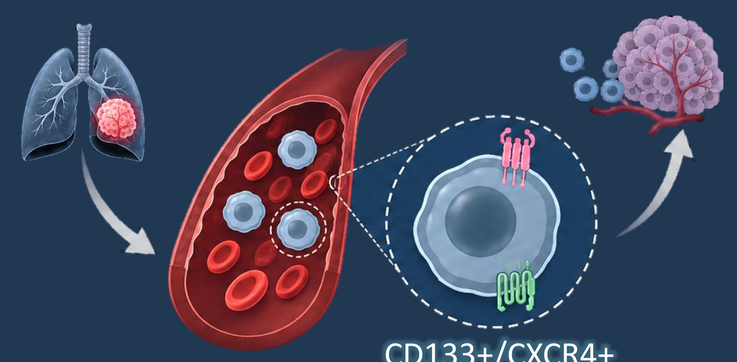
Metabolic and Lipidomic Remodeling during Lung Cancer Progression

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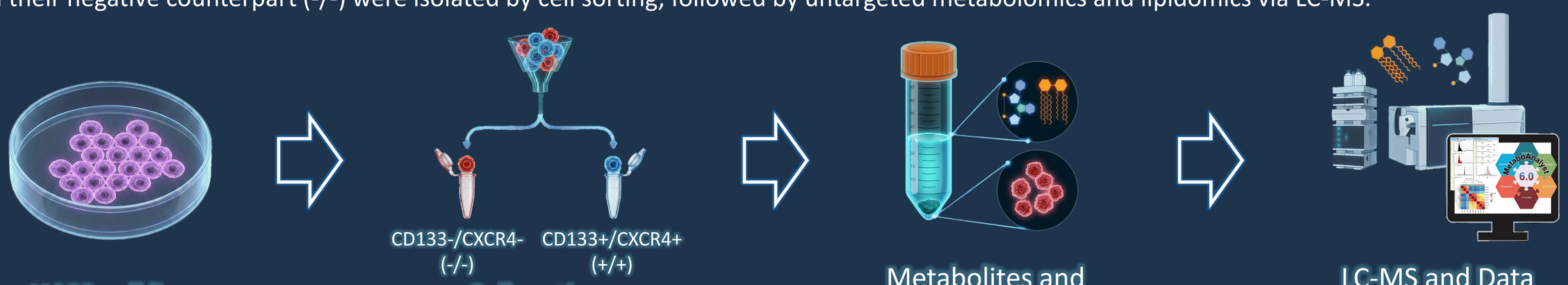
Background

Lung cancer is the leading cause of cancer-related mortality, mainly due to metastatic dissemination. A rare subpopulation of circulating tumor cells (CTCs) with stem-like and metastasis-initiating features is thought to drive tumor spread. In lung cancer, cells co-expressing CD133 and CXCR4 have been identified as metastasis-initiating cells (MICs). Emerging evidence links metastatic competence to profound metabolic rewiring, but the metabolic phenotype of MICs remains poorly characterized.



Aim and Workflow

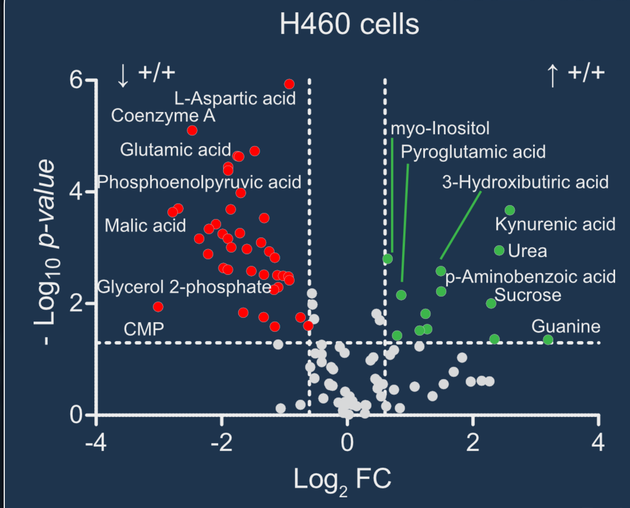
To characterize the metabolic and lipidomic profile of MICs, we used the H460 lung cancer cell line as experimental model. $CD133^{+}/CXCR4^{+}$ cells (+/+) and their negative counterpart (-/-) were isolated by cell sorting, followed by untargeted metabolomics and lipidomics via LC-MS.



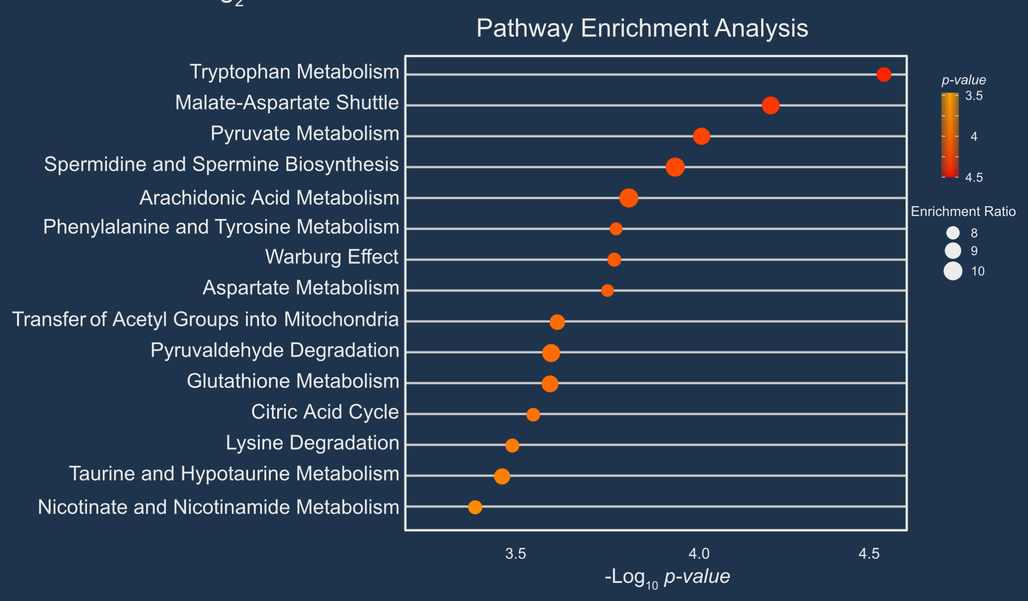
H460 cell line → Cell sorting → Metabolites and lipids extraction → LC-MS and Data analysis

Results

Polar metabolites

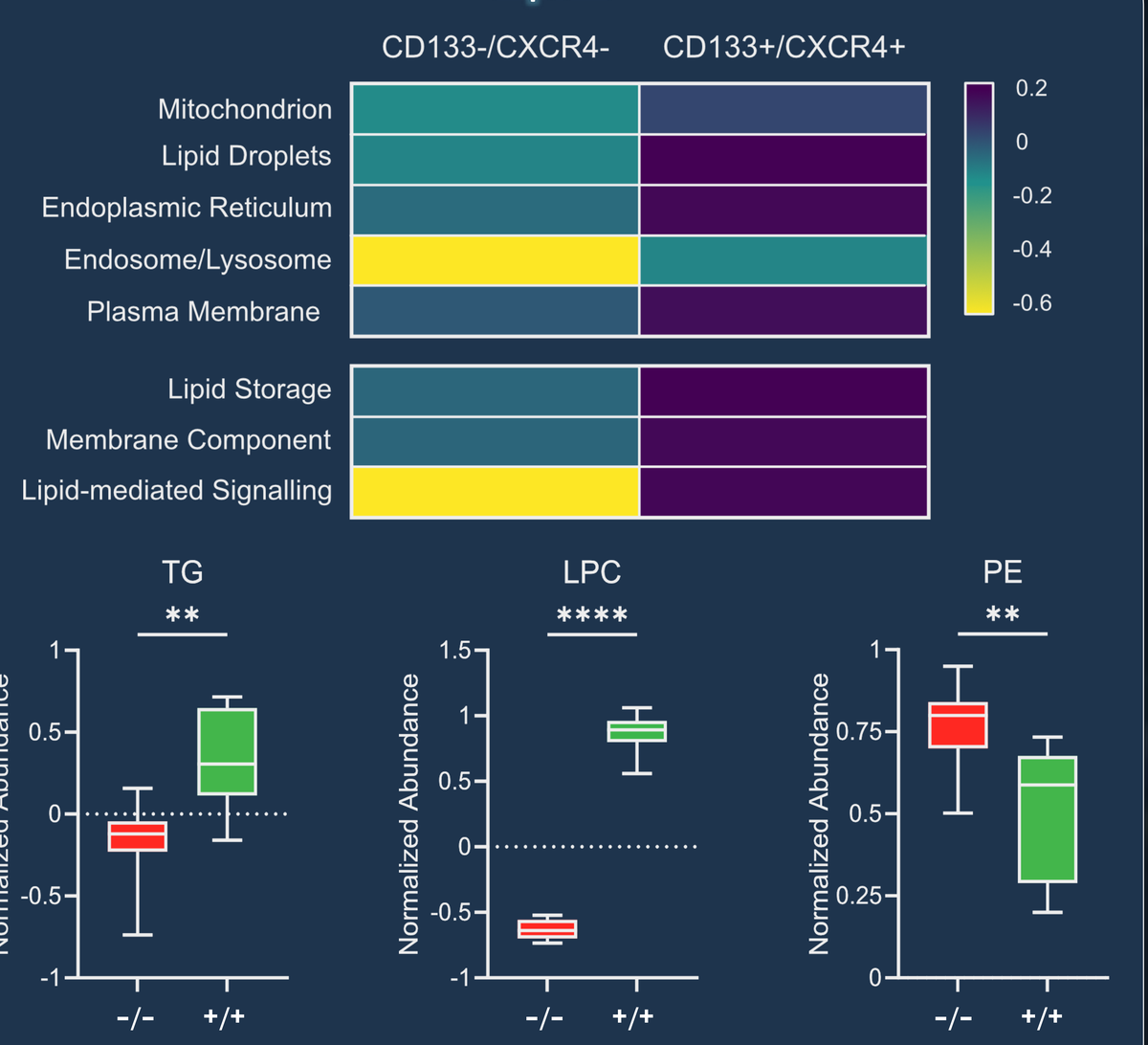


Volcano plot of polar metabolites in H460 $CD133^{+}/CXCR4^{+}$ vs $CD133^{-}/CXCR4^{-}$ cells. Green and red dots represent significantly upregulated and downregulated metabolites in +/+, respectively (FC ± 1.5, $p < 0.05$). The plot shows reduced glycolytic intermediates and increased kynurenic acid in +/+ cells.



Pathway enrichment analysis in H460 $CD133^{+}/CXCR4^{+}$ vs $CD133^{-}/CXCR4^{-}$ cells. Top enriched pathways are shown according to their statistical significance ($-\log_{10}$*p-value*). Tryptophan metabolism, malate-aspartate shuttle, pyruvate metabolism and spermine biosynthesis are among the most significantly enriched pathways in +/+ vs -/- comparison.

Lipids



Lipid ontology enrichment and key lipid class alterations in H460 $CD133^{+}/CXCR4^{+}$ vs $CD133^{-}/CXCR4^{-}$ cells. Heatmap shows enrichment of lipids in different cellular compartments and of lipids involved in biological functions. Box plots highlight significant changes in major lipid classes: increased triacylglycerols (TG) and lysophosphatidylcholines (LPC), decreased phosphatidylethanolamines (PE) in +/+ cells.

Conclusions

H460 CD133+/CXCR4+ cells exhibit a unique metabolic phenotype characterized by increased concentration of metabolites involved in kynurenine pathway and of lipid storage. These metabolic and lipidomic remodeling may support survival in bloodstream, promote membrane plasticity and increase their metastatic potential.

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