NMR STUDIES OF THE INTERACTION AND MULTIPLE BINDING MODES BETWEEN MANNOSE OLIGOSACCHARIDES AND DC-SIGN.

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DC-SIGN is a C-type lectin presenting a Carbohydrate Recognition Domain (CRD), that recognizes specifically high glycosylated structures present at the surface of several pathogens such as HIV, Hepatitis C, Ebola, etc.

A structural study of the interaction between the CRD of the DC-SIGN and simple mannose di- and trisaccharides contained in high mannose glycans of infective agents has been performed by NMR. Functionalized glycodendrimers are capable of inhibit viral infection by blocking the interaction between the viral glycoprotein and DC-SIGN [1, 2] .Understanding the binding mode of this lectin will permit the design of new and more selective ligands.

A first conformational analysis of the free ligand has confirmed that their structures are similar to those from the natural oligosaccharide and show moderate flexibility. The interaction with the lectin was analyzed by Saturation Transfer Difference spectroscopy whereby making possible to analyze the binding mode of a mannose disaccharide to DC-SIGN, which exhibits multiple binding modes. STD-NMR is sensitive to this effect and it is possible to compare experimental data and theoretical predictions based on CORCEMA-ST [3, 4] using STD initial growing rates for the evaluation. This research have refined previous crystallographic studies [5] determining the precise structure and orientation in the minor binding mode of the disaccharide within the DC-SIGN binding pocket. In this binding mode the disaccharide fit into the same binding sub-site as the major complex but the sense (reducing to non-reducing end) imposed by the coordination of the mannose with the Ca^{2+} atom is the opposite. This observation could be useful for further interactions studies and design of new ligands for DC-SIGN.

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