Modeling vascular inflammation with immune cell-vessel crosstalk in hiPSC-derived 3D vessels-on-chip

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Stellingen behorende bij het proefschrift getiteld

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1. Organ-on-chip platforms are emerging as predictive tools for human biology and disease modeling; their future impact relies on addressing current limitations and aligning with regulatory and translational goals. **— *This thesis***

2. An entirely hiPSC-derived vessel-on-chip model that replicates endothelial–mural cell interactions and hemodynamic flow enables physiologically relevant leukocyte transmigration and paves the way for accurate modeling of disease-specific inflammatory responses using patient-derived hiPSCs. ***—This thesis***

3. Inflammatory stimulation exacerbates endothelial–mural cell interaction deficiencies specific to HHT1, which are revealed in 3D hiPSC-derived self-assembling vessel-on-chip model. **— *This thesis***

4. The integration of hiPSC-derived macrophages into self-assembling Vessel-on-Chip model represents a promising step toward studying perivascular macrophage-specific functions, including their role in modulating inflammatory responses in a healthy or diseased vascular environment. ***—This thesis***

5. Fundamental differences in immune cell composition, cytokine signaling, and receptor expression between mice and humans limit the translational relevance of murine models and underscore the need for human-based platforms to study immune responses. **— *Mestas, J., and Hughes, C.C.W. (2004). Journal of Immunology.***

6. Organ-on-chip technologies replicate human organ-level physiology and disease mechanisms, offering predictive, human-relevant platforms that have the potential to transform drug development and precision medicine beyond the limitations of traditional animal models. **— *Ingber, D.E. (2022). Nature Reviews Genetics.***

7. Endothelial mechanotransduction via shear stress regulates gene expression, barrier integrity, and inflammatory responses—key processes that define vascular function and dysfunction. **— *Chien, S. (2007). American Journal of Physiology, Heart and Circulatory Physiology***

8. Leukocyte migration through the vascular wall involves coordinated interactions with endothelial cells, mural cells, and extracellular matrix components, each forming sequential barriers that are actively navigated during inflammation. **— *Nourshargh et al. (2010). Nature Reviews Molecular Cell Biology.***

9. Understanding a question is half an answer. **— *Socrates (470-399 BCE).*** *Science progresses by asking the right question at the right moment, but comprehending its meaning is the key to success.*

10. I have not failed. I've just found 10,000 ways that won't work. **— *Thomas A. Edison (1921).*** *In microfluidic cell culture systems, failure teaches you more than you think.*

11. Bilim, insanın kendine yaptığı yolculuktur. **— *Aziz Sancar (2015).*** *Science is a journey one takes into oneself — a transformative path that reshapes both the self and one's understanding of life.*

12. Dünyada her şey için, hayat için, başarı için en hakiki mürşit ilimdir. **— *Mustafa Kemal Atatürk (1924).*** *For everything in the world, the truest guide is science — this vision from one of the greatest minds has shaped my early education and academic path; for that, I am forever grateful.*