BACTERIAL LECTINS AND DYNAMICS OF GLYCOLIPIDS IN HOST MEMBRANES

Anne Imberty

Centre de Recherche sur les Macromolécules Végétales, CNRS and Université Grenoble Alpes, Grenoble, France

anne.imberty@cermav.cnrs.fr

Due to their interactions with glycoproteins, glycolipids and oligosaccharides, lectins play the crucial role of deciphering the glycocode. Furthermore, their multivalency is proposed to play a role in their strong avidity for glycosylated cell surfaces and also in their ability to affect membrane dynamics by clustering glycosphingolipids. Bacterial lectins are able to bind to glycoconjugates on human tissues and are therefore thought to be involved in the first step of infection. The role of lectins in membrane invagination indicates that they could also play a role in internalization of intracellular pathogens.

Lectins with modified valency were designed from the β-propeller fold of *Ralstonia solanacearum* lectin (RSL) that presents six fucose binding sites. After identification of key amino acids by molecular dynamics calculations, engineered lectins (neoRSLs) with reduced valency were produced and analysed. In a second step, neolectins have been designed with complete control of the number and the position of each of the binding sites. Whereas the avidity only depends on the presence of at least two binding sites, the ability to curve domains and invaginate membranes critically depends on the distance between two adjacent binding sites.

LecA, a *Pseudomonas aeruginosa specific* lectin specific for glycosphingolipid, is also able to invaginate membrane. LecA was demonstrated to be necessary for internalization of the bacteria in epithelial cells. Bivalent ligands, identified by focused galactoside-conjugates library, are able to cluster the two neighboring sites of LecA. Such high affinity ligands prevent *P. aeruginosa* invasion of human lung epithelial cells.