The branching of life: human iPSC-based angiogenesis-on-chip

Urdaneta González, K.E.

Stellingen behorende bij het proefschrift getiteld
"The Branching of Life: Human iPSC-Based Angiogenesis-on-Chip".

1. First, the branching of neovasculature, known as "angiogenesis," is a complex process to recapitulate. Second, the use of heterogeneous hiPSC-derived Endothelial Cells comprises an extra layer of difficulty. Third, organ-on-chip tech is not yet widely standardized. Hence, there are countless challenges to overcome and too little to conclude *(This thesis, derived from chapters 1-4).*

2. The optimization of the microenvironment allows for the hiPSC-derived Endothelial Cells to shape measurable sprouting structures within 3D microfluidic platforms. However, their reproducibility and performance linger at the edge of current QC standards, longing for refinement *(This thesis, derived from chapter 2).*

3. HiPSC-derived vascular derivatives represent a bridge between reductionist 2D cultures and animal-based studies of angiogenesis, providing another layer of human relevance to generate predictive data, ethically sensitive but also directly translatable to human biology *(This thesis, derived from chapters 3-4).*

4. In organ-on-chip, all problems are small – *last famous words – F. van den Hil.*
   Paradoxically, why does the recapitulation of angiogenesis continue failing?
   The central challenge is balancing the increasing biological complexity of these models with the need for sufficient throughput and scalability for robust preclinical studies *(This thesis, derived from chapters 1-4).*

5. The usefulness of emergent angiogenesis assays lies in evaluating their application as fit-for-purpose tools to address, in a more specific, faster, and cost-effective manner, the research questions unfeasible to elucidate with conventional or animal models *(Supported by Nahon et al., Nat Biomed Eng 2024).*

6. All models are wrong only if used assuming they should be perfect replicas of reality, but become powerful when employed in a fit-for-purpose manner, aware of their intrinsic limitations" *(Supported by Box and Drapper N. J Am Stat Assoc 1976).*

7. In the pursuit of engineering vascular growth on a *chip in a more humane and human-relevant manner (Inspired and supported by van Duinen et al., Int J Mol Sci 2020; and Soragni et al., Angiogenesis 2023)*, this work has, above all, engineered patience (*The author).*

8. Critical cues intrinsic to animal models are widely used to study angiogenesis due to their unique ability to capture biological systemic complexity, such as organ-to-organ interplay, which current advanced *in vitro* assays are still unable to fully recapitulate *(Supported by Staton et al., Int J Exp Pathol 2009; Stryker et al., Biomedicines 2019; and Weijts et al., Nat Commun 2018).*

9. Organ-on-chip systems powered by appropriate vascular cells can provide a powerful lens into the disease mechanisms underlying Hereditary Hemorrhagic Telangiectasia *(Supported by Orlova et al., Stem Cell Reports 2022; and Faughnan et al., Angiogenesis 2019).*

10. In another multiverse, organ-on-chip tech has been fully implemented in translational medicine and drug testing. However, in this universe, we still need to work hard to make it true. Luckily, as time and space are relative, in a jump, we might soon reach that multiverse *(The author).*

11. The PhD life is an endless series of glitches; some are solved, others are to be solved, but many will never be solved, and we need to learn how to live with it, move on, or be stubborn until it is solved *(The author).*

12. "If I have the gift of prophecy and can fathom all mysteries and all knowledge, and if I have a faith that can move mountains, but do not have love, I am nothing."

    1 Corinthians 13:2, The bible.

    A reminder that while science gives us knowledge, power, and technology to shape the world, only love gives our lives purpose *(The author).*