

Propositions/Stellingen

1. Variants in *TFAP2B* have pleiotropic effects with varying phenotypes and severities, which also include intestinal dysmotility. **(This thesis)**
2. Loss of function of *TFAP2B* results in a reduction of enteric neuronal progenitors and delayed intestinal transit time, leading to paediatric intestinal pseudo-obstruction (PIPO). **(This thesis)**
3. Absence of the long *FLNA* isoform leads to impaired intestinal smooth muscle contractility, which affects intestinal development and function, ultimately resulting in a myopathic form of PIPO. **(This thesis)**
4. Differential DNA methylation profiling is observed in enteric neural cells isolated from Hirschsprung disease (HSCR) patients and controls. **(This thesis)**
5. Patient-derived iPSCs are a valuable *in vitro* disease model to study defects in proliferation, migration, and differentiation of enteric neural progenitors, characteristic of HSCR. **(This thesis)**
6. Human inducible pluripotent stem cells carry unique genetic information, which reflects the genetic complexity of an individual.
7. Targeting epigenetic modifications may offer a more effective approach than gene therapy given their significant role in driving disease pathogenesis.
8. The future of personalized medicine will increasingly rely on patient-derived *in vitro* models, potentially reducing the need for *in vivo* animal studies.
9. While basic research may not immediately benefit patients, its cumulative contributions over time are pivotal for sustained progress in healthcare innovation.
10. Genomics and epigenomics functional research present both challenges and opportunities driving scientific breakthroughs.
11. *Memayu hayuning bawana* (Javanese philosophy)- To live is to do good for the world.