Studies of the reaction mechanism of xylanase and the ration design to increase activities in extreme conditions

Qun Wan

College of Science
Nanjing Agricultural University, Nanjing 210095, P.R. China
Email: qunwan@njau.edu.cn

Glycoside hydrolases (GHs) commonly use the retaining or inverting mechanisms to hydrolyze carbohydrates, and the rates of catalysis are usually pH dependent. Deep understanding of these pH-dependent reaction mechanisms is of great importance for protein engineering and drug design. We used high-resolution X-ray crystallography to analyze the sugar ring configurations of an oligosaccharide ligand during hydrolysis for the family 11 GH, and the results support the $^{1}S_{3}\rightarrow{}^{4}H_{3}\rightarrow{}^{4}C_{1}$ conformational itinerary. These results indicate that sugar ring flexibility may help to distort and break the glycosidic bond. Constant pH molecular dynamics simulations and neutron crystallography demonstrate that the catalytic glutamate residue (E177) has alternate conformational changes to transfer a proton to cleave the glycosidic bond. Furthermore, a neutron crystallography analysis shows that the H-bond length between E177 and its nearby tyrosine residue (Y88) is shortened when the pH increases, preventing E177 from rotating downward and obtaining a proton from the solvent for catalysis. This result indicates that the H-bond length variation may play a key role in the pH-dependent reaction mechanism. In summary, our results demonstrate that both sugar ring flexibility and protein dynamics are important in the pH-dependent reaction mechanism and may help to engineer GHs with different pH optima.

Qun Wan, Ph.D.
Professor, Department of Physics, College of Science, Nanjing Agricultural University
1 Weigang, Nanjing, Jiangsu Province, China 210095
Email: qunwan@njau.edu.cn

Research Field:

Protein engineering using structural biology, zymology and molecular dynamic simulation

Education

2002. 1 – 2008.2: Ph.D., Department of Molecular Physiology and Biophysics, College of Medicine, University of Vermont, Burlington, Vermont, USA, 05405.

1996.9 – 1999.8: M.S., College of Bioengineering, East China University of Science and Technology, Shanghai, China, 200237

1991.9 - 1994.8: B.S., Food Science, Jinling University of Science and Technology, Nanjing, China

Work Experience

- 2015.7 – present: Professor, Department of Physics, College of Science, Nanjing Agricultural University, Nanjing, China
- 2013.6 – 2015.6: Professor, College of Medicine, Yangzhou University, Yangzhou, China
- 2012.3 – 2013.6: Postdoctoral fellow in the Biology and Soft Matter Division, Oak Ridge National Lab, Oak Ridge, Tennessee, USA.
- 2011.6 – 2012.3: Director in the Drug Discovery Division, Shanghai Medicilon Inc., Shanghai, China.
- 2008. 3 – 2011.6: Postdoctoral fellow in the Department of Pharmacology, Case Western Reserve University, Cleveland, Ohio, USA.
- 2000. 8 – 2002. 1: Technician in the Department of Molecular Physiology and Biophysics, University of Vermont, Burlington, Vermont, USA.
- 2000. 2 – 2000. 8: Lab assistant in the Department of Biochemistry, Hong Kong University of Science and Technology, Hong Kong, China.

Research Projects

- Reaction mechanism and protein engineering of xylanase
- Reaction mechanism and drug design using the drug target, dihydrofolate reductase (DHFR)

Selected publications

1) Li, Z., Zhang, X., Wang, Q., Li, C., Zhang, N., Zhang, X., Xu, B., Ma, B., Schrader, T., Coates, L., Kovalevsky, A., Huang, Y.*, **Wan, Q***. ***ACS Catalysis***, 2018, 8, 8058-8068

2) **Wan Q.**, Parks J.M., Hanson B.L., Fisher S.Z., Ostermann A., Schrader T.E., Graham D., Coates L., Langan P., Kovalevsky, A. Direct determination of protonation states and visualization of hydrogen bonding in a glycoside hydrolase with neutron crystallography. ***Proc Natl Acad Sci USA,*** 112(40): 12384-12389.

3) **Wan Q.,** Bennett C.B.,Wilson A.W., Kovalevsky A., Langan P., Howell E., Dealwis C.G. Toward resolving the catalytic mechanism of dihydrofolate reductase using neutron and ultrahigh resolution X-ray crystallography. ***Proc Natl Acad Sci USA,*** 111(51):18225-18230.