Engineering polymerases for designed glycans and glycoconjugates

S-02.4-1

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An impressive diversity of glycopolymers and glycoconjugates exists in nature. They present biological, chemical and physico-chemical properties that open a vast application field in health, nutrition, cosmetic and biomaterial sectors. In addition, their native structures can also be subsequently transformed or can serve as model in biomimetic approaches. With this in mind, identifying glycan-synthesizing enzymes is a key step to access to new structures and this is largely facilitated by the flow of carbohydrate-active enzymes sequences arising in databases. Combining enzyme discovery to enzyme engineering and protein design further expands tremendously the scope of accessible catalytic reactions allowing to better control glycan-based architectures .

As an illustration of the power of these approaches, we will focus the presentation on glucansucrases a class of naturally very efficient transglucosylases, which use sucrose as a simple substrate to catalyze the formation of a broad variety of polymers[1]. We will show how sequence mining allowed the isolation of atypical enzymes with new product specificities and how structure function investigations combined with computer-assisted engineering enabled us to better understand and engineer glucansucrase processivity and specificity to open access to well-controlled architectures of polymers, glycosurfactants , new prebiotic and antigenic glycoligosaccharides and glycoconjugates.

1- Claire Moulis, David Guieysse, Sandrine Morel, Etienne Séverac, Magali Remaud-Siméon (2021) Natural and engineered transglycosylases: Green tools for the enzyme-based synthesis of glycoproducts. Current Opinion in Chem Biol. 61: 96-106.