



UKE Paper of the Month July 2012,

Journal of the National Cancer Institute, ([PMID: 22745469](#))

Role of Interleukin 16 in Multiple Myeloma

Djordje Atanackovic, York Hildebrandt, Julia Templin, Yanran Cao, Christiane Keller, Jens Panse, Sabrina Meyer, Henrike Reinhard, Katrin Bartels, Nesrine Lajmi, Orhan Sezer, Axel R. Zander, Andreas H. Marx, Ria Uhlig, Jozef Zustin, Carsten Bokemeyer, Nicolaus Kröger

ABSTRACT: Background: Multiple myeloma is a malignancy characterized by the expansion of a plasma cell clone that localizes to the human bone marrow. Myeloma cells and bone marrow stroma cells both produce soluble factors promoting the survival and progression of multiple myeloma. Interleukin-(IL)-16 is involved in regulating migration and proliferation of normal leukocytes, however, it is unclear whether IL-16 also plays a role in the pathophysiology of human cancers. Methods: We investigated IL-16 expression in cell lines and in the bone marrow of myeloma patients by quantitative RT-PCR, western blot, ELISA, flow cytometry, and immunohistochemistry. Using transfection of siRNA constructs we achieved downregulation of IL-16 in myeloma cells and investigated its influence on apoptosis by flow cytometry, proliferation by BrdU incorporation, and colony formation. Neutralization assays were performed using a monoclonal antibody against C-terminal IL-16. Results: We found IL-16 to be strongly overexpressed in the bone marrow of myeloma patients. Myeloma cell lines as well as primary tumor cells from myeloma patients constitutively expressed IL-16 and its receptors CD4 and/or CD9 and spontaneously secreted soluble IL-16. Silencing of IL-16 had an anti-proliferative effect on the tumor cells which was reversed by the addition of a recombinant C-terminal IL-16 peptide. Most importantly, the application of a monoclonal antibody directed against IL-16 or its receptors had a strong growth-inhibiting influence on myeloma cells. Conclusions: These findings indicate that cytokine IL-16 is an important growth-promoting factor in multiple myeloma and a candidate for novel diagnostic, prognostic and therapeutic applications for this incurable human malignancy.

STATEMENT: *“This is the first paper to describe an important role of cytokine IL-16 in the biology of multiple myeloma. It is also the first work to suggest that therapies targeting IL-16, i.e. monoclonal antibodies, may be developed into powerful weapons against cancer.”*

BACKGROUND: This work was performed solely at UKE. It was mainly conducted by members of the Laboratory for Tumor Immunology headed by Dr. Atanackovic who is a physician/researcher at the Medical Clinic II at UKE. The project represents a collaboration between his clinic and the Department for Stem Cell Transplantation headed by Prof. Nicolaus Kröger. Both scientists have long-standing interest and international reputation in translational research and therapy of multiple myeloma.