COPII-mediated vesicle formation at a glance

Devon Jensen and Randy Schekman*

Department of Molecular and Cell Biology, and Howard Hughes Medical Institute, University of California at Berkeley, Berkeley, CA 94720, USA

*Author for correspondence (schekman@berkeley.edu)

Journal of Cell Science 124, 1-4

doi:10.1242/jcs.069773

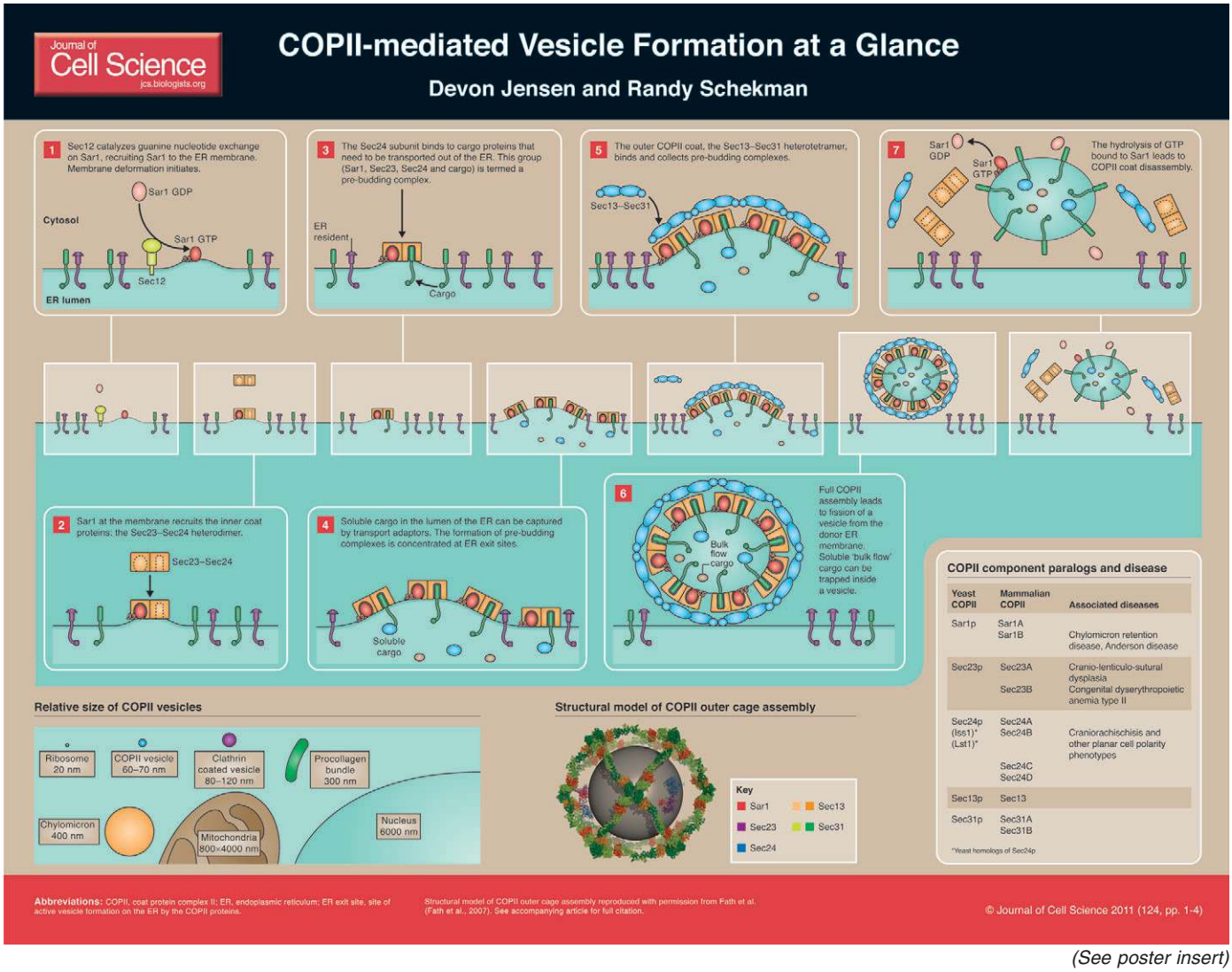
Introduction

Eukaryotic cells contain a number of different membrane compartments that have specialized roles. Each compartment depends on a specific mixture of proteins for its identity and function. For many compartments, proteins arrive by way of small membrane vesicles that travel through the cell from an originating compartment (Bonifacino and Glick, 2004; Gürkan et al., 2007). Small membrane vesicles are created by the action of coat proteins that deform membranes into the shape of vesicles and simultaneously select 'cargo' proteins for inclusion into these vesicles (Kirchhausen, 2000; Bonifacino and Lippincott-Schwartz, 2003). Coat protein complex II (COPII) is a set of highly conserved proteins that is responsible for creating small membrane vesicles that originate from the endoplasmic reticulum (ER) (Lee et al., 2004; Barlowe et al., 1994). The formation and movement of these COPII-derived vesicles is a crucial first step in the cellular secretion pathway, through which membrane and lumenal cargo proteins are transported from their site of synthesis at the ER on to other membrane compartments in the cell.

In this Cell Science at a Glance article, we first consider the five proteins that constitute the conserved core of the COPII vesicle creation machinery and take a look at how they are able to shape membranes, select cargo proteins that need to be transported, and form a polymeric coat that results in a vesicle. Then, we examine more recent discoveries that show how deficiencies in COPII can lead to disease. Finally, we briefly explore how additional factors can work with the COPII proteins to enhance transport efficiency in particular cases. Together with the accompanying poster, we hope that this brief overview will be useful and encourage readers to consider how efficient or deficient forward transport can affect the activity of the proteins they study.

The five core COPII proteins and vesicle formation

The COPII coat machinery consists of five cytosolic proteins: Sar1, Sec23, Sec24, Sec13 and Sec31. In cells, Sec23 and Sec24 are found in tight heterodimers, which form the inner COPII coat, whereas Sec13 and Sec31 are found



(See poster insert)

in stable heterotetramers of two subunits of each, which form the outer COPII coat (Barlowe et al., 1994). Sar1 and these two types of stable complexes are sequentially recruited to the ER membrane and work together to create a complete COPII vesicle. In most eukaryotic organisms, this recruitment to the membrane does not occur spontaneously across the entire surface of the ER. Instead, COPII proteins from the cytosol and cargo proteins on the membrane are recruited to discrete regions of the ER membrane, called ER exit sites or transitional ER (tER) (Budnik and Stephens, 2009; Bannykh et al., 1996). These exit sites are microdomains of high COPII activity and they label strongly with antibodies against COPII proteins when visualized by immunofluorescence microscopy (Fig. 1). Localization of COPII activity into these microdomains probably helps to maintain a crucial concentration of COPII proteins and enables the efficient recycling of these coat proteins as they are recruited back to the membrane for use in subsequent rounds of COPII budding (Orci et al., 1991).

Sar1 is the first COPII component recruited to the ER membrane, and it begins the process of vesicle formation. Sar1 is a small GTPase, whose activity, similarly to that of other small G proteins, is controlled by the state of the nucleotide to which it is bound (Pucadyil and Schmid, 2009). In its GDP-bound state, Sar1 is cytosolic and dormant, but when bound to GTP, Sar1 activates by exposing an amphipathic N-terminal α-helix, which embeds into the ER membrane (Lee and Miller, 2007; Bielli et al., 2005). This activity is restricted to the ER membrane, because Sec12, the guanine nucleotide exchange factor (GEF) that activates Sar1, is only found at the ER (Weissman et al., 2001). By embedding this α-helix, Sar1 anchors the forming coat complex on the membrane, but it also initiates membrane budding. In fact, activated Sar1 can, by itself, stimulate tubulation and membrane fission on synthetic liposomes (Lee et al., 2005; Bielli et al., 2005). Acting as a membrane-bound anchor for the other COPII components, activated Sar1 directly binds and recruits the next COPII sub-complex, the Sec23–Sec24 heterodimer.

The Sec23–Sec24 sub-complex arrives at the scene by virtue of the direct interaction between Sar1 and Sec23 (Bi et al., 2002). This interaction serves not only a structural role in assembling the inner coat complex on the membrane, but also a catalytic role. Sec23 is a GTPase-activating protein (GAP) for Sar1, accelerating the meager intrinsic GTPase activity of Sar1; full GTPase activity, however, is not realized until the complete COPII coat is assembled following the arrival of the Sec13–Sec31 outer coat (Yoshihisa et al., 1993; Antonny et al., 2001). This additive GTPase catalytic activity is thought to provide a built-in timing mechanism for the ordered assembly of the coat components, the cycle of vesicle formation and the eventual disassembly of the coat from the membrane of a completed COPII vesicle (Lee and Miller, 2007).

Sec24 is considered to be the primary subunit responsible for binding to membrane cargo proteins at the ER and concentrating them into the forming vesicle (Miller et al., 2002). Many cargo proteins have specific export-signal sequences in their cytoplasmic domains to mark them for COPII transport. Types of COPII signal sequences include di-hydrophobic, di-acidic, C-terminal hydrophobic and aromatic motifs (Wendeler et al., 2007; Barlowe, 2003). A number of cargo-binding pockets and the corresponding signal sequences they bind have been identified on the surface of Sec24 and have been termed the A-, B- and C-sites (Miller et al., 2003). Not all proteins that need to leave the ER contain a signal for direct binding to Sec24. Some proteins might interact with a transport adaptor, and thus be included in the COPII vesicle through an indirect interaction (Baines and Zhang, 2007). Still other proteins might passively enter COPII vesicles by simple diffusion – a process called bulk flow (Thor et al., 2009). Of those cargo proteins tested, several are found in COPII vesicles at concentrations higher than a bulk-flow model would suggest, indicating that concentrative sorting by Sec24 might be the rule (Malkus et al., 2002). Sec24 is brought to sites of COPII vesicle formation through its interaction with Sec23. Altogether, the set of proteins consisting of a membrane-bound Sar1 along with a cargo-loaded Sec23–Sec24 dimer has been termed a 'pre-budding complex' – a complex that is ready for the activity of Sec13–Sec31 to complete the formation of the vesicle.

The Sec13–Sec31 heterotetramer completes the process of membrane cargo sorting and vesicle fission. This outer layer of the coat collects pre-budding complexes and shapes the membrane to form a bud enriched in cargo molecules. To accomplish this task, the Sec13–Sec31 complexes polymerize, whereas Sec31 directly interacts with Sec23 and Sar1 (Bi et al., 2007). Under certain in vitro conditions, the elongated Sec13–Sec31 molecules can polymerize at vertices to form the edges of round 'empty cages', illustrating their potential to provide a structural framework for the shape of the vesicle as it buds off the donor ER membrane (Stagg et al., 2006; Fath et al., 2007). With the full complement of COPII proteins assembled into a polymerized coat, the extruded membrane is separated from the donor ER membrane by fission to form an intact vesicle. Unlike some other vesicle coats, COPII does not require a specialized GTPase, such as dynamin, to constrict the neck of the forming vesicle and release it from the membrane. Purified COPII components alone are able to form small vesicles from synthetic liposome membrane (Matsuoka et al., 1998). The end result of this process is a spherical membrane vesicle roughly 60–70 nm in size that carries cargo proteins to the ER–Golgi intermediate compartment or, in yeast, possibly directly to the *cis*-Golgi membrane. This process works well for the wide variety of cargo proteins trafficked from the ER, but what would happen if one of these five core COPII proteins was missing or mutated?

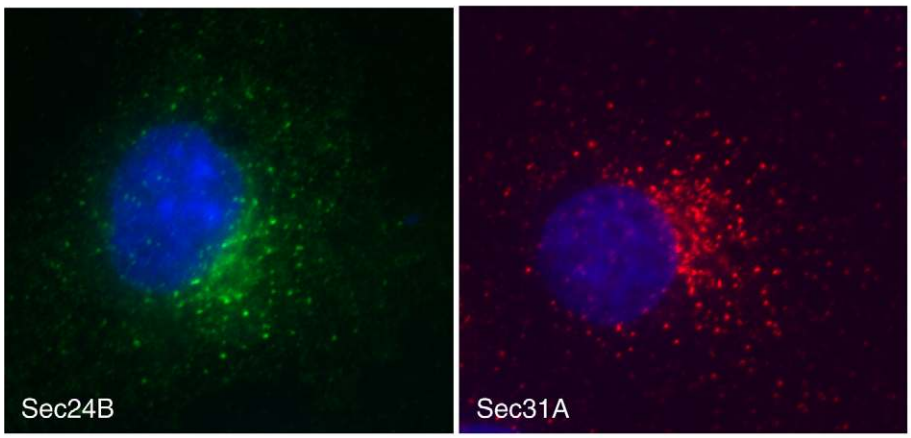


Fig. 1. ER exit sites. Members of both the inner (Sec24B) and outer (Sec31A) COPII coat are found concentrated at punctae on the ER membrane called ER exit sites. Image of Sec31A kindly provided by Soomin Shim (University of California at Berkeley, Berkeley, CA, USA).

COPII proteins linked to disease

COPII transport in the mammalian system has diversified, because gene-duplication events have created multiple paralogs for four out of the five COPII proteins. The mammalian repertoire

consists of: two Sar1 paralogs, Sar1A and Sar1B; two Sec23 paralogs, Sec23A and Sec23B; four Sec24 paralogs, Sec24A, Sec24B, Sec24C and Sec24D; a single Sec13; and two Sec31 paralogs, Sec31A and Sec31B. In recent years, one of the challenges for the field has been to elucidate the reason that these multiple paralogs have been conserved among higher organisms. Are the COPII paralogs functionally redundant but expressed in different tissues? Or have some of the paralogs become specialized to transport different cargo? Examples of developmental disorders and human diseases caused by mutations in Sar1B, Sec23A, Sec23B and Sec24B have begun to shed light on these questions.

Several different mutations in Sar1B have been associated with two related fat-malabsorption diseases: chylomicron retention disease and Anderson disease (Jones et al., 2003). Affected individuals are deficient in fat-soluble vitamins, have low blood cholesterol levels and show a lack of chylomicrons in their blood. Chylomicrons, one of the major types of circulating lipoprotein, are produced in the ER of intestinal epithelial cells and are secreted by those cells into the bloodstream. Interestingly, chylomicrons range in size from 75 to 450 nm in diameter (Hussain, 2000). So how can COPII vesicles, which are typically only 60–70 nm, accommodate such a large cargo molecule? Is Sar1B specialized to enable the transport of chylomicrons and perhaps other large cargo molecules such as pro-collagen? These issues remain unresolved (Fromme and Schekman, 2005).

A single missense mutation in Sec23A (F382L) has been found to lead to an autosomal-recessive disease called cranio-lenticulo-sutural dysplasia (CLSD) (Boyadjiev et al., 2006). The disease is marked by skeletal defects, cataracts and facial dysmorphisms. The molecular nature of this amino acid change has been studied in detail, and it was found that the mutation is near the part of Sec23A that binds and recruits Sec31 (Bi et al., 2007). Failure to recruit Sec31 leads to a large reduction in the packaging of cargo proteins in vitro, and is accompanied by swelling of the ER with untransported cargo in vivo (Fromme et al., 2007). Additionally, the tissues that are most affected by the disease appear to express low levels of the paralog Sec23B, suggesting that these tissues do not have enough fully functional Sec23 overall.

Many separate mutations in Sec23B were found in patients with a disease called congenital dyserythropoietic anemia type II (CDAII) (Schwarz et al., 2009; Bianchi et al., 2009). The symptoms of this disease appear to be largely due to defective erythropoiesis, in which red-blood-cell progenitors are often multinucleate and circulating red blood cells are morphologically abnormal. Various proteins in these red blood cells show immature glycosylation, indicating transport defects, but how this might be related to the cytokinesis defect in the multinucleate progenitor cells is unclear. Analysis of gene expression during wild-type erythroid differentiation detected an increase in RNA expression for Sec23B that was 5–7-fold greater than that for Sec23A (Schwarz et al., 2009). As with the Sec23A mutation, it seems that the Sec23B mutations only affect a specific tissue. It might be that Sec23A and Sec23B are functionally redundant, and able to largely compensate for one another in unaffected tissues where they are normally both expressed.

Recent reports demonstrate that two distinct premature stop codons in Sec24B lead to major neural tube defects in mice (Merte et al., 2010; Wansleeben et al., 2010). Homozygous mutant mice developed craniorachischisis and several other phenotypes indicative of defects within the tissue-organizing planar cell polarity pathway. A candidate-based approach looking at cargo proteins involved in establishing planar cell polarity revealed that the membrane protein Vangl2 appears to be specifically packaged by Sec24B. The entry of Vangl2 into COPII vesicles in vitro showed that the packaging was specifically enhanced in the presence of recombinant Sec24B and not the other Sec24 paralogs (Merte et al., 2010). In vivo analysis of mutant primary fibroblasts also showed a selective defect in the transport of Vangl2 (Wansleeben et al., 2010). Sec24 is a versatile protein but, in this case, Sec24B appears to have specific binding activity for at least one important cargo protein that cannot be compensated for by the presence of other Sec24 paralogs.

Perspectives

Recent developments have made this an opportune time to review the study of COPII-mediated vesicle transport. The past couple of years have seen a transition in the field, from the original understanding of the basic mechanisms of COPII in simpler organisms, to establishing the roles of the multiple COPII paralogs that drive COPII transport in the more complex mammalian system. This new knowledge comes with examples of deficiencies in COPII that cause developmental disorders and human disease.

Apart from the core components of the COPII machinery discussed here, there are several other exciting areas of study in the ER exit field. One such area is the way in which additional adaptors work together with the COPII proteins. These adaptors can have cargo-selective roles to further broaden the repertoire of proteins included in forming COPII vesicles. For instance, TANGO1 is found at ER exit sites and helps to load collagen VII, and perhaps other bulky cargo, into COPII vesicles (Saito et al., 2009). Additional recent examples of cargo-selective adaptors include GRASP65, and Erv26p/Svp26 (D'Angelo et al., 2009; Bue et al., 2006; Noda and Yoda, 2010). Another protein, ALG-2, stabilizes Sec31 at ER exit sites and might regulate the timing of COPII vesicle homotypic fusion (Bentley et al., 2010). Other COPII-interacting proteins, such as the signal-transducing adaptor molecules STAM1 and STAM2, and Sec23IP, affect ER-to-Golgi transport, but their mechanism of action is not clear (Rismanchi et al., 2009; McGary et al., 2010). The core COPII proteins accommodate many different cargos but, given the thousands of cargo molecules that must be accommodated in mammalian cells and tissues, it is not surprising that other factors are involved in specific cases.

Another topic of emerging interest is the protein and lipid components that comprise the structure and organization of the ER exit sites. Sec16 has been identified as a peripheral membrane protein found at these sites. Although Sec16 is apparently not directly required for vesicle formation (Matsuoka et al., 1998), it has been shown to interact with the COPII components Sec23 (Espenshade et al., 1995) and Sec13 (Hughes et al., 2009). In addition, kinase and phospholipase D activity near ER exit sites suggest that specific lipids mark exit sites and contribute to their identity and function (Aridor and Balch, 2000; Pathre et al., 2003).

In the future, we expect to learn more details about how an ER exit site is structurally organized. We think that knockout studies in mice and other model organisms will supply information about the specific roles of other COPII paralogs. Additionally, insight into the mechanism for packaging of large cargos and additional factors that enable efficient COPII transport will hopefully be found.

We apologize to those authors whose work could not be cited due to space limitations. Thanks to Soomin Shim for the immunofluorescence image of Sec31A. R.S. is an investigator of the HHMI.

References

Antonny, B., Madden, D., Hamamoto, S., Orci, L. and Schekman, R. (2001). Dynamics of the COPII coat with GTP and stable analogues. *Nat. Cell Biol.* **3**, 531-537.

Aridor, M. and Balch, W. E. (2000). Kinase signaling initiates coat complex II (COPII) recruitment and export from the mammalian endoplasmic reticulum. *J. Biol. Chem.* **275**, 35673-35676.

Baines, A. C. and Zhang, B. (2007). Receptor-mediated protein transport in the early secretory pathway. *Trends Biochem. Sci.* **32**, 381-388.

Bannykh, S. I., Rowe, T. and Balch, W. E. (1996). The organization of endoplasmic reticulum export complexes. *J. Cell Biol.* **135**, 19-35.
Barlowe, C. (2003). Signals for COPII-dependent export from the ER: What's the ticket out? *Trends Cell Biol.* **13**, 295-300.
Barlowe, C., Orci, L., Yeung, T., Hosobuchi, M., Hamamoto, S., Salama, N., Rexach, M. F., Ravazzola, M., Amherdt, M. and Schekman, R. (1994). COPII: A membrane coat formed by sec proteins that drive vesicle budding from the endoplasmic reticulum. *Cell* **77**, 895-907.
Bentley, M., Nycz, D. C., Joglekar, A., Fertschai, I., Malli, R., Graier, W. F. and Hay, J. C. (2010). Vesicular calcium regulates coat retention, fusogenicity, and size of pre-golgi intermediates. *Mol. Biol. Cell* **21**, 1033-1046.
Bi, X., Corpina, R. A. and Goldberg, J. (2002). Structure of the Sec23/24-Sar1 pre-budding complex of the COPII vesicle coat. *Nature* **419**, 271-277.
Bi, X., Mancias, J. D. and Goldberg, J. (2007). Insights into COPII coat nucleation from the structure of Sec23.Sar1 complexed with the active fragment of Sec31. *Dev. Cell.* **13**, 635-645.
Bianchi, P., Fermo, E., Vercellati, C., Boschetti, C., Barcellini, W., Iurlo, A., Marcello, A. P., Righetti, P. G. and Zanella, A. (2009). Congenital dyserythropoietic anemia type II (CDAII) is caused by mutations in the SEC23B gene. *Hum. Mutat.* **30**, 1292-1298.
Bielli, A., Haney, C. J., Gabreski, G., Watkins, S. C., Bannykh, S. I. and Aridor, M. (2005). Regulation of Sar1 NH2 terminus by GTP binding and hydrolysis promotes membrane deformation to control COPII vesicle fission. *J. Cell Biol.* **171**, 919-924.
Bonifacino, J. S. and Glick, B. S. (2004). The mechanisms of vesicle budding and fusion. *Cell* **116**, 153-166.
Bonifacino, J. S. and Lippincott-Schwartz, J. (2003). Coat proteins: Shaping membrane transport. *Nat. Rev. Mol. Cell Biol.* **4**, 409-414.
Boyadjiev, S. A., Fromme, J. C., Ben, J., Chong, S. S., Nauta, C., Hur, D. J., Zhang, G., Hamamoto, S., Schekman, R., Ravazzola, M. et al. (2006). Cranio-lenticulo-sutural dysplasia is caused by a SEC23A mutation leading to abnormal endoplasmic-reticulum-to-golgi trafficking. *Nat. Genet.* **38**, 1192-1197.
Budnik, A. and Stephens, D. J. (2009). ER exit sites-localization and control of COPII vesicle formation. *FEBS Lett.* **583**, 3796-3803.
Bue, C. A., Bentivoglio, C. M. and Barlowe, C. (2006). Erv26p directs pro-alkaline phosphatase into endoplasmic reticulum-derived coat protein complex II transport vesicles. *Mol. Biol. Cell* **17**, 4780-4789.
D'Angelo, G., Prencipe, L., Iodice, L., Beznoussenko, G., Savarese, M., Marra, P., Di Tullio, G., Martire, G., De Matteis, M. A. and Bonatti, S. (2009). GRASP65 and GRASP55 sequentially promote the transport of C-terminal valine-bearing cargos to and through the golgi complex. *J. Biol. Chem.* **284**, 34849-34860.
Espenshade, P., Gimeno, R. E., Holzmacher, E., Teung, P. and Kaiser, C. A. (1995). Yeast SEC16 gene encodes a multidomain vesicle coat protein that interacts with Sec23p. *J. Cell Biol.* **131**, 311-324.
Fath, S., Mancias, J. D., Bi, X. and Goldberg, J. (2007). Structure and organization of coat proteins in the COPII cage. *Cell.* **129**, 1325-1336.
Fromme, J. C. and Schekman, R. (2005). COPII-coated vesicles: flexible enough for large cargo? *Curr. Opin. Cell Biol.* **17**, 345-352.
Fromme, J. C., Ravazzola, M., Hamamoto, S., Al-Balwi, M., Eyaid, W., Boyadjiev, S. A., Cosson, P., Schekman, R. and Orci, L. (2007). The genetic basis of a craniofacial disease provides insight into COPII coat assembly. *Dev. Cell.* **13**, 623-634.
Gurkan, C., Koulov, A. V. and Balch, W. E. (2007). An evolutionary perspective on eukaryotic membrane trafficking *Adv. Exp. Med. Biol.* **607**, 73-83.
Hughes, H., Budnik, A., Schmidt, K., Palmer, K. J., Mantell, J., Noakes, C., Johnson, A., Carter, D. A., Verkade, P., Watson, P. et al. (2009). Organisation of human ER-exit sites: requirements for the localisation of Sec16 to transitional ER. *J. Cell Sci.* **122**, 2924-2934.
Hussain, M. M. (2000). A proposed model for the assembly of chylomicrons. *Atherosclerosis* **148**, 1-15.
Jones, B., Jones, E. L., Bonney, S. A., Patel, H. N., Mensenkamp, A. R., Eichenbaum-Voline, S., Rudling, M., Myrdal, U., Annesi, G., Naik, S. et al. (2003). Mutations in a Sar1 GTPase of COPII vesicles are associated with lipid absorption disorders. *Nat. Genet.* **34**, 29-31.
Kirchhausen, T. (2000). Three ways to make a vesicle. *Nat. Rev. Mol. Cell Biol.* **1**, 187-198.
Lee, M. C. and Miller, E. A. (2007). Molecular mechanisms of COPII vesicle formation. *Semin. Cell Dev. Biol.* **18**, 424-434.
Lee, M. C., Miller, E. A., Goldberg, J., Orci, L. and Schekman, R. (2004). Bi-directional protein transport between the ER and golgi. *Annu. Rev. Cell Dev. Biol.* **20**, 87-123.
Lee, M. C., Orci, L., Hamamoto, S., Futai, E., Ravazzola, M. and Schekman, R. (2005). Sar1p N-terminal helix initiates membrane curvature and completes the fission of a COPII vesicle. *Cell* **122**, 605-617.
Malkus, P., Jiang, F. and Schekman, R. (2002). Concentrative sorting of secretory cargo proteins into COPII-coated vesicles. *J. Cell Biol.* **159**, 915-921.
Matsuoka, K., Orci, L., Amherdt, M., Bednarek, S. Y., Hamamoto, S., Schekman, R. and Yeung, T. (1998). COPII-coated vesicle formation reconstituted with purified coat proteins and chemically defined liposomes. *Cell* **93**, 263-275.
McGary, K. L., Park, T. J., Woods, J. O., Cha, H. J., Wallingford, J. B. and Marcotte, E. M. (2010). Systematic discovery of nonobvious human disease models through orthologous phenotypes. *Proc. Natl. Acad. Sci. USA* **107**, 6544-6549.
Merte, J., Jensen, D., Wright, K., Sarsfield, S., Wang, Y., Schekman, R. and Ginty, D. D. (2010). Sec24b selectively sorts Vangl2 to regulate planar cell polarity during neural tube closure. *Nat. Cell Biol.* **12**, 41-46.
Miller, E., Antonny, B., Hamamoto, S. and Schekman, R. (2002). Cargo selection into COPII vesicles is driven by the Sec24p subunit. *EMBO J.* **21**, 6105-6113.
Miller, E. A., Beilharz, T. H., Malkus, P. N., Lee, M. C., Hamamoto, S., Orci, L. and Schekman, R. (2003). Multiple cargo binding sites on the COPII subunit Sec24p ensure capture of diverse membrane proteins into transport vesicles. *Cell* **114**, 497-509.
Noda, Y. and Yoda, K. (2010). Svp26 facilitates endoplasmic reticulum-to-golgi transport of a set of mannosyltransferases in saccharomyces cerevisiae. *J. Biol. Chem.* **285**, 15420-15429.
Orci, L., Ravazzola, M., Meda, P., Holcomb, C., Moore, H. P., Hicke, L. and Schekman, R. (1991). Mammalian Sec23p homologue is restricted to the endoplasmic reticulum transitional cytoplasm. *Proc. Natl. Acad. Sci. USA* **88**, 8611-8615.
Pathre, P., Shome, K., Blumental-Perry, A., Bielli, A., Haney, C. J., Alber, S., Watkins, S. C., Romero, G. and Aridor, M. (2003). Activation of phospholipase D by the small GTPase Sar1 is required to support COPII assembly and ER export. *EMBO J.* **22**, 459-469.
Pucadyil, T. J. and Schmid, S. L. (2009). Conserved functions of membrane active GTPases in coated vesicle formation. *Science* **325**, 1217-1220.
Rismanchi, N., Puertollano, R. and Blackstone, C. (2009). STAM adaptor proteins interact with COPII complexes and function in ER-to-golgi trafficking. *Traffic* **10**, 201-217.
Saito, K., Chen, M., Bard, F., Chen, S., Zhou, H., Woodley, D., Polischuk, R., Schekman, R. and Malhotra, V. (2009). TANGO1 facilitates cargo loading at endoplasmic reticulum exit sites. *Cell* **136**, 891-902.
Schwarz, K., Iolascon, A., Verissimo, F., Trede, N. S., Horsley, W., Chen, W., Paw, B. H., Hopfner, K. P., Holzmann, K., Russo, R. et al. (2009). Mutations affecting the secretory COPII coat component SEC23B cause congenital dyserythropoietic anemia type II. *Nat. Genet.* **41**, 936-940.
Stagg, S. M., Gurkan, C., Fowler, D. M., LaPointe, P., Foss, T. R., Potter, C. S., Carragher, B. and Balch, W. E. (2006). Structure of the Sec13/31 COPII coat cage. *Nature* **439**, 234-238.
Thor, F., Gautschi, M., Geiger, R. and Helenius, A. (2009). Bulk flow revisited: Transport of a soluble protein in the secretory pathway. *Traffic* **10**, 1819-1830.
Wansleeben, C., Feitsma, H., Montcouquiol, M., Kroon, C., Cuppen, E. and Meijlink, F. (2010). Planar cell polarity defects and defective Vangl2 trafficking in mutants for the COPII gene Sec24b. *Development* **137**, 1067-1073.
Weissman, J. T., Plutner, H. and Balch, W. E. (2001). The mammalian guanine nucleotide exchange factor mSec12 is essential for activation of the Sar1 GTPase directing endoplasmic reticulum export. *Traffic* **2**, 465-475.
Wendeler, M. W., Paccaud, J. P. and Hauri, H. P. (2007). Role of Sec24 isoforms in selective export of membrane proteins from the endoplasmic reticulum. *EMBO Rep.* **8**, 258-264.
Yoshihisa, T., Barlowe, C. and Schekman, R. (1993). Requirement for a GTPase-activating protein in vesicle budding from the endoplasmic reticulum. *Science* **259**, 1466-1468.

Cell Science at a Glance on the Web
Electronic copies of the poster insert are available in the online version of this article at jcs.biologists.org. The JPEG images can be downloaded for printing or used as slides.