IMPRS "Multiscale Biosystems" Project:
Design of high affinity carbohydrate binding proteins

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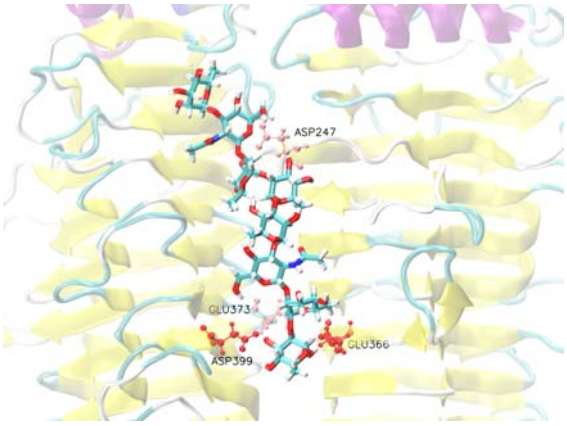
Project description: Carbohydrate-protein interactions are ubiquitous in nature and mediate the exchange of specific information. Understanding this language, however, might go beyond the traditional *key-lock* principle (1). The internal flexibility of carbohydrates and their extensive hydration considerably tune the strength and the dynamics of the interaction with proteins. Studying the various driving forces for these recognition events is very important to understand and possibly predict in which way structural features of a protein-carbohydrate complex influence the thermodynamics and the mechanism of binding (2). Only a few case studies exist from which general rules for the interaction of two amphiphilic partners, *i.e.* proteins and carbohydrates, in aqueous solution might be deduced. Goal of this project is the rational design of a carbohydrate binding site on a suitable protein scaffold in a systematic way, using both experimental and theoretical approaches (3). During a first stage, the candidate will create mutations on a protein surface and probe binding of oligosaccharides with docking procedures *in silico*. Successful protein mutants will then be purified and screened in the laboratory for high affinity binding to oligosaccharides with spectroscopic as well as calorimetric methods. Molecular details of the carbohydrate-ligand binding mechanisms can be studied with molecular dynamics techniques (4). This might also yield important insights for understanding and developing systems for the detection of bacterial pathogens.



Octasaccharide of *Shigella flexneri* serogroup Y O-antigen modeled into the binding site of Sf6 tailspike protein, the surface recognition organelle of bacteriophage Sf6 (3). Tailspike proteins are robust protein scaffolds for carbohydrate binding and hydrolysis.

References:

1. DeMarco, M. L., and Woods, R. J. (2008) *Glycobiology* **18**, 426-440.
2. Broeker, N. K., Gohlke, U., Müller, J. J., Uetrecht, C., Heinemann, U., Seckler, R., and Barbirz, S. (2012) *Glycobiology*, doi 10.1093/glycob/cws126.
3. Muller, J. J., Barbirz, S., Heinle, K., Freiberg, A., Seckler, R., and Heinemann, U. (2008) *Structure* **16**, 766-775
4. Wehle, M.; Vilotijevic, I.; Lipowsky, R.; Seeberger, P. H.; Varon Silva, D.; Santer, M. (2012) *JACS*, doi 10.1021/ja302803r

Required background: The candidate should have a strong biochemical background and motivation for both biophysical theoretical and experimental work as well as good communicative and networking skills for the interdisciplinary project.
Paper to read before the interview: Reference 1.
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