

COLLOQUIA IN CELLULAR SIGNALLING

Venue: Medical University Vienna, Center for Physiology and Pharmacology,
Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**".

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Friday **14.6.2013** **11:00 s.t.** **Erwin Ivessa** (host: M. Hohenegger)
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***"The sweet and the bitter: N-linked glycans in ER quality control
and ER-associated glycoprotein degradation"***

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Abstract:

An important and early step in the biogenesis of proteins that are imported into the endoplasmic reticulum (ER) is their quality control of protein folding. This process is mediated by a set of molecular chaperones, and in the case of N-glycosylated proteins, in addition by several lectins, glycosidases and glycosyl transferases. The function of the quality control system is highly dependent on the interplay between these proteins and precise oligosaccharide structures on the newly synthesized glycoproteins. Those glycoproteins that remain terminally misfolded are subject to a process termed ER-associated degradation (ERAD), involving their retrograde transport from the lumen of the ER to the cytosol, deglycosylation by N-glycanase, polyubiquitylation, and degradation by the 26S proteasome.

We are studying ERAD using mostly a luminal ER model protein expressed in selected cell lines with defects in the N-glycosylation pathway that resemble those found in certain congenital disorders of glycosylation (CDGs). In addition, we employ inhibitors of proteasomal degradation and of N-glycan processing to reveal requirements for ERAD to occur. I will present an overview on our current understanding of ERAD in terms of mechanistic aspects of the process and its intracellular localization and discuss future challenges in this field.