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ER–Golgi transport could occur in the absence of COPII vesicles

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In the Review article (Organization of the ER–Golgi interface for membrane traffic control. *Nature Rev. Mol. Cell Biol.* **14**, 382–392 (2013))[1], Brandizzi and Barlowe presented data in favour of the vesicular model of endoplasmic reticulum (ER)–Golgi transport. However, there are several observations suggesting that there could also be non-vesicular mechanisms of transport. For instance, it is now known that several organisms have no coat protein complex II (COPII)-coated buds, including microsporidia[2] and algae *Ostreococcus tauri*. In the latter case, three-dimensional structures were visualized by cryo-electron tomography and no membrane buds coated with COPII were found on the ER[3]. In some plant cells, COPII-coated buds are absent[4]. COPII-coated buds were not found on the ER in yeast[5].

Several observations suggest that in the absence of COPII vesicles, COPII function and even of the COPII coat, the ER–Golgi transport of several cargoes was not affected. In mammalian cells, cell growth and intracellular transport are not affected by: knockdown of both secretion-associated RAS-related 1 (SAR1) isoforms alone or together with simultaneous depletion of SEC23A and SEC23B[6]; all four isoforms of SEC24 (REF. 7) or blocked synthesis of SEC13 (REF. 8). In the absence of SAR1A and SAR1B or SEC13, only transport of procollagen I was blocked[6,8]. In zebrafish, elimination of both Sec23A and Sec23B does not kill cells or disrupt their ability to divide[9]. In yeast, deletion of Sec13 together with bypass of Sec thirteen 1 (BST1), BST2 (also known as EMP24) or BST3 did not cause cell death, although the removal of just Sec13 cells was lethal[10]. In *Saccharomyces cerevisiae*, in the absence of Sec24, soluble cargo can exit out of the ER[11]. In *Caenorhabditis elegans* that contain only a single isoform of SEC-23, deletion of this single *sec-23* gene did not induce cell lethality; procollagen I transport is inhibited, whereas other extracellular matrix proteins can be secreted[12]. By contrast, in mammalian cells, knockdown of both isoforms of SEC23 alone induced blockage of vesicular stomatitis virus glycoprotein (VSVG) transport[13]. One explanation for this could lie in the fact that SEC23 functions as the GTPase-activating protein (GAP) protein for SAR1. Therefore, in the absence of SEC23, SAR1 cannot hydrolyse GTP and remains in the GTP-bound form, leading to similar effects to those observed after transfection of cells with a SAR1p mutant trapped in the GTP-bound state[14]. Additionally, conventional cargoes are depleted in COPII-dependent vesicles[15]. Although these studies provide only indirect evidence that transport can occur when COPII vesicles are absent, I would argue that most evidence in favour of the role of COPII vesicles as transport carriers is also indirect. In any case, balanced discussion of these issues would be helpful for this research field.

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Competing interests statement
The authors declare no competing interests.