Universität Basel

Research Project

Carbohydrate-Lectin Interactions: New Antagonists guided by NMR

Third-party funded project

Project title Carbohydrate-Lectin Interactions: New Antagonists guided by NMR
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Department
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Our research is focused on elucidating the molecular nature of the interactions of lectins with their physiological carbohydrate ligands. Currently, our projects center on three types of lectins: The myelin-associated glycoprotein (MAG), the selectins and the asialoglycoprotein receptor (ASGP-R). These three targets were selected based on their significant pharmaceutical relevance, which results from their involvement in important biological processes such as neuronal repair, inflammation, infection and metabolism.

Carbohydrate-protein interactions are usually exceptionally weak, making the development of drug candidates starting from the physiological ligands a challenging task. Additionally, carbohydrates have very poor pharmacokinetic properties, which further complicates the development of carbohydrate mimetics. Our group utilizes state-of-the-art tools, such as NMR, surface plasmon resonance (SPR, Biacore) and molecular modeling techniques [MacroModel (free-energy perturbation), Sybyl, GrowMol] for the design of drug-like carbohydrate mimics. The compounds identified by these approaches are synthesized by chemical, chemo-enzymatic and combinatorial techniques.

In this R'EQUIP proposal we request a contribution towards the costs of a new console for our NMR spectrometer. With this new console, we can use our NMR for analytical purposes as well as the study of ligand-receptor interactions. The NMR is therefore indispensable to the progress of our research projects. Due to the improved electronics and hardware, the upgrade of our NMR will both greatly enhance the quality of measurements as well as permit a larger range of experiments to be performed. In addition, the upgrade from the Bruker DMX console to the AVANCE III console is required for future compatibility. The new console will enable our group to evaluate protein folding and to control protein, to determine protein structures, to localize binding sites on receptors, to measure binding epitopes through STD-NMR, to screen second-site fragments, to determine conformations of ligands bound to the target protein and study binding modes of mimetics through ^{19}F-NMR.

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