1. Abstract

The Golgi complex is the central station along the secretory pathway to sort proteins and lipids to their final destinations. It exists of a series of flattened cisternal membranes that are aligned in parallel to form polarized stacks. This structure is actively maintained amid a large flow of biosynthetic transports through the organelle. Cytosolic oriented Golgi-associated proteins including matrix proteins and a spectrin/ankyrin framework have been identified that may coordinate or maintain the Golgi architecture. Posttranslational modification of these proteins such as occurring during mitosis or apoptosis results in fragmentation of the Golgi complex and demonstrates the dynamic properties of this organelle. The Golgi complex is also a platform to integrate different signaling cascades, which may regulate the unique structure of the Golgi complex.

Recently, Golgi-derived lipid rafts were isolated. At the plasma membrane, lipid rafts are considered to play an important role in the coordination of signal transduction processes. Characterization of the protein components of Golgi-derived lipid rafts revealed the distinct identity of these microdomains at the Golgi complex rather than being the precursors of lipid rafts at the plasma membrane. Described in this thesis is a novel protein component of these microdomains. By use of degenerate PCR, combined with phage display, the complete coding sequence of this protein was cloned. Its primary structure and subsequent characterizations show that it is GPI-anchored and therefore a luminal protein. It is a Golgi resident protein and has a Brefeldin A-sensitive Golgi localization. Therefore, this protein was annotated GREG for Golgi-resident GPI-anchored protein. Mapping the Golgi-targeting signal in GREG shows a requirement of the EQ tandem repeat for its Golgi localization. Inhibition of GREG expression by double-strand RNA-mediated interference (dsRNAi) reveals an essential role for GREG in maintenance of the Golgi integrity. Expression of GPI anchor-deficient GREG mutant proteins results in vesiculation of the Golgi complex. These results imply the involvement of a luminal protein in maintenance of the Golgi structure.