Divergent Effects of Hypoxia on Polyamine Metabolism

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The intricate relationship between hypoxia and cellular metabolism has emerged as a central focus in understanding physiological responses and pathological states. Hypoxia serves as a potent driver of metabolic reprogramming, influencing key processes such as glycolysis, oxidative phosphorylation, and nutrient sensing. Through diverse signaling cascades, cells adapt to oxygen scarcity by altering their metabolic landscape, a phenomenon with profound implications for tissue homeostasis and disease progression.

In parallel, there is a growing interest on the role of polyamines as major drivers of processes ranging from gene expression to protein synthesis and cell proliferation. Recent evidence suggests a reciprocal relationship between hypoxia and polyamine metabolism, wherein hypoxic conditions regulate polyamine biosynthesis and catabolism, while polyamines modulate cellular responses to oxygen deprivation. Most of these studies uniformly agree that hypoxia promotes both the uptake of exogenous polyamines and the polyamine biosynthesis through the induction of ODC1, one of the rate-limiting enzymes in this pathway.

Here, we will present our latest findings showing that hypoxia, through a transcriptional regulation, reduces the polyamine biosynthesis pathway as well as polyamine (putrescine and spermidine) content in prostate cancer and beyond. By unraveling the dynamic interplay between hypoxia and polyamine metabolism, we aim to uncover new insights in health and disease.