

**Acute lymphoblastic leukemia (ALL)** is a blood cell-derived malignancy occurring either in adults or in children. The treatment is based on a multi-drug chemotherapy, which is effective for most children but significantly fewer adult patients are cured. Deaths due to leukemia progression or relapses are usually associated with certain genetic changes leading to enhanced proliferation and survival of leukemic cells. In addition, due to the non-selective, systemic activity, chemotherapy of ALL is associated with numerous, often long-term side effects. Novel, more selective and effective treatment options are needed, in particular for these ALL cases which harbor genetic defects associated with poor prognosis.

Such innovative, selective methods include **targeted therapies**. They are more specifically toxic to cancer cells, therefore are usually associated with fewer side effects. Therapeutic **monoclonal antibodies** are an example of targeted therapy. They bind proteins present on cancer cells and trigger several mechanisms leading to cancer elimination. Acute lymphoblastic leukemia cells are derived from immature B cells, which have characteristic proteins on their surface that can serve as therapeutic targets for monoclonal antibodies. One of such proteins, selectively present on B lymphocytes, is the CD20 antigen. Monoclonal antibodies directed against the CD20 antigen have been already used in the treatment of other malignant neoplasms, are well-tolerated and have minor side-effects.

In recent years, anti-CD20 antibodies have also been introduced into the treatment protocols for adults with B cell acute lymphoblastic leukemia, but only in those patients whose cancer cells express CD20 (approximately 50% of patients). In children with this type of leukemia, anti-CD20 antibodies are not currently used. The amount of CD20 protein on the surface of leukemic cells is heterogeneous and in many cases may be insufficient for effective treatment. Molecular mechanisms regulating the amount of CD20 protein in acute lymphoblastic leukemia are poorly understood. Our preliminary results suggest that genetic changes, which are associated with resistance to therapy and poor prognosis, can also regulate CD20 levels on leukemic cells. **The aim of this study is to better understand the mechanisms regulating the amount of CD20 and to identify signaling pathways that increase CD20 levels on leukemic cells.** The project will include preclinical studies in cellular models, mainly derived from cells isolated from patients, as well as in mouse models. Understanding the signaling pathways regulating the amount of CD20 in B cell acute lymphoblastic leukemia cells may improve the therapeutic efficacy of anti-CD20 antibodies and possibly result in better outcome for patients who underwent this type of immunotherapy.