Golgi dysfunction. For example, cancer cells have fragmented Golgi, which may be the reason why these cells have reduced cell attachment, changes on cell surface glycan, and secretion of lysosomal enzymes, all of which could be caused by Golgi dysfunction.

Methods: A unique multidisciplinary approach. We have developed a unique multidisciplinary approach employing biochemistry, cell biology, electron microscopy, and proteomics and glycomics, combined with a novel in vitro reconstitution assay, to provide a mechanistic explanation for Golgi structure formation and function. This allowed us to reveal that stack formation directly involves the Golgi stacking protein GRASP65 and GRASP55, which play complementary and essential roles in Golgi cisternal stacking by forming mitotically regulated trans-oligomers (3-5).

Results: Golgi cisternal stacking is required for accurate glycosylation. We have explored the functional consequences of Golgi unstacking by the depletion of GRASP55, GRASP65 or both. We found that Golgi cisternal unstacking stimulates COPI vesicle budding and thus enhances protein transport. Golgi fragmentation, however, impairs protein sorting and alters the glycosylation of cell surface proteins. Subsequently, cell adhesion and migration were reduced when the Golgi was unstacked. Furthermore, total protein synthesis and the proliferation of cells with unstacked Golgi were enhanced. We propose that Golgi stack formation is a flux regulator for protein trafficking and thereby functions as a quality control mechanism for protein sorting and modifications, e.g. glycosylation (Figure 1) (6, 7). This work has significant impact in understanding human diseases in which the Golgi becomes abnormal.

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