Metagenomic sequencing in clinical virology: advances in pathogen detection and future prospects

Carbo, E.C.

List of Publications / Publicaties

1. Glen R. Monroe, Gerardus W. Frederix, Sanne M.C. Savelberg, Tamar I. de Vries, Karen J. Duran, Jasper J. van der Smagt, P.A. Terhal, Peter M. van Hasselt, Hester Y. Kroes, Nanda M. Verhoeven-Duif, Ies J. Nijman, **Ellen C. Carbo**, Koen L. van Gassen, Nine V.A.M. Knoers, Anke M. Hövels, Mieke M. van Haelst, Gepke Visser, Gijs van Haaften. Effectiveness of whole-exome sequencing and costs of the traditional diagnostic trajectory in children with intellectual disability. Genetics in medicine: official journal of the American College of Medical Genetics. 2016. Sep;18(9):949-56.
DOI: 10.1038/gim.2015.200.

2. Iris M. de Lange, Marco J. Koudijs, Ruben van 't Slot, Boudewijn Gunning, Anja C.M. Sonsma, Lisette J.J.M van Gemert, Flip Mulder, **Ellen C. Carbo**, Marjan J.A. van Kempen, Nienke E. Verbeek, Ies J. Nijman, Robert F. Ernst, Sanne M.C.Savelberg, Nine V.A.M., Knoers, Eva H. Brilstra, Bobby P.C. Koeleman. Mosaicism of de novo pathogenic SCN1A variants in epilepsy is afrequent phenomenon that correlates with variable phenotypes. Epilepsia. 2018. Vol. 59, issue 3.
DOI: 10.1111/epi.14021.

3. Marielle E. Van Gijn, Isabella Ceccherini, Yael Shinar, **Ellen C. Carbo**, Mariska Slofstra, Juan I. Arostegui, Guillaume Sarrabay, Dorota Rowczenio, Ebun Omoyımn, Banu Balci-Peynircioglu, Hal M. Hoffman, Florian Milhavet, Morris A. Swertz, Isabelle Touitou. New workflow for classification of genetic variants' pathogenicity applied to hereditary recurrent fevers by the International Study Group for Systemic Autoinflammatory Diseases (INSAID). Journal of Medical Genetics. 2018. 2018;55:530–537.
DOI: 10.1136/jmedgenet-2017-105216

4. Iris M. de Lange, Marco J. Koudijs, Ruben van 't Slot, Anja C. M. Sonsma, Flip Mulder, **Ellen C. Carbo**, Marjan J.A. van Kempen, Isaac J. Nijman, Robert F. Ernst, Sanne M.C. Savelberg, Nine V.A.M. Knoers, Eva H. Brilstra, Bobby P.C. Koeleman. Assessment of parental mosaicism in SCN1A-related epilepsy by single-molecule molecular inversion probes and next-generation sequencing. Journal of Medical Genetics. 2019. 2019;56:75-80.
DOI: 10.1136/jmedgenet-2018-105672

5. Benjamin Kant, **Ellen C. Carbo**, Iris Kokmeijer, Jelske J.M. Oosterman, Joost Frenkel, Morris A. Swertz, Johannes K. Ploos van Amstel, Juan I. Aróstegui, Marco J. Koudijs, Mariëlle E. van Gijn. Gene Mosaicism Screening Using Single-Molecule Molecular Inversion Probes in Routine Diagnostics for Systemic Autoinflammatory Diseases. The Journal of Molecular Diagnostics. 2019. Vol. 21, No. 6.
DOI: 10.1016/j.jmoldx.2019.06.009

6. Anneloes L. van Rijn, Sander van Boheemen, Igor Sidorov, **Ellen C. Carbo**, Nikos Pappas, Hailiang Mei, Mariet Feltkamp, Marianne Aanerud, Per Bakke, Eric C. J. Claas, Tomas M. Eagan, Pieter S. Hiemstra, Aloys C. M. Kroes, Jutte J. C. de Vries. The respiratory virome and exacerbations in patients with chronic obstructive pulmonary disease. PLoS ONE. 2019. 14(10): e0223952.
DOI: 10.1371/journal.pone.0223952

7. Sander van Boheemen, Anneloes L. van Rijn, Nikos Pappas, **Ellen C. Carbo**, Ruben H.P. Vorderman, Igor Sidorov, Peter J. van `t Hof, Hailiang Mei, Eric C.J. Claas, Aloys C.M. Kroes, Jutte J.C. de Vries. Retrospective Validation of a Metagenomic Sequencing Protocol for Combined Detection of RNA and DNA Viruses Using Respiratory Samples from Pediatric Patients. The Journal of Molecular Diagnostics. 2020. Vol. 22, No. 2.
DOI: 10.1016/j.jmoldx.2019.10.007

8. **Ellen C. Carbo**, Emilie P. Buddingh, Evita Karelioti, Igor A. Sidorov, Mariet C.W. Feltkamp, Peter A. von dem Borne, Jan J.G.M. Verschuuren, Aloys C.M. Kroes, Eric C.J. Claas, Jutte J.C. de Vries. Improved diagnosis of viral encephalitis in adult and pediatric hematological patients using viral metagenomics. Journal of Clinical Virology. 2020. Vol.130, 104566.
DOI: 10.1016/j.jcv.2020.104566.

9. Tehmina Bharucha, Clarissa Oeser, Francois Balloux, Julianne R. Brown, **Ellen C. Carbo**, Andre Charlett, Prof. Charles Y. Chiu, Eric C. J. Claas, Marcus C. de Goffau, Jutte J. C. de Vries, Prof. Marc Eloit, Susan Hopkins, Jim F. Huggett, Duncan MacCannell, Sofia Morfopoulou, Prof. Avindra Nath, Denise M. O'Sullivan, Lauren B. Reoma, Liam P. Shaw, Igor Sidorov, Patricia J. Simner, Le Van Tan, Prof Emma C. Thomson, Lucy van Dorp, Michael R. Wilson, Prof. Judith Breuer, Nigel Field. STROBE-metagenomics: a STROBE extension statement to guide the reporting of metagenomics studies. The Lancet Infectious Diseases. 2020. Vol. 20, Issue 10, E251-E260.
DOI: 10.1016/S1473-3099(20)30199-7

10. **Ellen C. Carbo**, Igor A. Sidorov, Jessica C. Zevenhoven-Dobbe, Eric J. Snijder, Eric C. Claas, Jeroen F.J. Laros, Louis C.M. Kroes, Jutte J.C. de Vries. Coronavirus discovery by metagenomic sequencing: a tool for pandemic preparedness. Journal of Clinical Virolology. 2020. Vol. 131, 104594.
DOI: 10.1016/j.jcv.2020.104594.

11. Jutte J.C. de Vries, Julianne R. Brown, Natacha Couto, Martin Beer, Philippe Le Mercier, Igor Sidorov, Anna Papa, Nicole Fischer, Bas B. Oude Munnink, Christophe Rodriquez, Maryam Zaheri, Arzu Sayiner, Mario Hönemann, Alba Pérez-Cataluña, **Ellen C. Carbo**, Claudia Bachofen, Jakub Kubacki, Dennis Schmitz, Katerina Tsioka, Sébastien Matamoros, Dirk Höper, Marta Hernandez, Elisabeth Puchhammer-Stöckl, Aitana Lebrand, Michael Huber, Peter Simmonds, Eric C.J. Claas, F. Xavier López-Labrador. Recommendations for the introduction of metagenomic next-generation sequencing in clinical virology, part II: bioinformatic analysis and reporting, Journal of Clinical Virology. 2021. Vol. 138, 104812, ISSN 1386-6532.
DOI: 10.1016/j.jcv.2021.104812.

12. Alhena Reyes, **Ellen C. Carbo**, Johan S. van Harinxma thoe Slooten, Margriet E.M. Kraakman, Igor A. Sidorov, Eric C.J. Claas, Aloys C.M. Kroes, Leo G. Visser, Jutte J.C. de Vries. Viral metagenomic sequencing in a cohort of international travellers returning with febrile illness. Journal of Clinical Virology. 2021. Volume 143, 104940.
DOI: 10.1016/j.jcv.2021.104940.

13. **Ellen C. Carbo**, Ivar Blankenspoor, Jelle J. Goeman, Aloys C.M. Kroes, Eric C.J. Claas, Jutte J.C. de Vries. Viral metagenomic sequencing in the diagnosis of meningoencephalitis: a review of technical advances and diagnostic yield. Expert Review of Molecular Diagnostics. 2021. 21:11, 1139-1146. DOI: 10.1080/14737159.2021.1985467.

14. **Ellen C. Carbo**, Anne Russcher, Margriet E.M. Kraakman, Caroline S. de Brouwer, Igor A. Sidorov, Mariet C.W. Feltkamp, Aloys C.M. Kroes, Eric C.J. Claas, Jutte J.C. de Vries. Longitudinal Monitoring of DNA Viral Loads in Transplant Patients Using Quantitative Metagenomic Next-Generation Sequencing. Pathogens. 2022. 11, 236. DOI: 10.3390/pathogens11020236

15. **Ellen C. Carbo**, Igor A. Sidorov, Anneloes L. van Rijn-Klink, Nikos Pappas, Sander van Boheemen, Hailang Mei, Pieter S. Hiemstra, Tomas M. Eagan, Eric C.J. Claas, Aloys C.M. Kroes, Jutte J.C. de Vries. Performance of Five Metagenomic Classifiers for Virus Pathogen Detection Using Respiratory Samples from a Clinical Cohort. Pathogens. 2022. 11, 340. DOI: 10.3390/pathogens11030340

16. **Ellen C. Carbo**, Kees Mourik, Stefan A. Boers, Bas Oude Munnink, David Nieuwenhuijse, Marcel Jonges, Matthijs R.A. Welkers, Sebastien Matamoros, Joost van Harinxma thoe Slooten, Margriet Kraakman, Evita Karelioti, David van der Meer, Karin Ellen Veldkamp, Aloys C.M. Kroes, Igor A. Sidorov, Jutte J.C. de Vries. A comparison of five Illumina, Ion torrent, and nanopore sequencing technology-based approaches for whole genome sequencing of SARS-CoV-2. European Journal of Clinical Microbiol Infectious Diseases. 2023. DOI: 10.1007/s10096-023-04590-0

Curriculum Vitae

Ellen Carbo was born in Utrecht, the Netherlands, on February 26th, 1982. She finished her secondary education at the 'Niels Stensen College' in 2001, after which she went to the Technical University of Eindhoven to study Architecture and Civil Engineering. After first pursuing a career in the field of building engineering, she decided to change direction and started an undergraduate study of 'Life Sciences' at the Hogeschool Utrecht. During her Bachelor studies she completed two internships: one at the Department of Clinical Genetics at the University Medical Center Utrecht (UMCU), sequencing a novel breast cancer mutation gene, and one at the Department of Human Genetics at UMCU, working on next-generation sequencing (NGS) of ion channel genes in epilepsy patients. In 2013 she obtained her Bachelor degree in 'Biomolecular Research', after which she was hired at the place of her first internship at the UMCU to work on next-generation sequencing at the Department of Clinical Genetics.

While working at the Department of Clinical Genetics at the UMCU, she was eager to continue studying, so she started a part-time postgraduate study in biostatistics and epidemiology at the University of Amsterdam. Meanwhile, she focused her efforts on NGS data analysis ('dry lab'), instead of laboratory work ('wet lab'), and she gained experience in bioinformatics. For her postgraduate internship she combined her interest in genetics with her biostatistics and epidemiology study and worked on complex trait analysis. This research was performed on a large cohort of ALS patients at the UMCU Department of Neurogenetics, all while still working for the Department of Clinical Genetics at both the 'wet' and 'dry' laboratory. She obtained her Master of Science degree in 2016, after which she started working on a PhD project on auto inflammatory diseases for the Departments of Clinical Genetics at both the UMCU and the UMCG in Groningen.

To focus again on her original preferred subjects of NGS and bioinformatics, in 2018 she switched to a PhD project on viral metagenomic sequencing at the Department of Medical Microbiology at the Leiden University Medical Center (LUMC). Previously ignorant about the world of microbiology or viruses, besides occasionally experiencing annoying infections herself, she decided to dive into this new field and new adventure. She found out that she loved to unravel the nucleotides of all species, from viruses as well as bacteria, and from cucumber to her own human

genome (that she analyzed herself in 2020). During her PhD she worked on improving the laboratory and bioinformatics protocols of viral metagenomics and on the clinical application of this novel approach.

Ellen is also the coordinator of the Dutch special interest group of bioinformatics in medical microbiology, as a part of the *Dutch Society of Medical Microbiology*. This group was created to form an expertise network to improve the bioinformatics within the field, and for this group she organizes symposia, online meetings, and develops courses for experts at a national level. Recently, she started at the Department of Medical Microbiology & Infection Prevention at the Amsterdam University Medical Centers and began her training as a medical molecular microbiologist. In this role, she will continue to work in both the 'wet' and 'dry' laboratory to support patient care.

We do not follow maps to buried treasure,

and "X" never, ever marks the spot.

Indiana Jones, Indiana Jones and the Last Crusade, 1989