

SIGLEC-GLYCAN INTERACTIONS IN IMMUNE REGULATION

June Ereño-Orbea

CIC bioGUNE, Bizkaia Technology Park Building 801A, 48160 (Derio), Spain
jereo@cicbiogune.es

Hypersialylation, an aberrant increase in the expression of sialic acid, profoundly impacts tumor cell interactions with their microenvironment. Siglecs, immune receptors that recognize cell surface sialic acids, play a pivotal role in immune surveillance within the tumor microenvironment. Our group has studied the interaction between glycans containing sialic acids (sialoglycans) and Siglec receptors on immune cells, demonstrating that this pathway can be targeted to regulate immune responses and control tumor growth. Leveraging structural biology techniques, including X-ray crystallography, NMR, and molecular dynamics, we have scrutinized the molecular details governing their specificities for sialoglycans [1-5]. This information offers opportunities for developing novel molecules targeting Siglecs through modified sialic acids. Our research also focuses on uncovering structural insights on anti-Siglec antibodies to refine antibody-based therapies.

Acknowledgements: I thank AEI & MICIU (Spain), EU-GlycoTwining, EU-Glytunes, BBVA Leonardo, Caixa Foundation, Ramon Areces and Mizutani for funding, and all my collaborators and colleagues from Cancer Glycoimmunology and Chemical Glycobiology labs from CIC bioGUNE, who are contributing to this research.

References:

1. J. Ereño-Orbea, T. Sicard, T. H. Cui, M.T. Mazhab-Jafari, S. Benlekbir, A. Guarné, J. Rubinstein, J.P. Julien, *Nat. Commun.* **2017**, 8 (764), 764.
2. J. Ereño-Orbea, X. Liu, T. Sicard, I. Kucharska, W. Li, D. Borovsky, H. Cui, Y. Feng, D.S. Dimitrov, J.P. Julien, *J. Biol. Chem.* **2021**, 297 (2), 100966.
3. M.P. Lenza, U. Atxabal, C. Nycholat, I. Oyenarte, A. Franconetti, J.I. Quintana, S. Delgado, R. Núñez-Franco, C.T. Garnica Marroquín, H. Coelho, et al. *JACS Au.* **2022**, 3 (1), 204-215.
4. M.P. Lenza, L. Egia-Mendikute, A. Antofana-Vildosola, C.O. Soares, H. Coelho, F. Corzana, A. Bosch, P. Manisha, J.I. Quintana, I. Oyenarte, et al, J. Jiménez-Barbero, A. Palazon, J. Ereño-Orbea, *Nat. Commun.* **2023**, 14 (1), 3496.
5. U. Atxabal, C. Nycholat, J. Pröpster, et al, J. C. Paulson, J. Jiménez-Barbero, J. Ereño-Orbea, *ACS Chem. Biol.* **2024**, 19 (2), 483-496