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Differential dependence of the TCA cycle in triple-negative breast cancer cells

Statement of the Problem: Despite the demonstrated role of glutamine in the growth and survival of Triple-Negative Breast Cancer (TNBC) cells, how glutamine is utilized in TNBC cells remains unclear. The tricarboxylic acid (TCA) cycle is a central route for oxidative phosphorylation in cells, and fulfills their bioenergetic, biosynthetic, and redox balance requirements. Our research aims to understand whether TNBC cells metabolize glutamine via the TCA cycle (i.e., glutamine anaplerosis). The key cycle intermediate α-ketoglutarate (α-KG) serves as the entry point for glutamine anaplerosis. α-KG can then be converted to succinyl-CoA by the α-KG dehydrogenase complex (KGDHC) through oxidative phosphorylation, or to isocitrate by isocitrate dehydrogenase (IDH2) through reductive carboxylation pathways.

Findings: Here, we show that glutamine anaplerosis is critical for survival and growth of human TNBC cells. However, the dependence of human TNBC cells on KGDHC and IDH2 varies. In our presentation, we will discuss the potential mechanisms underlying the differential dependence of glutamine anaplerosis in human TNBC cells.

Conclusion & Significance: Overall, our studies provide compelling evidence to support metabolic dependence of TNBC cells on the TCA cycle, and also reveal the various pathways they may utilize in the TCA cycle.

Biography

Hui Feng has her expertise in Zebrafish Genetics and Cancer Therapeutics. Her application of innovative Zebrafish model system led to uncovery of novel metabolic pathways important for survival and proliferation of MYC-dependent leukemic cells. She has expanded her studies of this metabolic pathway into multiple MYC-driven cancers, including triple-negative breast cancer.

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