B cell malignancies

It is our aim to increase the insight of the pathogenesis causing human B cell lymphoproliferative malignancies like acute and chronic lymphoid leukaemia (ALL and CLL), multiple myeloma (MM) and lymphomas of Hodgkin or non-Hodgkin type (HS and NHL). As can be seen in the figure below, the diseases have been linked to different stages of the B cell differentiation.

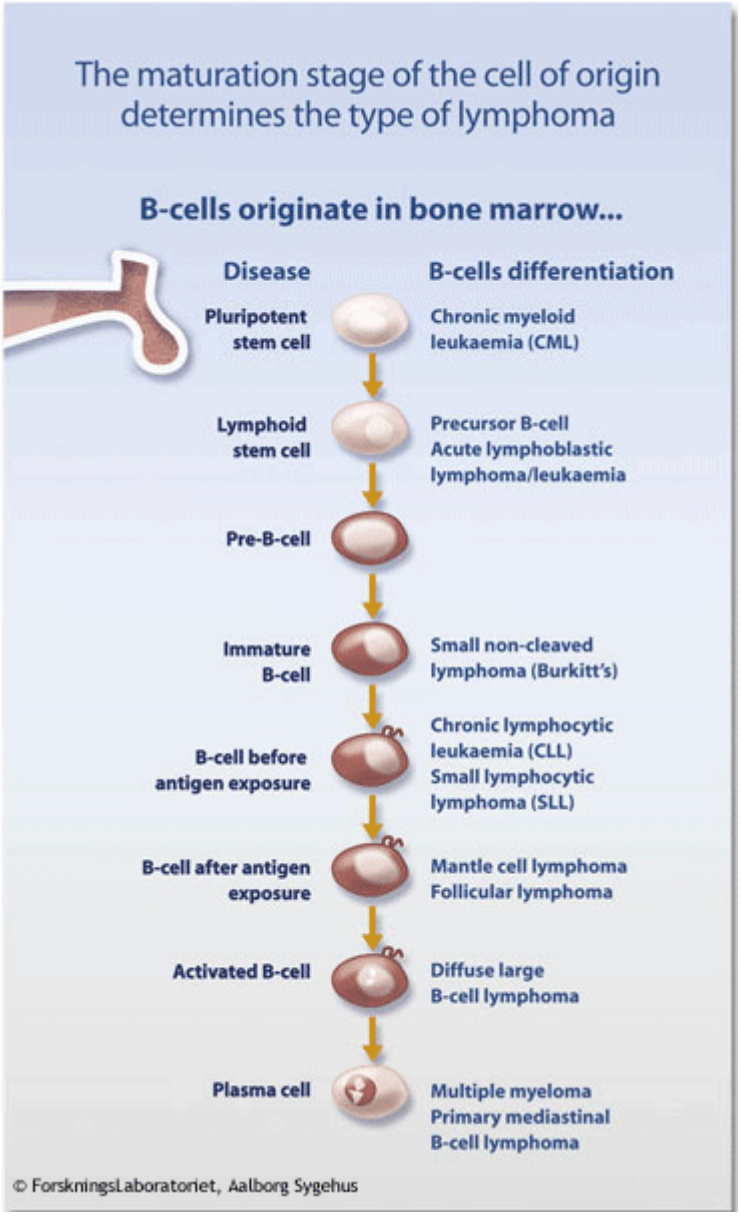
Normal B-cell development

Normal B-cell development takes place in well defined differentiation steps: 1) lymphoid stem cell (committed lymphoid progenitor), 2) pro-B-cell, 3) pre-B-cell, 4) immature/naive B-cell. The pre-B-cell is characterised by rearrangement of immunoglobin heavy chains, whereas the naïve B-cell is characterised by rearrangement of the immunoglobin light chain as well as expression of a functional B-cell receptor. After antigen exposure, further differentiation takes place in the lymph nodes where B-cells undergo somatic hyper-mutations and class switching. Finally B-cells differentiate into memory B-cells or immunoglobin secreting plasma cells.

B-cell malignancies

The cause of the lymphoproliferative diseases is still unknown, but during recent years a better understanding of the underlying molecular mechanisms has emerged. This includes linking translocations and mutations to cancerous genes that control cell division, apoptosis and DNA repair. The hypothesis is that the mechanisms behind rearrangement of immunogobin genes and somatic hypermutations - normal aspects of B-cell development – increase the likelihood of translocations and mutations to take place on other chromosomes in the B-cell.

The diversity in B-cell malignancies reflects the stages in the B-cell development from which the cancer originates (see figure). For example in "acute lymphoblastic lymphomas", there is no rearrangement of light chains and the cancer cells have surface markers in common with pro- and pre-B-cells. This indicates that the disease has developed from early stages in the B-cell development. "Diffuse large B-cell lymphoma" on the other hand, stems from mature B-cells that have undergone antigen exposure and have undergone somatic hypermutations.



Diagnosis and treatment

The diagnosis is based on biopsies from bone marrow, blood or lymph nodes using cell or gene specific tests. These tests are based directly on the latest knowledge on the malignant pathogenesis mechanisms of B cells. In this way the prognosis and thereby the treatment is revealed.

The treatment includes chemo- and radiation therapy following predefined principles where the overall condition of the patient and the sub-classification of the disease are taken into account.