

## Propositions (Stellingen)

### **A Step Forward: Lentiviral Gene Therapy as a Cure for Pompe Disease**

1. The conventional view of Pompe disease as a sole muscle disease has been challenged recently by impairment of the central nervous system in classic infantile patients. Therefore, brain targeting should be one of the prerequisites for an effective and curative therapy. (*this thesis*)
2. *Ex vivo* lentiviral gene therapy with IGFII tagged GAA protein shows improved tissue targeting compared with untagged GAA, and has the potential to fully correct the phenotype in a murine Pompe model. (*this thesis*)
3. Enhanced efficacy of lentiviral gene therapy improves the safety profile because it requires less vector integrations and allows the usage of a mild promoter. (*this thesis*)
4. Effective immunomodulatory reagents to eliminate or prevent immunity against rhGAA will be the key for future implementation of lentiviral gene therapy in classical infantile Pompe patients. (*this thesis*)
5. While gene addition by *ex vivo* lentiviral gene therapy holds great promise for development as a future treatment for Pompe patients, investigation should proceed in the field of gene editing, as a precise correction of genetic mutations is the ultimate goal for gene therapy. (*this thesis*)
6. It is immensely rewarding and a testimony to the transformative power of science that 20 years after the original work, a deadly virus that has plagued humankind and claimed millions of lives has been turned into a beneficial tool that now helps to relieve the suffering of people affected by debilitating maladies. (adapted from *Naldini, et al., Science, 2016*)
7. Characterizing gene expression profiles across multiple samples and species is instrumental for determining the extent to which the biology of a given organism can be extrapolated to another. (*Breschi, et al., Nature Reviews Genetics, 2017*)
8. The story of how a mysterious prokaryotic viral defense system became one of the most powerful and versatile platforms for engineering biology highlights the importance of basic science research. (*Hsu, et al., Cell, 2015*)
9. Discovery consists of looking at the same thing as everyone else and thinking something different. (*Albert Szent-Györgyi, 1937 Nobel Laureate*)
10. We keep moving forward, opening new doors, and doing new things, because we're curious and curiosity keeps leading us down new paths. (*Walt Disney*)
11. 上医治未病, 中医治欲病, 下医治已病。(《黄帝内经》)  
An ounce of prevention is worth a pound of cure. The supreme healer cures the illness that is still obscure. The good healer cures the illness that is about to break out. The mediocre healer is only able to cure when the illness is fully manifested. (*Huangdi Neijing, the oldest medical classic of ancient China*)