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Targeting Siglec–Sialoglycan Interactions: Structural Insights and Therapeutic Opportunities in Cancer



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12.00 pm

CIC biomaGUNE - Seminar Room

Glycans are complex sugar molecules abundantly displayed on the surface of human cells, forming the glycocalyx. These glycans are attached to proteins and lipids and play essential roles in processes such as cell adhesion, communication, and immune recognition. Importantly, glycan structures are dynamic and can change depending on the state of the cell and its environment. In cancer, this flexibility often results in aberrant or novel glycosylation patterns, which contribute to disease progression and immune evasion.

One of the most striking glycan alterations in cancer is hypersialylation, the overexpression of sialic acids on cell surfaces, which impacts how tumor cells interact with their microenvironment. Siglecs (sialic acid-binding immunoglobulin-like lectins), a family of immune receptors that recognize sialylated glycans, are central to modulating immune surveillance in tumors. Our research focuses on the sialoglycan–Siglec axis, demonstrating that it can be therapeutically targeted to regulate immune activity and control tumor growth.

Using structural biology techniques such as X-ray crystallography, NMR spectroscopy, and molecular dynamics simulations, we have dissected the molecular basis of Siglec binding specificity. These insights are guiding the design of synthetic ligands and modified sialic acids to modulate Siglec signalling. In parallel, we are uncovering structural features of anti-Siglec antibodies to improve antibody-based immunotherapies. Together, our work aims to translate glycobiological knowledge into new strategies for reprogramming the immune response in cancer.