Golgi membrane proteins YIPF3 and YIPF4 regulate turnover of the Golgi apparatus through autophagy

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Autophagy is a fundamental process for degrading and recycling cytosolic components. Autophagic substrates are degraded in a nonselective manner, but also specific organelles and proteins are selectively targeted through autophagy receptors. performing quantitative proteomic analysis of *Atg5*-deficient mouse brain identified YIPF3/YIPF4, Golgi membrane proteins with no known function, as candidate factors. Since these factors have a characteristic sequence (LIR motif) required for autophagy receptors, it may act as a receptor for Golgi selective autophagy called Golgiphagy.

First, we observed the localization of YIPF3 and YIPF4 during autophagy induction. These proteins formed punctate structures, which were colocalized with the puncta of the autophagosome marker and the proteins of each Golgi subcompartment (cis-, medial-, and trans-Golgi proteins). Moreover, we found that the Golgi protein interacted with specific ATG8s through LIR motif, similarly to other autophagy receptors. We, therefore, investigated whether these proteins function as a receptor for Golgiphagy.

For this purpose, we have developed two novel Golgiphagy-reporter systems for imaging and biochemical analysis, because few assays have been established to evaluate Golgiphagic activity. Using a Golgi-targeting motif, we fused tandem fluorescent tags, GFP-RFP and Halo-GFP, to this motif. This enables us to perform Golgiphagy analysis more easily and precisely. Using this system, we demonstrated that YIPF3 and YIPF4 are required for Golgi degradation by autophagy in an LIR motif-dependent manner.

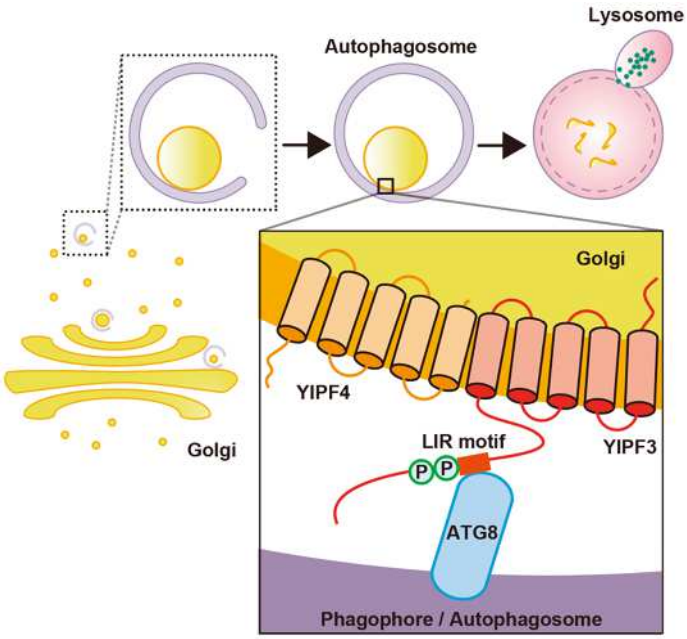

Figure. Model of how YIPF3–YIPF4-mediated Golgiphagy occurs and is regulated.