Advancing cardiac safety and drug discovery screening using human stem cell-derived cardiomyocytes

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Stellingen behorend bij het proefschrift getiteld

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1. The presence of both cardiac endothelial cells and cardiac fibroblasts is essential for cardiomyocyte maturation via tri-cellular crosstalk – *Giacomelli, Meraviglia, Campostrini et al. (2020), Cell Stem Cell*
2. Cardiac microtissues are capable of capturing both negative and positive inotropic drug responses with high accuracy, highlighting their potential for cardiac safety pharmacology – *This thesis*
3. Robotic workflows enable reproducible, large-scale production, maintenance, and analysis of cardiac microtissues, critical for high-throughput screening applications – *This thesis*
4. The greatest challenge in CPVT genetics is not identifying RYR2 variants, but proving their pathogenicity amid gene complexity and variant rarity – *Priori et al. (2021), JACC*
5. dbcAMP reliably induces arrhythmic events in cardiac microtissues containing hiPSC-CMs with mutations causing CPVT1, demonstrating its utility as a trigger in disease modeling – *This thesis*
6. Integrating hiPSC-CM-based *in vitro* data with *in silico* modelling through digital twins improves our ability to link preclinical findings to clinical cardiovascular risk – *This thesis*
7. "If you accept that the reality is not black or white, but uncertain, you are more acceptable to novel methodologies" – *Thomas Hartung (2024), accepting uncertainty is key to embracing non-traditional models and technologies.*
8. The FDA's plan to phase out animal testing marks a regulatory turning point; now the scientific community must deliver validated human-relevant alternatives that regulators can trust – *FDA press release (2025)*
9. "The devil is in the details" – *Christine Mummery, the success of translational science depends not just on big ideas, but on mastering experimental nuance.*
10. "Le travail comme le vin a besoin de se reposer et quand le vin est reposé il recommence à travailler" – *Jacques Pré'vert (1946), like wine, productive scientific work requires periods of rest and reflection to reach its full potential.*
11. "Life is what happens to you, while you're busy making other plans" – *John Lennon (1980), life rarely follows our plans; flexibility and openness often lead to the most meaningful discoveries.*
12. "This is science that affects everyone, so it's important to stay informed" – *Notebook LM (AI-generated interpretation of the outcome of chapter 7 of this thesis), the societal impact of (this) research underscores the need for transparency and accessible communication.*