Up-regulation of hexokinase II in myeloma cells: targeting myeloma cells with 3-bromopyruvate.

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Abstract
Hexokinase II (HKII), a key enzyme of glycolysis, is widely over-expressed in cancer cells. However, HKII levels and its roles in ATP production and ATP-dependent cellular process have not been well studied in hematopoietic malignant cells including multiple myeloma (MM) cells. We demonstrate herein that HKII is constitutively over-expressed in MM cells. 3-bromopyruvate (3BrPA), an inhibitor of HKII, promptly and substantially suppresses ATP production and induces cell death in MM cells. Interestingly, cocultures with osteoclasts (OCs) but not bone marrow stromal cells (BMSCs) enhanced the activation of glycolysis in MM cells by OCs via the PI3K-Akt-HKII pathway. Although BMSCs and OCs stimulate MM cell growth and survival, 3BrPA induces cell death in MM cells even in cocultures with OCs as well as BMSCs. Furthermore, HKII levels and lactate production in MM cells were mostly abrogated by the PI3K inhibitor LY294002, suggesting phosphorylation of Akt along with an increase in HKII levels and lactate production in MM cells. The enhancement of HKII activity in MM cells. Interestingly, cocultures with osteoclasts (OCs) but not bone marrow stromal cells (BMSCs) enhanced the up-regulation of hexokinase II in myeloma cells with 3-bromopyruvate. Related citations in PubMed

Role of mitochondria-associated hexokinase [Biochim Biophys Acta. 2009]
Evaluation of the role of hexokinase type II in cellular proliferation [J Nucl Med. 2009]
Glycolysis inhibition inactivates ABC transporters to restore [PLoS One. 2011]
3-Bromopyruvate: targets and outcomes. [J Bioenerg Biomembr. 2012]
Hexokinase-2 bound to mitochondria. [Semin Cancer Biol. 2009]

Selected references
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