Butyrate activates the monocarboxylate transporter MCT4 expression in breast cancer cells and enhances the antitumor activity of 3-bromopyruvate.


Abstract
Most malignant tumors exhibit the Warburg effect, which consists in increased glycolysis rates with production of lactate, even in the presence of oxygen. Monocarboxylate transporters (MCTs), maintain these glycolytic rates, by mediating the influx and/or efflux of lactate and are overexpressed in several cancer cell types. The lactate and pyruvate analogue 3-bromopyruvate (3-BP) is an inhibitor of the energy metabolism, which has been proposed as a specific antitumor agent. In the present study, we aimed at determining the effect of 3-BP in breast cancer cells and evaluated the putative role of MCTs on this effect. Our results showed that the three breast cancer cell lines used presented different sensitivities to 3-BP: ZR-75-1 ER (+)>MCF-7 ER (+)>SK-BR-3 ER (-). We also demonstrated that 3-BP reduced lactate production, induced cell morphological alterations and increased apoptosis. The effect of 3-BP appears to be cytotoxic rather than cytostatic, as a continued decrease in cell viability was observed after removal of 3-BP. We showed that pre-incubation with butyrate enhanced significantly 3-BP cytotoxicity, especially in the most resistant breast cancer cell line, SK-BR-3. We observed that butyrate treatment induced localization of MCT1 in the plasma membrane as well as overexpression of MCT4 and its mark of oxidative stress in cancer-related "lactate shuttle" in human tumor [Cell Cycle. 2011]

Evidence for a stromal-epithelial "lactate shuttle" in human tumor [Cell Cycle. 2011]

Monocarboxylate transporter 4 regulates maturation and traffic [Cancer Res. 2007]

Role of monocarboxylate transporters [J Bioenerg Biomembr. 2012]

Nutrient transporters in cancer: relevance to Warburg hypothesis and the art.

MCT1 and hypoxia-inducible MCT4 is critical for energetics and growth of cancer cells. CD147 subunit of lactate/H+ symporters [Proc Natl Acad Sci U S A. 2011]

Butyrate activates the monocarboxylate transporter MCT4. Influenza Virus

OMIM (calculated)

Cancer Res. 2007

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