

JOINT EVENT

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Mixing enzyme discovery with engineering for sucrose-derived bioproducts: The case of GH13 and GH70 polymerases

The exploration of the natural diversity, through data mining, functional genomics and/or metagenomics is an efficient mean to discover enzymes showing new functions or improved performances. These approaches can be further completed or run in parallel with semi-rational protein engineering based on structure/function studies or directed molecular evolution inspired from nature. Which of these alternatives are the best ones, in terms of effort, rapidity and efficiency? This is an open question to which a definite answer can be hardly formulated a priori. For illustration, we will take a few examples from our most recent work on glucansucrases from GH13 and GH70 families. These enzymes are naturally very efficient transglucosylases. They use sucrose as substrate and catalyze polymerization of its glucosyl units as a main reaction. Depending on their specificity, structures varying in size as well as in glycosidic linkage types can be obtained, thus giving access to an interesting panel of biopolymers. A campaign of genome sequencing and data mining allowed the isolation of atypical enzymes with new product specificities. In particular, a hyper efficient polymerase producing a gel-like polymer and, in contrast an enzyme synthesizing directly from sucrose a polymer of well-controlled low molar mass could be characterized. Structure-function studies combined with mutagenesis assays allowed us to decipher some of the molecular mechanisms behind the control of the polymer size and enzyme processivity. Another key property of these catalysts is coming from their ability to glucosylate a broad spectrum of hydroxylated molecules. Computational protein design, structurally-guided engineering and also random approaches such as neutral evolution was implemented for a fine tuning of their acceptor specificity toward non-natural acceptors such chemically protected disaccharides for vaccinal applications, polyol, flavonoids, or various chemicals. These various approaches will be described and discussed with regard to the engineering objectives.



Figure 1: Example of product diversity obtained with glucansucrases from GH13 and GH70 family

Recent Publications

1. Claverie M et al. (2017) Investigations on the determinants responsible for low molar mass dextran formation by DSR-M dextransucrase. ACS Catal. 7(10):7106-7119.

2. Vuillemin M et al. (2017) A dextran with unique rheological properties produced by the dextransucrase from *Oenococcus kitaharae* DSM 17330. *Carbohydr. Polym.* 179:10-18.
3. M Vuillemin et al. (2016) Characterization of the first α -(1 \rightarrow 3) branching sucrases of GH70 family. *J Biol Chem.* 291(14):7687-702.
4. Salamone S et al. (2015) Programmed chemo-enzymatic synthesis of the oligosaccharide component of a carbohydrate-based antibacterial vaccine candidate. *Chem. Comm.* 51(13):2581-2584.
5. Verges A et al. (2015) Computer-aided engineering of a transglucosylase for the glucosylation of an unnatural disaccharide of relevance for bacterial antigen synthesis. *ACS Catalysis.* 5(2):1186-1198.

Biography

Magali Rемаud Simeon is Professor at the National Institute of Applied Sciences of Toulouse and is head of the Catalysis and Enzyme Molecular Engineering group of the "Laboratoire d'Ingénierie des Systèmes Biologiques and Procédé (LISBP)". She received her PhD in Biochemistry from the University of Toulouse and was Post-Doc at the University of Pennsylvania. She has co-authored more than 150 papers and is co-inventor of 22 patents. Her research activities focus on Enzyme Engineering for white biotechnology, green chemistry, health, food/feed industries and synthetic biology. They cover enzyme structure/activity relationship studies, kinetic resolution, evolution combining both rational and combinatorial approaches, and applications to the synthesis of glycans, glycoconjugates and various synthons of interest. Her work is currently focused on the search and generation of enzymes displaying new specificities and improved catalytic properties. Her objective is to open new trajectories for biomass transformation. To this end, she specifically targets the integration of tailored enzymes in chemo-enzymatic cascades, new metabolic pathways or enzyme-based processes.

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