IMPRS on Multiscale Biosystems

Project description

Title:

Unraveling carbohydrate/lectin interactions molecularly and targeting lectins *in vivo*

PI: Dr. Bernd Lepenies, MPI-KG; **In collaboration with**: Dr. Stefanie Barbirz, Universität Potsdam

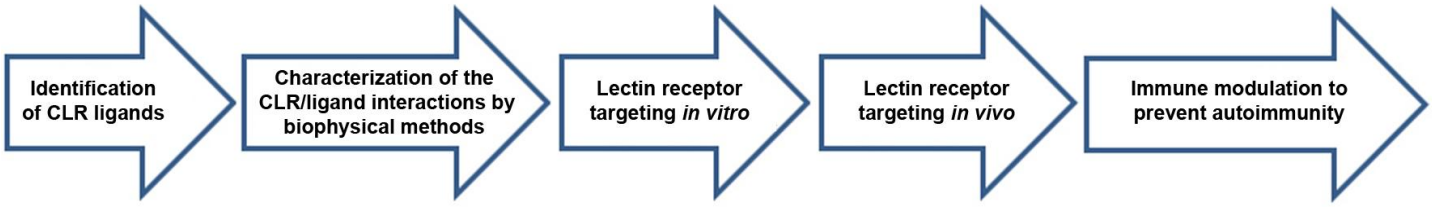
Project description:

Understanding the role that carbohydrates play in biological processes is of crucial importance to develop drugs and therapeutic agents for the treatment of human diseases. Particularly, interactions of carbohydrates with glycan-binding receptors (so-called lectins) are of interest, since these receptors may be exploited to inhibit binding of natural ligands competitively or to deliver drugs specifically into cells expressing the respective lectins [1]. Since lectin receptors usually exhibit low affinities for their ligands, multivalent presentation of the lectin ligands is often a prerequisite to induce biological effects [1]. Recent studies have shown that cell-specific targeting of lectin receptors *in vitro* as well as *in vivo* can indeed be achieved [2].

This interdisciplinary project is centered at the interface between biophysics, chemical biology, and immunology. The focus of the project is to characterize the interaction of carbohydrates with C-type lectin receptors (CLRs), a family of receptors expressed by cells of the innate immunity, on the molecular level and to target those with multivalent carbohydrate ligands. CLRs recognize glycan structures from pathogens such as bacteria, viruses, and fungi in a Ca^{2+}-dependent manner (Sancho & Reis e Sousa, *Annu. Rev. Immunol.* 2012, 30, 491).

In this collaborative project, carbohydrates binding to members of a C-type lectin receptor library previously generated in the Lepenies group will be identified by glycan array. The carbohydrate/protein interactions will then be characterized on the molecular level regarding affinity and specificity by biophysical methods such as isothermal titration calorimetry (ITC), surface plasmon resonance (SPR) or co-crystallization studies (Dr. Stefanie Barbirz, UP). The final goal of the project is to use synthetic carbohydrates for C-type lectin targeting during the course of inflammation. For this purpose, mouse models of inflammation will be employed that have been established in the Lepenies group. In conclusion, in this PhD project carbohydrate ligands of CLRs will be identified and the carbohydrate/lectin interactions will be further characterized by biophysical methods as well as suitable *in vitro* and *in vivo* models (see Workflow).

Workflow of the project:



Required background:
Diploma or M.Sc. in Biochemistry or any related discipline; preferentially experience or interest in biochemistry, cell biology and/or immunology

Papers to read before the interview:
[1] Lepenies, B.; Yin, J.; Seeberger, P.H.: Applications of synthetic carbohydrates to chemical biology. *Curr. Opin. Chem. Biol.* **2010**, 14, 404-411.
[2] Kikkeri, R.; Lepenies, B.; Adibekian, A.; Laurino, P.; Seeberger, P.H.: In vitro imaging and in vivo liver targeting with carbohydrate capped quantum dots. *JACS* **2009**, 131, 2110-2.

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