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**Supplementary Data**

**Characteristics of replication and pathogenicity of SARS-CoV-2 Alpha and Delta isolates**

**Xiao-Li Feng a,1, Dandan Yu a,b,f,1, Mi Zhang c,1, Xiaohong Li b,1, Qing-Cui Zou a, Wentai Ma d, Jian-Bao Han a, Ling Xu a,b,f, Cuixian Yang c, Wang Qu a, Zhong-Hua Deng a, Junyi Long a, Yanghaopeng Long a, Mingkun Li d,e, Yong-Gang Yao a,b,f,g, Xing-Qi Dong c,\*, Jianxiong Zeng a,b,f,g,h,\*, Ming-Hua Li a,\***

*a Kunming National High-level Biosafety Research Center for Non-Human Primates, Center for Biosafety Mega-Science, Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, 650107, China*

*b Key Laboratory of Animal Models and Human Disease Mechanisms of the Chinese Academy of Sciences, and KIZ-CUHK Joint Laboratory of Bioresources and Molecular Research in Common Diseases, Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, 650201, China*

*c Department of Infectious Diseases, Yunnan Provincial Infectious Diseases Hospital, Kunming, 650301, China*

*d Key Laboratory of Genomic and Precision Medicine, Beijing Institute of Genomics, Chinese Academy of Sciences, and China National Center for Bioinformation, Beijing, 100101, China.*

*e Center for Excellence in Animal Evolution and Genetics, Chinese Academy of Sciences, Kunming, 650201, China*

*f National Resource Center for Non-Human Primates, National Research Facility for Phenotypic & Genetic Analysis of Model Animals (Primate Facility), Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, 650107, China*

*g Kunming College of Life Science, University of Chinese Academy of Sciences, Kunming, 650204, China*

*h Yunnan Key Laboratory of Biodiversity Information, Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, 650201, China*

\* Corresponding authors.

*E-mail addresses*: dongxq8001@126.com (X.Q. Dong), zengjianxiong@mail.kiz.ac.cn (J. Zeng), limh@mail.kiz.ac.cn (M.H. Li)

1 Xiao-Li Feng, Dandan Yu, Mi Zhang and Xiaohong Li contributed equally to this work.

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**Supplementary Fig. S1** Phylogenetic tree of the Alpha isolate.Phylogenetic analysis of the Spike sequences of the Alpha isolate (red circle) within the existed SARS-CoV-2 Alpha variants (purple circle) by Nextstrain (Dated on 8 Feb 2022).

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**Supplementary Fig. S2** Phylogenetic tree of the Delta isolate.Phylogenetic analysis of the Spike sequences of the Delta isolate (red circle) within the existed SARS-CoV-2 Delta variants (blue circle) by Nextstrain (Dated on 8 Feb 2022).

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**Supplementary Fig. S3** Body weight of infected hACE2 transgenic mice and hamsters. **A, B** Body weight was monitored at 3 dpi and indicated by percentage of starting body weight for the prototype SARS-CoV-2-, Alpha- and Delta-infected hACE2 transgenic mice (**A**) and hamsters (**B**). The uninfected animals were used as control. Data were shown as mean ± standard deviaion (n = 6). Statistical analysis was performed by one-way ANOVA with Bonferroni’s *post hoc* test. n.s., not significant, \*\**P* < 0.01.

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**Supplementary Fig. S4** Spike K417N mutation in SARS-CoV-2 variants.Diagram of spike mutations including K417N of indicated SARS-CoV-2 variants.