

## Supporting Information for

### Mouse models susceptible to HCoV-229E and HCoV-NL63 and cross protection from challenge with SARS-CoV-2

Donglan Liu, Chunke Chen, Dingbin Chen, Airu Zhu, Fang Li, Zhen Zhuang, Chris Ka Pun Mok, Jun Dai, Xiaobo Li, Yingkang Jin, Zhao Chen, Jing Sun, Yanqun Wang, Yuming Li, Yanjun Zhang, Liyan Wen, Zhaoyong Zhang, Jianfen Zhuo, Junxiang Wang, Wei Ran, Dong Wang, Shengnan Zhang, Yanhong Tang, Suxiang Li, Xiaoming Lai, Peilan Wei, Jinwei Yuan, Fangli Chen, Shuxiang Huang, Fangfang Sun, Zhaohui Qian, Wenjie Tan, Jingxian Zhao, Malik Peiris, Jincun Zhao

Jingxian Zhao

Email: [zhaojingxian@gird.cn](mailto:zhaojingxian@gird.cn)

Malik Peiris

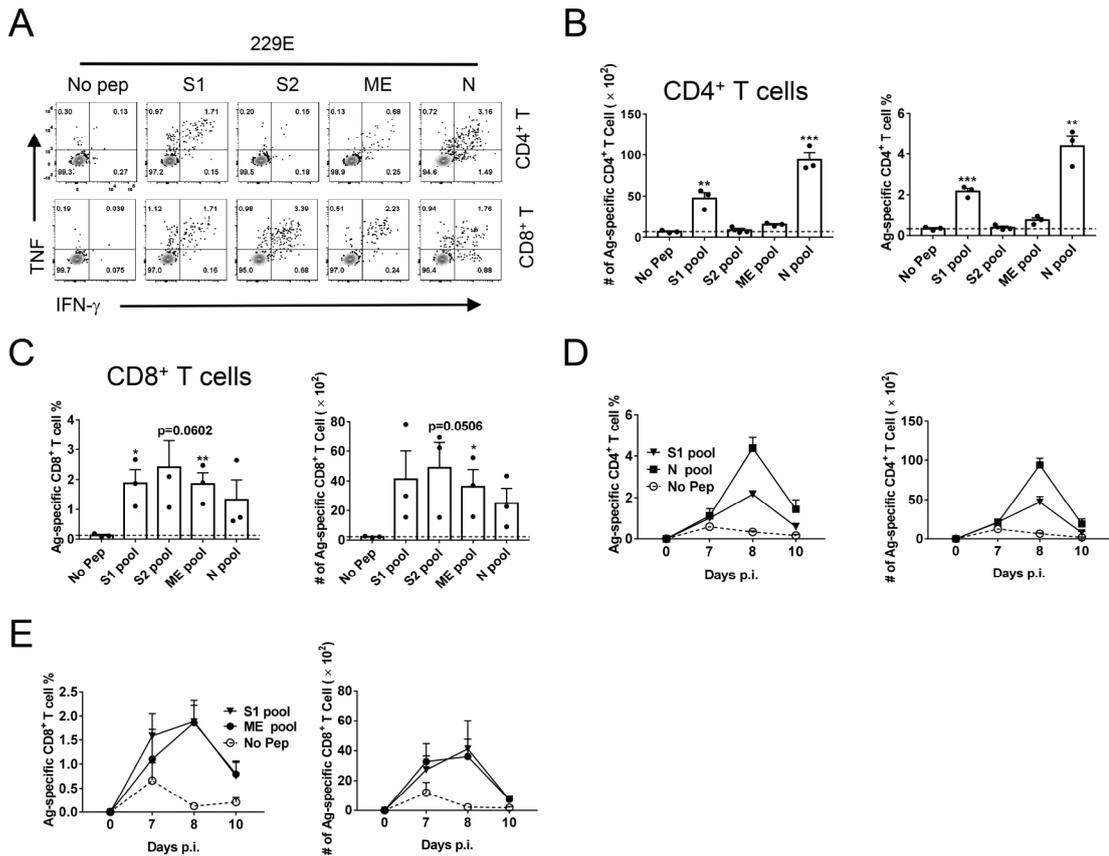
Email: [malik@hku.hk](mailto:malik@hku.hk)

Jincun Zhao

Email: [zhaojincun@gird.cn](mailto:zhaojincun@gird.cn)

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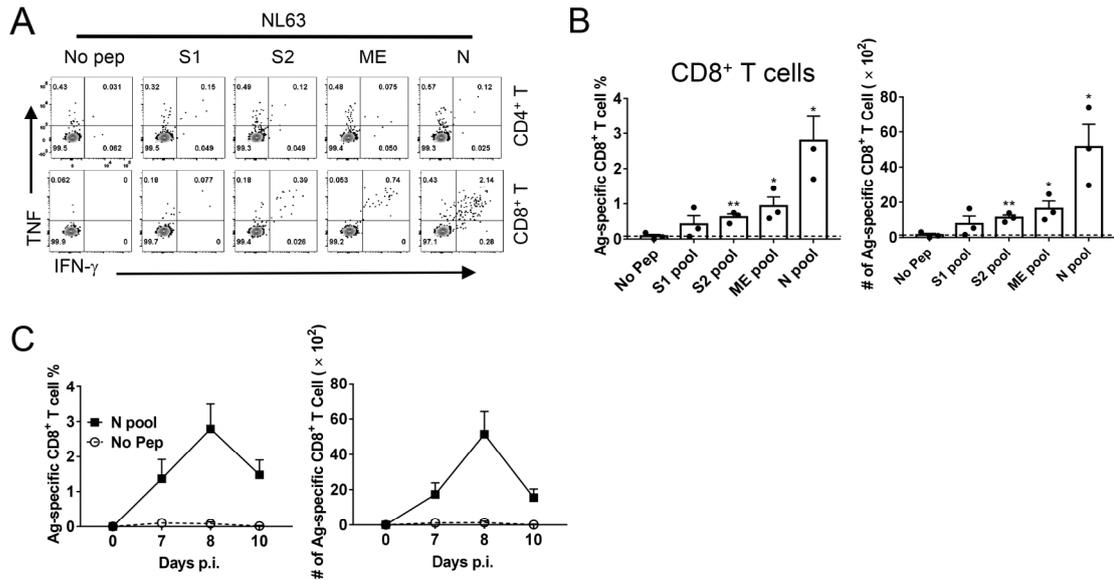
Figures S1 to S3



**Fig. S1. 229E infection induced virus specific T cell response in IFNAR<sup>-/-</sup>BALB/c mice.**

(A-C) Ad5-hAPN-transduced IFNAR<sup>-/-</sup>BALB/c mice were infected with  $1.5 \times 10^5$  TCID<sub>50</sub> of 229E. To identify 229E T-cell responses, single-cell suspensions were prepared from the BALF of transduced/ infected IFNAR<sup>-/-</sup> BALB/c mice and stimulated with 2  $\mu$ M structural protein peptide pools for 5-6 h in the presence of brefeldin A. Flow plots ((A), 8 d.p.i.), and summary of frequencies and cell numbers of 229E specific CD4<sup>+</sup> (B) and CD8<sup>+</sup> T cells (C) (determined by IFN- $\gamma$  intracellular staining) are shown (n = 3 mice per time point).

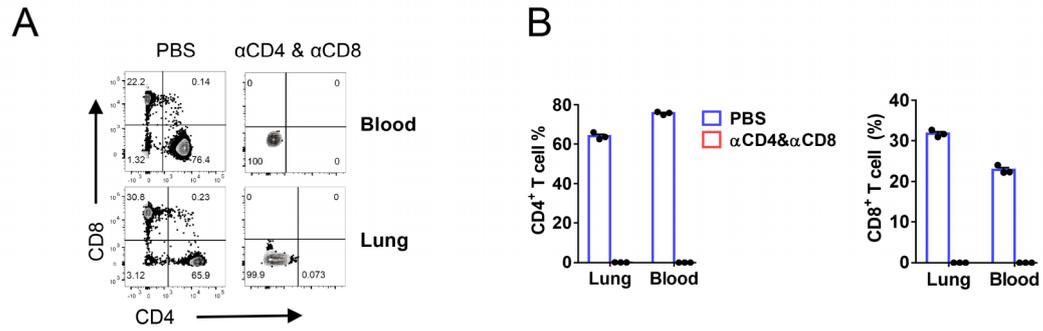
(D and E) To determine the kinetics of virus-specific T cell responses in 229E infected IFNAR<sup>-/-</sup>BALB/c mice, single-cell suspensions were prepared from the BALF of transduced/ infected IFNAR<sup>-/-</sup> BALB/c mice at indicated time points and stimulated with 2  $\mu$ M S1, ME or N protein peptide pools for 5-6 h in the presence of brefeldin A. The frequencies (left panel) and cell numbers (right panel) of 229E-specific CD4<sup>+</sup> (D) and CD8<sup>+</sup>T(E) cells from BALF are shown (n= 3 mice per time point).



**Fig. S2. NL63 infection induced virus specific T cell response in IFNAR<sup>-/-</sup> BALB/c mice.**

(A and B) Ad5-hACE2-transduced IFNAR<sup>-/-</sup>BALB/c mice were infected with  $1.0 \times 10^4$  PFU of NL63. To identify NL63 T-cell responses, single-cell suspensions were prepared from the BALF of transduced/infected IFNAR<sup>-/-</sup> BALB/c mice and stimulated with 2  $\mu$ M structural protein peptide pools for 5-6 h in the presence of brefeldin A. Flow plots ((A), 8 d.p.i.), and summary of frequencies and cell numbers of NL63 specific CD8<sup>+</sup> T cells (B) (determined by IFN- $\gamma$  intracellular staining) are shown (n = 3 mice per time point).

(C) To determine the kinetics of virus-specific T cell responses in IFNAR<sup>-/-</sup> BALB/c mice, single-cell suspensions were prepared from the BALF of transduced/infected IFNAR<sup>-/-</sup> BALB/c mice at indicated time points and stimulated with 2  $\mu$ M N protein peptide pools for 5-6 h in the presence of brefeldin A. The frequencies (left panel) and cell numbers (right panel) of NL63 specific CD8<sup>+</sup> T cells from BALF are shown (n= 3 mice per time point).



**Fig. S3. T cells depletion by anti-CD4 and anti-CD8 antibody in mice.**

(A and B) To determine T-cell depletion efficacy in mice, mice were treated intraperitoneally with 500  $\mu\text{g}$  anti-CD4 and 100  $\mu\text{g}$  anti-CD8 antibody. Two days later, single-cell suspensions were prepared from blood and lungs. Flow plots (A) and summary of frequencies of CD4<sup>+</sup> and CD8<sup>+</sup> T cells (B) in blood and lungs are shown (n = 3 mice).