Project Title: Bone marrow modeling for platelet production

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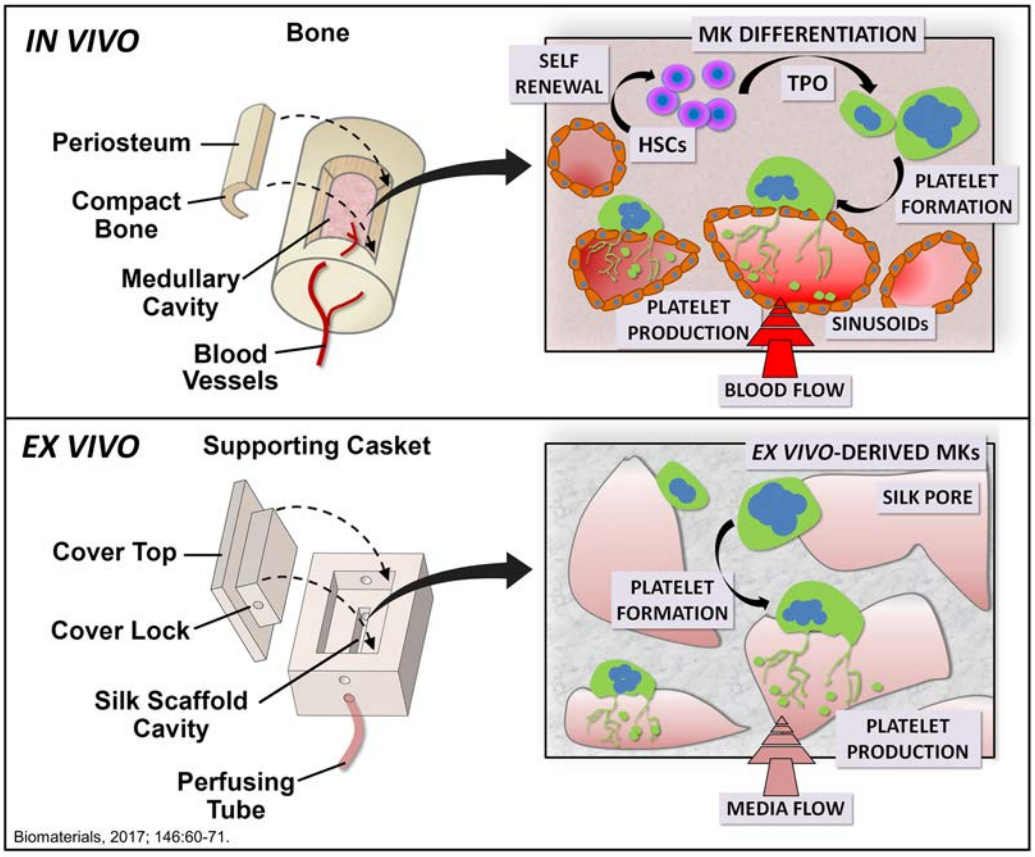
Research Theme: Clinical Biochemistry, Haematopoiesis

Abstract:



Megakaryocytes in the bone marrow are responsible for the continuous production of platelets in the blood. Under- or over-production of platelets has major clinical implications for many diseases, including thrombocytopenia and myeloproliferative neoplasms, where life-threatening side effects with incurable outcomes are common. The scientific and clinical communities are actively searching for new modes to generate functional platelets ex vivo to address clinical needs as well as for insight into fundamental studies of mechanisms. We hypothesize that engineering a 3D bone marrow mimic will propel mechanistic understanding of platelet shedding and determine future protocols for therapeutic inquiry.

Based on our previous publications, the candidate will utilize non-thrombogenic silk protein biomaterial to perfect an ex vivo three-dimensional (3D) tissue model of the bone marrow to study platelet release from megakaryocytes derived from human induced pluripotent stem cells. Megakaryocytes receive cues from the bone marrow environment including cell-cell contact, contact with extracellular matrix components, and physical characteristics of the tissue (topography

and rigidity of the extracellular space) as well as shear stress generated by the blood flow in the vessels. By refining the environment in the 3D silk-based bone marrow system the aim will be to provide all the physical and biochemical characteristics necessary to improve ex vivo platelet release by megakaryocytes. The outcome of these studies is expected to be the design of new tools to mimic the bone marrow niches *ex vivo* gaining insight into the mechanisms that control platelet release in a physiologically relevant manner.

Techniques

Cell culture, bioengineering techniques, confocal microscopy, western blotting, flow cytometry, molecular biology.