SCIENTIFIC SEMINAR

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Secondary sites and allosteric regulation of C-type lectins

The C-type lectin protein family is the largest and most complex family of mammalian carbohydrate-binding proteins. They are explored as therapeutic targets in various disease settings such as infectious diseases, immunotherapy, allergies, vaccine development and drug delivery in general. Consequently, there is a broad interest in developing specific ligands that could modulate the function of C-type lectins. However, selective chemical probes are limited. This is due to the shallow, polar, and promiscuous carbohydrate binding sites in many C-type lectins. For a number of the members of the C-type lectin family the presence of distant allosteric secondary sites has been implied by previous research. For a few lectins, this has been explored even further and probes are being developed to expand our insights into the mechanism and function of these sites. Taken together, this approach could offer increased druggability and selectivity while regulating receptor activity.

In this presentation, I will outline our ongoing efforts in leveraging the structural flexibility inherent to C-type lectins to develop small molecule modulators of their receptor functions. To illustrate the practical application of our ligands, I will provide insights from our latest research focused on DC-SIGN and Langerin. Furthermore, I will discuss a Python-based computational approach to predict and characterize allosteric secondary sites in C-type lectins. Here, we identified 20 structurally conserved pockets, at least four of which were predicted to have allosteric potential. These pockets overlapped with known binding sites for ligands and protein-protein interactions, suggesting a conserved function that could be explored for targeting C-type lectins.

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Atrio 800
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