Cell Reports, Volume *40*

Supplemental information

Vaccine-associated enhanced respiratory pathology in COVID-19 hamsters after T_H2-biased immunization

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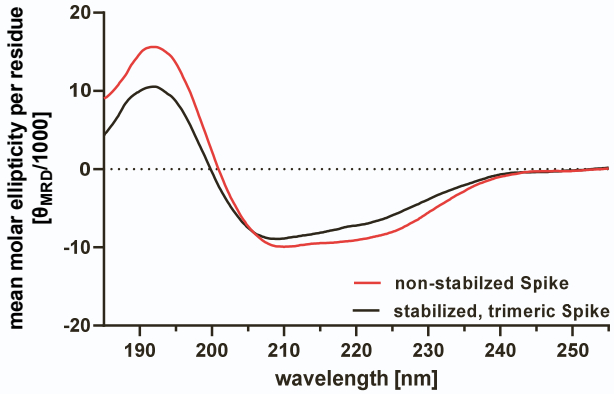
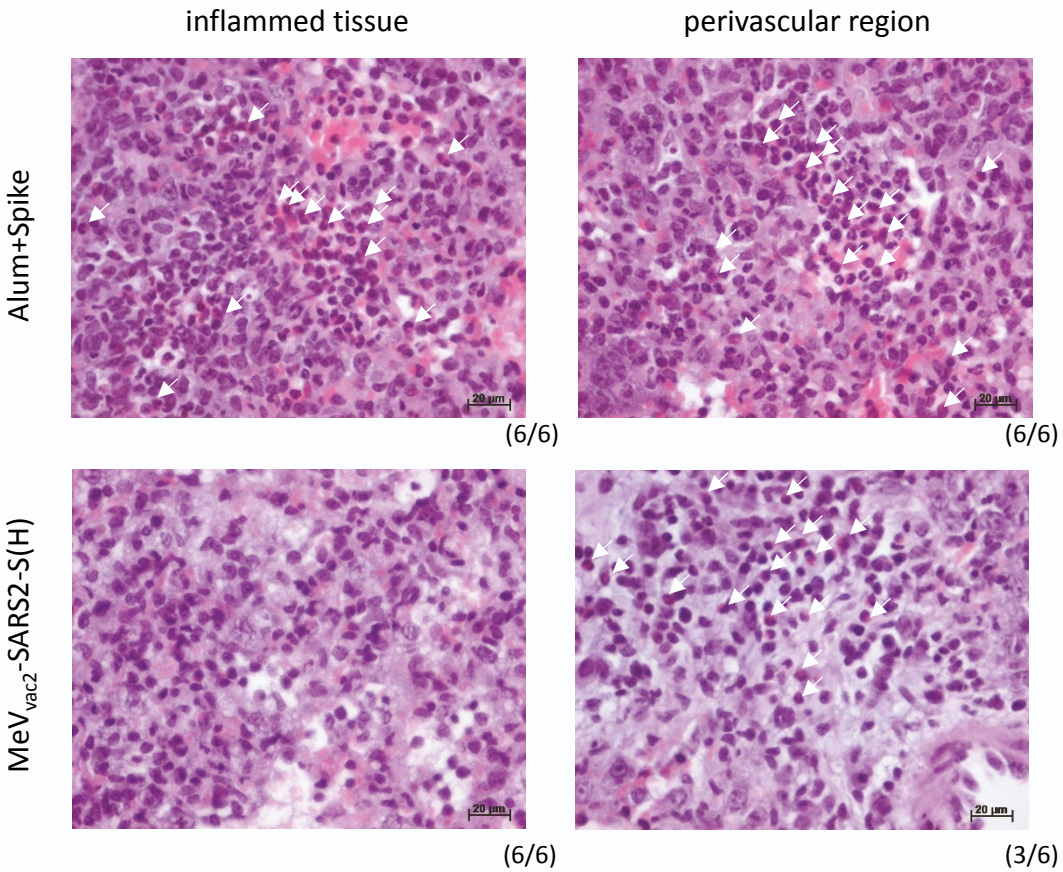
Figure S1. Relative secondary structural elements of S determined by circular dichroism (CD), Related to Figure 1



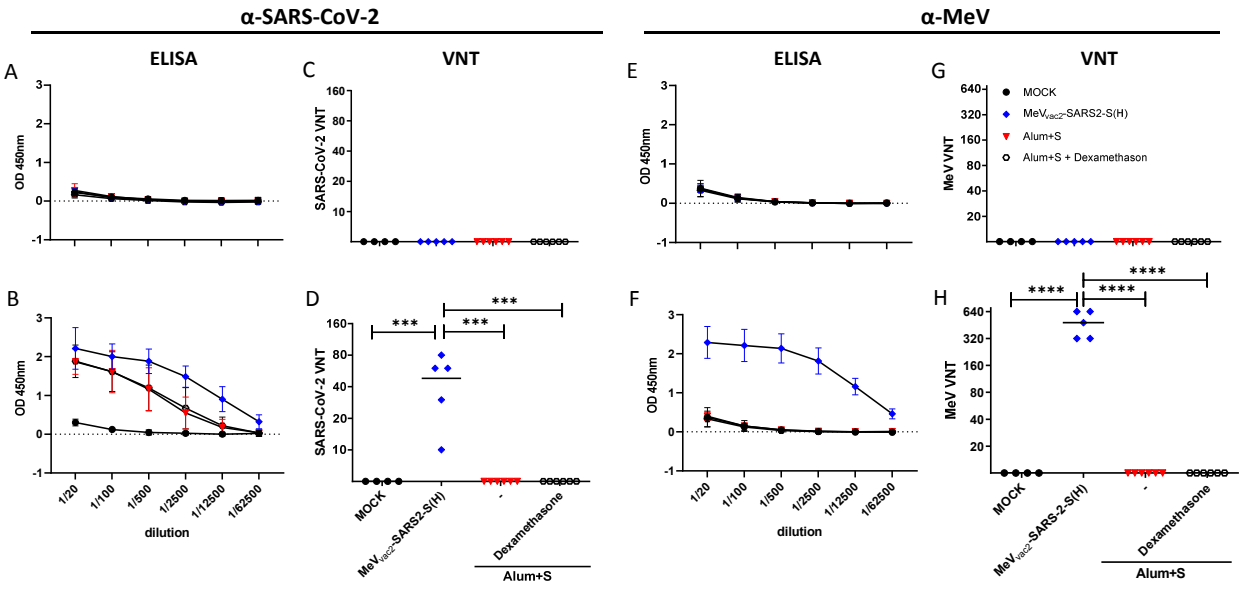
Suppl. Fig. S1: Relative secondary structural elements of S determined by circular dichroism (CD). To determine misfolding of recombinant Spike used for vaccination, spectra of non-stabilized recombinant S used for vaccination (red; Sino Biological, Cat.-No. 40589-V08B1) and soluble S stabilized in the native conformation (black; NIBSC, Cat.-No. 101007), secondary structure of the proteins was determined by CD spectroscopy. CD spectra of both proteins were recorded at room temperature from 255 nm – 185 nm by accumulating 10 runs, blotted and analysed for relative content of α-helical and β-sheet secondary structural elements.

Figure S2. Eosinophil infiltration into tissue of infected hamster lungs. Related to Figure 1



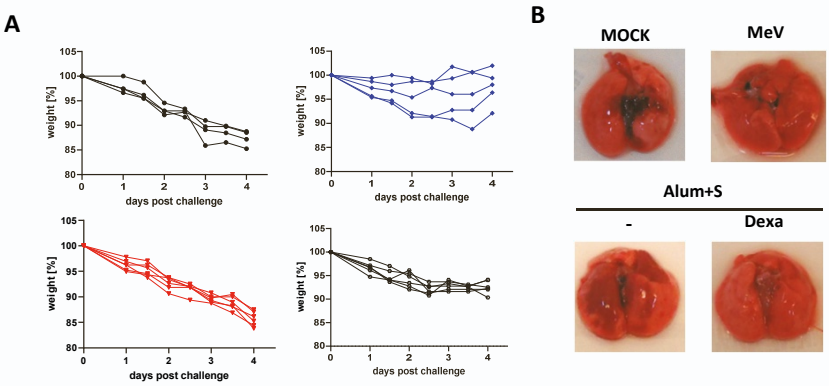
Suppl. Fig. S2: Eosinophil infiltration into tissue of infected hamster lungs. Haematoxilin and Eosin-staining of fixed lung slices of hamsters infected with SARS-CoV-2 after vaccination with Aluminum-adjuvanted Spike protein (upper panel) or MeV$_{vac2}$-SARS2-S(H) (lower panel) revealed eosinophil infiltration into inflammed tissue (left panel) of Alum+S, but not MeV$_{vac2}$-SARS2-S(H) immunized animals´. While eosinophils became evident in the perivascular region of samples of all animals vaccinated with protein before infection, only half (3/6) of the MeV-vaccinated animals revealed this phenotype. N = 6; representative pictures for the fraction of animals indicated below each picture. White arrows depict single eosinophils. Scale bar, 20 µm.

Figure S3. : Induction of α-SARS-CoV-2 S and α-MeV specific antibodies. Related to Figure 4



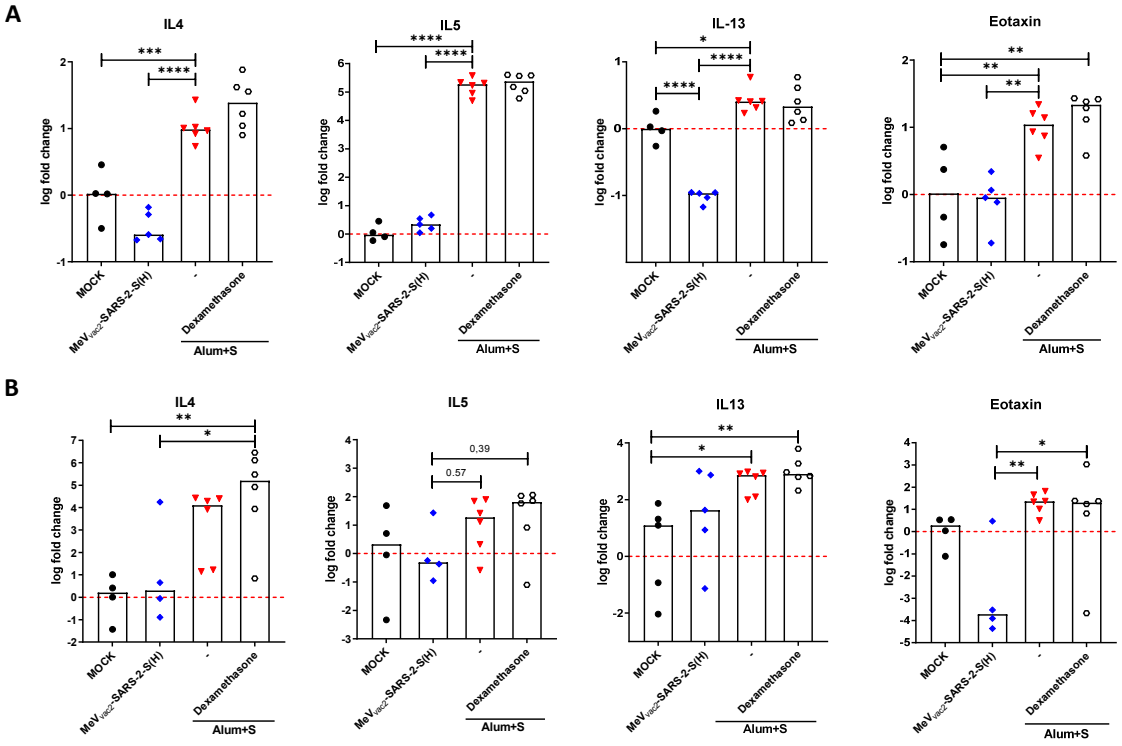
Suppl. Fig. S3: Induction of α-SARS-CoV-2 S and α-MeV specific antibodies. Sera of hamsters vaccinated on days 0 and 21 with MeV$_{vac2}$-SARS2-S(H) (blue diamonds) or Alum-adjuvanted S protein (red triangles, open circles) were collected on days 0 (A, C, E, G) and 31 (B, D, F, H) and analyzed for antibodies specific for SARS-CoV-2 S or MeV. Medium-inoculated hamsters (black circles) served as mock. Pan-IgG binding to recombinant SARS-CoV-2 S (A, B) or MeV bulk antigen (E, F) were determined by ELISA via the specific OD 450 nm value. Depicted are means and the respective standard deviation of each group (n = 4 - 6). Virus-neutralizing titers (VNT) in vaccinated hamsters for SARS-CoV-2 (C, D) or MeV (G, H) were calculated as the reciprocal of the highest dilution abolishing infectivity. For statistical analysis, ordinary one-way ANOVA was applied with Tukey's multiple comparisons test. ns, not significant ($p>0.05$), *, $p<0.05$; **, $p<0.01$;***, $p<0.001$;****, $p<0.0001$.

Figure S4. Gross pathology in vaccinated hamsters after challenge. Related to Figure 4



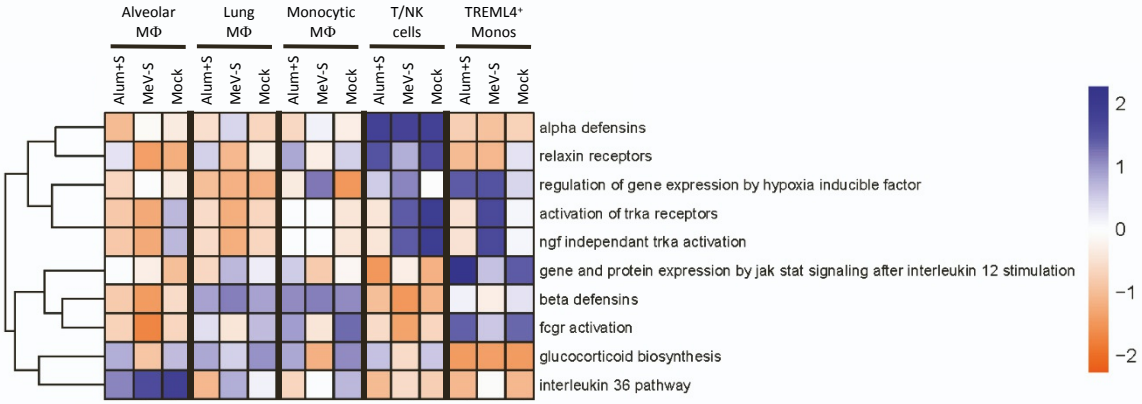
Suppl. Fig. S4: Gross pathology in vaccinated hamsters after challenge. Hamster were vaccinated at days 0 and 21 and challenged on day 35 with low-passage SARS-CoV-2. **(A)** Body weight changes of animals vaccinated with medium (upper left, black circles), MeV_{vac2}-SARS2-S(H) (upper right, blue diamonds), Alum+S without (lower left, red triangles) or with dexamethasone-treatment after challenge (lower right, open circles). **(B)** Macroscopic pathology of Syrian hamster lungs after SARS-CoV-2 infection and indicated vaccination or treatment on day 4 pi.

Figure S5. Deregulation of T_H2 cytokines in lungs (A) and BAL cells (B) of SARS-CoV-2 infected, vaccinated Syrian hamsters 4 dpi. Related to Figure 5.



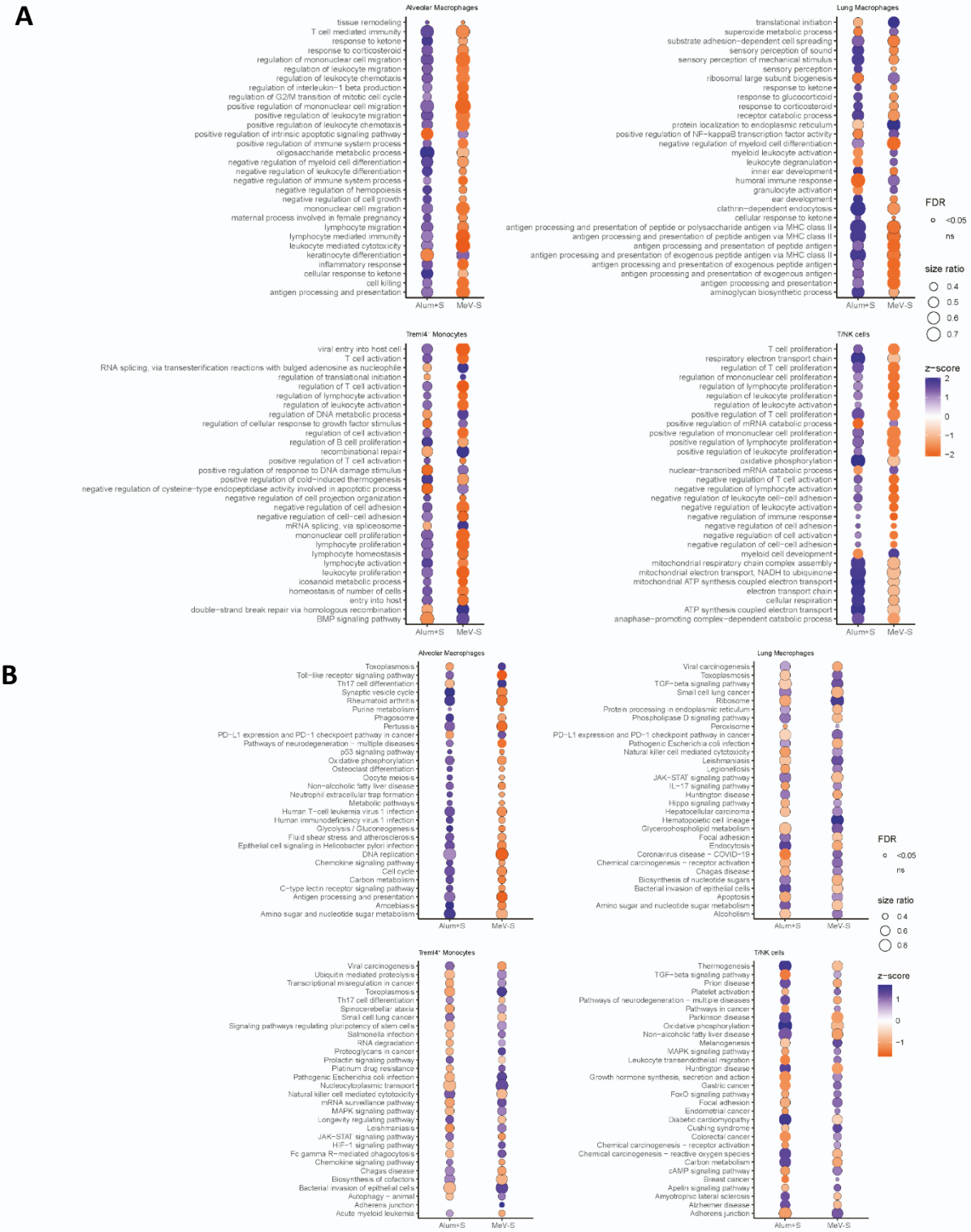
Suppl. Fig. S5: Deregulation of T_H2 cytokines in lungs (A) and BAL cells (B) of SARS-CoV-2 infected, vaccinated Syrian hamsters 4 dpi. Depicted are data of animals already displayed in Fig. 4**.** Relative fold-change expression of mRNAs encoding IL-4, IL-5, or IL-13 was determined using quantitative RT-PCR and the ΔΔct method. mRNA encoding RPL18 was used as housekeeping gene for normalization. Median of samples from mock-treated hamsters served as reference to normalize relative gene expression. Dots represent individual animals; mock-vaccinated hamsters, black circles; MeV$_{vac2}$-SARS2-S(H)-vaccinated hamsters, blue diamonds; protein-vaccinated hamsters, red triangles. For statistical analysis, ordinary one-way ANOVA was applied with Tukey‘s multiple comparisons test. ns, not significant (p>0.05), *, p<0.05; **, p<0.01;***, p<0.001;****, p<0.0001.

Figure S6. SARS-CoV-2 infection triggers cell-type specific induction of REACTOME pathways which differ depending on vaccination type and prior immune status. Related to Figure 6.



Suppl. Fig. S6: SARS-CoV-2 infection triggers cell-type specific induction of REACTOME pathways which differ depending on vaccination type and prior immune status. Heat map is derived from scRNA-seq data and highlights selected REACTOME pathways which exhibit differential activation or suppression triggered by infection. Differences are dependent on prior immune status or vaccination type, and are cell-type specific. Cell population specific activation or suppression of pathways observed in alveolar macrophages (MΦ), interstitial macrophages, monocytic macrophages, Treml4^{+} monocytes, and T/NK cells is presented. Heat map is colored relative to the activation z-score gradient presented in the scale bar**.**

Figure S7. SARS-CoV-2 infection induces cell-type specific enrichment of GO terms and activation or suppression of KEGG pathways, which differ dependent on prior vaccination type. Related to Figure 6.



Suppl. Fig. S7: SARS-CoV-2 infection induces cell-type specific enrichment of GO terms and activation or suppression of KEGG pathways, which differ dependent on prior vaccination type. Dot plots highlight enriched (A) GO categories or (B) KEGG pathways that exhibit differential activation status dependent on prior vaccination with either Alum+S or MeVvac2-SARS2-S(H). Individual comparison plots are derived from scRNA-seq data and represent differential enrichment observed in alveolar macrophages, interstitial macrophages, Treml4^{+} monocytes and T/NK cells. Enriched categories are labelled on the y-axes. Circle size represents the ratio of significantly dysregulated genes relative to the total gene number in a specific GO term or KEGG pathway. Circles are colored relative to activation z-score gradient presented in the scale bar, with significantly enriched categories or pathways (FDR $p<0.05$) highlighted with a black boarder. ns: non-significant

Table S1. Histopathological analysis of lung tissue of vaccinated Syrian hamsters batch #1 upon challenge with SARS-CoV-2. Related to Figure 1. Hamsters were vaccinates with medium (MOCK), MV_{vac2}-ATU(P) as measles-only vector control (MeV), MeV_{vac2}-SARS2-S(H) (MeV-S), or Alum-adjuvanted Spike protein (Alum+S). The left lobe of vaccinated hamster lungs was dissected 4 dpi. H& E staining revealed histopathological changes and immune cell infiltration assessed by a trained pathologist in a blinded manner. DIC, disseminated intravascular coagulation.

Animal-No.	Vaccine group	% Dense Area	Bronchia	Vessels	DIC	Dense Area	Fibrosis	Syncytia
47	MOCK	< 50% dense areas, clearly bronchial-associated	Marked purulent bronchitis (granulocytes and lymphocytes in the lumen), bronchial epithelium sometimes with inflammatory infiltration.	Vascular walls with inflammatory infiltration, Single-cell necrosis in the vessel wall, multiple hemorrhages in the tissue, 2 x edema around vessels	No	mostly lymphocytes and macrophages, less with granulocytes, sporadic eosinophils, proliferation of type II pneumocytes, often karyorrhexis	No	No
48	MOCK	30% dense areas, Bronchial- and vessel- associated	Bronchitis (lymphocytes and only very few granulocytes in the lumen), bronchial epithelium with little inflammatory infiltration and damage.	Vascular walls with inflammatory infiltration, Single-cell necrosis in the vessel wall, no bleeding or edema	No	mostly lymphocytes, macrophages, pneumocytes, isolated eosinophils, often karyorrhexis	No	No
49	MOCK	approximately 50% dense areas, clearly bronchial-associated	Bronchitis (lymphocytes and granulocytes in the lumen), bronchial epithelium sporadically with inflammatory infiltration, little damage.	Vascular walls with inflammatory infiltration, multiple hemorrhages in the tissue, 2 x edema around vessels	No	mostly lymphocytes, macrophages, pneumocytes, no granulocytes, eosinophils not increased, Foci with massive karyorrhexis	No	No
50	MOCK	approximately 33% dense areas, clearly bronchial-associated	Bronchitis (lymphocytes and granulozytes in the lumen), bronchial epithelium with little inflammatory infiltration and damage (karyorrhexis).	Vascular walls with inflammatory infiltration (also eosinophils), multiple hemorrhages in the tissue, 2 x edema around vessels	No	mostly lymphocytes, macrophages, pneumocytes, isolated eosinophils, foci with karyorrhexis	No	No
51	MOCK	approximately 33% dense areas, clearly bronchial-associated	Bronchitis (lymphocytes and granulocytes in the lumen), bronchial epithelium sporadically with inflammatory infiltration, little damage.	Vascular walls with inflammatory infiltration (also eosinophils), multiple hemorrhages in the tissue, 2 x edema around vessels	No	mostly lymphocytes, macrophages, pneumocytes, isolated eosinophils, frequent karyorrhexis	No	No
52	MOCK	approximately 33% dense areas (macroscopic), bronchial- and vessel-associated, diffuse distribution	Bronchitis (only few lymphocytes and granulocytes in the lumen) bronchial epithelium with inflammatory infiltration, little damage	Vascular walls with inflammatory infiltration, clear single cell necrosis in the vessel wall, several hemorrhages in the tissue.	No	diffused distributed, mostly lymphocytes, macrophages, pneumocytes, Isolated eosinophils, frequent karyorrhexis	No	No
53	Alum+S	approximately 33% dense areas (macroscopic), bronchial- and vessel-associated, diffuse distribution	Bronchitis (only few lymphocytes, granulocytes and little karyorrhexis in the lumen) bronchial epithelium with little inflammatory infiltration, marked proliferation of the bronchial epithelium, clear damage	Vessel walls only sporadically infiltrated with inflammation, hemorrhages in the tissue	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils, frequent karyorrhexis	No	No

Animal-No.	Vaccine group	% Dense Area	Bronchia	Vessels	DIC	Dense Area	Fibrosis	Syncytia
54	Alum+S	30% dense areas, bronchial- and vessel-associated	Bronchitis (lymphocytes and granulocytes in the lumen), bronchial epithelium: foci of inflammatory infiltration, marked proliferation of the bronchial epithelium,clear damage	Vessel walls only very slightly infiltrated, several hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils, frequent karyorrhexis	No	Yes
55	Alum+S	40% dense areas, not bronchial- or vessel- associated	Bronchitis (Lymphocytes and granulocytes in the lumen), bronchial epithelium: foci of inflammatory infiltration, marked proliferation of the bronchial epithelium, clear damage	Vascular walls with inflammatory infiltration, significant single cell necrosis in the vascular wall, 1 x hemorrhages in the tissue, 1 x edema around vessels.	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils, frequent karyorrhexis	No	Suspicion
56	Alum+S	80% dense areas, not clearly bronchial or vessel associated.	Bronchitis (lymphocytes and granulocytes in the lumen), bronchial epithelium: foci of inflammatory infiltration, marked proliferation of the bronchial epithelium, clear damage	Vascular walls with inflammatory infiltration, isolated single cell necrosis in the vascular wall, multiple hemorrhages in tissue, slight edema around vessels.	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils, only sporadic karyorrhexis	No	No
57	Alum+S	50% dense areas, not clearly bronchial or vessel associated.	Bronchitis (lymphocytes, granulocytes and karyorrhexis in the lumen), bronchial epithelium with very little inflammatory infiltration, no karyorrhexis, little damage	Vascular walls with inflammatory infiltration, isolated single cell necrosis in the vascular wall, sporadic hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils, only sporadic karyorrhexis	No	No
58	Alum+S	40% dense areas, not clearly bronchial or vessel associated.	Bronchitis (lymphocytes, granulocytes and karyorrhexis in the lumen), bronchial epithelium: Foci of inflammatory infiltration, very few karyorrhexis, little damage	Vascular walls with inflammatory infiltration, 1 x single cell necrosis in the vascular wall, 2 x hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils, only sporadic karyorrhexis	No	No
59	MeV	50% dense areas, not clearly bronchial or vessel associated, diffuse distribution	Bronchitis (lymphocytes, granulocytes and karyorrhexis in the lumen), bronchial epithelium with focal inflammatory infiltration, no karyorrhexis, little damage	Vascular walls with inflammatory infiltration, sporadic single cell necrosis in the vascular wall, multiple hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, few eosinophils, more neutrophils	No	No
61	MeV	40% dense areas, bronchial associated, diffuse distribution	Bronchitis (lymphocytes, granulocytes and karyorrhexis in the lumen), bronchial epithelium: foci of inflammatory infiltration, no karyorrhexis, little damage	Vascular walls with inflammatory infiltration, sporadic single cell necrosis in the vascular walls, edema around the vascular wall, multiple hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, no eosinophils, more neutrophils sporadic karyorrhexis	No	No

Animal-No.	Vaccine group	% Dense Area	Bronchia	Vessels	DIC	Dense Area	Fibrosis	Syncytia
62	MeV	approximately 20% dense areas (macroscopical), bronchial and vessel associated, diffuse distribution	Bronchitis (lymphocytes, granulocytes and karyorrhexis in the lumen), Bronchial epithelium: foci of inflammatory infiltration, no karyorrhexis, little damage	Vascular walls with inflammatory infiltration, sporadic single cell necrosis in the vascular walls, multiple hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, eosinophile involved, sporadic karyorrhexis	No	No
63	MeV	50% dense areas, not clearly bronchial or vessel associated, diffuse distribution	Bronchitis (lymphocytes and karyorrhexis in the lumen), bronchial epithelium: foci of inflammatory infiltration, sporadic karyorrhexis, proliferation?	Vascular walls with inflammatory infiltration, sporadic single cell necrosis in the vascular walls, edema around the vascular walls, several hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, eosinophile involved, sporadic karyorrhexis	No	No
64	MeV	60% dense areas, not clearly bronchial or vessel associated, diffuse distribution	Bronchitis (little in the lumen), bronchial epithelium with focal inflammatory infiltration, proliferation?	Vascular walls with inflammatory infiltration (especially veins), several hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, no eosinophils, sporadic karyorrhexis	No	No
65	MeV-S	20% dense areas (microscopic), clearly bronchial associated	Bronchitis (little in the lumen), bronchial epithelium hardly affected.	Vascular walls with very little inflammatory infiltration, 2 x hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, isolated eosinophils, no karyorrhexis (1 x ?)	No	No
66	MeV-S	10% dense areas, clearly bronchial associated	Bronchitis (little in the lumen), bronchial epithelium hardly affected.	Vascular walls without inflammatory infiltration, several hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, isolated eosinophils, sporadic karyorrhexis	No	No
67	MeV-S	25% dense areas, clearly bronchial associated	Mild bronchitis (mostly little in the lumen), bronchial epithelium with sporadic inflammatory infiltration, otherwise not affected.	Vascular walls with infiltration of eosinophils, several hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils around vessels, no karyorrhexis	No	No
68	MeV-S	50% dense areas, clearly bronchial-associated	Mild bronchitis (mostly little in the lumen), bronchial epithelium with focal inflammatory infiltration otherwise not affected.	Vascular walls infiltration of eosinophils, several hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, massive eosinophils around vessels, no karyorrhexis	No	No
69	MeV-S	30% dense areas, clearly bronchial associated	Mild bronchitis (lymphocytes and karyorrhexis in the lumen), bronchial epithelium with focal inflammatory infiltration, significant damage to the bronchial epithelium	Vascular walls with inflammatory infiltration, karyorrhexis in the vascular wall, edema around vessels, massive hemorrhage in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, significant amount of eosinophils, foci with karyorrhexis	No	Yes
70	MeV-S	60% dense areas, not clearly bronchial associated	Mild bronchitis (lymphocytes, karyorrhexis in the lumen), bronchial epithelium with focal inflammatory infiltration; significant damage to the bronchial epithelium.	Vascular walls with inflammatory infiltration, edema in the vascular wall, edema around the vessels, massive hemorrhages in the tissue.	No	mostly lymphocytes, macrophages, pneumocytes, isolated eosinophils, sporadic karyorrhexis	No	No

Table S2. Histopathological analysis of lung tissue of vaccinated Syrian hamsters batch #2 upon challenge with SARS-CoV-2. Related to Figure 4. Hamsters were vaccinates with medium (MOCK), MV_{vac2}-ATU(P) as measles-only vector control (MeV), MeV_{vac2}-SARS2-S(H) (MeV-S), or Alum-adjuvanted Spike protein (Alum+S). The left lobe of vaccinated hamster lungs was dissected 4 dpi. H& E staining revealed histopathological changes and immune cell infiltration assessed by a trained pathologist in a blinded manner. DIC, disseminated intravascular coagulation**.**

Animal-No.	Vaccine group	% Dense Area	Bronchia	Vessels	DIC	Dense Area	Fibrosis	Syncitia
#93	MOCK	about 30% dense areas, mostly bronchial associated	Bronchial epithelium with inflammatory infiltration, granulocytes in the lumen, partial erythrocytes, some bronchial epithelium in the surrounding tissue	Vascular walls sporadically infiltrated with inflammation, marked hemorrhages	No	few densed areas infiltrated with macrophages, pneumocytes, lymphocytes and granulocytes, no eosinophils, moderate karyorrhexis	No	No
#98	MOCK	max. 10%, small foci, not bronchial associated	slightly altered; low inflammatory infiltration, some inflammatory cells in the lumen	prominent endothelium, minor hemorrhage	No	with increased eosinophils; macrophages and lymphocytes	No	No
#105	MOCK	max. 10%, in a single condensed area, not bronchial associated	slightly altered; low inflammatory infiltration underneath the epithelium	prominent endothelium, minor hemorrhage	No	1 x dense area with macrophages and lymphocytes, hardly any granulocytes, no eosinophils. moderate karyorrhexis.	No	No
#109	MOCK	about 30%, dense areas not clearly bronchial associated	slightly altered; epithelium sporadically with inflammatory infiltration; granulocytes in the lumen	prominent endothelium, hemorrhage	No	Macrophages, pneumocytes, lymphocytes, hardly any granulocytes and eosinophils. Isolated foci with karyorrhexis.	No	No
#113	MOCK	max. 10%, in a single condensed area,	Epithelium clearly altered; scattered inflammatory infiltration, no granulocytes in the lumen	prominent endothelium, significant bleeding	No	Macrophages, pneumocytes, lymphocytes, hardly any granulocytes and eosinophils. Isolated foci with karyorrhexis.	No	No
#91	MeV-S	max. 10%, clear relation to bronchi.	Marked proliferation of the epithelium into the surrounding tissue. Epithelium with inflammatory infiltration	Prominent endothelium, minor hemorrhage?	No	Some eosinophils around vessels, macrophages, pneumocytes, lymphocytes and granulocytes, hardly any karyorrhexis.	No	No
#95	MeV-S	10% dense areas, small multiple foci, bronchial associated	Epithelium not signifiantly altered.	Prominent endothelium, scattered karyorrhexis in vessel walls, only 1 x hemorrhage	No	Some eosinophils in dense area, macrophages, pneumocytes, lymphocytes and granulocytes, hardly any karyorrhexis,	No	No
#99	MeV-S	minimal; only 3 small foci, strictly bronchial associated	Epithelium not significantly altered. Scattered Epithelium in the surrounding tissue.	Prominent endothelium, no hemorrhage	No	Some eosinophils in dense area, macrophages, pneumocytes, lymphocytes and granulocytes, no karyorrhexis.	No	No
#102	MeV-S	minimal; only smallest foci, bronchial associated	Regular	Prominent endothelium, no hemorrhage	No	Some eosinophils in dense area, macrophages, pneumocytes, lymphocytes and granulocytes, no karyorrhexis.	No	Suspected

Animal-No.	Vaccine group	% Dense Area	Bronchia	Vessels	DIC	Dense Area	Fibrosis	Syncitia
#114	MeV-S	30% dense areas, bronchial associated	Bronchitis, lymphocytes and a few granulocytes in the lumen; inflammatory infiltration of the epithelium. Epithelium in the surrounding tissue.	Prominent endothelium, perivasculitis with some eosinophils, hemorrhage in the surrounding area.	No	Macrophages, pneumocytes, lymphocytes. Hardly any granulocytes and eosinophils. Sporadic karyorrhexis.	No	No
#94	Alum+S / Dexa	10% dense areas, not bronchial associated	Bronchitis, epithelium with inflammatory infiltration	Vasculitis, prominent endothelium, low inflammatory infiltration of the vessel walls	No	Some eosinophils especially around vessels (poorly visible due to hemorrhages) Macrophages, pneumocytes, lymphocytes and granulocytes.	No	No
#97	Alum+S	50% dense areas, not bronchial associated	Bronchitis, epithelium with inflammatory infiltration, granulocytes and lymphocytes in the lumen, bronchial epithelium in the surrounding tissue	Marked vasculitis with inflammatory infiltration of the wall (incl. eosinophils), many eosinophils in the surrounding of the vessel walls	No	Many eosinophils especially around vessels. Macrophages, pneumocytes, lymphocytes and granulocytes.	No	No
#101	Alum+S	50% dense areas, not bronchial associated	Epithelium not infiltrated by inflammation, blood in the lumen	Marked vasculitis with inflammatory infiltration of the vessel wall, no edema around vessels, massive hemorrhage in the surrounding tissue.	No	Massive foci of eosinophils (vessels?), macrophages, pneumocytes, lymphocytes and granulocytes.	No	No
#104	Alum+S	60% dense areas, not bronchial associated	Epithelium little affected; granulocytes in the lumen	Marked vasculitis with inflammatory infiltration of the wall.	No	Massive foci of eosinophils (vessels?), macrophages, pneumocytes, lymphocytes and granulocytes.	No	No
#106	Alum+S	70% dense areas, not bronchial associated	Bronchitis, epithelium with little inflammatory infiltration, epithelium irregular, granulocytes (eosinophils) in the lumen	Marked vasculitis with low infiltration of eosinophils in the vessel wall, massive hemorrhage in the surrounding tissue.	No	Many eosinophils especially around vessels. Macrophages, pneumocytes, lymphocytes and granulocytes. Karyorrhexis.	No	No
#107	Alum+S / Dexa	30% dense areas, not bronchial associated	Bronchitis, epithelium with little inflammatory infiltration, epithelium irregular, granulocytes (eosinophils) in the lumen	Marked vasculitis with inflammatory infiltration of the vessel wall, hemorrhage in the surrounding area.	No	Some eosinophils, but more granulocytes, macrophages, pneumocytes, lymphocytes.	No	No
#111	Alum+S / Dexa	20% dense areas, bronchial associated	Epithelium hardly affected, single eosinophils in lumen	Prominent endothelium, hemorrhages.	No	Mild Infektion, Eosinophils present, often focal, Macrophages, pneumocytes, lymphocytes, granulocytes, karyorrhexis.	No	No
#112	Alum+S	60% dense areas, not bronchial-associated, highly condensed	Epithelium hardly affected, Detritus and granulocytes in the lumen	Prominent endothelium, sporadic inflammatory inflammation in the vessel wall, massive perivascular lymphatic infiltration.	No	Some eosinophils, granulocytes, macrophages, pneumocytes, lymphocytes low karyorrhexis.	No	No

Animal-No.	Vaccine group	% Dense Area	Bronchia	Vessels	DIC	Dense Area	Fibrosis	Syncitia
#116	Alum+S / Dexa	minimal; only smallest foci, strictly bronchial associated	Regular	Prominent endothelium, sporadic inflammatory infiltration.	No	Eosinophils clearly present, macrophages, pneumocytes, lymphocytes.	No	No
#117	Alum+S / Dexa	20% dense areas, not clearly bronchial associated	Epithelium appears disorganized; no infiltration of epithelium	Prominent endothelium, vessel wall infiltrated with eosinophils. Massive eosinophils in lumen + surrounding tissues.	No	Many eosinophils, macrophages, pneumocytes, lymphocytes, granulocytes.	No	No
#118	Alum+S	70% dense areas, not bronchial associated, highly condensed	Epithelium appears disorganized; no infiltration of epithelium low amount of inflammatory cell in the lumen	Prominent endothelium massive lymphatic sheath, massive eosinophils in the lumen + around the vessels, hemorrhages.	No	Massive eosinophils present, macrophages, pneumocytes, lymphocytes, granulocytes.	No	No
#120	Alum+S / Dexa	40% dense areas, not bronchial associated	Epithelium clearly altered; occasional inflammatory infiltration, granulocytes in the lumen; epithelium in the surrounding tissue	Prominent endothelium, inflammatory infiltration (eosinophils) of the wall, no hemorrhage.	No	Some eosinophils, granulocytes, macrophages, pneumocytes, lymphocytes low karyorrhexis.	No	Suspected
hamster #1	naive	Regular	Regular	Regular.	No	Regular.	No	No
hamster #2	naive	Regular	Regular	Regular.	No	Regular.	No	No

Table S3. Statistical evaluation of selected scRNA-Seq data sets. Related to Figure 6. scRNA data concerning relevant selectively up-regulated gene sets in depicted annotared cell types between differently vaccinated hamster cohorts were analysed to reveal statistical significance of de-regulated genes as depicted in Fig. 6D and 6F. Differential expression of the selected cytokines in different celltype compartments between treatment groups was performed using the FindMarkers function from Seurat with the default parameters. *, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001. MΦ, macrophages; DC, dendritic cells; NK, natural killer cells; ILC, innate lymphoid cells.

all cells	*Il4*			*Il5*			*IL13*			*IL19*			*CCL11*		
	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock
AT1/AT2															
Endothelial cells															
B cells															
Alveolar MΦ															
Lung MΦ										****	****		****	****	
Monocytic MΦ											*		***	****	
Treml4^{+} MΦ															
Neutrophils															
T/NK cells	*	****	***	****	****	****	****	****	***						
Myeloid DCs															
Plasmacytoid DC															
Fibroblasts															

T/NK cell compartment	*Il4*			*Il5*			*IL13*		
	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock	Alum+S vs. Mock	Alum+S vs. MeV	MeV vs. Mock
Naive									
Memory									
Activated		****	*	**	****	****	****	****	**
Regulatory									
NK									
ILC					***			**	

Table S4. Primer and Probe sets used. 6-Carboxyfluorescein (6FAM), BlackBerry® Quencher (BBQ), Cyanine 5 (Cy5).

Name	Sequenz	Reference
E_Sarbeco_F	5´-ACAggTACgTTAATAgTTAATAgCgT-3´	Corman et al., 2020
E_Sarbeco_R	5´-ATATTgCAgCAgTACgCACACA-3´	Corman et al., 2020
E_Sarbeco probe	5‘-(6FAM)-ACACTAgCCATCCTTACTgCgCTTCg(BBQ)-3‘	Corman et al 2020
IL-5_For	5’-gCCgTAgCCATggAgATC-3’	Mendlovic et al., 2014
IL-5 Seq Rev	5’-CgATgCACAgCTggTgCT-3’	This Paper
IL-5 probe	5’-(Cy5)-AgCTgTCCACTCACCgAGCTCTACTGAC (BBQ)-3`	This Paper
RPL18 F	5‘-gTTTATgAgTCgCACTAACCg-3‘	Zivcec et al., 2011
RPL18 R	5‘-TgTTCTCTCggCCAggAA-3‘	Zivcec et al., 2011
RPL18 probe	5‘-(Cy5)-TCTgTCCCTgTCCCggATgATC(BBQ)-3‘	Zivcec et al., 2011
Eotaxin forward	5’- AgAgAgCCTgAgACCAACAC-3’	Stanelle-Bertram et al., 2020
Eotaxin reverse	5’-AACTgggATAgAgCCTgggTg-3’	Stanelle-Bertram et al., 2020
Eotaxin-probe	5’-(6FAM)-TTgTggCCACTgCCTTCACCTC (BBQ)-3’	This Paper
IL-4-F	5'-ACAgAAAAAgggACACCATgCA-3'	Espitia et al., 2010
IL-4-R	5'-gAAgCCCTgCAgATgAggTCT-3'	Espitia et al., 2010
IL-4 probe	5'-(6FAM)-AgACgCCCTTTCAgCAAggAAgAACTCC-(BBQ)-3'	Espitia et al., 2010
IL-13-F	5'-AAATggCgggTTCTgTgC-3'	Espitia et al., 2010
IL-13-R	5'-AATATCCTCTgggTCTTgTAgATgg-3'	Espitia et al., 2010
IL-13 probe	5'-(Cy5)-TggATTCCCTgACCAACATCTCTAgTTgC (BBQ)-3'	Espitia et al., 2010