BMC Proceedings

POSTER PRESENTATION Open Access

Metalloproteinase inhibitors as a potential therapeutic approach in multiple myeloma: a preliminary study

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From 16th International Charles Heidelberger Symposium on Cancer Research
Coimbra, Portugal. 26–28 September 2010

Multiple Myeloma (MM) is one of the B-cell malignancies with a poor prognosis, characterized by the clonal expansion of neoplastic plasma cells within the bone marrow, elevated serum immunoglobulin, and osteolytic bone disease. The first pathogenic step is a premalignant monoclonal gamopathy of undetermined significance (MGUS). With progression of MGUS to myeloma, complex genetic/epigenetic events occur in the neoplastic plasma cell, and in the bone marrow microenvironment. The resultant interactions of myeloma cells, bone marrow stromal cells, and microvessels contribute to persistence of the tumour and resistance to drugs. Matrix metalloproteinases (MMPs) play a critical rule in bone remodeling (osteolitic lesions) and tumor invasion, and could be a new therapeutic target in MM.

The aim of this study is to evaluate the therapeutic potential of a metalloproteinase inhibitor, batimastat (BB-94), in a multiple myeloma cell line in culture.

For this purpose a MM cell line, the NCI-H929 [H929] cells were cultured in absence and presence of different concentrations of the MMP inhibitor, BB-94, during different periods of time. Cell viability and death was determined by the alamar blue assay and by flow cytometry using the annexin V/propidium iodide incorporation.

Our preliminary results show that BB-94 has, along a broad concentration range, an antiproliferative effect in MM cells that is accompanied by a cytotoxic effect as results of increased apoptosis levels as the concerntratio increases from 1 to 5μM.

This study suggests that batimastat could be a new therapeutic approach in multiple myeloma in monotherapy.

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Published: 24 September 2010

doi:
Cite this article as: Pais *et al.*: Metalloproteinase inhibitors as a potential therapeutic approach in multiple myeloma: a preliminary study. *BMC Proceedings* 2010 **4**(Suppl 2):P50.

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