# Activity-based protein profiling probes reveal the mode of action of the biofilm degrading PslG

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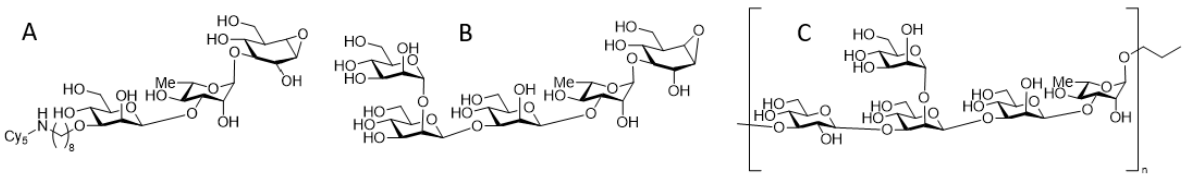
*Pseudomonas aeruginosa* are opportunistic bacteria causing chronic infections in cystic fibrosis and immune compromised patients.[1,2,3]Depending on the environment, *P. aeruginosa* can produce a biofilm that consists of a combination of DNA, proteins and polysaccharides.[4] This biofilm shields the bacteria from the host immune system and antibiotics. One of these polysaccharides is Psl, a polysaccharide built up from pentameric repeating units, consisting of mannose, rhamnose and glucose.[5] It has previously been shown that PslG can cleave Psl, making *P. aeruginosa* susceptible for antibiotics.[6] However, the mode of action of PslG remains enigmatic. We studied PslG using synthetic trisaccharide cyclophellitol-type probes and inhibitors based on different frameshifts of the Psl repeating unit. We show that PslG is actually an endo-glucosidase instead of a postulated[6] endo-mannosidase. This finding is further substantiated with hydrolytic experiments using synthetic pentameric and decameric Psl fragments. Structural studies are underway with the aim to prove the binding mode of inhibitor B, to unambiguously establish the endoglucosidase activity of PslG and provide structural insight into its hydrolytic mechanism. In all, our studies may pave the way for the design of new *P. aeruginosa*-targeting antibiotics.




A. One of the synthesized probes B. One of the synthesized inhibitors C. The synthesized Psl fragment, n = 1 or 2

Bibliographic references:

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