Bone marrow-on-chip as a model for thrombopoiesis research

The bone marrow is one of the major locations in the human body where platelets are produced[1]. To have a better understanding of which processes are involved in thrombopoiesis a bone marrow-on-chip model is proposed to systematically study all components. One of the most interesting interactions during the formation is the one between the megakaryocyte and endothelial cells[2–4]. This interplay leads to the maturation of megakaryocyte and subsequently the migration through the endothelial barrier and release of platelets[5,6]. Besides the role of the endothelial cells the extracellular matrix (ECM) also plays a crucial role in the homeostasis of megakaryocytes and their maturation. While collagen I is the main ECM component that ensures quiescence, collagen III, IV, fibronectin and fibrinogen lead to platelet formation/maturation[7]. Combining all these components into a single system gives us the opportunity to see the interplay between all these factors and investigate their individual roles (Fig. 1).

To create the bone marrow on-chip model we first need to determine the culture conditions for megakaryocytes based on protocols previously used and further optimise if needed[8]. In parallel we want to determine megakaryocyte viability and differentiation phase inside the chip by culturing megakaryocytes within an ECM gel. As a final step we want to introduce endothelial cells in the lumen of the chip to see if we can promote megakaryocyte migration and maturation in a physiological manner, which would lead to the production of (pro)platelets.

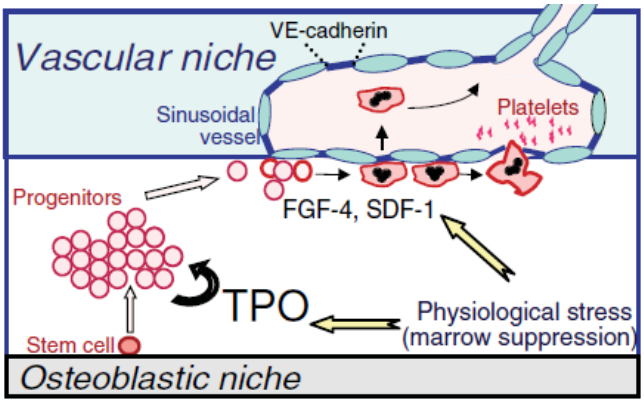

Figure 1: Overview of the process for platelet production, adapted from [9]. Schematic representation of the various steps from megakaryocyte to platelet production in the bone marrow as well as key influencers.

To achieve this goal the following steps have to be taken:

- Train basic skillset for working with chips
- Optimise megakaryocyte culture protocol
- Define matrix concentration and composition
- Characterise megakaryocyte differentiation and thrombopoiesis
    - Use CD41a/CD42 to determine differentiation phase
    - Optically observe the formation of possibly proplatelets and platelets.
- Determine the influence of endothelial cells on megakaryocytes and thrombopoiesis.

Techniques and skills required for this project:

- Cell culture (primary)
- Interest in microfluidics/ organ-on-chip technology
- Confocal microscopy
- Widefield microscopy
- Image analysis
- Immunocytochemistry
- Biochemistry

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Project duration: at least 6 months

Background: cell biology with an interest in organ-on-chip technology

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