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## **Glycosylation profiling with mass spectrometry: method development and application to cancer biomarker studies**

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## Curriculum Vitae

Geertruida (Gerda) Cornelia Maria Vreeker was born on July 20<sup>th</sup>, 1992 in Hoorn, the Netherlands. After she finished primary and secondary school she started her bachelor Chemistry at Vrije Universiteit Amsterdam, the Netherlands. After successfully obtaining her bachelor degree in 2013, she continued her studies with the master Chemistry at Vrije Universiteit Amsterdam/University of Amsterdam (combined program) with a specialization in Analytical Sciences. Next to her studies, Gerda has been involved in promotion activities of the studies, tutored at practical courses and was a member of the Program Committee Chemistry for two years.

During her masters she performed two internships. The first was in 2014 at the Medicinal Chemistry department at Vrije Universiteit Amsterdam and together with corresponding courses, this internship was extra-curricular and thus added to a complete analytical chemistry master. To gain more insights in molecules and chemical reactions she performed her internship on a subject related to drug design and synthesis. Besides the performance of synthesis experiments, she was also able to use her background in analytical chemistry to fully purify and characterize the synthesized molecules with liquid chromatography (LC), thin layer chromatography (TLC), infrared (IR) spectroscopy, UV detection, nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS). At the end of 2014 she started her second internship at the Center for Proteomics and Metabolomics (CPM) at Leiden University Medical Center (LUMC), Leiden, the Netherlands. Here she focused on method development for glycosylation analysis and did a cohort analysis on an automated platform under the supervision of dr. Karli R. Reiding and prof. dr. Manfred Wuhler.

In February 2016 Gerda started her PhD in a bridging position between the CPM and the department of Surgery (HLK) under the supervision of prof. dr. Manfred Wuhler (CPM), prof. dr. Rob A. E. M. Tollenaar (HLK), dr. Wilma E. Mesker (HLK) and dr. Yuri E. M. van der Burgt (CPM). Her research project focused on the MS method development for the analysis of protein glycosylation from blood-based samples and the application of these methods to cancer biomarker studies.

## List of publications (in this thesis)

- ❖ **Vreeker, G.C.M.**, Vangangelt, K.M.H., Bladergroen, M.R., Nicolardi, S., Mesker, W.E., Wuhrer, M., Van der Burgt, Y.E.M., Tollenaar, R.A.E.M.: Serum *N*-glycan profiles differ for various breast cancer subtypes. *Glycoconj. J.* (2021). doi:10.1007/s10719-021-10001-3
- ❖ **Vreeker, G.C.M.\***, Hanna-Sawires, R.G.\*, Mohammed, Y., Bladergroen, M.R., Nicolardi, S., Dotz, V., Nouta, J., Bonsing, B.A., Mesker, W.E., Van der Burgt, Y.E.M., Wuhrer, M.\*\*, Tollenaar, R.A.E.M.\*\*: Serum *N*-Glycome Analysis Reveals Pancreatic Cancer Disease Signatures. *Cancer med.* (2020). doi:10.1002/cam4.3439
- ❖ **Vreeker, G.C.M.**, Nicolardi, S., Madunic, K., Kotsias, M., Van der Burgt, Y.E.M., Wuhrer, M.: *O*- and *N*-glycosylation analysis from of cell lines by ultrahigh resolution MALDI-FTICR-MS. *Int. J. Mass Spectrom.* 448, 116267 (2020). doi:10.1016/j.ijms.2019.116267
- ❖ **Vreeker, G.C.M.**, Bladergroen, M.R., Nicolardi, S., Mesker, W.E., Tollenaar, R.A.E.M., van der Burgt, Y.E.M., Wuhrer, M.: Dried blood spot *N*-glycome analysis by MALDI mass spectrometry. *Talanta.* 205, 120104 (2019). doi:10.1016/j.talanta.2019.06.104
- ❖ **Vreeker, G.C.M.**, Nicolardi, S., Bladergroen, M.R., van der Plas, C.J., Mesker, W.E., Tollenaar, R.A.E.M., van der Burgt, Y.E.M., Wuhrer, M.: Automated Plasma Glycomics with Linkage-Specific Sialic Acid Esterification and Ultrahigh Resolution MS. *Anal. Chem.* 90, 11955–11961 (2018). doi:10.1021/acs.analchem.8b02391

\* *These authors share first authorship*

\*\* *These authors share last authorship*

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## List of publications (not in this thesis)

- ❖ Singh, S.S.\*, Naber, A.\*, Dotz, V., Schoep, E., Memarian, E., Slieker, R.C., Elders, P.J.M., **Vreeker, G.C.M.**, Nicolardi, S., Wuhrer, M., Sijbrands, E.J.G., Lieveise, A.G., 't Hart, L.M., van Hoek, M. Metformin and statin use associate with plasma protein *N*-glycosylation in people with type 2 diabetes. *BMJ Open Diabetes Research and Care*. 8, e001230 (2020). doi:10.1136/bmjdr-2020-001230
- ❖ Hauwert, N.J., Mocking, T.A.M., Da Costa Pereira, D., Kooistra, A.J., Wijnen, L.M., **Vreeker, G.C.M.**, Verweij, E.W.E., De Boer, A.H., Smit, M.J., De Graaf, C., Vischer, H.F., de Esch, I.J.P., Wijtmans, M., Leurs, R.: Synthesis and Characterization of a Bidirectional Photoswitchable Antagonist Toolbox for Real-Time GPCR Photopharmacology. *J. Am. Chem. Soc.* 140, 4232–4243 (2018). doi:10.1021/jacs.7b11422
- ❖ 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.: Serum Protein *N*-Glycosylation Changes with Rheumatoid Arthritis Disease Activity during and after Pregnancy. *Front. Med.* 4, 1–11 (2018). doi:10.3389/fmed.2017.00241
- ❖ **Vreeker, G.C.M.**, Wuhrer, M.: Reversed-phase separation methods for glycan analysis. *Anal. Bioanal. Chem.* 409, 359–378 (2017). doi:10.1007/s00216-016-0073-0
- ❖ Bladergroen, M.R., Reiding, K.R., Hipgrave Ederveen, A.L., **Vreeker, G.C.M.**, Clerc, F., Holst, S., Bondt, A., Wuhrer, M., van der Burgt, Y.E.M.: Automation of High-Throughput Mass Spectrometry-Based Plasma *N* -Glycome Analysis with Linkage-Specific Sialic Acid Esterification. *J. Proteome Res.* 14, 4080–4086 (2015). doi:10.1021/acs.jproteome.5b00538

## PhD Portfolio

### PhD training

#### Mandatory courses

PhD Introductory Meeting	2016
Basic Methods and Reasoning in Biostatistics	2016
BROK Course	2017

#### Generic/disciplinary courses

Quantitative LC-MS	2016
Summer course Glycosciences - <i>incl. poster presentation</i>	2016
Basic and Translational Oncology	2016
Communication in Science	2018
Clinical Diagnostics: Translational Mass Spectrometry	2018
Journal club on the chapters of "Essentials of Glycobiology"	2018
Introduction to GLP Regulations and Bioanalytical Method Validation by LC-MS/MS	2019

#### Attended lectures, LUMC presentations, participation in meetings

GlycoCan kickoff meeting	2016
Meeting Genootschap Keukenhof - <i>incl. presentation</i>	2016, 2017
LAP Career Event	2019
BCF Career Event	2019

#### Congress attendance and poster or oral presentations

CASA master event VU-UvA	2016
JP-NL Glycobiology meeting - <i>incl. poster</i>	2016
27th Glycobiology meeting Nijmegen - <i>incl. oral and poster</i>	2016
Symposium Clinical Mass Spectrometry Imaging	2017
American Society for Mass Spectrometry (ASMS) conference - <i>incl. oral</i>	2018
Nederlandse Vereniging voor Massaspectrometrie (NVMS) symposium - <i>incl. oral</i>	2018
NVMS conference attendance	2019
American Society for Mass Spectrometry (ASMS) conference - <i>incl. poster</i>	2019
Chains 2019 - <i>incl. poster</i>	2019

**Other activities**

Lab tour Rotary Club Noordwijk	2016
Lab tour Feadship - <i>incl. presentation</i>	2017
Clinical internship Oncology	2019

**Teaching activities****Lecturing, lab assistance, student supervision**

FOS course CPM – lab assistance	2016
FOS course Surgery - lecture	2016, 2017, 2018, 2019
Student supervision: Corné van der Plas	2017
Student supervision: Jennifer Heikamp	2017
Science4U project of Stedelijk Gymnasium Leiden	2017, 2018, 2019
FOS course Parasitology – lab assistance	2019

**Parameters of esteem****Personal grants**

NVMS conference attendance grant	2017
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**Organizational Experience****Social activities**

Sinterklaas celebration CPM	2016, 2017, 2018, 2019
Borrel committee CPM	2016, 2017
Labouting CPM	2016
Christmas dinner CPM	2017

## Acknowledgements

Here, at the end of this thesis I would like to thank all colleagues, friends and family for the support they gave me during my PhD.

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Also, I would like to thank Yuri van der Burgt for the support in writing the manuscripts and completing revisions. I want to thank Marco Bladergroen for his technical support with the automated pipetting platform and the creation of many of the beautiful figures found in this thesis. For the technical support with the MALDI-FTICR-MS I would like to thank Simone Nicolardi.

In addition, I want to thank my paranymphs Jan Nouta and Annelies Vlaar and all (former) colleagues and students from both the Center for Proteomics and Metabolomics and the Surgery department for the collaborations and support you provided. A special thanks to all co-authors of the chapters in this thesis for their contributions to my thesis. Additionally, I would like to thank all colleagues I shared an office with for the great times we had and the support you gave me in the ups and downs of my PhD trajectory.

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*Thank you,*

*Gerda van Dalen-Vreeker*