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STRUCTURAL CHARACTERIZATION OF GLYCOMIMETIC MOLECULES BINDING TO DC-SIGN LECTIN. A CRUCIAL STEP FOR RATIONAL DESIGN OF NEW ANTI-INFECTIVE DRUGS

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DC-SIGN (Dendritic Cell-Specific ICAM-3 Grabbing Non-integrin) is a C-type lectin mainly expressed by immature dendritic cells (DCs), located in the skin or peripheral mucosal tissues. It is a tetrameric transmembrane protein containing a Carbohydrate Recognition Domain (CRD) at the C-terminus that specifically recognizes, in a Ca^{2+}-dependent manner, highly glycosylated structures present at the surface of a broad spectrum of pathogens (viruses, bacteria, yeasts, and parasites). For instance, HIV-1 exploits the internalization pathway of DC-SIGN to facilitate trans-infections of T cells and to invade the host immune system. Therefore, this receptor is considered an interesting target for the design of inhibitors and anti-infective agents.

A full understanding of the molecular recognition of ligands by DC-SIGN represent an essential step for the rational design and optimization of glycomimetic drugs capable of blocking this lectin with high affinity. We performed detailed interaction studies between the ECD (extracellular domain) of DC-SIGN and glycomimetic molecules[1], designed to reproduce some salient features of the natural ligands. The binding events were fully investigated by Saturation Transfer Difference (STD) NMR[2] in solution, combined with X-ray results and CORCEMA-ST protocol[3].

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