 0.0000064665 | 0.0049922 |
| ENSG00000165799 | *RNASE7* | 76.05592952 | 2.591086011 | 0.578846 | 4.476294 | 0.0000075950 | 0.0055702 |
| ENSG00000158825 | *CDA* | 31.30464651 | 3.126427907 | 0.70532 | 4.432636 | 0.0000093088 | 0.0060990 |
| ENSG00000172005 | *MAL* | 315.8263003 | 2.780102998 | 0.629321 | 4.417623 | 0.0000099792 | 0.0060990 |
| ENSG00000188100 | *FAM25A* | 52.79654449 | 3.385115694 | 0.766093 | 4.418675 | 0.0000099308 | 0.0060990 |
| ENSG00000178734 | *LMO7DN* | 7.032824408 | 2.363797695 | 0.534435 | 4.422982 | 0.0000097348 | 0.0060990 |
| ENSG00000256618 | *MTRNR2L1* | 31.19207611 | 4.405844562 | 1.017059 | 4.331946 | 0.0000147797 | 0.0078477 |
| ENSG00000166396 | *SERPINB7* | 133.8826024 | 1.568727074 | 0.362378 | 4.328974 | 0.0000149805 | 0.0078477 |
| ENSG00000105427 | *CNFN* | 357.4556348 | 2.628314998 | 0.606082 | 4.336567 | 0.0000144726 | 0.0078477 |
| ENSG00000169035 | *KLK7* | 460.4004676 | 3.236932356 | 0.746379 | 4.336849 | 0.0000144540 | 0.0078477 |
| ENSG00000177243 | *DEFB103B* | 12.86752713 | 4.068667323 | 0.94596 | 4.301099 | 0.0000169953 | 0.0083096 |
| ENSG00000176797 | *DEFB103A* | 12.86752713 | 4.068667323 | 0.94596 | 4.301099 | 0.0000169953 | 0.0083096 |
| ENSG00000196805 | *SPRR2B* | 12.46642556 | 4.007415528 | 0.94584 | 4.236884 | 0.0000226643 | 0.0105675 |
| ENSG00000255823 | *MTRNR2L8* | 99.96331934 | -2.063829514 | 0.487551 | -4.23305 | 0.0000230542 | 0.0105675 |
| ENSG00000185966 | *LCE3E* | 18.55284064 | 4.403689631 | 1.044843 | 4.214692 | 0.0000250120 | 0.0111174 |
| ENSG00000269741 | *KLK9* | 38.39528424 | 3.634649191 | 0.869249 | 4.181368 | 0.0000289761 | 0.0125006 |
| ENSG00000163202 | *LCE3D* | 21.85709696 | 3.766259743 | 0.907597 | 4.149703 | 0.0000332906 | 0.0136037 |
| ENSG00000172382 | *PRSS27* | 235.5149533 | 2.146835495 | 0.51743 | 4.149036 | 0.0000333878 | 0.0136037 |
| ENSG00000265590 | *AP000275.65* | 13.45435781 | -2.313482025 | 0.565829 | -4.08866 | 0.0000433880 | 0.0172004 |
| ENSG00000163221 | *S100A12* | 117.0760162 | 2.42404596 | 0.595909 | 4.067813 | 0.0000474564 | 0.0183182 |
| ENSG00000115602 | *IL1RL1* | 44.99164745 | 2.186332063 | 0.544735 | 4.01357 | 0.0000598072 | 0.0224936 |
| ENSG00000185873 | *TMPRSS11B* | 162.1426424 | 2.930935532 | 0.738498 | 3.968781 | 0.0000722414 | 0.0264909 |
| ENSG00000183307 | *CECR6* | 16.55877878 | 1.882385854 | 0.478856 | 3.93101 | 0.0000845897 | 0.0302625 |
| ENSG00000178172 | *SPINK6* | 11.19634078 | 3.736066016 | 0.960846 | 3.88831 | 0.0001009446 | 0.0352537 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ENSG00000169509 | *CRCT1* | 124.6713786 | 3.255307448 | 0.839868 | 3.875975 | 0.0001061984 | 0.0353209 |
| ENSG00000087128 | *TMPRSS11E* | 856.279728 | 2.335954629 | 0.603236 | 3.872373 | 0.0001077807 | 0.0353209 |
| ENSG00000235568 | *NFAM1* | 385.2546016 | 2.109095274 | 0.544836 | 3.871064 | 0.0001083611 | 0.0353209 |
| ENSG00000143631 | *FLG* | 60.85365689 | 2.707724203 | 0.703833 | 3.847112 | 0.0001195184 | 0.0381108 |
| ENSG00000059728 | *MXD1* | 3049.682399 | 1.568764572 | 0.411317 | 3.814 | 0.0001367357 | 0.0407370 |
| ENSG00000204421 | *LY6G6C* | 11.23753312 | 2.015579995 | 0.530386 | 3.800212 | 0.0001445722 | 0.0407370 |
| ENSG00000137558 | *PI15* | 7.292990874 | 2.650754443 | 0.696318 | 3.806818 | 0.0001407663 | 0.0407370 |
| ENSG00000188373 | *C10orf99* | 11.24888949 | 3.740112396 | 0.980735 | 3.813582 | 0.0001369669 | 0.0407370 |
| ENSG00000125910 | *S1PR4* | 174.6183595 | 2.16060284 | 0.569216 | 3.795754 | 0.0001471953 | 0.0407370 |
| ENSG00000186474 | *KLK12* | 66.90156166 | 2.810027115 | 0.739856 | 3.798075 | 0.0001458243 | 0.0407370 |
| ENSG00000101210 | *EEF1A2* | 8.860473621 | 1.927591183 | 0.50611 | 3.808641 | 0.0001397326 | 0.0407370 |
| ENSG00000261272 | *MUC22* | 53.13744678 | 2.376412656 | 0.628685 | 3.779973 | 0.0001568455 | 0.0418293 |
| ENSG00000154262 | *ABCA6* | 91.04472433 | 0.918131079 | 0.242831 | 3.780947 | 0.0001562332 | 0.0418293 |
| ENSG00000162384 | *C1orf123* | 400.5115764 | -0.274660048 | 0.072946 | -3.76525 | 0.0001663849 | 0.0435810 |
| ENSG00000180871 | *CXCR2* | 559.0871712 | 2.296300313 | 0.613115 | 3.745302 | 0.0001801766 | 0.0447868 |
| ENSG00000196549 | *MME* | 223.9783358 | 2.350426949 | 0.628268 | 3.74112 | 0.0001832022 | 0.0447868 |
| ENSG00000136943 | *CTSV* | 169.9791044 | 1.651903131 | 0.441093 | 3.745024 | 0.0001803766 | 0.0447868 |
| ENSG00000204020 | *LIPN* | 40.67847121 | 2.99211748 | 0.797534 | 3.751711 | 0.0001756320 | 0.0447868 |
| ENSG00000135636 | *DYSF* | 374.8411619 | 2.317309474 | 0.621536 | 3.728362 | 0.0001927284 | 0.0462954 |
| ENSG00000113749 | *HRH2* | 69.49149917 | 2.193258848 | 0.588972 | 3.723878 | 0.0001961854 | 0.0462954 |
| ENSG00000204021 | *LIPK* | 6.857510391 | 2.959242988 | 0.798168 | 3.707544 | 0.0002092793 | 0.0462954 |
| ENSG00000068976 | *PYGM* | 17.33765035 | 2.050543859 | 0.552144 | 3.713782 | 0.0002041850 | 0.0462954 |
| ENSG00000211448 | *DIO2* | 155.321791 | 1.510686245 | 0.406436 | 3.716914 | 0.0002016710 | 0.0462954 |
| ENSG00000128917 | *DLL4* | 11.45535912 | 2.447852976 | 0.660082 | 3.708409 | 0.0002085653 | 0.0462954 |
| ENSG00000188897 | *CTD-3088G3.8* | 323.1906061 | 1.78061636 | 0.480706 | 3.70417 | 0.0002120839 | 0.0462954 |
| ENSG00000125810 | *CD93* | 601.1405142 | 1.759188231 | 0.475308 | 3.701152 | 0.0002146229 | 0.0462954 |
| ENSG00000178150 | *ZNF114* | 7.989085047 | 2.029484872 | 0.549584 | 3.692762 | 0.0002218314 | 0.0471569 |
| ENSG00000149564 | *ESAM* | 18.14827649 | 1.523369052 | 0.41299 | 3.688637 | 0.0002254587 | 0.0472433 |
| ENSG00000203710 | *CR1* | 411.1933018 | 2.299624216 | 0.627107 | 3.667037 | 0.0002453771 | 0.0481389 |
| ENSG00000163464 | *CXCR1* | 453.8760438 | 2.616490966 | 0.712521 | 3.672159 | 0.0002405100 | 0.0481389 |
| ENSG00000120129 | *DUSP1* | 6115.128063 | 1.732263316 | 0.473872 | 3.655551 | 0.0002566297 | 0.0481389 |
| ENSG00000152137 | *HSPB8* | 900.9324017 | 1.778499688 | 0.487281 | 3.649845 | 0.0002623991 | 0.0481389 |
| ENSG00000184508 | *HDDC3* | 101.6802136 | -0.391065227 | 0.106941 | -3.65684 | 0.0002553462 | 0.0481389 |
| ENSG00000206172 | *HBA1* | 9.437796303 | 3.255644841 | 0.885269 | 3.677576 | 0.0002354608 | 0.0481389 |
| ENSG00000141096 | *DPEP3* | 8.922090167 | 2.600257498 | 0.709629 | 3.66425 | 0.0002480641 | 0.0481389 |
| ENSG00000076662 | *ICAM3* | 139.9038075 | 2.270536264 | 0.620081 | 3.661675 | 0.0002505716 | 0.0481389 |
| ENSG00000244482 | *LILRA6* | 189.3604241 | 2.418416833 | 0.662635 | 3.649695 | 0.0002625518 | 0.0481389 |
| ENSG00000170373 | *CST1* | 131.6759055 | -3.542321735 | 0.97027 | -3.65086 | 0.0002613632 | 0.0481389 |
| ENSG00000171476 | *HOPX* | 495.7867843 | 1.529493784 | 0.420797 | 3.634752 | 0.0002782483 | 0.0503870 |
| ENSG00000254415 | *SIGLEC14* | 45.14160974 | 1.877309137 | 0.517712 | 3.626168 | 0.0002876585 | 0.0514558 |
| ENSG00000081237 | *PTPRC* | 4546.785921 | 1.738982361 | 0.480872 | 3.616312 | 0.0002988305 | 0.0519840 |
| ENSG00000107736 | *CDH23* | 109.6230575 | 0.860731249 | 0.238059 | 3.615619 | 0.0002996305 | 0.0519840 |
| ENSG00000142347 | *MYO1F* | 1440.496128 | 1.976436605 | 0.546849 | 3.614228 | 0.0003012436 | 0.0519840 |
| ENSG00000188404 | *SELL* | 592.631915 | 1.4423354 | 0.40133 | 3.593889 | 0.0003257790 | 0.0523150 |

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| ENSG00000163219 | *ARHGAP25* | 554.8197482 | 1.597820813 | 0.44492 | 3.591254 | 0.0003290910 | 0.0523150 |
| ENSG00000132965 | *ALOX5AP* | 361.1835711 | 1.581896625 | 0.440738 | 3.5892 | 0.0003316943 | 0.0523150 |
| ENSG00000132359 | *RAP1GAP2* | 213.009783 | 1.296496824 | 0.360265 | 3.598735 | 0.0003197694 | 0.0523150 |
| ENSG00000185862 | *EVI2B* | 461.495179 | 1.699127547 | 0.472435 | 3.596531 | 0.0003224895 | 0.0523150 |
| ENSG00000276070 | *CCL4L2* | 68.6673633 | 1.767519198 | 0.491474 | 3.596362 | 0.0003226984 | 0.0523150 |
| ENSG00000239998 | *LILRA2* | 156.1708969 | 2.41359626 | 0.67145 | 3.594603 | 0.0003248862 | 0.0523150 |
| ENSG00000156282 | *CLDN17* | 49.71152413 | 3.337239908 | 0.926759 | 3.600977 | 0.0003170233 | 0.0523150 |
| ENSG00000163563 | *MNDA* | 868.6380366 | 2.092578113 | 0.58443 | 3.580547 | 0.0003428759 | 0.0523886 |
| ENSG00000100908 | *EMC9* | 129.5613142 | -0.518890144 | 0.14484 | -3.5825 | 0.0003403253 | 0.0523886 |
| ENSG00000124126 | *PREX1* | 1676.142545 | 1.370895286 | 0.382525 | 3.583807 | 0.0003386230 | 0.0523886 |
| ENSG00000116741 | *RGS2* | 2515.481448 | 2.068800406 | 0.579639 | 3.569118 | 0.0003581852 | 0.0525386 |
| ENSG00000159884 | *CCDC107* | 36.05187668 | -0.506034534 | 0.141596 | -3.57379 | 0.0003518523 | 0.0525386 |
| ENSG00000077420 | *APBB1IP* | 243.778356 | 1.64456222 | 0.460633 | 3.570225 | 0.0003566752 | 0.0525386 |
| ENSG00000185201 | *IFITM2* | 1123.511188 | 1.573639347 | 0.440251 | 3.574411 | 0.0003510174 | 0.0525386 |
| ENSG00000198576 | *ARC* | 12.59565389 | 1.921251953 | 0.54003 | 3.557676 | 0.0003741507 | 0.0543370 |
| ENSG00000012779 | *ALOX5* | 542.1569197 | 1.341197064 | 0.3777 | 3.55096 | 0.0003838295 | 0.0551962 |
| ENSG00000147408 | *CSGALNACT1* | 47.32334612 | 1.736073692 | 0.489823 | 3.544287 | 0.0003936766 | 0.0552874 |
| ENSG00000127084 | *FGD3* | 488.0688261 | 1.329285081 | 0.375463 | 3.540387 | 0.0003995406 | 0.0552874 |
| ENSG00000160593 | *AMICA1* | 1529.369162 | 1.427087059 | 0.402968 | 3.541442 | 0.0003979461 | 0.0552874 |
| ENSG00000184922 | *FMNL1* | 417.2457271 | 1.543935634 | 0.435267 | 3.547097 | 0.0003895014 | 0.0552874 |
| ENSG00000203786 | *KPRP* | 5.488623737 | 3.534762474 | 1.000553 | 3.532808 | 0.0004111703 | 0.0563649 |
| ENSG00000115008 | *IL1A* | 41.13563665 | 2.044716665 | 0.579827 | 3.526423 | 0.0004212131 | 0.0572070 |
| ENSG00000085514 | *PILRA* | 213.260431 | 1.839828677 | 0.522145 | 3.523597 | 0.0004257310 | 0.0572901 |
| ENSG00000015285 | *WAS* | 196.6610082 | 1.566856851 | 0.445876 | 3.514111 | 0.0004412283 | 0.0588358 |
| ENSG00000204305 | *AGER* | 31.35634892 | 1.115269179 | 0.317594 | 3.511616 | 0.0004453905 | 0.0588557 |
| ENSG00000081041 | *CXCL2* | 121.8368299 | 1.121447805 | 0.320025 | 3.504247 | 0.0004578998 | 0.0599685 |
| ENSG00000117115 | *PADI2* | 311.0156325 | 1.595711216 | 0.455678 | 3.501843 | 0.0004620517 | 0.0599768 |
| ENSG00000186806 | *VSIG10L* | 112.6784624 | 1.836473622 | 0.524908 | 3.498656 | 0.0004676100 | 0.0601658 |
| ENSG00000123329 | *ARHGAP9* | 479.2259745 | 1.504954786 | 0.430779 | 3.493566 | 0.0004766144 | 0.0607911 |
| ENSG00000197405 | *C5AR1* | 1048.994493 | 2.117769646 | 0.606742 | 3.490394 | 0.0004823089 | 0.0609871 |
| ENSG00000111181 | *SLC6A12* | 40.50839526 | 1.247431148 | 0.357807 | 3.486322 | 0.0004897108 | 0.0612578 |
| ENSG00000169715 | *MT1E* | 513.315856 | -0.685757788 | 0.196795 | -3.48464 | 0.0004928019 | 0.0612578 |
| ENSG00000132510 | *KDM6B* | 579.8129011 | 1.305400127 | 0.375133 | 3.479832 | 0.0005017278 | 0.0618432 |
| ENSG00000189051 | *RNF222* | 48.81576384 | 2.238886942 | 0.643902 | 3.477063 | 0.0005069389 | 0.0619648 |
| ENSG00000130775 | *THEMIS2* | 767.653598 | 1.653998209 | 0.477286 | 3.465427 | 0.0005293899 | 0.0625580 |
| ENSG00000016602 | *CLCA4* | 2436.442163 | 1.817346604 | 0.523652 | 3.470523 | 0.0005194464 | 0.0625580 |
| ENSG00000151702 | *FLI1* | 244.7806654 | 1.307265921 | 0.377325 | 3.464563 | 0.0005310932 | 0.0625580 |
| ENSG00000126860 | *EVI2A* | 228.3966342 | 1.699506437 | 0.489786 | 3.469899 | 0.0005206545 | 0.0625580 |
| ENSG00000127507 | *ADGRE2* | 416.7557519 | 1.753547713 | 0.506288 | 3.463541 | 0.0005331160 | 0.0625580 |
| ENSG00000059804 | *SLC2A3* | 905.4839017 | 2.010343885 | 0.581013 | 3.460064 | 0.0005400461 | 0.0628682 |
| ENSG00000114268 | *PFKFB4* | 165.0457522 | 1.460312211 | 0.422942 | 3.452745 | 0.0005549131 | 0.0635896 |
| ENSG00000155926 | *SLA* | 742.9187908 | 1.459286381 | 0.422635 | 3.452832 | 0.0005547350 | 0.0635896 |
| ENSG00000159337 | *PLA2G4D* | 13.88198456 | 1.569829037 | 0.455069 | 3.44965 | 0.0005613144 | 0.0638245 |
| ENSG00000171608 | *PIK3CD* | 776.2463976 | 1.270669369 | 0.368994 | 3.443601 | 0.0005740223 | 0.0647674 |

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|---|---|---|---|---|---|---|---|
| ENSG00000132334 | *PTPRE* | 1056.794435 | 1.364429099 | 0.396935 | 3.437411 | 0.0005873037 | 0.0657601 |
| ENSG00000148841 | *ITPRIP* | 553.3588369 | 1.316881276 | 0.383757 | 3.431554 | 0.0006001332 | 0.0659737 |
| ENSG00000129353 | *SLC44A2* | 3678.47438 | 0.488097138 | 0.142286 | 3.430394 | 0.0006027045 | 0.0659737 |
| ENSG00000101187 | *SLCO4A1* | 160.6016704 | 1.311705529 | 0.382227 | 3.431743 | 0.0005997159 | 0.0659737 |
| ENSG00000124216 | *SNAI1* | 7.696103487 | 1.970326867 | 0.574818 | 3.427739 | 0.0006086298 | 0.0661288 |
| ENSG00000152518 | *ZFP36L2* | 658.0270618 | 0.533612565 | 0.155805 | 3.424877 | 0.0006150775 | 0.0663379 |
| ENSG00000140678 | *ITGAX* | 1565.747602 | 1.594065917 | 0.465752 | 3.42256 | 0.0006203438 | 0.0664175 |
| ENSG00000082074 | *FYB* | 991.9259765 | 1.340812758 | 0.392852 | 3.413019 | 0.0006424741 | 0.0665579 |
| ENSG00000197081 | *IGF2R* | 4115.112231 | 0.870500071 | 0.254689 | 3.41789 | 0.0006310867 | 0.0665579 |
| ENSG00000106780 | *MEGF9* | 783.34156 | 1.002450648 | 0.293299 | 3.417844 | 0.0006311927 | 0.0665579 |
| ENSG00000178372 | *CALML5* | 227.8365785 | 1.723079938 | 0.505537 | 3.408413 | 0.0006534185 | 0.0665579 |
| ENSG00000033327 | *GAB2* | 587.0589028 | 1.009740964 | 0.2958 | 3.413589 | 0.0006411326 | 0.0665579 |
| ENSG00000091592 | *NLRP1* | 904.1310348 | 0.92872128 | 0.272274 | 3.410982 | 0.0006472944 | 0.0665579 |
| ENSG00000092929 | *UNC13D* | 348.5835282 | 1.30726178 | 0.383488 | 3.40887 | 0.0006523250 | 0.0665579 |
| ENSG00000183091 | *NEB* | 147.948048 | 1.165209102 | 0.342494 | 3.402126 | 0.0006686381 | 0.0676385 |
| ENSG00000095370 | *SH2D3C* | 124.8445678 | 1.396717987 | 0.410791 | 3.40007 | 0.0006736854 | 0.0676823 |
| ENSG00000105329 | *TGFB1* | 135.7183389 | 1.026453687 | 0.30292 | 3.388533 | 0.0007026760 | 0.0701146 |
| ENSG00000151726 | *ACSL1* | 3497.092379 | 1.115803771 | 0.329795 | 3.383326 | 0.0007161359 | 0.0709749 |
| ENSG00000213190 | *MLLT11* | 34.96655406 | 0.991937175 | 0.293853 | 3.375624 | 0.0007364847 | 0.0720184 |
| ENSG00000128016 | *ZFP36* | 2290.304626 | 1.418453692 | 0.420154 | 3.376035 | 0.0007353859 | 0.0720184 |
| ENSG00000183625 | *CCR3* | 42.86315786 | 2.443863244 | 0.726592 | 3.363461 | 0.0007697164 | 0.0728125 |
| ENSG00000120738 | *EGR1* | 617.768747 | 2.058619948 | 0.613673 | 3.354587 | 0.0007948363 | 0.0728125 |
| ENSG00000057657 | *PRDM1* | 535.5767203 | 1.000608405 | 0.298692 | 3.349963 | 0.0008082233 | 0.0728125 |
| ENSG00000181016 | *LSMEM1* | 44.37615442 | 1.542909674 | 0.460244 | 3.35237 | 0.0008012297 | 0.0728125 |
| ENSG00000120156 | *TEK* | 12.27850013 | 2.088865477 | 0.62069 | 3.365391 | 0.0007643512 | 0.0728125 |
| ENSG00000107796 | *ACTA2* | 21.98390633 | -1.229083585 | 0.36527 | -3.36486 | 0.0007658134 | 0.0728125 |
| ENSG00000066336 | *SPI1* | 474.2143771 | 1.539695642 | 0.4568 | 3.370612 | 0.0007500137 | 0.0728125 |
| ENSG00000168010 | *ATG16L2* | 754.9539635 | 1.226851569 | 0.366626 | 3.346334 | 0.0008188782 | 0.0728125 |
| ENSG00000161638 | *ITGA5* | 427.2568365 | 1.294966403 | 0.385826 | 3.356348 | 0.0007897905 | 0.0728125 |
| ENSG00000166501 | *PRKCB* | 420.2501617 | 1.554013311 | 0.462873 | 3.357318 | 0.0007870255 | 0.0728125 |
| ENSG00000167916 | *KRT24* | 2397.09258 | 2.331361408 | 0.692022 | 3.368913 | 0.0007546513 | 0.0728125 |
| ENSG00000172081 | *MOB3A* | 500.967832 | 1.077518538 | 0.322239 | 3.343849 | 0.0008262464 | 0.0728125 |
| ENSG00000099308 | *MAST3* | 289.4385807 | 1.096338807 | 0.327958 | 3.342928 | 0.0008289942 | 0.0728125 |
| ENSG00000175489 | *LRRC25* | 220.170772 | 1.705010136 | 0.508146 | 3.355353 | 0.0007926364 | 0.0728125 |
| ENSG00000171777 | *RASGRP4* | 169.2813114 | 2.401692932 | 0.718349 | 3.343353 | 0.0008277259 | 0.0728125 |
| ENSG00000105501 | *SIGLEC5* | 68.90107457 | 2.374748837 | 0.709128 | 3.348828 | 0.0008115406 | 0.0728125 |
| ENSG00000177663 | *IL17RA* | 892.8199897 | 0.919762481 | 0.273986 | 3.356964 | 0.0007880339 | 0.0728125 |
| ENSG00000166535 | *A2ML1* | 1002.086654 | 1.450167898 | 0.434398 | 3.33834 | 0.0008428066 | 0.0730048 |
| ENSG00000110876 | *SELPLG* | 498.0963179 | 1.383877919 | 0.414676 | 3.337251 | 0.0008461152 | 0.0730048 |
| ENSG00000128383 | *APOBEC3A* | 456.5435759 | 1.968695343 | 0.589511 | 3.339542 | 0.0008391660 | 0.0730048 |
| ENSG00000091106 | *NLRC4* | 63.59447992 | 1.595926681 | 0.479431 | 3.32879 | 0.0008722405 | 0.0732848 |
| ENSG00000115165 | *CYTIP* | 605.0026885 | 1.549162056 | 0.465529 | 3.327745 | 0.0008755193 | 0.0732848 |
| ENSG00000173559 | *NABP1* | 3508.644402 | 1.454169197 | 0.437143 | 3.326532 | 0.0008793378 | 0.0732848 |
| ENSG00000175315 | *CST6* | 43.40935031 | 1.437118927 | 0.431248 | 3.332468 | 0.0008607948 | 0.0732848 |

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|---|---|---|---|---|---|---|---|
| ENSG00000133246 | *PRAM1* | 42.79085834 | 1.154190513 | 0.346598 | 3.330052 | 0.0008682973 | 0.0732848 |
| ENSG00000198053 | *SIRPA* | 520.3180461 | 1.149634662 | 0.345046 | 3.331828 | 0.0008627758 | 0.0732848 |
| ENSG00000163209 | *SPRR3* | 9398.66207 | 1.892942748 | 0.569654 | 3.32297 | 0.0008906446 | 0.0733931 |
| ENSG00000188305 | *C19orf35* | 14.74118642 | 2.027840744 | 0.610195 | 3.323266 | 0.0008897002 | 0.0733931 |
| ENSG00000115590 | *IL1R2* | 359.8218257 | 2.191449718 | 0.661145 | 3.31463 | 0.0009176438 | 0.0747778 |
| ENSG00000124882 | *EREG* | 227.0051715 | 1.760952973 | 0.531171 | 3.315229 | 0.0009156795 | 0.0747778 |
| ENSG00000113070 | *HBEGF* | 280.9775264 | 1.604054578 | 0.484422 | 3.311273 | 0.0009287250 | 0.0752626 |
| ENSG00000178726 | *THBD* | 569.6998692 | 2.072148166 | 0.626151 | 3.30934 | 0.0009351605 | 0.0753678 |
| ENSG00000197943 | *PLCG2* | 550.1524259 | 0.988242075 | 0.299196 | 3.302994 | 0.0009565855 | 0.0766732 |
| ENSG00000162572 | *SCNN1D* | 52.00949878 | 0.779800895 | 0.236387 | 3.298826 | 0.0009709006 | 0.0768620 |
| ENSG00000158887 | *MPZ* | 43.30825426 | 1.239879961 | 0.376097 | 3.296706 | 0.0009782593 | 0.0768620 |
| ENSG00000214113 | *LYRM4* | 209.8049346 | -0.386119827 | 0.117153 | -3.29586 | 0.0009811975 | 0.0768620 |
| ENSG00000151948 | *GLT1D1* | 194.0027529 | 2.453177853 | 0.744772 | 3.293865 | 0.0009882004 | 0.0768620 |
| ENSG00000141527 | *CARD14* | 189.6181425 | 0.664607081 | 0.201809 | 3.293245 | 0.0009903816 | 0.0768620 |
| ENSG00000198342 | *ZNF442* | 55.29332415 | -0.633468395 | 0.191935 | -3.30043 | 0.0009653628 | 0.0768620 |
| ENSG00000163218 | *PGLYRP4* | 35.40514359 | 1.507393971 | 0.45914 | 3.283079 | 0.0010267976 | 0.0792688 |
| ENSG00000130475 | *FCHO1* | 85.17477418 | 1.396035122 | 0.426313 | 3.274673 | 0.0010578446 | 0.0812380 |
| ENSG00000167759 | *KLK13* | 432.5007784 | 2.177708944 | 0.667258 | 3.263671 | 0.0010997881 | 0.0840192 |
| ENSG00000143546 | *S100A8* | 10686.37567 | 2.151083123 | 0.659681 | 3.260795 | 0.0011110021 | 0.0843267 |
| ENSG00000213347 | *MXD3* | 159.4639724 | 1.254876515 | 0.385071 | 3.25882 | 0.0011187671 | 0.0843267 |
| ENSG00000101336 | *HCK* | 871.1965188 | 1.616043212 | 0.495987 | 3.258239 | 0.0011210598 | 0.0843267 |
| ENSG00000204542 | *C6orf15* | 6.203863346 | 3.043601347 | 0.935576 | 3.253185 | 0.0011411927 | 0.0853732 |
| ENSG00000110203 | *FOLR3* | 10.09684646 | 2.947475316 | 0.906403 | 3.251838 | 0.0011466131 | 0.0853732 |
| ENSG00000062282 | *DGAT2* | 385.1136643 | 1.889009237 | 0.582431 | 3.243316 | 0.0011814721 | 0.0875244 |
| ENSG00000133710 | *SPINK5* | 1396.236797 | 1.523517868 | 0.47005 | 3.241184 | 0.0011903453 | 0.0877386 |
| ENSG00000119535 | *CSF3R* | 3574.954552 | 2.277942108 | 0.706229 | 3.225502 | 0.0012575197 | 0.0899771 |
| ENSG00000159516 | *SPRR2G* | 8.900936315 | 2.970580876 | 0.920519 | 3.22707 | 0.0012506472 | 0.0899771 |
| ENSG00000154429 | *CCSAP* | 160.9765066 | 0.524627084 | 0.162647 | 3.225554 | 0.0012572927 | 0.0899771 |
| ENSG00000188549 | *C15orf52* | 151.2467778 | 0.785723445 | 0.243249 | 3.23012 | 0.0012373831 | 0.0899771 |
| ENSG00000160255 | *ITGB2* | 1285.404679 | 1.207525803 | 0.373976 | 3.22889 | 0.0012427170 | 0.0899771 |
| ENSG00000173638 | *SLC19A1* | 147.9920447 | 1.589686916 | 0.492758 | 3.2261 | 0.0012548962 | 0.0899771 |
| ENSG00000155307 | *SAMSN1* | 447.0759092 | 1.459101124 | 0.453116 | 3.220151 | 0.0012812317 | 0.0912287 |
| ENSG00000162747 | *FCGR3B* | 1127.66368 | 2.265580387 | 0.706557 | 3.206507 | 0.0013435703 | 0.0915786 |
| ENSG00000168918 | *INPP5D* | 539.7586028 | 0.759423223 | 0.236774 | 3.207374 | 0.0013395295 | 0.0915786 |
| ENSG00000188001 | *TPRG1* | 146.6351541 | 0.982323984 | 0.305399 | 3.216525 | 0.0012975312 | 0.0915786 |
| ENSG00000120318 | *ARAP3* | 312.6943691 | 0.880062277 | 0.274794 | 3.202629 | 0.0013617921 | 0.0915786 |
| ENSG00000152926 | *ZNF117* | 700.4702591 | 0.667203224 | 0.208406 | 3.201464 | 0.0013673106 | 0.0915786 |
| ENSG00000059377 | *TBXAS1* | 356.7962638 | 1.33421913 | 0.415333 | 3.212407 | 0.0013162757 | 0.0915786 |
| ENSG00000187479 | *C11orf96* | 14.69699214 | 1.958308711 | 0.611243 | 3.203816 | 0.0013561901 | 0.0915786 |
| ENSG00000171310 | *CHST11* | 408.7728418 | 1.186643045 | 0.370603 | 3.201929 | 0.0013651076 | 0.0915786 |
| ENSG00000131471 | *AOC3* | 22.77300856 | 1.226591369 | 0.381778 | 3.212835 | 0.0013143161 | 0.0915786 |
| ENSG00000173868 | *PHOSPHO1* | 209.3184166 | 2.627190768 | 0.818348 | 3.21036 | 0.0013256865 | 0.0915786 |
| ENSG00000160229 | *ZNF66* | 56.13988521 | 0.87651468 | 0.273497 | 3.204843 | 0.0013513616 | 0.0915786 |
| ENSG00000188505 | *NCCRP1* | 649.3820155 | 1.424720362 | 0.443692 | 3.211057 | 0.0013224755 | 0.0915786 |

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|---|---|---|---|---|---|---|---|
| ENSG00000100985 | *MMP9* | 105.0085456 | 1.801939784 | 0.560903 | 3.212569 | 0.0013155353 | 0.0915786 |
| ENSG00000189056 | *RELN* | 20.41484416 | 1.821826465 | 0.570354 | 3.194201 | 0.0014021827 | 0.0934873 |
| ENSG00000130592 | *LSP1* | 1872.970387 | 0.886506466 | 0.277959 | 3.189347 | 0.0014259475 | 0.0946416 |
| ENSG00000106541 | *AGR2* | 41664.02551 | -0.714062434 | 0.224157 | -3.18555 | 0.0014447875 | 0.0954601 |
| ENSG00000104894 | *CD37* | 157.4882807 | 1.249881462 | 0.393085 | 3.179671 | 0.0014744245 | 0.0969814 |
| ENSG00000146112 | *PPP1R18* | 570.9228967 | 1.216818205 | 0.382862 | 3.178213 | 0.0014818607 | 0.0970354 |
| ENSG00000112137 | *PHACTR1* | 270.347717 | 1.480915393 | 0.466756 | 3.17278 | 0.0015098686 | 0.0970487 |
| ENSG00000112195 | *TREML2* | 177.9198685 | 2.368986837 | 0.747134 | 3.170764 | 0.0015203883 | 0.0970487 |
| ENSG00000170423 | *KRT78* | 380.5887664 | 1.924890584 | 0.607367 | 3.169241 | 0.0015283781 | 0.0970487 |
| ENSG00000188215 | *DCUN1D3* | 490.9316317 | 0.865486098 | 0.27282 | 3.172375 | 0.0015119764 | 0.0970487 |
| ENSG00000101236 | *RNF24* | 802.5230879 | 0.95210711 | 0.300246 | 3.171085 | 0.0015187079 | 0.0970487 |
| ENSG00000087589 | *CASS4* | 294.9893157 | 1.73106507 | 0.544957 | 3.176515 | 0.0014905605 | 0.0970487 |
| ENSG00000147168 | *IL2RG* | 270.2098958 | 0.933031134 | 0.294288 | 3.170466 | 0.0015219465 | 0.0970487 |
| ENSG00000125378 | *BMP4* | 17.60094942 | -1.212353032 | 0.38289 | -3.16632 | 0.0015438084 | 0.0976060 |
| ENSG00000111052 | *LIN7A* | 40.68503686 | 1.801629323 | 0.569401 | 3.164079 | 0.0015557467 | 0.0979386 |
| ENSG00000115935 | *WIPF1* | 622.5961766 | 1.143319049 | 0.361607 | 3.161768 | 0.0015681439 | 0.0982972 |
| ENSG00000126233 | *SLURP1* | 62.95038101 | 1.64617095 | 0.521552 | 3.156293 | 0.0015978817 | 0.0997350 |

Table S3: Biological processes enriched at baseline between “Cold” and “No Cold” groups

| ID | Description | GeneRatio | BgRatio | *P*value | *P*.adjust | qvalue | geneID | Count |
|---|---|---|---|---|---|---|---|---|
| GO:0042119 | neutrophil activation | 0.157895 | 0.028536908 | 1.06E-15 | 2.36E-12 | 2.11E-12 | *PADI2/CDA/S100A12/S100A8/MNDA/FCGR3B/SELL/PTPRC/CR1/CXCR2/CXCR1/MME/IGF2R/CALML5/ALOX5/FOLR3/SLC2A3/ARHGAP9/OLFM4/ITGAX/UNC13D/PRAM1/SLC44A2/C5AR1/SIGLEC5/SIGLEC14/LILRA2/SIRPA/CD93/MMP9/PREX1/ITGB2/NFAM1* | 33 |
| GO:0002283 | neutrophil activation involved in immune response | 0.15311 | 0.027961567 | 4.04E-15 | 3.89E-12 | 3.48E-12 | *PADI2/CDA/S100A12/S100A8/MNDA/FCGR3B/SELL/PTPRC/CR1/CXCR2/CXCR1/MME/IGF2R/CALML5/ALOX5/FOLR3/SLC2A3/ARHGAP9/OLFM4/ITGAX/UNC13D/PRAM1/SLC44A2/C5AR1/SIGLEC5/SIGLEC14/LILRA2/SIRPA/CD93/MMP9/ITGB2/NFAM1* | 32 |
| GO:0002446 | neutrophil mediated immunity | 0.148325 | 0.02870951 | 5.47E-14 | 3.16E-11 | 2.83E-11 | *PADI2/CDA/S100A12/S100A8/MNDA/FCGR3B/SELL/PTPRC/CR1/CXCR2/CXCR1/MME/IGF2R/CALML5/ALOX5/FOLR3/SLC2A3/ARHGAP9/OLFM4/ITGAX/UNC13D/PRAM1/SLC44A2/C5AR1/SIGLEC5/SIGLEC14/SIRPA/CD93/MMP9/ITGB2/NFAM1* | 31 |
| GO:0043312 | neutrophil degranulation | 0.148325 | 0.027904033 | 2.54E-14 | 1.84E-11 | 1.64E-11 | *PADI2/CDA/S100A12/S100A8/MNDA/FCGR3B/SELL/PTPRC/CR1/CXCR2/CXCR1/MME/IGF2R/CALML5/ALOX5/FOLR3/SLC2A3/ARHGAP9/OLFM4/ITGAX/UNC13D/PRAM1/SLC44A2/C5AR1/SIGLEC5/SIGLEC14/SIRPA/CD93/MMP9/ITGB2/NFAM1* | 31 |
| GO:0008544 | epidermis development | 0.138756 | 0.02617801 | 2.02E-13 | 9.74E-11 | 8.70E-11 | *FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/EREG/SPINK5/SPINK6/CTSV/CALML5/LIPK/LIPN/CST6/KRT78/BMP4/KRT24/ZFP36/CNFN/KLK5/KLK7/KLK8/KLK12/KLK13/SNAI1/WAS* | 29 |
| GO:0050900 | leukocyte migration | 0.133971 | 0.027098556 | 2.94E-12 | 1.06E-09 | 9.50E-10 | *PIK3CD/PADI2/CSF3R/ECM1/S100A12/S100A8/SELL/IL1A/CXCR2/CXCR1/INPP5D/CXCL2/TEK/JAML/ESAM/ITGA5/SELPLG/ITGAX/ADGRE2/TGFB1/C5AR1/SIRPA/THBD/HCK/MMP9/PREX1/ITGB2/IL17RA* | 28 |
| GO:0043588 | skin development | 0.119617 | 0.023646511 | 2.89E-11 | 7.61E-09 | 6.80E-09 | *FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/ASPRV1/EREG/SPINK5/SPINK6/CTSV/LIPK/LIPN/KRT78/KRT24/ZFP36/CNFN/KLK5/KLK8/KLK12/KLK13/SNAI1* | 25 |
| GO:0009913 | epidermal cell differentiation | 0.114833 | 0.020079397 | 5.69E-12 | 1.65E-09 | 1.47E-09 | *FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/EREG/SPINK5/SPINK6/CTSV/LIPK/LIPN/KRT78/BMP4/KRT24/ZFP36/CNFN/KLK5/KLK8/KLK12/KLK13* | 24 |
| GO:0030216 | keratinocyte differentiation | 0.110048 | 0.017260227 | 1.74E-12 | 7.18E-10 | 6.42E-10 | *FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/EREG/SPINK5/SPINK6/CTSV/LIPK/LIPN/KRT78/KRT24/ZFP36/CNFN/KLK5/KLK8/KLK12/KLK13* | 23 |
| GO:0031424 | keratinization | 0.095694 | 0.013002704 | 3.83E-12 | 1.23E-09 | 1.10E-09 | *FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/SPINK5/SPINK6/LIPK/LIPN/KRT78/KRT24/CNFN/KLK5/KLK8/KLK12/KLK13* | 20 |

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|---|---|---|---|---|---|---|---|---|
| GO:0070268 | cornification | 0.086124 | 0.006501352 | 1.63E-15 | 2.36E-12 | 2.11E-12 | *FLG/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/SPINK5/SPINK6/LIPK/LIPN/KRT78/KRT24/KLK5/KLK8/KLK12/KLK13* | 18 |
| GO:0097530 | granulocyte migration | 0.062201 | 0.007134227 | 3.21E-09 | 7.75E-07 | 6.92E-07 | *PIK3CD/CSF3R/S100A12/S100A8/IL1A/CXCR2/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA* | 13 |
| GO:0002521 | leukocyte differentiation | 0.090909 | 0.027558829 | 5.55E-06 | 7.65E-04 | 6.83E-04 | *PIK3CD/PTPRC/CR1/ZFP36L2/INPP5D/EGR1/SPINK5/AGER/PRDM1/SPI1/GAB2/BMP4/DLL4/PLCG2/EVI2B/TGFB1/MMP9/PREX1/NFAM1* | 19 |
| GO:0002768 | immune response-regulating cell surface receptor signaling pathway | 0.08134 | 0.026350613 | 4.07E-05 | 3.37E-03 | 3.01E-03 | *PIK3CD/THEMIS2/MNDA/PTPRC/CR1/WIPF1/INPP5D/FYB1/GAB2/PRKCB/PLCG2/ICAM3/C5AR1/LILRA2/HCK/NFAM1/WAS* | 17 |
| GO:0002429 | immune response-activating cell surface receptor signaling pathway | 0.076555 | 0.024509522 | 6.00E-05 | 4.34E-03 | 3.88E-03 | *PIK3CD/THEMIS2/MNDA/PTPRC/CR1/WIPF1/INPP5D/FYB1/PRKCB/PLCG2/ICAM3/C5AR1/LILRA2/HCK/NFAM1/WAS* | 16 |
| GO:0042110 | T cell activation | 0.076555 | 0.02686842 | 1.74E-04 | 1.12E-02 | 9.99E-03 | *PIK3CD/PTPRC/CR1/ZFP36L2/EGR1/SPINK5/AGER/TREML2/PRDM1/APBB1IP/JAML/BMP4/DLL4/TGFB1/PREX1/WAS* | 16 |
| GO:0060326 | cell chemotaxis | 0.07177 | 0.015534204 | 9.89E-07 | 1.51E-04 | 1.35E-04 | *PIK3CD/PADI2/CSF3R/S100A12/S100A8/CXCR2/CXCR1/CXCL2/HBEGF/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA* | 15 |
| GO:0030098 | lymphocyte differentiation | 0.07177 | 0.018871181 | 1.07E-05 | 1.23E-03 | 1.10E-03 | *PIK3CD/PTPRC/CR1/ZFP36L2/INPP5D/EGR1/SPINK5/PRDM1/SPI1/BMP4/DLL4/PLCG2/TGFB1/PREX1/NFAM1* | 15 |
| GO:0031349 | positive regulation of defense response | 0.07177 | 0.025947874 | 3.80E-04 | 1.93E-02 | 1.72E-02 | *PGLYRP4/S100A12/S100A8/NLRC4/IL1RL1/EREG/PLCG2/ICAM3/TGFB1/KLK5/KLK7/LILRA2/HCK/ITGB2/IL17RA* | 15 |
| GO:0040017 | positive regulation of locomotion | 0.07177 | 0.028191704 | 8.91E-04 | 3.30E-02 | 2.95E-02 | *PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/AGER/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1* | 15 |
| GO:0030595 | leukocyte chemotaxis | 0.066986 | 0.01167942 | 1.70E-07 | 3.07E-05 | 2.75E-05 | *PIK3CD/PADI2/CSF3R/S100A12/S100A8/CXCR2/CXCR1/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA* | 14 |
| GO:1901342 | regulation of vasculature development | 0.066986 | 0.017662965 | 2.18E-05 | 2.10E-03 | 1.88E-03 | *ECM1/IL1A/CCR3/EGR1/SPINK5/NOS3/TEK/ITGA5/BMP4/DLL4/PRKCB/SERPINB7/C5AR1/ITGB2* | 14 |
| GO:0002697 | regulation of immune effector process | 0.066986 | 0.023128704 | 3.76E-04 | 1.93E-02 | 1.72E-02 | *PTPRC/CR1/SPINK5/AGER/GAB2/UNC13D/PRAM1/ADGRE2/TGFB1/C5AR1/KLK5/KLK7/ITGB2/WAS* | 14 |
| GO:0051346 | negative regulation of hydrolase activity | 0.066986 | 0.024394454 | 6.37E-04 | 2.63E-02 | 2.35E-02 | *ECM1/RGS2/CR1/NLRC4/SPINK5/SPINK6/SPINK7/NOS3/PI15/CST6/A2ML1/SERPINB7/CST1/MMP9* | 14 |

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|---|---|---|---|---|---|---|---|---|
| GO:0052547 | regulation of peptidase activity | 0.066986 | 0.024509522 | 6.67E-04 | 2.72E-02 | 2.43E-02 | *ECM1/S100A8/CR1/NLRC4/SPINK5/SPINK6/SPINK7/PI15/CST6/A2ML1/NLRP1/SERPINB7/CST1/MMP9* | 14 |
| GO:0030335 | positive regulation of cell migration | 0.066986 | 0.025430067 | 9.52E-04 | 3.37E-02 | 3.02E-02 | *PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1* | 14 |
| GO:1903706 | regulation of hemopoiesis | 0.066986 | 0.025775272 | 1.08E-03 | 3.71E-02 | 3.32E-02 | *CSF3R/CR1/ZFP36L2/INPP5D/SPINK5/AGER/PRDM1/SPI1/BMP4/PRKCB/EVI2B/ZFP36/TGFB1/NFAM1* | 14 |
| GO:2000147 | positive regulation of cell motility | 0.066986 | 0.026465681 | 1.39E-03 | 4.30E-02 | 3.84E-02 | *PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1* | 14 |
| GO:0051272 | positive regulation of cellular component movement | 0.066986 | 0.027213624 | 1.80E-03 | 4.97E-02 | 4.44E-02 | *PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1* | 14 |
| GO:0097529 | myeloid leukocyte migration | 0.062201 | 0.010298602 | 2.61E-07 | 4.45E-05 | 3.98E-05 | *PIK3CD/CSF3R/S100A12/S100A8/IL1A/CXCR2/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA* | 13 |
| GO:0042742 | defense response to bacterium | 0.062201 | 0.016684886 | 5.13E-05 | 3.81E-03 | 3.40E-03 | *PGLYRP4/S100A12/S100A8/NLRC4/SPINK5/DEFB103B/DEFB103A/C10orf99/RNASE7/NLRP1/C5AR1/KLK5/KLK7* | 13 |
| GO:0045861 | negative regulation of proteolysis | 0.062201 | 0.020021863 | 3.13E-04 | 1.71E-02 | 1.53E-02 | *ECM1/CR1/NLRC4/IL1R2/SPINK5/SPINK6/SPINK7/PI15/CST6/A2ML1/SERPINB7/CST1/MMP9* | 13 |
| GO:0030099 | myeloid cell differentiation | 0.062201 | 0.022438295 | 9.09E-04 | 3.32E-02 | 2.96E-02 | *PIK3CD/CSF3R/INPP5D/SPI1/GAB2/FLI1/BMP4/PRKCB/EVI2B/RASGRP4/ZFP36/TGFB1/MMP9* | 13 |
| GO:0002683 | negative regulation of immune system process | 0.062201 | 0.023704045 | 1.49E-03 | 4.31E-02 | 3.85E-02 | *PADI2/MNDA/PTPRC/CR1/IL1RL1/INPP5D/SPINK5/PRDM1/BMP4/ZFP36/TGFB1/LILRA2/SAMSN1* | 13 |
| GO:0071621 | granulocyte chemotaxis | 0.057416 | 0.00632875 | 8.34E-09 | 1.86E-06 | 1.66E-06 | *PIK3CD/CSF3R/S100A12/S100A8/CXCR2/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA* | 12 |
| GO:0010466 | negative regulation of peptidase activity | 0.057416 | 0.015131465 | 8.45E-05 | 5.82E-03 | 5.20E-03 | *ECM1/CR1/NLRC4/SPINK5/SPINK6/SPINK7/PI15/CST6/A2ML1/SERPINB7/CST1/MMP9* | 12 |
| GO:0050673 | epithelial cell proliferation | 0.057416 | 0.020769806 | 1.46E-03 | 4.30E-02 | 3.84E-02 | *ECM1/CCR3/EREG/SLURP1/TEK/JAML/BMP4/DLL4/ZFP36/TGFB1/C5AR1/KLK8* | 12 |
| GO:1990266 | neutrophil migration | 0.052632 | 0.005810943 | 3.61E-08 | 7.45E-06 | 6.66E-06 | *PIK3CD/CSF3R/S100A12/S100A8/IL1A/CXCR2/CXCL2/JAML/C5AR1/PREX1/ITGB2* | 11 |
| GO:1904018 | positive regulation of vasculature development | 0.052632 | 0.009665727 | 6.07E-06 | 7.98E-04 | 7.13E-04 | *ECM1/IL1A/CCR3/EGR1/NOS3/TEK/ITGA5/PRKCB/SERPINB7/C5AR1/ITGB2* | 11 |
| GO:0030217 | T cell differentiation | 0.052632 | 0.01294517 | 9.07E-05 | 6.11E-03 | 5.46E-03 | *PIK3CD/PTPRC/CR1/ZFP36L2/EGR1/SPINK5/PRDM1/BMP4/DLL4/TGFB1/PREX1* | 11 |
| GO:0042113 | B cell activation | 0.052632 | 0.015591738 | 4.54E-04 | 2.15E-02 | 1.92E-02 | *PIK3CD/MNDA/PTPRC/ZFP36L2/INPP5D/PRDM1/PRKCB/PLCG2/TGFB1/SAMSN1/NFAM1* | 11 |
| GO:0045765 | regulation of angiogenesis | 0.052632 | 0.015706806 | 4.83E-04 | 2.25E-02 | 2.01E-02 | *ECM1/IL1A/CCR3/SPINK5/NOS3/TEK/ITGA5/DLL4/PRKCB/C5AR1/ITGB2* | 11 |

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|---|---|---|---|---|---|---|---|---|
| GO:0032103 | positive regulation of response to external stimulus | 0.052632 | 0.016167079 | 6.14E-04 | 2.57E-02 | 2.30E-02 | *S100A12/S100A8/IL1RL1/CXCL2/AGER/TGFB1/C5AR1/KLK5/KLK7/THBD/IL17RA* | 11 |
| GO:0050678 | regulation of epithelial cell proliferation | 0.052632 | 0.017662965 | 1.26E-03 | 4.01E-02 | 3.59E-02 | *ECM1/CCR3/EREG/SLURP1/TEK/JAML/BMP4/DLL4/ZFP36/TGFB1/C5AR1* | 11 |
| GO:0032496 | response to lipopolysaccharide | 0.052632 | 0.018180772 | 1.59E-03 | 4.55E-02 | 4.06E-02 | *S100A8/CXCL2/PRDM1/NOS3/PLCG2/ZFP36/TGFB1/C5AR1/LILRA2/THBD/HCK* | 11 |
| GO:0006959 | humoral immune response | 0.052632 | 0.018468443 | 1.80E-03 | 4.97E-02 | 4.44E-02 | *PGLYRP4/S100A12/S100A8/CR1/SPINK5/DEFB103B/DEFB103A/RNASE7/C5AR1/KLK5/KLK7* | 11 |
| GO:0030593 | neutrophil chemotaxis | 0.047847 | 0.005178068 | 1.26E-07 | 2.43E-05 | 2.18E-05 | *PIK3CD/CSF3R/S100A12/S100A8/CXCR2/CXCL2/JAML/C5AR1/PREX1/ITGB2* | 10 |
| GO:0002703 | regulation of leukocyte mediated immunity | 0.047847 | 0.009493125 | 3.15E-05 | 2.68E-03 | 2.40E-03 | *PTPRC/CR1/AGER/GAB2/UNC13D/PRAM1/ADGRE2/TGFB1/ITGB2/WAS* | 10 |
| GO:0051091 | positive regulation of DNA binding transcription factor activity | 0.047847 | 0.014153386 | 8.11E-04 | 3.17E-02 | 2.83E-02 | *S100A12/S100A8/NLRC4/AGER/RELN/PRKCB/CARD14/TGFB1/ITGB2/NFAM1* | 10 |
| GO:0010951 | negative regulation of endopeptidase activity | 0.047847 | 0.014383522 | 9.17E-04 | 3.32E-02 | 2.96E-02 | *CR1/NLRC4/SPINK5/SPINK6/SPINK7/CST6/A2ML1/SERPINB7/CST1/MMP9* | 10 |
| GO:1902105 | regulation of leukocyte differentiation | 0.047847 | 0.014613659 | 1.03E-03 | 3.61E-02 | 3.22E-02 | *CR1/ZFP36L2/INPP5D/SPINK5/AGER/PRDM1/BMP4/EVI2B/TGFB1/NFAM1* | 10 |
| GO:0050851 | antigen receptor-mediated signaling pathway | 0.047847 | 0.014786261 | 1.13E-03 | 3.80E-02 | 3.40E-02 | *PIK3CD/THEMIS2/MNDA/PTPRC/INPP5D/FYB1/PRKCB/PLCG2/NFAM1/WAS* | 10 |
| GO:0019730 | antimicrobial humoral response | 0.043062 | 0.006041079 | 4.90E-06 | 7.09E-04 | 6.34E-04 | *PGLYRP4/S100A12/S100A8/SPINK5/DEFB103B/DEFB103A/RNASE7/KLK5/KLK7* | 9 |
| GO:0045766 | positive regulation of angiogenesis | 0.043062 | 0.008457511 | 7.27E-05 | 5.13E-03 | 4.59E-03 | *ECM1/IL1A/CCR3/NOS3/TEK/ITGA5/PRKCB/C5AR1/ITGB2* | 9 |
| GO:0018149 | peptide cross-linking | 0.038278 | 0.003394511 | 5.01E-07 | 8.05E-05 | 7.19E-05 | *FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F* | 8 |
| GO:0051092 | positive regulation of NF-kappaB transcription factor activity | 0.038278 | 0.008054772 | 2.94E-04 | 1.64E-02 | 1.46E-02 | *S100A12/S100A8/NLRC4/AGER/PRKCB/CARD14/TGFB1/ITGB2* | 8 |
| GO:0050864 | regulation of B cell activation | 0.038278 | 0.008917784 | 5.81E-04 | 2.51E-02 | 2.24E-02 | *MNDA/PTPRC/ZFP36L2/INPP5D/PRDM1/TGFB1/SAMSN1/NFAM1* | 8 |

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|---|---|---|---|---|---|---|---|---|
| GO:0045619 | regulation of lymphocyte differentiation | 0.038278 | 0.008975318 | 6.06E-04 | 2.57E-02 | 2.30E-02 | *CR1/ZFP36L2/INPP5D/SPINK5/PRDM1/BMP4/TGFB1/NFAM1* | 8 |
| GO:0050866 | negative regulation of cell activation | 0.038278 | 0.010010931 | 1.23E-03 | 3.99E-02 | 3.57E-02 | *MNDA/INPP5D/PRDM1/NOS3/BMP4/TGFB1/THBD/SAMSN1* | 8 |
| GO:0007492 | endoderm development | 0.033493 | 0.004545193 | 4.58E-05 | 3.49E-03 | 3.12E-03 | *DUSP1/ARC/ITGA5/BMP4/TGFB1/MMP9/ITGB2* | 7 |
| GO:0001704 | formation of primary germ layer | 0.033493 | 0.007249295 | 8.30E-04 | 3.20E-02 | 2.86E-02 | *DUSP1/ITGA5/BMP4/KDM6B/MMP9/SNAI1/ITGB2* | 7 |
| GO:0050777 | negative regulation of immune response | 0.033493 | 0.0075945 | 1.09E-03 | 3.71E-02 | 3.32E-02 | *PTPRC/CR1/IL1RL1/INPP5D/SPINK5/TGFB1/SAMSN1* | 7 |
| GO:0002819 | regulation of adaptive immune response | 0.033493 | 0.007767102 | 1.24E-03 | 3.99E-02 | 3.57E-02 | *PTPRC/CR1/IL1RL1/AGER/TGFB1/SAMSN1/WAS* | 7 |
| GO:0001906 | cell killing | 0.033493 | 0.007997238 | 1.47E-03 | 4.30E-02 | 3.84E-02 | *PGLYRP4/S100A12/PTPRC/AGER/DEFB103B/DEFB103A/UNC13D* | 7 |
| GO:0072006 | nephron development | 0.033493 | 0.007939704 | 1.41E-03 | 4.30E-02 | 3.84E-02 | *EGR1/CALB1/TEK/ACTA2/BMP4/SERPINB7/TGFB1* | 7 |
| GO:0050832 | defense response to fungus | 0.028708 | 0.002301364 | 7.68E-06 | 9.66E-04 | 8.63E-04 | *S100A12/S100A8/C10orf99/RNASE7/TGFB1/IL17RA* | 6 |
| GO:0009620 | response to fungus | 0.028708 | 0.003106841 | 4.49E-05 | 3.49E-03 | 3.12E-03 | *S100A12/S100A8/C10orf99/RNASE7/TGFB1/IL17RA* | 6 |
| GO:0061844 | antimicrobial humoral immune response mediated by antimicrobial peptide | 0.028708 | 0.003106841 | 4.49E-05 | 3.49E-03 | 3.12E-03 | *PGLYRP4/S100A12/SPINK5/RNASE7/KLK5/KLK7* | 6 |
| GO:0050830 | defense response to Gram-positive bacterium | 0.028708 | 0.005235602 | 8.02E-04 | 3.17E-02 | 2.83E-02 | *PGLYRP4/DEFB103B/DEFB103A/C10orf99/RNASE7/C5AR1* | 6 |
| GO:0050853 | B cell receptor signaling pathway | 0.028708 | 0.005293136 | 8.50E-04 | 3.21E-02 | 2.87E-02 | *PIK3CD/MNDA/PTPRC/PRKCB/PLCG2/NFAM1* | 6 |
| GO:0007613 | memory | 0.028708 | 0.006098613 | 1.77E-03 | 4.97E-02 | 4.44E-02 | *HRH2/RELN/CALB1/ARC/ITGA5/KLK8* | 6 |
| GO:0072012 | glomerulus vasculature development | 0.023923 | 0.001438352 | 1.05E-05 | 1.23E-03 | 1.10E-03 | *EGR1/TEK/ACTA2/BMP4/SERPINB7* | 5 |
| GO:0061437 | renal system vasculature development | 0.023923 | 0.00155342 | 1.56E-05 | 1.56E-03 | 1.39E-03 | *EGR1/TEK/ACTA2/BMP4/SERPINB7* | 5 |
| GO:0061440 | kidney vasculature development | 0.023923 | 0.00155342 | 1.56E-05 | 1.56E-03 | 1.39E-03 | *EGR1/TEK/ACTA2/BMP4/SERPINB7* | 5 |

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|---|---|---|---|---|---|---|---|---|
| GO:0002886 | regulation of myeloid leukocyte mediated immunity | 0.023923 | 0.0025315 | 1.78E-04 | 1.12E-02 | 9.99E-03 | *GAB2/UNC13D/PRAM1/ADGRE2/ITGB2* | 5 |
| GO:0043300 | regulation of leukocyte degranulation | 0.023923 | 0.0025315 | 1.78E-04 | 1.12E-02 | 9.99E-03 | *GAB2/UNC13D/PRAM1/ADGRE2/ITGB2* | 5 |
| GO:0045123 | cellular extravasation | 0.023923 | 0.002876704 | 3.27E-04 | 1.74E-02 | 1.56E-02 | *PIK3CD/IL1A/JAML/SELPLG/ITGB2* | 5 |
| GO:0031663 | lipopolysaccharide-mediated signaling pathway | 0.023923 | 0.003049307 | 4.30E-04 | 2.14E-02 | 1.91E-02 | *PRDM1/NOS3/TGFB1/LILRA2/HCK* | 5 |
| GO:0045576 | mast cell activation | 0.023923 | 0.003221909 | 5.56E-04 | 2.48E-02 | 2.22E-02 | *PIK3CD/S100A12/GAB2/UNC13D/ADGRE2* | 5 |
| GO:0006968 | cellular defense response | 0.023923 | 0.003452045 | 7.65E-04 | 3.07E-02 | 2.75E-02 | *MNDA/CXCR2/CCR3/LSP1/C5AR1* | 5 |
| GO:0032835 | glomerulus development | 0.023923 | 0.003624648 | 9.56E-04 | 3.37E-02 | 3.02E-02 | *EGR1/TEK/ACTA2/BMP4/SERPINB7* | 5 |
| GO:0032945 | negative regulation of mononuclear cell proliferation | 0.023923 | 0.003969852 | 1.44E-03 | 4.30E-02 | 3.84E-02 | *MNDA/INPP5D/PRDM1/BMP4/TGFB1* | 5 |
| GO:0050672 | negative regulation of lymphocyte proliferation | 0.023923 | 0.003969852 | 1.44E-03 | 4.30E-02 | 3.84E-02 | *MNDA/INPP5D/PRDM1/BMP4/TGFB1* | 5 |
| GO:1900004 | negative regulation of serine-type endopeptidase activity | 0.019139 | 0.000747943 | 1.33E-05 | 1.43E-03 | 1.28E-03 | *CR1/SPINK5/SPINK6/SPINK7* | 4 |
| GO:1902572 | negative regulation of serine-type peptidase activity | 0.019139 | 0.000747943 | 1.33E-05 | 1.43E-03 | 1.28E-03 | *CR1/SPINK5/SPINK6/SPINK7* | 4 |
| GO:0072109 | glomerular mesangium development | 0.019139 | 0.000863011 | 2.50E-05 | 2.19E-03 | 1.96E-03 | *EGR1/ACTA2/BMP4/SERPINB7* | 4 |
| GO:1900003 | regulation of serine-type endopeptidase activity | 0.019139 | 0.000863011 | 2.50E-05 | 2.19E-03 | 1.96E-03 | *CR1/SPINK5/SPINK6/SPINK7* | 4 |
| GO:1902571 | regulation of serine-type peptidase activity | 0.019139 | 0.000863011 | 2.50E-05 | 2.19E-03 | 1.96E-03 | *CR1/SPINK5/SPINK6/SPINK7* | 4 |
| GO:0045577 | regulation of B cell differentiation | 0.019139 | 0.001495886 | 2.47E-04 | 1.49E-02 | 1.33E-02 | *ZFP36L2/INPP5D/PRDM1/NFAM1* | 4 |

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|---|---|---|---|---|---|---|---|---|
| GO:0001958 | endochondral ossification | 0.019139 | 0.00155342 | 2.87E-04 | 1.63E-02 | 1.45E-02 | *CSGALNACT1/TEK/BMP4/PHOSPHO1* | 4 |
| GO:0036075 | replacement ossification | 0.019139 | 0.00155342 | 2.87E-04 | 1.63E-02 | 1.45E-02 | *CSGALNACT1/TEK/BMP4/PHOSPHO1* | 4 |
| GO:0061311 | cell surface receptor signaling pathway involved in heart development | 0.019139 | 0.001610954 | 3.32E-04 | 1.74E-02 | 1.56E-02 | *BMP4/DLL4/TGFB1/SNAI1* | 4 |
| GO:1900271 | regulation of long-term synaptic potentiation | 0.019139 | 0.001726023 | 4.36E-04 | 2.14E-02 | 1.91E-02 | *AGER/RELN/CALB1/ARC* | 4 |
| GO:0050869 | negative regulation of B cell activation | 0.019139 | 0.001783557 | 4.96E-04 | 2.28E-02 | 2.03E-02 | *MNDA/INPP5D/PRDM1/SAMSN1* | 4 |
| GO:0043616 | keratinocyte proliferation | 0.019139 | 0.002243829 | 1.20E-03 | 3.99E-02 | 3.57E-02 | *EREG/SLURP1/ZFP36/KLK8* | 4 |
| GO:0090184 | positive regulation of kidney development | 0.019139 | 0.002301364 | 1.32E-03 | 4.16E-02 | 3.72E-02 | *EGR1/BMP4/SERPINB7/TGFB1* | 4 |
| GO:0002820 | negative regulation of adaptive immune response | 0.019139 | 0.002358898 | 1.45E-03 | 4.30E-02 | 3.84E-02 | *PTPRC/CR1/IL1RL1/SAMSN1* | 4 |
| GO:0072110 | glomerular mesangial cell proliferation | 0.014354 | 0.000575341 | 1.93E-04 | 1.19E-02 | 1.06E-02 | *EGR1/BMP4/SERPINB7* | 3 |
| GO:0072672 | neutrophil extravasation | 0.014354 | 0.000632875 | 2.63E-04 | 1.55E-02 | 1.39E-02 | *PIK3CD/IL1A/JAML* | 3 |
| GO:1901722 | regulation of cell proliferation involved in kidney development | 0.014354 | 0.000747943 | 4.48E-04 | 2.15E-02 | 1.92E-02 | *EGR1/BMP4/SERPINB7* | 3 |
| GO:0090192 | regulation of glomerulus development | 0.014354 | 0.000805477 | 5.66E-04 | 2.48E-02 | 2.22E-02 | *EGR1/BMP4/SERPINB7* | 3 |
| GO:1900424 | regulation of defense response to bacterium | 0.014354 | 0.000805477 | 5.66E-04 | 2.48E-02 | 2.22E-02 | *SPINK5/KLK5/KLK7* | 3 |
| GO:0030889 | negative regulation of B cell proliferation | 0.014354 | 0.000920545 | 8.55E-04 | 3.21E-02 | 2.87E-02 | *MNDA/INPP5D/PRDM1* | 3 |
| GO:0097709 | connective tissue replacement | 0.014354 | 0.001035614 | 1.22E-03 | 3.99E-02 | 3.57E-02 | *IL1A/AGER/TGFB1* | 3 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| GO:0072111 | cell proliferation involved in kidney development | 0.014354 | 0.001150682 | 1.68E-03 | 4.76E-02 | 4.26E-02 | *EGR1/BMP4/SERPINB7* | 3 |

Table S4: Molecular functions enriched at baseline between “Cold” and “No Cold” groups

| ID | Description | GeneRatio | BgRatio | *P*value | *P*.adjust | qvalue | geneID | Count |
|---|---|---|---|---|---|---|---|---|
| GO:0017171 | serine hydrolase activity | 0.0591133 | 0.015961738 | 1.06E-04 | 7.29E-03 | 6.50E-03 | *TMPRSS11B/TMPRSS11E/RELN/CTSV/PRSS27/KLK5/KLK6/KLK7/KLK8/KLK12/KLK13/MMP9* | 12 |
| GO:0008236 | serine-type peptidase activity | 0.0591133 | 0.01567362 | 8.93E-05 | 7.29E-03 | 6.50E-03 | *TMPRSS11B/TMPRSS11E/RELN/CTSV/PRSS27/KLK5/KLK6/KLK7/KLK8/KLK12/KLK13/MMP9* | 12 |
| GO:0004252 | serine-type endopeptidase activity | 0.054187192 | 0.014060159 | 1.45E-04 | 8.28E-03 | 7.38E-03 | *TMPRSS11B/TMPRSS11E/CTSV/PRSS27/KLK5/KLK6/KLK7/KLK8/KLK12/KLK13/MMP9* | 11 |
| GO:0061134 | peptidase regulator activity | 0.054187192 | 0.012561945 | 5.33E-05 | 7.29E-03 | 6.50E-03 | *NLRC4/MAL/SPINK5/SPINK6/SPINK7/PI15/CST6/A2ML1/NLRP1/SERPINB7/CST1* | 11 |
| GO:0030414 | peptidase inhibitor activity | 0.044334975 | 0.010487496 | 2.97E-04 | 1.36E-02 | 1.21E-02 | *NLRC4/SPINK5/SPINK6/SPINK7/PI15/CST6/A2ML1/SERPINB7/CST1* | 9 |
| GO:0019955 | cytokine binding | 0.039408867 | 0.005819984 | 2.43E-05 | 5.01E-03 | 4.47E-03 | *CSF3R/IL1R2/IL1RL1/CXCR2/CXCR1/CCR3/ZFP36/IL2RG* | 8 |
| GO:0004896 | cytokine receptor activity | 0.039408867 | 0.005243748 | 1.13E-05 | 4.66E-03 | 4.15E-03 | *CSF3R/IL1R2/IL1RL1/CXCR2/CXCR1/CCR3/IL17RA/IL2RG* | 8 |
| GO:0070851 | growth factor receptor binding | 0.034482759 | 0.007606316 | 9.29E-04 | 3.15E-02 | 2.81E-02 | *ECM1/IL1A/IL36G/EREG/HBEGF/AGR2/ITGA5* | 7 |
| GO:0005154 | epidermal growth factor receptor binding | 0.019704433 | 0.001901579 | 5.70E-04 | 2.14E-02 | 1.90E-02 | *EREG/HBEGF/AGR2/ITGA5* | 4 |
| GO:0019956 | chemokine binding | 0.019704433 | 0.001382966 | 1.61E-04 | 8.28E-03 | 7.38E-03 | *CXCR2/CXCR1/CCR3/ZFP36* | 4 |
| GO:0001848 | complement binding | 0.019704433 | 0.001210096 | 9.31E-05 | 7.29E-03 | 6.50E-03 | *CR1/C5AR1/CD93/ITGB2* | 4 |
| GO:0001846 | opsonin binding | 0.014778325 | 0.00080673 | 5.22E-04 | 2.14E-02 | 1.90E-02 | *CR1/CD93/ITGB2* | 3 |
| GO:0004175 | endopeptidase activity | 0.068965517 | 0.02702547 | 1.28E-03 | 3.52E-02 | 3.14E-02 | *CLCA4/ASPRV1/MME/TMPRSS11B/TMPRSS11E/CTSV/PRSS27/KLK5/KLK6/KLK7/KLK8/KLK12/KLK13/MMP9* | 14 |
| GO:0061135 | endopeptidase regulator activity | 0.039408867 | 0.010314625 | 1.24E-03 | 3.52E-02 | 3.14E-02 | *NLRC4/SPINK5/SPINK6/SPINK7/CST6/A2ML1/SERPINB7/CST1* | 8 |
| GO:0004866 | endopeptidase inhibitor activity | 0.039408867 | 0.009968883 | 9.95E-04 | 3.15E-02 | 2.81E-02 | *NLRC4/SPINK5/SPINK6/SPINK7/CST6/A2ML1/SERPINB7/CST1* | 8 |

| **Mediator**<br>($\log_{10}$ pg/ml) | **Cold** (n=23, unless otherwise stated)<br>Median | **No Cold** (n=25, unless otherwise stated)<br>Median | *P*-value |
|---|---|---|---|
| IFN-α | 0.046 | 0.046 | 0.176 |
| IFN-β | 1.866 | 0.856 | 0.617 |
| IFN-γ | 0 | 0 | 0.314 |
| IL-1β | 1.193 | 0.870 | 0.086 |
| IL-6 | 0.991 | 0.659 | 0.103 |
| IL-8 | 3.170 | 2.923 | 0.356 |
| IL-10 | 0.803 | 0.803 | 0.068 |
| IL-15 | 0.419 | 0.329 | 0.391 |
| IL-17A | 0.609 | 0.144 | 0.039* |
| CXCL10<br>(IP-10) | 1.991 | 1.715 | 0.054 |
| LCN-2 | 6.704 (n=10) | 5.875 (n=9) | 0.017* |
| MIP-1α | 0.903 | 0.732 | 0.192 |
| MPO | 6.758 (n=10) | 5.861 (n=9) | 0.010* |
| CCL5 (RANTES) | 0.254 | 0.369 | 0.665 |
| TNF-α | 0 | 0 | 0.692 |

**Table S5: Day 0 cytokine levels in infected and uninfected volunteers** Day 0 mediator levels in the upper respiratory tract were determined in participants who subsequently developed symptomatic RSV infection (Cold, n=23) and those that did not (No Cold, n=25). Statistical analyses used two-tailed Mann Whitney *U* tests; **P*<0.05.

Table S6: DEGs between day 3 and day 0 in the “No Cold” group (*P*-value<0.01, LFC>0.5)

| | GeneName | baseMean | $\log^2$Fold Change | lfcSE | stat | *P*value | Padj |
|---|---|---|---|---|---|---|---|
| ENSG00000268173 | *AC007192.4* | 34.09618 | 10.71285 | 1.946479 | 5.503707 | 3.72E-08 | 0.000546 |
| ENSG00000163734 | *CXCL3* | 149.3781 | 1.440807 | 0.321685 | 4.478942 | 7.50E-06 | 0.055023 |
| ENSG00000081041 | *CXCL2* | 174.802 | 1.436306 | 0.349674 | 4.107556 | 4.00E-05 | 0.195535 |
| ENSG00000177606 | *JUN* | 1314.332 | 0.725754 | 0.189651 | 3.826781 | 0.00013 | 0.274872 |
| ENSG00000163739 | *CXCL1* | 1567.606 | 1.058814 | 0.272342 | 3.887809 | 0.000101 | 0.274872 |
| ENSG00000159231 | *CBR3* | 89.53077 | -0.80421 | 0.21029 | -3.82427 | 0.000131 | 0.274872 |
| ENSG00000140519 | *RHCG* | 205.5315 | 2.384514 | 0.629577 | 3.787487 | 0.000152 | 0.279058 |
| ENSG00000143536 | *CRNN* | 332.3173 | 2.42925 | 0.700976 | 3.465527 | 0.000529 | 0.644422 |
| ENSG00000137331 | *IER3* | 1131.598 | 0.773632 | 0.225847 | 3.425471 | 0.000614 | 0.644422 |
| ENSG00000123119 | *NECAB1* | 17.4312 | 1.396028 | 0.40761 | 3.424915 | 0.000615 | 0.644422 |
| ENSG00000196993 | *NPIPB9* | 90.3268 | -0.60766 | 0.177412 | -3.42512 | 0.000615 | 0.644422 |
| ENSG00000169203 | *RP11-231C14.4* | 249.1964 | -0.64802 | 0.187268 | -3.46041 | 0.000539 | 0.644422 |
| ENSG00000280893 | *AC009133.23* | 9.701738 | -2.5609 | 0.758312 | -3.3771 | 0.000733 | 0.691727 |
| ENSG00000067082 | *KLF6* | 1426.194 | 0.520046 | 0.157306 | 3.305947 | 0.000947 | 0.694302 |
| ENSG00000186474 | *KLK12* | 25.34081 | 1.839293 | 0.551663 | 3.334085 | 0.000856 | 0.694302 |
| ENSG00000113070 | *HBEGF* | 259.5387 | 1.320102 | 0.402212 | 3.282104 | 0.00103 | 0.719647 |
| ENSG00000091128 | *LAMB4* | 79.02638 | 1.205408 | 0.370164 | 3.256417 | 0.001128 | 0.719647 |
| ENSG00000132932 | *ATP8A2* | 24.55841 | 0.602019 | 0.184236 | 3.267642 | 0.001084 | 0.719647 |
| ENSG00000139318 | *DUSP6* | 775.636 | 0.686782 | 0.215349 | 3.189164 | 0.001427 | 0.807516 |
| ENSG00000203852 | *HIST2H3A* | 311.1639 | 1.57602 | 0.502519 | 3.136242 | 0.001711 | 0.838019 |
| ENSG00000165794 | *SLC39A2* | 27.49601 | 1.602373 | 0.51099 | 3.135821 | 0.001714 | 0.838019 |
| ENSG00000154734 | *ADAMTS1* | 34.50457 | 1.779 | 0.565144 | 3.147873 | 0.001645 | 0.838019 |
| ENSG00000183336 | *BOLA2* | 5.369005 | -9.99524 | 3.22335 | -3.10089 | 0.001929 | 0.913049 |
| ENSG00000121742 | *GJB6* | 75.14953 | 1.351585 | 0.437849 | 3.086874 | 0.002023 | 0.923257 |
| ENSG00000265590 | *AP000275.65* | 33.19193 | -1.87079 | 0.607592 | -3.07902 | 0.002077 | 0.923257 |
| ENSG00000169509 | *CRCT1* | 43.10019 | 2.246315 | 0.786001 | 2.857904 | 0.004264 | 0.971488 |
| ENSG00000090104 | *RGS1* | 260.8477 | 0.758897 | 0.261628 | 2.900676 | 0.003724 | 0.971488 |
| ENSG00000263961 | *C1orf186* | 9.726597 | 1.104421 | 0.381009 | 2.898677 | 0.003747 | 0.971488 |
| ENSG00000143878 | *RHOB* | 1806.952 | 0.509216 | 0.179492 | 2.83699 | 0.004554 | 0.971488 |
| ENSG00000115602 | *IL1RL1* | 51.0304 | 1.606061 | 0.559536 | 2.870347 | 0.0041 | 0.971488 |
| ENSG00000185873 | *TMPRSS11B* | 126.1337 | 2.320712 | 0.77744 | 2.98507 | 0.002835 | 0.971488 |
| ENSG00000124875 | *CXCL6* | 692.2134 | 0.849458 | 0.286733 | 2.962539 | 0.003051 | 0.971488 |
| ENSG00000145879 | *SPINK7* | 90.93384 | 2.305832 | 0.75561 | 3.051617 | 0.002276 | 0.971488 |
| ENSG00000112394 | *SLC16A10* | 25.4085 | 1.106001 | 0.3716 | 2.976325 | 0.002917 | 0.971488 |
| ENSG00000155918 | *RAET1L* | 74.83194 | 1.296183 | 0.451471 | 2.871022 | 0.004091 | 0.971488 |
| ENSG00000197181 | *PIWIL2* | 16.37803 | 0.889869 | 0.298332 | 2.982817 | 0.002856 | 0.971488 |
| ENSG00000104368 | *PLAT* | 1629.246 | 1.266039 | 0.433067 | 2.923424 | 0.003462 | 0.971488 |
| ENSG00000111215 | *PRR4* | 92.77336 | -0.82179 | 0.277502 | -2.96137 | 0.003063 | 0.971488 |
| ENSG00000018236 | *CNTN1* | 68.40497 | 0.892821 | 0.307411 | 2.904322 | 0.00368 | 0.971488 |
| ENSG00000279777 | *AC004813.1* | 52.62626 | -0.60351 | 0.20639 | -2.92413 | 0.003454 | 0.971488 |
| ENSG00000128965 | *CHAC1* | 76.63318 | 0.803606 | 0.281341 | 2.856341 | 0.004286 | 0.971488 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ENSG00000185864 | *NPIPB4* | 335.7528 | -0.52362 | 0.177264 | -2.95391 | 0.003138 | 0.971488 |
| ENSG00000171401 | *KRT13* | 3674.625 | 1.533781 | 0.527322 | 2.908621 | 0.00363 | 0.971488 |
| ENSG00000175906 | *ARL4D* | 476.1744 | 0.578185 | 0.203438 | 2.842066 | 0.004482 | 0.971488 |
| ENSG00000269404 | *SPIB* | 27.53031 | 0.814364 | 0.278475 | 2.924367 | 0.003452 | 0.971488 |
| ENSG00000169035 | *KLK7* | 193.8601 | 1.85068 | 0.640657 | 2.888722 | 0.003868 | 0.971488 |
| ENSG00000129455 | *KLK8* | 26.1473 | 2.13996 | 0.750293 | 2.852164 | 0.004342 | 0.971488 |
| ENSG00000088882 | *CPXM1* | 53.04393 | 0.761404 | 0.266631 | 2.855645 | 0.004295 | 0.971488 |
| ENSG00000156282 | *CLDN17* | 19.61386 | 2.754695 | 0.950417 | 2.898406 | 0.003751 | 0.971488 |
| ENSG00000128342 | *LIF* | 164.0332 | 0.589717 | 0.206526 | 2.855406 | 0.004298 | 0.971488 |
| ENSG00000163751 | *CPA3* | 103.1778 | 1.764197 | 0.637979 | 2.765291 | 0.005687 | 0.990244 |
| ENSG00000188818 | *ZDHHC11* | 88.32456 | -0.54877 | 0.198388 | -2.76616 | 0.005672 | 0.990244 |
| ENSG00000136943 | *CTSV* | 147.4117 | 0.920501 | 0.328398 | 2.803004 | 0.005063 | 0.990244 |
| ENSG00000188070 | *C11orf95* | 136.192 | 0.50528 | 0.181364 | 2.785993 | 0.005336 | 0.990244 |
| ENSG00000170426 | *SDR9C7* | 8.854919 | 2.309243 | 0.821713 | 2.81028 | 0.00495 | 0.990244 |
| ENSG00000166211 | *SPIC* | 20.23969 | 0.594662 | 0.215019 | 2.765632 | 0.005681 | 0.990244 |
| ENSG00000165799 | *RNASE7* | 49.36023 | 1.409505 | 0.504665 | 2.792952 | 0.005223 | 0.990244 |
| ENSG00000197253 | *TPSB2* | 75.30485 | 1.871105 | 0.675495 | 2.769975 | 0.005606 | 0.990244 |
| ENSG00000198156 | *NPIPB6* | 98.34868 | -0.54924 | 0.198827 | -2.76241 | 0.005738 | 0.990244 |
| ENSG00000269711 | *CTD-3214H19.16* | 10.41424 | 10.46232 | 3.708287 | 2.821336 | 0.004782 | 0.990244 |
| ENSG00000105427 | *CNFN* | 181.4197 | 1.277771 | 0.454088 | 2.813927 | 0.004894 | 0.990244 |
| ENSG00000022556 | *NLRP2* | 93.76168 | 1.077863 | 0.386322 | 2.790064 | 0.00527 | 0.990244 |
| ENSG00000142619 | *PADI3* | 97.15799 | 0.547472 | 0.20942 | 2.614223 | 0.008943 | 1 |
| ENSG00000143556 | *S100A7* | 630.9285 | 1.955151 | 0.744234 | 2.627063 | 0.008613 | 1 |
| ENSG00000196754 | *S100A2* | 4500.136 | 1.346063 | 0.492669 | 2.732187 | 0.006292 | 1 |
| ENSG00000179914 | *ITLN1* | 48.25683 | -1.69569 | 0.651444 | -2.60297 | 0.009242 | 1 |
| ENSG00000135919 | *SERPINE2* | 144.2735 | 1.144279 | 0.440156 | 2.599711 | 0.00933 | 1 |
| ENSG00000132465 | *JCHAIN* | 62.01675 | 0.908242 | 0.345234 | 2.630798 | 0.008518 | 1 |
| ENSG00000118785 | *SPP1* | 24.56759 | 1.089926 | 0.412914 | 2.639595 | 0.008301 | 1 |
| ENSG00000120738 | *EGR1* | 360.8778 | 1.082594 | 0.406853 | 2.660894 | 0.007793 | 1 |
| ENSG00000254245 | *PCDHGA3* | 16.88847 | -0.81997 | 0.308613 | -2.65694 | 0.007885 | 1 |
| ENSG00000253159 | *PCDHGA12* | 23.25894 | -0.70802 | 0.257928 | -2.74503 | 0.006051 | 1 |
| ENSG00000133710 | *SPINK5* | 1205.992 | 0.789563 | 0.296293 | 2.664807 | 0.007703 | 1 |
| ENSG00000120149 | *MSX2* | 27.93288 | 0.635925 | 0.244592 | 2.599942 | 0.009324 | 1 |
| ENSG00000276180 | *HIST1H4I* | 123.343 | 0.605086 | 0.230213 | 2.62837 | 0.00858 | 1 |
| ENSG00000170667 | *RASA4B* | 32.38069 | -0.65927 | 0.252296 | -2.61307 | 0.008973 | 1 |
| ENSG00000164604 | *GPR85* | 21.83782 | 0.745677 | 0.286781 | 2.600157 | 0.009318 | 1 |
| ENSG00000107984 | *DKK1* | 176.808 | 0.807979 | 0.297051 | 2.720003 | 0.006528 | 1 |
| ENSG00000117983 | *MUC5B* | 72.21829 | -1.39958 | 0.515548 | -2.71474 | 0.006633 | 1 |
| ENSG00000175518 | *UBQLNL* | 18.33565 | -0.77311 | 0.288423 | -2.68046 | 0.007352 | 1 |
| ENSG00000165474 | *GJB2* | 526.7655 | 0.911625 | 0.347925 | 2.620178 | 0.008788 | 1 |
| ENSG00000134901 | *KDELC1* | 36.77971 | 0.505743 | 0.196205 | 2.577628 | 0.009948 | 1 |
| ENSG00000249240 | *AC069368.3* | 5.588089 | -1.7672 | 0.665496 | -2.65546 | 0.00792 | 1 |
| ENSG00000188508 | *KRTDAP* | 20.60571 | 2.121478 | 0.781522 | 2.714549 | 0.006637 | 1 |
| ENSG00000102313 | *ITIH6* | 35.36962 | -0.71756 | 0.263563 | -2.72252 | 0.006479 | 1 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ENSG00000268089 | *GABRQ* | 21.23443 | 1.933114 | 0.706636 | 2.73566 | 0.006226 | 1 |
| ENSG00000198763 | *MT-ND2* | 2776.095 | -0.57408 | 0.215711 | -2.66133 | 0.007783 | 1 |

Table S7: DEGs between day 3 and day 0 in the “Cold” group (*P*-*v*alue<0.01, LFC>0.5)

| | GeneName | baseMean | log$^2$Fold Change | lfcSE | stat | *P*value | *P*adj |
|---|---|---|---|---|---|---|---|
| ENSG00000125378 | *BMP4* | 22.04009 | 1.543324 | 0.297741 | 5.183448 | 2.18E-07 | 0.003195 |
| ENSG00000132326 | *PER2* | 1311.424 | -0.66742 | 0.14176 | -4.70814 | 2.50E-06 | 0.018336 |
| ENSG00000140006 | *WDR89* | 150.7693 | 0.632335 | 0.15182 | 4.165032 | 3.11E-05 | 0.114173 |
| ENSG00000184313 | *MROH7* | 105.3837 | -0.78921 | 0.204508 | -3.85906 | 0.000114 | 0.271157 |
| ENSG00000129757 | *CDKN1C* | 101.3036 | 0.671943 | 0.17645 | 3.80812 | 0.00014 | 0.271157 |
| ENSG00000173451 | *THAP2* | 76.44963 | 0.624654 | 0.165438 | 3.775758 | 0.00016 | 0.271157 |
| ENSG00000277117 | *ICOSLG* | 38.58432 | 1.309042 | 0.340901 | 3.839948 | 0.000123 | 0.271157 |
| ENSG00000127129 | *EDN2* | 292.3299 | 2.41171 | 0.668713 | 3.606497 | 0.00031 | 0.281593 |
| ENSG00000135045 | *C9orf40* | 111.4209 | 0.591656 | 0.163835 | 3.611298 | 0.000305 | 0.281593 |
| ENSG00000153485 | *TMEM251* | 175.3835 | 0.621159 | 0.172678 | 3.597203 | 0.000322 | 0.281593 |
| ENSG00000206172 | *HBA1* | 21.72477 | -3.39372 | 0.944417 | -3.59346 | 0.000326 | 0.281593 |
| ENSG00000204172 | *AGAP9* | 156.9233 | -0.68697 | 0.193771 | -3.54528 | 0.000392 | 0.287681 |
| ENSG00000198929 | *NOS1AP* | 147.7733 | -0.72025 | 0.209007 | -3.44607 | 0.000569 | 0.31136 |
| ENSG00000118508 | *RAB32* | 180.2051 | 0.58683 | 0.17011 | 3.449702 | 0.000561 | 0.31136 |
| ENSG00000196859 | *KRT39* | 38.21066 | 0.952273 | 0.274481 | 3.469356 | 0.000522 | 0.31136 |
| ENSG00000152284 | *TCF7L1* | 33.26154 | -0.7667 | 0.230403 | -3.32767 | 0.000876 | 0.3195 |
| ENSG00000240583 | *AQP1* | 61.98687 | -1.05708 | 0.322695 | -3.2758 | 0.001054 | 0.3195 |
| ENSG00000175164 | *ABO* | 228.5686 | -0.58983 | 0.178901 | -3.29698 | 0.000977 | 0.3195 |
| ENSG00000006327 | *TNFRSF12A* | 480.2161 | 0.932948 | 0.2811 | 3.318923 | 0.000904 | 0.3195 |
| ENSG00000172000 | *ZNF556* | 17.04258 | 0.87804 | 0.266582 | 3.293689 | 0.000989 | 0.3195 |
| ENSG00000198342 | *ZNF442* | 63.13852 | 0.754397 | 0.227406 | 3.317401 | 0.000909 | 0.3195 |
| ENSG00000225828 | *FAM229A* | 41.86062 | -0.5085 | 0.156767 | -3.24367 | 0.00118 | 0.320019 |
| ENSG00000185880 | *TRIM69* | 1353.204 | 0.629862 | 0.194459 | 3.239051 | 0.001199 | 0.320019 |
| ENSG00000132881 | *RSG1* | 106.1672 | 0.534104 | 0.167607 | 3.186653 | 0.001439 | 0.338339 |
| ENSG00000221886 | *ZBED8* | 178.3149 | 0.656915 | 0.206286 | 3.184482 | 0.00145 | 0.338339 |
| ENSG00000163359 | *COL6A3* | 109.9409 | -1.36855 | 0.436338 | -3.13645 | 0.00171 | 0.349108 |
| ENSG00000122641 | *INHBA* | 71.23154 | 1.845157 | 0.586767 | 3.144618 | 0.001663 | 0.349108 |
| ENSG00000129474 | *AJUBA* | 371.5591 | 0.690348 | 0.222181 | 3.107139 | 0.001889 | 0.355797 |
| ENSG00000188290 | *HES4* | 312.5322 | 0.669324 | 0.224127 | 2.986357 | 0.002823 | 0.360848 |
| ENSG00000179914 | *ITLN1* | 71.80596 | 1.857605 | 0.620404 | 2.994186 | 0.002752 | 0.360848 |
| ENSG00000164404 | *GDF9* | 21.44236 | 0.717419 | 0.240885 | 2.97826 | 0.002899 | 0.360848 |
| ENSG00000036448 | *MYOM2* | 36.698 | 0.731788 | 0.245223 | 2.984168 | 0.002844 | 0.360848 |
| ENSG00000123411 | *IKZF4* | 100.528 | -0.51143 | 0.171315 | -2.98534 | 0.002833 | 0.360848 |
| ENSG00000132481 | *TRIM47* | 188.1067 | 0.510921 | 0.172017 | 2.970178 | 0.002976 | 0.360848 |
| ENSG00000187187 | *ZNF546* | 84.94763 | 0.720698 | 0.233248 | 3.089832 | 0.002003 | 0.360848 |
| ENSG00000159885 | *ZNF222* | 88.79954 | 0.594934 | 0.200539 | 2.966677 | 0.00301 | 0.360848 |
| ENSG00000261221 | *ZNF865* | 88.98932 | -0.55707 | 0.187852 | -2.96546 | 0.003022 | 0.360848 |
| ENSG00000132801 | *ZSWIM3* | 109.449 | 0.520946 | 0.174892 | 2.978677 | 0.002895 | 0.360848 |
| ENSG00000177854 | *TMEM187* | 153.3936 | 0.525238 | 0.17367 | 3.024343 | 0.002492 | 0.360848 |
| ENSG00000278705 | *HIST1H4B* | 594.7796 | 0.677645 | 0.231015 | 2.933342 | 0.003353 | 0.369876 |
| ENSG00000203724 | *C1orf53* | 43.69044 | 0.605087 | 0.208161 | 2.906826 | 0.003651 | 0.374903 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ENSG00000232040 | *ZBED9* | 37.2166 | 0.83489 | 0.285474 | 2.924569 | 0.003449 | 0.374903 |
| ENSG00000104267 | *CA2* | 209.3763 | 0.919822 | 0.315283 | 2.917449 | 0.003529 | 0.374903 |
| ENSG00000122254 | *HS3ST2* | 22.89722 | 1.033907 | 0.354774 | 2.914269 | 0.003565 | 0.374903 |
| ENSG00000177606 | *JUN* | 1569.743 | 0.662493 | 0.234252 | 2.828126 | 0.004682 | 0.384771 |
| ENSG00000164082 | *GRM2* | 20.58784 | -0.7129 | 0.250317 | -2.84799 | 0.0044 | 0.384771 |
| ENSG00000163536 | *SERPINI1* | 52.52468 | 0.54397 | 0.196048 | 2.774681 | 0.005526 | 0.384771 |
| ENSG00000019991 | *HGF* | 57.15752 | 0.646882 | 0.228819 | 2.827044 | 0.004698 | 0.384771 |
| ENSG00000090266 | *NDUFB2* | 674.9224 | 0.514751 | 0.180961 | 2.844548 | 0.004447 | 0.384771 |
| ENSG00000255823 | *MTRNR2L8* | 88.69851 | 0.80221 | 0.284671 | 2.818019 | 0.004832 | 0.384771 |
| ENSG00000135094 | *SDS* | 374.6442 | 0.833066 | 0.295145 | 2.82257 | 0.004764 | 0.384771 |
| ENSG00000175985 | *PLEKHD1* | 84.74293 | -0.67052 | 0.240603 | -2.78682 | 0.005323 | 0.384771 |
| ENSG00000108821 | *COL1A1* | 144.2349 | -0.83705 | 0.296719 | -2.82103 | 0.004787 | 0.384771 |
| ENSG00000261857 | *MIA* | 203.7857 | 0.827884 | 0.292163 | 2.833632 | 0.004602 | 0.384771 |
| ENSG00000142530 | *FAM71E1* | 19.35397 | 0.555792 | 0.197434 | 2.815074 | 0.004877 | 0.384771 |
| ENSG00000170775 | *GPR37* | 104.9986 | 0.566107 | 0.206773 | 2.737821 | 0.006185 | 0.389828 |
| ENSG00000197019 | *SERTAD1* | 621.5665 | 0.515149 | 0.188775 | 2.728909 | 0.006354 | 0.391678 |
| ENSG00000078401 | *EDN1* | 78.41643 | 1.222486 | 0.448687 | 2.724583 | 0.006438 | 0.392048 |
| ENSG00000040608 | *RTN4R* | 19.66314 | 0.599538 | 0.220824 | 2.715001 | 0.006628 | 0.392048 |
| ENSG00000113209 | *PCDHB5* | 15.93101 | 0.681644 | 0.252213 | 2.702646 | 0.006879 | 0.393004 |
| ENSG00000196345 | *ZKSCAN7* | 91.34475 | 0.52829 | 0.195666 | 2.699956 | 0.006935 | 0.393055 |
| ENSG00000165917 | *RAPSN* | 21.05145 | -0.63449 | 0.236171 | -2.68658 | 0.007219 | 0.400593 |
| ENSG00000145632 | *PLK2* | 1570.018 | 0.505878 | 0.18918 | 2.67406 | 0.007494 | 0.401224 |
| ENSG00000198939 | *ZFP2* | 25.53408 | 0.761238 | 0.284628 | 2.674505 | 0.007484 | 0.401224 |
| ENSG00000186480 | *INSIG1* | 1680.1 | 0.590828 | 0.220892 | 2.674736 | 0.007479 | 0.401224 |
| ENSG00000198670 | *LPA* | 68.50585 | -0.60768 | 0.227745 | -2.66823 | 0.007625 | 0.40529 |
| ENSG00000214756 | *METTL12* | 90.15136 | 0.507306 | 0.190443 | 2.663816 | 0.007726 | 0.407007 |
| ENSG00000149243 | *KLHL35* | 30.62397 | 0.540832 | 0.203969 | 2.651538 | 0.008013 | 0.407759 |
| ENSG00000239282 | *GATSL3* | 163.1875 | 0.518584 | 0.195348 | 2.65467 | 0.007939 | 0.407759 |
| ENSG00000088538 | *DOCK3* | 53.29586 | -0.54609 | 0.207448 | -2.6324 | 0.008478 | 0.414453 |
| ENSG00000241360 | *PDXP* | 67.81247 | 0.52209 | 0.19822 | 2.633894 | 0.008441 | 0.414453 |
| ENSG00000242866 | *STRC* | 49.76977 | -0.67549 | 0.257248 | -2.62583 | 0.008644 | 0.418498 |
| ENSG00000162772 | *ATF3* | 603.2502 | 0.697791 | 0.268797 | 2.595975 | 0.009432 | 0.420723 |
| ENSG00000187094 | *CCK* | 60.47584 | 0.800681 | 0.309839 | 2.584187 | 0.009761 | 0.420723 |
| ENSG00000198785 | *GRIN3A* | 14.96359 | 1.201367 | 0.460333 | 2.60978 | 0.00906 | 0.420723 |
| ENSG00000187720 | *THSD4* | 175.5152 | -0.56348 | 0.218724 | -2.57622 | 0.009989 | 0.420723 |
| ENSG00000280006 | *AC009060.2* | 90.4094 | -0.81421 | 0.315713 | -2.57896 | 0.00991 | 0.420723 |

## Table S8: Biological Processes Enriched in “Cold” group (d0 vs d3)

| **ID** | **Description** | **Gene Ratio** | **BgRatio** | ***P*value** | ***P*.adjust** | **Qvalue** | **geneID** | **Count** |
|---|---|---|---|---|---|---|---|---|
| GO:0044057 | Regulation of system process | 0.148 | 0.0295106 | 6.99E-05 | 2.16E-02 | 1.75E-02 | *EDN2/NOS1AP/PER2/CCK/GDF9/EDN1/AQP1/INHBA/HGF* | 9 |
| GO:0010035 | Response to inorganic substance | 0.131 | 0.0272913 | 2.40E-04 | 3.67E-02 | 2.97E-02 | *JUN/EDN1/AQP1/HGF/GPR37/CA2/HBA1/COL1A1* | 8 |
| GO:0042326 | Negative regulation of phosphorylation | 0.131 | 0.0248321 | 1.26E-04 | 3.33E-02 | 2.69E-02 | *JUN/ATF3/INHBA/HGF/CDKN1C/AJUBA/BMP4/RTN4R* | 8 |
| GO:0015711 | Organic anion transport | 0.115 | 0.0190139 | 1.52E-04 | 3.53E-02 | 2.85E-02 | *PER2/CCK/GRM2/EDN1/AQP1/CA2/HBA1* | 7 |
| GO:0000302 | Response to reactive oxygen species | 0.115 | 0.0122961 | 9.54E-06 | 5.89E-03 | 4.76E-03 | *JUN/EDN1/AQP1/HGF/GPR37/HBA1/COL1A1* | 7 |
| GO:0042542 | Response to hydrogen peroxide | 0.098 | 0.0071377 | 4.70E-06 | 4.35E-03 | 3.52E-03 | *JUN/AQP1/HGF/GPR37/HBA1/COL1A1* | 6 |
| GO:0042476 | Odontogenesis | 0.098 | 0.0068378 | 3.66E-06 | 4.35E-03 | 3.52E-03 | *EDN1/AQP1/INHBA/CA2/BMP4/COL1A1* | 6 |
| GO:2001236 | Regulation of extrinsic signalling pathway | 0.082 | 0.009237 | 2.47E-04 | 3.67E-02 | 2.97E-02 | *ATF3/INHBA/HGF/BMP4/TNFRSF12A* | 5 |
| GO:0044070 | Regulation of anion transport | 0.066 | 0.0050384 | 2.51E-04 | 3.67E-02 | 2.97E-02 | *PER2/CCK/EDN1/CA2* | 4 |
| GO:0050886 | Endocrine process | 0.066 | 0.0046785 | 1.89E-04 | 3.67E-02 | 2.97E-02 | *EDN2/GDF9/EDN1/INHBA* | 4 |
| GO:0060395 | SMAD protein signal transduction | 0.066 | 0.0034789 | 5.94E-05 | 2.16E-02 | 1.75E-02 | *JUN/GDF9/INHBA/BMP4* | 4 |
| GO:0015669 | Gas transport | 0.049 | 0.0011396 | 4.33E-05 | 2.01E-02 | 1.62E-02 | *AQP1/CA2/HBA1* | 3 |

## Table S9: Biological Processes Enriched in “No Cold” group (d0 vs d3)

| **ID** | **Description** | **Gene Ratio** | **BgRatio** | ***P*value** | ***P*.adjust** | **Qvalue** | **geneID** | **Count** |
|---|---|---|---|---|---|---|---|---|
| GO:0008544 | Epidermis development | 0.116 | 0.017694 | 2.87E-05 | 5.48E-03 | 4.73E-03 | *CRCT1/S100A7/SPINK5/MSX2/CTSV/DKK1/CNFN/KLK7* | 8 |
| GO:0043588 | Skin development | 0.116 | 0.014335 | 6.24E-06 | 2.09E-03 | 1.80E-03 | *CRCT1/S100A7/SPINK5/MSX2/CTSV/DKK1/ATP8A2/CNFN* | 8 |
| GO:0042742 | Defense response to bacterium | 0.101 | 0.015055 | 7.86E-05 | 8.76E-03 | 7.57E-03 | *S100A7/JCHAIN/CXCL6/SPINK5/MUC5B/RNASE7/KLK7* | 7 |
| GO:0002687 | Positive regulation of leukocyte migration | 0.072 | 0.006358 | 7.69E-05 | 8.76E-03 | 7.57E-03 | *S100A7/CXCL6/CXCL1/CXCL3/CXCL2* | 5 |
| GO:0002688 | Regulation of leukocyte chemotaxis | 0.072 | 0.005638 | 4.33E-05 | 6.77E-03 | 5.85E-03 | *S100A7/CXCL6/CXCL1/CXCL3/CXCL2* | 5 |
| GO:0002690 | Positive regulation of leukocyte chemotaxis | 0.072 | 0.004679 | 1.75E-05 | 3.90E-03 | 3.37E-03 | *S100A7/CXCL6/CXCL1/CXCL3/CXCL2* | 5 |
| GO:0019730 | Antimicrobial humoral response | 0.058 | 0.003239 | 7.27E-05 | 8.76E-03 | 7.57E-03 | *JCHAIN/SPINK5/RNASE7/KLK7* | 4 |
| GO:0019731 | Antibacterial humoral response | 0.058 | 0.002879 | 4.56E-05 | 6.77E-03 | 5.85E-03 | *JCHAIN/SPINK5/RNASE7/KLK7* | 4 |
| GO:0071622 | Regulation of granulocyte chemotaxis | 0.058 | 0.002219 | 1.60E-05 | 3.90E-03 | 3.37E-03 | *S100A7/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0001893 | Maternal placenta development | 0.058 | 0.001739 | 5.90E-06 | 2.09E-03 | 1.80E-03 | *SPP1/CTSV/GJB2/LIF* | 4 |
| GO:0071624 | Positive regulation of granulocyte chemotaxis | 0.058 | 0.0015 | 3.18E-06 | 2.09E-03 | 1.80E-03 | *S100A7/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0046697 | Decidualization | 0.058 | 0.00114 | 9.94E-07 | 1.33E-03 | 1.15E-03 | *SPP1/CTSV/GJB2/LIF* | 4 |

## Table S10: Molecular Functions Enriched in “No Cold” group (d0 vs d3)

| ID | Description | GeneRatio | BgRatio | *P*value | *P*.adjust | qvalue | geneID | Count |
|---|---|---|---|---|---|---|---|---|
| GO:0030545 | receptor regulator activity | 0.114 | 0.027947 | 7.26E-04 | 1.11E-02 | 9.74E-03 | *CXCL6/CXCL1/CXCL3/CXCL2/SPP1/HBEGF/DKK1/LIF* | 8 |
| GO:0004175 | endopeptidase activity | 0.114 | 0.027025 | 5.83E-04 | 9.80E-03 | 8.58E-03 | *TMPRSS11B/PLAT/CTSV/TPSB2/KLK7/KLK8/KLK12/ADAMTS1* | 8 |
| GO:0048018 | receptor ligand activity | 0.114 | 0.026276 | 4.84E-04 | 9.80E-03 | 8.58E-03 | *CXCL6/CXCL1/CXCL3/CXCL2/SPP1/HBEGF/DKK1/LIF* | 8 |
| GO:0017171 | serine hydrolase activity | 0.100 | 0.015962 | 1.24E-04 | 3.81E-03 | 3.34E-03 | *TMPRSS11B/PLAT/CTSV/TPSB2/KLK7/KLK8/KLK12* | 7 |
| GO:0008236 | serine-type peptidase activity | 0.100 | 0.015674 | 1.11E-04 | 3.81E-03 | 3.34E-03 | *TMPRSS11B/PLAT/CTSV/TPSB2/KLK7/KLK8/KLK12* | 7 |
| GO:0004252 | serine-type endopeptidase activity | 0.100 | 0.01406 | 5.62E-05 | 3.45E-03 | 3.02E-03 | *TMPRSS11B/PLAT/CTSV/TPSB2/KLK7/KLK8/KLK12* | 7 |
| GO:0005125 | cytokine activity | 0.086 | 0.012677 | 2.59E-04 | 5.95E-03 | 5.21E-03 | *CXCL6/CXCL1/CXCL3/CXCL2/SPP1/LIF* | 6 |
| GO:0005539 | glycosaminoglycan binding | 0.086 | 0.012274 | 2.17E-04 | 5.71E-03 | 5.00E-03 | *SERPINE2/JCHAIN/CXCL6/HBEGF/RNASE7/ADAMTS1* | 6 |
| GO:0004867 | serine-type endopeptidase inhibitor activity | 0.057 | 0.005474 | 5.86E-04 | 9.80E-03 | 8.58E-03 | *SERPINE2/SPINK5/SPINK7/ITIH6* | 4 |
| GO:0042379 | chemokine receptor binding | 0.057 | 0.003457 | 9.98E-05 | 3.81E-03 | 3.34E-03 | *CXCL6/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0008009 | chemokine activity | 0.057 | 0.002766 | 4.13E-05 | 3.45E-03 | 3.02E-03 | *CXCL6/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0045236 | CXCR chemokine receptor binding | 0.057 | 0.000922 | 4.26E-07 | 7.84E-05 | 6.86E-05 | *CXCL6/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0042834 | peptidoglycan binding | 0.029 | 0.000807 | 1.41E-03 | 2.00E-02 | 1.75E-02 | *JCHAIN/RNASE7* | 2 |

## Table S11: KEGG Pathways Enriched in “No Cold” group (d0 vs d3)

| ID | Description | GeneRatio | BgRatio | *P*value | *P*.adjust | qvalue | geneSymbol | Count |
|---|---|---|---|---|---|---|---|---|
| hsa04657 | IL-17 signaling pathway | 0.226 | 0.012515 | 7.88E-08 | 7.25E-06 | 6.14E-06 | *JUN/S100A7/CXCL6/CXCL1/CXCL3/CXCL2/MUC5B* | 7 |
| hsa04060 | Cytokine-cytokine receptor interaction | 0.194 | 0.039564 | 1.16E-03 | 2.67E-02 | 2.26E-02 | *IL1RL1/CXCL6/CXCL1/CXCL3/CXCL2/LIF* | 6 |
| hsa04668 | TNF signaling pathway | 0.161 | 0.014803 | 8.11E-05 | 3.73E-03 | 3.16E-03 | *JUN/CXCL1/CXCL3/CXCL2/LIF* | 5 |
| hsa05132 | Salmonella infection | 0.129 | 0.011573 | 4.15E-04 | 1.27E-02 | 1.08E-02 | *JUN/CXCL1/CXCL3/CXCL2* | 4 |
| hsa05120 | Epithelial cell signaling in Helicobacter pylori infection | 0.097 | 0.009151 | 2.74E-03 | 4.21E-02 | 3.56E-02 | *JUN/CXCL1/HBEGF* | 3 |
| hsa05134 | Legionellosis | 0.097 | 0.007401 | 1.49E-03 | 2.74E-02 | 2.32E-02 | *CXCL1/CXCL3/CXCL2* | 3 |

## Table S12: Molecular Functions enriched in the WGCNA “Brown” module

| ID | Description | GeneRatio | BgRatio | *P*value | *P*.adjust | qvalue | geneID | Count |
|---|---|---|---|---|---|---|---|---|
| GO:0004175 | endopeptidase activity | 0.29 | 0.027025 | 4.25E-04 | 3.72E-03 | 2.80E-03 | *TMPRSS11B/KLK7/KLK8/KLK12* | 4 |
| GO:0017171 | serine hydrolase activity | 0.29 | 0.015962 | 5.60E-05 | 6.54E-04 | 4.92E-04 | *TMPRSS11B/KLK7/KLK8/KLK12* | 4 |
| GO:0008236 | serine-type peptidase activity | 0.29 | 0.015674 | 5.22E-05 | 6.54E-04 | 4.92E-04 | *TMPRSS11B/KLK7/KLK8/KLK12* | 4 |
| GO:0004252 | serine-type endopeptidase activity | 0.29 | 0.01406 | 3.42E-05 | 6.54E-04 | 4.92E-04 | *TMPRSS11B/KLK7/KLK8/KLK12* | 4 |

## Table S13: Molecular Functions enriched in the WGCNA “Turquoise” module

| ID | Description | GeneRatio | BgRatio | *P*value | *P*.adjust | qvalue | geneID | Count |
|---|---|---|---|---|---|---|---|---|
| GO:1901681 | sulfur compound binding | 0.15 | 0.0133687 | 2.27E-03 | 2.36E-02 | 1.64E-02 | *SERPINE2/HBEGF/ADAMTS1* | 3 |
| GO:0061134 | peptidase regulator activity | 0.15 | 0.0125619 | 1.90E-03 | 2.26E-02 | 1.57E-02 | *SERPINE2/SPINK5/ITIH6* | 3 |
| GO:0005539 | glycosaminoglycan binding | 0.15 | 0.0122738 | 1.78E-03 | 2.26E-02 | 1.57E-02 | *SERPINE2/HBEGF/ADAMTS1* | 3 |
| GO:0030414 | peptidase inhibitor activity | 0.15 | 0.0104875 | 1.13E-03 | 1.88E-02 | 1.31E-02 | *SERPINE2/SPINK5/ITIH6* | 3 |
| GO:0061135 | endopeptidase regulator activity | 0.15 | 0.0103146 | 1.08E-03 | 1.88E-02 | 1.31E-02 | *SERPINE2/SPINK5/ITIH6* | 3 |
| GO:0004866 | endopeptidase inhibitor activity | 0.15 | 0.0099689 | 9.80E-04 | 1.88E-02 | 1.31E-02 | *SERPINE2/SPINK5/ITIH6* | 3 |
| GO:0008201 | heparin binding | 0.15 | 0.0092198 | 7.81E-04 | 1.88E-02 | 1.31E-02 | *SERPINE2/HBEGF/ADAMTS1* | 3 |
| GO:0004867 | serine-type endopeptidase inhibitor activity | 0.15 | 0.0054742 | 1.69E-04 | 1.41E-02 | 9.80E-03 | *SERPINE2/SPINK5/ITIH6* | 3 |

# Table S14: Molecular Functions enriched in the WGCNA “Blue” module

| ID | Description | GeneRatio | BgRatio | *P*value | *P*.adjust | qvalue | geneID | Count |
|---|---|---|---|---|---|---|---|---|
| GO:0030545 | receptor regulator activity | 0.43 | 0.027947 | 1.15E-06 | 1.17E-05 | 4.63E-06 | *CXCL6/CXCL1/CXCL3/CXCL2/SPP1/LIF* | 6 |
| GO:0048018 | receptor ligand activity | 0.43 | 0.026276 | 8.00E-07 | 9.76E-06 | 3.87E-06 | *CXCL6/CXCL1/CXCL3/CXCL2/SPP1/LIF* | 6 |
| GO:0005125 | cytokine activity | 0.43 | 0.012677 | 1.07E-08 | 3.26E-07 | 1.30E-07 | *CXCL6/CXCL1/CXCL3/CXCL2/SPP1/LIF* | 6 |
| GO:0005126 | cytokine receptor binding | 0.36 | 0.015443 | 1.51E-06 | 1.32E-05 | 5.23E-06 | *CXCL6/CXCL1/CXCL3/CXCL2/LIF* | 5 |
| GO:0001228 | transcriptional activator activity, RNA polymerase II transcription regulatory region | 0.29 | 0.023683 | 2.57E-04 | 1.74E-03 | 6.91E-04 | *JUN/EGR1/KLF6/SPIB* | 4 |
| GO:0001664 | G-protein coupled receptor binding | 0.29 | 0.015097 | 4.51E-05 | 3.44E-04 | 1.37E-04 | *CXCL6/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0042379 | chemokine receptor binding | 0.29 | 0.003457 | 1.26E-07 | 1.92E-06 | 7.62E-07 | *CXCL6/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0008009 | chemokine activity | 0.29 | 0.002766 | 5.05E-08 | 1.03E-06 | 4.08E-07 | *CXCL6/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0045236 | CXCR chemokine receptor binding | 0.29 | 0.000922 | 4.80E-10 | 2.93E-08 | 1.16E-08 | *CXCL6/CXCL1/CXCL3/CXCL2* | 4 |
| GO:0000982 | transcriptional activator activity, RNA polymerase II core promoter proximal region sequence | 0.21 | 0.023049 | 3.66E-03 | 1.49E-02 | 5.91E-03 | *JUN/EGR1/KLF6* | 3 |
| GO:0001158 | enhancer sequence-specific DNA binding | 0.14 | 0.005301 | 2.43E-03 | 1.23E-02 | 4.90E-03 | *JUN/SPIB* | 2 |
| GO:0000980 | RNA polymerase II distal enhancer sequence-specific DNA binding | 0.14 | 0.004149 | 1.50E-03 | 8.29E-03 | 3.29E-03 | *JUN/SPIB* | 2 |
| GO:0070412 | R-SMAD binding | 0.07 | 0.001325 | 1.84E-02 | 4.68E-02 | 1.86E-02 | *JUN* | 1 |
| GO:0001965 | G-protein alpha-subunit binding | 0.07 | 0.001095 | 1.52E-02 | 4.04E-02 | 1.60E-02 | *RGS1* | 1 |
| GO:0071837 | HMG box domain binding | 0.07 | 0.001037 | 1.44E-02 | 4.00E-02 | 1.59E-02 | *JUN* | 1 |
| GO:0001134 | transcription factor activity, transcription factor recruiting | 0.07 | 0.000807 | 1.12E-02 | 3.26E-02 | 1.30E-02 | *LIF* | 1 |
| GO:0033549 | MAP kinase phosphatase activity | 0.07 | 0.000807 | 1.12E-02 | 3.26E-02 | 1.30E-02 | *DUSP6* | 1 |
| GO:0017017 | MAP kinase tyrosine/serine/threonine phosphatase activity | 0.07 | 0.000749 | 1.04E-02 | 3.26E-02 | 1.30E-02 | *DUSP6* | 1 |
| GO:0035497 | cAMP response element binding | 0.07 | 0.000749 | 1.04E-02 | 3.26E-02 | 1.30E-02 | *JUN* | 1 |