NOVEL REGULATION OF POSTTRANSLATIONAL MODIFICATIONS IN THE GOLGI APPARATUS: FROM BASIC SCIENCE TO DISEASES

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In eukaryotes half of cellular proteins are secreted or membrane bound. Both groups of proteins are synthesized on membrane bound polysomes, translocated into the lumen of the endoplasmic reticulum (ER), transported first to the Golgi apparatus (GA) and thereafter to their final destination within or outside the cell. In the lumens of the ER and GA eighty percent of these proteins become glycosylated, sulfated and phosphorylated by enzyme catalyzed reactions using as substrates nucleotide-sugars, nucleotide-sulfate and ATP. These nucleotide derivatives must be transported into the lumens of the above organelles from the cytosol, the site where most are synthesized. Transport of these substrates into the lumen of the GA is mediated by specific transporters, which are antiporters with the corresponding nucleoside monophosphate. While the initially characterized transporters were specific for one substrate recent studies have shown that others may be multisubstrate. Mutants in these transporters have been characterized in uni- and multi-cellular eukaryotes such as yeast, *Leishmania*, *Entamoeba*, *Drosophila*, nematodes, plants and mammals. In many of these organisms mutations of transporter proteins result in striking developmental phenotypes including diseases such as Leukocyte Adhesion Deficiency Syndrome II which affects growth and brain development. Very recent studies with *C. elegans* suggest tissue functional redundancy of these transporters.

Key words: glycosylation, protein secretion, membrane biogenesis