

Nasal mucosa exploited by SARS-COV-2 for replicating and shedding during
reinfection

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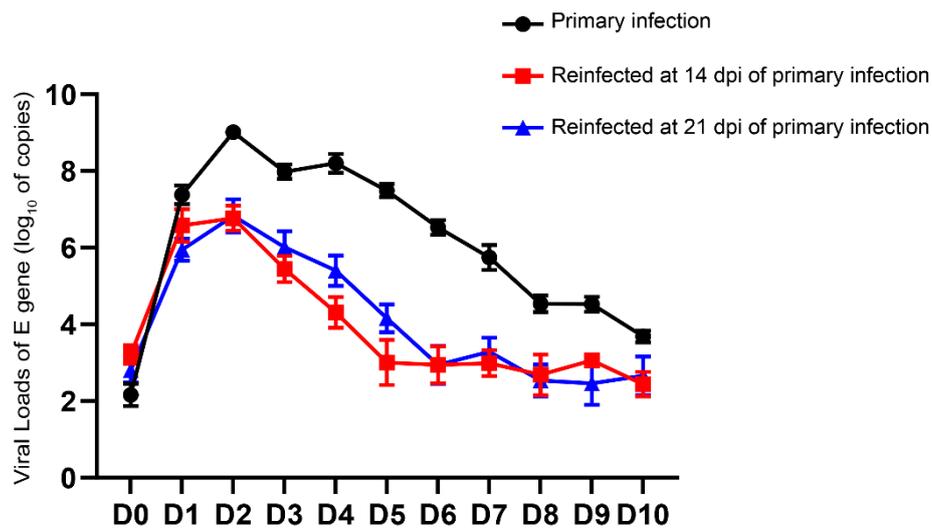


Figure S1. Viral shedding in 1 ml nasal washes from 0 dpi to 10 dpi in the primary infection and reinfection.

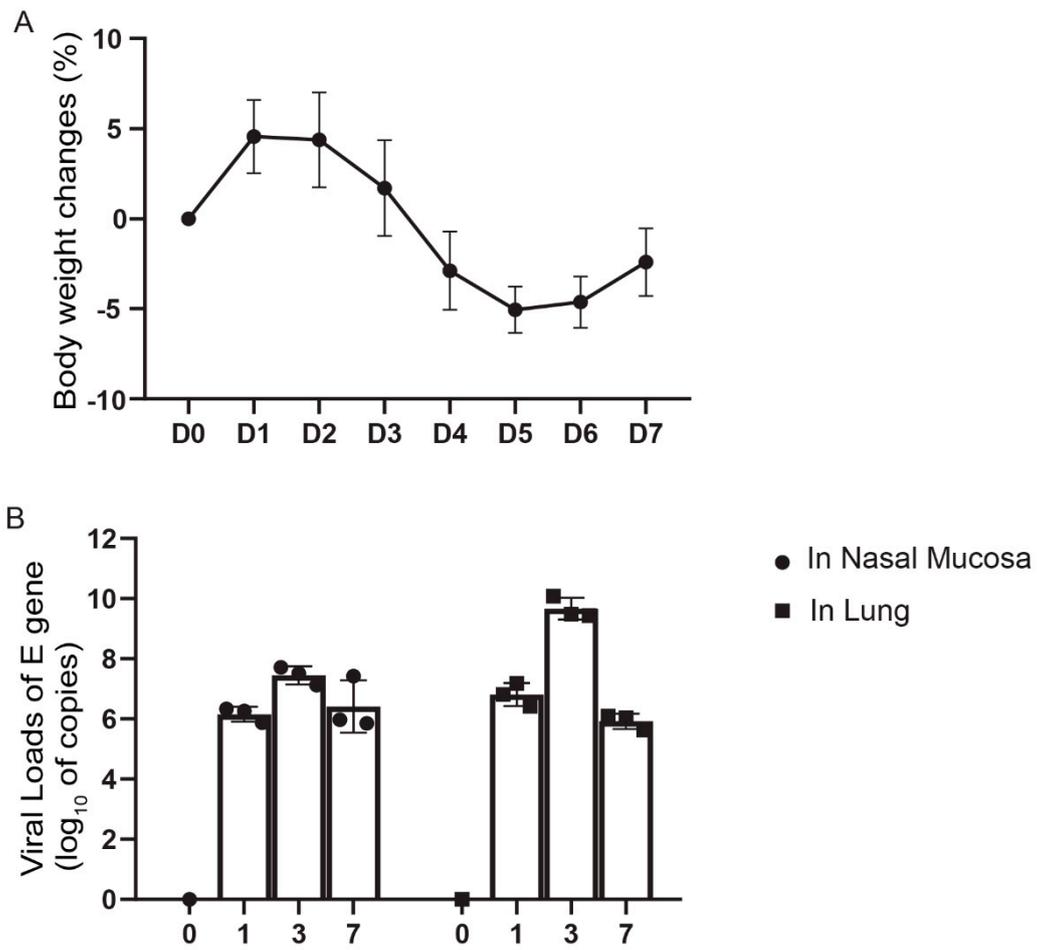


Figure S2. The infectivity in healthy Syrian hamsters of the shedding from upper respiratory tract in the primary infection and reinfection.

Primary infection	TTGTTTGTTCCTGTTTATTGCCACTAGTCTCTAGTCAGTGTGTTAATCTTACAACCGAAGTCAATACCOCCTGCATACACTAATCTTTCACAC	100
Reinfection at 14 dpi	TTGTTTGTTCCTGTTTATTGCCACTAGTCTCTAGTCAGTGTGTTAATCTTACAACCGAAGTCAATACCOCCTGCATACACTAATCTTTCACAC	100
Reinfection at 21 dpi	TTGTTTGTTCCTGTTTATTGCCACTAGTCTCTAGTCAGTGTGTTAATCTTACAACCGAAGTCAATACCOCCTGCATACACTAATCTTTCACAC	99
Consensus	atggttggttttctgtttttattggccactagctctctagtcagtggttaattcttaaacacagaactcaattaccocctgcatacactaattctttccacac	
Primary infection	GTGGTGTATTACCGTGCAAAAGTTTCAGATCTCAGTTTTACATCAACTCAGGACTGTTCCTACCTTTCTTTCCAAATGTACTTGGTTCGATCG	200
Reinfection at 14 dpi	GTGGTGTATTACCGTGCAAAAGTTTCAGATCTCAGTTTTACATCAACTCAGGACTGTTCCTACCTTTCTTTCCAAATGTACTTGGTTCGATCG	200
Reinfection at 21 dpi	GTGGTGTATTACCGTGCAAAAGTTTCAGATCTCAGTTTTACATCAACTCAGGACTGTTCCTACCTTTCTTTCCAAATGTACTTGGTTCGATCG	199
Consensus	gtgggtgtttataccctgcaaaagtcttcagatctcagttttacatccaactcaggactgttcttaccctttcttccaatgttacttggttccatgct	
Primary infection	TATACATGCTCTGGGACCAATGTAAGAGGTTGATAACCCGTCTCAACATTTAATGATGGTGTATTTTGGTCCACTGAGAAGTCTACACATA	300
Reinfection at 14 dpi	TATACATGCTCTGGGACCAATGTAAGAGGTTGATAACCCGTCTCAACATTTAATGATGGTGTATTTTGGTCCACTGAGAAGTCTACACATA	300
Reinfection at 21 dpi	TATACATGCTCTGGGACCAATGTAAGAGGTTGATAACCCGTCTCAACATTTAATGATGGTGTATTTTGGTCCACTGAGAAGTCTACACATA	299
Consensus	tatacatgtctctgggaccaaaggtaagaggtttgataacccgtctcaacatttaatgatgggtttattttggctccactgagaagctcaacata	
Primary infection	ATAAGAGGCTGGATTTTGGTACTACTTAGATTCGAAGACCCAGTCCCTACTTATTGTTAATAACGCTACTAATGTGTTATTAAAGCTGTGAATTC	400
Reinfection at 14 dpi	ATAAGAGGCTGGATTTTGGTACTACTTAGATTCGAAGACCCAGTCCCTACTTATTGTTAATAACGCTACTAATGTGTTATTAAAGCTGTGAATTC	400
Reinfection at 21 dpi	ATAAGAGGCTGGATTTTGGTACTACTTAGATTCGAAGACCCAGTCCCTACTTATTGTTAATAACGCTACTAATGTGTTATTAAAGCTGTGAATTC	399
Consensus	ataagaggctggatttttggtagtacttttagatcgaagaccagctccctacttattgtaataacgctactaattgttattaaagctgtgaatttc	
Primary infection	AAITTTGTAATGATCCATTTTGGGTGTTTATTACCAAAAAACAACAAAGTTGGATGGAAGTGAGTTCAGAGTTTATTCTAGTCCGAATAATTGCAC	500
Reinfection at 14 dpi	AAITTTGTAATGATCCATTTTGGGTGTTTATTACCAAAAAACAACAAAGTTGGATGGAAGTGAGTTCAGAGTTTATTCTAGTCCGAATAATTGCAC	500
Reinfection at 21 dpi	AAITTTGTAATGATCCATTTTGGGTGTTTATTACCAAAAAACAACAAAGTTGGATGGAAGTGAGTTCAGAGTTTATTCTAGTCCGAATAATTGCAC	499
Consensus	aaatgttgatgatccattttgggtggtttattaccacaaaacaaagttggatggaaagtgagttcagagtttattctagtcgcaataattgcac	
Primary infection	TTTTGAATATGCTCTCAGCCCTTTCTTATGGACCTTGAAGGAAAACAGGGTAATTTCAAAAATCTTAGGGATTTGTTTAAAGAAATTTAGTGGTAT	600
Reinfection at 14 dpi	TTTTGAATATGCTCTCAGCCCTTTCTTATGGACCTTGAAGGAAAACAGGGTAATTTCAAAAATCTTAGGGATTTGTTTAAAGAAATTTAGTGGTAT	600
Reinfection at 21 dpi	TTTTGAATATGCTCTCAGCCCTTTCTTATGGACCTTGAAGGAAAACAGGGTAATTTCAAAAATCTTAGGGATTTGTTTAAAGAAATTTAGTGGTAT	599
Consensus	ttttgaatgtctctcagccctttcttattggaccttgaaggaacacaggttaattcaaaaatcttagggaatttggtttgaagaatattgatggttat	
Primary infection	TTTAAATATATCTAAGCACAGCCCTAATTAATTTAGTGGGTGATCTCCCTCAGGGTTTTCCGGCTTTAGAACCATTGGTAGATTTGCCAATAGGTATTA	700
Reinfection at 14 dpi	TTTAAATATATCTAAGCACAGCCCTAATTAATTTAGTGGGTGATCTCCCTCAGGGTTTTCCGGCTTTAGAACCATTGGTAGATTTGCCAATAGGTATTA	700
Reinfection at 21 dpi	TTTAAATATATCTAAGCACAGCCCTAATTAATTTAGTGGGTGATCTCCCTCAGGGTTTTCCGGCTTTAGAACCATTGGTAGATTTGCCAATAGGTATTA	699
Consensus	tttaaatatattctaaagcacagccctaatatttagtgggtgactctccctcagggttttccggctttagaaccattggtagatttgcacaataggtatta	
Primary infection	ACATCACTAGGTTCAAACTTTACTTCTTACATAGAAGTATTGACTCTGGTATCTTCTCAGGTTGACAGCTGGTGCAGCTTATTAATG	800
Reinfection at 14 dpi	ACATCACTAGGTTCAAACTTTACTTCTTACATAGAAGTATTGACTCTGGTATCTTCTCAGGTTGACAGCTGGTGCAGCTTATTAATG	800
Reinfection at 21 dpi	ACATCACTAGGTTCAAACTTTACTTCTTACATAGAAGTATTGACTCTGGTATCTTCTCAGGTTGACAGCTGGTGCAGCTTATTAATG	799
Consensus	acatacactaggttcaaaactttacttctctacatagaagtatttgaactctgggtgattctctccaggttggacagctgggtcagctcagattatgt	
Primary infection	GGTTTATCTCAACCTAGGACTTTCTATTAATAATATAAATAAATGAAATGGAACATTACAGATGCTGTAGACTGTGCACCTTCTCAGAAACAAG	900
Reinfection at 14 dpi	GGTTTATCTCAACCTAGGACTTTCTATTAATAATATAAATAAATGAAATGGAACATTACAGATGCTGTAGACTGTGCACCTTCTCAGAAACAAG	900
Reinfection at 21 dpi	GGTTTATCTCAACCTAGGACTTTCTATTAATAATATAAATAAATGAAATGGAACATTACAGATGCTGTAGACTGTGCACCTTCTCAGAAACAAG	899
Consensus	gggttattcttcaacctaggactttcttataaataatataaataaataaataaataaataaataaataaataaataaataaataaataaataaataaataa	
Primary infection	TGTACGTTGAAATCCTCAGCTGTAGAAAAGGAATCTATCAAACTTCAACTTTAGAGTCCAAACCAACAGAAATCTATTGTTAGATTTCCATAATTACAA	1000
Reinfection at 14 dpi	TGTACGTTGAAATCCTCAGCTGTAGAAAAGGAATCTATCAAACTTCAACTTTAGAGTCCAAACCAACAGAAATCTATTGTTAGATTTCCATAATTACAA	1000
Reinfection at 21 dpi	TGTACGTTGAAATCCTCAGCTGTAGAAAAGGAATCTATCAAACTTCAACTTTAGAGTCCAAACCAACAGAAATCTATTGTTAGATTTCCATAATTACAA	999
Consensus	tgtacgttgaaatcctcactgtagaaaaggaatctatcaaaacttcaacttttagagtccaaccaacagaatctattgttagatttccataattacaa	
Primary infection	ACITTTGCCCTTTTGGTGAAGTTTTTAACGCCACAGATTTGCATCTGTTTATGCTTGGAAACAGGAAGAAATCAGCAACTGTGTCTGATATTCTGT	1100
Reinfection at 14 dpi	ACITTTGCCCTTTTGGTGAAGTTTTTAACGCCACAGATTTGCATCTGTTTATGCTTGGAAACAGGAAGAAATCAGCAACTGTGTCTGATATTCTGT	1100
Reinfection at 21 dpi	ACITTTGCCCTTTTGGTGAAGTTTTTAACGCCACAGATTTGCATCTGTTTATGCTTGGAAACAGGAAGAAATCAGCAACTGTGTCTGATATTCTGT	1099
Consensus	acttggcccttttgggtgaagttttaaaccgccacagatttgcattctggtttatgcttggaaacaggaagagaatcagcaactgtgttctgctgattctgt	
Primary infection	CCATATAATTCGCGATCATTTTCCACTTTTAAAGTGTATGGAAGTGTCTCTACTAATTAATTAATGATCTCTGCTTTACTAATGCTATAGCAGATTCATT	1200
Reinfection at 14 dpi	CCATATAATTCGCGATCATTTTCCACTTTTAAAGTGTATGGAAGTGTCTCTACTAATTAATTAATGATCTCTGCTTTACTAATGCTATAGCAGATTCATT	1200
Reinfection at 21 dpi	CCATATAATTCGCGATCATTTTCCACTTTTAAAGTGTATGGAAGTGTCTCTACTAATTAATTAATGATCTCTGCTTTACTAATGCTATAGCAGATTCATT	1199
Consensus	ccatataatctcgcgatcattttccactttttaaaggttattggaagtgctctactaataatataatgactctgctttactaatgtctatgctgagattcatt	
Primary infection	GTAAATGAGTGTAGTGAAGTCAGCAAAATGCTCTCAGGCAAACTGGAAGAGATTGCTGATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAAT	1300
Reinfection at 14 dpi	GTAAATGAGTGTAGTGAAGTCAGCAAAATGCTCTCAGGCAAACTGGAAGAGATTGCTGATTAATTAATTAATTAATTAATTAATTAATTAATTAAT	1300
Reinfection at 21 dpi	GTAAATGAGTGTAGTGAAGTCAGCAAAATGCTCTCAGGCAAACTGGAAGAGATTGCTGATTAATTAATTAATTAATTAATTAATTAATTAATTAAT	1299
Consensus	gtaattagaggtgatgagtcagacaaatgctctcagggcaaaactggaagattgctgattataatataaataaataaataaataaataaataaataaataa	
Primary infection	TAGCTTGGAAATCTCAACAATCTTGAATTAAGGTTTGGTGAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAAT	1400
Reinfection at 14 dpi	TAGCTTGGAAATCTCAACAATCTTGAATTAAGGTTTGGTGAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAAT	1400
Reinfection at 21 dpi	TAGCTTGGAAATCTCAACAATCTTGAATTAAGGTTTGGTGAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAAT	1399
Consensus	tagcttggaaattctcaacaatcttgaattaaaggtttgggtgaattataatctctgatatagattgttttaggaagcttaactcaaacctttttgagagaga	
Primary infection	TATTTCAACTGAAATCTATCAGGCCGTTAGCACACTTGTAAATGGTGTGGAAGTTTTAATTTGTTACTTTCCCTTACAACTCATATGTTTCCAAACCCACT	1500
Reinfection at 14 dpi	TATTTCAACTGAAATCTATCAGGCCGTTAGCACACTTGTAAATGGTGTGGAAGTTTTAATTTGTTACTTTCCCTTACAACTCATATGTTTCCAAACCCACT	1500
Reinfection at 21 dpi	TATTTCAACTGAAATCTATCAGGCCGTTAGCACACTTGTAAATGGTGTGGAAGTTTTAATTTGTTACTTTCCCTTACAACTCATATGTTTCCAAACCCACT	1499
Consensus	tatttcaactgaaatctatcagggcggtagcacacttgttaaggtgtggaagttttaaattgttacttcttccaactcatatgcttcttccaact	
Primary infection	AATGGTGTGGTTACCAACCATACAGAGTAGTAGTACTTTCTTTGAACCTTCTACATGCACCAGCACTGTTTGGGACCTAAAAAGTCTACTAATTTGG	1600
Reinfection at 14 dpi	AATGGTGTGGTTACCAACCATACAGAGTAGTAGTACTTTCTTTGAACCTTCTACATGCACCAGCACTGTTTGGGACCTAAAAAGTCTACTAATTTGG	1600
Reinfection at 21 dpi	AATGGTGTGGTTACCAACCATACAGAGTAGTAGTACTTTCTTTGAACCTTCTACATGCACCAGCACTGTTTGGGACCTAAAAAGTCTACTAATTTGG	1599
Consensus	aatgggtgtggttaccacacatacagagtagtagtactttctttgaaccttctacatgcaccagcaactgtttgggacctaaaaagctactaatttgg	
Primary infection	TTAAAAACAATGTGTCAATTTCAACTTCAATGGTTTAAACAGGCACAGGTGTTCTTACTGAGTCTAACAAAAAGTTTCTGGCTTTCCAAACATTTGGCAG	1700
Reinfection at 14 dpi	TTAAAAACAATGTGTCAATTTCAACTTCAATGGTTTAAACAGGCACAGGTGTTCTTACTGAGTCTAACAAAAAGTTTCTGGCTTTCCAAACATTTGGCAG	1700
Reinfection at 21 dpi	TTAAAAACAATGTGTCAATTTCAACTTCAATGGTTTAAACAGGCACAGGTGTTCTTACTGAGTCTAACAAAAAGTTTCTGGCTTTCCAAACATTTGGCAG	1699
Consensus	ttaaaaacaatgtgtcaatttcaacttcaatggttttaaaccagccacaggtgttcttactgagctaacaaaaagtttctggctttccaacaatttggcag	
Primary infection	AGCATTGCTGACACTACTGATGCTGCTCCGTGATCCACAGACACTGAGATTTGACATTACACCATGTTCTTTGGTGGTGCAGTGTATAACACCA	1800
Reinfection at 14 dpi	AGCATTGCTGACACTACTGATGCTGCTCCGTGATCCACAGACACTGAGATTTGACATTACACCATGTTCTTTGGTGGTGCAGTGTATAACACCA	1800
Reinfection at 21 dpi	AGCATTGCTGACACTACTGATGCTGCTCCGTGATCCACAGACACTGAGATTTGACATTACACCATGTTCTTTGGTGGTGCAGTGTATAACACCA	1799
Consensus	agcattgctgacactactgatgctgctccgtgattccacagacactgagatttgcattacacatggttcttttgggtgctcaggtgtataacacca	
Primary infection	GGAAACAATCTTCAACAGGTTGCTGTTCTTTACAGGAATGTTAACTGCACAGAGTCCCTGTTGCTATTATGAGATCAACTTACTCTACTTGGC	1900
Reinfection at 14 dpi	GGAAACAATCTTCAACAGGTTGCTGTTCTTTACAGGAATGTTAACTGCACAGAGTCCCTGTTGCTATTATGAGATCAACTTACTCTACTTGGC	1900
Reinfection at 21 dpi	GGAAACAATCTTCAACAGGTTGCTGTTCTTTACAGGAATGTTAACTGCACAGAGTCCCTGTTGCTATTATGAGATCAACTTACTCTACTTGGC	1899
Consensus	ggaaacaatcttcaacagggtgctgttctttacaggaattgtaactgcacagagtcctctgttgcattatcagcagatcaacttactctactctggtc	
Primary infection	GTGTTTATTTACAGGTTCTAATGTTTTTCAAACAGTGCAGGCTGTTTAAATAGGGGCTGAACATGTCAACAATCATATGAGTGTGACATACCCATTGG	2000
Reinfection at 14 dpi	GTGTTTATTTACAGGTTCTAATGTTTTTCAAACAGTGCAGGCTGTTTAAATAGGGGCTGAACATGTCAACAATCATATGAGTGTGACATACCCATTGG	2000
Reinfection at 21 dpi	GTGTTTATTTACAGGTTCTAATGTTTTTCAAACAGTGCAGGCTGTTTAAATAGGGGCTGAACATGTCAACAATCATATGAGTGTGACATACCCATTGG	1999
Consensus	gtgtttattctcaggtttctaagtgttttcaaacagctgagctgttttaataggggctgaacatgtcaacaactcatatgagtgacataccattgg	
Primary infection	TGCAGGTATATGCGCTAGTTATCAGACTCAGACTAATTTCTCC	2045
Reinfection at 14 dpi	TGCAGGTATATGCGCTAGTTATCAGACTCAGACTAATTTCTCC	2043
Reinfection at 21 dpi	TGCAGGTATATGCGCTAGTTATCAGACTCAGACTAATTTCTCC	2043
Consensus	tgcaggtatattgctgtagttatcagactcagactaattctctcc	

Figure S3: No difference in the S1 gene sequence from the nasal washes between the

primary infection and reinfection.

Table S1. *p*-value among viral loads in various tissues in the primary and secondary infection by SPSS PASW statistical software version 18.0

		Viral load in nose	Viral load in nasal mucosa	Viral load in lung	Viral load in trachea	Viral load in bulbous olfactorius	Viral load in cerebrum	Viral load in jaw	Viral load in NALF	Viral load in BALF	sgRNA in nose	sgRNA in nasal mucosa
D 0	B A	0.000	0.000	0.000							0.386	
	C A	0.000	0.000	0.000							0.001	
	B C	0.360	0.000	0.014							0.001	
D 3	B A	0.000	0.000	0.000	0.000	0.000	0.000	0.081	0.000	0.000	0.019	0.155
	C A	0.000	0.000	0.000	0.000	0.000	0.000	0.005	0.000	0.000	0.010	0.007
	B C	0.863	0.891	0.001	0.003	0.362	0.380	0.061	0.066	0.473	0.592	0.054
D 5	B A	0.000	0.000	0.000	0.000	0.000	0.000	0.009	0.000	0.000	0.000	0.000
	C A	0.000	0.000	0.000	0.004	0.000	0.000	0.001	0.000	0.000	0.000	0.000
	B C	0.007	0.006	0.080	0.038	0.236	0.000	0.037	0.000	1.000	0.219	0.000
D 7	B A	0.000	0.000	0.000	0.000	0.000	0.000	0.005	0.003	0.001	0.000	0.000
	C A	0.000	0.000	0.000	0.014	0.000	0.001	0.003	0.002	0.000	0.000	0.000
	B C	0.006	0.698	0.050	0.002	0.210	0.279	0.747	0.703	0.783	0.297	1.000
D 10	B A	0.000	0.009	0.000	0.001	0.037	0.038	0.043		0.037	0.558	0.000
	C A	0.000	0.001	0.000	0.061	0.007	0.035	0.023		0.004	0.063	0.000
	B C	0.071	0.089	0.015	0.010	0.237	0.952	0.646		0.113	0.027	1.000

A Primary infection; B Reinfected at 14 dpi of primary infection; C Reinfected at 21 dpi of primary infection

NALF were nasal pharyngeal larvage fluid, BALF were bronchoalveolar larvage fluid.

Table S2. Histology score standards of the lung damage

Categories	Score
Pulmonary parenchymal	0 none
	1 The lung structure was clear, and the alveolar septum was slightly thickened, very few inflammatory cells infiltrate
	2 Local edema, local alveolar septum thickening, alveolar cells had slightly exfoliated necrosis, a small amount of inflammatory cell infiltration
	3 Some alveolar septum was thickened, accompanied by mild parenchymal lesions, a small amount of alveolar cell degeneration necrosis, moderate amount of inflammatory cell infiltration
	4 Large area of the alveolar septum was thickened, some substantial lesions, large area of alveolar structure has disappeared, alveolar

	<p>cells have degeneration and necrosis, a large number of inflammatory cell infiltration</p> <p>5 Lung structure disappeared with extensive consolidation and diffuse infiltration of inflammatory cells</p>
Bronchus and Bronchiole	<p>0 none</p> <p>1 Local tracheal epithelium was slightly diseased with slight cell abscission</p> <p>2 Part of trachea epithelial cells were shed, and mild amount of exudate was observed in the lumen</p> <p>3 The cells were denaturated and necrotic, part of the mucosa is detached, and a large number of inflammatory exudates and tissue fragments could be seen in the lumen</p> <p>4 The cells were denaturated and necrotic, and a large number of mucosa detached, part of the lumen was blocked</p> <p>5 The cells were denaturated and necrotic, and a large number of the mucosa was detached, A large area or the total lumen was blocked</p>
Pulmonary vasculitis	<p>0 none</p> <p>1 Mild edema and hyperemia, minimal inflammatory cell infiltrated around the lumen</p> <p>2 Vascular edema, local endothelial cells were necrotic, a small number of inflammatory cell infiltration</p> <p>3 Endothelial cells were denaturated and necrotic with vascular wall hyperplasia, inflammatory cell infiltration</p> <p>4 Vascular wall cells were denaturated and necrotic, with lumen stenosis and inflammatory cell infiltration</p> <p>5 Vascular structures were ruptured or many cells were denaturated and necrotic, diffuse infiltration of inflammatory cells</p>

Table S3. Sequences of primers for real time RT-qPCR detection of mRNA gene expression of host cytokines

Gene name	Forward primer (5' to 3')	Reverse Primer (5' to 3')
<i>β-actin</i>	ATGGCCAGGTCATCACCATT G	CAGGAAGGAAGGCTGGAAAA G
<i>IL-1β</i>	GTGGACAACAAAGCTCGTG G	AGCCCGTCAACCTCAAAGAA
<i>IL-6</i>	TGTCTTCTTGGGACTGCTGC	CCAAACCTCCGACTTGTTGA
<i>TNF-α</i>	CACCCACCGTCAAGGATTCA	TTGGCTGGGCAATGAAGAGT
<i>IFN-α</i>	AGACTGGGAGTTGCCTGTGA	GAGGAATCCAGGGCTTTCCAG
<i>IFN-γ</i>	TGCATCTTGGCTTTGTTGCTC	TCCCCTCCATTACGACATC
<i>MIP-1α</i>	GGTCCAAGAGTACGTCGCTG	GAGTTGTGGAGGTGGCAAGG
<i>RANTES</i>	TCAGCTTGGTTTGGGAGCAA	TGAAGTGCTGGTTTCTTGGGT

<i>IP-10</i>	TACGTCGGCCTATGGCTACT	TTGGGGACTCTTGTCACTGG
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