

Editorial: Glycolysis as a target for cancer therapy

Tuhin Subhra Chakraborty, Ph.D Molecular and Integrative Physiology, University of Michigan, MI 48109, USA E-mail: tchakrab@umich.edu

Cancer is a highly heterogeneous disease and each cancer has its individual metabolic fingerprint. Even within a single cancer, its constituent cells are heterogeneous and the metabolic fingerprint varies from one cell to another (Jie Zheng 2012). Unlike normal cells, glycolysis is enhanced in cancer cells (Warburg 1927, 1956; Robert A. Gatenby et.al. 2004; Jie Zheng 2012). This was first described by German scientist Otto Warburg in the 1920s. Following Warburg's observations that cancer cells have a higher rate of glycolysis than normal cells, interest in the metabolic property of cancers has steadily increased. In recent years, understanding the features and complexity of the metabolism and energetics of cancer cells has been rekindled, mainly because therapy targeting metabolism hits the "core" of the cancer and has the potential to cripple a cancer cell's ability to self-renew.

Upregulated glycolysis is the hallmark of a vast majority of invasive cancers in humans. Although metabolic control over glycolysis can be applied during multiple steps in the glycolytic pathway, most studies support the hypothesis that control over glycolytic flux primarily occurs during glucose transport. Control may also occur during the phosphorylation of key glycolytic enzymes (Robert A. Gatenby et.al. 2004). This demonstrates the clinical importance of glucose metabolism and makes glycolytic phenotype a mainstream target for clinical oncology. Importantly, increased tumor aggressiveness is also correlated with increased glucose uptake. In fact glycolytic phenotype is positively correlated with a transition from pre-malignant lesions to invasive cancers (Robert A. Gatenby et.al. 2004). This extraordinary preference of enhanced glycolysis in cancer cells indicates new avenues for better treatment options using pharmacological agents to inhibit the emergence of glycolytic phenotype and

therefore retard the progression of the early lesion.

In his [article](#), Postdoc of the Month winner Dr. Dhruv Kumar, pointed out that upregulated glycolysis was associated with the incidence of metastasis in head and neck cancer. Moreover, when many glycolytic regulators were over expressed, the survival rate in patients suffering from head and neck squamous cell carcinoma (HNSCC) was reduced. One way to measure glycolysis in cancer is to visualize tumors by positron emission tomography (PET) using the glucose analogue tracer, fluorodeoxyglucose (FdG). Individuals suffering from cancer have shown significantly increased glucose uptake during FdGPET imaging. Increased glucose uptake as seen during FdGPET is largely dependent on the rate of glycolysis. Indeed, FdG uptake occurs through glucose transporters such as GLUT1. In their article, Dhruv and Thomas speculated that inhibition of GLUT1 activity could reduce the glycolytic phenotype, which, in turn, could affect the progression of the disease. Apart from GLUT1, hexokinases are also key molecules regulating glycolytic flux and could be targeted with specific inhibitors.

It seems well worthwhile to explore the glycolytic phenotype of cancers as this could likely lead to targeted therapies. Regulating glycolytic flux using pharmacological agents as described by Dhruv and Thomas could reduce the glycolytic phenotype in HNSCC and prevent metastasis or death. In order to discover better treatment options, a more complete understanding of the molecular basis of HNSCC glycolysis is required. Thus, finding markers for HNSCC glycolysis is crucial for therapeutic success as summarized in the current [article](#) by Dr. Dhruv Kumar.

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