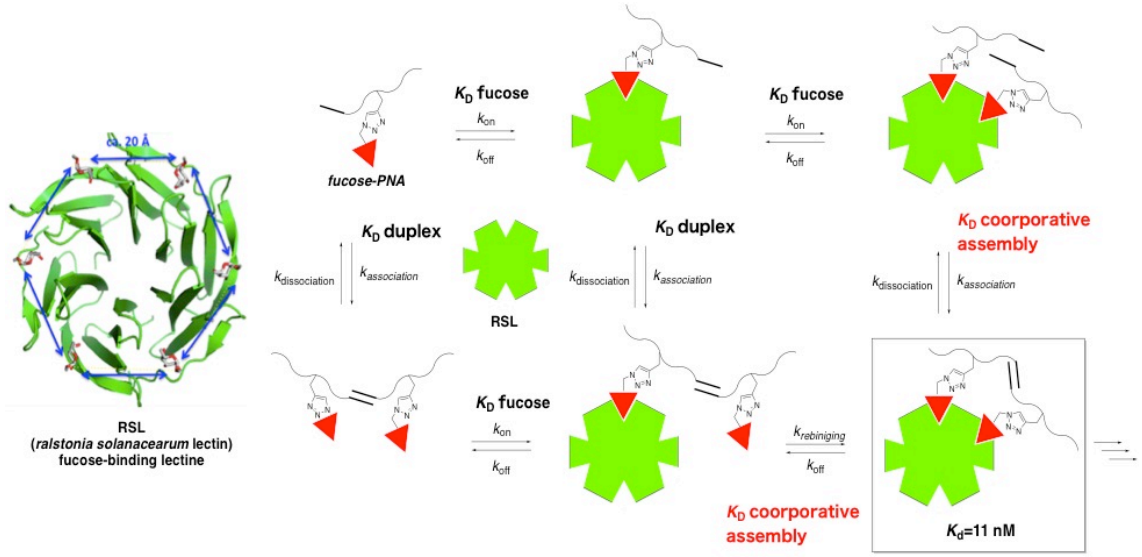
Dynamic cooperative glycan assembly blocks binding of bacterial lectins to epithelial cells

T. Machida[1], A. Novoa[1], É. Gillon [2], S. Zheng[3], J. Claudinon[3], T. Eierhoff[3], A. Imberty[2], W. Römer[3], N. Winssinger[1]*

[1]Department of Organic Chemistry, NCCR Chemical Biology, University of Geneva, 30 quai Ernest Ansermet, 1211 Geneva, Switzerland, [2]CERMAV UPR5301, CNRS, and Université Grenoble Alpes, BP 53, 38041 Grenoble cedex 9, France, [3]Faculty of Biology, Albert-Ludwigs-University Freiburg, Schänzlestraße 1, and Centre for Biological Signalling Studies (BIOSS), Albert-Ludwigs-University Freiburg, Schänzlestraße 18, 79104 Freiburg, G

Pathogenic bacterial infection to the host frequently utilizes lectin which recognizes glycan on cell surface of host. Lectin usually has multiple glycan-binding pockets and the multivalent inhibitor which simultaneously blocks multiple pockets is potent anti-bacterial medication strategy.

RSL was successfully blocked by conjugate with fucose and short peptide nucleic acid (PNA) with palindromic sequence (K_D=11 nM) in which neither fucose nor PNA had comparable affinity (fucose: K_D=2200 nM. PNA: GGCC, self hybridization K_D=3800 nM). That suggested that host protein stabilize beneficial dimer formation. This conjugate had IC_{50} of 555 nM to inhibit the binding of fucose-binding lectin BambL to epithelial cells with efficiency of more than 700-hold compared to L-fucose.



1) T. Machida, A. Novoa, É. Gillon, S. Zheng, J. Claudinon, T. Eierhoff, A. Imberty, W. Römer, N. Winssinger, *Angew. Chem. Int. Ed*. **2017**, *in press.*