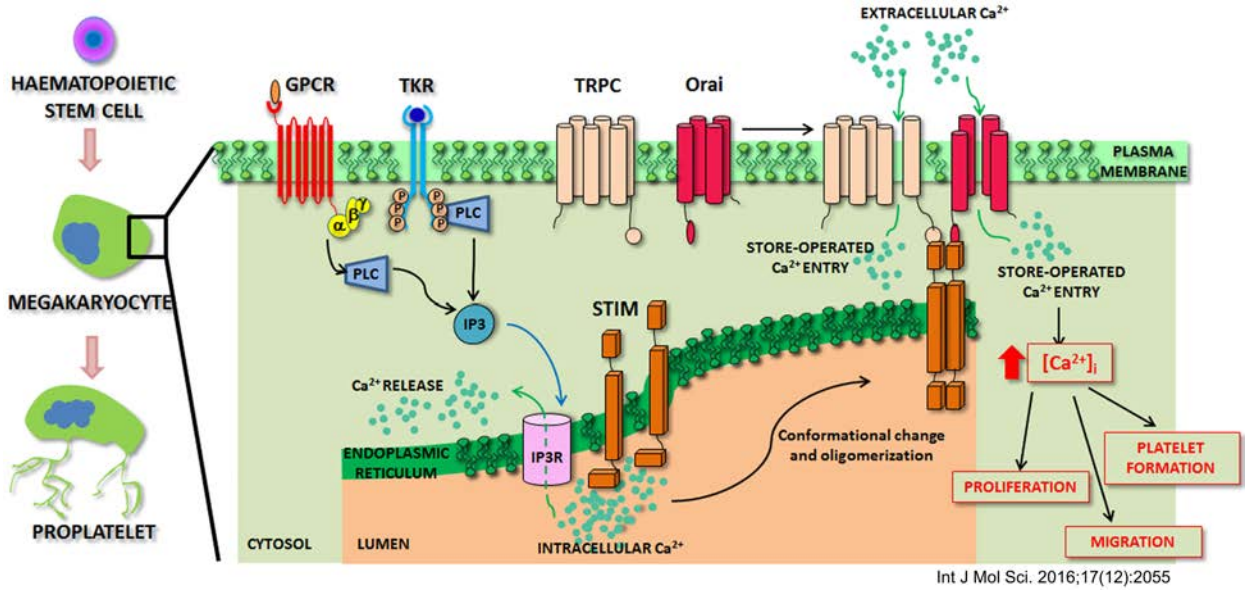
Project Title: Calcium signaling networks in physiological and pathological megakaryopoiesis
Supervisor: Christian Di Buduo
Laboratory: Laboratory of studies on megakaryocyte function, Department of Molecular Medicine
Research Theme: Clinical Biochemistry, Haematopoiesis

Abstract:



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Bone marrow megakaryocytes are derived from haematopoietic stem cells to produce blood platelets. Calcium (Ca^{2+}) plays fundamental and diversified roles along the route of human haematopoietic stem cells to platelets. Our group demonstrated that cytosolic Ca^{2+} concentration in megakaryocytes is under the control of plasma membrane and subcellular Ca^{2+}-sensitive channels. Also, we showed that Ca^{2+} signaling networks are activated by cytokines and growth factors that regulate the spatiotemporal patterns of intracellular pathways involved in megakaryocyte differentiation. Any impairments of Ca^{2+} homeostasis in megakaryocytes result in profound functional alterations that may result in haematological diseases, such as Myeloproliferative Neoplasms,

Based on our previous publications, the candidate will perform primary cell cultures of human healthy and diseased megakaryocytes to further exploit the role of the Ca^{2+} signaling in megakaryopoiesis. By using modern approaches of live-cell imaging, the candidate will characterize the role and contribution of cation channels and cytoplasmic organelles to the shaping of Ca^{2+} flows and their impact on platelet production.

By the end of the Ph.D. program, we expect the candidate to be able to provide new mechanistic insights into the role of the Ca^{2+} signaling networks and their regulatory pathways in physiological and pathological megakaryopoiesis with the aim of identifying new possible therapeutic targets for megakaryocyte-related diseases.

Techniques

Cell culture, live-cell imaging, immunofluorescence microscopy, western blotting, flow cytometry, molecular biology.