Poster

Structural enzymology for the synthesis and functionalization of biopolymers

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Polymers play a central role in our modern society where they are used as base materials in the manufacture of countless everyday products or they find more sophisticated applications in medicine, diagnostics and fine chemistry. However, less than 1% of the 350 megatons/y of manufactured polymers are bio-based, with the vast majority still being of fossil origin. Environmental as well as sustainability concerns are driving research into renewable and recyclable bio-derived polymers that can replace petroleum-based polymers and that are biocompatible and/or possibly bioactive depending on the targeted applications.[1] Carbohydrate polymerases are tools of choice to meet these expectations and the same is true for decorating enzymes that can modify an existing polysaccharide by glycosylation, oxidation, phosphorylation and sulfation.[2-3] For enzyme engineering, a detailed understanding of the catalytic mechanism of these enzymes is essential to control the structure of the reaction products in term of linkage specificity, chain length and degree of functionalization. However, understanding how these enzymes, generally composed of multiple domains, interact with their substrates is far from trivial as the enzyme-polymer interactions as well as the synthesis dynamics (multi-chain vs. single-chain?) are still poorly understood. In the Biocatalysis team of TBI we are developing an integrative approach for the characterization of these enzymes using a combination of structural biology techniques including X-ray diffraction, small-angle X-ray scattering, NMR and cryo-electron microscopy, complemented with biochemical characterization and molecular modelling. Here, the recent structural studies targeting selected enzyme classes such as glucansucrases, glycoside-phosphorylases and polysaccharide kinases will be presented. The complementarity of these techniques will be discussed, in particular when studying the enzyme dynamics that occur during the catalysis.

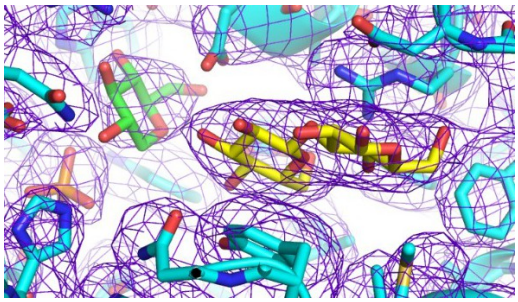

Image: Active site of a carbohydrate phosphorylase as obtained by cryo-EM.

[1] Zhu Y., Romain C. & Williams C.K., "*Sustainable polymers from renewable resources"*, (2016) Nature 540, 354 (2016).

[2] Molina M., Cioci G., Moulis C., Séverac E. & Remaud-Siméon M., *"Bacterial α-Glucan and Branching Sucrases from GH70 Family: Discovery, Structure-Function Relationship Studies and Engineering",* (2021) *Microorganisms,* Jul 28;9(8):1607. doi: 10.3390/microorganisms9081607.

[3] Li A., Benkoulouche M., Ladeveze S., Durand J., Cioci G., Laville E. & Potocki-Veronese G., *"Discovery and Biotechnological Exploitation of Glycoside-Phosphorylases"*, (2022) Int J Mol Sci. Mar 11;23(6):3043. doi: 10.3390/ijms23063043.