

Cleaving like a pro: specificity, structure, and function of Pro-Pro endopeptidases

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Curriculum vitae

Bart Claushuis was born on the 24th of July in 1996 in The Hague, the Netherlands. After obtaining his VWO/Gymnasium diploma from the 'Segbroek College' in 2014, he started the bachelor's program Biology at Leiden University. During his last year internship, he studied the genetic instability in *Streptomyces coelicolor* under the supervision of dr. Daniel Rozen. After obtaining his bachelor's degree, Bart enrolled for the master's program Molecular Genetics and Biotechnology at Leiden University and graduated *cum laude* in 2020. During his Msc, he studied bacterial cell-cell fusion using L-form cells at the Microbial Sciences department of the Institute of Biology Leiden under the supervision of prof. dr. Dennis Claessen. During his second internship at the department of Medical Microbiology at the Leiden University Medical Center, Bart studied the regulation of *htrA* transcription in *Clostridioides difficile* under the supervision of dr. ir. Jeroen Corver.

After obtaining his MSc degree, Bart started his PhD research at the Center for Proteomics and Metabolomics at the Leiden University Medical Center under the supervision of dr. Paul Hensbergen, dr. ir. Jeroen Corver, and prof. dr. Manfred Wuhrer. During his PhD research, he studied Pro-Pro endopeptidases (PPEPs), a group of bacterial proteases with a unique cleavage specificity, using molecular biology techniques and mass spectrometry-based proteomics approaches. He helped to develop a new assay that allowed for a detailed characterization of PPEP specificity and developed a personal interest in structural biology. Upon completing his PhD, Bart will continue his career as a researcher outside of academia.

List of publications

In chronological order

Mutational meltdown of putative microbial altruists in *Streptomyces coelicolor* colonies

Z. Zhang, S. Shitut, <u>B. Claushuis</u>, D. Claessen & D.E. Rozen Nature Communications, 2022, 13:1, 1-9 (not part of this thesis)

Generating Heterokaryotic Cells via Bacterial Cell-Cell Fusion

S. Shitut, M. Shen, <u>B. Claushuis</u>, R.J.E. Derks, M. Giera, D.E. Rozen, D. Claessen, A. Kros Microbiology Spectrum, 2022, 10, 4 (not part of this thesis)

In-Depth Specificity Profiling of Endopeptidases Using Dedicated Mix-and-Split Synthetic Peptide Libraries and Mass Spectrometry

<u>B. Claushuis</u>, R.A. Cordfunke, A.H. de Ru, A. Otte, H.C. van Leeuwen, O.I. Klychnikov, P.A. van Veelen, J. Corver, J.W. Drijfhout, P.J. Hensbergen Analytical Chemistry, 2023, 95, 31, 11621 – 11631 (Chapter 4)

Revised Model for the Type A Glycan Biosynthetic Pathway in *Clostridioides difficile* Strain 630Δ*erm* Based on Quantitative Proteomics of *cd0241–cd0244* Mutant Strains

<u>B. Claushuis</u>, A.H. de Ru, S.A. Rotman, P.A. van Veelen, L.F. Dawson, B.W. Wren, J. Corver, W.K. Smits, P.J. Hensbergen ACS Infectious Diseases, 2023, 9, 12, 2665 – 2674 (Chapter 2)

Non-prime- and Prime-side Profiling of Pro-Pro Endopeptidase Specificity Using Synthetic Combinatorial Peptide Libraries and Mass Spectrometry

<u>B. Claushuis</u>, R.A. Cordfunke, A.H. de Ru, J. van Angeren, U. Baumann, P.A. van Veelen, M. Wuhrer, J. Corver, J.W. Drijfhout, P.J. Hensbergen The FEBS journal, 2024, 17160 (Chapter 5)

Characterization of the *Clostridioides difficile* 630∆*erm* putative Pro-Pro endopeptidase CD1597

<u>B. Claushuis</u>, A.H. de Ru, P.A. van Veelen, P.J. Hensbergen, and J. Corver Accepted for publication in Access Microbiology (Chapter 3)

Biochemical and structural characterization of PPEP-3 from *Geobacillus* thermodenitrificans

<u>B. Claushuis</u>[§], F. Wojtalla[§], H.C. van Leeuwen, J. Corver, U. Baumann[¶], Paul J. Hensbergen[¶] In preparation [§] and [¶]: Authors contributed equally to this work (Chapter 6)

Protease specificity profiling using synthetic combinatorial peptide libraries and mass spectrometry

<u>B. Claushuis</u>, R.A. Cordfunke, A.H. de Ru, P.A. van Veelen, J. Corver, J.W. Drijfhout, P.J. Hensbergen

In preparation for publishing in Methods in Molecular Biology book series (Springer) (not part of this thesis)

PhD portfolio

PhD student	Bart Claushuis
PhD period	2020-2024
Promotor	prof. dr. Manfred Wuhrer
Copromotors	dr. Paul J. Hensbergen and dr. ir. Jeroen Corver
Leiden University Medical Center, Center for Proteomics and Metabolomics	

Courses

- Basiscursus Regelgeving en Organisatie voor Klinisch onderzoekers (BROK)
- Basic Methods and Reasoning in Biostatistics
- PhD Introductory Meeting
- Academic Writing for PHDs
- Using R for Data Analysis
- Use Your Brain
- Job Orientation
- Job Search skills

Conferences and presentations

- International Clostridium Difficile Symposium, Online, 2020. Attendance
- ClostPath 2021, Online, 2021. Poster presentation
- Netherlands Proteomics Platform, Utrecht, The Netherlands, 2022. Oral presentation
- GRC Proteolytic Enzymes and Their Inhibitors, Lucca, Italy, 2022. Poster presentation
- Netherlands Proteomics Platform, Utrecht, The Netherlands, 2032. Attendance
- ClostPath 2023, Banff, Canada, 2023. Poster presentation

Supervision of students

2023 Erawan van der Veere Leiden University Medical Center

Teaching activities

- 2021 Lecture on proteomics, proteases and N-terminomics (LUMC)
- 2022 Young Scientist 4 a Day (Stedelijk Gymnasium Leiden, the Netherlands)
- 2022 Workgroup Infectious Agents and Immunity (LUMC)
- 2023 Science4U (Stedelijk Gymnasium Leiden, the Netherlands)
- 2023 Lecture on N-terminomics and combinatorial peptide libraries (LUMC)
- 2024 Science4U (Stedelijk Gymnasium Leiden, the Netherlands)

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Paul, due to your endless time and energy, I went from a mass spec rookie to a mass spec expert in no time and we have spent many hours together behind a PC, looking at peaks, peptides, and proteins. I greatly appreciate that your door was always open and that I was always welcome to annoy you with yet another question.

I would like to thank Manfred for being my promotor and for the opportunity to work at the Center for Proteomics and Metabolomics. Your guidance and advice throughout my years at CPM and your support as I completed my PhD are greatly appreciated.

My thanks go to all my colleagues from both the CPM and LUCID for all their assistance in the lab, for sharing their knowledge, and for the fun times together. I especially want to thank Peter, Arnoud, and Rayman, who were there from the start of my PhD and had a great part in realizing this thesis. Rayman, I'm also grateful to you for being my paranymph and your support during and around my defense. I also want to thank Sarah, Jordy, Annemarie, and George for all their contributions, as well as Wiep Klaas and Annemieke for their help with experiments and for all their valuable insights.

I'm also thankful to Uli and Fabian, our collaborators from Cologne, for our fruitful discussions via Skype and for solving the PPEP-3 structure. My interest in structural biology grew significantly during my PhD, and I am grateful to you for sharing your knowledge and the assistance you provided in my analyses.

Also, a big thank you to all my friends for supporting me during my PhD. You guys have helped me a lot with all the great times we had. Luc, I'm glad that you, as my oldest friend, can be part of this thesis by designing the cover. Justin, I want to thank you for being my paranymph. Kirsten, I owe you a great amount of thanks as well. Over the past four years, you have always believed in me and provided a lot of support. The final months of writing this thesis were a little stressful at times, and I am grateful for your patience and understanding during those moments.

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