Enzymatic Sugar Mastery

Induction of glycan conformations by CAZymes

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In Short

- Carbohydrate-active enzymes (CAZymes) are diverse enzymes crucial for handling sugars in biological processes
- Understanding CAZymes, especially key enzymes like (α)-mannosidase II (GMII), is vital for drug development, including cancer treatments targeting abnormal sugar patterns on cancer cells.
- The use of advanced computational techniques like REST-RECT offers insights into how CAZymes like GMII function

Carbohydrate-active enzymes (CAZymes) are a diverse group of enzymes responsible for handling carbohydrates like sugars and their complex forms found in various biological processes. Think of them as the workers in a busy kitchen, where they chop, mix, and modify different ingredients to create various dishes. CAZymes can be categorized into three main classes based on their tasks: glycoside hydrolases (GHs), which break down sugars; glycosyltransferases (GTs), which help build complex sugar molecules; and polysaccharide lyases (PLs), which are involved in cutting long sugar chains. These enzymes play critical roles in processes like building cell walls, producing energy, and interacting with pathogens. To handle the wide range of sugar structures they encounter, CAZymes come equipped with nearly 300 different folds that allow them to bind to specific sugars effectively. One fascinating aspect of CAZymes, especially GHs, is how they work on sugar molecules. When sugars bind to these enzymes, they undergo changes in shape, which help the enzymes break down the sugar bonds more efficiently. This shape-shifting ability is crucial for the enzyme to grab onto the sugar tightly and perform its job effectively. Understanding the mechanics of how these enzymes work is not only intriguing but also essential for various applications, including drug development. For example, in cancer research, scientists have found that certain types of cancer cells display abnormal sugar patterns on their surfaces. By targeting the enzymes responsible for these patterns, there is hope to develop treatments that can stop cancer cells from spreading. However, developing such treatments is challenging. While there have been efforts to design drugs that specifically target these enzymes, finding ones that work without causing harmful side effects has proven difficult. Therefore, it is required to constantly explore new techniques and methodologies to better understand how these enzymes function and how they can be targeted effectively. One such approach involves using advanced computer simulations to study how these enzymes interact with sugars at the molecular level. By simulating these interactions, we can gain insights into how the enzymes distort sugar molecules and use this knowledge to design better drugs. We here focus on a specific enzyme called (α)-mannosidase II (GMII), which plays a crucial role in modifying sugar molecules within cells (Figure 1). By studying GMII and its interactions with sugars, we aim to uncover the fundamental mechanisms behind sugar distortion and how this process could be targeted for therapeutic purposes. Using a rather

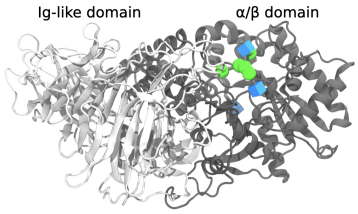

***Figure 1:** Structure of GMII in complex with its substrate M5G0 (PDB entry: 3CZN). The globular structure consists of an Ig-like domain, harboring β-sheets (white), and an α/β domain with the catalytic site (gray).*

new computational technique called REST-RECT 1, we try to shed light on how GMII works and how the flexibility of the glycan in the binding site can help in the conformational rearrangements. In summary, CAZymes are like molecular chefs, intricately involved in shaping and modifying sugars in biological systems. By unraveling the mysteries of how these enzymes work, we hope to uncover new strategies for treating diseases and improving human health.

WWW

https://www.hmi.uni-bremen.de/Grothaus/grothaus_ home.html

More Information

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DFG Subject Area

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