Metabolic state of glioma stem cells and nontumorigenic cells.


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Abstract

Gliomas contain a small number of treatment-resistant glioma stem cells (GSCs), and it is thought that tumor regrowth originates from GSCs, thus rendering GSCs an attractive target for novel treatment approaches. Cancer cells rely more on glycolysis than on oxidative phosphorylation for glucose metabolism, a phenomenon used in 2-[(18)F]fluoro-2-deoxy-D-glucose positron emission tomography imaging of solid cancers, and targeting metabolic pathways in cancer cells has become a topic of considerable interest. However, if GSCs are indeed important for tumor control, knowledge of the metabolic state of GSCs is needed. We hypothesized that the metabolism of GSCs differs from that of their progeny. Using a unique imaging system for GSCs, we assessed the oxygen consumption rate, extracellular acidification rate, intracellular ATP levels, glucose uptake, lactate production, PKM1 and PKM2 expression, radiation sensitivity, and cell cycle duration of GSCs and their progeny in a panel of glioma cell lines. We found GSCs and progenitor cells to be less glycolytic than differentiated glioma cells. GSCs consumed less glucose and produced less lactate while maintaining higher ATP levels than their differentiated progeny. Compared with differentiated cells, GSCs were radiosensitive, and this correlated with a higher mitochondrial reserve capacity. Glioma cells expressed both isoforms of pyruvate kinase, and inhibition of either glycolysis or oxidative phosphorylation had minimal effect on energy production in GSCs and progenitor cells. We conclude that GSCs rely mainly on oxidative phosphorylation. However, if challenged, they can use additional metabolic pathways. Therefore, targeting glycolysis in glioma may spare GSCs.

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