

SIGNALING PATHWAYS AS THERAPEUTIC TARGETS IN PEDIATRIC B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

1. RAS pathway mutations are more frequent in pediatric B-cell precursor acute lymphoblastic leukemia than previously assumed, often occur in a minor fraction of cells at diagnosis and may serve as biomarker to select patients for intensified therapy or treatment with MEK inhibitors (this thesis).
2. JAK2 can have primary and secondary oncogenic functions in pediatric B-cell precursor acute lymphoblastic leukemia, and distinct limitations will apply for JAK2-directed therapy in these two patient populations (this thesis).
3. *PDGFRA* is highly expressed in ERG-deleted leukemia but not affected by genetic aberrations or related to cell survival (this thesis).
4. Mutations of the FGFR pathway are rare in pediatric BCP-ALL but FGF signaling decreases the response to prednisolone (this thesis).
5. The membrane protein EMP1 is a novel biomarker for prednisolone resistance and links cell adhesion to cellular drug resistance (this thesis).
6. (...) Advancements to link cancer genomic and proteomic data will become valuable resources for dealing with the intrinsic complexities of tumors. Creixell et al., *Cell* 2015, 163 (1): 202-217
7. Those designing and conducting new leukemia treatment protocols face challenges that come from success: a radical change in treatment for all patients could jeopardize past gains in outcome, whereas modest changes are unlikely to yield significant improvements. Pui and Evans, *Semin. Hematol.* 2013, 50 (3): 185-196
8. The essential question for personalized cancer medicine is whether any therapeutic strategy could provide cure or long-term remission despite the presence of intratumor heterogeneity. Tannock and Hickman, *N Engl J Med* 2016, 375 (13): 1289-94.
9. One day, we imagine that cancer biology and treatment—at present, a patchwork quilt of cell biology, genetics, histopathology, biochemistry, immunology, and pharmacology—will become a science with a conceptual structure and logical coherence that rivals that of chemistry or physics. Hanahan and Weinberg, *Cell* 2000, 144 (5): 646-74
10. There is no heartache like a sick child, and no greater gift than the chance to help one. *Nature* 2017, 543 (7647), 590
11. Afstand scheidt enkel de lichamen, niet de geesten. Desiderius Erasmus