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Spatial Metabolomic Mapping of Fibrosis-Associated Metabolites in the UUO Kidney

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Objectives : This study aimed to identify fibrosis-related metabolites and visualize their spatial distribution in the kidney using spatial metabolomics in a unilateral ureteral obstruction (UUO) mouse model.
Methods : UUO was induced in 8-week-old male C57BL/6 mice by ligation of the left ureter, and kidneys were harvested 7 days after surgery. Untargeted metabolomic profiling was performed using liquid chromatography–mass spectrometry (LC-MS) (sham, n=11; UUO, n=13). Spatial metabolite imaging was conducted using Orbitrap secondary ion mass spectrometry (OrbiSIMS) and time-of-flight secondary ion mass spectrometry (TOF-SIMS).
Results : LC-MS analysis identified significant alterations in several metabolites in UUO kidneys compared with the sham group, including increased levels of p-cresol sulfate and trimethylamine-N-oxide (TMAO). Lipidomic analysis revealed revealed increased levels of triglycerides and cholesteryl esters, whereas ceramides, sphingomyelins, phosphatidylcholines, and phosphatidylethanolamines were decreased in UUO kidneys. OrbiSIMS imaging detected 272,404 distinct mass-to-charge (m/z) ion signals across kidney sections, enabling high-resolution spatial metabolite mapping. Phosphatidylethanolamines were predominantly distributed in cortical tubular regions and showed reduced signals in UUO kidneys, consistent with LC-MS findings. In contrast, phosphatidylcholines showed localized increases in specific kidney regions despite an overall decrease observed by LC-MS.
Conclusions : Spatial metabolomics using OrbiSIMS and TOF-SIMS enabled high-resolution mapping of fibrosis-associated metabolites in the UUO kidney model. The combined use of LC-MS and SIMS imaging provides complementary information on metabolite abundance and spatial localization, offering new insights into metabolic remodeling during renal fibrosis.

Figure1.PNG

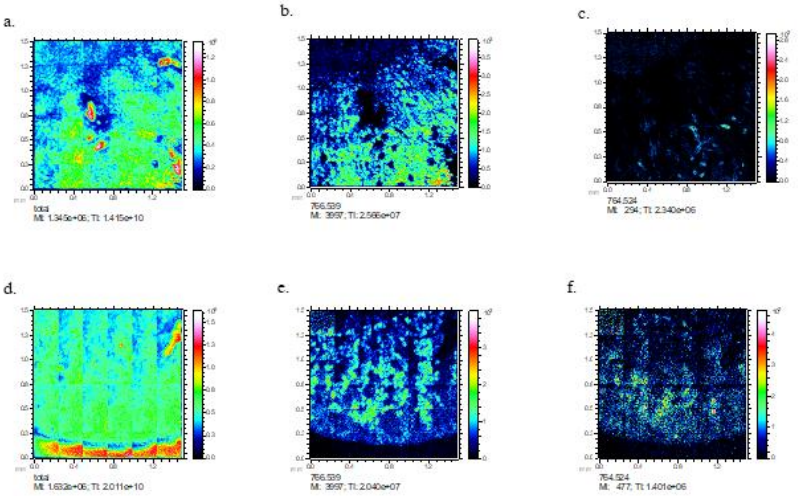

Fig. 1. Representative cryo-section OrbiSIMS images of kidney tissue in sham and UUO mice.
a. Sham group: total ion distribution of all detected molecules (m/z 80–1200).
b. Sham group: ion image of phosphatidylethanolamine 38:4 (PE 38:4; m/z 766.5384).
c. Sham group: ion image of phosphatidylcholine 36:5 (PC 36:5; m/z 764.5227).
d. UUO group: total ion distribution of all detected molecules (m/z 80–1200).
e. UUO group: ion image of PE 38:4 (m/z 766.5384).
f. UUO group: ion image of PC 36:5 (m/z 764.5227).
MI: Maximum Intensity, TI: Total Intensity.

Figure1.PNG

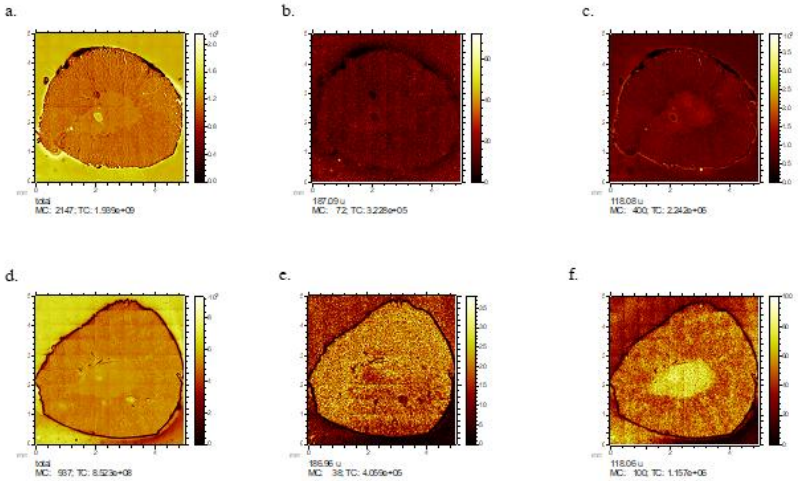

Fig. 2. Representative cryo-section TOF-SIMS images of kidney tissue under different sample preparation conditions.
a. Sham group: total ion distribution of all detected molecules (m/z 0–1200) in lyophilized samples.
b. Sham group: negative ion image of cresol sulfate (m/z 187.09) in lyophilization sample.
c. Sham group: positive ion image of betaine (m/z 118.10) in lyophilization sample.
d. Sham group: total ion distribution of all detected molecules (m/z 0–1200) in fresh cryo-section samples scanned immediately after sectioning.
e. Sham group: negative ion image of cresol sulfate (m/z 187.09) in none treatment sample.
f. Sham group: positive ion image of betaine (m/z 118.10) in none treatment sample.
MC, Maximum Counts ; TC, Total Counts.