



## UKE Paper of the Month July 2012,

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### Role of Interleukin 16 in Multiple Myeloma

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**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.