2. PROBLEM STATEMENT

In the course of work on this thesis the transcription factors influencing the commitment and differentiation of myeloid cells were analyzed, in particular Icsbp and Klf4.

It has already been described that Icsbp plays a pivotal role in the lineage commitment of bipotent granulocyte-monocyte progenitors (GMPs), directing them toward macrophage lineage. However, the underlying mechanism of this switch is not fully understood. The global gene expression analysis of GMPs from Icsbp$^{+/+}$ and Icsbp$^{-/-}$ mice revealed strong down-regulation of the transcription factor *Klf4* in the absence of Icsbp. *Klf4* is highly expressed exclusively in the progenitors of the myeloid lineage (Terszowski et al., 2005). However, the role of Klf4 in the development of myeloid cells has not been studied yet.

In addition, several eosinophil-specific genes were strongly down-regulated in the Icsbp$^{-/-}$ GMPs, indicating perturbed eosinophilopoiesis in the absence of Icsbp. This aspect of myeloid development in Icsbp$^{-/-}$ mice has not yet been studied.

This work answers the following questions:

- Is Klf4 downstream target of Icsbp or do these two factors function independently in myelopoiesis?

- Is it possible to rescue (in part or completely) the defective macrophage differentiation of Icsbp$^{-/-}$ progenitors by reintroducing Klf4?

- Does the deletion of Klf4 cause defective myelopoiesis in mice? For this purpose, study of the hematopoietic system of mice with conditional Klf4 deletion was performed.

- How does Klf4 regulate myelopoiesis and what are the possible downstream targets?

- Does Icsbp, in addition to its documented involvement in the development of monocytes and neutrophilic granulocytes, play a role in the development of eosinophilic granulocytes? For this purpose, the eosinophil representation and function was analyzed in Icsbp$^{-/-}$ mice.