

# Biomimetic reconstruction of a human embryonic aorta-on-chip for the generation of transplantable hematopoietic stem and progenitor cells

PhD Project IPV /nLife

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## Abstract

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In vertebrates, the aorta–gonad–mesonephros (AGM) region is the first intraembryonic niche where hematopoietic stem and progenitor cells (HSPCs) emerge through the endothelial-to-hematopoietic transition (EHT). During this process, specialized hemogenic endothelial cells (HECs) lose their endothelial phenotype and acquire a hematopoietic fate under the influence of mechanical forces such as shear stress, cell–matrix interactions, and molecular signaling within the aortic microenvironment. In humans, this event occurs between 27 and 36 days post-fertilization and establishes the definitive hematopoietic system that underpins curative bone marrow transplantation. However, the molecular and biophysical mechanisms governing human EHT remain poorly understood, hindered by limited access to embryonic tissues and inadequate in vitro models.

This PhD project aims to recreate the human embryonic aorta-on-chip, a microfluidic system that mimics the structure, flow dynamics, and mechanical cues of the AGM niche to promote functional EHT and the generation of transplantable HSPCs. Using human induced pluripotent stem cells (hiPSCs) and primary stromal populations, the project will integrate controlled extracellular matrix composition, stiffness, and hemodynamic parameters to study and optimize hematopoietic emergence.

The research plan includes: (1) deriving and characterizing hiPSC-derived HECs using flow cytometry, imaging, and multi-omics tools; (2) developing a 3D microfluidic aorta-on-chip model combining endothelial and mesenchymal cells under defined shear stress; and (3) inducing and monitoring EHT in this system through functional assays, lineage tracing, and biosensors for real-time analysis.

This interdisciplinary approach—bridging stem cell biology, mechanobiology, and microengineering—seeks to provide fundamental insight into human developmental hematopoiesis and establish a scalable platform for generating patient-specific HSCs, with major implications for regenerative medicine and transplantation.

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