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SCIENCE IS OUR MEDICINE

Multiplexed and spatial biology: connecting anatomical scales

Danube Symposium 2023/09/22

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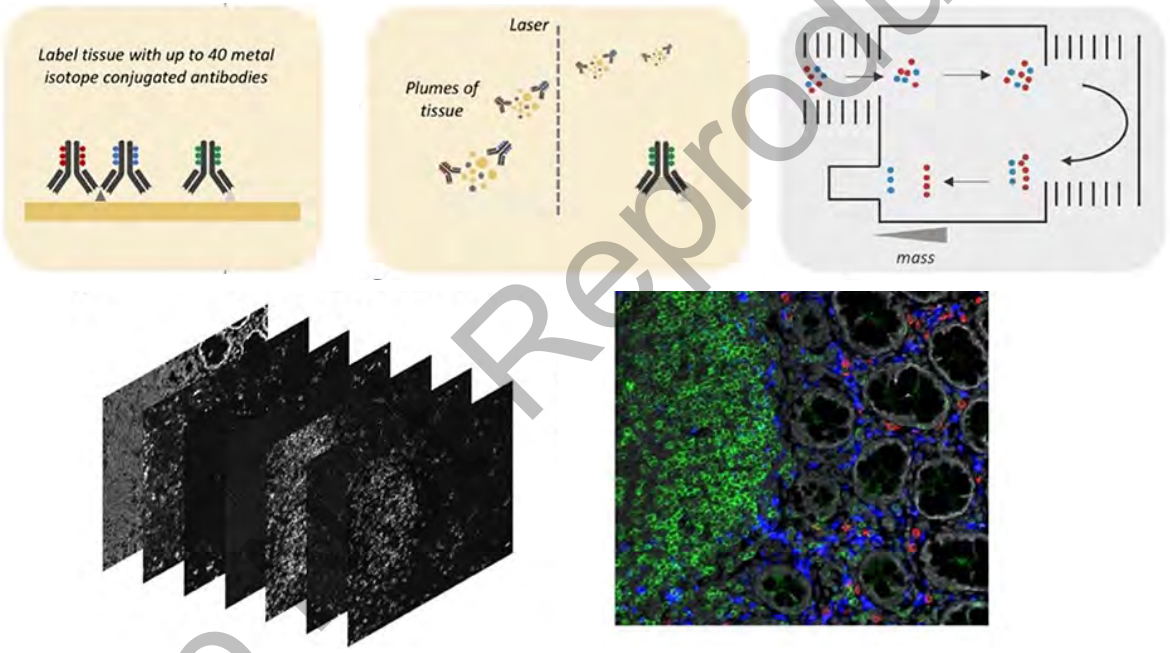
Multiplexed imaging: omics with spatial context



Depicted: Imaging mass cytometry (IMC)

Similar methods: CODEX, MIBI, IBEX, ...

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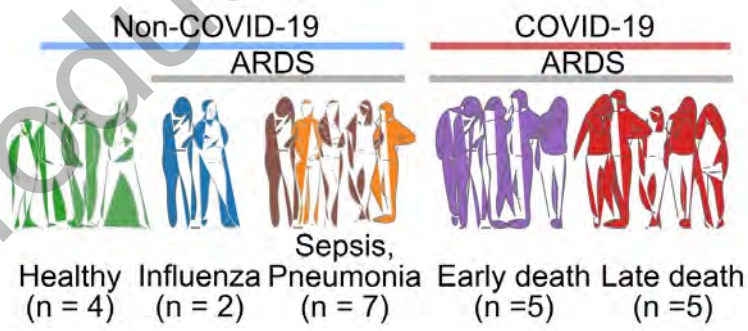
The spatial landscape of lung pathology in COVID-19

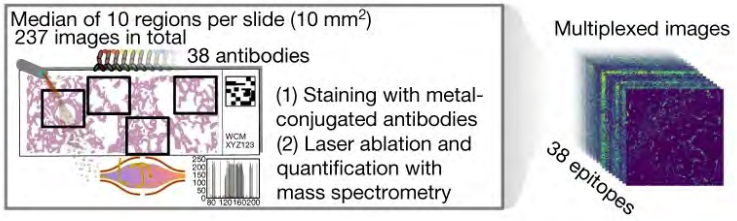
Cohort of 23 individuals with various lung infections:

- “Early” COVID-19 (succumbed 1-5 days after onset)
- “Late” COVID-19 (>30 days after disease onset)
- ARDS (influenza, bacterial pneumonia, sepsis)



Multiplexed imaging of lung tissue:

- 37 marker antibody panel for imaging mass cytometry
- 247 images, ~1mm2 each



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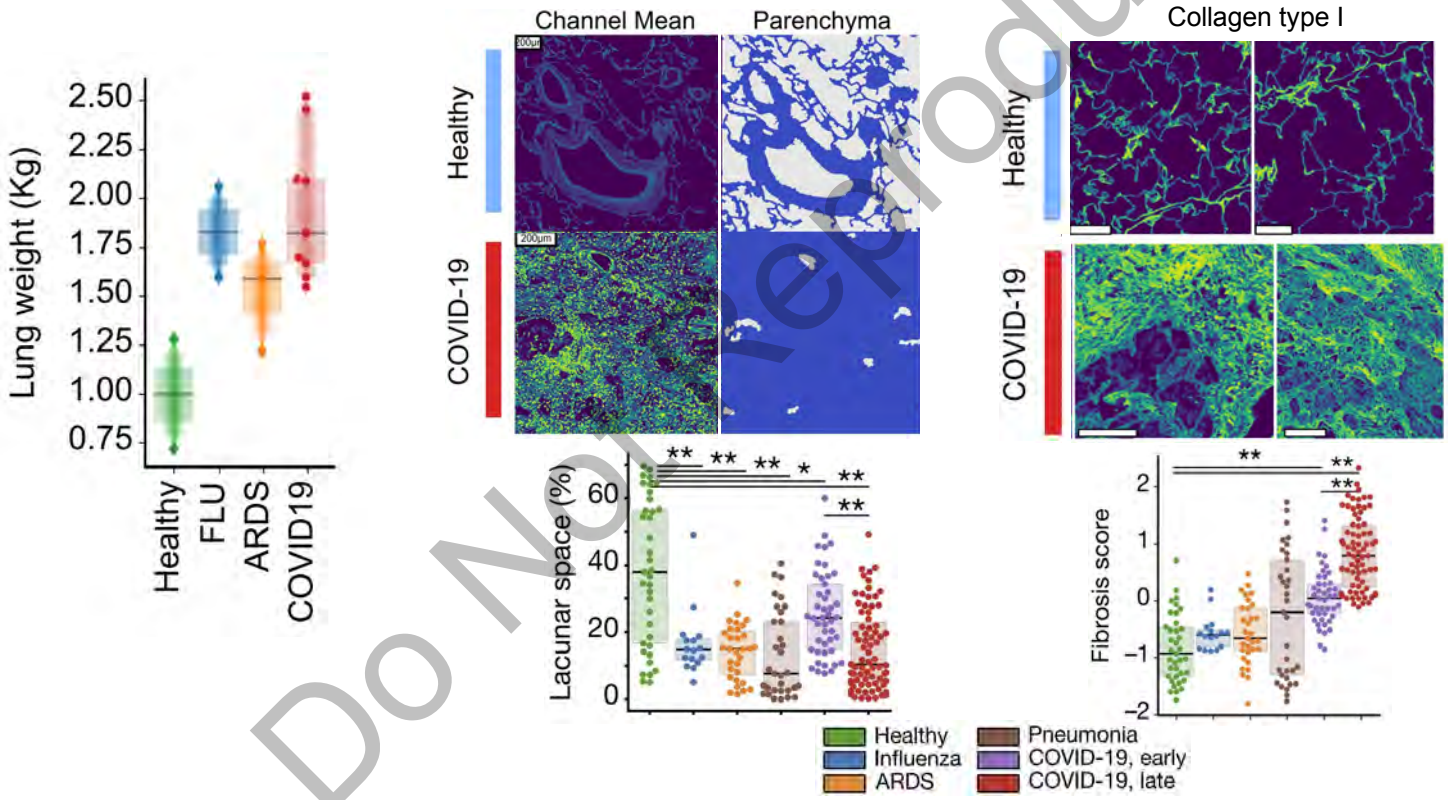
Quantification of lung pathology at micro-anatomical level



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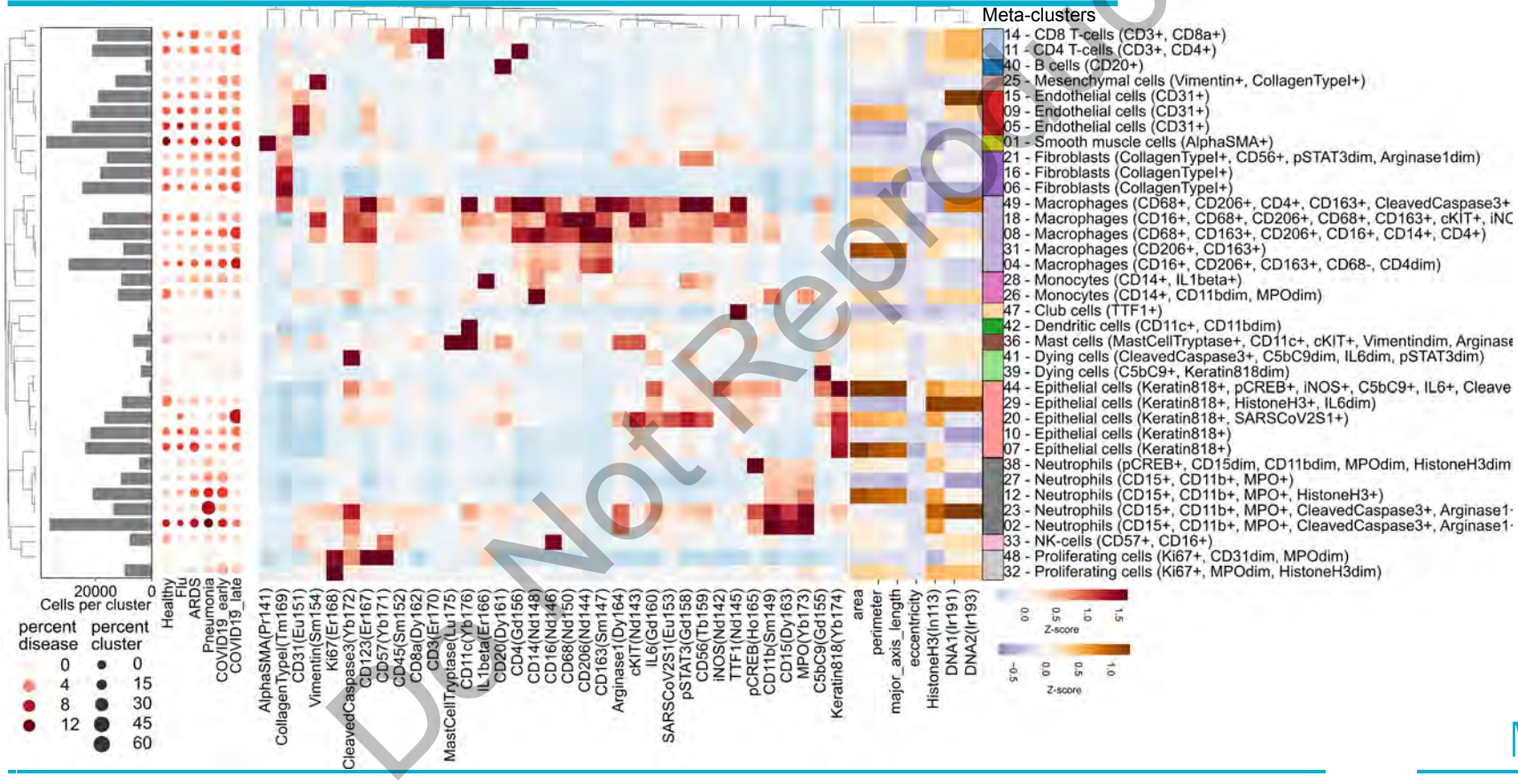
Cellular quantification and phenotyping



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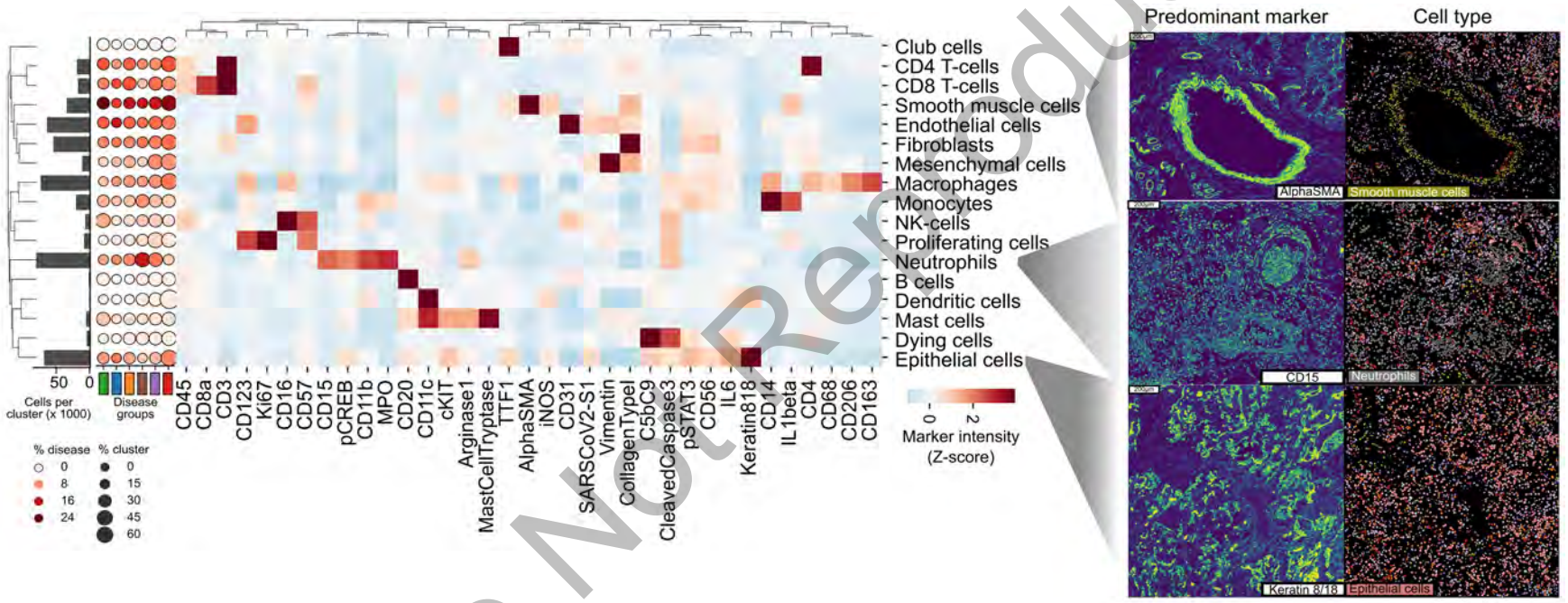
Clusters

Cellular quantification and phenotyping



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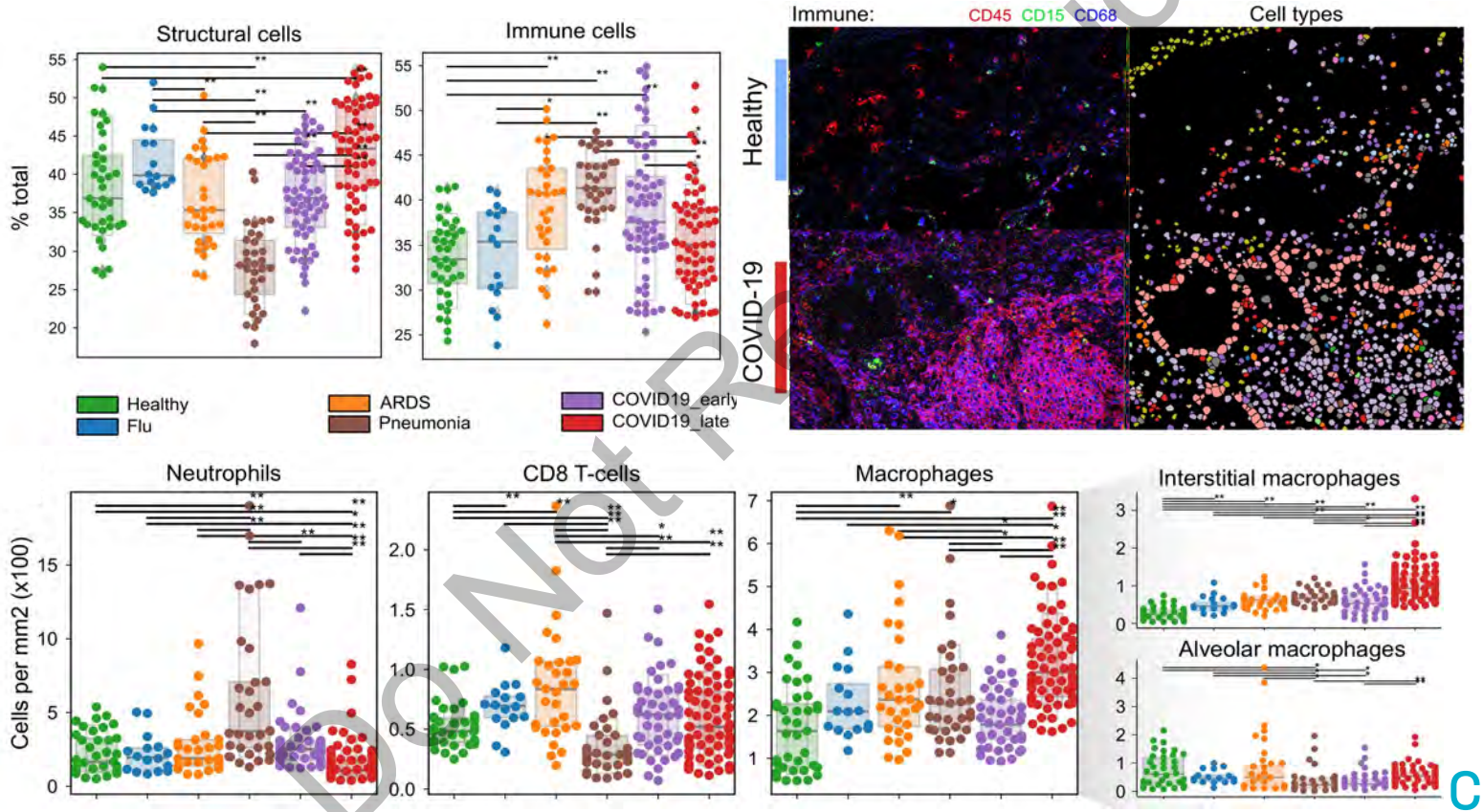
Infiltration of interstitial macrophages in severe COVID-19



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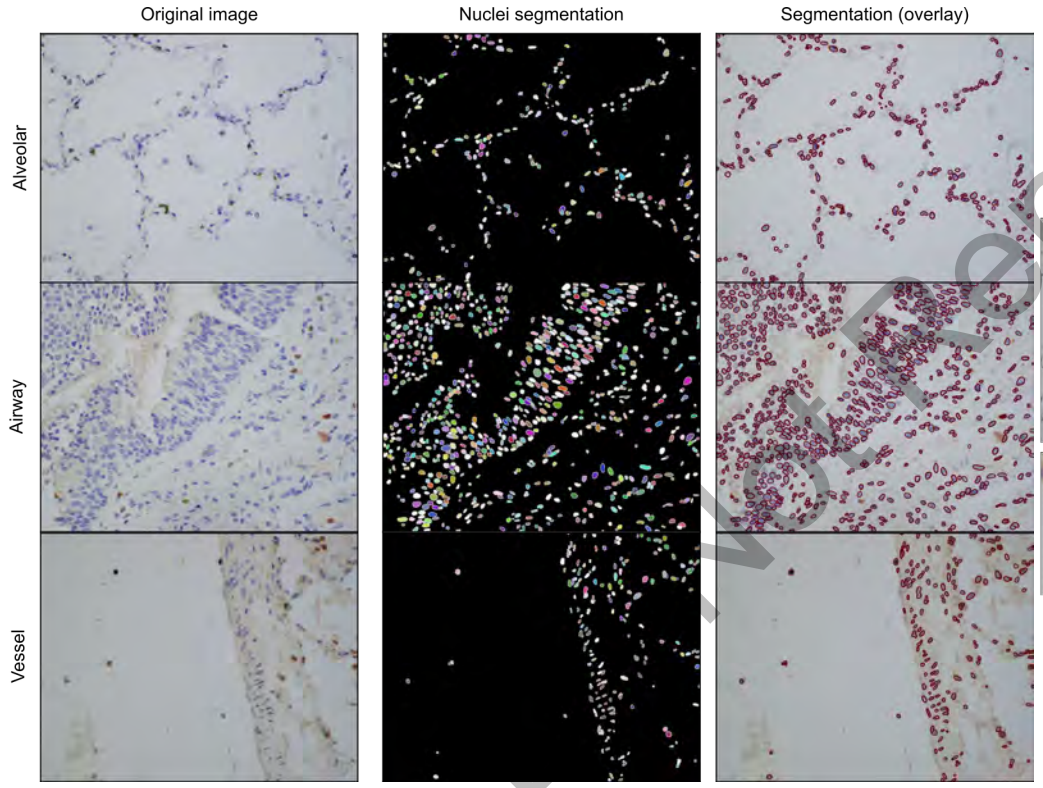
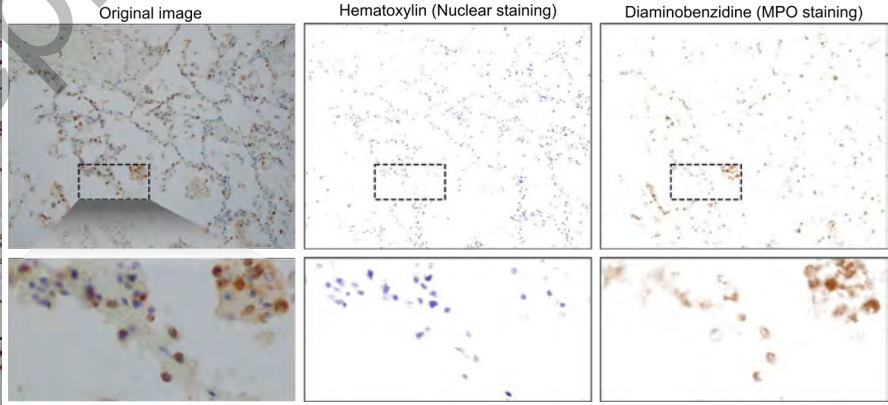
Validation with immunohistochemistry

Hematoxylin segmentation



Color decomposition and quantification



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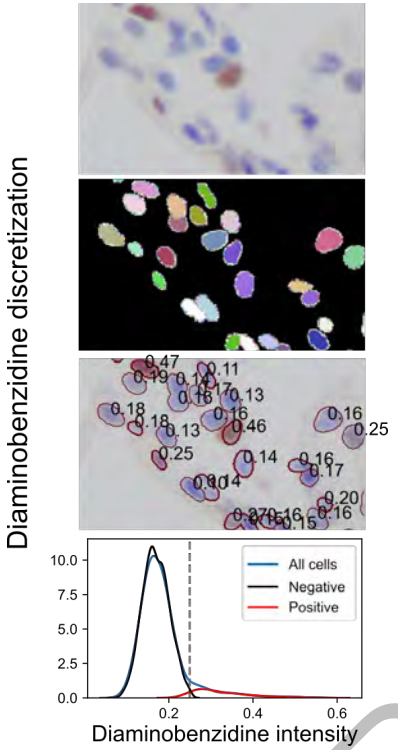
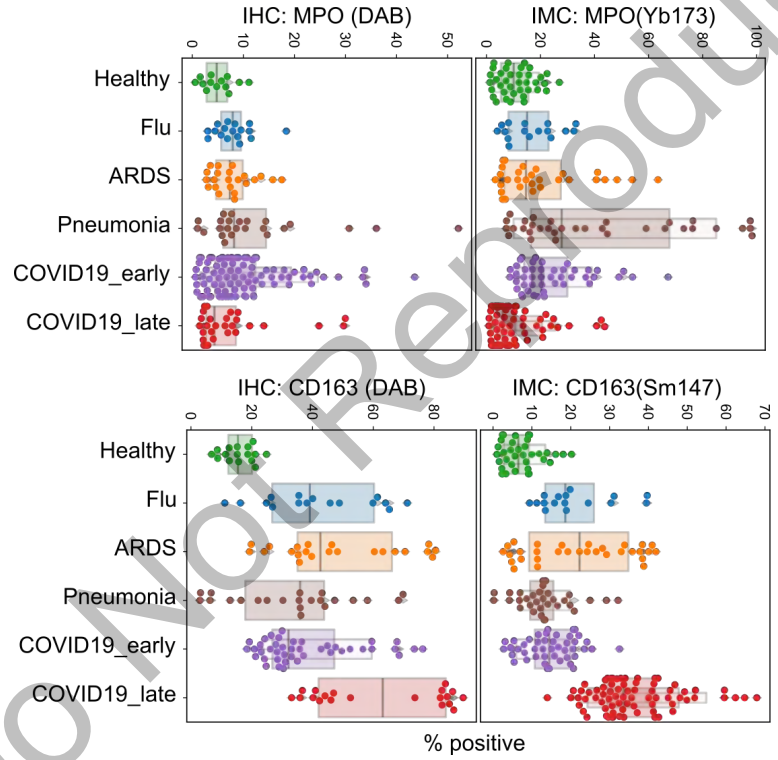
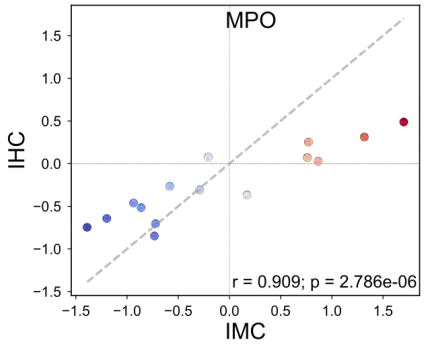
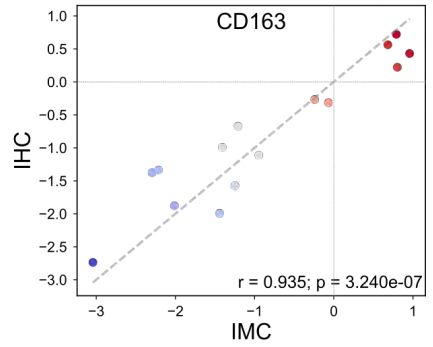
Good agreement of immunohistochemistry and multiplexed imaging









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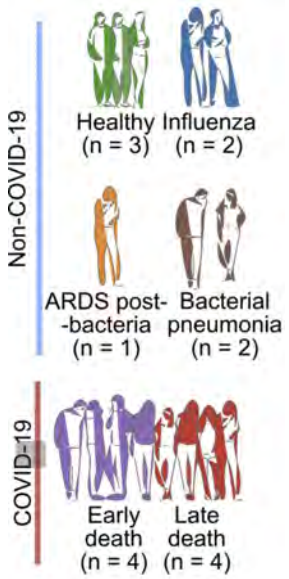
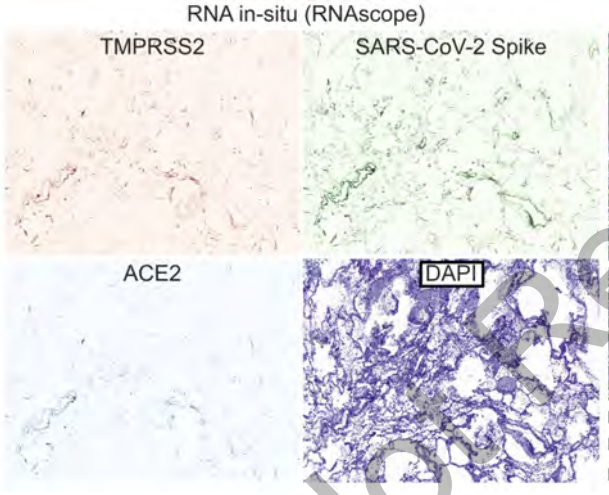
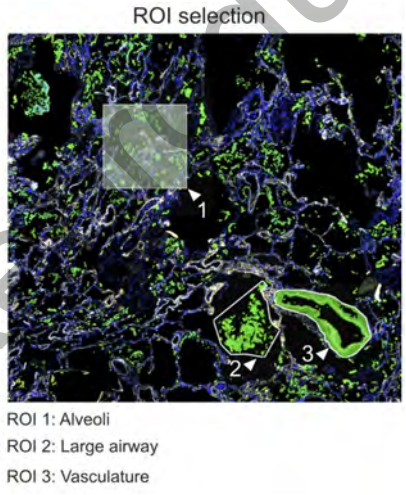
Targeted spatial transcriptomics of COVID-19







GeoMx targeted spatial transcriptomics (1666 targets)

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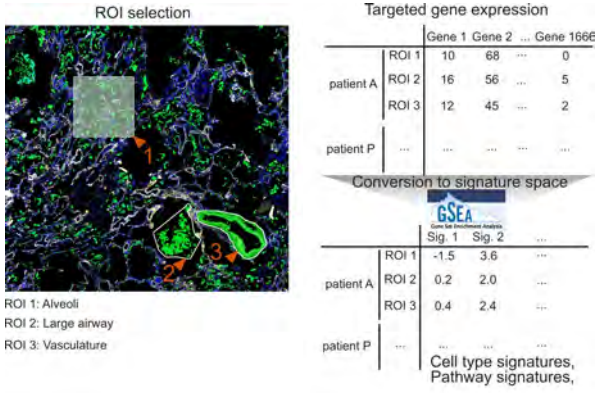
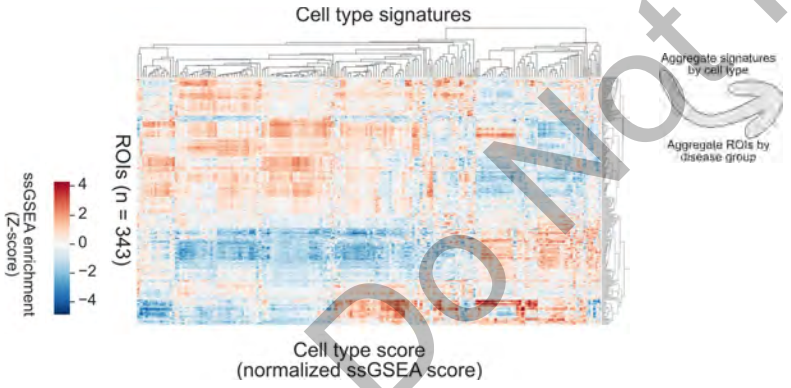
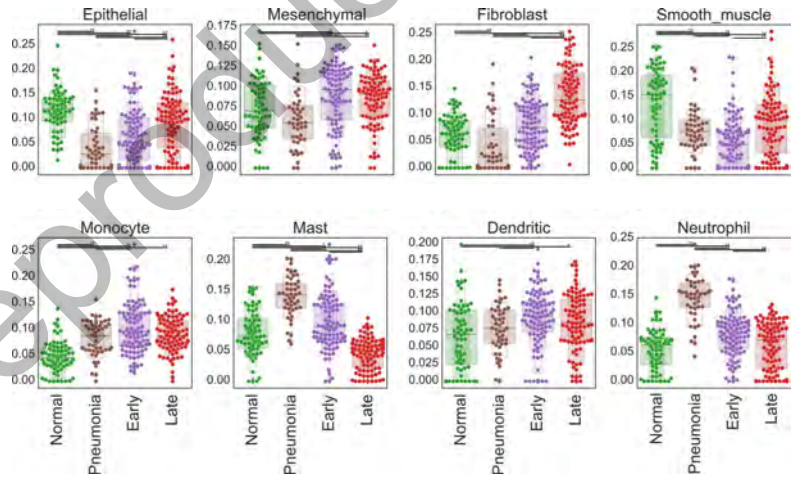
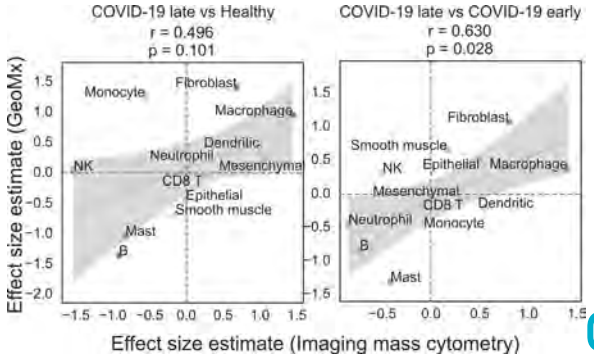
Good agreement of spatial transcriptomics and multiplexed imaging









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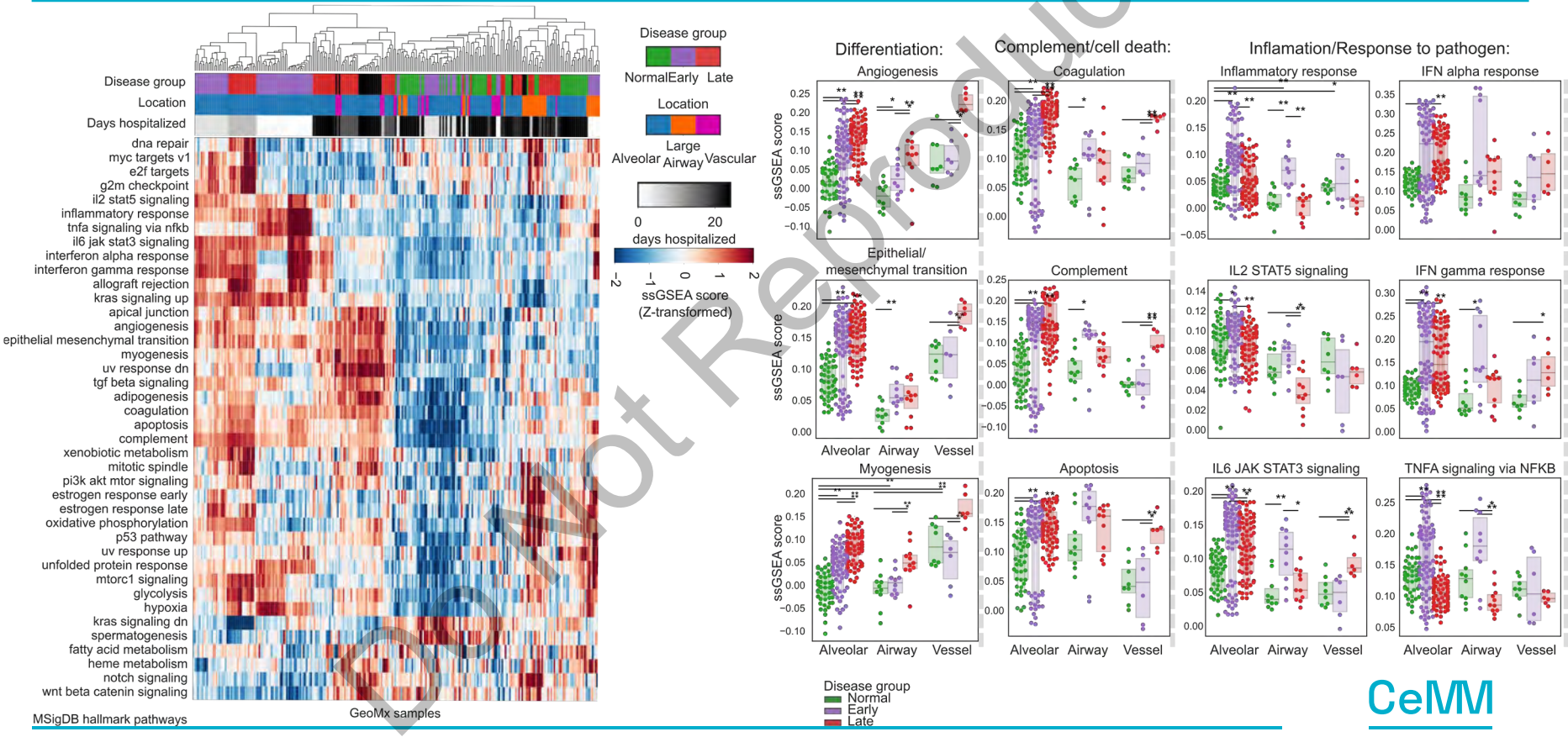
Complementary information between spatial transcriptomics and multiplexed imaging



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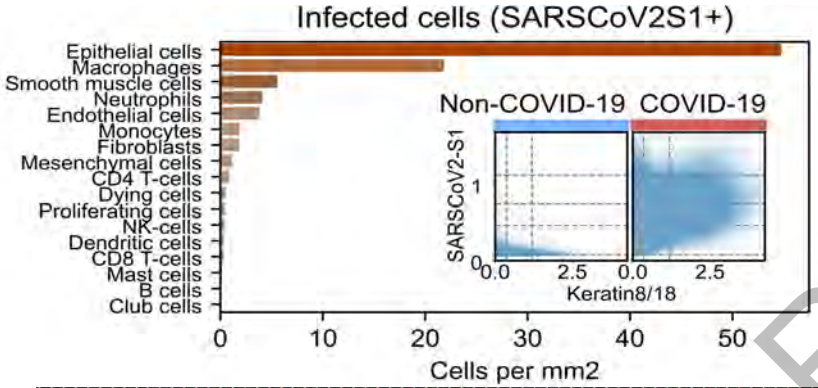
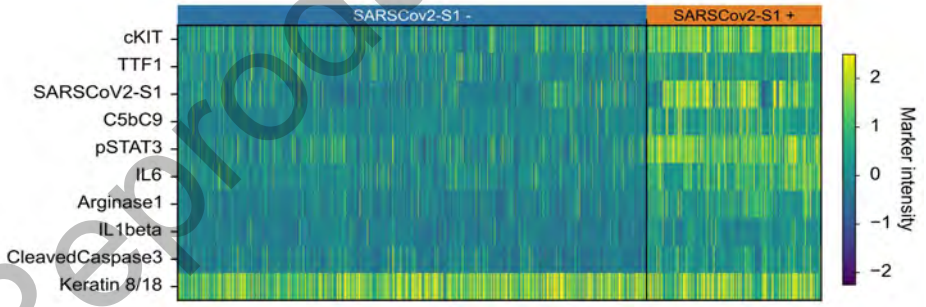
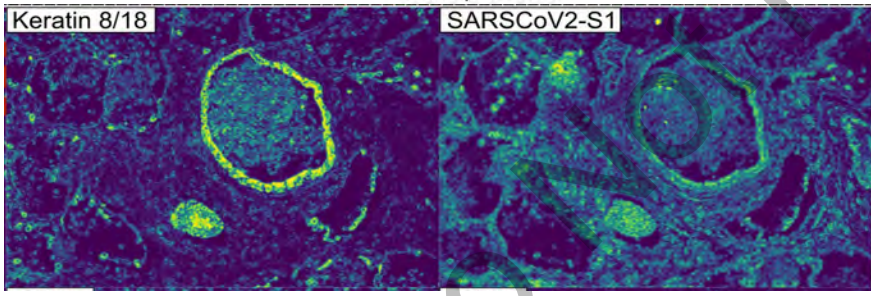
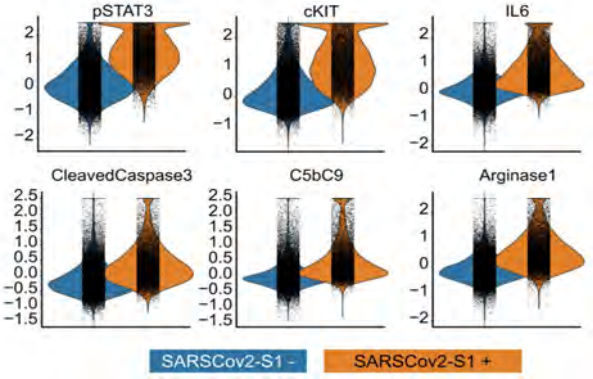
Detection and characterization of infected cells









SARS-CoV-2 Spike protein (S1) antibody included in IMC panel

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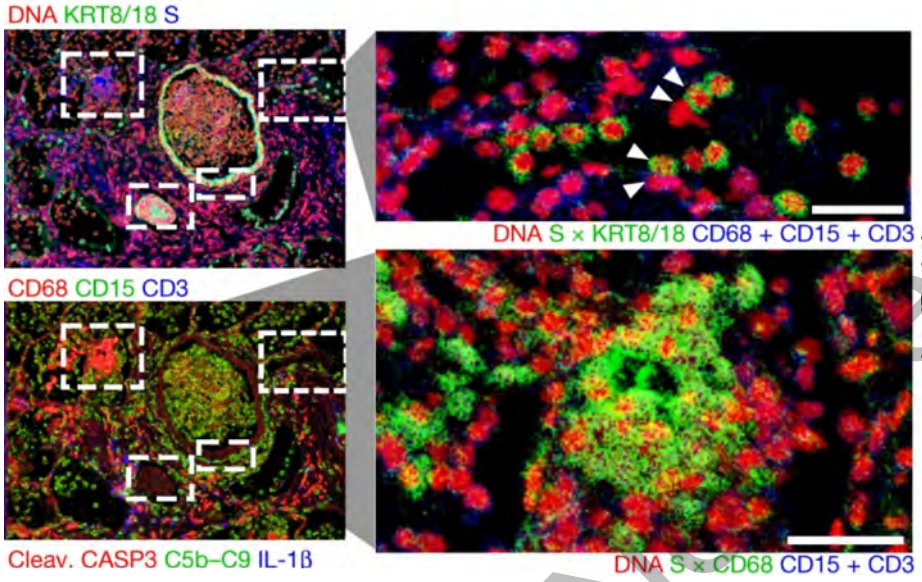
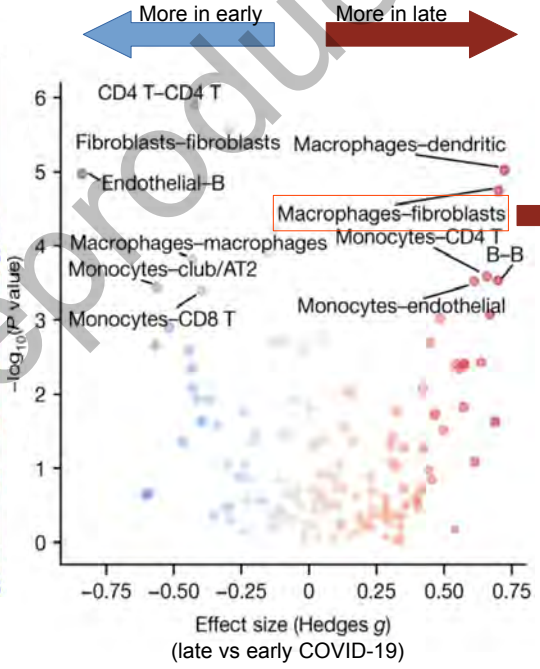
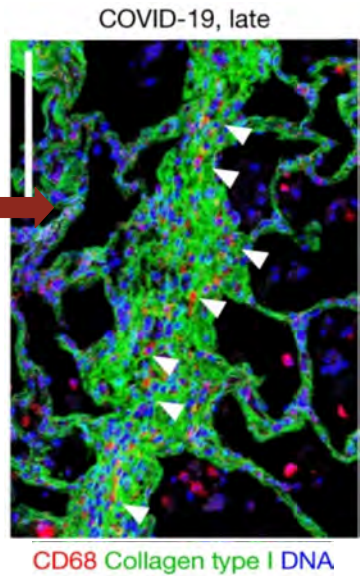
Infiltration of interstitial macrophages during fibrosis







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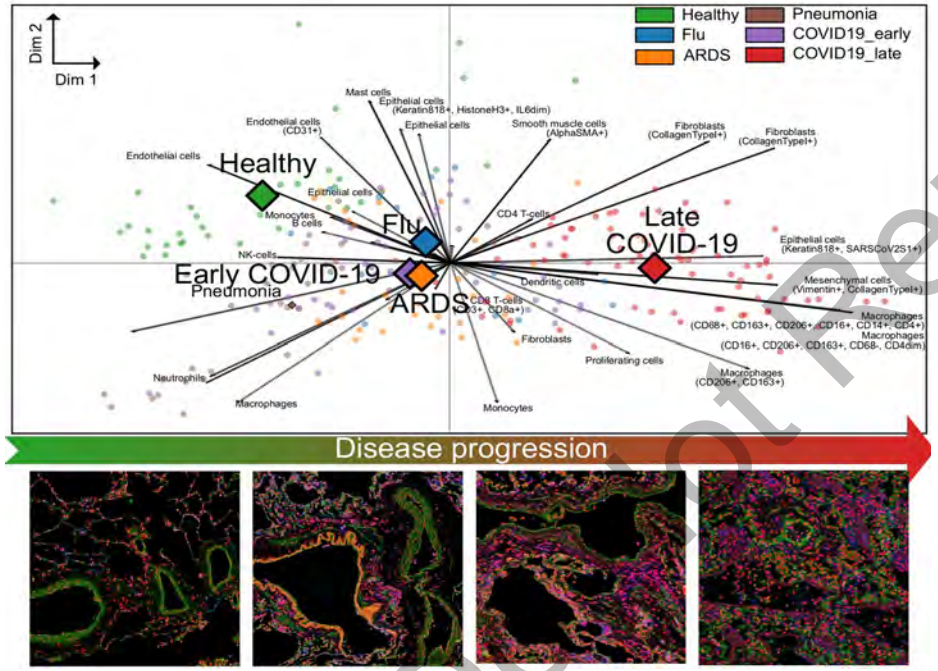
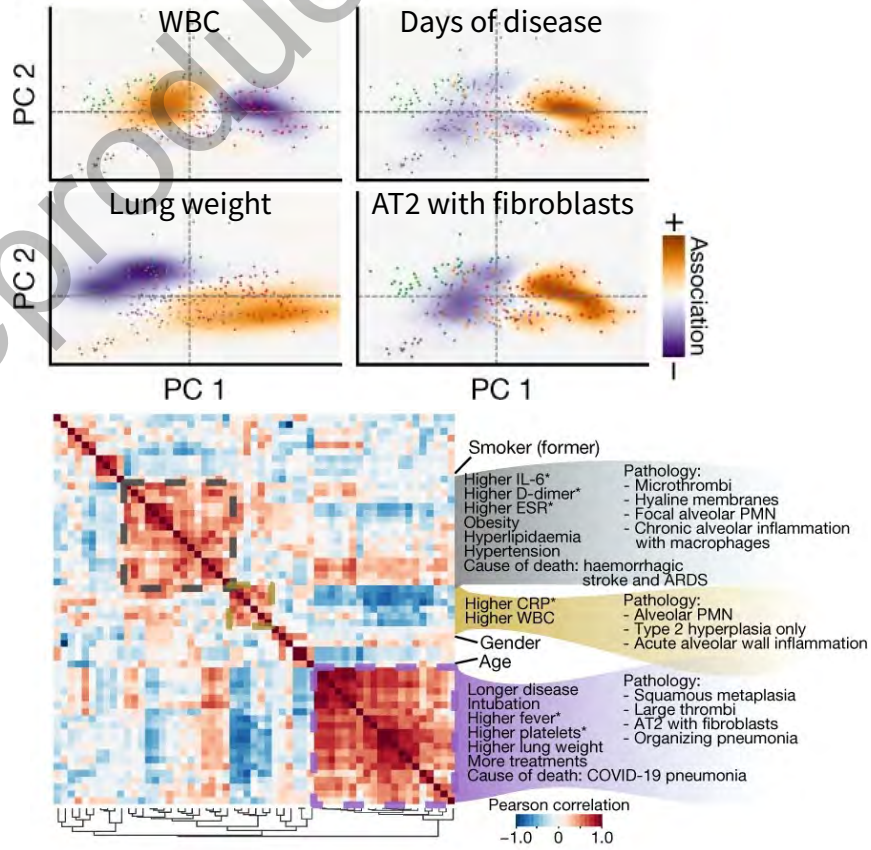
Augmenting spatial atlases with clinical interpretability





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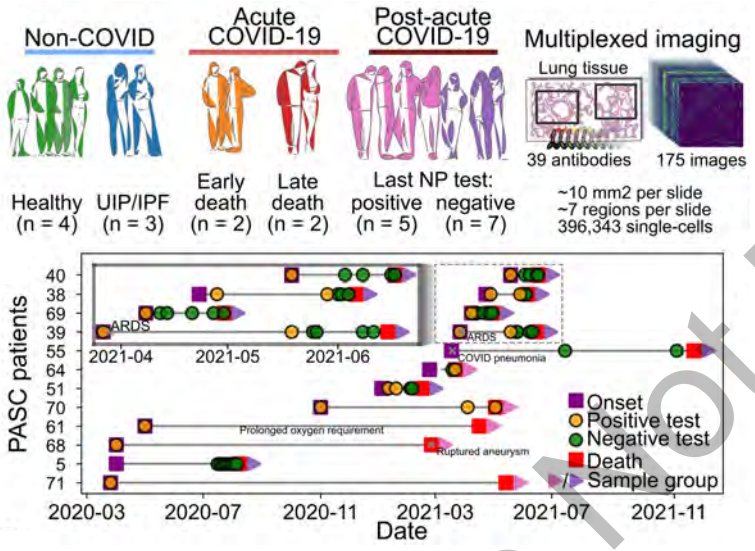
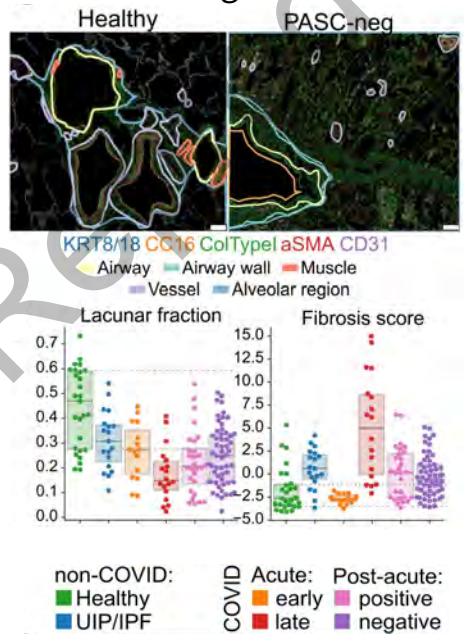
Persistent dysfunction of post-acute COVID-19 lung

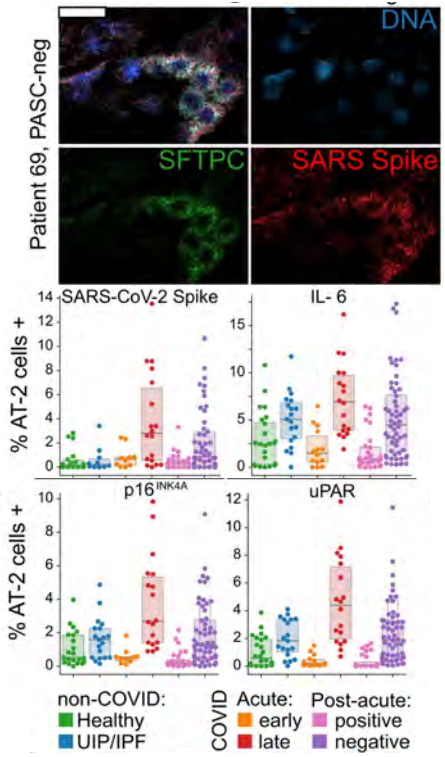
PASC/post-acute COVID-19 patients
followed up to 359 days with incidental death



Persistent lung structural derangement



Persistent SARS-CoV-2 and AT-2 cell senescence



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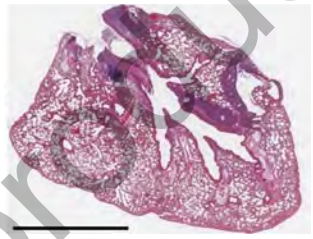
Rendeiro et al., medRxiv (2022), doi:10.1101/2022.11.28.22282811

The cross anatomical scale impact of aging

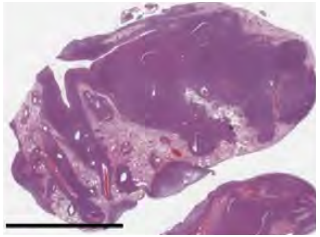
20 years old

102 years old

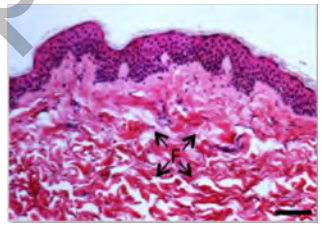
Ludvík Chybík, photographed by Jan Langer, "Faces of Century" project



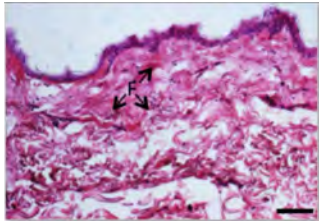
Young mouse lung



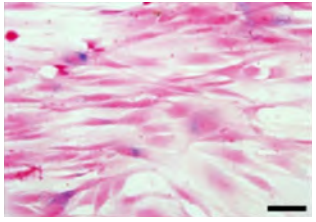
Older mouse lung



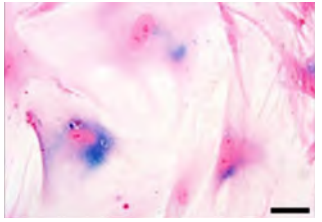
Young skin (28 years old)



Older skin (69 years old)



Young fibroblasts



Aged fibroblasts

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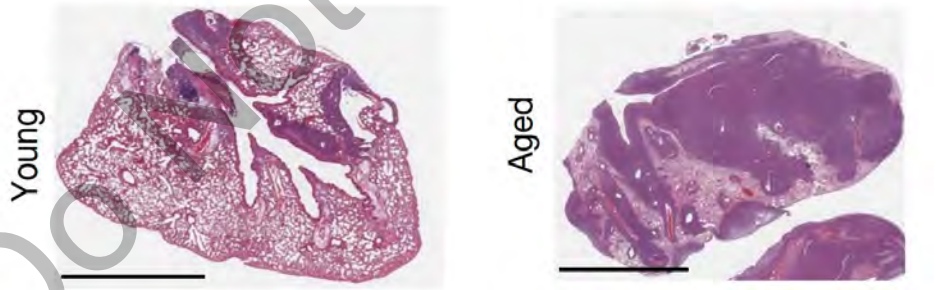
Microanatomical manifestations of aging

The aging process and age-related diseases manifest at the micro-anatomical tissue level, progressively resulting in loss of tissue integrity and function.

We are interested in:

- Spatial distribution of cells and cell states and their organization in healthy and aging tissue.
- Using tissue images/features to predict biological age and risk of disease onset.



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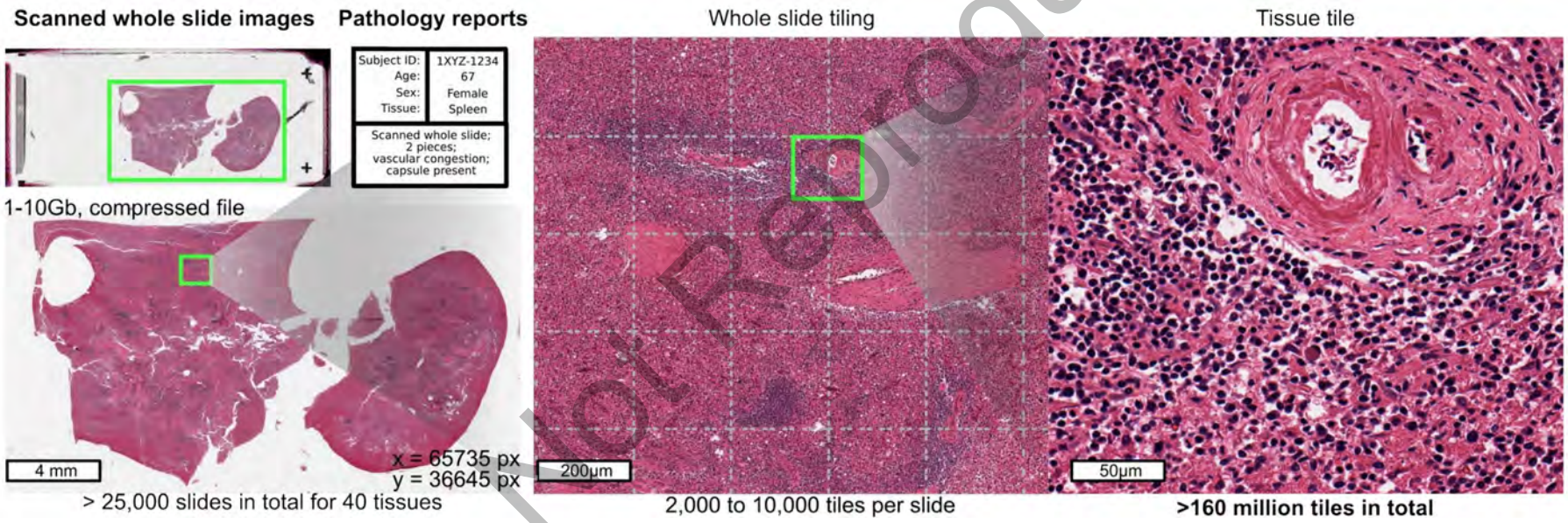
Unappreciated biomedical goldmine: histopathological images



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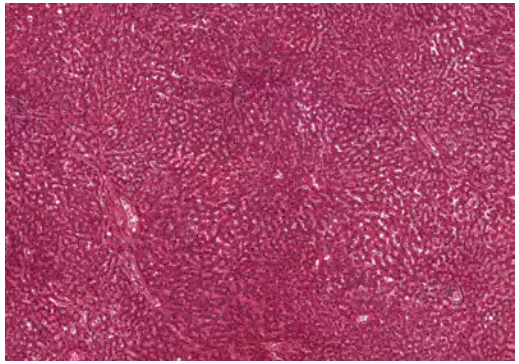
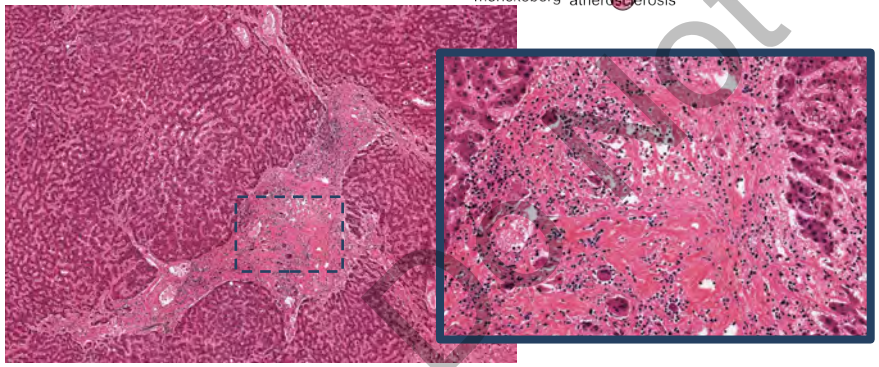
Pathological annotation of 40 human tissues



GTEX-12WSD-1426; Age bracket: 60-69; no major abnormalities



GTEX-111VG-0826; Age bracket: 60-69; chronic inflammation and fibrosis

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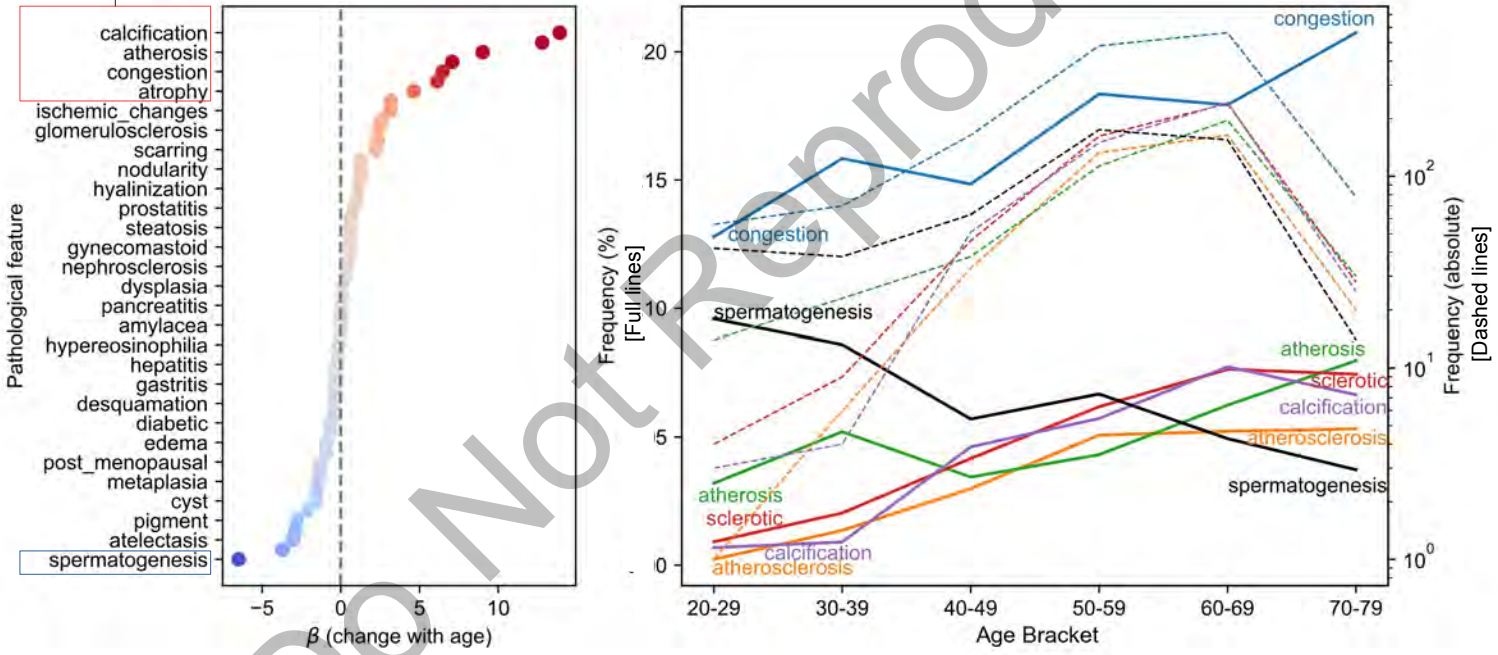
Changes in tissue pathology over the human lifespan



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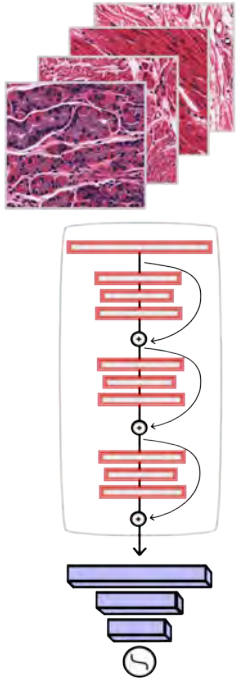
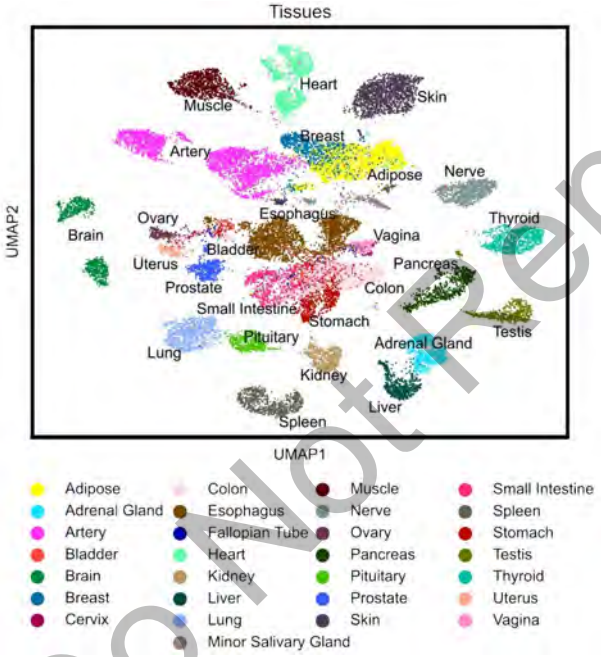
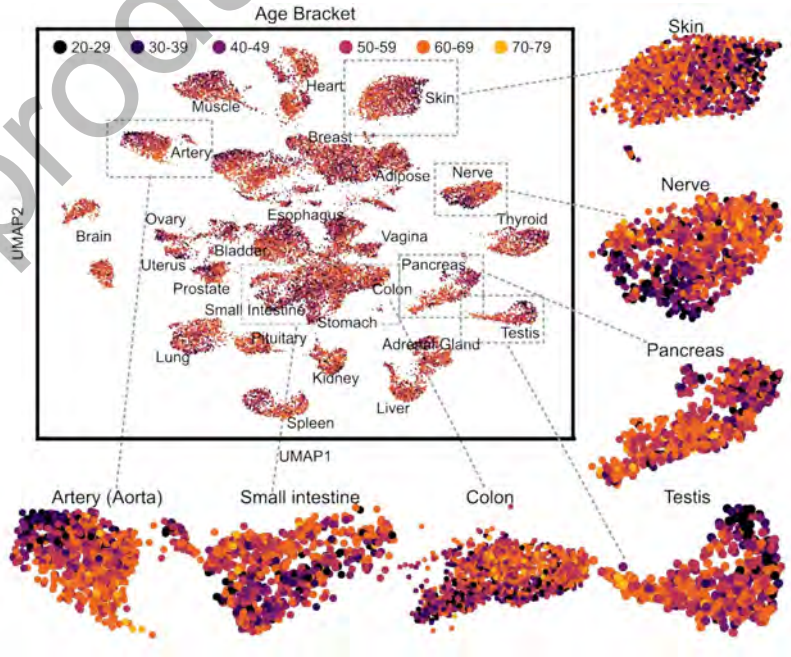
Comprehensive representation of H&E images using deep learning models

Fine-tuning of vision models for tissue classification



Extraction of tissue relevant features for downstream analysis





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Training data balanced for tissue type, age and sex.

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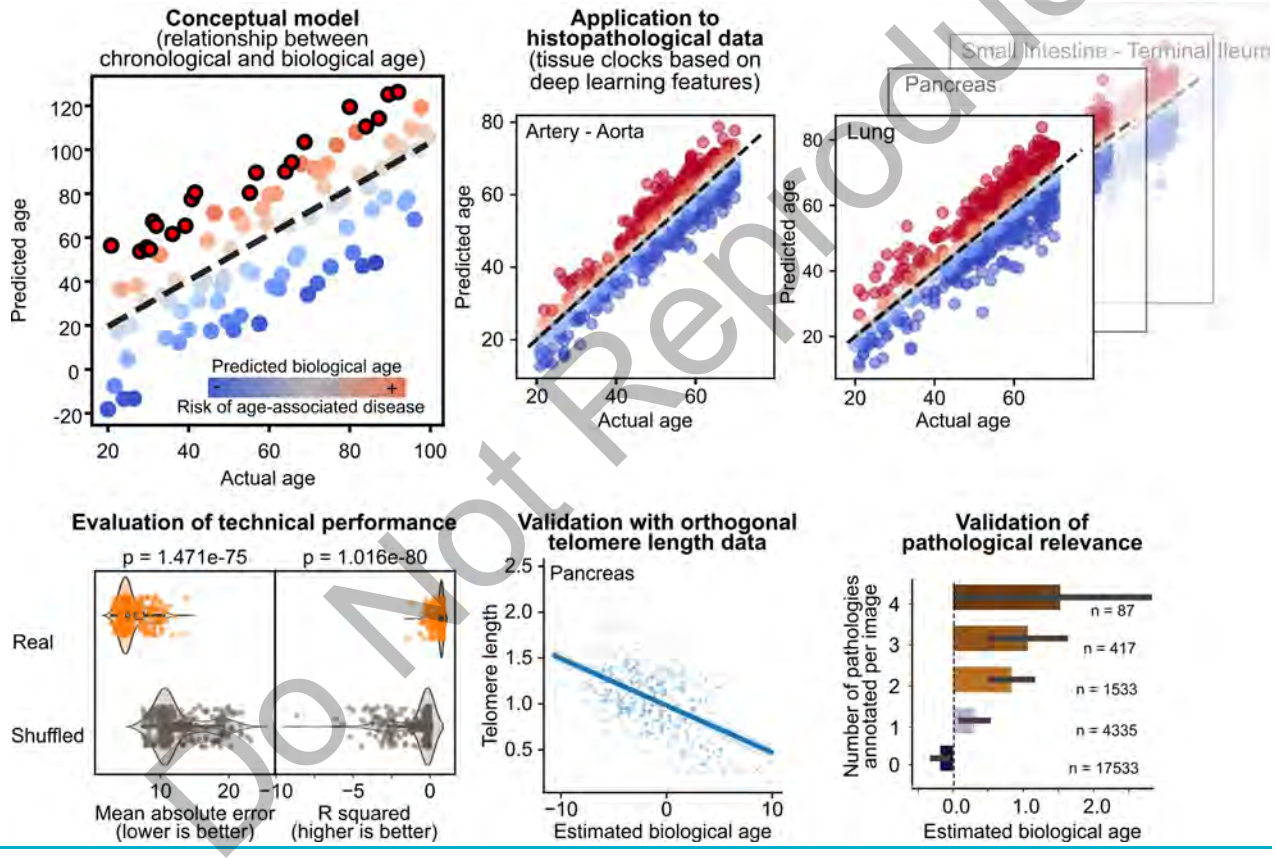
Predictors of biological aging from tissue images



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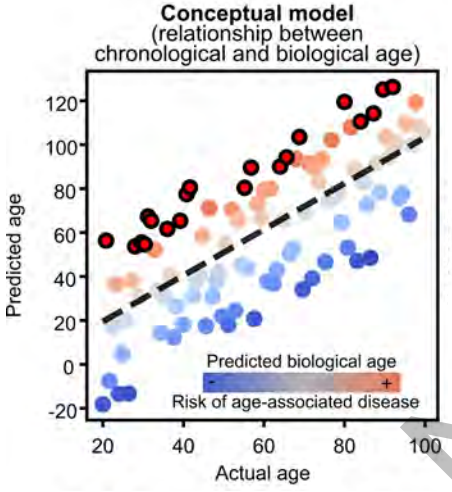
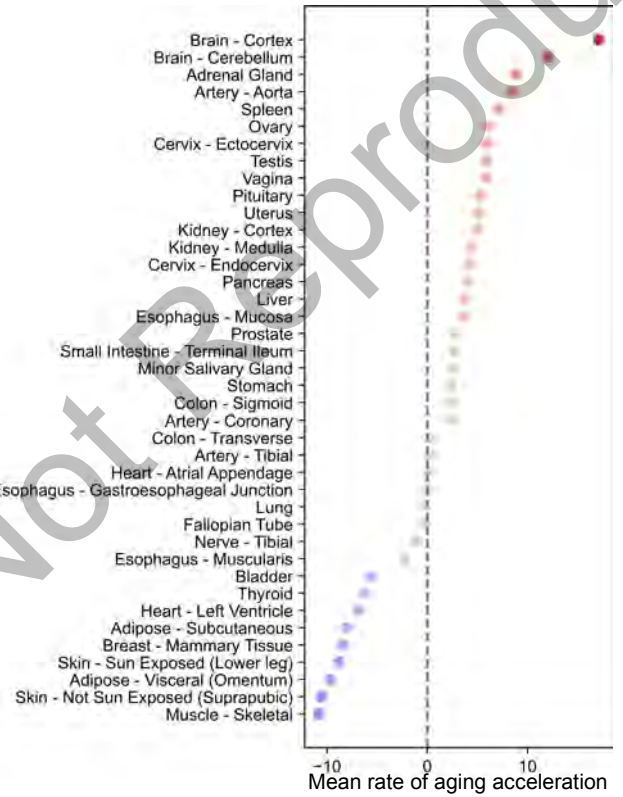
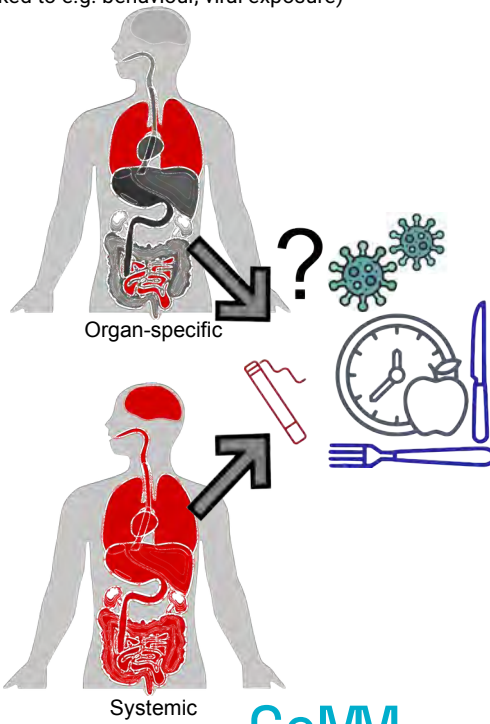
Cross-tissue/organ comparison of rates of aging



Ranking tissues by rate of accelerated aging



Identification of organ-specific vs systemic aging
(linked to e.g. behaviour, viral exposure)



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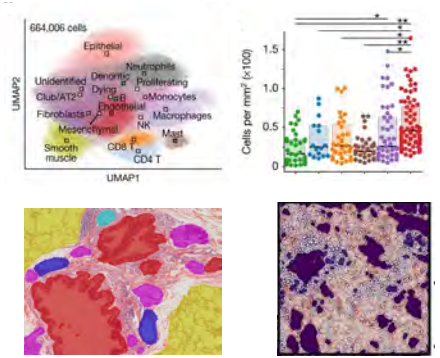
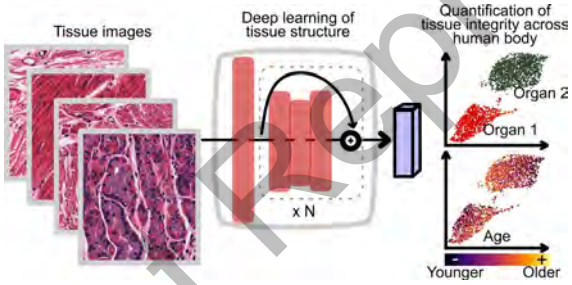
Rendeiro lab: spatial and computational biology of aging

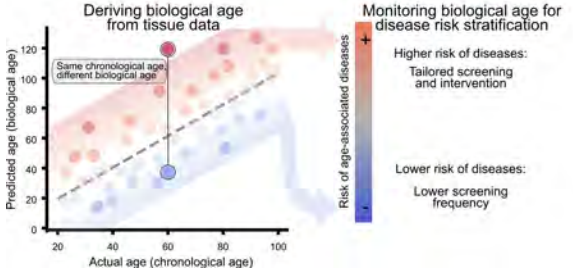
Quantification of cell phenotypes, cell communication and tissue organization



Detection of age-related tissue organization changes



Understanding relationship between loss of tissue integrity and disease onset



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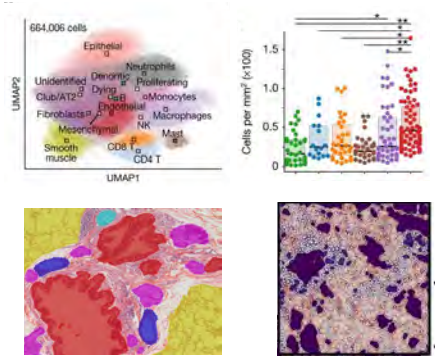
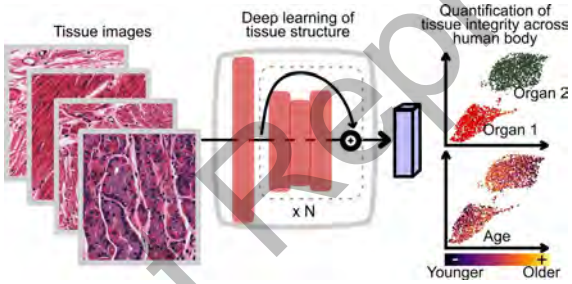
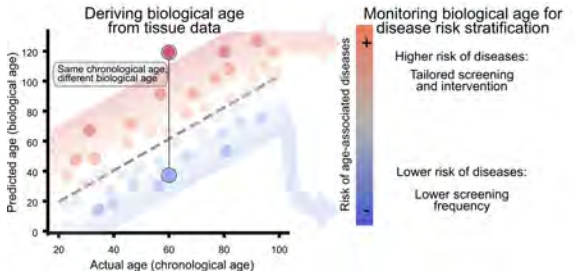
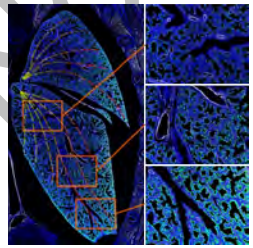




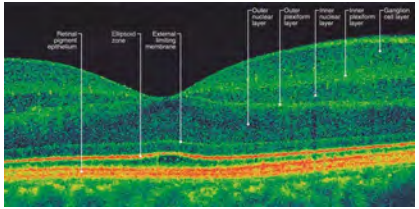


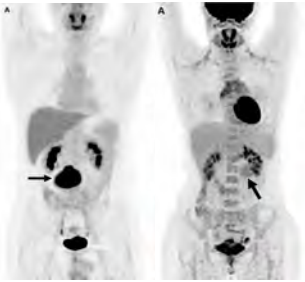
Perhaps with you?

Organ-scale gradients of tissue organization



Integration of/translation to in vivo/non-invasive imaging





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