Molecular cartography of human organs: recent advances in multimodal imaging and omics approaches to map the molecular universe of tissues

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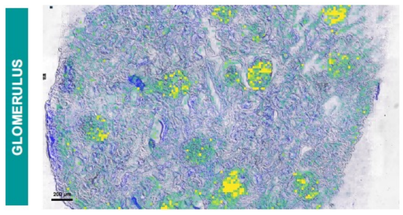
KPMP

Within the Kidney Precision Medicine Project (KPMP), our Tissue Interrogation Site (TIS) has developed a number of matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI)-based spatial omics methods for assaying kidney biopsies obtained from Tissue Recruitment Sites nationwide (USA). We integrate our data with data obtained from other TISs in effort to create a kidney tissue atlas, with the goal of identifying critical cells, pathways, and targets for novel therapies.

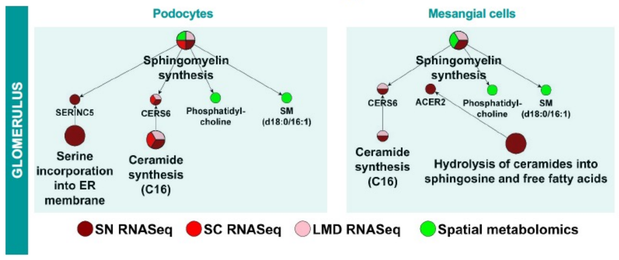
Spatial lipidomics identified a key molecular marker of glomerular biology

MALDI-MS lipidomics found that podocytes were the synthesis site for glomerular sphingomyelin (SM) d18:0/16:1, where *CerS6* in podocytes was confirmed by nuclear RNA, cytosolic RNA, and protein expression.



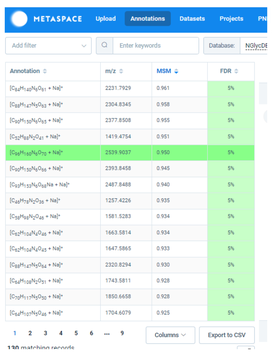
Hansen, J., et. al. *Science Advances* **2022**, *8*, eabn4965

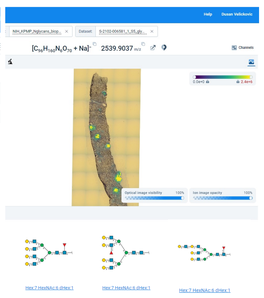
CERS6 is also expressed in mesangial cell, though only detected by the snRNAseq dataset.



Rapid spatial N-glycomics data annotation and visualization in METASPACE

We created NGlycDB-v1, a public database of naturally occurring N-glycans, that can be used in METASPACE.



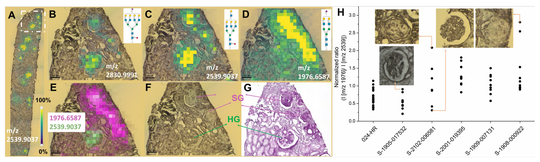


Veličković et. al., *Anal. Chem* **2021**, 93, 13421

NGlycDB is available for public use in METASPACE for processing and visualizing MSI-based N-glycomics data. It can provide FDR controlled annotations and results in <10 min.

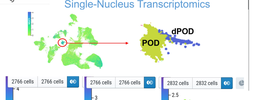
Correlative multi-omics data reveals N-glycan changes in glomerulosclerosis

Our MALDI-MSI workflow identified specific N-glycans related to glomerulosclerosis, and integration of snSeq and regional proteomics data supported dysregulation of key enzymes related to N-glycan maturation within these tissue functional units.

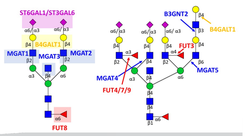


Kidney Mapping Atlas

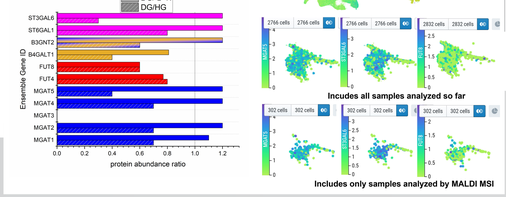
Single-Nucleus Transcriptomics



Key enzymes involved in specific biosynthetic steps during N-glycan maturation

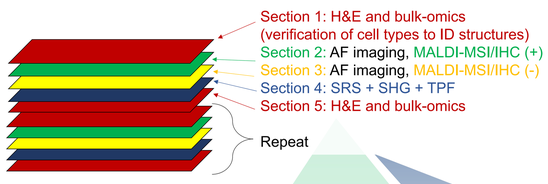


Regional Proteomics



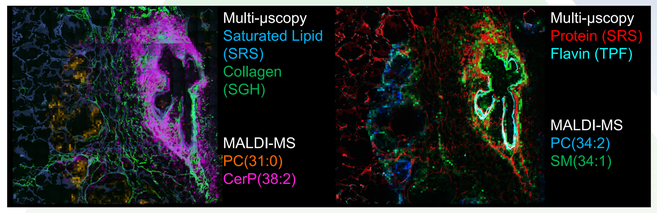
LungMAP HuBMAP Human BioMolecular Atlas Program

For the LungMAP and HuBMAP projects, we have developed a multi-section, multi-omics approach for mapping the molecular profile of the human lung. Our team can obtain comprehensive molecular information from our metabolite, protein, and lipid extraction (MPLEx) protocol, determine the spatial location of these molecules within different cells and tissue functional units using our MALDI-MSI assays, and correlate these findings using multimodal microscopy that combines high lateral resolution stimulated Raman scattering (SRS), second harmonic generation (SHG), and two-photon fluorescence (TPF).



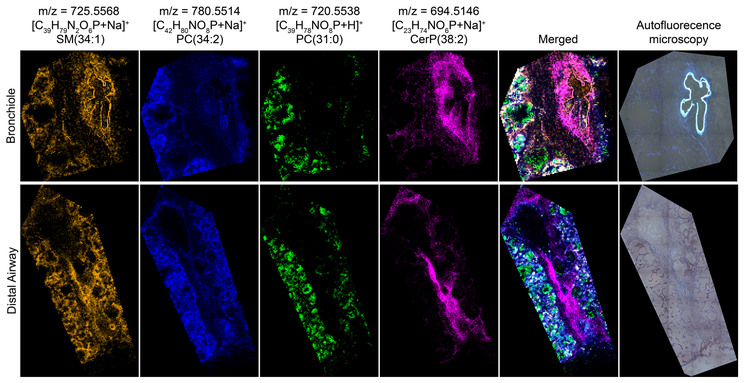
Multi-omics imaging using MALDI-MS + multimodal microscopy of lung tissue

Correlated MALDI-MS lipidomics and high lateral resolution multimodal microscopy show the interaction of lipids with metabolite and protein distributions in lung tissue.



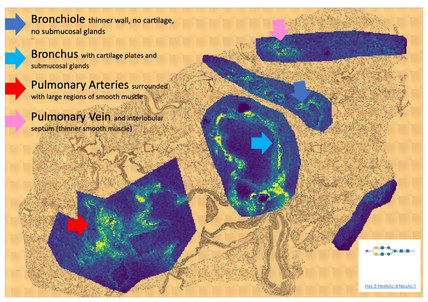
MALDI-MS lipid imaging of human lung tissue

Representative ion images of lung tissue illustrate the distribution of various lipid species within bronchiole and distal tubules. Autofluorescence images allow the identification of structures prior to MALDI-MSI.

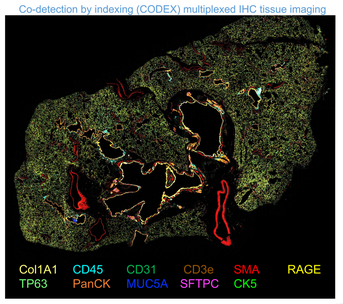


Spatial N-glycomics + IHC of human lung tissue

Using our MALDI-MSI workflow for mapping N-glycans, we can visualize the distribution of these molecules in large human lung tissue sections at pre-defined locations and match them with cell specific markers defined by IHC analysis on the same tissue section.



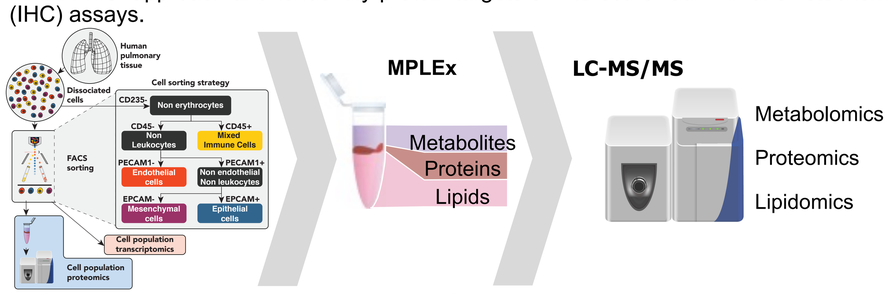
Co-detection by indexing (CODEX) multiplexed IHC tissue imaging

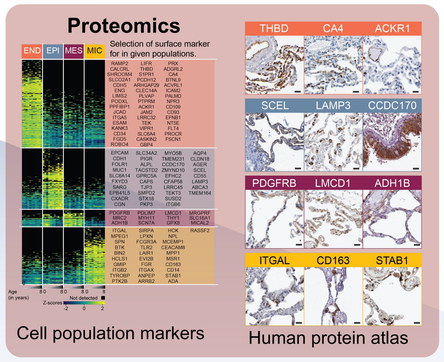


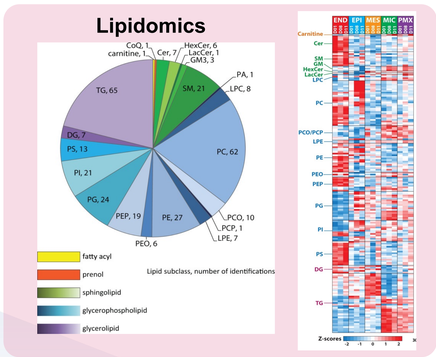
Post-doc position available!
Cool science, industry competitive salary, and in the US Pacific Northwest!

Cell-specific lipidomics and proteomics

Our MPLEx protocol provides broad molecular coverage, with high confidence molecular annotations of metabolites, lipids, and proteins within the human lung. We utilize this information to increase confidence in the molecular species we measure in our untargeted MALDI-MSI approach and to identify protein targets of interest for our immunohistochemical (IHC) assays.

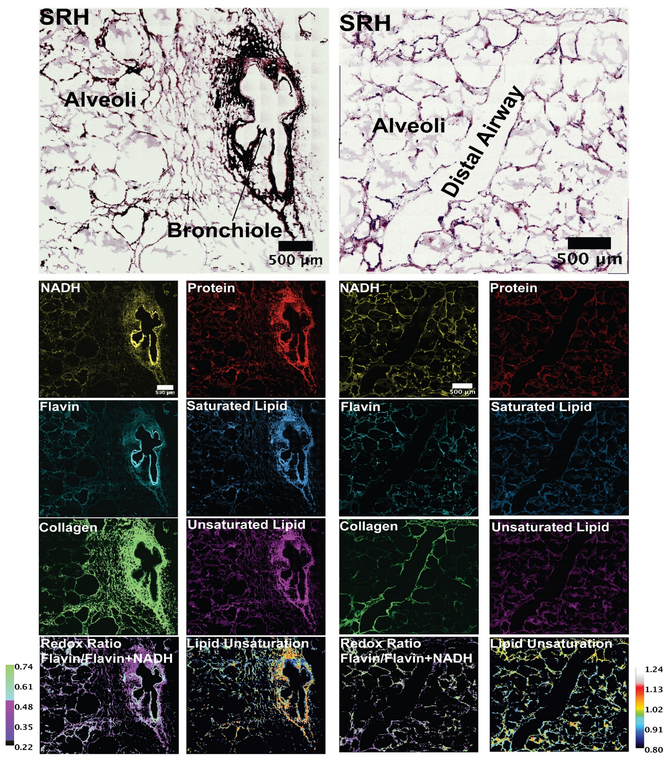






Multimodal microscopy with SRS x SHG x TPF

Investigation of bronchopulmonary disease (BPD) in the human lung, specifically in the vicinity of the bronchioles and distal tubules, using multimodal imaging. This approach may reveal distinctive metabolic variations, providing evidence of the heterogeneity present in BPD, which can be correlated with our molecular findings from analysis of serial sections using our MALDI-MSI-based assays.



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