

MOLECULAR EXPLOITATION OF NEISSERIA GONORRHOEAE LOS **RECOGNITION BY THE THERAPEUTIC MONOCLONAL ANTIBODY 2C7**

Masi Alessandro Antonio^a, Di Carluccio Cristina^a, Tiemblo Mártin Marta^a, Peter A. Rice^b, Benjamin P. Beernink^c, Molinaro Antonio^a, Marchetti Roberta^a, Sanjay Ram^b Silipo Alba^a

^a Department of Chemical Sciences, University of Naples Federico II, Via Cinthia 4, 80126. Naples. Italv alessandroantonio.masi@unina.it

^b Department of Infectious Diseases and Immunology, University of Massachusetts Chan Medical School, Worcester, Massachusetts 01605, USA

^c Department of Pediatrics, University of California San Francisco, Oakland, California 94609, USA

Glycan-protein interactions play a pivotal role in immunomodulation and offer promising therapeutic avenues for bacterial infections, tumors, and viral diseases. In this study, we employed a multidisciplinary approach to investigate both exogenous and endogenous ligands, underscoring the crucial role of glycans in immunotherapy [1,2].

On one hand, we characterized the lipooligosaccharide (LOS) of Neisseria gonorrhoeae strain 15253, focusing on the conserved 2C7 epitope, which is specifically recognized by the monoclonal antibody 2C7[3]. Biophysical, computational and spectroscopical (NMR) binding studies [4] revealed that the recognition is predominantly mediated by the β-chain, with a specific epitope involving the terminal β -Gal residue of the core region. MD (Molecular dynamics) simulations and ITC (isothermal titration calorimetry) experiments proved stability and property of the 3D complex and the energetics of the interaction. Moreover, the synthetic terminal tetrasaccharide from *N. gonorrhoeae* core LOS further demonstrated recognition by 2C7, paving the way for new strategies to combat infections in an era of increasing antibiotic resistance [5].

Overall, our results remark the importance of studying glycans as a transversal immunotherapeutic target, providing a solid foundation for the development of interventions that exploit glycan-protein interactions—both exogenous and endogenous—for the treatment of bacterial infections and cancer diseases.

References:

1. Rice P.A., Shafer W.M., Ram S., Jerse A.E. Annu Rev Microbiol. 2017, 8, 665-686.

- 2. Beernink PT, Di Carluccio C, JACS Au. 2024, 7, 2617-2629.
- 3. Di Carluccio C, Forgione MC, Silipo A. Carbohydr Res. 2021, 503, 108313.
- 4. Nieto-Fabregat F, Lenza MP, J Org Chem. 2024, 20, 2084-2107.
- 5. Di Carluccio C, Cerofolini L, Moreira M, ACS Cent Sci. 2024, 10, 447-459.