Stellingen behorende bij het proefschrift

Identification of Novel Therapeutic Strategies Against *MLL*-rearranged Acute Lymphoblastic Leukemia in Infants

1. SN-38, and its pro-drug irinotecan, inhibit *MLL*-rearranged infant ALL *in vitro* and induce profound remission in xenograft models, showing promise for clinical application. (*This thesis*)

2. MEK inhibitor trametinib inhibits *MLL*-rearranged infant ALL *in vivo* at specific niche sites and reduces ERK phosphorylation, making it a promising therapeutic candidate. (*This thesis*)

3. The synergy between MEK inhibitors and prednisolone constitutes a promising therapeutic strategy against *MLL*-rearranged infant ALL, both with and without *RAS* mutations. (*This thesis*)

4. S-adenosylhomocysteine hydrolase inhibitor 3-deazaneplanocin is effective against *MLL*-rearranged infant ALL cells and at a molecular level, but whether it could be of added value to the treatment of *MLL*-rearranged infant ALL remains to be determined. (*This thesis*)

5. Drug repurposing is an important tool for finding therapeutics against rare diseases and diseases in children. (*This thesis*)

6. The prognostic significance of infant age differs between ALL and AML: in ALL, infants fare far worse than older children, whereas outcomes for infants with AML are similar to those for older children. (*Brown, Hematology Am Soc Hematol Educ Program, 2013*).

7. *MLL*-rearranged infant ALL contains remarkably few somatic mutations, having one of the lowest somatic coding mutation rates observed in a human cancer. (*Andersson et al., Nature Genetics, 2015*)

8. A drug that fails in animal trials will not necessarily fail in human trials. (*Vogelstein et al., Science, 2013*)

9. The heterogeneity and rarity of infant ALL is the major limitation for clinical trials, resulting in slow accrual over long time periods and limiting study power. (*Kotecha et al., Blood Cancer Journal, 2014*)

10. Freely accessible databases with Absorption, Distribution, Metabolism, Exctretion, Toxicity (ADMET) and adverse event information of approved drugs are important to make drug development more efficient and to reduce late stage attrition. (*Legehar, Journal of Cheminformatics, 2016*)

11. Together the human and AI can outperform any human, but they can also outperform any algorithm. (*Andrew Hopkins*)

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