

Immunoglobulin G glycosylation as a modulator of antiviral immunity

From acute respiratory virus infection to maternal and infant RSV immunisation

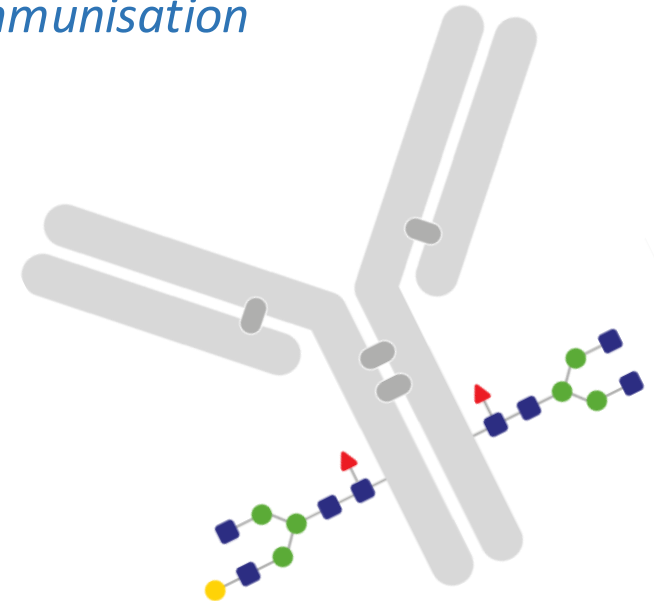
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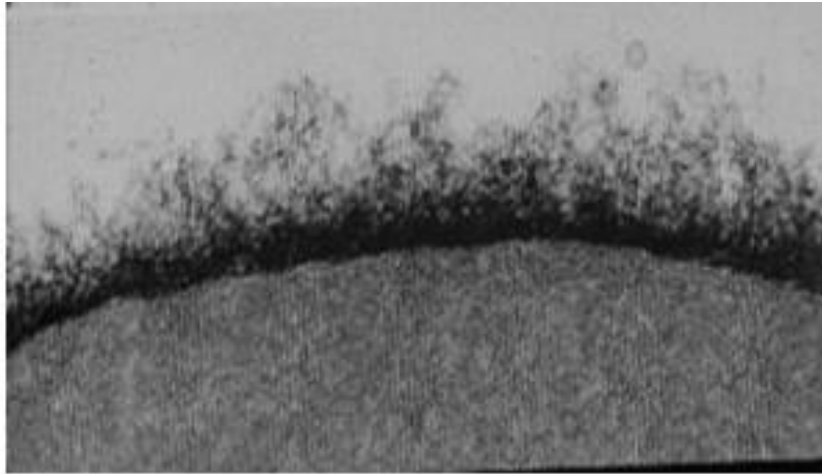
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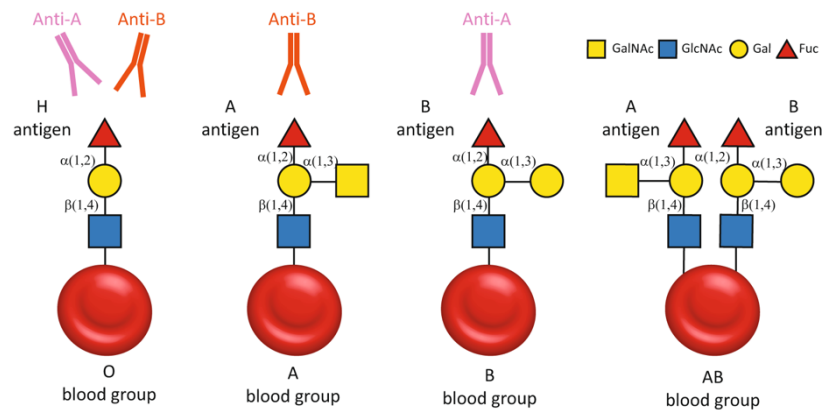


Protein glycosylation

- The most elaborate post-translational modification

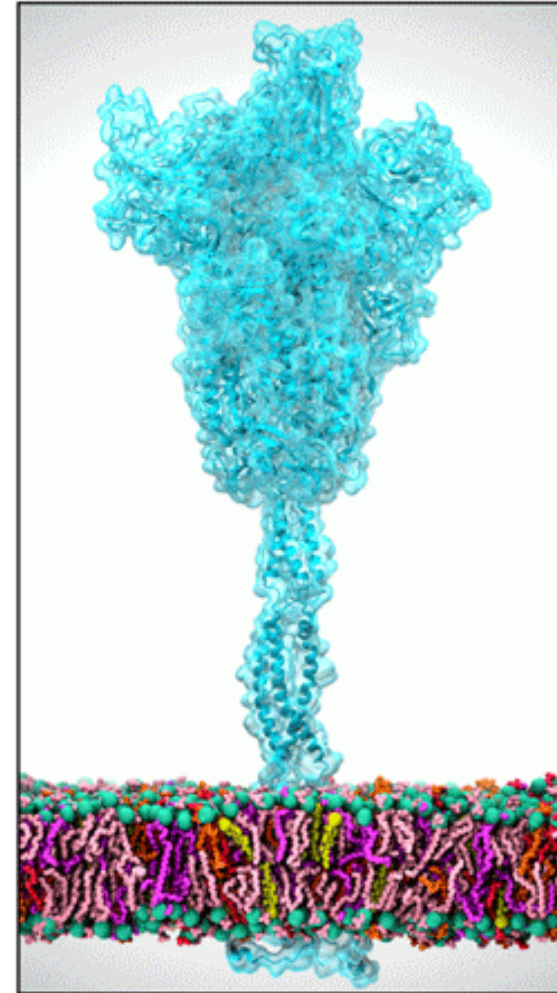


Voet and Voet, Biochemistry 4th edition. 2010



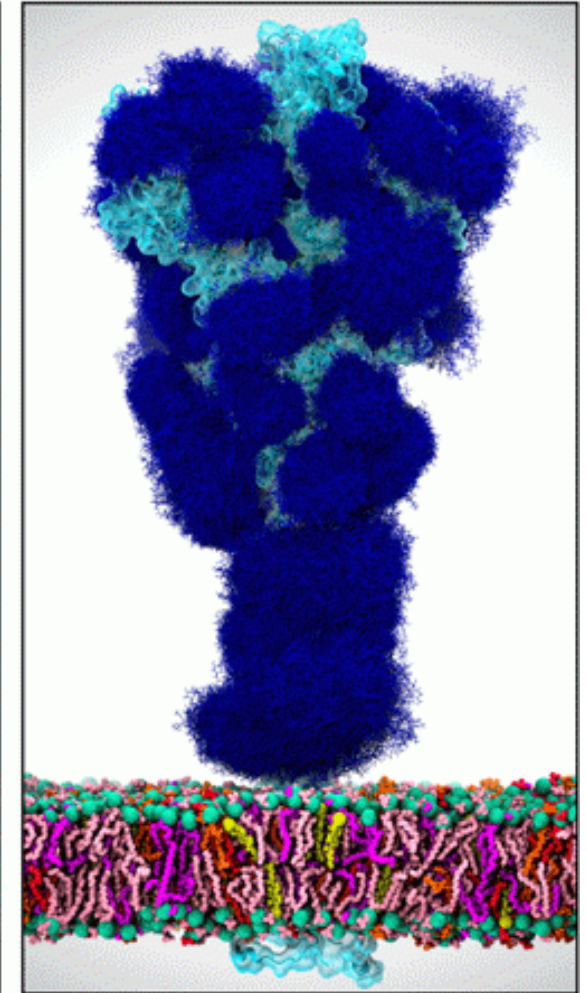
Anso et al. Nat Comm 2023

This is the **Spike**



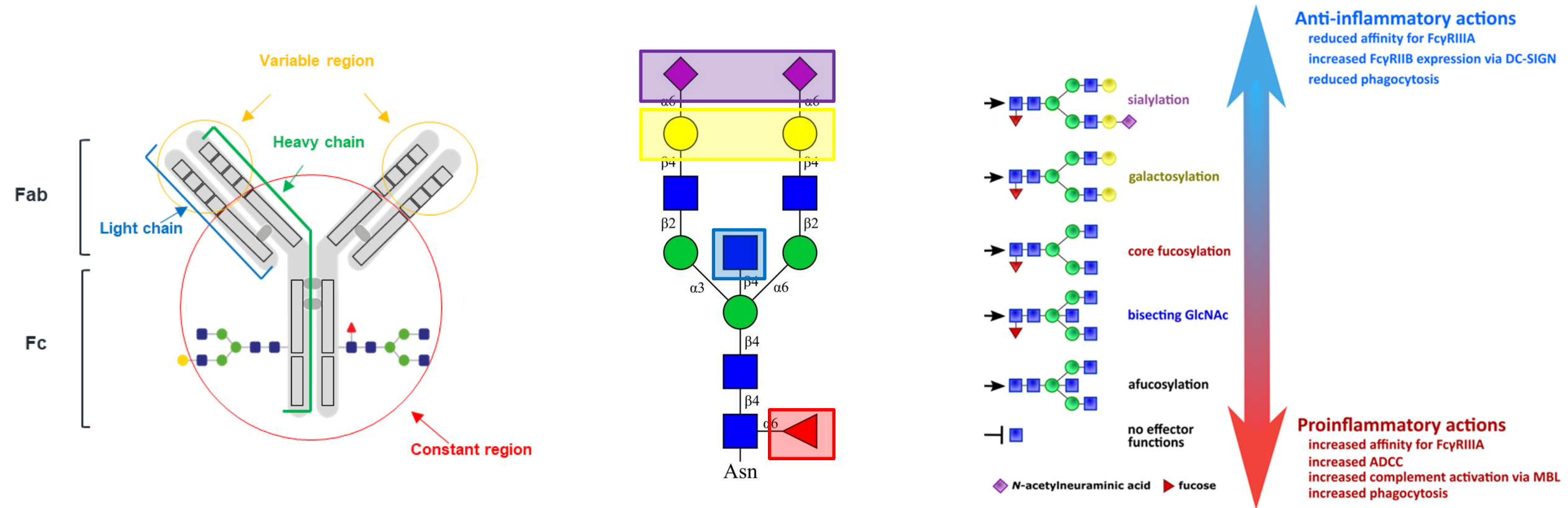
Casalino et al., ACS Cent. Sci. 2020

This is the **Spike** with **glycans**

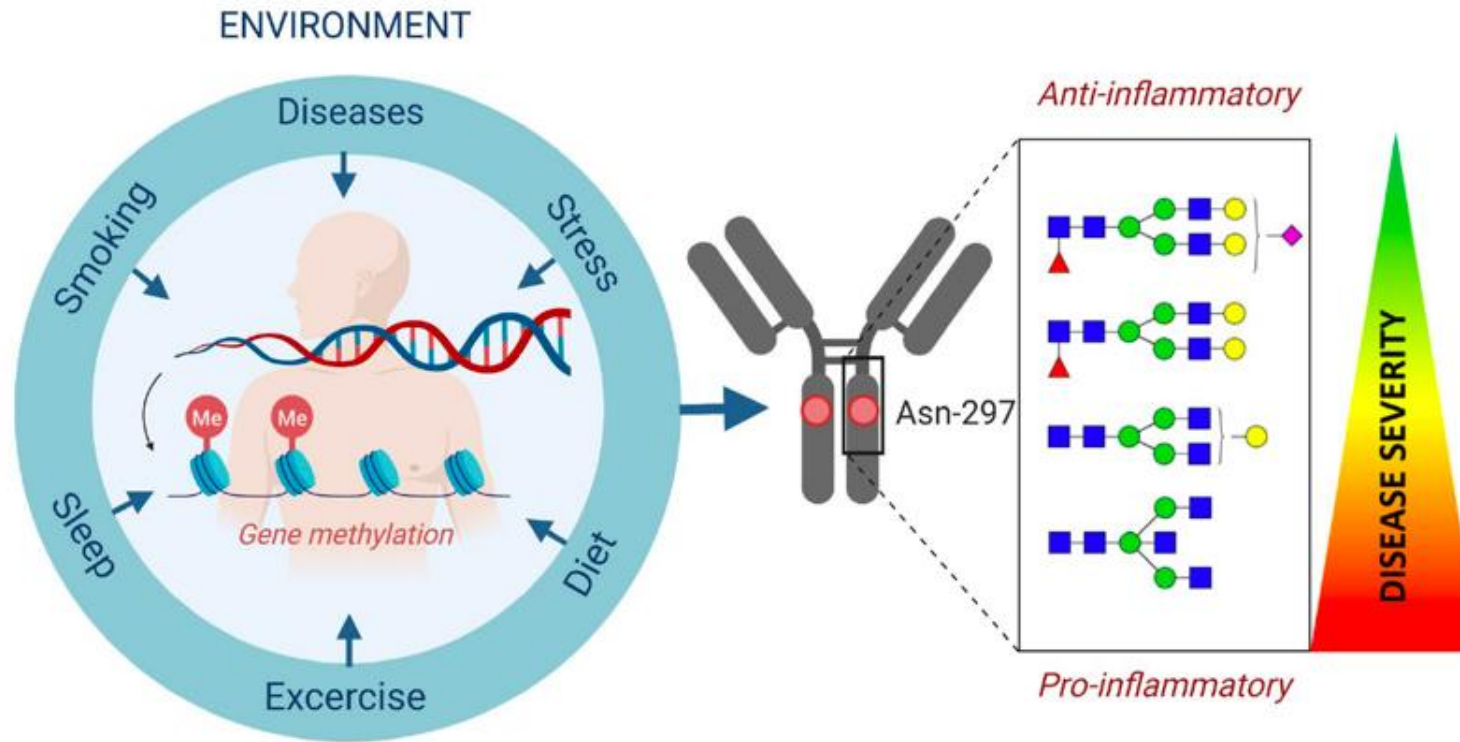


Every IgG carries a functional N-glycan at Asn297

- Each IgG heavy chain carries a conserved N-glycan at Asn297 of the Fc region.
- A biantennary core is variably decorated with galactose, sialic acid, core fucose and bisecting GlcNAc



The IgG glycome is a modifiable readout of immune status



- Regulated by large gene networks pleiotropic with age- and inflammation-related disease.
- Shifted by environment and lifestyle (smoking, stress, diet, sleep, exercise).
- IgG glycome changes track, and can precede, ageing-related and inflammatory disease.



The IgG glycome **changes up to a decade before** people are diagnosed with diabetes, CVD or inflammatory diseases

Diabetes Care



Plasma N-Glycans as Emerging Biomarkers of Cardiometabolic Risk: A Prospective Investigation in the EPIC-Potsdam Cohort Study

<https://doi.org/10.2337/dc19-1507>

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Diabetes
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& Care

Plasma N-glycome shows continuous deterioration as the diagnosis of insulin resistance approaches

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Original research



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N-glycans as functional effectors of genetic and epigenetic disease risk



Immunoglobulin G N-Glycosylation Signatures in Incident Type 2 Diabetes and Cardiovascular Disease

<https://doi.org/10.2337/dc22-0833>

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Markus Perola,^{10,11} Samira Mora,^{5,6}
Matthias B. Schulze,^{1,2,12}
Gordan Lauc,^{4,7} and
Clemens Wittenbecher^{1,3,13}



Glycosylation of Immunoglobulin G Associates With Clinical Features of Inflammatory Bowel Diseases

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Gastroenterology 2018;154:1320–1333

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Glycosylation Profile of Immunoglobulin G Is Cross-Sectionally Associated With Cardiovascular Disease Risk Score and Subclinical Atherosclerosis in Two Independent Cohorts

Gastroenterology 2018;155:829–843

Protein Glycosylation as a Diagnostic and Prognostic Marker of Chronic Inflammatory Gastrointestinal and Liver Diseases

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Gastroenterology 2020;158:95–110

Editorial

Glycomics and Cardiovascular Disease Advancing Down the Path Towards Precision

Patrick R. Lawler

Plasma N-Glycan Signatures Are Associated With Features of Inflammatory Bowel Diseases

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Gordan Lauc,² and Manfred Wuhrer¹



The IgG glycome in COVID-19

► Engineering (Beijing). 2022 Sep 6. doi: 10.1016/j.eng.2022.08.007. Online ahead of print.

Differences in Immunoglobulin G Glycosylation Between Influenza and COVID-19 Patients

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PMID: 36093331 PMCID: PMC9446557 DOI: 10.1016/j.eng.2022.08.007

► Glycobiology. 2021 May 3;31(4):372-377. doi: 10.1093/glycob/cwaa102.

Composition of the immunoglobulin G glycome associates with the severity of COVID-19

Tea Petrović¹, Inês Alves^{2 3 4}, Dario Bugada^{5 6}, Julio Pascual⁷, Frano Vučković¹, Andrea Skelin¹, Joana Gaifem^{2 3}, Judit Villar-Garcia⁷, Manuel M Vicente^{2 3 8}, Ângela Fernandes^{2 3}, Ana M Dias^{2 3}, Ivan-Christian Kurolt⁹, Alemka Markotić⁹, Dragan Primorac^{10 11 12 13 14 15}, Adriana Soares¹⁶, Luis Malheiro^{4 17}, Irena Trbojević-Akmačić¹, Miguel Abreu^{8 18}, Rui Sarmento E Castro^{8 18}, Silvia Bettinelli¹⁹, Annapaola Callegaro¹⁹, Marco Arosio¹⁹, Lorena Sangiorgio¹⁹, Luca F Lorini⁵, Xavier Castells⁷, Juan P Horcajada⁷, Salomé S Pinho^{2 3 4 8}, Massimo Allegri^{20 6}, Clara Barrios⁷, Gordan Lauc^{1 21}

Affiliations + expand

PMID: 33174592 PMCID: PMC7717252 DOI: 10.1093/glycob/cwaa102

► Eur J Immunol. 2022 Jun;52(6):946-957. doi: 10.1002/eji.202149491. Epub 2022 Apr 4.

Altered IgG glycosylation at COVID-19 diagnosis predicts disease severity

Manuel M Vicente^{1 2 3 4}, Inês Alves^{1 4 5}, Joana Gaifem^{1 4}, Cláudia S Rodrigues^{1 2 4}, Ângela Fernandes^{1 4}, Ana M Dias^{1 4}, Jerko Štambuk⁶, Tea Petrović⁶, Pedro Oliveira², Frederico Ferreira-da-Silva^{1 7}, Adriana Soares⁸, Nair Seixas⁹, Tiago Teixeira⁹, Luis Malheiro¹⁰, Miguel M Abreu¹¹, Gordan Lauc¹², Rui Sarmento E Castro¹¹, Salomé S Pinho^{1 2 4 5}

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PMID: 35307819 PMCID: PMC9087392 DOI: 10.1002/eji.202149491

Review

► Glycoconj J. 2021 Oct;38(5):611-623. doi: 10.1007/s10719-021-10021-z.

Epub 2021 Sep 20.

SARS-CoV-2 S glycoprotein binding to multiple host receptors enables cell entry and infection

Irena Trbojević-Akmačić¹, Tea Petrović², Gordan Lauc^{2 3}

Affiliations + expand

PMID: 34542788 PMCID: PMC8450557 DOI: 10.1007/s10719-021-10021-z

► Adv Exp Med Biol. 2021;1325:239-264. doi: 10.1007/978-3-030-70115-4_12.

The Importance of Glycosylation in COVID-19 Infection

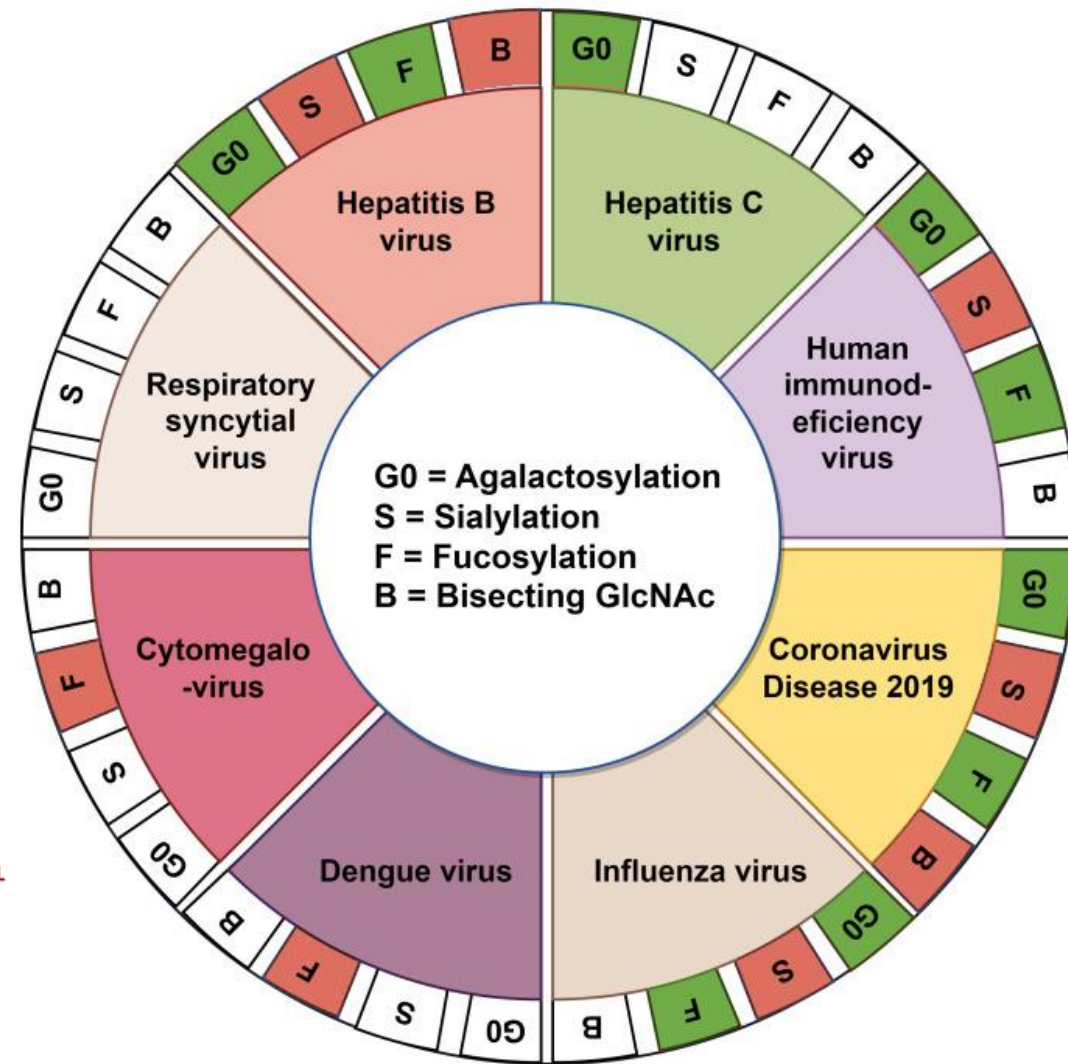
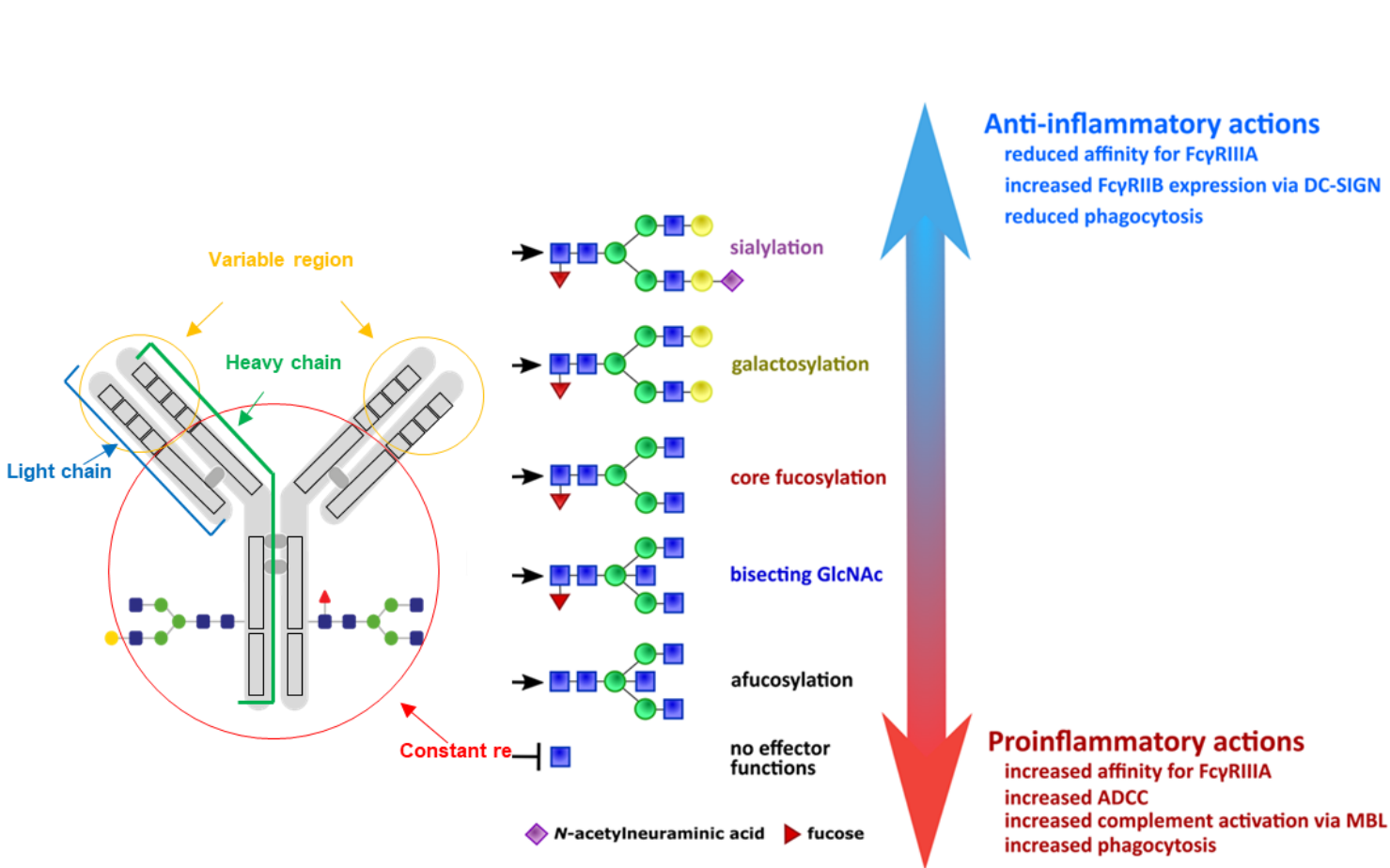
Tea Petrović¹, Gordan Lauc^{1 2}, Irena Trbojević-Akmačić³

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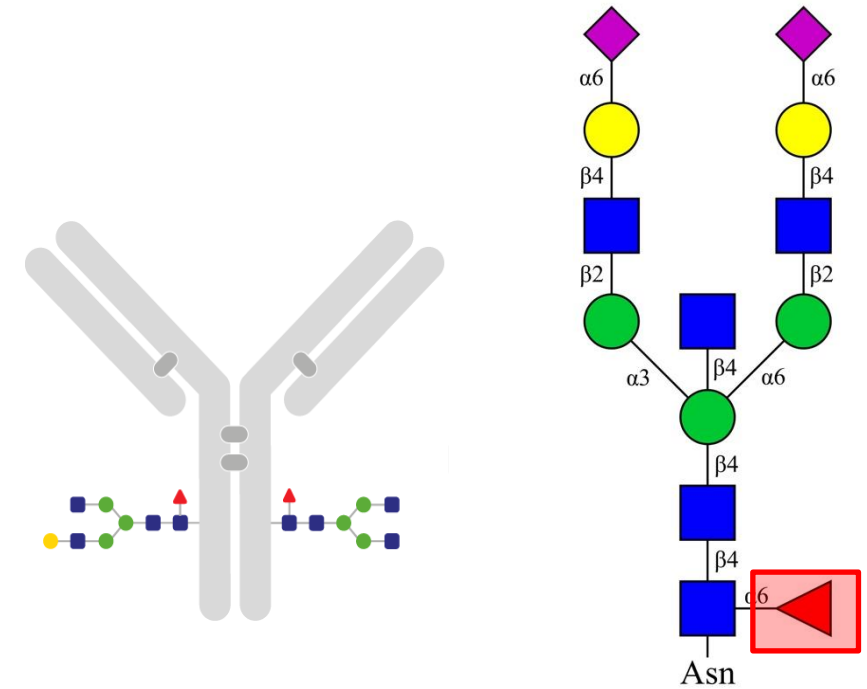
PMID: 34495539 DOI: 10.1007/978-3-030-70115-4_12



IgG glycosylation differs depending on the virus



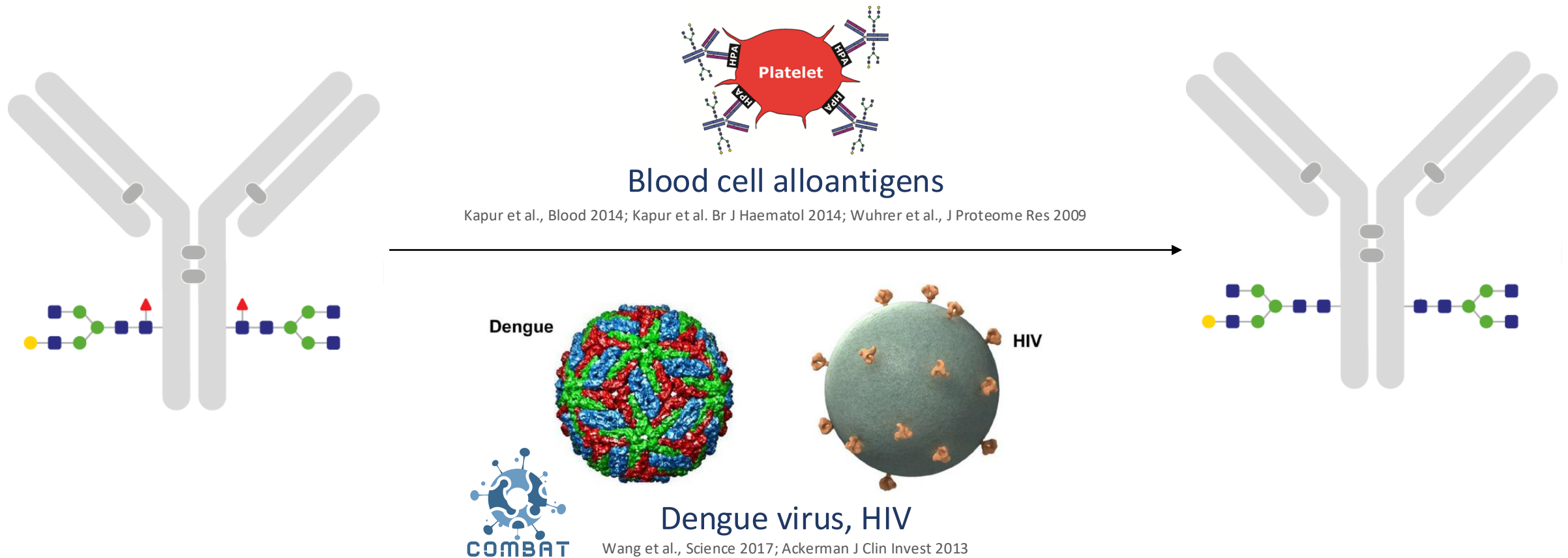
The fucosylation case



- Exceptionally stable
- Considered a protective mechanism
- Absence causes 30-40x stronger binding to FcγRIIIa



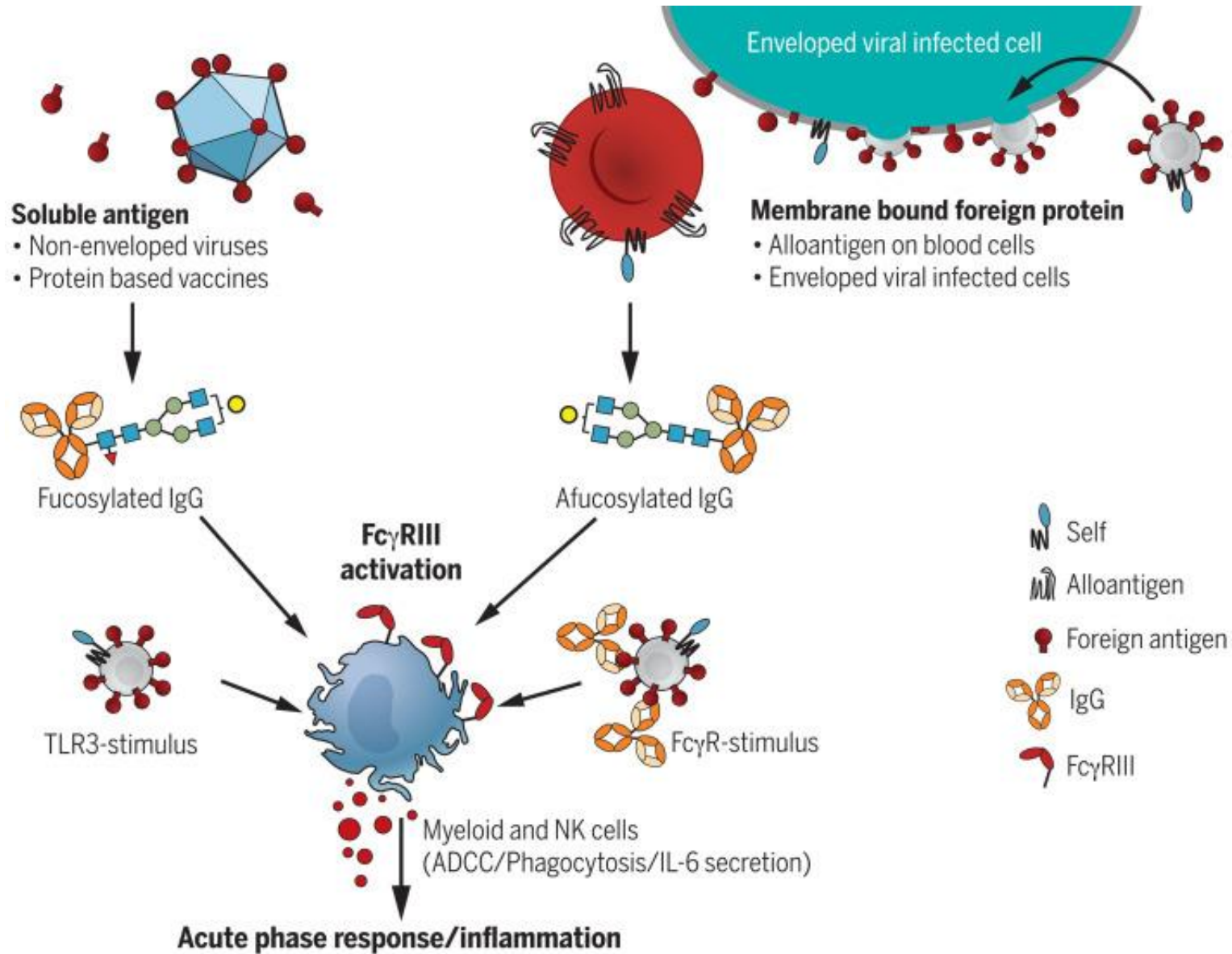
The fucosylation case



The IgG glycome shifts from ~95% to as low as ~10% core fucosylated



Afucosylated IgG: a hallmark of enveloped-virus responses



Open question: does vaccination reshape the same glyco-features?

PIPELINE (Pregnancy and Infant PrEparedness pLatform IN Europe) *glycomics in maternal & infant RSV immunisation*

- Horizon Europe adaptive platform trial for pandemic preparedness; the RSV trial focuses on RSV prevention in pregnancy and infancy: maternal vaccine (RSVpreF) vs infant mAb (nirsevimab) vs both.
- Genos hop-on adds high-throughput IgG and IgA Fc glycomics as a new molecular layer on the 90-infant immunity substudy.
- Infants depend on maternally derived IgG in the first months of life; Fc glycans set placental transfer efficiency and effector function.
- Whether maternal vaccination or infant monoclonal antibody reshapes the same effector-relevant glycan traits is unknown.

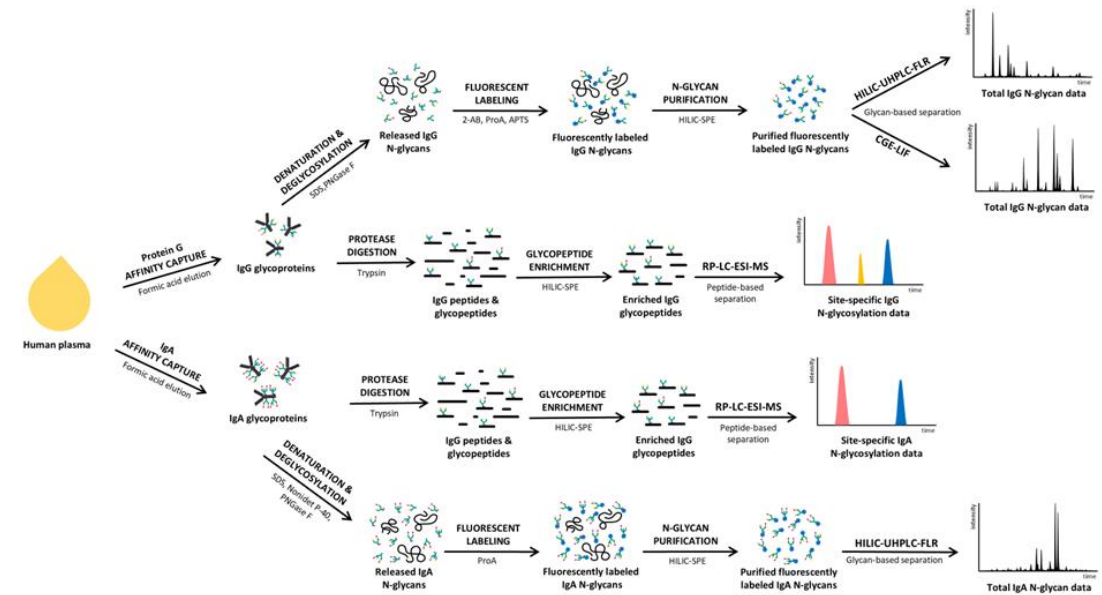


Figure 1. Schematics of various glycoanalytical workflows available in GENOS.

Why it matters

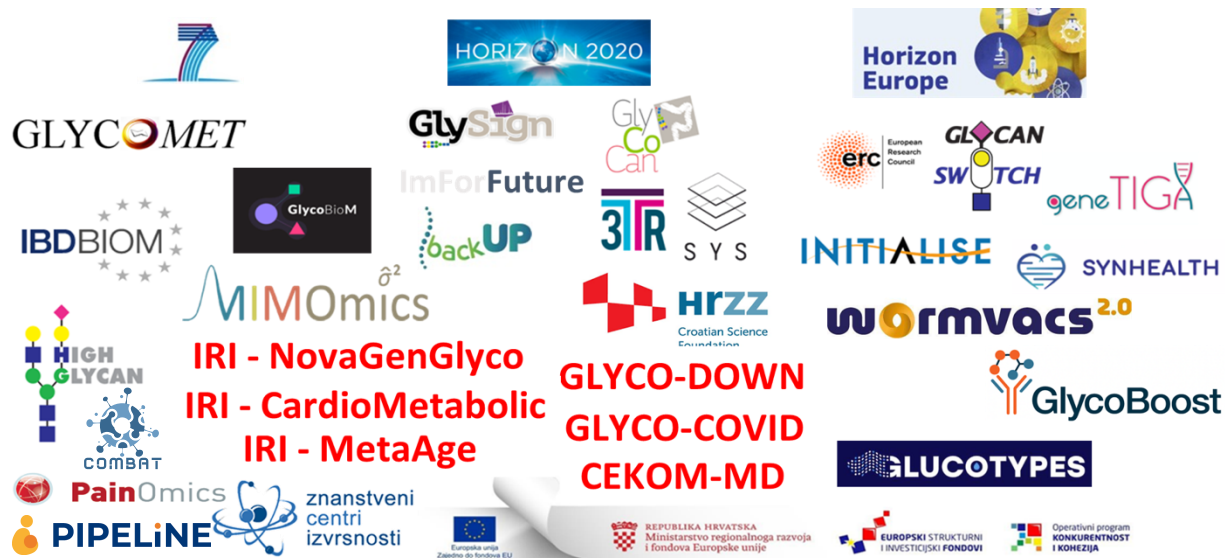
Functional, quantitative antibody phenotyping at scale, for RSV today and for emerging pathogens tomorrow.



Genos: high-throughput glycomics at scale

- > 200,000 individual glycomes analysed over the past decade.
- > 80% of glycomes published in major clinical and epidemiological studies come from Genos.
- **Platform:** 7 UHPLC systems, LC-MS and CGE; up to 200 samples/day; CE-IVDR IgG glycome kit.
- **Reach:** €40M+ competitive funding, >300 publications, global cohort collaborations (institutional data).

Funding



Collaborators



Genos team

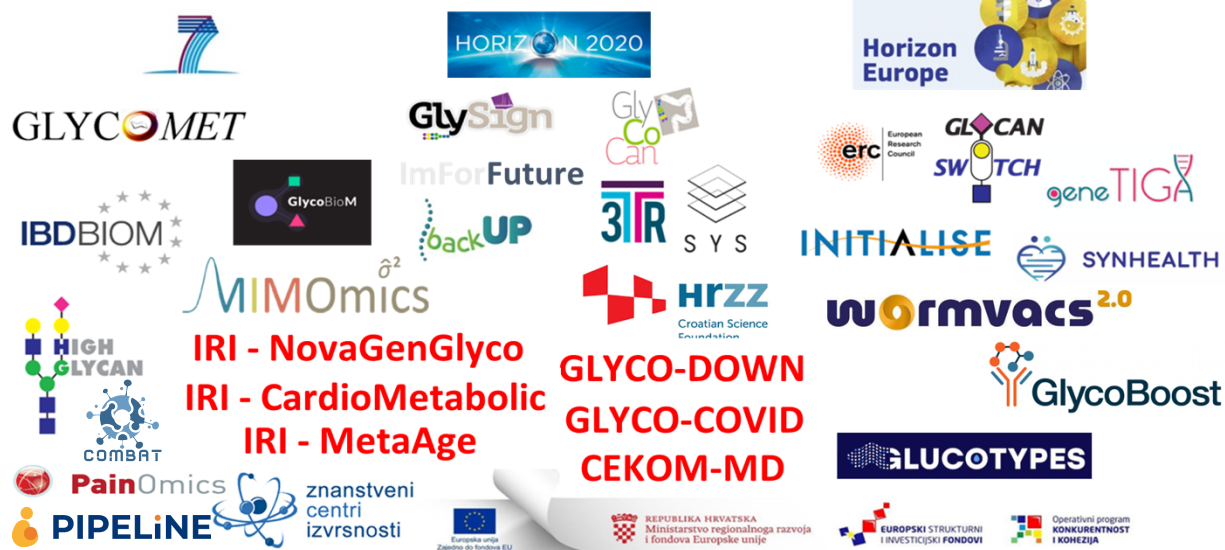


Thank you

Let's collaborate!

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Funding



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