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Structural basis for substrate recognition mechanism of ER glucosidase II

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The endoplasmic reticulum (ER) possesses a sophisticated quality control system to proofread newly synthesized proteins. A series of N-linked oligosaccharide intermediates attached on the nascent proteins serves as specific tags for the quality control system. In this system, glucosidase II is involved in trimming of non-reducing terminal glucose residue of N-glycan intermediates. Glucosidase II consists of approximately 110 kDa catalytic α subunit (GIIα) and 60 kDa non-catalytic regulatory β subunit (GIIβ). It has been shown that GIIα alone can hydrolyze a small α-glycosidase model substrate (pNP-glucose), while it cannot catalyze deglucosylation of the N-linked oligosaccharide substrates unless it makes a complex with GIIβ. In this study, we determined the first crystal structure of GIIα in the absence and presence of its inhibitor 1-deoxynojirimycin at 1.6-Å resolution. The crystal structure revealed that GIIα has a characteristic segment at the N-terminus as compared with the cognate glycoside hydrolases (GH31). Interestingly, the N-terminal segment was accommodated on the substrate-binding pocket. Based on these results, we suggest that the N-terminal segment of GIIα undergoes structural rearrangement through interaction with GIIβ, thereby promoting the substrate-binding capacity for the N-linked oligosaccharide substrates.

Keywords: protein X-ray crystallography, glycoside hydrolase, quality control system