# HIGHLIGHTS



MEMBRANE TRAFFIC

## A coat with many pockets

The coat protein (COP)II is responsible for budding transport vesicles containing SNAREs and cargo from the endoplasmic reticulum (ER), but how it interacts with SNARE and cargo molecules has remained unclear. However, two papers in *Cell* now shed light on COPII interactions and show that it is a coat with many pockets.

In yeast, the SNARE proteins Sed5, Bos1 and Sec22 form the t-SNARE (target-membrane SNARE) and Bet1 is the v-SNARE (vesicle-membrane SNARE) of the SNARE complex that is needed for ER–Golgi transport. This SNARE complex is packaged into ER-derived vesicles by the COPII coat, which contains the subunit Sec23/Sec24.

In the first paper, Goldberg and colleagues studied COPII–SNARE interactions. They showed that Sec23/24 interacts with Sed5, Sec22 and Bet1 (but not Bos1) through three distinct binding sites. Sec23/24 binds to a bipartite motif in Sed5 — that is, the A site of Sec23/24 binds YNNSNPF and the B site binds LXXME. Sec23/24 also binds to an LXXLE motif in Bet1, and to the DXE signal of the cargo molecule Sys1, through its B site. Finally, Sec23/24 binds to Sec22 through a third spatially distinct site.

The COPII-binding motifs identified by Goldberg and co-workers are in strategically important regions of the SNARE proteins and the authors showed that the "…COPII coat seems to be a specific conductor of the fusogenic forms of these SNAREs". They showed that COPII selects the uncomplexed form of Bet1, because the LXXLE sequence is inaccessible in the SNARE complex. Furthermore, they found that COPII favours Sed5 when it is part of the t-SNARE complex, because t-SNARE assembly exposes the YNNSNPF motif. So, it seems that the specificity of vesicle fusion might be programmed during vesicle budding.

In the second paper, Schekman and colleagues investigated cargo recruitment by Sec24. They identified the same site as Goldberg and colleagues on Sec24 that binds Bet1 and showed that mutating this site disrupts the packaging of various cargo molecules. Interestingly, the cargo molecules that were affected did not all share a common sorting signal, and those that did were not affected to the same extent. Furthermore, the vesicles generated in the presence of mutant Sec24 contained other cargo molecules, such as pro-α-factor, which indicates that additional cargo-interaction sites are present on Sec24.

When they tested the effect of mutating the Bet1-binding site *in vivo*, Schekman and co-workers found that the Sec24 homologues Lst1 and Iss1 could cooperate to facilitate intracellular transport in the presence of mutant Sec24. In fact, they showed that the same binding site is conserved as a cargo-interaction domain on Lst1, although this site can only select a subset of the cargo molecules that the Sec24 site can.

In the final part of their study, Schekman and colleagues identified a binding site on Sec24 that is specific for Sec22. This work therefore supports a model in which Sec24 contains "…multiple independent cargo binding domains that allow for recognition of a diverse set of sorting signals", and together these papers have given us valuable insights into COPII coat interactions.

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### References and links

**ORIGINAL RESEARCH PAPERS** Mossessova, E. *et al*. SNARE selectivity of the COPII coat. *Cell* **114**, 483–495 (2003) | Miller, E. A. *et al*. Multiple cargo binding sites on the COPII subunit Sec24p ensure capture of diverse membrane proteins into transport vesicles. *Cell* **114**, 497–509 (2003)