High-throughput mass spectrometric N-glycomics

Reiding, K.R.

Acknowledgements

First of all, I would like to thank Manfred, my promotor and guide. I could not have wished for better supervision. You have allowed me to find my place in the group and in research, and for that, I am very grateful.

I also want to thank André, my second promotor, who has shown faith in me from the first day. Although retirement has limited our eventual interaction, I very much appreciate your time and dedication to bring me to the finish line.

Of course I would like to thank the fantastic group in Leiden (although whose constituents have changed and grown to such a degree that individual naming is becoming quite the affair). I can hardly believe my luck to have stumbled upon you. I regard many of you as friend, and because of you, I rarely consider the things I do to be work.

Thank you, very much, those of you that wanted me at their side during their own defenses, Niels, Rosina, Albert, and Bas. Paying it forward, I am grateful to my own paranymfs Noortje and David, whose scientific and personal lifes kept crossing with mine.

Furthermore, I would like to thank my collaborators, and the many people I was allowed to work with abroad, which took me in and showed me the larger world of science. Rene, Erdmann and the others in Magdeburg, Maja, Genadij, Gordan and the others in Zagreb, and Mili and Daryl and the others in Culham. It is great to be a part of the international community you have created.

Op persoonlijk vlak wil ik mijn reisgenoten bedanken: Niels (dezelfde), Remco, Mark, Timo, Thijs en Julius. Onze expedities door de wildernis hebben een belangrijke indruk op mij achtergelaten, inclusief faliekante misrekeningen in de voedselvoorraad, geothermisch smeltende schoenen, en de viering van het verdaguurtje. Alleen het vangen van die orka is er nog niet van gekomen.

Vanzelfsprekend kan dit dankwoord niet compleet zijn zonder mijn ouders te noemen. Jullie hebben hard gewerkt om mij, onzelfzuchtig, alle kansen in het leven te geven, en daar ben ik jullie zeer dankbaar voor. Het boekje dat voor jullie ligt is minstens zoveel jullie verdienste als het mijne.

Bovenal wil ik Wietske bedanken, zonder wiens aanwezigheid dit hele wetenschappelijke avontuur waarschijnlijk niet had plaatsgevonden. Wat ik doe, dat doe ik voor jou. Jij bent de drijvende kracht in mijn leven.

Curriculum Vitae

Karli Robert Reiding was born October 7th 1985 in Rotterdam, The Netherlands. He quickly developed a broad interest in understanding the world, and enjoyed his explorations into the natural sciences, history, and philosophy.

After finishing his primary and secondary education he studied Biomedical Sciences at Leiden University, obtaining his Bachelor's degree in 2008 and his Master's degree in 2011. The education was broadly focused on different aspects of biomedical research, including biological knowledge and technical skills, as well as study design, statistical analysis, and the art of writing and presenting. During his Master's, Karli specialized into the research track. As optional courses, he found an interest in bioinformatics and biostatistics, giving him experience with several of the programming languages commonly found in science, including R and Python. In addition, he followed a minor in science-based business, which detailed on project management, strategic marketing, financial management, and other aspects of business administration.

During his internships, Karli had the opportunity to gain hands-on experience with a wide variety of subjects. His graduation internship focused on the identification of new genes involved in mismatch repair at the Leiden University Medical Center, Department of Toxicology, within the group of Prof.dr. Marcel Tijsterman. Two other internships covered the (epi)genetic mechanisms behind protein S deficiency (Thrombosis and Hemostasis, Prof.dr. Pieter H. Reitsma), and HLA-G expression in throphoblast cells (Immunohematology and Blood Transfusion, Prof.dr. Peter J. van den Elsen).

Karli proceeded to do his PhD education at the Leiden University Medical Center Biomolecular Mass Spectrometry Unit (later the Center for Proteomics and Metabolomics) under the supervision of Prof.dr. André M. Deelder and Prof.dr. Manfred Wuhrer. His research focused on the development and application of high-throughput methodology for mass spectrometric glycosylation analysis, which has led to more than two dozen publications in peer-reviewed journals, as well as a patent application on linkage-specific sialic acid derivatization for MALDI-MS analysis.

Currently, Karli is employed as a post-doctoral researcher at Biomolecular Mass Spectrometry and Proteomics, Utrecht University, within the group of Prof.dr. Albert Heck, where he is deepening his understanding of proteomics and mass spectrometric native (glyco)protein analysis.

Publications and submitted manuscripts

1. **Reiding, K. R.**, Blank, D., Kuijper, D. M., Deelder, A. M., and Wuhrer, M. (2014) High-throughput profiling of protein *N*-glycosylation by MALDI-TOF-MS employing linkage-specific sialic acid esterification. *Anal Chem* 86, 5784-5793.

2. Bondt, A., Rombouts, Y., Selman, M. H., Hensbergen, P. J., **Reiding, K. R.**, Hazes, J. M., Dolhain, R. J., and Wuhrer, M. (2014) Immunoglobulin G (IgG) Fab glycosylation analysis using a new mass spectrometric high-throughput profiling method reveals pregnancy-associated changes. *Mol Cell Proteomics* 13, 3029-3039.

3. **Reiding, K. R.**, Bladergroen, M. R., Hipgrave Ederveen, A. L., Vreeker, G. C., Clerc, F., Holst, S., Bondt, A., Wuhrer, M., and van der Burgt, Y. E. (2015) Automation of high-throughput mass spectrometry-based plasma *N*-glycome analysis with linkage-specific sialic acid esterification. *J Proteome Res* 14, 4080-4086.

4. Borelli, V., Vanhooren, V., Lonardi, E., **Reiding, K. R.**, Capri, M., Libert, C., Garagnani, P., Salvioli, S., Franceschi, C., and Wuhrer, M. (2015) Plasma *N*-glycome signature of Down Syndrome. *J Proteome Res* 14, 4232-4245.

5. de Haan, N., **Reiding, K. R.**, Haberger, M., Reusch, D., Falck, D., and Wuhrer, M. (2015) Linkage-specific sialic acid derivatization for MALDI-TOF-MS profiling of IgG glycopeptides. *Anal Chem* 87, 8284-8291.

6. Jansen, B. C., **Reiding, K. R.**, Bondt, A., Hipgrave Ederveen, A. L., Palmblad, M., Falck, D., and Wuhrer, M. (2015) MassyTools: a high-throughput targeted data processing tool for relative quantitation and quality control developed for glycomic and glycoproteomic MALDI-MS. *J Proteome Res* 14, 5088-5098.

7. Shubhakar, A., **Reiding, K. R.**, Gardner, R. A., Spencer, D. I., Fernandes, D. L., and Wuhrer, M. (2015) High-throughput analysis and automation for glycomics studies. *Chromatographia* 78, 321-333.

8. Breen, L. D., Pucic-Bakovic, M., Vuckovic, F., **Reiding, K.R.**, Trbojevic-Akmacic, I., Srajer Gajdosik, M., Cook, M. I., Lopez, M. J., Wuhrer, M., Camara, L. M., Andjelkovic, U., Dupuy, D. E., and Josic, D. (2016) IgG and IgM glycosylation patterns in patients undergoing image-guided tumor ablation. *Biochim Biophys Acta* 1860, 1786-1794.

9. **Reiding, K. R.**, Lonardi, E., Hipgrave Ederveen, A. L., and Wuhrer, M. (2016) Ethyl esterification for MALDI-MS analysis of protein glycosylation. *Methods Mol Biol* 1394, 151-162.

10. Clerc, F., **Reiding, K. R.**, Jansen, B. C., Kammeijer, G. S., Bondt, A., and Wuhrer, M. (2016) Human plasma protein *N*-glycosylation. *Glycoconj J* 33, 309-343.

11. de Haan, N., **Reiding, K. R.**, Driessen, G., van der Burg, M., and Wuhrer, M. (2016) Changes in healthy human IgG Fc-glycosylation after birth and during early childhood. *J Proteome Res* 15, 1853-1861.

12. Jansen, B. C., Bondt, A., **Reiding, K. R.**, Lonardi, E., de Jong, C. J., Falck, D., Kammeijer, G. S., Dolhain, R. J., Rombouts, Y., and Wuhrer, M. (2016) Pregnancy-associated serum *N*-glycome changes studied by high-throughput MALDI-TOF-MS. *Sci Rep* 6, 23296.

13. Jansen, B. C., Bondt, A., **Reiding, K. R.**, Scherjon, S. A., Vidarsson, G., and Wuhrer, M. (2016) MALDI-TOF-MS reveals differential *N*-linked plasma- and IgG-glycosylation profiles between mothers and their newborns. *Sci Rep* 6, 34001.

14. Klasic, M., Kristic, J., Korac, P., Horvat, T., Markulin, D., Vojta, A., **Reiding, K. R.**, Wuhrer, M., Lauc, G., and Zoldos, V. (2016) DNA hypomethylation upregulates expression of the MGAT3 gene in HepG2 cells and leads to changes in *N*-glycosylation of secreted glycoproteins. *Sci Rep* 6, 24363.

15. Kozak, R. P., Urbanowicz, P. A., Punyadeera, C., **Reiding, K. R.**, Jansen, B. C., Royle, L., Spencer, D. I., Fernandes, D. L., and Wuhrer, M. (2016) Variation of human salivary O-glycome. *PLoS One* 11, e0162824.

16. Meyer, S., Nederend, M., Jansen, J. H., **Reiding, K. R.**, Jacobino, S. R., Meeldijk, J., Bovenschen, N., Wuhrer, M., Valerius, T., Ubink, R., Boross, P., Rouwendal, G., and Leusen, J. H. (2016) Improved in vivo anti-tumor effects of IgA-Her2 antibodies through half-life extension and serum exposure enhancement by FcRn targeting. *MAbs* 8, 87-98.

17. **Reiding, K. R.**, Hipgrave Ederveen, A. L., Rombouts, Y., and Wuhrer, M. (2016) Murine plasma *N*-glycosylation traits associated with sex and strain. *J Proteome Res* 15, 3489-3499.

18. Shubhakar, A., Kozak, R. P., **Reiding, K. R.**, Royle, L., Spencer, D. I., Fernandes, D. L., and Wuhrer, M. (2016) Automated high-throughput permethylation for glycosylation analysis of biologics using MALDI-TOF-MS. *Anal Chem* 88, 8562-8569.

19. Rombouts, Y., Jonasdottir, H. S., Hipgrave Ederveen, A. L., **Reiding, K. R.**, Jansen, B. C., Freysdottir, J., Hardardottir, I., Ioan-Facsinay, A., Giera, M., and Wuhrer, M. (2016) Acute phase inflammation is characterized by rapid changes in plasma/peritoneal fluid *N*-glycosylation in mice. *Glycoconj J* 33, 457-470.

20. Rouwendal, G. J., van der Lee, M. M., Meyer, S., **Reiding, K. R.**, Schouten, J., de Roo, G., Egging, D. F., Leusen, J. H., Boross, P., Wuhrer, M., Verheijden, G. F., Dokter, W. H., Timmers, M., and Ubink, R. (2016) A comparison of anti-HER2 IgA and IgG1 in vivo efficacy is facilitated by high *N*-glycan sialylation of the IgA. *MAbs* 8, 74-86.

21. de Haan, N., **Reiding, K. R.**, and Wuhrer, M. (2017) Sialic Acid Derivatization for the rapid subclass- and sialic acid linkage-specific MALDI-TOF-MS analysis of IgG Fc-glycopeptides. *Methods Mol Biol* 1503, 49-62.

22. **Reiding, K. R.**, Ruhaak, L. R., Uh, H. W., El Bouhaddani, S., van den Akker, E. B., Plomp, R., McDonnell, L. A., Houwing-Duistermaat, J. J., Slagboom, P. E., Beekman, M., and Wuhrer, M. (2017) Human plasma *N*-glycosylation as analyzed

by MALDI-FTICR-MS associates with markers of inflammation and metabolic health. *Mol Cell Proteomics* 16, 228-242.

23. de Haan, N., **Reiding, K. R.**, Kristic, J., Hipgrave Ederveen, A. L., Lauc, G., Wuhrer, M. (2017) The *N*-glycosylation of mouse IgG-Fc differs between IgG subclasses and strains. *Front Immunol* 8, 608.

24. Plomp, R., Ruhaak, L. R., Uh, H. W., **Reiding, K. R.**, Selman, M. H., Houwing-Duistermaat, J. J., Slagboom, P. E., Beekman, M., Wuhrer, M. (2017) Subclass-specific IgG glycosylation is associated with markers of inflammation and metabolic health. *Sci Rep* 7, 12325.

25. Ferrantelli, E., Farhat, K., Hipgrave Ederveen, A. L., **Reiding, K. R.**, Beelen, R. H. J., van Ittersum, F. J., Wuhrer, M., Dotz, V. (2018) Effluent and serum protein *N*-glycosylation is associated with inflammation and transport characteristics in peritoneal dialysis patients. *Sci Rep* 8, 979.

26. **Reiding, K. R.**, Vreeker, G. C. M., Bondt, A., Bladergroen, M. R., Hazes, J. M. W., van der Burgt, Y. E. M., Wuhrer, M., Dolhain, R. J. E. M. (2018) Serum protein *N*-glycosylation changes with rheumatoid arthritis disease activity during and after pregnancy. *Front Med* 4, 241.

27. Jacobino, S. R., Nederend, M., Reijneveld, J. F., Augustijn, D., Jansen, J. H. M., Meeldijk, J., **Reiding, K. R.**, Wuhrer, M., Coenjaerts, F. E. J., Hack, C. E., Bont, L. J., Leusen, J. H. W. (2018) Reformatting palivizumab and motavizumab from IgG to human IgA impairs their efficacy against RSV infection *in vitro* and *in vivo*. *MAbs*. *Manuscript accepted*.

28. **Reiding, K. R.**, Bondt, A., Hennig, R., Gardner, R. A., O'Flaherty, R., Trbojević-Akmačić, I., Shubhakar, A., Hazes, J. M. W., Reichl, U., Fernandes, D. L., Pučić-Baković, M., Rapp, E., Spencer, D. I. R., Dolhain, R. J. E. M., Rudd, P. M., Lauc, G., Wuhrer, M. High-throughput serum *N*-glycomics: method comparison and application to study rheumatoid arthritis and pregnancy-associated changes. *Manuscript under review*.

29. Clerc, F., Novokmet, M., Dotz, V., **Reiding, K. R.**, de Haan, N., Kammeijer, G. S. M., Dalebout, H., Bladergroen, M. R., Vukovic, F., Rapp, E., IBD-BIOM consortium, Targan, S. R., Barron, G., Manetti, N., Latiano, A., McGovern, D. P. B., Annese, V., Lauc, G., Wuhrer, M. Plasma *N*-glycan signatures of inflammatory bowel diseases. *Manuscript submitted*.

30. de Haan, N., Boeddha, N. P., Ekinci, E., **Reiding, K. R.**, Emonts, M., Hazelzet, J. A., Wuhrer, M., Driessen, G. J. Differences in IgG Fc glycosylation are associated with outcome of pediatric meningococcal sepsis. *Manuscript submitted*.

31. Dotz, V., Lemmers, R. F. H., **Reiding, K. R.**, Hipgrave Ederveen, A. L., Lieverse, A. G., Mulder, M. T., Sijbrands, E. J. G., Wuhrer, M. van Hoek, M. Plasma protein *N*-glycan signatures of type 2 diabetes. *Manuscript submitted*.