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## **Supplemental Information**

## A Mouse Model of SARS-CoV-2

## **Infection and Pathogenesis**

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Figure S1. Weight change of mice infected with SARS-CoV-2. Wild-type C57BL/6 mice, young (4.5 weeks old) and aged (30 weeks old) hACE2 humanized mice (n=3) were intranasally infected with  $4 \times 10^5$  pfu of SARS-CoV-2 and monitored daily for weight change. Related to Figure 2.



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Figure S2. Immunostaining of brain section in SARS-CoV-2 infected hACE2 mice. (A) Immunofluorescence staining of mouse brain paraffin sections for SARS-Cov-2 S protein (green) and DAPI (blue). Immunofluorescence staining analysis for the mainly infected cell types in the brain. (B) Immunofluorescence staining of tissue paraffin sections for SARS-Cov-2 S protein (green), neuron marker NeuN (gold), astrocyte marker GFAP (red) and microglial cell marker Iba1 (white). Related to Figure 2.

Table S1. Cytokine levels in the serum of SARS-CoV-2 infected mice. Related to Figure 3.

		IL-3	IL-1β	TNF-α	IL-9	IFN-γ	IL-2	IL-13	IL-6 IL-4	MCP-1	IL-5	IL-1α	G-CSF	RANTES	IL-10	кс	IL-17A	GM-CSF	Eotaxin	ΜΙΡ-1β	IL-12p40	MIP-1α	IL-12p70
wt	NO.1	1.6	4.1	74.9	37.5	24.7	2.4	61.5	2.6 2.1	101.0	5.5	8.3	61.0	4.3	31.1	29.9	31.8	33.8	25.8	58.1	64.4	8.4	111.1
	NO.2	3.0	7.3	112.0	43.9	26.5	4.1	98.9	3.6 3.5	136.1	10.2	11.2	55.1	7.3	58.8	34.5	27.4	43.2	19.8	45.5	45.8	7.4	136.8
	NO.3	2.2	5.5	82.7	33.7	23.9	1.9	65.3	3.2 2.9	279.6	10.0	7.8	71.9	5.4	45.6	34.5	36.4	37.1	19.9	33.8	67.7	15.9	146.4
hACE2- young	NO.1	2.9	6.6	92.2	46.2	28.8	3.9	84.3	3.3 4.1	130.9	9.1	8.3	56.9	6.6	52.7	37.8	24.2	42.1	21.6	68.0	51.8	4.1	169.7
	NO.2	2.1	5.3	93.1	40.4	25.4	3.3	77.4	2.9 3.1	114.3	7.8	6.0	41.7	5.1	38.8	34.0	30.4	38.6	19.5	59.6	26.4	4.2	141.2
	NO.3	1.7	4.7	69.0	37.8	22.1	2.5	61.5	2.5 2.6	105.3	6.5	5.3	45.7	3.4	39.5	30.9	30.3	36.2	15.5	51.8	37.2	3.3	140.0
hACE2- aged	NO.1	1.9	4.2	77.7	33.9	21.3	3.1	48.3	3.0 2.2	117.7	6.9	4.3	71.2	7.3	40.1	25.4	41.7	34.9	47.8	46.5	69.8	4.6	123.2
	NO.2	2.2	6.5	124.5	48.3	34.0	0.7	87.8	7.5 4.1	159.8	11.0	8.3	445.9	8.5	47.4	61.7	35.3	44.8	44.8	65.9	43.5	6.0	152.5
	NO.3	4.8	14.1	184.9	203.4	161.0	6.6	143.8	6.5 6.3	276.5	13.4	9.9	114.2	13.1	83.1	64.9	31.3	66.1	106.5	174.6	83.9	9.0	210.0

Primer/Probe name	Primer/Probe sequence							
L-GT-F1	ggtgatgtaaatatttgcccacaggt							
L-GT-R1	cacgacattcaacagaccttgvatt							
R-GT-F1	taacgttactggccgaagccgctt							
R-GT-R1	ctcagagatggtttcagcaaacagc							
ehACE2 F1	cgaagccgaagacctgttcta							
ehACE2 R1	gggcaagtgtggactgttcc							
emACE2-F1	tccagactccgatcatcaagc							
emACE2-R1	tgctcatggtgttcagaattgt							
CoV-F3	tcctggtgattcttcttcaggt							
CoV-R3	tctgagagagggtcaagtgc							
CoV-P3	agctgcagcaccagctgtcca							

Table S2. Primers and probes used for PCR or qRT-PCR analysis.