Multi-Modal Mass Spectrometry Imaging of an Animal Model of High-Grade Serous Ovarian Cancer Provides Deeper Coverage

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Introduction

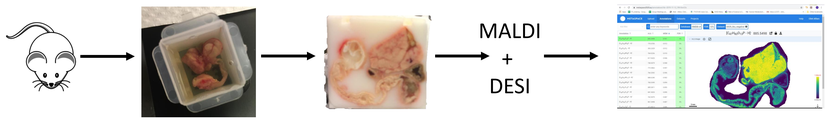
Mass spectrometry imaging is a powerful technique to study the spatial organization of chemicals in biological tissues. Matrix assisted laser desorption ionization (MALDI) and desorption electrospray ionization (DESI) are two popular MS imaging techniques for lipid imaging. In this study, MALDI and DESI were utilized to investigate samples from a mouse model (triple knockout, TKO) of high-grade serous ovarian cancer (HGSC). The chemical coverage of the methods was compared based on unique and shared METASPACE annotations. The combined use of MALDI and DESI is shown to provide a more thorough lipidomic coverage, leading to a better potential for discovering critical biomarkers of HGSC and a better assessment of the metabolic aberrations underpinning the disease.

Study Goals

- Annotate the different molecules detected from DESI and MALDI MSI of TKO-control and TKO-HGSC samples
- Investigate the extent to which the complementary chemical coverage observed in MALDI and DESI provide additional insight into the progression of HGSC

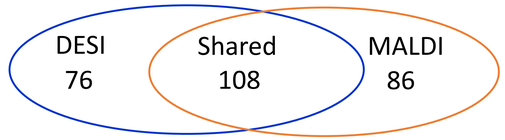
Methods

- Two mice, 1-TKO-Control and 1-TKO-HGSC, were sacrificed and reproductive systems extracted.
- The tissues were embedded in a 10% gelatin, 5% carboxymethylcellulose solution, and cryosectioned to 10 µm.
- Adjacent tissue sections were imaged with DESI on an Orbitrap QExactive, and with MALDI on a Bruker SolariX 12T FTICR and a Bruker RapifleX MALDI-TOF, in negative ion mode.
- DESI-MS solvent was 1:1 DMF-ACN, flow rate 1.2µL/minute, *m/z* range 80-1500, resolving power 140K at *m/z* 200, and pixel size was 240 µm.
- MALDI matrix was 10 mg/mL 1,5-diaminonaphthalene (1,5-DAN), dissolved in 65:20:15 acetonitrile-methanol-chloroform, and was applied with an iMatrixSpray system. The SolariX was operated with datasize set to 4M, transient time of 2.4sec, 150 µm raster size, and *m/z* range 200-1500. The RapifleX was operated in reflectron mode, *m/z* range 200-1500, and 100 µm raster size.
- Images were uploaded to METASPACE for peak annotation, using the HMDB database as a reference, and a 10% false discovery rate.
- The annotation lists were analyzed in Microsoft Excel. DESI-MS ion images were normalized and plotted in MATLAB. MALDI-MS images were visualized using SCiLS Lab software.

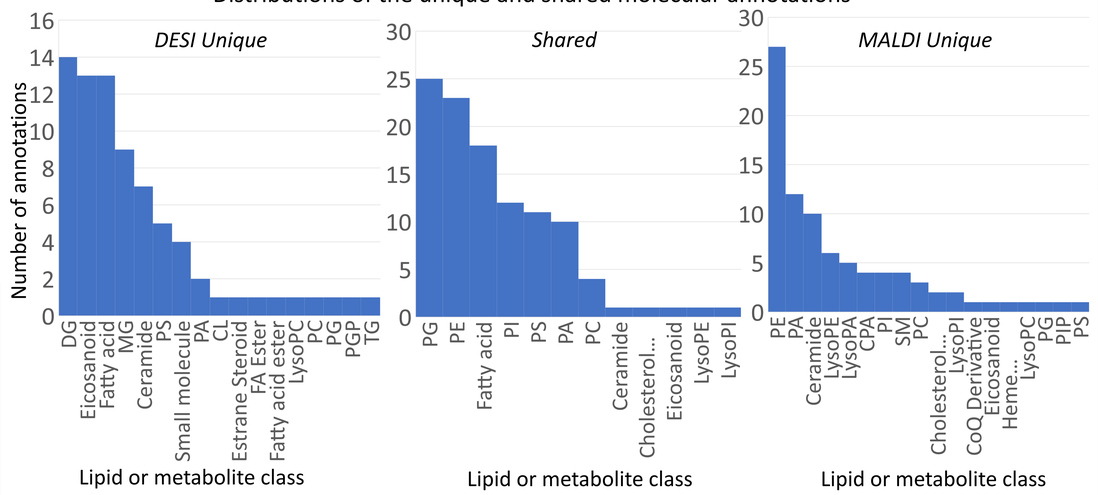


Results

Unique and shared METASPACE annotations observed with MALDI and DESI



Distributions of the unique and shared molecular annotations

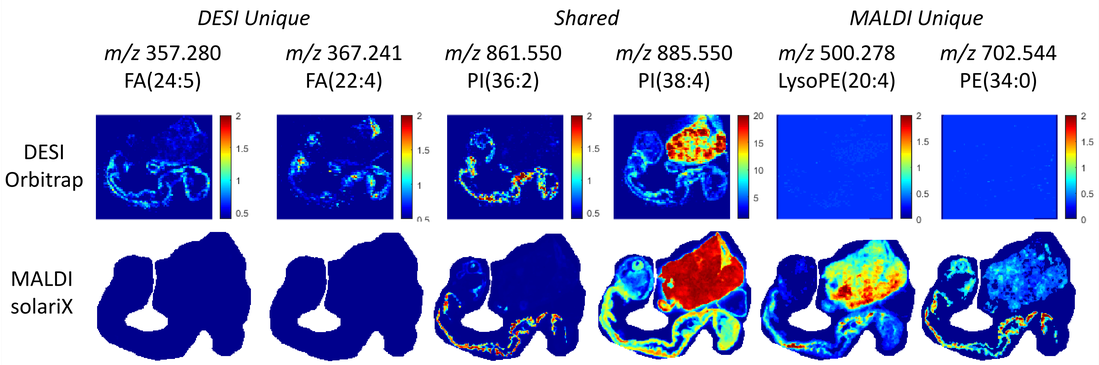


Greater number of diacylglycerols (DGs), eicosanoids, fatty acids, and monoacylglycerols (MGs) were detected with DESI.

Several phosphatidylglycerols, phosphatidylethanolamines, fatty acids, and other phospholipids, were annotated in both the DESI and MALDI datasets, among others.

Many phosphatidylethanolamines were uniquely annotated in the MALDI-MS data, along with some phosphatidic acid lipids and ceramides, and others.

Ion images of select annotations that are unique or shared



Conclusions

- Tissue imaging with MALDI and DESI provides a deeper and complementary lipidomic coverage that surpasses a single modality.
- Annotations were based on MS[1] data only and need to be verified with on-tissue MS[2], and possibly LC-MS analysis of tissue microextractions.
- Integration of MALDI and DESI MSI with other imaging modalities would provide more insight into HGSC progression in the TKO mouse model.
- Application of MALDI and DESI to a larger cohort of TKO mice with different stages of HGSC is needed to verify the annotations and support any biological conclusions.

References

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