Intra-Golgi and retrograde Golgi-to-ER traffic

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https://reactome.org
**Introduction**

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**Literature references**


Reactome database release: 83

This document contains 4 pathways (see Table of Contents)

https://reactome.org
Intra-Golgi and retrograde Golgi-to-ER traffic

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The mammalian Golgi complex, a central hub of both anterograde and retrograde trafficking, is a ribbon of stacked cisterna with biochemically distinct compartments (reviewed in Glick and Nakano, 2009; Szul and Sztul, 2011). Anterograde cargo from the ERGIC and ER is received at the cis-Golgi, trafficked through the medial- and trans-Golgi and released through the trans-Golgi network (TGN) to the endolysosomal system and the plasma membrane. Although still under debate, current models of Golgi trafficking favour the cisternal maturation model, where anterograde cargo remain associated with their original lipid membrane during transit through the Golgi and are exposed to sequential waves of processing enzymes by the retrograde movement of Golgi resident proteins. In this way, cis-cisterna mature to medial- and trans-cisterna as the early acting Golgi enzymes are replaced by later acting ones (reviewed in Pelham, 2001; Storrie, 2005; Glick and Nakano, 2009; Szul and Sztul, 2011). More recently, a kiss-and-run (KAR) model for intra-Golgi trafficking has been proposed, which marries aspects of the cisternal maturation model with a diffusion model of transport (reviewed in Mironov et al, 2103).

Like the anterograde ERGIC-to Golgi transport step, intra-Golgi trafficking between the cisterna appears to be COPI-dependent (Storrie and Nilsson, 2002; Szul and Sztul, 2011). Numerous snares and tethering complexes contribute to the targeting and fusion events that are required to maintain the specificity and directionality of these trafficking events (reviewed in Chia and Gleeson, 2014). Golgi tethers include long coiled coiled proteins like the Golgins, as well as multisubunit tethers like the COG complex. These tethers make numerous interactions with other components of the secretory system including RABs, SNAREs, motor and coat proteins as well as components of the cytoskeleton (reviewed in Munro, 2011; Willet et al, 2013).

Retrograde traffic from the cis-Golgi back to the ERGIC and ER depends on both the COPI-dependent pathway, which appears to be important for recycling of KDEL receptors, and a more recently described COPI-independent pathway that relies on RAB6 (reviewed in Szul and Sztul, 2011; Heffernan and...
Simpson, 2014). RAB6 and RAB9 also play roles at the TGN side of the Golgi, where they are implicated in the docking of vesicles derived from the endolysosomal system and the plasma membrane (reviewed in Pfeffer, 2011)

**Literature references**


**Editions**

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The trans-Golgi network is the docking site for retrograde cargo from the endolysosomal system and the plasma membrane. Typical cargo includes recycling resident TGN proteins such as TGOLN2 (also known as TGN46), receptors such as the mannose-6-phosphate receptors and toxins like Shiga, cholera and ricin which use the retrograde trafficking machinery to 'hitchhike' back through the secretory system for release into the cytoplasm (reviewed in Johannes and Popoff, 2008; Pfeffer, 2011; Sandvig et al, 2013). These cargo are trafficked from the endocytic system in a clathrin- and AP1-dependent manner that is described in more detail in the "Trans-Golgi network budding pathway" (just not yet). In general, it appears that vesicles are uncoated prior to their tethering and fusion at the TGN. At the TGN, at least 2 distinct tethering pathways exist. A RAB6-dependent pathway contributes to the fusion and docking of vesicles from the early endocytic pathway. These vesicles, which carry cargo such as TGOLN2 and toxins, dock at the TGN through interactions with TGN-localized Golgin tethers and with the multisubunit tethering complexes COG and GARP (reviewed in Bonafacino and Rojas, 2006; Bonafacino and Hierro, 2011; Pfeffer, 2011). In contrast, mannose-6-phosphate receptors appear to traffic from late endosomes to the TGN through a RAB9- and PLIN3-dependent pathway. Vesicles are recruited to the TGN through interaction of RAB9 with the atypical RHO GTPase RHOBTB3, and tethered by virtue of interaction with TGN-localized Gorgins and the GARP complex (Perez-Victoria et al, 2008; Perez-Victoria et al, 2009; Diaz et al, 1999; reviewed in Pfeffer, 2011; Chia and Gleeson, 2014).

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The mammalian Golgi consists of at least three biochemically distinct cisternae, cis-, medial- and trans (reviewed in Szul and Sztul, 2011; Day et al, 2013). The structure and function of the Golgi are tightly interconnected, such that proteins that are required for protein transport through the Golgi are often also required for the organization of the Golgi stacks, and vice versa (reviewed in Liu and Storrie, 2012; Liu and Storrie, 2015; Chia and Gleeson, 2014; Munro, 2011). Newly synthesized proteins from the ER and ER-GIC are received at the cis face of the Golgi and flow through to the trans-Golgi before being released to the trans-Golgi network (TGN) for further secretion to the endolysosomal system, plasma membrane or extracellular region. Retrograde flow from the trans- to cis-cisternae moves endocytosed cargo from the extracellular region, the plasma membrane and the endolysosomal system back towards the ER. Intra-Golgi retrograde traffic also returns resident Golgi proteins to their appropriate cisternae, in this way facilitating cisternal remodeling or maturation (reviewed in Boncompain and Perez, 2013; Day et al, 2013). Intra-Golgi traffic in both directions is mediated by COPI carriers, with specificity of transport being determined at least in part by the complement of SNAREs, RABs and tethering proteins involved (reviewed in Szul and Sztul, 2011; Spang 2013; Willet et al, 2013; Chia and Gleeson, 2014).

**Literature references**


Golgi-to-ER retrograde transport

**Location:** Intra-Golgi and retrograde Golgi-to-ER traffic

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Retrograde traffic from the cis-Golgi to the ERGIC or the ER occurs through either COPI-coated vesicles or through a less well characterized RAB6-dependent route that makes use of tubular carriers (reviewed in Lord et al, 2013; Spang et al, 2013; Heffernan and Simpson, 2014). The balance between these two pathways may be influenced by cargo type and concentration and membrane composition, though the details remain to be worked out (reviewed in Heffernan and Simpson, 2014).

**Literature references**


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