STELLINGEN BEHOREND BIJ HET PROEFSCHRIFT:

Relevance of Signal Transduction Pathway Mutations in Pediatric T-ALL

1. *TLX3*-rearranged T-ALL is associated with strongly activating *NOTCH1* mutations whereas the incidence of NOTCH-activating mutations is reduced in *TAL1*- or *LMO2*-rearranged pediatric T-ALL patients. *(this thesis)*

2. Some seemingly wild-type *NOTCH1* or *FBXW7* T-ALL patients express an activated NOTCH1-driven expression signature, implying that not all NOTCH1-activating mutational mechanisms have been revealed yet. *(this thesis)*

3. *PTEN/AKT* mutations and NOTCH1-activating mutations are nearly mutual exclusive genetic events in pediatric T-ALL that are each associated with specific T-ALL genetic subtypes. *(this thesis)*

4. Micro-deletions represent a novel, RAG-mediated PTEN inactivational event in pediatric T-cell leukemic cells and thymocytes of healthy individuals. *(this thesis)*

5. The immature T-ALL subtype as identified by unsupervised gene expression profiling analysis, is strongly predicted by the early T-cell precursor ALL gene signature and thus both reflect a single disease entity. *(this thesis)*

6. A uniform prognostic factor for pediatric T-ALL has not been identified yet.

7. RAG activity is associated with a developing immune system in children and thus may explain the increased incidence of lymphatic leukemia in children compared to adults.

8. Biologists typically concentrate on fold change, statisticians on *p*-value.

9. Great discoveries and improvements invariably involve the cooperation of many minds. *(Alexander Graham Bell)*

10. Don't let perfection get in the way of progress. *(Tony Bombacino)*

11. Er zijn meer volwassenen bang in het licht, dan kinderen in het donker. *(van Kooten en de Bie)*