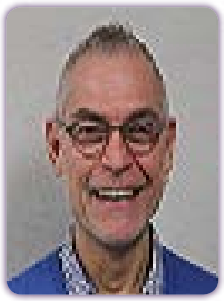
5th International Conference on
GLYCOBIOLOGY & GLYCOPROTEOMICS
&
3rd International Conference on
MOLECULAR BIOLOGY & NUCLEIC ACIDS
August 27-28, 2018 | Toronto, Canada



Jose Kovensky

University of Picardie Jules Verne, France

Multivalent sugar-lectin interactions from glycoclusters on oligosaccharide scaffolds to self-assembling structures

Carbohydrates play an essential role in several biological functions associated with selective interactions with cellular proteins that govern a wide variety of life processes. In living organisms, these high-affinity carbohydrate-protein interactions occur through multivalent contacts, characterized by an enhancement of the affinity when the sugar ligand is presented in a cluster rather than alone. Several biomimetic approaches have been developed in order to prepare synthetic multivalent neoglycoconjugates to interfere with a series of pathological events such as infections due to viruses and bacteria, tumor progression and migration, and inflammation processes. We constructed multivalent glycoconjugates on oligosaccharide scaffolds, to obtain structures with improved hydrophilicity and pharmacokinetics, as compared to peptidic, aromatic, or polymeric scaffolds. We were able to perform regioselective oxidation of mono-, di-, trisaccharides and cyclodextrins. We started preparing multimannosides, galactosides, and lactosides, synthesized by coupling the corresponding alkynyl glycosides to the azido modified oligosaccharides by CuAAC. We obtain a considerable gain in affinity to model lectins as Concanavalin A and PNA. Some of our glycoclusters were able to inhibit galectins 1 and 3. Afterward, we synthesized other glycoclusters exposing thiosugars, showing higher stability towards glycosyl hydrolases than O-glycosides. S-galactosides, S-lactosides, 3-deoxy-S-lactosides, and analogs of dithiogalactoside (a commonly used galectin inhibitor) afforded new multivalent probes to analyze sugar-lectin interactions. We finally explored a supramolecular approach for the construction of multivalent architectures, able to interact with proteins, through the design and synthesis of thiolactose-based amphiphiles. Interestingly, two compounds which only differ in the length of the spacer connecting the sugar fragments to the scaffold showed different properties. In this presentation, we will present the synthesis and affinities of different glycoclusters, and we discuss the influence several parameters as the triazole moiety, the length of the spacer, the ability for crosslinking of our glycoclusters, and the self-assembling properties of sugar-based amphiphiles.

Biography

Professor Jose Kovensky has PhD from the Universidad de Buenos Aires (Argentina, 1992). He did his postdoctoral research at the Ecole Normale Superieure (Paris, France, 1994-1995). After being Professor of Organic Chemistry in Argentina, he got a Full Professor position in Amiens in 2002. He has been the principal investigator of several projects financed by the Regional Council or Picardie Region, binational projects France-Germany, France-Argentine, and partner in European Projects. He has directed or co-directed 12 PhD theses. He is a co-author of more than 80 publications (articles, book chapters, patents). He has a wide experience in the synthesis and modification of oligosaccharides, in particular, uronic acid containing oligosaccharides, sulfonated oligosaccharides, glycosaminoglycans, multivalent glycoclusters, and sugar-based surfactants.

jose.kovensky@u-picardie.fr

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