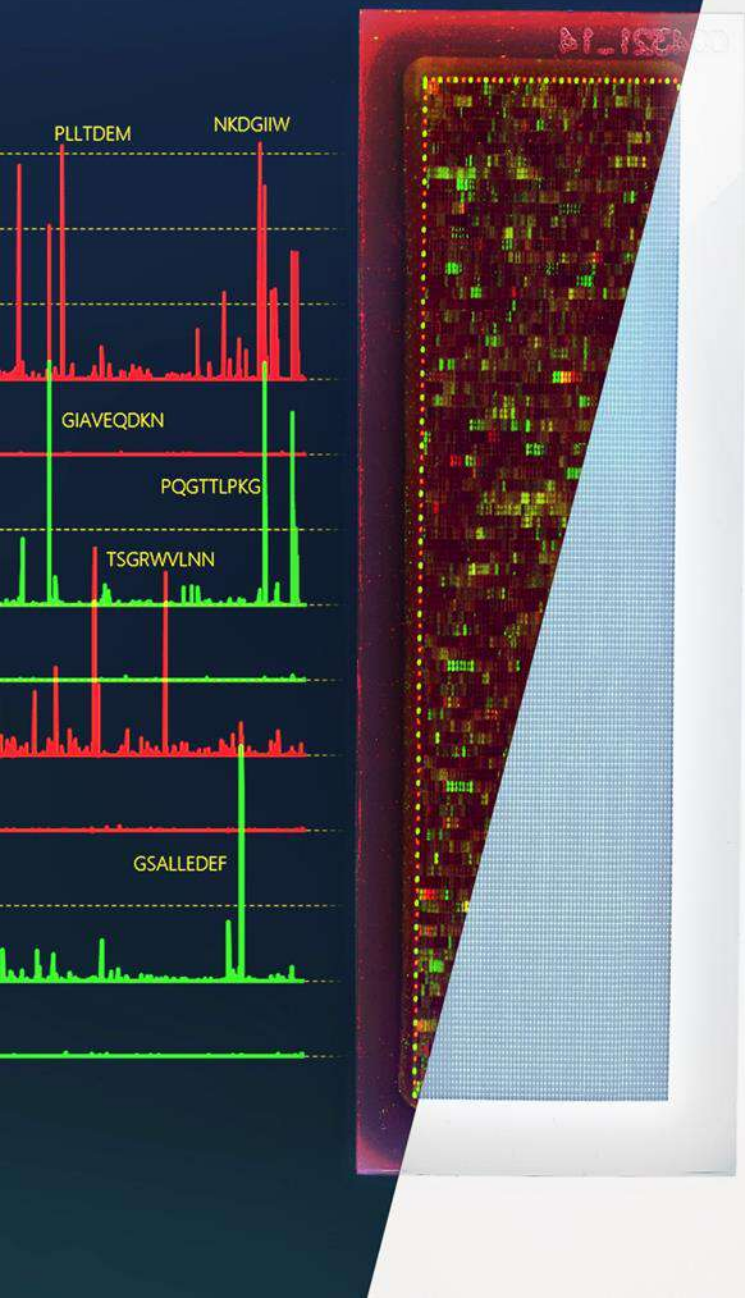

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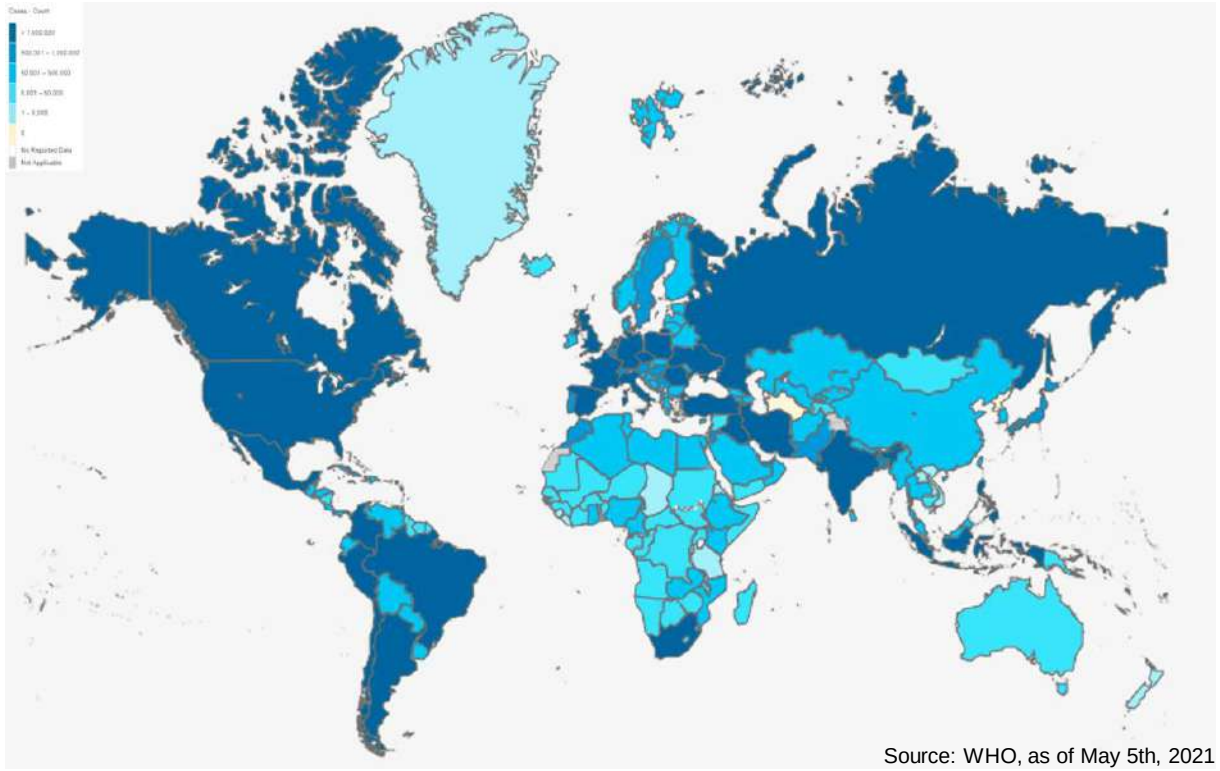
Uncovering antibody epitope signatures in COVID-19 patients by high-density peptide microarray screening

Dr. Kirsten Heiss
Research & Development
PEPperPRINT GmbH

June 2021

Coronavirus disease (COVID-19)

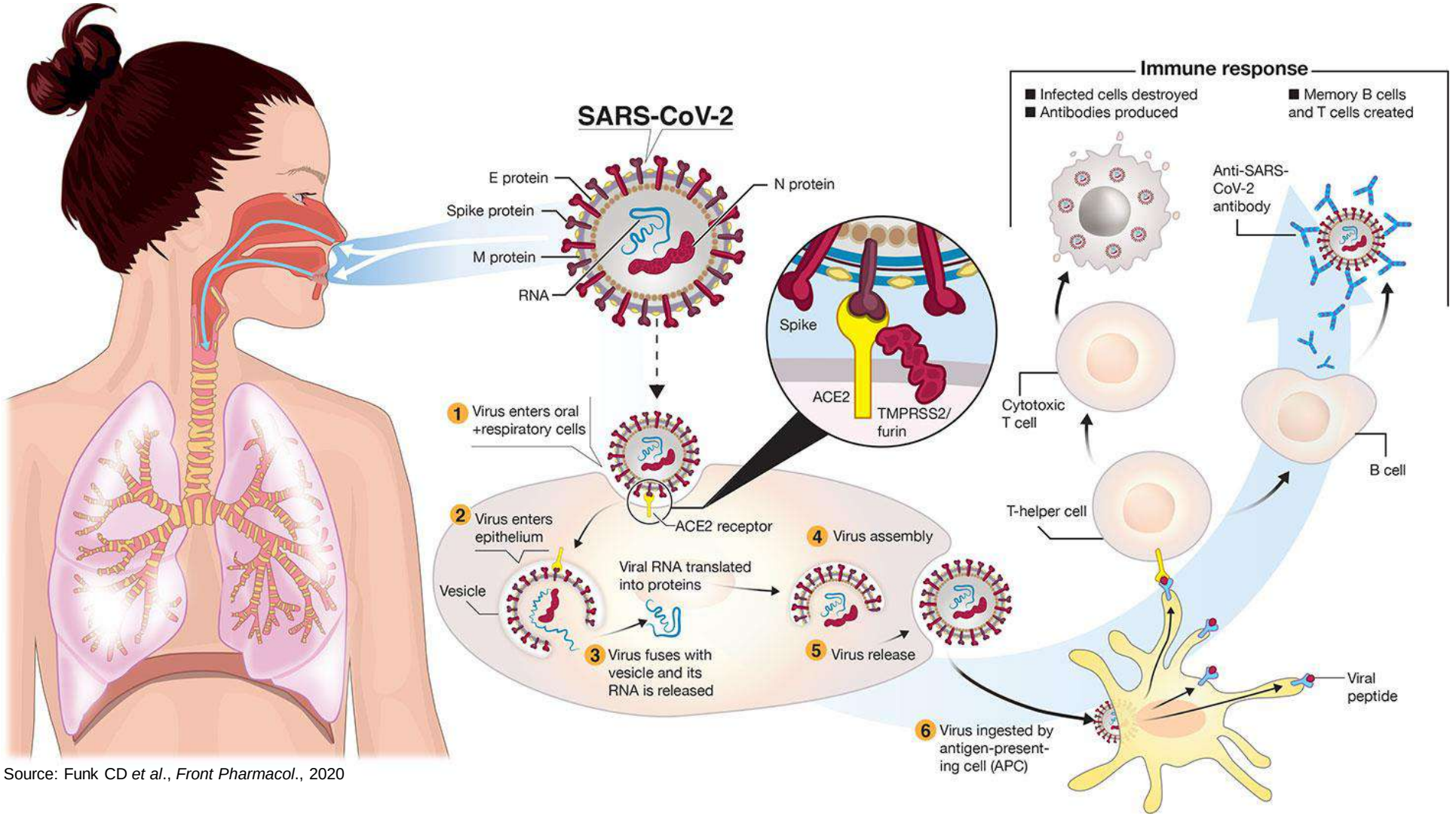


Source: WHO, as of May 5th, 2021

Globally > 170 million confirmed cases

- respiratory illness
- course of disease varies in symptoms and severity
- possible long-term effects (long COVID) in convalescents
- caused by a newly emerged coronavirus, SARS-CoV-2
- multiple SARS-CoV-2 variants are circulating globally

Understanding the host immune defense



Source: Funk CD *et al*., *Front Pharmacol*., 2020

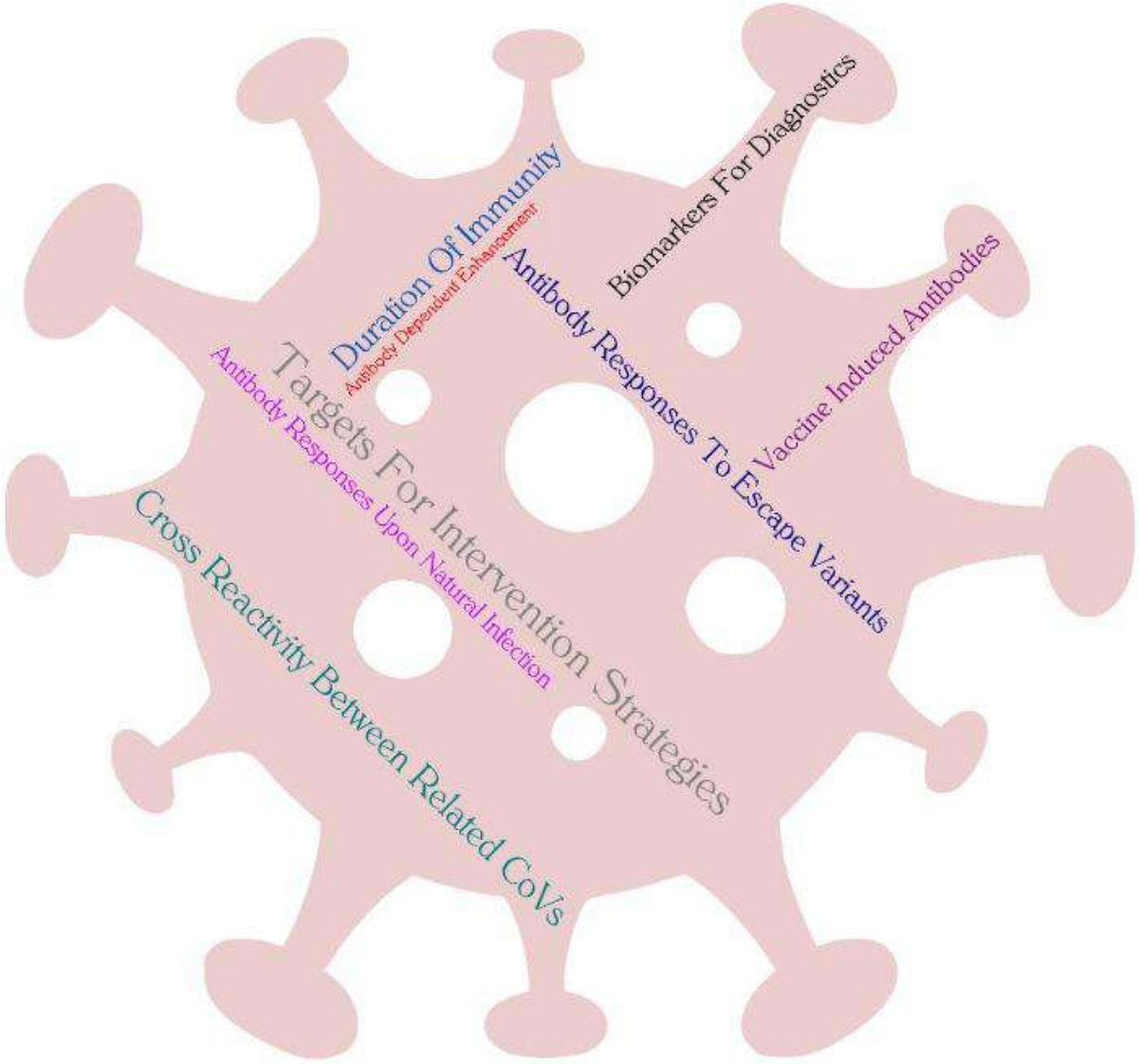
Antibody responses to SARS-CoV-2

Essential for anti-viral defense:

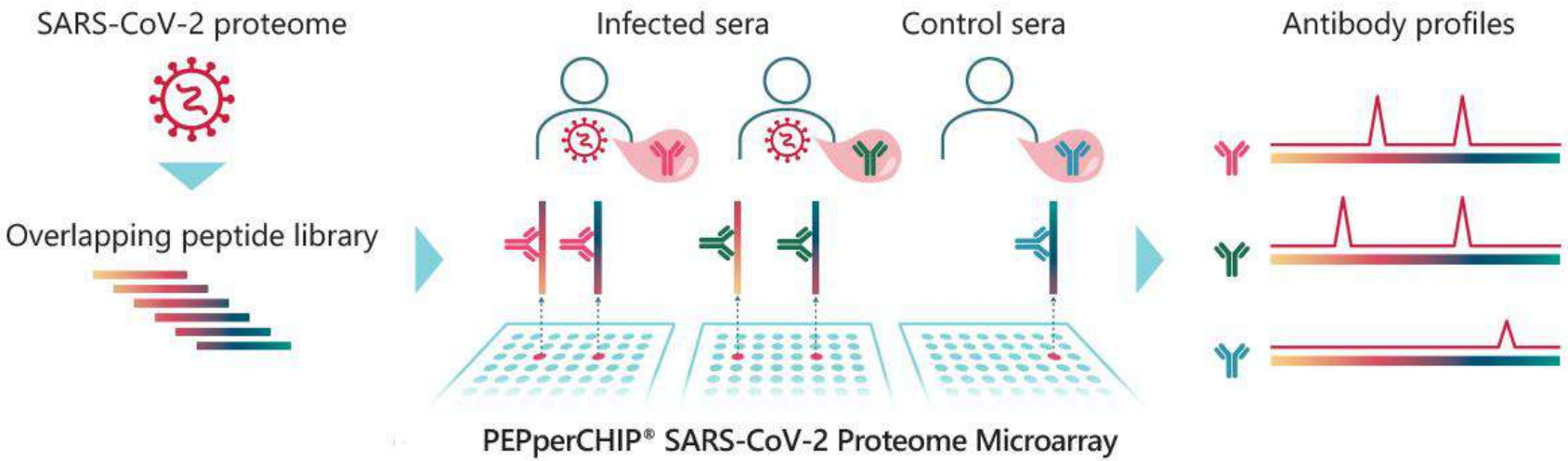
- virus neutralization

Significance to understand humoral responses:

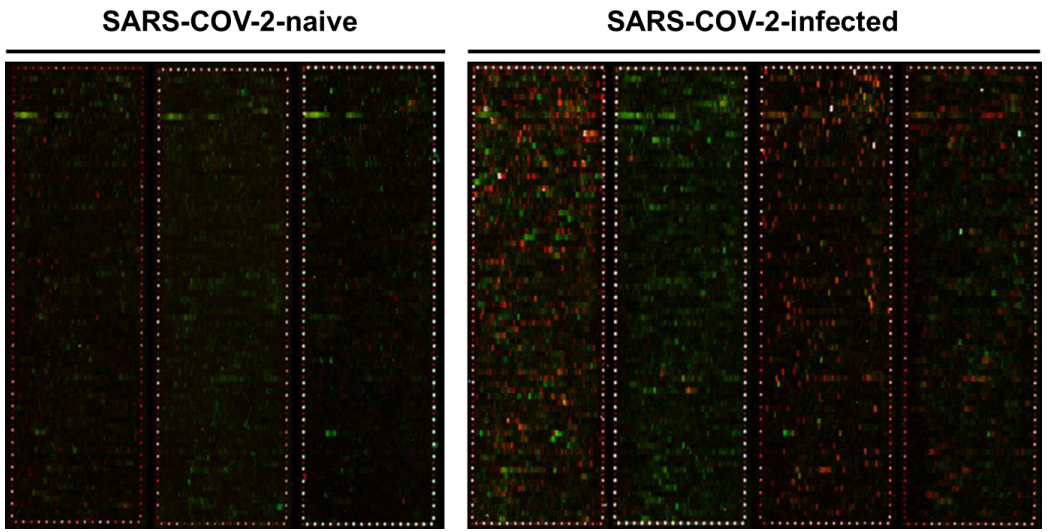
- strategies for active and passive immunization
- accurate serological diagnostics
- epidemiological studies



Proteome-wide antibody screening



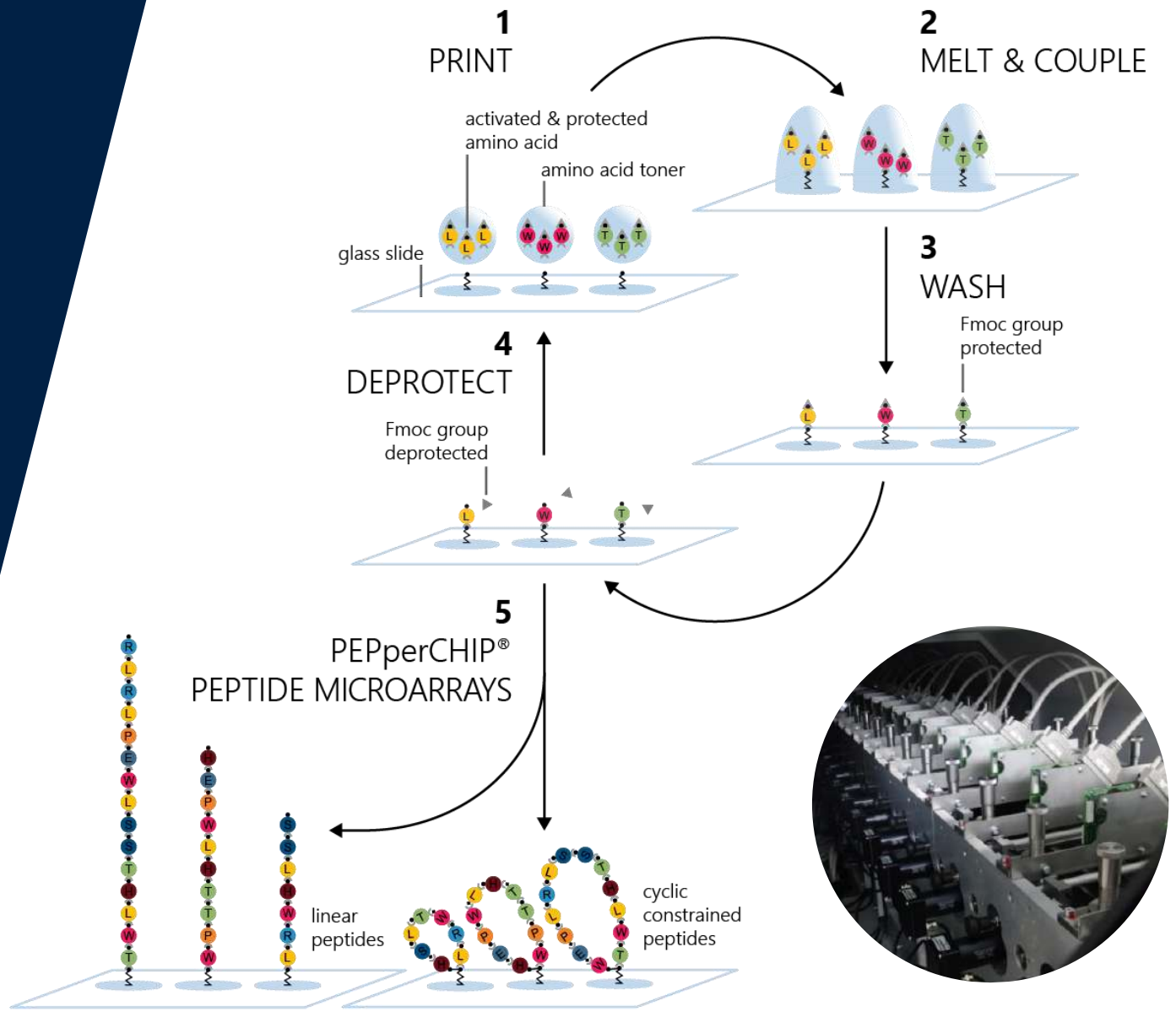
Whole proteome of SARS-CoV-2 isolate Wuhan-Hu-1 (GenBank ID: MN908947.3) translated into 4,883 individual peptides



Epitope-resolved view of antibody responses

Our Platform Technology

- High spot density (1,200 peptides/cm^2)
- Digital printing flexibility: multiple formats with high scalability
- Fast production times
- High peptide quality with routine double couplings
- Very low material consumption



SARS-CoV-2 proteome-wide antibody screening

frontiers in Immunology

ORIGINAL RESEARCH
published: 23 March 2021
doi: 10.3389/fimmu.2021.629185

SARS-CoV-2 Proteome-Wide Analysis Revealed Significant Epitope Signatures in COVID-19 Patients

Tatjana Schwarz[1†], Kirsten Heiss[2†], Yuvaraj Mahendran[2], Fiordiligie Casilag[2], Florian Kurth[3], Leif E. Sander[3], Clemens-Martin Wendtner[4], Manuela A. Hoechstetter[4], Marcel A. Müller[1], Renate Sekul[2], Christian Drosten[1,5], Volker Stadler[2‡] and Victor M. Corman[1,5*‡]*

[1] Institute of Virology, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany, [2] PEPperPRINT GmbH, R&D unit, Heidelberg, Germany, [3] Department of Infectious Diseases and Respiratory Medicine, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany, [4] Munich Clinic Schwabing, Academic Teaching Hospital, Ludwig-Maximilians University (LMU), Munich, Germany, [5] German Centre for Infection Research, Associated Partner Charité, Berlin, Germany

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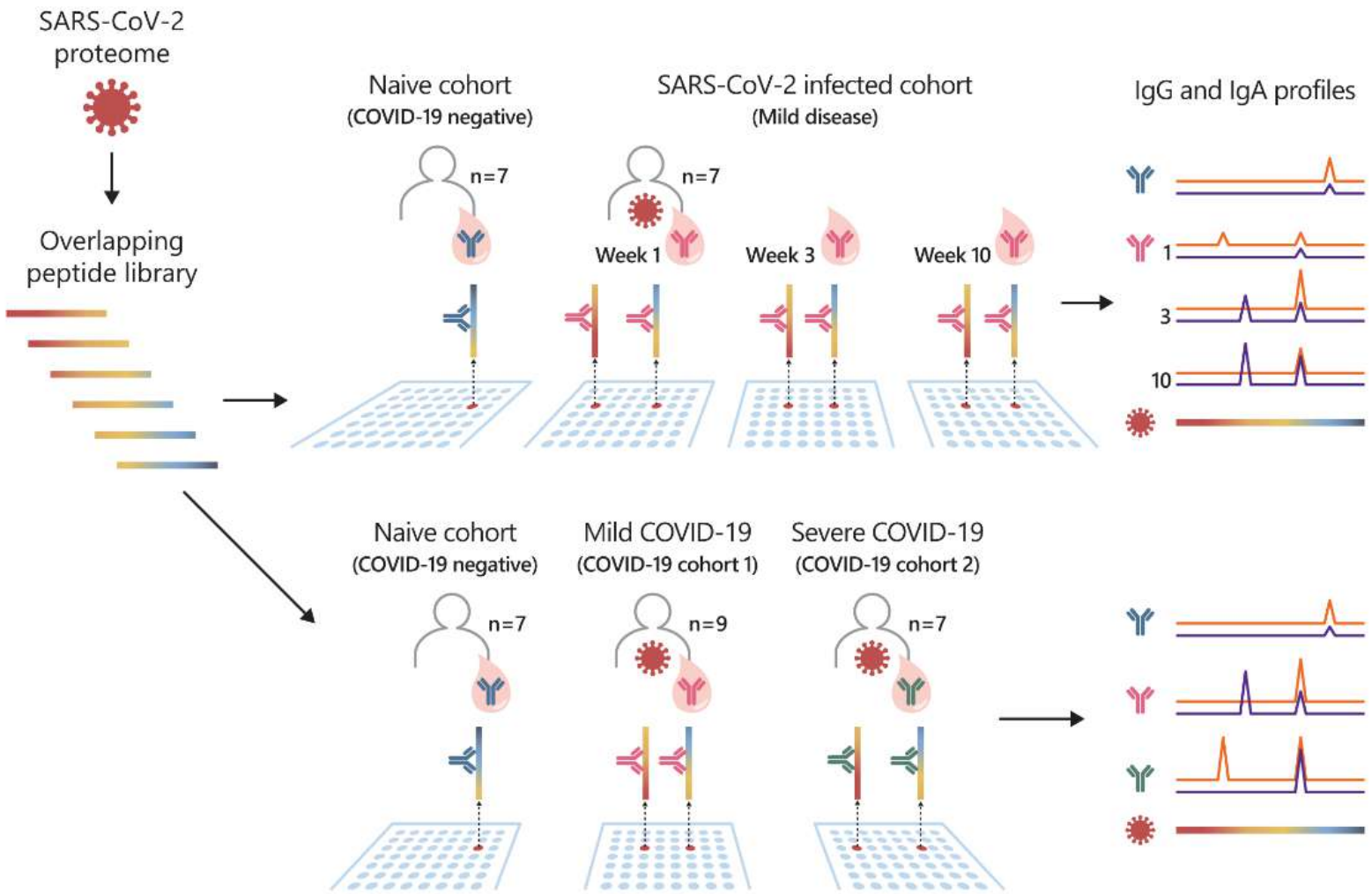
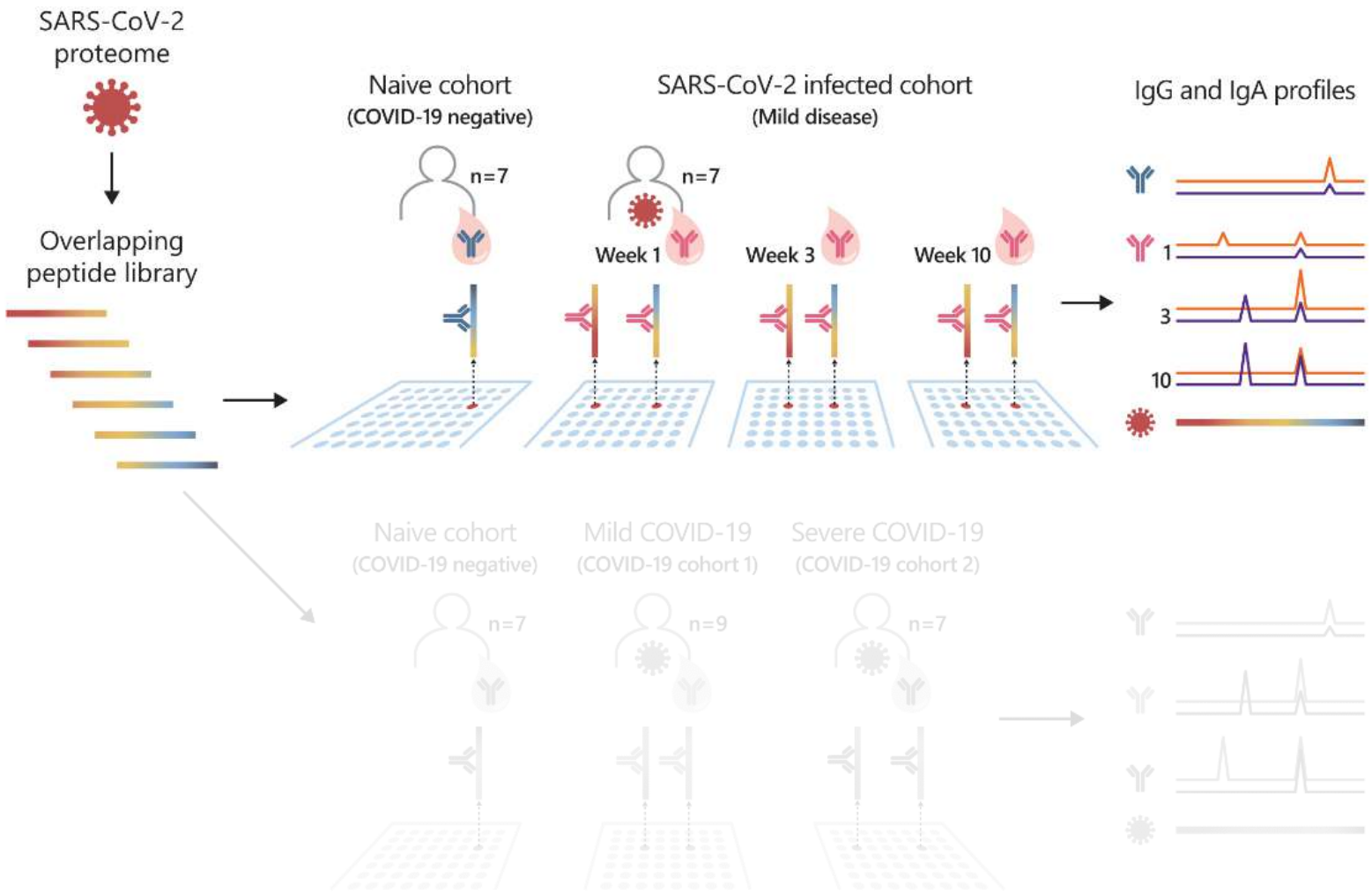
Edited by:
Sean X. Leng,
Johns Hopkins University,
United States

SARS-CoV-2 proteome-wide antibody screening



Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

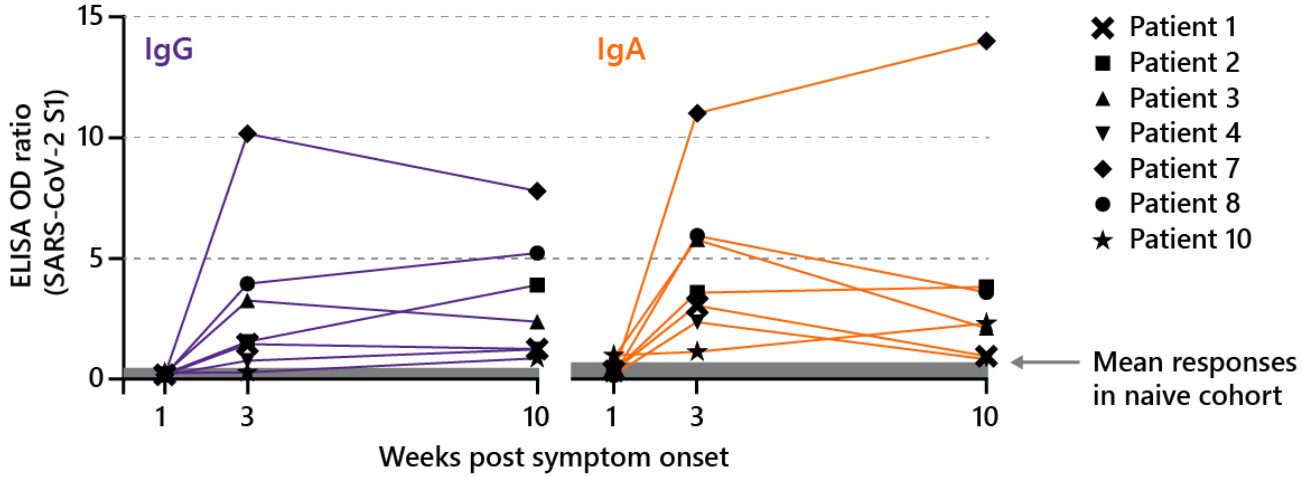
SARS-CoV-2 proteome-wide antibody screening



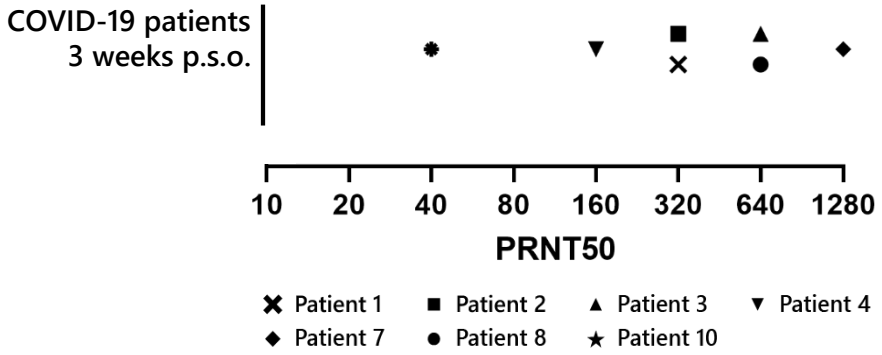
Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

Longevity of epitope-specific antibody responses

- **Longitudinal antibody response to SARS-CoV-2 Spike S1**

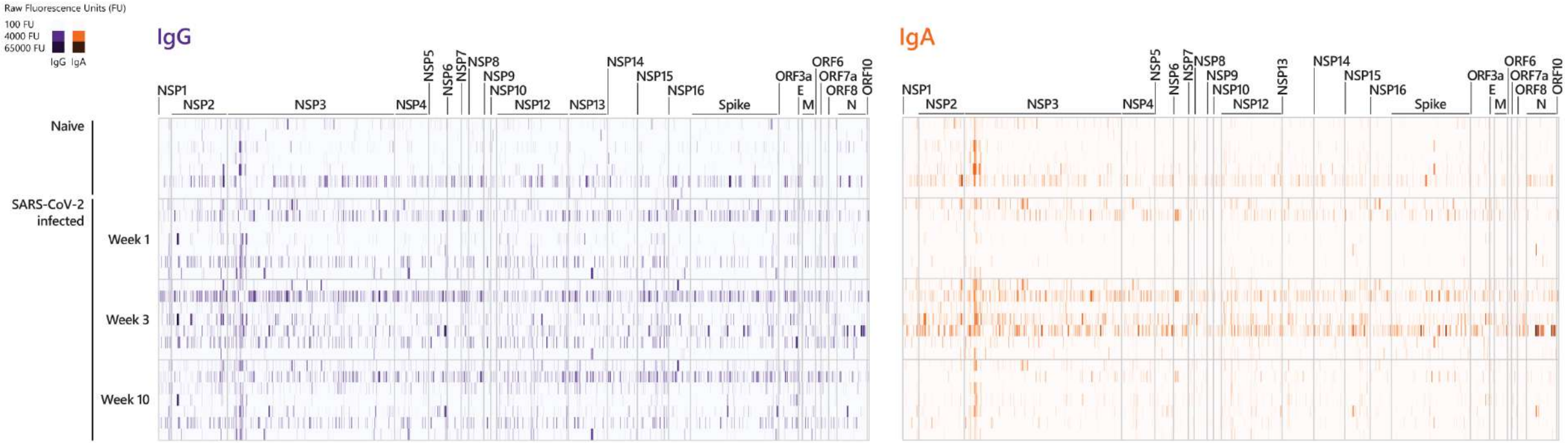


- **Neutralization titers**



Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185; Wölfel R. *et al*., (2020) *Nature* 581,465-469.

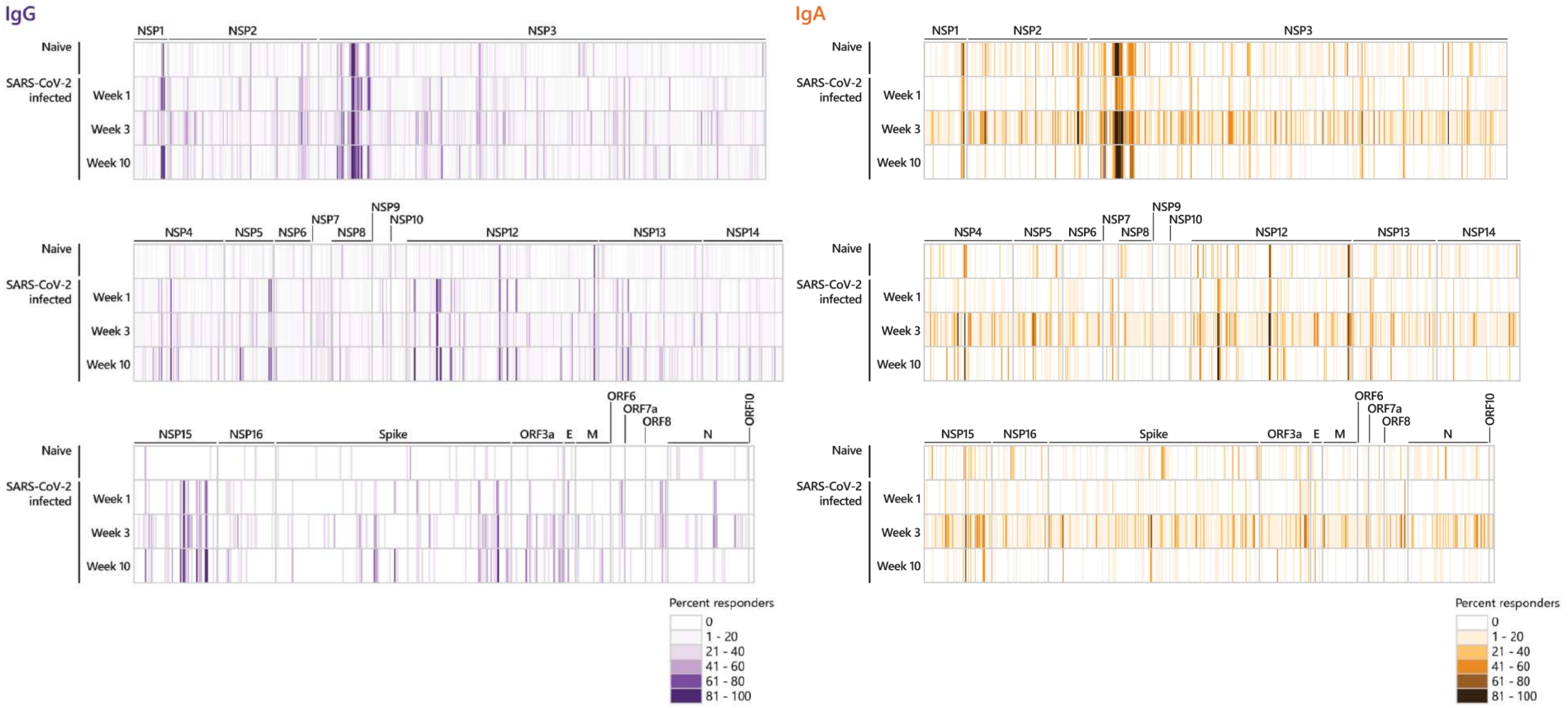
Longevity of epitope-specific antibody responses



- Heterogeneous breadth of antibody responses across COVID-19 patients for both IgG and IgA
- IgG: increasing epitope-specific antibody responses in most instances towards later time points
- IgA: early responses rather weak; peak in antibody responses 3 weeks p.s.o. before declining for most of the epitopes

Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

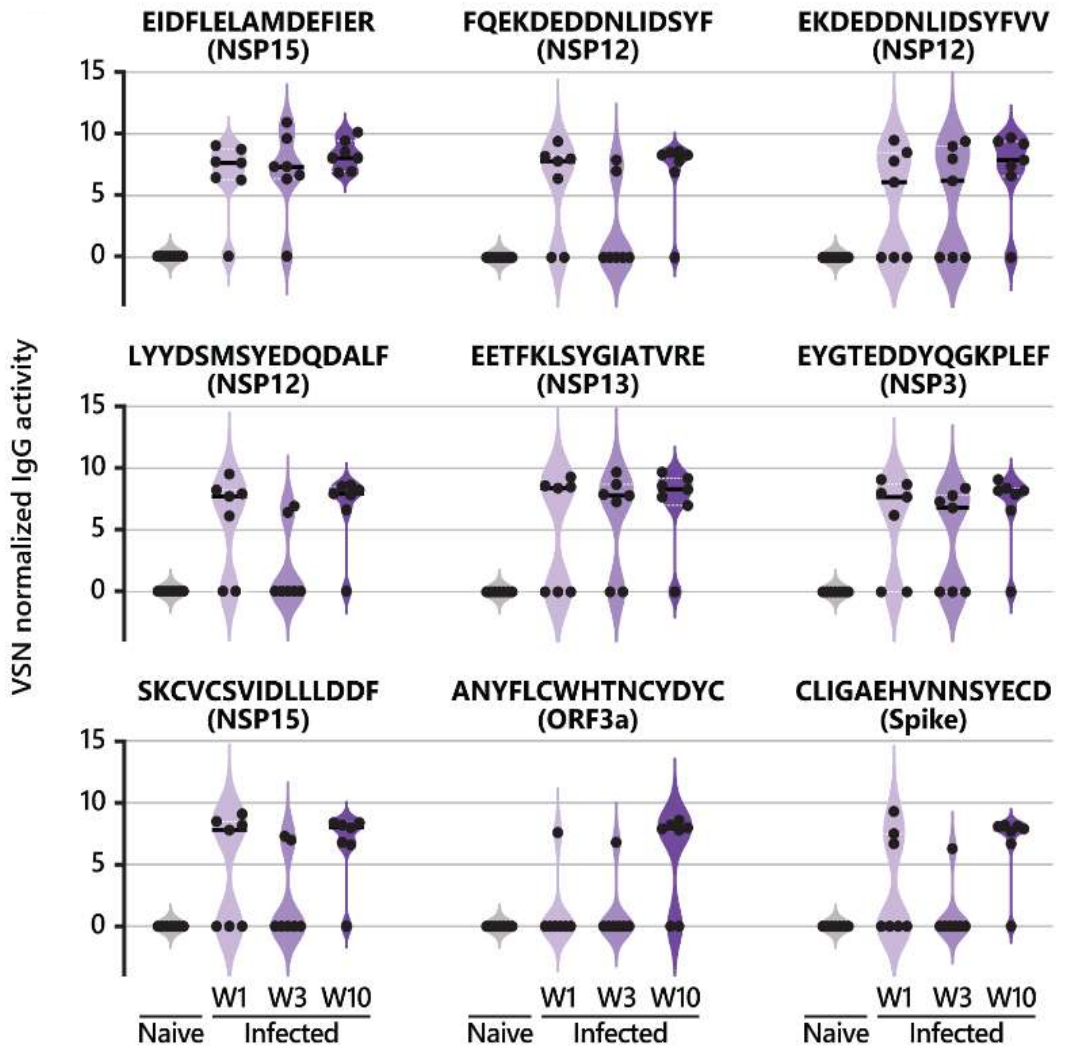
Longevity of epitope-specific antibody responses



Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

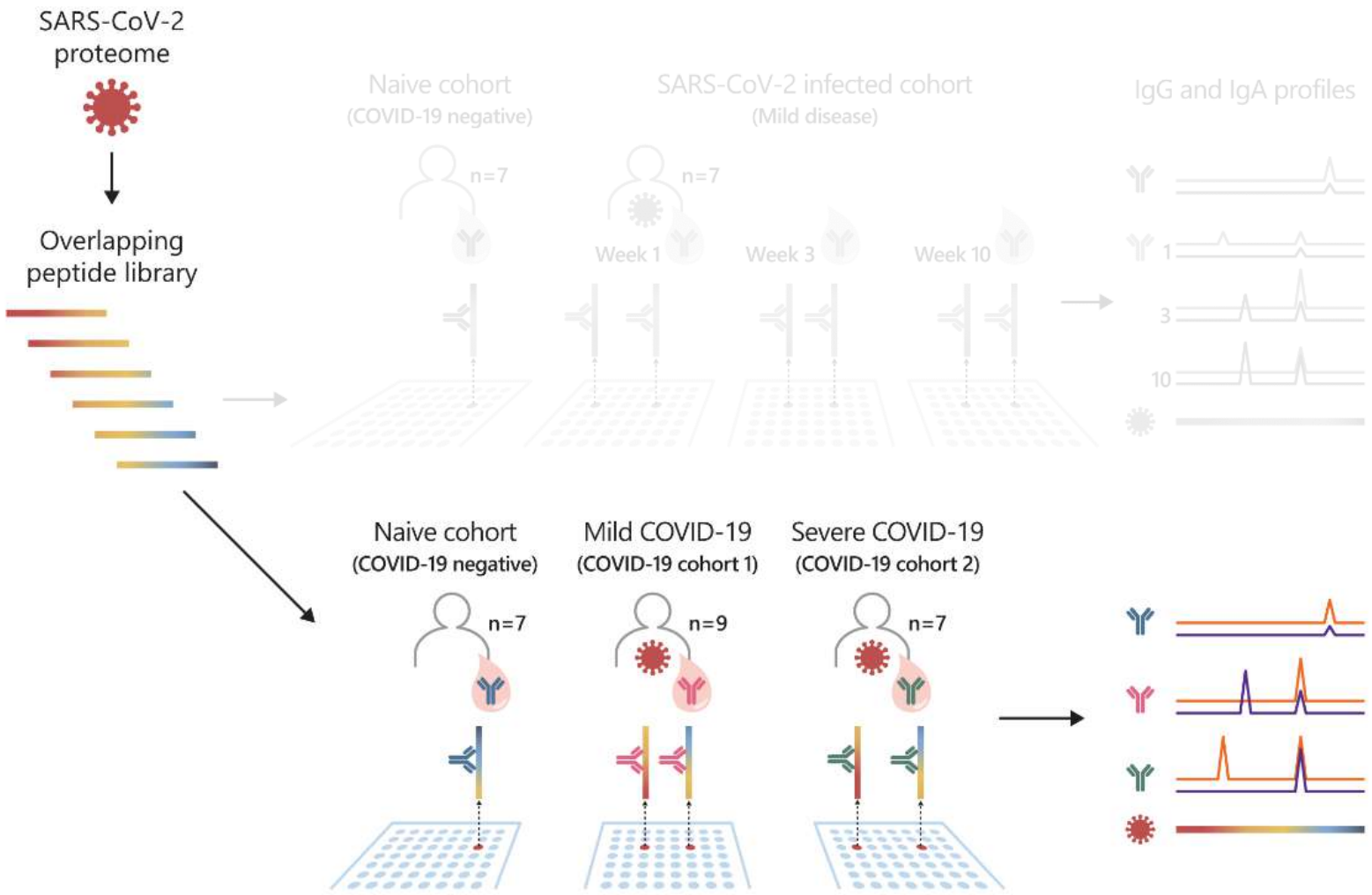
E_{6662}-R_{6676}: a potential serological marker

- Most epitopes could be assigned to proteins located in the ORF1a/b polyprotein
- Significant reactivity against a NSP15-derived peptide (E_{6662}-R_{6676}) across the entire time span of analysis
- The other peptides were only significant at the late convalescent phase
- Spike protein-derived epitope C_{649}-D_{663} is located in the S1 domain, adjacent to the S1/S2 cleavage site



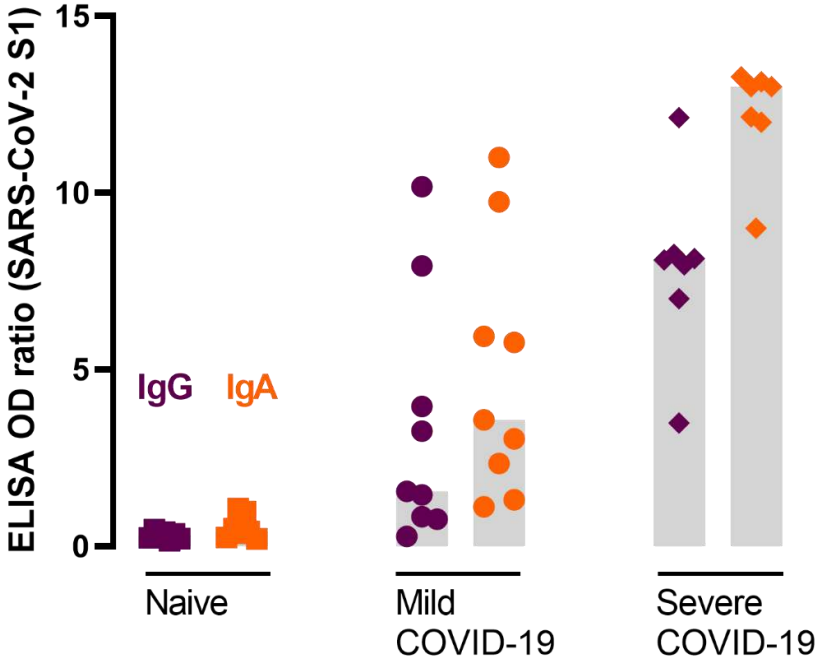
Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

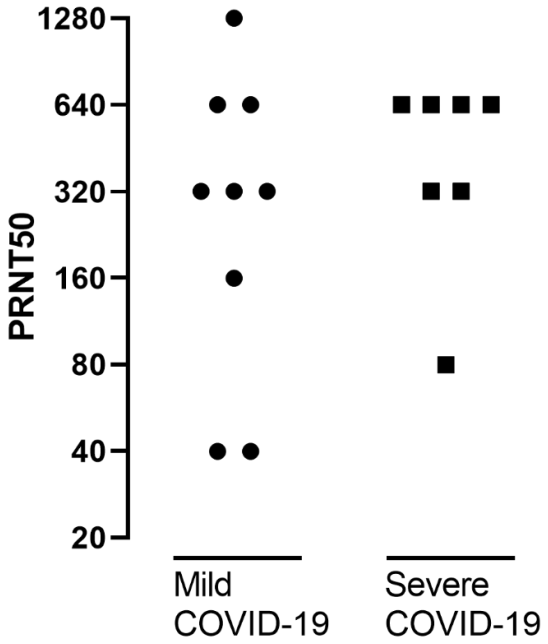
SARS-CoV-2 proteome-wide antibody screening



Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

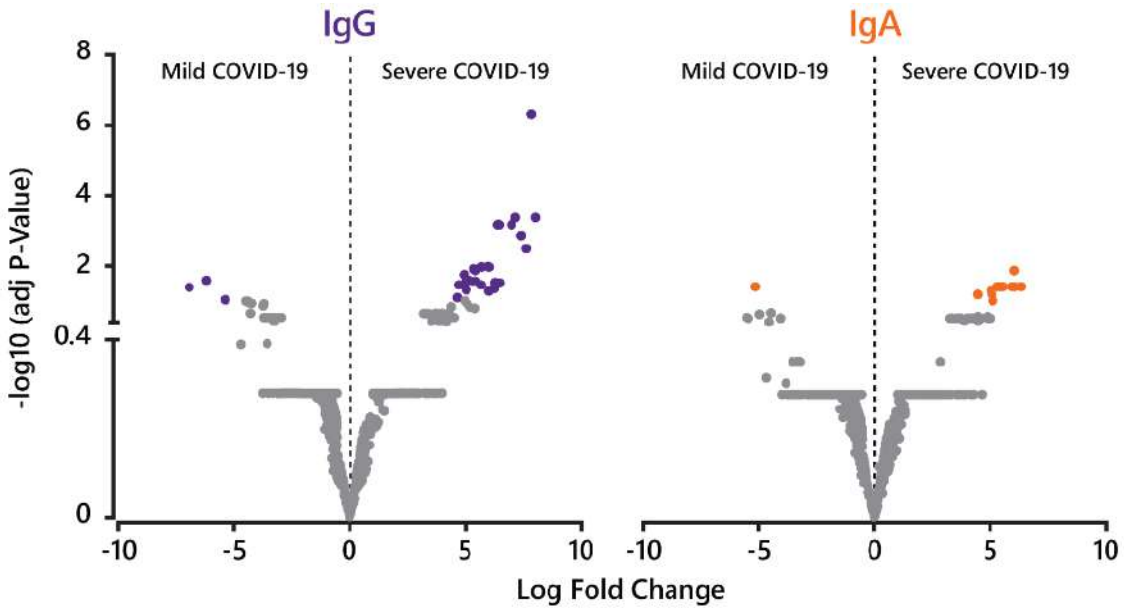
Higher antibody response against S1 in severe COVID-19

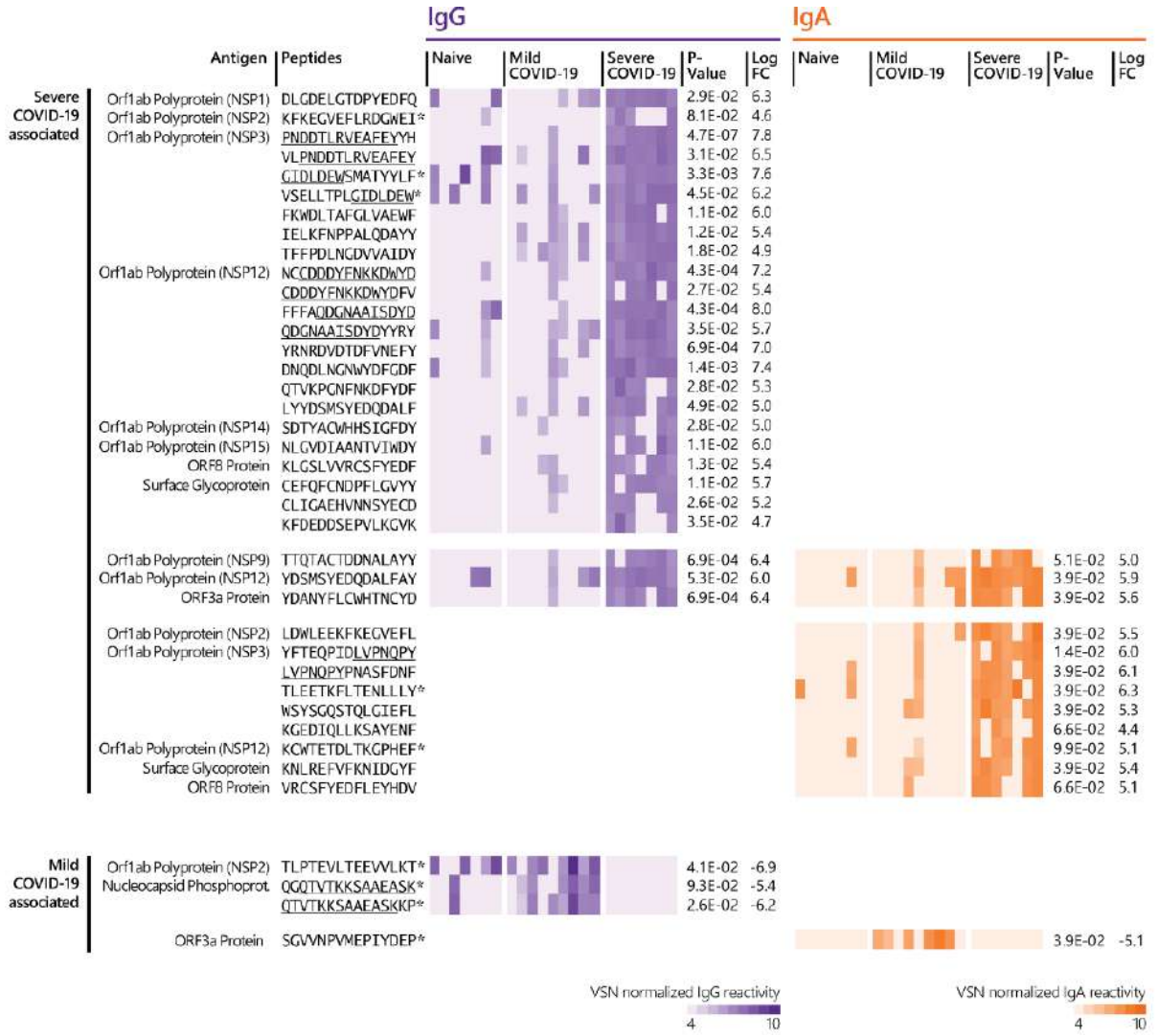




Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

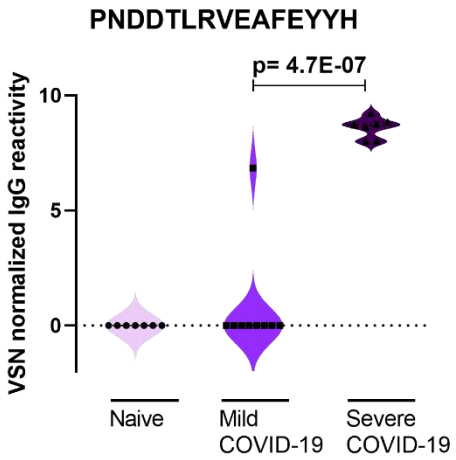
Epitope signatures in mild & severe COVID-19

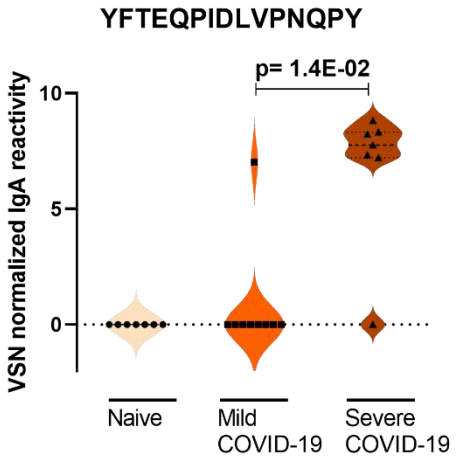


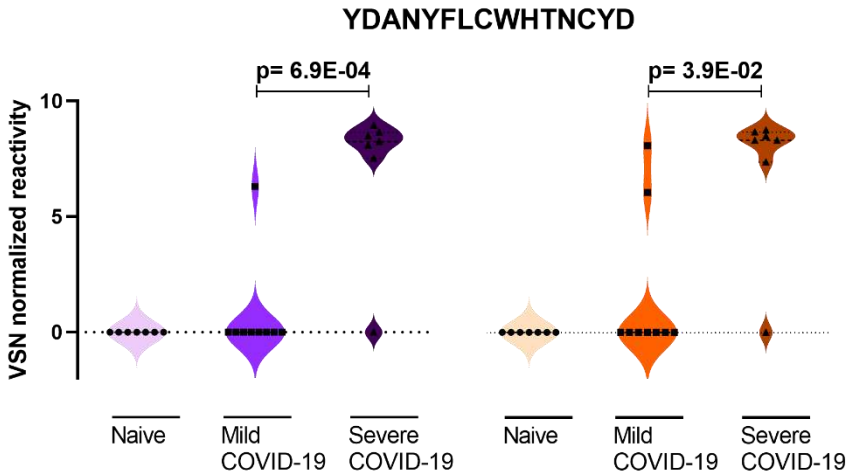


Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

Epitope recognition associated with severe COVID-19







Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

Conclusions

SARS-CoV-2 proteome-wide antibody screening identified:

- Antibody responses to linear B cell epitopes potentially applicable as serological markers of early and/or late SARS-CoV-2 infection
- Antibody responses to a Spike S1 epitope, which may interfere with furin-mediated cleavage
- Epitopes as potential biomarkers able to discriminate severe from mild COVID-19 disease courses
- Further validation of suitability as serological markers needed (e.g. larger patient cohorts)

Schwarz T., Heiss K., *et al*., (2021) *Front. Immunol*. 12:629185.

SARS-CoV-2 customer studies

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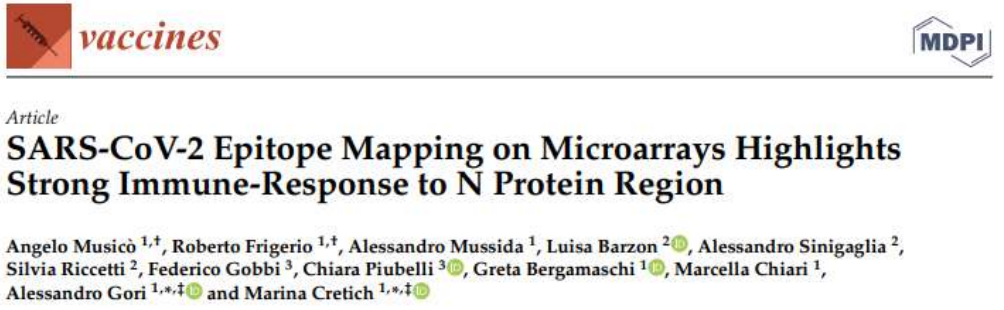
Vaccines and Antiviral Agents

SARS-CoV-2 spike protein stabilized in the closed state induces potent neutralizing responses.

George W. Carnell, Katarzyna A. Ciazynska, David A. Wells, Xiaoli Xiong, Ernest T. Aguinam, Stephen H. McLaughlin, Donna Mallery, Soraya Ebrahimi, Lourdes Ceron-Gutierrez, Benedikt Asbach, Sebastian Einhauser, Ralf Wagner, Leo C. James, Rainer Doffinger, Jonathan L. Heeney, John A. G. Briggs

DOI: 10.1128/JVI.00203-21

MRC Laboratory of Molecular Biology, anti-Spike responses


vaccines

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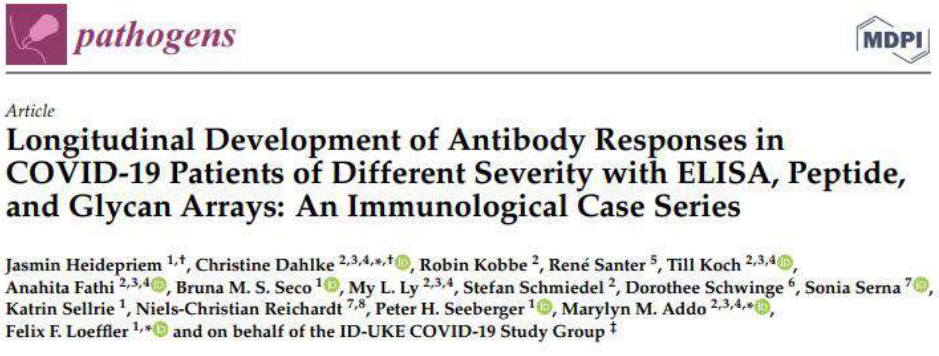
Article

SARS-CoV-2 Epitope Mapping on Microarrays Highlights Strong Immune-Response to N Protein Region

Angelo Musicò [1,†], Roberto Frigerio [1,†], Alessandro Mussida [1], Luisa Barzon [2], Alessandro Sinigaglia [2], Silvia Riccetti [2], Federico Gobbi [3], Chiara Piubelli [3], Greta Bergamaschi [1], Marcella Chiari [1], Alessandro Gori [1,*,‡] and Marina Cretich [1,*,‡]

National Research Council of Italy, proteome-wide screening


pathogens

MDPI

Article

Longitudinal Development of Antibody Responses in COVID-19 Patients of Different Severity with ELISA, Peptide, and Glycan Arrays: An Immunological Case Series

Jasmin Heidepriem [1,†], Christine Dahlke [2,3,4,*,†], Robin Kobbe [2], René Santer [5], Till Koch [2,3,4], Anahita Fathi [2,3,4], Bruna M. S. Seco [1], My L. Ly [2,3,4], Stefan Schmiedel [2], Dorothee Schwinge [6], Sonia Serna [7], Katrin Sellrie [1], Niels-Christian Reichardt [7,8], Peter H. Seeberger [1], Marylyn M. Addo [2,3,4,*], Felix F. Loeffler [1,*] and on behalf of the ID-UKE COVID-19 Study Group [‡]

MPI of Colloids and Interfaces, proteome-wide screening


Hindawi
Journal of Immunology Research
Volume 2020, Article ID 9465398, 8 pages
https://doi.org/10.1155/2020/9465398

Hindawi

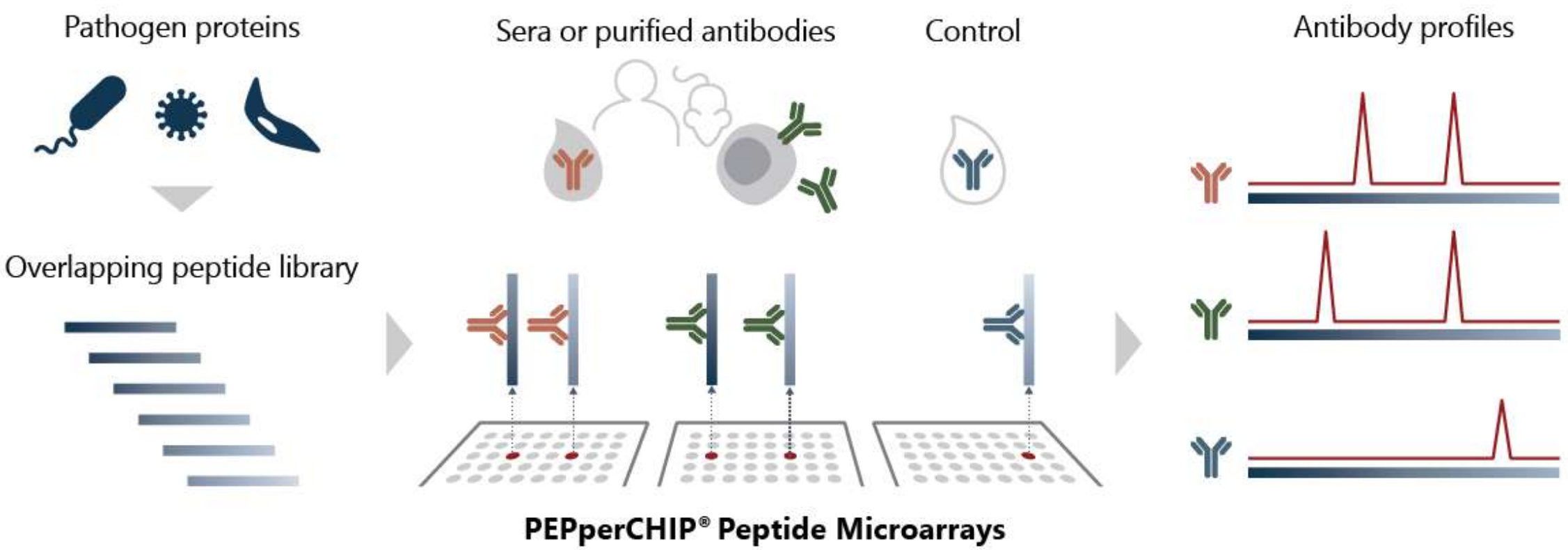
Research Article

Generation of Chicken IgY against SARS-COV-2 Spike Protein and Epitope Mapping

Yan Lu [1], Yajun Wang [2], Zhen Zhang [3], Jingliang Huang [4], Meicun Yao [5], Guobin Huang [6], Yuanyuan Ge [6], Peichun Zhang [1], Huaxin Huang [1], Yong Wang [7], Huiliang Li [2] and Wen Wang [1]

Huamin Medicine Co Ltd, anti-Spike responses

Applications for peptide microarrays



Vaccine development & monitoring

Discriminative epitope biomarkers for diagnostics

Epitope mapping

Vaccine development & monitoring

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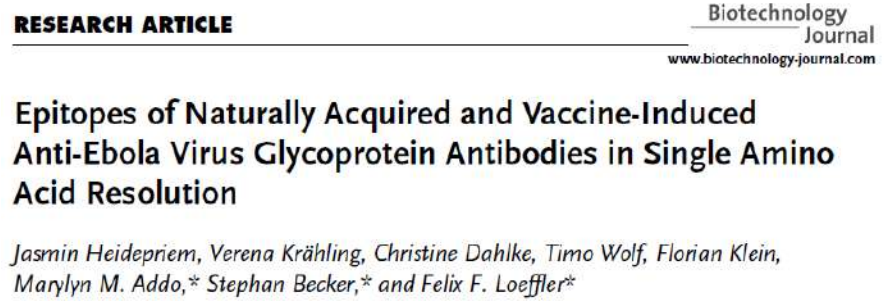
www.nature.com/npjvaccines

ARTICLE OPEN

Immunization with full-length *Plasmodium falciparum* merozoite surface protein 1 is safe and elicits functional cytophilic antibodies in a randomized first-in-human trial

Antje Blank[1,9], Kristin Fürle[2,9], Anja Jäschke[2,9], Gerd Mikus[1], Monika Lehmann[3], Johannes Hüsing[3], Kirsten Heiss[4], Thomas Giese[5], Darrick Carter[6], Ernst Böhnlein[7], Michael Lanzer[2,10*], Walter E. Haefeli[1,10*] and Hermann Bujard[7,8,10]

Heidelberg Hospital & Sumaya Biotech, Malaria Vaccine Phase 1 Trial



RESEARCH ARTICLE

Biotechnology Journal
www.biotechnology-journal.com

Epitopes of Naturally Acquired and Vaccine-Induced Anti-Ebola Virus Glycoprotein Antibodies in Single Amino Acid Resolution

Jasmin Heidepriem, Verena Krähling, Christine Dahlke, Timo Wolf, Florian Klein, Marylyn M. Addo, Stephan Becker,* and Felix F. Loeffler**

BNI for Tropical Medicine, EBOV Antibody Signatures

npj | Vaccines

www.nature.com/npjvaccines

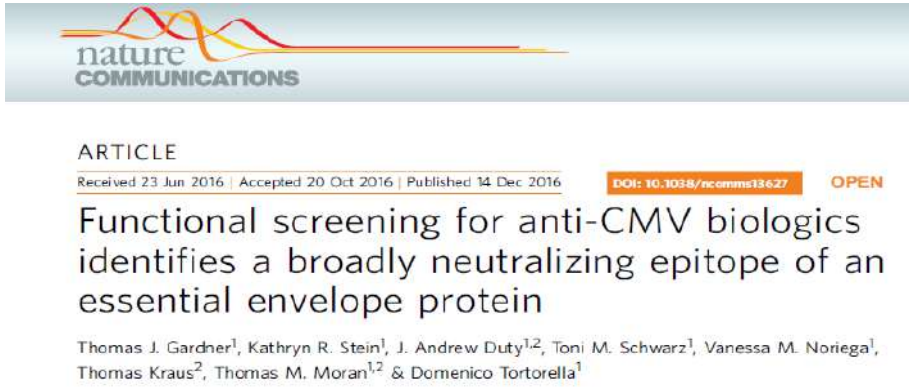
ARTICLE OPEN

Check for updates

Immunization of mice with chimeric antigens displaying selected epitopes confers protection against intestinal colonization and renal damage caused by Shiga toxin-producing *Escherichia coli*

David A. Montero[1,2], Felipe Del Canto[1], Juan C. Salazar[1], Sandra Céspedes[1], Leandro Cádiz[1], Mauricio Arenas-Salinas[3], José Reyes[4], Ángel Oñate[4] and Roberto M. Vidal[1,5]

Universidad de Chile, Epitope Screening for Antigen Design



nature COMMUNICATIONS

ARTICLE

Received 23 Jun 2016 | Accepted 20 Oct 2016 | Published 14 Dec 2016

DOI: 10.1038/ncomms13627 OPEN

Functional screening for anti-CMV biologics identifies a broadly neutralizing epitope of an essential envelope protein

Thomas J. Gardner[1], Kathryn R. Stein[1], J. Andrew Duty[1,2], Toni M. Schwarz[1], Vanessa M. Noriega[1], Thomas Kraus[2], Thomas M. Moran[1,2] & Domenico Tortorella[1]

Icahn School of Medicine, Immunotherapeutics and Vaccines

Biomarker discovery & epitope mapping

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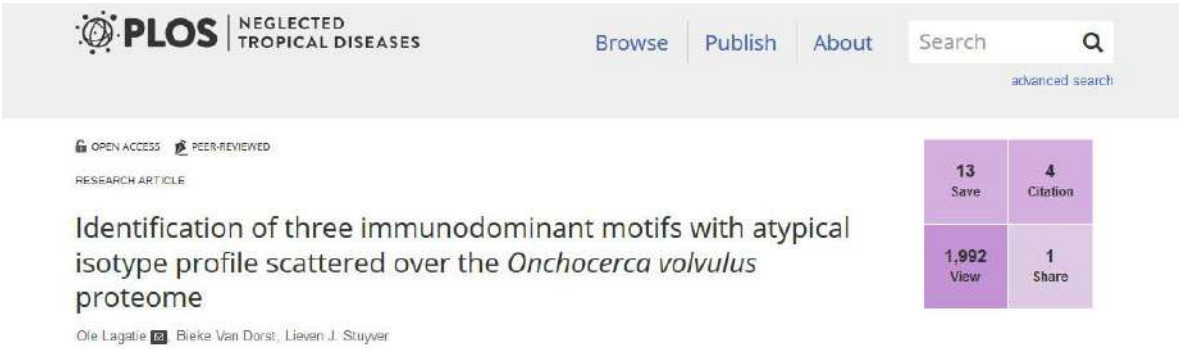
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RESEARCH ARTICLE

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Ole Lagatie, Bieke Van Dorst, Lieven J. Stuyver

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Janssen Diagnostics, Proteome-wide Epitope Mappings


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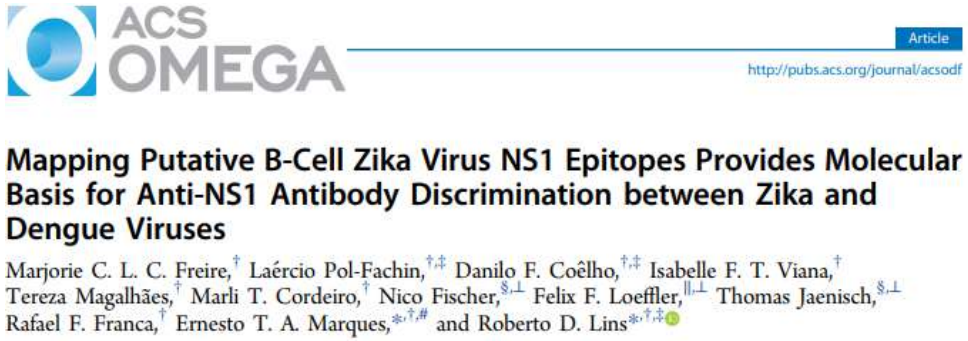
Identification of a Zika NS2B epitope for which absence of IgG response is associated with severe neurological symptoms and the design of a biomarker capable of discriminatory diagnostics between severe and non-severe clinical phenotypes

Felix F. Loeffler[a,¶], Isabelle F.T. Viana[b,¶], Nico Fischer[c], Danilo F. Coêlho[b,d], Carolina S. Silva[e], Antônio F. Purificação Jr.[b], Catarina M.C.S. Araújo[b], Bruno H.S. Leite[b], Ricardo Durães-Carvalho[f], Tereza Magalhães[g], Clarice N.L. Morais[b], Marli T. Cordeiro[b], Roberto D. Lins[2,&], Ernesto T.A. Marques[b,h,&] and Thomas Jaenisch[c,i,&,*]

Heidelberg Hospital & Aggeu Magalhães Institute, Epitope mapping


ACS OMEGA

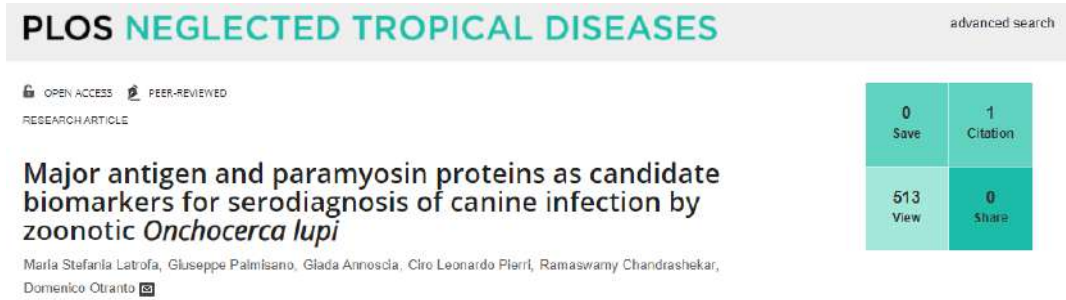
Article

http://pubs.acs.org/journal/acsodf

Mapping Putative B-Cell Zika Virus NS1 Epitopes Provides Molecular Basis for Anti-NS1 Antibody Discrimination between Zika and Dengue Viruses

Marjorie C. L. C. Freire,[†] Laércio Pol-Fachin,[†,‡] Danilo F. Coêlho,[†,‡] Isabelle F. T. Viana,[†] Tereza Magalhães,[†] Marli T. Cordeiro,[†] Nico Fischer,[§,⊥] Felix F. Loeffler,[∥,⊥] Thomas Jaenisch,[§,⊥] Rafael F. Franca,[†] Ernesto T. A. Marques,[*,†,#] and Roberto D. Lins[*,†,‡]

Aggeu Magalhães Institute & Federal University of Pernambuco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RESEARCH ARTICLE

Major antigen and paramyosin proteins as candidate biomarkers for serodiagnosis of canine infection by zoonotic *Onchocerca lupi*

Maria Stefania Latrofa, Giuseppe Palmisano, Giada Annoscia, Ciro Leonardo Pierri, Ramaswamy Chandrashekar, Domenico Otranto

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University of Bari & Bu-Ali Sina University, Epitope mapping

Applications for peptide microarrays

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TARGET BINDER

ALLERGY RESEARCH

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Thank you for joining the webinar

Contact

Dr. Kirsten Heiss

Research & Development

PEPperPRINT GmbH
Tullastrasse 2
69126 Heidelberg, Germany

Visit us: www.pepperprint.com

Get in touch: info@pepperprint.com

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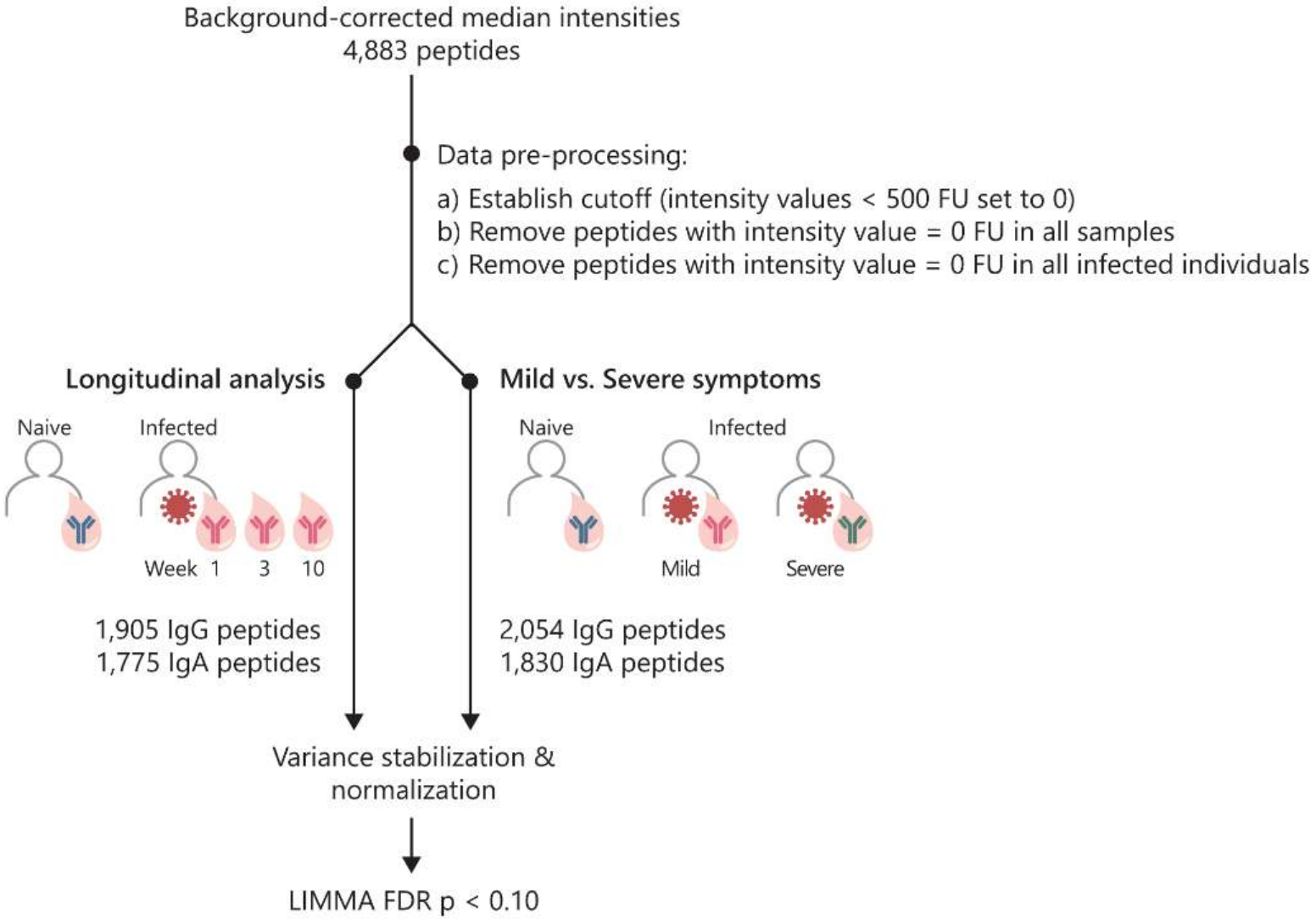
Appendix

Workflow for statistical analysis



FU=Fluorescence intensity units