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To cite this version:

Yamini Ravichandran, Bruno Goud, Jean-Baptiste Manneville. The Golgi apparatus and cell polarity: Roles of the cytoskeleton, the Golgi matrix, and Golgi membranes. Current Opinion in Cell Biology, 2020, 62, pp.104-113. 10.1016/j.ceb.2019.10.003 . hal-02399472

HAL Id: hal-02399472

https://hal.science/hal-02399472

Submitted on 11 Dec 2019

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The Golgi apparatus and cell polarity: roles of the cytoskeleton, the Golgi matrix and Golgi membranes

Yamini Ravichandran[1,2,3], Bruno Goud[1,2], Jean-Baptiste Manneville[1,2,+]

[1] Institut Curie, PSL Research University, CNRS, UMR 144, 26 rue d'Ulm F-75005, Paris, France

[2] Sorbonne Université, UPMC University Paris 06, CNRS, UMR 144, 26 rue d'Ulm F-75005, Paris, France

[3] Institut Pasteur, CNRS, UMR 3691, 25 rue du Docteur Roux F-75014, Paris, France

+: to whom correspondence should be addressed (email: Jean-Baptiste.Manneville@curie.fr, phone: 33 1 56 24 65 64, fax: 33 1 56 24 64 21)

Running head: The Golgi apparatus in cell polarity

Keywords: trafficking, microtubules, actin, signaling, golgin, centrosome, forces

Word count: 3167 words

Summary

Membrane trafficking plays a crucial role in cell polarity by directing lipids and proteins to specific subcellular locations in the cell and sustaining a polarized state. The Golgi apparatus, the master organizer of membrane trafficking, can be subdivided into three layers that play different mechanical roles: a cytoskeletal layer, the so-called Golgi matrix and the Golgi membranes. First, the outer regions of the Golgi apparatus interact with cytoskeletal elements, mainly actin and microtubules, which shape, position and orient the organelle. Closer to the Golgi membranes, a matrix of long coiled-coiled proteins not only selectively captures transport intermediates but also participates in signaling events during polarization of membrane trafficking. Finally, the Golgi membranes themselves serve as active signaling platforms during cell polarity events. We review here the recent findings that link the Golgi apparatus to cell polarity, focusing on the roles of the cytoskeleton, the Golgi matrix and the Golgi membranes.

Introduction

The Golgi apparatus is the transformation and sorting factory of most proteins and plays a pivotal role in membrane trafficking. In the secretory pathway, the Golgi apparatus receives *de novo* synthesized molecules from the endoplasmic reticulum (ER), post-translationally processes lipids and proteins, and sorts cargoes to their ultimate destination [1,2]. Cell polarity, the process by which a cell defines an oriented axis for instance to migrate, divide or differentiate, strongly depends on membrane trafficking [3]. Over the past three decades, evidence has accumulated showing that the structure, organization and positioning of the Golgi apparatus are implicated in maintaining a polarized cell state [2,4–6]. In polarized cells, cellular materials are transported along the polarity axis. This requires polarization of membrane trafficking from the Golgi apparatus. Conversely, the position of the Golgi inside the cell can dictate the directionality of membrane trafficking and the proper localization of polarity cues. This 'chicken-and-egg' problem is typical of feedback loops involved in symmetry breaking during establishment of cell polarity. In the case of Golgi-dependent membrane trafficking, the orientation of the Golgi apparatus in the direction of the polarity axis targets transport towards a given region of the cell, for example, towards the leading edge plasma membrane during cell migration (front-rear polarity), in the apical process of neural stem cells (radial polarity), towards the apical compartment of epithelial cells or towards the immunological synapse (Fig. 1). In all these examples and despite intensive research, it is still not clear whether and how external polarity cues are transduced inside the cell to polarize transport from the Golgi apparatus, and conversely, whether and how the Golgi apparatus could be driving cell polarization. One historical example is given by the small G protein CDC42. CDC42 was identified as an evolutionary conserved polarity protein in several organisms, from yeast to humans [7]. In mammalian cells, beside its functions in cell protrusion formation and cell migration as a plasma membrane-associated protein, CDC42 also operates in intracellular vesicle trafficking [8,9]. Consistently, CDC42 not only localizes at the plasma membrane but also at the Golgi apparatus where it interacts with the Golgi matrix [8], coat proteins [10–12], microtubule motors and the actin polymerization machinery [11]. However the precise role of CDC42 at the Golgi apparatus, how the Golgi associated pool of CDC42 interacts with the plasma membrane-associated pool and whether these interactions impact on cell polarity remains to be determined [8].

We focus here on the machineries localized at the Golgi apparatus which have been shown or hypothesized to participate in establishing directional membrane trafficking during cell polarization in mammalian cells. The Golgi apparatus can be viewed structurally as a three-layered organelle constituted of membrane-enclosed Golgi cisternae, the so-called Golgi matrix and cytoskeletal elements. Because of its

organization in *cis*, *median* and *trans* compartments, the Golgi apparatus possesses an intrinsic polarity. Intra-Golgi trafficking is in itself a polarized process, whether it is described in terms of a vesicular transport or a cisternal maturation model [13]. In mammalian cells, Golgi stacks are tethered laterally to form a Golgi ribbon typically found in tight association with the centrosome. Current models suggest that the assembly of the Golgi ribbon is an actin and microtubule (MT) dependent process. Maintenance of the Golgi architecture depends on the cytoskeleton and is coordinated at least in part by Rho and Rab GTPases [14,15]. In the following, we review recent work on the molecular players acting at the Golgi apparatus and relevant for the mechanical aspects of cell polarization, such as the generation of forces involved in Golgi positioning. For clarity, we have separated the description of the molecular mechanisms in three parts each corresponding to one structural component of the Golgi apparatus – the Golgi matrix, the Golgi-associated cytoskeleton and Golgi membranes – even if these three components are linked and interact with one another.

Golgi matrix proteins and cell polarity

In mammalian cells, Golgi membranes are organized as an interconnected ribbon typically positioned adjacent to the centrosome in the perinuclear region. This proximity is usually disrupted by conditions that perturb Golgi organization. The functional significance of the proximity between the Golgi apparatus and the centrosome is not fully understood. Several studies have linked the spatial connection between the centrosome and the Golgi apparatus with directed protein transport or directional migration [16–18]. In front-rear cell polarity models, such as directed cell migration, centrosomal reorientation towards the leading edge is known to align the Golgi apparatus towards the leading edge (Fig. 1A).

Strikingly a number of proteins belonging to the Golgi matrix [19,20] are not only critical for maintaining the typical Golgi architecture and its positioning close to the centrosome, but also for cell polarity. For instance, Golgi reassembly and stack proteins (GRASPs) link Golgi stacks together. Depletion of GRASP55 or GRASP65 perturbs Golgi organization and function [21] and the phosphorylation of GRASP65 is required for both Golgi and centrosome reorientation during directed cell migration [22]. Depletion of GRASP65 and GRASP55 also reduces the level of $\alpha 5\beta 1$ integrin and consequently decreases adhesion, migration and invasion of HeLa cells and of the breast cancer cell line MDA-MB-231 [23]•.

Similarly, the Golgi matrix protein GM130, a GRASP65 binding partner, has been implicated in cell polarity. GM130 recruits and activates the kinase YSK1 which phosphorylates downstream cell polarity targets [24]. Consistently, expressing inactive YSK1 blocks both Golgi and centrosome reorientation during cell migration [24]. In

addition, GM130 may also control cell migration through the activation of both YSK1 and CDC42 [24–26]. More recently, deletion of GM130 in Purkinje neurons has been shown to induce Golgi fragmentation and defects in Golgi positioning [27]••. In contrast, a study carried out in GM130 knock out (KO) retinal pigment epithelial (RPE-1) cells shows that the physical proximity between the centrosome and the Golgi apparatus is not necessary for protein transport, cell migration, or ciliogenesis [28]•. While these results further strengthen the proposed role of GM130 in Golgi ribbon formation and in associating the Golgi apparatus to the centrosome by recruiting AKAP450 (A-kinase anchoring protein of 450 kDa, also known as AKAP350, AKAP9, or CG-NAP) [29], they question whether a connection between the Golgi apparatus and the centrosome is required for cell polarity during directed migration (Fig.1A) [16].

Golgi-associated cytoskeletal elements

The actin and microtubule network and their associated molecular motors play a key role in maintaining Golgi architecture and positioning during cell polarization by generating forces and mechanical tension [30–32]. In particular, the microtubule minus-end directed motor dynein has been shown both to anchor microtubule plus-ends at the plasma membrane and to concentrate at the Golgi apparatus. During directed cell migration activation of CDC42 at the leading edge plasma membrane recruits and anchors dynein at the cell cortex via the Par polarity complex [33,34]. Dynein in turn pulls on astral microtubules to reorient the centrosome towards the leading edge [33,35–37]. The Golgi apparatus probably reorients via the same mechanism through its mechanical link with the centrosome. Dynein is also found at the cis-Golgi where it associates with the actin cytoskeleton and coat proteins [11]. Together with results showing the role of the CDC42/COPI interaction in directed intra-Golgi trafficking [10], these observations suggest that Golgi-localized dynein could also participate in redirecting membrane trafficking during establishment of cell polarity. In addition to this physical link between the dynein motor and the Golgi apparatus, recent studies have mostly focused on the role of Golgi-nucleated microtubules and on actin-generated tension to link the Golgi apparatus with cell polarity.

The Golgi apparatus as a polarized non-centrosomal microtubule organizing center

The Golgi apparatus is a site that can nucleate and stabilize non-centrosomal microtubules [5,31,38,39]. Microtubule nucleating and/or stabilizing factors accumulate at Golgi membranes and act as molecular scaffolds. Golgi-derived microtubule arrays are polarized and can therefore induce cell asymmetry facilitating polarized transport of post-Golgi cargoes in a specific direction [16,40,41] during cell migration and

differentiation [42–45]. Recently better characterization of the molecular machineries associated both at the plus and minus-ends of Golgi-derived microtubules involved in their nucleation, dynamics, stabilization and regulation has led to a model clarifying the role of these microtubules in the polarization of membrane trafficking (Fig. 2).

First, the identification of the *cis*-Golgi localized protein AKAP450 as a key player in Golgi-derived microtubule nucleation transformed the field of Golgi-derived microtubules [46,47]. AKAP450 recruits two γ-TuRC-binding homologous proteins namely CEP215 and myomegalin (MMG) which in turn recruit γ-TuRC (Fig. 2A) [48–51]. Simultaneously several studies showed that recruitment of cytoplasmic linker-associated proteins (CLASPs) to the *trans*-Golgi by the golgin GCC185 was also essential for the nucleation and organization of Golgi-derived microtubules [52,53]. CLASPs are microtubule plus-end tracking proteins (+TIPs) that stabilize microtubules [54] (Fig. 2B). Both AKAP450 and CLASPs associate with the microtubule lattice-binding protein MTCL1, which promotes microtubule association with the Golgi apparatus [55]. Therefore, the initial models of Golgi-derived microtubules involved tethering of microtubules regulatory proteins at both *cis*- and *trans*-Golgi compartments. How these differently localized groups of proteins could collaborate in the same pathway to generate polarized microtubule arrays was unclear, especially in the absence of microtubule stabilizing proteins essential for anchoring microtubule minus-ends to Golgi membranes.

Depletion of the calmodulin-regulated spectrin-associated protein CAMSAP2 in mammalian RPE-1 cells leads to the loss of most non-centrosomal microtubules [56], suggesting that CAMSAP2 participates in microtubule stabilization at Golgi membranes. Subsequently, CAMSAP2 was shown to be essential for tethering, but not for nucleation, of non-centrosomal microtubules at the Golgi apparatus [57]••. AKAP450 is thought to play a dual function by organizing Golgi microtubules at the *cis*-Golgi, initially by anchoring CAMSAP2-bound microtubule minus-ends, and then by enhancing microtubule nucleation through γ-TURC recruitment (Fig. 2B, C). Through their roles in organizing Golgi-anchored microtubules, AKAP450 and CAMSAP2 contribute to Golgi reorientation during cell polarization and migration. Interestingly, Golgi-anchored microtubules also appear to participate in Golgi fragmentation during Golgi reorientation, probably by exerting pulling forces on Golgi membranes [57]••.

Similar mechanisms may be at play in other polarity models. For instance, non-centrosomal microtubules control cell polarity in endothelial cells migrating in 2D and 3D models and during vessel development in Zebrafish [58]•. Interestingly, another CAMSAP family member, CAMSAP3, has been involved in apico-basal polarity in epithelial cells (Fig. 1B) [59]. Here CAMSAP3 tethers microtubule minus-ends to the apical cortex, resulting in pulling forces which may orient the microtubule array in the

apico-basal direction and lead to the polarized intracellular organization and positioning organelles typical of epithelial cells.

Associated with CAMSAP2, the end binding proteins (EBs) EB1, EB2 and EB3 which form the core components of microtubule plus-end tracking protein (+TIPs) complexes, have been implicated in tethering microtubules to the Golgi apparatus, in Golgi morphology and reorientation during directed cell migration. The current model for EB-dependent polarized organization of microtubules at the Golgi apparatus involves the interaction between AKAP450 and MMG. MMG recruits EBs along microtubules to induce dispersion of Golgi stacks via plus-end tracking. MMG also recruits CAMSAP2 in an EB-dependent manner at microtubule minus-ends to favor Golgi compaction probably via dynein-mediated transport [60]• (Fig. 2C).

Linking actin and the Golgi apparatus

The Golgi apparatus is a hub for a wide array of actin regulatory proteins. CDC42, WHAMM, WAVE, Arp2/3 complex, cortactin, cofilin, profilin II and several myosins (II, VI, 18, 1b) localize at the Golgi apparatus and the *trans*-Golgi network (TGN) [30]. In addition to the evident role of microtubules, the actin cytoskeleton is also emerging as a key factor in the assembly and maintenance of the Golgi architecture, in Golgi mechanics and in Golgi-dependent membrane trafficking [30,61,62]. Golgi reorientation during cell migration depends on Rho-associated protein kinase (ROCK), a main regulator of acto-myosin contractility [63]. Aside from the Arp2/3 complex which generates branched actin networks, three actin nucleators belonging to the formin family have been linked to the Golgi apparatus, mDia1, INF2 and FMNL1 isoform γ [6,64]. In addition, recent work shows that the formin family members FMNL2 and -3, CDC42 effectors known to regulate cell edge protrusion during migration and invasion, localize and function at the Golgi apparatus [65]••. Consistent with the role of CDC42 in regulating anterograde transport through the Golgi apparatus via cargo sorting and carrier formation [66], FMNL2/3 depletion also affects anterograde trafficking from the Golgi apparatus to the plasma membrane [65]••. Such a link between FMNL2/3 and the actin-dependent functions of CDC42 could be of particular importance during polarization of membrane trafficking (Fig. 3A).

Deciphering the link between actin driven migration and Golgi apparatus reorientation is key to understanding how both processes are coupled in space and time during cell polarization. Golgi phosphoprotein 3 (GOLPH3) is one such pivotal link required for Golgi to plasma membrane trafficking that bridges the Golgi apparatus to the actin cytoskeleton [67–70]. GOLPH3 is known to bind to phosphatidylinositol-4-phosphate (PtdIns(4)P), a lipid enriched in *trans*-Golgi membranes. Most importantly,

GOLPH3 binds the unconventional myosin, myosin 18A (MYO18A), which links the Golgi apparatus to F-actin. The GOLPH3/MYO18A/F-actin pathway is thought to exert a tensile force on Golgi cisternae and to participate in Golgi reorientation during cell polarization [71]• [72,73] (Fig. 3B). However the role of GOLPH3 as one of the main Golgi-associated actor driving polarization of membrane trafficking has been recently questioned by the finding that MYO18A does not display any motor activity [74]••.

Interactions between actin and Golgi-derived microtubules

The actin and microtubule cytoskeletons interactions occur at several subcellular locations, for instance at focal adhesions at the plasma membrane (see [75,76] for a recent review) or at the nuclear envelope [77]. Not surprisingly, these interactions are also observed at the Golgi apparatus. A distinct connection between Golgi membranes, actin filaments and Golgi-derived microtubules has been recently proposed. The formin protein FHDC1/IFN1 is thought to coordinate actin and microtubule dynamics during Golgi ribbon formation, and to establish intrinsic Golgi polarity [78]•.

Golgi membranes

Golgi membranes are located at the crossroads between the anterograde secretory route and the retrograde route. Golgi lipids and membrane proteins are thus ideally situated to be involved in a large number of signaling pathways, among which is signaling involved in cell polarity. Polarity proteins such as CDC42 localize at the Golgi apparatus, although their function there is still not clear. Other Golgi-localized GTPases have been recently shown to mediate trafficking events potentially involved in cell polarization, such as Arf1 in response to cell-matrix adhesion cues [79], Arl5 during amino acids-stimulated retrograde trafficking [80] or Rab6 in targeting secretion to focal adhesions [81]. We focus below on the less studied role of Golgi lipids and lipid metabolism in polarization processes.

Golgi lipids: new roles for PtdIns(4)P

PtdIns(4)P initiates the recruitment of the GOLPH3/MYO18A/F-actin machinery at Golgi membranes to shape the Golgi ribbon during cell polarization. Recently, two studies point to new roles for PtdIns(4)P and GOLPH3 in membrane trafficking and cell polarity. First, elegant *in vitro* experiments with liposomes and purified proteins confirm that PtdIns(4)P is required for GOLPH3 binding to membranes and demonstrate that GOLPH3 binding to PtdIns(4)P-containing membranes induces membrane curvature

and tubulation in a PtdIns(4)P-dependent manner [82]•. Second, a developmental biology study has demonstrated a new role for PtdIns(4)P during neurogenesis [83]••. A lipid signaling pathway involving Phosphatidylinositol transfer proteins (PITPs), PtdIns(4)P, GOLPH3 and ceramide transfer protein (CERT) at the Golgi apparatus appears to regulate apically directed membrane trafficking in neural stem cells during neocortex development in mice. CERT also plays an important role in Golgi positioning in these cells via a PtdIns(4)P-dependent mechanism [83]•• (Fig. 3B).

Lipid metabolism and mechanosensitivity

Cell polarity is often triggered by mechanical cues induced by cell-cell or cell-matrix adhesion. Such mechanical cues have recently been shown to impact on the organization and mechanical properties of the Golgi apparatus [79],[84]•. Mechanotransduction events at the Golgi apparatus may influence cell polarity. For instance, contractile forces induced by adhesion to the extracellular matrix were shown to modulate lipid metabolism through a pathway involving the sterol regulatory element binding protein (SREBP), a regulator of lipogenesis, and the Lipin-1 phosphatidate phosphatase that converts phosphatidic acid (PA) to diacylglycerol (DAG) [84]•. Since the rigidity of the Golgi apparatus also correlates with the level of acto-myosin contractility [61],[84]•, the physical properties of the Golgi apparatus may regulate the binding and/or activity of some of the components of this metabolic pathway. For instance, the level of DAG could influence membrane curvature [85] and in turn the binding of Arf1 or the activity of Lipin-1. Although not demonstrated yet, mechanosensitive pathways such as the Lipin-1/DAG/Arf1/SREBP pathway may be involved in polarity events activated by cell-matrix adhesion cues.

Concluding remarks and open questions

The Golgi apparatus plays a pivotal role in polarized cell functions. For instance, Golgi positioning and orientation control polarized membrane transport during cell migration or T-cell immunological synapse formation (Fig.1A,C). We have described here the main molecular pathways controlling Golgi-driven polarity, according to which element of the Golgi is involved, Golgi-associated cytoskeleton and motors, the Golgi matrix or Golgi membranes. As these pathways are likely to interact, understanding how the actors identified so far work in concert and mechanically couple the different constituents of the Golgi apparatus is the main challenge for the coming years. Accordingly, a physical link

between the Golgi matrix and the actin cytoskeleton implicating the golgin GCC88 and the CDC42 guanine exchange factor (GEF) ITSN-1 has recently been identified [86]• (Fig. 3A). Interesting novel targets could also emerge. For instance, as part of the cytoskeleton, spectrins [87], septins [88],[89]•• and intermediate filaments [90] may fill some missing links in current models. While they are known to interact with the Golgi apparatus and participate in Golgi organization and membrane trafficking [87,90], it is not known whether their interaction with the Golgi apparatus is directly involved in cell polarity. Technical developments such as optogenetics, FRET-based probes or laser ablation, should be instrumental to better decipher how forces are generated at the Golgi apparatus during cell polarization. It is also tempting to speculate that mechanosensitive properties of the Golgi apparatus are key during establishment of cell polarity.

Finally, since cell polarity is deregulated in cancer, not surprisingly several polarity regulators associated with the Golgi apparatus have been implicated in cancer and invasion. The epithelial-to-mesenchymal transition (EMT) was recently shown to increase rearward positioning of the Golgi apparatus at the back of the nucleus in migrating breast cancer cells [91]. However, the increased migration of the cells correlates more with a stable positioning of the Golgi apparatus than with its position at the back or at the front of the nucleus [91]. GOLPH3 has been identified as an oncogene [68,92]. By driving Golgi reorientation and polarized trafficking, GOLPH3 enhances cell migration and cellular transformation [71]. Another protein implicated in cancer progression is Intraflagellar transport 20 (IFT20), which affects the nucleation of Golgi-derived microtubules and promotes intra-Golgi transport to induce invadopodia and tumor invasion [93]. On the contrary, perturbing Golgi-derived microtubules by depleting CAMSAP2-AKAP450 in highly invasive fibrosarcoma cells diminishes their ability to migrate [57]••. These findings point to polarity pathways associated with the Golgi apparatus as potential targets in cancer therapy.

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Following their previous work on GOLPH3, the authors identify PtdIns(4)P as a critical Golgi lipid for anterograde trafficking from the Golgi apparatus to the plasma membrane by allowing GOLPH3 binding to Golgi membranes and subsequent membrane deformation. *In vitro* reconstitution experiments demonstrate that PtdIns(4)P is required for membrane curvature induced by GOLPH3.

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The authors show that a duo of Phosphatidylinositol transfer proteins (PITPs), PITPNA and PITPNB, drives the PtdIns(4)P-dependent recruitment of GOLPH3 in a redundant manner and also possibly recruits ceramide transfer protein (CERT) to Golgi membranes. The PITP/PtdIns(4)P/GOLPH3/CERT lipid signaling pathway appears to regulate apically directed membrane trafficking rather than bulk membrane trafficking in neural stem cells during neocortex development in mice. Interestingly CERT also plays an important role in Golgi positioning in these cells via a PtdIns(4)P-dependent mechanism. Downregulating CERT by shRNA perturbs both Golgi positioning and radial alignment phenocopying PITPNA/PITPNB or GOLPH3 deficiency phenotypes. However

CERT does not operate via the GOLPH3/actin pathway and the downstream effectors of CERT associated with Golgi reorientation and/or polarity proteins remain to be identified.

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The authors identify a pathway involving the sterol regulatory element binding protein (SREBP), a regulator of lipogenesis, and the Lipin-1 phosphatidate phosphatase that converts phosphatidic acid (PA) to diacylglycerol (DAG) as a key mechanosensitive pathway linking extracellular physical constraints to the Golgi apparatus. High acto-myosin contractility increases Lipin-1 activity and consequently DAG and Arf1 levels on Golgi membranes, preventing SREBP from shuttling from the ER to Golgi apparatus. Interestingly, a force directly applied on the Golgi apparatus using optical tweezers increases the amount of DAG on Golgi membranes mimicking the effects of increased contractility. Conversely, under reduced acto-myosin contractility, Lipin-1 is inhibited, SREBP accumulates in the Golgi apparatus where it is cleaved and then translocates to the nucleus where SREBP transcription factors are activated to promote lipid synthesis.

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This study investigates the potential involvement of septins in the structure and function of the Golgi apparatus. The authors show that septin 1 promotes Golgi positioning and anterograde trafficking by localizing at the cis-Golgi in a GM130-dependent manner, facilitating nucleation of microtubules and recruiting centrosomal proteins at the Golgi surface.

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Figure legends

Figure 1 – Positioning of the Golgi apparatus in different contexts of cell polarity
A. In most (but not all) migrating cell types, the Golgi apparatus is positioned with the centrosome in front of the nucleus in the direction of migration. Leucocytes are a notable exception. **B.** Epithelial cells exhibit baso-lateral polarity which relies on polarized membrane trafficking. In these cells, the Golgi apparatus is located between the nucleus and the apical surface. **C.** During the formation of an immunological synapse between a T-cell and a target antigen-presenting cell, the T-cell polarizes and its Golgi apparatus reorients towards the synapse to maintain polarized membrane trafficking towards establishing a target cell-T-cell contact. **D.** Transport in the axon from the cell body to the growth cone is crucial to maintain the polarized organization of neuronal cells. In pyramidal neurons, the position of the Golgi apparatus in the cell body correlates with the position of the main axon. **E.** Radial glial cells display a non-pericentrosomal Golgi positioning. The centrosome localizes close to the ventral side, while the Golgi apparatus is shifted towards the basal lamina close to the nucleus. Vesicular trafficking is mostly oriented perpendicular to the polarity axis in these cells.

Figure 2 – Golgi-associated microtubules
A. The Golgi matrix protein GM130 bound to AKAP450 recruits the γ-TuRC binding proteins CEP215 and myomegalin (MMG). γ–TuRC subsequent binding to CEP215 and MMG induces microtubule nucleation at the surface of the Golgi apparatus. **B.** The elongation of microtubules is associated with several microtubule-stabilizing proteins such as CLASPs. **C**. CAMSAP2 and end-binding proteins EB1/3 tether microtubules to the Golgi apparatus therefore regulating Golgi positioning and reorientation during directed cell migration. Abbreviation: MT, microtubule.

Figure 3 – Golgi-associated actin
A. A number of actin regulators have been identified to localize at the Golgi apparatus. Among them, the formin family members FMLNL2/3 are regulated by CDC42, nucleate actin polymerization at the surface of the Golgi apparatus and participate in cell polarity. **B.** A main pathway involving Golgi-associated actin in Golgi architecture and in the polarization of membrane trafficking is the GOLPH3/MYO18A/F-actin pathway. Phosphatidylinositol-4-phosphate (PtdIns(4)P) and upstream lipid transfer proteins (PITPs and CERT) regulate this pathway.

Acknowledgements

Y.Ravichandran is funded by the Polarnet ITN (Innovative Training Network) part of the European Commission and the Fondation pour la Recherche Médicale (FRM). We apologize to colleagues whose work we could not cite due to space limitations. The authors declare no conflict of interest.

Conflict of interest

The authors declare no conflict of interest.

Figure 1

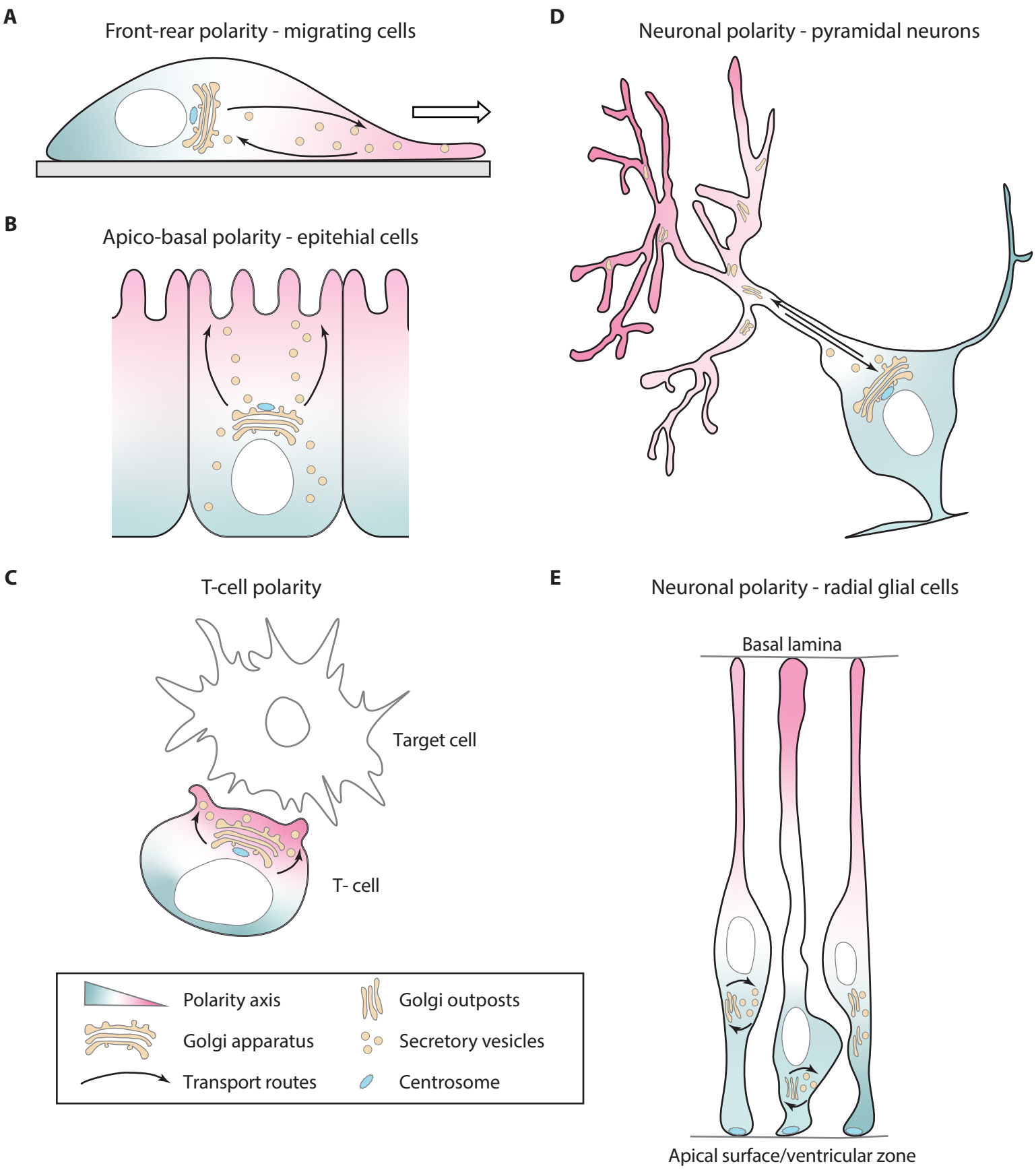
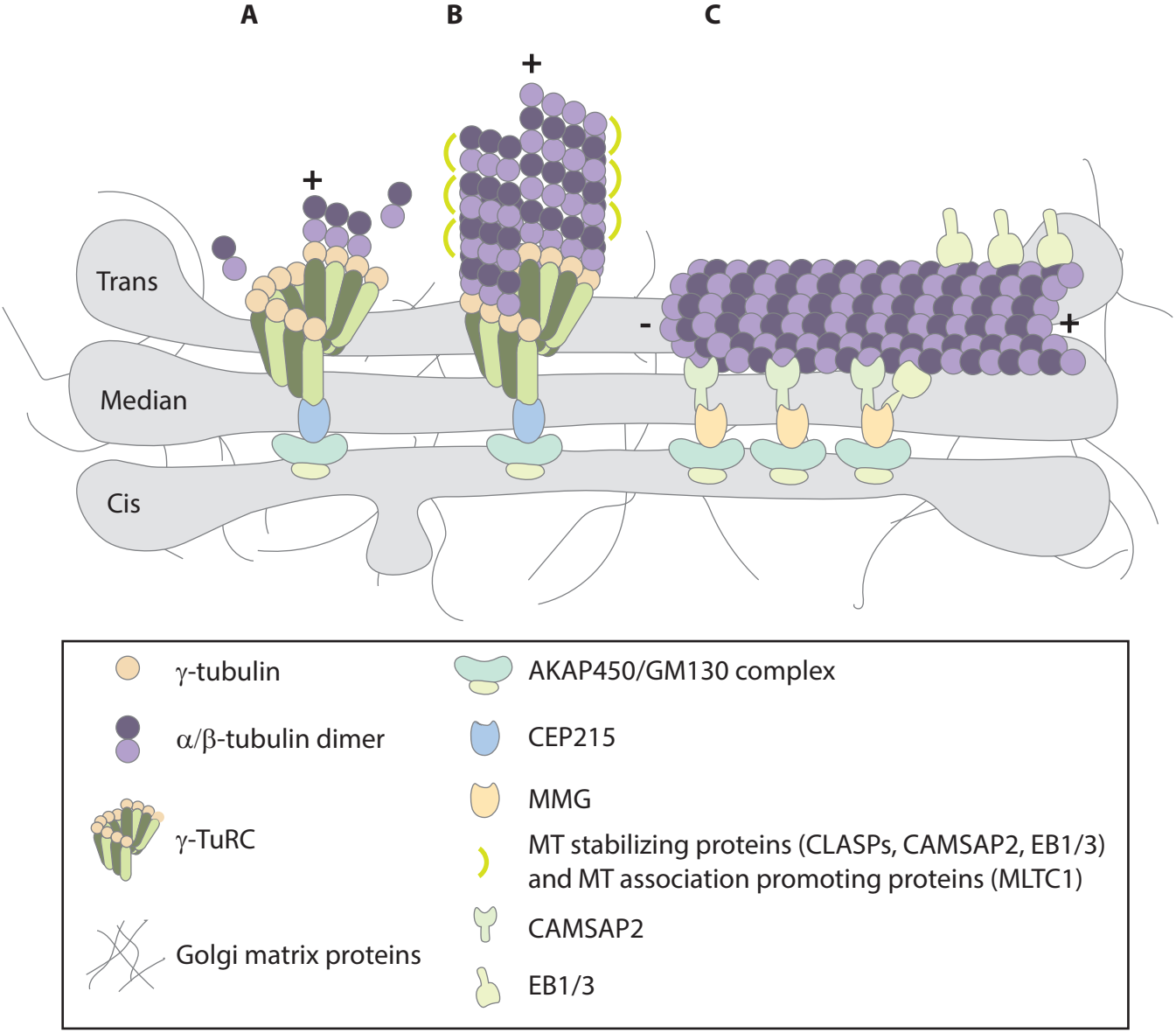

A
Front-rear polarity - migrating cells
B
Apico-basal polarity - epitehial cells
C
T-cell polarity
Target cell
T- cell
D
Neuronal polarity - pyramidal neurons
E
Neuronal polarity - radial glial cells
Basal lamina
Apical surface/ventricular zone
Polarity axis
Golgi apparatus
Transport routes
Golgi outposts
Secretory vesicles
Centrosome

Figure 2


A
B
C
+
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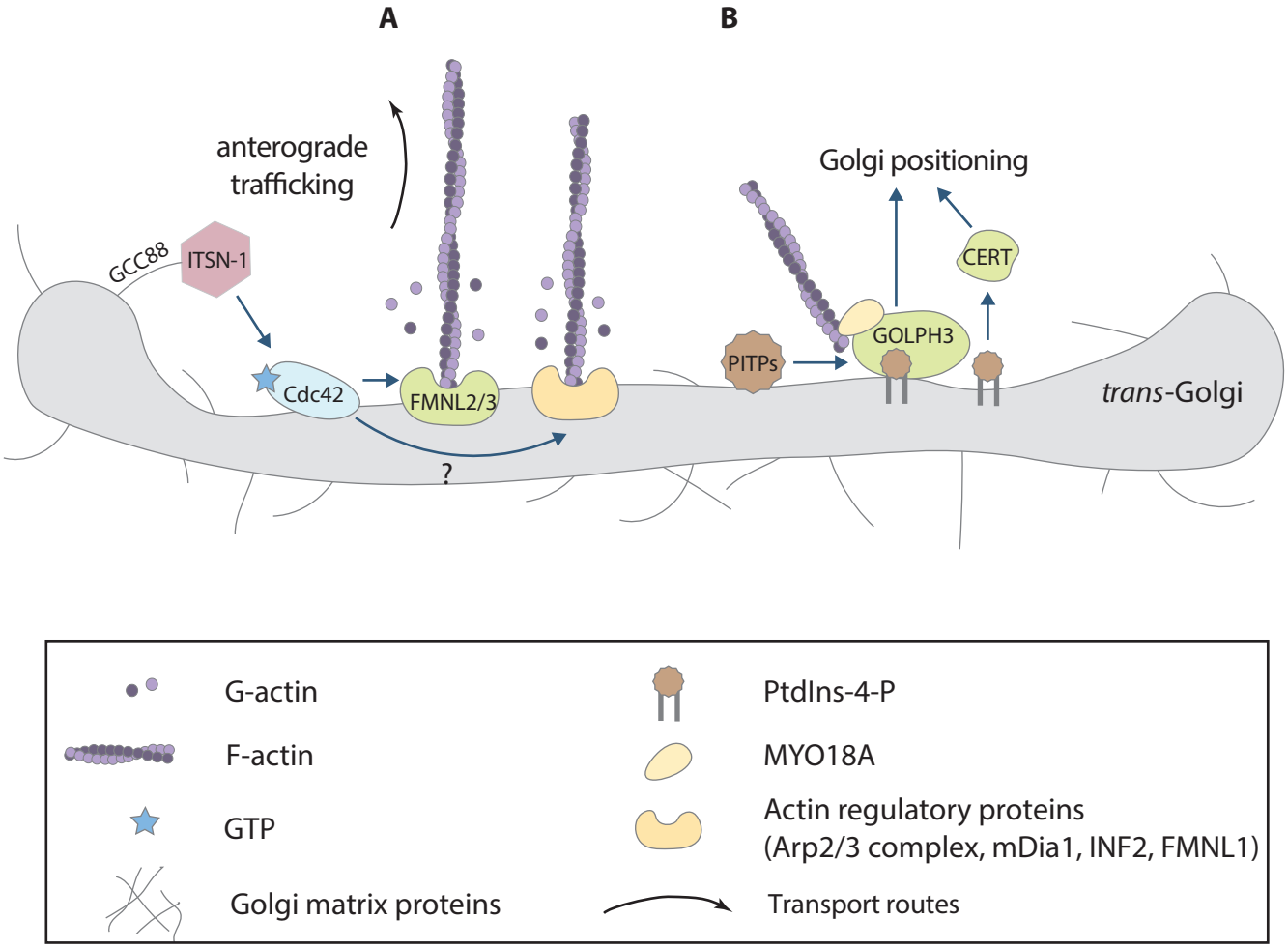
Trans
Median
Cis
γ-tubulin
α/β-tubulin dimer
γ-TuRC
Golgi matrix proteins
AKAP450/GM130 complex
CEP215
MMG
MT stabilizing proteins (CLASPs, CAMSAP2, EB1/3) and MT association promoting proteins (MLTC1)
CAMSAP2
EB1/3

Figure 3


A
B
anterograde trafficking
GCC88
ITSN-1
Cdc42
FMNL2/3
?
Golgi positioning
CERT
GOLPH3
PITPs
trans-Golgi
G-actin
F-actin
GTP
Golgi matrix proteins
PtdIns-4-P
MYO18A
Actin regulatory proteins
(Arp2/3 complex, mDia1, INF2, FMNL1)
Transport routes