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Synthetic Tools to interact with Antigen Presenting Cells (APCs)

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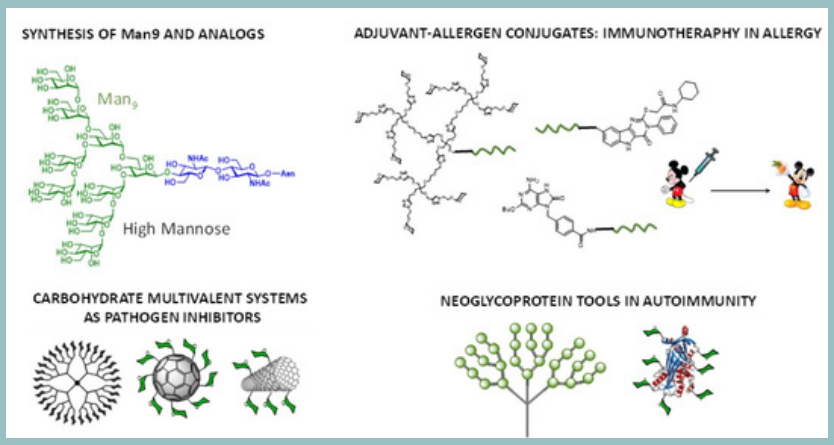
CIC biomaGUNE - Seminar Room

Antigen Presenting Cells (APCs) are essential for innate and adaptive immunity as well as self-immune tolerance. To exert their functions, these cells are equipped with a series of receptors capable to recognize conserved molecular structures present in pathogens. Among these APCs, Dendritic cells (DCs) are one of the most important representatives. These cells express different families of receptors, mainly C-type lectins (CTLs) and Toll-like receptors (TLRs), to accomplish this goal.

One research line in our group is devoted to develop carbohydrate multivalent systems to interact with DC-SIGN, a CTL presents at the surface of DCs that recognize mannosylated and fucosylated oligosaccharides. To construct these multivalent systems, we have used different scaffolds including small organic molecules, dendrimers and dendrons, carbon nanoforms, proteins, etc. We have tested the corresponding carbohydrate multivalent systems in infection assays to evaluate the capacity that they have to block DC-SIGN and inhibit infection processes



Being the branched nonasaccharide of mannoses (Man9) the main epitope of the high mannose glycan (Man9GlcNAc2) recognized by DC-SIGN, we have implemented a synthetic strategy to prepare efficiently this oligosaccharide and some analogs. With these oligosaccharides on hand, we have used them as tools to understand the recognition process of high mannose by DC-SIGN. This will help to select better mimetics of this high mannose oligosaccharide and to prepare adequate glycoconjugates to interact with DC-SIGN.

A second research line is focused on the development of adjuvant-allergen conjugates with the aim to modulate the immune response, inducing long-term tolerance to the allergen. To achieve this goal, different adjuvants based on ligands to DC-SIGN, TLR4 and TLR7 receptors were conjugated to allergen T-cell epitopes. These conjugates have been evaluated using dendritic cells from allergic patients and in animal models to confirm their capacity to induce tolerance.[