Chapter 2

The Golgi Complex

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DISTRIBUTION AND BASIC STRUCTURAL CHARACTERISTICS

Camillo Golgi's unexpected staining of an "internal reticular apparatus" of spinal neurons with silver nitrate made the Golgi Complex (GC) first visible as a "black reaction" at the very end of the last century. Ironically, neither the basis of this reduction of heavy metal salts, nor the reason why the GC is so conspicuous in neurons, is adequately understood. What is well-established, however, is that the GC exists in all animal, plant, and fungal cells which contain rough endoplasmic reticulum (RER). The GC is now known as a station along both the secretory and endocytic paths where an impressive number of covalent and non-covalent post-

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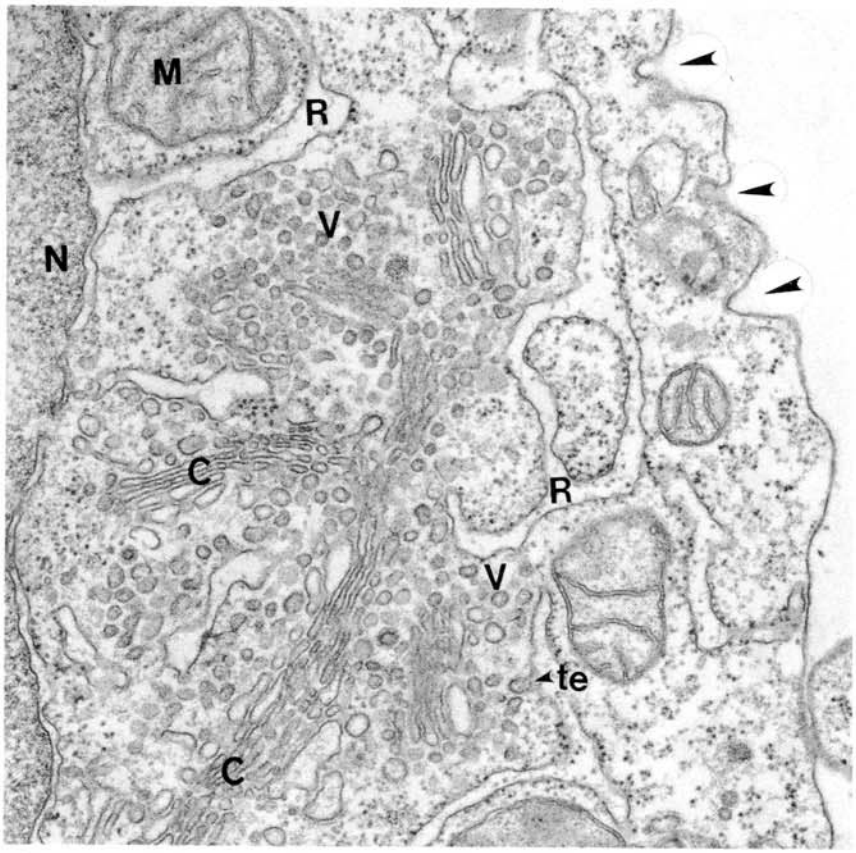

Figure 1. Thin section of the Golgi region of a myeloma cell fixed with glutaraldehyde followed by osmium tetroxide. Note the rough endoplasmic reticulum (R), transitional elements (te), conspicuous stacked cisternae (C) and associated vesicles (V). (N) nucleus, (M) mitochondrion. Arrowheads designate coated pits at the cell surface.

translational modifications occur and where macromolecules are sorted to a variety of destinations.

The ultrastructural hallmark of the GC is the set of 3–30 elongated, closely-apposed cisternae (Figure 1) which in three dimensions constitute a pile of somewhat saucer-shaped closed membrane-bounded saccules. Individual cisternae are often perforated by pores, and small smooth-surfaced vesicles are found in the vicinity of the cisternae. The cisternae closest to the RER are generally referred to as "cis," "proximal" or "forming," while cisternae further removed are called "trans," "distal" or "mature." Beyond the most distal of the closely apposed cisternae are immature secretion granules (condensing vacuoles, Figure 2) and additional anas-

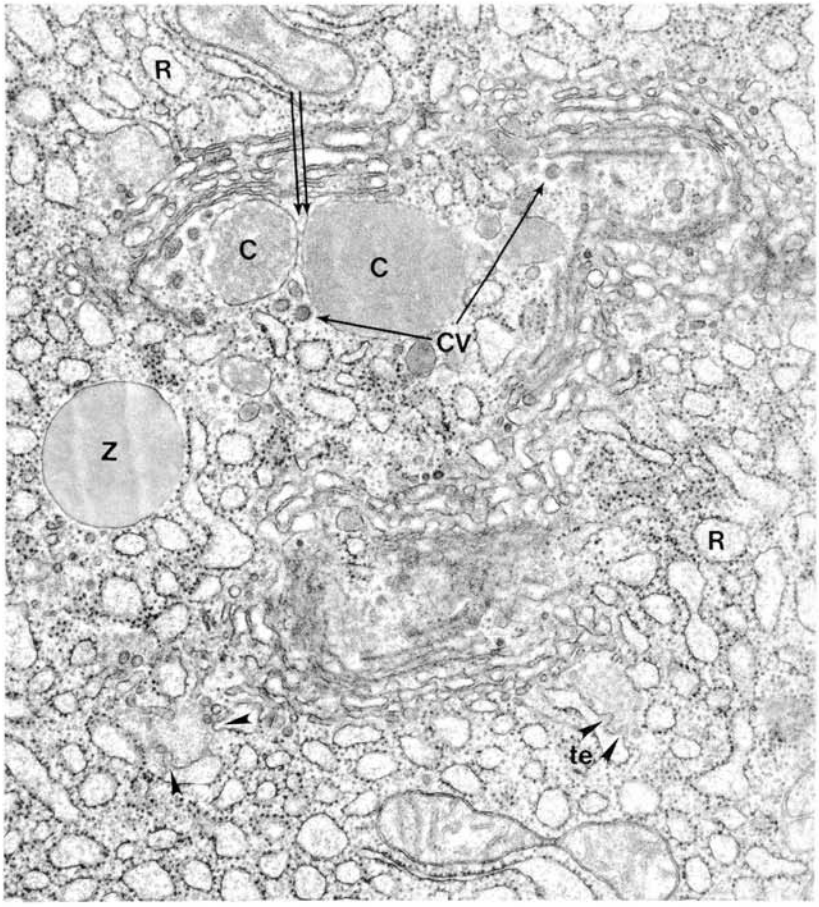

Figure 2. Thin section of a guinea pig exocrine pancreatic cell. Mature secretion granules [zymogen granules] (Z) and immature granules [condensing vacuoles] (C) are adjacent to the Golgi cisternae, some of which contain visibly concentrated content (arrowhead). CV: coated vesicles. (te) designates transitional elements of the RER. The large double arrow indicates the proximal-to-distal axis across the stack of Golgi cisternae. Unlike the cell types illustrated in Figure 1, exocrine pancreatic cells secrete primarily via the "regulated" secretory path, i.e., after concentration of their secretory products in the secretion granules.

tomosing and tubular smooth cisternae, known as GERL, Trans-Golgi Network, or Trans-Golgi Reticulum (Figure 3). These latter structures are best characterized in cells, such as fibroblasts, which do not store secretory products in granules. Their exact identification must await the development of suitable reagents (e.g., antibod-

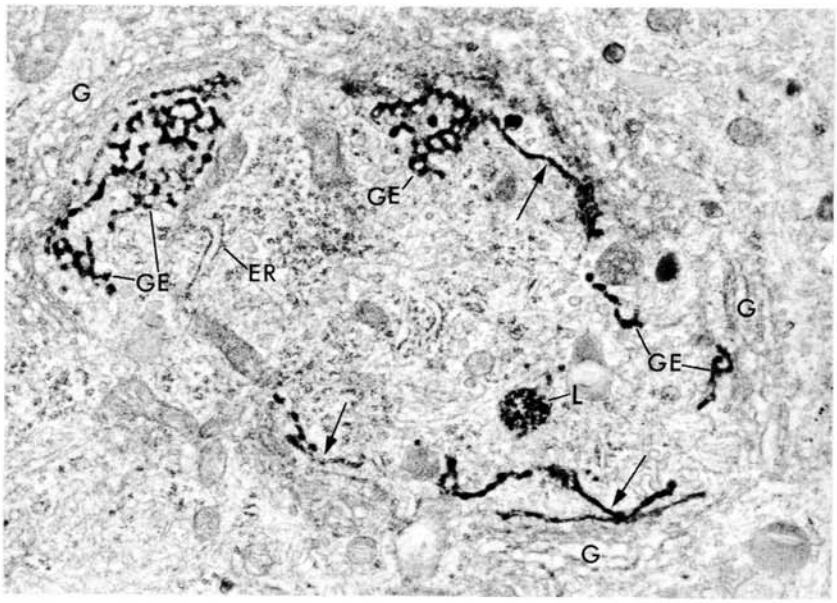

Figure 3. Electron micrograph of a rat dorsal root ganglia neuron incubated for acid phosphatase activity. Electron-opaque reaction product delineates the anastomosing and cisternal portions of GERL (GE and arrows, respectively). Acid phosphatase activity is not present in the cisternal stacks of the Golgi (G). (From P. Novikoff, with permission.)

ies) for their systematic recognition in distinct cell types; however, available information indicates that key sorting events occur in these structures (see below).

The GC of animal cells is found during interphase near the centrosome, on the apical side of the nucleus with its distal face (which is usually convex) toward the apex of the cell. The proximal face is usually closely associated with specialized areas of the RER (transitional elements) from which small smooth-surfaced vesicles appear to bud. Systematic examination of sections with the electron microscope indicates that most animal cells contain one—or certainly no more than a few—stacks of Golgi cisternae. By contrast, in plant cells and in certain insect cells many discrete small Golgi stacks are found scattered throughout the cytoplasm without obvious relation to the RER.

Subcellular fractions enriched in Golgi-derived vesicles and cisternae have been obtained from several cells and tissues. Since the membranes of the GC have a density which is similar to that of other smooth membranes (plasma membrane, outer mitochondrial membrane, etc.), it is only in the case of cells whose GC

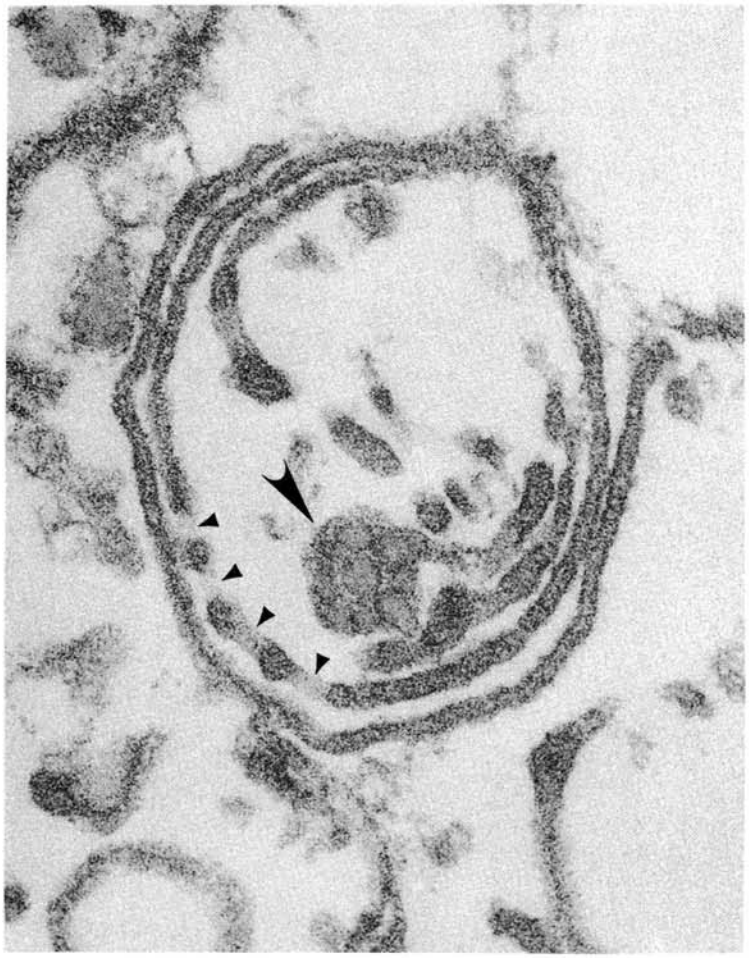

Figure 4. Thin section of an isolated "stacked" Golgi-rich fraction recovered from a rat liver homogenate. Note the abundant secretory lipoprotein content (large arrowhead). The small arrowheads indicate pores in cisternae.

contains secretory products of very low density (e.g., the abundant secretory lipoproteins of the hepatocyte) that the isolated fractions are especially pure (Figure 4). The prospect for obtaining comparably enriched fractions from other cell types is sure to improve as immunoaffinity methods are increasingly applied to isolation of organelles. In the liver, and in a few other tissues, isolated Golgi-enriched

fractions retain a characteristic stacked organization of their cisternae. It is not known what "glue" holds the individual cisternae so firmly together that they withstand the trauma of homogenization. Related materials may be important for the targeting of vesicles to, and their fusion with, Golgi cisternae.

STRUCTURE

No resident proteins are known to be present in both the membranes of the GC and the membranes of other organelles. No soluble macromolecules of the cisternal space of the GC have been identified except for macromolecules which are undergoing transport. The membrane lipids of the GC have not been studied in great detail; however, cholesterol and phospholipids are major components (cholesterol is essentially missing from the RER), with glycosphingolipids also being readily detected, possibly because this is their site of synthesis.

Although the composition of the cisternal space of the GC cannot at present be studied directly, indirect evidence suggests that the ionic composition is distinct from that of the ground substance of the cytoplasm and cisternal space of the ER. For example, when carboxylic ionophores such as monensin are added to living cells, Golgi cisternae dilate within seconds, while the RER is unaffected (Figure 5). This ionophore is known to promote equilibration of sodium, potassium, and proton concentrations across membranes. There is also cytochemical evidence suggesting that the cisternal pH of distal cisternae is somewhat acid.

It is not known why the GC has its characteristic centrosomal location in animal cells; however, an intimate relation exists between the GC and the tubulin-based cytoskeleton. Thus, when cells are treated with drugs which block tubulin polymerization, the GC fragments and becomes widely distributed throughout the cytoplasm as miniature stacks of cisternae (Figure 6). Macromolecular transport through the GC persists, although certain sorting operations may be disturbed.

A striking feature of the GC which has been intensively studied by electron microscopists is its cytochemical heterogeneity (Figure 7). For example, in many cells: 1) intense osmication produces a metallic deposit within proximal cisternae; 2) light fixation followed by incubation with substrates of nucleoside diphosphatase (uridine diphosphate, thiamine pyrophosphate) in the presence of heavy metal salts which precipitate inorganic phosphates ("capture reagents") produces a deposit in distal cisternae; and 3) incubation with substrates of acid phosphatase and comparable capture reagents produces a deposit in the GERL. These cytochemical staining patterns, which are curiously somewhat variable from one cell type and one cell to the next, were identified long before the complexity of the participation of the GC in glycosylation reactions was known. It is now clear, as mentioned below, that the enzymes responsible for glycosylation are also subcompartmentalized across the GC, and that the above-mentioned phosphatases are thought to be important for allowing glycosylation to proceed.

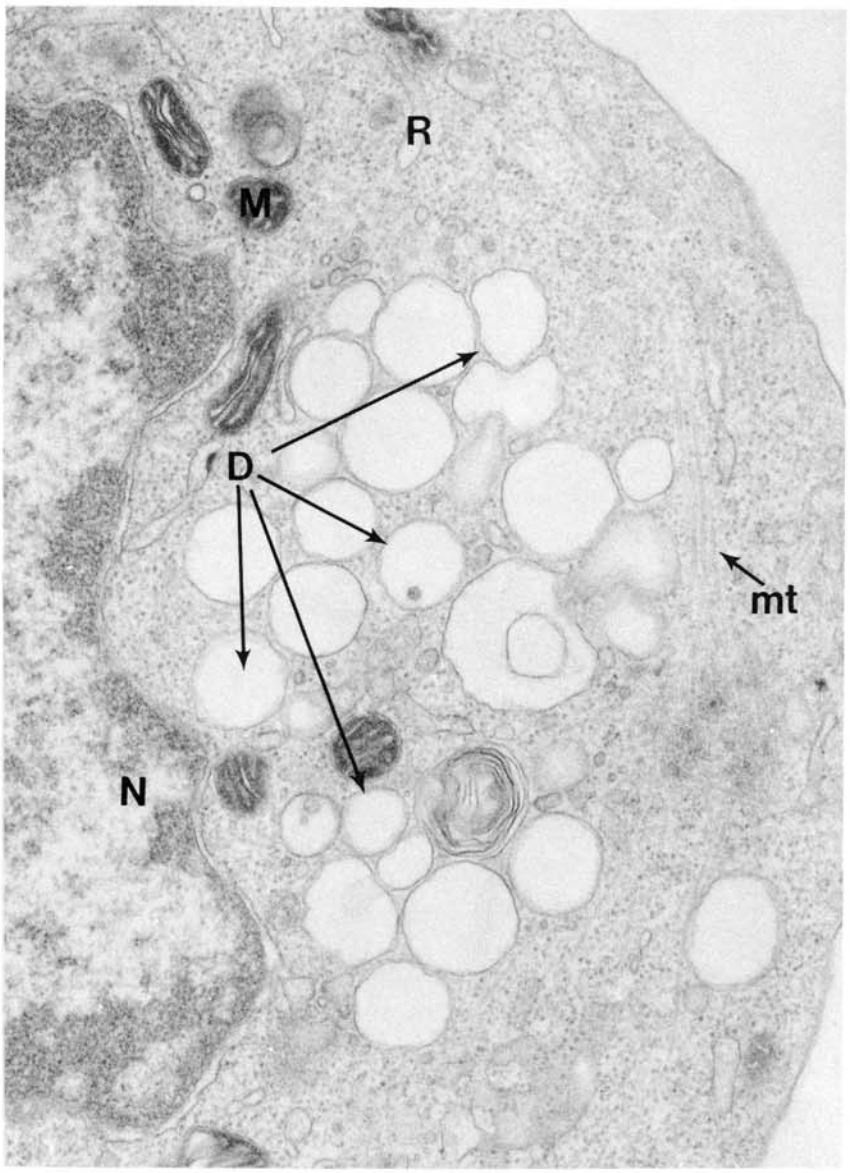

Figure 5. Thin section of a mouse thymoma cell treated for 1 hr with the carboxylic ionophore, monensin. Note the dilated Golgi elements (D), microtubules (mt), mitochondria (M), the RER (R) and the nucleus (N). The dilation is accompanied by major slowing of transport across the Golgi. Both effects are slowly reversible. (Micrograph courtesy of M. Detraz.)

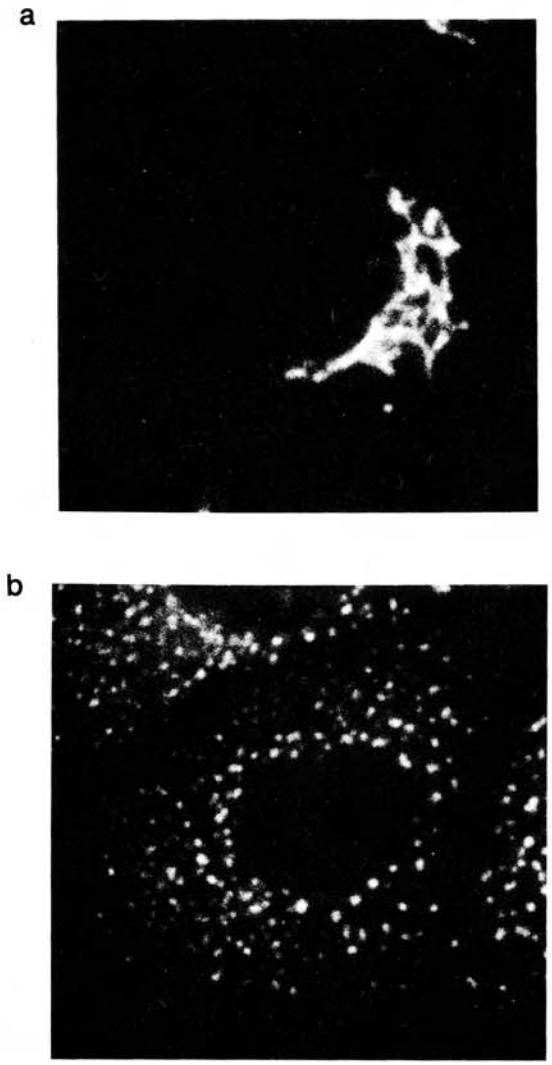

Figure 6. Depolymerization of microtubules results in scattering of the Golgi Complex. Bovine kidney cells in culture were treated with nocodazole for 2 hr at 37 °C and fixed with formaldehyde. Galactosyl transferase was revealed in both control (**a**) and nocodazole-treated (**b**) cells, using immunofluorescent reagents in the presence of detergent to permeabilize all membranes. All staining in the control is juxtanuclear. The gross dispersal of Golgi elements seen in (**b**) is totally reversible upon withdrawal of the drug.

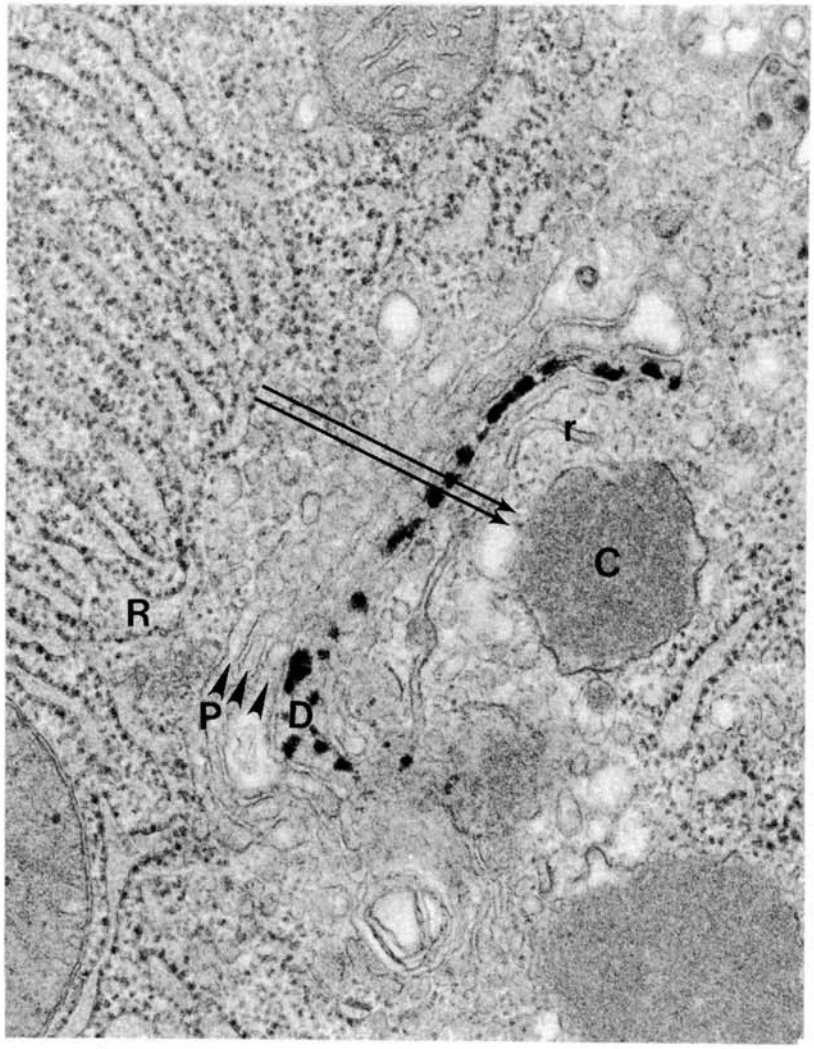

Figure 7. Thin section of the guinea pig exocrine pancreas after cytochemical detection of nucleoside diphosphatase activity. The reaction product is confined to distal cisternae (D) and appears as a black (electron-scattering) deposit. Rough endoplasmic reticulum (R), proximal Golgi cisternae (P) and condensing vacuole (C). The detection procedure involves light fixation with aldehydes, incubation with uridine diphosphate in the presence of lead nitrate (which produces the lead phosphate precipitate at sites of enzyme activity), post-fixation with osmium tetroxide and routine dehydration, embedding, sectioning and examination.

POSTTRANSLATIONAL MODIFICATIONS

Table 1 lists modifications of macromolecules which occur while they pass through the GC along the secretory path. The identified enzymes responsible for these modifications are integral membrane proteins. In a few cases genetic engineering experiments have made it possible to identify the peptide sequences which account for these enzymes residing in the GC.

The best-characterized covalent modifications are involved with glycan addition and maturation. In higher eukaryotes, especially the biosynthesis of N-glycans (whose core is added to asparagine residues in the RER) has been extensively studied. For example, typical N-glycans (Figure 8) are radically remodeled to "complex" structures due to both sugar removal by glycosidases and "terminal" sugar addition in the GC. The presence of immature *vs.* complex units can be readily judged from their differential sensitivity to endoglycosidases.

The biological roles of N-glycans can be studied by use of: a) a sugar analogue (tunicamycin) to interrupt addition of the glycans in the RER, b) sugar analogues which block glycosidase action (nojirimycins, etc.), or c) cell mutants which lack individual oligosaccharide processing activities.

Certain of the enzymes responsible for N-glycan maturation have been localized at the electron microscopic level by immunocytochemistry. In general, the anatomic distribution of the enzymes matches the order of their enzymologic function (the first of the GlcNAc transferases has been detected in medial cisternae, galactosyl and sialyl transferase have been detected in distal and postcisternal structures etc.). Nevertheless, judging from a still small number of cell types which have been studied, as with the distribution of GC phosphatases, transferase and glycosidase distributions do vary among cell types. In yeast there is a further class of oligosaccharide added to N-glycans of many secretory and membrane proteins during Golgi traversal. These are massive phosphate-containing polymannose units. Mutants are available which fail to add complete polymannose units.

For many O-glycans (which are linked to the polypeptide via the hydroxyl of serine or threonine residues), even the addition of the first sugar, N-acetyl galac-

Table 1. Posttranslational Modifications which Occur During Golgi Traversal

Trimming and elongation of N-glycans
Initiation and elongation of O-glycans
Initiation and elongation of glycosaminoglycans
Elongation of glycolipids
Sulfation of glycans
Phosphorylation of glycans
Proteolysis at dibasic amino acids
Acylation?
Concentration of content
Non-covalent addition of lipid to secretory lipoproteins

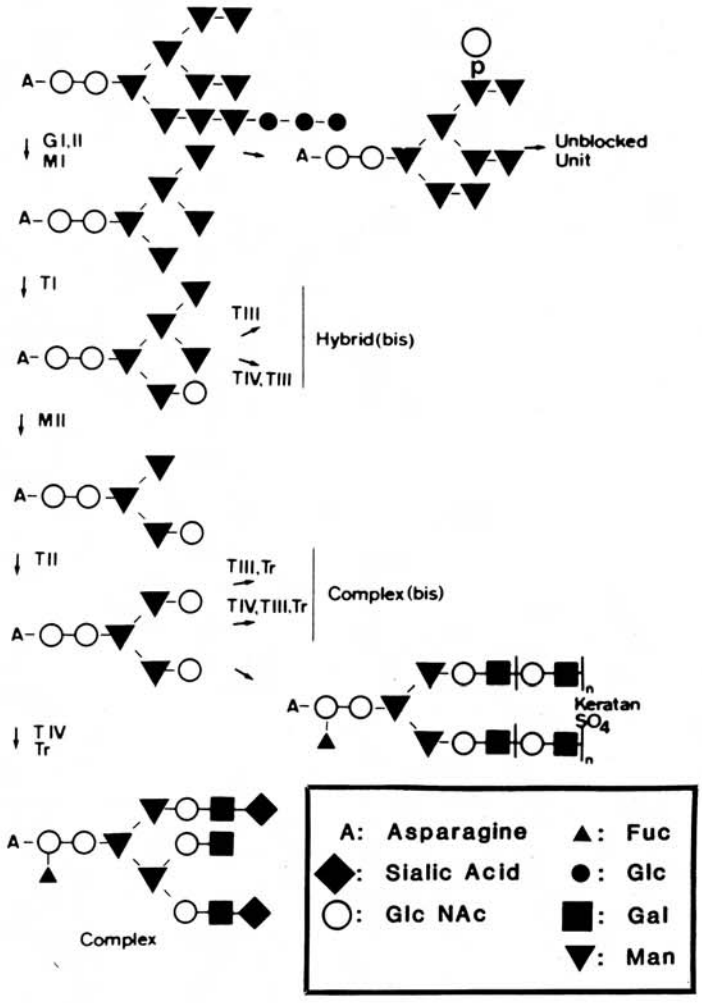

Figure 8. Structural and biosynthetic relations among asparagine-linked oligosaccharides. The parent oligosaccharide (upper left) is donated from a dolichol-linked precursor. Only a few of the processing options are indicated. G, glucosidase; M, mannosidase; T, GlcNAc transferase; Tr, terminal sugar (galactose, fucose, sialic acid) transferases. In hybrid structures, one branch retains terminal nonreducing mannose; in complex units, bi-, tri- or tetra-antennary elongation occurs; in bisected units (bis) additional GlcNAc is added to the innermost mannose. The "unblocked unit" bears the mannose-6-phosphate signal which is responsible for targeting of many acid hydrolases to lysosomes. All steps after G1, II and M1 occur in the Golgi complex. Reproduced with permission from Tartakoff, A., The Secretory and Endocytic Paths, J. Wiley Interscience, 1987.

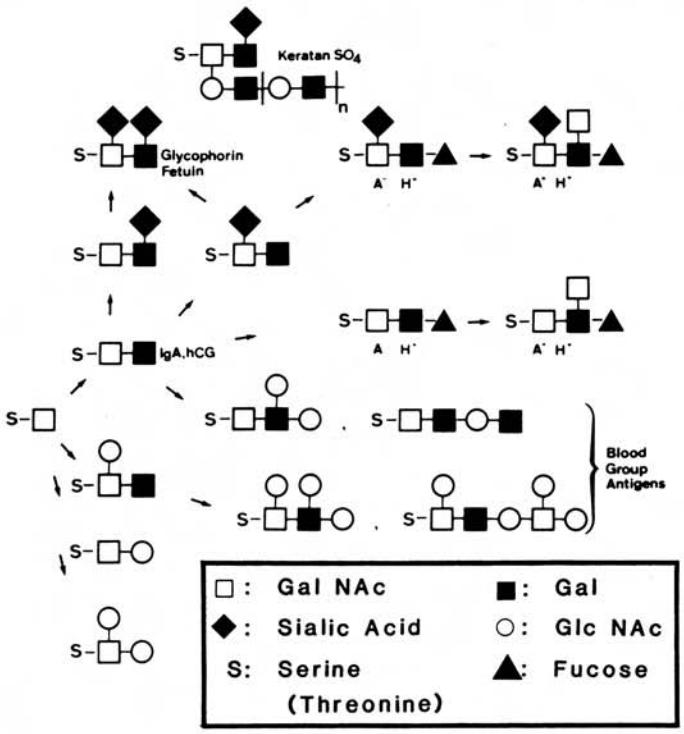

Figure 9. Structural and biosynthetic relations among N-acetylgalactosamine-linked oligosaccharides. A limited number of the many processing options are indicated. A and H blood group specificities are noted. Reproduced with permission from Tartakoff, A., The Secretory and Endocytic Paths, J. Wiley Interscience, 1987.

tosamine, occurs in the GC. Such units (Figure 9) are found on many cell surface proteins (e.g., glycophorin and the low density lipoprotein receptor) and secretory proteins (e.g., chorionogonadotrophin, mucins). The role of O-glycans is difficult to study, since specific inhibitors comparable to those used for analysis of N-glycan structure are not available. One option is to make use of CHO cell mutants which fail to add the initiating of GalNAc.

Initiation of O-linked glycan chains of glycosaminoglycans (Figure 10) is also thought to occur in the GC. In this case a characteristic tetrasaccharide composed of xylose, two residues of galactose, and glucuronic acid is added to selected serine and threonine residues. The more distally located repeating disaccharides, which, along with their polypeptide backbones, distinguish the several classes of proteoglycans, are also added during traversal of the GC. Before exit from the GC, these units undergo sulfation and, in the case of heparin sulfate, epimerization of glucuronic acid to iduronic acid. Sulfation of many O-glycans, N-glycans, and

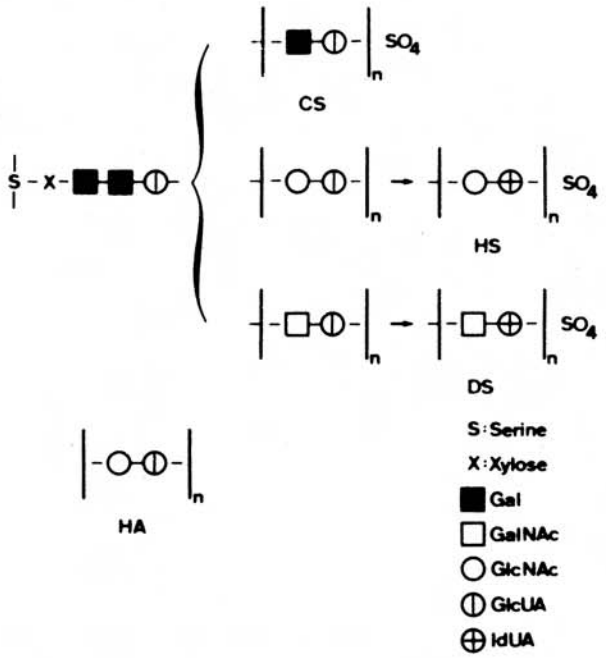

Figure 10. Structural and biosynthetic relations among xylose-linked glycosaminoglycans and hyaluronic acid. CS, chondroitin sulfate; HS, heparin sulfate; DS, dermatan sulfate; HA, hyaluronic acid. Reproduced with permission from Tartakoff, A., The Secretory and Endocytic Paths, J. Wiley Interscience, 1987.

glycolipids also occurs during Golgi traversal. As with O-glycans, the construction of glycosaminoglycan chains fails to occur in selected CHO cell mutants.

Phosphorylation of selected N-glycan chains also occurs during GC traversal. This is of known importance for the lysosomal acid hydrolases of fibroblasts and a number of other cell types. In these cases, one or more mannose residues per glycan chain (there may be many glycan chains per polypeptide and their structures may be different) acquires a blocked phosphate unit composed of phosphodiester-linked N-Acetylglucosamine. A specific phosphodiesterase then releases the terminal GlcNAc, leaving a mannose-6-phosphate unit(s). The significance of this terminal unit is that it can interact with the mannose phosphate receptors (two are known: 215,000 and 46,000 Daltons), which are concentrated in the GC. This interaction leads to the segregation of many such hydrolases from the secretory path and their delivery to lysosomes (see Figure 14B). In the fatal human disease, Mucolipidosis II ("I-Cell Syndrome"), which is characterized by major disorders of connective tissue and neurological function, the enzyme activity responsible for addition of the blocked phosphate unit is missing, massive secretion of acid

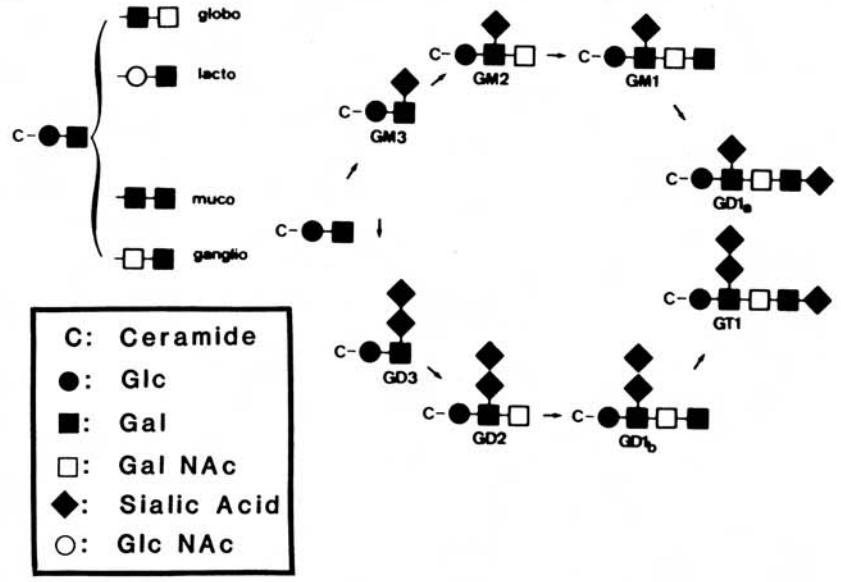

Figure 11. Structural and biosynthetic relations among simpler glycolipids. The ganglio series (characterized by sialic acid) is given in detail. Reproduced with permission from Tartakoff, A., The Secretory and Endocytic Paths, J. Wiley Interscience, 1987.

hydrolases occurs, and lysosomes become engorged by the accumulation of indigestible substrates.

The major glycolipids of animal cells are derivatives of sphingosine. Unlike phospholipids, which are built on glycerophosphate and contain two acyl chains, sphingolipids (Figure 11) bear only one acyl substituent and lack phosphate. The addition of their terminal sugars, and possibly their first sugar glucose/galactose, occurs during Golgi traversal. When the sugar residues bear sulfate or terminal sialic acid, they are known as sulfatides or gangliosides, respectively. Both residues are added during GC transit. The numerous sugar transferases in the GC function effectively because Golgi membranes are equipped with specific ports which allow entry of activated sugars (sugar nucleotides such as uridinediphospho-galactose, cytidinemonophospho-sialic acid, etc.), which are synthesized in the cytoplasm or, in the latter case, in the nucleus. These ports in fact accomplish 1-to-1 exchange of sugar nucleotides for nucleoside phosphates (uridinemonophosphate, cytidinemonophosphate, etc.), which are among the products of the sugar transferase reactions. A port has also been identified for entry of the activated sulfate donor, phosphoadenosinephosphosulfate. Additional ports presumably exist which allow exit of monosaccharides produced by glycosidase action.

Major proteolytic events occur during and after traversal of the stack of Golgi cisternae. For example, many hormones (insulin, glucagon, ACTH, etc.) are

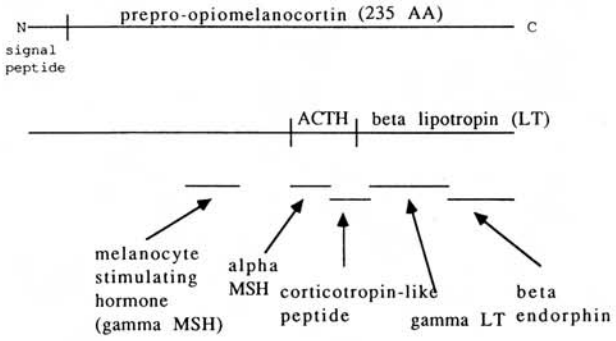

Figure 12. A dramatic example of the extent of proteolysis which can occur during transit of hormones through the Golgi Complex and condensing vacuoles. Proopiomelanocortin is synthesized in the anterior and intermediary lobes of the pituitary and undergoes extensive cleavage at sites marked by pairs of basic amino acids. The upper processing scheme (including ACTH) is characteristic of the anterior pituitary, while the lower scheme pertains to the intermediary lobe.

synthesized at the level of the RER as pro-hormones (proinsulin, proglucagon, proopiomelanocortin, etc.). While in the GC and/or condensing vacuoles they are cut by endoproteases (which have been best identified in yeast) at sites of single or (more often) paired basic amino acids (Figure 12). Exopeptidases also participate in liberating the final product.

The Golgi is responsible for the massive non-covalent addition of lipids to secretory lipoproteins; for example, the low and high density lipoproteins secreted by hepatocytes. The extent of addition of cores of cholesterol and phospholipids to these lipoproteins is so great that they become visible within Golgi cisternae after osmium fixation (Figure 4). Although the situation is not well understood, this lipid addition implies that RER and/or Golgi membranes must flip-flop the component lipids with great efficiency from the endodomain (cytoplasmic face), where lipid synthesis occurs, to the ectodomain and beyond. Apart from sugar addition to glycolipids, other steps of lipid synthesis are not known to occur in the GC.

The Golgi posttranslational modification which first caught the attention of electron microscopists is the impressive ability of distal Golgi elements to concentrate their macromolecular content to the point of producing essentially solid protein. These events of concentration are conspicuous in cells engaged in genesis of secretion granules or specialized lysosomes (endocrine and exocrine cells of the pancreas, pituitary cell types, granulocytes, etc.). The final stages of concentration occur in condensing vacuoles, downstream from Golgi cisternae themselves (Figure 2). This thermodynamically improbable event is not understood, but may involve extensive charge neutralization of secretory protein content (by small and macromolecular ions) and active ion extrusion, followed by water efflux. Judging

from indirect cytochemical measurements, the condensing vacuoles, as well as secretion granules, endosomes and lysosomes, have an acidic interior.

MECHANISMS OF TRANSPORT ALONG THE SECRETORY PATH

Golgi-associated vesicular transport along the secretory path involves: 1) receiving soluble and membrane proteins from the RER, 2) transit from proximal to distal cisternae, 3) exit to the cell surface(s), and 4) exit to lysosomes. The minimum time required for delivery of newly-synthesized proteins to their destinations is about 30 minutes; however, many proteins require as much as several hours.

Passage of RER content and membrane proteins to the GC is thought to be mediated by smooth surfaced "transit vesicles" which bud from the transitional elements of the RER. This event requires ongoing ATP production, GTP and a temperature in excess of 10 °C, but is not affected by inhibitors of protein synthesis. Although direct evidence is lacking, it is likely that a vesicular shuttle is involved and that "empty" vesicles return repeatedly from the GC to encapsulate and transport successive quanta of RER materials. This return leg of transport requires intact microtubules. In the presence of brefeldin A it rapidly causes Golgi membranes to relocate to the RER.

Exit from the RER is selective. Many RER membrane proteins (such as those involved in protein synthesis and drug detoxification), as well as certain proteins which appear to be soluble in the RER content, do not exit efficiently. These include the heavy chain binding protein (also known as BiP) which associates with free heavy chains of immunoglobulin and other incompletely folded polypeptides. Moreover, proteins do not exit at a uniform rate: half-times for RER exit vary from minutes to hours. It has been argued that all proteins exit except for those that bear retention signals. A deeper analysis of RER exit should be forthcoming with the availability of *in vitro* models (cell-free or using perforated cells) as well as multiple yeast mutants in which exit is reversibly blocked at 37 °C.

The mechanism of transit from proximal to distal cisternae has been much discussed. A trivial explanation—direct cisternal continuity—is ruled out by electron microscopy. Two further models (Figure 13) which are able to account for transit are: 1) a "dissociative" model in which vesicles bud from and target hierarchically to successive cisternae, and 2) a model of "cisternal progression," according to which entire cisternae move in a proximal-to-distal direction. The first model has received considerable experimental support from both cell fusion studies and from cell-free analysis of N-glycan maturation of membrane glycoproteins in transit across the Golgi stack. For the cell-free studies, pairs of stacked Golgi fractions are mixed with appropriate supernatant factors. A set of soluble and membrane-associated proteins (coatamers) have been identified and implicated in vesicle formation, targeting, and fusion. This model requires an impressive degree of precision of vesicle targeting in successive rounds of membrane fission and

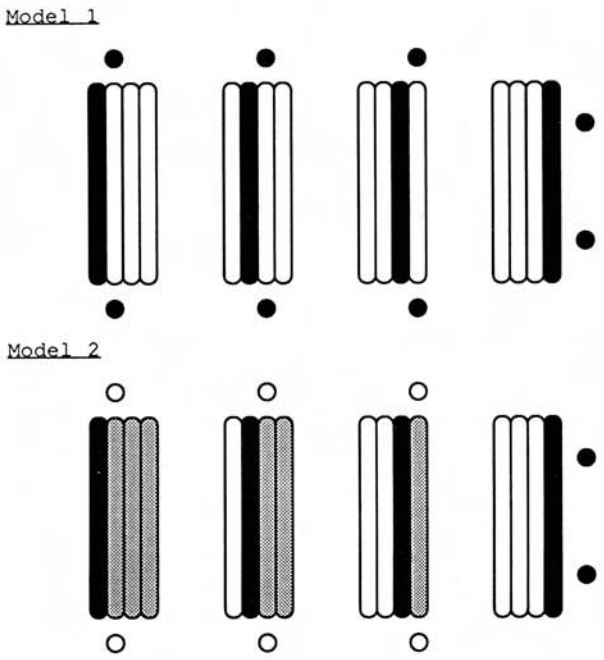

Figure 13. Two models which seek to explain how secretory protein content passes from the proximal face (left) of the Golgi stack to the distal face (right). Each model is illustrated as a sequence of time frames to describe the passage of a cohort of secretory content across the Golgi stack. In Model 1, passage from one cisterna to the next is accomplished by small vesicles which depart from a given cisternae carrying quanta of content and target specifically to the ext cisternae. In Model 2, the entire cisternae move in a proximal-to-distal direction, finally releasing vesicles at the distal face. According to this model, proximal cisternae must continually be regenerated. These newly-created cisternae are white.

fusion. The budding and targeting is thought to occur at the rims (extremities) of cisternae. The second model has the advantage of avoiding this issue of exquisite vesicle targeting specificities, but has difficulty accounting for the progressive modification of the composition of successive cisternae (see above) and must postulate that the most proximal cisternae are continually being regenerated. The strongest evidence for this model comes from study of a specialized (and possibly atypical) system: the genesis of surface scales by certain marine algae. The scales which mature within Golgi cisternae are so large that they could not be encapsulated by small transit vesicles.

Transit across the GC requires ATP, GTP, and fatty acyl CoA and proceeds effectively only above 20 °C. It is dramatically slowed, for unknown reasons, by the carboxylic ionophore, monensin (See Figure 5).

MACROMOLECULAR SORTING

Figure 14 gives an overview of the macromolecular sorting options which are executed by the GC.

Exit from the GC of constitutively secreted proteins and membrane proteins which are constitutively delivered to the plasma membrane occurs after their transit through the most distal cisternae, which house the terminal sugar transferases, judging from the extent of maturation of their N-glycans. The putative carrier vesicles responsible for their delivery to the cell surface have been only partly characterized.

Secretory glycoproteins which are massively stored in secretion granules also bear "matured" N-glycans. As mentioned above, their concentration begins in distal Golgi cisternae and is completed as condensing vacuoles are converted to secretion granules. In the case of cells which produce secretion granules, both constitutively secreted proteins and those destined for storage may be present in condensing vacuoles, but constitutively transported proteins are not stored in secretion granules. As with RER exit, it is thought that a given protein will be constitutively secreted unless it bears a critical (yet undefined) signal which leads to its being retained and concentrated. This sorting decision is upset by agents such as chloroquine or ammonium chloride which dissipate the relative acidity of membrane-bounded compartments. It is therefore thought that the acidity of condensing vacuoles is essential.

In the best-studied animal cells, the exit of acid hydrolases from the GC occurs after addition of the mannose-phosphate units (described above) and involves mannose-phosphate receptors. Subcellular fractionation studies of the liver indicate that the enzymes responsible for mannose-phosphate addition are in relatively proximal Golgi cisternae. Immunocytochemical studies of the larger receptor show that its sub-GC location varies from one cell type to the next and that it can be detected in endosomes but not in lysosomes. It is therefore thought that the cytologic site of acid hydrolase exit from the GC may be variable and that hydrolase arrival in lysosomes follows passage through endosomes. As with many cell surface receptors, the affinity of the mannose-phosphate receptors for mannose-phosphate bearing ligands is high at neutral pH and low at acidic pH. Thus, the acid hydrolase ligand should be released upon arrival in the endosome.

This entire trajectory of acid hydrolase delivery is upset in I-Cell Disease, since mannose-phosphate units are not added to the hydrolases (see above). The result is that they are secreted.

In selected cell types, such as the hepatocyte and in yeast, accurate targeting of acid hydrolases can be accomplished in the absence of mannose phosphate units. Polypeptide determinants are presumably responsible. This is also true for lysosomal membrane proteins, which do not bear mannose-phosphate units.

Constitutive exit to the cell surface may lead to more than a single plasma membrane domain. In hepatocytes and other polarized epithelial cells (e.g., kidney

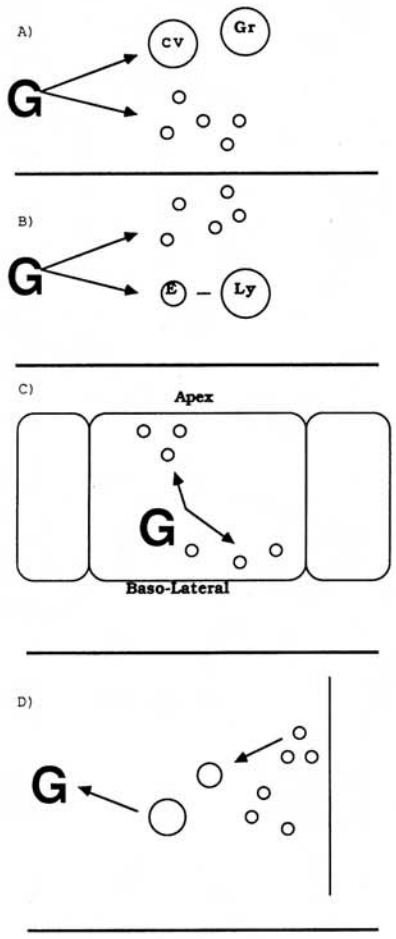

Figure 14. Enumeration of multiple sorting/transport options accomplished by the Golgi Complex. **A**) Delivery of secretory products to both constitutively discharged secretion vesicles and, via condensing vacuoles (CV), to secretion granules (Gr). **B**) Delivery of products to both secretion vesicles and to lysosomes (Ly) via endosomes (E). For simplicity, only one of the secretory options indicated in (**A**) is included. **C**) Delivery of membrane or secretory proteins to both the apical and baso-lateral surfaces of polarized cells. **D**) Receipt of vesicular traffic from the cell surface(s), possibly followed by return to the cell surface.

or intestinal epithelial cells), the functions and composition of the apical plasma membrane are distinctly different from those of the basolateral surface. These differences are critical for many functions of epithelial cells; for example in transepithelial ion transport. Much effort has been devoted to elucidating the path(s) taken by membrane glycoproteins and glycolipids as they exit from post-GC

elements toward these two domains. For experimental simplicity, much of the analysis has been based on following viral envelope glycoproteins (of Vesicular Stomatitis Virus, Semliki Forest Virus, Influenza Virus, etc.). The site at which sorting of apical vs. basolateral membrane proteins occurs varies according to cell type: in kidney epithelial cells, the VSV glycoprotein (G) proceeds directly from the GC to the basolateral surface (where this virus buds) and the hemagglutinin of Influenza proceeds directly from the GC to the apical surface (where this virus buds). In hepatocytes, by contrast, all membrane and secretory proteins appear to move from the GC to the sinusoidal surface (equivalent of the basolateral surface), from which some membrane proteins subsequently pass to the bile canalicular front.

GOLGI FUNCTIONS IN ENDOCYTOSIS

Morphologic studies of endocytosis of some (but certainly not all) soluble tracers and biochemical studies of labeled cell surface glycoproteins have documented a route of vesicular transport from the cell surface to Golgi cisternae (See Figure 14). The data indicate that this endocytic route is followed less often than transit from the cell surface to lysosomes or return to the cell surface (diacytosis); nevertheless, cumulatively, the plasma membrane-to-Golgi transport of both proteins and lipids may account for a large fraction of GC membrane traffic and be responsible for important remodeling of surface glycoconjugates. The diacytotic route is believed to be essential for antigen presentation by cells of the immune system and for recycling of cell surface receptors.

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