

Glycoproteomics characterization of immunoglobulins in health and disease

Plomp, H.R.

Citation

Plomp, H. R. (2017, May 31). *Glycoproteomics characterization of immunoglobulins in health and disease*. Retrieved from https://hdl.handle.net/1887/49752

Version: Not Applicable (or Unknown)

License: License agreement concerning inclusion of doctoral thesis in the

Institutional Repository of the University of Leiden

Downloaded from: https://hdl.handle.net/1887/49752

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle http://hdl.handle.net/1887/49752 holds various files of this Leiden University dissertation

Author: Plomp, H.R.

Title: Glycoproteomics characterization of immunoglobulins in health and disease

Issue Date: 2017-05-31

List of abbreviations

AA 2-aminobenzoic acid

AAV ANCA-associated vasculitis
ABC ammonium bicarbonate

ACN acetonitrile

ACPA anti-citrullinated protein antibodies
ADCC antibody-dependent cellular cytotoxicity
ANCA anti-neutrophil cytoplasmic antibodies

C1q complement component 1 q

CDC complement-dependent cellular cytotoxicity

CE capillary electrophoresis

CGE-LIF capillary gel electrophoresis with laser-induced fluorescence

CH conserved heavy chain
CID collision-induced dissociation

CMV cytomegalovirus CRP c-reactive protein

DC-SIGN dendritic cell-specific intercellular adhesion molecule-3 grabbing non-

integrin

DHB 2,5-dihydroxybenzoic acid

DTT dithiothreitol

EGPA eosinophilic granulomatosis with polyangiitis

ELISA enzyme-linked immunosorbent assay

Endo S endoglycosidase S
ER endoplasmic reticulum
ERLIC electrostatic repulsion HILIC
ESI electrospray ionization
ETD electron-transfer dissociation

FA formic acid

Fab fragment antigen binding
Fc fragment crystallizable
FcεR Fc-epsilon receptor
FcγR Fc-gamma receptor

FEIA fluorescent-enzyme immune assay

FRS Framingham risk score
GBP glycan-binding protein
GC glucocorticosteroid therapy

GDob1 chimeric MN12H2 antibodies with V genes from the human

monoclonal IgG2 antibody DOB1

GlcNAc *N*-acetylglucosamine

GPA granulomatosis with polyangiitis
HDLC high density lipoprotein cholesterol

HEK human embryonic kidney

Hex hexose

HexNAc N-acetylhexosamine

HILIC hydrophilic interaction liquid chromatography

HIV human immunodeficiency virus

HPLC high performance liquid chromatography

HR hazard ratio

Ig immunoglobulin IL interleukin IT ion trap

IVIg intravenous Immunoglobulin LC liquid chromatography

LDLC low density lipoprotein cholesterol
LEMS lambert-Eaton Myasthenic Syndrome
MALDI matrix-assisted laser desorption ionization

MBL mannose-binding lectin
MPA microscopic polyangiitis
MPO myeloperoxidase

MRM multiple reaction monitoring

MS mass spectrometry

NCGN necrotizing glomerulonephritis
NeuAc N-acetylneuraminic acid
PBS phosphate buffered saline

PR3 proteinase 3 PNGase F N-glycosidase F

PTM post-translational modification

qTOF quadropole TOF RA rheumatoid arthritis

ROC receiver operating characteristic

RP reversed phase

RSD relative standard deviation

SA sialic acid

SIGN-R1

SD standard deviation

SDS-PAGE sodium dodecyl sulfate polyacrylamide gel electrophoresis

specific intercellular adhesion molecule-3 grabbing non-integrin

related 1

t-ITP transient isotachophoresis

T3 triiodothyronine
TC total cholesterol
TFA trifluoroacetic acid
TG triglycerides

TNP trinitrophenol TOF time-of-flight

UHPLC ultra high performance liquid chromatography

ZIC HILIC zwitterionic HILIC

Acknowledgements

Looking back at the past 5 years, my PhD at the Center for Proteomics and Metabolomics has been a wonderful experience surrounded by great people. I remember having a lot of doubts before I started, wondering whether a PhD was the right fit for me. I can now say I have much enjoyed doing research and it has been a very fulfilling experience. I would like to express my gratitude to the many people who helped me along the way and brought me to where I am now, at the end of my thesis.

First of all I would like to thank my promotor Manfred, for his dedication and his guidance. While he had plenty on his plate, first as head of the glyco group, professor at the VU Amsterdam and finally head of the CPM, he was always available for questions and discussions. When I sent him a manuscript I would always get detailed feedback within a few days, often at odd hours of the night. Thank you for your direction and encouragement!

I would also like to thank André, my original promotor. Although he left soon after I started, from what I've heard he was the driving force behind my selection despite my admittedly not stellar job interview. I would like to thank him for his confidence in me.

I would like to thank Paul, my co-promotor, for his help in shaping my thesis and propositions, and for sharing his knowledge of proteomics.

I would further like to thank Carolien, Agnes and Irina for their guidance in the lab and their supervision of the machinery which enabled me and everyone in the group to measure tens of thousands of samples. At the same time I would like to apologize for all of the mistakes which I've made, after which I came running to you for help; thank you for having my back!

My current colleagues I owe a great deal due to their contributions to both my development as a researcher and the friendly and encouraging environment in the group. Karli started just two weeks before me and was always game for fun discussions, glyco-related or not. I would like to thank him for all his technical and bioinformatic support. Noortje joined us later and was also frequently subjected to my questions, as well as many friendly conversations. In addition, I would like to thank her for the organisational skills she shared with me when we organised a small lab outing. Thank you both for being my paranymphs! Albert guided me during my first experiment as a PhD student; I would like to thank him for his guidance, as well as for the Christmas tree which now adorns my desk. Further thanks to David who has boosted my understanding of analytics and introduced me to new and exciting board games. Stephi, thank you for the organisational skills which helped support the literal backbone of

this thesis! Bas, thank you for all the technical support, and sorry for all of the bugs I encountered which should not have been possible! Further thanks to Viktoria, Guinevere, Gerda, Kathrin, Florent, Cees, and all of the others at the CPM!

I would also like to thank my former colleagues, Yoann, Gerhild and Maurice, for showing me the ropes of glycoanalysis. Yoann aided me in writing several publications and gave me a lot of useful advice. Gerhild taught me how to interpret mass spectrometric data and Maurice was always ready to impart (an often lengthy monologue of) his vast repository of knowledge.

In addition, I would like to thank Hae-Won, Marian, Jeanine and Eline for expanding my view on statistics and aiding in the processing of large datasets.

To my collaborators in Amsterdam and Maastricht: it was a pleasure to work with you! Michael, Gillian, Myrthe and Sanne: thank you for your contributions to my thesis and good luck with yours as well! Gestur, Theo and Jan Willem: thank you for your guidance.

I would also like to thank the students I had the pleasure of supervising: Lisette, Shivani and Jayshri. I learned a lot from supervising you, as I hope you did too!

I would further like to thank Manu for guiding me through the bureaucratic jungle known as 'Converis'.

Finally, I would like to address the support I got from home, from Jan and my family. Thank you for the afternoons and evenings when you looked after Leander so that I could work on my thesis, and for the second opinions on various pieces of writing. I would also like to thank Jan for all of his encouragement and for the confidence he has given me.

Curriculum Vitae

Henriëtte Rosina Plomp was born on Friday the 13th of November, 1987 in Leiderdorp, The Netherlands. After receiving the bulk of her primary education in international schools, she attended the Stedelijk Gymnasium Leiden and graduated in 2006. During the next three years, she was enrolled in the Bachelor program Life Science and Technology, a collaboration between Leiden University and the Technical University Delft. In her final year there, she followed an internship at the Department of Molecular Cell Biology at the Leiden University Medical Center, supervised by Dr. A. Zaldumbide and Prof. Dr. R. C. Hoeben, investigating the migration of human mesenchymal stem cells from different biological sources.

Following that, Rosina enrolled in the Master study Forensic Science at the University of Amsterdam, receiving a degree in 2011. In that year she also performed an internship at the Department of Forensic Molecular Biology at the Erasmus Medical Center, supervised by Dr. K. Ackermann and Prof. Dr. M. Kayser. During this time she conducted research into the expression of circadian biomarkers in human blood.

In 2012 Rosina joined the Center for Proteomics and Metabolomics at the Leiden University Medical Center as a PhD student under the supervision of Prof. Dr. M. Wuhrer, Prof. Dr. A.M. Deelder and Dr. P. Hensbergen. During her PhD, which was funded by the HighGlycan Project of the European Union's Seventh Framework Programme, Rosina investigated glycosylation of immunoglobulins using a mass spectrometry-based proteomics approach, which resulted in this thesis. Since completing her thesis, she has continued in the field of glycoproteomics as a post-doctoral researcher in the same group.

List of publications

- 1. Ackermann, K., **Plomp, R.**, Lao, O., Middleton, B., Revell, V. L., Skene, D. J., and Kayser, M. (2013) Effect of sleep deprivation on rhythms of clock gene expression and melatonin in humans. *Chronobiol Int* 30, 901-909
- 2. **Plomp, R.**, Hensbergen, P. J., Rombouts, Y., Zauner, G., Dragan, I., Koeleman, C. A., Deelder, A. M., and Wuhrer, M. (2014) Site-specific N-glycosylation analysis of human immunoglobulin e. *J Proteome Res* 13, 536-546
- 3. Huffman, J. E., Pucic-Bakovic, M., Klaric, L., Hennig, R., Selman, M. H., Vuckovic, F., Novokmet, M., Kristic, J., Borowiak, M., Muth, T., Polasek, O., Razdorov, G., Gornik, O., **Plomp, R.**, Theodoratou, E., Wright, A. F., Rudan, I., Hayward, C., Campbell, H., Deelder, A. M., Reichl, U., Aulchenko, Y. S., Rapp, E., Wuhrer, M., and Lauc, G. (2014) Comparative performance of four methods for high-throughput glycosylation analysis of immunoglobulin G in genetic and epidemiological research. *Mol Cell Proteomics* 13, 1598-1610
- 4. Nagelkerke, S. Q., Dekkers, G., Kustiawan, I., van de Bovenkamp, F. S., Geissler, J., **Plomp, R.**, Wuhrer, M., Vidarsson, G., Rispens, T., van den Berg, T. K., and Kuijpers, T. W. (2014) Inhibition of FcγR-mediated phagocytosis by IVIg is independent of IgG-Fc sialylation and FcγRIIb in human macrophages. *Blood* 124, 3709-3718
- 5. **Plomp, R.**, Dekkers, G., Rombouts, Y., Visser, R., Koeleman, C. A., Kammeijer, G. S., Jansen, B. C., Rispens, T., Hensbergen, P. J., Vidarsson, G., and Wuhrer, M. (2015) Hinge-Region O-Glycosylation of Human Immunoglobulin G3 (IgG3). *Mol Cell Proteomics* 14, 1373-1384
- 6. Falck, D., Jansen, B. C., **Plomp, R.**, Reusch, D., Haberger, M., and Wuhrer, M. (2015) Glycoforms of Immunoglobulin G Based Biopharmaceuticals Are Differentially Cleaved by Trypsin Due to the Glycoform Influence on Higher-Order Structure. *J Proteome Res* 14, 4019-4028
- 7. Stavenhagen, K., **Plomp, R.**, and Wuhrer, M. (2015) Site-Specific Protein N- and O-Glycosylation Analysis by a C18-Porous Graphitized Carbon-Liquid Chromatography-Electrospray Ionization Mass Spectrometry Approach Using Pronase Treated Glycopeptides. *Anal Chem* 87, 11691-11699
- 8. **Plomp, R.**, Bondt, A., de Haan, N., Rombouts, Y., and Wuhrer, M. (2016) Recent Advances in Clinical Glycoproteomics of Immunoglobulins (Igs). *Mol Cell Proteomics* 15, 2217-2228
- 9. Dekkers, G., **Plomp, R.**, Koeleman, C. A., Visser, R., von Horsten, H. H., Sandig, V., Rispens, T., Wuhrer, M., and Vidarsson, G. (2016) Multi-level glyco-engineering techniques to generate IgG with defined Fc-glycans. *Sci Rep* 6, 36964

- 10. Sonneveld, M. E., Koelewijn, J., de Haas, M., Admiraal, J., **Plomp, R.**, Koeleman, C. A., Hipgrave Ederveen, A. L., Ligthart, P., Wuhrer, M., van der Schoot, C. E., and Vidarsson, G. (2016) Antigen specificity determines anti-red blood cell IgG-Fc alloantibody glycosylation and thereby severity of haemolytic disease of the fetus and newborn. Br J Haematol 176(4), 651-660
- 11. 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. (2016) Human plasma N-glycosylation as analyzed by MALDI-FTICR-MS associates with markers of inflammation and metabolic health. *Mol Cell Proteomics* 16(2), 228-242
- 12. Kemna, M. J., **Plomp**, R., van Paassen, P., Koeleman, C. A. M., Jansen, B. C., Damoiseaux, J. G. M. C., Tervaert J. W., Wuhrer, M. (in press) Galactosylation and sialylation levels of IgG predict relapse in patients with PR3-ANCA associated vasculitis. *EBioMedicine* 17, 108-118
- 13. **Plomp**, R., Ruhaak, L. R., Uh, H., Reiding, K. R., Selman, M., 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. Manuscript submitted for publication.