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Train trip into the cell: the Golgi Apparatus as the central station of the intracellular membrane traffic

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ABSTRACT

Cellular membranes are crucial for the cells. The eukaryotic cell is made up of the plasma membrane that isolates it from the external world, and of intracellular membranes, which form compartments that give rise to the organelles. This subdivision allows the cell to adapt to changing external conditions, and to perform specific functions depending on the tissue. Cell membranes are made up of (glyco)lipids and (glyco)proteins that once synthesized are sorted and transported to their specific subcellular destination. Mistakes in this process may compromise cell survival and, consequently, the whole organism. Hence, the control and regulation of intracellular transport is a crucial process for the survival of the cell. The Golgi complex, or Golgi apparatus, is the organelle responsible for such regulation and control. It can be compared to the Grand Central station on the intracellular rail trip in which travellers, carriages, wheels, traffic lights, motors and tracks help us to understand how the intracellular membrane traffic takes place.

Introduction

The cell is protected from external environment by a surrounding membrane called plasma membrane. In certain cell types, this membrane presents domains that are clearly differentiated in function and morphology (cilia, flagella, microvilli), e.g. polarized cells like neurones and epithelial cells (renal and intestinal). Other cell types lack these specialized structures e.g. non-polarized cells like fibroblasts.

The functional evolution of the eukaryotic cell is parallel to the appearance of new intracellular compartments. This structural and functional compartmentalization is determined by the different distribution of the cell membrane components, lipids and proteins. Their correct distribution in the plasma membrane and in intracellular membranes allows the cell to fulfil its genetically determined functions properly. Otherwise serious pathological disorders would take place. Therefore, the knowledge of the signals that guide lipids and proteins to their proper destinies (endoplasmic reticulum, Golgi apparatus, lysosomes, chloroplasts, mitochondria, peroxisomes, plasma membrane) is crucial to understand the function of the cell. This line of research is included in the field that studies the intracellular traffic of membranes.

The great routes of the intracellular traffic of membranes

The intracellular traffic of membranes directs lipids and proteins to their destination. It has several pathways (Fig. 1):

1. The secretory, biosynthetic or exocytic pathway. This intracellular route is followed by the molecules synthesized in the endoplasmic reticulum (ER) that are transported to (a) other subcellular compartments (such as the Golgi apparatus, the lysosomes, the cloroplats, etc), (b) the plasma membrane, and (c) the extracellular medium. We distinguish two types of secretion:

1.1. Constitutive secretion. As soon as lipids and proteins are synthesized, they are continuously transported and secreted to their final destination. This secretion happens in all cells. An example for a protein that follows is contitutively secreted is given in a recent review by Ureña & Arribas (2000)[1].

1.2. Regulated secretion. It takes place only in response to specific signals e.g. certain ions or as a consequence of the hormone-receptor interaction. Once the products susceptible to regulated secretion have been synthesized, they are stored in spherical membrane structures called vesicles or granules, depending on their size. This secretion is only reported in certain cell types such as endocrine and exocrine cells, macrophages, some leukocytes and neurons.

[1] Como ejemplo de una proteína de secreción constitutiva ver el artículo de Ureña & Arribas (2000).

2. The endocytic pathway. This is the route by which soluble and membrane components enter into the cell. This includes:

2.1. The receptor-mediated endocytosis. The molecules that enter into the cell first bind to either a cell surface receptor or to a receptor stored in intracellular compartments that rapidly migrate to the plasma membrane in response to specific signals. For instance, the glucose receptor GLUT4 is stored in vesicles just localized bellow the plasma membrane. Increase in the plasma concentration of glucose leads to the secretion of insulin, which binds to cell surface receptors. This binding induces the vesicles to fuse with the plasma membrane where the receptors are incorporated. Free glucose is then taken up by these receptors and both re-enter the cell, glucose is then released and GLUT4 receptors can be used in a new cycle. The uncoupling between the this signalling and trafficking processes results in insulin-independent diabetes mellitus.

2.2. Endocytosis by pinocytosis. This allows the entry of macromolecules and fluids, which renews the plasma membrane every 30-60 min.

2.3. Endocytosis by caveolae. This mechanism uses vesicles that carry mainly caveolin and capture small hydrophobic molecules such as cholesterol and folic acid. Caveolae are involved in intracellular signal transduction.

2.4. Phagocytosis is a specialized form of endocytosis that incorporates large particles such as viruses, bacteria, intracellular parasites and inert complexes. It takes place only in certain cell types such as macrophages and neutrophils.

3. The recycling pathway. Certain membrane components enter the cell but once the load is released, they are returned to the plasma membrane so that they can be used again. This is what happens with most membrane receptors. In fact, it is a combination of the endocytic (internalising) and the secretory (return to the cell surface) pathways.

Regarding the amount of intracellular membrane, secretion and endocytosis are highly equilibrated. Any alteration would compromise cell survival. However, we will not focus on the mechanisms that are involved or that regulate these pathways, since they are beyond the scope of this text.

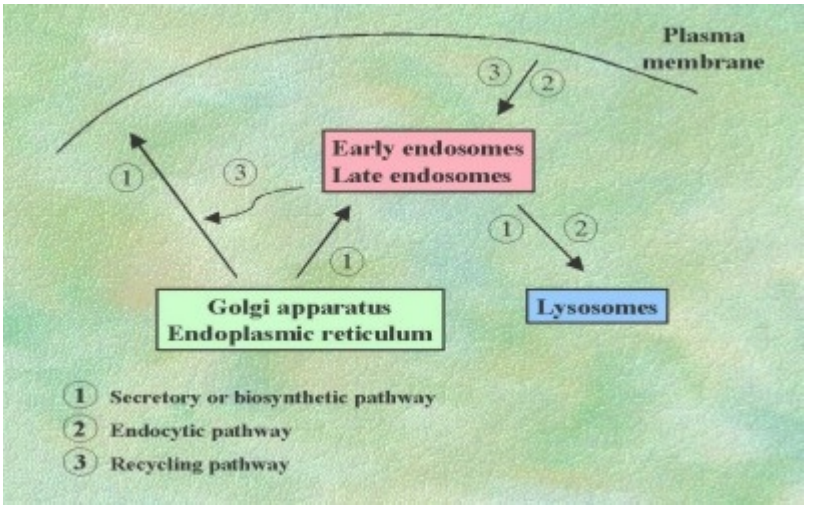

Fig.1. Intracellular pathways of membrane trafficking.

Train trip into the cellTrain trip into the cell

The organelles and molecular components involved in membrane traffic can be compared to a train journey and itemized as follows: passengers would stand for lipids and proteins, carriages for transport vesicles and stations for organelles (endoplasmic reticulum, lysosomes, endosomes, plasma membrane). We will focus on the intracellular Grand Central Station: the Golgi apparatus.

The endoplasmic reticulum as the hangar, factory and assembly line of intracellular trains

Lipids and proteins are synthesized in the ER, which consists of a continuous net of cisternae covered by ribosomes and extends through all the cytoplasm. Protein synthesis occurs on ribosomes, where the genetic message encoded in mRNA is translated. mRNA results from the transcription of DNA in the nucleus and is then transported to the cytoplasm. It encodes for cellular proteins, which may remain in the cytoplasm or else be transferred to the ER. Among the latter, some are free or soluble inside the ER cisternae (lumen) and some are membrane-bound. They could be referred to as standing passengers (soluble or luminal proteins) and seated passengers (membrane proteins). They comprise on the one hand proteins of the ER, which have to be retained,

and on the other hand proteins that must end up in other compartments to function and proteins that are to be secreted to the outside of the cell.

All proteins have a three-dimensional structure that is achieved by a continuous folding. Only properly folded proteins can be transported. Spontaneous twisting often brings about errors that may inactivate the protein. To prevent this from happening, a set of proteins of the ER lumen called chaperones help their mates in the contortion exercises. They contribute to the slow and ordered folding of proteins and to the packaging of their different subunits (Ellgaard et al, 1999). However, the most essential item in a journey is the ticket. What is the ticket? Which passengers are allowed to travel and which not? Unlike real passengers, certain molecular passengers can travel free! However, others must pay. What does this mean? According to the bulk-flow theory of exit (Wieland et al, 1987), the departure of soluble and membrane-bound proteins (both termed as cargo) from the ER does not need specific signals. However, recent data suggest that certain proteins present a signal sequence at the carboxyl terminal end that consists of two phenylalanines or, at least, two acidic amino acids (Nishimura & Balch, 1997). The signal sequences that determine whether the ER proteins stay there are better characterized: di-lysine and di-arginine are required at the carboxyl terminal end for type I and type II membrane proteins, respectively (Nilsson et al, 1989; Jackson et al, 1990; Schutze et. al, 1994), and lysine-asparagine-glutamic acid-leucine (KDEL) at the carboxyl terminal end for soluble proteins (Munro & Pelham, 1987). In principle, all the proteins that lack these ER retention signals will leave the ER towards the Golgi apparatus. However, the ER and the Golgi are not physically connected and so membrane intermediaries or transport vesicles are needed to make this intracellular journey.

Transport vesicles or the formation and assembly of intracellular wagons

Both the soluble and membrane-bound proteins that follow the secretory pathway leave the ER towards the Golgi apparatus, where their molecular structure is completed (glycosylation, phosphorylation) and they are packaged and sorted to their appropriate final destination. Export from the ER is extensively studied and there are more data on the molecular machinery involved than on its regulation. The ER is bigger than the Golgi apparatus, which means that the ER proteins are diluted and must concentrate throughout their journey to the Golgi. This is achieved in parallel to the formation of

transport vesicles, which takes place in specific ribosome-free areas of the ER called exiting sites. Thus not all the ER is able to accumulate cargo and form transport vesicles. The wagons (vesicles) can only be found at platforms (exiting sites).

Two relevant facts are associated with transport: (1) the loading of the cargo and (2) the deformation of the membrane at the exit sites and the subsequent separation that lead to the formation of the vesicle. Passengers (proteins and lipids) are scattered around the station and when the time of departure of the train (vesicles) approaches, they gather on the platform (exiting sites). The auto-assembly of several coats of multiproteic complexes deforms the donor membrane to form COP (coat proteins)-coated vesicles. There are COPI- and COPII-coated vesicles (Kreis and Pepperkok, 1994). These vesicles are generated in tandem (Nickel et al., 1998), i.e. COPII vesicles are originated in the ER first, then they fuse to each other giving rise to the vesicular-tubular transport complex (VTC) from where COPI vesicles are formed. These VTCs are considered a labile pleomorphic organelle that is also known like endoplasmic reticulum-Golgi intermediate compartment (ERGIC; Hauri et al, 2000) (Fig. 2). The VTC or ERGIC is a mobile membrane structure that carries and concentrate secretory components (Martínez-Menárguez et al, 1999). For further details about the molecular machinery required for the formation of COP-coated vesicles, see specialized reviews (Rothman & Wieland, 1996; Schekman and Orci, 1996; Wieland & Harter, 1999; Springer et al, 1999). There is another coat called clathrin that operates in the intracellular traffic. It is the association of three heavy and three light chains that form the so-called tryskelion units and are linked as polyhedrons like the net in basketball. They were first associated with receptor-mediated endocytosis but they have also been reported in the transport of proteins from the Golgi apparatus to lysosomes (Le Borgue & Hoflack, 1998).

The formation of vesicles is regulated to a great extent by other molecules, most of which are also directly involved in intracellular signaling processes (Stow, 1995; De Camilli et al, 1996). This allows the cell to regulate its intracellular traffic according to specific external signals, just as given events (sports, political, musical, etc) and times of the year (height of the season, off season) determine the travel demand. In order to meet such demand, the number of wagons, their size and the frequency of trains have to be carefully regulated so that they neither stop the traffic nor waste membranes or energy since the formation of vesicles requires ATP.

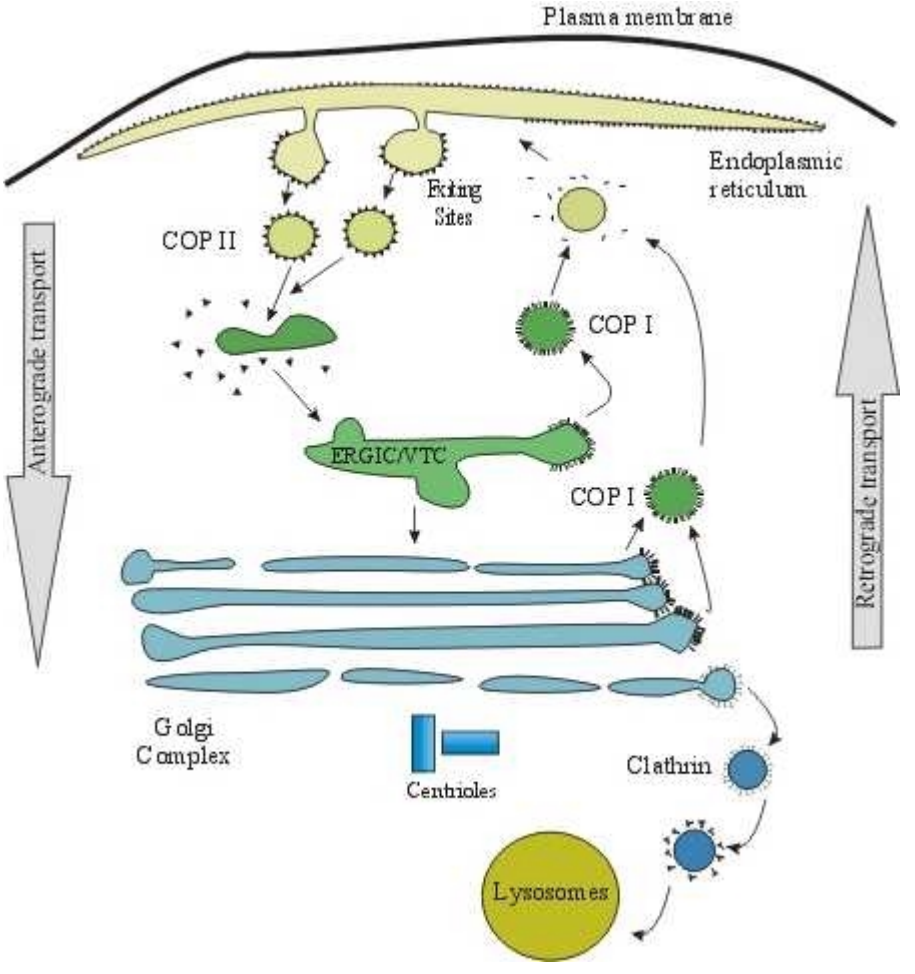

Fig. 2. Diagram of the intracellular transport in the endoplasmic reticulum and the Golgi apparatus. The latter is surrounded by the ER and is organized around the centrioles. Between the Golgi and the ER, several tubular and vesicular structures form a pleomorphic and dynamic compartment termed as ERGIC (endoplasmic reticulum-Golgi intermediate compartment) or VTC (vesicular-tubular transport complex).

The Golgi apparatus: the Grand central station of intracellular traffic in eukaryotic cells

In most non-polarized animal cells, the Golgi apparatus is an active and a single-copy organelle. It consists of a set of stacks made up of highly flat cisternae with dilated rims. These stacks are interconnected by means of

tubules and vesicles (Rambourg y Clermont, 1990). The Golgi apparatus is responsible for most the post-translational modifications of proteins (Driouch & Staehelin, 1997; Farquhar & Palade, 1998). The most frequent is glycosylation that gives rise to glycolipids and glycoproteins, and it consists in extensive modifications of the carbohydrate groups (glycans or saccharides) that have been previously added en block to the proteins synthesized in the ER. Phosphorylation is also another post-translational modification that occurs in the Golgi apparatus, which is essential for the sorting of luminal proteins to lysosomes, as well as the sulfatation of proteoglycans and some proteolytic reactions that are crucial for certain hormones.

In animal cells, the Golgi apparatus is localized close to the nucleus and around the centrosome (the cytoplasmic organelle where microtubules are formed) (Fig. 3A). The ER surrounds the Golgi apparatus (Fig. 2) (Note: in the Cell and Molecular Biology, and Biochemistry textbooks, the Golgi is located between the ER and the plasma membrane to simplify the secretory pathway, which does not reflect the real intracellular arrangement in non-polarized cells, frequently leading to errors of interpretation).

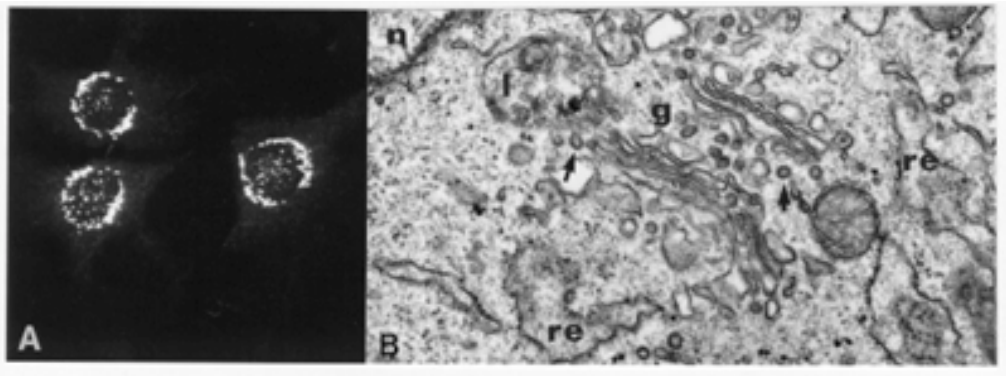

Fig. 3. (A) The Golgi apparatus of mammalian cells cultured with antibodies against one of its resident protein (mannosidase II) as visualized under the fluorescence microscope. The Golgi shows a reticular morphology that extends around the nucleus. (B) The Golgi apparatus (g) seen under the transmission electron microscope. This organelle consists of a stack of flat cisternae and is surrounded by ribosome-attached cisternae from the endoplasmic reticulum (re). The arrows show COPI-coated vesicles.(n, nucleus; l, lysosome).

In both animal and plant cells, a stack of the Golgi consists of flat cisternae (central zone) with an entry (cis) and an export area (trans) (Fig. 3A). Each area is linked to a net of tubular and vesicular structures: one of entry (cis-Golgi network, CGN) and one of exit (trans-Golgi network, TGN)

(Rambourg y Clermont, 1990) (Fig. 2). The morphologic polarity of the Golgi apparatus results in functional polarity and vectorial traffic. During this journey, the lipids and proteins passing through the Golgi undergo several sequential modifications determined by the molecular composition of the enzymes unevenly distributed in the cisternae (Roth, 1997; Varki, 1998). In contrast to the well-characterized signal sequences of the ER, the sequences added by glycosyltransferases or the structural requirements that allow their retention in specific cisternae of the Golgi are unclear.

Assembly and maintenance of the Golgi apparatus in eukaryotic cells. Vesicular and cisternal-maturation transport models.

The Golgi apparatus is also composed by membranes. Therefore, in spite of the intense entry and export traffic, its size and shape remain constant. This requires a finely regulated equilibrium of the input and output flows to prevent the hypertrophy and the atrophy of the Golgi, which would compromise the cell survival. Thus the integrity of the Golgi apparatus results from the equilibrium between the incoming (anterograde) and the outgoing (retrograde) traffic (Fig. 2). The former is the membrane flow that enters and is then destined for the plasma membrane. The latter refers to the flow that arrives at and originates in the Golgi or passes through it and is then directed to the ER. The retrograde route is used by membrane and soluble proteins that have left the ER for the Golgi by mistake and then should returned to the ER. To this end, they need specific receptors that recognize the motifs for ER retention (the receptors of the K(H)DEL sequence mentioned above) (Lewis & Pelham, 1990). It is also the pathway used by certain toxins (e.g. the cholera and Shiga toxins) to reach the ER and exert their toxic effect. In this case, the Golgi apparatus is an unavoidable checkpoint before reaching the ER (Sandvig et al, 1992).

However, what determines and regulates the specificity and consistency of both flows? Or, in other words, which are the traffic lights and the points that govern the arrival and departure of intracellular trains? The specificity of recognition and of membrane fusion is due to the molecular interaction between a series of multiproteic complexes, as suggested by the SNARE hypothesis of vesicular transport (Rothman and Warren, 1994). According to this model, there is a molecular interaction between a group of proteins such as the NSF (NEM-sensitive fusion protein), the SNAPs (soluble NSF-binding proteins) and the SNAREs (receptors of SNAPs). The latter are present at both the donor (vSNARE) and the acceptor (tSNARE) membranes,

such as a transport vesicle and a Golgi cisternae or plasma membrane, respectively. The interplay between vSNARE and tSNARE should be unique and should ensure the specifity of the fusion. Several SNAREs have been identified in certain compartments. They could be regarded as the points that switch each train to its corresponding platform. However, they are not totally specific and so require the help of a family of proteins termed Rabs (Novick and Zerial, 1997). These proteins attach to membranes after activation by binding to GTP. Each compartment has a specific Rab protein, which represents the signal that avoids train collisions during the switching of rails and errors in the location of trains at platforms. There are other minor traffic regulators but they are beyond the scope of this text. Whatever the direction, transport is mediated by vesicles (Rothman, 1994) (Fig. 4A). The size of these structures is 60-80 nm and the SNARE and Rab proteins determine their specificity and consistency. The vesicular model is a good candidate for the transport of most lipids and proteins, since the sizes agree. Moreover, the volume/area ratio is high, which increases the carrying capacity. However, the cell also secretes large molecules and proteins e.g. the scales of certain algae, the procollagen synthesized by fibroblasts and the multiproteic complexes between apoprotein E and albumin in the hepatocyte, none of which fits in vesicles. In these cases, an alternative model has been suggested: the cisternal-maturation (Fig. 4B) (Mironov et al, 1997; Glick and Malhotra, 1998). According to this hypothesis, a cisterna is formed in the cis site of the Golgi apparatus by continuous fusion of VTCs formed in the exiting sites of the ER (Fig. 4B). This results in the cis-most cisterna of the Golgi. Posterior transport to the plasma membrane is favored by the progressive shift of cisternae to the trans site of the Golgi. Transported proteins in such a way would never be removed from cisternae and Golgi-resident proteins (glycosyltransferases) would be transported back to adjacent cisternae by vesicles. Finally, in the trans-most site of the Golgi (TGN), the mature cisterna would either be transported as such or split giving rise to tubules in order to merge with the plasma membrane.

Mitosis is frequently used as a model for the study of the molecular mechanisms of assembly and disassembly of the Golgi apparatus (Warren & Malhotra, 1998). This is the process of division that results in the production of daughter cells genetically identical to the parent cell from which they arose and with the same organelles. During mitosis, the Golgi apparatus is extensively fragmented and homogenously distributed through the cytoplasm so that it is equitably distributed to each daughter cell. At the end of the division, these fragments are re-assembled to achieve the classical

morphology of the Golgi (Lowe et al, 1998). However, this is exclusive to mammalian cells. In yeast, another major model for the study of the molecular mechanisms involved in intracellular traffic (Duden & Schekman, 1997), Drosophila (Stanley et al., 1997), and plant cells (Driouich & Staehelin, 1997) the Golgi virtually remains unaltered during mitosis.

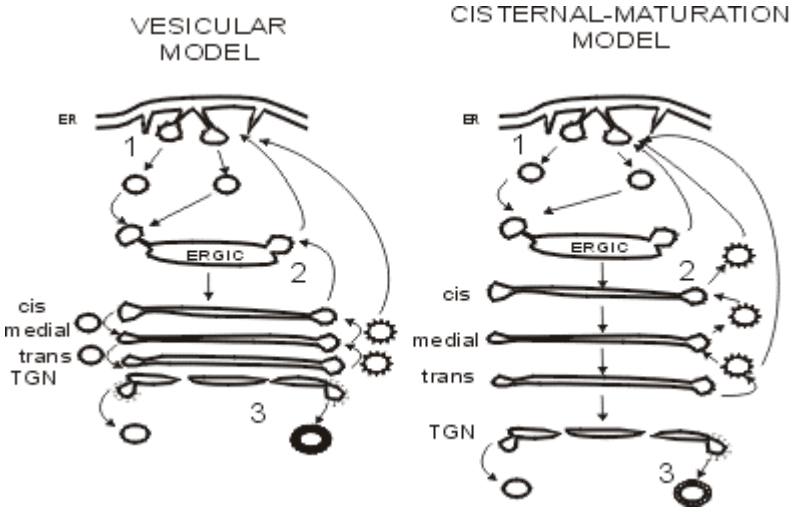

Fig. 4. General diagram of two models of intracellular transport: the vesicular (A) and the cisternal-maturation (B) models. See text for further details. Partially adapted from Glick and Malhotra (1998).

High- and low-speed routes for intracellular transport: the cytoskeleton and its association with the Golgi apparatus

In sum, intracellular traffic is mainly mediated by vesicles, which requires the sorting of the cargo in the specific membrane domains of each compartment, followed by transport and subsequent fusion of the vesicle and the membrane of the receptor compartment.. We have also described the molecular mechanisms that regulate these processes (COPI and COPII coats; SNAREs, rabs). In addition, another set of proteins establish and maintain the shape of compartments, retain the organelles at specific sites of the cell and favour the fusion and movement of vesicles so that they end up in the appropriate compartments. We are going to talk now about motors, wheels and rails.

All cells present a cytoskeleton that is involved in the subcellular organization of the cell, that maintains the shape of the cell, and it consists of microtubules (Fig. 5A), intermediate filaments and actin microfilaments (Fig. 5B).

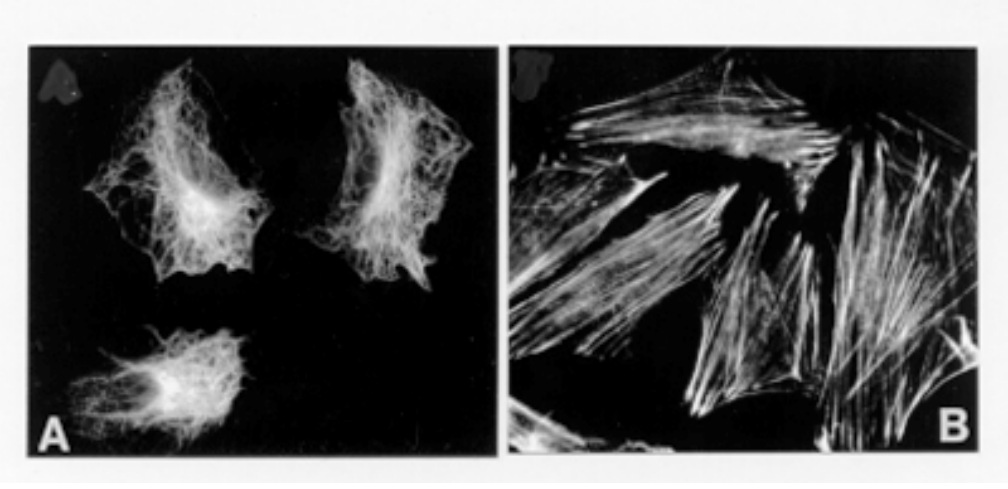

Fig. 5. The cytoskeleton in eukaryotic cells. (A) The microtubular net as visualized using anti-□-tubulin antibodies. (B) The actin cytoskeleton (stress fibres) as visualized using the phalloidin toxin.

Microtubules are linear structures composed of tubulin units that point to the periphery of the cell from the centriole. As has been pointed out, the Golgi apparatus is located around centrioles (Fig. 5A) centralizing the membrane flow originated in the ER (Fig. 2) (Cole and Lippincott-Schwartz, 1995). The Golgi apparatus is connected to cytoskeleton (Kreis et al, 1997). The factors that affect the structure of microtubules also alter the integrity and localization of the Golgi apparatus (Fig. 5A) by splitting it into small pieces or ministacks that are dispersed throughout the cytosplasm (Fig. 5B). Both the Golgi and the transport vesicles interact with microtubules through a family of proteins called dyneins and kinesins, which are able to transform ATP into movement. They are thus referred to as motor proteins (Allan, 1996). In non-polarized cells, dynein allows movement towards the centrosome, whereas kinesin do it to the plasma membrane (Lane & Allan, 1998). It is just as the wheels (vesicles) move on the rails (microtubules). Since this is a direct and rapid means of transport, microtubules represent the intracellular high-speed routes. However, the Golgi apparatus remains attached to microtubules when the motor function is inactivated. This shows that there must be a specific set of proteins to ensure a continuous attachment between the Golgi and the

microtubules (Infante et al, 1999). These proteins may behave as the brakes of organelles and, in this case, of the Golgi apparatus.

On the other hand, the Golgi also interacts with the actin microfilaments (Valderrama et al, 1998, 2000). Microfilaments are also composed of polymerized actin units and their diameter and length are lower than those of microtubules and they have numerous ramifications. They thus form a dense, flexible, dynamic cytoplasmatic network that is responsible for the motion of cells. The breaking of actin microfilaments brings on the compactness of the Golgi apparatus (Fig. 5C).

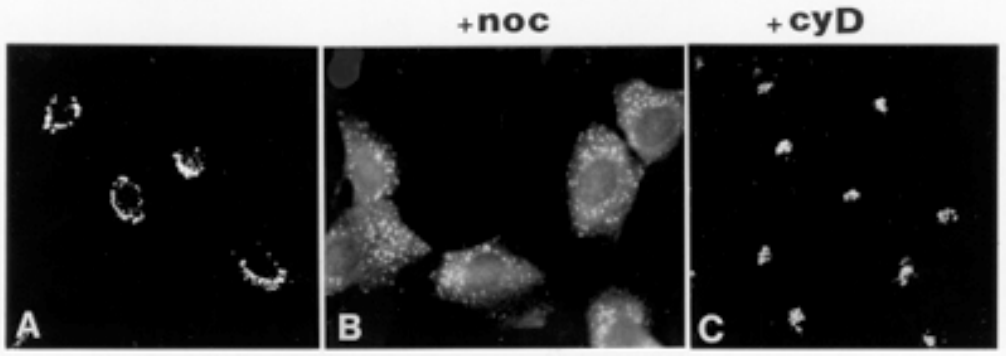

Fig. 6. The subcellular localization and morphology of the Golgi apparatus (A) depend on the cytoskeleton. The disruption of microtubules by nocodazole (noc) leads to the fragmentation of the Golgi and its spreading throughout the cytoplasm (B), whereas the disruption of the actin microfilaments by cytochalasin D (cyD) leads to its compactation (C).

Microfilaments are also associated with another type of motor proteins termed myosins (Sellers, 1999). The rate of transport through microfilaments (low-speed route) is lower than through microtubules. However, the reticular organization allows access to every area of the cell, reminiscent of suburban trains, which cover short distances and have frequent stops.

Finally, the Golgi also contains spectrin and ankyrin isoforms (Holleran and Holzbaur, 1998), which are thought to behave as scaffolds. The cytoskeleton of the erythrocytesis based upon spectrin, which accounts for the flexibility of these cells in passing the narrow capillaries of the blood microflow. However, although the role of such proteins in the Golgi apparatus is unknown, they could be involved in the flat shape of cisternae rather than in intracellular transport.

APENDIX

Is the Golgi apparatus a dependent or independent organelle with respect to the ER?

Recent data on the Golgi apparatus have given rise to a strong controversy. The Golgi apparatus was understood to be an organelle that was tightly associated with the ER, with which it maintained a fine dynamic membrane balance. However, two recent articles suggest that this is not the case, and that the Golgi is an independent organelle. If the biogenesis and physiology of the Golgi apparatus depend on the ER, one might assume that a functional Golgi could be re-built from the ER. Using microsurgery techniques, Pelletier et al. (2000) obtained subcellular fragments that contained solely ER membranes. They observed that such fragments were able to synthesize and transport cargo out the ER. However, this cargo was not secreted but retained in the ER exiting sites since no Golgi membranes were present in these subcellular fragments. To assess whether the ER was essential to the formation of the Golgi apparatus, in another study Seemann et al. (2000) treated cells with a drug (brefeldin A) that reversibly induces the merging of Golgi and ER membranes. When brefeldin A was withdrawal in cells that expressed a negative mutant of Sar1 (a crucial protein for the formation of COPII-coated vesicles from the ER), they observed the appearance of a Golgi-like structure that contained known Golgi matrix proteins but was devoid of the Golgi glycosyltranferases. The latter were still retained in the exiting sites of the ER as a consequence of the inhibitory effect of the Sar1 mutant protein. Taken together, these experiments indicate that the ER is neither necessary nor sufficient for the formation and function of the Golgi apparatus. Hence, they indicate that this organelle is independent of the ER (Kumplerman, 2000). Immediately afterwards, new Golgi transport models appeared (Pelham and Rothman, 2000; Stephens and Pepperkok, 2001).

Camilo Golgi discovered the Golgi apparatus a little over 100 years ago (Golgi, 1898). Over the last 20 years the field of intracellular traffic has seen tremendous advances towards the identification of the relevant molecular machineries. Proteins involved in budding, fission, fusion, and sorting have been discovered, and, in some cases, a picture of how such proteins are assembled and work has been glimpsed. In contrast, perhaps surprisingly, a satisfactory understanding of how transport occurs in vivo at the organelle level has not been achieved. The novel combination of GFP (green fluorescent

protein) technology and advanced higher resolution quantitative video microscopy with correlative light-electron microscopy will doubtless provide new and relevant information about the transport into, through and from the Golgi apparatus (Lippincott-Schwartz et al., 1998; Polishchuk et al., 2000; Keller et al., 2001). We trust we will not have to wait another century for the complete understanding of this complex and dynamic organelle.

Acknowledgements

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Pointers of Interest

Citoskeleton

1. TM Terry's Laboratory (Universidad de Connecticut, Storrs)
http://cmgm.stanford.edu/theriot/movies.htm

2. Joel Swanson (Univ. Michigan, Ann Harbor, USA)
http://www.umich.edu/~jswanlab/Movies/movies.html

3. Phagocytosis
http://www.umich.edu/~jswanlab/Images/images.html.

4. Microtubule dynamics during mitosis, motility and membrane traffiqking (Salmon Lab Movies)
http://www.unc.edu/depts/salmlab/salmonlabmovies.html

Motors

1. Molecular motors (Molecular Motors Group at the University of York, UK)
http://motility.york.ac.uk:85/

2. Kinesine Superfamily (Laboratorio de N. Hirokawa, Tokyo, Japón)
http://cb.m.u-tokyo.ac.jp/

3. Ron Vale's molecular motors lab
http://cmp.ucsf.edu/valelab/

4. Kinesine Movements along a microtubule
http://math.lbl.gov/~hwang/animation/walk9.mpeg
http://www.bio.brandeis.edu/~gelles/kamppnp/index.html

5. Myosine
http://www.mrc-lmb.cam.ac.uk/myosin/myosin.html

6. Myosine II during cell division and migration
http://www.stc.cmu.edu/CLMIBhp/Imggallpg/

7. Force generated by myosine II on an actine microfilament
http://cmgm.stanford.edu/~wshih/gif.html

8. Vesicular transport along skid giant axon microtubules and microfilaments (Laboratory de M. Langford)
http://www.dartmouth.edu/~langford/

9. Microtubules and microfilaments cellular motility, axonal growth, and melanophores (Laboratorio de G. Borisy)
http://borisy.bocklabs.wisc.edu/pages/movies.html

10. Complete list of cytoeskeleton labs
http://vl.bwh.harvard.edu/labs.shtml#cytoskeleton

El complejo de Golgi y tráfico intracelular

1. Golgi complex in Plants
http://cs3.brookes.ac.uk/schools/bms/research/molcell/hawes/gfp/gfp.html

2. Images from the Viki Allan's lab web page

http://www.biomed2.man.ac.uk/allan/

3. Images from the Jennifer Lippincott-Schwartz's lab
http://dir.nichd.nih.gov/CBMB/uobhome.htm
http://dir.nichd.nih.gov/cbmb/pb1labob.html

4. Images from the Graham Warren's lab
http://info.med.yale.edu/cellbio/Warren.html

5. Derek Toomre's lab
http://www.livingroomcell.com/

6. Rainer Pepperkok's lab
http://www.embl-heidelberg.de/ExternalInfo/pepperko/index.html
http://www.rpi.edu/~plourj/cellbiol/er-golgi.htm

7. Bruno Goud's lab
http://www.curie.fr/sr/cdrom/equipes/goude.htm

5. Kai Simons' lab
http://www.mpi-cbg.de/content.php3?lang=en&aktID=simons
http://www.embl-heidelberg.de/ExtrenalInfo/simons/movies.html

6. Felix Wieland's lab
http://www.uni-heidelberg.de/zentral/bzh/wieland.html

7. Golgi Apparatus' 3D Organization
http://bio3d.colorado.edu/

8. Clatrine mediated endocytosis
http://www.hms.harvard.edu/news/clathrin/index.html

9. Thomas Kreis's lab
http://www.unige.ch/keris-lab/FP/FP_Video.html

Miscellaneous

1. General web page for Cellular biologists (P. Lafont)
http://www.unige.ch/sciences/biochimie/Lafont/WA_CB.html

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