The Activation Of The Inflammasome Conditions Leukemia And Lymphoma Cell Proliferation

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Hematological Malignancies have recently become curable for 30-60% of patients. Although it is possible to cure the symptoms with chemotherapy and eliminate the tumor cells via the ionizing radiation, the remission rate is still low. The main goal of this study was to understand the role of inflammatory patterns in leukemia and lymphoma cells. To this purpose Peripheral and Bone-marrow-derived blood was collected and peripheral blood mononuclear cells (PBMCs) were isolated by means of Ficoll’s gradient. The stimulation with IL-1β significantly increased the levels of IL-17A in PBMCs obtained from non-Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL) patients compared to healthy cells. In order to understand the earlier steps following the production of the endogenous IL-1β, PBMCs were treated with LPS, a Toll-like receptor (TLR)-4 ligand, that is well known to induce the activation of the inflammasome in the presence of ATP. The stimulation with LPS+ATP induced higher release of IL-1β from NHL- and CLL-derived compared to healthy PBMCs. Similarly, IFN was highly produced after the activation of the inflammasome in both NHL- and CLL-derived PBMCs. Moreover, the stimulation with IL-1β increased tumour cell proliferation in both NHL and CLL samples. In sharp contrast the administration of IL-1Ra, soluble receptor for IL-1β, significantly reduced IL-1β-mediated proliferation of PBMCs from NHL and CLL patients but not in healthy cells. These data support the role of the NLRP-3 inflammasome and more specifically of IL-1β on hematopoietic tumor progression.

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