

## *Supplementary Material*

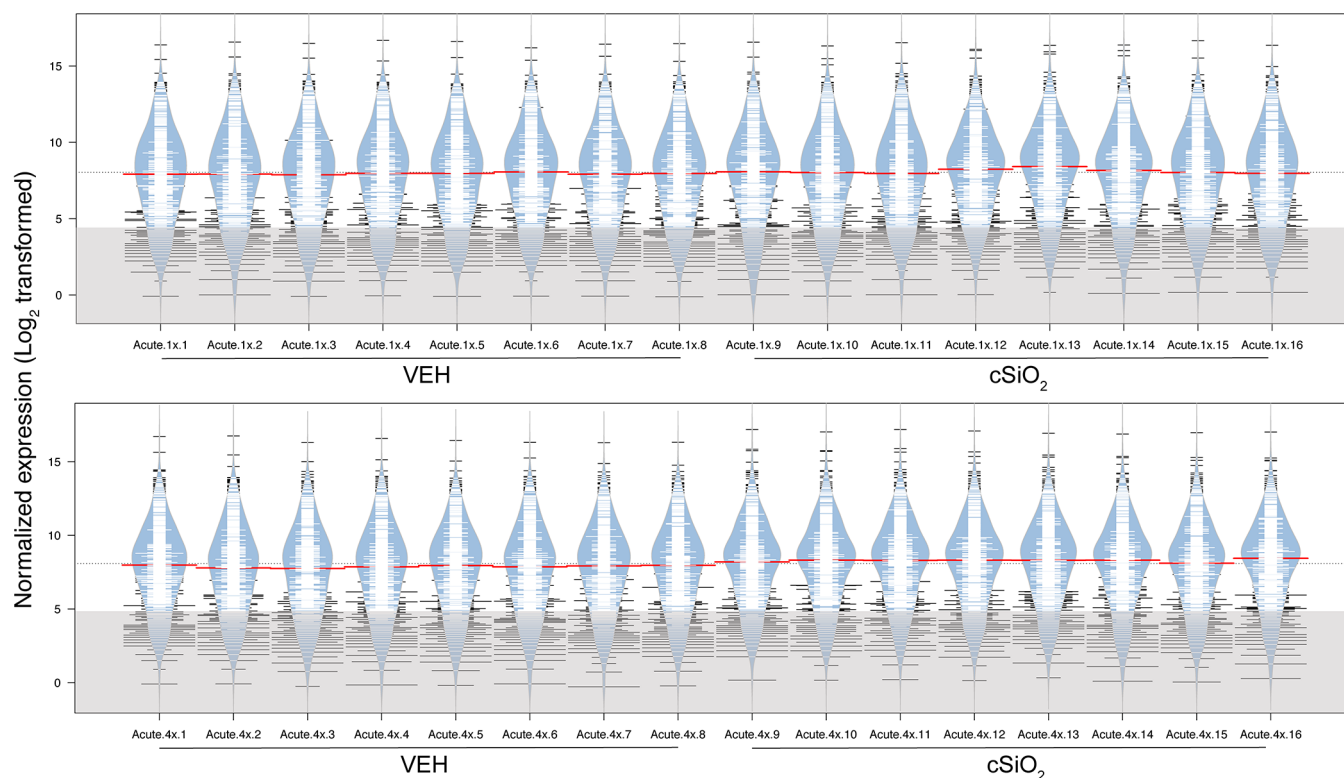
Mapping of Dynamic Transcriptome Changes Associated with Silica-Triggered Autoimmune Pathogenesis in the Lupus-Prone NZBWF1 Mouse

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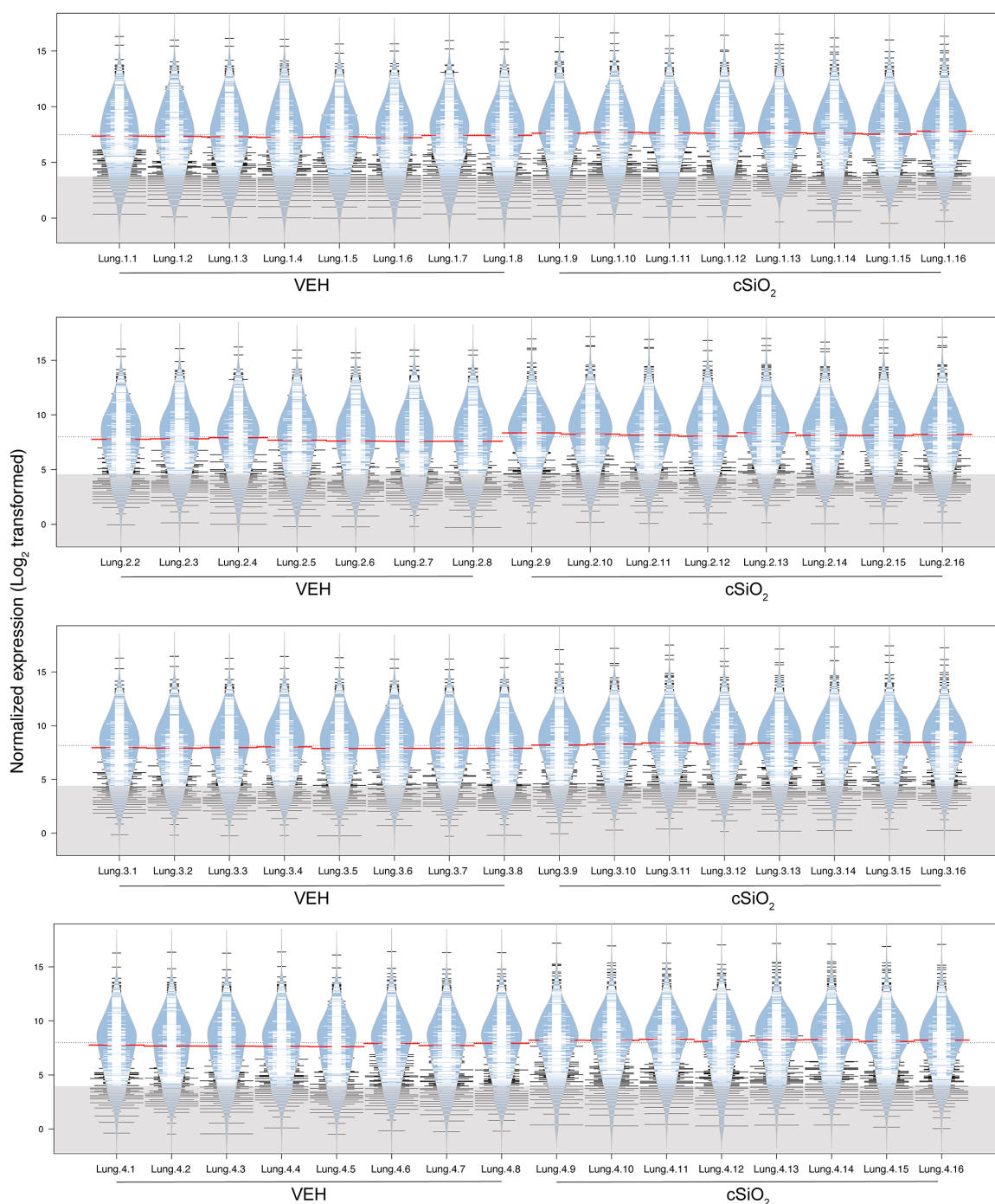
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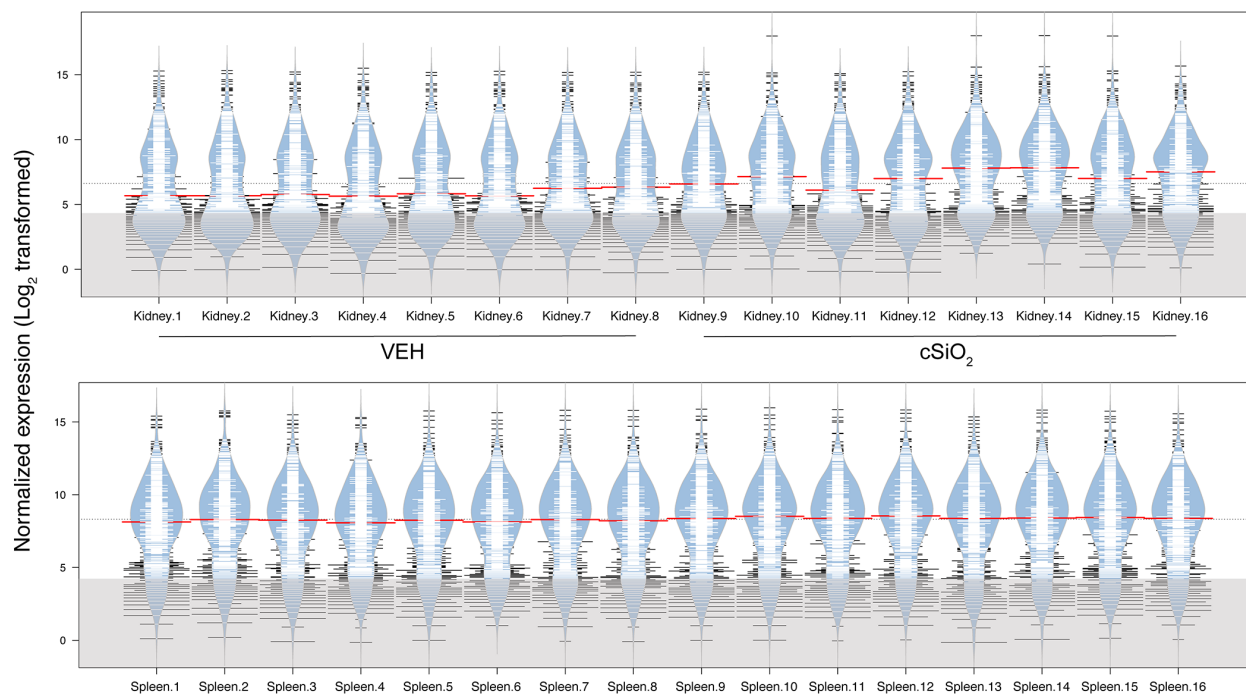
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**Supplementary figure 1. Beanplots depicting distribution of normalized expression of nanoString PanCancer Immune gene panel – acute response in lung (experiments 1 and 2).** Samples are named by dosing regimen (Acute.1x, single instillation; Acute.4x, four weekly instillations) and sample numbers, for which 1-8 correspond to vehicle controls (VEH) and numbers 9-16 correspond to cSiO<sub>2</sub>-exposed mice. Red lines show the medians, white/black lines represent individual data points (line width indicates number of genes at that expression level), and blue polygons represent the estimated density of the data. The shaded region indicates genes excluded because of low signal. Plots were generated using BoxPlotR ([shiny.chemgrid.org/boxplotr/](https://shiny.chemgrid.org/boxplotr/)).

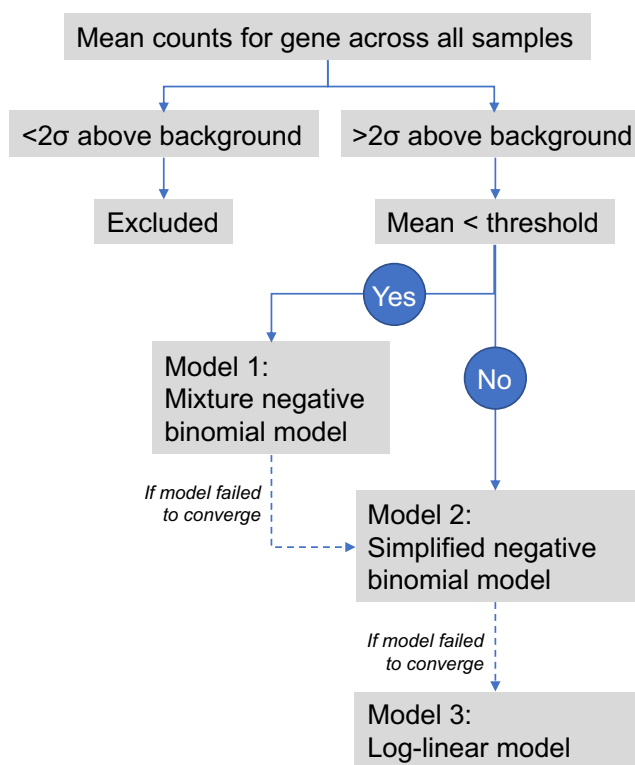


**Supplementary figure 2. Beanplots depicting distribution of normalized expression of nanoString PanCancer Immune gene panel – chronic response in lung (experiment 3).** Samples are named by “tissue.cohort.ID”. Cohorts 1, 2, 3, and 4 correspond to samples obtained 1, 5, 9, or 13 weeks post instillation with cSiO<sub>2</sub>. Sample ID numbers 1-8 correspond to vehicle controls (VEH), and numbers 9-16 correspond to cSiO<sub>2</sub>-exposed mice. Red lines show the medians, white/black lines represent individual data points (line width indicates number of genes at that expression level), and blue polygons represent the estimated density of the data. The shaded region indicates genes excluded because of low signal. Plots were generated using BoxPlotR ([shiny.chemgrid.org/boxplotr/](http://shiny.chemgrid.org/boxplotr/)).



**Supplementary figure 3. Beanplots depicting distribution of normalized expression of nanoString PanCancer Immune gene panel – chronic response in kidney and spleen.** Samples are named by tissue (kidney or spleen) and sample numbers, for which 1-8 correspond to vehicle controls (VEH) and numbers 9-16 correspond to cSiO<sub>2</sub>-exposed mice. Red lines show the medians, white/black lines represent individual data points (line width indicates number of genes at that expression level), and blue polygons represent the estimated density of the data. The shaded region indicates genes excluded because of low signal. Plots were generated using BoxPlotR ([shiny.chemgrid.org/boxplotr/](http://shiny.chemgrid.org/boxplotr/)).

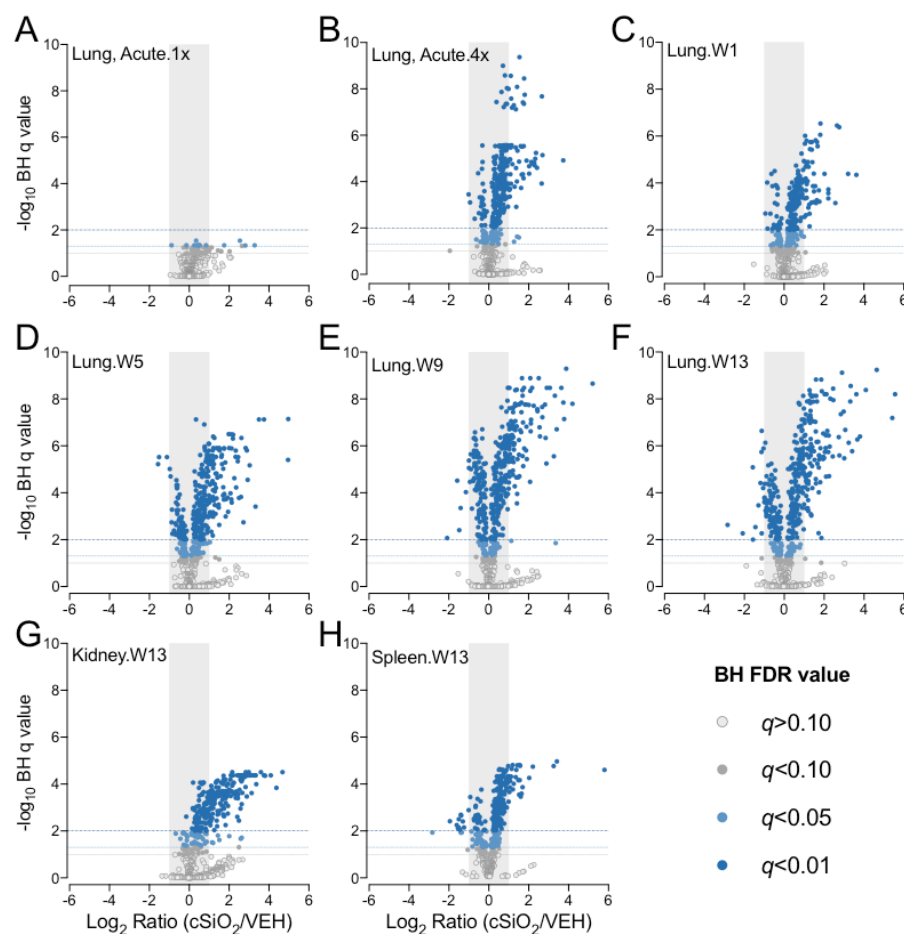




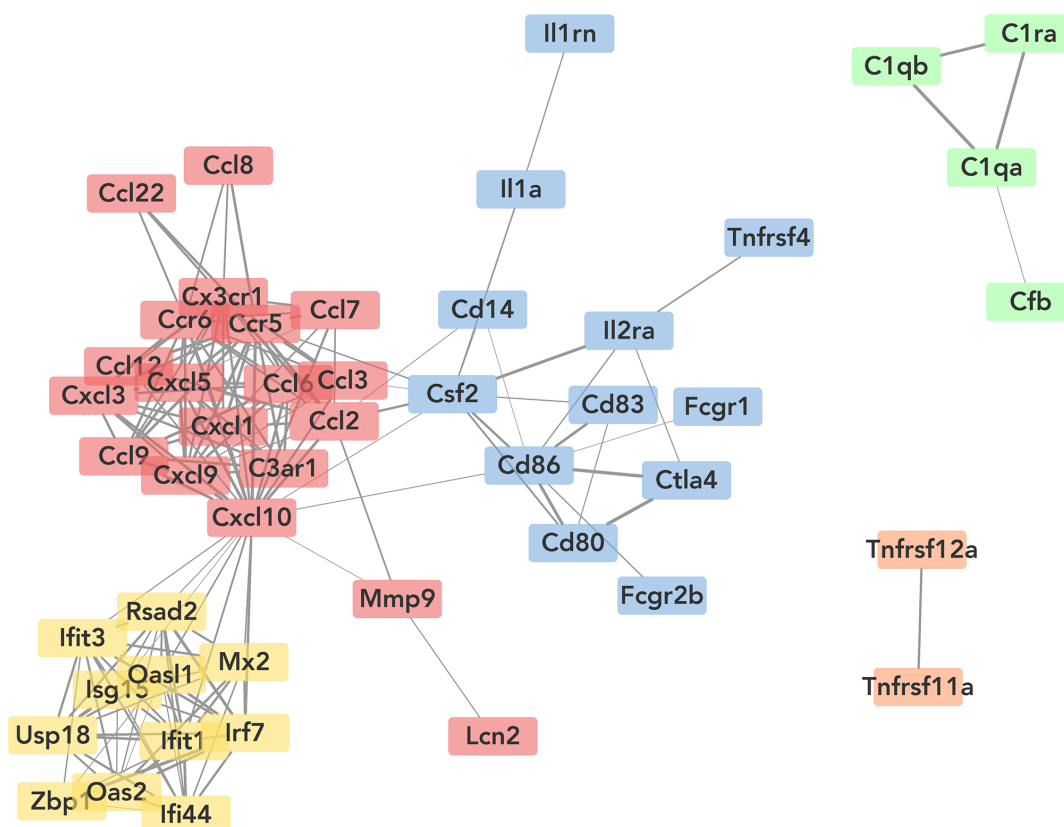
**Supplementary figure 4. Process flow for differential gene expression analysis using nSolver.** As outlined by the supplied user manual<sup>1</sup>, the mean of the gene across all samples was compared against the threshold, which is set as 10 times the background signal. If the gene mean was below the threshold, the mixture negative binomial (*MLE* function in R, Wald test to calculate a *p* value) was applied; if model 1 did not converge, the simplified model in 2 (*glm.nb* function in R/Mass) was applied instead. If the gene mean was above the threshold, the mixture model in 1 was simplified to model 2. If model 2 did not converge, the log-linear model 3 was used (*lm* function in R). For each gene, the optimal model applied for each gene is provided in Supplementary File 2 (model 1, “Wald”; model 2, “lm.nb”; model 3, “loglinear”).

<sup>1</sup> NanoString Technologies, Inc. (2018) nCounter Advanced Analysis 2.0 Plugin for nSolver Software User Manual, vers. Jan 2018 (MAN-10030-03). Accessed at [www.nanostring.com](http://www.nanostring.com)

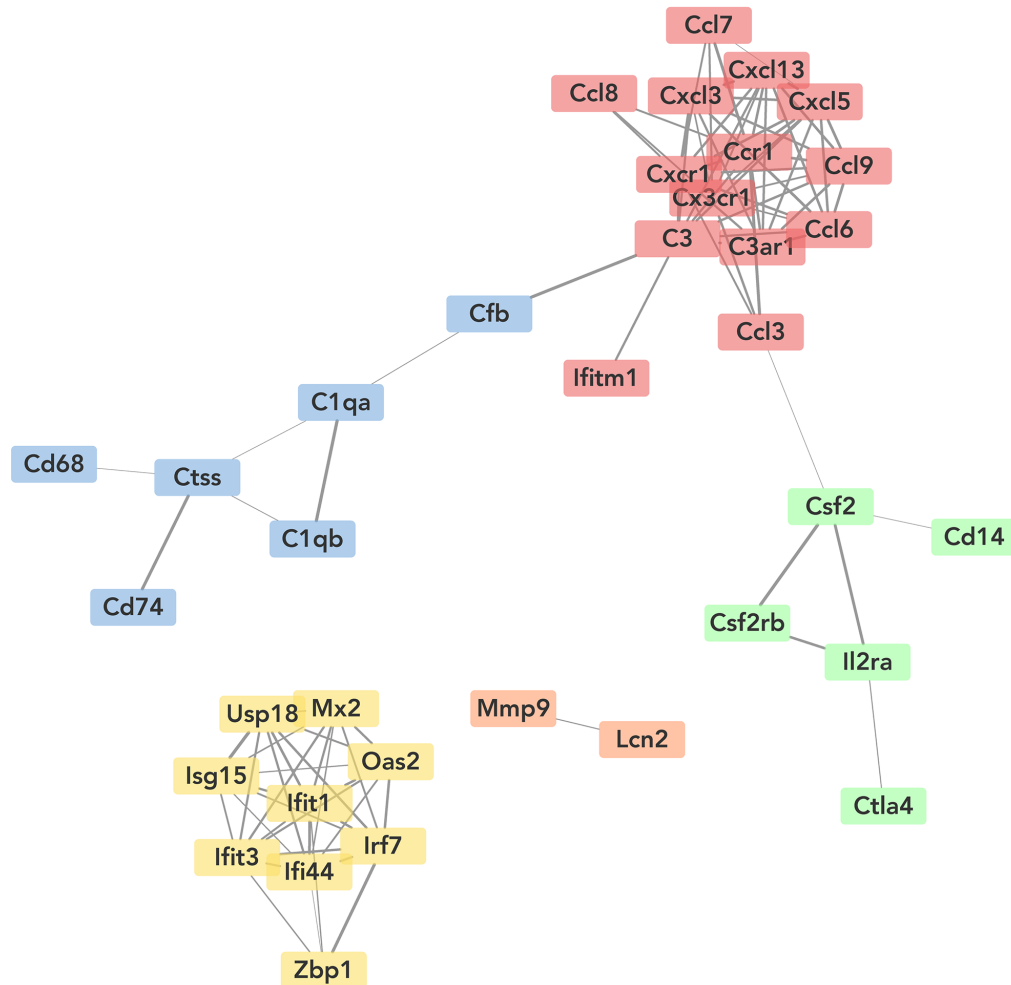




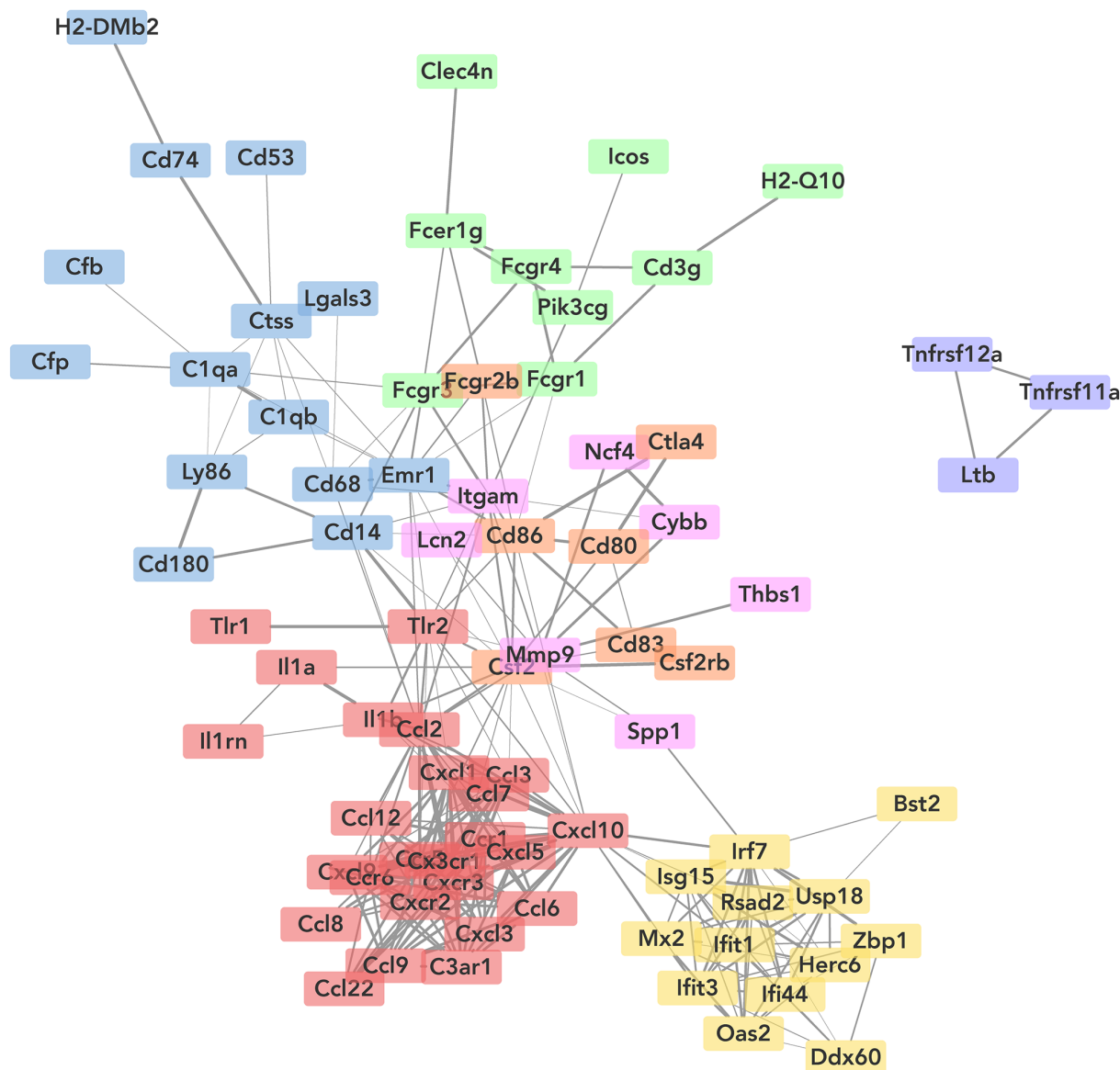
**Supplementary figure 5. Volcano plots depicting immune-related mRNA expression as measured using the nanoString Mouse PanCancer Immune Panel.** Values shown are the  $\log_2$  ratios of cSiO<sub>2</sub> treatment with respect to vehicle (VEH) controls plotted against the  $-\log_{10}$  Benjamini-Hochberg false discovery rate  $q$  value. A significant difference in gene expression was inferred for genes with BH  $q$  value  $<0.05$  and  $\log_2$  ratio  $>1$  or  $<-1$ . Horizontal lines indicate  $q$  value cutoffs of 0.1, 0.05 and 0.01, and the vertical shaded region indicates expression values that do not meet the fold change cutoff for significance. (A) Acute.1x, lung tissues from mice 1 day post single cSiO<sub>2</sub> instillation versus dosing-matched VEH control. (B) Acute.4x, lung tissues from mice 1 day post four weekly cSiO<sub>2</sub> instillations versus dosing-matched VEH control; (C-F) Lung.W1, Lung.W5, Lung.W9, and Lung.W13, lung tissues from cSiO<sub>2</sub>-treated (four weekly instillations) at 1, 5, 9, or 13 weeks post final instillation compared to time-matched VEH controls; (G) Kindey.W13, kidney tissues from cSiO<sub>2</sub>-treated (four weekly instillations) at 13 weeks post final instillation compared to tissue-matched VEH controls; (H) Spleen.W13, spleen tissues from cSiO<sub>2</sub>-treated (four weekly instillations) at 13 weeks post final instillation compared to tissue-matched VEH controls.



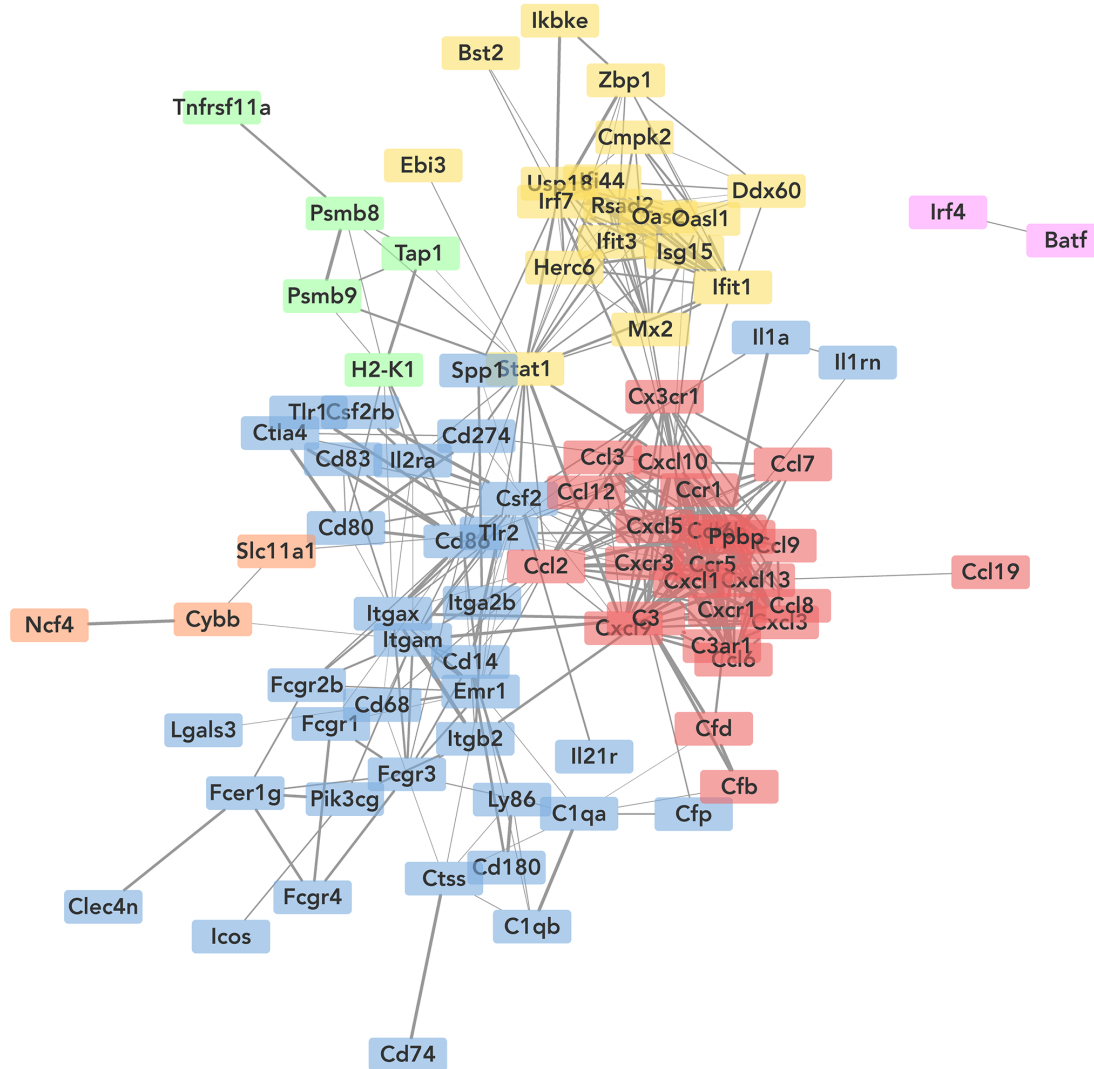
**Supplementary figure 6. Network visualization of significant differentially expressed immune response genes in lung tissues of mice treated with cSiO<sub>2</sub> (four weekly doses) compared to dosing-matched vehicle controls 1 day post instillation (Acute.4x).** Network interactions were modeled using the STRING database ([string-db.org](http://string-db.org)) with a minimum required interaction score  $\geq 0.7$ , and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape, and edge widths reflect the combined interaction score (thicker edges indicate higher score). Note, a network for mice treated only once with cSiO<sub>2</sub> was not made, as only five significant genes in that treatment group were identified. Major groupings include transcripts associated with interferon signaling (yellow), cytokine and chemokines (red), and innate and adaptive immune response (blue). See Supplementary file 6 for protein-protein interactions and functional annotations obtained from the STRING database.



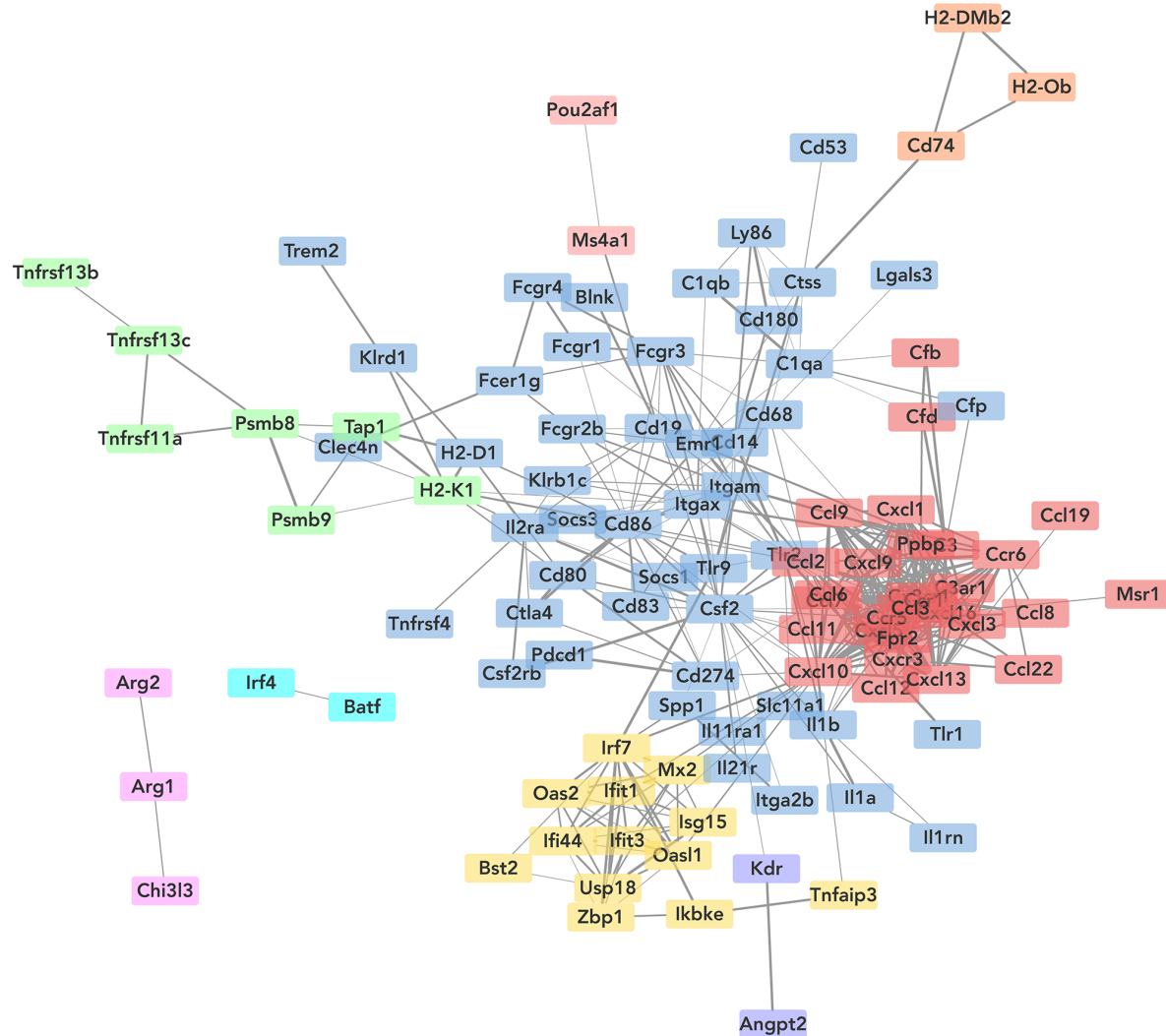
**Supplementary figure 7. Network visualization of significant differentially expressed immune response genes in lung tissues of mice treated with cSiO<sub>2</sub> (four weekly doses) compared to time-matched vehicle controls 1 week post instillation (Lung.W1).** Network interactions were modeled using the STRING database ([string-db.org](http://string-db.org)) with a minimum required interaction score  $\geq 0.7$ , and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape, and edge widths reflect the combined interaction score (thicker edges indicate higher score). Major groupings include transcripts associated with interferon signaling (yellow), cytokine and chemokines (red), complement (green), and innate and adaptive immune response (blue). See Supplementary file 6 for protein-protein interactions and functional annotations obtained from the STRING database.



**Supplementary figure 8. Network visualization of significant differentially expressed immune response genes in lung tissues of mice treated with cSiO<sub>2</sub> (four weekly doses) compared to time-matched vehicle controls 5 weeks post instillation (Lung.W5).** Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score  $\geq 0.7$ , and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape, and edge widths reflect the combined interaction score (thicker edges indicate higher score). Major groupings include transcripts associated with interferon signaling (yellow), cytokine and chemokines (red), complement (green), and innate and adaptive immune response (blue & green). See Supplementary file 6 for protein-protein interactions and functional annotations obtained from the STRING database.

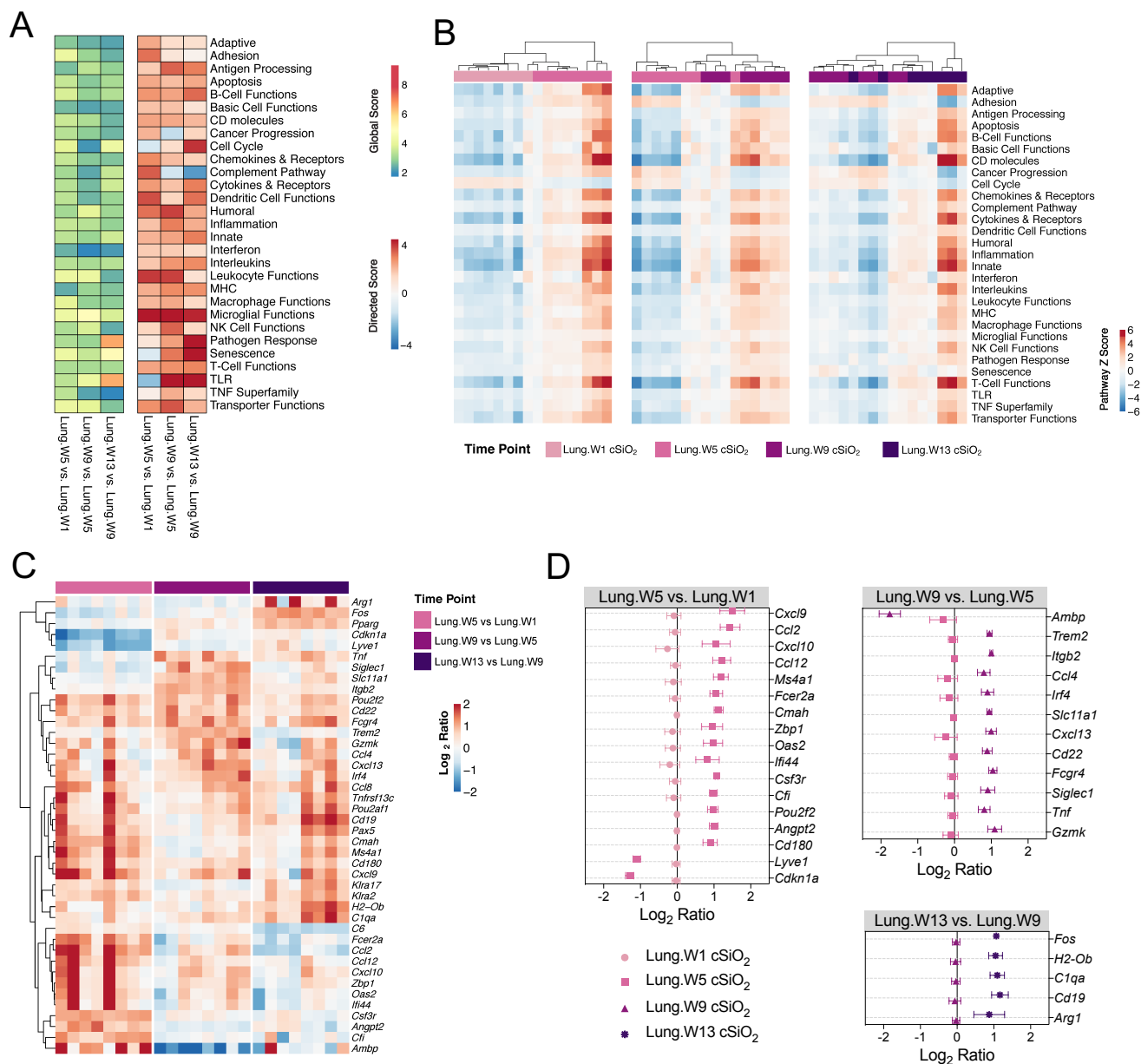


**Supplementary figure 9. Network visualization of significant differentially expressed immune response genes in lung tissues of mice treated with cSiO<sub>2</sub> (four weekly doses) compared to time-matched vehicle controls 9 weeks post instillation (Lung.W9).** Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score  $\geq 0.7$ , and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape, and edge widths reflect the combined interaction score (thicker edges indicate higher score). See Supplementary file 6 for protein-protein interactions and functional annotations obtained from the STRING database.

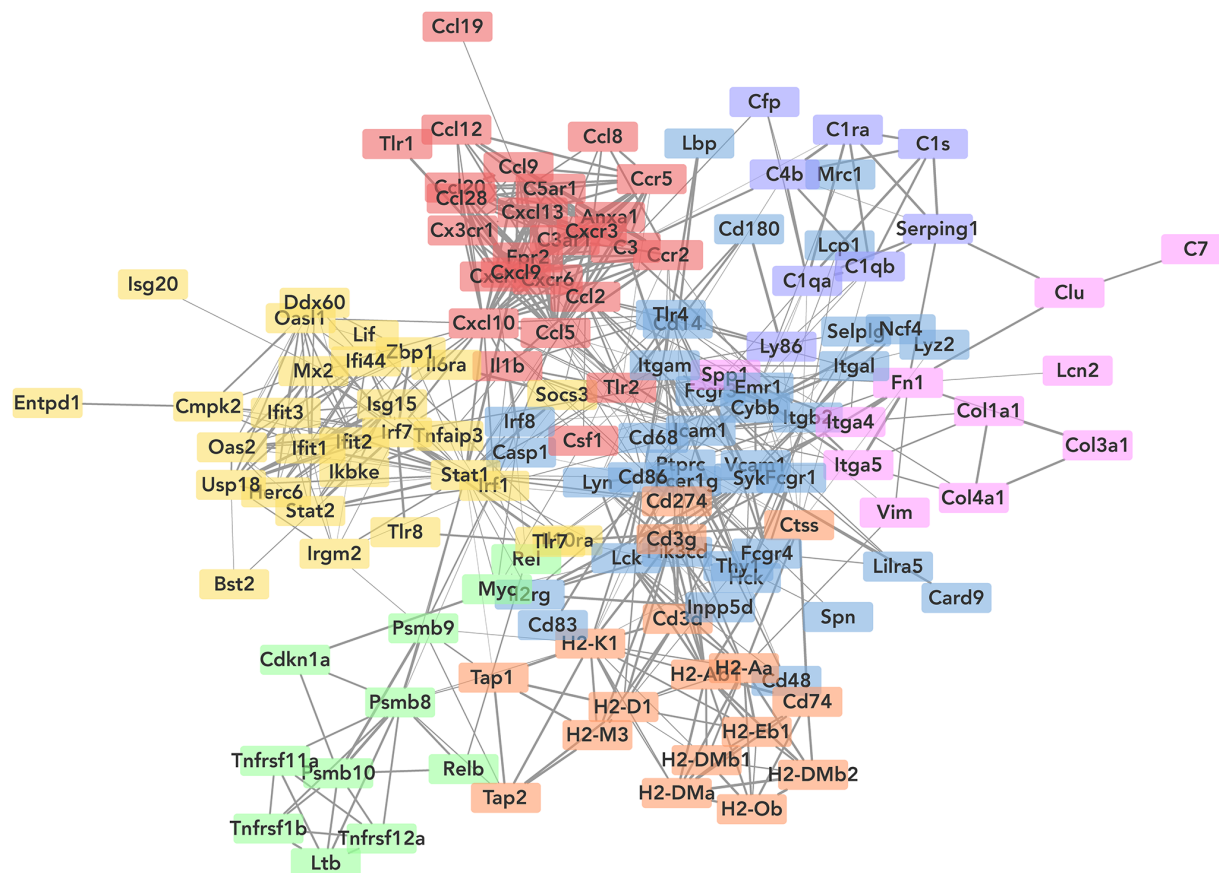


**Supplementary figure 10. Network visualization of significant differentially expressed immune response genes in lung tissues of mice treated with cSiO<sub>2</sub> (four weekly doses) compared to time-matched vehicle controls 13 weeks post instillation (Lung.W13).** Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score  $\geq 0.7$ , and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape, and edge widths reflect the combined interaction score (thicker edges indicate higher score). See Supplementary file 6 for protein-protein interactions and functional annotations obtained from the STRING database.

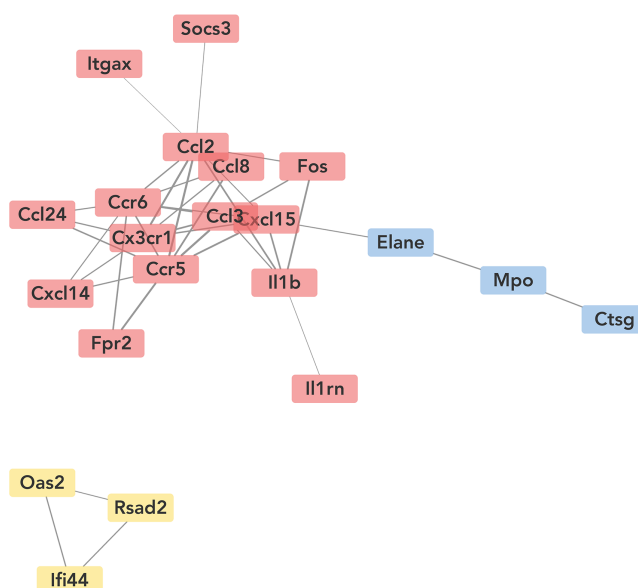




**Supplementary figure 11. Comparison of transcriptional response by time point in lung tissues of cSiO<sub>2</sub>-exposed mice.** Mice received four repeated weekly doses of cSiO<sub>2</sub> via intranasal instillation, and gene expression was determined in lung tissues obtained at 1, 5, 9, or 13 weeks post instillation. (A) Heatmaps depicting either global or directed significance scores for immune-related pathways (see Materials and Methods for details on calculation of significance scores). (B) Heatmap depicting individual pathway Z scores of each immune pathway when comparing time points progressively: W1 vs W5, W9 vs W5, W13 vs W9. (C) Heatmap depicting gene expression for differentially expressed genes for any of the time point comparisons. Values shown are the log<sub>2</sub> ratio compared to the average expression for the previous time point, as indicated. (D) Selected differentially expressed genes for each time point comparison are shown as dot plots for the average log<sub>2</sub> ratio expression  $\pm$  SEM for each comparison indicated.



**Supplementary figure 12. Network visualization of significant differentially expressed immune response genes in kidney tissues of mice treated with cSiO<sub>2</sub> (four weekly doses) compared to tissue-matched vehicle controls 13 weeks post instillation (Kidney.W13).** Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score  $\geq 0.7$ , and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape, and edge widths reflect the combined interaction score (thicker edges indicate higher score). See Supplementary file 6 for protein-protein interactions and functional annotations obtained from the STRING database.



**Supplementary figure 13. Network visualization significant differentially expressed immune response genes in spleen tissues of mice treated with cSiO<sub>2</sub> (four weekly doses) compared to tissue-matched vehicle controls 13 weeks post instillation (Spleen.W13).** Network interactions were modeled using the STRING database ([string-db.org](http://string-db.org)) with a minimum required interaction score  $\geq 0.7$ , and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape, and edge widths reflect the combined interaction score (thicker edges indicate higher score). See Supplementary file 6 for protein-protein interactions and functional annotations obtained from the STRING database.

**Supplementary Table 1. Significant differentially expressed genes in lung tissues of mice following single cSiO<sub>2</sub> dose (experiment 1)**

<b>Gene symbol</b>	<b>Log<sub>2</sub> ratio cSiO<sub>2</sub>/VEH</b>	<b>SEM</b>	<b>95% CI</b>	<b>FDR <i>q</i> value</b>	<b>Associated pathways</b>
<i>Ccl24</i>	3.28	0.767	1.78, 4.79	0.0459	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Arg1</i>	2.82	0.674	1.50, 4.14	0.0465	Basic Cell Functions
<i>Chil3</i>	2.65	0.641	1.39, 3.91	0.0481	Basic Cell Functions
<i>Cxcl5</i>	2.54	0.466	1.62, 3.45	0.0288	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Leukocyte Functions
<i>Lcn2</i>	1.76	0.391	0.995, 2.53	0.0459	Apoptosis, Innate, Transporter Functions

*Note:* Values shown are the calculated mean log<sub>2</sub> ratios, SEM and 95% confidence intervals of transcript counts for lung tissues obtained from cSiO<sub>2</sub>-treated mice with respect to dosing-matched (single dose) vehicle treated mice 1 day post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected *q* values are shown. Pathway associations for each significant gene are also shown.

**Supplementary Table 2. Significant differentially expressed genes in lung tissues of mice following four cSiO<sub>2</sub> doses (experiment 2).**

<b>Gene symbol</b>	<b>Log<sub>2</sub> ratio cSiO<sub>2</sub>/VEH</b>	<b>SEM</b>	<b>95% CI</b>	<b>FDR <i>q</i> value</b>	<b>Associated pathways</b>
<i>Cxcl5</i>	3.74	0.462	2.83, 4.64	1.22E-05	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Leukocyte Functions
<i>Cxcl1</i>	2.70	0.314	2.08, 3.31	7.23E-06	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Transporter Functions
<i>Ctla4</i>	2.67	0.236	2.20, 3.13	1.24E-06	B-Cell Functions, CD molecules, T-Cell Functions
<i>Cxcl10</i>	2.66	0.430	1.81, 3.50	1.20E-04	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate, Leukocyte Functions
<i>Oasl1</i>	2.42	0.328	1.78, 3.06	2.54E-05	Basic Cell Functions
<i>Ccl2</i>	2.37	0.270	1.85, 2.90	5.77E-06	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, NK Cell Functions, Pathogen Response, T-Cell Functions
<i>Lcn2</i>	2.33	0.283	1.77, 2.88	1.04E-05	Apoptosis, Innate, Transporter Functions
<i>Irf7</i>	2.30	0.303	1.70, 2.89	2.01E-05	Adaptive, Innate, Interferon, Senescence
<i>Mx2</i>	2.28	0.291	1.71, 2.85	1.50E-05	Innate
<i>Ifi44</i>	2.18	0.282	1.63, 2.73	1.68E-05	Interferon
<i>Oas2</i>	2.14	0.272	1.61, 2.68	1.43E-05	Basic Cell Functions, Interferon
<i>Isg15</i>	2.03	0.271	1.50, 2.56	2.18E-05	Basic Cell Functions, Innate, Interferon
<i>Ccl3</i>	2.03	0.293	1.46, 2.60	4.48E-05	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Ccl7</i>	1.90	0.236	1.44, 2.37	1.23E-05	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions
<i>Csf2</i>	1.81	0.158	1.50, 2.12	1.17E-06	Adaptive, Cytokines & Receptors, Innate, Interleukins, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Clec5a</i>	1.78	0.138	1.51, 2.05	4.69E-07	Apoptosis, Cytokines & Receptors, Innate
<i>Trem2</i>	1.77	0.166	1.44, 2.09	1.75E-06	Basic Cell Functions, Humoral
<i>Marco</i>	1.76	0.184	1.40, 2.13	2.91E-06	Innate, Transporter Functions
<i>Ifit1</i>	1.75	0.266	1.22, 2.27	7.17E-05	Interferon, Transporter Functions
<i>Il2ra</i>	1.72	0.160	1.40, 2.03	1.75E-06	Adaptive, B-Cell Functions, CD molecules, Inflammation, T-Cell Functions
<i>Mmp9</i>	1.71	0.249	1.22, 2.20	4.83E-05	Adhesion, Apoptosis, Cancer Progression

<i>C3ar1</i>	1.67	0.178	1.32, 2.02	3.12E-06	Adaptive, Cancer Progression, Complement Pathway, Inflammation, Macrophage Functions
<i>Zbp1</i>	1.65	0.241	1.17, 2.12	5.03E-05	Innate
<i>Il1rn</i>	1.62	0.279	1.08, 2.17	1.87E-04	Cytokines & Receptors, Inflammation, Interleukins
<i>Cfb</i>	1.60	0.168	1.28, 1.93	2.91E-06	Complement Pathway, Innate
<i>C1qa</i>	1.54	0.102	1.34, 1.74	2.82E-07	Complement Pathway, Innate
<i>Ccl12</i>	1.52	0.191	1.15, 1.90	1.37E-05	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Cxcl9</i>	1.51	0.523	0.484, 2.54	2.55E-02	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate
<i>Msr1</i>	1.44	0.161	1.13, 1.76	4.66E-06	CD molecules, Macrophage Functions, Transporter Functions
<i>Cxcl3</i>	1.42	0.484	0.468, 2.37	2.37E-02	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>C1qb</i>	1.42	0.117	1.19, 1.65	8.30E-07	Complement Pathway, Innate
<i>Usp18</i>	1.41	0.223	0.974, 1.85	9.82E-05	Basic Cell Functions
<i>Rsad2</i>	1.38	0.298	0.798, 1.97	1.23E-03	Basic Cell Functions
<i>Siglec1</i>	1.37	0.186	1.00, 1.73	2.60E-05	Adhesion, CD molecules, Transporter Functions
<i>Ccl9</i>	1.36	0.134	1.10, 1.63	2.38E-06	Chemokines & Receptors, Cytokines & Receptors
<i>Clec4n</i>	1.35	0.146	1.07, 1.64	3.38E-06	Cytokines & Receptors, Innate
<i>Ifit3</i>	1.30	0.219	0.87, 1.73	1.66E-04	Interferon
<i>Ccl8</i>	1.27	0.482	0.325, 2.22	3.87E-02	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Fcgr1</i>	1.26	0.120	1.03, 1.50	1.85E-06	Antigen Processing, CD molecules, Innate, MHC, Transporter Functions
<i>Ccr5</i>	1.19	0.155	0.886, 1.49	1.76E-05	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Icos</i>	1.17	0.114	0.948, 1.39	2.14E-06	CD molecules, T-Cell Functions
<i>Tnfrsf4</i>	1.15	0.115	0.924, 1.37	2.69E-06	B-Cell Functions, CD molecules, Cytokines & Receptors, Inflammation, T-Cell Functions, TNF Superfamily
<i>Tnfrsf11a</i>	1.13	0.102	0.930, 1.33	1.42E-06	Adaptive, CD molecules, Cytokines & Receptors, Interleukins, TNF Superfamily
<i>Cd83</i>	1.12	0.115	0.894, 1.34	2.77E-06	B-Cell Functions, CD molecules, Dendritic Cell Functions, Humoral, Interleukins, T-Cell Functions
<i>Slc11a1</i>	1.12	0.183	0.766, 1.48	1.24E-04	Adaptive, Antigen Processing, Transporter Functions

<i>Cd80</i>	1.11	0.119	0.875, 1.34	3.37E-06	Adaptive, CD molecules, T-Cell Functions
<i>Cx3cr1</i>	1.11	0.084	0.949, 1.28	4.51E-07	Chemokines & Receptors, Cytokines & Receptors, Macrophage Functions, Microglial Functions
<i>Cd14</i>	1.09	0.159	0.779, 1.4	4.83E-05	CD molecules, Cytokines & Receptors, Inflammation, Innate, Pathogen Response, Transporter Functions
<i>Fcgr2b</i>	1.08	0.132	0.822, 1.34	1.10E-05	Antigen Processing, B-Cell Functions, CD molecules, Inflammation, Interleukins, MHC, Transporter Functions
<i>Ccr6</i>	1.07	0.186	0.710, 1.44	2.03E-04	Adaptive, CD molecules, Chemokines & Receptors, Humoral, Innate, T-Cell Functions
<i>Il1a</i>	1.06	0.201	0.668, 1.46	4.45E-04	Adaptive, Cytokines & Receptors, Inflammation, Innate, Interleukins
<i>Cd86</i>	1.05	0.128	0.796, 1.30	1.11E-05	Adaptive, B-Cell Functions, CD molecules, Dendritic Cell Functions, T-Cell Functions, TLR
<i>Ccl22</i>	1.04	0.183	0.685, 1.40	2.28E-04	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Ccl6</i>	1.01	0.104	0.809, 1.21	2.77E-06	Chemokines & Receptors, Cytokines & Receptors
<i>C1ra</i>	1.00	0.084	0.839, 1.17	8.30E-07	Complement Pathway, Innate

*Note:* Values shown are the calculated mean log<sub>2</sub> ratios, SEM and 95% confidence intervals of transcript counts for lung tissues of cSiO<sub>2</sub>-treated mice with respect to dosing-matched (four weekly doses) vehicle-treated mice 1 day post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected  $q$  values are shown. Pathway associations for each significant gene are also shown.

**Supplementary Table 3. Significant differentially expressed genes in lung tissues of mice at 1 week post cSiO<sub>2</sub> instillation (experiment 3).**

<b>Gene symbol</b>	<b>Log<sub>2</sub> ratio cSiO<sub>2</sub>/VEH</b>	<b>SEM</b>	<b>95% CI</b>	<b>FDR <i>q</i> value</b>	<b>Associated pathways</b>
<i>Cxcl5</i>	3.63	0.472	2.71, 4.56	4.43E-05	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Leukocyte Functions
<i>Cxcl3</i>	3.21	0.413	2.40, 4.02	4.09E-05	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Lcn2</i>	2.77	0.204	2.37, 3.17	4.13E-07	Apoptosis, Innate, Transporter Functions
<i>Ctla4</i>	2.66	0.188	2.29, 3.03	3.52E-07	B-Cell Functions, CD molecules, T-Cell Functions
<i>Chil3</i>	2.58	0.498	1.61, 3.56	7.11E-04	Basic Cell Functions
<i>Slc11a1</i>	2.22	0.354	1.53, 2.92	1.85E-04	Adaptive, Antigen Processing, Transporter Functions
<i>Irf7</i>	2.22	0.372	1.49, 2.95	2.68E-04	Adaptive, Innate, Interferon, Senescence
<i>Mmp9</i>	2.22	0.401	1.43, 3.00	4.58E-04	Adhesion, Apoptosis, Cancer Progression
<i>Marco</i>	2.03	0.261	1.52, 2.54	4.09E-05	Innate, Transporter Functions
<i>Cfb</i>	1.83	0.120	1.59, 2.06	2.90E-07	Complement Pathway, Innate
<i>Il1rn</i>	1.82	0.145	1.53, 2.10	8.66E-07	Cytokines & Receptors, Inflammation, Interleukins
<i>Ccl8</i>	1.78	0.335	1.13, 2.44	6.13E-04	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Ccl3</i>	1.75	0.284	1.20, 2.31	2.03E-04	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Trem2</i>	1.68	0.159	1.36, 1.99	2.71E-06	Basic Cell Functions, Humoral
<i>Clec5a</i>	1.65	0.148	1.36, 1.94	1.77E-06	Apoptosis, Cytokines & Receptors, Innate
<i>Mx2</i>	1.64	0.302	1.04, 2.23	5.43E-04	Innate
<i>Isg15</i>	1.60	0.308	1.00, 2.21	7.00E-04	Basic Cell Functions, Innate, Interferon
<i>C3ar1</i>	1.58	0.136	1.31, 1.84	1.52E-06	Adaptive, Cancer Progression, Complement Pathway, Inflammation, Macrophage Functions
<i>Oas2</i>	1.56	0.237	1.09, 2.02	1.34E-04	Basic Cell Functions, Interferon
<i>Siglec1</i>	1.50	0.247	1.02, 1.98	2.28E-04	Adhesion, CD molecules, Transporter Functions
<i>Cxcr1</i>	1.49	0.189	1.12, 1.86	4.00E-05	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Interleukins



<i>Ifi44</i>	1.48	0.280	0.93, 2.03	6.52E-04	Interferon
<i>Msr1</i>	1.45	0.221	1.02, 1.88	1.34E-04	CD molecules, Macrophage Functions, Transporter Functions
<i>Ccl9</i>	1.42	0.159	1.11, 1.73	1.29E-05	Chemokines & Receptors, Cytokines & Receptors
<i>Clqa</i>	1.39	0.125	1.14, 1.63	1.77E-06	Complement Pathway, Innate
<i>Csf2</i>	1.39	0.137	1.12, 1.66	3.77E-06	Adaptive, Cytokines & Receptors, Innate, Interleukins, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Ifit1</i>	1.37	0.262	0.856, 1.88	6.92E-04	Interferon, Transporter Functions
<i>Clqb</i>	1.32	0.119	1.08, 1.55	1.77E-06	Complement Pathway, Innate
<i>Ccl6</i>	1.30	0.127	1.05, 1.55	3.54E-06	Chemokines & Receptors, Cytokines & Receptors
<i>Ccl7</i>	1.28	0.284	0.728, 1.84	2.04E-03	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions
<i>Cxcl13</i>	1.28	0.341	0.614, 1.95	7.13E-03	Adaptive, B-Cell Functions, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, T-Cell Functions
<i>Slc7a11</i>	1.26	0.248	0.771, 1.74	8.37E-04	Transporter Functions
<i>Clec4n</i>	1.23	0.145	0.942, 1.51	2.02E-05	Cytokines & Receptors, Innate
<i>Zbp1</i>	1.22	0.250	0.732, 1.71	1.11E-03	Innate
<i>Ctss</i>	1.20	0.133	0.935, 1.46	1.27E-05	Innate
<i>Cx3cr1</i>	1.18	0.167	0.856, 1.51	8.30E-05	Chemokines & Receptors, Cytokines & Receptors, Macrophage Functions, Microglial Functions
<i>Cd14</i>	1.14	0.130	0.887, 1.40	1.52E-05	CD molecules, Cytokines & Receptors, Inflammation, Innate, Pathogen Response, Transporter Functions
<i>Cd74</i>	1.14	0.169	0.806, 1.47	1.11E-04	Antigen Processing, B-Cell Functions, CD molecules, Innate, MHC, T-Cell Functions
<i>Ccr1</i>	1.14	0.204	0.742, 1.54	4.26E-04	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Innate, Leukocyte Functions, Transporter Functions
<i>C3</i>	1.13	0.0988	0.940, 1.33	1.55E-06	Cancer Progression, Complement Pathway, Inflammation, Innate, Transporter Functions
<i>Fcgr1</i>	1.10	0.178	0.750, 1.45	2.03E-04	Antigen Processing, CD molecules, Innate, MHC, Transporter Functions
<i>Ifit3</i>	1.10	0.248	0.615, 1.59	2.35E-03	Interferon
<i>Il2ra</i>	1.09	0.147	0.800, 1.38	6.40E-05	Adaptive, B-Cell Functions, CD molecules, Inflammation, T-Cell Functions
<i>Csf2rb</i>	1.09	0.155	0.791, 1.40	8.43E-05	CD molecules, Cancer Progression, Cytokines & Receptors

<i>Cd68</i>	1.08	0.127	0.829, 1.33	2.02E-05	CD molecules
<i>Ifitm1</i>	1.06	0.0871	0.892, 1.23	9.87E-07	CD molecules, Innate, Interferon
<i>Slamf7</i>	1.06	0.191	0.682, 1.43	4.57E-04	CD molecules, Innate, NK Cell Functions
<i>Icos</i>	1.05	0.0975	0.862, 1.24	2.11E-06	CD molecules, T-Cell Functions
<i>Cd33</i>	1.04	0.115	0.818, 1.27	1.22E-05	Adhesion, CD molecules
<i>Usp18</i>	1.03	0.238	0.564, 1.50	2.82E-03	Basic Cell Functions

*Note:* Values shown are the calculated mean log<sub>2</sub> ratios, SEM and 95% confidence intervals of transcript counts for lung tissues of cSiO<sub>2</sub>-treated mice with respect to time-matched vehicle-treated mice 1 week post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected  $q$  values are shown. Pathway associations for each significant gene are also shown.

Supplementary Table 4. Significant differentially expressed genes in lung tissues of mice at 5 weeks post cSiO<sub>2</sub> instillation (experiment 3).

Gene symbol	Log <sub>2</sub> ratio cSiO <sub>2</sub> /VEH	SEM	95% CI	FDR <i>q</i> value	Associated pathways
<i>Cxcl5</i>	4.96	0.270	4.43, 5.49	7.12E-08	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Leukocyte Functions
<i>Cxcl3</i>	4.95	0.515	3.94, 5.95	3.96E-06	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Ccl3</i>	3.75	0.228	3.30, 4.20	7.35E-08	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Lcn2</i>	3.50	0.210	3.09, 3.91	7.35E-08	Apoptosis, Innate, Transporter Functions
<i>Cxcl10</i>	3.32	0.601	2.14, 4.50	3.93E-04	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate, Leukocyte Functions
<i>Ccl2</i>	3.03	0.338	2.36, 3.69	6.73E-06	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, NK Cell Functions, Pathogen Response, T-Cell Functions
<i>Ccl8</i>	2.93	0.383	2.18, 3.68	2.81E-05	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Il1rn</i>	2.89	0.266	2.36, 3.41	1.56E-06	Cytokines & Receptors, Inflammation, Interleukins
<i>Cxcl1</i>	2.83	0.247	2.35, 3.32	1.24E-06	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Transporter Functions
<i>Cxcl9</i>	2.72	0.607	1.53, 3.91	1.80E-03	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate
<i>Clec5a</i>	2.62	0.199	2.23, 3.01	4.58E-07	Apoptosis, Cytokines & Receptors, Innate
<i>Irf7</i>	2.60	0.413	1.79, 3.41	1.50E-04	Adaptive, Innate, Interferon, Senescence
<i>Ccl7</i>	2.49	0.402	1.70, 3.28	1.66E-04	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions
<i>Msr1</i>	2.45	0.248	1.96, 2.94	3.05E-06	CD molecules, Macrophage Functions, Transporter Functions
<i>C3ar1</i>	2.43	0.260	1.92, 2.94	4.59E-06	Adaptive, Cancer Progression, Complement Pathway, Inflammation, Macrophage Functions
<i>Ifi44</i>	2.35	0.336	1.69, 3.01	5.91E-05	Interferon
<i>Ctla4</i>	2.33	0.217	1.91, 2.76	1.58E-06	B-Cell Functions, CD molecules, T-Cell Functions
<i>Marco</i>	2.32	0.232	1.86, 2.77	2.98E-06	Innate, Transporter Functions
<i>Oas2</i>	2.26	0.291	1.69, 2.83	2.38E-05	Basic Cell Functions, Interferon
<i>Mmp9</i>	2.20	0.160	1.89, 2.52	3.28E-07	Adhesion, Apoptosis, Cancer Progression

<i>Cfb</i>	2.19	0.170	1.85, 2.52	4.85E-07	Complement Pathway, Innate
<i>Isg15</i>	2.13	0.365	1.41, 2.84	2.61E-04	Basic Cell Functions, Innate, Interferon
<i>Clec4n</i>	2.12	0.153	1.82, 2.42	3.27E-07	Cytokines & Receptors, Innate
<i>Trem2</i>	2.12	0.189	1.75, 2.49	1.30E-06	Basic Cell Functions, Humoral
<i>Ccl12</i>	2.11	0.347	1.43, 2.78	1.92E-04	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Zbp1</i>	2.07	0.315	1.45, 2.69	1.05E-04	Innate
<i>Csf2</i>	2.00	0.176	1.65, 2.34	1.24E-06	Adaptive, Cytokines & Receptors, Innate, Interleukins, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Ccl9</i>	1.98	0.140	1.71, 2.26	3.16E-07	Chemokines & Receptors, Cytokines & Receptors
<i>Chil3</i>	1.95	0.376	1.21, 2.69	6.48E-04	Basic Cell Functions
<i>Ccr6</i>	1.92	0.308	1.32, 2.52	1.57E-04	Adaptive, CD molecules, Chemokines & Receptors, Humoral, Innate, T-Cell Functions
<i>Ifit1</i>	1.85	0.303	1.25, 2.44	1.88E-04	Interferon, Transporter Functions
<i>Mx2</i>	1.83	0.377	1.09, 2.57	1.02E-03	Innate
<i>Spp1</i>	1.81	0.195	1.43, 2.19	5.09E-06	Adhesion, Apoptosis, Cytokines & Receptors, T-Cell Functions
<i>Fcgr1</i>	1.76	0.270	1.23, 2.29	1.13E-04	Antigen Processing, CD molecules, Innate, MHC, Transporter Functions
<i>Il1a</i>	1.75	0.156	1.45, 2.06	1.30E-06	Adaptive, Cytokines & Receptors, Inflammation, Innate, Interleukins
<i>Clqa</i>	1.75	0.156	1.44, 2.06	1.30E-06	Complement Pathway, Innate
<i>Usp18</i>	1.74	0.286	1.17, 2.30	1.94E-04	Basic Cell Functions
<i>Ccl6</i>	1.70	0.197	1.32, 2.09	9.26E-06	Chemokines & Receptors, Cytokines & Receptors
<i>Clec7a</i>	1.70	0.241	1.23, 2.17	5.69E-05	Inflammation, Innate, Leukocyte Functions, Transporter Functions
<i>Blnk</i>	1.69	0.264	1.17, 2.20	1.31E-04	B-Cell Functions, Humoral
<i>Sl00a8</i>	1.64	0.181	1.29, 2.00	5.98E-06	Adaptive, Basic Cell Functions, Inflammation
<i>Clqb</i>	1.63	0.157	1.32, 1.93	2.38E-06	Complement Pathway, Innate
<i>Ccr1</i>	1.61	0.162	1.30, 1.93	2.98E-06	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Innate, Leukocyte Functions, Transporter Functions
<i>Ctss</i>	1.57	0.197	1.18, 1.95	1.95E-05	Innate

<i>Cd14</i>	1.52	0.139	1.25, 1.79	1.56E-06	CD molecules, Cytokines & Receptors, Inflammation, Innate, Pathogen Response, Transporter Functions
<i>Fcgr2b</i>	1.50	0.131	1.25, 1.76	1.24E-06	Antigen Processing, B-Cell Functions, CD molecules, Inflammation, Interleukins, MHC, Transporter Functions
<i>Rsad2</i>	1.50	0.346	0.820, 2.17	2.34E-03	Basic Cell Functions
<i>Ccr5</i>	1.48	0.272	0.952, 2.02	4.31E-04	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Ccl22</i>	1.47	0.258	0.962, 1.98	3.16E-04	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Cd83</i>	1.44	0.129	1.18, 1.69	1.32E-06	B-Cell Functions, CD molecules, Dendritic Cell Functions, Humoral, Interleukins, T-Cell Functions
<i>Icos</i>	1.41	0.180	1.06, 1.77	2.23E-05	CD molecules, T-Cell Functions
<i>Slamf7</i>	1.41	0.252	0.919, 1.91	3.51E-04	CD molecules, Innate, NK Cell Functions
<i>Tlr2</i>	1.37	0.118	1.13, 1.60	1.24E-06	CD molecules, Inflammation, Innate, Leukocyte Functions, TLR
<i>Arg2</i>	1.37	0.168	1.04, 1.70	1.52E-05	Basic Cell Functions
<i>H2-DMb2</i>	1.37	0.222	0.931, 1.80	1.75E-04	Antigen Processing, MHC
<i>Il1b</i>	1.34	0.133	1.07, 1.60	2.98E-06	Adaptive, Chemokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, Pathogen Response, T-Cell Functions, Transporter Functions
<i>Fcgr3</i>	1.34	0.193	0.964, 1.72	6.21E-05	Antigen Processing, CD molecules, MHC, Transporter Functions
<i>Ly86</i>	1.32	0.162	1.01, 1.64	1.52E-05	Humoral, Inflammation, Innate, Pathogen Response
<i>Ifit3</i>	1.32	0.262	0.804, 1.83	8.00E-04	Interferon
<i>Cd80</i>	1.28	0.175	0.935, 1.62	4.30E-05	Adaptive, CD molecules, T-Cell Functions
<i>Emr1</i>	1.28	0.191	0.907, 1.65	8.61E-05	Basic Cell Functions
<i>Cd180</i>	1.28	0.226	0.833, 1.72	3.33E-04	CD molecules, Inflammation, Innate
<i>Cd68</i>	1.26	0.096	1.07, 1.44	4.59E-07	CD molecules
<i>Cd86</i>	1.24	0.137	0.974, 1.51	6.08E-06	Adaptive, B-Cell Functions, CD molecules, Dendritic Cell Functions, T-Cell Functions, TLR
<i>Ly9</i>	1.24	0.205	0.833, 1.64	2.04E-04	Adhesion, CD molecules
<i>Ncf4</i>	1.21	0.106	1.00, 1.42	1.24E-06	Basic Cell Functions, Innate
<i>Cd53</i>	1.20	0.089	1.02, 1.37	3.97E-07	CD molecules

<i>Pik3cg</i>	1.20	0.138	0.927, 1.47	8.98E-06	Apoptosis, Inflammation, Innate
<i>Cx3cr1</i>	1.20	0.200	0.806, 1.59	2.08E-04	Chemokines & Receptors, Cytokines & Receptors, Macrophage Functions, Microglial Functions
<i>Ddx60</i>	1.20	0.248	0.715, 1.69	1.05E-03	Basic Cell Functions
<i>Cd200r1</i>	1.19	0.124	0.948, 1.44	3.96E-06	B-Cell Functions
<i>Cfp</i>	1.19	0.175	0.850, 1.54	7.66E-05	Cancer Progression, Complement Pathway, Innate
<i>Clec4a2</i>	1.19	0.189	0.821, 1.56	1.50E-04	Innate
<i>Slamf6</i>	1.19	0.230	0.734, 1.64	6.81E-04	CD molecules
<i>Fcer1g</i>	1.18	0.108	0.964, 1.39	1.56E-06	Antigen Processing, Interleukins, MHC, Transporter Functions
<i>Ifitm1</i>	1.18	0.116	0.955, 1.41	2.64E-06	CD molecules, Innate, Interferon
<i>Irf4</i>	1.18	0.321	0.548, 1.81	6.63E-03	Interleukins, T-Cell Functions, TLR
<i>Cxcr2</i>	1.17	0.155	0.863, 1.47	3.19E-05	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate, Interleukins
<i>Ebi3</i>	1.16	0.123	0.915, 1.40	4.56E-06	Cytokines & Receptors, Humoral, Interleukins
<i>Cybb</i>	1.15	0.127	0.896, 1.39	6.37E-06	Innate, Transporter Functions
<i>Ms4a1</i>	1.15	0.236	0.691, 1.62	9.91E-04	B-Cell Functions, CD molecules, Humoral
<i>Fcgr4</i>	1.14	0.229	0.694, 1.59	8.54E-04	CD molecules, T-Cell Functions
<i>Tnfrsf11a</i>	1.12	0.152	0.823, 1.42	3.95E-05	Adaptive, CD molecules, Cytokines & Receptors, Interleukins, TNF Superfamily
<i>H2-Q10</i>	1.11	0.284	0.551, 1.67	4.58E-03	Adaptive, Antigen Processing, B-Cell Functions, MHC
<i>Ltb</i>	1.09	0.179	0.737, 1.44	1.94E-04	Cytokines & Receptors, Interleukins, TNF Superfamily
<i>Cd74</i>	1.07	0.105	0.861, 1.27	2.64E-06	Antigen Processing, B-Cell Functions, CD molecules, Innate, MHC, T-Cell Functions
<i>Tlr1</i>	1.07	0.209	0.661, 1.48	7.04E-04	CD molecules, Inflammation, Innate, Interleukins, Macrophage Functions, TLR
<i>Herc6</i>	1.06	0.206	0.659, 1.47	6.73E-04	Basic Cell Functions
<i>Itgam</i>	1.04	0.144	0.761, 1.32	4.50E-05	Adaptive, CD molecules, Innate, Leukocyte Functions, T-Cell Functions, Transporter Functions
<i>Bst2</i>	1.04	0.204	0.644, 1.44	7.10E-04	CD molecules, Humoral, Innate
<i>Cxcr3</i>	1.04	0.317	0.417, 1.66	1.29E-02	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Innate, T-Cell Functions

<i>Lgals3</i>	1.02	0.108	0.812, 1.23	4.25E-06	Innate, T-Cell Functions
<i>Csf2rb</i>	1.01	0.174	0.669, 1.35	2.66E-04	CD molecules, Cancer Progression, Cytokines & Receptors
<i>Cd84</i>	1.00	0.082	0.841, 1.16	8.07E-07	Adhesion, CD molecules
<i>Cd5</i>	1.00	0.157	0.695, 1.31	1.33E-04	Apoptosis, CD molecules, T-Cell Functions
<i>Cd3g</i>	1.00	0.164	0.680, 1.32	1.84E-04	Apoptosis, CD molecules, T-Cell Functions, Transporter Functions
<i>Tnfrsf12a</i>	-1.12	0.113	-1.34, -0.897	3.05E-06	Adhesion, Apoptosis, CD molecules, TNF Superfamily
<i>Cdkn1a</i>	-1.51	0.152	-1.80, -1.21	3.05E-06	B-Cell Functions, Cancer Progression, Cell Cycle, Senescence
<i>Thbs1</i>	-1.56	0.172	-1.90, -1.22	5.98E-06	Adaptive, Cell Cycle, Inflammation, Macrophage Functions

*Note:* Values shown are the calculated mean  $\log_2$  ratios, SEM and 95% confidence intervals of transcript counts for lung tissues of cSiO<sub>2</sub>-treated mice with respect to time-matched vehicle-treated mice 5 weeks post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected  $q$  values are shown. Pathway associations for each significant gene are also shown.

Supplementary Table 5. Significant differentially expressed genes in lung tissues of mice at 9 weeks post cSiO<sub>2</sub> instillation (experiment 3).

Gene symbol	Log <sub>2</sub> ratio cSiO <sub>2</sub> /VEH	SEM	95% CI	FDR <i>q</i> value	Associated pathways
<i>Cxcl5</i>	5.22	0.284	4.66, 5.77	3.34E-09	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Leukocyte Functions
<i>Ccl2</i>	4.20	0.283	3.64, 4.75	1.64E-08	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, NK Cell Functions, Pathogen Response, T-Cell Functions
<i>Lcn2</i>	3.89	0.186	3.53, 4.26	1.28E-09	Apoptosis, Innate, Transporter Functions
<i>Ccl7</i>	3.79	0.301	3.20, 4.38	7.59E-08	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions
<i>Cxcl10</i>	3.75	0.248	3.26, 4.23	1.42E-08	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate, Leukocyte Functions
<i>Cxcl11</i>	3.65	0.211	3.23, 4.06	3.99E-09	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Transporter Functions
<i>Oasl1</i>	3.41	0.299	2.82, 4.00	1.97E-07	Basic Cell Functions
<i>Cxcl3</i>	3.36	1.090	1.22, 5.50	1.45E-02	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Ccl3</i>	3.32	0.206	2.92, 3.72	7.29E-09	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Cxcl9</i>	3.27	0.379	2.53, 4.01	2.78E-06	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate
<i>Il1rn</i>	3.07	0.168	2.74, 3.40	3.34E-09	Cytokines & Receptors, Inflammation, Interleukins
<i>C3ar1</i>	2.92	0.166	2.59, 3.24	3.34E-09	Adaptive, Cancer Progression, Complement Pathway, Inflammation, Macrophage Functions
<i>Ccl8</i>	2.90	0.363	2.18, 3.61	5.82E-06	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Irf7</i>	2.86	0.273	2.32, 3.39	4.54E-07	Adaptive, Innate, Interferon, Senescence
<i>Msr1</i>	2.83	0.194	2.45, 3.21	1.72E-08	CD molecules, Macrophage Functions, Transporter Functions
<i>Isg15</i>	2.70	0.213	2.28, 3.11	7.12E-08	Basic Cell Functions, Innate, Interferon
<i>Ccl12</i>	2.69	0.191	2.31, 3.06	2.29E-08	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Trem2</i>	2.60	0.107	2.39, 2.81	5.11E-10	Basic Cell Functions, Humoral
<i>Oas2</i>	2.58	0.242	2.11, 3.06	3.87E-07	Basic Cell Functions, Interferon



<i>Ifi44</i>	2.55	0.222	2.12, 2.99	1.86E-07	Interferon
<i>Clec5a</i>	2.51	0.130	2.26, 2.77	2.19E-09	Apoptosis, Cytokines & Receptors, Innate
<i>Zbp1</i>	2.45	0.182	2.10, 2.81	3.49E-08	Innate
<i>Cfb</i>	2.44	0.180	2.09, 2.8	3.31E-08	Complement Pathway, Innate
<i>Ccr5</i>	2.26	0.159	1.95, 2.57	2.21E-08	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Spp1</i>	2.18	0.123	1.94, 2.42	3.34E-09	Adhesion, Apoptosis, Cytokines & Receptors, T-Cell Functions
<i>Fcgr1</i>	2.13	0.172	1.80, 2.47	8.74E-08	Antigen Processing, CD molecules, Innate, MHC, Transporter Functions
<i>Ifit1</i>	2.12	0.175	1.77, 2.46	1.18E-07	Interferon, Transporter Functions
<i>Mx2</i>	2.11	0.190	1.74, 2.48	2.59E-07	Innate
<i>Clec4n</i>	2.09	0.102	1.89, 2.28	1.28E-09	Cytokines & Receptors, Innate
<i>Clqa</i>	2.09	0.129	1.84, 2.34	7.29E-09	Complement Pathway, Innate
<i>Cxcl13</i>	2.08	0.315	1.47, 2.70	3.38E-05	Adaptive, B-Cell Functions, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, T-Cell Functions
<i>Clqb</i>	2.02	0.140	1.75, 2.30	1.89E-08	Complement Pathway, Innate
<i>Marco</i>	1.92	0.229	1.47, 2.36	3.65E-06	Innate, Transporter Functions
<i>Csf2</i>	1.90	0.162	1.58, 2.22	1.52E-07	Adaptive, Cytokines & Receptors, Innate, Interleukins, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Fcgr2b</i>	1.89	0.129	1.63, 2.14	1.72E-08	Antigen Processing, B-Cell Functions, CD molecules, Inflammation, Interleukins, MHC, Transporter Functions
<i>Siglec1</i>	1.88	0.206	1.48, 2.28	1.60E-06	Adhesion, CD molecules, Transporter Functions
<i>Il1a</i>	1.83	0.126	1.58, 2.07	1.79E-08	Adaptive, Cytokines & Receptors, Inflammation, Innate, Interleukins
<i>Slamf7</i>	1.79	0.193	1.42, 2.17	1.33E-06	CD molecules, Innate, NK Cell Functions
<i>Ccl9</i>	1.78	0.100	1.58, 1.97	3.34E-09	Chemokines & Receptors, Cytokines & Receptors
<i>Cxcr1</i>	1.74	0.224	1.30, 2.18	7.34E-06	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Interleukins
<i>Cd14</i>	1.73	0.142	1.45, 2.01	1.09E-07	CD molecules, Cytokines & Receptors, Inflammation, Innate, Pathogen Response, Transporter Functions
<i>Slc11a1</i>	1.70	0.110	1.48, 1.91	1.17E-08	Adaptive, Antigen Processing, Transporter Functions
<i>Usp18</i>	1.70	0.196	1.32, 2.09	2.67E-06	Basic Cell Functions

<i>Ctss</i>	1.69	0.100	1.50, 1.89	4.42E-09	Innate
<i>Cd68</i>	1.67	0.081	1.51, 1.82	1.28E-09	CD molecules
<i>Ccl6</i>	1.64	0.110	1.42, 1.85	1.58E-08	Chemokines & Receptors, Cytokines & Receptors
<i>Cd74</i>	1.00	0.085	0.836, 1.17	1.46E-07	Antigen Processing, B-Cell Functions, CD molecules, Innate, MHC, T-Cell Functions
<i>Fcgr4</i>	1.64	0.123	1.40, 1.88	3.63E-08	CD molecules, T-Cell Functions
<i>Ifit3</i>	1.63	0.148	1.34, 1.92	2.64E-07	Interferon
<i>Arg2</i>	1.58	0.141	1.30, 1.86	2.39E-07	Basic Cell Functions
<i>Tlr2</i>	1.56	0.106	1.35, 1.77	1.72E-08	CD molecules, Inflammation, Innate, Leukocyte Functions, TLR
<i>Ctla4</i>	1.54	0.220	1.11, 1.97	2.03E-05	B-Cell Functions, CD molecules, T-Cell Functions
<i>Ccr1</i>	1.52	0.149	1.23, 1.81	5.69E-07	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Innate, Leukocyte Functions, Transporter Functions
<i>Blnk</i>	1.52	0.174	1.18, 1.86	2.53E-06	B-Cell Functions, Humoral
<i>Plau</i>	1.51	0.103	1.31, 1.71	1.72E-08	Adhesion, Senescence
<i>Irf4</i>	1.48	0.214	1.06, 1.90	2.21E-05	Interleukins, T-Cell Functions, TLR
<i>Il2ra</i>	1.45	0.173	1.11, 1.79	3.65E-06	Adaptive, B-Cell Functions, CD molecules, Inflammation, T-Cell Functions
<i>Rsad2</i>	1.43	0.248	0.947, 1.92	1.15E-04	Basic Cell Functions
<i>Ccr6</i>	1.42	0.274	0.882, 1.95	3.07E-04	Adaptive, CD molecules, Chemokines & Receptors, Humoral, Innate, T-Cell Functions
<i>Cd200r1</i>	1.41	0.083	1.25, 1.57	4.25E-09	B-Cell Functions
<i>Cx3cr1</i>	1.41	0.120	1.18, 1.65	1.48E-07	Chemokines & Receptors, Cytokines & Receptors, Macrophage Functions, Microglial Functions
<i>Il21r</i>	1.39	0.201	0.995, 1.78	2.23E-05	CD molecules, Cytokines & Receptors
<i>Lgals3</i>	1.36	0.095	1.17, 1.54	1.96E-08	Innate, T-Cell Functions
<i>Fcer1g</i>	1.34	0.079	1.18, 1.49	4.25E-09	Antigen Processing, Interleukins, MHC, Transporter Functions
<i>Clec7a</i>	1.34	0.108	1.13, 1.55	8.74E-08	Inflammation, Innate, Leukocyte Functions, Transporter Functions
<i>Itgam</i>	1.34	0.119	1.11, 1.57	2.14E-07	Adaptive, CD molecules, Innate, Leukocyte Functions, T-Cell Functions, Transporter Functions
<i>Csf2rb</i>	1.33	0.089	1.16, 1.51	1.58E-08	CD molecules, Cancer Progression, Cytokines & Receptors

<i>Cxcr3</i>	1.31	0.208	0.901, 1.71	5.27E-05	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Innate, T-Cell Functions
<i>Bst2</i>	1.30	0.132	1.04, 1.56	8.07E-07	CD molecules, Humoral, Innate
<i>Ada</i>	1.27	0.139	1.00, 1.55	1.54E-06	Adhesion, B-Cell Functions, T-Cell Functions
<i>Tnfrsf11a</i>	1.26	0.109	1.05, 1.48	1.64E-07	Adaptive, CD molecules, Cytokines & Receptors, Interleukins, TNF Superfamily
<i>Ly9</i>	1.26	0.130	1.00, 1.51	9.40E-07	Adhesion, CD molecules
<i>Cmpk2</i>	1.00	0.102	0.80, 1.20	8.56E-07	Basic Cell Functions
<i>Icos</i>	1.25	0.154	0.949, 1.55	4.94E-06	CD molecules, T-Cell Functions
<i>Cd83</i>	1.24	0.118	1.01, 1.48	4.32E-07	B-Cell Functions, CD molecules, Dendritic Cell Functions, Humoral, Interleukins, T-Cell Functions
<i>Emr1</i>	1.23	0.088	1.06, 1.41	2.45E-08	Basic Cell Functions
<i>Cd274</i>	1.23	0.096	1.05, 1.42	5.96E-08	CD molecules, T-Cell Functions
<i>Tap1</i>	1.23	0.125	0.987, 1.48	7.71E-07	Antigen Processing, MHC, T-Cell Functions, Transporter Functions
<i>Fcgr3</i>	1.22	0.087	1.04, 1.39	2.45E-08	Antigen Processing, CD molecules, MHC, Transporter Functions
<i>Clec4a2</i>	1.22	0.101	1.02, 1.41	1.20E-07	Innate
<i>Cd180</i>	1.22	0.107	1.01, 1.43	1.93E-07	CD molecules, Inflammation, Innate
<i>Il1b</i>	1.22	0.144	0.936, 1.50	3.30E-06	Adaptive, Chemokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, Pathogen Response, T-Cell Functions, Transporter Functions
<i>Ddx60</i>	1.22	0.164	0.897, 1.54	1.12E-05	Basic Cell Functions
<i>Slamf6</i>	1.22	0.171	0.884, 1.55	1.71E-05	CD molecules
<i>Cd86</i>	1.19	0.101	0.992, 1.39	1.52E-07	Adaptive, B-Cell Functions, CD molecules, Dendritic Cell Functions, T-Cell Functions, TLR
<i>H2-K1</i>	1.19	0.116	0.964, 1.42	5.46E-07	Antigen Processing, MHC, T-Cell Functions
<i>Nlrc5</i>	1.19	0.145	0.905, 1.47	4.57E-06	Innate, Interferon, MHC
<i>Ncf4</i>	1.18	0.109	0.965, 1.39	3.61E-07	Basic Cell Functions, Innate
<i>Herc6</i>	1.18	0.144	0.899, 1.46	4.57E-06	Basic Cell Functions
<i>Chil3</i>	1.14	0.362	0.432, 1.85	1.18E-02	Basic Cell Functions
<i>Itgax</i>	1.13	0.093	0.953, 1.32	1.00E-07	Adhesion, CD molecules, Innate, T-Cell Functions

<i>Ikbke</i>	1.07	0.122	0.836, 1.31	2.28E-06	Apoptosis, Innate
<i>Cfp</i>	1.07	0.146	0.781, 1.35	1.33E-05	Cancer Progression, Complement Pathway, Innate
<i>Psmb9</i>	1.06	0.105	0.851, 1.26	6.64E-07	Antigen Processing
<i>Itgb2</i>	1.05	0.059	0.937, 1.17	3.34E-09	CD molecules, Humoral, Inflammation, Leukocyte Functions, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Cybb</i>	1.05	0.076	0.90, 1.20	2.67E-08	Innate, Transporter Functions
<i>C3</i>	1.05	0.090	0.875, 1.23	1.52E-07	Cancer Progression, Complement Pathway, Inflammation, Innate, Transporter Functions
<i>Psmb8</i>	1.05	0.092	0.867, 1.23	1.97E-07	Antigen Processing
<i>Ly86</i>	1.05	0.099	0.859, 1.25	3.87E-07	Humoral, Inflammation, Innate, Pathogen Response
<i>Sh2b2</i>	1.05	0.093	0.867, 1.23	4.06E-07	B-Cell Functions, Cytokines & Receptors
<i>Stat1</i>	1.05	0.110	0.834, 1.26	1.02E-06	Adaptive, Cytokines & Receptors, Innate, T-Cell Functions
<i>Cd80</i>	1.05	0.152	0.753, 1.35	2.20E-05	Adaptive, CD molecules, T-Cell Functions
<i>Pik3cg</i>	1.04	0.113	0.820, 1.26	1.45E-06	Apoptosis, Inflammation, Innate
<i>Ebi3</i>	1.03	0.123	0.788, 1.27	3.65E-06	Cytokines & Receptors, Humoral, Interleukins
<i>Batf</i>	1.02	0.102	0.817, 1.22	7.09E-07	
<i>Xaf1</i>	1.02	0.125	0.774, 1.27	4.85E-06	Apoptosis
<i>Tlr1</i>	1.02	0.155	0.712, 1.32	3.68E-05	CD molecules, Inflammation, Innate, Interleukins, Macrophage Functions, TLR
<i>Ccl19</i>	1.01	0.164	0.689, 1.33	6.63E-05	Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Leukocyte Functions, T-Cell Functions
<i>Itga2b</i>	-1.14	0.192	-1.51, -0.759	9.37E-05	Adhesion, CD molecules, Leukocyte Functions
<i>Ppbp</i>	-1.40	0.282	-1.95, -0.843	4.54E-04	Chemokines & Receptors
<i>Camp</i>	-1.47	0.392	-2.24, -0.703	3.90E-03	Adaptive, Cancer Progression, Inflammation, Innate
<i>Hamp</i>	-1.57	0.236	-2.03, -1.11	3.19E-05	Basic Cell Functions, Innate
<i>Cfd</i>	-2.08	0.628	-3.31, -0.849	8.83E-03	Complement Pathway, Innate

*Note:* Values shown are the calculated mean log<sub>2</sub> ratios, SEM and 95% confidence intervals of transcript counts for lung tissues of cSiO<sub>2</sub>-treated mice with respect to time-matched vehicle-treated mice 9 weeks post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected  $q$  values are shown. Pathway associations for each significant gene are also shown.

Supplementary Table 6. Significant differentially expressed genes in lung tissues of mice at 13 weeks post cSiO<sub>2</sub> instillation (experiment 3).

Gene symbol	Log <sub>2</sub> ratio cSiO <sub>2</sub> /VEH	SEM	95% CI	FDR <i>q</i> value	Associated pathways
<i>Cxcl5</i>	5.56	0.332	4.91, 6.21	6.37E-09	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Leukocyte Functions
<i>Cxcl3</i>	5.42	0.420	4.59, 6.24	6.46E-08	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Ccl2</i>	4.64	0.203	4.24, 5.03	5.77E-10	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, NK Cell Functions, Pathogen Response, T-Cell Functions
<i>Ccl7</i>	4.09	0.229	3.64, 4.54	4.18E-09	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions
<i>Ccl8</i>	3.80	0.353	3.10, 4.49	3.98E-07	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Lcn2</i>	3.79	0.134	3.52, 4.05	6.32E-11	Apoptosis, Innate, Transporter Functions
<i>Cxcl10</i>	3.67	0.351	2.98, 4.36	5.37E-07	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate, Leukocyte Functions
<i>Cxcl11</i>	3.62	0.216	3.19, 4.04	6.37E-09	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Transporter Functions
<i>Cxcl9</i>	3.40	0.366	2.68, 4.11	1.69E-06	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate
<i>Ccl3</i>	3.33	0.177	2.98, 3.68	2.83E-09	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Ccl12</i>	3.31	0.218	2.88, 3.74	1.28E-08	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Cxcl13</i>	3.23	0.320	2.60, 3.86	7.47E-07	Adaptive, B-Cell Functions, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, T-Cell Functions
<i>Clqa</i>	3.06	0.266	2.54, 3.58	2.11E-07	Complement Pathway, Innate
<i>Pdcd1</i>	3.01	0.351	2.32, 3.70	3.40E-06	Apoptosis, CD molecules, Humoral, T-Cell Functions
<i>C3ar1</i>	2.98	0.218	2.56, 3.41	3.49E-08	Adaptive, Cancer Progression, Complement Pathway, Inflammation, Macrophage Functions
<i>Il1rn</i>	2.90	0.133	2.63, 3.16	7.57E-10	Cytokines & Receptors, Inflammation, Interleukins
<i>Clqb</i>	2.84	0.212	2.43, 3.26	4.50E-08	Complement Pathway, Innate
<i>Oasl1</i>	2.77	0.313	2.16, 3.38	2.56E-06	Basic Cell Functions

<i>Ccr5</i>	2.74	0.257	2.24, 3.25	4.31E-07	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Trem2</i>	2.46	0.160	2.15, 2.77	1.12E-08	Basic Cell Functions, Humoral
<i>Msr1</i>	2.45	0.134	2.18, 2.71	3.60E-09	CD molecules, Macrophage Functions, Transporter Functions
<i>Irf7</i>	2.43	0.277	1.88, 2.97	2.80E-06	Adaptive, Innate, Interferon, Senescence
<i>Cfb</i>	2.31	0.148	2.02, 2.60	9.84E-09	Complement Pathway, Innate
<i>Isg15</i>	2.28	0.233	1.82, 2.74	1.08E-06	Basic Cell Functions, Innate, Interferon
<i>Pou2af1</i>	2.25	0.313	1.63, 2.86	1.94E-05	Basic Cell Functions, Humoral
<i>Fcgr4</i>	2.23	0.205	1.83, 2.63	3.66E-07	CD molecules, T-Cell Functions
<i>Slamf7</i>	2.21	0.241	1.74, 2.69	1.83E-06	CD molecules, Innate, NK Cell Functions
<i>Spp1</i>	2.16	0.190	1.79, 2.53	2.28E-07	Adhesion, Apoptosis, Cytokines & Receptors, T-Cell Functions
<i>Clec5a</i>	2.12	0.127	1.87, 2.37	6.37E-09	Apoptosis, Cytokines & Receptors, Innate
<i>Ccr6</i>	2.10	0.294	1.52, 2.67	2.02E-05	Adaptive, CD molecules, Chemokines & Receptors, Humoral, Innate, T-Cell Functions
<i>Zbp1</i>	2.09	0.192	1.71, 2.47	3.56E-07	Innate
<i>Fcgr1</i>	2.08	0.216	1.66, 2.50	1.22E-06	Antigen Processing, CD molecules, Innate, MHC, Transporter Functions
<i>Oas2</i>	2.04	0.222	1.60, 2.47	1.81E-06	Basic Cell Functions, Interferon
<i>Clec4n</i>	2.03	0.123	1.79, 2.28	6.37E-09	Cytokines & Receptors, Innate
<i>Blnk</i>	2.00	0.232	1.55, 2.46	3.31E-06	B-Cell Functions, Humoral
<i>Marco</i>	1.97	0.226	1.52, 2.41	2.93E-06	Innate, Transporter Functions
<i>Ctss</i>	1.96	0.177	1.62, 2.31	2.97E-07	Innate
<i>Ifi44</i>	1.95	0.228	1.50, 2.39	3.62E-06	Interferon
<i>Cd14</i>	1.89	0.108	1.67, 2.10	4.68E-09	CD molecules, Cytokines & Receptors, Inflammation, Innate, Pathogen Response, Transporter Functions
<i>Chil3</i>	1.87	0.553	0.781, 2.95	8.45E-03	Basic Cell Functions
<i>Fcgr2b</i>	1.86	0.093	1.67, 2.04	1.49E-09	Antigen Processing, B-Cell Functions, CD molecules, Inflammation, Interleukins, MHC, Transporter Functions
<i>Csf2</i>	1.82	0.189	1.45, 2.19	1.27E-06	Adaptive, Cytokines & Receptors, Innate, Interleukins, Macrophage Functions, T-Cell Functions, Transporter Functions

<i>Il21r</i>	1.81	0.269	1.28, 2.34	3.55E-05	CD molecules, Cytokines & Receptors
<i>Ifit1</i>	1.77	0.201	1.38, 2.17	2.69E-06	Interferon, Transporter Functions
<i>Ada</i>	1.76	0.208	1.35, 2.17	3.84E-06	Adhesion, B-Cell Functions, T-Cell Functions
<i>Siglec1</i>	1.75	0.197	1.37, 2.14	2.51E-06	Adhesion, CD molecules, Transporter Functions
<i>Irf4</i>	1.74	0.222	1.31, 2.18	8.33E-06	Interleukins, T-Cell Functions, TLR
<i>Tnfrsf13c</i>	1.74	0.287	1.18, 2.30	9.52E-05	B-Cell Functions, CD molecules, T-Cell Functions, TNF Superfamily
<i>Arg1</i>	1.73	0.475	0.796, 2.66	5.21E-03	Basic Cell Functions
<i>Slc11a1</i>	1.70	0.166	1.38, 2.03	6.61E-07	Adaptive, Antigen Processing, Transporter Functions
<i>Cxcr3</i>	1.66	0.204	1.26, 2.06	5.76E-06	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Innate, T-Cell Functions
<i>Arg2</i>	1.64	0.109	1.43, 1.85	1.28E-08	Basic Cell Functions
<i>Clec4a2</i>	1.62	0.159	1.31, 1.93	6.74E-07	Innate
<i>Ccl9</i>	1.60	0.099	1.41, 1.80	7.45E-09	Chemokines & Receptors, Cytokines & Receptors
<i>Cd68</i>	1.59	0.079	1.44, 1.75	1.47E-09	CD molecules
<i>Slamf6</i>	1.59	0.239	1.12, 2.06	3.95E-05	CD molecules
<i>Il1b</i>	1.58	0.140	1.31, 1.86	2.46E-07	Adaptive, Chemokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, Pathogen Response, T-Cell Functions, Transporter Functions
<i>Ctla4</i>	1.58	0.226	1.13, 2.02	2.59E-05	B-Cell Functions, CD molecules, T-Cell Functions
<i>Plau</i>	1.56	0.126	1.31, 1.80	9.38E-08	Adhesion, Senescence
<i>Usp18</i>	1.52	0.180	1.17, 1.88	3.95E-06	Basic Cell Functions
<i>Tnfrsf4</i>	1.49	0.161	1.17, 1.80	1.69E-06	B-Cell Functions, CD molecules, Cytokines & Receptors, Inflammation, T-Cell Functions, TNF Superfamily
<i>Ccr1</i>	1.48	0.092	1.30, 1.67	7.47E-09	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Innate, Leukocyte Functions, Transporter Functions
<i>Cd200r1</i>	1.45	0.097	1.26, 1.64	1.32E-08	B-Cell Functions
<i>Cd83</i>	1.44	0.116	1.21, 1.67	8.89E-08	B-Cell Functions, CD molecules, Dendritic Cell Functions, Humoral, Interleukins, T-Cell Functions
<i>Il1a</i>	1.41	0.145	1.12, 1.69	1.11E-06	Adaptive, Cytokines & Receptors, Inflammation, Innate, Interleukins

<i>Tlr9</i>	1.41	0.222	0.972, 1.84	6.32E-05	CD molecules, Chemokines & Receptors, Inflammation, Innate, Interleukins, TLR, Transporter Functions
<i>Cfp</i>	1.40	0.176	1.05, 1.74	7.21E-06	Cancer Progression, Complement Pathway, Innate
<i>Tlr2</i>	1.37	0.086	1.20, 1.54	7.82E-09	CD molecules, Inflammation, Innate, Leukocyte Functions, TLR
<i>Tap1</i>	1.36	0.146	1.07, 1.64	1.69E-06	Antigen Processing, MHC, T-Cell Functions, Transporter Functions
<i>Mx2</i>	1.36	0.293	0.782, 1.93	9.36E-04	Innate
<i>Ikbke</i>	1.34	0.134	1.08, 1.61	8.34E-07	Apoptosis, Innate
<i>Cd19</i>	1.34	0.285	0.782, 1.90	8.22E-04	B-Cell Functions, CD molecules
<i>Emr1</i>	1.33	0.103	1.13, 1.54	6.46E-08	Basic Cell Functions
<i>H2-K1</i>	1.33	0.126	1.08, 1.58	5.00E-07	Antigen Processing, MHC, T-Cell Functions
<i>Cd74</i>	1.33	0.142	1.05, 1.61	1.58E-06	Antigen Processing, B-Cell Functions, CD molecules, Innate, MHC, T-Cell Functions
<i>Socs3</i>	1.33	0.149	1.03, 1.62	2.56E-06	T-Cell Functions
<i>Cd80</i>	1.32	0.096	1.13, 1.51	3.15E-08	Adaptive, CD molecules, T-Cell Functions
<i>Itgax</i>	1.31	0.089	1.13, 1.48	1.51E-08	Adhesion, CD molecules, Innate, T-Cell Functions
<i>Cd274</i>	1.31	0.099	1.11, 1.50	4.95E-08	CD molecules, T-Cell Functions
<i>Cd86</i>	1.31	0.105	1.10, 1.52	8.75E-08	Adaptive, B-Cell Functions, CD molecules, Dendritic Cell Functions, T-Cell Functions, TLR
<i>Fpr2</i>	1.30	0.078	1.14, 1.45	6.37E-09	Adaptive, Basic Cell Functions, Inflammation
<i>Ccl6</i>	1.30	0.106	1.09, 1.51	1.04E-07	Chemokines & Receptors, Cytokines & Receptors
<i>Il2ra</i>	1.30	0.158	0.988, 1.61	5.51E-06	Adaptive, B-Cell Functions, CD molecules, Inflammation, T-Cell Functions
<i>Ccl19</i>	1.30	0.176	0.959, 1.65	1.46E-05	Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Leukocyte Functions, T-Cell Functions
<i>Lgals3</i>	1.27	0.072	1.13, 1.42	4.23E-09	Innate, T-Cell Functions
<i>Csf2rb</i>	1.26	0.083	1.10, 1.43	1.20E-08	CD molecules, Cancer Progression, Cytokines & Receptors
<i>Ncf4</i>	1.26	0.099	1.07, 1.46	6.72E-08	Basic Cell Functions, Innate
<i>Cx3cr1</i>	1.25	0.129	0.994, 1.50	1.22E-06	Chemokines & Receptors, Cytokines & Receptors, Macrophage Functions, Microglial Functions
<i>Ly9</i>	1.25	0.173	0.912, 1.59	1.78E-05	Adhesion, CD molecules
<i>Fcer1g</i>	1.23	0.095	1.05, 1.42	6.36E-08	Antigen Processing, Interleukins, MHC, Transporter Functions



<i>Psmb8</i>	1.23	0.142	0.949, 1.50	3.13E-06	Antigen Processing
<i>C3</i>	1.22	0.097	1.03, 1.41	8.12E-08	Cancer Progression, Complement Pathway, Inflammation, Innate, Transporter Functions
<i>Ly86</i>	1.21	0.177	0.859, 1.55	3.19E-05	Humoral, Inflammation, Innate, Pathogen Response
<i>Ccl22</i>	1.21	0.183	0.854, 1.57	4.17E-05	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Tlr1</i>	1.21	0.248	0.728, 1.70	6.04E-04	CD molecules, Inflammation, Innate, Interleukins, Macrophage Functions, TLR
<i>Ccl11</i>	1.20	0.216	0.78, 1.63	2.04E-04	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation, T-Cell Functions
<i>Nlrc5</i>	1.19	0.163	0.867, 1.50	1.66E-05	Innate, Interferon, MHC
<i>H2-DMb2</i>	1.18	0.188	0.809, 1.55	7.18E-05	Antigen Processing, MHC
<i>H2-Ob</i>	1.18	0.232	0.724, 1.63	4.54E-04	Antigen Processing, MHC
<i>Batf</i>	1.17	0.123	0.929, 1.41	1.33E-06	
<i>Tnfrsf11a</i>	1.15	0.076	1.00, 1.30	1.28E-08	Adaptive, CD molecules, Cytokines & Receptors, Interleukins, TNF Superfamily
<i>Bst2</i>	1.14	0.127	0.890, 1.39	2.35E-06	CD molecules, Humoral, Innate
<i>Cd180</i>	1.13	0.169	0.801, 1.46	3.69E-05	CD molecules, Inflammation, Innate
<i>Psmb9</i>	1.11	0.124	0.868, 1.35	2.28E-06	Antigen Processing
<i>Ifit3</i>	1.11	0.190	0.737, 1.48	1.36E-04	Interferon
<i>Itgam</i>	1.10	0.161	0.787, 1.42	3.10E-05	Adaptive, CD molecules, Innate, Leukocyte Functions, T-Cell Functions, Transporter Functions
<i>Ms4a1</i>	1.10	0.217	0.670, 1.52	4.72E-04	B-Cell Functions, CD molecules, Humoral
<i>Fcgr3</i>	1.09	0.082	0.931, 1.25	4.60E-08	Antigen Processing, CD molecules, MHC, Transporter Functions
<i>Tnfrsf13b</i>	1.09	0.154	0.785, 1.39	2.26E-05	B-Cell Functions, CD molecules, TNF Superfamily
<i>Tnfaip3</i>	1.08	0.105	0.87, 1.28	6.62E-07	Apoptosis, B-Cell Functions, Inflammation, Innate
<i>Cd53</i>	1.06	0.097	0.874, 1.25	3.35E-07	CD molecules
<i>Socs1</i>	1.06	0.148	0.771, 1.35	1.97E-05	Cytokines & Receptors, T-Cell Functions
<i>Icos</i>	1.05	0.164	0.732, 1.38	5.72E-05	CD molecules, T-Cell Functions
<i>Pou2f2</i>	1.04	0.133	0.783, 1.31	8.33E-06	Humoral, T-Cell Functions
<i>Cxcl16</i>	1.03	0.084	0.862, 1.19	1.06E-07	Chemokines & Receptors, Cytokines & Receptors, Innate, Interferon

<i>H2-D1</i>	1.01	0.093	0.827, 1.19	3.77E-07	Antigen Processing, MHC, T-Cell Functions
<i>H2-Ea-ps</i>	1.01	0.113	0.786, 1.23	2.51E-06	Antigen Processing
<i>Klrd1</i>	-1.04	0.109	-1.26, -0.828	1.29E-06	NK Cell Functions
<i>Kdr</i>	-1.06	0.167	-1.39, -0.733	6.27E-05	Adhesion, Apoptosis, Cancer Progression
<i>Lrrn3</i>	-1.13	0.100	-1.33, -0.939	2.28E-07	CD molecules
<i>Itga2b</i>	-1.13	0.312	-1.74, -0.516	5.39E-03	Adhesion, CD molecules, Leukocyte Functions
<i>Txk</i>	-1.14	0.124	-1.38, -0.897	1.83E-06	Adaptive, Cytokines & Receptors, Interleukins, T-Cell Functions
<i>Angpt2</i>	-1.19	0.177	-1.53, -0.838	3.82E-05	Adhesion, Cancer Progression
<i>Il11ra1</i>	-1.29	0.246	-1.77, -0.806	3.49E-04	Cytokines & Receptors, Interleukins, NK Cell Functions
<i>Ppbp</i>	-1.44	0.364	-2.16, -0.730	2.91E-03	Chemokines & Receptors
<i>Camp</i>	-1.56	0.475	-2.49, -0.625	1.01E-02	Adaptive, Cancer Progression, Inflammation, Innate
<i>Klrb1c</i>	-1.57	0.200	-1.97, -1.18	8.11E-06	NK Cell Functions
<i>Hamp</i>	-2.08	0.576	-3.21, -0.949	5.43E-03	Basic Cell Functions, Innate
<i>Cfd</i>	-2.84	0.694	-4.20, -1.48	2.34E-03	Complement Pathway, Innate

*Note:* Values shown are the calculated mean log<sub>2</sub> ratios, SEM and 95% confidence intervals of transcript counts for lung tissues of cSiO<sub>2</sub>-treated mice with respect to time-matched vehicle-treated mice 13 weeks post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected  $q$  values are shown. Pathway associations for each significant gene are also shown.

**Supplementary Table 7. Significant differentially expressed genes in kidney tissues of mice at 13 weeks post cSiO<sub>2</sub> instillation (experiment 3).**

<b>Gene symbol</b>	<b>Log<sub>2</sub> ratio cSiO<sub>2</sub>/VEH</b>	<b>SEM</b>	<b>95% CI</b>	<b>FDR <i>q</i> value</b>	<b>Associated pathways</b>
<i>Fpr2</i>	4.68	0.460	3.78, 5.58	3.11E-05	Adaptive, Basic Cell Functions, Inflammation
<i>Lcn2</i>	4.38	0.682	3.04, 5.71	1.45E-04	Apoptosis, Innate, Transporter Functions
<i>Itgam</i>	4.09	0.468	3.17, 5.00	4.21E-05	Adaptive, CD molecules, Innate, Leukocyte Functions, T-Cell Functions, Transporter Functions
<i>Clec4a2</i>	3.81	0.496	2.84, 4.79	4.42E-05	Innate
<i>Ccl12</i>	3.75	0.457	2.85, 4.64	4.21E-05	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation
<i>Fcgr4</i>	3.60	0.394	2.83, 4.37	3.11E-05	CD molecules, T-Cell Functions
<i>Ccl5</i>	3.36	0.500	2.38, 4.34	1.01E-04	Adaptive, Cancer Progression, Chemokines & Receptors, Dendritic Cell Functions, Inflammation, Innate, Macrophage Functions, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Tlr8</i>	3.33	0.426	2.50, 4.17	4.21E-05	CD molecules, Inflammation, Innate, Interleukins, Pathogen Response, TLR
<i>Fcgr1</i>	3.31	0.388	2.55, 4.07	4.21E-05	Antigen Processing, CD molecules, Innate, MHC, Transporter Functions
<i>C3ar1</i>	3.21	0.386	2.45, 3.97	4.21E-05	Adaptive, Cancer Progression, Complement Pathway, Inflammation, Macrophage Functions
<i>Ccr5</i>	3.13	0.530	2.09, 4.17	2.40E-04	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Klra2</i>	3.09	0.363	2.38, 3.80	4.21E-05	NK Cell Functions
<i>Ccl2</i>	3.05	0.371	2.33, 3.78	4.21E-05	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, NK Cell Functions, Pathogen Response, T-Cell Functions
<i>Il1b</i>	2.99	0.308	2.39, 3.59	3.11E-05	Adaptive, Chemokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, Pathogen Response, T-Cell Functions, Transporter Functions
<i>Ccl9</i>	2.95	0.379	2.21, 3.69	4.21E-05	Chemokines & Receptors, Cytokines & Receptors
<i>Irf7</i>	2.89	0.371	2.17, 3.62	4.21E-05	Adaptive, Innate, Interferon, Senescence
<i>Col1a1</i>	2.89	0.519	1.88, 3.91	3.35E-04	Cancer Progression, Transporter Functions
<i>Hck</i>	2.84	0.308	2.23, 3.44	3.11E-05	Inflammation, Innate
<i>Oasl1</i>	2.83	0.434	1.97, 3.68	1.32E-04	Basic Cell Functions

<i>Ctss</i>	2.80	0.370	2.07, 3.52	4.84E-05	Innate
<i>Clqb</i>	2.73	0.347	2.05, 3.41	4.21E-05	Complement Pathway, Innate
<i>Oas2</i>	2.71	0.329	2.07, 3.36	4.21E-05	Basic Cell Functions, Interferon
<i>Zbp1</i>	2.68	0.338	2.02, 3.35	4.21E-05	Innate
<i>Fcgr3</i>	2.67	0.362	1.96, 3.38	6.24E-05	Antigen Processing, CD molecules, MHC, Transporter Functions
<i>Cxcl9</i>	2.67	0.450	1.79, 3.55	2.34E-04	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate
<i>Pou2f2</i>	2.66	0.346	1.98, 3.34	4.42E-05	Humoral, T-Cell Functions
<i>Clqa</i>	2.65	0.338	1.99, 3.31	4.21E-05	Complement Pathway, Innate
<i>Ccl28</i>	2.64	0.524	1.61, 3.67	7.19E-04	Chemokines & Receptors, Cytokines & Receptors
<i>Lif</i>	2.64	0.870	0.939, 4.35	1.94E-02	Cytokines & Receptors
<i>Cx3cr1</i>	2.63	0.334	1.98, 3.28	4.21E-05	Chemokines & Receptors, Cytokines & Receptors, Macrophage Functions, Microglial Functions
<i>Emr1</i>	2.63	0.373	1.90, 3.37	7.69E-05	Basic Cell Functions
<i>Isg15</i>	2.61	0.358	1.91, 3.31	6.46E-05	Basic Cell Functions, Innate, Interferon
<i>Mx2</i>	2.60	0.356	1.90, 3.30	6.46E-05	Innate
<i>Ccl8</i>	2.59	0.880	0.867, 4.31	2.15E-02	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Ifit1</i>	2.57	0.339	1.91, 3.24	4.84E-05	Interferon, Transporter Functions
<i>Cxcl10</i>	2.57	0.356	1.88, 3.27	6.46E-05	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate, Leukocyte Functions
<i>Cxcl11</i>	2.57	0.539	1.51, 3.63	1.11E-03	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Transporter Functions
<i>Fcer1g</i>	2.52	0.320	1.89, 3.15	4.21E-05	Antigen Processing, Interleukins, MHC, Transporter Functions
<i>Mrc1</i>	2.52	0.403	1.73, 3.31	1.76E-04	CD molecules
<i>H2-DMb2</i>	2.49	0.623	1.27, 3.71	3.64E-03	Antigen Processing, MHC
<i>Socs3</i>	2.49	0.997	0.541, 4.45	4.89E-02	T-Cell Functions
<i>Ncf4</i>	2.46	0.294	1.88, 3.04	4.21E-05	Basic Cell Functions, Innate
<i>C7</i>	2.46	0.424	1.63, 3.29	2.69E-04	Complement Pathway, Innate
<i>Col3a1</i>	2.44	0.451	1.56, 3.33	4.05E-04	Adhesion, Cancer Progression, Cytokines & Receptors

<i>C5ar1</i>	2.41	0.296	1.83, 2.99	4.21E-05	Chemokines & Receptors, Complement Pathway, Humoral
<i>Vcam1</i>	2.41	0.429	1.57, 3.25	3.24E-04	Adhesion, CD molecules, Leukocyte Functions, T-Cell Functions
<i>Cxcl13</i>	2.41	0.570	1.29, 3.53	2.46E-03	Adaptive, B-Cell Functions, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, T-Cell Functions
<i>Cd84</i>	2.40	0.414	1.59, 3.21	2.69E-04	Adhesion, CD molecules
<i>Ccr2</i>	2.36	0.387	1.61, 3.12	2.06E-04	Adaptive, CD molecules, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Humoral, Inflammation, Interleukins, Macrophage Functions, T-Cell Functions
<i>Klra17</i>	2.33	0.428	1.49, 3.17	3.89E-04	NK Cell Functions
<i>Runx1</i>	2.25	0.387	1.49, 3.00	2.64E-04	
<i>Cd48</i>	2.24	0.323	1.6, 2.87	8.56E-05	CD molecules, T-Cell Functions
<i>Cd14</i>	2.24	0.383	1.49, 2.99	2.58E-04	CD molecules, Cytokines & Receptors, Inflammation, Innate, Pathogen Response, Transporter Functions
<i>Ly86</i>	2.21	0.324	1.58, 2.84	9.16E-05	Humoral, Inflammation, Innate, Pathogen Response
<i>Cd68</i>	2.20	0.278	1.66, 2.75	4.21E-05	CD molecules
<i>Cybb</i>	2.17	0.268	1.64, 2.69	4.21E-05	Innate, Transporter Functions
<i>Itgal</i>	2.16	0.233	1.71, 2.62	3.11E-05	Adhesion, CD molecules, Leukocyte Functions, T-Cell Functions
<i>Il10ra</i>	2.16	0.328	1.52, 2.81	1.17E-04	CD molecules
<i>Lyz2</i>	2.15	0.350	1.46, 2.84	2.05E-04	Transporter Functions
<i>Itgb2</i>	2.09	0.266	1.57, 2.61	4.21E-05	CD molecules, Humoral, Inflammation, Leukocyte Functions, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Nlrc5</i>	2.08	0.369	1.35, 2.80	3.22E-04	Innate, Interferon, MHC
<i>Spn</i>	2.07	0.285	1.52, 2.63	6.46E-05	Adhesion, Apoptosis, CD molecules, T-Cell Functions
<i>Tlr7</i>	2.06	0.336	1.40, 2.72	2.06E-04	Chemokines & Receptors, Inflammation, Innate, Interleukins, Microglial Functions, Pathogen Response, TLR
<i>Ddx60</i>	2.02	0.322	1.39, 2.65	1.76E-04	Basic Cell Functions
<i>Syk</i>	2.01	0.321	1.38, 2.64	1.76E-04	B-Cell Functions, Innate, Interleukins, Leukocyte Functions, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Ccl20</i>	2.01	0.642	0.753, 3.27	1.64E-02	Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Selp1g</i>	2.00	0.328	1.36, 2.65	2.06E-04	Adhesion, CD molecules, Leukocyte Functions
<i>Ptpnc</i>	1.96	0.289	1.40, 2.53	9.57E-05	B-Cell Functions, CD molecules, Cytokines & Receptors, T-Cell Functions

<i>Ifit3</i>	1.96	0.325	1.32, 2.59	2.18E-04	Interferon
<i>Cxcr6</i>	1.95	0.395	1.17, 2.72	8.51E-04	CD molecules, Chemokines & Receptors, Innate
<i>Spp1</i>	1.94	0.437	1.08, 2.79	1.82E-03	Adhesion, Apoptosis, Cytokines & Receptors, T-Cell Functions
<i>Cd74</i>	1.93	0.339	1.27, 2.60	2.93E-04	Antigen Processing, B-Cell Functions, CD molecules, Innate, MHC, T-Cell Functions
<i>Tap1</i>	1.88	0.285	1.32, 2.44	1.17E-04	Antigen Processing, MHC, T-Cell Functions, Transporter Functions
<i>Usp18</i>	1.88	0.304	1.29, 2.48	1.95E-04	Basic Cell Functions
<i>Psmb8</i>	1.85	0.310	1.25, 2.46	2.21E-04	Antigen Processing
<i>H2-Eb1</i>	1.85	0.328	1.21, 2.49	3.19E-04	Antigen Processing, Interleukins, MHC
<i>C4b</i>	1.85	0.337	1.19, 2.51	3.62E-04	Complement Pathway, Humoral, Inflammation, Innate
<i>Cxcl11</i>	1.84	0.358	1.14, 2.54	6.34E-04	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate
<i>Il2rg</i>	1.83	0.253	1.34, 2.33	6.46E-05	B-Cell Functions, CD molecules, Cytokines & Receptors, Interleukins, T-Cell Functions
<i>Cd3g</i>	1.83	0.488	0.871, 2.79	5.62E-03	Apoptosis, CD molecules, T-Cell Functions, Transporter Functions
<i>H2-Aa</i>	1.82	0.335	1.16, 2.48	4.00E-04	Antigen Processing, Interferon, MHC, T-Cell Functions
<i>H2-Ab1</i>	1.80	0.323	1.17, 2.44	3.32E-04	Antigen Processing, Interferon, MHC, T-Cell Functions
<i>H2-K1</i>	1.78	0.306	1.18, 2.38	2.64E-04	Antigen Processing, MHC, T-Cell Functions
<i>Lilra5</i>	1.76	0.247	1.27, 2.24	7.52E-05	CD molecules, Innate
<i>Pik3cd</i>	1.76	0.292	1.18, 2.33	2.18E-04	Inflammation, Innate
<i>C3</i>	1.76	0.414	0.953, 2.57	2.34E-03	Cancer Progression, Complement Pathway, Inflammation, Innate, Transporter Functions
<i>H2-Ea-ps</i>	1.75	0.317	1.13, 2.37	3.48E-04	Antigen Processing
<i>Cxcr3</i>	1.75	0.369	1.03, 2.48	1.11E-03	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Innate, T-Cell Functions
<i>Gbp5</i>	1.74	0.286	1.18, 2.30	2.06E-04	Interferon
<i>Tnfrsf1b</i>	1.73	0.225	1.29, 2.17	4.42E-05	CD molecules, Inflammation, TNF Superfamily
<i>Itga4</i>	1.73	0.238	1.26, 2.20	6.46E-05	Adhesion, CD molecules, Leukocyte Functions
<i>Tnfrsf12a</i>	1.73	0.403	0.938, 2.52	2.24E-03	Adhesion, Apoptosis, CD molecules, TNF Superfamily
<i>Clec7a</i>	1.72	0.350	1.03, 2.40	8.85E-04	Inflammation, Innate, Leukocyte Functions, Transporter Functions

<i>Cd180</i>	1.71	0.306	1.11, 2.31	3.32E-04	CD molecules, Inflammation, Innate
<i>Fnl</i>	1.71	0.391	0.946, 2.48	1.96E-03	Adhesion, Apoptosis
<i>Bst2</i>	1.70	0.245	1.22, 2.18	8.56E-05	CD molecules, Humoral, Innate
<i>H2-DMa</i>	1.70	0.306	1.10, 2.29	3.43E-04	Antigen Processing, MHC, T-Cell Functions
<i>Xaf1</i>	1.69	0.250	1.20, 2.18	9.98E-05	Apoptosis
<i>Psmb9</i>	1.69	0.273	1.15, 2.22	1.99E-04	Antigen Processing
<i>Amica1</i>	1.66	0.312	1.05, 2.27	4.74E-04	Adhesion, Transporter Functions
<i>Cd86</i>	1.65	0.290	1.08, 2.22	2.99E-04	Adaptive, B-Cell Functions, CD molecules, Dendritic Cell Functions, T-Cell Functions, TLR
<i>Casp1</i>	1.64	0.269	1.11, 2.16	2.06E-04	Cytokines & Receptors, Innate, Interleukins, Microglial Functions
<i>H2-DMb1</i>	1.62	0.327	0.984, 2.26	7.96E-04	Antigen Processing, MHC
<i>Lcp1</i>	1.60	0.231	1.15, 2.05	8.56E-05	T-Cell Functions, Transporter Functions
<i>Cdkn1a</i>	1.58	0.339	0.913, 2.24	1.29E-03	B-Cell Functions, Cancer Progression, Cell Cycle, Senescence
<i>Cfp</i>	1.57	0.273	1.03, 2.10	2.82E-04	Cancer Progression, Complement Pathway, Innate
<i>Herc6</i>	1.55	0.304	0.956, 2.15	6.55E-04	Basic Cell Functions
<i>Tnfrsf14</i>	1.51	0.249	1.03, 2.00	2.06E-04	CD molecules, T-Cell Functions, TNF Superfamily
<i>Inpp5d</i>	1.51	0.267	0.985, 2.03	3.13E-04	Apoptosis, B-Cell Functions, Interleukins
<i>Ltb</i>	1.51	0.525	0.485, 2.54	2.40E-02	Cytokines & Receptors, Interleukins, TNF Superfamily
<i>Vim</i>	1.49	0.259	0.980, 1.99	2.82E-04	Cancer Progression
<i>Icam1</i>	1.48	0.229	1.03, 1.93	1.39E-04	Adaptive, Antigen Processing, CD molecules, Leukocyte Functions, T-Cell Functions, Transporter Functions
<i>H2-Ob</i>	1.48	0.334	0.825, 2.14	1.82E-03	Antigen Processing, MHC
<i>Lck</i>	1.44	0.460	0.535, 2.34	1.57E-02	Apoptosis, B-Cell Functions, T-Cell Functions
<i>Cd83</i>	1.43	0.200	1.04, 1.83	7.10E-05	B-Cell Functions, CD molecules, Dendritic Cell Functions, Humoral, Interleukins, T-Cell Functions
<i>Irf1</i>	1.43	0.236	0.970, 1.89	2.06E-04	Interleukins, T-Cell Functions
<i>Ifit2</i>	1.42	0.309	0.816, 2.03	1.41E-03	Interferon
<i>Anxa1</i>	1.42	0.327	0.784, 2.06	2.01E-03	Cell Cycle, Inflammation, T-Cell Functions, Transporter Functions
<i>H2-M3</i>	1.41	0.254	0.911, 1.91	3.43E-04	Antigen Processing, MHC, NK Cell Functions, T-Cell Functions

<i>Clu</i>	1.40	0.382	0.655, 2.15	6.32E-03	Apoptosis, Cancer Progression, Innate
<i>Thy1</i>	1.38	0.347	0.705, 2.06	3.64E-03	Adhesion, CD molecules, T-Cell Functions
<i>Irgm2</i>	1.37	0.193	0.987, 1.74	7.69E-05	Innate, Interferon
<i>Stat1</i>	1.35	0.209	0.946, 1.76	1.35E-04	Adaptive, Cytokines & Receptors, Innate, T-Cell Functions
<i>Csf1</i>	1.34	0.195	0.962, 1.73	8.63E-05	Cytokines & Receptors, Inflammation, Innate, Macrophage Functions, Transporter Functions
<i>H2-D1</i>	1.32	0.224	0.882, 1.76	2.44E-04	Antigen Processing, MHC, T-Cell Functions
<i>Ikbke</i>	1.28	0.240	0.807, 1.75	4.69E-04	Apoptosis, Innate
<i>Serping1</i>	1.27	0.248	0.781, 1.75	6.45E-04	Complement Pathway, Innate
<i>Relb</i>	1.26	0.249	0.772, 1.75	7.01E-04	Antigen Processing, Dendritic Cell Functions, T-Cell Functions
<i>Il34</i>	1.26	0.364	0.546, 1.97	9.07E-03	Cytokines & Receptors, Inflammation, Innate, Macrophage Functions
<i>Psmb10</i>	1.25	0.223	0.813, 1.69	3.27E-04	Humoral, T-Cell Functions
<i>Entpd1</i>	1.22	0.205	0.814, 1.62	2.35E-04	CD molecules
<i>Myc</i>	1.21	0.253	0.717, 1.71	1.06E-03	Apoptosis, Cell Cycle, Senescence
<i>Ada</i>	1.20	0.213	0.783, 1.62	3.17E-04	Adhesion, B-Cell Functions, T-Cell Functions
<i>Cd3d</i>	1.20	0.439	0.336, 2.06	3.22E-02	CD molecules, T-Cell Functions
<i>Stat2</i>	1.19	0.195	0.805, 1.57	2.06E-04	Basic Cell Functions
<i>Tlr4</i>	1.18	0.223	0.739, 1.61	5.01E-04	Adaptive, CD molecules, Chemokines & Receptors, Inflammation, Innate, Interleukins, Pathogen Response, T-Cell Functions, TLR
<i>Tnfrsf11a</i>	1.18	0.268	0.660, 1.71	1.83E-03	Adaptive, CD molecules, Cytokines & Receptors, Interleukins, TNF Superfamily
<i>Tlr2</i>	1.16	0.281	0.607, 1.71	2.89E-03	CD molecules, Inflammation, Innate, Leukocyte Functions, TLR
<i>Axl</i>	1.15	0.210	0.742, 1.57	3.63E-04	Inflammation, Innate, NK Cell Functions, Transporter Functions
<i>Il18r1</i>	1.15	0.418	0.334, 1.97	3.03E-02	CD molecules, Innate, T-Cell Functions
<i>Tnfaip3</i>	1.14	0.194	0.761, 1.52	2.47E-04	Apoptosis, B-Cell Functions, Inflammation, Innate
<i>Irf8</i>	1.13	0.179	0.777, 1.48	1.73E-04	Interferon, Interleukins, T-Cell Functions
<i>Itga5</i>	1.13	0.226	0.686, 1.57	7.68E-04	Adhesion, CD molecules, Innate, Leukocyte Functions
<i>Rel</i>	1.11	0.168	0.778, 1.44	1.18E-04	Cytokines & Receptors, Interleukins, T-Cell Functions



<i>Il16</i>	1.11	0.268	0.581, 1.63	2.85E-03	Chemokines & Receptors, Cytokines & Receptors, Interleukins, Leukocyte Functions
<i>Ifi44</i>	1.10	0.188	0.734, 1.47	2.53E-04	Interferon
<i>C1ra</i>	1.10	0.210	0.692, 1.52	5.20E-04	Complement Pathway, Innate
<i>Isg20</i>	1.09	0.276	0.548, 1.63	3.94E-03	Basic Cell Functions, Innate, Interferon
<i>C1s1</i>	1.08	0.226	0.640, 1.53	1.06E-03	Complement Pathway, Innate
<i>Tlr1</i>	1.07	0.226	0.625, 1.51	1.17E-03	CD molecules, Inflammation, Innate, Interleukins, Macrophage Functions, TLR
<i>Rrad</i>	1.07	0.286	0.508, 1.63	5.70E-03	Basic Cell Functions
<i>Tap2</i>	1.06	0.222	0.629, 1.50	1.06E-03	Antigen Processing, MHC, Transporter Functions
<i>Cd274</i>	1.05	0.176	0.709, 1.40	2.21E-04	CD molecules, T-Cell Functions
<i>Ifi27</i>	1.04	0.169	0.703, 1.37	2.06E-04	Interferon, NK Cell Functions
<i>Ccl19</i>	1.04	0.262	0.529, 1.56	3.70E-03	Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Leukocyte Functions, T-Cell Functions
<i>Il6ra</i>	1.03	0.174	0.694, 1.37	2.29E-04	CD molecules, Chemokines & Receptors, Cytokines & Receptors, Interleukins
<i>Lbp</i>	1.03	0.244	0.556, 1.51	2.43E-03	Chemokines & Receptors, Inflammation, Innate, Leukocyte Functions, Macrophage Functions, Transporter Functions
<i>Cmpk2</i>	1.02	0.178	0.671, 1.37	2.82E-04	Basic Cell Functions
<i>Lyn</i>	1.02	0.178	0.667, 1.37	2.93E-04	B-Cell Functions, Cytokines & Receptors, Dendritic Cell Functions, Inflammation, Innate, Transporter Functions
<i>Sbno2</i>	1.01	0.196	0.627, 1.40	6.14E-04	Inflammation, Macrophage Functions
<i>Col4a1</i>	1.01	0.233	0.558, 1.47	2.03E-03	Cancer Progression

*Note:* Values shown are the calculated mean log<sub>2</sub> ratios, SEM and 95% confidence intervals of transcript counts for kidney tissues of cSiO<sub>2</sub>-treated mice with respect to time-matched vehicle-treated mice 13 weeks post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected  $q$  values are shown. Pathway associations for each significant gene are also shown.

**Supplementary Table 8. Significant differentially expressed genes in spleen tissues of mice at 13 weeks post cSiO<sub>2</sub> instillation (experiment 3).**

<b>Gene symbol</b>	<b>Log<sub>2</sub> ratio cSiO<sub>2</sub>/VEH</b>	<b>SEM</b>	<b>95% CI</b>	<b>FDR <i>q</i> value</b>	<b>Associated pathways</b>
<i>Cxcl14</i>	5.80	0.664	4.50, 7.10	2.50E-05	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Ccl8</i>	3.41	0.297	2.83, 3.99	1.09E-05	Adaptive, Cancer Progression, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Fcgr4</i>	3.25	0.343	2.58, 3.92	1.71E-05	CD molecules, T-Cell Functions
<i>Klra2</i>	2.21	0.237	1.74, 2.67	1.81E-05	NK Cell Functions
<i>Il1b</i>	2.03	0.266	1.51, 2.56	5.46E-05	Adaptive, Chemokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, Pathogen Response, T-Cell Functions, Transporter Functions
<i>Il21</i>	1.69	0.256	1.19, 2.19	1.35E-04	B-Cell Functions, Cytokines & Receptors, Interleukins, NK Cell Functions, T-Cell Functions
<i>Msr1</i>	1.64	0.269	1.11, 2.16	2.58E-04	CD molecules, Macrophage Functions, Transporter Functions
<i>Itgax</i>	1.60	0.274	1.07, 2.14	3.44E-04	Adhesion, CD molecules, Innate, T-Cell Functions
<i>Il1rn</i>	1.57	0.161	1.25, 1.88	1.68E-05	Cytokines & Receptors, Inflammation, Interleukins
<i>Ccl3</i>	1.55	0.152	1.25, 1.85	1.55E-05	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, NK Cell Functions, T-Cell Functions, Transporter Functions
<i>Ccl2</i>	1.55	0.210	1.14, 1.96	6.84E-05	Chemokines & Receptors, Cytokines & Receptors, Humoral, Inflammation, Innate, Interleukins, Macrophage Functions, NK Cell Functions, Pathogen Response, T-Cell Functions
<i>Fpr2</i>	1.52	0.253	1.02, 2.01	2.84E-04	Adaptive, Basic Cell Functions, Inflammation
<i>Socs3</i>	1.48	0.202	1.09, 1.88	6.86E-05	T-Cell Functions
<i>Lag3</i>	1.43	0.144	1.15, 1.72	1.59E-05	CD molecules, Interleukins, MHC, NK Cell Functions, T-Cell Functions
<i>Oas2</i>	1.38	0.161	1.06, 1.69	2.50E-05	Basic Cell Functions, Interferon
<i>Cx3cr1</i>	1.35	0.175	1.01, 1.70	5.06E-05	Chemokines & Receptors, Cytokines & Receptors, Macrophage Functions, Microglial Functions
<i>Ccr5</i>	1.25	0.182	0.894, 1.61	9.76E-05	Adaptive, CD molecules, Chemokines & Receptors, Cytokines & Receptors, Dendritic Cell Functions, Macrophage Functions, T-Cell Functions, Transporter Functions
<i>Fos</i>	1.21	0.189	0.84, 1.58	1.70E-04	Inflammation, Innate, Pathogen Response

<i>Ifi44</i>	1.20	0.115	0.972, 1.42	1.55E-05	Interferon
<i>Cfb</i>	1.15	0.127	0.903, 1.40	2.25E-05	Complement Pathway, Innate
<i>Tigit</i>	1.12	0.144	0.838, 1.40	4.79E-05	Interleukins, T-Cell Functions
<i>Dusp4</i>	1.08	0.149	0.786, 1.37	7.43E-05	Basic Cell Functions, Innate
<i>Batf</i>	1.06	0.162	0.746, 1.38	1.39E-04	
<i>Ccr6</i>	1.04	0.168	0.710, 1.37	2.18E-04	Adaptive, CD molecules, Chemokines & Receptors, Humoral, Innate, T-Cell Functions
<i>Xbp1</i>	1.02	0.129	0.773, 1.28	4.67E-05	
<i>Bcl2l1</i>	-1.01	0.207	-1.41, -0.601	1.30E-03	Apoptosis, Cytokines & Receptors, Innate
<i>Cd8b1</i>	-1.24	0.333	-1.89, -0.591	7.12E-03	CD molecules, T-Cell Functions
<i>Il1rl1</i>	-1.30	0.316	-1.92, -0.677	3.91E-03	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Innate, Interleukins, Macrophage Functions, Transporter Functions
<i>Mpo</i>	-1.35	0.394	-2.12, -0.578	1.16E-02	Basic Cell Functions
<i>Tal1</i>	-1.38	0.306	-1.98, -0.780	2.20E-03	Cell Cycle
<i>Ccl24</i>	-1.40	0.306	-2.00, -0.797	2.03E-03	Adaptive, Chemokines & Receptors, Cytokines & Receptors, Inflammation
<i>Sl100a8</i>	-1.40	0.410	-2.20, -0.595	1.18E-02	Adaptive, Basic Cell Functions, Inflammation
<i>Lcn2</i>	-1.44	0.401	-2.23, -0.658	8.73E-03	Apoptosis, Innate, Transporter Functions
<i>Elane</i>	-1.47	0.407	-2.27, -0.673	8.68E-03	Chemokines & Receptors, Cytokines & Receptors, Inflammation, Interleukins, Leukocyte Functions
<i>Tfrc</i>	-1.50	0.352	-2.19, -0.809	3.15E-03	CD molecules, Transporter Functions
<i>Rsad2</i>	-1.50	0.401	-2.29, -0.713	7.13E-03	Basic Cell Functions
<i>Camp</i>	-1.54	0.416	-2.35, -0.721	7.66E-03	Adaptive, Cancer Progression, Inflammation, Innate
<i>Ctsg</i>	-1.60	0.410	-2.40, -0.793	5.56E-03	Basic Cell Functions
<i>Icam4</i>	-1.95	0.473	-2.88, -1.02	3.82E-03	Adhesion, CD molecules
<i>Cxcl15</i>	-2.83	0.815	-4.43, -1.23	1.17E-02	Cell Cycle, Chemokines & Receptors, Cytokines & Receptors, Inflammation, Interleukins

*Note:* Values shown are the calculated mean log<sub>2</sub> ratios, SEM and 95% confidence intervals of transcript counts for spleen tissues of cSiO<sub>2</sub>-treated mice with respect to time-matched vehicle-treated mice 13 weeks post instillation. Statistical analysis was performed using nSolver software (nanoString) with the Benjamini-Hochberg method for control of false discoveries ( $\alpha=0.05$ ); FDR-corrected  $q$  values are shown. Pathway associations for each significant gene are also shown.