

# WEAVE SOFTWARE FOR SPATIAL MULTI-OMICS DATA **INTEGRATION - COMBINING MSI AND SRT TO INVESTIGATE** MOLECULAR HETEROGENEITY IN PROSTATE CANCER AND PARKINSON'S DISEASE

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### Introduction

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We describe a spatial multi-omics dataset integration pipeline, and cloud-based software suite of bioinformatics tools, allowing for combined visualisation and downstream analysis. This pipeline was applied to mass spectrometry imaging (MSI) and spatially resolved transcriptomics (SRT) measurements of human prostate cancer (PCa) and mouse models of Parkinson's disease (PD).

## **Methods**

After co-registration and granularity matching in the Weave platform, the MSI and SRT data were directly linked, obtaining a representative mass spectrum associated with a representative SRT spot, and matched spatial readouts. Detailed pathology annotations were transferred to the

# Materials

Matched prostate normal and tumour biopsies (8 x normal, 8 x tumour) were collected from PCa patients who had undergone radical prostatectomy, snap frozen, and stored at -80°C. Serial cryosections (10 µm) were used for SRT (Visium assay, 10X Genomics) and MALDI-2 MSI analysis.

MALDI-2 MSI for lipids was performed on an Orbitrap Elite mass spectrometer (Thermo Fisher Scientific) in positive ion mode. The SRT and MSI-measured sections were H&E stained according to recommended protocols and digitised for pathologist annotations<sup>[1]</sup>.

Non-embedded snap-frozen mouse PD brain tissue was sectioned onto Visium gene expression arrays. It was firstly imaged using a MALDI FTICR instrument (Bruker Daltonics) for neurotransmitters then followed by H&E staining for microscopy and SRT measurement<sup>[2]</sup>.

# shared SRT-MSI spatial coordinates.

# Results



Fig. 1. Strategy for co-registration and integration of different spatial multi-omics data layers generated on consecutive human prostate cancer tissue sections. To link SRT data with MSI data, UMAP visualizations of different modalities were co-registered in two steps based on the H&E stainings of the respective slides and MSI data, and a UMAP visualization of transformed MSI data was generated after granularity matching.



#### **Fig. 2**.

(A) Highly detailed annotations made by specialist prostate cancer pathologists, supported by the Weave platform annotation tool. Annotations were made on high resolution microscopy data from the MSI data section and transformed to the shared coordinate system via the spatial multiomics integration pipeline. This figure shows examples of the pathologist-assigned classes on this specific sample and their spatial distribution in the shared coordinate system.

(B) The H&E images were manually annotated based on tissue morphology (i.e., the Allen Brain Atlas) and dopamine expression. Mouse striatum and substantia nigra hemispheres were categorized into two groups, that is, 'intact' for the left hemisphere and 'lesioned' for the right.

#### Direct correlation analysis between spatially resolved transcriptomics and mass spectrometry imaging data

# Correlation:0.693 A Lipid: PE 40:6 [M+H]+ Gene:AGR2 GOLM1 FOLH1 ABCC4 AMACR TRPM8 HPGD NUCB2 KLK11 AGR2 MIA3 IDH1 CD164 TMEM45B MIPEP ACSM1 TFF3 ALDH1A3 DSCAM-AS1 ENTPD5 PLAT SMS CLGN TMSB15A ZNF350-AS Correlation:-0.631 Lipid: SM 34:1;O2 [M+H]+ Gene:AGR2 DNAH8 NEFH -MDK -EEF1A2 -RLN1 -TMEFF2 PC 30:1 PC 32:1 PE 40: PE 38:0 PC 40:7 PC 40:7 PC 40:7 PC 40:7 PC 40:7 PC 36:1 PC 30:1 PC 30:1 PC 32:1 PE 40:3 PE 40:3 PE 42:1 PE 42:1 PE 40:4 PE 38:1 PE 38:1 PE 38:1 PC 38:5 PC 38:5 PC 38:5 Lipids







Interactive visualizations of spatial multi-omics data via Weave platform

#### **Fig. 4**.

(A) Screenshot of interactive visualization for human prostate cancer samples. Overlay of a correlated pair (from serial sections): gene DSCAM-AS1 & lipid PE 40:3 (m/z 820.584) and MALDI-MSI H&E microscopy. In the right tumor sample, the correlated pair is also highly co-localized with annotated Prostatic Intraepithelial Neoplasia (PIN) region.

(B) Screenshot of interactive visualization for mouse model of Parkinson's disease. Overlay of dopamine (m/z 421.19), annotated intact Striatum region (ACB + CP regions), which are highly correlated with each other, and H&E microscopy.

Fig. 3. Hierarchically-clustered heatmap of the correlation matrix between MSI and SRT data for prostate cancer sample (A), and mouse brain sample (B). Examples of highly positively and negatively correlated ions and gene expression pairs from MSI and SRT data are shown on the right.

### Conclusion

• MSI-SRT data have both shared and complementary biochemical trends, many of which are highly colocalized with specific diseased regions.

• Spatial multi-omics integration pipeline supported via cloud-based Weave platform successfully combines multiple spatial molecular analysis approaches from both same and serial sections. The resulting aligned and matched spatial multi-omics dataset enables the direct comparison and correlation between gene expression and the distribution of lipids or neurotransmitters, providing a more complete picture and understanding of complex diseases such as high-risk prostate cancer and Parkinson's disease.

#### **References:**

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