Data S1

Materials and methods

H&E procedure. The biopsy lung tissues from the patient had already been placed in fixative with 10% neutral-buffered formalin, except for some fresh fragments directly stored in RNA preservation solution for genome analysis before reaching the surgical pathology laboratory. The H&E procedure was performed in the Department of Pathology of the Eighth Medical Center of the Chinese People's Liberation Army General Hospital (Beijing, China). After 16-20 h (overnight at room temperature) in fixative, the specimen was sectioned cautiously and gently, and transferred to tissue cassettes. After tissue cutting, the tissue cassettes were transferred to a tissue processor (DAKEWE HP300; Dakewe Biotech Co., Ltd.) for fixation, dehydration and clearing. Embedding was performed in a histological paraffin dispenser (HistoCore Arcadia H; Leica Microsystems Shanghai Ltd.). First, the cassette lid was snapped off and the cleared specimen was transferred into an appropriate preheated mold on the hot plate of the embedding station. Second, the tissue was orientated inside the mold to obtain the desired position and the melted paraffin was poured to entirely surround the edges of the tissue. Third, the mold was carefully transferred onto the cool plate so that paraffin returned to a solid phase. Finally, the mold was snapped off and the paraffin blocks were stored at room temperature for sectioning. Paraffin blocks were sections at the desired thickness (usually 4-5 μm) on a microtome and floated in a 40˚C water bath containing distilled water. A record of the orientation and sequence of the sections was kept. The sections were transferred onto poly-1-lysine-coated coverslips for drying overnight and the slides were stored at room temperature until ready for use.

For paraffinization/rehydration, the following steps were followed: i) Sections were washed with xylene three times for 3 min each; sections were washed twice with 100% ethanol for 3 min each; sections were washed twice with 95% ethanol for 3 min each; sections were washed once with 80% ethanol for 3 min; and sections were washed twice in dH_2O for 5 min each. For staining, the sections were cleaned with distilled water, and then the nuclei were stained with hematoxylin for ~5 min at room

temperature. The sections were rinsed under temperate running water, and the differentiator (0.3% acid alcohol) was used until the background became colorless. The slides were again rinsed under running tap water before flooding the smear with eosin for 30 sec to 2 min (room temperature). The smear was dehydrate in alcohol (70, 95 and 100%) for 3 min each and then rinsed with xylene three times for 1 min each. The slides were then mounted with a clean coverslip and observed under a light microscope.

IHC procedure. IHC was performed on paraffin-embedded sections created as aforementioned. Blocking reagent (cat. no. PV-9000; Reagent 1; Origene Technologies, Inc.) was diluted 1:10 and used to block non-specific binding by incubating with blocking buffer for 30-60 min at room temperature in a humidified chamber. The primary antibodies, including TTF-1 (cat. no. ZM-0270), Napsin A (cat. no. ZM-0473), cytokeratin 5/6 (cat. no. ZM-0313) and tumor protein 63 (cat. no. ZM-0406), were provided by Origene Technologies, Inc. 1X Phosphate-Buffered Saline plus 0.1% Tween (PBST) (cat. no. NBS7510, Shanghai Nonin Biological Technology Co. Ltd.) were applied to dilute the primary antibodies at a dilution ratio of 1:100. Next, the appropriate diluted antibody to the tissue sections on the slide and they were incubated for 1 h at room temperature in a humidified chamber. The slides were rinsed three times using PBST for 2 min each time. The appropriate response enhancer (cat. no. PV-9000; Reagent 2; Origene Technologies, Inc.) was applied to the tissue sections on the slide and incubated for 20 min at room temperature in a humidified chamber. The slides were rinsed three times using PBST for 2 min each time. The secondary antibody (cat. no. PV-9000; Reagent 3; Origene Technologies, Inc.), which was diluted in antibody buffer to a 1:200 dilution, was applied to the tissue sections on the slide and incubated for 30 min at room temperature. The slides were then rinsed three times in PBS for 2 min each time. The appropriate DAB solution (cat. no. DA1015; Beijing Suolaibao Technology Co. Ltd.) was applied to the slides for 5 min or until the desired color intensity was reached. The slide was then mounted with a clean coverslip and observed under a

light microscope.

Reverse transcription-quantitative (RT-q)PCR primer sequences. RT-qPCR was performed by an external company (Beijing Pushi Medical Laboratory Co., Ltd.). Briefly, before running the TaqMan qPCR assays, isolated total RNA was extracted from the serum sample of the patient using a Viral RNA Isolation Kit (cat. no. R0035S; RNAeasy™; Beyotime Institute of Biotechnology) and reverse transcribed to cDNA using a cDNA RT kit (cat. no. D7160M; BeyoRT™; Beyotime Institute of Biotechnology). The TaqMan qPCR assay was performed with a Novel Coronavirus (2019-nCoV) Real time RT-PCR Kit (cat. no. RR-0478-02; liferiver™; Shanghai ZJ Bio-Tech Co., Ltd.) and 2019-nCoV Nucleic acid detection Kit (cat. no. ABI 7500 fast; Thermo Fisher Scientific, Inc.). The qPCR primer sequences of COVID-19 and control (GAPDH) were as follows: COVID forward, 5'-CCCTGTGGGTTTTACACTTAA-3' and reverse, 5'-ACGATTGTGCATCAGCTGA-3'; and GAPDH forward, 5'-GATTCCACCCATGGCAAATTC-3' and reverse, 5'-CTGGAAGATGGTGATGGGATT-3'.

details of the next-generation sequencing (NGS) assay. The next-generation sequencing (NGS) assay was performed by Geneseeq Technology, Inc. DNA/RNA samples were prepared for sequencing by the Homgen Unversa DNA Library Prep kit (cat. no. PK10002HG-96; Shanghai Heyin Biotechnology Co., Ltd.). The quality/integrity of the processed samples was verified by Qsep100 Bioanalyzer (Hangzhou Houze Bio-technology Co., Ltd.). The type of sequencing was PE150 with the nucleotide length of 150 bp (paired ends). The sequencing kit was a NovaSeq 6000 S4 Reagent Kit v1.5 (cat. no. 20028312; Illumina Inc.). The loading concentration of the final library was 200-400 pM (RT-qPCR). The software used to analyze the data included blast software (bwa 0.7.17-r1188) and somatic mutation analysis software (strelka-2.9.10/Mutect2) (1-3).

References

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(3) Benjamin D, Sato T, Cibulskis K, et al. Calling somatic SNVs and indels with Mutect2[J]. BioRxiv, 2019: 861054.