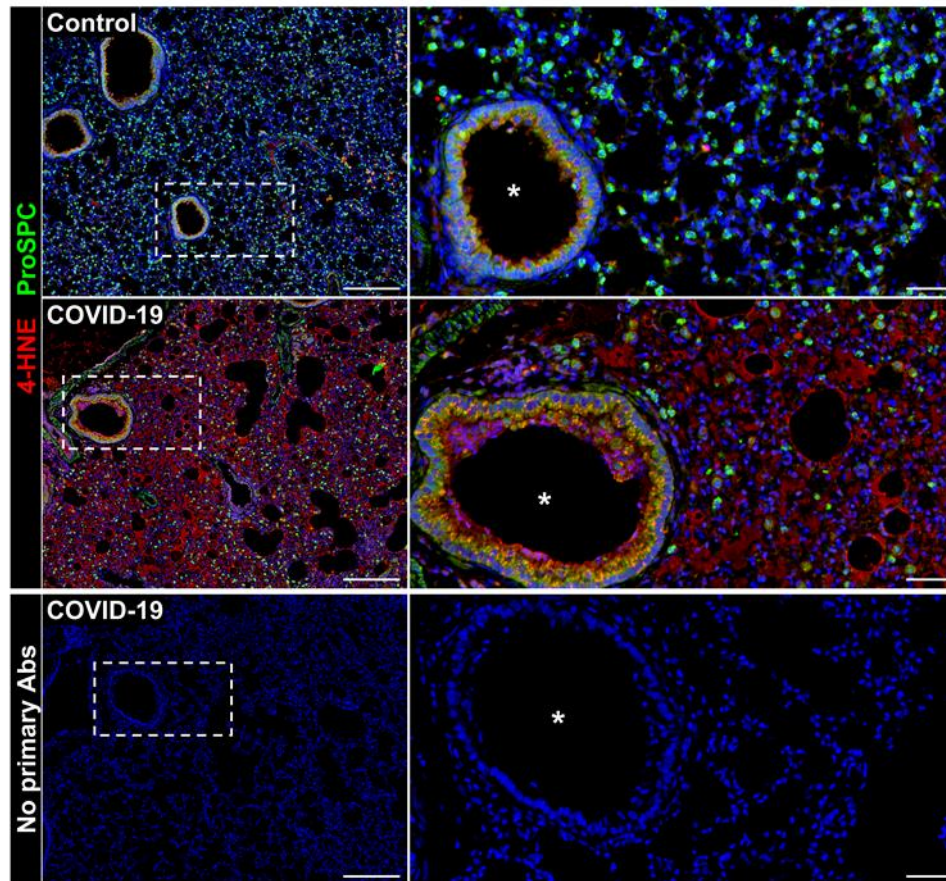


**Supplemental Results:****Supplemental Table S4**

Signaling pathways altered by SARS-CoV-2 in hamsters. KEGG pathways shown were observed from using the list of proteins with up or downward relative abundance having a P-value < 0.05 and  $\geq 3$  proteins. Protein abbreviations correspond to UniProt gene names.

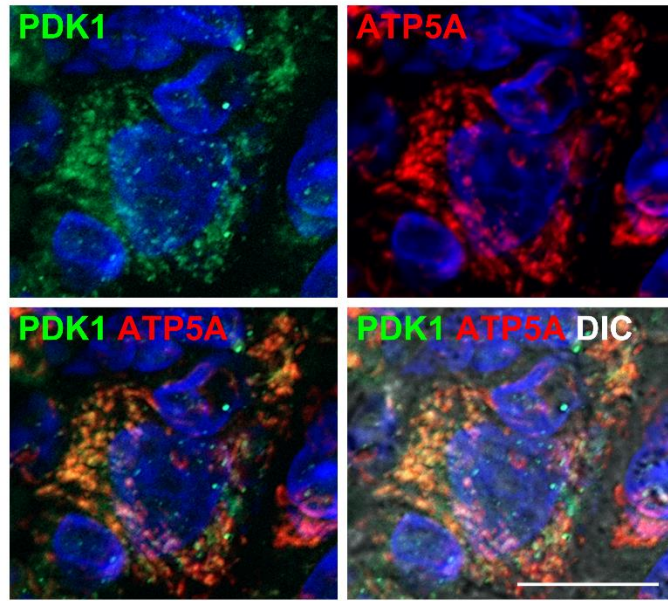
<b>Up-regulated Protein Pathways by SARS-CoV-2</b>	<b>Proteins</b>	<b>P-value</b>
Complement and coagulation cascades	VTN, FGA, FGG, KNG1	8.8E-6
Platelet activation	FGA, FGG, GNAI2	9.2E-4
Pathways in cancer	GSTM3, KNG1, GNAI2	0.048
<b>Down-regulated Protein Pathways by SARS-CoV-2</b>	<b>Proteins</b>	<b>P-value</b>
Alzheimer's disease	PSMA2, GAPDH, SLC25A4, PSMA7, RTN4	2.0E-4
Parkinson's disease	HSPA5, PSMA2, SLC25A4, PSMA7	5.0E-4
Prion disease	HSPA5, PSMA2, SLC25A4, PSMA7	7.0E-4
Spinocerebellar ataxia	PSMA2, SLC25A4, PSMA7	0.001
Pathways of neurodegeneration	HSPA5, PSMA2, SLC25A4, PSMA7	0.005
Huntington's disease	PSMA2, SLC25A4, PSMA7	0.011
Amyotrophic lateral sclerosis	HSPA5, PSMA2, PSMA7	0.017

## Supplemental Figures:

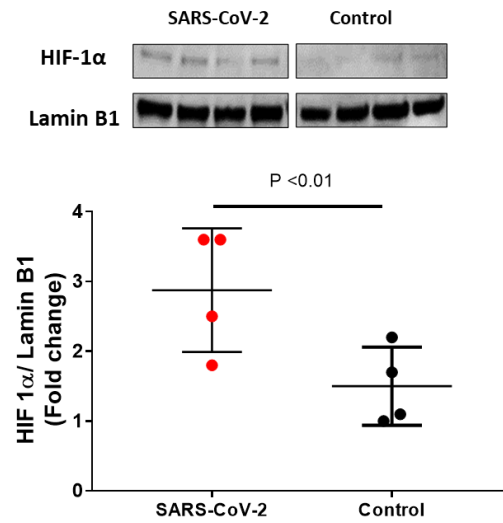


### Supplemental Figure S1. Increased 4-HNE deposition in SARS-CoV-2-infected lungs.

Double immunofluorescence imaging of 4-HNE (end-product of lipid peroxidation) and ProSPC in lung sections from an uninfected hamster (control) and a SARS-CoV-2-infected hamster at 4 dpi. Control sections show a normal distribution of ProSPC-positive AT2 cells and minimal 4-HNE staining. Infected lungs show extensive 4-HNE deposition in damaged epithelial areas with loss of ProSPC-expressing AT2 cells and in the cellular debris found along the inner lining of bronchioles. No primary antibody experiments showed negative staining in the same infected lung section. Scale bars: 250  $\mu$ m, 10  $\mu$ m (magnified panels); \* denotes the lumen of a bronchiole.

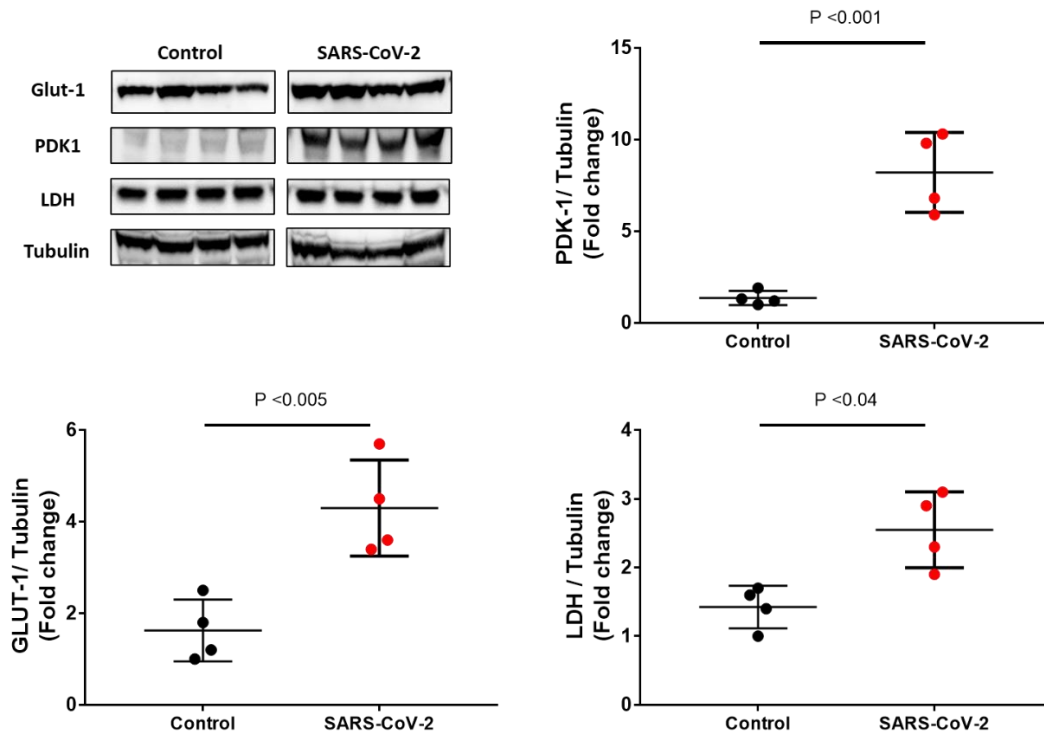


**Supplemental Figure S2. Mitochondrial localization of PDK1.** Double immunofluorescence imaging of PDK1 and the mitochondrial marker ATP5A in lung sections from a SARS-CoV-2-infected hamster at 4 dpi. Nuclei were counterstained with Hoechst 33342 (blue). Scale bars: 10  $\mu$ m. DIC = differential interference contrast.



**Supplemental Figure S3. Densitometric analysis for relative expression of HIF-1α.**

Immunoblotting showing HIF-1α expression in nuclear extracts from lung tissue lysates of SARS-CoV-2 infected and non-infected hamsters (upper panel) and Lamin B1 as loading control (lower panel). Densitometry was done by BioRad Image Lab 5.2.1 software.



**Supplemental Figure S4. Densitometric analyses for relative expressions of Glut-1, PDK1 and LDH.** Immunoblotting showing Glut-1, PDK1 and LDH levels in total lung homogenates of SARS-CoV-2 infected and non-infected hamsters. Equal protein loading was confirmed by probing with anti-tubulin antibody (lower panel). Densitometric analyses for relative expression of Glut-1, PDK1, LDH were done by BioRad Image Lab 5.2.1 software.