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**Metabolic interplay between glycolysis and mitochondrial oxidation: the reverse Warburg effect and its therapeutic implication**

Minjong Lee, Jung-Hwan Yoon

**Abstract**

Aerobic glycolysis, *i.e.*, the Warburg effect, may contribute to the aggressive phenotype of hepatocellular carcinoma. However, increasing evidence highlights the limitations of the Warburg effect, such as high mitochondrial respiration and low glycolysis rates in cancer cells. To explain such contradictory phenomena with regard to the Warburg effect, a metabolic interplay between glycolytic and oxidative cells was proposed, *i.e.*, the "reverse Warburg effect". Aerobic glycolysis may also occur in the stromal compartment that surrounds the tumor; thus, the stromal cells feed the cancer cells with lactate and this interaction prevents the creation of an acidic condition in the tumor microenvironment. This concept provides great heterogeneity in tumors, which makes the disease difficult to cure using a single



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