

**Stellingen behorende bij het proefschrift:**  
**Chronic lymphocytic leukemia: the B cell receptor and beyond**  
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1. Enhanced basal  $\text{Ca}^{2+}$  signaling is not a uniform feature of CLL cells, but is associated with the CLL IGHV mutational status, likely reflecting a distinct cellular origin. (*this thesis*)
2. The level of basal  $\text{Ca}^{2+}$  signaling in CLL cells is not correlated with the  $\text{Ca}^{2+}$  signaling of identical CLL-derived IgM BCR in TKO cells, indicating that high basal  $\text{Ca}^{2+}$  levels as seen in some CLL samples would result from cell-intrinsic changes rather than from BCR-dependent autonomous signaling. (*this thesis*)
3. Chronic lymphocytic leukemia cells with enhanced NF- $\kappa$ B signaling are associated with a lower responsive capacity towards B-cell receptor stimulation. (*this thesis*)
4. Although stereotypic B cell receptors can already be detected in cord blood B cells, their frequency in healthy control B cells increases with age. (*this thesis*)
5. Similarities in the clonal B cell receptor repertoire in familial CLL suggest that BCR responsiveness may contribute to CLL formation in addition to genetic predisposition. (*this thesis and Crowther-Swanepoel, Blood 2008*)
6. Profiling of CAR-T cells from responding CLL patients showed over-time a CAR-T cell population with a memory phenotype, whilst for non-responding patients the CAR-T cell population had a phenotype associated with exhaustion. (*adapted from Fraietta, J.A., Nature Medicine 2018*)
7. To breed a jumping sport horse that excels in the highest levels of competition, not only genetic factors should be taken into account, but also environmental factors, such as the rider–horse interaction. (*adapted from Bartolomé et al., J Anim Breed Genet 2018*)
8. In reference to an evolutionary system, continuing adaptation is needed in order for a species to maintain its relative fitness amongst the systems it is co-evolving with. (*The red queen hypothesis” based on “Now, here, you see, it takes all the running you can do, to keep in the same place” from Lewis Carroll, Alice in Wonderland, Through the looking glass*) (*Leigh Van Valen, Evolutionary Theory 1973*)
9. Research on malignant hematological diseases, either clinical or fundamental, is generally based on cohorts, but in the end the individual patient needs to be treated.
10. Without basic scientific research, such as on CRISPR-Cas9, the flow of translational research will eventually dry up. This is precisely why basic research needs to be better funded.
11. Life is like riding a bicycle. To keep your balance you must keep moving. (*Albert Einstein*)