Establishing a pipeline for analysis of T-cell receptor sequencing data and characterizing the impact of the T-cell repertoire on the clinical outcome of bladder cancer

Master´s thesis (30 ECTS)

Asbjørn Kjær | 201709022

Bioinformatics Research Centre (BiRC)

Aarhus University

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Supervisor:

Nicolai Juul Birkbak

Associate professor

Department of Molecular Medicine (MOMA)

Aarhus University

Abstract

T-cells play a crucial role in the fight against cancer, as they can recognize the mutated proteins of the cancer and target the malignant cells for destruction. This contact is mediated through the T-cell receptor (TCR), which has a distinct nucleotide sequence for each T-cell clone. Sequencing of this receptor through T-cell receptor sequencing (TCRseq) can thus be used to characterize the composition of the T-cell repertoire, which can provide insights into the state of the cancer. In this thesis a pipeline for assembling TCRseq data into unique TCR clones was implemented and tested. This pipeline was then used to characterize the impact of the peripheral TCR repertoire on the clinical outcome of bladder cancer in two local cohorts. This analysis revealed that a more diverse TCR repertoire is associated with better prognosis. Patients with good clinical outcome are distinguished by a change in diversity during treatment, while patients with recurrence have a repertoire characterized by constant diversity and a high degree of clonal overlap through time, both when treated with chemotherapy or immunotherapy. This study highlights the importance of the systemic immune system in the fight against cancer and calls for further investigation into using the state of the immune system as a biomarker to guide cancer treatment.

Abbreviations

Bacillus Calmette-Guérin	(BCG)
Complementarity-determining region	(CDR)
Clonal hematopoiesis of intermediate potential	(CHIP)
High-grade free survival	(HGFS)
Humant leukocyt antigen	(HLA)
Major histocompatibility complex	(MHC)
Muscle invasive bladder cancer	(MIBC)
Neoadjuvant chemotherapy	(NAC)
Non muscle invasive bladder cancer	(NMIBC)
Recurrence free survival	(RFS)
Recover T Cell Receptor	(RTCR)
T-cell receptor	(TCR)