

Glycosylation Helps Cellulase Enzymes Bind to Plant Cell Walls

Computer simulations suggest a new strategy to design enhanced enzymes for biofuels production.

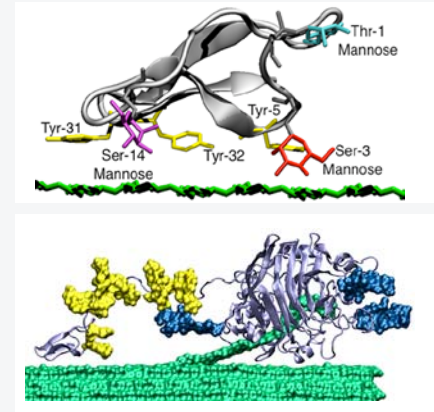
Large-scale computer simulations predict that the addition of glycosylation on carbohydrate-binding modules can dramatically improve the binding affinity of these protein domains over amino acid mutations alone. These simulations suggest that glycosylation can be used as a protein engineering tool to enhance the activity of cellulase enzymes, which are a key component in the conversion of cellulose to soluble sugars in the production of biofuels.

Glycosylation is the covalent attachment of carbohydrate molecules to protein side chains, and is present in many proteins across all kingdoms of life. Moreover, glycosylation is known to serve a wide variety of functions in biological recognition, cell signaling, and metabolism. Cellulase enzymes, which are responsible for deconstructing cellulose found in plant cell walls to glucose, contain glycosylation that when modified can affect enzymatic activity—often in an unpredictable manner.

To gain insight into the role of glycosylation on cellulase activity, scientists at the National Renewable Energy Laboratory (NREL) used computer simulation to predict that adding glycosylation on the carbohydrate-binding module of a cellulase enzyme dramatically boosts the binding affinity to cellulose—more than standard protein engineering approaches in which amino acids are mutated. Because it is known that higher binding affinity in cellulases leads to higher activity, this work suggests a new route to designing enhanced enzymes for biofuels production. More generally, this work suggests that tuning glycosylation in cellulase enzymes is a key factor to consider when engineering biochemical conversion processes, and that more work is needed to understand how glycosylation affects cellulase activity at the molecular level.

Technical Contact: Gregg Beckham, gregg.beckham@nrel.gov

Reference: Taylor, C.B.; Talib, M.F.; McCabe, C.; Bu, L.; Adney, W.S.; Himmel, M.E.; Crowley, M.F.; Beckham, G.T. (2012). "Computational Investigation of Glycosylation Effects on a Family 1 Carbohydrate-Binding Module." *J. Biol. Chem.* 287(5), pp. 3147-55.



Top: The carbohydrate-binding module from *Trichoderma reesei* Cel7A with O-glycosylation (mannose in red at Serine-3, blue at Threonine-1, and purple at Serine-14). The green surface is cellulose. Bottom: The *T. reesei* Cel7A enzyme catalytically engaged on a cellulose crystal with the carbohydrate-binding module shown on the left end of the protein. The glycans on the carbohydrate-binding module are shown in yellow spacefill.

Key Research Results

Achievement

Using NREL's RedMesa supercomputer and the National Science Foundation's supercomputers, NREL researchers predicted that adding glycosylation to the carbohydrate-binding module of cellulase enzymes can dramatically improve the binding affinity of the enzyme.

Key Result

Once experimentally validated, the predictions may provide a new avenue for improving cellulase enzyme activity through glycoprotein engineering.

Potential Impact

This approach may ultimately aid in lowering cellulase costs for biofuels production.