Re: Regulation of Cancer Cell Metabolism

Cairns RA, Harris IS, Mak TW

The Campbell Family Cancer Research Institute, Toronto, Ontario, Canada


EDITORIAL COMMENT

For basic needs of dividing cells, three main molecular mechanisms include rapid adenosine triphosphate (ATP) generation for providing energy, increased biosynthesis of macromolecules, and maintenance of appropriate cellular redox status. Metabolic changes in cancer cells have not been well described yet. The best described metabolic mechanism observed in tumour cells is the Warburg effect which is a shift from ATP generation through oxidative phosphorylation to ATP generation through glycolysis, even under normal oxygen concentrations. This effect is regulated by several pathways such as the phosphatidylinositol 3-kinase pathway, hypoxia-inducible factor, p53, MYC and AMP-activated protein kinase (AMPK). The tumor microenvironment is characterized by hypoxia, low extracellular pH and low glucose concentration. Mutations in oncogenes and tumor suppressor genes cause alterations in intracellular signalling pathways that affect tumour cell metabolism. A key molecule produced as a result of altered cancer metabolism is reduced nicotinamide adenine dinucleotide phosphate (NADPH), which functions as a cofactor and provides reducing power in many enzymatic reactions crucial for macromolecular biosynthesis. NADPH is also an antioxidant and forms part of the defense against reactive oxygen species (ROS) produced during rapid proliferation. High levels of ROS can cause damage to macromolecules, which can induce apoptosis. These antioxidant systems rely on the reducing power of NADPH to maintain their activities. In the near future, anticancer treatments will focus on energy metabolism of the cancer cell.

Fehmi Narter, MD, PhD