



## Editorial

## Glycomedicine: Unveiling the Paracentral Dogma

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*Life relies on the coordination of nucleic acids and proteins, yet glycans—one of the four fundamental building blocks of life—are gradually revealing their pivotal role beyond the central dogma of molecular biology, linking nucleic acids, proteins, and lipids to regulate life activities.*

Among the four equally essential pillars of life, nucleic acids (DNA and RNA), proteins, carbohydrates (glycans), and lipids, the first two follow the well-established “central dogma” of transcription (DNA to RNA) and translation (RNA to protein), while the regulatory logic of glycans and lipids has long remained underexplored. Today, advances in glycobiology highlight the core roles of glycans in physiology (i.e., structural support, energy supply, and signal transduction) and pathology (e.g., cancer progression, immune dysregulation, and host–pathogen interactions), prompting a critical question: Is there a definitive “paracentral dogma” governing the interactions between DNA, RNA, glycans, and lipids? Do glycans serve as the third life code, after nucleic acids and amino acids, that defines the material basis of cells?

To address these questions and explore glycans' pivotal functions in disease mechanisms, we are privileged to present this special issue, titled *Glycomedicine: Unveiling the Paracentral Dogma*. The special issue includes one Views & Comments article and ten original Research articles covering diverse subtopics, each con-

tributing unique insights to glycoscience and its clinical translation:

- “Can DNA Be Glycosylated?” by Wei Wang
- “New Avenues for Human Blood Plasma Biomarker Discovery via Improved In-Depth Analysis of the Low-Abundant N-Glycoproteome” by Frania J. Zuniga-Banuelos et al.
- “GlycoPro: A High-Throughput Sample Processing Platform for Multi-Glycosylation-Omics Analysis” by Xuejiao Liu et al.
- “Ablation of *ST6Gal-I* Downregulates BACE1 Expression and Suppresses Production of A $\beta$ <sub>42</sub> Plaques in Alzheimer’s Disease” by Kangkang Yang et al.
- “IgG Fucosylation: An Emerging Key Player in the Treatment of Severe COVID-19” by Caiping Zhao et al.
- “Contrasting Macroevolutionary Patterns in the Human N-Glycosylation Pathway” by Domagoj Kifer et al.
- “Deep Reinforcement Learning-Driven Multi-Omics Integration for Constructing gtAge: A Novel Aging Clock from the IgG N-Glycome and Blood Transcriptome” by Yao Xia et al.
- “Absolute Quantification of Aging-Associated Glycans in IgG for Biological Age Prediction: Insights from Glycomics and Transcriptomics” by Huijuan Zhao et al.
- “The Serum-Derived Extracellular Vesicle N-Glycome as a New Biosignature for Childhood Epilepsy” by Yuanyuan Liu et al.
- “A Comparative Mechanistic Study of Live-Cell Glycocalyx Engineering: Improving Adoptive Cell Therapies Against B Lymphoma” by Yuxin Li et al.
- “Fucosylated IgG Contributes to Adipose Tissue Dysfunction During Aging” by Jingyu Wang et al.

These articles discuss recent progress at the frontier of glycoscience, including the following topics:

- Glycomedicine and health, covering neurodegenerative diseases (Alzheimer’s disease), infectious diseases (COVID-19), metabolic aging (adipose tissue dysfunction), biological aging (gtAge clock, aging-related glycan quantification), and pediatric neurological disorders (childhood epilepsy), expanding glycomedicine’s application across multiple organ systems;

- Glycobiology technology innovation, including a deep analysis of low-abundance N-glycoproteomes, the GlycoPro high-throughput platform, and live-cell glycocalyx engineering, providing more efficient and precise tools for translating basic glycomics research into clinical practice;
- Novel directions in glycosylation, focusing on DNA glycosylation to break substrate limitations in traditional glycosylation research and expand the understanding of the life regulatory network;
- Glycosylation in disease regulation, uncovering glycans' roles in cancer immunity (B lymphoma therapy), neuropathology ( $A\beta_{42}$  plaque suppression), immune responses (severe COVID-19 treatment), and metabolic regulation (adipose tissue function),

deepening insights into how glycans synergize with other biomolecules to regulate diseases under the “paracentral dogma.”

This special issue also offers expert recommendations for basic glycomics research and its application in glycomedicine, guiding researchers into the new era of glycomedicine: a discipline that leverages glycomics approaches to achieve precise disease diagnosis, targeted drug discovery, and personalized treatment, ultimately advancing preventive, predictive, and precision medicine.

We believe the findings in this special issue will inject new vitality into glycoscience, facilitate further elucidation of the “paracentral dogma,” and open new glycan-targeted paths for human health and disease prevention.