Serious clinical problems are hematologic diseases, including acute myelogenous leukemia, chronic myelogenous leukemia, aplastic anemia and immune disorders. The method used in the treatment of these diseases are allo- or autotransplantation of hematopoietic stem/progenitor cells (HSPCs). The cell suspension containing hematopoiesis progenitors form the transplantation material obtained from the donor peripheral blood (PB) after administration of mobilization agent - granulocyte colony stimulating factor (G-CSF) or CXCR4 antagonist (AMD3100). The effectiveness of the transplantation depends on many factors, including the number of transplanted HSPCs. Therefore, knowledge of the factors and phenomena associated with migration of these cells is crucial to optimize clinical results associated with therapies based on HSPCs. The role of SDF-1 (stromal derived factor) in the retention of HSPCs is indisputable, there are however observations suggest the existence of other factors acting as chemoattractant in the process. One of them is a sphingosine-1-phosphate (S1P), a bioactive sphingolipid present in the cell membrane, which is involved in several processes, including stimulation of cell growth and proliferation as well as affect the egress of HSPCs from bone marrow microenvironment during mobilization process.

Sphingosine kinases are key enzymes regulating the production of S1P. So far, the two isoforms have been characterized: SphK1 and SphK2, and a numerous of differences between them include derived from two separate genes, pathways of formation, tissue-specific expression and localization within the cell, as well as various kinetic properties suggest that they are involved in different physiological processes. Studies on SphK2 deficient mice had significantly higher levels of S1P in the PB. On the other hand, the administration of an SphK1 inhibitor dynamically reduces endogenous S1P in mice peripheral blood. It proposed the theory that in addition to synthesizing S1P in cells, SphK2 also acts in the removal of this bioactive lipid from blood. This intriguing mechanism has not been clarified and SphK role is not fully understood.

Based on the expression pattern of S1P in peripheral blood of mice with defective of SphK1 and SphK2 and due to the properties of this lipid in retention of HSPCs, I hypothesized that mice SphK1-KO show a poor mobilizing of these cells, and this process will be increased in animals SphK2-KO.

Evaluation of pharmacological mobilization of hematopoietic stem/progenitor cells of mice with a sphingosine kinase type 1 (SphK1-KO) and 2 (SphK2-KO) defect will be performed using a granulocyte colony stimulating factor (G-CSF) and a CXCR4 antagonist (AMD3100). The activity of the mobilization process will be determined based on the number of leukocyte, $Lin^{-}Sca\text{-}1^{+}c\text{-}Kit^{+}$ and $Lin^{-}Sca\text{-}1^{+}CD45^{+}$ cells by flow cytometry and the amount of circulating hematopoietic progenitors (CFU-GM) in clonogeneic assays *in vitro*.

Results obtained in this project can shed new light on the HSPCs retention, expanding knowledge about this phenomenon. If the assumptions made in the project were to prove correct, my experiment will confirm the key role of S1P and not the SDF-1 in the mobilization of HSPCs from bone marrow niche to peripheral blood.