Synthesis and binding interactions of secondary cell wall polysaccharide fragments of paenibacillus

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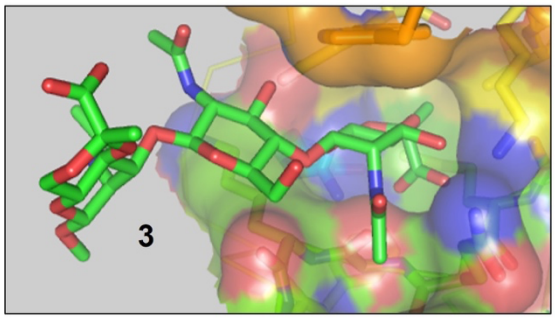
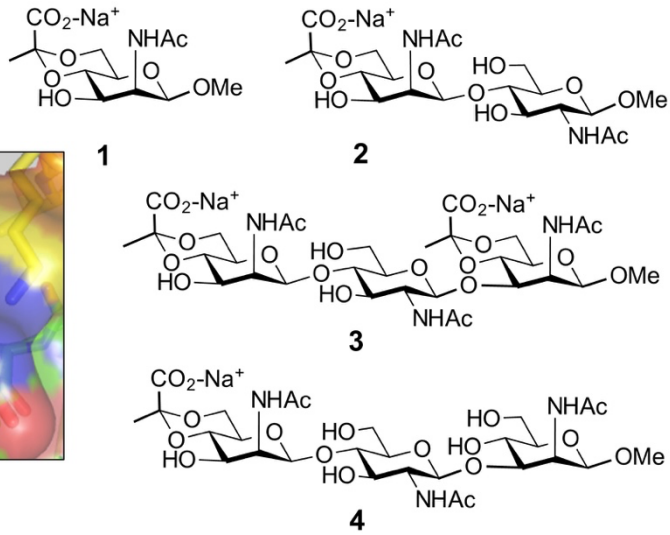
Surface (S-) layer proteins of *Paenibacillus alvei* are non-covalently bound through the pyruvyl anchor of its secondary cell wall polysaccharide (SCWP) [-3)[4,6-*O*-pyruvyl]-β-D-ManNAc-(1-4)-β-D-GlNAc-(1-. Aiming at an in-depth study of SCWP biosynthesis and the molecular details of the binding interaction with the N-terminal S-layer homology (SLH) domain trimer, we have set out to synthesize defined oligomeric ligands to be used for crystallographic and ITC binding studies of the wild-type SLH domain trimer as well as select mutants. For the preparation of the challenging β-D-ManNAc linkage, two approaches have been studied.

Inversion at C-2 of a β-linked glucopyranosyl unit followed by azide introduction and conversion into acetamido groups was used for the assembly of ligands **1**-**3**.[1,2] For the synthesis of a tetrasaccharide ligand, hydrogen bond mediated aglycon delivery[3] was employed using a 2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-picoloyl-protected mannosyl thioglycoside donor. Binding of ligands (in a nanomolar K_D range) was mainly driven by the terminal pyruvylated ManNAc residue as shown for trisaccharide **3** (pdb 7sv4), thus opening future perspectives to inhibit bacterial cell wall assembly.[4]





Bibliographic references:

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Financial Support from Austrian Science Fund (P27374-B, P32521-B to C.S. and P.K.)