A competitive binding assay for RNA ligand discovery

Wintermans, S.E.L.

Curriculum vitae

Sophie Wintermans was born on July 16th, 1997 in Wageningen, the Netherlands. She attended high school from 2009 to 2015 (VWO at Rembrandt College in Veenendaal) where she chose the specializations Natuur & Gezondheid and Natuur & Techniek, in combination with the visual and performing arts. Sophie continued her education with the bachelor Molecular Life Sciences at Wageningen University & Research, in which she also obtained a qualification for teaching chemistry in high school. She completed her BSc thesis in the BioNanoTechnology group under supervision of prof.dr. A.H. Velders, focusing on the synthesis of silver nanoparticles for detecting Lyme's disease.

Sophie continued her studies with the master Molecular Life Sciences at Wageningen University & Research, in the specialization track Biomedical Research. She did her research internship at MercaChem (now Symeres) under the supervision of dr. M. Scheepstra and dr. A. Bunschoten, in which she synthesized novel small molecule inhibitors for Cyclin Dependent Kinase 16. During her MSc thesis under supervision of dr. J.F. Keijzer and dr. H.B. Albada, Sophie worked on enhanced protein modification by hemin/G-quadruplex DNAzymes and nucleoapzymes, which resulted in a first author paper in *ChemCatChem* (2021). During her BSc and MSc, Sophie was highly involved in the programme committee of the BSc/MSc Molecular Life Sciences, where she first served as a student member and later as chair of the committee.

After graduation from her master in 2020, she joined the Medical Biochemistry lab at Leiden University to initiate her doctoral studies under the supervision of dr. M.E. Artola Perez de Azanza, dr. R.C.L. Olsthoorn and prof.dr. J.M.F.G. Aerts. The goal of the project was to develop new small-molecule drugs targeting RNA tertiary structures. For this, she developed a novel high-throughput assay to screen for potential RNA-binding molecules, which can be applied to different RNA structures, with the aim of finding new antimicrobial compounds. The research covered in this thesis was presented as a poster at IUPAC-CHAINS (2023 in Den Haag, The Netherlands, best poster presentation prize), Reedijk Symposium (2023 and 2024 in Leiden, The Netherlands), EMBO-EMBL The Complex Life of RNA (2024 in Heidelberg, Germany), as well as oral presentations at NWO CHAINS (2022 in Veldhoven, The Netherlands), the LED3 PhD/PD Symposium (2024 in Leiden, The Netherlands), and ChemBio VII (2024 in Sevilla, Spain, best oral communication prize). Moreover, Sophie was a co-applicant on three awarded grants that supported her research: a Kiem grant (€10.000 from Leiden University, 2023), a Kiem Seed

Funding (€15.000 from Una Europa, 2024) and an NWO XS grant (€50.000 from NWO, 2025).

Besides research, Sophie followed several courses offered by the Graduate School of Leiden University, including *Time Management*, *Managing Your Brain*, *Speed Reading* and *Scientific Conduct for PhDs*. She supervised three bachelor students and three master students and assisted in practicals of *Life Sciences* from the study programme Life Science & Technology (LST), *Biochemistry 1* from Biopharmaceutical Sciences (BFW) and *Leren Onderzoeken 1* from Molecular Sciences & Technology (MST).

Furthermore, Sophie was founder and chair of the LIC73 PhD/PD board of the Leiden Institute of Chemistry, organized the first LED3 PhD/PD Symposium in 2024 and attended the Science Communication Summer School 2024 from the Department of Science Communication & Society of Leiden University. Since 2025, Sophie works as a science communicator for the Pandemic and Disaster Preparedness Center (PDPC), a client of the science communication company Philogirl.

List of publications

- **S.E.L. Wintermans**, J.F. Keijzer, M. Dros, H. Zuilhof, B. Albada. Aptamer-Assisted Bioconjugation of Tyrosine Derivatives with Hemin/G-Quadruplex (hGQ) DNAzyme Nucleoapzyme Nanostructures. *ChemCatChem.* **2021**, 13 (21).

- **S.E.L. Wintermans**, J.S. Hoffmann, V. van Kuijk, Y. Durmus, M.D. Tacoma, I. Broekhuizen, A.P.A. Janssen, H. van den Elst, B.R. van Doodewaerd, P.P. Geurink, M.E. Artola, R.C.L. Olsthoorn. High-Throughput Competitive Binding Assay for Targeting RNA Tertiary Structures with Small Molecules: Application to Pseudoknots and G-Quadruplexes. *Nucleic Acids Research.* **2025**, 53 (16).

- **S.E.L. Wintermans**, C. Berges, J.S. Hoffmann, Y. Durmus, B.R. van Doodewaerd, L. van Berkom, J. Benningshof, P.P. Geurink, R.C.L. Olsthoorn, M.E. Artola. Discovery of New SARS-CoV-2 Pseudoknot and G-Quadruplex Ligands as Potential Antiviral Drugs. *(manuscript in preparation)*

Acknowledgements

After graduating from my master and having been uncomfortably close to a burn out, I was not sure if I could survive a PhD project. At the interview for this PhD position, I was told that the project would be high-risk, high-reward, and that it could just as easily fail completely. While I had many reasons not to take up the project, I felt that it was a risk worth taking. I am now writing these acknowledgements with a smile on my face, knowing that it was the best decision that I could have taken.

This thesis would not have been possible without the support and guidance of my fantastic supervisors **Marta**, **René** and **Hans**. You created an environment where I felt challenged and encouraged, where I could be creative and make mistakes without feeling like a failure. **René**, you are a large part of the genius behind this thesis. Your knowledge of RNA has been invaluable, and your expertise guided us to some very fortuitous decisions that shaped the outcome of my research. In other words, behind my serendipity was your wisdom. You gave me freedom and confidence – I loved having you as my supervisor. **Marta**, even though I barely did any chemistry and most of my thesis was about a topic you weren't familiar with – you taught me *so* much. You showed me the importance of being critical of your own work and remembering the 'Why?' behind research questions. In addition, you helped me turn my anxiety into curiosity – the sign of a true scientist. You were (and *are*) a genuine role model for me – even though I know you wouldn't describe yourself as such. Your resilience and strength are nothing short of aspirational. **Hans**, thank you for your guidance and wisdom. It means a lot to me that you are my promotor. During my first presentation at the Medical Biochemistry group meeting, you told me that you did your thesis with prof.dr.ir. Sjef Wintermans – my grandfather. With his signature on your diploma, I feel so very honoured to have yours on mine: truly a full-circle moment.

I would like to thank all the brilliant and kind **members** and **former members** of Medical Biochemistry group and the people of the DE1/CE1 hallways. Even though I was on my own RNA-targeting island, you made me feel at home and helped me elevate my research with your suggestions and ideas. Thank you for tolerating my singing and Eurovision Song Contest music in the lab. Special thanks to all (former and unofficial) members of Kantoor Koelkast, a.k.a. party office: **Max**, **Bas**, **Jeroen**, **Martijn**, **Bart**, **Klara, Eva** and **Mats**. We had some great nonsensical, scientific and political discussions, during the long days and at the Friday drinks. You made the difficult times a lot less difficult. **Max**, you

fantastic human being, I am so happy to have met you. Throughout my PhD, you were my rock – both for scientific and personal problems. I sincerely believe we both deserve a diploma in psychology to go along with our PhDs. Also, a big thanks to the many students that have passed through the MBIOC laboratory, in particular **Jackelien**, **Tijn**, **Saskia** and **Deborah**, with whom I shared many laughs and glasses of a wine-based cocktail that shall not be named.

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This PhD was high-risk, high-reward, and *girl*, did it pay off. Thank you all.

\- Sophie