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Significance of macrophage inflammatory protein-1 alpha (MIP-1α) in multiple myeloma.

저자: Terpos, Evangelos^{1,2} (AUTHOR) e.terpos@imperial.ac.uk, eterpos@hotmail.com
Politou, Marianna² (AUTHOR)
Viniou, Nora³ (AUTHOR)
Raheemulla, Amin² (AUTHOR)

제공처: Leukemia & Lymphoma Dec2005, Vol. 46 Issue 12, p1699-1707. 9p.

문서 유형: Article

주제어: *MULTIPLE myeloma
*MACROPHAGES
*B cell lymphoma
*MONOCLONAL gammopathies
*PLASMACYTOMA

저자 제공 키워드: bone disease
Macrophage inflammatory protein 1-alpha (MIP-1α#03B1)
Macrophage inflammatory protein 1-alpha (MIP-1α)
multiple myeloma
osteoclasts

초록: Macrophage inflammatory protein-1 alpha (MIP-1α) is a member of the CC chemokine family and is primarily associated with cell adhesion and migration. It is produced by myeloma (MM) cells and directly stimulates osteoclast formation and differentiation in a dose dependent way. MIP-1α protein levels were elevated in the bone marrow plasma of MM patients and correlated with disease stage and activity. MIP-1α was elevated in the serum of myeloma patients with severe bone disease and correlated positively with bone resorption markers providing evidence for a causal role of MIP-1α in the development of lytic bone lesions. MIP-1α has also been found to stimulate proliferation, migration and survival of plasma cells. Mice, which were inoculated with myeloma cells and treated with a monoclonal rat anti-mouse MIP-1α antibody, showed a reduction of both paraprotein and lytic lesions. In addition, MIP-1α enhanced adhesive interactions between myeloma and marrow stromal cells, increasing the expression of RANKL and IL-6, which further increased bone destruction and tumor burden. Myeloma patients with high MIP-1α serum levels have poor prognosis. The positive correlation between MIP-1α and β2-microglobulin that has been observed in MM patients at diagnosis further supports the notion that MIP-1α is not only a chemokine with osteoclast activity function but is also implicated in myeloma growth and survival. Therefore, MIP-1α pathway may serve as a development of novel anti-myeloma therapies. [ABSTRACT FROM AUTHOR]

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Leukemia & Lymphoma, December 2005; 46(12): 1699-1707 Taylor & Francis Informa

Significance of macrophage inflammatory protein-1 alpha (MIP-1α) in multiple myeloma

EVANGELOS TERPOS^{1,2}, MARIANNA POLITOU², NORA VINIOU³, & AMIN RAHEMTULLA³

¹Department of Hematology, 251 General Airforce Hospital, Athens, Greece, ²Department of Hematology, Faculty of Medicine, Imperial College London, Hammersmith Hospital, London, UK, & ³First Department of Internal Medicine, University of Athens School of Medicine, Athens, Greece

Abstract
Macrophage inflammatory protein-1 alpha (MIP-1α) is a member of the CC chemokine family and is primarily associated with cell adhesion and migration. It is produced by myeloma (MM) cells and directly stimulates osteoclast formation and differentiation in a dose dependent way. MIP-1α protein levels were elevated in the bone marrow plasma of MM patients and correlated with disease stage and activity. MIP-1α was also elevated in the serum of myeloma patients with severe bone disease and correlated positively with bone resorption markers providing evidence for a causal role of MIP-1α in the development of lytic bone lesions in MM. MIP-1α has also been found to stimulate proliferation, migration and survival of plasma cells. Mice, which were inoculated with myeloma cells and treated with a monoclonal rat anti-mouse MIP-1α antibody, showed a reduction of both paraprotein and lytic lesions. In addition, MIP-1α enhanced adhesive interactions between myeloma and marrow stromal cells, increasing the expression of RANKL and IL-6, which further increased bone destruction and tumor burden. Myeloma patients with high MIP-1α serum levels have poor prognosis. The positive correlation between MIP-1α and β2-microglobulin that has been observed in MM patients at diagnosis further supports the notion that MIP-1α is not only a chemokine with osteoclast activity function but is also implicated in myeloma growth and survival. Therefore, MIP-1α pathway may serve as a target for the development of novel anti-myeloma therapies.

Keywords: Macrophage inflammatory protein 1-alpha (MIP-1α), multiple myeloma, bone disease, osteoclasts

Introduction
MIP-1α is a member of the C-C chemokine family, which is characterized by the absence of an intervening amino acid between the first 2 of the 4 cysteine residues that are conserved in the chemokine superfamily. Each chemokine has 4 conserved cysteine residues and they can be classified into 4 types: C chemokines, CC chemokines, CXC chemokines and CXXX chemokines, depending on the number of amino acids

a dose-dependent way [7]. Furthermore, it has been found elevated in the bone marrow plasma of myeloma patients and correlates with the presence of bone lytic lesions and survival [8-10]. Therefore, it is involved in the pathogenesis of myeloma bone disease, which is a major complication of MM. In addition, MIP-1α enhances adhesive interactions between myeloma cells and marrow stromal cells increasing the expression of receptor activator of nuclear factor-κB ligand (RANKL) and interleukin-6

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