

Stellingen behorende bij het proefschrift:

Propositions associated with the thesis:

**Bruton's tyrosine kinase
signaling in
health and disease:
a molecular perspective.**

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1. The expression and activity of signaling molecules in B cells, together with the balance between activating and inhibitory pathways, are crucial for the outcome of BCR signaling. (*this thesis*)
2. Tec limits the activation of the Akt signaling pathway and might act to restrain Btk activating capacity. (*this thesis*)
3. Toll-like receptor signaling and T cell interaction are crucial for the development of Btk-mediated autoimmune disease. (*this thesis*)
4. Btk inhibition may have more far reaching effects than previously anticipated, as it also affects proximal upstream BCR signaling and rewires the entire BCR signaling cascade. (*this thesis*)
5. Next to BCR signaling, co-stimulatory stimulation strongly contributes to the proliferation signature observed in CLL B cells. (*this thesis*)
6. Combinatorial approaches of epigenetic drugs with immunotherapy may synergize to reshape the tumor microenvironment and restore an effective antitumor response. (*Villanueva et al., Trends in Immunology 2020*)
7. The sensitivity to a specific inhibitor is influenced by the type of BCR signaling upon which malignant B cells depend and the pathways that can be diverted to bypass the block imposed by targeted agents. (*Burger J.A. and Wiestner A., Nature Reviews Cancer 2018*)
8. Altered B cell signaling programmes increase the risk of autoimmunity by modulating positive and negative selection during B cell development, culminating in an increase in the proportion of mature B cells that exhibit autoreactivity. (*Rawlings D.J. et al., Nature Reviews Immunology 2017*)
9. Early global sharing of scientific data is vitally important to understand the complexities of the B cell and T cell responses in COVID-19 and to elucidate which immune responses provide protection from both the initial infection and reinfection. (*Cox R.J. and Brokstad K.A., Nature Reviews Immunology 2020*)
10. If your experiment needs statistics, you ought to have done a better experiment. (*Ernest Rutherford*)
11. Nothing great was ever achieved without enthusiasm. (*Ralph Waldo Emerson*)