## **Supplementary Data Description file**

## Integrated histopathology, spatial and single cell transcriptomics resolve cellular drivers of early and late alveolar damage in COVID-19

Jimmy Tsz Hang Lee<sup>1,\*</sup>, Sam N. Barnett<sup>2,3\*</sup>, Kenny Roberts<sup>1</sup>, Helen Ashwin<sup>4</sup>, Luke Milross<sup>5</sup>, Jae-Won Cho<sup>6</sup>, Alik Huseynov<sup>2</sup>, Benjamin Woodhams<sup>1,7</sup>, Alexander Aivazidis<sup>1</sup>, Tong Li<sup>1</sup>, Joaquim Majo<sup>8</sup>, Patricia Chaves<sup>2</sup>, Michael Lee<sup>2</sup>, Antonio M. A. Miranda<sup>2</sup>, Zuzanna Jablonska<sup>2</sup>, Vincenzo Arena<sup>9</sup>, Brian Hanley<sup>10</sup>, Michael Osborn<sup>10</sup>, Virginie Uhlmann<sup>7</sup>, Xiao-Ning Xu<sup>11</sup>, Gary R. McLean<sup>2,12</sup>, Sarah A. Teichmann<sup>1,13</sup>, Anna M. Randi<sup>2,3</sup>, Andrew Filby<sup>14</sup>, Paul M. Kaye<sup>4</sup>, Andrew J. Fisher<sup>5,15,\*\*,#</sup>, Martin Hemberg<sup>6,\*\*,#</sup>, Michela Noseda<sup>2,3\*\*,#</sup>, Omer Ali Bayraktar<sup>1,\*\*,#</sup>

\* These authors contributed equally

\*\* These authors jointly supervised this work

# corresponding authors: <u>a.j.fisher@newcastle.ac.uk</u>, <u>mhemberg@bwh.harvard.edu</u>, <u>m.noseda@imperial.ac.uk</u>, <u>ob5@sanger.ac.uk</u>

- 1. Cellular Genetics Programme, Wellcome Sanger Institute, Wellcome Genome Campus, Hinxton, UK.
- 2. National Heart and Lung Institute, Imperial College London, London, UK.
- 3. British Heart Foundation Centre of Research Excellence, Imperial College London, London, UK.
- 4. York Biomedical Research Institute, Hull York Medical School, University of York, York, UK.
- 5. Newcastle University Translational and Clinical Research Institute, Newcastle upon Tyne, UK.
- 6. The Gene Lay Institute of Immunology and Inflammation, Brigham and Women's Hospital, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA.
- 7. European Bioinformatics Institute, European Molecular Biology Laboratory (EMBL), Cambridge, UK.
- 8. Department of Cellular Pathology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.
- 9. Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Istituto di Anatomia Patologica, Università Cattolica Del Sacro Cuore, Rome, Italy.
- 10. Department of Cellular Pathology, Northwest London Pathology, Imperial College London NHS Trust, London, UK
- 11. Department of Infectious Disease, Imperial College London, London, UK.
- 12. London Metropolitan University, London, UK.
- 13. Cambridge Stem Cell Institute & Department of Medicine, University of Cambridge, Cambridge, UK.
- 14. Biosciences Institute and Innovation, Methodology and Application Research Theme, Newcastle University, Newcastle upon Tyne, UK.
- 15. Institute of Transplantation, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.

Supplementary Data 1: COVID-19 patient metadata used for snRNA-seq / RNAscope.

Supplementary Data 2: Datasets used for generation of COVID-19 sc-/snRNA-seq object.

Supplementary Data 3: Cell state abbreviations.

**Supplementary Data 4**: Cell state differential gene expression analysis. Differentially expressed genes were calculated using the Wilcoxon Rank Sum Test with Benjamini-Hochberg adjustment.

**Supplementary Data 5**: EdgeR Pseudobulk analysis of sc-/snRNA-seq data (COVID-19 vs. Healthy / cell state). Differentially expressed genes were calculated using QLF (Quasi-Likelihood F-test).

**Supplementary Data 6**: MSigDB Pathway enrichment analysis in EP.AT1 (COVID-19 vs. Healthy / cell state).

**Supplementary Data 7**: MSigDB Pathway enrichment analysis in EP.AT2 (COVID-19 vs. Healthy / cell state).

Supplementary Data 8: COVID-19 patient metadata used for WTA profiling.

**Supplementary Data 9**: EdgeR Pseudobulk analysis of EDAD vs ODAD spatial WTA. Differentially expressed genes were calculated using QLF (Quasi-Likelihood F-test). P values were adjusted for multiple comparisons using the Benjamini-Hochberg method.

**Supplementary Data 10**: EdgeR Pseudobulk analysis of EDAD vs PRES spatial WTA. Differentially expressed genes were calculated using QLF (Quasi-Likelihood F-test). P values were adjusted for multiple comparisons using the Benjamini-Hochberg method.

**Supplementary Data 11**: EdgeR Pseudobulk analysis of ODAD vs PRES spatial WTA. Differentially expressed genes were calculated using QLF (Quasi-Likelihood F-test). P values were adjusted for multiple comparisons using the Benjamini-Hochberg method.

**Supplementary Data 12**: EdgeR Pseudobulk analysis of MDAD vs PRES spatial WTA. Differentially expressed genes were calculated using QLF (Quasi-Likelihood F-test). P values were adjusted for multiple comparisons using the Benjamini-Hochberg method.

**Supplementary Data 13:** SVG format of Supplementary Figure 1D.