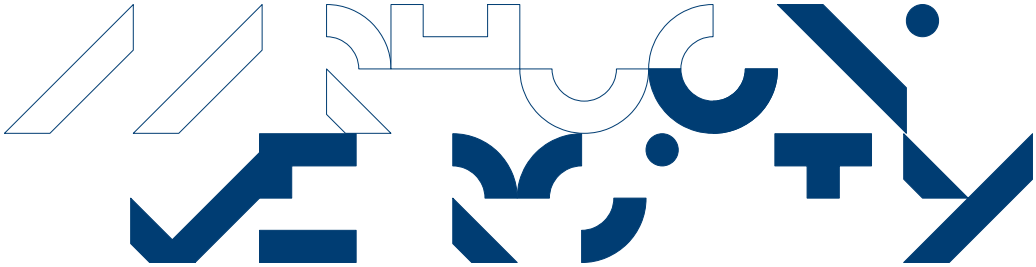

Investigating the B-Cell Receptor in bladder and kidney cancer to understand its role in anti-cancer immunity and its potential implications for cancer treatment and outcomes

Liliane Zoe Bader
M.Sc. Thesis
June 15th, 2025

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This document was typeset in LaTeX.

ABSTRACT

B cells and their receptors (BCRs) play an increasingly recognized role in anti-tumor immunity, complementing the more extensively studied T-cell responses. This thesis investigates the BCR repertoires in bladder and kidney cancers, aiming to characterize their clonality, diversity and gene usage patterns, and to explore their associations with clinical outcomes. Utilizing high-throughput immune repertoire sequencing data from over 350 patient samples, including healthy controls, comprehensive bioinformatic and statistical analyses were conducted. Key findings include increased clonotype expansion and reduced diversity in cancer samples compared to healthy controls, along with distinct V(D)J gene usage patterns. Importantly, lower BCR diversity correlated with adverse clinical outcomes, such as reduced survival. UMAP-based dimensionality reduction and correlation heatmaps were applied to reveal associations between specific immunoglobulin gene segments and clinical variables, suggesting potential biomarkers for disease prognosis. These results emphasize the relevance of B cells in cancer immunology and support the integration of BCR repertoire analysis into future diagnostic and therapeutic strategies.

PREFACE

This thesis was written with the Cancer Evolution & Immunology Group at the Department of Molecular Medicine (MoMa), Aarhus University Hospital. I am very grateful to my supervisor, Professor Nicolai Juul Birkbak, head of the research group, for his guidance and support throughout the project. I would also like to thank the other members of the group, especially Postdoc Randi Istrup Juul, PhD student Asbjørn Kjær and Postdoc Ragnhild Liborius Laursen, for their valuable support.

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Thesis submitted:

June 15th, 2025

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Pages: 60
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ABBREVIATIONS

BCR	B-Cell Receptor
BH	Benjamini–Hochberg
BMI	Body Mass Index
CDR	Complementarity-Determining Region
CNV	Copy Number Variation
CRP	C-Reactive Protein
CSR	Class Switch Recombination
ctDNA	Circulating Tumor DNA
DNA	Deoxyribonucleic Acid
GC	Germinal Center
HR	Hazard Ratio
HPC	High Performance Computing
IgH	Immunoglobulin Heavy Chain
IgK	Immunoglobulin Kappa
IgL	Immunoglobulin Lambda
LDH	Lactate Dehydrogenase
NGS	Next-Generation Sequencing
ORF	Open Reading Frame
PCA	Principal Component Analysis
PCR	Polymerase Chain Reaction
QC	Quality Control
SHM	Somatic Hypermutation
TCR	T-Cell Receptor
TIL-Bs	Tumor-Infiltrating B Lymphocytes
TLS	Tertiary Lymphoid Structures
UMAP	Uniform Manifold Approximation and Projection
UMI	Unique Molecular Identifier