

## ENGINEERING TRANSGLUCOSIDASES REGIOSPECIFICITY FOR PROGRAMMED CHEMO-ENZYMATIC SYNTHESIS OF COMPLEX BACTERIAL CARBOHYDRATES

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An innovative strategy is described for the chemo-enzymatic synthesis of complex microbial oligosaccharides. The concept is based on the exploitation of enzyme engineering technologies to circumvent sugar organic synthesis boundaries and create new glyco-enzymes designed on purpose to enter a programmed chemo-enzymatic pathway. A semi-rational engineering approach allowed the design of  $\alpha$ -transglucosidases with new and tremendously enhanced specificities toward non-natural protected acceptors, compatible with subsequent chemical elongation. Focused on the synthesis of serotype-specific *Shigella flexneri* oligosaccharide haptens, a biological model of importance for human health, glucosylation products were used at an early stage of the chemo-enzymatic pathway and evolved into building blocks serving as intermediates for the synthesis of the desired motifs. To our knowledge, this is the first report of successful engineering of  $\alpha$ -transglucosidase acceptor specificity. Our approach demonstrates the potential of appropriate combinations of planned chemo-enzymatic pathway and enzyme engineering in glycochemistry.

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