STRUCTURAL INSIGHTS INTO CARBOHYDRATE-LECTIN INTERACTIONS

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Carbohydrates represent a crucial class of molecules that are generally exhibited on cell's surface, covalently attached on proteins, lipid or RNA [1]. The presence of these carbohydrates plays an essential role in cellular communication and regulate the immune responses. As example, they enable immune system to distinguish between self and non-self, such as pathogens or tumour cells [2].
The interaction between glycans and immune cells is mediated by a class of proteins called lectins, which are capable of binding to specific carbohydrate structures. Lectins, including Siglecs (Sialic acid-binding Ig-like lectins) and Galectins, play a pivotal role in recognizing and interpreting the information encoded in surface carbohydrates. These lectins bind to specific carbohydrate motifs, triggering downstream signalling events that modulate immune function [3]. For instance, Siglecs can bind to sialic acid-containing glycans on the surface of cells, regulating immune cell activation and cytokine production [4].
Herein, we combined Nuclear Magnetic Resonance (NMR) spectroscopy, computational and biophysical techniques to gain structural insights into the molecular recognition processes between modified carbohydrates and lectins. One notable example is Siglec-8, which plays a key role in regulating allergic responses [5]. We elucidated the binding mechanism of four high-affinity analogues of Sialoglycans, demonstrating that sialic acid binds to the classic sialyl binding pocket of the Siglec receptor family. Notably, compounds with sulfonate groups and 9-naphthyl sulfonate exhibited the highest affinity, as determined by NMR and biophysical experiments.
These findings provide valuable insights for the rational design of the next generation of Siglec-8 inhibitors. By understanding the structural determinants of carbohydrate-lectin interactions, we can develop novel therapeutic strategies that target these interactions to modulate immune responses and treat diseases associated with dysregulated immune function.

References:
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