

## Propositions (Stellingen)

### ‘ Exploring the Spectrum of Pituitary Hormone Deficiencies: Genotype, molecular mechanisms and phenotypic variability ’

1. Isolated Growth Hormone Deficiency may be due to a mutation in *HMGGA2* (this thesis).
2. Mutations in genes involved in the Hedgehog pathway may explain part of the phenotype of patients with Combined Pituitary Hormone Deficiency (this thesis).
3. *OTX2* is a good candidate gene for genetic screening in patients with Isolated Growth Hormone Deficiency or Combined Pituitary Hormone Deficiency, in whom mutations in the classical candidate genes have been ruled out, especially in patients with ocular problems (this thesis).
4. Heterozygous *OTX2* mutations may cause Combined Pituitary Hormone Deficiency by exerting a dominant negative effect (this thesis).
5. The same mutation in *GHR* may produce variable degrees in phenotypic severity due to nonsense mediated decay (this thesis).
6. Yet unidentified genetic variants may play a role in the etiology of Combined Pituitary Hormone Deficiency presently diagnosed as “idiopathic” (this thesis).
7. It is important to use primary cultures established from cells of patients for functional studies (Fang *et al*, J. Clin. Endocrinol. Metab. 2009).
8. Genetic defects may result in a range of clinical phenotypes depending on the degree of disturbance of key endocrine mechanisms (David *et al*, Endocr. Rev. 2011).
9. Next-generation exome sequencing has become a powerful new approach for identifying genes that underlie Mendelian disorders and perhaps for complex traits as well (Bamshad *et al*, Nat. Rev. Genet. 2011).
10. The factors involved in deciding human stature are numerous. They interact with each other to produce the single character we call height (William Bateson 1909).
11. We don't know a millionth of one percent about anything (Thomas A. Edison).

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