UNRAVELLING THE GLYCAN RECOGNITION PROPERTIES OF HUMAN GALECTIN-9

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Galectin-9 is a tandem-repeat galectin that has been reported to have a major role in many biological processes such as cell growth, differentiation, communication, and death [1]. Moreover, it has been proposed as a possible biomarker for many pathologies due to its immunomodulatory capacity [2]. In view of the biological importance, its molecular recognition properties have been analyzed during this work. As a tandem-repeat galectin, Galectin-9 is composed of two carbohydrate recognition domains (CRDs) covalently linked by a peptide linker. Herein, the NMR backbone assignment of both the C-domain and N-domain of Galectin-9 has been achieved, instrumental for obtaining site-specific information by defining the protein residues implicated in oligosaccharide binding. Additionally, ligand-observed techniques such as STD and STD-HSQC experiments have been performed. In particular, the binding to Lactosamine (LacNAc), the B- and the A-antigen tetrasaccharide type 2 (B-type 2 and A-type 2) [3], 3-Sialyl Lactosamine (3-S'LacNAc), and polylactosamine (PLNA) [4] oligosaccharides has been compared. Specifically PLNA structures have been found in both glycoproteins and glycolipids acting as elongated scaffolds to provide recognition by glycan binding proteins (GBPs). Besides, they have also been associated to key biological processes, mainly related to immune regulation [5], making it important the study of the interaction between Galectin-9 and PLNA structures. Finally, affinity values were confirmed by isothermal titration calorimetry (ITC), and molecular dynamics (MD) simulations were performed to obtain 3D atomic resolution complexes, providing the impetus for disentangling the glycan-lectin interaction.

References:

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