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3-Bromopyruvate: targets and outcomes.

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Abstract

The pyruvate mimetic 3-bromopyruvate (3-BP) is generally presented as an inhibitor of glycolysis and has shown remarkable efficacy in not only preventing tumor growth, but even eradicating existant tumors in animal studies. We here review reported molecular targets of 3-BP and suggest that the very range of possible targets, which pertain to the altered energy metabolism of tumor cells, contributes both to the efficacy and the tumor specificity of the drug. Its in vivo efficacy is suggested to be due to a combination of glycolytic and mitochondrial targets, as well as to secondary effects affecting the tumor microenvironment. The cytotoxicity of 3-BP is less due to pyruvate mimicry than to alkylation of, e.g., key thiols. Alkylation of DNA/RNA has not been reported. More research is warranted to better understand the pharmacokinetics of 3-BP, and its potential toxic effects to normal cells, in particular those that are highly ATP-/mitochondrion-dependent.

PMID: 22298255 [PubMed - indexed for MEDLINE]

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