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Decoding telomere gene variation through saturation genome editing: from functional genomics to clinical interpretation

Obolenski, S.

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Curriculum vitae

Sofia Obolenski was born on the 17th of March 1997. After completing her secondary education in Cologne (Germany), she began the Bachelor's program in Biomedical Sciences at Maastricht University (The Netherlands) in 2016, where she developed a growing interest in cancer genetics and molecular biology. Alongside her studies, she worked as a student assistant in the university library for two years. In 2018, she completed an extracurricular research internship at the School for Mental Health and Neuroscience, Maastricht University, focusing on autoantibodies in neurological and psychiatric disorders. Later that year, she was awarded an Erasmus+ travel grant and completed a six-month exchange semester at the University of Exeter (UK). In 2019, she completed her Bachelor's thesis at the School for Oncology and Developmental Biology, Maastricht University, investigating the role of NDRG4 in the enteric nervous system in colorectal cancer.

She continued with the Master's programme in Biomedical Sciences at Maastricht University, specialising in tumour immunology, and graduated with distinction in 2021. During her Master's, she also worked as a seminar tutor in the Biomedical Sciences Bachelor programme, teaching courses including immunology, human genetics, and anatomy. She also gained international research experience, first at the University of Oxford (UK) under the supervision of Dr. David N. Church and later at the Wellcome Sanger Institute in Cambridge (UK), working with Dr. David J. Adams and Dr. Andrew J. Waters.

Inspired by the topic of cancer predisposition genetics and by the research environment within the Adams team, Sofia chose to continue this line of work. An opportunity arose to stay on as a PhD student and further contribute to the optimization and application of saturation genome editing on tumour suppressor genes implicated in familial melanoma, in collaboration with Leiden University Medical Center. The main findings of this research are presented in this thesis.

In 2026, Sofia is embarking on a new scientific endeavour at the MRC Laboratory of Molecular Biology in Cambridge as a postdoctoral fellow within the Synthetic Human Genome Project, where she will extend her PhD work in telomere biology and functional genomics to explore large-scale genome engineering and synthetic human genome biology, with a particular focus on how engineered genomic changes affect telomere function.

PhD Portfolio

Courses and workshops

2021	LUMC course: Workshop Scientific conduct
2021	LUMC course: Communication in Science for PhDs
2021	WSI course: Introduction to Regulatory Compliance
2021	WSI course: Introduction to Entrepreneurship and Innovation
2021	WSI course: Communicating your science - an introduction to Public Engagement
2021	WSI course: Scientific writing & writing an academic report
2021	Next Generation Sequencing
2022	WSI course: The use of human materials in research - regulatory awareness
2022	WSI course: Current ethical issues in genomics
2022	LUMC course: Basic Methods and Reasoning in Biostatistics
2022	WSI course: Flow Cytometry Course
2025	Edinburgh University: Variant Analysis Workshop
2025	WSI course: Risk Management Training
2025	WSI course: Responsible Research and Innovation (RRI)
2025	Utrecht University course: Responsible Conduct of Research

Conferences attended

2022	Mutational Scanning Symposium Toronto (CN)
2022	CRISPR and Beyond: Perturbations at Scale to Understand Genomes in Cambridge (UK)
2023	Telomeres & Telomerase 2023 CSHL in Boston (USA)
2023	Curating the Clinical Genome (Presenter) in Cambridge (UK)
2023	Mutational Scanning Symposium (Flash Talk & Poster) in Cambridge (UK)
2023	ACGS Conference Birmingham (Presenter)

2023	GenoMel Meeting (Presenter)
2024	MGC Symposium in Leiden, NL (Presenter)
2025	Festival of Genomics & Biodata in London, UK (Poster)
2025	GenoMel Meeting in Amsterdam, NL

List of Publications

Discordant prognosis of mismatch repair deficiency in colorectal and endometrial cancer reflects variation in antitumour immune response and immune escape

Mark A. Glaire, Neil A. J. Ryan, Marieke E. Ijsselsteijn, Katarzyna Kedzierska, [Sofia Obolenski](#), Reem Ali, Emma J. Crosbie, Tjalling Bosse, Noel F. C. C. de Miranda, David N. Church

The Journal of Pathology. 2022;256(2):196–208. DOI: 10.1002/path.5894

Population-based analysis of POT1 variants in a cutaneous melanoma case-control cohort

Irving Simonin-Wilmer, Raul Ossio, Emmett M. Leddin, Mark Harland, Karen A. Pooley, Mauricio Gerardo Martil de la Garza, [Sofia Obolenski](#), James Hewinson, Chi C. Wong, Vivek Iyer, John C. Taylor, Julia A. Newton-Bishop, D. Timothy Bishop, Gerardo Andrés Cisneros, Mark M. Iles, David J. Adams, Carla Daniela Robles-Espinoza

Journal of Medical Genetics. 2023;60(6):470–478. DOI: 10.1136/jmg-2022-108776

Analyzing the functional effects of DNA variants with gene editing

Sarah Cooper, [Sofia Obolenski](#), Andrew J. Waters, Andrew R. Bassett, Matthew A. Coelho

Cell Reports Methods. 2024;4(6):100776. DOI: 10.1016/j.crmeth.2024.100776

Saturation genome editing of BAP1 functionally classifies somatic and germline variants

Andrew J. Waters, Timothy Brendler-Spaeth, Danielle Smith, Victoria Offord, Hong Kee Tan, Yajie Zhao, [Sofia Obolenski](#), Maartje Nielsen, Remco van Doorn, Jo-Ellen Murphy, Prashant Gupta, Charlie F. Rowlands, Helen Hanson, Erwan Delage, Mark Thomas, Elizabeth J. Radford, Sebastian S. Gerety, Clare Turnbull, John R. B. Perry, Matthew E. Hurles, David J. Adams

Nature Genetics. 2024;56:1462–1472. DOI: 10.1038/s41588-024-01799-3

Protocol for the functional evaluation of genetic variants using saturation genome editing

Sofia Obolenski, Roberto Olvera-León, Dongyu Sun, David J. Adams, Andrew J. Waters

STAR Protocols. 2025;6(2):103710. DOI: 10.1016/j.xpro.2025.103710

POT1 genetic testing in melanoma-prone families in Sweden: germline variant prevalence and tumor spectrum in identified carriers

Konstantinos Papadakis, Anna Karlsson, Christina Hirsch, Jakob Lamecker, Emilia Häggström, Sofia Obolenski, Mark Harland, David J. Adams, Hildur Helgadóttir

Acta Oncologica. 2025;64(2):205–214. DOI: 10.2340/1651-226X.2025.44048

SPARKI: a tool for the statistical analysis of pathogen identification results

Jacqueline M. Boccacino, Martin Del Castillo Velasco-Herrera, Mathew A. Beale, Jamie Billington, Ian Vermes, Sofia Obolenski, Kim Wong, Laura Torrens, Sarah Moody, Sandra Perdomo, Saamin Cheema, Bailey Francis, Victoria Offord, Adam P. Butler, David J. Adams

Bioinformatics. 2025;41(11):btaf596. DOI: 10.1093/bioinformatics/btaf596

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I thank Dr. Andrew Waters, whose contribution to this thesis was invaluable. Our collaboration spanned every chapter, and I am deeply grateful for his guidance, generosity, and for teaching me the foundations of saturation genome editing from day one. His calm and supportive approach helped me navigate challenges, and his scientific insight and mentorship made this journey both productive and enjoyable. Beyond the science, I will always appreciate his impeccable book and film recommendations.

I thank Prof. Remco van Doorn for his openness, generosity, and for welcoming me as his external PhD student. He guided me through the PhD system at the LUMC with great care, kindly introducing me to his team. His guidance through the LUMC PhD system, thoughtful collaboration, trust, and genuine enthusiasm for my project were invaluable, and I am very grateful for his support throughout this journey. I also thank Dr Thomas Potjer, who has been involved since the start, both as a member of my thesis guidance committee and as a key collaborator on the *POT1* and *TINF2* projects. His thoughtful feedback and enthusiasm for connecting SGE functional data to clinical interpretation were invaluable. I thank the PhD thesis advisory committee members for their time, feedback, and scientific input.

I am grateful to Prof. Elizabeth Berry at Oregon Health & Science University for her sustained engagement with the *POT1* project and for inviting me to take part in the GenoMEL Consortium, which provided invaluable clinical perspective and broadened my understanding of telomere biology beyond the lab. I thank Dr. Matthew Coelho and Dr. Sarah Cooper at the Wellcome Sanger Institute for their collaboration on the *Cell Reports* review, which was an exceptional learning experience. I also thank Dr. Yajie Zhao at the Changping Laboratory in Beijing for their outstanding support and expertise in conducting the UK Biobank analysis of *POT1*, which greatly strengthened this work. I thank Dr. Charlie Rowlands and Prof. Clare Turnbull at the Institute of Cancer Research for their guidance on the ACMG/AMP framework.

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