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Neutron diffraction for deciphering lectin-carbohydrate interactions in bacterial infection

Content

Lectins are carbohydrate-binding proteins that play important roles in cell recognition and host-pathogen interactions. Many pathogenic bacteria produce lectins that are specific for glycans present on the host surface and that participate in adhesion in the early stages of infection. Lectin-carbohydrate interactions are mostly formed by hydrogen bonds but other types of interactions can also be involved including CH-π stacking, hydrophobic interactions, water-bridging or metal coordination.

Neutron macromolecular crystallography (NMX) offers unique insights into the hydrogen-bonding network as it directly locates and visualizes all hydrogen (or deuterium) atoms. Perdeuteration where all hydrogen atoms are replaced by deuterium atoms enhances their visibility in the neutron maps. While perdeuteration of recombinant proteins is almost routinely carried out in dedicated facilities, the production of perdeuterated sugars is still very challenging.

Using NMX, we have unravelled the details of protein-carbohydrate interactions in two fucose-specific lectins, with the unique feature of producing perdeuterated monosaccharide fucose using a glyco-engineered strain of *E. coli* bacteria for preparation of co-crystals. PLL lectin from bacteria *Photorhabdus luminescens* was chosen as a model system for a detailed description of the H-bonding network involved in sugar recognition, including direct and water-bridged hydrogen bonds as well as CD-π stacking interactions.

LecB lectin from *Pseudomonas aeruginosa*, a human opportunistic pathogen that causes lethal infections in cystic fibrosis patients, is currently viewed as a potential drug target for glycomimetic compounds with antiadhesive properties. The neutron study enabled a complete description of the hydrogen-bonding network and the protonation states of charged amino acids involved in the sugar binding including the observation of a low-barrier hydrogen bond between fucose and the protein.

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