

**Project:** Initial Training Network for Neurological Disorders orchestrated by cytokines (NeuroKine)

**Research Topic:** Development of a novel single-cell T cell receptor profiling platform using next-generation sequencing (NGS)



The clinical outcome of infection, autoimmunity and malignancy is highly determined by T-cell activity. The diverse TCR repertoire of an individual shifts rapidly in response to disease, therapy or vaccination: a shift reflective of altered adaptive immune system function. NGS is being increasingly used to sequence TCR repertoires during health and disease to provide a time point-specific snapshot of the adaptive immune system. TCR sequencing can help develop disease biomarkers and facilitate the discovery of interesting T cell clones, including TILs, which can be used for (individualized) immunotherapy and diagnostic applications.

In existing TCR sequencing technologies, the loss of alpha-beta chain pairing specificity during bulk T cell mRNA or DNA extraction is compensated for by ignoring the TCR alpha chain or carrying out-frequency based matching, which does not identify T cell clones below a certain threshold level. Therefore, the aim of this thesis is to develop a single-cell based TCR profiling platform allowing the accurate identification of functional i.e. paired alpha and beta chains of a multitude of single T cells in a high-throughput manner through the use of barcode technology. The platform under development incorporates molecular and conceptual properties that minimize cost, time consumption and amplification bias.



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