Cancer metabolism — an emerging hallmark of cancer

The past decade has witnessed remarkable progress toward understanding the hallmarks of cancer, including sustaining proliferation signaling, enabling replicative immortality, evading growth suppressors, escape from cell death, inducing angiogenesis, and activating following invasion and metastasis, etc., comprising major biological capabilities facilitating the development of human cancers (Hanahan, et al., 2011). Recently, disordered metabolism has become another emerging hallmark of cancer. About ninety years ago, Otto Warburg pioneered quantitative investigations of cancer metabolism and discovered that cancer cells have increased glycolysis even under aerobic conditions, known as the Warburg effect (Warburg, 1956; Vander Heiden, et al., 2009). The deregulation of metabolism in cancer cells was attributed to the malfunctions of oncogenes and mutated tumor suppressor genes (Cairns, et al., 2011). However, current studies show that interference with glycolysis, a glucose metabolism process, promotes oncogenic mutations (Yun, et al., 2009). In fact, obese and diabetic patients have higher incidences of cancer, indicating that metabolic changes contribute to tumorigenesis (Forte, et al., 2012). Therefore, disordered metabolism may not only be an effect, but also a cause in tumorigenesis. In other words, cancer may be classified as a metabolic disease (DeBerardinis, 2008). Recently, numerous studies focusing on the Warburg effect show that upregulated glycolysis in cancer cells is not only utilized to produce ATP to compensate reduced ATP output from mitochondria, but also to provide biosynthetic molecules precursors and to build up a balanced redox homeostasis facilitating rapid cell proliferation (Gatenby, et al., 2004; Cairns, et al., 2011). In addition, lactate, which was erroneously thought of as a waste product from cancer metabolism, has been demonstrated to form a unique microenvironment to facilitate the development of cancer (Semenza, et al., 2008). Recognition and understanding of the impact of cancer metabolism will increasingly and positively affect the development of novel anti-cancer therapeutics (Hanahan, et al., 2011).

References:


