Golgins in the structure and dynamics of the Golgi apparatus

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Golgins are a family of coiled-coil proteins associated with the Golgi apparatus necessary for tethering events in membrane fusion and as structural supports for Golgi cisternae. Recent work has shown that golgins such as GM130, golgin-45 and p115 bind to Rab GTPases via their coiled-coil domains, and that GM130, rather than being part of a static structural matrix, is in dynamic exchange between the membrane surface and the cytoplasm. Golgins such as bicaudal-D1 and -D2 bind to Rab6, but, rather than tethering membranes together, link vesicles to the cytoskeleton, thus adding a new function for this class of proteins. Other golgins containing the Golgi targeting GRIP domain, rather than binding Rabs, interact with and are recruited to membranes by another class of GTPase, the Arls. Current evidence therefore suggests that golgins function in a variety of membrane–membrane and membrane–cytoskeleton tethering events at the Golgi apparatus, and that all these are regulated by small GTPases of the Rab and Arl families.

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Abbreviations

ARF	ADP-ribosylation factor
Arl	ARF-like GTPase
CASP	CCAAT-displacement protein alternatively spliced product
GRASP	Golgi reassembly and stacking protein
GRIP	conserved domain present in golgin-97, RanBP2α, Imh1 and p230/golgin-245
SNARE	soluble *N*-ethylmaleimide sensitive factor attachment protein receptor
TGN	*trans*-Golgi network

Introduction

In most animal and plant cells, the Golgi apparatus is an array of cisternal membrane structures arranged in a stack [1]. These stacks can then organise end to end into a larger ribbon structure, as in animal cells, or can remain as discrete stacks, as in plant cells. Fungi, including yeasts, typically show a lesser degree of Golgi organisation, and Golgi cisternae are highly motile structures often found singly as well as in stacked structures. Despite this high degree of organisation, Golgi stacks are extremely dynamic structures through which large amounts of secretory material and membrane passes on its way to many destinations within the cell.

In this review, we focus on the functions of different golgins in various aspects of Golgi structure and dynamics in animal cells.

What is a golgin?

Golgins were originally identified as a group of Golgi-localised antigens recognised by sera from patients with a variety of autoimmune conditions, and they are differentiated by their molecular weight (as determined by denaturing polyacrylamide gel electrophoresis) [1–3]. They share a common predicted structural feature, the presence of long regions of coiled-coil, a motif known to form an extended rod-like structure [4]. To date, the significance of their discovery as autoantigens remains unclear but might be a consequence of these repetitive coiled-coil domains generating multiple antigenic fragments during apoptotic and necrotic cell death, thus causing sustained autoantibody production [5]. More recently, several other Golgi-localised proteins have been identified that can also be categorised as golgins because of the presence of predicted coiled-coil domains and similarity with known golgins, despite the fact that they were not originally identified as autoantigens (Table 1).

Another feature of many of these proteins is their interaction with Rab-family small GTPases that typically function in controlling recognition processes between vesicles and their target membranes [6]. In light of this, it seems reasonable to classify all Golgi-localised proteins with predicted coiled-coil domains as golgins (summarised in Table 1), other than those such as the SNARE (soluble *N*-ethylmaleimide sensitive factor attachment protein receptor) proteins, which clearly fall into a category of their own.

What do golgins do?

The discovery of the golgins coincided with the observation that under certain conditions Golgi membranes could be extracted with detergent to leave a proteinaceous skeleton that retained the three-dimensional organisation of Golgi cisternae [7]. Building on older studies that identified proteinaceous material linking Golgi cisternae, this is commonly referred to as the Golgi matrix [8–10]. Golgins such as GM130/golgin-95 and p115 were found to be components of this matrix, and, together with their predicted elongated structure, this was interpreted as evidence that golgins function in the maintenance and

Table 1

Mammalian golgins and their interacting partners.

Name	Features	GTPases	Interactions	References
GM130/golgin-95	P	Rab1, Rab2, Rab33b	p115, GRASP65	[3,11,20•,56•,57•,58]
p115	P	Rab1	GM130	[12,15,58]
Golgin-45	P	Rab2	GRASP55	[20•]
GRASP55	N-Myr		Golgin-45	[20•,36]
GRASP65	N-Myr		GM130	[17,18]
Giantin/gcp372/macrogolgin	TMD		p115, GM130	[26–28,59]
Golgin-84	TMD	Rab1	OCRL(?)	[29,34•]
Golgin-67	TMD*			[30]
CASP	TMD			[32•]
gcp60	P		Giantin	[31]
Golgin-160/gcp170/mea-2	P			[3,60,61]
Bicaudal-D1, -D2	P	Rab6	Dynactin, p50–dynamitin	[40•,41•]
GMAP-210	P		Microtubules	[43,44]
Golgin-97	GRIP	Arl1/3		[47–49,50•,62]
Golgin-240, -245, -256/p230	GRIP	Arl1/3		[2,47–49,50•,63]
GCC88	GRIP	Arl1/3		[51]
GCC135	GRIP	Arl1/3		[51]

GRIP, conserved domain present in golgin-97, RanBP2α, Imh1 and p230/golgin-245; N-Myr, amino-terminal myristoylation; OCRL, Ocular cerebro renal syndrome of Lowe; P, peripheral membrane protein; TMD, transmembrane domain. *Predicted.

establishment of Golgi structure [11]. In many ways, this was a rediscovery of some slightly earlier work, since p115 was already known to function in Golgi transport, most likely by attaching vesicles to their target membrane before membrane fusion [12]. The tethering hypothesis of Waters and Pfeffer encapsulates these findings [6], and essentially explains what golgins do at a molecular level: they bind to and link adjacent membranes in vesicle docking during protein transport, and cisternae during Golgi stack formation [13,14].

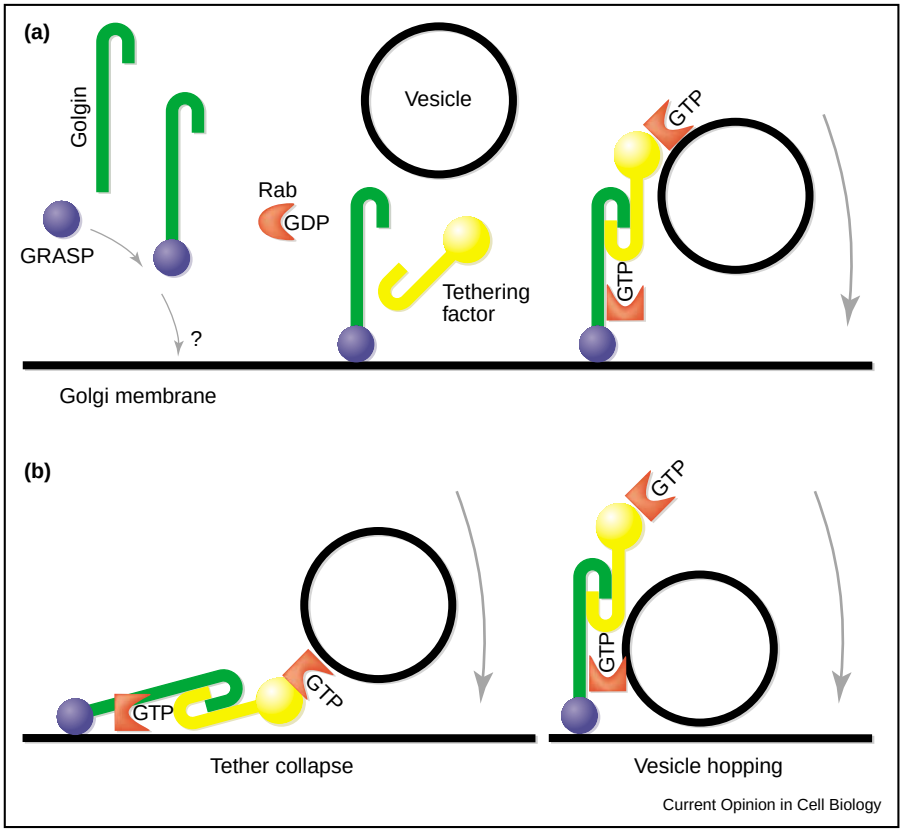
The paradigm for this tethering event on Golgi membranes is the *cis*-Golgi-localised tethering system comprising p115, its *cis*-Golgi membrane receptor GM130, and Rab1 (Figure 1a). p115 is recruited on to COPII-coated ER-to-Golgi transport vesicles or vesicle clusters via an interaction with Rab1 [15], or alternatively onto COPI-coated Golgi recycling vesicles via the integral membrane protein giantin [13]. It is thought that p115 then interacts with GM130 and its membrane anchor GRASP65 to link these vesicles to the *cis*-Golgi. In the case of COPI vesicles, it has been shown that golgin-mediated tethering precedes and then directs the cognate vesicle and target SNARE complex assembly necessary for membrane fusion [16•]. To date, this explanation of golgin function still remains valid, although, as we will discuss later, some additional definitions of the tethering events carried out might be necessary.

The Golgi matrix

As mentioned above, several golgins were identified as components of a putative structural Golgi matrix. Subsequently, the GM130-interacting protein GRASP65 was discovered using a functional assay to identify additional structural components involved in Golgi stack formation [17]. GRASP65 has been shown to bind to the extreme carboxyl terminus of GM130 and to directly target it to the *cis*-Golgi [18,19•]. More recently, a related complex on the medial-Golgi comprising GRASP55 and golgin-45 was identified [20•]. When golgin-45 is depleted using RNA interference, secretory protein transport is blocked, the Golgi structure collapses, and Golgi enzymes are relocated to the ER, although Golgi matrix proteins such as the GRASPs and GM130 remain in small remnant structures discrete from the ER [20•]. This is reminiscent of findings that treatment of cells with brefeldin A or dominant-negative forms of the Sar1 GTPase causes most proteins to be recycled to the ER, but Golgi-like structures containing golgins such as GM130 can still be observed under the light microscope [21,22••]. These results suggest that some golgins and their interacting partners are necessary for both giving identity to and maintaining Golgi structure (Figure 2 [23]).

To carry out its function, any structural matrix would need to be highly dynamic, to allow rapid remodelling as vast amounts of membrane and secretory cargo pass through the Golgi. For example, it is estimated that in the exocrine pancreas more secretory material enters the Golgi from the ER every five minutes than there is protein within the Golgi ([1] and references therein). In this light, it is intriguing to note that many of the golgins and their interacting partners are peripheral and not integral membrane proteins, which means that they can potentially be rapidly recycled via the cytoplasm from one part of the Golgi membrane to another. Experimental data obtained using photobleaching-based techniques to estimate the mobility of green fluorescent protein (GFP)-tagged proteins suggest that the GRASP65–GM130 complex undergoes a cycle of rapid membrane association and

Figure 1



Models for vesicle tethering at the *cis*-Golgi. **(a)** Newly synthesised GRASP65 (blue) and the GM130 ('Golgin', green) assemble into a complex in the cytoplasm, then directly target to Golgi membranes. The mechanism by which the *cis*-Golgi membrane is recognised is not known but may involve interactions between GRASP65 and transmembrane proteins. Rab1–GTP (Rab) is loaded onto an incoming vesicle and recruits the tethering factor p115 (yellow). The acidic carboxyl terminus of p115 binds to the basic amino terminus of GM130 and tethers the vesicle to the Golgi membrane. **(b)** Once tethered, the vesicle should fuse with the target membrane; however, the intervening events and further functions of the Rab proteins are unclear. The tether could collapse or bend, pulling the vesicle on to the Golgi membrane surface, or the vesicle could hop along the tether. In both cases, Rab proteins might regulate the sequence of events.

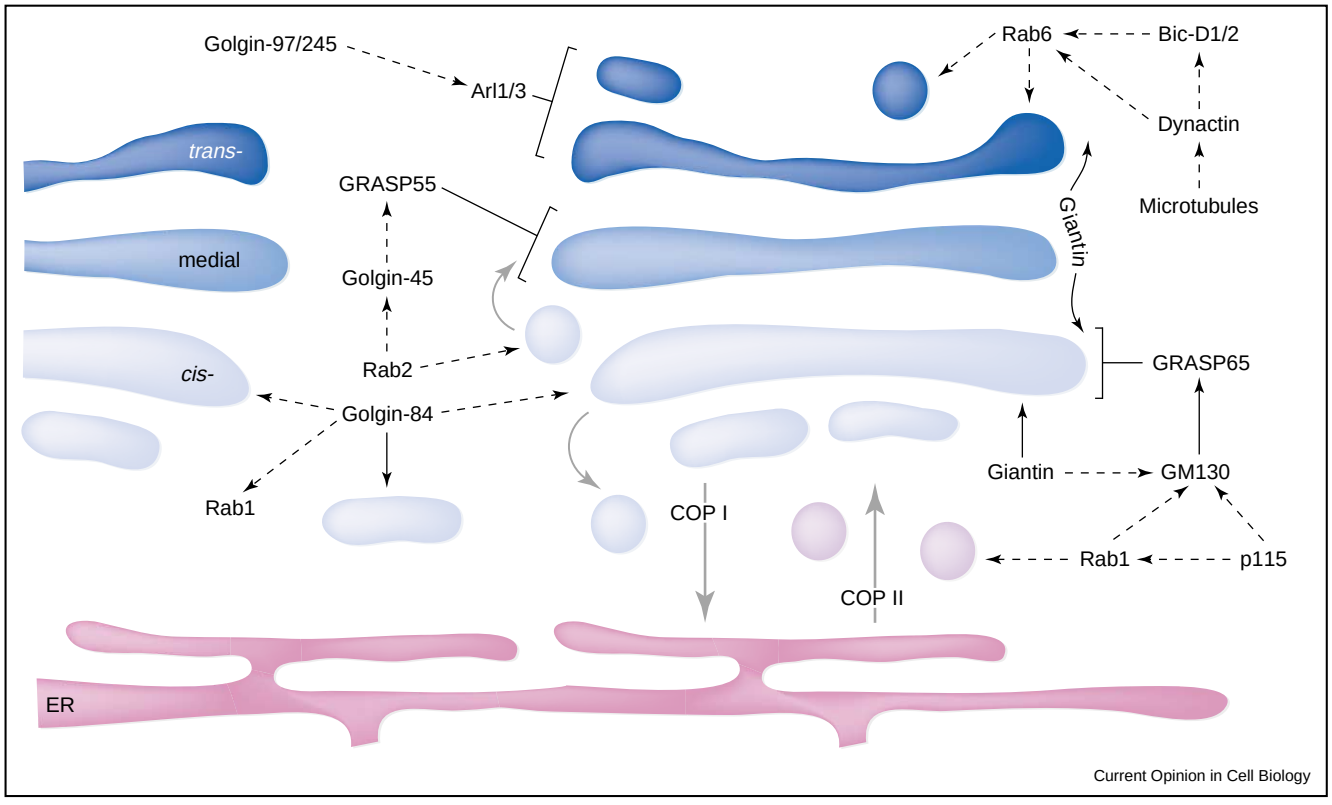
dissociation [22••]. Biochemical data show that this complex associates directly with Golgi membranes with high affinity, but how this process is regulated and the identity of the receptor on Golgi membranes remains unclear [17,19•,22••]. One possibility is that membrane proteins recycling between the ER and the Golgi, and transported membrane proteins in general, are the receptors for this complex. The identification of the p24 cargo receptor proteins in association with GRASPs supports this idea [24]. Biochemical and two-hybrid data show that GRASPs bind the cytoplasmic domains of these membrane proteins and can discriminate oligomeric from monomeric forms of the signal [24]. Whether or not this is used *in vivo* to discriminate the Golgi-localised fraction of these proteins from, say, the ER pool requires further investigation.

Rabs and the regulation of golgins

Simply holding two membranes together at the ends of an extended arm or rod structure or covering the membrane surface with a proteinaceous matrix, although suitable mechanisms for the organisation of Golgi cisternae into stacks, do not at first glance appear to be good ways to encourage membrane fusion. Regulation of tethers and matrix proteins must therefore take place to allow the membranes to approach sufficiently close that vesicle and target SNAREs can engage when fusion should occur. A common property of many golgins is that they bind to Rab GTPases often via coiled-coil domains: p115 binds Rab1, GM130 binds Rab1, Rab2 and Rab33b, golgin-84 binds Rab1, and golgin-45 binds Rab2 (Table 1; Figure 2).

What is the purpose of these interactions? In the case of p115, it makes sense that Rab1 acts as its vesicle-localised receptor, as discussed above; but GM130 and golgin-45 are already attached to the membrane via the GRASPs. One possibility is that although GRASPs can directly and stably attach to the membrane surface by their myristic acid anchor, the Rabs regulate the initial membrane

Figure 2



Golgin dynamics and Golgi structure. Golgins and their binding partners localise to discrete complexes on the surface of the different subcompartments of the Golgi. Golgins and Rab GTPases form a dynamic network of interacting partners that specify, shape and organise Golgi membranes. Solid lines are used for irreversible or high-affinity binding reactions; dashed lines indicate dynamic interactions. Multiple lines do not indicate that all interactions can occur to the same molecule simultaneously. Golgin-97 and golgin-245 are taken as indicative of GRIP-domain proteins.

association of GRASP–golgin complexes. On the basis of current knowledge, however, there is a more likely possibility. The Rab-binding properties of GM130 and golgin-45 might simply be a part of the tethering reaction, whereby multiple components of the tethering complex recognise the correct Rab protein on the vesicle surface to give high-affinity binding downstream of initial attachment programmed by p115 or a related molecule. It is also worth considering what we mean by 'regulation' in this context. Rabs undergo a conformational change upon GTP binding, which is relaxed on GTP hydrolysis. The active or GTP-bound form of the Rab becomes membrane-associated and is thought to act as a timer, regulating specific vesicle docking by controlling the association of tethering factors with the membrane [6]. In this model, Rabs are essentially viewed as passive receptors that recruit effectors to the membrane, but Rab binding could also induce conformational change in the binding partner or effector molecule, thus activating or inhibiting its function. Accordingly, the fact that multiple golgins in the same tethering complex bind Rab GTPases might indicate cooperativity to ensure specificity.

There are other options worthy of consideration, however. Rabs might regulate the conformation of the tethering complex, perhaps collapsing the captured vesicle onto its target, or the vesicle might hop along the components of the tether, by means of the Rab-binding sites, towards the target (Figure 1b). The ability of Rabs to recruit factors such as p115 to vesicles from the cytoplasm suggests another possible function: organising already membrane-associated complexes such as GRASP65–GM130 within the two-dimensional plane of the membrane.

None of these models is necessarily mutually exclusive and however speculative these proposals seem, they illustrate the point that Rabs may be more than simple tethering factor receptors. Coiled-coil proteins are often thought of as rigid structures, but this is a simplification of what is in fact a highly versatile protein-folding motif able to form both rigid and dynamic structures [4]. The coiled-coil predictions for golgins all display breaks or potential hinge regions, so they could form jointed arm structures, and it is therefore certainly possible that Rabs could regulate the conformation of golgins. Few, if any, structural

measurements of golgins have been made, and this remains a poorly understood aspect of their properties, but one that is likely to be crucial for understanding their function and the role of Rab proteins.

Rabs are not the only regulators of golgins, and, as in most other cellular events, protein phosphorylation is an important regulatory modification in both interphase and mitosis [25]. Phosphorylation during mitosis as a mechanism for disassembling the Golgi apparatus has been studied extensively, and several golgins are known to be mitotic phosphoproteins [25]; however, the action of kinases is also needed to maintain Golgi structure in interphase. The interaction of GM130 with giantin, mediated by p115, is enhanced by phosphorylation of p115 by an unidentified casein kinase II-like enzyme [26]. Essentially, nothing is known about the phosphorylation of other golgins and their binding partners during interphase.

Is that golgin function all tied up?

So, do all golgins form a matrix and act as tethers; and if not, what do they do? At a recent ESF/EMBO workshop in Tomar, Portugal, Sean Munro (Cambridge, UK) proposed that a wider range of functions should be considered for these proteins. Many potential functions can be envisaged, including negative regulation of membrane fusion events by keeping membranes apart, providing transient binding sites for vesicles to attach to limit their diffusion, compartmentalisation and organisation of membrane proteins, and cytoskeletal interaction or linking, to name a few. As we discuss below, there is emerging evidence for some of the non-tethering functions of golgins.

Integral membrane golgins and their partners

There are four type-II transmembrane golgins in animal cells, giantin, golgin-84, golgin-67 and CASP (CCAAT-displacement protein alternatively spliced product) (Table 1). The prototypic transmembrane golgin is giantin, a 400 kDa dimeric protein, disulphide bonded in the small Golgi lumenal domain, with the bulk of the protein predicted to form an extended coiled-coil structure in the cytoplasm [27,28]. Golgin-84 was the second transmembrane golgin to be described, and has a similar structure to giantin, although with a much smaller cytoplasmic domain [29]. It was found as an interacting partner of OCRL1 (Ocular cerebro renal syndrome of Lowe 1), a Golgi phosphatidylinositol 5-phosphatase, in a yeast two-hybrid screen [29]. Golgin-67 is similar to GM130 but does not bind GRASPs; instead, it has a predicted transmembrane domain [30], although unlike golgin-84 and giantin it has not been proven to be an integral membrane protein and might therefore target to the Golgi by another mechanism. Giantin function in COPI vesicle tethering has been described above, and the only thing to add to this story is a peripheral membrane golgin, GCP60, which is well conserved between flies, worms and mammals. GCP60 interacts with the carboxy-terminal region of giantin adjacent to the transmembrane domain, and although it is not known what GCP60 does at a molecular level its overexpression disrupts the Golgi and blocks ER-to-Golgi transport [31].

The carboxy-terminal regions of giantin, golgin-84 and CASP containing the transmembrane domains and approximately 100 amino acids adjacent to this are sufficient to target these proteins to the Golgi [29,32•,33]. Strikingly, all three proteins share sequence similarity within the transmembrane domains. In particular, key tyrosine and histidine residues are absolutely conserved [32•]. When this tyrosine in CASP is mutated to leucine, Golgi localisation is lost and the protein accumulates in the ER [32•], demonstrating the importance of this sequence conservation. Whether this indicates that CASP was unable to leave the ER or was not retained in the Golgi was not determined, but the latter possibility implies that CASP might normally recycle between the ER and Golgi.

The analysis of the yeast CASP COY1 (CASP of yeast 1) revealed that although not essential for cell growth it shows genetic interactions with SNAREs needed for ER-to-Golgi transport [32•]. A yeast strain with a temperature-sensitive defect in the gene encoding the ER-to-Golgi SNARE Sec22p, *sec22-3*, has a growth defect at 34°C that is restored by overexpression of Coy1p. The opposite effect was seen with the ER-to-Golgi SNARE Gos1p: while deleting the gene has little effect, overexpression of Coy1p in this background significantly reduces cell growth despite having no obvious effect in wild-type cells. This effect was lost with a form of Coy1p mutated at either the conserved tyrosine or histidine residues [32•]. These results suggest that interactions with the transmembrane domain are critical for the function of Coy1p, and by extension the functions of giantin and golgin-84. One possible explanation for these findings is that Coy1p functions directly in vesicle tethering, organising SNARE proteins to regions of Golgi cisternae where vesicles are tethered by means of interactions with its transmembrane domain. This does not exclude other possibilities, for example that Coy1p is needed for efficient SNARE recycling or as a SNARE regulator.

Golgin-84 is essential for normal Golgi structure in animal cells, and when depleted the ER becomes enlarged and Golgi stacks fragment into many smaller structures [34•]. Unlike similar experiments with golgin-45, protein transport is reduced but not blocked under these conditions, and Golgi enzymes remain in these Golgi structures [20•]. When cells are treated with the drug brefeldin A, Golgi matrix proteins such as GM130 and the GRASPs redistribute to small punctate cytoplasmic structures discrete

from the ER [11,21]. Golgin-84 and CASP, in contrast, do relocalise to the ER on brefeldin A treatment, indicating that they are not part of the GM130-containing Golgi matrix [34•,32•]. The localisation of golgin-84 to *cis*-Golgi-associated tubulo-vesicular profiles and to cisternae in cryo-electron microscopy discrete from GM130 is consistent with this [34•,35•]. By contrast, GM130 and its binding partner GRASP65 are present only on the *cis*-most Golgi cisternae [36]. It is therefore unlikely that golgin-84 is involved in giving identity to cisternae, although it is clearly important for normal Golgi function. Somewhat contradicting this view, golgin-84 does bind Rab1, again by a coiled-coil domain, and antibodies to golgin-84 reduce stacking of Golgi cisternae in a cell-free assay, suggesting some involvement in Rab-mediated tethering [34•,35•].

Tethering events are not, by definition, positive; 'negative tethering' might be equally important to prevent vesicles fusing with the wrong target until the right one comes along. This might be an important mechanism in the Golgi apparatus with its stack of related cisternal membranes through which content should pass vectorially, or for the recycling of vesicles from the Golgi to specific subdomains of the ER. A soluble fragment of golgin-84 that might be expected to inhibit Golgi stack formation actually causes an increase in cisternal length without changing other aspects of Golgi stack formation [35•], supporting the idea that golgin-84 has a negative regulatory function. An alternative hypothesis of Lowe and colleagues is that golgin-84 is needed to laterally organise Golgi stacks into the larger ribbon structure characteristic of animal cells [34•]. This is an interesting idea, bringing together tethering and recognition events in a way that could be important for regulating cargo flux through the Golgi and high-level Golgi organisation, and would also explain why golgin-84 is not essential for ER-to-Golgi or intra-Golgi transport. This can even be partially reconciled with the function of Coy1p in yeast, which, although lacking this ribbon-like organisation of Golgi stacks, presumably do regulate lateral fusion of their Golgi cisternae.

Tethering Golgi membranes to the cytoskeleton

Golgi membranes are collected in the pericentriolar region of animal cells, in part by the action of the dynein motor protein [37,38]. Bicaudal-D proteins are a family of coiled-coil proteins that localise to the *trans*-Golgi region and associated vesicles and interact with dynactin, an adaptor for the dynein motor protein [39•]. On the basis of a series of recent publications, we propose that the bicaudal-D proteins should be considered golgins, owing to their Golgi localisation, conserved coiled-coil domains and Rab6-binding properties [40•,41•]. Like other golgins, bicaudal-D1 and -D2 bind to Rab6 by a carboxy-terminal coiled-coil domain, and in this case the interaction is necessary for targeting them to Golgi membranes [40•,41•]. The purpose of this interaction is believed to be to link or tether vesicles and *trans*-Golgi membranes to microtubules via the dynein–dynactin complex. This interaction might be the 'capture' part of the dynein and microtubule search/capture system that collects Golgi membranes in the pericentriolar region in animal cells [38,42••], although this remains to be proven. The details of Rab6 function are discussed in more detail elsewhere in this issue (see the review by Sannerud, Jaakko Saraste and Goud, this issue).

Another Golgi-associated coiled-coil protein with microtubule-binding properties that can be termed a golgin is GMAP210 [43,44]. This localises to the *cis*-Golgi, and when overexpressed causes a total disassembly of the Golgi and a block in anterograde and retrograde transport between the ER and Golgi [44]. Whether or not the coiled-coil domain of GMAP210 binds to any Rab GTPases still remains to be investigated. Not all Golgi–microtubule interactions are mediated by golgins; two other known Golgi-localised microtubule-binding proteins are Hook3 on the *cis*-Golgi and CLIPR-59 on the *trans*-Golgi [45,46]. Although Hook3 is a member of a family of coiled-coil proteins, other family members localise to other cellular structures and it therefore cannot really be termed a golgin [45]. CLIPR-59 is part of the CLIP-170 family of organelle–cytoskeleton linker proteins, clearly discrete from the golgin family of proteins [46].

The GRIP domain

The GRIP domain was originally identified as a conserved carboxy-terminal domain present in a group of Golgi-localised proteins from yeast and mammals that otherwise showed little homology [47–49]. It is characterised by an invariant tyrosine residue at position 4, followed eight amino acids later by a phenylalanine or tyrosine residue. Initially, this domain was reported to bind the Rab6 on farwestern blots, and, together with data on the yeast GRIP-domain protein Imh1, this suggested a function in vesicle tethering [48]. It has recently become apparent that the GRIP domain binds the ARF-like GTPases Arl1 and Arl3 with significantly higher affinity than Rab6 in both yeast two-hybrid and biochemical assays [50•] (see also Update). In itself, this does not shed much light on the function of GRIP-domain proteins because it is not known what Arl GTPases do; but it does imply that we need to consider non-tethering functions for them.

By analogy with the functions of the different ARF proteins, Arls can either recruit vesicle coat proteins or other membrane adaptor or signalling molecules to membranes [50•]. The GRIP-domain proteins p230/golgin-245, GCC88p and GCC135p in animal cells are associated with the surface of *trans*-Golgi-derived tubulo-vesicular carriers and the *trans*-Golgi network (TGN), and it has

been suggested they might function as vesicle coats or in the organisation of membrane subcompartments of the TGN [51,52]. It is also possible that the various GRIP-domain proteins have different Golgi-associated functions, and that the GRIP domain is merely a device to localise them to the TGN.

Golgins and Golgi dysfunction

Several golgins and their associated proteins are cleaved at an early stage during programmed cell death in animal cells. Amongst these are golgin-160, GRASP65 and p115 [53–55]. Golgin-160 is cleaved by caspase-2 at a unique site, and expression of a mutant form of golgin-160 resistant to cleavage slows apoptotic Golgi fragmentation (see also the review by Maag, Hicks and Machamer, this issue) [53]. Similarly, GRASP65 is cleaved by caspase-3, and expression of a cleavage-resistant GRASP65 slows apoptotic Golgi fragmentation [54]. If nothing else, this tells us that both golgin-160 and GRASP65 are important for the maintenance of normal Golgi structure. Something different is suggested from studies of p115 during apoptosis, where the carboxy-terminal cleavage product translocates into the nucleus and has an apparent pro-apoptotic effect that can be mimicked by overexpression of the same fragment in transfection experiments [55].

But why should the state of the Golgi be important for apoptosis in animal cells? The cleavage of these proteins during apoptosis could be necessary to abolish Golgi function and protein transport, something that might be important in the response to virus infection, for example. At present, this remains largely speculation, albeit one in keeping with the original identification of golgins as antigens in autoimmune diseases.

Conclusions

Golgins are modular proteins, comprising a central coiled-coil domain separating different types of interaction motif for Rab and Arl family GTPases, membrane anchoring, and the recruitment of other proteins, which in many cases are other golgins. Owing to their extensive and repetitive coiled-coil structures, golgins from different organisms, or even in closely related organisms, are not always easily identified on the basis of sequence similarity. Many golgins function in tethering interactions between membranes, or membranes and the cytoskeleton, and this is a dynamic, regulated process controlled by the Rab GTPases. It is important to remember that tethering is more than just linking vesicles with their target membranes it includes stacking of Golgi cisternae, and interactions with the cytoskeleton. It is also important to note that not all golgins are proven or even likely to be tethering factors. In future, reconstitutions of these tethering events *in vitro* using purified components is likely to be the key to understanding both the function of golgins and the Rab and Arl GTPases that regulate them.

Update

Further evidence for a link between the Arl1 GTPases and coiled-coil vesicle-tethering factors containing GRIP domains is provided by two recent studies in yeast [64,65]. Arl1p was shown to bind yeast GRIP-domain proteins, whereas Arl3p was needed for Golgi localisation of Arl1p. The authors of one of these studies [64] suggest that rather than acting as simple recruitment factors, Arls act in a regulatory cascade to control recruitment of GRIP-domain proteins to the Golgi apparatus.

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- •• of outstanding interest

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