



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

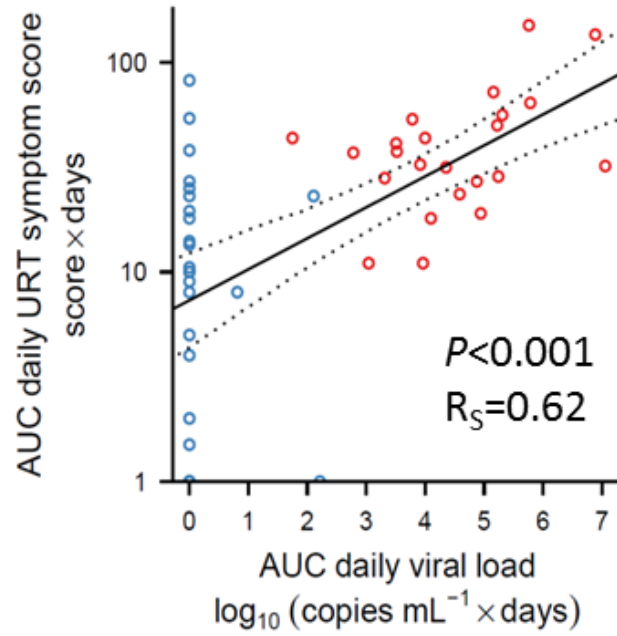


Fig. S1: Correlation between total upper respiratory tract symptom scores and viral load.

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.

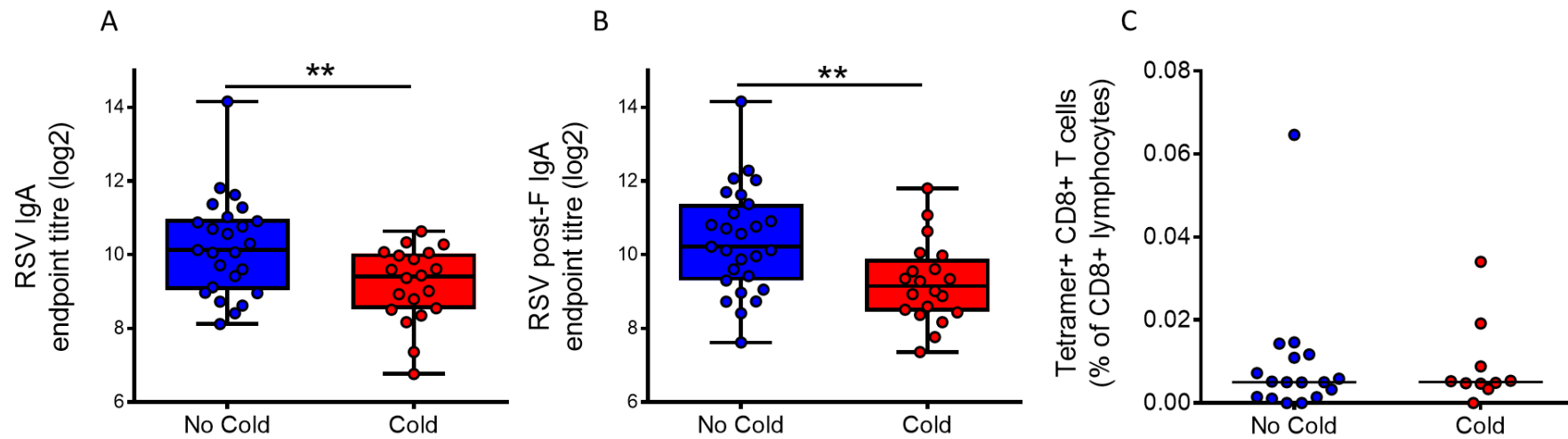


Fig. S2: Pre-inoculation nasal anti-RSV antibody levels, but not anti-RSV CD8⁺ T cell proportions, are associated with protection from infection.

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.

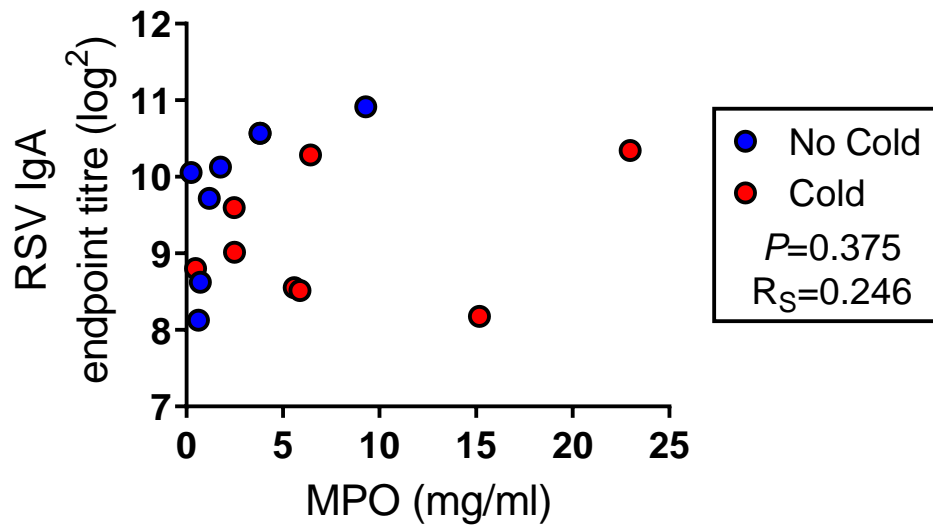


Fig. S3: Pre-inoculation nasal anti-RSV antibody levels are not associated with measures of neutrophilic inflammation.

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.

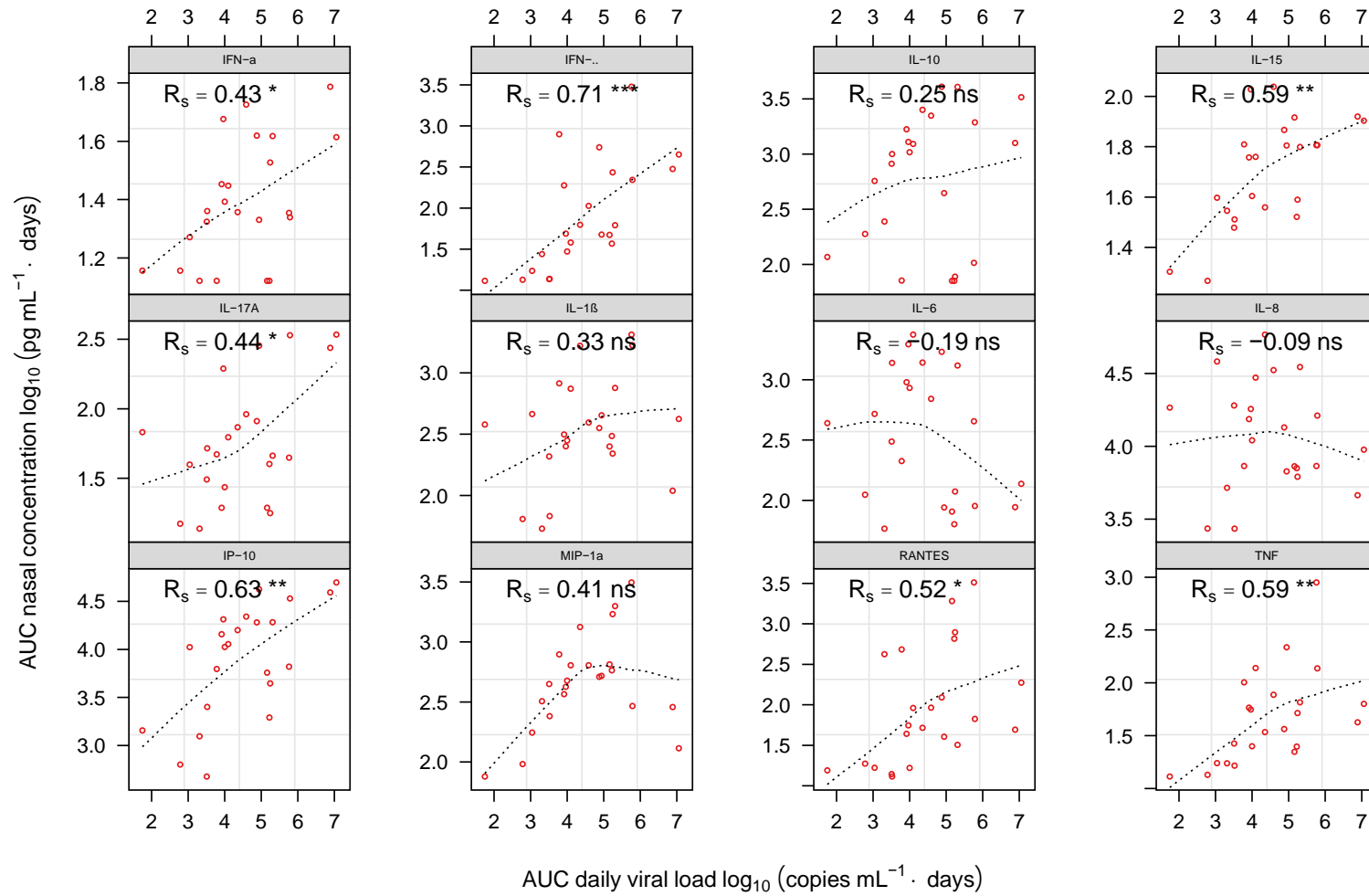


Fig. S4: Cumulative viral load correlates with the levels of several inflammatory mediators.

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-1 β , (F) CCL3/MIP-1 α , (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.

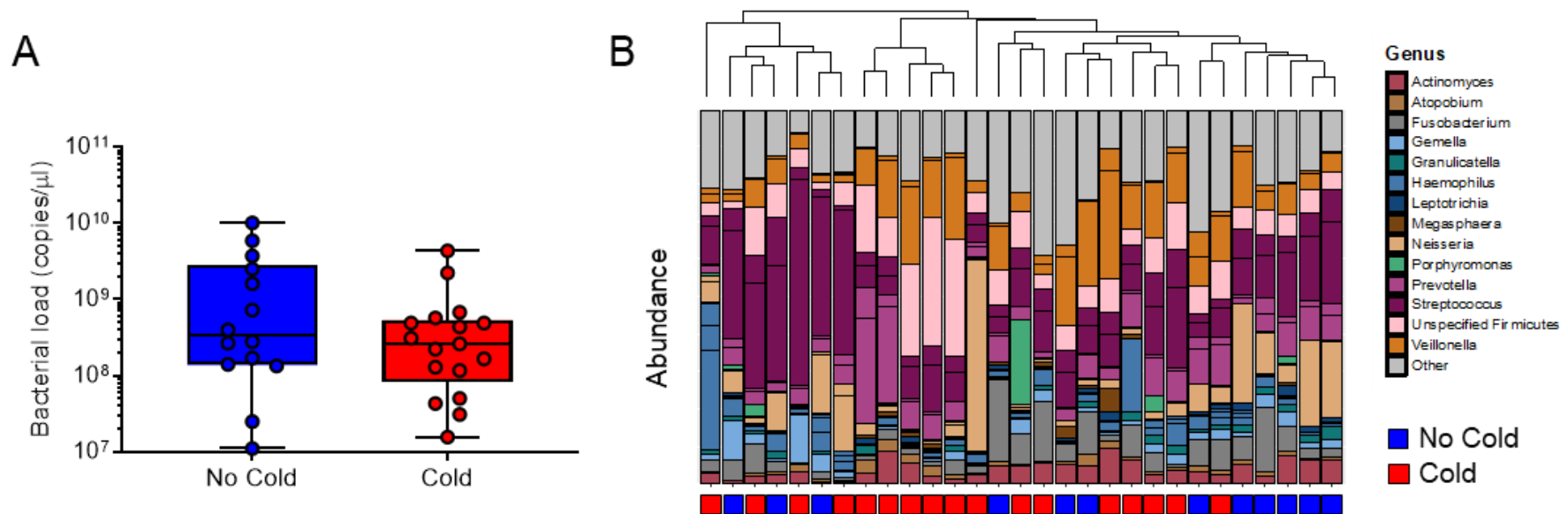
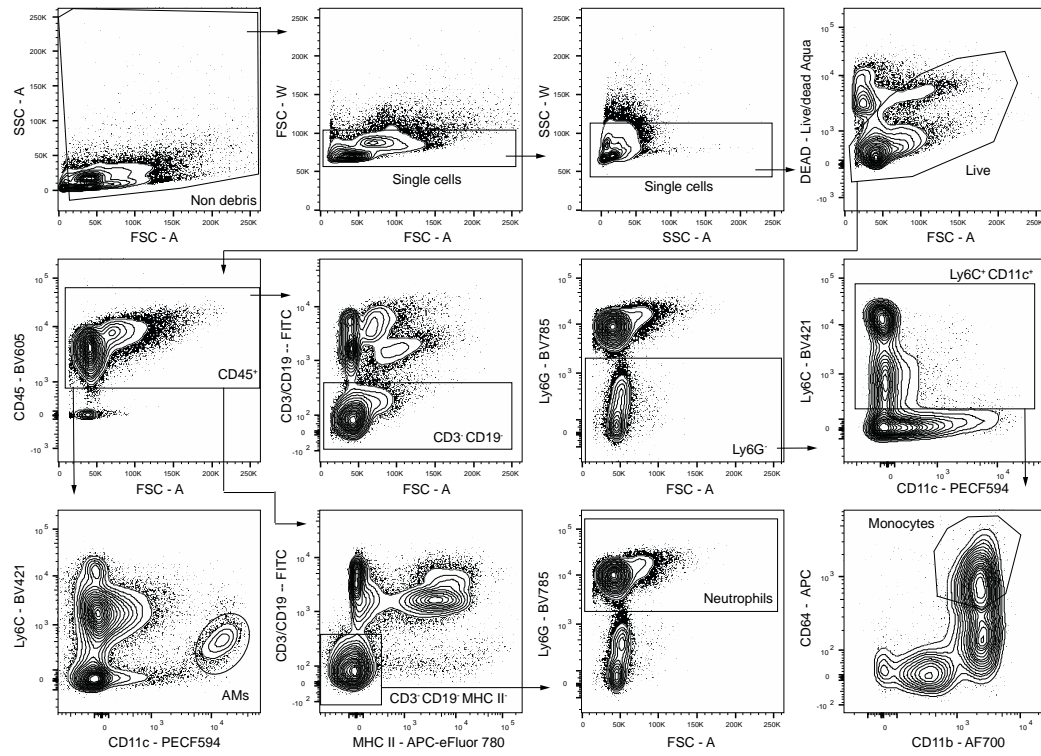


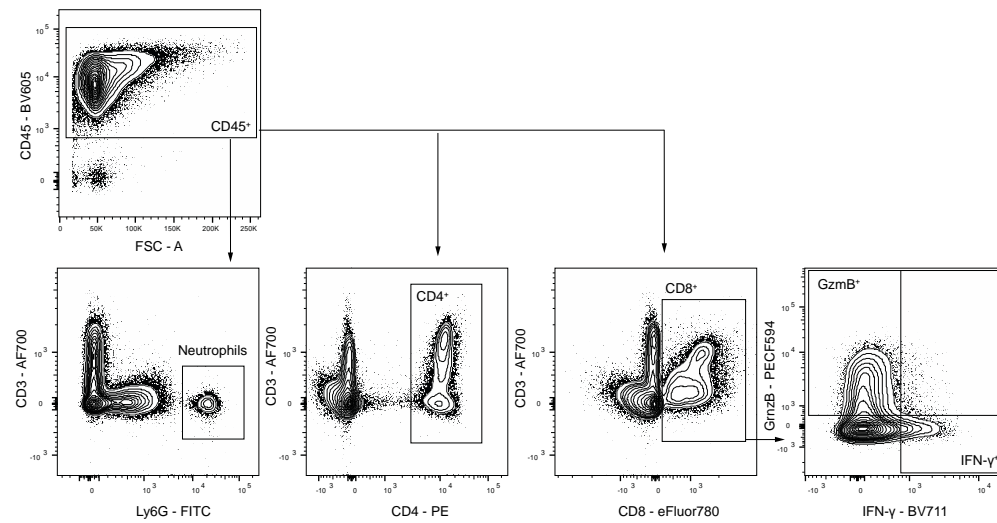
Fig. S5: The airway microbiome at point of virus exposure is not associated with susceptibility to infection.

(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)

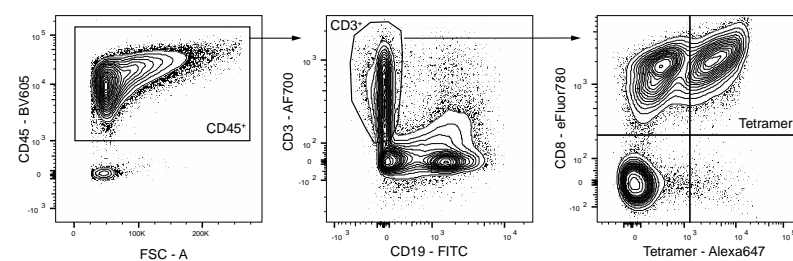


Fig. S6: Gating strategies for identifying murine lung cells.

(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.

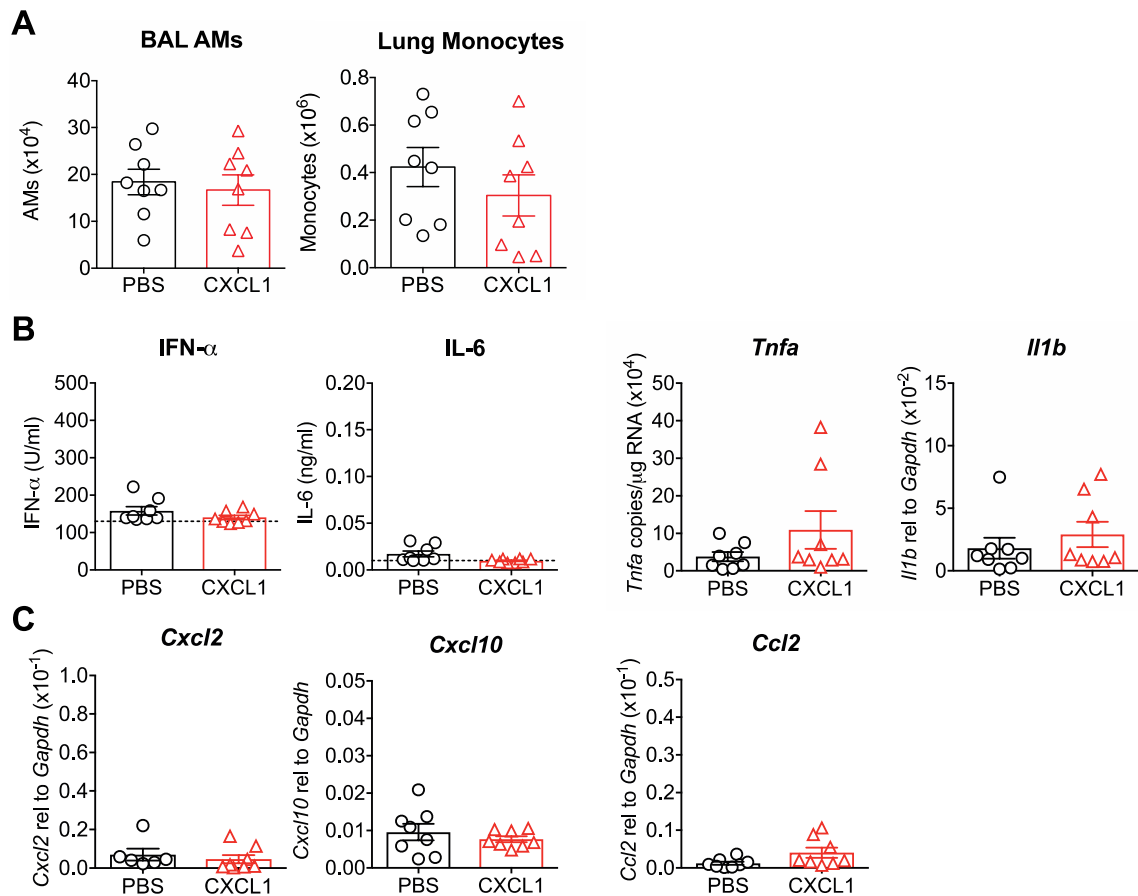


Fig. S7: Treatment with rCXCL1 alone causes no change in alveolar macrophages, monocytes or inflammatory mediators in the lung.

Mice were treated with mock (PBS) or 10 μ g 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 \pm 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.

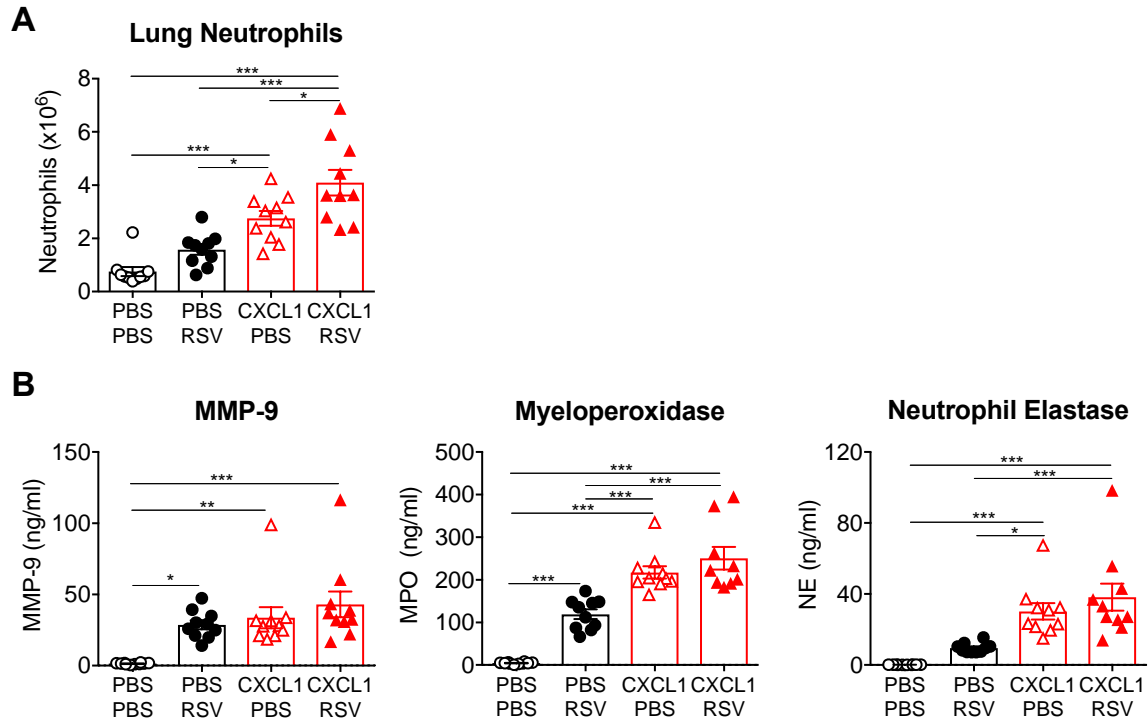


Fig. S8: RSV infection of rCXCL1 pre-treated mice enhances the early production of neutrophil markers.

Mice were treated with mock (PBS) or 5 μ g 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 \pm 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. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

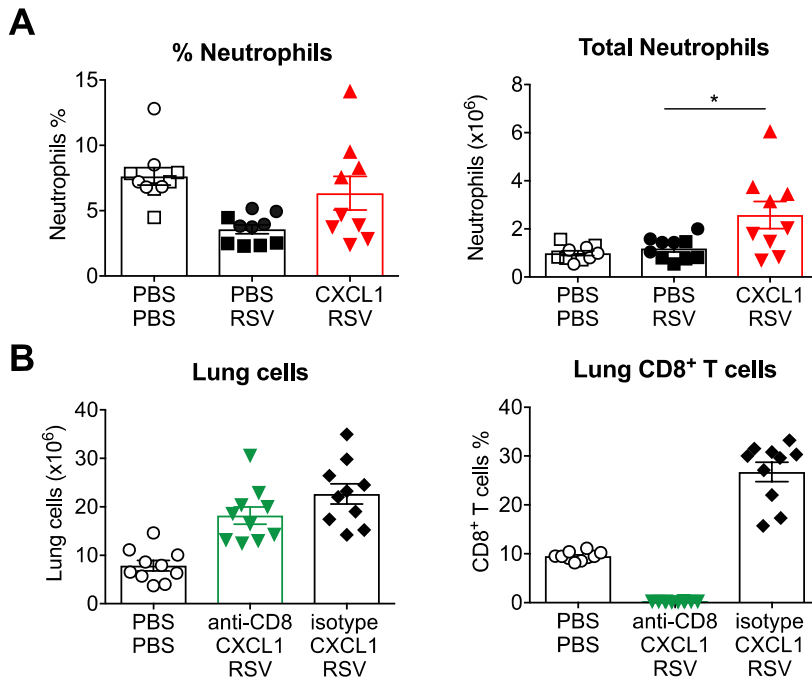


Fig. S9: Treatment with rCXCL1 pre-RSV infection does not result in an increase in neutrophil frequency on day 8 p.i. and treatment with anti-CD8 antibodies is sufficient to remove CD8⁺ T cells during RSV infection.

Mice were treated with mock (PBS) or 8 μ g or 10 μ g 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 μ g 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 \pm SEM of 10 (PBS/PBS, PBS/RSV) or 9 (CXCL1/RSV) mice, pooled from two independent experiments - repeat 1 (10 μ g CXCL1; circles) and repeat 2 (8 μ g CXCL1; squares). Data from (B) are presented as mean \pm 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)	<i>P</i> -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	Pvalue	Padj
ENSG00000129455	<i>KLK8</i>	64.04073471	4.50463631	0.725538	6.208681	0.0000000005	0.0000078
ENSG00000140519	<i>RHCG</i>	327.2661994	3.899687376	0.687333	5.673651	0.0000000140	0.0001025
ENSG00000143536	<i>CRNN</i>	717.7315072	3.961919136	0.710893	5.573155	0.0000000250	0.0001124
ENSG00000136688	<i>IL36G</i>	119.3575404	3.485458598	0.629406	5.537698	0.0000000306	0.0001124
ENSG00000203785	<i>SPRR2E</i>	549.5597617	3.759191643	0.694542	5.412479	0.0000000622	0.0001823
ENSG00000244617	<i>ASPRV1</i>	201.6683348	2.541982486	0.473897	5.363995	0.0000000814	0.0001990
ENSG00000163216	<i>SPRR2D</i>	493.240127	3.489918519	0.673736	5.179946	0.0000002219	0.0004651
ENSG00000172137	<i>CALB2</i>	7.432513115	3.827424619	0.744758	5.139154	0.0000002760	0.0005060
ENSG00000102837	<i>OLFM4</i>	9.018542922	2.379694573	0.485505	4.901481	0.0000009512	0.0015502
ENSG00000164867	<i>NOS3</i>	39.06236907	2.172068356	0.455328	4.770338	0.0000018392	0.0024524
ENSG00000104327	<i>CALB1</i>	97.2215325	3.213472664	0.672135	4.780991	0.0000017443	0.0024524
ENSG00000145879	<i>SPINK7</i>	214.5721968	3.777459369	0.795095	4.750953	0.0000020246	0.0024747
ENSG00000167755	<i>KLK6</i>	219.7775905	3.749018528	0.793685	4.723561	0.0000023175	0.0026149
ENSG00000143369	<i>ECM1</i>	368.3426926	2.548748229	0.543078	4.693155	0.0000026902	0.0028186
ENSG00000088386	<i>SLC15A1</i>	58.06521529	1.444700757	0.309249	4.671646	0.0000029880	0.0029218
ENSG00000167754	<i>KLK5</i>	58.04069283	4.183165833	0.901151	4.642025	0.0000034501	0.0031629
ENSG00000244094	<i>SPRR2F</i>	174.9314565	3.559094351	0.769266	4.62661	0.0000037170	0.0032071
ENSG00000197948	<i>FCHSD1</i>	433.0477186	0.555918016	0.122298	4.545597	0.0000054780	0.0044639
ENSG00000188508	<i>KRTDAP</i>	56.82226766	4.12052942	0.913535	4.510532	0.0000064665	0.0049922
ENSG00000165799	<i>RNASE7</i>	76.05592952	2.591086011	0.578846	4.476294	0.0000075950	0.0055702
ENSG00000158825	<i>CDA</i>	31.30464651	3.126427907	0.70532	4.432636	0.0000093088	0.0060990
ENSG00000172005	<i>MAL</i>	315.8263003	2.780102998	0.629321	4.417623	0.0000099792	0.0060990
ENSG00000188100	<i>FAM25A</i>	52.79654449	3.385115694	0.766093	4.418675	0.0000099308	0.0060990
ENSG00000178734	<i>LMO7DN</i>	7.032824408	2.363797695	0.534435	4.422982	0.0000097348	0.0060990
ENSG00000256618	<i>MTRNR2L1</i>	31.19207611	4.405844562	1.017059	4.331946	0.0000147797	0.0078477
ENSG00000166396	<i>SERPINB7</i>	133.8826024	1.568727074	0.362378	4.328974	0.0000149805	0.0078477
ENSG00000105427	<i>CNFN</i>	357.4556348	2.628314998	0.606082	4.336567	0.0000144726	0.0078477
ENSG00000169035	<i>KLK7</i>	460.4004676	3.236932356	0.746379	4.336849	0.0000144540	0.0078477
ENSG00000177243	<i>DEFB103B</i>	12.86752713	4.068667323	0.94596	4.301099	0.0000169953	0.0083096
ENSG00000176797	<i>DEFB103A</i>	12.86752713	4.068667323	0.94596	4.301099	0.0000169953	0.0083096
ENSG00000196805	<i>SPRR2B</i>	12.46642556	4.007415528	0.94584	4.236884	0.0000226643	0.0105675
ENSG00000255823	<i>MTRNR2L8</i>	99.96331934	-2.063829514	0.487551	-4.23305	0.0000230542	0.0105675
ENSG00000185966	<i>LCE3E</i>	18.55284064	4.403689631	1.044843	4.214692	0.0000250120	0.0111174
ENSG00000269741	<i>KLK9</i>	38.39528424	3.634649191	0.869249	4.181368	0.0000289761	0.0125006
ENSG00000163202	<i>LCE3D</i>	21.85709696	3.766259743	0.907597	4.149703	0.0000332906	0.0136037
ENSG00000172382	<i>PRSS27</i>	235.5149533	2.146835495	0.51743	4.149036	0.0000333878	0.0136037
ENSG00000265590	<i>AP000275.65</i>	13.45435781	-2.313482025	0.565829	-4.08866	0.0000433880	0.0172004
ENSG00000163221	<i>S100A12</i>	117.0760162	2.42404596	0.595909	4.067813	0.0000474564	0.0183182
ENSG00000115602	<i>IL1RL1</i>	44.99164745	2.186332063	0.544735	4.01357	0.0000598072	0.0224936
ENSG00000185873	<i>TMPRSS11B</i>	162.1426424	2.930935532	0.738498	3.968781	0.0000722414	0.0264909
ENSG00000183307	<i>CECR6</i>	16.55877878	1.882385854	0.478856	3.93101	0.0000845897	0.0302625
ENSG00000178172	<i>SPINK6</i>	11.19634078	3.736066016	0.960846	3.88831	0.0001009446	0.0352537

ENSG00000169509	<i>CRCT1</i>	124.6713786	3.255307448	0.839868	3.875975	0.0001061984	0.0353209
ENSG00000087128	<i>TMPRSS11E</i>	856.279728	2.335954629	0.603236	3.872373	0.0001077807	0.0353209
ENSG00000235568	<i>NFAM1</i>	385.2546016	2.109095274	0.544836	3.871064	0.0001083611	0.0353209
ENSG00000143631	<i>FLG</i>	60.85365689	2.707724203	0.703833	3.847112	0.0001195184	0.0381108
ENSG00000059728	<i>MXD1</i>	3049.682399	1.568764572	0.411317	3.814	0.0001367357	0.0407370
ENSG00000204421	<i>LY6G6C</i>	11.23753312	2.015579995	0.530386	3.800212	0.0001445722	0.0407370
ENSG00000137558	<i>PII5</i>	7.292990874	2.650754443	0.696318	3.806818	0.0001407663	0.0407370
ENSG00000188373	<i>C10orf99</i>	11.24888949	3.740112396	0.980735	3.813582	0.0001369669	0.0407370
ENSG00000125910	<i>SIPR4</i>	174.6183595	2.16060284	0.569216	3.795754	0.0001471953	0.0407370
ENSG00000186474	<i>KLK12</i>	66.90156166	2.810027115	0.739856	3.798075	0.0001458243	0.0407370
ENSG00000101210	<i>EEF1A2</i>	8.860473621	1.927591183	0.50611	3.808641	0.0001397326	0.0407370
ENSG00000261272	<i>MUC22</i>	53.13744678	2.376412656	0.628685	3.779973	0.0001568455	0.0418293
ENSG00000154262	<i>ABCA6</i>	91.04472433	0.918131079	0.242831	3.780947	0.0001562332	0.0418293
ENSG00000162384	<i>C1orf123</i>	400.5115764	-0.274660048	0.072946	-3.76525	0.0001663849	0.0435810
ENSG00000180871	<i>CXCR2</i>	559.0871712	2.296300313	0.613115	3.745302	0.0001801766	0.0447868
ENSG00000196549	<i>MME</i>	223.9783358	2.350426949	0.628268	3.74112	0.0001832022	0.0447868
ENSG00000136943	<i>CTSV</i>	169.9791044	1.651903131	0.441093	3.745024	0.0001803766	0.0447868
ENSG00000204020	<i>LIPN</i>	40.67847121	2.99211748	0.797534	3.751711	0.0001756320	0.0447868
ENSG00000135636	<i>DYSF</i>	374.8411619	2.317309474	0.621536	3.728362	0.0001927284	0.0462954
ENSG00000113749	<i>HRH2</i>	69.49149917	2.193258848	0.588972	3.723878	0.0001961854	0.0462954
ENSG00000204021	<i>LIPK</i>	6.857510391	2.959242988	0.798168	3.707544	0.0002092793	0.0462954
ENSG00000068976	<i>PYGM</i>	17.33765035	2.050543859	0.552144	3.713782	0.0002041850	0.0462954
ENSG00000211448	<i>DIO2</i>	155.321791	1.510686245	0.406436	3.716914	0.0002016710	0.0462954
ENSG00000128917	<i>DLL4</i>	11.45535912	2.447852976	0.660082	3.708409	0.0002085653	0.0462954
ENSG00000188897	<i>CTD-308G3.8</i>	323.1906061	1.78061636	0.480706	3.70417	0.0002120839	0.0462954
ENSG00000125810	<i>CD93</i>	601.1405142	1.759188231	0.475308	3.701152	0.0002146229	0.0462954
ENSG00000178150	<i>ZNF114</i>	7.989085047	2.029484872	0.549584	3.692762	0.0002218314	0.0471569
ENSG00000149564	<i>ESAM</i>	18.14827649	1.523369052	0.41299	3.688637	0.0002254587	0.0472433
ENSG00000203710	<i>CRI</i>	411.1933018	2.299624216	0.627107	3.667037	0.0002453771	0.0481389
ENSG00000163464	<i>CXCR1</i>	453.8760438	2.616490966	0.712521	3.672159	0.0002405100	0.0481389
ENSG00000120129	<i>DUSP1</i>	6115.128063	1.732263316	0.473872	3.655551	0.0002566297	0.0481389
ENSG00000152137	<i>HSPB8</i>	900.9324017	1.778499688	0.487281	3.649845	0.0002623991	0.0481389
ENSG00000184508	<i>HDDC3</i>	101.6802136	-0.391065227	0.106941	-3.65684	0.0002553462	0.0481389
ENSG00000206172	<i>HBA1</i>	9.437796303	3.255644841	0.885269	3.677576	0.0002354608	0.0481389
ENSG00000141096	<i>DPEP3</i>	8.922090167	2.600257498	0.709629	3.66425	0.0002480641	0.0481389
ENSG00000076662	<i>ICAM3</i>	139.9038075	2.270536264	0.620081	3.661675	0.0002505716	0.0481389
ENSG00000244482	<i>LILRA6</i>	189.3604241	2.418416833	0.662635	3.649695	0.0002625518	0.0481389
ENSG00000170373	<i>CST1</i>	131.6759055	-3.542321735	0.97027	-3.65086	0.0002613632	0.0481389
ENSG00000171476	<i>HOPX</i>	495.7867843	1.529493784	0.420797	3.634752	0.0002782483	0.0503870
ENSG00000254415	<i>SIGLEC14</i>	45.14160974	1.877309137	0.517712	3.626168	0.0002876585	0.0514558
ENSG00000081237	<i>PTPRC</i>	4546.785921	1.738982361	0.480872	3.616312	0.0002988305	0.0519840
ENSG00000107736	<i>CDH23</i>	109.6230575	0.860731249	0.238059	3.615619	0.0002996305	0.0519840
ENSG00000142347	<i>MYO1F</i>	1440.496128	1.976436605	0.546849	3.614228	0.0003012436	0.0519840
ENSG00000188404	<i>SELL</i>	592.631915	1.4423354	0.40133	3.593889	0.0003257790	0.0523150

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

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

ENSG00000133246	<i>PRAMI</i>	42.79085834	1.154190513	0.346598	3.330052	0.0008682973	0.0732848
ENSG00000198053	<i>SIRPA</i>	520.3180461	1.149634662	0.345046	3.331828	0.0008627758	0.0732848
ENSG00000163209	<i>SPRR3</i>	9398.66207	1.892942748	0.569654	3.32297	0.0008906446	0.0733931
ENSG00000188305	<i>C19orf35</i>	14.74118642	2.027840744	0.610195	3.323266	0.0008897002	0.0733931
ENSG00000115590	<i>ILIR2</i>	359.8218257	2.191449718	0.661145	3.31463	0.0009176438	0.0747778
ENSG00000124882	<i>EREG</i>	227.0051715	1.760952973	0.531171	3.315229	0.0009156795	0.0747778
ENSG00000113070	<i>HBEGF</i>	280.9775264	1.604054578	0.484422	3.311273	0.0009287250	0.0752626
ENSG00000178726	<i>THBD</i>	569.6998692	2.072148166	0.626151	3.30934	0.0009351605	0.0753678
ENSG00000197943	<i>PLCG2</i>	550.1524259	0.988242075	0.299196	3.302994	0.0009565855	0.0766732
ENSG00000162572	<i>SCNN1D</i>	52.00949878	0.779800895	0.236387	3.298826	0.0009709006	0.0768620
ENSG00000158887	<i>MPZ</i>	43.30825426	1.239879961	0.376097	3.296706	0.0009782593	0.0768620
ENSG00000214113	<i>LYRM4</i>	209.8049346	-0.386119827	0.117153	-3.29586	0.0009811975	0.0768620
ENSG00000151948	<i>GLT1D1</i>	194.0027529	2.453177853	0.744772	3.293865	0.0009882004	0.0768620
ENSG00000141527	<i>CARD14</i>	189.6181425	0.664607081	0.201809	3.293245	0.0009903816	0.0768620
ENSG00000198342	<i>ZNF442</i>	55.29332415	-0.633468395	0.191935	-3.30043	0.0009653628	0.0768620
ENSG00000163218	<i>PGLYRP4</i>	35.40514359	1.507393971	0.45914	3.283079	0.0010267976	0.0792688
ENSG00000130475	<i>FCHO1</i>	85.17477418	1.396035122	0.426313	3.274673	0.0010578446	0.0812380
ENSG00000167759	<i>KLK13</i>	432.5007784	2.177708944	0.667258	3.263671	0.0010997881	0.0840192
ENSG00000143546	<i>SI00A8</i>	10686.37567	2.151083123	0.659681	3.260795	0.0011110021	0.0843267
ENSG00000213347	<i>MXD3</i>	159.4639724	1.254876515	0.385071	3.25882	0.0011187671	0.0843267
ENSG00000101336	<i>HCK</i>	871.1965188	1.616043212	0.495987	3.258239	0.0011210598	0.0843267
ENSG00000204542	<i>C6orf15</i>	6.203863346	3.043601347	0.935576	3.253185	0.0011411927	0.0853732
ENSG00000110203	<i>FOLR3</i>	10.09684646	2.947475316	0.906403	3.251838	0.0011466131	0.0853732
ENSG00000062282	<i>DGAT2</i>	385.1136643	1.889009237	0.582431	3.243316	0.0011814721	0.0875244
ENSG00000133710	<i>SPINK5</i>	1396.236797	1.523517868	0.47005	3.241184	0.0011903453	0.0877386
ENSG00000119535	<i>CSF3R</i>	3574.954552	2.277942108	0.706229	3.225502	0.0012575197	0.0899771
ENSG00000159516	<i>SPRR2G</i>	8.900936315	2.970580876	0.920519	3.22707	0.0012506472	0.0899771
ENSG00000154429	<i>CCSAP</i>	160.9765066	0.524627084	0.162647	3.225554	0.0012572927	0.0899771
ENSG00000188549	<i>C15orf52</i>	151.2467778	0.785723445	0.243249	3.23012	0.0012373831	0.0899771
ENSG00000160255	<i>ITGB2</i>	1285.404679	1.207525803	0.373976	3.22889	0.0012427170	0.0899771
ENSG00000173638	<i>SLC19A1</i>	147.9920447	1.589686916	0.492758	3.2261	0.0012548962	0.0899771
ENSG00000155307	<i>SAMSN1</i>	447.0759092	1.459101124	0.453116	3.220151	0.0012812317	0.0912287
ENSG00000162747	<i>FCGR3B</i>	1127.66368	2.265580387	0.706557	3.206507	0.0013435703	0.0915786
ENSG00000168918	<i>INPP5D</i>	539.7586028	0.759423223	0.236774	3.207374	0.0013395295	0.0915786
ENSG00000188001	<i>TPRG1</i>	146.6351541	0.982323984	0.305399	3.216525	0.0012975312	0.0915786
ENSG00000120318	<i>ARAP3</i>	312.6943691	0.880062277	0.274794	3.202629	0.0013617921	0.0915786
ENSG00000152926	<i>ZNF117</i>	700.4702591	0.667203224	0.208406	3.201464	0.0013673106	0.0915786
ENSG00000059377	<i>TBXAS1</i>	356.7962638	1.33421913	0.415333	3.212407	0.0013162757	0.0915786
ENSG00000187479	<i>C11orf96</i>	14.69699214	1.958308711	0.611243	3.203816	0.0013561901	0.0915786
ENSG00000171310	<i>CHST11</i>	408.7728418	1.186643045	0.370603	3.201929	0.0013651076	0.0915786
ENSG00000131471	<i>AOC3</i>	22.77300856	1.226591369	0.381778	3.212835	0.0013143161	0.0915786
ENSG00000173868	<i>PHOSPHO1</i>	209.3184166	2.627190768	0.818348	3.21036	0.0013256865	0.0915786
ENSG00000160229	<i>ZNF66</i>	56.13988521	0.87651468	0.273497	3.204843	0.0013513616	0.0915786
ENSG00000188505	<i>NCCRP1</i>	649.3820155	1.424720362	0.443692	3.211057	0.0013224755	0.0915786

ENSG00000100985	<i>MMP9</i>	105.0085456	1.801939784	0.560903	3.212569	0.0013155353	0.0915786
ENSG00000189056	<i>RELN</i>	20.41484416	1.821826465	0.570354	3.194201	0.0014021827	0.0934873
ENSG00000130592	<i>LSP1</i>	1872.970387	0.886506466	0.277959	3.189347	0.0014259475	0.0946416
ENSG00000106541	<i>AGR2</i>	41664.02551	-0.714062434	0.224157	-3.18555	0.0014447875	0.0954601
ENSG00000104894	<i>CD37</i>	157.4882807	1.249881462	0.393085	3.179671	0.0014744245	0.0969814
ENSG00000146112	<i>PPP1R18</i>	570.9228967	1.216818205	0.382862	3.178213	0.0014818607	0.0970354
ENSG00000112137	<i>PHACTR1</i>	270.347717	1.480915393	0.466756	3.17278	0.0015098686	0.0970487
ENSG00000112195	<i>TREML2</i>	177.9198685	2.368986837	0.747134	3.170764	0.0015203883	0.0970487
ENSG00000170423	<i>KRT78</i>	380.5887664	1.924890584	0.607367	3.169241	0.0015283781	0.0970487
ENSG00000188215	<i>DCUN1D3</i>	490.9316317	0.865486098	0.27282	3.172375	0.0015119764	0.0970487
ENSG00000101236	<i>RNF24</i>	802.5230879	0.95210711	0.300246	3.171085	0.0015187079	0.0970487
ENSG00000087589	<i>CASS4</i>	294.9893157	1.73106507	0.544957	3.176515	0.0014905605	0.0970487
ENSG00000147168	<i>IL2RG</i>	270.2098958	0.933031134	0.294288	3.170466	0.0015219465	0.0970487
ENSG00000125378	<i>BMP4</i>	17.60094942	-1.212353032	0.38289	-3.16632	0.0015438084	0.0976060
ENSG00000111052	<i>LIN7A</i>	40.68503686	1.801629323	0.569401	3.164079	0.0015557467	0.0979386
ENSG00000115935	<i>WIPF1</i>	622.5961766	1.143319049	0.361607	3.161768	0.0015681439	0.0982972
ENSG00000126233	<i>SLURP1</i>	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	Pvalue	P.adjust	qvalue	geneID	Count
GO:0042119	neutrophil activation	0.157895	0.028536908	1.06E-15	2.36E-12	2.11E-12	<i>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</i>	33
GO:0002283	neutrophil activation involved in immune response	0.15311	0.027961567	4.04E-15	3.89E-12	3.48E-12	<i>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</i>	32
GO:0002446	neutrophil mediated immunity	0.148325	0.02870951	5.47E-14	3.16E-11	2.83E-11	<i>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</i>	31
GO:0043312	neutrophil degranulation	0.148325	0.027904033	2.54E-14	1.84E-11	1.64E-11	<i>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</i>	31
GO:0008544	epidermis development	0.138756	0.02617801	2.02E-13	9.74E-11	8.70E-11	<i>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</i>	29
GO:0050900	leukocyte migration	0.133971	0.027098556	2.94E-12	1.06E-09	9.50E-10	<i>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</i>	28
GO:0043588	skin development	0.119617	0.023646511	2.89E-11	7.61E-09	6.80E-09	<i>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</i>	25
GO:0009913	epidermal cell differentiation	0.114833	0.020079397	5.69E-12	1.65E-09	1.47E-09	<i>FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/EREG/SPINK5/SPINK6/CTSV/LIPK/LIPN/KRT78/BMP4/KRT24/ZFP36/CNFN/KLK5/KLK8/KLK12/KLK13</i>	24
GO:0030216	keratinocyte differentiation	0.110048	0.017260227	1.74E-12	7.18E-10	6.42E-10	<i>FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/EREG/SPINK5/SPINK6/CTSV/LIPK/LIPN/KRT78/KRT24/ZFP36/CNFN/KLK5/KLK8/KLK12/KLK13</i>	23
GO:0031424	keratinization	0.095694	0.013002704	3.83E-12	1.23E-09	1.10E-09	<i>FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/SPINK5/SPINK6/LIPK/LIPN/KRT78/KRT24/CNFN/KLK5/KLK8/KLK12/KLK13</i>	20

GO:0070268	cornification	0.086124	0.006501352	1.63E-15	2.36E-12	2.11E-12	<i>FLG/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F/SPRR2G/SPINK5/SPINK6/LIPK/LIPN/KRT78/KRT24/KLK5/KLK8/KLK12/KLK13</i>	18
GO:0097530	granulocyte migration	0.062201	0.007134227	3.21E-09	7.75E-07	6.92E-07	<i>PIK3CD/CSF3R/S100A12/S100A8/IL1A/CXCR2/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA</i>	13
GO:0002521	leukocyte differentiation	0.090909	0.027558829	5.55E-06	7.65E-04	6.83E-04	<i>PIK3CD/PTPRC/CR1/ZFP36L2/INPP5D/EGR1/SPINK5/AGER/PRDM1/SPI1/GAB2/BMP4/DLL4/PLCG2/EVI2B/TGFB1/MMP9/PREX1/NFAM1</i>	19
GO:0002768	immune response-regulating cell surface receptor signaling pathway	0.08134	0.026350613	4.07E-05	3.37E-03	3.01E-03	<i>PIK3CD/THEMIS2/MNDA/PTPRC/CR1/WIPF1/INPP5D/FYB1/GAB2/PRKCB/PLCG2/ICAM3/C5AR1/LILRA2/HCK/NFAM1/WAS</i>	17
GO:0002429	immune response-activating cell surface receptor signaling pathway	0.076555	0.024509522	6.00E-05	4.34E-03	3.88E-03	<i>PIK3CD/THEMIS2/MNDA/PTPRC/CR1/WIPF1/INPP5D/FYB1/PRKCB/PLCG2/ICAM3/C5AR1/LILRA2/HCK/NFAM1/WAS</i>	16
GO:0042110	T cell activation	0.076555	0.02686842	1.74E-04	1.12E-02	9.99E-03	<i>PIK3CD/PTPRC/CR1/ZFP36L2/EGR1/SPINK5/AGER/TREML2/PRDM1/APBB1P/JAML/BMP4/DLL4/TGFB1/PREX1/WAS</i>	16
GO:0060326	cell chemotaxis	0.07177	0.015534204	9.89E-07	1.51E-04	1.35E-04	<i>PIK3CD/PADI2/CSF3R/S100A12/S100A8/CXCR2/CXCR1/CXCL2/HBEGF/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA</i>	15
GO:0030098	lymphocyte differentiation	0.07177	0.018871181	1.07E-05	1.23E-03	1.10E-03	<i>PIK3CD/PTPRC/CR1/ZFP36L2/INPP5D/EGR1/SPINK5/PRDM1/SPI1/BMP4/DLL4/PLCG2/TGFB1/PREX1/NFAM1</i>	15
GO:0031349	positive regulation of defense response	0.07177	0.025947874	3.80E-04	1.93E-02	1.72E-02	<i>PGLYRP4/S100A12/S100A8/NLRC4/IL1RL1/EREG/PLCG2/ICAM3/TGFB1/KLK5/KLK7/LILRA2/HCK/ITGB2/IL17RA</i>	15
GO:0040017	positive regulation of locomotion	0.07177	0.028191704	8.91E-04	3.30E-02	2.95E-02	<i>PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/AGER/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1</i>	15
GO:0030595	leukocyte chemotaxis	0.066986	0.01167942	1.70E-07	3.07E-05	2.75E-05	<i>PIK3CD/PADI2/CSF3R/S100A12/S100A8/CXCR2/CXCR1/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA</i>	14
GO:1901342	regulation of vasculature development	0.066986	0.017662965	2.18E-05	2.10E-03	1.88E-03	<i>ECM1/IL1A/CCR3/EGR1/SPINK5/NOS3/TEK/ITGA5/BMP4/DLL4/PRKCB/SERPINB7/C5AR1/ITGB2</i>	14
GO:0002697	regulation of immune effector process	0.066986	0.023128704	3.76E-04	1.93E-02	1.72E-02	<i>PTPRC/CR1/SPINK5/AGER/GAB2/UNC13D/PRAM1/ADGRE2/TGFB1/C5AR1/KLK5/KLK7/ITGB2/WAS</i>	14
GO:0051346	negative regulation of hydrolase activity	0.066986	0.024394454	6.37E-04	2.63E-02	2.35E-02	<i>ECM1/RGS2/CR1/NLRC4/SPINK5/SPINK6/SPINK7/NOS3/PII5/CST6/A2ML1/SERPINB7/CST1/MMP9</i>	14

GO:0052547	regulation of peptidase activity	0.066986	0.024509522	6.67E-04	2.72E-02	2.43E-02	<i>ECM1/S100A8/CR1/NLRC4/SPINK5/SPINK6/SPINK7/PII5/CST6/A2ML1/NLRP1/SERPINB7/CST1/MMP9</i>	14
GO:0030335	positive regulation of cell migration	0.066986	0.025430067	9.52E-04	3.37E-02	3.02E-02	<i>PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1</i>	14
GO:1903706	regulation of hemopoiesis	0.066986	0.025775272	1.08E-03	3.71E-02	3.32E-02	<i>CSF3R/CR1/ZFP36L2/INPP5D/SPINK5/AGER/PRDM1/SPI1/BMP4/PRKCB/EVI2B/ZFP36/TGFB1/NFAM1</i>	14
GO:2000147	positive regulation of cell motility	0.066986	0.026465681	1.39E-03	4.30E-02	3.84E-02	<i>PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1</i>	14
GO:0051272	positive regulation of cellular component movement	0.066986	0.027213624	1.80E-03	4.97E-02	4.44E-02	<i>PIK3CD/PTPRC/IL1A/CXCL2/HBEGF/RELN/TEK/ITGA5/BMP4/TGFB1/C5AR1/MMP9/PREX1/SNAI1</i>	14
GO:0097529	myeloid leukocyte migration	0.062201	0.010298602	2.61E-07	4.45E-05	3.98E-05	<i>PIK3CD/CSF3R/S100A12/S100A8/IL1A/CXCR2/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA</i>	13
GO:0042742	defense response to bacterium	0.062201	0.016684886	5.13E-05	3.81E-03	3.40E-03	<i>PGLYRP4/S100A12/S100A8/NLRC4/SPINK5/DEFB103B/DEFB103A/C10orf99/RNASE7/NLRP1/C5AR1/KLK5/KLK7</i>	13
GO:0045861	negative regulation of proteolysis	0.062201	0.020021863	3.13E-04	1.71E-02	1.53E-02	<i>ECM1/CR1/NLRC4/IL1R2/SPINK5/SPINK6/SPINK7/PII5/CST6/A2ML1/SERPINB7/CST1/MMP9</i>	13
GO:0030099	myeloid cell differentiation	0.062201	0.022438295	9.09E-04	3.32E-02	2.96E-02	<i>PIK3CD/CSF3R/INPP5D/SPI1/GAB2/FLI1/BMP4/PRKCB/EVI2B/RASGRP4/ZFP36/TGFB1/MMP9</i>	13
GO:0002683	negative regulation of immune system process	0.062201	0.023704045	1.49E-03	4.31E-02	3.85E-02	<i>PADI2/MNDA/PTPRC/CR1/IL1RL1/INPP5D/SPINK5/PRDM1/BMP4/ZFP36/TGFB1/LILRA2/SAMSN1</i>	13
GO:0071621	granulocyte chemotaxis	0.057416	0.00632875	8.34E-09	1.86E-06	1.66E-06	<i>PIK3CD/CSF3R/S100A12/S100A8/CXCR2/CXCL2/JAML/ADGRE2/C5AR1/PREX1/ITGB2/IL17RA</i>	12
GO:0010466	negative regulation of peptidase activity	0.057416	0.015131465	8.45E-05	5.82E-03	5.20E-03	<i>ECM1/CR1/NLRC4/SPINK5/SPINK6/SPINK7/PII5/CST6/A2ML1/SERPINB7/CST1/MMP9</i>	12
GO:0050673	epithelial cell proliferation	0.057416	0.020769806	1.46E-03	4.30E-02	3.84E-02	<i>ECM1/CCR3/EREG/SLURP1/TEK/JAML/BMP4/DLL4/ZFP36/TGFB1/C5AR1/KLK8</i>	12
GO:1990266	neutrophil migration	0.052632	0.005810943	3.61E-08	7.45E-06	6.66E-06	<i>PIK3CD/CSF3R/S100A12/S100A8/IL1A/CXCR2/CXCL2/JAML/C5AR1/PREX1/ITGB2</i>	11
GO:1904018	positive regulation of vasculature development	0.052632	0.009665727	6.07E-06	7.98E-04	7.13E-04	<i>ECM1/IL1A/CCR3/EGR1/NOS3/TEK/ITGA5/PRKCB/SERPINB7/C5AR1/ITGB2</i>	11
GO:0030217	T cell differentiation	0.052632	0.01294517	9.07E-05	6.11E-03	5.46E-03	<i>PIK3CD/PTPRC/CR1/ZFP36L2/EGR1/SPINK5/PRDM1/BMP4/DLL4/TGFB1/PREX1</i>	11
GO:0042113	B cell activation	0.052632	0.015591738	4.54E-04	2.15E-02	1.92E-02	<i>PIK3CD/MNDA/PTPRC/ZFP36L2/INPP5D/PRDM1/PRKCB/PLCG2/TGFB1/SAMSN1/NFAM1</i>	11
GO:0045765	regulation of angiogenesis	0.052632	0.015706806	4.83E-04	2.25E-02	2.01E-02	<i>ECM1/IL1A/CCR3/SPINK5/NOS3/TEK/ITGA5/DLL4/PRKCB/C5AR1/ITGB2</i>	11

GO:0032103	positive regulation of response to external stimulus	0.052632	0.016167079	6.14E-04	2.57E-02	2.30E-02	<i>S100A12/S100A8/IL1RL1/CXCL2/AGER/TGFB1/C5AR1/KLK5/KLK7/THBD/IL17RA</i>	11
GO:0050678	regulation of epithelial cell proliferation	0.052632	0.017662965	1.26E-03	4.01E-02	3.59E-02	<i>ECM1/CCR3/EREG/SLURP1/TEK/JAML/BMP4/DLL4/ZFP36/TGFB1/C5AR1</i>	11
GO:0032496	response to lipopolysaccharide	0.052632	0.018180772	1.59E-03	4.55E-02	4.06E-02	<i>S100A8/CXCL2/PRDM1/NOS3/PLCG2/ZFP36/TGFB1/C5AR1/LILRA2/THBD/HCK</i>	11
GO:0006959	humoral immune response	0.052632	0.018468443	1.80E-03	4.97E-02	4.44E-02	<i>PGLYRP4/S100A12/S100A8/CR1/SPINK5/DEFB103B/DEFB103A/RNASE7/C5AR1/KLK5/KLK7</i>	11
GO:0030593	neutrophil chemotaxis	0.047847	0.005178068	1.26E-07	2.43E-05	2.18E-05	<i>PIK3CD/CSF3R/S100A12/S100A8/CXCR2/CXCL2/JAML/C5AR1/PREX1/ITGB2</i>	10
GO:0002703	regulation of leukocyte mediated immunity	0.047847	0.009493125	3.15E-05	2.68E-03	2.40E-03	<i>PTPRC/CR1/AGER/GAB2/UNC13D/PRAM1/ADGRE2/TGFB1/ITGB2/WAS</i>	10
GO:0051091	positive regulation of DNA binding transcription factor activity	0.047847	0.014153386	8.11E-04	3.17E-02	2.83E-02	<i>S100A12/S100A8/NLRC4/AGER/RELN/PRKCB/CARD14/TGFB1/ITGB2/NFAM1</i>	10
GO:0010951	negative regulation of endopeptidase activity	0.047847	0.014383522	9.17E-04	3.32E-02	2.96E-02	<i>CR1/NLRC4/SPINK5/SPINK6/SPINK7/CST6/A2ML1/SERPIN7/CST1/MMP9</i>	10
GO:1902105	regulation of leukocyte differentiation	0.047847	0.014613659	1.03E-03	3.61E-02	3.22E-02	<i>CR1/ZFP36L2/INPP5D/SPINK5/AGER/PRDM1/BMP4/EVI2B/TGFB1/NFAM1</i>	10
GO:0050851	antigen receptor-mediated signaling pathway	0.047847	0.014786261	1.13E-03	3.80E-02	3.40E-02	<i>PIK3CD/THEMIS2/MNDA/PTPRC/INPP5D/FYB1/PRKCB/PLCG2/NFAM1/WAS</i>	10
GO:0019730	antimicrobial humoral response	0.043062	0.006041079	4.90E-06	7.09E-04	6.34E-04	<i>PGLYRP4/S100A12/S100A8/SPINK5/DEFB103B/DEFB103A/RNASE7/KLK5/KLK7</i>	9
GO:0045766	positive regulation of angiogenesis	0.043062	0.008457511	7.27E-05	5.13E-03	4.59E-03	<i>ECM1/IL1A/CCR3/NOS3/TEK/ITGA5/PRKCB/C5AR1/ITGB2</i>	9
GO:0018149	peptide cross-linking	0.038278	0.003394511	5.01E-07	8.05E-05	7.19E-05	<i>FLG/LCE3E/LCE3D/SPRR3/SPRR2D/SPRR2B/SPRR2E/SPRR2F</i>	8
GO:0051092	positive regulation of NF-kappaB transcription factor activity	0.038278	0.008054772	2.94E-04	1.64E-02	1.46E-02	<i>S100A12/S100A8/NLRC4/AGER/PRKCB/CARD14/TGFB1/ITGB2</i>	8
GO:0050864	regulation of B cell activation	0.038278	0.008917784	5.81E-04	2.51E-02	2.24E-02	<i>MNDA/PTPRC/ZFP36L2/INPP5D/PRDM1/TGFB1/SAMSN1/NFAM1</i>	8

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

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

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

GO:0072111	cell proliferation involved in kidney development	0.014354	0.001150682	1.68E- 03	4.76E- 02	4.26E- 02	<i>EGR1/BMP4/SERPINB7</i>	3
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Table S4: Molecular functions enriched at baseline between “Cold” and “No Cold” groups

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

Mediator (log ₁₀ pg/ml)	Cold (n=23, unless otherwise stated) Median	No Cold (n=25, unless otherwise stated) Median	<i>P</i> -value
IFN- α	0.046	0.046	0.176
IFN- β	1.866	0.856	0.617
IFN- γ	0	0	0.314
IL-1 β	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 (IP-10)	1.991	1.715	0.054
LCN-2	6.704 (n=10)	5.875 (n=9)	0.017*
MIP-1 α	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	Pvalue	Padj
ENSG00000268173	<i>AC007192.4</i>	34.09618	10.71285	1.946479	5.503707	3.72E-08	0.000546
ENSG00000163734	<i>CXCL3</i>	149.3781	1.440807	0.321685	4.478942	7.50E-06	0.055023
ENSG00000081041	<i>CXCL2</i>	174.802	1.436306	0.349674	4.107556	4.00E-05	0.195535
ENSG00000177606	<i>JUN</i>	1314.332	0.725754	0.189651	3.826781	0.00013	0.274872
ENSG00000163739	<i>CXCL1</i>	1567.606	1.058814	0.272342	3.887809	0.000101	0.274872
ENSG00000159231	<i>CBR3</i>	89.53077	-0.80421	0.21029	-3.82427	0.000131	0.274872
ENSG00000140519	<i>RHCG</i>	205.5315	2.384514	0.629577	3.787487	0.000152	0.279058
ENSG00000143536	<i>CRNN</i>	332.3173	2.42925	0.700976	3.465527	0.000529	0.644422
ENSG00000137331	<i>IER3</i>	1131.598	0.773632	0.225847	3.425471	0.000614	0.644422
ENSG00000123119	<i>NECAB1</i>	17.4312	1.396028	0.40761	3.424915	0.000615	0.644422
ENSG00000196993	<i>NPIP9</i>	90.3268	-0.60766	0.177412	-3.42512	0.000615	0.644422
ENSG00000169203	<i>RP11-231C14.4</i>	249.1964	-0.64802	0.187268	-3.46041	0.000539	0.644422
ENSG00000280893	<i>AC009133.23</i>	9.701738	-2.5609	0.758312	-3.3771	0.000733	0.691727
ENSG00000067082	<i>KLF6</i>	1426.194	0.520046	0.157306	3.305947	0.000947	0.694302
ENSG00000186474	<i>KLK12</i>	25.34081	1.839293	0.551663	3.334085	0.000856	0.694302
ENSG00000113070	<i>HBEGF</i>	259.5387	1.320102	0.402212	3.282104	0.00103	0.719647
ENSG00000091128	<i>LAMB4</i>	79.02638	1.205408	0.370164	3.256417	0.001128	0.719647
ENSG00000132932	<i>ATP8A2</i>	24.55841	0.602019	0.184236	3.267642	0.001084	0.719647
ENSG00000139318	<i>DUSP6</i>	775.636	0.686782	0.215349	3.189164	0.001427	0.807516
ENSG00000203852	<i>HIST2H3A</i>	311.1639	1.57602	0.502519	3.136242	0.001711	0.838019
ENSG00000165794	<i>SLC39A2</i>	27.49601	1.602373	0.51099	3.135821	0.001714	0.838019
ENSG00000154734	<i>ADAMTS1</i>	34.50457	1.779	0.565144	3.147873	0.001645	0.838019
ENSG00000183336	<i>BOLA2</i>	5.369005	-9.99524	3.22335	-3.10089	0.001929	0.913049
ENSG00000121742	<i>GJB6</i>	75.14953	1.351585	0.437849	3.086874	0.002023	0.923257
ENSG00000265590	<i>AP000275.65</i>	33.19193	-1.87079	0.607592	-3.07902	0.002077	0.923257
ENSG00000169509	<i>CRCT1</i>	43.10019	2.246315	0.786001	2.857904	0.004264	0.971488
ENSG00000090104	<i>RGS1</i>	260.8477	0.758897	0.261628	2.900676	0.003724	0.971488
ENSG00000263961	<i>C1orf186</i>	9.726597	1.104421	0.381009	2.898677	0.003747	0.971488
ENSG00000143878	<i>RHOB</i>	1806.952	0.509216	0.179492	2.83699	0.004554	0.971488
ENSG00000115602	<i>IL1RL1</i>	51.0304	1.606061	0.559536	2.870347	0.0041	0.971488
ENSG00000185873	<i>TMPRSS11B</i>	126.1337	2.320712	0.77744	2.98507	0.002835	0.971488
ENSG00000124875	<i>CXCL6</i>	692.2134	0.849458	0.286733	2.962539	0.003051	0.971488
ENSG00000145879	<i>SPINK7</i>	90.93384	2.305832	0.75561	3.051617	0.002276	0.971488
ENSG00000112394	<i>SLC16A10</i>	25.4085	1.106001	0.3716	2.976325	0.002917	0.971488
ENSG00000155918	<i>RAET1L</i>	74.83194	1.296183	0.451471	2.871022	0.004091	0.971488
ENSG00000197181	<i>PIWIL2</i>	16.37803	0.889869	0.298332	2.982817	0.002856	0.971488
ENSG00000104368	<i>PLAT</i>	1629.246	1.266039	0.433067	2.923424	0.003462	0.971488
ENSG00000111215	<i>PRR4</i>	92.77336	-0.82179	0.277502	-2.96137	0.003063	0.971488
ENSG00000018236	<i>CNTN1</i>	68.40497	0.892821	0.307411	2.904322	0.00368	0.971488
ENSG00000279777	<i>AC004813.1</i>	52.62626	-0.60351	0.20639	-2.92413	0.003454	0.971488
ENSG00000128965	<i>CHAC1</i>	76.63318	0.803606	0.281341	2.856341	0.004286	0.971488

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

ENSG00000268089	<i>GABRQ</i>	21.23443	1.933114	0.706636	2.73566	0.006226	1
ENSG00000198763	<i>MT-ND2</i>	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 -value<0.01, LFC>0.5)

	GeneName	baseMean	log ² Fold Change	lfcSE	stat	Pvalue	Padj
ENSG00000125378	<i>BMP4</i>	22.04009	1.543324	0.297741	5.183448	2.18E-07	0.003195
ENSG00000132326	<i>PER2</i>	1311.424	-0.66742	0.14176	-4.70814	2.50E-06	0.018336
ENSG00000140006	<i>WDR89</i>	150.7693	0.632335	0.15182	4.165032	3.11E-05	0.114173
ENSG00000184313	<i>MROH7</i>	105.3837	-0.78921	0.204508	-3.85906	0.000114	0.271157
ENSG00000129757	<i>CDKN1C</i>	101.3036	0.671943	0.17645	3.80812	0.00014	0.271157
ENSG00000173451	<i>THAP2</i>	76.44963	0.624654	0.165438	3.775758	0.00016	0.271157
ENSG00000277117	<i>ICOSLG</i>	38.58432	1.309042	0.340901	3.839948	0.000123	0.271157
ENSG00000127129	<i>EDN2</i>	292.3299	2.41171	0.668713	3.606497	0.00031	0.281593
ENSG00000135045	<i>C9orf40</i>	111.4209	0.591656	0.163835	3.611298	0.000305	0.281593
ENSG00000153485	<i>TMEM251</i>	175.3835	0.621159	0.172678	3.597203	0.000322	0.281593
ENSG00000206172	<i>HBA1</i>	21.72477	-3.39372	0.944417	-3.59346	0.000326	0.281593
ENSG00000204172	<i>AGAP9</i>	156.9233	-0.68697	0.193771	-3.54528	0.000392	0.287681
ENSG00000198929	<i>NOS1AP</i>	147.7733	-0.72025	0.209007	-3.44607	0.000569	0.31136
ENSG00000118508	<i>RAB32</i>	180.2051	0.58683	0.17011	3.449702	0.000561	0.31136
ENSG00000196859	<i>KRT39</i>	38.21066	0.952273	0.274481	3.469356	0.000522	0.31136
ENSG00000152284	<i>TCF7L1</i>	33.26154	-0.7667	0.230403	-3.32767	0.000876	0.3195
ENSG00000240583	<i>AQP1</i>	61.98687	-1.05708	0.322695	-3.2758	0.001054	0.3195
ENSG00000175164	<i>ABO</i>	228.5686	-0.58983	0.178901	-3.29698	0.000977	0.3195
ENSG00000006327	<i>TNFRSF12A</i>	480.2161	0.932948	0.2811	3.318923	0.000904	0.3195
ENSG00000172000	<i>ZNF556</i>	17.04258	0.87804	0.266582	3.293689	0.000989	0.3195
ENSG00000198342	<i>ZNF442</i>	63.13852	0.754397	0.227406	3.317401	0.000909	0.3195
ENSG00000225828	<i>FAM229A</i>	41.86062	-0.5085	0.156767	-3.24367	0.00118	0.320019
ENSG00000185880	<i>TRIM69</i>	1353.204	0.629862	0.194459	3.239051	0.001199	0.320019
ENSG00000132881	<i>RSG1</i>	106.1672	0.534104	0.167607	3.186653	0.001439	0.338339
ENSG00000221886	<i>ZBED8</i>	178.3149	0.656915	0.206286	3.184482	0.00145	0.338339
ENSG00000163359	<i>COL6A3</i>	109.9409	-1.36855	0.436338	-3.13645	0.00171	0.349108
ENSG00000122641	<i>INHBA</i>	71.23154	1.845157	0.586767	3.144618	0.001663	0.349108
ENSG00000129474	<i>AJUBA</i>	371.5591	0.690348	0.222181	3.107139	0.001889	0.355797
ENSG00000188290	<i>HES4</i>	312.5322	0.669324	0.224127	2.986357	0.002823	0.360848
ENSG00000179914	<i>ITLN1</i>	71.80596	1.857605	0.620404	2.994186	0.002752	0.360848
ENSG00000164404	<i>GDF9</i>	21.44236	0.717419	0.240885	2.97826	0.002899	0.360848
ENSG000000036448	<i>MYOM2</i>	36.698	0.731788	0.245223	2.984168	0.002844	0.360848
ENSG00000123411	<i>IKZF4</i>	100.528	-0.51143	0.171315	-2.98534	0.002833	0.360848
ENSG00000132481	<i>TRIM47</i>	188.1067	0.510921	0.172017	2.970178	0.002976	0.360848
ENSG00000187187	<i>ZNF546</i>	84.94763	0.720698	0.233248	3.089832	0.002003	0.360848
ENSG00000159885	<i>ZNF222</i>	88.79954	0.594934	0.200539	2.966677	0.00301	0.360848
ENSG00000261221	<i>ZNF865</i>	88.98932	-0.55707	0.187852	-2.96546	0.003022	0.360848
ENSG00000132801	<i>ZSWIM3</i>	109.449	0.520946	0.174892	2.978677	0.002895	0.360848
ENSG00000177854	<i>TMEM187</i>	153.3936	0.525238	0.17367	3.024343	0.002492	0.360848
ENSG00000278705	<i>HIST1H4B</i>	594.7796	0.677645	0.231015	2.933342	0.003353	0.369876
ENSG00000203724	<i>C1orf53</i>	43.69044	0.605087	0.208161	2.906826	0.003651	0.374903

ENSG00000232040	<i>ZBED9</i>	37.2166	0.83489	0.285474	2.924569	0.003449	0.374903
ENSG00000104267	<i>CA2</i>	209.3763	0.919822	0.315283	2.917449	0.003529	0.374903
ENSG00000122254	<i>HS3ST2</i>	22.89722	1.033907	0.354774	2.914269	0.003565	0.374903
ENSG00000177606	<i>JUN</i>	1569.743	0.662493	0.234252	2.828126	0.004682	0.384771
ENSG00000164082	<i>GRM2</i>	20.58784	-0.7129	0.250317	-2.84799	0.0044	0.384771
ENSG00000163536	<i>SERPINI1</i>	52.52468	0.54397	0.196048	2.774681	0.005526	0.384771
ENSG00000019991	<i>HGF</i>	57.15752	0.646882	0.228819	2.827044	0.004698	0.384771
ENSG00000090266	<i>NDUFB2</i>	674.9224	0.514751	0.180961	2.844548	0.004447	0.384771
ENSG00000255823	<i>MTRNR2L8</i>	88.69851	0.80221	0.284671	2.818019	0.004832	0.384771
ENSG00000135094	<i>SDS</i>	374.6442	0.833066	0.295145	2.82257	0.004764	0.384771
ENSG00000175985	<i>PLEKHD1</i>	84.74293	-0.67052	0.240603	-2.78682	0.005323	0.384771
ENSG00000108821	<i>COL1A1</i>	144.2349	-0.83705	0.296719	-2.82103	0.004787	0.384771
ENSG00000261857	<i>MIA</i>	203.7857	0.827884	0.292163	2.833632	0.004602	0.384771
ENSG00000142530	<i>FAM71E1</i>	19.35397	0.555792	0.197434	2.815074	0.004877	0.384771
ENSG00000170775	<i>GPR37</i>	104.9986	0.566107	0.206773	2.737821	0.006185	0.389828
ENSG00000197019	<i>SERTAD1</i>	621.5665	0.515149	0.188775	2.728909	0.006354	0.391678
ENSG00000078401	<i>EDN1</i>	78.41643	1.222486	0.448687	2.724583	0.006438	0.392048
ENSG00000040608	<i>RTN4R</i>	19.66314	0.599538	0.220824	2.715001	0.006628	0.392048
ENSG00000113209	<i>PCDHB5</i>	15.93101	0.681644	0.252213	2.702646	0.006879	0.393004
ENSG00000196345	<i>ZKSCAN7</i>	91.34475	0.52829	0.195666	2.699956	0.006935	0.393055
ENSG00000165917	<i>RAPSN</i>	21.05145	-0.63449	0.236171	-2.68658	0.007219	0.400593
ENSG00000145632	<i>PLK2</i>	1570.018	0.505878	0.18918	2.67406	0.007494	0.401224
ENSG00000198939	<i>ZFP2</i>	25.53408	0.761238	0.284628	2.674505	0.007484	0.401224
ENSG00000186480	<i>INSIG1</i>	1680.1	0.590828	0.220892	2.674736	0.007479	0.401224
ENSG00000198670	<i>LPA</i>	68.50585	-0.60768	0.227745	-2.66823	0.007625	0.40529
ENSG00000214756	<i>METTL12</i>	90.15136	0.507306	0.190443	2.663816	0.007726	0.407007
ENSG00000149243	<i>KLHL35</i>	30.62397	0.540832	0.203969	2.651538	0.008013	0.407759
ENSG00000239282	<i>GATSL3</i>	163.1875	0.518584	0.195348	2.65467	0.007939	0.407759
ENSG00000088538	<i>DOCK3</i>	53.29586	-0.54609	0.207448	-2.6324	0.008478	0.414453
ENSG00000241360	<i>PDXP</i>	67.81247	0.52209	0.19822	2.633894	0.008441	0.414453
ENSG00000242866	<i>STRC</i>	49.76977	-0.67549	0.257248	-2.62583	0.008644	0.418498
ENSG00000162772	<i>ATF3</i>	603.2502	0.697791	0.268797	2.595975	0.009432	0.420723
ENSG00000187094	<i>CCK</i>	60.47584	0.800681	0.309839	2.584187	0.009761	0.420723
ENSG00000198785	<i>GRIN3A</i>	14.96359	1.201367	0.460333	2.60978	0.00906	0.420723
ENSG00000187720	<i>THSD4</i>	175.5152	-0.56348	0.218724	-2.57622	0.009989	0.420723
ENSG00000280006	<i>AC009060.2</i>	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	Pvalue	P.adjust	Qvalue	geneID	Count
GO:0044057	Regulation of system process	0.148	0.0295106	6.99E-05	2.16E-02	1.75E-02	<i>EDN2/NOS1AP/PER2/CCK/GDF9/EDN1/AQP1/INHBA/HGF</i>	9
GO:0010035	Response to inorganic substance	0.131	0.0272913	2.40E-04	3.67E-02	2.97E-02	<i>JUN/EDN1/AQP1/HGF/GPR37/CA2/HBA1/COL1A1</i>	8
GO:0042326	Negative regulation of phosphorylation	0.131	0.0248321	1.26E-04	3.33E-02	2.69E-02	<i>JUN/ATF3/INHBA/HGF/CDKN1C/AJUBA/BMP4/RTN4R</i>	8
GO:0015711	Organic anion transport	0.115	0.0190139	1.52E-04	3.53E-02	2.85E-02	<i>PER2/CCK/GRM2/EDN1/AQP1/CA2/HBA1</i>	7
GO:0000302	Response to reactive oxygen species	0.115	0.0122961	9.54E-06	5.89E-03	4.76E-03	<i>JUN/EDN1/AQP1/HGF/GPR37/HBA1/COL1A1</i>	7
GO:0042542	Response to hydrogen peroxide	0.098	0.0071377	4.70E-06	4.35E-03	3.52E-03	<i>JUN/AQP1/HGF/GPR37/HBA1/COL1A1</i>	6
GO:0042476	Odontogenesis	0.098	0.0068378	3.66E-06	4.35E-03	3.52E-03	<i>EDN1/AQP1/INHBA/CA2/BMP4/COL1A1</i>	6
GO:2001236	Regulation of extrinsic signalling pathway	0.082	0.009237	2.47E-04	3.67E-02	2.97E-02	<i>ATF3/INHBA/HGF/BMP4/TNFRSF12A</i>	5
GO:0044070	Regulation of anion transport	0.066	0.0050384	2.51E-04	3.67E-02	2.97E-02	<i>PER2/CCK/EDN1/CA2</i>	4
GO:0050886	Endocrine process	0.066	0.0046785	1.89E-04	3.67E-02	2.97E-02	<i>EDN2/GDF9/EDN1/INHBA</i>	4
GO:0060395	SMAD protein signal transduction	0.066	0.0034789	5.94E-05	2.16E-02	1.75E-02	<i>JUN/GDF9/INHBA/BMP4</i>	4
GO:0015669	Gas transport	0.049	0.0011396	4.33E-05	2.01E-02	1.62E-02	<i>AQP1/CA2/HBA1</i>	3

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

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

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

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

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

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

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

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

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

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

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

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