Controlling the C-type lectin receptors in infections & immunity: selective glycomimetic antagonists

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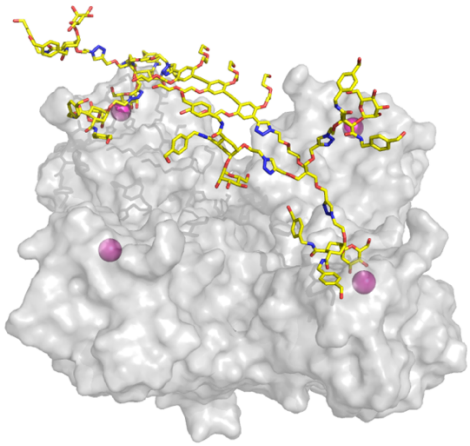
C-type lectin receptors (CLRs) are a large family of Pattern Recognition Receptors, dedicated to the detection of carbohydrate-based motifs, using a Ca^{2+} ion for recognition. Innate immune cells express a variety of CLRs, which shape the immune response, often in cross-talk with TLRs. Some pathogens have found strategies to circumvent CLR's role or even to use them in their infection process. This is the case of several deadly viruses, like HIV and SARS-CoV2. Subversion of several CLRs has been reported, including MGL, L-SIGN and especially DC-SIGN, which is the most widely reported co-receptors facilitating viral infection. During the past 15 years, our groups were engaged to develop glycomimetic ligands able to interfere with DC-SIGN recognition, thus inhibiting its role in viral infections.[1–3]This project took us from the design of glycomimetic able to mimic the monovalent oligosaccharide ligands of DC-SIGN[4], to the refinement of their activity by structural optimization[5] and of their multivalent presentation[6]. Biophysical methods were devised, optimized to produce structure-activity-relationship for the designed mimics and to account for the dynamic and the different topology of the receptors presentation[7,8]. Structures from crystallographic studies were used in the design to increase the affinity and selectivity of ligands for a specific lectin. In the process, we have developed general principles for the selective design of potent glycomimetic ligands for CLRs and tools for their study. This duo presentation will summarize the history of this scientific journey.



One of the possible chelation binding mode of Polyman26 on DC-SIGN tetramer

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