A novel approach based on tracking the fate of proteins that become ‘stapled’ to the walls of the Golgi yields insights into the long-sought mechanism of transport through this organelle.

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Related research article Lavieu G, Zheng H, Rothman JE. 2013. Stapled Golgi cisternae remain in place as cargo passes through the stack. eLife 2:e00558. doi: 10.7554/eLife.00558

Image Electron micrograph showing protein ‘staples’ (indicated by white arrows) distributed across the Golgi

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proteins that had been aggregated in precisely defined locations. They found that cargoes remained where they had been stapled, but without stapling, they moved to the cell surface.

The fact that the staples remain where they are generated strongly supports a model in which Golgi compartments are static, and cargo proteins move from one cisterna to the next during transport across the Golgi stack (Figure 1B). Nevertheless, there are important caveats. First, this experiment uses aggregates of an artificial protein, which ‘staples’ membrane compartments together. No natural cargo has ever been shown to behave in this way. Such aggregates could potentially inactivate entire subdomains of the Golgi itself. Lavieu et al. tried hard to control for this. They showed that Golgi complexes containing red fluorescent staples could still support the transport of a well-characterized cargo (GFP-labeled vesicular stomatitis virus G glycoprotein) to the cell surface. Cells harbouring stapled Golgi membranes were also able to deliver a larger cargo, collagen, from the Golgi to the cell surface, and to transport proteins to the ER upon addition of the fungal metabolite, brefeldin A. While these are excellent controls, the cells seem to dislike harbouring the chimeric proteins because they turn over in cells with a half life of about 6 hours (Lavieu et al., 2013). What cannot be determined with certainty is whether the control cargoes bypass a stapled microdomain.

Finally, the Yale team generated large aggregates of a cargo that did not become attached to the membrane, and showed that these aggregates moved through the membrane-stapled Golgi complex via the edges (or ‘rims’) of the cisternae. By contrast, the stapled membrane-associated proteins remained confined to the central regions of the Golgi (Figure 1B). Lavieu et al. conclude that rims progress forward from one cisterna to the next while the central regions of cisternae remain in place. This is reminiscent of an earlier study (Volchuk et al., 2000) that identified what appear to be ‘megavesicles’ carrying cargo from one region of the Golgi to another. Previous work from many labs has shown that a number of cargoes are found predominantly at the rims while Golgi enzymes seem to localize to the central domains of cisternae (see Cosson et al., 2002). Lavieu et al. suggest that others may have concluded that the Golgi matures because they were monitoring markers present at the rims; such analysis would have missed the fate of the central Golgi region. Lavieu et al. are careful not to over-interpret their findings but one conclusion seems quite clear: Golgi rims are distinct from static central regions, with broad implications for all models of Golgi transport.

Future work should focus on the mechanisms by which the cargo within Golgi rims moves forward and how it is segregated to the rim region. Rab family GTPases will surely be important (Mizuno-Yamasaki et al., 2012), and a cascade linking their functions may help contribute to the directionality of transport through the Golgi (Rivera-Molina and Novick, 2009; Pfeffer, 2010). Golgi rim transport also takes certain cargo backwards in a pathway to the ER. Thus, Golgi rims will need to accommodate the molecular machineries needed to separately package anterograde and retrograde cargoes. How Golgi residents are correctly localized and retained in the face of a large volume of secretory traffic remains an important question for future research.

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**Competing interests:** The author declares that no competing interests exist.

**Published** 11 June 2013

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