3-bromopiruvato. Em várias linhagens de células cancerosas o alvo principal do 3-bromopiruvato e a enzima gliceraldeído-3-fosfato dehidrogenase (GAPDH)

Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) is pyruvylated during 3-bromopyruvate mediated cancer cell death.

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Abstract

BACKGROUND: The pyruvic acid analog 3-bromopyruvate (3BrPA) is an alkylating agent known to induce cancer cell death by blocking glycolysis. The anti-glycolytic effect of 3BrPA is considered to be the inactivation of glycolytic enzymes. Yet, there is a lack of experimental documentation on the direct interaction of 3BrPA with any of the suggested targets during its anticancer effect. Methods and

RESULTS: In the current study, using radiolabeled ((14)C) 3BrPA in multiple cancer cell lines, glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was identified as the primary intracellular target of 3BrPA, based on two-dimensional (2D) gel electrophoretic autoradiography, mass spectrometry and immunoprecipitation. Furthermore, in vitro enzyme kinetic studies established that 3BrPA has marked affinity to GAPDH. Finally, Annexin V staining and active caspase-3 immunoblotting demonstrated that apoptosis was induced by 3BrPA.

CONCLUSION: GAPDH pyruvylation by 3BrPA affects its enzymatic function and is the primary intracellular target in 3BrPA mediated cancer cell death.

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