

# Acute Viral Respiratory Infection Rapidly Induces a CD8<sup>+</sup> T Cell Exhaustion–like Phenotype

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Acute viral infections typically generate functional effector CD8<sup>+</sup> T cells (T<sub>CD8</sub>) that aid in pathogen clearance. However, during acute viral lower respiratory infection, lung T<sub>CD8</sub> are functionally impaired and do not optimally control viral replication. T cells also become unresponsive to Ag during chronic infections and cancer via signaling by inhibitory receptors such as programmed cell death-1 (PD-1). PD-1 also contributes to T<sub>CD8</sub> impairment during viral lower respiratory infection, but how it regulates T<sub>CD8</sub> impairment and the connection between this state and T cell exhaustion during chronic infections are unknown. In this study, we show that PD-1 operates in a cell-intrinsic manner to impair lung T<sub>CD8</sub>. In light of this, we compared global gene expression profiles of impaired epitope-specific lung T<sub>CD8</sub> to functional spleen T<sub>CD8</sub> in the same human metapneumovirus-infected mice. These two populations differentially regulate hundreds of genes, including the upregulation of numerous inhibitory receptors by lung T<sub>CD8</sub>. We then compared the gene expression of T<sub>CD8</sub> during human metapneumovirus infection to those in acute or chronic lymphocytic choriomeningitis virus infection. We find that the immunophenotype of lung T<sub>CD8</sub> more closely resembles T cell exhaustion late into chronic infection than do functional effector T cells arising early in acute infection. Finally, we demonstrate that trafficking to the infected lung alone is insufficient for T<sub>CD8</sub> impairment or inhibitory receptor upregulation, but that viral Ag-induced TCR signaling is also required. Our results indicate that viral Ag in infected lungs rapidly induces an exhaustion-like state in lung T<sub>CD8</sub> characterized by progressive functional impairment and upregulation of numerous inhibitory receptors. *The Journal of Immunology*, 2015, 195: 4319–4330.

**C**D8<sup>+</sup> T cells (T<sub>CD8</sub>) possess critical functions that protect against intracellular pathogens and cancer, including cytotoxicity, cytokine production, and long-lived mem-

ory potential (1, 2). During acute infection, naive T<sub>CD8</sub> encounter Ag, acquire effector functions, and proliferate to clear the infection, after which 90–95% die whereas the remaining few become memory cells (2). Memory T<sub>CD8</sub> can rapidly reactivate their effector functions and proliferate upon pathogen re-encounter, contributing to protective immunity (3). During chronic infection, a different sequence of events occurs: pathogen-specific T<sub>CD8</sub> initially acquire effector functions, but they gradually become exhausted and fail to eliminate the infection (4). Proliferation and IL-2 production are lost early, followed by TNF, with IFN- $\gamma$  production failing weeks into exhaustion (5). Prolonged TCR stimulation by persistent viral or tumor Ags is thought to transcriptionally reprogram exhausted T<sub>CD8</sub>, resulting in these functional changes (6).

The paradigm that acute infection generates functional effector T cells followed by memory development, while chronic infection causes T cell exhaustion, is not generalizable to all infections. During acute viral lower respiratory infection (LRI) in mice, pulmonary T<sub>CD8</sub> become functionally impaired, rapidly losing cytotoxicity and cytokine production (7–11). In contrast to exhaustion, lung T<sub>CD8</sub> impairment during LRI occurs rapidly, with IFN- $\gamma$  production waning as early as day 7 (7). Additionally, only T<sub>CD8</sub> in the respiratory tract become impaired; T<sub>CD8</sub> in lymphoid organs maintain their effector functions, suggesting that the infected lung environment is critical for the development of impairment (12). LRI are typically cleared within 7–12 d even in the face of T<sub>CD8</sub> impairment, but the generation of protective immunity may be compromised by the rapid impairment of the primary and secondary anti-viral T<sub>CD8</sub> effector responses (13). Failure to generate a quality memory T<sub>CD8</sub> response may help explain the ability of respiratory viruses and other pathogens to repeatedly reinfect individuals despite minimal antigenic drift (14–16). A better understanding of the phenotype, functions, and mechanisms

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Received for publication December 9, 2014. Accepted for publication August 21, 2015.

This work was supported by National Institutes of Health Grants AI085062 (to J.V.W.), AI040079 (to S.J.), AI042284 (to S.J.), HL054977, HL121139, and Veterans Affairs Merit Award BX001444 (to S.J.), and GM007347 (to J.J.E.). The Vanderbilt Medical Center Flow Cytometry Shared Resource is supported by Vanderbilt Ingram Cancer Center Grant P30 CA68485 and by Vanderbilt Digestive Disease Research Center Grant DK058404. This work was also supported in part by the Vanderbilt Clinical and Translational Science Award Grant ULI RR024975-01 from the National Center for Research Resources/National Institutes of Health.

J.J.E. designed and performed the experiments, analyzed the results, and wrote the manuscript; P.L. and Y.S. assisted with data analysis; P.G. and S.J. provided critical reagents and experimental advice; S.W. and A.K.H. performed experiments, analyzed data, and wrote the manuscript; and J.V.W. designed the experiments, analyzed the results, and wrote the manuscript.

The microarray data presented in this article have been submitted to the Gene Expression Omnibus database (<http://www.ncbi.nlm.nih.gov/gds>) under accession number GSE53349.

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The online version of this article contains supplemental material.

Abbreviations used in this article: A34R, A34R<sub>82–90</sub>; Arm, lymphocytic choriomeningitis virus Armstrong; B6, C57BL/6; CI-13, lymphocytic choriomeningitis virus clone 13; DC, dendritic cell; F528, H2-D<sup>b</sup>/F<sub>528–536</sub> (SGVTNNGFI); FDR, false discovery rate; HMPV, human metapneumovirus; ICS, intracellular cytokine staining; i.n., intranasal(ly); LCMV, lymphocytic choriomeningitis virus; LRI, lower respiratory infection; M195, HLA-B\*0702/M<sub>195–203</sub> (APYAGLIMI); N11, H2-K<sup>b</sup>/N<sub>11–18</sub> (LSY-KHAIL); PD-1, programmed cell death-1; PD-L1, programmed cell death ligand-1; p.i., postinfection; RSV, respiratory syncytial virus; T<sub>CD8</sub>, CD8<sup>+</sup> T cell; WT, wild-type.

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controlling lung T<sub>CD8</sub> activity during LRI is needed to design new and effective therapeutics and vaccines.

We previously uncovered a role for the inhibitory receptor programmed cell death-1 (PD-1) in mediating lung T<sub>CD8</sub> impairment during human metapneumovirus (HMPV) and influenza virus infection (12). Blocking PD-1 during LRI resulted in increased T<sub>CD8</sub> degranulation, IFN- $\gamma$  production, and ability to clear the infection. A recent study showed that during respiratory syncytial virus (RSV) infection, PD ligand-1 (PD-L1) expression by lung dendritic cells (DCs) primarily mediated lung T<sub>CD8</sub> impairment (17). PD-1 has been proposed to play a role during other acute infections, including rabies (18), histoplasmosis (19), and bacterial sepsis (20, 21). However, PD-1 expression by APCs (e.g., microglia, macrophages, DCs) was found to be primarily important in mediating early susceptibility to these pathogens. Recently, it was shown that PD-1 expression on lung T<sub>CD8</sub> correlated with disease severity caused by different strains of influenza virus and PD-1 blockade improved survival, but this was not associated with restored T<sub>CD8</sub> functionality (22). Therefore, the intrinsic ability of PD-1 to regulate adaptive immune responses during acute LRI remains unclear.

PD-1 blockade restores function to exhausted T<sub>CD8</sub> during HIV infection in humans (23) and chronic lymphocytic choriomeningitis virus (LCMV) clone 13 infection of mice (24). PD-1 is not the sole mediator of exhaustion, however, as additionally inhibitory receptors, including TIM-3 (25), LAG-3 (26), 2B4 (27), and others (28), also contribute. The PD-1-mediated functional impairment in both acute viral LRI and chronic systemic infection suggests that additional similarities may exist during these seemingly disparate infections. However, whether additional inhibitory receptors are expressed, what drives their expression, and whether they play a role in lung T<sub>CD8</sub> impairment during acute viral LRI are unknown.

We addressed these issues by first determining that PD-1 regulates lung T<sub>CD8</sub> in a cell-intrinsic manner during HMPV infection. This then allowed us to more directly study the phenotype of impaired lung T<sub>CD8</sub>. We compared the global gene expression profiles of impaired virus-specific lung T<sub>CD8</sub> to unimpaired spleen T<sub>CD8</sub> in the same HMPV-infected mice. Gene expression analysis has uncovered numerous pathways regulating effector and memory T<sub>CD8</sub> development during acute infection (29) and exhaustion during chronic infection (4, 30). Given the functional differences that exist between effector T<sub>CD8</sub> present during most acute infections, exhausted T<sub>CD8</sub> during chronic infections, and impaired lung T<sub>CD8</sub> during LRI, we hypothesized that each population would possess a unique gene expression profile that may provide insights into the mechanisms governing each functional state. Surprisingly, we found that the lung T<sub>CD8</sub> gene expression signature was similar to T<sub>CD8</sub> early in the exhaustion process; however, when focusing solely on genes with known immune functions, impaired lung T<sub>CD8</sub> were most similar to fully exhausted cells. We confirmed that impaired lung T<sub>CD8</sub> coexpress these inhibitory receptors to a greater degree than do spleen T<sub>CD8</sub>. Finally, we show that T<sub>CD8</sub> inhibitory receptor expression is driven by Ag-dependent TCR signaling, and without TCR stimulation, T<sub>CD8</sub> remain functional with very low inhibitory receptor expression. Our results indicate that acute viral LRI induces an exhaustion-like state in lung T<sub>CD8</sub> characterized by rapid functional impairment and Ag-dependent upregulation of numerous inhibitory receptors.

## Materials and Methods

### Mice and viral infection

C57BL/6 (B6) and congenic Thy1.1<sup>+</sup> mice were purchased from The Jackson Laboratory. B6-Kb<sup>0</sup>Db<sup>0</sup>;B7.2 transgenic mice were obtained with permission from Drs. Alexander Sette (La Jolla Institute for Allergy and

Immunology, La Jolla, CA) and François Lemonnier (Institut Pasteur, Paris, France). PD-1<sup>-/-</sup> mice were obtained with permission from Dr. Tasuku Honjo (Kyoto University, Kyoto, Japan). All animals were bred and maintained in specific pathogen-free conditions in accordance with the Vanderbilt Institutional Animal Care and Use Committee. Six- to twelve-week-old age- and gender-matched animals were used in all experiments. Mixed bone marrow chimeric mice were generated by irradiating Thy1.1<sup>+</sup> recipients with two doses of 5 Gy, 4 h apart, followed by reconstitution with 1  $\times$  10<sup>6</sup> wild-type (WT; Thy1.1<sup>+</sup>) and 1  $\times$  10<sup>6</sup> PD-1<sup>-/-</sup> (Thy1.2<sup>+</sup>) bonemarrow cells 24 h later. Mice were rested for 8 wk and then bled to check reconstitution before use in experiments. HMPV (pathogenic clinical strain TN/94-49, genotype A2) was grown and titered in LLC-MK2 cells as previously described (31). For all experiments, mice were anesthetized with ketamine-xylazine and infected intranasally (i.n.) with 1  $\times$  10<sup>6</sup> PFU HMPV.

### Flow cytometry staining

Tetramers were generated for the following viral epitopes as previously described (12, 32): HLA-B\*0702/M<sub>195-203</sub> (M195) (APYAGLIMI), H2-D<sup>b</sup>/F<sub>528-536</sub> (F528) (SGVTNNGFI), and H2-K<sup>b</sup>/N<sub>11-18</sub> (N11) (LSY-KHAIL). Lymphocytes were isolated from spleens and lungs of infected animals and stained as previously described (12). Cells were stained with PE- or allophycocyanin-labeled tetramers (0.1–1  $\mu$ g/ml), anti-CD8 $\alpha$  (clone 53-6.7, BD Biosciences), and anti-CD19 (clone 1D3, iCyt). In some experiments, cells were also stained for the inhibitory receptors PD-1 (clone RMP1-30), TIM-3 (clone RMT3-23), LAG-3 (clone C9B7W), and 2B4 [clone m2B4 (B6)458.1] or with appropriate isotype controls (all from BioLegend). For mixed bone marrow chimera experiments, cells were stained for Thy1.1 (clone OX-7, BD Biosciences) and Thy1.2 (clone 53-2.1, BD Biosciences). Surface/tetramer staining was performed for 1 h at room temperature in PBS containing 1% FBS and 50 nM dasatinib. Intracellular cytokine staining (ICS) was performed in parallel with tetramer staining as previously described (12). Flow cytometric data were collected using an LSR II or LSRFortessa (BD Biosciences) and analyzed with FlowJo software (Tree Star). Boolean gating in FlowJo was used to assess inhibitory receptor coexpression, and patterns were visualized using the SPICE program (National Institute of Allergy and Infectious Diseases).

### Generation of bone marrow-derived DCs and immunizations

Bone marrow-derived DCs were generated as previously described (12). To obtain secondary M195-specific T<sub>CD8</sub>, mice were primed i.n. with 2  $\times$  10<sup>6</sup> M195-loaded, LPS-matured DCs and then challenged with HMPV 3 wk later. For generation of lung-infiltrating vaccinia virus A34R<sub>82-90</sub> (A34R)-specific T<sub>CD8</sub>, mice were immunized i.n. with A34R DCs and then challenged 7 d later with HMPV and were treated daily i.n. during the infection with either 50  $\mu$ g A34R peptide or an irrelevant HLA-B\*0702-restricted peptide. To study splenic T<sub>CD8</sub> response to systemically administered Ag, mice were immunized s.c. with A34R-specific DCs, challenged 7 d later with HMPV, and injected daily s.c. and i.p. during the infection with either 50  $\mu$ g (via each route) A34R peptide or mock peptide.

### Cell sorting

To obtain sufficient quantities of primary epitope-specific T<sub>CD8</sub>, on day 7 after HMPV infection the spleens and lungs from three mice were pooled together after processing. Samples were stained, sorted, and RNA purified on separate days in independent experiments. Cells were processed in ice-cold R10 media containing 10 nM dasatinib to prevent activation and TCR signaling. Lung cells were processed as before. Splenocytes were depleted of B cells by incubation on goat anti-mouse IgG- and IgM-coated (100  $\mu$ g/ml) (SouthernBiotech) T-75 flasks at 10<sup>6</sup> cells/ml for 1 h at 37°C and then processed as before. Both lung and spleen cells were stained for viability, CD19, CD8, and M195 tetramers (both PE and allophycocyanin conjugated). Splenocytes were also stained for CD44 (clone IM-7; BD Biosciences) and CD62L (MEL-14; BD Biosciences) to obtain control naive cells. Dual tetramer<sup>+</sup> T<sub>CD8</sub> were sorted using a BD FACSAria III. Samples were maintained at 4°C for the entirety of the sort and purity was 97–99% for all populations.

### RNA amplification and hybridization

Total RNA was isolated from sorted naive, spleen, lung, and secondary lung M195-specific T<sub>CD8</sub> using an RNeasy kit (Qiagen) according to the manufacturer's instructions. On-column DNase digestion was performed, and eluted RNA was quantified and checked for integrity using an Agilent 2100 Bioanalyzer. RNA was amplified using a WT Ovation Pico kit (NuGEN) and then converted to cDNA. Amplified samples were again checked for

integrity and then hybridized to mouse gene 1.1 ST microarrays (Affymetrix) and scanned on the GeneTitan instrument (Affymetrix).

### Microarray data analysis

**HMPV  $T_{CD8}$  data analysis.** Microarray data were processed using the oligonucleotide package implementation of rma in R software (33). For microarray analysis, four groups (naive, spleen, lung, and secondary lung) were compared using the limma package (34). Significantly changed probes were identified by ANOVA. The  $p$  values were adjusted for multiple comparisons using the false discovery rate (FDR) method (35). The thresholds for significance were set to control the expected FDR at values  $<10\%$  and the fold-change at 2.

**HMPV data versus LCMV data.** GSE41867 data (26) were downloaded from the National Center for Biotechnology Information Gene Expression Omnibus database. The microarray data files from the present study and GSE41867 were processed separately using the oligonucleotide package implementation of rma in R software. The batch effect of two data sets was corrected using ComBat package (36). In one analysis, five groups (spleen and lung are from the HMPV data set and the additional three groups are from GSE41867 data) were selected to a subset (top 50% based on the coefficient of variation) of the original data and 10 pairwise comparisons were done using the limma package in BioConductor (34). The differentially expressed probes/genes were refined to the gene list based on two criteria: adjusted  $p$  value  $<0.1$  and fold-change  $>2$ . Analysis of similarity was also performed as previously described (37). In a separate analysis, all groups were compared using ANOVA with the same cutoffs for significance and a heat map was generated.

### Ingenuity Pathway Analysis

Ingenuity Pathway Analysis (<http://www.ingenuity.com>) was used to compare different biological processes in spleen versus lung  $T_{CD8}$  and to identify all immune genes present in each data set.

### Accession numbers

The microarray data have been submitted to the Gene Expression Omnibus database (<http://www.ncbi.nlm.nih.gov/gds>) under the accession number GSE53349.

### Statistical analysis

Comparisons between tetramer staining and ICS within the same animals were performed using a paired  $t$  test or Wilcoxon signed rank test. Comparisons between two independent groups were performed using an unpaired Student  $t$  test or Wilcoxon rank sum test. Multiple group comparisons were performed using one-way ANOVA with a Bonferroni posttest for comparison of individual groups. A  $p$  value  $<0.05$  was considered statistically significant by convention. All  $p$  values should be for two-sided tests and unadjusted for multiple comparisons unless otherwise noted. Error bars on each graph represented the SEM unless otherwise noted. All analyses were conducted using R software version 2.16.

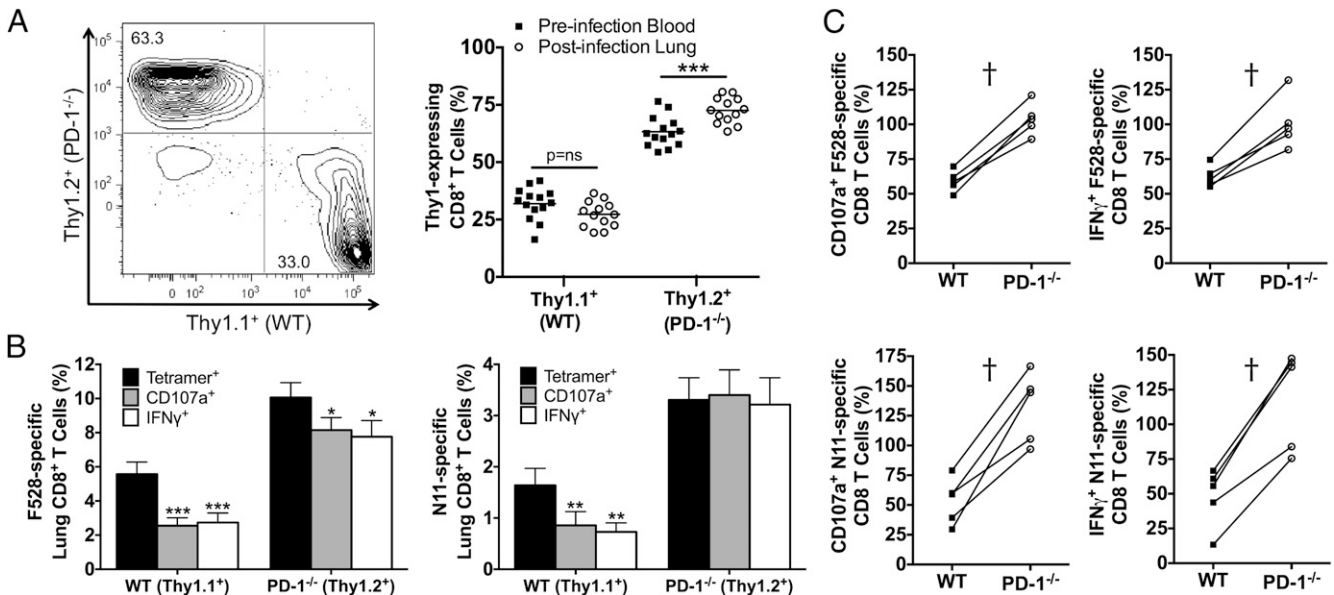
### Study approval

All animals were maintained in accordance with the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* and were handled according to protocols approved by the Vanderbilt University subcommittee on animal care (Institutional Animal Care and Use Committee).

## Results

### Lung $T_{CD8}$ impairment is cell-intrinsically regulated by PD-1

We have previously shown that blockade or genetic ablation of PD-1 reverses functional impairment (12). However, it was unclear whether PD-1 caused impairment via direct signaling on the  $T_{CD8}$  surface or whether its effects were indirectly mediated by other immune cells. To answer this question, we generated WT:PD-1<sup>-/-</sup> bone marrow chimeric mice. After reconstitution of irradiated recipients with either 1:1 WT (Thy1.1<sup>+</sup>):PD-1<sup>-/-</sup> (Thy1.2<sup>+</sup>) donor bone marrow cells (Fig. 1) or 4:1 WT:PD-1<sup>-/-</sup> cells (not shown), the  $T_{CD8}$  compartment consisted of approximately twice as many PD-1<sup>-/-</sup> as WT cells (Fig. 1A). This was true in both the preinfection blood and the postinfection lung compartments (Fig. 1A), indicating a stable ratio of WT:PD-1<sup>-/-</sup> T cells following HMPV infection.



**FIGURE 1.** Lung  $T_{CD8}$  impairment is cell-intrinsically regulated by PD-1. (A–C) WT (Thy1.1<sup>+</sup>):PD-1<sup>-/-</sup> (Thy1.2<sup>+</sup>) mixed bone marrow chimeric mice were checked for immune reconstitution in the blood before and in the lung after HMPV infection. (A) A representative flow cytometry plot gated on live/CD19<sup>-</sup>/CD3<sup>+</sup>/CD8<sup>+</sup> lymphocytes is shown. In the graph, each symbol represents an individual mouse and the horizontal bar indicates the mean. Ratios of WT:PD-1<sup>-/-</sup>  $T_{CD8}$  in preinfection blood (■) and postinfection lungs (○) sum to 100%. (B) Mixed bone marrow chimeric mice were infected with HMPV and the lung F528- and N11-specific  $T_{CD8}$  responses were quantified via tetramer staining (black bars), CD107a mobilization (gray bars), and intracellular IFN- $\gamma$  production (white bars) at day 7 p.i. Data are combined from three independent experiments with four to five mice per experiment. (C) The percentage of functional HMPV-specific  $T_{CD8}$  was calculated by dividing the percentage that degranulated or made IFN- $\gamma$  by the percentage that stained tetramer<sup>+</sup>. Lines connect data points from WT and PD-1<sup>-/-</sup>  $T_{CD8}$  within the same mouse. Data are representative of one out of three independent experiments with five mice per experiment. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , unpaired  $t$  test; † $p < 0.05$ , paired  $t$  test.

We quantified the total F528 and N11 epitope-specific T<sub>CD8</sub> response on day 7 postinfection (p.i.) via tetramer staining, and in parallel their effector functions via brief peptide restimulation followed by intracellular cytokine staining. We have previously shown that direct comparison of these assays allows for the accurate quantification of the functionality of epitope-specific lung T<sub>CD8</sub> in a manner that is not influenced by variations in lung APCs or in vitro stimulation conditions (12, 13, 38). The percentage of tetramer<sup>+</sup> T<sub>CD8</sub> was greater among PD-1<sup>-/-</sup> cells (Fig. 1B), likely reflecting the increased precursor frequencies due to greater overall numbers of cells. More importantly, we observed greater frequencies of degranulating (i.e., CD107a<sup>+</sup>) or IFN- $\gamma$ -producing PD-1<sup>-/-</sup> versus WT T<sub>CD8</sub>. To control for the greater overall T<sub>CD8</sub> response by PD-1<sup>-/-</sup> cells, we calculated the percentage of T<sub>CD8</sub> capable of degranulating or making IFN- $\gamma$  and compared WT and PD-1<sup>-/-</sup> cells within the same mouse. Lung T<sub>CD8</sub> were more functional in PD-1<sup>-/-</sup> compared with WT cells for both epitopes and both effector functions measured (Fig. 1C). WT T<sub>CD8</sub> remained impaired in this experiment despite the presence of PD-1<sup>-/-</sup> hematopoietic cells of different lineages, namely APCs such as DCs. Therefore, these data show that PD-1 functions in a cell-intrinsic manner to impair lung T<sub>CD8</sub> during viral LRI.

#### Gene expression analysis of impaired lung T<sub>CD8</sub> and unimpaired spleen T<sub>CD8</sub>

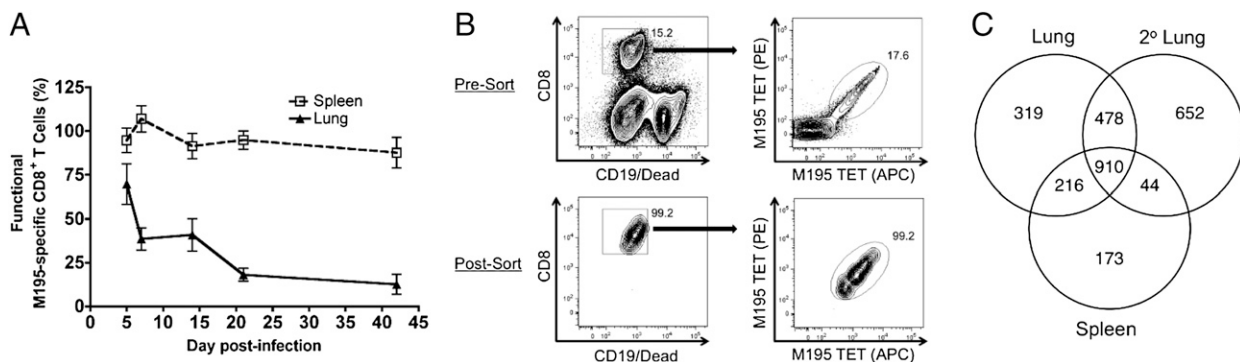
Given the cell-intrinsic nature of PD-1-mediated lung T<sub>CD8</sub> impairment, we reasoned that a more thorough examination of anti-viral T<sub>CD8</sub> might reveal other mechanisms regulating their function in the respiratory tract. We previously showed that HMPV-specific T<sub>CD8</sub> in different environments within the same infected mouse have different levels of functionality (12). We found that HMPV-specific lung T<sub>CD8</sub> rapidly lose the ability to produce IFN- $\gamma$  (Fig. 2A) or degranulate (not shown), although these effector functions are maintained in the spleen over time. HMPV is cleared from the lungs by day 10 (12), yet T<sub>CD8</sub> exhibited progressive functional decline long after infection. Secondary lung T<sub>CD8</sub> are also highly impaired in their ability to degranulate or make cytokines following challenge of previously infected mice or mice immunized with HMPV-specific class I-restricted epitopes (12, 13).

We hypothesized that the infected lung environment influences T<sub>CD8</sub> functionality at a transcriptional level to balance the need for viral control with prevention of immune-mediated pathology. To test this, we compared global gene expression differences between virus-specific, impaired lung T<sub>CD8</sub> and functional spleen T<sub>CD8</sub>

from the same HMPV-infected mice. We infected B6-Kb<sup>0</sup>Db<sup>0</sup>;B7.2 transgenic mice, in which T<sub>CD8</sub> only recognize epitopes restricted by the human MHC class I molecule HLA-B\*0702 (39). The T<sub>CD8</sub> response in B6-Kb<sup>0</sup>Db<sup>0</sup>;B7.2 transgenic mice is dominated by cells recognizing the M195 epitope, which accounts for ~60% of anti-viral T<sub>CD8</sub> (12). At day 7 p.i., the time at which lung T<sub>CD8</sub> impairment begins (Fig. 2A), we sorted spleen and lung M195-specific T<sub>CD8</sub> as well as secondary lung M195-specific T<sub>CD8</sub> from mice primed with M195-loaded DCs then challenged with HMPV. M195-specific T<sub>CD8</sub> were sorted to high purity (Fig. 2B) and gene expression analysis was performed. Two samples were deemed outliers based on principal component analysis and excluded from further study (Supplemental Fig. 1).

We quantified the gene expression differences of these populations and compared them to naive T<sub>CD8</sub> to make direct comparisons between the three groups. Approximately 900 genes were up- or downregulated by all three populations of M195-specific T<sub>CD8</sub> compared with naive T<sub>CD8</sub> (Fig. 2C), which reflect many genes associated with T cell activation and differentiation (Table I). More than 1300 genes were differentially expressed by both primary and secondary lung T<sub>CD8</sub> (Supplemental Table I). Despite large numbers of overlapping genes between these groups, each population contained numerous genes uniquely identifying them: 173 for spleen, 319 for primary lung, and 652 for secondary lung T<sub>CD8</sub> (Fig. 2C). A total of 370 genes differed between the impaired lung and unimpaired spleen T<sub>CD8</sub> from the same infected mice, indicating that lung anti-viral T<sub>CD8</sub> exhibit a unique gene expression profile while combating infection.

Activated spleen and lung T<sub>CD8</sub> up- and downregulated numerous genes compared with naive T<sub>CD8</sub> (Fig. 3A, Table I) in concordance with previous studies (29, 40). Some of these genes were shared by both spleen and lung T<sub>CD8</sub>, but lung T<sub>CD8</sub> also upregulated numerous unique genes. Gene clustering demonstrated that primary and secondary lung T<sub>CD8</sub> were most closely related, with numerous additional genes only expressed during challenge infection (Fig. 3A). To broadly compare which biological processes were altered in lung compared with spleen anti-viral T<sub>CD8</sub>, we performed gene ontology analysis (Fig. 3B). Numerous pathways were substantially altered in primary lung T<sub>CD8</sub>; “cellular function and maintenance” was the most significantly changed. Other pathways with known immune functions were altered in lung T<sub>CD8</sub>, including “hematological system development and function,” “immune cell trafficking,” “inflammatory response,” and “cell death and survival.” Genes were then sorted by functional classification and biological process so that just the



**FIGURE 2.** Isolation of epitope-specific lung and spleen T<sub>CD8</sub> and comparison of gene expression. **(A)** Time course of HMPV M195-specific T<sub>CD8</sub> functionality (IFN- $\gamma$  production) in the lung and the spleen. **(B)** Pre- and postsort analysis of lung M195-specific T<sub>CD8</sub> at day 7 p.i. **(C)** Total number of genes differentially expressed for the indicated M195-specific T<sub>CD8</sub> populations compared with naive T<sub>CD8</sub>. Naive spleen T<sub>CD8</sub>, spleen M195-specific T<sub>CD8</sub>, lung M195-specific T<sub>CD8</sub>, and 2° lung M195-specific T<sub>CD8</sub> are shown. Genes were considered significantly different when the fold-change was >2 and the FDR was <10%.

Table I. Genes differentially regulated between M195-specific T<sub>CD8</sub> compared with naive T<sub>CD8</sub>

Gene	Other Names	Spl	Lu 1o	Lu 2o	Gene	Other Names	Spl	Lu 1o	Lu 2o	Gene	Other Names	Spl	Lu 1o	Lu 2o	Gene	Other Names	Spl	Lu 1o	Lu 2o
<b>I. Activating/Inhibitory Receptors</b>					<b>V. Chemotaxis/Movement</b>					<b>VIII. Innate Immunity</b>					<b>X. Transcriptional Regulation (cont.)</b>				
CD200	OX2	1.6	4.2	4.6	CAPG		7.0	14.7	25.3	BST2	Tethrin	1.3	4.2	1.5	IRF4		4.9	10.7	6.7
CD244	2B4	1.5	4.4	15.1	CCL1		1.0	8.1	21.2	CD14		1.6	3.4	4.2	IRF7		1.2	2.5	0.8
FGL2		5.1	39.4	84.5	CCL4		11.1	73.6	60.1	CYBB		1.9	6.3	5.2	IRF8		1.9	10.5	3.4
HAVCR2	TIM-3	11.0	34.8	23.8	CCL7		1.1	2.2	1.8	CYSLTR2		2.6	5.5	5.6	JUN		6.5	1.1	2.1
LAG3	CD223	18.9	50.8	39.2	CCR7		3.3	11.1	40.5	HP	Haptoglobin	1.0	3.2	1.9	MYB		1.4	3.1	15.5
PDCD1	PD-1	26.4	29.3	23.7	CCR8		1.6	6.8	47.9	ISG15		3.2	12.2	2.7	MYC		1.3	2.8	2.0
TNFRSF4	OX40	1.0	2.2	1.4	CCRL2		2.8	9.7	5.9	ISG20		1.9	9.9	8.4	PRDM1	BLIMP-1	4.4	12.4	7.3
TNFRSF9	4-1BB	4.4	9.7	1.2	CXCL3		1.0	1.2	1.8	MGST1		1.1	3.1	3.6	RBPJ		1.3	1.6	2.5
TREML2		10.5	5.2	9.8	CXCL9		1.4	8.7	1.5	RSAD2	Viperin	2.3	10.3	2.3	SOCS2		2.0	4.5	9.0
					CXCL10		8.4	26.8	2.2	SCGB1A1	Uteroglobin	1.4	207	69.2	STAT2		1.2	3.3	1.9
					HRH4		7.1	3.3	3.9	TLR7		1.6	1.5	1.2	TCF7		1.8	3.9	4.6
					XCL1		3.9	26.2	25.2	UBE2L6		2.6	6.3	2.7					
<b>II. Adhesion</b>					<b>VI. Cytokines</b>					<b>IX. Signaling</b>					<b>XI. Miscellaneous</b>				
AMICA1		2.8	8.4	7.0	IFNG		43.1	125	84.0	CD38		3.7	8.7	10.5	ATP6V0D2		1.1	2.0	8.6
BGN		1.1	3.3	3.0	IL10		2.2	25.7	3.2	FGR		1.9	4.5	3.9	C3		1.0	4.1	5.4
CD93		1.1	2.4	2.0	IL10RA		7.4	17.7	10.1	LAT2		1.5	3.0	7.3	CD36		1.1	5.4	9.6
CDH1		1.4	4.6	32.4	IL12RB1		2.8	5.8	5.2	MUC1		1.5	3.8	2.2	CD74		2.5	5.1	8.3
CDH5		1.2	3.3	2.1	IL12RB2		4.3	1.8	1.1	RGS16		6.5	21.1	14.5	FABP5		1.1	2.5	4.0
SPARC	Osteonectin	1.1	5.7	11.0	IL2		1.5	3.9	4.1	TNIP1		1.1	2.5	2.5	FCER1G		2.1	6.9	12.9
					IL2RA		14.9	34.9	18.8	GADD45B		1.8	6.8	5.0	GCNT1		2.8	8.8	2.7
					IL7R		2.4	6.6	1.8	GADD45G		1.6	13.1	9.8	PLSCR1		8.3	18.3	15.1
					LIF		1.1	2.1	1.6	TYROBP		2.4	5.6	7.3	PRF1	Perforin	2.3	6.0	3.5
					OSM		1.1	2.2	3.4					RORA		4.2	2.0	2.2	
					TGFBI		1.2	3.5	4.4					SERPING1		1.1	7.7	3.4	
					TNF		2.3	5.6	7.5					THBD		1.1	3.1	2.3	
														ZBTB32		16.6	33.7	8.1	
<b>III. Apoptosis</b>					<b>VII. Cytokine Signaling</b>					<b>X. Transcriptional Regulation</b>									
BCL2L11		1.2	2.0	3.7	CISH		3.5	10.7	16.4	AFF1		1.8	4.4	6.3					
BCL3		1.4	2.9	1.2	ENG	Endoglin	4.3	1.8	3.5	ATF3		0.6	6.6	12.8					
CDKN1A		3.3	8.1	5.2	SFTPA1		1.1	4.0	3.3	BACH2		2.8	6.4	7.6					
IER3		3.2	11.2	9.2	TIMP3		1.1	2.8	1.7	BATF3		1.2	2.1	1.6					
PLAC8		1.5	3.6	2.5						EGR2		1.5	1.8	3.4					
PRMT2		1.5	1.3	3.0						EPAS1	HIF-2A	2.1	5.0	5.8					
TNFSF10	TRAIL	1.6	7.2	15.8						FOS		3.2	1.5	1.8					
										ID3		2.6	1.7	1.2					
<b>IV. Cellular Growth</b>																			
CCND3	Cyclin D3	1.7	3.4	3.5															
CDC20		2.1	4.4	3.1															
CD63		1.6	6.8	32.3															
CD81		1.3	2.2	3.6															
GRN	Granulin	2.0	4.7	6.8															
P2RX7		1.1	2.1	14.4															
S1PR1		1.4	3.2	7.2															

Green indicates downregulated; red indicates upregulated.

subset of immune genes could be compared. This analysis revealed that spleen T<sub>CD8</sub> very closely resemble naive T<sub>CD8</sub>, indicating a state of immune immaturity (Fig. 3C). Conversely, lung T<sub>CD8</sub> upregulated the expression of dozens of additional immune genes, suggesting that lung-homing virus-specific T<sub>CD8</sub> adopt a significantly more differentiated state to combat viral infection. These results indicate that lung T<sub>CD8</sub> are immunologically more mature than spleen T<sub>CD8</sub> and display a distinct gene expression profile.

*Genes encoding several inhibitory receptors and pathways are upregulated in impaired lung T<sub>CD8</sub>*

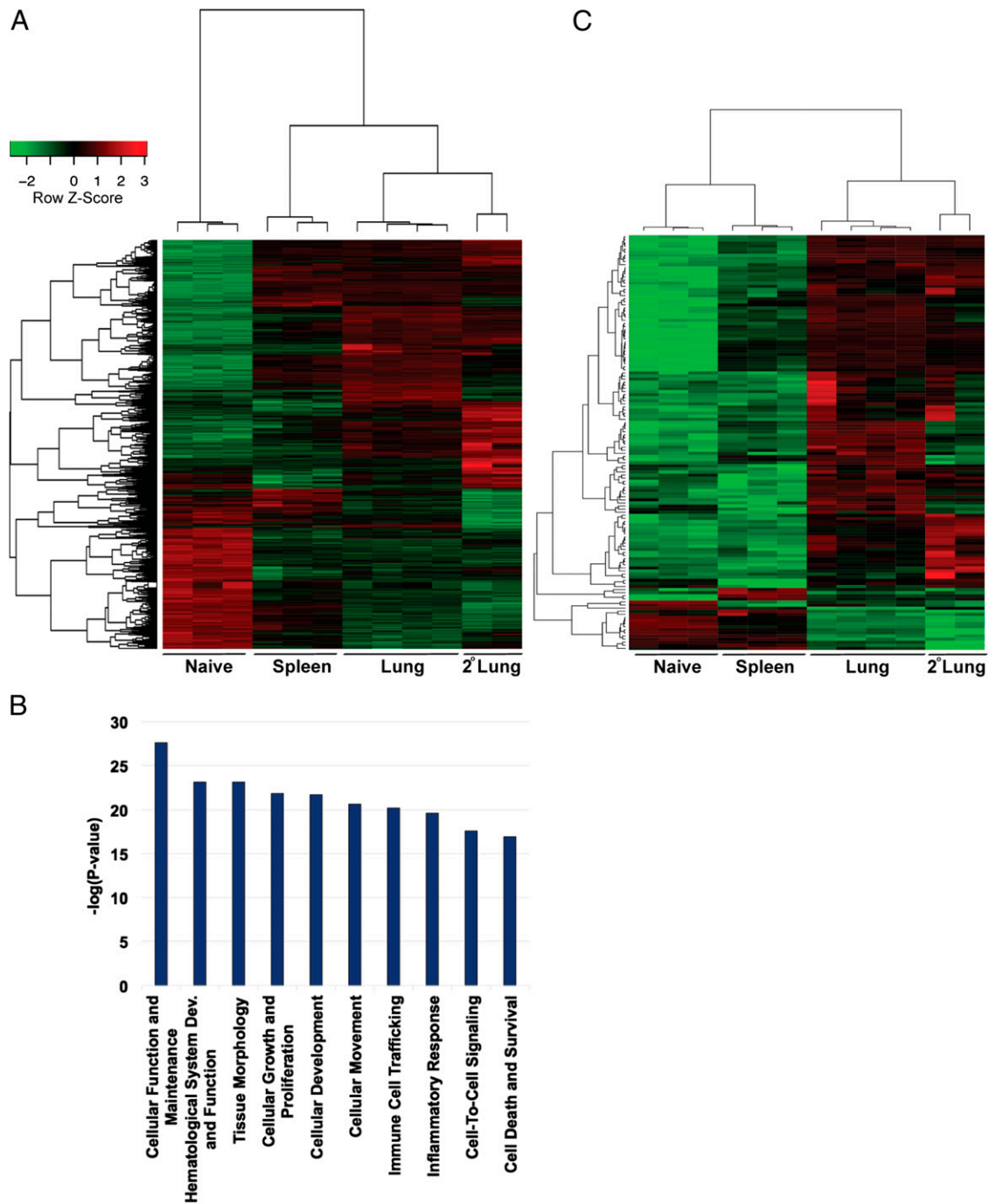
Several genes encoding inhibitory receptors, which can contribute to T cell exhaustion during chronic infection, were highly expressed by impaired lung T<sub>CD8</sub> (Fig. 3C, Table I). These genes encode the receptors TIM-3 (*Havr2*), LAG-3 (*Cd233*), and 2B4 (*Cd244*). *Pdcd1*, the gene that encodes PD-1, was not differentially expressed between spleen and lung T<sub>CD8</sub>, which may reflect either recent activation of spleen T<sub>CD8</sub> or migration from the infected lung where they had encountered Ag. FGL2, an inhibitory

molecule expressed by regulatory T cells that has been shown to inhibit adaptive immunity (41) and also promote T cell exhaustion during chronic LCMV infection (42), was also highly upregulated by lung T<sub>CD8</sub>. Interestingly, other known inhibitory receptors, such as CTLA-4, CD160, and BTLA, were not different between any of the groups. The activating receptors OX40 and 4-1BB were upregulated in the lung compared with the spleen, but not as dramatically. Of note, many genes encoding adhesion molecules, cytokines, chemokines, and various others were also significantly different (Supplemental Table I, Table I). In summary, impaired lung T<sub>CD8</sub> displayed coordinated upregulation of several genes associated with T cell exhaustion.

*Impaired lung T<sub>CD8</sub> adopt an exhaustion-like state during viral LRI*

Functional impairment in association with upregulation of inhibitory receptors has also been observed in exhausted T<sub>CD8</sub> during chronic infection. However, important differences exist, including the speed with which lung T<sub>CD8</sub> impairment versus exhaustion develops (days versus weeks). We sought to determine whether

GREEN = Downregulated  
RED = Upregulated



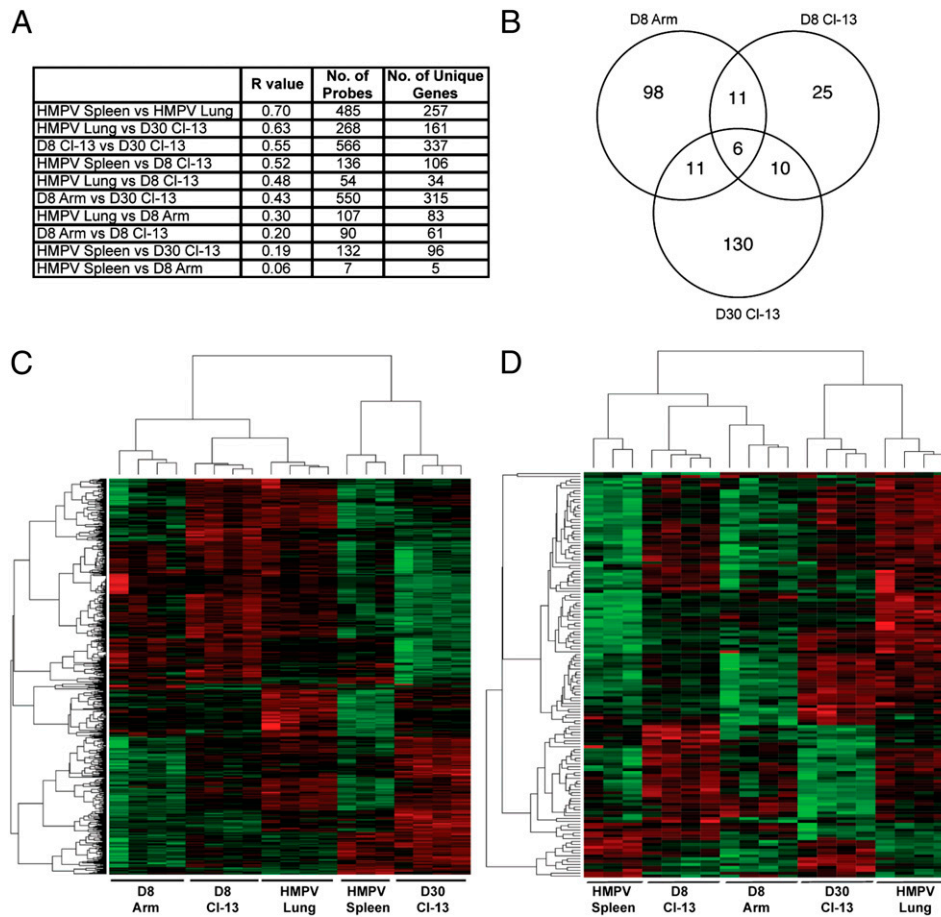
**FIGURE 3.** Lung T<sub>CD8</sub> differentially regulate numerous immune-related genes compared with spleen T<sub>CD8</sub>. **(A)** Heat map of ANOVA analysis of the gene expression profiles of naive T<sub>CD8</sub> as well as spleen, lung, and secondary lung (2° lung) M195-specific T<sub>CD8</sub>. Each row represents a unique gene whereas each column is an individual sample. **(B)** Enrichment of gene ontology categories (biological processes) for genes differentially expressed in the lung versus the spleen. The top 10 categories are shown. **(C)** Immunity-related genes were identified using Ingenuity Pathway Analysis and are displayed in a heat map comparing all four groups. Genes were considered significantly different when the fold-change was >2 and the FDR was <10%.

impaired lung T<sub>CD8</sub> resemble exhausted T cells at a global transcriptional level by comparing the gene expression differences of lung T<sub>CD8</sub> during acute viral LRI to functional effector T<sub>CD8</sub> during acute LCMV Armstrong (Arm) infection as well as exhausted T<sub>CD8</sub> during chronic LCMV clone 13 (Cl-13) infection (30). We found that anti-HMPV spleen and lung T<sub>CD8</sub> gene expression differed by 257 genes ( $R = 0.70$ ) in this analysis, whereas anti-LCMV T<sub>CD8</sub> at day 8 during Arm infection and day 30 during Cl-13 infection differed by 337 genes ( $R = 0.43$ ) (Fig. 4A). Interestingly, anti-HMPV lung T<sub>CD8</sub> differed by only 34 genes

compared with anti-LCMV T<sub>CD8</sub> at day 8 during Cl-13 infection ( $R = 0.48$ ), which increased to 161 genes at day 30 p.i. ( $R = 0.63$ ). Compared to effector T<sub>CD8</sub> at day 8 after Arm infection, anti-HMPV lung T<sub>CD8</sub> differed by 83 genes ( $R = 0.31$ ) whereas anti-HMPV spleen T<sub>CD8</sub> differed by only 5 genes ( $R = 0.06$ ). These results suggest that impaired lung T<sub>CD8</sub> gene expression most closely resembles exhausted T<sub>CD8</sub> early during chronic infection.

In a separate analysis, we compared each T<sub>CD8</sub> population based on patterns of gene expression. This experiment also revealed that lung T<sub>CD8</sub> most closely resemble T<sub>CD8</sub> early during Cl-13 infec-





**FIGURE 4.** Lung  $T_{CD8}$  possess an exhaustion-like gene expression profile. Lung and spleen M195-specific  $T_{CD8}$  gene expression was directly compared with that of spleen gp33-specific  $T_{CD8}$  during acute (Arm) or chronic (CI-13) LCMV infection (data from Doering et al. in Ref. 30). LCMV samples include early acute (day 8 [D8] Arm), early chronic (D8 CI-13), and late chronic (day 30 [D30] CI-13). Batch effect was compensated for before further analysis. Genes were considered significantly different when the fold change was  $>2$  and the FDR was  $<10\%$ . **(A)** Pairwise comparisons were made based on the coefficient of variation. The total number of probes, genes, and unique genes plus corresponding similarity score ( $R$  value) are shown. **(B)** In a separate analysis, all groups were compared using ANOVA, and the total number of genes found differentially expressed for the indicated anti-LCMV  $T_{CD8}$  populations compared with lung M195-specific  $T_{CD8}$  is shown. **(C)** Heat map resulting from the analysis in **(B)** shows the gene expression profiles of each  $T_{CD8}$  population. **(D)** Immune genes were identified using Ingenuity Pathway Analysis and are displayed in a heat map for each group of anti-HMPV or -LCMV  $T_{CD8}$ .

tion (day 8 p.i.), followed by functional effectors during Arm infection (Fig. 4B). However, each LCMV group differentially regulated numerous genes compared with lung  $T_{CD8}$ . The number of genes differentially expressed in these groups was similar to what we found when comparing the groups head-to-head, which showed that lung  $T_{CD8}$  exhibited gene regulation patterns with features of both early CL-13 and late CI-13 (Fig. 4C). Out of the total gene set for this analysis, we next compared only the genes with known immune functions. We found that anti-HMPV lung  $T_{CD8}$  most closely resemble exhausted anti-LCMV  $T_{CD8}$  at day 30 after CI-13 infection (Fig. 4D). In this analysis, anti-HMPV spleen  $T_{CD8}$  were more closely related to D8 CI-13 and Arm  $T_{CD8}$ . Of note, when comparing all genes or just immune genes, anti-HMPV lung  $T_{CD8}$  also uniquely express numerous genes that are not shared by any of the other populations (Fig. 4B, 4C, Supplemental Table II). These results indicate that lung  $T_{CD8}$  global gene expression closely resembles  $T_{CD8}$  that are destined to become exhausted (day 8 CI-13), whereas the lung  $T_{CD8}$  immunophenotype most closely resembles fully exhausted  $T_{CD8}$  (day 30 CI-13). Therefore, the infected lung environment rapidly induces a transcriptional state associated with exhaustion in lung  $T_{CD8}$ .

To confirm that increased inhibitory receptor gene expression during acute LRI corresponds to increased cell surface expression, we performed flow cytometric analysis of lung and spleen M195-specific  $T_{CD8}$  at day 7 after HMPV infection. Despite similar *Pdcd1* mRNA levels (Table I), surface PD-1 expression was greater on lung  $T_{CD8}$  at day 7 (Fig. 5A). The same was true for TIM-3 and LAG-3. 2B4 expression was also higher in the lung. Additionally, we found considerable coexpression of these inhibitory receptors on lung  $T_{CD8}$ , with most lung  $T_{CD8}$  expressing two or more inhibitory receptors by day 7 p.i.; in contrast, most splenic  $T_{CD8}$  expressed one or no inhibitory receptors (Fig. 5B). Thus, impaired lung  $T_{CD8}$  are associated with the coexpression of multiple inhibitory receptors.

#### *Viral Ag-mediated $T_{CD8}$ functional impairment is lung specific*

Ag-induced TCR signaling is associated with PD-1 upregulation during chronic infections (23, 24, 43, 44). To determine whether viral Ag is necessary for lung  $T_{CD8}$  impairment and inhibitory receptor upregulation, we took advantage of the fact that i.n. DC immunization elicits unimpaired, PD-1<sup>low</sup>  $T_{CD8}$  directly in the lung (12). We immunized mice i.n. with LPS-matured bone marrow-derived DCs loaded with the vaccinia virus-derived

epitope A34R, challenged them with HMPV a week later, and delivered cognate A34R peptide i.n. to induce TCR signaling or a control (mock) HLA-B\*0702–restricted peptide (Fig. 6A). Of note, mice receiving mock peptide did not lose weight during the infection (HMPV does not cause clinical disease in mice), whereas those receiving A34R peptide lost nearly 25% of their body weight (Fig. 6B). The endogenous M195 response was greatly diminished in A34R-treated mice and so was not included in the following analysis. Heterologous A34R-specific T<sub>CD8</sub> in mice receiving mock peptide were minimally impaired, whereas M195-specific T<sub>CD8</sub> in the same infected lungs were impaired (Fig. 6C). In contrast, A34R-specific T<sub>CD8</sub> in mice receiving cognate peptide expanded in number but were severely impaired (Fig. 6C).

Compared to M195-specific cells, fewer A34R-specific T<sub>CD8</sub> in mock-treated mice expressed PD-1, TIM-3, LAG-3 (Fig. 7A), or 2B4 (not shown). However, A34R-specific T<sub>CD8</sub> expressed very high levels of inhibitory receptors in mice treated with cognate Ag A34R peptide (Fig. 7A). Furthermore, in the mock peptide-treated mice, inhibitory receptor coexpression was low in A34R-specific T<sub>CD8</sub> (Fig. 7B), with most cells expressing one or no receptors. A34R-specific T<sub>CD8</sub> in A34R peptide-treated mice highly coexpressed all four of the inhibitory receptors we analyzed. Their expression eclipsed that of even the M195-specific T<sub>CD8</sub> that also were exposed to the presence of cognate Ag due to HMPV infection. Therefore, the large degree of functional impairment observed in A34R peptide-treated mice (Fig. 6) was associated with a dramatic increase in inhibitory receptor coexpression. Thus, cognate Ag-induced TCR signaling in the context of pulmonary infection promotes lung T<sub>CD8</sub> impairment and inhibitory receptor coexpression.

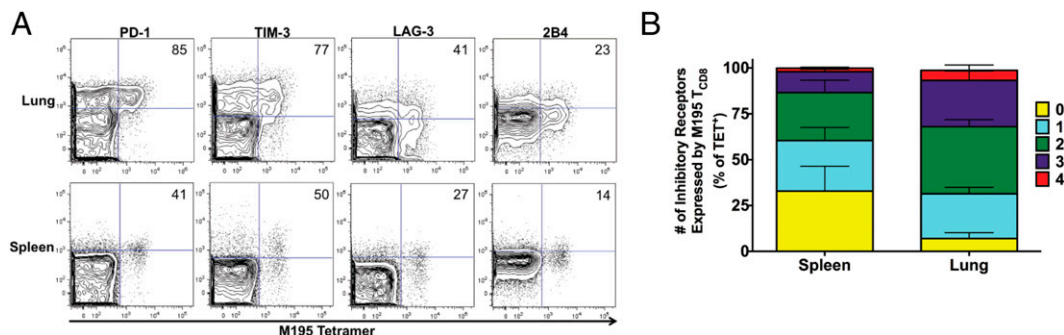
To show that this phenomenon is specific to the lung environment, we systemically immunized mice with A34R-specific DCs via the s.c. route and then injected them daily s.c. and i.p. with either A34R or mock peptide during HMPV infection (Fig. 8A). In mice treated with either mock or A34R peptide, the A34R-specific spleen T<sub>CD8</sub> were equally functional as measured by CD107a mobilization and IFN- $\gamma$  production (Fig. 8B). Splenic T<sub>CD8</sub> specific for the HMPV epitope M195 were unimpaired, as shown previously (12, 45). A34R-specific T<sub>CD8</sub> in mice treated with mock peptide had low expression of PD-1, TIM-3, LAG-3, and 2B4 (Fig. 8C and not shown) and most of these cells expressed one or no inhibitory receptors (Fig. 8D). Splenic M195-specific T<sub>CD8</sub> treated with mock peptide (but exposed to cognate Ag through HMPV infection) upregulated inhibitory receptor expression despite retaining functionality. However, A34R-specific

T<sub>CD8</sub> in mice treated with cognate A34R peptide increased expression of PD-1, TIM-3, LAG-3, and 2B4. As in the lung (Fig. 7A), A34R-specific T<sub>CD8</sub> in mice treated with Ag A34R peptide expressed higher levels of TIM-3 and LAG-3 than did M195-specific T<sub>CD8</sub>. Moreover, these cells exhibited substantial coexpression of multiple inhibitory receptors, with 70% coexpressing two or more inhibitory receptors. These results confirm that Ag-induced TCR signaling mediates inhibitory receptor expression, but more conclusively demonstrate that the location of T<sub>CD8</sub> in the lung is critical for the development of the exhaustion-like phenotype, because splenic T<sub>CD8</sub> remain functional despite Ag stimulation and upregulation of inhibitory receptors.

## Discussion

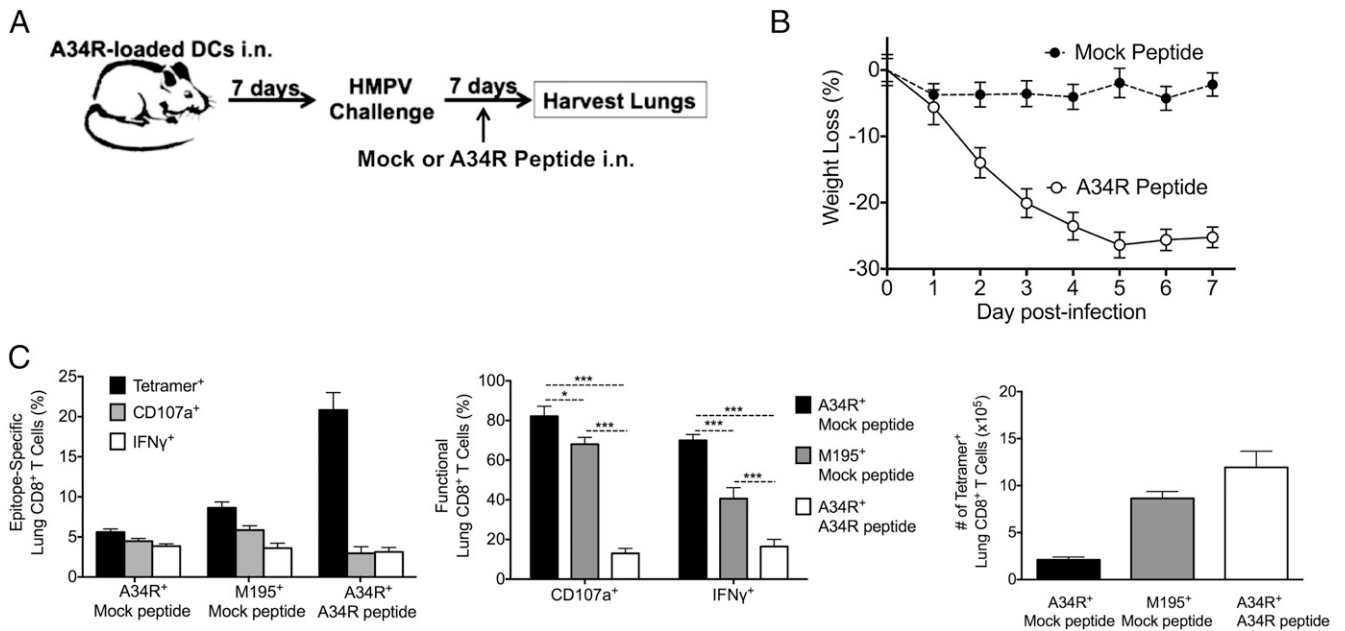
In this study, we sought to further elucidate mechanisms of T<sub>CD8</sub> impairment during acute viral LRI and better define the dysfunctional effector state observed in pulmonary T<sub>CD8</sub>. We first determined that lung T<sub>CD8</sub> impairment was cell-intrinsically regulated by PD-1. Importantly, this excluded a role for other PD-1–expressing cell types in mediating T<sub>CD8</sub> functional impairment. PD-1 signaling has been shown to affect multiple immune cells (e.g., macrophages and DCs) during other acute infections (20, 21). A T<sub>CD8</sub>-intrinsic role for PD-1 was suggested by in vitro studies showing that blocking PD-L1 on epithelial cells during RSV infection (46) or microglial cells during coronavirus infection (47) resulted in increased IFN- $\gamma$  production by memory T<sub>CD8</sub>. Bone marrow chimeric experiments confirmed an intrinsic role for PD-1 in impairing T<sub>CD8</sub> memory development and secondary responses after VACV infection (48). In the present study, we used bone marrow chimeric mice to show that PD-1 cell-intrinsically regulates T<sub>CD8</sub> functions during acute viral LRI. The contribution of T<sub>CD8</sub>-intrinsic PD-1 signaling to viral clearance cannot be assessed using this model, so the possibility exists that PD-1 expression by other immune cells is responsible for the increased viral replication observed in PD-1–expressing mice (12).

Several studies have shown that HMPV and RSV infection of DCs impaired the ability of these DCs to prime an effective T cell response; however, none of these studies reported on inhibitory ligand expression by DCs (49–52). We found previously that PD-L1 and other inhibitory receptors are expressed at substantially different levels by different subsets of APCs in the lung, and this expression was partially modulated by type I IFN expression (38). Yao et al. (17) recently reported that during RSV infection, inflammatory DC-derived PD-L1 directly inhibits cytokine production by effector T cells in vitro and in vivo. Thus, inhibitory



**FIGURE 5.** Lung T<sub>CD8</sub> coexpress numerous inhibitory receptors. **(A)** Multiparameter flow cytometry was used to quantify expression of the inhibitory receptors PD-1, TIM-3, LAG-3, and 2B4 on M195-specific lung and spleen T<sub>CD8</sub> at day 7 after HMPV infection. Numbers indicate percentage tetramer<sup>+</sup> T<sub>CD8</sub> expressing the receptor in the lung or spleen. Representative flow plots are shown. **(B)** Boolean gating analysis for the coexpression of inhibitory receptors on M195-specific T<sub>CD8</sub> at day 7 p.i. The number of receptors expressed by lung and spleen T<sub>CD8</sub> is shown. Data are representative of one out of independent experiments.





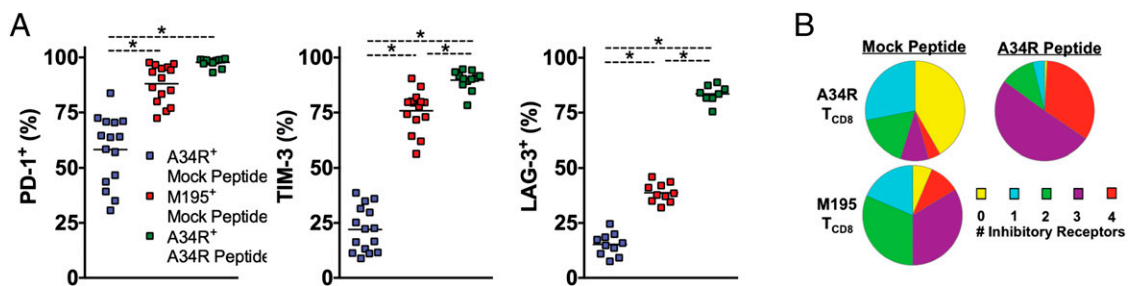
**FIGURE 6.** Cognate Ag is required for lung T<sub>CD8</sub> impairment. **(A)** Experimental design: mice were immunized i.n. with A34R-loaded DCs and challenged 7 d later with HMPV. During infection, mice were given either cognate (A34R) or mock (irrelevant HLA-B7–restricted epitope) peptide i.n. daily. Lung T<sub>CD8</sub> response was quantified at day 7 p.i. **(B)** Weight loss during HMPV infection of DC-immunized, peptide-treated mice. **(C)** Tetramer staining and ICS for the A34R and M195 T<sub>CD8</sub> epitopes at day 7 p.i. The percentage of tetramer<sup>+</sup>/IFN- $\gamma$ <sup>+</sup>/CD107a<sup>+</sup> (left), functional epitope-specific T<sub>CD8</sub> (middle), and the total number of tetramer<sup>+</sup> T<sub>CD8</sub> (right) were calculated. For each bar, the epitope analyzed is given with the treatment directly below. A34R<sup>+</sup> and M195<sup>+</sup> T<sub>CD8</sub> responses in mock-treated mice are from the same infected animals. Results are combined from three independent experiments with five mice per group. \**p* < 0.05, \*\*\**p* < 0.001, unpaired *t* test.

ligand expression by APCs may contribute to lung T<sub>CD8</sub> impairment. However, several lines of evidence support persistence of the intrinsic T<sub>CD8</sub> impaired phenotype induced by respiratory virus infection. First, in our initial study describing lung T<sub>CD8</sub> impairment, we showed that HMPV-specific lung T<sub>CD8</sub> were impaired at numerous time points after infection and after reinfection, whereas splenic T<sub>CD8</sub> remained functional at all time points (12). However, mice i.n. immunized with bone marrow–derived DCs did not exhibit lung T<sub>CD8</sub> impairment. Additionally, mice infected with HMPV and subsequently challenged with either HMPV or peptide-loaded bone marrow–derived DCs exhibited the same degree of impairment in both groups of mice, indicating that additional DCs could not rescue the phenotype. Genetic ablation or Ab blockade of PD-1 in vivo and in vitro (which did not affect APC numbers) restored T<sub>CD8</sub> functionality in the ICS assay (12, 13). Taken together, these data support a cell-intrinsic role for PD-1 in lung T<sub>CD8</sub> impairment.

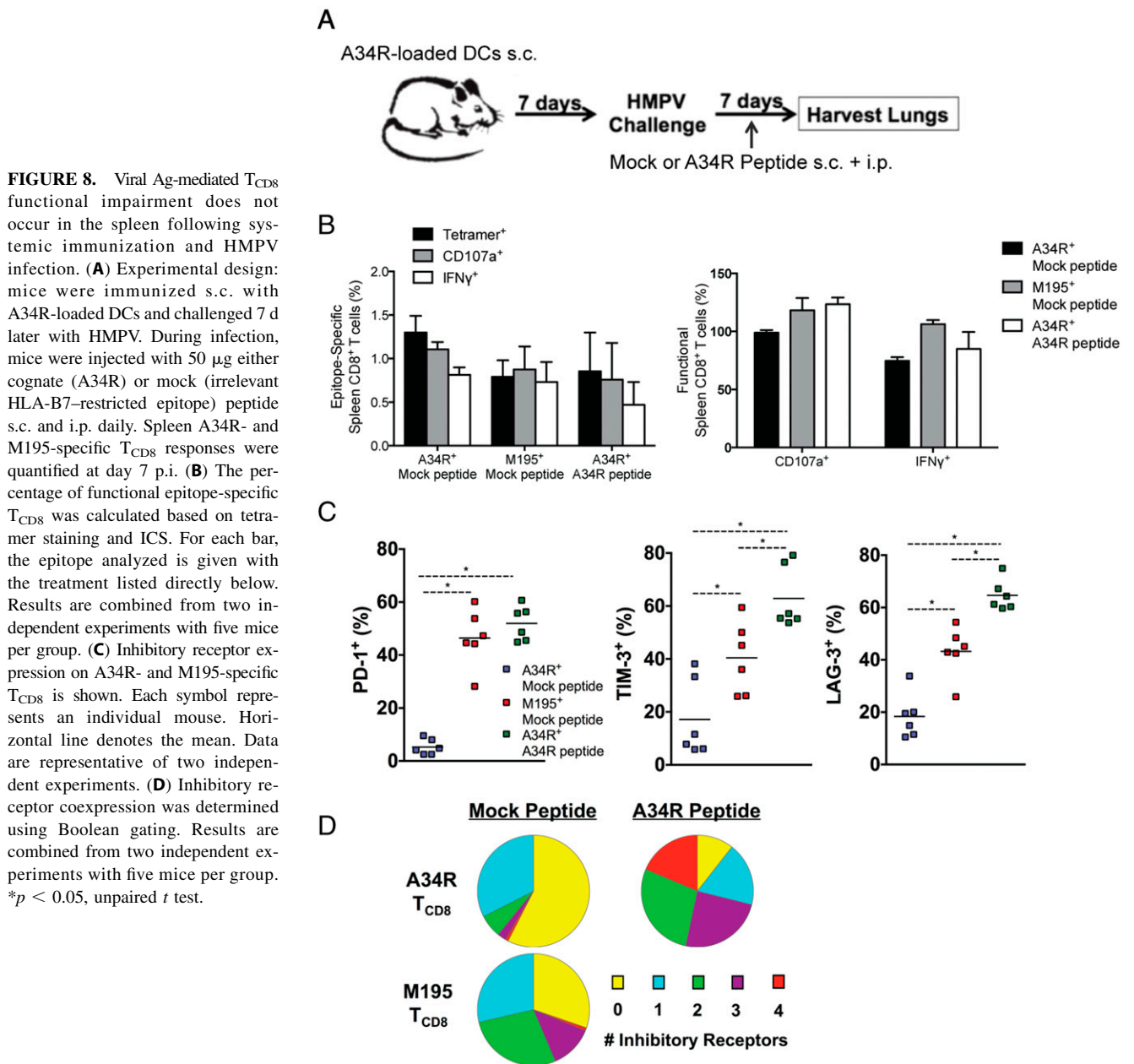
We then profiled global gene expression in impaired lung versus unimpaired spleen epitope-specific T<sub>CD8</sub> to identify pathways that

might explain the stark difference in functionality observed between these two populations. Lung T<sub>CD8</sub> exhibited a more diverse pattern of gene expression, suggesting that exposure to viral Ag in the infected milieu drives further differentiation, which was confirmed by subsequent experiments showing the upregulation of inhibitory receptors in response to cognate Ag-induced TCR signaling. Lung T<sub>CD8</sub> exhibited a more diverse pattern of gene expression than did spleen T<sub>CD8</sub>, expressing an additional 319 genes. They upregulated expression of numerous genes encoding chemokines, including CCL1, CCL3, CCL4, CXCL9, and CXCL15, suggesting a role for lung T<sub>CD8</sub> in recruiting other inflammatory cells to the infected lung. They transcribed more *Ifng*, *Tnfa*, and *Ii2* mRNA despite a decreased ability to produce these cytokines, suggesting posttranscriptional regulation of gene expression, which has been observed during exhaustion (4).

Recently the transcriptional circuitry that regulates effector, memory, and exhausted T<sub>CD8</sub> has been defined (reviewed by Kaech and Cui in Ref. 1). T-bet, which supports effector T<sub>CD8</sub> function and prevents exhaustion (53), and Eomes, which promotes exhaustion



**FIGURE 7.** Viral Ag mediates lung T<sub>CD8</sub> inhibitory receptor expression. Mice were immunized and treated as in Fig. 6. **(A)** Inhibitory receptor expression on A34R- and M195-specific T<sub>CD8</sub> is shown. Each symbol represents an individual mouse. Horizontal line denotes the mean. **(B)** Inhibitory receptor coexpression was determined for both epitopes via Boolean gating. Data are displayed as a pie chart. Results are combined from three independent experiments with five mice per group. \**p* < 0.05, unpaired *t* test.



**FIGURE 8.** Viral Ag-mediated T<sub>CD8</sub> functional impairment does not occur in the spleen following systemic immunization and HMPV infection. **(A)** Experimental design: mice were immunized s.c. with A34R-loaded DCs and challenged 7 d later with HMPV. During infection, mice were injected with 50  $\mu$ g either cognate (A34R) or mock (irrelevant HLA-B7–restricted epitope) peptide s.c. and i.p. daily. Spleen A34R- and M195-specific T<sub>CD8</sub> responses were quantified at day 7 p.i. **(B)** The percentage of functional epitope-specific T<sub>CD8</sub> was calculated based on tetramer staining and ICS. For each bar, the epitope analyzed is given with the treatment listed directly below. Results are combined from two independent experiments with five mice per group. **(C)** Inhibitory receptor expression on A34R- and M195-specific T<sub>CD8</sub> is shown. Each symbol represents an individual mouse. Horizontal line denotes the mean. Data are representative of two independent experiments. **(D)** Inhibitory receptor coexpression was determined using Boolean gating. Results are combined from two independent experiments with five mice per group. \* $p < 0.05$ , unpaired  $t$  test.

(54), were not differentially expressed between spleen and lung T<sub>CD8</sub> in our study. Fos and Jun, two proteins that form the heterodimeric transcription factor AP-1, were both more highly expressed in lung T<sub>CD8</sub>. AP-1 was recently described as a transcriptional activator of PD-1 (55) and so may represent a link between Ag-induced TCR signaling and PD-1. The genes encoding transcription factors *Id2* and *Id3* were more highly expressed in lung T<sub>CD8</sub>. *Id2* supports development of terminal effectors (56) whereas *Id3* promotes survival of long-lived memory cells (57). *Id2* could contribute during early effector differentiation of lung T<sub>CD8</sub>, but the contribution of each of these transcriptional regulators to impairment remains to be defined. Additionally, the *Prdm1* gene, which encodes the transcriptional repressor BLIMP-1, was upregulated in lung T<sub>CD8</sub>, whereas BCL-6, which opposes BLIMP-1 activity, was downregulated in both lung and spleen T<sub>CD8</sub>. During acute infections, high BLIMP-1 expression enhances T cell functions and the formation of KLRG1<sup>high</sup>IL-7R<sup>low</sup> terminal effectors (58). During chronic infection, BLIMP-1 is highly expressed in association with the upregulation of inhibitory receptors (40).

During viral LRI, a role for BLIMP-1 has been described in the generation of IL-10–producing effector T<sub>CD8</sub> (60). Given the high expression of inhibitory receptors on lung T<sub>CD8</sub>, BLIMP-1 in these cells may promote functional impairment, but further experiments are necessary to explore this possibility.

Lung T<sub>CD8</sub> expression of T-bet, BLIMP-1, AP-1, and *Id2* during acute viral LRI all imply an effector phenotype. Indeed, lung T<sub>CD8</sub> are effectors that produce cytokines, degranulate, and kill infected cells. However, they rapidly lose these effector functions in conjunction with coordinated upregulation of several inhibitory receptors. These inhibitory receptors temper immune responses in a number of settings (54), and their roles in LRI are not well understood. TIM-3, which is coexpressed by PD-1<sup>+</sup> T cells during chronic infections (25) and cancer (61), also impairs T cell responses during acute viral infections (62, 63). 2B4 can be either inhibitory or stimulatory (64), but in the setting of chronic infection it contributes to the rapid impairment of memory T<sub>CD8</sub> (27). Lung T<sub>CD8</sub> also expressed higher levels of *Il10* and *Il10ra* mRNA. T cells are the primary producers of IL-10 during LRI

(65), and it has been proposed that their expression of IL-10R facilitates an intrinsic T<sub>CD8</sub> counterregulatory mechanism (60), suggesting that IL-10 may also be a key mediator of T<sub>CD8</sub> impairment. However, unlike during chronic infection where IL-10 blockade enables clearance of an established infection (66), blocking IL-10 during acute infection only serves to increase inflammation and not accelerate viral clearance (60), so its application in therapeutic approaches may be limited.

Interestingly, we observed a significant overlap in the gene expression profile of impaired lung T<sub>CD8</sub> during acute viral LRI and exhausted T<sub>CD8</sub> during chronic viral infection. This was especially true when examining genes with known immune functions. Notably, impaired lung T<sub>CD8</sub> resemble exhausted cells more than they do functional splenic cells or even effector splenic T<sub>CD8</sub> during acute LCMV infection. It is unlikely that lung T<sub>CD8</sub> exist in other states of unresponsiveness, such as anergy or senescence, as genes associated with these conditions were not upregulated. Previous reports have also described exhaustion as unique from these states (4).

The functional impairment, upregulation of similar inhibitory receptors, and overlapping gene expression profiles shared by lung T<sub>CD8</sub> during acute viral LRI and T<sub>CD8</sub> during chronic LCMV infection suggest a similar functional state. This has been described as exhaustion, which is secondary to repetitive TCR stimulation during chronic infection and cancer. However, this paradigm may need revising given our results that exhaustion can develop rapidly in the right setting, namely, acute viral infection of an organ with critical importance with regard to survival. A similar functional state of anti-viral T<sub>CD8</sub> may exist in acute CNS infections, such as that seen during rabies (18) and coronavirus (47) infection. A key similarity in all these settings is the exposure of T<sub>CD8</sub> to viral Ag during infection. However, the degree to which viral Ag alone mediates exhaustion is unclear. It is likely that varying levels of Ag are expressed at different times and in different organs during these acute infections and also during chronic infections. A key future direction will be to explore the factors present in each organ during infection that mediate exhaustion. Understanding these processes will allow for more targeted therapies, especially now that PD-1 blockade is being used clinically for cancer treatment. The effects of these treatments may vary widely based on the local environment in the target tissue with differing levels of Ag, inhibitory receptors, immunomodulatory ligands, and cytokines.

Whereas the gene expression profile of lung T<sub>CD8</sub> shares many similarities with exhausted T<sub>CD8</sub>, it also preserves a core signature of unique genes. For example, lung T<sub>CD8</sub> more highly express the transcription factors ID3, IRF8, and AP-1 than do early effector, early exhausted, or late exhausted T<sub>CD8</sub>. Some of the unique transcripts may represent networks of genes required to exist in the lung environment, and many of them are immune genes with well-characterized functions. It will be interesting to decipher the role of these and other gene products in enforcing T<sub>CD8</sub> impairment versus allowing for control of respiratory virus infections.

In summary, we have shown that PD-1 cell-intrinsically regulates lung T<sub>CD8</sub> impairment and that lung T<sub>CD8</sub> rapidly acquire a gene expression profile resembling the exhausted state observed during chronic infection. Their differentiation state comprises elements of both effector and exhausted T cells that may allow them to balance control of pathogen spread with prevention of immune-mediated tissue damage. We confirmed coexpression of PD-1, TIM-3, LAG-3, and 2B4 by lung T<sub>CD8</sub> with a relative lack of these receptors by functional spleen T<sub>CD8</sub>. Our results indicate that acute viral LRI induces an exhaustion-like state in lung T<sub>CD8</sub> characterized by rapid functional impairment and Ag-dependent upregulation of numerous inhibitory receptors. Further exploration

of the roles of these inhibitory receptors in T cell impairment may yield novel targets for therapeutics or vaccine strategies against respiratory virus infections.

## Acknowledgments

We thank D. Flaherty, B. Matlock, and K. Weller at the Vanderbilt Flow Cytometry Shared Resource for invaluable assistance with sorting cells and analyzing flow cytometry data. We also thank Drs. A. Sette, F. Lemonnier, and T. Honjo for providing mice used in these experiments. We are grateful to Mark Boothby and Stokes Peebles for helpful discussions of the work.

## Disclosures

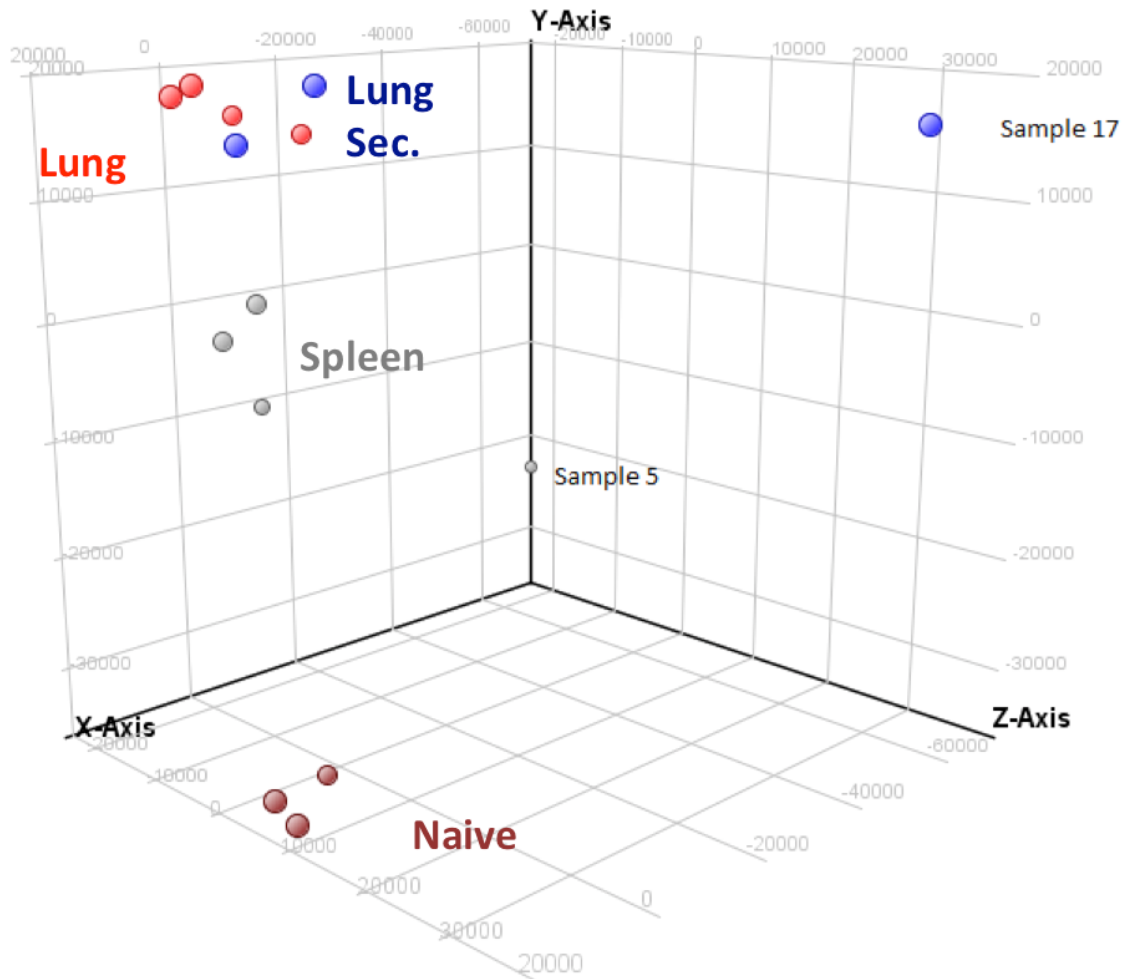
J.V.W. serves on the Scientific Advisory Board of Quidel, which activity has no conflict with the present work. The other authors have no financial conflicts of interest.

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## SUPPLEMENTARY FIGURE



**Figure S1. Gene Expression Profile of Lung T<sub>CD8</sub> Is Unique Compared to Naïve, Splenic or Memory T<sup>CD8</sup> During HMPV Infection**

From Figure 2. Gene expression data is plotted on three principal component axes. Sample #5 (spleen M195-specific T<sub>CD8</sub>) and Sample #17 (secondary lung M195-specific T<sub>CD8</sub>) were excluded from further analysis.



**Supplemental Table 1.** Genes differentially expressed comparing spleen, lung primary, and lung secondary CD8 to naive CD8.

Gene	Naïve Spl CD8 #1	Naïve Spl CD8 #2	Naïve Spl CD8 #3	HMPV Spl #1	HMPV Spl #2	HMPV Spl #3	HMPV Lung #1	HMPV Lung #2	HMPV Lung #3	HMPV Lung #4	HMPV Lung 2o #1	HMPV Lung 2o #2
AFF1	9.626	9.466	9.164	8.477	8.637	8.495	7.284	7.239	7.403	7.260	6.677	6.861
AMICA1	4.422	4.714	4.280	6.243	5.904	5.743	7.665	7.576	7.316	7.603	7.254	7.324
ATF3	4.457	4.643	3.669	5.154	4.962	5.157	6.686	6.872	7.096	7.277	8.078	7.788
ATP6V0D2	2.898	2.563	2.586	2.471	2.727	2.463	2.897	3.838	3.622	4.270	7.082	4.480
BACH2	7.051	7.165	7.291	5.534	6.113	5.436	4.567	4.578	4.410	4.424	4.042	4.452
BAG3	6.512	6.896	7.047	6.591	6.744	6.780	7.282	7.860	8.059	7.704	8.171	8.061
BATF3	4.317	4.285	3.992	3.861	3.911	4.089	5.177	5.471	5.168	5.248	5.204	4.576
BCL2L11	9.654	9.235	9.378	9.429	9.633	9.877	8.233	8.315	8.588	8.578	7.330	7.706
BCL3	8.095	8.022	7.566	8.680	8.087	8.343	9.177	9.696	9.570	9.348	8.328	8.085
BGN	4.351	3.736	3.827	4.030	3.484	4.143	5.213	4.785	6.133	6.619	6.257	4.808
BST2	8.214	8.681	8.719	9.231	8.513	9.132	10.686	10.590	10.450	10.732	8.968	9.188
C3	4.774	4.672	4.466	4.379	4.696	4.798	6.575	6.291	6.764	7.111	7.847	6.318
CAPG	5.842	5.691	5.634	8.720	8.080	8.805	9.575	9.739	9.480	9.603	10.424	10.347
CCL1	3.712	3.938	3.597	4.074	3.364	3.940	6.383	7.010	6.816	6.866	7.834	8.469
CCL4	4.784	5.170	5.373	8.642	8.669	8.417	11.147	11.372	11.335	11.388	10.817	11.222
CCL7	4.666	4.692	4.759	4.706	4.962	4.676	5.461	5.687	5.789	6.476	5.837	5.236
CCND3	6.877	7.355	7.160	8.107	7.530	8.033	8.870	8.994	8.753	9.018	8.868	8.998
CCR7	11.154	11.148	10.922	9.339	9.115	9.551	7.865	7.574	7.585	7.407	6.021	5.446
CCR8	3.679	3.468	3.212	3.892	3.941	4.598	6.424	6.333	5.820	6.258	8.875	9.197
CCRL2	3.211	3.563	4.052	5.545	4.889	4.908	6.985	7.050	6.394	7.147	6.500	5.841
CD14	3.193	3.159	2.843	3.698	3.518	3.934	4.261	4.400	4.996	5.683	6.417	3.821
CD200	4.281	4.283	4.266	5.006	4.936	4.946	6.369	6.459	5.940	6.605	6.366	6.582
CD244	3.971	3.577	3.276	4.162	4.329	4.170	5.617	5.838	5.409	6.090	7.602	7.438
CD36	2.724	3.002	2.864	2.713	3.031	3.117	4.834	4.572	5.317	6.420	6.957	5.301
CD38	4.333	4.630	4.439	6.228	6.438	6.349	7.571	7.604	7.610	7.573	7.868	7.842
CD63	2.798	3.168	3.078	3.594	3.230	4.153	5.713	5.360	5.380	6.641	9.054	6.999
CD69	8.503	8.267	7.817	8.114	7.882	7.990	9.523	9.348	9.229	9.271	8.660	8.740
CD7	9.261	9.397	9.474	10.282	10.294	10.482	9.326	9.103	9.359	9.084	9.474	9.199
CD74	5.223	4.965	5.627	5.834	7.165	6.800	6.995	7.409	7.560	8.523	9.459	7.198
CD81	5.021	4.778	4.910	3.938	4.261	5.329	5.512	5.681	6.122	6.907	7.018	6.510
CD93	3.264	3.613	3.800	3.490	3.213	3.750	4.401	4.325	4.612	5.939	5.100	4.015
CDC20	5.094	5.310	5.608	6.236	6.412	6.500	7.414	7.628	7.310	7.563	7.100	6.844
CDH1	4.580	4.315	4.511	3.718	4.125	4.000	7.109	6.279	6.373	6.925	9.473	9.498
CDH5	3.504	3.050	3.849	4.028	3.409	3.855	4.516	4.528	5.411	6.262	4.910	4.169
CDKN1A	5.893	6.370	5.625	7.385	7.670	7.948	8.816	8.994	8.924	9.205	8.593	8.110
CDKN2D	7.687	7.439	7.220	7.249	6.518	7.171	8.291	8.211	7.947	8.346	8.159	8.133
CFLAR	7.244	6.794	6.825	6.571	6.653	6.487	7.318	7.644	7.529	7.679	7.183	7.384
CHD7	7.694	7.863	7.867	8.378	8.451	7.726	7.586	7.537	7.805	7.385	6.659	6.635

Gene	Naïve Spl CD8 #1	Naïve Spl CD8 #2	Naïve Spl CD8 #3	HMPV Spl #1	HMPV Spl #2	HMPV Spl #3	HMPV Lung #1	HMPV Lung #2	HMPV Lung #3	HMPV Lung #4	HMPV Lung 2o #1	HMPV Lung 2o #2
CISH	5.125	5.066	5.329	7.214	6.807	6.886	8.706	8.720	8.542	8.392	9.146	9.278
CLIC4	7.577	7.466	7.549	8.463	8.073	8.490	9.321	9.343	9.307	9.486	9.083	8.467
CXCL10	4.076	5.089	5.133	8.260	7.774	7.473	9.587	9.764	9.230	9.469	5.918	5.933
CXCL3	2.683	2.786	2.604	2.794	2.756	2.683	2.816	2.990	3.004	2.797	3.984	3.067
CXCL9	3.735	4.196	3.225	4.315	4.123	4.270	5.922	6.967	6.529	7.963	4.852	3.844
CYBB	3.500	2.866	2.847	4.298	3.800	4.005	5.368	5.760	5.166	6.573	6.972	3.909
CYSLTR2	5.072	4.601	4.936	6.369	5.723	6.576	7.458	7.142	7.140	7.546	7.488	7.224
DCN	2.904	3.262	3.232	3.032	2.943	3.059	3.619	3.589	4.332	4.907	3.923	3.607
DDIT3	7.520	7.578	7.529	7.298	7.889	7.501	8.542	8.597	8.554	8.806	7.863	7.942
DUSP1	9.868	9.867	9.807	9.367	9.391	9.115	10.709	10.290	10.209	10.759	10.449	10.678
EGR2	6.371	6.600	6.571	5.867	5.992	5.999	7.181	7.437	7.300	7.660	8.434	8.136
ENG	5.967	6.285	6.167	3.865	3.832	4.379	4.730	5.067	5.681	5.620	4.537	4.090
EPAS1	5.173	5.382	5.066	6.612	5.923	6.255	7.112	6.976	7.836	8.173	7.692	7.792
FABP5	5.441	5.819	5.805	5.822	5.344	6.231	6.990	6.976	6.789	7.332	8.646	6.743
FCER1G	4.007	4.252	4.683	4.959	5.590	5.616	6.489	6.830	6.917	8.139	9.037	6.981
FGL2	3.767	2.924	3.578	5.698	5.943	5.691	8.997	8.552	8.609	8.737	9.690	9.958
FGR	3.946	4.072	4.753	4.562	5.805	5.237	6.510	6.364	6.251	6.611	6.479	5.947
FHL2	4.038	4.613	4.760	6.648	6.606	7.033	7.999	7.649	7.740	7.734	7.043	7.436
FOS	7.528	7.799	7.840	6.031	6.045	6.024	8.672	8.180	8.112	8.372	8.529	8.617
GADD45B	7.321	7.200	6.880	8.269	7.276	8.499	9.863	10.079	9.708	9.977	9.600	9.292
GADD45G	3.794	3.489	4.234	4.733	4.223	4.595	7.365	7.640	7.624	7.563	7.185	7.064
GCNT1	3.975	4.232	4.337	5.772	5.305	5.949	7.397	7.492	7.031	7.358	5.501	5.687
GRN	5.664	5.889	5.770	6.906	6.908	6.600	8.115	7.802	7.786	8.294	8.996	8.085
HAVCR2	4.006	3.018	3.105	6.990	6.321	7.211	8.329	8.688	8.345	8.630	7.927	7.966
HP	3.486	3.669	3.926	4.016	3.802	3.276	5.490	4.856	4.962	6.267	5.373	3.824
HRH4	3.642	3.929	3.421	6.764	6.741	5.989	5.266	5.600	5.522	5.097	5.178	6.042
HSPH1	7.538	7.668	8.014	8.157	8.170	8.048	9.237	9.815	10.233	9.789	9.742	9.763
ID3	6.137	6.331	6.271	4.824	4.176	5.531	6.592	7.202	7.088	7.047	6.072	5.814
IER3	4.598	4.514	4.210	5.750	6.537	6.035	7.796	7.934	8.036	7.914	7.812	7.465
IFNG	3.567	4.187	3.481	9.363	9.037	9.125	10.658	10.745	10.762	10.666	10.089	10.185
IL10	2.905	3.313	2.979	4.108	4.062	4.383	7.548	7.718	8.098	7.646	4.660	4.786
IL10RA	4.009	4.567	4.068	6.998	7.340	6.981	8.386	8.381	7.923	8.761	7.557	7.556
IL12RB1	4.118	4.232	4.545	5.772	5.773	5.851	6.874	6.894	6.593	6.960	6.596	6.730
IL12RB2	7.224	6.081	6.701	8.295	8.900	9.106	7.595	7.430	7.754	7.427	6.470	7.132
IL2	3.237	4.159	4.241	4.885	4.397	4.178	5.710	6.486	5.336	5.860	5.744	6.054
IL2RA	3.958	3.849	4.242	8.039	7.662	8.031	8.903	9.406	9.246	9.016	8.398	8.104
IL7R	10.719	10.588	10.690	9.263	9.593	9.350	8.100	7.948	8.039	7.717	9.742	9.902
IRF1	7.596	8.061	7.942	7.287	7.391	7.040	8.138	8.504	8.464	8.309	7.557	7.546
IRF4	4.467	5.177	4.726	7.748	7.410	6.119	8.038	8.324	8.283	8.185	7.523	7.535

Gene	Naïve Spl CD8 #1	Naïve Spl CD8 #2	Naïve Spl CD8 #3	HMPV Spl #1	HMPV Spl #2	HMPV Spl #3	HMPV Lung #1	HMPV Lung #2	HMPV Lung #3	HMPV Lung #4	HMPV Lung 2o #1	HMPV Lung 2o #2
IRF7	8.087	8.126	8.091	8.476	8.074	8.582	9.526	9.462	9.181	9.515	7.513	8.188
IRF8	4.739	4.853	4.924	5.897	5.685	5.686	7.835	8.498	8.301	8.292	6.811	6.424
ISG15	5.194	5.638	5.620	7.357	6.774	7.304	9.082	9.331	9.013	8.936	6.759	7.083
ISG20	6.616	7.062	6.419	7.817	7.380	7.569	10.144	10.111	9.822	9.935	9.774	9.759
JAK3	6.068	6.322	6.260	6.230	5.983	5.849	6.969	6.875	6.905	6.903	6.848	6.987
JUN	8.839	8.612	8.711	6.180	6.011	5.851	8.822	8.862	8.865	8.835	9.703	9.842
LAG3	3.300	3.357	3.603	7.860	7.738	7.389	9.028	9.265	9.051	9.004	8.646	8.781
LAT2	5.046	4.922	4.717	5.560	5.339	5.523	6.664	6.723	6.246	6.332	7.728	7.798
LDLR	5.157	5.383	5.647	4.965	4.843	4.434	6.356	5.887	6.062	6.029	6.430	5.941
LIF	3.124	2.655	3.009	2.743	2.515	3.004	4.303	3.753	3.474	4.370	3.789	3.378
MGST1	2.528	2.822	2.740	2.468	2.446	2.937	4.266	3.511	4.130	5.458	6.088	2.978
MUC1	3.766	3.975	3.470	4.576	4.343	4.167	5.625	5.569	5.786	5.670	5.038	4.751
MXI1	8.150	7.703	7.679	7.815	7.990	8.475	7.325	7.055	7.131	7.160	7.170	7.348
MYB	9.284	9.065	9.066	8.530	8.643	8.938	7.411	7.552	7.692	7.423	5.207	5.170
MYC	7.199	7.987	7.965	7.641	7.521	6.797	9.165	9.373	9.231	9.043	8.720	8.704
NFKB2	8.417	8.738	8.450	9.012	9.065	9.278	8.165	8.059	8.011	8.083	7.599	7.696
NUDCD2	5.964	6.017	5.712	5.163	4.873	5.573	6.473	6.667	6.159	6.413	6.199	6.241
OSM	3.815	4.367	4.517	4.095	4.685	4.290	5.206	5.619	5.269	5.413	6.428	5.537
P2RX7	3.673	4.236	4.120	3.949	4.355	3.984	5.138	4.772	5.214	5.277	8.028	7.684
PLAC8	8.763	8.729	8.799	9.403	9.071	9.526	10.699	10.552	10.577	10.555	10.116	10.076
PLSCR1	3.410	3.207	3.230	6.524	5.755	6.734	7.521	7.552	7.407	7.439	7.110	7.290
PRDM1	3.749	3.840	4.245	6.352	6.163	5.686	7.590	7.534	7.619	7.556	6.800	6.836
PRF1	7.118	6.977	7.219	8.408	8.129	8.376	9.678	9.747	9.654	9.724	9.224	8.616
PRMT2	5.045	4.547	4.358	4.215	4.007	3.934	5.070	4.719	5.132	5.317	5.921	6.548
RBPJ	5.498	5.439	5.357	5.108	4.921	5.279	6.190	6.049	5.933	6.096	6.814	6.700
RGS16	6.314	6.619	5.712	9.001	8.455	9.285	10.666	10.591	10.540	10.669	9.882	10.255
RHOB	6.064	5.765	6.256	3.824	3.572	4.404	5.322	5.020	4.734	5.439	6.356	6.095
RORA	6.375	6.377	6.261	8.563	8.324	8.351	7.458	7.200	7.501	7.239	7.455	7.473
RSAD2	4.142	4.398	4.426	5.772	5.201	5.631	7.891	7.833	7.363	7.664	5.278	5.778
S1PR1	11.140	10.916	10.973	10.468	10.408	10.565	9.442	9.348	9.133	9.361	8.101	8.241
SCGB1A1	2.689	2.602	2.560	2.997	3.356	2.934	10.010	10.001	10.556	10.677	8.904	8.557
SERPINE2	3.329	3.159	2.894	3.051	3.054	3.460	4.537	4.071	4.406	4.880	4.705	4.624
SERPING1	3.076	3.156	2.907	3.099	3.003	3.386	5.758	5.344	5.869	6.976	5.403	4.182
SFTPA1	4.156	3.254	4.041	3.334	3.960	3.749	5.711	4.985	5.726	6.795	5.882	5.237
SLC34A2	2.957	3.281	3.683	3.423	3.138	3.228	4.223	3.830	4.440	5.823	4.434	3.642
SOCS1	5.779	5.836	5.495	5.611	5.520	5.451	6.560	6.624	6.677	6.507	6.058	6.492
SOCS2	4.337	4.149	4.142	5.374	5.127	5.234	6.093	6.318	6.774	6.318	7.366	7.377
SPARC	4.024	4.067	3.689	4.037	4.078	4.267	5.947	5.941	6.314	7.501	7.833	6.951
STAT2	6.498	6.737	6.119	6.808	6.779	6.704	8.041	8.213	8.158	8.230	7.281	7.507

Gene	Naïve Spl CD8 #1	Naïve Spl CD8 #2	Naïve Spl CD8 #3	HMPV Spl #1	HMPV Spl #2	HMPV Spl #3	HMPV Lung #1	HMPV Lung #2	HMPV Lung #3	HMPV Lung #4	HMPV Lung 2o #1	HMPV Lung 2o #2
TAF4B	8.375	8.440	8.459	7.213	7.492	7.302	5.962	5.987	6.034	5.600	5.232	5.354
TCF7	10.967	11.004	10.872	10.096	9.968	10.245	8.906	8.960	8.960	9.057	8.579	8.941
TGFBI	4.067	3.920	3.937	4.331	3.959	4.304	5.199	5.494	5.672	6.784	7.278	4.945
THBD	3.252	2.830	3.056	3.396	3.216	3.034	4.095	4.228	4.410	5.947	4.499	3.996
TIMP3	4.176	3.752	3.940	3.747	4.065	3.723	4.828	5.434	5.098	6.494	5.147	4.240
TLR7	3.528	3.175	3.270	2.675	2.561	2.597	4.032	4.216	3.203	4.082	3.242	2.920
TNF	5.978	5.676	5.902	7.071	7.177	6.867	8.448	8.582	8.254	8.091	8.699	8.826
TNFRSF4	6.401	6.225	6.411	5.988	6.151	6.780	7.517	7.473	7.876	7.126	7.098	6.585
TNFRSF9	5.080	5.412	5.367	7.418	6.860	8.015	8.399	8.831	8.458	8.539	5.142	5.861
TNFSF10	4.169	4.711	4.277	5.333	4.790	5.134	7.436	7.337	6.796	7.402	8.217	8.510
TNIP1	8.667	8.896	8.679	8.767	8.623	8.377	7.681	7.360	7.304	7.362	7.564	7.318
TREML2	7.481	7.522	7.431	4.402	3.775	4.065	4.977	5.235	4.882	5.334	4.426	3.956
TYROBP	5.102	4.877	5.256	6.623	6.110	6.289	6.700	7.436	7.657	8.440	9.350	6.532
UBE2L6	3.423	4.570	4.428	5.577	5.679	5.247	6.866	6.748	6.514	7.086	5.944	5.241
ULK1	7.636	7.608	7.653	7.417	7.505	7.509	6.057	6.313	6.281	6.125	5.822	6.158
XCL1	5.910	6.292	5.487	8.128	7.028	8.393	10.482	10.666	10.552	10.740	10.441	10.657
ZBTB32	4.147	4.440	3.293	8.279	8.173	7.592	8.766	9.299	9.070	8.999	7.213	6.732
ZFP36	8.437	8.424	8.295	8.142	8.133	8.023	9.307	9.286	9.100	9.209	8.812	8.808

**Supplemental Table 2.** Genes differentially expressed comparing HMPV spleen and lung CD8 to LCMV CD8.

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10465840	Scgb1a1	1.22489924	1.097489037	0.196440685	7.19901952	0.895983116	0.160372934	5.87723405	0.178991023	6.559536609	36.64729391	9.35E-08
10403821	Tcrg-V3	25.67251527	10.71535554	2.529109792	18.9162109	0.417386276	0.098514297	0.736827331	0.23602668	1.765336748	7.479394907	1.34E-07
10519983	Fgl2	2.455319484	1.382718719	0.716013102	3.626916692	0.563152261	0.291617082	1.477166909	0.517829904	2.6230329	5.065433413	1.46E-07
10394054	Cd7	7.738213034	5.031780271	5.348796871	1.549479567	0.650250936	0.691218612	0.200237388	1.06300287	0.307938639	0.289687495	2.47E-07
10548513	Klra9	9.950055502	8.176211773	4.042649417	4.455294082	0.821725243	0.406294157	0.447765752	0.4944404	0.54490933	1.102072829	2.47E-07
10359697	Xcl1	10.14102383	2.611025901	1.111656151	8.937049617	0.257471627	0.109619716	0.881276858	0.425754548	3.422811552	8.039401037	4.23E-07
10349603	Ii10	2.504294679	2.099665878	0.694299772	4.695603725	0.838426043	0.27724364	1.875020446	0.330671551	2.236357591	6.763078304	1.81E-06
10437224	Mx2	2.276091305	1.781463072	0.710173672	4.091848635	0.782685241	0.31201458	1.797752413	0.398646306	2.296903427	5.761757717	1.81E-06
10421387	Sftpc	0.999298967	1.067890091	0.267814675	4.421806844	1.068639242	0.268002554	4.42490885	0.250788613	4.140694704	16.51069658	1.81E-06
10530615	Ociad2	6.948335631	1.580656314	1.554003173	3.409081591	0.227487041	0.223651138	0.490632832	0.983137928	2.156750687	2.193741719	1.82E-06
10523182	Areg	8.08023602	3.880274164	1.694742675	6.462140074	0.480217924	0.209739254	0.79974645	0.436758488	1.665382342	3.813050894	2.47E-06
10589994	Eomes	2.307139857	2.894083932	1.896685622	1.767821195	1.254403335	0.822093908	0.766239285	0.655366488	0.610839643	0.932058099	2.47E-06
10574259	Gpr56	1.768171898	1.649469468	0.862672894	2.606438848	0.932867144	0.487889721	1.474086796	0.523000219	1.580167986	3.021352435	2.47E-06
10554240	Isg20	2.285765557	1.235104132	0.732910983	2.846101619	0.540345937	0.320641363	1.245141528	0.593400155	2.304341427	3.883284168	2.47E-06
10590620	Ccr9	1.065345624	0.387498288	0.779777398	0.682871646	0.363730116	0.731947811	0.640986015	2.01233766	1.762257195	0.87572639	2.75E-06
10405211	Gadd45g	0.821870973	1.065669626	0.456802304	2.123096664	1.296638598	0.555807808	2.583248142	0.428652833	1.992265343	4.647736327	2.84E-06
10548879	Mgp	0.977996775	1.135837099	0.307750472	3.872981058	1.161391457	0.314674322	3.960116392	0.270945959	3.409803272	12.58480949	3.00E-06
10407126	Plk2	1.895742583	1.463073943	1.01744548	2.022617986	0.771768254	0.53670023	1.066926493	0.695416308	1.382444131	1.987937463	3.00E-06
10521678	Cd38	2.198041841	1.662857011	1.044390344	2.434790582	0.756517451	0.475145798	1.107708933	0.628069844	1.464221257	2.331303231	3.09E-06
10462618	Ifit3	4.174211072	1.274049782	0.890330612	3.859280458	0.3052193	0.213293146	0.924553261	0.698819328	3.02914416	4.334659961	3.09E-06
10531724	Plac8	0.572701926	0.474532635	0.446135558	1.029247169	0.828585715	0.779001323	1.797177769	0.9401578	2.168970253	2.307027878	3.09E-06
10503334	Gem	2.489438705	1.587724113	0.759593377	3.678509824	0.637783975	0.305126363	1.477646273	0.478416477	2.316844465	4.842735513	4.19E-06
10379721	Ccl4	2.433525938	2.14805753	0.826140433	3.942649653	0.882693501	0.339482896	1.620138742	0.384598839	1.835448817	4.77237222	5.29E-06
10526410	Hspb1	0.87591493	1.029397122	0.442551645	2.304761191	1.175224998	0.505245007	2.631261453	0.429913428	2.238942719	5.207892044	5.29E-06
10482795	Ernm	0.668656635	0.24601174	0.52927951	0.558658109	0.367919388	0.791556506	0.835493257	2.151440052	2.270859554	1.055506777	5.43E-06
10390186	Abi3	1.261126057	1.424834539	0.758292553	2.01596544	1.129811354	0.601282123	1.598543959	0.53219692	1.414876876	2.658558932	5.91E-06
10477187	Tpx2	0.382840776	0.307931751	0.336587152	0.749925899	0.804333736	0.879183131	1.958845417	1.093057634	2.435363989	2.228028891	5.91E-06
10548504	Klra8	4.301773466	5.331474094	2.953999869	2.582157347	1.239366539	0.686693498	0.600254143	0.554068128	0.484323341	0.874122363	6.23E-06
10399710	Rsad2	2.786604934	1.189530313	0.789612424	3.066408606	0.426874401	0.283360018	1.100410241	0.663801851	2.577831412	3.883435105	6.23E-06
10385248	Hmmr	0.366802728	0.28411474	0.313746209	0.753098274	0.774570958	0.855354078	2.053142512	1.10429402	2.650683568	2.400342228	6.38E-06
10566366	Trim30d	3.027029317	1.315911666	0.983435688	2.776321729	0.434720489	0.324884758	0.91717702	0.747341721	2.109808585	2.823084176	6.38E-06
10389064	Ccl1	1.037582487	1.159091249	0.546561325	2.260391318	1.117107569	0.526764216	2.178517224	0.471542965	1.950140957	4.135659102	7.79E-06
10551989	Tmem149	1.189516733	1.195026556	0.720959336	1.803878803	1.004631985	0.60609432	1.516480394	0.603299845	1.509488466	2.502053464	1.03E-05
10547769	Ptpn6	0.450624184	0.449706822	0.408494116	0.877663757	0.997964242	0.906507309	1.947662351	0.908356503	1.951635409	2.148534637	1.09E-05
10420413	Lats2	1.875400098	2.319723504	2.237795207	0.975332954	1.236921927	1.193236158	0.520066601	0.96468187	0.420452245	0.435845492	1.16E-05
10587350	Ddx43	6.094543529	5.061960911	2.590422695	3.799919181	0.830572608	0.425039658	0.623495289	0.511742928	0.750681257	1.466910859	1.25E-05
10576034	Irf8	0.849894718	0.707261379	0.460326035	1.642492499	0.832175285	0.541627128	1.932583489	0.650857022	2.322327427	3.568106893	1.25E-05
10350733	Rgs16	3.553339008	0.765404169	0.721507141	2.879628994	0.215404206	0.203050466	0.810400862	0.942648565	3.762233226	3.991130275	1.26E-05
10516246	Cdca8	0.384603755	0.353237571	0.410094996	0.644332878	0.918445456	1.06627923	1.675316138	1.160960864	1.824077987	1.571179566	1.83E-05
10351867	Aim2	4.055766008	2.216028164	1.363256535	3.416579489	0.54638955	0.336128005	0.842400543	0.615180149	1.541758153	2.506189701	2.00E-05
10515836	Ccnb1	0.331230807	0.248600145	0.274453687	0.74901073	0.75053449	0.828587441	2.261295488	1.103996487	3.012913487	2.729096988	2.00E-05



ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10389231	Ccl3	3.571793177	1.630686532	0.748198907	4.976924164	0.45654562	0.209474309	1.393396515	0.458824484	3.052042233	6.651873074	2.51E-05
10360834	Hlx	0.912418881	0.973809252	0.656960666	1.454873474	1.0672831	0.720020902	1.594523638	0.674629723	1.494002518	2.214551875	2.79E-05
10511416	Tox	7.13669789	1.847940017	1.967099137	2.689864228	0.258934881	0.275631555	0.376905996	1.064482136	1.455601482	1.367426876	2.79E-05
10369290	Ddit4	1.055603161	0.878733944	0.612604938	1.647615715	0.832447246	0.5803364	1.560828706	0.697144958	1.87498813	2.689524051	3.47E-05
10533198	Oas2	1.438121437	1.044477166	0.623132084	2.243886711	0.726278838	0.433295873	1.560290149	0.596597134	2.148334865	3.600980868	3.51E-05
10434778	Rtp4	3.880387275	1.13582407	1.015328736	2.839937102	0.292708946	0.261656547	0.731869502	0.893913734	2.500331853	2.797061682	3.66E-05
10444890	Ier3	2.245779807	2.374085859	1.011052482	3.234738316	1.057132071	0.450201075	1.440363078	0.425870226	1.362519516	3.199377256	3.84E-05
10524621	Oasl2	1.6294411	0.830140806	0.667321197	2.003452181	0.509463525	0.409539932	1.229533355	0.803865069	2.413388387	3.002230698	3.84E-05
10459905	Setbp1	4.082032187	2.074196489	1.129364091	4.171757499	0.508128401	0.27666712	1.02198055	0.544482693	2.011264372	3.693899543	3.84E-05
10539135	Capg	0.662413142	0.329259594	0.386709019	0.925257204	0.497060781	0.583788266	1.396797777	1.174480643	2.81011464	2.39264449	4.38E-05
10351644	Cd244	3.977882881	1.88267205	1.176944053	3.657837738	0.473284937	0.295871972	0.91954385	0.625145549	1.942896926	3.107911314	4.83E-05
10545528	Pigp	3.486102049	2.82110984	1.892136253	2.365806961	0.809244767	0.542765595	0.678639618	0.670706339	0.838608596	1.250336469	5.14E-05
10557895	Ilgax	0.24526862	0.325184732	0.396180487	0.434506218	1.325830967	1.615292189	1.771552421	1.218324379	1.336182715	1.096738059	5.30E-05
10429564	Ly6a	1.002397573	0.616871488	0.60481293	1.308525426	0.615396031	0.603366315	1.305395645	0.980452074	2.121228574	2.16352092	5.30E-05
10523670	Aff1	2.176243053	1.845417858	2.29062628	0.940658542	0.847983342	1.052559951	0.432239653	1.241250739	0.509726584	0.410655614	5.70E-05
10428796	Fbxo32	1.577809665	1.803624719	1.997221074	0.832978814	1.143119325	1.265818761	0.527933649	1.107337382	0.461835994	0.417068909	5.94E-05
10462973	Hells	0.633551814	0.46338125	0.533781221	0.88134212	0.731402295	0.84252181	1.39111293	1.15192667	1.901980537	1.651129873	5.94E-05
10368199	Myb	0.782640495	0.404413322	0.953359883	0.386309908	0.516729361	1.218132578	0.49359816	2.357389904	0.955235366	0.405208898	5.94E-05
10390763	Ccr7	1.319621328	1.283156663	1.632919428	0.689585156	0.972367327	1.237415154	0.522562906	1.272579939	0.537413066	0.42230201	6.10E-05
10462866	Cep55	0.484306175	0.402131265	0.497662596	0.684278559	0.830324464	1.027578466	1.412904882	1.237562555	1.701629836	1.374984908	6.49E-05
10575052	Cdh1	1.132442337	1.260623588	0.620609427	2.13896476	1.113190091	0.548027398	1.888806776	0.492303518	1.696751338	3.446555381	6.76E-05
10428536	Trps1	2.781621857	1.473402722	1.640518372	1.467886187	0.529691956	0.589770449	0.527708748	1.113421571	0.996255922	0.894769733	6.90E-05
10569017	Ifitm3	1.797699751	0.904292595	0.601783801	2.67482581	0.503027602	0.334752119	1.48791577	0.665474653	2.957920726	4.44482853	6.97E-05
10346960	Ccny1	2.874782781	1.705194166	1.375139488	2.105669267	0.59315583	0.478345528	0.732462042	0.806441586	1.234856011	1.531240492	7.92E-05
10437687	Litaf	2.372298214	1.372014967	1.106239766	2.031569004	0.578348438	0.466315643	0.856371679	0.80628841	1.480719273	1.836463547	8.85E-05
10437080	Ttc3	2.398295782	1.99033575	1.771444879	1.527669889	0.829895864	0.738626525	0.636981435	0.890023143	0.767543812	0.862386353	9.08E-05
10389151	Sifn10-ps	1.98530078	1.384460832	1.028309984	2.022460994	0.697355709	0.517961809	1.018717675	0.742751229	1.460829332	1.966781442	9.47E-05
10579532	Bst2	1.465615892	0.808717502	0.668662221	1.707483962	0.551793622	0.456232922	1.16502828	0.826818042	2.111347854	2.553582223	9.74E-05
10531415	Cxcl10	4.972590421	1.893921733	1.087841488	4.349561518	0.380872256	0.218767563	0.874707376	0.574385662	2.296589897	3.998341271	9.74E-05
10547906	Lag3	1.789483556	0.799776958	0.711021389	1.861325163	0.446931717	0.39733329	1.040146559	0.889024599	2.327305312	2.617818804	9.75E-05
10419323	Dlgap5	0.541792034	0.396008898	0.446128571	0.839191232	0.73092418	0.823431397	1.54891763	1.126561988	2.119122164	1.881052428	9.81E-05
10393936	Cbr2	0.925491505	1.078262752	0.556695775	1.89806806	1.165070393	0.601513652	2.050875723	0.516289536	1.760301983	3.409524814	1.05E-04
10462623	Ifit1	5.658767957	1.77527719	0.932173853	5.615678816	0.313721503	0.164730885	0.99238542	0.525086368	3.163268726	6.024282702	1.07E-04
10548314	Klr1b	1.489110412	0.353893497	0.835053952	0.762615875	0.237654303	0.560773698	0.512128495	2.359619376	2.154930456	0.913253416	1.07E-04
10482528	Neb	1.608366022	0.902560967	0.777204092	1.760478942	0.561166398	0.483225883	1.094576059	0.861109798	1.950537422	2.265143686	1.17E-04
10557156	Plk1	0.50340794	0.44192276	0.408352777	0.940877078	0.877862117	0.811176671	1.869015171	0.924036537	2.129053226	2.304079048	1.20E-04
10374560	Zrsr1	2.334985518	2.280160228	1.823410555	1.632633564	0.976520073	0.780908721	0.699205006	0.799685274	0.716017034	0.89537354	1.20E-04
10402347	Ifi272a	1.863500797	0.86074027	1.008769658	1.337411034	0.461894232	0.541330414	0.717687396	1.171979158	1.553791637	1.325784359	1.29E-04
10572906	Mcm5	0.568529471	0.486730602	0.644689088	0.631581961	0.856122026	1.133958961	1.110904524	1.324529596	1.297600682	0.979669073	1.29E-04
10585778	Sema7a	0.845966689	0.601657016	0.511260334	1.307744497	0.711206509	0.604350431	1.545858145	0.849753796	2.173571423	2.557883745	1.29E-04
10541307	Usp18	2.193076015	1.119681155	0.571425052	3.654896755	0.510552825	0.260558707	1.66656182	0.510346226	3.264229946	6.396108717	1.34E-04

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10466224	Ms4a3	0.92766958	0.416806334	0.726912695	0.712742231	0.449304734	0.783590096	0.76831476	1.744005876	1.710008158	0.980505961	1.65E-04
10521913	Rbpj	1.232023387	0.893892562	0.677447877	1.653722791	0.725548371	0.549866086	1.34228198	0.757862753	1.850024109	2.441107051	2.01E-04
10501020	Chi3l3	1.174480246	0.14841066	0.187010278	2.039973611	0.126362841	0.159228117	1.736916068	1.260086556	13.74546552	10.90835027	2.04E-04
10346298	Coq10b	2.801491458	1.804300619	1.732791927	1.622595986	0.644050016	0.618524794	0.579190053	0.96036764	0.899293593	0.936405555	2.16E-04
10573172	Clgn	3.258370256	2.312643928	1.928107984	1.962804968	0.7097548	0.59173999	0.60238856	0.833724535	0.848727702	1.017995353	2.22E-04
10427454	Card6	1.55364347	2.167872971	1.836618367	1.097562031	1.395347783	1.182136315	0.706443951	0.847198333	0.506285214	0.597599398	2.23E-04
10573823	Chd9	2.029064213	1.946611448	1.594288891	1.543557148	0.959364142	0.785726189	0.760723657	0.819007251	0.792945685	0.968179077	2.23E-04
10514466	Jun	1.006276851	1.248614744	0.542073627	2.414205561	1.240826263	0.538692336	2.399146476	0.434140018	1.933507171	4.453648801	2.23E-04
10571984	Ddx60	3.568499973	1.650436761	1.090477146	3.278560097	0.462501548	0.305584182	0.918750209	0.660720345	1.986480291	3.006537192	2.43E-04
10548535	Klra3	3.63501621	2.36766296	2.100809026	1.969947872	0.651348666	0.577936632	0.541936475	0.887292263	0.832022085	0.937709162	2.44E-04
10389606	Prr11	0.393845531	0.329715292	0.321579482	0.846788082	0.837169057	0.816511696	2.150051266	0.975324743	2.568240247	2.633215515	2.44E-04
10449652	Dnahc8	2.333579509	2.208343544	2.038771249	1.257448837	0.946333106	0.873666932	0.538849794	0.923212901	0.569408162	0.616767986	2.45E-04
10381697	Hexim1	2.081791485	1.425192925	1.76715867	1.019274072	0.684599267	0.848864395	0.489613911	1.239943477	0.715183225	0.576786957	2.49E-04
10436095	Retnla	1.095710787	1.138067216	0.55642843	2.184062755	1.038656578	0.507824178	1.993283976	0.488924047	1.919098208	3.925145874	2.53E-04
10441233	Mx1	1.665122225	0.934461881	0.623699891	2.317605237	0.561197171	0.374567033	1.391852924	0.667442839	2.480149575	3.715898097	2.58E-04
10430113	Arhgap39	1.115547516	0.963572368	0.706536528	1.514200036	0.863766316	0.633354041	1.357360412	0.733246979	1.57144402	2.143130577	2.70E-04
10383204	Rnf213	2.355229636	0.945317974	0.884686511	1.928483151	0.401369769	0.375626435	0.818808969	0.935861303	2.040036478	2.179849162	2.73E-04
10504838	Nr4a3	2.208215153	1.234169194	1.816958935	0.900658602	0.558898979	0.822817891	0.407867232	1.472212192	0.729769149	0.495695629	2.75E-04
10542205	Klre1	3.576527528	6.218589437	2.1376224	3.728983615	1.738722654	0.597680958	1.042626846	0.343747151	0.599651039	1.744453845	2.78E-04
10561679	Psmc8	0.493890672	0.511843827	0.592440851	0.642623209	1.036350463	1.199538448	1.301144657	1.157464093	1.255506417	1.08470442	2.78E-04
10512774	Coro2a	0.952049508	0.722416203	0.571937471	1.447919376	0.758801089	0.600743413	1.520844624	0.791700779	2.004273118	2.531604326	2.78E-04
10399360	Rhob	1.745469154	1.359789233	0.971434608	1.987844743	0.779039395	0.55654642	1.138859853	0.714400868	1.461877102	2.046298049	2.78E-04
10409278	Nfil3	2.538648834	1.417048974	1.236874587	1.923892184	0.558190229	0.487217677	0.757841005	0.872852392	1.357675154	1.555446449	2.82E-04
10411728	Cenph	0.481697579	0.343282661	0.437913175	0.722206286	0.71265183	0.909103957	1.499293992	1.275663542	2.103823957	1.649199721	2.91E-04
10570434	Ifitm1	0.375019897	0.301448444	0.36813905	0.609770882	0.803819867	0.981652047	1.625969413	1.22123387	2.022803216	1.656360232	2.91E-04
10522051	Klf3	1.061334087	2.001909785	1.653481321	0.84869295	1.886220191	1.557927274	0.799647312	0.825951965	0.423941656	0.513276406	2.91E-04
10556113	Rbm3	0.579491912	0.463931212	0.67834809	0.576386364	0.800582721	1.170591126	0.994640911	1.462173859	1.242396177	0.849691142	2.91E-04
10389143	Slnf8	2.313771009	1.222494623	0.843282245	2.608263503	0.528355926	0.364462275	1.12727815	0.689804461	2.133558262	3.092989944	2.91E-04
10546853	Srgap3	4.338108623	2.088161338	1.932207721	2.203201191	0.48135294	0.44540326	0.507871375	0.925315341	1.055091458	1.140250692	2.91E-04
10380174	Mpo	0.966829529	0.390825837	0.735305314	0.696001483	0.404234485	0.760532536	0.719880249	1.881414289	1.780848187	0.946547604	3.17E-04
10397645	Gpr65	2.044284074	1.32682839	1.022452787	2.080102474	0.649043059	0.500152009	1.017521244	0.770599118	1.56772533	2.034423987	3.30E-04
10475866	Bcl2l11	2.349061307	0.979528532	1.904603827	0.725857899	0.416987215	0.81079358	0.308999129	1.944408728	0.741027826	0.381107025	3.35E-04
10357043	Bcl2	2.526919178	1.449910319	1.158713911	2.179800092	0.573785791	0.45854807	0.862631504	0.79916247	1.503403392	1.881223717	3.39E-04
10594774	Ccnb2	0.507299165	0.381767197	0.543789376	0.593475333	0.752548442	1.071930359	1.169872481	1.424400475	1.554547741	1.091369855	3.44E-04
10417734	Nr1d2	2.089565573	1.968231321	2.227075552	1.003229144	0.941933264	1.065807927	0.480113741	1.131511082	0.509710994	0.450469291	3.44E-04
10587792	Plscr1	2.420001581	1.779205031	1.099622476	2.456882944	0.73520821	0.454389156	1.015240223	0.618041461	1.380888038	2.234296768	3.44E-04
10410931	Vcan	1.17487048	0.509816308	0.816550089	0.858962202	0.433934052	0.695012857	0.731112252	1.601655491	1.684846461	1.051940615	3.44E-04
10449284	Dusp1	2.326766685	1.696859425	1.047932257	2.447450926	0.729277858	0.450381323	1.051867788	0.61757164	1.442341593	2.335504904	3.52E-04
10357488	Cd55	2.396050975	1.526331334	2.260901235	0.870920168	0.637019558	0.943594798	0.363481486	1.481265034	0.570597058	0.385209294	3.53E-04
10574023	Mt2	0.793830442	0.428878316	0.399699982	1.282911598	0.540264386	0.503508005	1.616102798	0.931965938	2.991318399	3.209686404	3.55E-04
10425321	Apobec3	0.553610439	0.424343764	0.47095686	0.804508943	0.76650246	0.850700829	1.453204069	1.109847487	1.895889634	1.708243391	3.55E-04

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10395039	Cmpk2	1.244093604	0.810969651	0.68863751	1.48395217	0.651855815	0.553525481	1.192797845	0.849153245	1.829849204	2.154910454	3.55E-04
10420302	Gzmc	0.799520149	0.40354129	0.38340854	1.31087842	0.504729355	0.479548315	1.639581468	0.950109815	3.24843691	3.419012054	3.55E-04
10509163	Id3	1.189360432	1.136825066	0.682037857	1.863087505	0.955828894	0.573449258	1.56646165	0.5999497	1.638851535	2.73164823	3.55E-04
10356082	Plscr1	2.184689925	1.690239526	1.047661033	2.378462929	0.773674793	0.479546787	1.088695884	0.619829922	1.407175074	2.270259992	3.55E-04
10433088	Cbx5	0.489628845	0.455454799	0.531560769	0.697754214	0.930204181	1.085640224	1.425067621	1.167098844	1.531994427	1.312651825	3.62E-04
10344713	Ahcy	0.348510806	0.415453087	0.580279778	0.411168543	1.192080934	1.665026644	1.179787069	1.396739597	0.989687055	0.708569483	3.66E-04
10437040	Chaf1b	0.646240691	0.455618259	0.553802209	0.809353358	0.705028738	0.85695967	1.252402347	1.215496083	1.776384819	1.46144841	3.70E-04
10450367	Hspa1a	0.367756812	0.752936202	0.167682365	2.938422126	2.047375268	0.455959915	7.990122896	0.222704612	3.902617669	17.52373978	3.84E-04
10411739	Ccnb1	0.371315502	0.272251913	0.307423494	0.751266538	0.733209122	0.827930676	2.023256593	1.129187636	2.759453655	2.443751213	3.97E-04
10521602	Cpeb2	2.865642842	2.335709856	2.402020835	1.279202193	0.81507361	0.838213611	0.446392752	1.028390075	0.547671702	0.532552497	4.05E-04
10452633	Tgif1	1.746075709	0.851784447	1.458263663	0.763435273	0.487827901	0.835166342	0.437229193	1.712010202	0.896277545	0.523523484	4.23E-04
10563597	Saa3	2.768018304	1.179743011	0.976743592	2.469100242	0.426204917	0.352867461	0.892010085	0.827929119	2.092913641	2.527889881	4.24E-04
10562637	Ccnb1	0.332163944	0.235774799	0.272054813	0.71576667	0.709814546	0.819037762	2.154859622	1.153875709	3.035806515	2.630964922	4.32E-04
10378068	Xaf1	2.064464753	0.857994682	0.771285044	1.977258475	0.415601517	0.37360049	0.957758408	0.898939189	2.304511339	2.563589805	4.32E-04
10531980	Gbp9	1.851042828	1.040215499	0.889988145	1.834888232	0.561961875	0.480803648	0.991272705	0.855580546	1.763950099	2.061699634	4.34E-04
10484463	Serping1	1.030872586	1.104720929	0.577203959	1.983283025	1.071636732	0.559917846	1.923887638	0.52248848	1.79527967	3.436017712	4.37E-04
10543067	Asns	0.968492224	0.52068957	0.492752694	1.405961386	0.537629066	0.508783325	1.451701264	0.94634639	2.700191185	2.853279955	4.52E-04
10439762	Ahcy	0.455776897	0.53490157	0.663270752	0.531435944	1.173603958	1.455253121	1.166000179	1.239986549	0.993521001	0.801235306	4.60E-04
10366630	Tmbim4	0.745262461	0.458051891	0.537497897	0.973720881	0.614618225	0.721219604	1.306547602	1.173443244	2.125787274	1.811580821	4.60E-04
10452980	Eif2ak2	2.043251867	0.940885642	0.877363816	1.889532831	0.460484416	0.429395822	0.924767456	0.932487197	2.008249192	2.153648004	4.72E-04
10590494	Kif15	0.583775153	0.369290698	0.512968887	0.699071784	0.63259064	0.878709696	1.197501778	1.389065282	1.893012167	1.362795682	5.15E-04
10523156	Cxcl2	5.079701073	3.277235986	1.439264075	4.982741722	0.645163158	0.283336372	0.980912391	0.439170106	1.520409804	3.462006597	5.17E-04
10375443	Havcr2	0.809247715	0.391605444	0.402038224	1.256107173	0.483912944	0.496804892	1.552191188	1.026641049	3.20758353	3.12434763	5.17E-04
10374197	Ramp3	0.997132669	1.031553371	1.440665702	0.547625653	1.034519682	1.444808446	0.549200393	1.396598317	0.530874765	0.380119866	5.21E-04
10597279	Ccr1	2.560189297	1.318241712	0.876388362	2.863848361	0.514900095	0.342313892	1.118608051	0.664816136	2.172475908	3.267784564	5.23E-04
10587829	Plod2	2.395924426	2.261455161	1.553747427	1.987142443	0.943875832	0.648496009	0.829384442	0.687056482	0.878700793	1.278935307	5.32E-04
10391461	Brca1	0.711411828	0.452314636	0.599239141	0.770764364	0.635798587	0.842323837	1.083429222	1.324828103	1.704044714	1.28623835	5.45E-04
10548525	Klra10	6.252471259	5.163918302	3.265207897	2.96598845	0.825900366	0.522226774	0.474370585	0.632312075	0.574367811	0.908361288	5.65E-04
10399087	Ncapg2	0.525442185	0.334618867	0.525465076	0.581849663	0.636832893	1.000043565	1.107352397	1.570339056	1.738842965	1.107304157	5.96E-04
10590631	Ccr2	0.366465251	0.425911008	0.482819317	0.592037766	1.1622139	1.317503682	1.615535894	1.133615493	1.390050399	1.226209775	6.24E-04
10353420	Mcm3	0.549374352	0.47745482	0.553962165	0.720117631	0.869088298	1.008350978	1.31079587	1.160239967	1.508242457	1.299940098	6.24E-04
10405874	Cbx3	0.541624223	0.480953036	0.597054867	0.687078119	0.887982878	1.102341517	1.268551314	1.241399518	1.428576322	1.15077886	6.26E-04
10410207	Cbx3	0.541624223	0.480953036	0.597054867	0.687078119	0.887982878	1.102341517	1.268551314	1.241399518	1.428576322	1.15077886	6.26E-04
10527009	Chst12	1.964328875	1.471389796	1.781663309	0.972193887	0.74905471	0.907008665	0.494924195	1.210871052	0.660731704	0.545666447	6.54E-04
10458195	Cdc25c	0.541250034	0.360491125	0.400983467	0.880256008	0.666034369	0.740847006	1.626338941	1.11232549	2.441824352	2.195242647	6.61E-04
10533569	Kdm2b	0.990867111	0.845646821	1.249576057	0.594236744	0.853441205	1.261093484	0.599713864	1.477657133	0.702700855	0.47555068	6.61E-04
10446771	Lclat1	3.149171972	1.412205277	1.529328982	1.660593308	0.448437014	0.48562892	0.527311091	1.082936743	1.175886633	1.085831321	6.61E-04
10498367	P2ry13	1.030619976	0.45099325	0.682576246	0.909372865	0.437594129	0.662296736	0.882355171	1.51349548	2.016377994	1.33226562	6.61E-04
10389877	Wfikkn2	0.182721727	0.326827467	0.420281571	0.327589801	1.78866231	2.300118204	1.792834412	1.285943239	1.002332526	0.779453164	6.65E-04
10451287	lsg15	1.606905896	0.945108153	0.694879106	2.000078474	0.588154014	0.43243298	1.24467679	0.735237659	2.116242959	2.87831143	6.72E-04
10478525	Wfdc2	0.979619766	1.02287113	0.547687689	1.929211897	1.044151175	0.559081909	1.969347662	0.535441536	1.886075225	3.522467157	6.88E-04

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10490104	Aurka	0.576497927	0.644068798	0.515006829	1.055155401	1.117209219	0.893336827	1.830284815	0.799614622	1.638265049	2.048818272	7.19E-04
10531994	Mpa2l	1.968509114	0.887255012	0.773157081	2.024734363	0.450724361	0.392762764	1.028562352	0.871403453	2.282020768	2.618787841	7.37E-04
10360382	Ifi204	1.507186031	0.621326134	0.578013088	1.862337326	0.412242498	0.383504807	1.235638659	0.930289354	2.99735875	3.221963937	7.70E-04
10411611	Naip5	3.408869989	2.436101021	1.985041022	1.955340355	0.714635943	0.582316436	0.573603676	0.814843475	0.802651589	0.985037757	7.98E-04
10551293	Cyp2f2	0.956106726	1.12387412	0.562374982	1.964301499	1.175469317	0.588192684	2.054479323	0.500389654	1.747794939	3.492867861	8.16E-04
10418193	Plac9	1.006138676	1.122028034	0.693765835	1.63299932	1.115182291	0.689533015	1.623036028	0.618314172	1.45539975	2.353819168	8.16E-04
10526972	Nudt1	0.458866919	0.364872507	0.39605656	0.805566576	0.795159755	0.863118572	1.755556004	1.085465614	2.20780289	2.03396852	8.71E-04
10373454	Pa2g4	0.50568527	0.473429769	0.557974266	0.691544248	0.936214276	1.103402254	1.367538842	1.178578752	1.460711374	1.239383767	8.71E-04
10473022	Plp2	0.554801299	0.396941456	0.534549569	0.652491758	0.715465982	0.963497328	1.176081887	1.346671054	1.643798471	1.220638452	9.00E-04
10418180	Plac9	1.008061526	1.114519286	0.695485879	1.625312197	1.105606411	0.689924039	1.612314482	0.624023189	1.458307826	2.336944927	9.37E-04
10418205	Plac9	1.008061526	1.114519286	0.695485879	1.625312197	1.105606411	0.689924039	1.612314482	0.624023189	1.458307826	2.336944927	9.37E-04
10392221	Pecam1	0.733718603	0.391082138	0.667623559	0.61005925	0.533013797	0.909917722	0.831462154	1.707118515	1.559926137	0.913777294	9.52E-04
10452316	C3	1.071682606	0.621371313	0.527415266	1.613263551	0.579809086	0.492137563	1.505355729	0.848792429	2.596295513	3.058810874	9.57E-04
10454077	Taf4b	2.092736017	1.362302034	2.041996474	0.785510424	0.650966975	0.975754447	0.375350936	1.498930798	0.57660519	0.384677659	9.95E-04
10368289	Enpp1	2.083817434	0.900266393	1.52971609	0.891178414	0.432027479	0.734093143	0.427666263	1.6991816	0.989905234	0.582577656	9.96E-04
10548401	Klrc2	2.097958988	1.722107864	1.768326052	1.231753985	0.820849156	0.842879228	0.587120145	1.026838149	0.715259485	0.696564971	1.02E-03
10462796	Kif11	0.509140263	0.359736287	0.497792941	0.643404412	0.706556352	0.977712778	1.263707584	1.383771831	1.78854465	1.292514134	1.07E-03
10404439	Serpib9b	0.944250829	0.376771227	0.77635009	0.619904191	0.39901604	0.822186294	0.656503729	2.060534444	1.645306613	0.798485372	1.08E-03
10582997	Casp4	3.255773968	1.847504872	1.319517443	2.635831683	0.567454894	0.405285335	0.809586817	0.714215948	1.426698096	1.997572443	1.15E-03
10397346	Fos	1.555604645	1.574750285	0.743050786	2.605975438	1.012307523	0.477660432	1.675217059	0.471853089	1.654849955	3.507129642	1.15E-03
10346365	Sgol2	0.688077934	0.465342844	0.500901362	1.008529624	0.676293805	0.727971843	1.465720051	1.076413591	2.167282976	2.013429591	1.16E-03
10546855	Srgap3	2.121442121	1.074547844	1.25238243	1.363916457	0.506517634	0.59034485	0.642919476	1.165497132	1.269293373	1.089057483	1.16E-03
10482772	Nr4a2	4.953035317	1.816833068	2.431762748	1.544635698	0.366812056	0.490964145	0.311856387	1.338462399	0.850180308	0.635191776	1.17E-03
10474769	Bub1b	0.507214515	0.37256157	0.441221771	0.77093853	0.734524663	0.869891848	1.519945719	1.184292225	2.069291605	1.747281254	1.19E-03
10575873	Osgin1	1.015883979	1.160505915	0.728074321	1.601306691	1.142360681	0.716690425	1.576269262	0.627376657	1.37983501	2.199372571	1.21E-03
10541729	Cdca3	0.576981543	0.449920079	0.567795873	0.697668991	0.779782445	0.984079785	1.209170378	1.261992741	1.550650935	1.228732056	1.23E-03
10524631	Oasl1	1.119861166	1.046744378	0.730774146	1.61851604	0.93470906	0.652557807	1.445282764	0.698140025	1.546238102	2.214796527	1.24E-03
10349102	Bcl2	2.695166895	1.759659984	1.452507451	2.011243045	0.652894627	0.538930429	0.746240631	0.825447793	1.142972542	1.384669692	1.27E-03
10590242	Ccr8	0.809808445	0.957576448	0.556102975	1.556779913	1.182472786	0.686709281	1.922405134	0.58074003	1.625750002	2.799445396	1.27E-03
10542911	Samd9l	2.830153609	1.34839207	1.065792923	2.471213623	0.476437768	0.376584833	0.873172967	0.790417674	1.832711478	2.318662067	1.27E-03
10411359	Plp2	0.598803149	0.444776952	0.563332864	0.715081793	0.742776575	0.940764699	1.194185092	1.266551383	1.607731224	1.269377023	1.28E-03
10474902	Rad51	0.496168096	0.326815072	0.456875796	0.647724558	0.658678127	0.920808493	1.305453865	1.397964278	1.981929886	1.417725701	1.33E-03
10428534	Trps1	4.088241682	1.427472736	1.151764949	3.184590961	0.349165447	0.281726238	0.778963478	0.806856005	2.230929447	2.764966032	1.33E-03
10525464	Orai1	1.712015211	1.252181569	1.652108514	0.854411883	0.731407969	0.965008081	0.499067927	1.319384149	0.682338651	0.517164505	1.38E-03
10451763	Satb1	0.416451151	0.348577097	0.570138272	0.444417918	0.837017971	1.369039972	1.067154975	1.635615984	1.274948701	0.779491466	1.38E-03
10462613	Ifit2	1.124094335	0.692933266	0.538444666	1.754069388	0.616436935	0.479003095	1.56042899	0.777051258	2.531368421	3.257659512	1.38E-03
10474875	Casc5	0.56410532	0.409445805	0.541428737	0.708148542	0.7258322	0.959800799	1.255348102	1.322345302	1.729529363	1.307925668	1.43E-03
10523145	Cxcl15	0.998817346	1.100872626	0.519105458	2.198508075	1.102176119	0.519720107	2.201111229	0.471539982	1.997059445	4.235185819	1.46E-03
10376326	Irgm2	1.122252203	0.715794704	0.640971679	1.472372296	0.637819825	0.571147624	1.311979867	0.895468597	2.056975677	2.297094152	1.47E-03
10533549	Anapc5	0.561294577	0.458183719	0.662546964	0.570737319	0.81629814	1.180390816	1.016823148	1.44602904	1.245651677	0.861429227	1.47E-03
10555695	Rrm1	0.43743635	0.353660954	0.437368928	0.655901533	0.808485519	0.999845872	1.49942165	1.236689896	1.854605452	1.499652789	1.48E-03

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10394978	Rrm2	0.599184319	0.456242136	0.540075861	0.783730369	0.761438712	0.901351795	1.307995462	1.183748319	1.717794803	1.451148674	1.48E-03
10569102	Irf7	2.032301137	0.942564409	0.831778656	1.856006938	0.463791705	0.409279236	0.913253899	0.882463467	1.969103566	2.2313712	1.48E-03
10538590	Herc6	2.265780134	1.232336227	0.915246475	2.399728056	0.543890472	0.403943199	1.059117793	0.742692177	1.947299774	2.621947336	1.49E-03
10588577	Cish	1.555626444	1.344285233	0.809854205	2.030624009	0.864143984	0.520596837	1.305341663	0.602442239	1.510560377	2.507394535	1.49E-03
10441956	Fam120b	2.011958752	1.524535673	1.363176801	1.550052841	0.757737042	0.677537151	0.770419791	0.894158677	1.016737665	1.13708863	1.49E-03
10509568	Camk2n1	2.356152749	2.220857254	1.825010135	1.58802152	0.942577791	0.77457208	0.673989206	0.821759315	0.715048893	0.870143946	1.50E-03
10466521	Gcnt1	1.462766496	1.283534557	0.831137591	1.841314327	0.877470574	0.568195671	1.258788967	0.647538149	1.434565448	2.215414567	1.50E-03
10607870	Tlr7	2.536576357	1.244062735	1.117882068	2.054223576	0.490449551	0.440705073	0.809841017	0.89857371	1.651221854	1.837603121	1.50E-03
10476989	Gins1	0.552570309	0.343544354	0.455680363	0.737378165	0.621720618	0.824655895	1.334451296	1.326409117	2.146384177	1.618191664	1.53E-03
10359890	Nuf2	0.46060867	0.328942699	0.423089076	0.692918067	0.714147867	0.918543449	1.504353071	1.286209049	2.106500826	1.637759295	1.61E-03
10538356	Chn2	3.557088751	1.922236972	1.447029097	2.562880749	0.540396124	0.406801516	0.720499523	0.752783927	1.333280332	1.771132836	1.65E-03
10591494	S1pr5	1.010612248	2.999090794	1.242337582	1.709564585	2.967597909	1.22929203	1.69161277	0.41423807	0.570027619	1.37608699	1.65E-03
10492628	Serpini1	2.783043392	2.062845931	1.961277538	1.554756871	0.741219464	0.704724024	0.558653478	0.950762977	0.753695101	0.792726598	1.85E-03
10554445	Prc1	0.404562673	0.361622795	0.361653499	0.823576594	0.893860998	0.893936893	2.035720666	1.000084907	2.277446571	2.277253217	1.89E-03
10435920	Cd200r4	2.764663503	2.051167989	1.539440849	2.067737192	0.741923199	0.556827566	0.747916406	0.750519147	1.008077936	1.343174175	1.91E-03
10419154	Ear1	1.628168094	1.009424042	0.693989465	2.250249841	0.619975324	0.426239445	1.382074645	0.687510338	2.229241376	3.242484152	1.91E-03
10397895	Ubr7	0.701970359	0.49345856	0.659383887	0.738621316	0.702962103	0.939332949	1.052211546	1.336249769	1.49682542	1.120168889	1.91E-03
10444927	Nrm	0.418418087	0.463252505	0.653678848	0.446678833	1.107152198	1.562262407	1.067541883	1.411063818	0.964223243	0.683330712	1.95E-03
10411126	Jmy	2.412850846	1.879768124	2.500218806	0.878066594	0.779065199	1.036209433	0.363912504	1.330067669	0.467114312	0.3511959	1.98E-03
10586244	Dennd4a	2.87655449	1.023810648	1.942119658	0.875436312	0.355915611	0.67515483	0.304335035	1.896952001	0.855076389	0.450763324	1.98E-03
10352954	Hmgb3	0.687771357	0.475743668	0.701856437	0.660696092	0.691717769	1.020479306	0.960633334	1.47528277	1.388764866	0.941355037	2.01E-03
10419288	Gch1	5.250608635	2.081106774	2.637245753	1.589961333	0.396355341	0.502274295	0.302814672	1.267232314	0.763997961	0.602887058	2.02E-03
10408243	Hist1h4a	0.414586311	0.492843286	0.528887356	0.616264251	1.188759187	1.275699032	1.486455858	1.073134951	1.250426389	1.165208894	2.02E-03
10368277	Rps12	2.704342637	2.888134447	1.53573019	2.686369099	1.067961732	0.567875597	0.993353824	0.531737777	0.930139905	1.749245484	2.04E-03
10436662	Mir155	2.265118028	2.641829189	1.622894955	2.045369837	1.166309727	0.716472579	0.902985987	0.6143073	0.774224861	1.260321767	2.14E-03
10435907	Cd200r1 // Cd200r1	2.305003271	2.059187287	1.606931854	1.704574957	0.893355473	0.69714949	0.739510863	0.78037188	0.827790152	1.060763687	2.15E-03
10543239	Tcfec	0.837340508	0.453346908	0.692859761	0.772641786	0.541412846	0.827452816	0.92273308	1.528321357	1.704305848	1.115148879	2.18E-03
10382998	Birc5	0.492521779	0.357118406	0.427392097	0.749538223	0.725081451	0.867762839	1.521837725	1.196779806	2.098850718	1.75374844	2.20E-03
10366586	Irfng	1.141770226	0.811655091	0.660630419	1.561902807	0.710874283	0.578601897	1.367965963	0.813929989	1.924343019	2.364261109	2.20E-03
10362275	Samd3	1.884269796	2.523088916	1.616555111	1.670547431	1.339027416	0.857921257	0.886575497	0.640704773	0.662104066	1.033399616	2.20E-03
10487577	Ckap2l	0.699826827	0.490462244	0.555571451	0.919082805	0.700833728	0.793869897	1.313300334	1.132750702	1.873911432	1.654301718	2.21E-03
10409190	Cenpp	0.67495212	0.42421036	0.624086069	0.668268167	0.628504374	0.924637542	0.990097144	1.471171211	1.575322598	1.070794878	2.26E-03
10497520	Ect2	0.534305521	0.381607565	0.430792996	0.850679294	0.714212281	0.806267162	1.592121475	1.128890084	2.229199241	1.974682277	2.26E-03
10359434	Fasl	2.244763196	1.637183115	1.644458267	1.3609192	0.729334443	0.732575387	0.606264038	1.004443701	0.831256557	0.827579044	2.31E-03
10518145	Prdm2	2.299094314	1.799093986	2.195890924	1.015792759	0.782522916	0.955111285	0.441823005	1.220553757	0.564613504	0.462587986	2.31E-03
10414315	Cdkn3	0.623052713	0.421207137	0.50564917	0.835012447	0.676037723	0.811567239	1.340195508	1.200476263	1.982427107	1.651367186	2.34E-03
10508151	Clsn	0.601444149	0.452445341	0.640935729	0.634593629	0.75226493	1.06566126	1.055116473	1.416603669	1.402586283	0.990104935	2.34E-03
10424400	Myc	1.425774096	0.886586428	0.658688746	1.8828227	0.621828121	0.461986754	1.320561725	0.742949278	2.123676431	2.85844067	2.34E-03
10361091	Atf3	1.580818986	1.464554498	0.822397733	2.270518994	0.926453004	0.520235233	1.436292842	0.561534401	1.550313762	2.760852691	2.35E-03
10408074	Hist1h4k	0.424490794	0.497702034	0.540409371	0.627974103	1.17246838	1.273076775	1.479358591	1.085809047	1.261747111	1.162034074	2.35E-03
10492815	Tmem154	0.479052096	0.566913766	0.758598642	0.492470886	1.183407338	1.583541014	1.028011129	1.338119989	0.868687472	0.649185035	2.40E-03



ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10563085	Fcgrt	0.490505165	0.799869952	0.859835989	0.565514816	1.630706482	1.752960113	1.152923265	1.074969734	0.707008452	0.657700798	2.46E-03
10570000	Gpi1	0.433710542	0.468691752	0.608494488	0.515330088	1.080655659	1.402996767	1.188188982	1.298282904	1.099507482	0.8468936	2.47E-03
10443463	Cdkn1a	1.040171819	0.684093709	0.625397128	1.278237035	0.657673758	0.60124406	1.22887105	0.91419804	1.868511607	2.043880566	2.48E-03
10365344	Tcp11l2	1.31406386	1.618135853	1.70156935	0.825767432	1.231398185	1.294890912	0.628407383	1.051561491	0.510320212	0.485297547	2.56E-03
10438378	Cdc45	0.616162182	0.493152963	0.576765801	0.784835994	0.800362269	0.936061669	1.273749049	1.169547471	1.591465637	1.360753348	2.56E-03
10422227	Spry2	2.668387558	2.086961398	2.024584427	1.433453257	0.782105805	0.758729526	0.537198299	0.970111105	0.686861414	0.708023453	2.65E-03
10558134	Plekha1	2.717216684	2.081460114	1.520258483	2.069749267	0.766026547	0.559491075	0.761716678	0.73038079	0.994373735	1.36144563	2.79E-03
10364950	Gadd45b	1.293231807	0.67367114	0.555583413	1.671003754	0.52092064	0.429608528	1.292114643	0.824710129	2.480444322	3.007655943	2.81E-03
10594911	Tex9	0.903768904	0.671442336	0.594623487	1.340285409	0.742935869	0.657937537	1.482995712	0.885591293	1.996128837	2.254006845	2.81E-03
10530100	Arap2	1.69645348	1.059171254	1.572068707	0.84525137	0.624344414	0.926679526	0.498246123	1.484244122	0.798030882	0.537668211	2.85E-03
10404132	Cmah	0.489004448	0.534607287	0.872554186	0.397255748	1.09325649	1.784348158	0.812376554	1.632140466	0.743079562	0.455279173	2.85E-03
10345074	Cetn4	0.949854876	0.36855479	0.584855666	0.885970877	0.388011684	0.615731604	0.932743412	1.586889336	2.403905475	1.514853884	2.85E-03
10550326	Ap2s1	0.425108568	0.428529572	0.533075635	0.554949431	1.008047364	1.253975278	1.305429888	1.243964642	1.295008483	1.041033193	2.88E-03
10367224	Stat2	1.396967142	0.973477986	0.752072563	1.666760043	0.696851026	0.538360954	1.193127593	0.772562476	1.712170247	2.216222377	2.88E-03
10548532	Klra9	5.549867082	5.693545585	2.819820075	3.467864547	1.025888639	0.508087857	0.624855424	0.495266093	0.609086991	1.229817667	2.94E-03
10350392	Aspm	0.6953865	0.487499118	0.610637009	0.812012362	0.701047717	0.878126062	1.167713728	1.252591002	1.665669398	1.32977915	2.97E-03
10360985	Cenpf	0.605036839	0.396109507	0.459705946	0.896458034	0.654686594	0.759798275	1.481658598	1.160552672	2.263157078	1.950068388	3.00E-03
10521731	Ncapg	0.606327606	0.408327191	0.533919223	0.766032321	0.673443179	0.880578779	1.26339674	1.30757695	1.876025742	1.434734485	3.00E-03
10392207	Tex2	0.809479804	0.464085073	0.962866825	0.459304675	0.573312726	1.189488385	0.567407207	2.074763615	0.989699306	0.477017863	3.15E-03
10502791	Ifi44	1.790134338	0.867884417	0.845786595	1.735054	0.484815245	0.472471019	0.96923117	0.974538289	1.999176348	2.051408725	3.16E-03
10496822	Gng5	2.158334206	1.485422982	1.391882984	1.5777302	0.688226586	0.644887608	0.730994391	0.937028039	1.062142042	1.133522155	3.18E-03
10356299	Gpr55	0.623487129	0.479848349	0.741501037	0.545947425	0.769620297	1.189280424	0.875635437	1.545282042	1.137749928	0.736273313	3.18E-03
10363475	Prf1	1.135839865	0.854782867	0.682723624	1.475358978	0.752555791	0.601073835	1.298914595	0.798709999	1.726004386	2.16099008	3.18E-03
10403980	Hist1h2bj	0.231369764	0.206965313	0.292244187	0.411880526	0.894521865	1.263104489	1.780183025	1.412044286	1.990094479	1.40937115	3.18E-03
10365933	Eea1	2.331841364	1.127109866	1.522918582	1.160143645	0.483356151	0.653096993	0.497522543	1.35117137	1.029308393	0.761789671	3.21E-03
10439651	Cd200	1.220376392	1.105728013	0.785250821	1.637965891	0.906054903	0.643449699	1.342180906	0.710166345	1.48134611	2.085914266	3.24E-03
10487392	Kcnp3	1.714412449	2.040212314	1.562405118	1.438390526	1.190035872	0.911335612	0.838999114	0.76580516	0.70502002	0.920625842	3.24E-03
10412345	Parp8	2.538643314	1.793225168	2.162597515	1.107520399	0.706371453	0.851871353	0.436264674	1.205982134	0.617613682	0.512125068	3.31E-03
10531407	Cxcl9	0.742153015	0.490448583	0.365970567	1.58289821	0.660845638	0.493120098	2.132846164	0.746195585	3.227449861	4.325206322	3.36E-03
10394735	Pdia6	0.52302611	0.437943426	0.434119422	0.890953373	0.837326126	0.830014819	1.703458691	0.991268269	2.034402891	2.052323224	3.37E-03
10469278	Il2ra	0.593280988	0.33919575	0.355905992	0.988472934	0.571728669	0.599894484	1.666112607	1.049264304	2.914166628	2.777342769	3.43E-03
10606770	Zmat1	2.18471468	2.123507232	1.662741055	1.602304148	0.971983779	0.76107927	0.733415747	0.783016431	0.754555541	0.963652244	3.43E-03
10446074	Uhrf1	0.525895957	0.489513044	0.562841011	0.698394498	0.930817279	1.070251642	1.328008875	1.14979778	1.426712744	1.24083797	3.45E-03
10455961	ligp1	1.4628641	0.585367673	0.502440268	2.067149087	0.40015178	0.343463394	1.413083476	0.85833279	3.531368715	4.114218581	3.54E-03
10468885	Zfp826	2.176030959	1.662777889	1.673758846	1.381211764	0.764133379	0.769179703	0.634739023	1.006603983	0.830665222	0.825215513	3.55E-03
10408210	Hist1h2bf	0.233988127	0.21683686	0.298974477	0.420924029	0.926700271	1.277733538	1.798911914	1.378799142	1.941201455	1.407892851	3.55E-03
10408070	Hist1h2bl	0.226936632	0.200049359	0.290328789	0.395653323	0.88152079	1.279338583	1.74345287	1.451285775	1.977778505	1.362776745	3.55E-03
10403948	Hist1h2bn	0.238139155	0.212187713	0.298176879	0.423553353	0.891024042	1.252111939	1.778596018	1.405250453	1.996125731	1.420476846	3.55E-03
10544133	Parp12	1.649845804	1.083822026	0.849202833	1.815678543	0.656923225	0.514716485	1.100514083	0.783526089	1.675255254	2.138097605	3.55E-03
10368612	Gapdh	0.500359333	0.453494772	0.575435465	0.612649034	0.90633819	1.150044434	1.224418122	1.268891068	1.3509506	1.064670274	3.57E-03
10483110	Ifih1	2.80657878	1.394967423	1.110357724	2.383444787	0.497034836	0.39562678	0.849234949	0.795973946	1.708602472	2.146555776	3.63E-03

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10403978	Hist1h2bk	0.221890907	0.198123223	0.283568292	0.398337755	0.892885722	1.277962655	1.795196391	1.43127236	2.010555601	1.40473306	3.71E-03
10547590	Klrg1	0.257059266	0.418556756	0.466950936	0.472356085	1.628250021	1.81651081	1.837537667	1.115621549	1.128535325	1.01157541	3.71E-03
10406423	Mblac2	1.565092667	2.154249241	1.228749629	1.961254168	1.376435586	0.785097046	1.253123352	0.570384153	0.910411911	1.596138157	3.76E-03
10380067	4-Sep	2.405945385	2.69193643	1.534666035	2.327364274	1.118868469	0.637864036	0.96733878	0.570097428	0.864568809	1.516528171	3.84E-03
10491091	Tnfsf10	1.619872135	1.360970413	0.743495164	2.436182353	0.840171507	0.458983859	1.503934971	0.546297816	1.790033296	3.276662003	3.91E-03
10356866	Pdcd1	3.407189136	1.154541263	1.407135123	1.622094917	0.338854468	0.412990024	0.476080092	1.218782878	1.404969202	1.152764145	3.94E-03
10503281	Gxylt1	2.064318761	1.485018886	1.508168498	1.368726583	0.719374795	0.730588961	0.663040325	1.015588766	0.921689681	0.907542218	3.97E-03
10429568	Ly6c1	0.565081601	0.488949979	0.557189358	0.766947577	0.865273226	0.986033446	1.35723332	1.139563108	1.568560404	1.376457691	3.97E-03
10406581	Dhfr	0.67444148	0.443981307	0.48530029	0.945185463	0.658294782	0.719558782	1.40143436	1.09306469	2.128885718	1.947630124	4.08E-03
10511363	Penk	5.737633755	3.501975627	1.979746418	3.860715178	0.610351894	0.345045798	0.672875848	0.565322729	1.102439191	1.950105903	4.13E-03
10403957	Hist1h4m	0.394677811	0.502112673	0.514251677	0.624632804	1.272209025	1.302965767	1.58263978	1.024175856	1.244009238	1.214644175	4.14E-03
10408092	Hist1h4m	0.394677811	0.502112673	0.514251677	0.624632804	1.272209025	1.302965767	1.58263978	1.024175856	1.244009238	1.214644175	4.14E-03
10346790	Ctla4	2.252162249	0.756470068	0.993325723	1.37693321	0.335886133	0.441054246	0.611382777	1.313106447	1.820208451	1.386184993	4.17E-03
10549102	Kcnj8	2.462396806	4.333034102	2.485890484	1.840851431	1.759681499	1.00954098	0.747585209	0.573706651	0.424841205	0.740519923	4.17E-03
10404036	Hist1h2bg	0.322779742	0.50291873	0.359416851	0.893723956	1.558086411	1.11350498	2.768835335	0.714661891	1.777074311	2.486594477	4.23E-03
10603346	Plp2	0.665246776	0.484684877	0.60401928	0.761900327	0.72857907	0.907962731	1.14528977	1.246210286	1.571949863	1.261384119	4.23E-03
10591556	Spc24	0.589511532	0.37553398	0.434736162	0.880913144	0.637025673	0.737451497	1.494310281	1.157648001	2.345761475	2.026316697	4.23E-03
10473240	Eno1	0.457862464	0.4384976	0.475167831	0.706782527	0.957705936	1.037795994	1.543656846	1.083626982	1.611827585	1.487437662	4.29E-03
10346668	Fam117b	1.756050775	1.273650631	1.713280466	0.858370731	0.725292599	0.975644037	0.488807467	1.345173021	0.673945201	0.501010049	4.31E-03
10404067	Hist1h4b	0.422800884	0.502650505	0.532516673	0.636912906	1.188858691	1.259497539	1.506413375	1.059417363	1.267108856	1.196043127	4.31E-03
10490150	Zbp1	0.943191335	0.616490534	0.591899239	1.21866109	0.653621923	0.627549488	1.292061371	0.960110831	1.976771778	2.058899572	4.36E-03
10455389	Scgb3a2	0.96518972	1.009831814	0.515885781	2.00734343	1.046252144	0.534491582	2.079739752	0.51086307	1.987799753	3.891061752	4.42E-03
10412298	Itga1	0.499099883	0.412560095	0.44327805	0.803926136	0.826608277	0.888154987	1.610752003	1.074456924	1.948627962	1.813593377	4.47E-03
10593492	Zc3h12c	1.540725576	0.729345438	1.085277443	0.980500377	0.4733779	0.704393735	0.63638872	1.488015672	1.344356632	0.903455963	4.49E-03
10558295	Zranb1	2.734264293	1.918179483	2.300127233	1.107019159	0.701534043	0.841223447	0.404869113	1.199119923	0.577119696	0.481286054	4.49E-03
10440393	Samsn1	2.144415748	1.458565352	1.215270906	1.775014961	0.68016911	0.566714224	0.827738261	0.833196061	1.2169595	1.460591999	4.56E-03
10380571	Gngt2	1.458509075	1.514899156	0.951309396	1.963786337	1.038662825	0.652247842	1.346434089	0.627968794	1.296314893	2.064298267	4.57E-03
10548307	Klrb1c	1.379559509	0.489508781	0.95251248	0.802423501	0.354829769	0.690446823	0.581651966	1.945853715	1.639242301	0.842428333	4.63E-03
10581813	Mlkl	1.240190943	0.64136264	0.648658748	1.431556082	0.517148301	0.523031354	1.154302964	1.011375949	2.232054057	2.20694793	4.66E-03
10380551	Phb	0.53363487	0.440169654	0.533579303	0.703429348	0.824851745	0.999895871	1.31818475	1.212212833	1.598086878	1.318322026	4.71E-03
10499431	Syt11	2.666002509	1.380279403	1.317803932	1.795206348	0.517733723	0.494299584	0.673370089	0.954737083	1.300610835	1.362271203	4.73E-03
10411622	Naip6	2.045960304	2.051107368	1.557273962	1.633645831	1.00251572	0.761145736	0.798473865	0.759235711	0.796470168	1.049042025	4.87E-03
10385518	Tgtp1	1.102776812	0.813916319	0.670033575	1.495850571	0.738060785	0.607587653	1.356439993	0.823221699	1.837843198	2.232500918	4.87E-03
10439321	Slc15a2	2.194486768	1.554028199	1.658743446	1.278387214	0.708151091	0.755868511	0.582544964	1.067383106	0.822628068	0.770696166	4.88E-03
10406968	Cenpk	0.906214938	0.531368206	0.624114298	1.083375473	0.586360016	0.688704491	1.19549505	1.174542043	2.038841354	1.735860684	4.92E-03
10469151	Itih5	1.431858428	0.554597453	0.793853005	1.099848971	0.387327016	0.554421435	0.768126897	1.431403986	1.983148256	1.385456709	4.92E-03
10545135	Il12rb2	0.619813053	0.343712991	0.880003908	0.328790166	0.554543002	1.419789247	0.53046667	2.560287017	0.956583471	0.373623529	5.04E-03
10372648	Lyz2	1.027486185	0.457136251	0.291254503	2.491657235	0.444907443	0.283463181	2.42500315	0.637128432	5.450578968	8.554914043	5.04E-03
10606554	Nap1l3	2.068403063	2.052594038	1.594670059	1.632562161	0.992356894	0.770966785	0.789286281	0.776904751	0.795365343	1.023761719	5.09E-03
10533729	Vps37b	1.8155033	1.191032046	1.60875029	0.851141162	0.656034085	0.886118075	0.468818295	1.350719568	0.714624904	0.52906978	5.27E-03
10414202	Sftpa1	0.91934384	1.036288902	0.619644903	1.694754896	1.127204922	0.674007783	1.843439661	0.597946096	1.635407746	2.735042099	5.28E-03

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10467637	Arhgap19	0.643534407	0.456354773	0.629282849	0.685371911	0.70913811	0.97785424	1.06501207	1.378933421	1.501840127	1.089131719	5.29E-03
10385533	Tgtp1	0.908172138	0.665108577	0.56682144	1.347738123	0.732359592	0.624134364	1.484011749	0.852223921	2.026343021	2.377711972	5.41E-03
10449581	Mtch1	0.577912282	0.486381619	0.72741015	0.538595611	0.841618416	1.25868609	0.931967754	1.495554358	1.107351903	0.740429057	5.64E-03
10355312	Ikzf2	2.718834426	1.526780063	2.007634268	1.162453289	0.561556838	0.73841726	0.427555749	1.31494661	0.761375732	0.579016461	5.71E-03
10452516	Ankrd12	2.571997499	1.903589005	2.146827785	1.188989233	0.740120862	0.834692797	0.462282422	1.127779042	0.624603961	0.553835404	5.75E-03
10445338	Enpp5	2.095237728	1.778680268	1.454447721	1.708369496	0.848915731	0.694168352	0.815358311	0.817711731	0.960470258	1.174582951	5.79E-03
10601011	Kif4	0.536031217	0.334995371	0.479472863	0.655625471	0.624954966	0.894486827	1.223110614	1.431282053	1.957118	1.367388067	5.81E-03
10511282	Tnfrsf4	1.60195151	0.828581523	0.771311848	1.61533877	0.517232586	0.481482644	1.008356845	0.93088227	1.949523042	2.094274545	5.81E-03
10508651	Sdc3	0.959782414	1.025081617	0.70122784	1.466968457	1.068035423	0.730611261	1.528438566	0.684070252	1.431074787	2.091999738	5.83E-03
10548333	Cd69	1.873987531	1.247683726	0.899036232	2.157788994	0.665790836	0.479745045	1.151442557	0.720564205	1.729435873	2.400113496	5.83E-03
10447317	Epas1	0.705064055	0.456089967	0.458655598	1.064351383	0.64687735	0.650516212	1.509581116	1.005625274	2.333643491	2.320589539	5.84E-03
10408200	Hist1h4f	0.268491362	0.368982045	0.361525922	0.561257775	1.374279017	1.346508579	2.090412782	0.979792722	1.521097795	1.552468967	5.87E-03
10594540	Plekho2	0.528672908	0.592449826	0.488895663	0.967167756	1.120635873	0.924760198	1.829425607	0.82521024	1.632488885	1.97827027	5.92E-03
10487340	Ncaph	0.575780381	0.419970443	0.617332325	0.594144341	0.729393459	1.072166307	1.031894036	1.469942313	1.414728942	0.96243841	5.92E-03
10399391	Gen1	0.507232721	0.306716727	0.424385926	0.697487963	0.604686397	0.836669065	1.375084718	1.383641287	2.274046059	1.643522841	6.06E-03
10573261	Asf1b	0.59760083	0.474744516	0.516451308	0.830378362	0.79441743	0.864207815	1.389520094	1.087851025	1.74910575	1.607854118	6.10E-03
10491300	Skil	2.253125785	1.476346478	1.487991924	1.401979549	0.655243701	0.660412275	0.622237586	1.007888017	0.949627726	0.94219567	6.15E-03
10592201	Chek1	0.660895256	0.475638386	0.588803361	0.791922968	0.719688002	0.890917821	1.198257909	1.237922292	1.664968578	1.344970188	6.18E-03
10385500	Irgm1	0.959451344	0.523481641	0.533970656	1.23409131	0.545605199	0.556537504	1.286246893	1.020037024	2.357468175	2.311159419	6.18E-03
10377429	Snord118	2.611846733	3.192130324	0.859372939	5.415624738	1.222173676	0.329028855	2.073484891	0.26921612	1.696555024	6.30183299	6.18E-03
10380059	Rnu3b1	0.777521892	1.947021407	0.61641038	2.426607208	2.504137088	0.792788455	3.120950332	0.316591475	1.246317683	3.936674798	6.18E-03
10588007	Tfdp2	2.020212493	1.101077221	1.505073438	1.0870799	0.545030399	0.74500749	0.538101761	1.366909977	0.987287612	0.722276981	6.18E-03
10494407	Hist2h2bb	0.347910407	0.516193318	0.627547763	0.442343187	1.483696112	1.80376255	1.271428442	1.215722367	0.85693319	0.704875729	6.18E-03
10573082	Inpp4b	2.093014762	1.293901525	1.01363954	1.984292879	0.618199904	0.484296412	0.94805489	0.783397747	1.533573337	1.957592223	6.27E-03
10438445	Klhl6	0.468673054	0.520429351	0.758522384	0.466246159	1.110431562	1.618446755	0.994821773	1.457493475	0.895887515	0.614676862	6.32E-03
10533246	Oas1g	1.380725587	0.890021824	0.749136518	1.610170986	0.644604426	0.542567274	1.166177408	0.841705785	1.809136519	2.149369235	6.42E-03
10435501	Stfa1	1.19455885	0.546401913	0.873485613	0.868171603	0.457408953	0.731220244	0.726771731	1.598613755	1.588888295	0.993916317	6.42E-03
10510580	Tnfrsf9	1.578787524	0.700395968	0.725107889	1.501793504	0.443629024	0.459281492	0.951232184	1.035282786	2.144206383	2.071131106	6.45E-03
10379615	Slfn5	1.504107616	0.812965265	0.695152161	1.747858492	0.540496742	0.462169165	1.162056806	0.855082241	2.1499793	2.514353821	6.48E-03
10463704	As3mt	0.649496518	1.91571565	1.268128047	0.841331184	2.949539524	1.952478593	1.295359037	0.661960478	0.439173311	0.663443401	6.60E-03
10443690	Glp1r	2.183546701	2.134998378	1.422295277	1.987214093	0.9777663	0.651369296	0.910085455	0.666180964	0.930780142	1.397188141	6.64E-03
10494411	Rnu1b1	0.473645303	1.173073894	0.527008408	1.418150252	2.476692759	1.112664696	2.994118683	0.449254229	1.208918091	2.690944264	6.70E-03
10450796	Armcx5	2.262570434	1.658419192	1.737809986	1.283968501	0.732980139	0.7680689	0.567482223	1.047871367	0.774212278	0.73884286	6.77E-03
10590267	Snora62	0.600247075	1.213967165	0.799581778	1.03906329	2.02244578	1.332087753	1.731059314	0.658651899	0.855923719	1.299508467	6.78E-03
10372781	Irak3	0.631656344	0.346624616	0.598527087	0.610923278	0.548755062	0.947551769	0.967176668	1.726729894	1.762492477	1.020711162	6.82E-03
10504470	Melk	0.669567623	0.476657515	0.610034037	0.767454024	0.711888536	0.911086522	1.146193451	1.279816258	1.610074321	1.258051155	6.85E-03
10508723	Snora61	1.759065035	2.010441195	1.153415737	2.138122036	1.142903278	0.655698177	1.215487769	0.573712745	1.063508866	1.853730591	6.85E-03
10507112	Stil	0.716960627	0.394211809	0.63121938	0.643052501	0.549837458	0.880410103	0.896914666	1.601218851	1.631236018	1.018746448	6.85E-03
10362674	Rnu3a	0.367331888	1.337906933	0.373804968	1.905318046	3.642229213	1.017621884	5.186911644	0.279395344	1.424103575	5.097091292	6.99E-03
10555510	Pde2a	1.285094647	1.241482837	1.637302967	0.666564879	0.966063348	1.274071891	0.518689328	1.318828516	0.536910265	0.407111507	7.00E-03
10497646	Phc3	2.008943005	1.903155058	1.815758423	1.320317922	0.947341489	0.903837699	0.657220199	0.954078027	0.693752155	0.727144044	7.25E-03

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10518561	Apitd1	0.541521039	0.453079928	0.483561121	0.832239081	0.836680194	0.892968298	1.536854564	1.06727553	1.836848267	1.721062851	7.46E-03
10515431	Kif2c	0.498210906	0.412198141	0.481107298	0.727510243	0.827356721	0.965669946	1.46024552	1.167174837	1.76495275	1.512157985	7.46E-03
10430372	Rac2	0.457377157	0.54202843	0.621240732	0.587300389	1.185079801	1.358267947	1.28406148	1.146140493	1.083523219	0.945366842	7.52E-03
10450363	Snord52	0.396230362	0.800413719	0.355490664	1.427841713	2.020071645	0.897181787	3.603564618	0.444133647	1.78387961	4.016537866	7.53E-03
10497971	Sclt1	2.320792072	1.281467095	1.307810405	1.59106291	0.55216799	0.56351899	0.685568918	1.020557149	1.241594823	1.216585297	8.09E-03
10584841	Amica1	1.020807521	0.678052246	0.533516697	1.543330147	0.664231241	0.522641817	1.511871842	0.78683715	2.276122756	2.892749478	8.34E-03
10353674	Lsm5	0.719568398	0.500892965	0.51051422	1.040176329	0.69610195	0.70947282	1.445555881	1.019208206	2.076643919	2.037507062	8.34E-03
10375880	Nhp2	0.486546083	0.440514683	0.502730491	0.701071114	0.90539149	1.033263875	1.440914107	1.141234356	1.591481831	1.394526744	8.34E-03
10563260	Snmp70	0.482598636	0.582731458	0.688966143	0.580076687	1.207486749	1.427617263	1.201985758	1.182304704	0.995444265	0.841952384	8.37E-03
10389395	Brip1	0.63686796	0.405602665	0.517872519	0.806751579	0.63687089	0.81315524	1.266748572	1.276797625	1.989019426	1.557818865	8.39E-03
10531987	Gbp4	1.377217202	0.884487436	0.75412489	1.631057091	0.64222799	0.5475715	1.184313621	0.852612326	1.84407039	2.162847445	8.39E-03
10581306	Rps2	0.556569804	0.462639899	0.596358669	0.658690977	0.831234278	1.071489442	1.183483136	1.289034235	1.423766039	1.104521509	8.71E-03
10496204	Cenpe	0.747861925	0.470943716	0.561142951	0.944739729	0.62972014	0.750329616	1.263254215	1.191528694	2.006056555	1.683599032	8.78E-03
10346722	Nbeal1	2.385857552	1.618743781	1.734425898	1.343342845	0.678474614	0.726961212	0.563044027	1.07146413	0.829867494	0.77451729	8.88E-03
10487480	Bub1	0.600330116	0.342599791	0.469304102	0.768471473	0.570685665	0.781743394	1.280081497	1.369831839	2.243058788	1.63747018	8.90E-03
10531972	Gbp8	1.80128493	1.35466139	0.970447843	2.021040662	0.752052808	0.538753102	1.121999429	0.716376691	1.491915749	2.082585557	8.95E-03
10472235	Dapl1	1.559136868	1.906182764	1.931864009	0.827673679	1.222588473	1.239059923	0.530853767	1.013472604	0.434204786	0.428432682	9.14E-03
10345752	Il1r2	2.451746705	0.751026816	1.017693297	1.505840166	0.306323167	0.415089085	0.614190757	1.355069187	2.00504181	1.479660101	9.19E-03
10606532	Acp1	0.505347426	0.402822695	0.509966285	0.68133997	0.797120305	1.009139967	1.348260491	1.265982011	1.69141406	1.336049047	9.37E-03
10499639	Cks1b	0.575227526	0.43833598	0.504240356	0.832965216	0.762021913	0.876592883	1.448062163	1.15035128	1.900289399	1.651920967	9.43E-03
10535904	Hsph1	0.752425263	0.93542034	0.584068517	1.428050251	1.243206981	0.776247882	1.897929695	0.624391508	1.526640152	2.445004669	9.47E-03
10358408	Rgs1	2.405053378	1.8778976	1.420120378	1.903007089	0.780813273	0.590473538	0.791253577	0.756228869	1.013371064	1.340032238	9.47E-03
10351095	Tnfsf4	2.209448011	1.499913791	1.384198658	1.618911026	0.678863582	0.626490712	0.732721937	0.922852144	1.07933605	1.169565522	9.53E-03
10382701	Sap30bp	0.498578566	0.456663252	0.592054311	0.61465079	0.915930374	1.187484485	1.232806285	1.296478988	1.345960698	1.038166226	9.54E-03
10359982	Atf6	0.64363763	0.491113619	0.62327185	0.742682902	0.763028133	0.968358314	1.153883594	1.269099096	1.512242529	1.191587429	9.71E-03
10563780	E2f8	0.597866866	0.404272572	0.568497874	0.656528364	0.676191633	0.950877038	1.098117995	1.4062242	1.623974538	1.154847526	9.96E-03
10416945	Mir17hg	2.445077568	1.729389139	1.987181739	1.221170105	0.707294182	0.812727484	0.499440231	1.149065699	0.706128006	0.614523614	9.99E-03
10395538	Pnpla8	2.457856189	1.350336372	2.116637638	0.898513482	0.549396005	0.861172288	0.365567964	1.567489169	0.665399748	0.42450038	9.99E-03
10372383	Zdhc17	2.669028479	2.050414321	1.541135182	2.085671527	0.768224969	0.577414289	0.781434722	0.751621351	1.017195162	1.353334575	9.99E-03
10391207	Dhx58	1.083786246	0.715616545	0.597865784	1.450390258	0.660293068	0.55164548	1.338262285	0.835455508	2.026770157	2.425946252	1.02E-02
10450325	Cfb	0.937825218	0.527044908	0.575513551	1.149971725	0.561986282	0.613668239	1.226211135	1.091963023	2.181923606	1.998166201	1.05E-02
10444658	Clic1	0.544499125	0.479050538	0.56544441	0.696302507	0.879800382	1.038467068	1.278794537	1.180343962	1.453505321	1.231425219	1.05E-02
10587508	Ttk	0.669456052	0.43878654	0.595380707	0.735350852	0.655437409	0.889349952	1.098430361	1.356880062	1.67587377	1.235093518	1.06E-02
10390535	Arl5c	0.779220577	0.939954753	1.205023688	0.558468185	1.206275579	1.546447467	0.716701023	1.282001803	0.594143689	0.463449964	1.08E-02
10384373	Figl1	0.536292792	0.426526639	0.492730756	0.793355393	0.795324205	0.918771915	1.479332566	1.15521684	1.860037149	1.610119489	1.08E-02
10604076	Snora69	3.254288523	2.870975453	2.012168046	2.147372093	0.882212942	0.618312738	0.65985916	0.700865639	0.747959057	1.067193218	1.08E-02
10375980	Aff4	1.989238157	1.301798311	1.730925082	0.954211631	0.654420541	0.870144721	0.479686973	1.329641518	0.732994983	0.551272635	1.08E-02
10369815	Cdk1	0.636598878	0.456519989	0.469641267	0.987431778	0.717123458	0.73773499	1.551105119	1.028741957	2.162954093	2.102523454	1.08E-02
10408094	Hist1h2ao	0.429246327	0.49911291	0.523136282	0.649814689	1.162765709	1.218732111	1.513850318	1.04813214	1.301939252	1.242151827	1.09E-02
10416037	Pbk	0.780098239	0.454633215	0.622101178	0.822832684	0.582789696	0.797465175	1.054780851	1.368358398	1.809882465	1.322666976	1.10E-02
10386058	Sparc	0.989431528	1.129338306	0.616194591	1.866972245	1.141401171	0.622776386	1.886914042	0.545624449	1.653155866	3.029841987	1.10E-02

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10404045	Hist1h2ad	0.429810032	0.503079729	0.525813408	0.648485927	1.170469954	1.223362344	1.508773361	1.04518902	1.289032116	1.233300476	1.11E-02
10595753	Trpc1	2.159091256	1.497905358	1.795834089	1.128177453	0.69376658	0.831754602	0.52252421	1.198896899	0.75317005	0.628219199	1.13E-02
10461152	Snhg1	0.899734267	1.671689553	0.799993908	1.822913072	1.857981421	0.889144647	2.02605718	0.478554111	1.090461485	2.278658693	1.14E-02
10422776	Phb	0.537546847	0.415289352	0.524431165	0.687875446	0.772564018	0.975600857	1.27965674	1.26280908	1.656376313	1.311660122	1.15E-02
10410560	Trip13	0.662482067	0.447151871	0.569790835	0.78390942	0.674964492	0.86008492	1.183291532	1.274266914	1.753116715	1.375784536	1.15E-02
10597871	Higd1a	2.101519537	1.923679032	1.211148601	2.281322192	0.915375279	0.57632041	1.085558403	0.629600147	1.185916234	1.883602219	1.17E-02
10514221	Plin2	0.920832079	0.499346007	0.598415278	1.056370536	0.542276945	0.649863631	1.147191285	1.198398045	2.115508128	1.765280023	1.19E-02
10373569	Rpsa	0.421775826	0.379288478	0.554130101	0.476529395	0.89926557	1.313802422	1.129816756	1.460972672	1.256377196	0.85995941	1.19E-02
10379636	Sifn4	1.519683009	0.696268567	0.781747645	1.392941398	0.458166975	0.514414941	0.916599969	1.122767394	2.000580615	1.781829991	1.19E-02
10347193	Atic	0.445622979	0.534225337	0.571252819	0.646797569	1.198828074	1.281919573	1.451445729	1.069310606	1.210720504	1.132243987	1.20E-02
10501629	Cdc14a	1.619132082	0.681789634	0.721395507	1.572724766	0.421083395	0.445544569	0.971338153	1.058091045	2.306759575	2.180114448	1.23E-02
10528090	Rundc3b	2.162245751	1.981286292	2.010205079	1.145727396	0.916309485	0.929683907	0.529878436	1.014595966	0.578274528	0.569955478	1.26E-02
10368970	Prdm1	1.255917451	1.057412391	0.752597326	1.730517681	0.841944182	0.599241077	1.377891262	0.711734922	1.63655892	2.299393875	1.27E-02
10516051	Cap1	0.43817415	0.436003263	0.447115669	0.745935427	0.995045608	1.020406314	1.702372054	1.025486979	1.710848268	1.668327636	1.27E-02
10492469	Mlf1	2.101886774	1.494231573	1.43041712	1.45384625	0.710900126	0.680539569	0.691686283	0.957292796	0.972972514	1.016379229	1.27E-02
10560260	Sae1	0.504446832	0.431879194	0.538694227	0.664405935	0.856144129	1.06789099	1.317098041	1.247326185	1.538406906	1.233363754	1.27E-02
10460359	Coro1b	0.489280039	0.578625012	0.569672199	0.722334979	1.182604982	1.164307051	1.476322192	0.984527436	1.248364597	1.267983554	1.30E-02
10350377	Zbtb41	2.106345913	1.209509743	1.360246444	1.333121627	0.574221801	0.645784928	0.632907263	1.124626281	1.102199991	0.980058895	1.32E-02
10582985	Casp1	2.443317421	2.084625193	1.397930331	2.224623345	0.853194585	0.57214438	0.910492974	0.670590731	1.067157469	1.591369252	1.32E-02
10352918	Mir29c	5.610280592	2.561354308	2.348585094	2.443045623	0.45654656	0.418621681	0.435458723	0.916930972	0.953810106	1.040220186	1.32E-02
10408118	Hist1h2ag	0.431434083	0.498216714	0.523820727	0.647072121	1.1547922	1.214138491	1.499816881	1.051391316	1.298776421	1.235293084	1.34E-02
10460376	Ppp1ca	0.431416816	0.456338933	0.486477875	0.687310575	1.057768071	1.127628449	1.593147392	1.066045081	1.506140557	1.41283008	1.34E-02
10364990	Eef2	0.487966142	0.550474628	0.691322723	0.546069971	1.128100047	1.416743219	1.119073484	1.255866644	0.991998438	0.789891541	1.34E-02
10442262	Zfp758	2.292147279	1.412952097	1.451551522	1.516754366	0.616431636	0.63327149	0.661717674	1.027318283	1.073464818	1.044919414	1.34E-02
10450605	Tubb5	0.448284226	0.384830662	0.449469523	0.671302092	0.858452382	1.002644074	1.497492112	1.167967025	1.744409059	1.493543073	1.35E-02
10385375	Thg1l	0.449430018	0.367812613	0.467019835	0.633194206	0.818397968	1.039138055	1.408882765	1.269722184	1.72151303	1.35581866	1.36E-02
10457205	Crem	2.668883537	1.495907782	1.796495469	1.272900081	0.56049946	0.673126213	0.476941037	1.200939985	0.850921492	0.708546224	1.36E-02
10419151	Ear1	1.032118398	1.056558153	0.61946086	1.799575609	1.023679217	0.600183914	1.743574781	0.586300771	1.703243313	2.905067496	1.38E-02
10591472	Cdc37	0.455953283	0.534508993	0.594332847	0.625058663	1.172288944	1.303495049	1.370883127	1.111923008	1.169407197	1.051697993	1.39E-02
10353034	Snord87	2.249551867	2.176058303	1.561340224	1.889618699	0.967329687	0.694067226	0.839997835	0.717508452	0.868367679	1.210254286	1.40E-02
10445894	Erh	0.541373238	0.439692845	0.5037118	0.76893589	0.812180608	0.930433507	1.42034337	1.145599265	1.748802369	1.52653936	1.41E-02
10408072	Hist1h2ai	0.419903566	0.493969726	0.519920266	0.635372833	1.176388501	1.23818969	1.513139885	1.052534677	1.286258651	1.222058217	1.45E-02
10496539	Gbp5	1.027085313	0.682694178	0.629913883	1.327510593	0.664690819	0.613302395	1.29250275	0.92268823	1.944517231	2.107447747	1.52E-02
10569014	Ifitm2	1.321134083	0.798959689	0.638505815	1.697297526	0.604752916	0.483301296	1.28472768	0.799171502	2.124384433	2.658233468	1.53E-02
10394674	Socs2	0.800461403	0.892780446	0.610173184	1.337955287	1.115332286	0.762276834	1.671480076	0.683452675	1.498638654	2.192746783	1.55E-02
10420668	Mir15a	2.964653132	0.824901022	1.414598872	1.195809075	0.278245375	0.477154935	0.403355476	1.714871037	1.449639463	0.845334391	1.57E-02
10408111	Hist1h2ah	0.422571912	0.497909882	0.521802645	0.639619451	1.178284377	1.234825673	1.513634563	1.04798612	1.284608871	1.225788057	1.57E-02
10403955	Hist1h2ao	0.422103133	0.495903053	0.521102351	0.637996657	1.174838597	1.234537984	1.511471029	1.050814969	1.286535046	1.224321203	1.57E-02
10368486	Rnf146	2.576151841	2.088941918	2.392570706	1.085257848	0.810876861	0.928738232	0.421270917	1.145350517	0.519525143	0.453594891	1.57E-02
10552418	Etfb	0.596435764	0.471696704	0.526781742	0.830698268	0.790859188	0.883216222	1.392770719	1.11678063	1.761085589	1.576930636	1.59E-02
10548565	Magohb	1.365716193	1.176375638	0.79035393	1.91205721	0.861361712	0.578710229	1.400039935	0.671855065	1.625379809	2.419241731	1.60E-02

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10586744	Anxa2	0.719983409	0.477237014	0.591078675	0.827513	0.662844461	0.820961522	1.149350096	1.238543234	1.733966509	1.400004829	1.61E-02
10496592	Gbp2	0.818753223	0.638263675	0.567568047	1.194217564	0.779555619	0.693210153	1.458580597	0.889237581	1.871041092	2.104095836	1.64E-02
10403938	Hist1h2ai	0.444774041	0.514791517	0.535421041	0.660441622	1.157422577	1.20380461	1.484892466	1.040073551	1.282930276	1.233499568	1.65E-02
10389214	Ccl9	1.803002884	2.058801588	1.377255219	1.806140042	1.141873708	0.763867452	1.001739963	0.668959664	0.87727737	1.31140548	1.66E-02
10358389	Rgs2	2.090360171	1.433515564	1.199991514	1.764148528	0.685774435	0.574059691	0.843944767	0.837096955	1.230644837	1.47013417	1.67E-02
10493259	Ssr2	0.391260533	0.332723689	0.494407731	0.483144379	0.85038909	1.263627912	1.234840568	1.485940879	1.452088912	0.977218496	1.67E-02
10540650	Arpc4	0.482220369	0.58619755	0.615404236	0.649601082	1.215621711	1.276188805	1.347104195	1.049823965	1.10816069	1.055568102	1.67E-02
10542470	Mgst1	1.560528043	0.592968531	0.606819451	1.733289142	0.379979414	0.388855204	1.110706821	1.023358608	2.92307104	2.856350664	1.76E-02
10515425	Snord38a	1.492087919	2.6952925	1.267614992	2.052120162	1.806389869	0.849557842	1.375334615	0.470307023	0.761371971	1.618882843	1.76E-02
10420877	Esco2	0.638492372	0.445642581	0.546389343	0.796873078	0.697960698	0.855749211	1.248054187	1.226070771	1.788143933	1.458434517	1.78E-02
10439312	Cd86	2.258242932	0.882290154	0.970944514	1.664143508	0.390697627	0.429955741	0.736919613	1.100482091	1.886163525	1.713942953	1.79E-02
10376778	Mfap4	1.042573861	1.265821535	0.714719511	1.736011995	1.214131278	0.685533695	1.66512135	0.564628972	1.371450831	2.428941659	1.80E-02
10374464	Spred2	2.503363468	1.412253003	1.642341454	1.332651082	0.564142211	0.656053935	0.532344223	1.162922968	0.943634801	0.811433626	1.81E-02
10392183	Ern1	0.708825687	0.478811291	0.825768612	0.545991986	0.675499351	1.164981219	0.770276806	1.724622263	1.140307248	0.661192467	1.81E-02
10394558	Rpl29	0.536319403	0.440542002	0.612571185	0.575651354	0.821417236	1.142176064	1.073336804	1.390494396	1.306688923	0.93972973	1.81E-02
10396068	Ppil5	0.571779336	0.46293912	0.538609925	0.786036283	0.809646468	0.94198914	1.37471964	1.163457357	1.697925816	1.4593795	1.82E-02
10565994	Art2b	2.265364895	1.629261566	1.262403071	2.066200005	0.719204915	0.557262573	0.912082645	0.774831431	1.268181886	1.636719723	1.84E-02
10463505	Dpcd	0.495834717	0.533753063	0.493927364	0.878094133	1.076473763	0.99615325	1.770941209	0.925385536	1.645131791	1.777779884	1.85E-02
10408085	Hist1h2an	0.400799485	0.480528345	0.500446516	0.62615545	1.198924558	1.248620657	1.562266103	1.041450564	1.30305622	1.251193542	1.89E-02
10493189	Mef2d	2.127224202	2.147875623	2.080821552	1.138796458	1.009708155	0.978186291	0.53534388	0.968781213	0.530196649	0.547282134	1.92E-02
10351509	Fcgr4	1.264946595	0.536830004	0.747810357	1.091808751	0.424389461	0.59117939	0.863126361	1.393011479	2.033807246	1.460007529	1.99E-02
10577190	Rasa3	0.556170336	0.569028362	0.913693931	0.42230883	1.023118865	1.642831113	0.759315632	1.605708945	0.742157787	0.462199447	2.00E-02
10580300	Asna1	0.460848448	0.544830047	0.472162058	0.831725898	1.182232574	1.024549525	1.804770964	0.866622648	1.526578613	1.76152633	2.00E-02
10568217	Dctpp1	0.570047161	0.504009435	0.487138638	0.918562794	0.884153926	0.854558486	1.611380352	0.966526823	1.822511108	1.885629104	2.00E-02
10363735	Egr2	1.541129494	1.27200788	0.817612244	2.023450071	0.825373783	0.530527933	1.31296564	0.64277294	1.59075278	2.474828484	2.00E-02
10404051	Hist1h4d	0.355849872	0.367291656	0.437023666	0.546704607	1.032153401	1.228112473	1.536334983	1.1898546	1.488475435	1.250972543	2.00E-02
10573198	Dnajb1	1.115539845	1.055612355	0.752298805	1.52236675	0.946279382	0.674380936	1.364690608	0.712665783	1.442164581	2.023619789	2.03E-02
10528207	Cd36	1.584590255	1.356469935	0.754062783	2.392326593	0.856038292	0.47587241	1.509744608	0.555900845	1.763641443	3.17258277	2.05E-02
10526838	Got2	0.57923357	0.486663678	0.725083162	0.538927442	0.840185554	1.251797546	0.930414724	1.489906057	1.107391956	0.74326294	2.06E-02
10404389	Irf4	1.260720887	0.654836685	0.667794303	1.311357853	0.519414481	0.529692424	1.040165089	1.019787557	2.002572372	1.963715245	2.08E-02
10591781	Anln	0.632513257	0.484624997	0.510462707	0.9301683	0.766189469	0.807038749	1.470590995	1.053314854	1.919356836	1.82220618	2.11E-02
10547943	Ncapd2	0.541302889	0.476204397	0.593862173	0.638747631	0.8797374	1.097097733	1.180018883	1.247074107	1.341330813	1.075582281	2.15E-02
10410295	Zfp595	2.251670722	1.649448044	1.420223829	1.682260457	0.732544074	0.630742237	0.747116548	0.861029745	1.019892965	1.184503753	2.15E-02
10546685	Eif4e3	1.240354984	0.810392861	0.740644301	1.496620585	0.653355589	0.597122848	1.206606661	0.91393241	1.846784019	2.020700873	2.15E-02
10497831	Ccna2	0.640936456	0.486342646	0.63283889	0.704674563	0.758800099	0.987366039	1.099445284	1.301220231	1.448926121	1.113513368	2.15E-02
10395259	Nampt	1.559336401	0.734486927	0.820943196	1.381302573	0.47102532	0.52646959	0.885827184	1.117709745	1.880636024	1.682579965	2.15E-02
10503315	Rad54b	0.734049442	0.485131462	0.595650927	0.862303138	0.660897529	0.811458865	1.174720788	1.227813435	1.777462823	1.447665233	2.18E-02
10445268	Gpr116	0.924671952	1.016467189	0.685057575	1.466607243	1.099273301	0.740865529	1.586083842	0.673959359	1.442847599	2.14085253	2.18E-02
10389719	Scpep1	0.68545093	0.470490113	0.817502324	0.500993354	0.686395033	1.192648939	0.730896016	1.737554735	1.064832905	0.612834165	2.19E-02
10414262	Ear2	2.089357396	0.917225466	0.744382111	2.248263653	0.438998837	0.356273232	1.076055087	0.811558487	2.451157035	3.020308547	2.19E-02
10360070	Fcer1g	1.569256563	0.765627925	0.689297846	1.801665533	0.487892129	0.439251211	1.148101321	0.900303951	2.353186809	2.613769277	2.22E-02

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Arms D8cl13.FC	D8Arms HMPVLung.FC	D8Arms HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungs HMPVSpleen.FC	adj.P.Val
10445067	Znrd1as	2.118860749	2.041485759	1.553155212	1.739401677	0.96348274	0.733014292	0.820913634	0.760796496	0.852027338	1.119914909	2.24E-02
10424676	Ly6e	0.625372928	0.431784479	0.566453746	0.697062993	0.690443189	0.905785525	1.114635704	1.311890014	1.614377143	1.230573544	2.25E-02
10499035	Mnd1	0.75822153	0.386151288	0.535606829	0.845618893	0.509285574	0.706398866	1.115266264	1.387038828	2.189864233	1.578805286	2.26E-02
10408081	Hist1h1b	0.293391907	0.421689863	0.449693048	0.502035085	1.437292078	1.532738422	1.711141561	1.066407062	1.190531547	1.116395033	2.26E-02
10578690	Neil3	0.736653247	0.462085597	0.659053173	0.732336758	0.627276944	0.894658614	0.994140406	1.426257768	1.584850864	1.111195255	2.26E-02
10425226	Eif3l	0.505898902	0.448036748	0.57737239	0.605082843	0.885625064	1.141280179	1.196054865	1.288671951	1.350520568	1.047994074	2.31E-02
10578515	Ankrd37	1.137030477	0.977915625	0.72561094	1.629184654	0.860061049	0.63816314	1.432841676	0.74199749	1.665976708	2.245259222	2.36E-02
10563099	Snord35b	0.429586	0.612094081	0.920766321	0.355583841	1.424846435	2.143380651	0.827736101	1.504288883	0.580930043	0.386182501	2.40E-02
10584580	Snord14e	0.732160154	1.227874627	0.46169197	2.327212449	1.677057432	0.630588769	3.178556546	0.376009048	1.895317647	5.040617121	2.40E-02
10408693	F13a1	1.180234916	0.588280942	0.826750602	0.97499683	0.49844394	0.700496647	0.826104038	1.405366965	1.657365997	1.179311908	2.41E-02
10368886	Foxo3	2.220157757	2.093988817	1.57468426	1.765617643	0.943171182	0.709266832	0.79526675	0.75200223	0.843183893	1.121251852	2.41E-02
10351825	Tagln2	0.483202463	0.589508363	0.505366876	0.824255542	1.220002812	1.045869828	1.705818174	0.857268375	1.398208396	1.631004288	2.42E-02
10376060	Irf1	0.830182927	0.688360803	0.585168678	1.206549625	0.829167621	0.704867155	1.453353935	0.850090064	1.752786649	2.061883469	2.45E-02
10583100	Mmp8	0.880775388	0.493900207	0.733085068	0.790009018	0.56075614	0.832317839	0.8969472	1.484277709	1.599531661	1.077649856	2.45E-02
10450145	Psbm9	0.67042954	0.473767209	0.49968117	0.954735575	0.706662192	0.745314967	1.424065495	1.054697669	2.01519978	1.910689518	2.48E-02
10501586	S1pr1	0.63738993	0.644683889	1.016592637	0.451127032	1.011443481	1.594930496	0.707772449	1.576885437	0.699764705	0.44376382	2.52E-02
10575733	Cenpn	0.634887524	0.481416194	0.684440692	0.622783015	0.758270048	1.078050309	0.980934404	1.42172345	1.293647832	0.909915239	2.55E-02
10404026	Hist1h2af	0.423196619	0.498137219	0.519167909	0.640406915	1.177082228	1.226777071	1.513260943	1.042218668	1.285603425	1.233525617	2.55E-02
10412207	Gpx8	1.086954022	3.671116832	1.479658712	1.63995192	3.377435254	1.361289146	1.508759236	0.403054106	0.446717442	1.108331203	2.55E-02
10583310	Taf1d	3.035151645	1.590260717	1.366862512	2.05249406	0.523947698	0.450344059	0.676241025	0.859521019	1.290665133	1.501609739	2.57E-02
10439299	Sifa3	0.92233709	0.323991043	0.651738696	0.645084702	0.351271836	0.706616598	0.699402322	2.011594796	1.991057208	0.989790395	2.60E-02
10480432	Mastl	0.649135648	0.362344531	0.65524445	0.537582122	0.558195398	1.009410671	0.828150669	1.808346459	1.483621457	0.820429874	2.61E-02
10473356	Ube2l6	1.242446281	1.103148419	0.793056016	1.601961385	0.887884197	0.638302056	1.289360683	0.718902372	1.452172126	2.019985163	2.63E-02
10421517	Cysltr2	2.035476021	1.033522447	0.863519366	2.073691539	0.507754666	0.424234605	1.018774732	0.835510993	2.00643106	2.401441844	2.72E-02
10536499	Cav1	0.92063375	1.27192837	0.67909477	1.689547298	1.381579123	0.737638361	1.83520026	0.533909603	1.328335257	2.487940376	2.78E-02
10403943	Hist1h2bm	0.310144356	0.355230464	0.367675436	0.578025313	1.145371363	1.185497748	1.863729911	1.035033515	1.627183961	1.572107509	2.78E-02
10456400	Tubb6	1.107573881	1.062156532	0.733841132	1.621058778	0.958993842	0.662566303	1.46361232	0.690897349	1.526195743	2.209005065	2.83E-02
10533256	Oas1a	1.744650774	1.226814187	0.792050186	2.245223743	0.703186108	0.453987811	1.286918721	0.645615444	1.830125349	2.834698841	2.89E-02
10505276	Slc31a1	0.737624898	0.428061858	0.683566649	0.628416771	0.580324578	0.926713091	0.851946257	1.596887547	1.468051311	0.919320408	2.89E-02
10500324	Hist2h2ac	0.4523965	0.516771556	0.558925922	0.632718505	1.142297866	1.235477998	1.398592839	1.081572535	1.2243679	1.132025694	3.01E-02
10445875	Btg3	2.094770029	1.454861552	1.229623803	1.778884444	0.694520894	0.586997039	0.849202738	0.845182692	1.222717338	1.446689987	3.02E-02
10419156	Ear10	1.595468511	0.997729294	0.815924654	1.821869621	0.625351919	0.51140129	1.141902587	0.817781595	1.826015965	2.232889534	3.03E-02
10346876	Snora41	3.972020787	2.039796641	1.458954035	2.894382153	0.51354128	0.367307754	0.7286926	0.715244846	1.418956231	1.983874807	3.09E-02
10362097	H6ob	2.309484767	1.108957618	2.082481288	0.746086925	0.480175333	0.901708172	0.323053408	1.877872746	0.672782181	0.358268249	3.10E-02
10404069	Hist1h1a	0.416310348	0.693751219	0.486207173	0.896916395	1.666427996	1.16789596	2.15444175	0.700837937	1.292850189	1.844720613	3.10E-02
10458382	Cd14	2.307436105	1.455973588	1.058325261	2.27332984	0.630991942	0.458658534	0.985218977	0.726884931	1.561381236	2.148044579	3.11E-02
10467124	Acta2	0.920684016	0.80618482	0.61746771	1.374321508	0.875636816	0.670661921	1.492717897	0.765913343	1.704722632	2.225738262	3.12E-02
10365482	Timp3	1.015275246	1.072960955	0.73551289	1.500830659	1.056817803	0.724446787	1.478250026	0.685498281	1.39877472	2.040522579	3.15E-02
10407792	Gpr137b-ps	2.304680533	1.532382137	1.941678261	1.074133153	0.664900022	0.842493453	0.466065963	1.267097948	0.700956457	0.553198321	3.16E-02
10440419	Btg3	2.040754655	1.42308962	1.209045662	1.753163853	0.697334987	0.592450278	0.859076249	0.849592074	1.231941986	1.450039405	3.25E-02
10405587	Tgfb1	0.984632432	0.60728056	0.576357985	1.334662592	0.616758641	0.585353444	1.355493227	0.949080248	2.197769334	2.315683355	3.26E-02

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10466210	Ms4a6d	1.25111049	0.687940512	0.67833541	1.472069199	0.549863915	0.542186654	1.176610068	0.986037889	2.139820483	2.170119939	3.28E-02
10351873	Pyhin1	1.490720049	1.004651347	0.813849511	1.738467775	0.673936966	0.545943896	1.166193329	0.81008154	1.730418996	2.136104713	3.28E-02
10466606	Anxa1	0.558562519	0.467278666	0.474817944	0.90143257	0.836573617	0.85007126	1.613843643	1.016134435	1.929111331	1.898480421	3.28E-02
10503833	Rplp1 // Rplp1	0.468962535	0.485591807	0.527225074	0.690576725	1.035459703	1.124237086	1.472562676	1.085737168	1.422134218	1.309832858	3.31E-02
10409220	Hist2h2aa1	0.453715976	0.526358336	0.565862593	0.634330592	1.160105363	1.247173615	1.398078591	1.075052021	1.205130702	1.120997569	3.32E-02
10494662	Ywhah	0.589519829	0.490629786	0.558310094	0.796662619	0.832253236	0.947059058	1.351375442	1.13794578	1.623755106	1.426917815	3.36E-02
10531931	Sparcl1	1.016498417	0.953929082	0.679606423	1.496063064	0.938446205	0.668575977	1.471781007	0.712428665	1.568316862	2.201366872	3.46E-02
10425049	Apol9b	1.269326699	1.295900153	0.831682243	1.771904574	1.020935078	0.655215276	1.395940521	0.64177957	1.367315661	2.130506679	3.48E-02
10603567	Dynlt3	2.440359488	1.312702907	1.446009623	1.488326516	0.537913743	0.592539595	0.60988003	1.101551323	1.133787781	1.0292646	3.51E-02
10567171	Snord14a	2.307898501	2.634362559	1.243484186	2.840012168	1.141455119	0.538795006	1.230561988	0.472024696	1.078064277	2.283914987	3.56E-02
10461162	Snord22	2.232664598	2.035655361	1.197681115	2.435376616	0.911760487	0.536435753	1.090793762	0.588351613	1.196359985	2.033409883	3.59E-02
10344819	Cspp1	2.030693543	2.061434873	1.799118694	1.320452767	1.01513834	0.88596268	0.650247189	0.872750684	0.64055032	0.73394422	3.63E-02
10544932	Inmt	0.983310328	1.093986929	0.680329333	1.561103195	1.112555108	0.691876525	1.587599713	0.621880678	1.426985235	2.294628674	3.76E-02
10440513	Cyyr1	1.091591323	1.137366085	0.73791233	1.672413369	1.041933974	0.675996881	1.532087452	0.648790516	1.470426621	2.266412013	3.90E-02
10364293	Ube2g2	0.486203899	0.663101351	0.542410904	0.879998796	1.36383388	1.115603772	1.809937759	0.81799095	1.327095466	1.622384045	3.97E-02
10546706	Rybp	2.325205308	1.532474925	1.817366515	1.106370489	0.659070801	0.781593999	0.475816258	1.185902937	0.721950142	0.608776755	4.05E-02
10433145	Gtsf1	0.906228263	0.463127805	0.66741619	0.853751285	0.511049836	0.736476908	0.94209298	1.441105851	1.843446401	1.279188756	4.08E-02
10451225	Polh	0.563214015	0.456480195	0.610457504	0.644321501	0.810491541	1.083881947	1.144008286	1.337314324	1.411499353	1.055473144	4.13E-02
10376455	Hist3h2a	0.459765371	0.471699629	0.445430253	0.840334132	1.025957279	0.968820797	1.827745597	0.944309102	1.781502635	1.88656726	4.13E-02
10375402	Adam19	1.115723141	0.780540534	0.665163476	1.402073349	0.699582634	0.596172519	1.256649879	0.852183131	1.796285124	2.107862805	4.18E-02
10373407	Esyt1	0.46405611	0.423710056	0.538273378	0.587297016	0.913057811	1.159931669	1.265573285	1.270381409	1.386082316	1.091075724	4.22E-02
10363070	Gp49a	2.706321601	1.300111801	1.097059312	2.190868192	0.480398117	0.405369159	0.809537267	0.843819209	1.685138301	1.997037141	4.39E-02
10500333	Hist2h4	0.466546873	0.543787984	0.551473936	0.678625144	1.165559165	1.182033292	1.454570127	1.014134098	1.247959066	1.230566124	4.39E-02
10402800	Gpr132	0.857574525	0.606249055	1.043025418	0.502390016	0.706934543	1.216250469	0.585826656	1.72045698	0.828685854	0.481666129	4.44E-02
10404061	Hist1h2bb	0.300696379	0.355776248	0.316023689	0.697795009	1.183174367	1.050972713	2.32059665	0.888265282	1.961331072	2.208046529	4.48E-02
10572932	Naa20	1.717612962	0.88260393	0.798400578	1.709844777	0.513854954	0.464831481	0.995477337	0.904596672	1.937273016	2.1415876	4.52E-02
10591816	Dpy19l1	0.496994314	0.432741387	0.49390457	0.732364819	0.870716977	0.99378314	1.473587924	1.141338882	1.692384509	1.482806322	4.58E-02
10427918	Fam105a	0.481210337	0.608875987	0.566145842	0.787821306	1.265301137	1.176503906	1.637166213	0.929821267	1.293894524	1.391551871	4.61E-02
10368144	Tnfaip3	2.098070555	1.302858309	1.649823014	1.041273687	0.620979264	0.786352494	0.496300606	1.266310391	0.79922251	0.631142661	4.67E-02
10582303	Cyba	0.406180004	0.424600001	0.45033558	0.647013099	1.045349345	1.10870938	1.592922088	1.06061135	1.523817942	1.436735466	4.68E-02
10420483	Phf11	1.20619063	0.848044875	0.726396541	1.479259887	0.703076988	0.602223664	1.226389802	0.856554367	1.744317938	2.036435755	4.70E-02
10497122	Depdc1a	0.809778262	0.480054019	0.631142932	0.82900718	0.592821568	0.779402166	1.023745905	1.314733147	1.726903946	1.313501488	4.78E-02
10559261	Cd81	0.706021317	0.619560928	0.521757065	1.179148234	0.877538558	0.739010356	1.670131207	0.84214004	1.903199798	2.259956431	4.80E-02
10453632	Rpl7a	0.573719595	0.480439458	0.571159537	0.734359403	0.837411623	0.995537789	1.279997073	1.188827288	1.528516009	1.285734291	4.88E-02
10523058	Elf5a	0.349257912	0.452667214	0.38229705	0.758437897	1.29608292	1.09459811	2.171569696	0.844543272	1.675486701	1.983896808	4.90E-02
10427628	Il7r	1.123441728	1.319915072	1.579298595	0.66544491	1.174885211	1.405768146	0.592327036	1.196515313	0.504157369	0.421354715	4.93E-02
10581605	Hp	1.157815048	0.66428872	0.614683418	1.484682487	0.573743381	0.530899489	1.282314035	0.92532569	2.234995781	2.415361214	4.93E-02
10576883	Shcbp1	0.753810431	0.395042559	0.511222473	0.92642272	0.524060881	0.678184398	1.228986337	1.294094679	2.345121303	1.812171351	4.93E-02
10404063	Hist1h2ab	0.20605657	0.258657365	0.247212246	0.539871253	1.255273562	1.199729987	2.620014747	0.955751816	2.087206188	2.18383701	4.94E-02
10593050	Il10ra	1.3249659	1.124933296	0.814250672	1.63745798	0.849028111	0.614544625	1.23584915	0.723821293	1.455604512	2.01099985	4.95E-02
10477167	Mcts2	2.162674355	1.366144948	1.760504072	1.045043055	0.631692397	0.814040296	0.483217944	1.288665653	0.764957669	0.593604452	4.95E-02



ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10344658	Rb1cc1	1.970923108	1.478607233	1.881256578	0.959091702	0.750210511	0.954505313	0.486620558	1.272316634	0.648645348	0.509814405	4.98E-02
10455015	Vaultrc5	0.861026113	0.944064099	0.596107338	1.437994272	1.096440728	0.692322021	1.670093682	0.631426763	1.52319559	2.412307615	5.11E-02
10480804	Phpt1	0.542308916	0.366897836	0.490488205	0.697522535	0.676547675	0.904444295	1.286208864	1.33685227	1.901135591	1.422098488	5.20E-02
10368616	Zufsp	2.820588673	1.557747019	1.428808092	1.846695037	0.552277272	0.506563791	0.654719724	0.9172273	1.185490978	1.292472409	5.26E-02
10577508	Ckap2	0.603779887	0.385019072	0.53495498	0.704097061	0.637681182	0.886009938	1.166148585	1.389424626	1.828732943	1.316180028	5.30E-02
10512487	Rmrp	0.335621862	0.733120094	0.431363698	0.86009438	2.184363344	1.285266982	2.562688776	0.588394319	1.173197116	1.993896063	5.40E-02
10363082	Lilrb4	2.715765289	1.259554287	1.066142089	2.19740126	0.4637935	0.392575196	0.809127825	0.846443937	1.744586384	2.061077301	5.43E-02
10382844	Snord1c	0.383946587	0.870013516	0.573969412	0.913944048	2.265975385	1.494919948	2.380393728	0.659724708	1.05049408	1.59232187	5.49E-02
10600169	Bgn	1.064872546	1.1068292	0.751656093	1.517753036	1.039400635	0.705864843	1.425290793	0.679107574	1.371262192	2.019212044	5.54E-02
10592058	Tuba1b	0.573092906	0.44619198	0.493958072	0.797405493	0.778568317	0.86191622	1.39140702	1.10705278	1.787135424	1.614318175	5.62E-02
10584578	Snord14c	0.425360189	1.048068472	0.362718665	1.790506463	2.463955253	0.852732989	4.209388911	0.346082985	1.708386914	4.936350491	5.62E-02
10476297	Mir103-2	2.96952519	1.02671168	1.524026322	1.322548593	0.345749443	0.513222224	0.445373758	1.484376142	1.288140204	0.867799049	5.67E-02
10406254	Eil2	1.677918601	0.881412963	1.535295495	0.719154202	0.525301384	0.914999985	0.428598981	1.741857176	0.815910626	0.468414194	5.72E-02
10425834	Samm50	0.622665582	0.497747792	0.626511719	0.711015339	0.799382214	1.00617689	1.141889578	1.258693116	1.428465079	1.134879552	5.80E-02
10461156	Snhg1	1.426941195	1.527439722	0.907234443	2.004208835	1.07042934	0.63578965	1.404549004	0.593957608	1.312136123	2.209141032	5.83E-02
10476106	Snord57	1.538601337	2.612774695	1.376847318	1.900358547	1.698149242	0.89486944	1.235120821	0.526967488	0.727333494	1.380224607	5.87E-02
10351039	Gas5	1.811536195	2.001428656	1.171498478	2.139490059	1.104823995	0.646687867	1.18103633	0.58533112	1.068981426	1.826284967	5.95E-02
10449303	Bak1	0.443922201	0.50455085	0.490498598	0.705885266	1.136574945	1.10492018	1.590110307	0.972148986	1.399036917	1.439117808	6.06E-02
10535025	Got2	0.573567177	0.465816789	0.635924794	0.598640228	0.812139899	1.108718942	1.043714236	1.36518221	1.285140943	0.941369535	6.14E-02
10371662	Spic	0.535717962	0.34702455	0.676050049	0.455300632	0.647774715	1.261951432	0.849888681	1.948133205	1.312012744	0.673471783	6.16E-02
10497337	Car1	0.570654636	0.274473003	0.496976574	0.597330887	0.480979187	0.870888525	1.046746753	1.810657403	2.176282846	1.201929665	6.20E-02
10492499	Mfsd1	0.517218611	0.430875669	0.506591051	0.736652629	0.833062963	0.97945248	1.424257778	1.175724433	1.709664024	1.45413668	6.25E-02
10406407	Arrdc3	2.318693374	1.709725605	1.479621125	1.648230969	0.737365977	0.63812712	0.710844732	0.865414381	0.964032453	1.113954742	6.31E-02
10446229	Tnfsf9	1.20102138	0.746836342	0.574712031	1.716045587	0.621834344	0.478519401	1.428821848	0.769528742	2.29775319	2.985922504	6.44E-02
10408225	Hist1h4c // Hist1h4c	0.288783703	0.401075564	0.366724742	0.613892151	1.388844175	1.269894176	2.125785301	0.914353243	1.530614693	1.673986181	6.75E-02
10457357	Mpp7	2.301794465	1.470536064	1.224947973	1.978470344	0.638865062	0.532170874	0.859533887	0.832994173	1.345407564	1.615146429	6.96E-02
10511290	Tnfrsf18	1.251491115	0.587366577	0.748740631	1.071529168	0.469333398	0.598278823	0.856201978	1.274741635	1.824293737	1.431108616	7.13E-02
10543118	Glccl1	2.026438071	1.323015375	1.492430614	1.218014162	0.652877279	0.736479755	0.601061626	1.128052359	0.920634926	0.816127832	7.29E-02
10395273	Gdap10	2.068254275	0.848376285	0.785001052	2.0277123	0.410189547	0.379547651	0.980397974	0.925298204	2.390109597	2.58306953	7.41E-02
10569020	Ifitm6	2.598738496	1.429102649	1.368790148	1.808534835	0.549921683	0.526713307	0.695927981	0.957796943	1.265503802	1.321265233	7.52E-02
10437673	Tnp2	0.965390014	0.893936944	0.67658624	1.387283914	0.925985282	0.700842385	1.437019126	0.756861258	1.551881173	2.050416978	7.57E-02
10407985	Gpr141	0.964355119	0.457763267	0.710870359	0.850366169	0.474683296	0.737145834	0.881797744	1.552921369	1.857654886	1.19623242	7.81E-02
10360406	Ifi205	1.733017795	0.575431223	0.704121383	1.539812924	0.332039997	0.406297838	0.888515356	1.223641254	2.675928698	2.18685721	7.84E-02
10456974	Arf1	0.462708923	0.42044227	0.543566042	0.56256991	0.908653904	1.174747265	1.215818155	1.292843468	1.338043175	1.034961469	8.01E-02
10547793	Rnu7	1.6162143	2.786201955	0.980334218	3.134480216	1.723906264	0.606562025	1.939396413	0.351853252	1.125001083	3.197358776	8.01E-02
10461154	Snhg1	1.134898655	1.597996593	0.858306865	1.857639694	1.40805224	0.756285032	1.63683311	0.537114328	1.162480385	2.164307161	8.01E-02
10408202	Hist1h3e	0.346940575	0.403334628	0.41749565	0.577206856	1.16254672	1.203363573	1.663705249	1.035109861	1.431086786	1.382545796	8.11E-02
10413596	Sfmbt1	2.164866276	1.436473199	1.447215848	1.43676162	0.663538998	0.668501267	0.663672226	1.007478489	1.000200784	0.992776318	8.12E-02
10571840	Hpgd	1.171505586	1.598030875	0.824369243	1.983888803	1.364083018	0.703683578	1.693452277	0.515865654	1.241458368	2.406553641	8.21E-02
10372652	Lyz1	1.113452807	0.921815699	0.697229591	1.634940714	0.827889331	0.626186926	1.468352052	0.756365498	1.773609102	2.344910107	8.23E-02
10486057	Rab5b	0.464082318	0.650841314	0.477050786	0.956153821	1.402426444	1.027944328	2.060310821	0.732975574	1.469104373	2.004301951	8.37E-02

ID	Gene.Symbol	D30cl13vs D8Arm.FC	D30cl13vs D8cl13.FC	D30cl13vs HMPVLung.FC	D30cl13vs HMPVSpleen.FC	D8Armvs D8cl13.FC	D8Armvs HMPVLung.FC	D8Armvs HMPVSpleen.FC	D8cl13vs HMPVLung.FC	D8cl13vs HMPVSpleen.FC	HMPVLungvs HMPVSpleen.FC	adj.P.Val
10482177	Strbp	2.060971057	1.616175924	1.678334635	1.295406647	0.784181766	0.814341681	0.628541892	1.038460362	0.801525767	0.771840502	8.40E-02
10447566	Atp5g2	0.479480427	0.411442588	0.450813267	0.74736208	0.858100904	0.940212032	1.558691528	1.095689361	1.816443172	1.657808532	8.45E-02
10402512	Scarna13	1.082821125	1.303624057	1.499703237	0.666906475	1.203914503	1.384996287	0.615897178	1.150410833	0.511578834	0.444692296	8.51E-02
10548552	Klra2	1.173424693	0.549293201	0.739225355	1.074806292	0.468111166	0.629972558	0.91595677	1.345775542	1.956707803	1.453962969	8.73E-02
10406928	Cd180	1.261043	0.620533577	0.817467298	1.086226489	0.492079633	0.648246965	0.861371491	1.317361909	1.750471737	1.328770572	8.81E-02
10496569	Gbp6	0.840064527	0.612831368	0.57509939	1.172593338	0.729505113	0.684589543	1.395837224	0.938430081	1.913402933	2.038940324	9.00E-02
10454512	Sft2d3	2.167380264	1.621769658	1.839244576	1.139599378	0.748262631	0.848602623	0.525795772	1.134097291	0.702688802	0.61960187	9.14E-02
10425799	Rnu12	0.752779477	1.245354293	0.660747281	1.527662269	1.654341451	0.877743484	2.029362269	0.530569722	1.226688885	2.312022028	9.20E-02
10408077	Hist1h2ak	0.39360033	0.505165335	0.435324013	0.745517908	1.283447436	1.106005202	1.894098788	0.861745616	1.475789919	1.712558661	9.36E-02
10404049	Hist1h3d	0.331260744	0.368400711	0.402725811	0.540865505	1.11211702	1.215736602	1.632748571	1.093173272	1.468144575	1.343011774	9.43E-02
10539091	Sftpb	0.922323002	1.09680198	0.702877	1.525524043	1.1891734	0.762072504	1.65400195	0.640842205	1.390883743	2.17039972	9.44E-02
10405927	Zfp455	2.251600085	1.943185507	1.443000101	1.879669808	0.863024264	0.640877619	0.834815126	0.742595134	0.967313621	1.302612389	9.48E-02
10565990	Art2a-ps	2.196570194	1.723410385	1.419293174	1.778376649	0.784591537	0.646140596	0.809615215	0.823537555	1.031893891	1.253001621	9.51E-02
10502655	Cyr61	0.963030519	1.145363265	0.734640528	1.536782798	1.189332261	0.762842417	1.595777879	0.641403955	1.341742699	2.091884043	9.57E-02
10548497	Klra6	2.133247055	1.720139542	1.387085397	1.810517273	0.806348021	0.650222577	0.848714296	0.806379577	1.05254093	1.305267345	9.65E-02
10526508	Fis1	0.584733102	0.489133703	0.579280986	0.724388084	0.836507633	0.990675889	1.23883543	1.184299879	1.480961297	1.250495186	9.78E-02