Protective role of glucose-6-phosphate dehydrogenase activity in the metabolic response of C6 rat glioma cells to polyunsaturated fatty acid exposure.

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Source

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Abstract

Polyunsaturated fatty acids (PUFAs) can influence tumor growth and migration, both in vitro and in vivo. The PUFA gamma-linolenic acid (GLA) has been reported to improve the poor prognosis associated with human gliomas, although its effects at sublethal concentrations on residual cells postsurgery are poorly understood. The study investigated the effects sublethal PUFAs doses (90 or 150 microM) may have on rat C6 glioma cell energy metabolism, since an adequate energy supply is essential for cell proliferation, migration, and apoptosis. Of note was the identification of mitochondrial heterogeneity in relation to the mitochondrial membrane potential (MMP), which has been suggested but unproven in previous studies. GLA and eicosapentaenoic acid (EPA) caused significant changes in cellular fatty acid composition and increased the percentage of cells with a low MMP after a 96-h exposure period. The presence of PUFAs inhibited C6 cell proliferation and migration, although apoptosis was not induced. The protein expression and activity of glucose-6-phosphate dehydrogenase was increased after 96-h incubation with 90 microM GLA and EPA and would allow redox regulation through increased NADPH production, permitting the maintenance of adequate intracellular reduced glutathione concentrations and limiting rates of lipid peroxidation and reactive oxygen species generation. Neither NADP(+)-isocitrate dehydrogenase nor NADP(+)-malate dehydrogenase activity responded to PUFAs, suggesting it is glucose-6-phosphate dehydrogenase that is the principal source of NADPH in C6 cells. These data compliment studies showing that higher concentrations of GLA induced glioma cell death and tumor regression and suggest that GLA treatment could be useful for the inhibition of residual cell proliferation and migration after surgical removal of the tumor mass.