

NMR and Calorimetric Study of Natural and Synthetic Human Milk Oligosaccharide Mimetics and Their Interactions with Galectin

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Human galectins are β -galactoside-binding proteins involved in key biological processes such as immune regulation, cell–cell communication, and host–pathogen interactions, where glycan recognition is central to their function^{1–3}. Subtle structural variations in glycans can significantly modulate binding selectivity and affinity, making them important systems for understanding molecular recognition in carbohydrate–protein interactions.

Human milk oligosaccharides (HMOs), such as 2'-fucosyllactose (2'FL), are abundant glycans present in breast milk and play important roles in infant health and modulation of the gut microbiota⁴. These naturally occurring structures provide biologically relevant scaffolds to investigate glycan recognition by lectins.

Understanding how small structural changes affect glycan–protein interactions is essential for elucidating the molecular basis of galectin selectivity and for guiding the design of stable glycomimetic tools^{5,6}. In particular, the introduction of non-natural linkages may modulate conformational behaviour and enzymatic stability while preserving recognition features.

In this study, a comparative multi-technique approach was employed to analyse natural and synthetic fucosylated lactose derivatives. Nuclear magnetic resonance (¹H NMR, STD-NMR, ROESY, and titration experiments) was used to investigate conformational properties and map ligand–galectin interaction epitopes across different galectins. In addition, isothermal titration calorimetry (ITC) provided quantitative binding affinities and thermodynamic profiles.

Overall, all ligands display a similar recognition mode across the galectin panel, with galactose as the main binding epitope. NMR and ITC data indicate comparable interaction profiles and affinities despite the structural modifications introduced in the synthetic analogues.

References:

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