Exploring the sarcoma immune landscape

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PHD PORTFOLIO

The PhD trajectory – an overview

I started my PhD in 2020 at the Department of Pathology at Leiden University Medical Center, where I joined a project within the Leiden Center for Computational Oncology under the supervision of Judith Bovée and Noel de Miranda. My research focused on characterizing the immune landscape of bone and soft tissue sarcomas, with the aim of identifying opportunities for immunotherapy in these rare malignancies.

At the beginning of my PhD, I established a strong methodological and computational foundation by completing courses in genomics and transcriptomics, biostatistics, and Linux programming. These courses enabled me to work with high-dimensional datasets and apply bioinformatic approaches in translational oncology. In parallel, I familiarized myself with the broader field by conducting a comprehensive review on immunity and genomics in sarcomas together with Debora Meijer, which resulted in our first peer-reviewed (**Chapter 2**). This work helped define key challenges and opportunities in the field and guided the direction of my subsequent research.

Building on this foundation, I investigated chordoma, a rare bone tumor with limited treatment options. Using multimodal and spatial profiling approaches, I characterized the tumor microenvironment and investigated immune cell interactions within these tumors. These studies required the integration of multiple data types and close collaboration with clinicians, pathologists, cancer biologists, and computational scientists. During the final stages of this first chordoma project, I was co-applicant on a grant awarded by the Cancer Research Institute and the Chordoma Foundation in 2023, which enabled us to further expand this research line. This ultimately resulted in two peer-reviewed publications (**Chapters 4** and **5**) and marked an important step in establishing a dedicated research line on chordoma immunology within our group. Through this work, I also developed close interactions with patient organizations, which strengthened my awareness of the direct clinical relevance of translational research for patients with rare cancers. Alongside this work, I studied the immunogenic features of undifferentiated pleomorphic sarcoma and myxofibrosarcoma using a similar approach to our first chordoma study. This project also resulted in a peer-reviewed publication (**Chapter 3**).

Beyond the projects included in this thesis, I contributed to additional studies on chordoma and other bone tumors, including high-grade osteosarcoma and osteofibrous dysplasia/OFD-like adamantinoma/adamantinoma. In these

projects, I applied similar spatial technologies to further characterize tumor microenvironments, broadening my expertise in sarcoma biology and strengthening my technical and analytical skills.

To support my scientific development, I actively participated in national and international conferences. I presented my work at meetings of CTOS, FORTRESS, CIMT, and specialized chordoma workshops. Over time, my role evolved from attendee to oral presenter and organizer of scientific events, particularly local symposia at Leiden University Medical Center. These experiences strengthened my ability to communicate complex findings to diverse audiences and engage with the international research community.

Collaboration was a central component of my PhD trajectory. My projects involved close interaction between multiple disciplines, including cancer biology, computational biology, pathology, radiotherapy, neurosurgery, and orthopedic surgery. These collaborations were essential for integrating diverse methodologies, collecting patient material and clinical data, and translating molecular findings into clinically meaningful insights.

My work was recognized through several awards and grants. I received the award for most relevant abstract for patients at the Dutch Sarcoma Group PhD Symposium in 2022 and the award for best presentation at the chordoma research symposium organized by the Bone Cancer Research Trust in 2024. In addition, I received a personal Skills Development Grant from the Bone Cancer Research Trust in 2024.

In addition to research, I contributed to education and supervision by mentoring bachelor's and master's students and participating in teaching activities within the Biomedical Sciences curriculum. These experiences further strengthened my ability to mentor junior researchers, communicate scientific concepts effectively, and foster enthusiasm for research.

Overall, my PhD trajectory reflects a progression from building a strong methodological foundation to leading complex, collaborative research projects in translational oncology, with a particular focus on improving our understanding of the immune landscape of rare cancers and identifying potential therapeutic opportunities.

CRediT statement for the Chapters in this thesis

CRediT table for the thesis of Siddh van Oost

Ch.	Type*	Short Title	Conceptualization	Data Curation	Formal Analysis	Funding Acquisition	Investigation	Methodology	Project Administration	Resources	Software	Supervision	Validation	Visualization	Writing – Original Draft	Writing – Review & Editing	Preregistered	Preprinted	Published with Peer Review
1	Introduction	General Introduction	■											■	■	■	☐	☐	☐
2	PhD project chapter	Review on immunity and genomics	■											■	■	■	☐	☐	☑
3	PhD project chapter	Immunogenic features of UPS and MFS	■	■	■		■	■	■		■	■	■	■	■	■	☐	☑	☑
4	PhD project chapter	Multimodal profiling of chordomas	■	■	■		■	■	■		■		■	■	■	■	☐	☑	☑
5	PhD project chapter	Spatial profiling of chordomas	■	■	■	■	■	■	■		■		■	■	■	■	☐	☑	☑
6	Discussion	Discussion and future perspectives	■												■	■	☐	☐	☐

**PhD project chapters are the direct result of the PhD project of the PhD candidate.*
Some theses also include Collaboration Chapters, to which the PhD candidate has contributed but fall outside the PhD project.

Dissemination table

1.	***van Oost S, Meijer DM, Kuijjer ML, Bovee J, de Miranda N. Linking Immunity with Genomics in Sarcomas: Is Genomic Complexity an Immunogenic Trigger?***	
	Chapter in this thesis	*2*
	Publication in peer-reviewed journal	*https://doi.org/10.3390/biomedicines9081048*
2.	***van Oost S, Meijer DM, Erdem ZB, IJsselsteijn ME, Roelands J, Lam SW, et al. Divergent therapeutic and prognostic impacts of immunogenic features in undifferentiated pleomorphic sarcoma and myxofibrosarcoma***	
	Chapter in this thesis	*3*
	Preprint	*https://doi.org/10.1101/2025.03.27.645727*
	Publication in peer-reviewed journal	*https://doi.org/10.1007/s00262-025-04123-y*
	Open access data	*RNA sequencing: GEO at GSE285944* *Imaging Mass Cytometry: BioStudies at S-BIAD1555* *GitLab: https://git.lumc.nl/bstp/papers/immunogenic-features-of-ups-and-mfs*
	Open access code	*GitHub: https://github.com/deMirandaLab/immunogenic-features-of-ups-and-mfs*
3.	***van Oost S, Meijer DM, IJsselsteijn ME, Roelands JP, van den Akker B, van der Breggen R, et al. Multimodal profiling of chordoma immunity reveals distinct immune contextures***	
	Chapter in this thesis	*4*
	Preprint	*https://doi.org/10.1101/2023.09.14.557579*
	Publication in peer-reviewed journal	*https://doi.org/10.1136/jitc-2023-008138*
	Open access data	*RNA sequencing: GEO at GSE239531* *Imaging Mass Cytometry: BioStudies at S-BIAD830* *GitLab: https://git.lumc.nl/bstp/papers/multimodal-profiling-of-chordomas*
	Open access code	*GitHub: https://github.com/deMirandaLab/multimodal-profiling-of-chordomas*
4.	***van Oost S, Ursem R, Erdem ZB, Cardoso S, Venneker S, van der Breggen R, et al. Immune infiltration is associated with distinct transcriptional states and metabolic profiles in chordomas***	
	Chapter in this thesis	*5*
	Preprint	*https://doi.org/10.1101/2025.11.04.686078*
	Publication in peer-reviewed journal	*https://doi.org/10.1016/j.isci.2026.115668*
	Open access data	*GeoMx DSP & MALDI-MSI (processed): https://figshare.com/s/4d52d0129b9e0f9c7a8c* *MALDI-MSI (raw): MassIVe at MSV000100742* *GitLab: https://git.lumc.nl/bstp/papers/spatial-profiling-of-chordomas*
	Open access code	*GitHub: https://github.com/deMirandaLab/spatial-profiling-of-chordomas*

Overview of completed courses and other training

Completed courses and other training		
Mandatory activities		
Year	**Description**	**Hours**
2021	*Leiden University Onboarding Program Inform & Connect*	*5*
2021	*Basic Methods and Reasoning in Biostatistics*	*42*
2024	*Responsible Research – eBROK*	*42*
Scientific courses, workshops, and other training activities		
Year	**Description**	**Hours**
2021	*MGC - Genomics & Transcriptomics*	*7*
2022	*Organization of the post-CTOS recap for LUMC Sarcoma Researchers*	*2*
2023	*Organization of the LUMC Sarcoma Research Night*	*5*
2023	*Supervision MSc student Biomedical Sciences*	*130*
2023	*CPM – A hitchhiker's guide to GALAXY*	*5*
2023	*CPM – MALDI-TOF-MSI Imaging Analysis*	*5*
2024	*Organization of the LUMC Chordoma Research Workshop*	*3*
2025	*Co-supervision BSc student Biomedical Sciences*	*24*
Transferable skills courses, workshops, and other training activities		
Year	**Description**	**Hours**
2021	*Practical Linux*	*4*

Dissemination, acknowledgement, esteem, and other relevant scientific activities

Other scientific activities related to this thesis		
Year	**Description**	**Linked to**
2022	*Oral presentation, Dutch Sarcoma Group (DSG) PhD Symposium, Utrecht*	*Chapter 4*
2022	*Most relevant abstract for patients award, DSG PhD Symposium, Utrecht*	*Chapter 4*
2022	*Oral presentation, Dutch Tumor Immunology Meeting (DTIM), Breukelen*	*Chapter 4*
2022	*Oral presentation, Connective Tissue Oncology Society, Vancouver, Canada*	*Chapter 4*
2023	*Poster presentation, FORTRESS Research Meeting, Essen, Germany*	*Chapter 4*
2023	*Oral presentation, DSG PhD Symposium, Utrecht*	*Chapter 3*
2023	*Oral presentation, LUMC Cancer Research Day, Leiden*	*Chapter 3*
2023	*Clinic and Laboratory Integration Program Grant, "Leveraging Natural Immunity in Chordomas for Tailored Immunotherapy", Cancer Research Institute & Chordoma Foundation, co-applicant*	*Chapter 4+5*
2023	*Oral presentation, Chordoma Foundation Research Workshop, Boston, US*	*Chapter 4*
2023	*Poster presentation, Cancer Immunotherapy (CIMT), Mainz, Germany*	*Chapter 3*
2023	*Oral presentation, CONDOR Symposium Microenvironment and Immunotherapy of Sarcomas, Bordeaux, France*	*Chapter 3*
2024	*Oral presentation, FORTRESS Research Meeting, Leuven, Belgium*	*Chapter 5*
2024	*Oral presentation, LUMC Cancer Research Day, Leiden*	*Chapter 5*
2024	*Skills Development Grant, Bone Cancer Research Trust (BCRT), personal grant*	*Chapter 5*
2024	*Oral presentation, BCRT Chordoma Research Symposium, London, UK*	*Chapter 5*
2024	*Best presentation award, BCRT Chordoma Research Meeting, London, UK*	*Chapter 5*
2025	*Oral presentation, FORTRESS Research Meeting, Essen, Germany*	*Chapter 3*