

Immunogenetics and proteomics for improved, minimally-invasive early detection of lymphoid malignancies

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1. Even high-risk chronic lymphocytic leukemia (CLL) subtypes may display a prolonged indolent preclinical stage, extending as far as 16 years before CLL diagnosis. – **Chapter 2, this thesis**
2. CLL pathogenesis is a stepwise process, where (autonomous) B-cell receptor signaling in genetically predisposed individuals results in a monoclonal expansion of B-cells, followed by accumulation of pathogenic somatic variants and progression to CLL. – **Chapter 3, this thesis**
3. Rheumatoid factor-like extranodal marginal zone lymphoma (eMZL) clonotypes are already present in both tissue biopsies and the peripheral blood of Sjögren patients several months to years prior to eMZL diagnosis. – **Chapter 5, this thesis**
4. Patient groups at increased risk of lymphoma will benefit from novel sensitive and specific early detection methods such as immunogenetic sequencing. – **Chapters 2, 5 and 6, this thesis**
5. Hidden Markov Modeling effectively captures unobserved pre-clinical stages of chronic disease by measuring fluctuations in the concentration of key biomarkers. – **Chapter 9, this thesis**
6. Novel methods aiming to reduce the occurrence of sequencing errors during next generation sequencing, such as duplex sequencing, are of vital importance to distinguish biological sequence variation from technical artefacts. – **Dillon et al. Haematologica (2023)**
7. Single cell sequencing technologies are the most promising source of novel insights into the early pathogenesis of non-Hodgkin's lymphoma subtypes.– **Nagler and Wu, Blood (2023)**
8. Our emerging understanding of the ways in which SF3B1 and ATM alterations induce replication stress will be crucial to the development of novel therapeutic strategies for leukemia. – **Cusan et al., J Clin Invest (2023), Bland et al., Nat Genet (2023)**
9. Exploration of the close link between aging and cancer will be essential to combat the rising incidence of various cancer subtypes in our aging population, as illustrated by the fact that four hallmarks of aging have very close parallels with four cancer determinants. – **López-Otín et al., Cell Metabolism (2023)**
10. Our understanding of the impact of environmental factors on chronic disease is too limited to combat the ever-increasing burden on society, highlighting the urgent need to profile these factors systematically to protect public health. – **Vermeulen et al. Science (2020)**
11. You can match a blood transfusion to a blood type — that was an important discovery. Matching a cancer cure to our genetic code could be as easy, just as standard.. – **President Barack Obama, 2015 State of the Union address on the Precision Medicine Initiative**