MS10 Protein-carbohydrate interactions

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Molecular recognition mechanism for the galactoside binding in a melibiose transporter MelB
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Abstract
The major facilitator superfamily (MFS) is one of the largest transporter families containing uniporters and secondary active transporters. *Salmonella typhimurium* melibiose transporter MelB<sub>St</sub> is a prototype of the Na<sup>+</sup>-coupled MFS transporters, and it catalyzes stoichiometric transport of galactosides with Na<sup>+</sup>, Li<sup>+</sup>, or H<sup>+</sup>. MelB<sub>St</sub> exhibits a loose sugar specificity with affinities for a wide range of galactosides of various modifications at the non-galactosyl moiety but with no affinity for glucose or glucosides. This sugar recognition mechanism was a long-unsolved puzzle till our crystal structures were resolved. We so far obtained seven structures of MelB<sub>St</sub> bound with different sugars or sugar analogs and deciphered the molecular recognition mechanism for the sugar binding. MelB<sub>St</sub> has a charged- and Trp residues-clustered narrow pocket to select for the specific galactosyl moiety and a large non-specific pocket to accommodate the chemically diverse non-galactosyl moieties. The cation-binding pocket is directly connected to the galactosyl-specific binding site, setting the structural basis for the coupled transport. These key structural findings have laid a solid foundation for understanding the cooperative binding and symport mechanisms in Na<sup>+</sup>-coupled MFS transporters, including eukaryotic transporters such as MFSD2A.

References