Preferential elimination of CLL B cells using personalized bispecific antibodies

May Palgi Shloosh

Under the supervision of Prof. Itai Benhar

Chronic lymphocytic leukemia (CLL) is characterized by the clonal proliferation and progressive accumulation of mature, naïve B lymphocytes in peripheral blood, lymphoid tissues, and bone marrow. Over the past two decades, significant advances have been made in CLL therapy, with the objective evolving from merely alleviating symptoms to achieving complete remission and enhancing patient survival. The most common therapeutic approaches for CLL are to eliminate the leukemic B cells, primarily by using monoclonal anti-CD20 antibodies, bispecific antibodies targeting pan-B-cell antigens, inhibition of B cell receptor (BCR) signaling or chimeric antigen receptor (CAR) T-cells. However, these approaches are not ideal, as they are not specific to the pathological B cells and inadvertently eliminate healthy B cells. This can lead in some cases to severe side effects as well as rendering the treated individuals partially immuno-compromised.

We hypothesize that preferential elimination of pathological B cells can be achieved through the application of bispecific biologics in a novel approach called BiSPEC (Bi-Specific antibody for Elimination of Pathological B Cells). These bispecific antibodies are comprised of one effector arm targeting CD20, and a personalized cell targeting arm recognizing the BCR of the pathological B cells (e.g., using an anti-idiotype antibody). With this approach, we aim to target and eliminate pathological B cells, thereby preserving healthy B cells and minimizing the risk of immunosuppression. Furthermore, we propose to evaluate the efficacy of the BiSPEC in both human and murine CLL models, *in vitro* and *in vivo*.