

## N-LINKED GLYCANS IN PROTEIN FOLDING AND QUALITY CONTROL

A. Helenius\*, P. Deprez, M. Gautschi, K. Quirin,  
C. Ritter, E. Frickel, and L. Ellgaard

*Swiss Federal Institute of Technology Zurich (ETH Zurich), Zurich, Switzerland*  
*ari.helenius@bc.biol.ethz.ch*

Newly synthesized proteins enter the ER co-translationally and undergo folding, oligomeric assembly, and quality control before transport to the Golgi complex and beyond. Folding begins co-translationally when a domain has emerged from the translocon complex. Several chaperones and folding enzymes including calnexin, calreticulin, ERp57, BiP, and PDI bind to growing nascent chains, and help the proteins fold during and after chain termination. If something goes wrong, the proteins are unable to exit to the Golgi complex, and get degraded. In the case of glycoproteins, the addition of N-linked glycans and their trimming is often essential for proper maturation because a panel of lectins and sugar modifying enzymes in the ER help to determine the fate of such proteins. Glucose- and mannose-trimming by ER-glycosidases is used as a 'timer' for protein entry into the calnexin/calreticulin cycle, a chaperone machinery specific for glycoproteins, and for degradation. Particularly important are two enzymes that regulate the on-and-off reactions in the calnexin/calreticulin cycle: glucosidase II (which removes two glucoses from the core oligosaccharide) and UDP-glc:glycoprotein glucosyltransferase (GT)(which adds back one glucose residue). Glucosidase II determines when and how a glycoprotein can enter the cycle, and GT is a folding sensor that decides whether a glycoprotein is ready to leave the cycle. In the lecture, the properties of these important enzymes will be described. Recent biochemical, structural, and cell biological results provide the basis for an increasingly detailed model for their action, and for the function of calnexin and calreticulin as glycoprotein specific chaperones in the ER.

PL  
1