26. Synthetic Approaches to Glycoprotein Quality Control System

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N-Glycosylation of Asn is a prominent modification of eukaryotic proteins. It occurs co-translationally in ER and then becomes a subject of further processing by a variety of glycosidases and glycosyltransferases to produce highly diverse structures. It is becoming clear that a number of intracellular proteins are in involved in this process. For instance, endoplasmic reticulum (ER) residing molecular chaperones calnexin (CNX) and calreticulin (CRT) are considered to recognize the oligosaccharide portion (Glc1Man9GlcNAc2) of glycoproteins and assist their folding. Other major players in glycoprotein quality control are glucosyl transferase (UGGT), mannosidase-like lectin (EDEM) and cargo receptors (VIP36, ERGIC-53) and ubiquitin ligase (Fbs1). All of these proteins likely recognize precisely different oligosaccharide structures, although molecular basis of these phenomena is unclear. We achieved the first chemical synthesis of dodecasaccharide (GlcMan9GlcNAc2), which is a putative ligand of CNX and CRT. Recently, we developed the first synthetic substrate of UGGT. A systematic study is in progress to 1) comprehensively prepare *N*-linked glycans and library of their partial structures, that may exist in ER and play roles in protein quality control, 2) synthesize glycoprotein having homogeneous glycan chain, and analyses of interactions between synthetic glycans and various proteins involved in glycoprotein quality control.