Stellingen behorende bij het proefschrift

Modeling of Pompe Disease using Induced Pluripotent Stem Cells for the Development of Novel Therapies

1. Prediction of splicing regulatory elements using *in silico* tools or minigenes often give false positive and false negative results (*this thesis*).

2. Assessment of endogenous pre-mRNA splicing is a prerequisite to demonstrate splicing modulation in response to gene variants or drug treatment (*this thesis*).

3. Treatment of skeletal muscle cells *in vitro* with AONs results in almost complete rescue of the IVS1 allele and it provides proof that the concept is sound to be explored in patients (*this thesis*).

4. Differentiation of iPSCs into an expandable and pure precursor population increases robustness and simplicity of *in vitro* disease modeling (*this thesis*).

5. Isogenic cell lines generated using gene correction are useful for the identification of cellular processes related to disorders, and can be used for filtering of genes that are differentially expressed due to genetic variation between donors (*this thesis*).

6. In many ways, the CRISPR story illustrates how science often works, with a fitting reminder that the basic microbiological processes driving the survival of bacteria often give rise to valuable molecular tools, enzymes and technologies, together with the historical involvement of a plethora of unsung heroes whom selflessly advance science for the benefits of humankind (*Barrangou et al,. Nature Review Microbiology 2017*).

7. Unintended uptake and toxicological challenges should be addressed in the very early stages of new AON development (*adapted from Godfrey et al,. EMBO Molecular Medicine, 2017*).

8. iPSCs represent a paradigm shift because they now allow us to directly observe and treat relevant patient cells (*Shi et al,. Nature Review Drug Discovery 2017*).

9. Oligonucleotide therapy does not have the safety and efficacy issues associated with expressed-vector gene therapy, and its use in some applications is advancing on the road to approval by the Food and Drug Administration (*Askari et al,. The New England Journal of Medicine 1996*).

10. Progress in considering hPSC-derived muscle as a valid source of cells for basic and translational research applications has been hindered by the lack of an efficient method to isolate muscle precursors (*Borchin et al,. Stem Cell Reports 2013*).

11. Even if you're not doing anything wrong, you are being watched and recorded (*Edward Snowden*).

Erik van der Wal
Rotterdam, October 12th, 2017