Clinical investigations into the metabolic pathways of early-stage hormone receptor positive/HER2 negative breast cancer.

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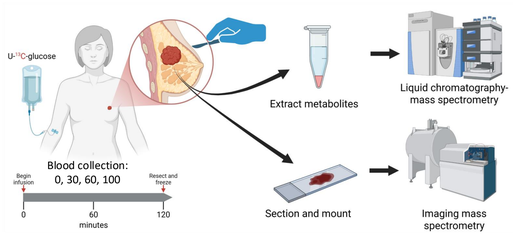
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Introduction

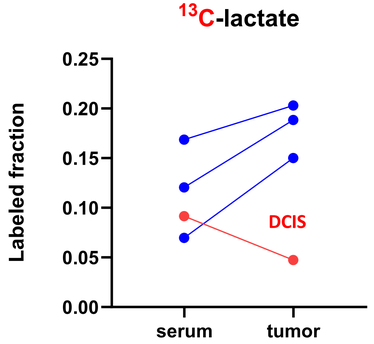
One of the recognized hallmarks of cancer cells is deregulated cellular metabolism, characterized by enhanced metabolic autonomy compared with non-transformed cells. Tumor cells display an overall increase in glucose metabolism, enhanced aerobic glycolysis and decreased oxidative phosphorylation, accompanied by a requirement for a high rate of protein, nucleotide, and fatty acid synthesis to provide the raw materials for cell division. Approximately 70-80% of all breast cancers (BC) are hormone receptor positive (HR+), and most HR+ breast cancers are HER2-negative (Her2-). The metabolic dependencies of HR+/Her2- BC and in particular, high-risk HR+ BC, are poorly understood. In depth analyses of *in vivo* metabolic processes by HR+ BC using carbon-13 labeled glucose (13C-glucose) infusions have never been done in humans. 13C-glucose is a stable isotope tracer that has been widely used *in vitro*, *in vivo*, and in patients in a variety of disease settings to study glucose, amino acid, and lipid metabolism. We hypothesize that HR+ breast cancers *in vivo* have altered use of metabolic pathways that can be determined by *in vivo* 13C isotope glucose labelling. The primary objective is to describe and discover new insights into the glucose, TCA cycle, amino acid, and lipid metabolic dependencies of HR+/Her2- BC, via liquid chromatography-mass spectrometry (LC-MS) and matrix-assisted laser desorption/ionization (MALDI) imaging mass spectrometry analysis of *in vivo* U-13C-glucose-labeled biopsy of tumor and benign adjacent tissue.

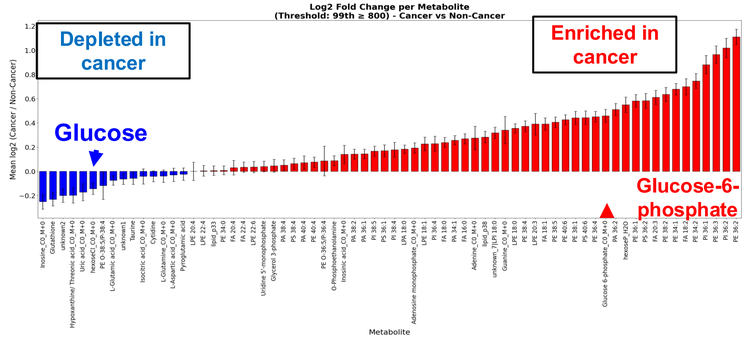
Schema

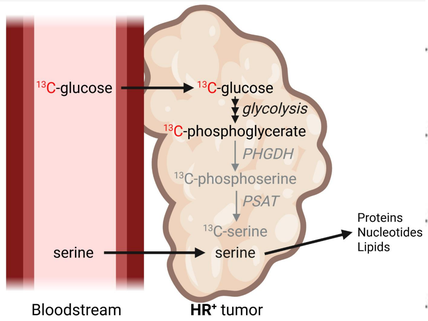


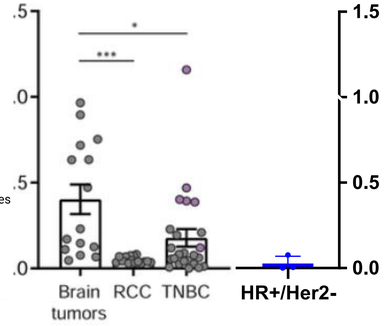
This is an ongoing pilot study that will enroll 16 patients with early stage I, II or III HR+/Her2- breast cancer who do not require neoadjuvant therapy and have planned curative primary resection. Demographic and clinicopathological information will be collected.ClinicalTrials.gov ID NCT05736367.

Results



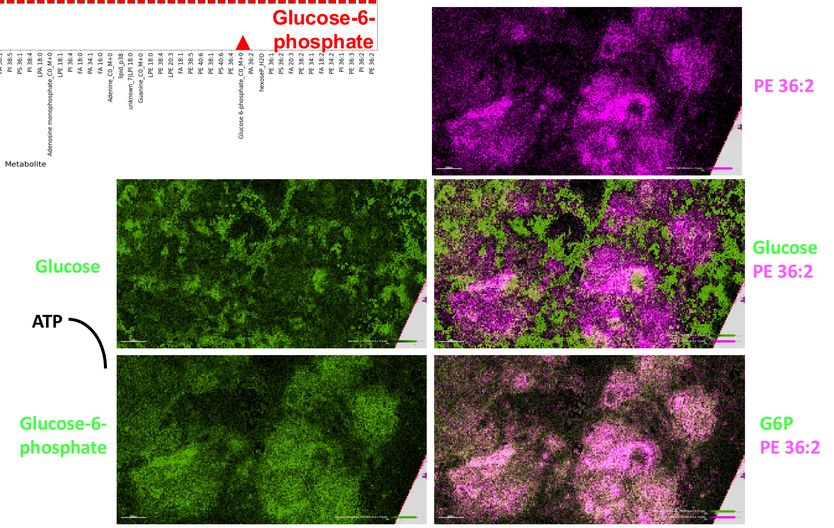






13C-serine synthesis from glucose

Spatial metabolomics of cancer vs. stroma



Cancerous ducts capture glucose more aggressively than surrounding stroma

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