Abstract

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Plasma cell survival: The impact of extracellular ATP

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ABSTRACT

Introduction: Multiple myeloma (MM) originates from the neoplastic transformation of long-lived plasma cells within the bone marrow niche. The tumour microenvironment (TME) has been implicated in MM progression, maintenance and treatment response. Osteoblasts in the bone marrow TME contribute to inducing MM cell dormancy and driving oncogenic cells out of their quiescent state via angiogenic switching, modulating to their re-activation and maintenance during relapse. A key secretory molecule produced by osteoblasts is extracellular adenosine triphosphate (e-ATP) which has conflicting evidence concerning its effect upon plasma cell survival. A recent murine study demonstrated a pro-survival effect, whereby e-ATP was reported to induce plasma cell maintenance and reflect characteristics of cell rescue. The aim of this project was to elucidate the impact of e-ATP exposure within the wider context of human plasma cell survival.

Methods: In-vitro human plasma cell culture systems were utilised to investigate the function of e-ATP as a proliferation modulating factor. Trials of e-ATP dose response during the differentiation of memory B cells to plasma cells in-vitro were carried out. The effect of e-ATP from a primary cellular source of osteoblasts was used to identify differences between a natural source compared to a formulation of e-ATP.

Results: A dose dependent killing effect with depletion in plasma cell numbers in vitro was demonstrated. These results were in contrast to those observed in the murine system but align with other published pro-apoptotic effects of e-ATP.

Conclusion: e-ATP demonstrates an apoptotic dose response effect on plasma cell survival.

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