LECTINS AND LECTOMES FOR DECIPHERING THE GLYCOCODE

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A large number of pathogenic microorganisms display receptors for specific recognition and adhesion to the glycoconjugates present on human tissues. In addition to membrane-bound adhesins, soluble lectins are involved in lung infections caused by the *bacteria Pseudomonas aeruginosa* and *Burkholderia cepacia* and by the fungus *Aspergillus fumigatus* that are responsible for hospital-acquired diseases. The multivalency of lectin is proposed to play a role in their strong avidity for glycosylated cell surfaces, in their specific binding to targeted human tissues, and also in their ability to affect membrane dynamics by clustering glycosphingolipids, resulting in some cases in internalization of intracellular pathogens.
Accumulated knowledge about the structures of the lectins and the interactions with host glycoconjugates has led to the design of powerful glyco-derived inhibitors that can serve as antimicrobial therapeutic agents, as a complement to or an alternative to antibiotic therapy. Several strategies are developed with development of glycoderivatives and/or multivalent glycostructures. The structural role of calcium present in the binding site of fucose and galactose specific lectins has been investigated through x-ray and neutron crystallography [1] and novel inhibition strategy with using carbohydrate glycomimetics and non-carbohydrate glycomimetics are being developed [2,3].
Structural information on lectins is now organized in databases with possibility for datamining of lectin sequences in genomes [4]. This opens the possibility to develop tools from bacterial lectins, that can be used for purification and labelling glycoconjugates, vectorisation or as glue for creating artificial tissue. Synthetic glycobiology offers innovative methods for building super-lectins as novel architectures [5].

References:

1. L. Gajdos, M.P. Blakeley, M. Haertlein, V.T. Forsyth, J.M. Devos, A. Imberty, *Nature Com.* **2022**,*13*,194.
2. E. Zahorska, L.M. Denig, S. Lienenklaus, S. Kuhaudomlarp, T. Tschernig, P. Lipp, A. Munder, E. Gillon, S. Minervini, V. Verkhova, A. Imberty, S. Wagner, A. Titz, *JACS Au* **2024**, *4*, 4715–4728.
3. S. Kuhaudomlarp, E. Siebs, E. Shanina, J. Topin, I. Joachim, P. da Silva Figueiredo Celestino Gomes, A. Varrot, D. Rognan, C. Rademacher, A. Imberty, A. Titz, *Angew. Chem.* **2021**, *60*, 2-13.
4. F. Bonnardel, J. Mariethoz, S. Perez, A. Imberty, F. Lisacek, *Nucleic Acids Res*. **2021**, *49*, D1548-D1554.
5. S. Notova, A. Imberty, *Curr. Opin. Chem. Biol.* **2023***, 73*, 102275.