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Soutenance de thèse

Vendredi 14 Déc. 2012

A 14h30 - Salle des séminaires du CERMAV

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Development of glycomimetic antagonists of the C-type lectin receptor DC-SIGN: a new anti-HIV preventive strategy

Thèse de Doctorat de l'Université Joseph Fourier

Dendritic cells routinely survey the peripheral tissues, capture and process the invading pathogens, and present the antigens to T cells to boost the pathogen specific adaptive immune responses. These cells recognize the foreign organisms with the help of multiple pattern recognition receptors (PRRs), which specifically bind molecules on the pathogen surfaces.

Among PRRs, C-type lectin receptors (CLRs) have an important role in pathogen recognition and capturing. However, one of these CLRs, DC-SIGN, is known to be hijacked by many pathogens including HIV to promote their infection.

This work aims to develop the antagonists of DC-SIGN in order to block the use of this receptor by pathogens. To achieve that, the strategy of the development of glycomimetic ligands of DC-SIGN and the multivalent presentation of the selected monovalent glycomimics has been employed.

The presented studies were accomplished in collaboration with several chemists groups, who have designed and synthesized different glycomimetic compounds as well as different multivalent platform. Using SPR the activity of the compounds to inhibit DC-SIGN was estimated. The compounds were also evaluated for their selectivity to DC-SIGN vs langerin, another CLR with a protective role from HIV infection. Some of the compounds were structurally characterized by X-ray crystallography and NMR spectrometry studies. The SPR studies of multivalent compounds confirmed the improved activity, but also revealed possible complications

Overall, these studies allowed to identify two new monovalent leads and to draw perspectives for their further improvement, and suggested the improvement of multivalent presentation platforms.