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Recent Advances in Tumor Metabolism: Illuminating Novel Pathways in Cancer Research

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Letter to Editor

Recent breakthroughs in the metabolism of tumors have revolutionized our comprehension of cancer research, presenting new sites for therapeutic exploration (Vander Heiden & DeBerardinis, 2017). Cancer cells show distinct metabolic adaptations to support their unbridled proliferation and survival. Investigating and analyzing these metabolic alterations has become a paramount focus of cancer research. In this editorial, we explore the most recent developments in tumor metabolism, highlighting their profound significance and potential bearing on the development of cancer therapies (Warburg, 1956).

The Warburg effect, which emphasizes how much cancer cells rely on glycolysis even in oxygen-rich environments, has traditionally been linked to cancer metabolism (Tang *et al*., 2023). This phenomenon is still valid, but recent research has shown that tumors have complex metabolic rewiring. The discovery of numerous metabolic pathways linked to tumorigenesis has been made possible by cutting-edge methods like metabolomics, flux analysis, and genomics (Suri *et al*., 2023). The use of alternative nutrient sources is a crucial aspect of tumor metabolism. To meet their energy needs, cancer cells exhibit the capacity to metabolize amino acids, fatty acids, and ketones in addition to glucose (Garcia-Bermudez *et al*., 2020). Furthermore, a promising metabolic vulnerability in some cancers the reliance on glutamine as a crucial nitrogen source for anabolic processes has emerged, opening the door for targeted interventions.

Cancer represents a complex ecosystem in which cancer cells interact with non-cancer cells through many communications. This includes intercellular interactions, paracrine signaling, and extracellular vesicles. Non-malignant cells such as cancer-associated fibroblasts, macrophages, granulocytes, natural killer cells, and lymphocytes contribute to the regulation of malignant characteristics (Vokurka *et al*., 2022). The interplay between cancer cell metabolism and the TME (Tumor microenvironment) has long been recognized, with researchers aiming to comprehend these interactions for improved diagnostics and novel anticancer strategies. Tumor cells exhibit adaptability in nutrient acquisition and utilization, supporting growth, migration, and bioenergetically demanding processes (Pavlova & Thompson, 2016). Throughout carcinogenesis, tumor cells adapt dominant metabolic pathways, enhancing flexibility to meet changing environmental demands (Folmes *et al*., 2012). Glioblastoma, a highly aggressive tumor, is influenced by non-transformed glial cells, impacting cancer cell metabolism, and growth (Virtuoso *et al*., 2021). FAP, expressed in glioblastoma cells, particularly the mesenchymal subtype, is important, linked to TGF-β1 (Transforming Growth Factor-beta 1) signaling (Smetana Jr & Masařík, 2022).

Metabolic reprogramming in cancer is intricately linked to dysregulated signaling pathways. Key oncogenic signaling pathways, including PI3K-AKT-mTOR and MYC (respectively Phosphatidylinositol 3-kinase, Protein kinase B, Mammalian target of rapamycin and A gene that encodes for the MYC protein), regulate metabolic processes to guarantee a sufficient supply of nutrients and energy for accelerated tumor proliferation (Vander Heiden & DeBerardinis, 2017). Additionally, the intersection of tumor metabolism and immune signaling has shed light on the potential of immune metabolism in cancer immunotherapy (Buck *et al*., 2015). The deepening understanding of tumor metabolism has opened doors for the development of novel therapeutic approaches. A complementary approach to conventional cytotoxic therapies is to take advantage of the metabolic weaknesses of cancer cells (Vander Heiden, 2011). In-depth research is currently being done on a variety of small molecules and inhibitors that target important metabolic pathways (Shen *et al*., 2021). Additionally, there is growing interest in the idea of metabolic reprogramming as a biomarker for patient stratification and treatment response forecasting. While the field of tumor metabolism progresses rapidly, several challenges lie ahead (Kouidhi *et al*., 2018). The complexity and heterogeneity of tumor metabolism necessitate a comprehensive understanding of context-specific metabolic adaptations. Additionally, the translation of these discoveries from bench to bedside mandates meticulous clinical validation and the formulation of effective therapeutic strategies (da Silva *et al*., 2023). Collaborative efforts among researchers, clinicians, and pharmaceutical industries will be pivotal in addressing these challenges and capitalizing on the potential of tumor metabolism-targeted therapies.

In summary, recent advances in tumor metabolism have unveiled novel pathways in cancer research, providing unprecedented insights into the metabolic rewiring of cancer cells. Redefining the way that oncogenic signaling, metabolic pathways, and immune responses are interconnected might fundamentally alter the way

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that cancer is treated. With ongoing efforts and collaborative research, the translation of these discoveries into effective therapies holds great promise for the future of cancer patients worldwide. The emerging field of tumor metabolism invites us to embark on a transformative journey toward precision oncology and personalized medicine.

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