**Popular Science Summary**

**The role of the P2X4 purinergic receptor in regulating mitochondrial metabolism and redox homeostasis in hematopoietic stem cells: insights from P2X4-knockout mice**

Hematopoietic stem progenitor cells are responsible for blood production and regeneration throughout life. Their ability to remain in a quiescent state, activate, and self-renew depends on proper mitochondrial metabolism and the maintenance of redox balance, which protect the cells from oxidative stress. Increasing evidence points to a key role of purinergic signaling—an evolutionarily ancient mechanism of intercellular communication based on molecules such as ATP—in regulating these processes. However, the precise mechanisms of this pathway in hematopoietic cells remain poorly understood. This project aims to investigate the role of the purinergic receptor P2X4 in regulating mitochondrial metabolism and the oxidative-reductive balance in hematopoietic stem progenitor cells.

The P2X4 receptor is a protein present on the surface and inside cells that responds to chemical signals related to energy and inflammation. We hypothesize that P2X4 acts as a “metabolic sensor” that helps stem cells adjust their activity and resistance to oxidative stress by regulating mitochondrial function. The absence of this receptor may disrupt energy balance and increase susceptibility to damage, leading to a reduced regenerative capacity of the cells.

Our hypothesis is that the lack of the P2X4 receptor impairs mitochondrial integrity, enhances oxidative stress, alters key metabolic pathways, and weakens the ability of hematopoietic stem and progenitor cells to regenerate, form colonies, and self-renew.

In this project, we will compare stem cells obtained from mice lacking the P2X4 gene with cells from healthy control mice. We will employ modern methods to study cellular metabolism, including measurements of mitochondrial respiration, determination of reactive oxygen species levels, and analyses of proteins and metabolites using advanced proteomic and metabolomic techniques. Additionally, we will assess the functional ability of the cells to proliferate and differentiate, which will allow us to determine the impact of P2X4 deficiency on their regenerative potential.

Understanding how the P2X4 receptor influences metabolism and the oxidative-reductive balance in stem cells is important not only from a basic biology perspective but also has clinical potential. The results may contribute to the development of new therapies that improve the efficiency of stem cell transplantation and the treatment of diseases related to oxidative damage and stem cell exhaustion, such as anemia or bone marrow failure.

The completion of this project will expand our knowledge of the primary signaling mechanisms linking cellular metabolism with their function and resistance to stress. This unique approach combines mitochondrial biology with immunology and hematology, creating a new research perspective that may impact the development of regenerative medicine.