4D-Metabolomics Profiling of Lung Adenocarcinoma using timsMetabo™ With Complementary Separation Techniques

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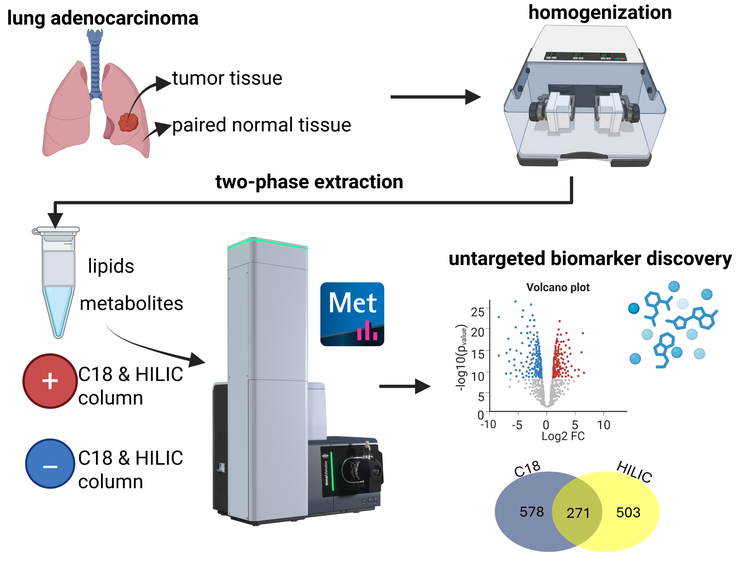
Introduction

Metabolite profiling is essential to understanding the molecular mechanisms of tumorigenesis in lung adenocarcinoma (LUAD), a common subtype of lung cancer.

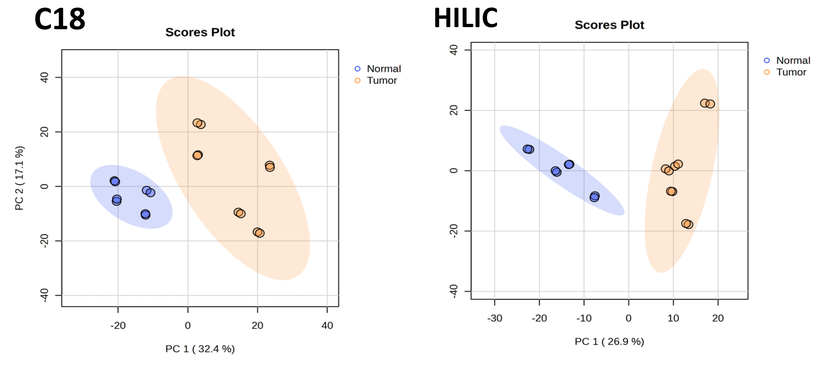
We profiled the polar metabolomes of lung tissue homogenates representing tumor and healthy tissue from human donors using a novel trapped ion mobility-mass spectrometer (TIMS-MS). Importantly, both reversed-phase (RP) and hydrophilic interaction (HILIC) liquid chromatography (LC) were applied, to cover both moderately and highly polar compounds.

The integration of LC-TIMS-MS/MS-based for untargeted 4D-metabolomics enables precise and selective metabolomic profiling of complex lung tissue extracts including data integration of complementary separation approaches.

Workflow



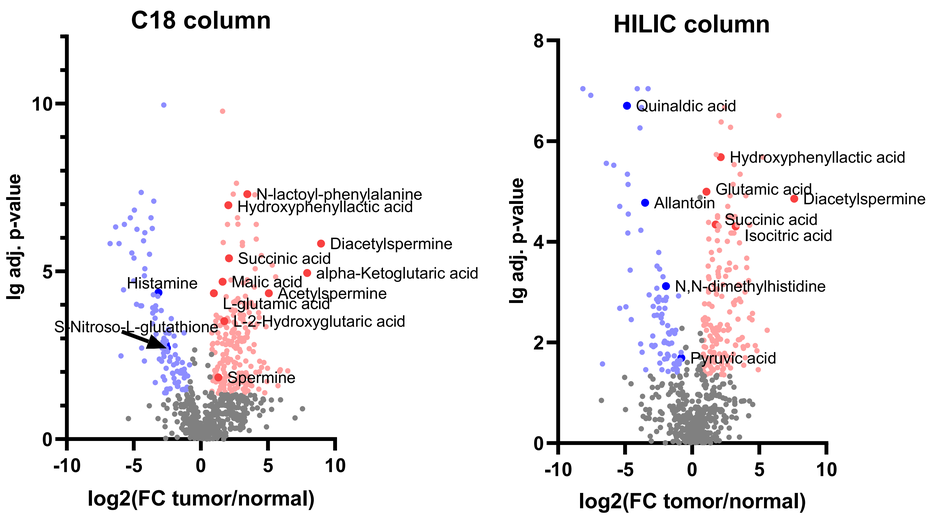
Statistical Analysis



The PCA analyses based on Bruker Bio-AQ C18 (15min) and Waters Acquity UPLC BEH HILIC data (21min), show consistency and reveal a clear separation between tumor and normal lung tissue, suggesting profound dysregulation in the respective global metabolomic profile.

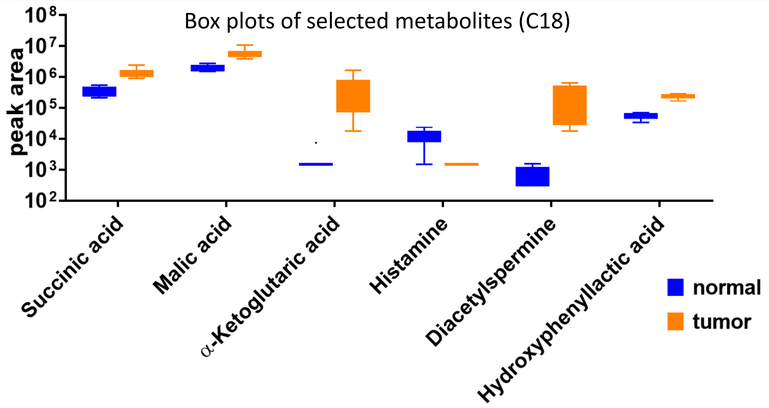
Metabolomic Biomarker Discovery

Volcano plot of differential metabolic features



Points in **red** indicate significantly up-regulated metabolites in tumor tissue (log2FC>0.8, adj. p<0.05), and points in **blue** indicate significantly down-regulated metabolites (log2FC<0.8, adj. p<0.05). Grey points represent features that did not meet the significance or fold-change criteria.

Box plots of selected metabolites (C18)



The upregulation of tricarboxylic acid (TCA) cycle intermediates, diacetylspermine, and hydroxyphenyllactic acid, reflect intensified energy metabolism and altered amino acid processing. The upregulated diacetylspermine derived from the rapid cell turnover and the accelerated polyamine metabolism essential for tumor proliferation. Conversely, the downregulation of histamine suggests a suppressed inflammatory response within the tumor microenvironment.

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Conflict of interest statement

ER, BR, StW and MRL are employees of Bruker Daltonics GmbH & Co. KG. Bruker Daltonics manufactures LC-MS instrumentation, consumables, and timsTOF instruments.

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