

Stellingen behorende bij het proefschrift

MOLECULAR DRIVERS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

Toward targeted therapy for children with ALL

1. Both leukemia-intrinsic characteristics and leukemia-extrinsic signals from the microenvironment should be studied to develop effective targeted therapy for children with acute lymphoblastic leukemia. [this thesis]
2. The induction of autophagy through upregulation of Vps34 is essential for the proliferation and survival of ETV6-RUNX1 positive leukemia, which makes targeted therapy in this subgroup plausible. [this thesis]
3. The LARG / RhoA axis is important in migration of ETV6-RUNX1 positive leukemic cells, which enables selective targeting of the leukemic niche with small molecule inhibitors. [this thesis]
4. Tunneling nanotubes are important in the formation of the supportive leukemic niche by inducing cytokine release, leukemic cell survival, and stroma-driven drug resistance. [this thesis]
5. CCR4 and CXCR1 / 2 ligands but not CXCR4 ligands, are upregulated by BCP-ALL cells in a self-reinforcing leukemic microenvironment. [this thesis]
6. Initiation of tumors is unavoidable, but their progression to malignancy can and should be controllable [Bissell & Hines, *Nature Medicine*, 2011]
7. Depictions of the intracellular circuitry governing cancer cell biology will need to be complemented by similar diagrams charting the complex interactions between the neoplastic and stromal cells within a tumor and the dynamic extracellular matrix that they collectively erect and remodel [Hanahan & Weinberg, *Cell*, 2011]
8. Given that many investigational anticancer drugs eventually fail, the animal models on which clinical trials are predicated must at best be limited in power, and at worst be wildly inaccurate. [Kamb, *Nature Reviews Drug Discovery*, 2005]
9. Precision medicine requires a different type of clinical trial that focuses on individual, not average, responses to therapy. [Schork, *Nature*, 2015]
10. Fact may not be truth, and truth may not be factual. [Murakami, *The Wind-Up Bird Chronicle*, 1994]
11. It does not do harm to the mystery to know a little more about it [Feynman, *The Feynman Lectures on Physics*, 1964]

Roel Polak
Rotterdam, November 2017