The Role of IL-21 In Waldenström Macroglobulinemia

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Cytokines within the tumor microenvironment play an important role in supporting the growth and survival of B cell malignancies. One such cytokine, IL-21, promotes the growth of myeloma and Hodgkin lymphoma cells while inducing apoptosis in chronic lymphocytic leukemia. However, the biologic significance of IL-21 has not been examined in Waldenström macroglobulinemia (WM), a B-cell lymphoma characterized by elevated serum IgM and a lymphoplasmacytic bone marrow infiltrate.

In recent work, we have confirmed the presence of IL-21 in the bone marrow of patients with WM and have identified activated T cells as the source of this cytokine. We readily detected the IL-21 receptor on malignant WM B cells and demonstrate that IL-21 significantly increases both IgM secretion and cellular proliferation of these cells with no effect on viability. IL-21 rapidly induces phosphorylation of STAT3 in WM cells, and treatment of the WM cell line MWCL-1 with a STAT3 inhibitor abolished the IL-21-mediated increases in cellular proliferation and IgM secretion. IL-21 also increased the expression of known STAT3 targets involved in B cell differentiation including BLIMP-1, XBP-1, IL-6 and IL-10.

Overall our data indicate that IL-21 in the bone marrow microenvironment significantly affects the biology of WM tumor cells through a STAT3-dependent mechanism.