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Journal Article

Glucose Metabolism Heterogeneity in Human and Mouse Malignant Glioma Cell Lines

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Renal Cell Cancer

Rosette, Jean J.M.C.H. de la, Sternberg, Cora N., Poppel,

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Summary The current study examined specific bioenergetic markers associated with the metabolic phenotype of several human and mouse glioma cell lines. Based on preliminary studies, we hypothesized that glioma cells would express one of at least two different metabolic phenotypes, possibly acquired through progression. The D-54MG and GL261 glioma cell lines displayed an oxidative phosphorylation (OXPHOS)-dependent phenotype, characterized by extremely long survival under glucose starvation, and low tolerance to poisoning of the electron transport chain (ETC). Alternatively, U-251MG and U-87MG glioma cells exhibited a glycolytic-dependent phenotype with functional OXPHOS. These cells displayed low tolerance to glucose starvation and were resistant to a ETC blocker. Moreover, these cells could be rescued in low glucose conditions by oxidative substrates (e.g., lactate, pyruvate). Finally, these two phenotypes could be distinguished by the differential expression of LDH isoforms. OXPHOS-dependent cells expressed both LDH-A and -B isoforms whereas glycolytic-dependent glioma cells expressed only LDH-B. In the latter case, LDH-B would be expected to be essential for the use of extracellular lactate to fuel cell activities. These observations raise the possibility that the heterogeneity in glucose metabolism and, in particular, the sole expression of LDH-B, might identify an important biological marker of glioma cells that is critical for their progression and that might afford a new target for anticancer drugs.

Keywords glioma - glucose metabolism - glucose starvation - lactate - LDH isoforms

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