[Abstract 57]

A NOVEL MURINE MODEL FOR HUMAN WALDENSTROM'S MACROGLOBULINEMIA

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The pre-clinical studies of investigational agents in Waldenstrom's Macroglobulinemia (WM) have been limited by the lack of an *in vivo* animal model which is representative of the disease in patients. We and others have previously demonstrated growth of primary myeloma cells in immunodeficient mice bearing a human bone marrow (huBM) implant (SCID-hu mice). We therefore evaluated the use of this model for propagation of WM tumor cells. Four weeks following implantation of human fetal bone chip in SCID mice, mononuclear cells obtained from BM aspirates of consenting WM patients were directly inoculated into the bone chip. Mice were then evaluated every 2 weeks for the presence of human immunoglobulins. Eight of 11 patient samples engrafted in mice 4 to 28 weeks after WM cell inoculation as confirmed through detection of circulating human IgM and/or human κ or λ chain of the same type as that from the patient from whom the BM aspirate was obtained. The levels of human paraproteins which were detected in murine sera showed time dependent progression. Importantly, immunohistological analysis of human bone chips retrieved from the mice showed diffuse infiltration of IgM^+ and/or κ^+ or λ^+ lymphoplasmacytic cells as well as mast cells, which we recently demonstrated provide growth and survival signals for WM cells (*JCO 2004 22:571S*). Consistent with our previous observations with the MM SCID-hu mouse model, hereto we did not observe infiltration of murine tissues by WM cells confirming the essential nature of the human BM microenvironment in supporting WM cell expansion. These studies therefore demonstrate the utility of using the SCID-hu mouse model for the study of WM, and provide a useful pre-clinical model for the investigation of novel drug agents for the treatment of WM.