Propositions (Stellingen)

GATA2-DEPENDENT MECHANISMS IN HEMATOPOIETIC STEM CELL BIOLOGY: A VOYAGE FROM ONTOGENY TO LINEAGE COMMITMENT AND FUNCTION

1. Gata2 is a master regulator of the transcriptional network involved in both formation and function of hematopoietic stem cells (HSCs). (*This thesis*)

2. Gata2 acts as a decision factor for HSCs in multiple processes: transition from endothelial to hematopoietic cell state and HSC maturation during embryonic development, and also lineage differentiation choice during adulthood. (*This thesis*)

3. The loss of Gata2 places HSCs in a constant state of proliferation. (*This thesis*)

4. Aging has an indirect but significant impact on the progression of a bone marrow failure phenotype in Gata2 haploinsufficiency syndromes. (*This thesis*)

5. Gata2 dosage has different effects on distinct cellular compartments constituting the hematopoietic system. (*This thesis*)

6. Understanding the mechanisms driving complex diseases is only possible with a comprehensive research approach consisting of various model systems that diversify our view of the problem.

7. Revisiting former questions in light of the advances in technology and information improves our knowledge about the biology of life.

8. Life is a study in contrasts between randomness and determinism: from the chaos of molecular compositions and interactions to the precise coordination of differentiation and developmental trajectories, living organisms are able to balance these two aspects to survive and evolve. (*Adapted from Raj and Oudenaarden, 2008*)

9. Genes have no intrinsic effects on phenotype. Genes affect phenotype as they affect dynamics of transcriptional networks and therefore cellular behavior and biophysics. (*Adapted from Hagolani et al., 2021*)

10. Complex phenotypic outcomes might result from a relatively small number of genetic causes, also known as the "law of the vital few." (*Adapted from Pareto principle*)

11. “Science is not only a discipline of reason but, also, one of romance and passion.” (*Stephen Hawking*)

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Rotterdam, 2022