

Mechanisms of humoral immune dysfunction in CLL

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Chronic lymphocytic leukaemia (CLL) is a low-grade non-Hodgkin lymphoma and the most common leukaemia in elderly individuals. One of the main features of CLL is an immunodeficiency, including a humoral deficiency, leading to frequent infections, which is a main cause of death in the patients. Our main goal is to identify and characterise the causes of this humoral immunodeficiency. We hypothesized that CLL B cells influence the composition of the normal residual B cell (NRB) compartment in the patients. We show significant changes in the subpopulations of the NRBs. We furthermore investigated the B cell receptor (BCR) repertoire of the NRBs to determine if an altered V-gene usage or mutation frequency could explain an impaired humoral immune response. Hence, we sort-purified different B cell subpopulations and performed deep sequencing of the IGHV-genes. Additionally, we performed functional assays analysing effects of soluble CLL-derived factors on the activation, proliferation and cell death of B cells of healthy individuals. We aim to understand further if and how NRBs are influenced by the CLL B cells and differ from normal B cells in healthy individuals.