

# Spatiotemporal Heterogeneity of the Pulmonary Host Response to SARS-CoV-2

## Background

- The relationship between COVID-19 disease severity and pulmonary infection by SARS-CoV-2 is poorly understood.
- FFPE samples from 24 deceased COVID-19 patients were analyzed by RNASeq, IHC, and DSP.

## Research Questions

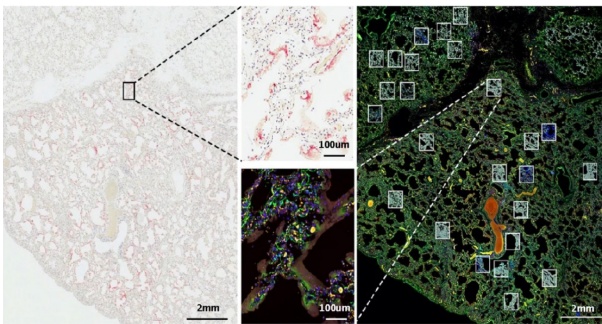
1. How does viral load and the immune infiltrate in infected lung tissue correlate with disease duration and/or severity?
2. What immune cells are recruited to infected lung tissue and how are they spatially organized?

## Experimental Setup

Sample Type	FFPE
Tissue Type	Human Lung
Assay	Cancer Transcriptome Atlas & Immuno-Oncology Protein Panel
Analytes	RNA and Protein
Readout	nCounter® Analysis System and NGS

*“The use of the GeoMx Digital Spatial Profiler has provided unprecedented spatial transcriptomic and proteomic analysis of the intrapulmonary heterogeneity of SARS-CoV-2 infection.”*

*-Desai et al.*



Geometric regions of interest (ROIs) were selected based on positive or negative RNA-ISH staining for SARS-CoV-2 (left) in a serial section as well as fluorescent staining (right) for CD45 (red), CD68 (yellow), PanCK (green), and DNA (blue). Figure reproduced with permission from Desai et al. Nat Commun 11, 6319 (2020) under the [Creative Commons license](#)

## Results & Conclusions

- Viral load and immune response are highly heterogeneous both within a given patient sample and between patient samples.
- Interferon stimulated genes (ISGs), the checkpoint protein PD-1, as well as markers associated with macrophages, chemokines, and cytokines were differentially expressed in SARS-CoV-2 positive ROIs
- Disease progression can be described in two phases: an early phase characterized by high viral load, IFN response, and acute cellular injury and a later phase characterized by viral clearance, a reduced IFN response, and tissue reorganization.
- Antiviral treatment would be most beneficial in the early stages of infection followed by treatment with steroids or JAK inhibitors in the later stages of COVID-19.

Desai, N., Neyaz, A., Szabolcs, A. et al. Temporal and spatial heterogeneity of host response to SARS-CoV-2 pulmonary infection. Nat Commun 11, 6319 (2020). <https://doi.org/10.1038/s41467-020-20139-7>

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