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Microenvironment regulation of the IL-23R/IL-23 axis overrides chronic lymphocytic leukemia indolence

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The development and progression of Chronic Lymphocytic Leukemia (CLL) require co-operation of both microenvironment and cytokines. Investigating the IL-23R/IL-23 axis we found that circulating cells of early-stage CLL patients with shorter time-to-treatment (but not of those with a more benign course) expressed a defective form of the IL-23R complex lacking the IL-12Rß1 chain. However, the cells from both patient groups expressed the com-plete IL-23R complex in tissue infiltrates and could be induced to express it when co-cultured with activated T cells or other CD40L-bearing cells. IL-23 production by CLL cells activated in vitro in this fashion and in lymphoid tissues was observed suggesting the exist-ence of an autocrine/paracrine loop causing CLL cell proliferation. Culture of CLL cells with stromal cells, nurse like cells and stimulation with anti IgM antibodies and IL-4 failed to activate this loop. Interference with the IL-23R/IL-23 axis using an anti-IL-23p19 anti-body proved effective in controlling disease onset/expansion in xenografted mice, suggesting potential therapeutic strategies.

Keywords
Chronic Lymphocytic Leukemia, IL23, microenvironment