Poster Presentation

BM.P49

Structure of the S.coelicolor A3(2) N-acetylhexosaminidase provides insight into GH20 catalysis

N. Thi Nguyen[1], N. Doucet[1]

[1]*INRS-Institut Armand-Frappier, Université du Québec, Laval, QC, Canada*

β-N-acetylhexosaminidases (HEX - EC 3.2.1.52) are glycosidases that catalyze the glycosidic linkage hydrolysis of gluco- and galacto-configurations of N-acetyl-β-D-hexosaminides. These enzymes have shown considerable interest due to their importance in human physiology and their potential use for the enzymatic synthesis of carbohydrates and glycomymetics. HEX can cleave the β-1,4-glycosidic bonds of polymers with long saccharide chains, and utilize a double-displacement retaining mechanism with neighboring group participation to yield an oxazolinium intermediate. In this study, the three-dimensional structure of the wild-type and catalytically impaired E302Q HEX variant from the soil bacterium Streptomyces coelicolor A3(2) (ScHEX-family GH20) were solved in ligand-free forms and in the presence of 6-acetamido-6-deoxy-castanospermine (6-Ac-Cas). The E302Q variant was also trapped as an intermediate with oxazoline bound to the active center. The complexed structures reveal an active pocket with multiple subsites packed with four Trp, providing a hydrophobic environment that forms a small active-site architecture suitable for holding polysaccharide chains and protecting the formed oxazolinium intermediate during catalysis. Crystallographic evidence highlights structural variations in the loop 3 environment, suggesting conformational heterogeneity for important active-site residues of this GH20 family member.

Keywords: glycosidase