Quality-controlled lipid-based protein sorting into selective endoplasmic reticulum exit sites by glycan remodeling

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GPI-anchored proteins (GPI-APs) exit the endoplasmic reticulum (ER) through a specialized export pathway in the yeast Saccharomyces cerevisiae. We have recently shown that very long acyl chain (C26) ceramides present in the ER membrane drives clustering and sorting of GPI-APs into selective ER exit sites (ERES). Here we found that this lipid-based ER sorting also involves the C26 ceramide as lipid moiety of GPI-APs, which is incorporated into the GPI anchor through a lipid remodeling process after protein attachment in the ER. Moreover, we also show that the presence of the C26 ceramide in the GPI anchor is monitored by the remodeling of the GPI-glycan. Therefore, our study reveals a novel quality control system that ensures lipid-based sorting of GPI-APs into selective ERES for differential ER export.

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