Somatic stem cells are required to maintain homeostasis in different tissues. In this context stem cells give rise to differentiating cells which replace cells getting lost in the lifetime of a multi-cellular organism. To fulfill this function over a long period of time, it is essential that the pool of stem cells remains a constant size. Since both the abnormal loss as well as the uncontrolled expansion of stem cells is fatal for organisms, the decision of self-renewal versus differentiation needs to be tightly regulated. The understanding of such mechanisms will not only be essential for the clinical use of these cells in regenerative medicine but will also increase our understanding of certain aspects of tumor formation and degenerative diseases.

At the example of the hematopoietic system, a few transcription factors, e.g. HoxB4, AML1/Runx1, SCL/Tal1, Meis1, have been identified, taking part in the decision process self-renewal versus differentiation of primitive hematopoietic stem cells. While loss of function of these transcription factors is generally associated with defects in the development of the hematopoietic system, the aberrant expression is often results in an expansion of primitive hematopoietic cells and seems to be connected to different forms of leukemia.

With the aim to identify additional transcription factors required for the self-renewal process of primitive human hematopoietic cells, we have performed genome wide GeneChipTM analyses of different cell fractions, containing either primitive or more mature hematopoietic cells. We identified a number of transcription factors encoding genes which are specifically expressed in the most primitive hematopoietic cell fractions, whose function has not yet been associated with hematopoiesis. In order to characterize the early hematopoietic function of some of these candidate genes we decided to perform over expression as well as RNAi mediated knock down experiments. We are using a lentiviral strategy to genetically manipulate primary human umbilical cord blood derived CD34+ cells and analyze effects on the cell fates of transduced cells in different functional read out systems.