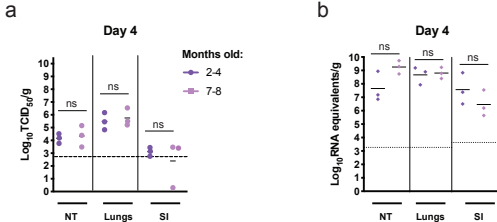


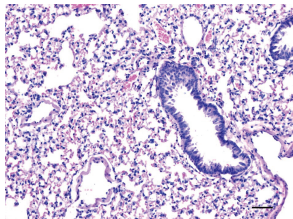
## **Supplementary Information**

### **SARS-CoV-2 infection and transmission in the North American deer mouse**

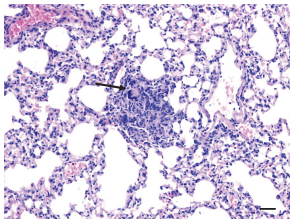


**Supplementary Figure 1: Viral burden in the tissues by age.** Eight to thirty two-week old male or female deer mice (*P. maniculatus*) were inoculated with  $1 \times 10^5$  TCID<sub>50</sub> of SARS-CoV-2 by an intranasal (i.n.) route of administration. **a**, Infectious viral load in the nasal turbinates, lung, and proximal small intestine at 4 dpi. **b**, Viral RNA load in the nasal turbinates, lung, and proximal small intestine at 4 dpi. Solid lines indicate means. Dashed lines and dotted lines indicate the limit of detection for the TCID50 assay and qRT-PCR assay, respectively. ns =  $P > 0.05$ , ANOVA with multiple comparison correction.

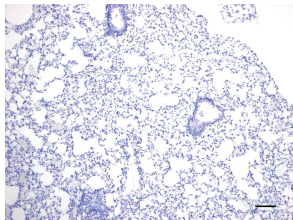
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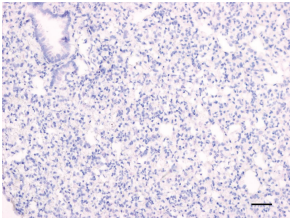
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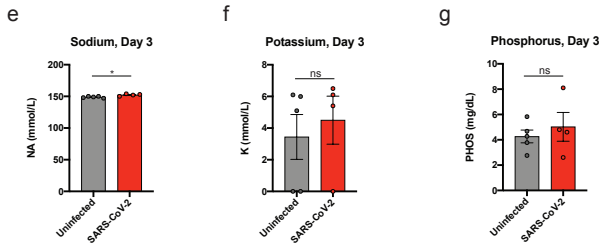
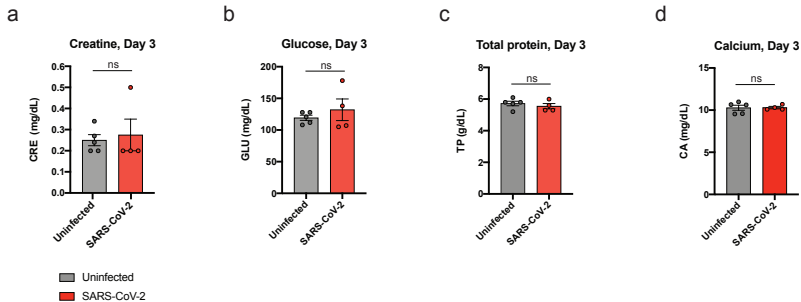
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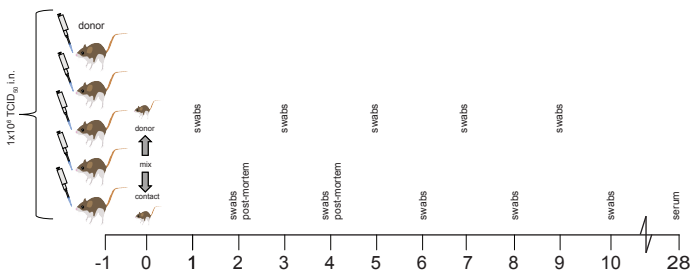
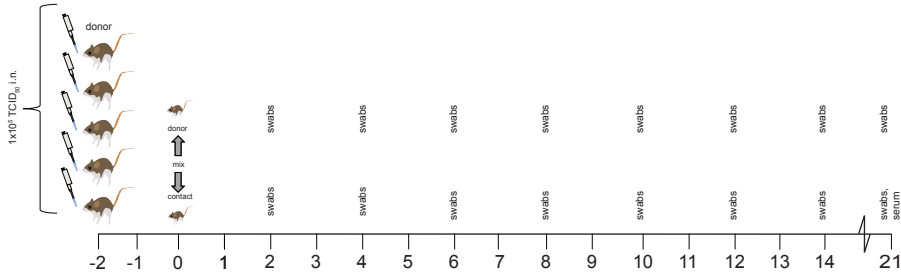


**Supplementary Figure 2: Histological analysis of lungs at 21 days following SARS-CoV-2 exposure.** Adult male and female deer mice were exposed to  $10^5$  TCID<sub>50</sub> SARS-CoV-2 by an i.n. route of infection. Lesions were not observed at this time point (a) except for a small focus of inflammation (b) with presence of syncytial cell (arrow). ISH using both anti-sense probe (c) and sense probe (d) was negative. Scale bars = 50  $\mu$ m (a-b) and 100  $\mu$ m (c-d). A total of three biological replicates (individual animals) were assessed at each time point, and the selected panels are representative of these findings.



**Supplementary Figure 3: Serum biochemical values.** Serum biochemistry were measured in uninfected and SARS-CoV-2-infected deer mice at 3 dpi ( $10^6$  TCID<sub>50</sub>, i.n. route). Bars indicate mean, error bars indicate SEM.  $n = 5/4$  biologically independent samples (individual animals) for uninfected/infected. \* =  $P < 0.05$ , ns =  $P > 0.05$ , two-tailed, unpaired t test with Welch's correction (e,  $P = 0.0176$ ).



**a****b**

**Supplementary Figure 4: Schematic of deer mouse SARS-CoV-2 transmissions study 1 & 2.** Adult male and female deer mice were exposed to **a)**  $1 \times 10^8$  TCID<sub>50</sub> or **b)**  $1 \times 10^8$  TCID<sub>50</sub> SARS-CoV-2 by i.n. route of infection. At **a)** 1 dpi or **b)** 2 dpi individual inoculated donor deer mice were transferred to a new cage and co-housed with a single naïve deer mouse (1:1 ratio) to assess SARS-CoV-2 transmission by direct contact. Deer mice were either maintained in direct contact throughout the study for serial swabbing or were humanely euthanized on 2 or 4 dpi for tissue collection.

Figure	Panel	Description	DPI	DM Cohort 1	DM Cohort 2	DM Cohort 3	DM Cohort 4	DM Cohort 5	DM Cohort 6	DM Cohort T1a	DM Cohort T1b	DM Cohort T2
				1x10 <sup>5</sup> TCID <sub>50</sub>	1x10 <sup>5</sup> TCID <sub>50</sub>	1x10 <sup>5</sup> TCID <sub>50</sub>	1x10 <sup>5</sup> TCID <sub>50</sub>	N/A	1x10 <sup>6</sup> TCID <sub>50</sub>	1x10 <sup>6</sup> TCID <sub>50</sub>	1x10 <sup>5</sup> TCID <sub>50</sub>	
				n = 6	n = 3	N/A	n = 3	n = 5	n = 5	N/A	N/A	N/A
				2-4 months (n = 3), 7-8 months (n = 3)	n = 6 (12 total)	n = 6	n = 5	N/A	n = 5 (10 total)	infected donor (n = 5), naïve (n = 5)	2x [infected donor (n = 5), naïve (n = 5)]	infected donor (n = 5), naïve (n = 5)
				M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F
				0-21/28 dpi	2/4 dpi	0/2/4/6/8 dpi (swabs); 0,7,14,21,28 (blood)	6 dpi	2 dpi	1/3 dpi	-1,1,3,5,7,9 (donor); 4,6 (donor);	2/4 (naïve)	0,2,4,6,8,10,12,14,21
2	a	Survival	0 - 21	X								
2	b	Weight	0 - 21	X								
2	c	Nasal Turbinates	2/4		X							
2	d	Lung	2/4		X							
2	e	Small Intestine	2/4		X							
2	f	Colon	2/4		X							
2	g	Oropharyngeal Swabs	0/2/4/6/8			X						
2	h	Rectal Swabs	0/2/4/6/8			X						
2	i	Nasal Wash*	6				X					
2	j	Urine	6					X		X (donor)		
2	k	Faeces	4					X		X (donor)		
2	l	Blood	1/3					X	X			
2	m	NT/Lung/SI	21	X								
3	a	H&E/ISH NT	2/4		X							
3	b	H&E/ISH Lungs	2/4		X							
4	a	Hematologic Values**	3						X			
4	b	NLR**	3						X			
4	c	ALT	3						X			
4	d	ALB	3						X			
4	e	BUN	3						X			
4	f	Lung Cytokines	2		X			X				
4	g	ELISA	0,7,14,21,28	X (uninfected)		X						
4	h	PRNT90	28	X (uninfected)		X						
5	a	Oropharyngeal Swabs (RNA)	-1 - 10 dpi/dpc							X		
5	b	Rectal Swabs (RNA)	-1 - 10 dpi/dpc							X		
5	c	Oropharyngeal Swabs (TCID <sub>50</sub> )	-1 - 10 dpi/dpc							X		
5	d	Rectal Swabs (TCID <sub>50</sub> )	-1 - 10 dpi/dpc							X		
5	e	Nasal wash, NT, lung	2 dpc								X	
5	f	Nasal wash, NT, lung	4 dpc								X	
5	g	ELISA	21 dpc							X		
5	h	Oropharyngeal Swabs (RNA)	0,2,4,6,8,10,12,14,21									X
5	i	Rectal Swabs (RNA)	0,2,4,6,8,10,12,14,21									X

Supplementary Table 1. Experimental design (Deer mouse cohorts, group sizes, doses).

DM: deer mouse  
dpi: days post-infection  
NT: nasal turbinates  
SI: small intestine  
ISH: In situ hybridization  
NLR: neutrophil-to-lymphocyte ratio  
ALT: alanine aminotransferase  
ALB: blood albumin  
BUN: blood urea nitrogen  
ELISA: enzyme-linked immunosorbent assay  
PRNT90: plaque reduction neutralization test 90%  
\* one sample not obtained  
\*\* two samples not obtained

<b>Primer name</b>	<b>Primer/probe sequence</b>
E_Sarbeco_F1	5'- ACAGGTACGTTAATAGTTAATAGCGT-3'
E_Sarbeco_R2	5'-ATATTGCAGCAGTACGCACACA-3'
E_Sarbeco_P1 (probe)	5'-FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ-3'

**Supplementary Table 2. Primer/probe sequences.**

FAM: Fluorescein amidite

BBQ: BlackBerry quencher