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Imaging metabolism and physiology in cancer

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Personal

Abstract

The metabolic adaptability of cancer cells on multiple energy pathways is thought to underlie tumorigenesis in vivo. Metabolism of the cancer cell is diverse with reliance on both aerobic glycolysis and oxidative phosphorylation to meet demands for building blocks and energy equivalents. Metabolic plasticity is also associated with developing resistance to treatment and distal metastases. While there is strong support for shift in cancer cell metabolism to aerobic glycolyses recent studies showed evidence for robust utilization of glucose through the TCA (tricarboxylic acid) cycle. Drugs targeting both these energy pathways have been developed and pre-clinical studies in mice showed promising results alone or in combination. Clinical studies were limited because of off-target toxicities.

Solid tumors have a microenvironment distinctly different from normal tissues. Many factors contribute to the distinct tumor microenvironment including altered metabolism, chaotic blood vessel network, conditions which cause acidotic and hypoxic conditions. The acidotic conditions can further be exacerbated by OxPhos inhibitors which force metabolism to aerobic glycolysis producing additional lactate. Tumor hypoxia can result from inadequate supply of oxygen through defective blood vessel network or from demand outstripping supply or both.