The Golgi apparatus and main discoveries in the field of intracellular transport

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In this chapter, we summarize important findings in the field of intracellular transport, which have considerably contributed to the understanding of the function and organization of the Golgi apparatus (GA). It is not possible to mention all authors in this huge field. We apologize for gaps and incompleteness, and are thankful for suggestions and corrections.

The GA is named after its discoverer Camillo Golgi, who first described the complex *apparato reticolare interno* in 1898 (Golgi 1898a,b; reviewed by Berger 1997; Dröscher 1998). Although Camillo Golgi had presented his discovery convincingly, for a long time his data have been considered as an artifact of cell staining (Farquhar and Palade 1981). Only after the electron microscopic confirmation of the existence of the GA in cells by Dalton in 1951, scientists started to believe in its reality. Therefore, we will not list the discoveries within the area of intracellular transport made in the time, before the existence of the GA was confirmed electron microscopically. However, the names of A. Negri, H. Fuch, A. Perroncito, S. Ramon y Cajal, D.N. Nassonov, R.H. Bowen, G.S. Carter, H.W. Beams and R.L. King, V.M. Emmel, H.W. Deane and E.M. Dempsey, W.C. Schneider et al. should be mentioned, because they have considerably contributed to the understanding of the Golgi function (reviewed in Berger 1997). Here, we want to address most important discoveries within the area of intracellular transport after 1951 (Table 1).

Additionally, we would like to mention further important contributions to this field. The hypothesis of lipid rafts was proposed and developed by van Meer and Simons. The Lodish group made the invention of the synchronization of the transport of cargoes. The role of lectins in ER-to-Golgi transport was discovered by H.-P. Hauri. The most important contribution to the characterization of Rab machinery (although in the endocytic pathway) was made by M. Zerial. W. Hong, R. Sheller and R. Jahn made important contributions to the understanding of the function of the SNARE machinery. R. Schekman and W. Balch deciphered the functions of the COPII coat. A. Rambourg, Y. Clermont, G. Griffiths, A. Staehelin and K. Howell made significant contributions to the 3D-analysis of the GA in different cell types. J. Slot and H. Geuze provided new insight into the morphology of the endocytic system and its interaction with exocytosis. The important contribution into the analysis of the kinetics of the plant GA was made by C. Hawes. The characterization of the 3D-structure of several proteins important for intracellular transport, and protein coat complexes in their crystal state is linked with W. Balch and J. Goldberg's names. We apologise again for possible

Table 1. The Golgi apparatus and main discoveries in the field of physiology of intracellular transport

1898	Discovery of the GA
1951	Confirmation of the presence of the GA (Dalton 1951)
1961	The regional distribution of the thiamine-pyrophosphatase activity within the GA (Novikoff and Goldfischer 1961)
1964	The *trans* ER (Novikoff 1964; Novikoff et al. 1964)
1964	GERL concept (Novikoff 1964)
1964	Isolation of Golgi membranes from cells (Morré and Mollenhauer 1964)
1964	The process of sulphation in the GA (Godman and Lane 1964)
1966	The sugar–nucleotide transport from the cytosol to the Golgi lumen across the Golgi membranes, the role of the GA in glycosylation (Neutra and Leblond 1966)
1966	The origin of lysosomes and the function of clathrin-coated vesicles during protein absorption (Bainton and Farquhar 1966; Friend and Farquhar 1967)
1967	The intracellular transport (Jamieson and Palade 1967a,b)
1969	Galactosyltransferase as a Golgi marker (Whur et al. 1969; Morré et al. 1969)
1976	Isolation of clathrin-coated vesicles (Pearse 1976)
1977	The PM-to-Golgi transport of the endogenously added marker (Herzog and Farquhar 1977)
1980	M6P-mediated sorting of Golgi enzymes at the GA (Tabas and Kornfeld 1980)
1981	Clathrin-coated buds in the *trans* side of the GA (Griffiths et al. 1981)
1982	Immunocytochemical localization of galactosyltransferase (Roth and Berger 1982)
1983	Topology of N-glycosylation (Dunphy and Rothman 1983)
1984	Reconstitution of intra-Golgi transport *in vitro* (Balch et al. 1984)
1984	The 15°C temperature block (Saraste and Kuismanen 1984)
1985	Clathrin-independent endocytosis (Moya et al. 1985; Sandvig et al. 1985)
1985–1987	The mitotic form of the GA and mechanisms of mitotic Golgi transformation in animal cells (Featherstone et al. 1985; Lucocq et al. 1987)
1986	The COPI-coated vesicles and characterization of molecular mechanisms involved into the function of COPI coat (Orci et al. 1986; Serafini et al. 1991)
1986	The structure and function of the TGN and the 20°C temperature block (Griffiths and Simons 1986)
1987	KDEL-signal for the retention of luminally located proteins (Munro and Pelham 1987)
1989	BFA was applied for the study of intra-Golgi transport (Doms et al. 1989; Lippincott-Schwartz et al. 1989)
1990	SNAREs (Newman et al. 1990)
1990	The main genes involved in intracellular transport, the genetic evidence in favour of the vesicular model of the transport in yeast (Kaiser and Schekman 1990)
1991	A Golgi retention signal in the membrane-spanning domain (Swift and Machamer 1991)
1993	The role of oligomerization for the retention of Golgi enzymes (Weisz et al. 1993)
1993	The role of PM-derived signalling for intra-Golgi transport (De Matteis et al. 1993)
1994	Golgi matrix (Slusarewicz et al. 1994) and *cis*-Golgin, GM130 (Nakamura et al. 1995)
1994	COPI-dependent retrieval sorting signals (Cosson and Letourneur 1994)

Table 1. *(Continued)*

1994	COPII coat. Isolation of COPII-dependent small vesicles in cell-free system (Barlowe et al. 1994)
1996	Application of GFP-technology for the study of the GA in living cells (Cole et al. 1996)
1996	Characterization of the ER exit sites (Bannykh et al. 1996)
1997	The AP3 and AP4 coats (Dell'Angelica et al. 1997, 1999)
1997	Characterization of ER-to-Golgi transport carriers in living cells (Presley et al. 1997; Scales et al. 1997; Mironov et al. 2003)
1997	Characterization of post-Golgi transport carriers in living cells (Wacker et al. 1997; Hirschberg et al. 1998; Polishchuk et al. 2000)
1998	Intra-Golgi transport of large cargo aggregates (Bonfanti et al. 1998)
1998	The role of endocytic TGN in the formation of the most-*trans* Golgi cisterna (Pavelka et al. 1998)
1998	Discovery of R- and Q-SNAREs (Fasshauer et al. 1998)
1999	Tomographic reconstruction of the GA (Ladinsky et al. 1999)
2001	The concentration of regulatory secretory proteins within the Golgi cisternae (Oprins et al. 2001)
2003	The understanding of the evolution of small GTPases had changed the model of the Golgi evolution (Jékely 2003)
2003	Characterization of Golgi-to-apical PM transport carriers in living cells (Kreitzer et al. 2003)
2004	Intercisternal connections in transporting GA (Marsh et al. 2004; Trucco et al. 2004)
2006	Characterization of the Golgi-to-endosome carriers in living cells (Polishchuk et al. 2006)
2006	The role of GM130 in the maintenance of the Golgi ribbon (Puthenveedu et al. 2006)
2007	The role of ER-to-Golgi transport in the maintenance of the Golgi ribbon (Marra et al. 2007)

gaps (all authors quoted in the consecutive chapters deserve to be listed here). The list is open for suggestions.

The development of the research in the field of intracellular transport has been comprehensively discussed in 1998 at the conference in Pavia devoted to the 100th anniversary of the Golgi discovery.

History of models of intracellular transport

Historically, the first mechanism that had been proposed for intracellular transport was the progression. The origin of the progression model (or the concept of *cis*-to-*trans* flow) links to Grasse's name (1957) who proposed that the continuous formation of *cis* Golgi cisternae balances the conversion of *trans* one into secretory granules. However, the first experimental data in favour of the progression concept were obtained in 1971 (Franke et al. 1971).

In 1967, it has been demonstrated that proteins newly synthesized in the ER appeared, after a few minutes, not only over Golgi stacks but also over

round profiles surrounding the GA and the conclusion that secretory proteins bypass the GA was made (Jamieson and Palade 1967a,b, 1968a,b). Then, in 1981, the vesicular model replaced the progression model because the main support for the progression model, the *cis–trans* movement of scales in algae has been considered to be a rare formula connected with unusual geometry and size of the product (Farquhar and Palade 1981). Ironically, the major supporting data for the vesicular model at that time was based on the isolation of Golgi-derived clathrin-coated vesicles (Rothman et al. 1980). However, after the discovery of coat protein I (COPI) (Orci et al. 1986), the vesicular model was changed, and instead of clathrin-dependent vesicles, COPI-dependent vesicles were proposed to serve as anterograde carriers. The strongest support for the vesicular model appeared from the experiments in yeast with the temperature sensitive *Sec* genes (Kaiser and Schekman 1990). The *in vitro* isolation of functional (containing VSVG and able to fuse with acceptor Golgi membranes) COPI-coated vesicles (Osterman et al. 1993) was interpreted as the second proof for the role of COPI-coated vesicles in the anterograde intra-Golgi transport. Importantly, however, that the first author of this paper later stressed, that actually, these data support the cisterna maturation model (Ostermann 2001).

On the other hand, it has also been demonstrated that 20 min after fusion of two (or more) cells (one cell is VSV-infected, another is a non-infected cell) and formation of a heterokaryon, VSVG seems to move from the GA derived from the infected cell to the GA derived from non-infected cells (Rothman et al. 1984). These results were interpreted as confirmation of the ability of vesicular carriers to diffuse through the cytosol of the heterokaryon from one GA to another. However, later, the Rothman group (Orci et al. 1998) laid less emphasis on the heterokaryon experiments, suggesting that those observations appeared as a result of the treatment of cells with an acidic medium. Instead, the “string theory” was proposed, according to which a proteinaceous-like string links vesicles to cisternal elements and prevents budded vesicles from diffusing away, while still allowing them to diffuse laterally.

With time, due to accumulation of contradictions, the current vesicular paradigm became less and less effective in the explanation of growing body of observations (Mironov et al. 1997). As a result, the original version of the vesicular paradigm began to be modified not only by the opponents of the vesicular model but also by its authors and proponents (Orci et al. 1998).

In order to resolve accumulated contradictions within the field, almost simultaneously several groups (Bannykh and Balch 1997; Mironov et al. 1997; Glick et al. 1997; Schekman and Mellman 1997) have published the cisterna maturation-progression model based on the COPI vesicles-mediated Golgi enzyme recycling.

The first experimental confirmation that large aggregated cargo, such as procollagen I, can be transported through the GA by maturation mechanism came in 1998 (Bonfanti et al. 1998). Previous stereological observations in

P. scheffelii suggesting that their scales being much too large to be packaged into vesicles are transported by the progression of Golgi cisternae towards the plasmalemma were published not in an original paper but in a review (Becker et al. 1995) and were not confirmed later because glycoprotein and polysaccharide synthesis are uncoupled during flagella regeneration (Perasso et al. 2000).

Next, it has been demonstrated (Mironov et al. 2001) that both diffusible and non-diffusible cargoes are transported in the same carriers through the Golgi stacks. It has been proved that vesicles are not transport carriers for cargo in the intra-Golgi transport not only *in situ*, but also *in vitro*, in cell-free assay (Happe and Weidman 1998). After these publications, there was a short period when the cisterna maturation model became dominant.

With time new contradictions not compatible with the cisterna maturation-progression model have accumulated (Mironov et al. 2005). The attempts to use transport models based on combination of basic principles were not successful (see Chapter 3.2). Therefore now, there is no consensus on the models of intra-Golgi transport. The existence of the maturation mechanism is almost finally established for the secretion of large polymeric structures incompatible in size with COPI-dependent vesicles in many types of cells and under the infection of some viruses.

References

Bainton DF, Farquhar MG (1966) Origin of granules in polymorphonuclear leukocytes. Two types derived from opposite faces of the Golgi complex in developing granulocytes. J Cell Biol 28(2): 277–301

Balch WE, Dunphy WG, Braell WA, Rothman JE (1984) Reconstitution of the transport of protein between successive compartments of the Golgi measured by the coupled incorporation of N-acetylglucosamine. Cell 39: 405–416

Bannykh SI, Rowe T, Balch WE (1996) The organization of endoplasmic reticulum export complexes. J Cell Biol 135: 19–35

Bannykh SI, Balch WE (1997) Membrane dynamics at the endoplasmic reticulum–Golgi interface. J Cell Biol 138: 1–4

Barlowe C, Orci L, Yeung T, Hosobuchi M, Hamamoto S, Salama N, Rexach MF, Ravazzola M, Amherdt M, Schekman R (1994) COPII: a membrane coat formed by Sec proteins that drive vesicle budding from the endoplasmic reticulum. Cell 77: 895–907

Becker B, Bolinger B, Melkonian M (1995) Anterograde transport of algal scales through the Golgi complex is not mediated by vesicles. Trends Cell Biol 5: 305–307

Berger EG (1997) The Golgi apparatus: from discovery to contemporary studies. In: Berger EG, Roth J (eds) The Golgi apparatus. Basel et al., Birkhauser Verlag, pp 1–35

Bonfanti L, Mironov AA Jr, Martínez-Menárguez JA, Martella O, Fusella A, Baldassarre M, Buccione R, Geuze HJ, Mironov AA, Luini A (1998) Procollagen traverses the Golgi stack without leaving the lumen of cisternae: evidence for cisternal maturation. Cell 95(7): 993–1003

Cole NB, Smith CL, Sciaky N, Terasaki M, Edidin M, Lippincott-Schwartz J (1996) Diffusional mobility of Golgi proteins in membranes of living cells. Science 273 (5276): 797–801

Cosson P, Letourneur F (1994) Coatomer interaction with di-lysine endoplasmic reticulum retention motif. Science 263: 1629–1631
Dalton AJ (1951) Observations of the Golgi substance with the electron microscope. Nature 168(4267): 244–245
De Matteis MA, Santini G, Kahn RA, Di Tullio G, Luini A (1993) Receptor and protein kinase C-mediated regulation of ARF binding to the Golgi complex. Nature 364: 818–821
Dell'Angelica EC, Ohno H, Ooi CE, Rabinovich E, Roche KW, Bonifacino JS (1997) AP-3: an adaptor-like protein complex with ubiquitous expression. EMBO J 16(5): 917–928
Dell'Angelica EC, Mullins C, Bonifacino JS (1999) AP-4, a novel protein complex related to clathrin adaptors. J Biol Chem 274: 7278–7285
Doms RW, Russ G, Yewdell JW (1989) Brefeldin A redistributes resident and itinerant Golgi proteins to the endoplasmic reticulum. J Cell Biol 109: 61–72
Dröscher A (1998) Camillo Golgi and the discovery of the Golgi apparatus. Histochem Cell Biol 109: 425–430
Dunphy WG, Rothman JE (1983) Compartmentation of asparagine-linked oligosaccharide processing in the Golgi apparatus. J Cell Biol 97(1): 270–275
Farquhar MG, Palade GE (1981) The Golgi apparatus (complex)-(1954–1981)-from artifact to center stage. J Cell Biol 91(3 Pt 2): 77s–103s
Fasshauer D, Sutton RB, Brunger AT, John R (1998) Conserved structural features of the synaptic fusion complex: SNARE proteins reclassified as Q- and R-SNAREs. Proc Natl Acad Sci USA 95(26): 15781–15786
Featherstone C, Griffiths G, Warren G (1985) Newly synthesized G protein of vesicular stomatitis virus is not transported to the Golgi complex in mitotic cells. J Cell Biol 101(6): 2036–2046
Franke WW, Morre DJ, Deumling B, Cheetham RD, Kartenbeck J, Jarasch E-D, Zengtraf HW (1971) Synthesis and turnover of membrane proteins in rat liver: an examination of the membrane flow hypothesis. Z Naturforsch 26b: 1031–1039
Friend DS, Farquhar MG (1967) Functions of coated vesicles during protein absorption in the rat vas deferens. J Cell Biol 35(2): 357–376
Glick BS, Elston T, Oster G (1997) A cisternal maturation mechanism can explain the asymmetry of the Golgi stack. FEBS Lett 414: 177–181
Godman GC, Lane N (1964) On the site of sulfation in the chondrocyte. J Cell Biol 21: 353–366
Golgi C (1898a) Intorno alla struttura della cellula nervosa. Boll Soc Med Chir Pavia 13: 1–14
Golgi C (1898b) Sur la structure des cellules nerveuses des ganglions spinaux. Arch Ital Biol 30: 60–71
Grasse PP (1957) Ultrastructure, polarity and reproduction of Golgi apparatus. C R Hebd Seances Acad Sci 245(16): 1278–1281
Griffiths G, Warren G, Stuhlfauth I, Jockusch BM (1981) The role of clathrin-coated vesicles in acrosome formation. Eur J Cell Biol 26(1): 52–60
Griffiths G, Simons K (1986) The *trans* Golgi network: sorting at the exit site of the Golgi complex. Science 34: 438–443
Happe S, Weidman P (1998) Cell-free transport to distinct Golgi cisternae is compartment specific and ARF independent. J Cell Biol 140(3): 511–523
Herzog V, Farquhar MG (1977) Luminal membrane retrieved after exocytosis reaches most Golgi cisternae in secretory cells. Proc Natl Acad Sci USA 74(11): 5073–5077
Hirschberg K, Miller CM, Ellenberg J, Presley JF, Siggia ED, Phair RB, Lippincott-Schwartz J (1998) Kinetic analysis of secretory protein traffic and characterization of Golgi to plasma membrane transport in living cells. J Cell Biol 143: 1485–1503

Jamieson JD, Palade GE (1967a) Intracellular transport of secretory proteins in the pancreatic exocrine cell. I. Role of the peripheral elements of the Golgi complex. J Cell Biol 34(2): 577–596

Jamieson JD, Palade GE (1967b) Intracellular transport of secretory proteins in the pancreatic exocrine cell. II. Transport to condensing vacuoles and zymogen granules. J Cell Biol 34(2): 597–615

Jamieson JD, Palade GE (1968a) Intracellular transport of secretory proteins in the pancreatic exocrine cell. 3. Dissociation of intracellular transport from protein synthesis. J Cell Biol 39(3): 580–588

Jamieson JD, Palade GE (1968b) Intracellular transport of secretory proteins in the pancreatic exocrine cell. IV. Metabolic requirements. J Cell Biol 39(3): 589–603

Jékely G (2003) Small GTPases and the evolution of the eukaryotic cell. Bioessays 25(11): 1129–1138

Kaiser CA, Schekman R (1990) Distinct sets of SEC genes govern transport vesicle formation and fusion early in the secretory pathway. Cell 61(4): 723–733

Kreitzer G, Schmoranzer J, Low SH, Li X, Gan Y, Weimbs T, Simon SM, Rodriguez-Boulan E (2003) Three-dimensional analysis of post-Golgi carrier exocytosis in epithelial cells. Nat Cell Biol 5(2): 126–136

Ladinsky MS, Mastronarde DN, McIntosh JR, Howell KE, Staehelin LA (1999) Golgi structure in three dimensions: functional insights from the normal rat kidney cell. J Cell Biol 144: 1135–1149

Lippincott-Schwartz J, Yuan LC, Bonifacino JS, Klausner RD (1989) Rapid redistribution of Golgi proteins into the ER in cells treated with Brefeldin A: evidence for membrane cycling from the Golgi to ER. Cell 56: 801–813

Lucocq JM, Pryde JG, Berger EG, Warren G (1987) A mitotic form of the Golgi apparatus in Hela cells. J Cell Biol 104: 865–874

Marra P, Salvatore L, Mironov A Jr, Di Campli A, Di Tullio G, Trucco A, Beznoussenko G, Mironov A, De Matteis MA (2007) The biogenesis of the Golgi ribbon: the roles of membrane input from the ER and of GM130. Mol Biol Cell 18(5): 1595–1608

Marsh BJ, Volkmann N, McIntosh JR, Howell KE (2004) Direct continuities between cisternae at different levels of the Golgi complex in glucose-stimulated mouse islet beta cells. Proc Natl Acad Sci USA 101(15): 5565–5570

Mironov AA, Weidman P, Luini A (1997) Variations on the intracellular transport theme: maturing cisternae and trafficking tubules. J Cell Biol 138: 481–484

Mironov AA, Beznoussenko GV, Nicoziani P, Martella O, Trucco A, Kweon HS, Di Giandomenico D, Polishchuk RS, Fusella A, Lupetti P, Berger EG, Geerts WJ, Koster AJ, Burger KN, Luini A (2001) Small cargo proteins and large aggregates can traverse the Golgi by a common mechanism without leaving the lumen of cisternae. J Cell Biol 155: 1225–1238

Mironov AA, Mironov AA Jr, Beznoussenko GV, Trucco A, Lupetti P, Smith JD, Geerts WJ, Koster AJ, Burger KN, Martone ME, Deerinck TJ, Ellisman MH, Luini A (2003) ER-to-Golgi carriers arise through direct en bloc protrusion and multistage maturation of specialized ER exit domains. Dev Cell 5: 583–594

Mironov AA, Beznoussenko GV, Polishchuk RS, Trucco A (2005) Intra-Golgi transport. A way to a new paradigm? BBA Mol Cell Res 1744: 340–350

Morré DJ, Mollenhauer HH (1964) Isolation of Golgi apparatus from plant cells. J Cell Biol 23: 295–305

Morré DJ, Merlin L, Keenan T (1969) Localization of glycosyl transferase activities in a Golgi apparatus-rich fraction isolated from rat liver. Biochem Biophys Res Commun 37(5): 813–819

Moya M, Dautry-Varsat A, Goud B, Louvard D, Boquet P (1985) Inhibition of coated pit formation in Hep2 cells blocks the cytotoxicity of diphtheria toxin but not that of ricin. J Cell Biol 101: 548–559

Munro S, Pelham HRB (1987) A C-terminal signal prevents secretion of luminal ER proteins. Cell 48: 899–907

Nakamura N, Rabouille C, Watson R, Nilsson T, Hui N, Slusarewicz P, Kreis TS, Warren G (1995) Characterization of a *cis*-Golgi matrix protein, GM130. J Cell Biol 131: 1715–1726

Neutra M, Leblond CP (1966) Radioautographic comparison of the uptake of galactose-H and glucose-H3 in the Golgi region of various cells secreting glycoproteins or mucopolysaccharides. J Cell Biol 30: 137–150

Newman AP, Shim J, Ferro-Novick S (1990) BET1, BOS1, and SEC22 are members of a group of interacting yeast genes required for transport from the endoplasmic reticulum to the Golgi complex. Mol Cell Biol 10(7): 3405–3414

Novikoff A, Goldfischer S (1961) Nucleosidediphosphatase activity in the Golgi apparatus and its usefulness for cytological studies. Proc Natl Acad Sci USA 47: 802–810

Novikoff AB (1964) GERL, its form and function in neurons of rat spinal ganglia. Biol Bull 127: 358

Novikoff AV, Essner E, Quintana N (1964) Golgi apparatus and lysosomes. Fed Proc 23: 1010–1022

Oprins A, Rabouille C, Posthuma G, Klumperman J, Geuze HJ, Slot JW (2001) The ER to Golgi interface is the major concentration site of secretory proteins in the exocrine pancreatic cell. Traffic 2: 831–838

Orci L, Glick BS, Rothman JE (1986) A new type of coated vesicular carrier that appears not to contain clathrin: its possible role in protein transport within the Golgi stack. Cell 46: 171–184

Orci L, Perrelet A, Rothman JE (1998) Vesicles on strings: morphological evidence for processive transport within the Golgi stack. Proc Natl Acad Sci USA 95(5): 2279–2283

Ostermann J, Orci L, Tani K, Amherdt M, Ravazzola M, Elazar Z, Rothman JE (1993) Stepwise assembly of functionally active transport vesicles. Cell 75(5): 1015–1025

Ostermann J (2001) Stoichiometry and kinetics of transport vesicle fusion with Golgi membranes. EMBO Rep 2(4): 324–329

Pavelka M, Ellinger A, Debbage P, Loewe C, Vetterlein M, Roth J (1998) Endocytic routes to the Golgi apparatus. Histochem Cell Biol 109: 555–570

Pearse BM (1976) Clathrin: a unique protein associated with intracellular transfer of membrane by coated vesicles. Proc Natl Acad Sci USA 73(4): 1255–1259

Perasso L, Grunow A, Brüntrup IM, Bölinger B, Melkonian M, Becker B (2000) The Golgi apparatus of the scaly green flagellate *Scherffelia dubia*: uncoupling of glycoprotein and polysaccharide synthesis during flagellar regeneration. Planta 210(4): 551–562

Polishchuk RS, Polishchuk EV, Marra P, Alberti S, Buccione R, Luini A, Mironov AA (2000) Correlative light-electron microscopy reveals the tubular–saccular ultrastructure of carriers operating between Golgi apparatus and plasma membrane. J Cell Biol 148 (1): 45–58

Polishchuk RS, San Pietro E, Di Pentima A, Tete S, Bonifacino JS (2006) Ultrastructure of long-range transport carriers moving from the *trans* Golgi network to peripheral endosomes. Traffic 7: 1092–1103

Presley JF, Cole NB, Schroer TA, Hirschberg K, Zaal KJ, Lippincott-Schwartz J (1997) ER-to-Golgi transport visualized in living cells. Nature 389: 81–85

Puthenveedu MA, Bachert C, Puri S, Lanni F, Linstedt AD (2006) GM130 and GRASP65-dependent lateral cisternal fusion allows uniform Golgi-enzyme distribution. Nat Cell Biol 8: 238–248

Roth J, Berger EG (1982) Immunocytochemical localization of galactosyltransferase in HeLa cells: codistribution with thiamine pyrophosphatase in *trans*-Golgi cisternae. J Cell Biol 93(1): 223–229

Roth J, Berger EG (eds) (1997) The Golgi apparatus. Basel. Birkhauser

Rothman JE, Bursztyn-Pettegrew H, Fine RE (1980) Transport of the membrane glycoprotein of vesicular stomatitis virus to the cell surface in two stages by clathrin-coated vesicles. J Cell Biol 86(1): 162–171

Rothman JE, Miller RL, Urbani LJ (1984) Intercompartmental transport in the Golgi complex is a dissociative process: facile transfer of membrane protein between two Golgi populations. J Cell Biol 99: 260–271

Sandvig K, Sundan A, Olsnes S (1985) Effect of potassium depletion of cells on their sensitivity to diphtheria toxin and pseudomonas toxin. J Cell Physiol 124: 54–56

Saraste J, Kuismanen E (1984) Pre- and post-Golgi vacuoles operate in the transport of Semliki Forest virus membrane glycoproteins to the cell surface. Cell 38(2): 535–549

Scales SJ, Pepperkok R, Kreis TE (1997) Visualization of ER-to-Golgi transport in living cells reveals a sequential mode of action for COPII and COPI. Cell 90: 1137–1148

Schekman R, Mellman I (1997) Does COPI go both ways? Cell 90: 197–200

Serafini T, Orci L, Amherdt M, Brunner M, Kahn RA, Rothman JE (1991) ADP-ribosylation factor is a subunit of the coat of Golgi-derived COP-coated vesicles: a novel role for a GTP-binding protein. Cell 67(2): 239–253

Slusarewicz P, Nilsson T, Hui N, Watson R, Warren G (1994) Isolation of a matrix that binds medial Golgi enzymes. J Cell Biol 124(4): 405–413

Swift AM, Machamer CE (1991) A Golgi retention signal in a membrane-spanning domain of coronavirus E1 protein. J Cell Biol 115(1): 19–30

Tabas I, Kornfeld S (1980) Biosynthetic intermediates of beta-glucuronidase contain high mannose oligosaccharides with blocked phosphate residues. J Biol Chem 255 (14): 6633–6639

Trucco A, Polishchuk RS, Martella O, Di Pentima A, Fusella A, Di Giandomenico D, San Pietro E, Beznoussenko GV, Polishchuk EV, Baldassarre M, Buccione R, Geerts WJ, Koster AJ, Burger KN, Mironov AA, Luini A (2004) Secretory traffic triggers the formation of tubular continuities across Golgi sub-compartments. Nat Cell Biol 6 (11): 1071–1081

Varki A, Cummings R, Esko J, Freeze H, Hart G, Marth J (1999) Essentials of glycobiology. Cold Spring Harbor Laboratory Press, Cold Spring Harbor

Wacker I, Kaether C, Kromer A, Migala A, Almers W, Gerdes HH (1997) Microtubule-dependent transport of secretory vesicles visualized in real time with a GFP-tagged secretory protein. J Cell Sci 110: 1453–1463

Weisz OA, Swift AM, Machamer CE (1993) Oligomerization of a membrane protein correlates with its retention in the Golgi complex. J Cell Biol 122(6): 1185–1196

Whur P, Herscovics A, Leblond CP (1969) Radioautographic visualization of the incorporation of galactose-3H and mannose-3H by rat thyroids in vitro in relation to the stages of thyroglobulin synthesis. J Cell Biol 43: 289–311