

## Abstract for general public

All blood cells in our organism are produced derived from hematopoietic stem cells. Hematopoietic stem cells self-renew their own population, and therefore they constitute the regeneration reservoir of blood throughout our lives. They also give rise to cells that subsequently differentiate to mature blood cells.

Hematopoietic stem cells reside in bone marrow. It is known, that their local microenvironment, referred to as the bone marrow niche, is crucial for their proper functioning. The niche is built from various types kind of cells, which provide adhesion and produce molecular factors that are necessary for hematopoietic stem cells. Alteration of the structure or function of the niche results in impairment of hematopoietic stem cells and leads to globally altered blood production.

The ability of the hematopoietic stem cells to self-renew may be also linked to negative consequences. During aging hematopoietic stem cells acquire mutations that may lead to malignant transformation to leukemic stem cells. Leukemic stem cells are the rare population among all leukemic cells, but drive the development of the disease.

Recent research postulate that common lack of efficiency of the current anti-leukemic therapies results from their low activity against leukemic stem cells. Therefore, it is suggested that new therapies should target the leukemic stem cells

The aim of this project is to identify and characterize the niches of hematopoietic and leukemic stem cells. We want to reveal what differs between these two niches and indicate the potential molecular mechanisms typical for niche of leukemic stem cells, but not active in the niche of hematopoietic stem cells. Identification of the niche of leukemic stem cells may lead to the definition of novel therapeutic targets. The alteration of interaction between leukemic stem cells with their niche may result in their elimination.

To precisely characterize the niches of hematopoietic and leukemic stem cells we propose a system, in which upon contact with niche cells, the stem cells will induce expression of fluorescent marker in the niche cells. Fluorescent marker will allow to sort out the niche cells, that contacted the investigated stem cells and to further analyze their gene expression. After identification of genes involved in interaction with the niche, we will attempt to inactivate these genes and see whether we altered their adhesion to the niche. The studies will be performed in vitro, using primary cultures of mesenchymal stromal cells, as well as in vivo using the mouse models.

Altogether, the project proposes new system for detection of cell-cell interactions to identify the niches of hematopoietic and leukemic stem cells. Successful completion of the project may lead to new therapeutic targets against leukemic stem cells.