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Nucleotide biosynthesis remodeling as a hallmark of tumor aggressiveness

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In recent years, the characterization of cancer-dependent metabolic remodeling has been the focus of a growing number of studies. In particular, the metabolic requirements for cell proliferation have been extensively studied. Within this project, the scientists are interest in unique metabolic processes that do not fall under the category of ?proliferation-dependent", but instead are more likely to be involved in the transition of cancer cells to a more aggressive state. By executing the epithelial-mesenchymal transition (EMT) program, carcinoma cells gain stem-like properties, such as enhanced survival, self-renewal, and anchorage-independent growth, all of which contribute to increased aggressiveness in vivo. Recently, the Shaul lab identified a set of metabolic genes that are up-regulated in mesenchymal-like cells. A subset of these gene were demonstrated to be essential for the EMT program. Among them are the pyrimidine degradation pathway and the tetrahydrobiopterin (BH4) biosynthesis pathway, which both uses nucleotides as their initial substrates. In this proposal, they hypothesize that remodeling of nucleotide metabolism plays a major role in regulating cancer cell plasticity. Specifically, using stable isotope-assisted metabolomics together with tumor biology studies they plan to characterize the synthesis and the destiny of nucleotides during tumor progression. Further understanding the role of nucleotides in regulating the EMT program may lead to the discovery of novel cellular mechanisms that require these molecules to promote anchorage-independent tumor growth. The proposed work will reveal a deeper understanding of essential metabolic processes in tumor cells and discover cellular mechanisms important for cancer progression.

Projektbeteiligte

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