Hematopoietic stem cells (HSCs) are crucial for maintaining balanced homeostasis in the human body. HSCs are pluripotent cells, which are able to give rise to many very different cells. HSCs can be found in fetal liver initially during organismal development where they expand and move to their more definitive location, the bone marrow, shortly before birth in humans and mice. HSCs possess to not only recapitulate themselves (self-renew) or proliferate and expand, but are also the first branching point from which subsequent multipotent progenitors and eventually all blood cell lineages are formed thus establishing specific and restricted terminal differentiation pathways. The irreversible decision to initiate and follow a specific differentiation pathway is designated as lineage commitment. The drivers of lineage commitment, which are a base of this thesis, are intrinsic as well as extrinsic factors acting within the stem cell niche, such as transcription factors, chromatin remodeling factors, and cytokines, which are essential for proliferation, survival, self-renewal and lineage commitment decisions. These regulatory factors, working either independently or in mutual coordination, maintain balanced homeostasis of HSC renewal and their differentiation. The goal of this thesis will be to ascribe the mechanisms of lineage commitment of HSCs with regard to the role that key regulation molecules play in this cell fate decision.