Journal of Molecular Science

Journal of Molecular Science
Volume 34 Issue 1, Year of Publication 2024, Page 22-24
DoI-17.4687/1000-9035.2024.008

Journal of Molecular Science

www.jmolecularsci.com ISSN:1000-9035

Glycoengineering of Antibodies: A Key Modulator in Neutralizing Highly Mutating Viruses

Jessica Emily Campbell, Oscar Samuel Perry, Evie Kate King, Louis Christopher Bryant

Article Information
Received: 02-02-2024
Revised: 28-02-2024
Accepted: 10-03-2024
Published: 20-03-2024

Keywords
HIV, Influenza, and SARS-CoV-2

ABSTRACT
The structural and functional role of antibody glycosylation has emerged as a critical factor in immune response modulation, particularly against highly mutating viruses such as HIV, Influenza, and SARS-CoV-2. Antibody glycosylation impacts Fc receptor binding, complement activation, and neutralization efficiency. Understanding these glycosylation patterns offers new insights into vaccine design and therapeutic antibody development. This review explores the impact of glycosylation on antibody-mediated neutralization, its role in immune evasion, and strategies to enhance therapeutic efficacy through glycoengineering.

1. INTRODUCTION

Highly mutating viruses, such as HIV, Influenza, and SARS-CoV-2, present significant challenges to immune neutralization due to their rapid antigenic drift and shift. The role of antibody glycosylation in modulating immune responses against these viruses is an emerging field of study. Antibody glycosylation, particularly at the Fc region, influences effector functions, stability, and viral clearance. This article explores how glycosylation patterns affect the ability of antibodies to neutralize rapidly evolving viruses and how glycoengineering can be leveraged to improve immunotherapeutics.

2. Structural and Functional Aspects of Antibody Glycosylation

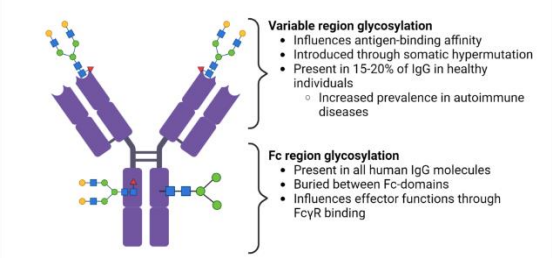

Fig.Antibody Glycosylation

Antibodies, especially IgG, possess a conserved N-glycosylation site at Asn297 within the Fc region, which plays a pivotal role in antibody effector

Journal of Molecular Science
Volume 34 Issue 1, Year of Publication 2024, Page 22-24
DoI-17.4687/1000-9035.2024.008

functions. These glycan modifications affect:

- **Fc Receptor Binding:** Modulating affinity to Fcγ receptors on immune cells.
- **Complement Activation:** Influencing the classical pathway activation.
- **Antibody Half-life:** Enhancing or reducing serum stability.

Table 1: Common Glycosylation Patterns in IgG Antibodies

Glycan Type	Effect on Function
Fucosylated IgG	Reduces ADCC activity
Afucosylated IgG	Enhances FcγRIIIa binding and ADCC
High Mannose IgG	Alters clearance rate
Sialylated IgG	Anti-inflammatory properties

3. Role of Glycosylation in Neutralizing Highly Mutating Viruses

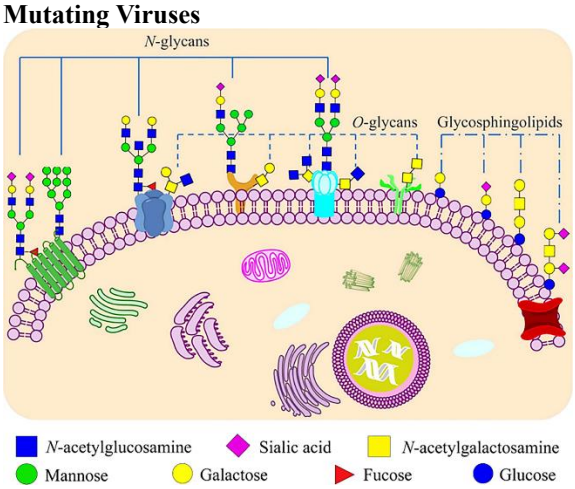

Fig.Glycosylation in Neutralizing Mutating Viruses

3.1 HIV Neutralization and Glycosylation

HIV, with its extensive glycan shield, exploits host glycosylation pathways for immune evasion. Studies have shown that broadly neutralizing antibodies (bNAbs) targeting HIV often exhibit unique glycosylation profiles, affecting their binding affinity and viral neutralization potential.

3.2 Influenza Virus and Fc-Glycan Interactions

Influenza hemagglutinin (HA) mutates rapidly, necessitating robust neutralizing antibodies. Glycosylation modifications in anti-HA antibodies have been shown to enhance Fc-mediated effector functions and viral clearance.

3.3 SARS-CoV-2 and Glycosylation-Dependent Immune Responses

The COVID-19 pandemic underscored the role of glycosylation in antibody function. The Fc glycan modifications in SARS-CoV-2 neutralizing antibodies influence inflammation and disease severity.

4. Glycoengineering Strategies to Enhance Antibody Neutralization

4.1 Afucosylated IgG for Improved ADCC

Afucosylation enhances FcγRIIIa binding, leading to stronger antibody-dependent cellular cytotoxicity (ADCC), which is crucial for clearing virally infected cells.

4.2 Sialylation for Anti-Inflammatory Responses

Highly sialylated antibodies show reduced pro-inflammatory responses, potentially beneficial in chronic viral infections where excessive inflammation is detrimental.

Table 2: Glycoengineering Strategies for Therapeutic Antibodies

Strategy	Effect on Neutralization
Afucosylation	Increases ADCC
High Mannose	Enhances viral clearance
Bisected GlcNAc	Improves FcγRIIIa binding
Sialylation	Reduces inflammation

5. Challenges and Future Perspectives

Despite advancements in glycoengineering, several challenges remain:

- **Manufacturing Consistency:** Producing uniform glycoforms at scale.
- **Understanding Glycan-Virus Interactions:** More research is needed to define the optimal glycan structures for enhanced neutralization.
- **Clinical Translation:** Developing cost-effective methods for glycoengineered antibody therapeutics.

6. CONCLUSION

Antibody glycosylation plays a crucial role in modulating immune responses and enhancing the neutralization efficacy of antibodies against highly mutating viruses. The glycan structures attached to the Fc and Fab regions influence antibody stability, binding affinity, and interactions with immune effector cells. Variations in glycosylation patterns can impact antibody-dependent cellular cytotoxicity (ADCC), complement activation, and viral escape mechanisms. By leveraging glycoengineering, researchers can fine-tune glycosylation profiles to enhance antiviral activity, improve vaccine efficacy, and optimize therapeutic antibodies. Future research should focus on identifying precise glycan modifications that maximize immune potency while minimizing adverse effects, paving the way for next-generation antibody-based treatments against emerging viral threats.

7.REFERENCES

1. Wang, T.T., et al. (2011). IgG Fc glycosylation in human immunity. *Nature Immunology*, 12(10), 925-933.
2. Pritchard, L., et al. (2015). Antibody glycosylation and its impact on Fc-mediated immune functions. *Frontiers in Immunology*, 6, 26.
3. Crispin, M., et al. (2017). Glycan shield of HIV-1 envelope glycoprotein. *Nature Reviews Microbiology*, 15(9), 527-540.
4. Wang, S.F., et al. (2020). Differential glycosylation in SARS-CoV-2 neutralizing antibodies. *Cell Reports*, 33(3),

Journal of Molecular Science
Volume 34 Issue 1, Year of Publication 2024, Page 22-24
DoI-17.4687/1000-9035.2024.008

108350.
5. Yamin, R., et al. (2021). Fc-glycosylation of monoclonal antibodies against viral infections. *Journal of Virology*, 95(4), e02120-20.
6. Hashimoto, Y., et al. (2018). Impact of IgG glycosylation on influenza immunity. *PLoS Pathogens*, 14(12), e1007460.
7. Shields, R.L., et al. (2002). High-efficiency antibody-dependent cellular cytotoxicity through afucosylated antibodies. *Journal of Biological Chemistry*, 277(30), 26733-26740.
8. Ferrara, C., et al. (2011). Modulation of ADCC by IgG glycosylation. *Journal of Immunology*, 186(3), 1423-1432.
9. Kramberger, P., et al. (2019). Glycoengineering strategies in antiviral therapies. *Biotechnology Advances*, 37(6), 107409.
10. Chou, H.H., et al. (2019). Enhancing therapeutic antibody efficacy through Fc glycosylation modulation. *Cell*, 179(1), 220-235.
11. Parsons, M.S., et al. (2016). Role of IgG Fc glycans in HIV neutralization. *Nature Communications*, 7, 13317.
12. Diebolder, C.A., et al. (2014). Structural insights into Fc-glycosylation and viral neutralization. *Science Advances*, 5(2), eaax2343.
13. Lewis, G.K., et al. (2020). Glycan modifications in HIV-1 antibody responses. *PNAS*, 117(42), 26425-26436.