

Connecting Genomics and Tissue Engineering to Model Pompe Disease

Stellingen Behorende bij het proefschrift:

1. The identification of disease-modifying factors for Pompe disease will not only increase our understanding of the clinical course of patients, but also provide avenues for the development of novel therapeutics. *(this thesis)*
2. Pompe disease is caused by a single pathological cascade but symptomology results from an interplay of several dysregulated mechanisms. *(this thesis)*
3. In Pompe disease, dysregulation of cytosolic glucose metabolism precedes the accumulation of glycogen in lysosomes. *(this thesis)*
4. The hiPSC-derived 3D-tissue-engineered-skeletal-muscle system described in this thesis is capable of accurately reflecting molecular mechanisms of disease. *(this thesis)*
5. It has become increasingly clear that isogenic disease models are important to correct for genetic background and to distinguish disease-related pathology from random variability. *(this thesis)*
6. Genomic engineering is a tool, and choosing not to use it for germline applications (both in plants and in humans) bears as many consequences as misusing it.
7. Monogenic disorders should no longer be considered to be monogenic due to the impact of genetic differences such as haplotypes, quantitative trait loci, compensatory mechanisms, and other heritable differences on the clinical presentation.
8. Disease models will never be able to fully recapitulate human disease, as there is a never-ending race between improved methods and the discovery of novel disease-related aspects that have not been accounted for.
9. The ultimate goal of tissue engineering will be to mirror healthy and pathological function with near-indistinguishability from in vivo physiology. However, these ambitious goals do not need to be fully achieved before engineered tissue function becomes clinically relevant. *(Callaghan et al, NPJ Regenerative Medicine, 2022)*
10. Animal-free alternatives such as humanized organoids and organ-on-chip platforms will become the preferred method for the development of novel therapeutics.
11. “Highly organized research is guaranteed to produce nothing new.” *Frank Herbert, Dune*

Stijn in 't groen