

# traducción

## síntesis de proteínas (2)

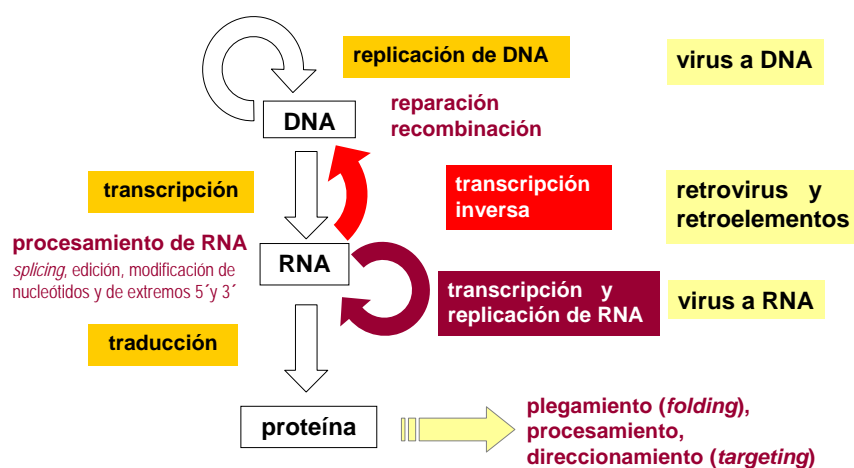
**modificaciones  
co- y pos-traduccionales**

**direccionamiento de proteínas**

1



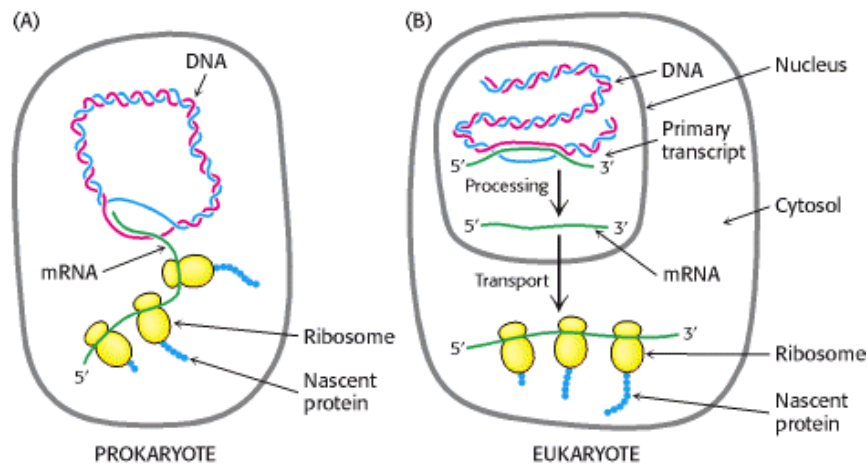
## “Dogma central de la biología molecular”



2

Víctor Romanowski

## transcripción y traducción en el mismo o en diferentes compartimientos



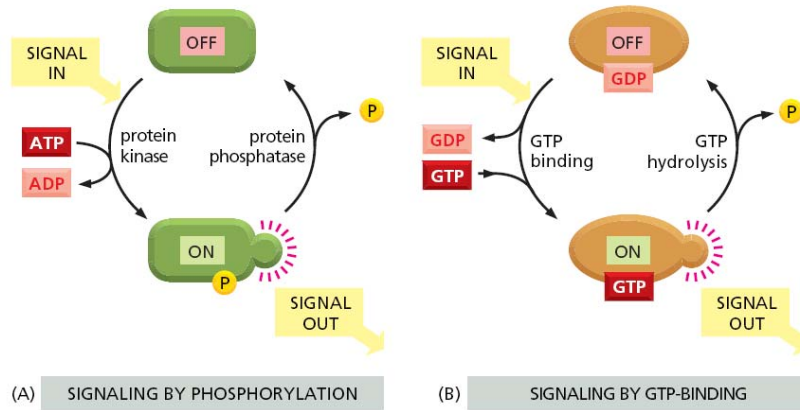
3

## Modificación de proteínas

1. las proteínas sufren modificaciones post-traduccionales (y co-traduccionales)
2. la actividad biológica puede depender de las modificaciones
3. la espectrometría de masas es uno de los mejores métodos para identificar las modificaciones

4

**Modificación de proteínas → covalente o no covalente → actividad**



**A comparison of the two major intracellular signaling mechanisms in eucaryotic cells.** In both cases, a signaling protein is activated by the addition of a phosphate group and inactivated by the removal of this phosphate. To emphasize the similarities in the two pathways, ATP and GTP are drawn as APPP and GPPP, and ADP and GDP as APP and GPP, respectively. The addition of a phosphate to a protein can also be inhibitory.

- **Protein Post-translational Modifications**

- 1. Folding and Processing of Proteins**

- During translation proteins fold as they exit ribosome
  - Some proteins can assume native 3D structure spontaneously
  - Other proteins may require chaperones



## Protein Post-translational Modifications

### 2. Amino-terminal and carboxyterminal modifications

- Cleavage of f-Met from bacterial proteins or Met from eukaryotic proteins. Other amino acids may be trimmed as well.
- Acetylation of Met or other N-terminal amino acids
- Removal of signal peptide for secreted or membrane proteins
- Removal of C-terminal amino acids.

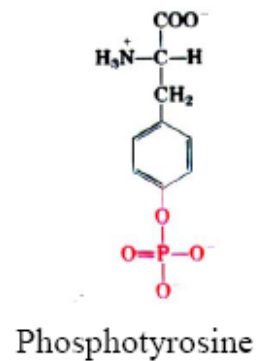
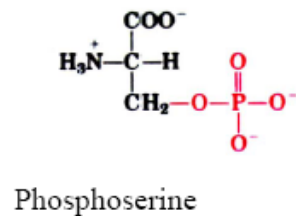
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## Protein Post-translational Modifications

### 3. Modification of Individual Amino Acids

#### a. Phosphorylation

- Enzymatic reaction by specific kinases
- Usually on Ser, Thr, Tyr



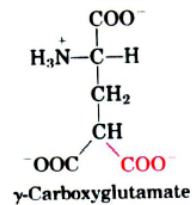
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- Protein Post-translational Modifications

### 3. Modification of Individual Amino Acids

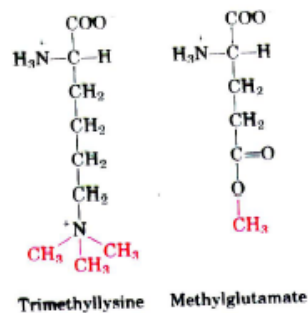
### b. Carboxylation

Addition of extra carboxyl groups to Asp and Glu



### c. Methylation

Addition of methyl groups to Lys and Glu

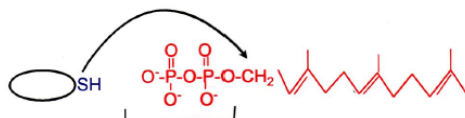


- Protein Post-translational Modifications

### 3. Modification of Individual Amino Acids

#### d. Isoprenylation

- Addition of an isoprenyl group to a protein at either the C-terminus or the N-terminus
- Derived from pyrophosphate intermediate in cholesterol biosynthesis



- **Protein Post-translational Modifications**

### **3. Modification of Individual Amino Acids**

#### **e. Addition of prosthetic groups**

Covalently bound prosthetic group – required for activity  
Example: Cytochrome C -- Heme group

11

## **Protein Post-translational Modifications**

### **3. Modification of Individual Amino Acids**

#### **f. Proteolytic Processing**

Some types of proteins are synthesized as a larger, inactive precursor protein and must be cleaved for activity

#### **g. Formation of disulfide bonds**

Spontaneous cross-linking at Cys residues  
Brought into proximity by folding  
Helps to stabilize 3D structure

12

- Protein Post-translational Modifications

### 3. Modification of Individual Amino Acids

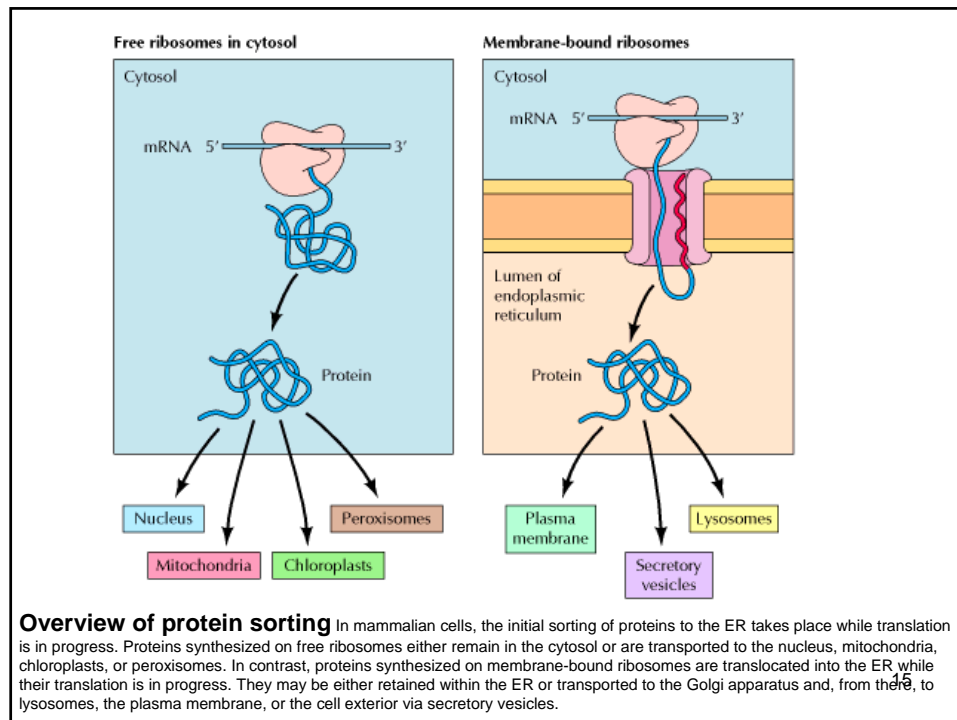
#### **h. Glycosylation (N)**

- Addition of oligosaccharides to proteins
- Usually at Asn
- Sugars are transferred from dolichol-P
- Present in ER

13

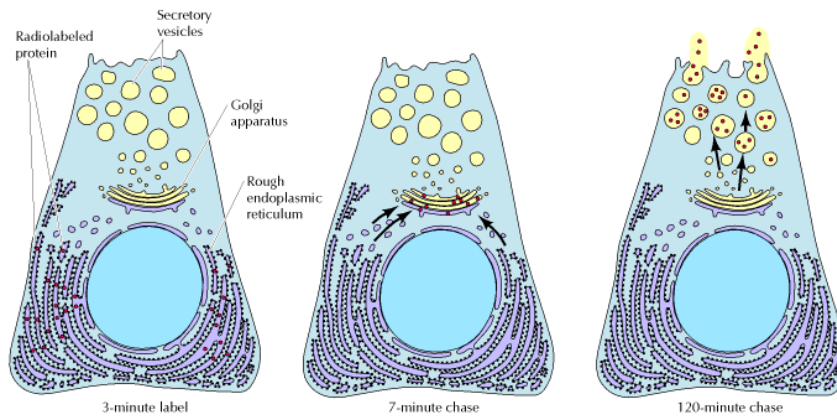
**Direccionamiento proteínas a  
diferentes compartimientos  
subcelulares**  
**protein targeting**

14

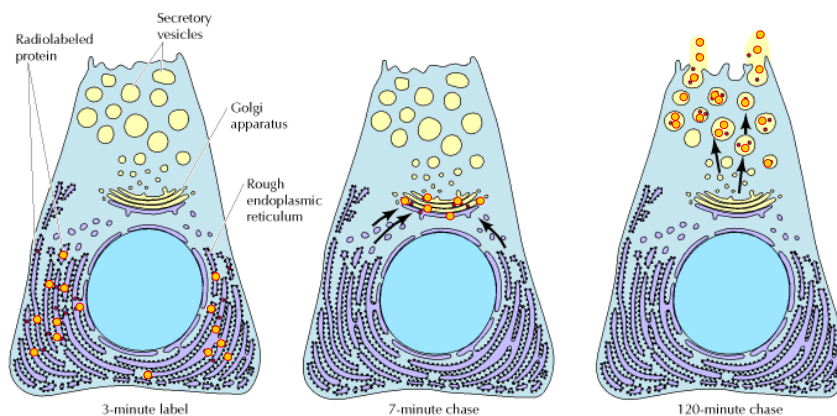


## proteínas de secreción: la vía secretoria secretory pathway

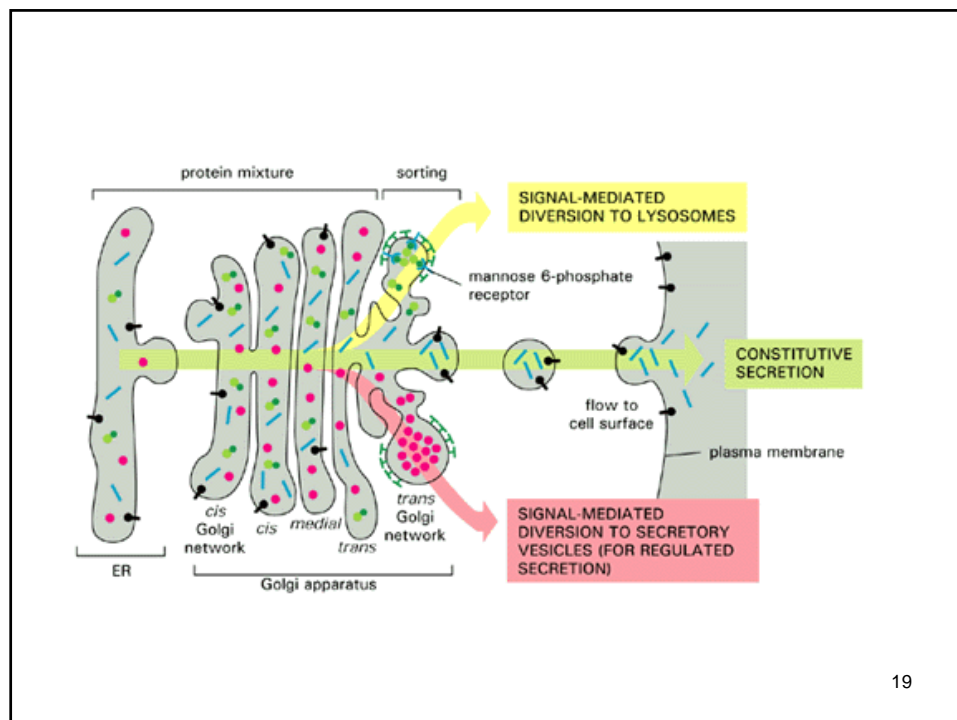




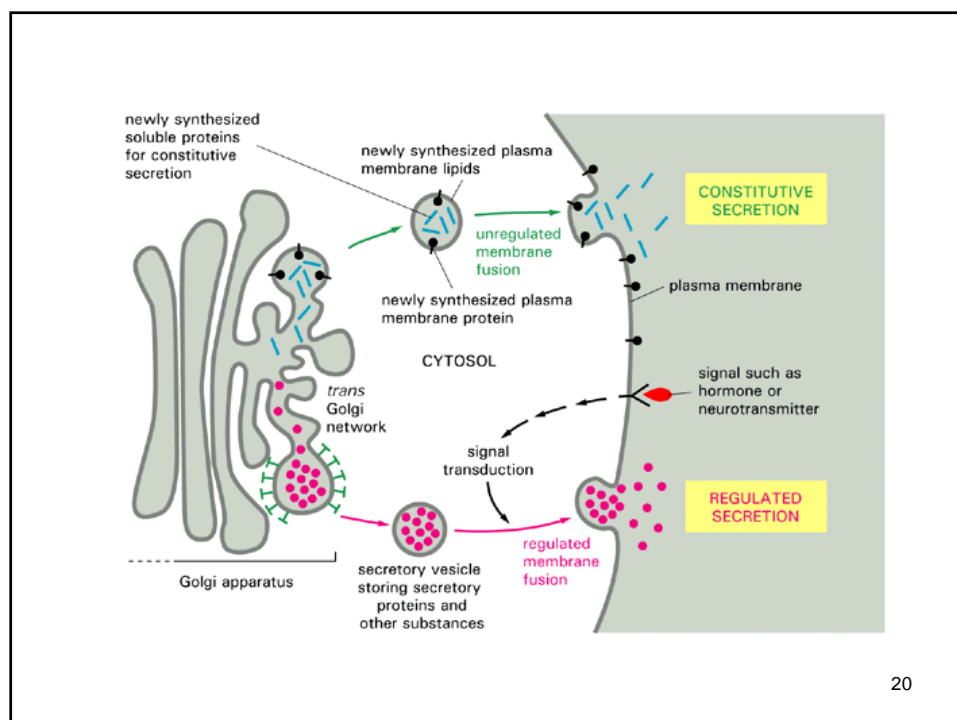
**The secretory pathway** Pancreatic acinar cells, which secrete most of their newly synthesized proteins into the digestive tract, were labeled with radioactive amino acids to study the intracellular pathway taken by secreted proteins. After a short incubation with radioactive amino acids (3-minute label), autoradiography revealed that newly synthesized proteins were localized to the rough ER. Following further incubation with nonradioactive amino acids (a chase), proteins were found to move from the ER to the Golgi apparatus and then, within secretory vesicles, to the plasma membrane and cell exterior.



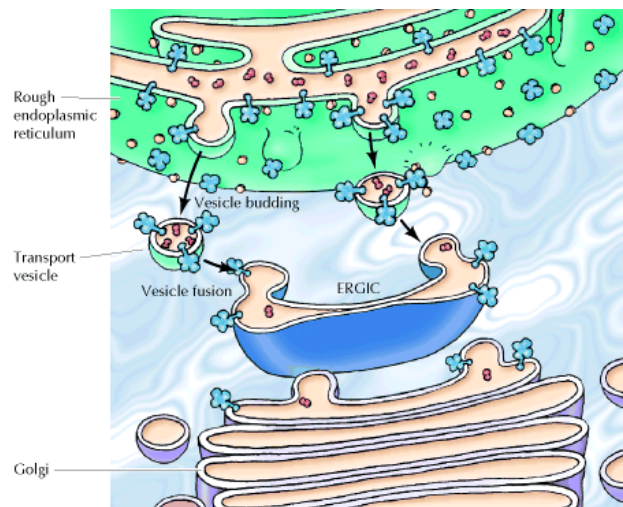
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19



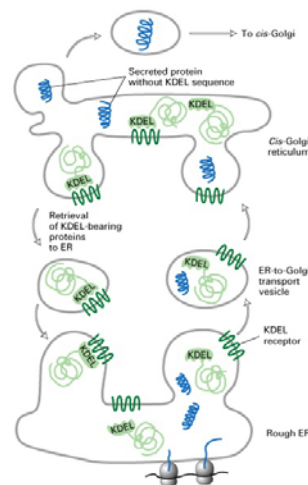
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**Figure 9.20. Vesicular transport from the ER to the Golgi** Proteins and lipids are carried from the ER to the Golgi in transport vesicles that bud from the membrane of the ER and then fuse to form the vesicles and tubules of the ER-Golgi intermediate compartment (ERGIC). Luminal ER proteins are taken up by the vesicles and released into the lumen of the Golgi. Membrane proteins maintain the same orientation in the Golgi as in the ER.

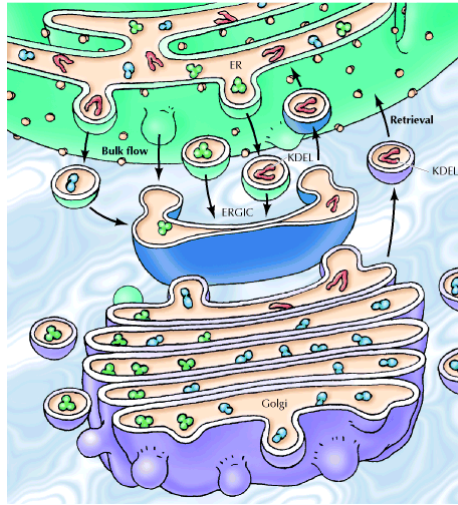
21

## ER-resident proteins often are retrieved from the *cis*-Golgi

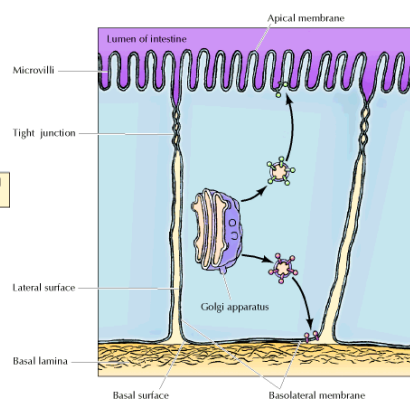
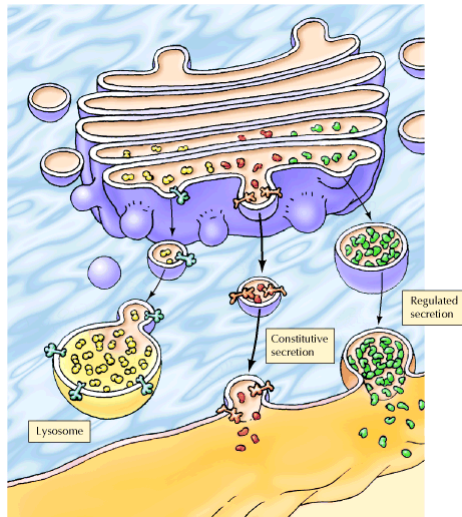


22

Lys-Asp-Glu-Leu (**KDEL**)  
C-terminal → RER

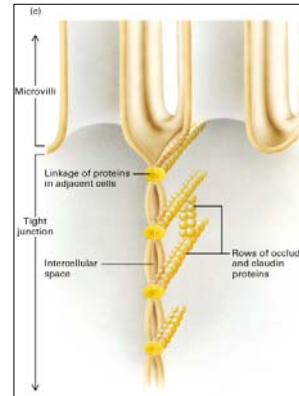
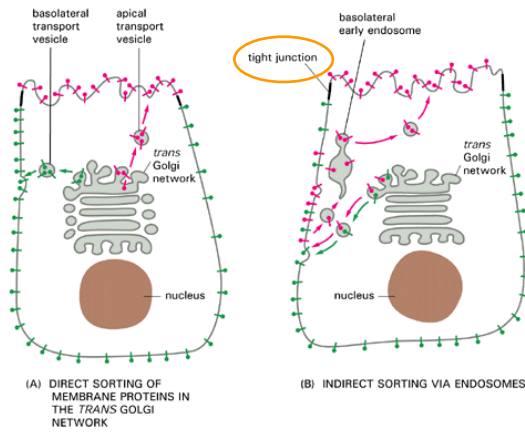


**Figure 9.21. Retrieval of resident ER proteins** Proteins destined to remain in the lumen of the ER are marked by the sequence Lys-Asp-Glu-Leu (KDEL) at their carboxy terminus. These proteins are exported from the ER to the Golgi in the nonselective bulk flow of proteins through the secretory pathway, but they are recognized by a receptor in the ER-Golgi intermediate compartment (ERGIC) or the Golgi apparatus and selectively returned to the ER.



**Figure 9.27. Transport from the Golgi apparatus** Proteins are sorted in the *trans* Golgi network and transported in vesicles to their final destinations. In the absence of specific targeting signals, proteins are carried to the plasma membrane by constitutive secretion. Alternatively, proteins can be diverted from the constitutive secretion pathway and targeted to other destinations, such as lysosomes or regulated secretion from the cells. **Figure 9.28. Transport to the plasma membrane of polarized cells** The plasma membranes of polarized epithelial cells are divided into apical and basolateral domains. In this example (intestinal epithelium), the apical surface of the cell faces the lumen of the intestine, the lateral surfaces are in contact with neighboring cells, and the basal surface rests on a sheet of extracellular matrix (the basal lamina). The apical membrane is characterized by the presence of microvilli, which facilitate the absorption of nutrients by increasing surface area. Specific proteins are targeted to either the apical or basolateral membranes in the *trans* Golgi network. Tight junctions between neighboring cells maintain the identity of the apical and basolateral membranes by preventing the diffusion of proteins between these domains.

direccionamiento a superficie apical y basolateral  
en células polarizadas (epitelios)



*tight junctions*  
uniones de oclusión  
o estancas

25



The Nobel Prize in  
Physiology or Medicine  
1999



**Günter Blobel**

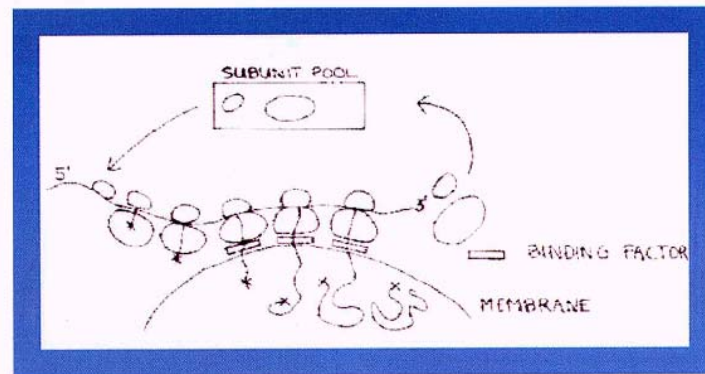
"for the discovery that proteins have intrinsic **signals** that govern their **transport and localization** in the cell"

Rockefeller University, New York, NY, USA;  
Howard Hughes Medical Institute

26

## Signal hypothesis

1971: “Las proteínas secretadas al espacio extracelular contienen una señal intrínseca que las dirige hacia y a través de las membranas”

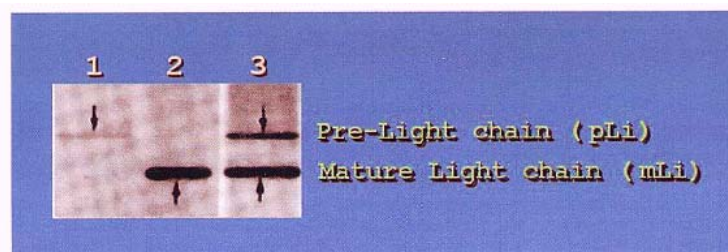


27

## Signal hypothesis

- La traducción de poly(A) mRNA de células de mieloma (principalmente mRNA de IgG) en un sistema libre de células **sin vesículas microsomales** genera una **proteína 2-3 kDa mayor**.
- El mapa peptídico indica que la extensión se encuentra en el **amino** terminal

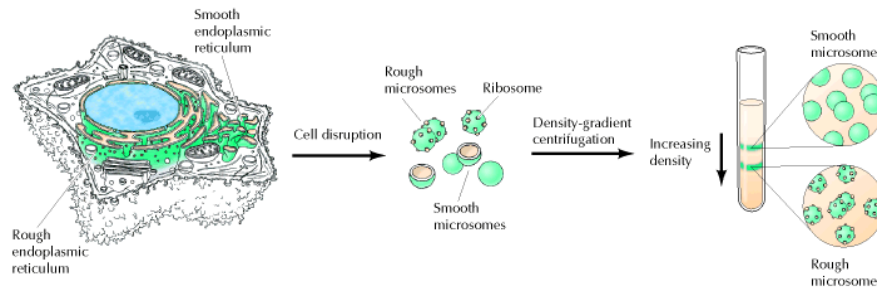
*Milstein, C. et al., Nature New Biology 239: 117-120, 1972*



28

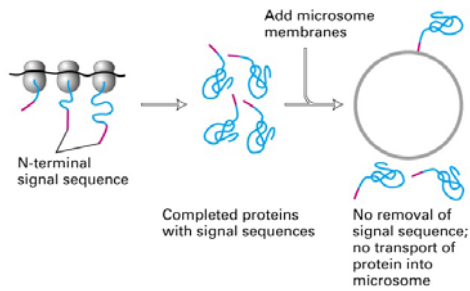


# preparación de microsomas



29

(a) Cell-free protein synthesis; no microsomes present

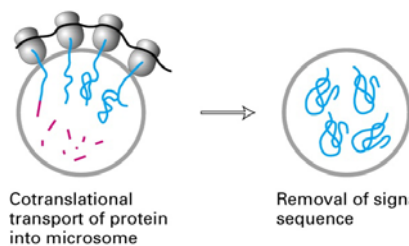


traducción *in vitro* en ausencia de microsomas

importación co-traducciona  
de las proteínas al RER:

traducción *in vitro*  
en presencia de microsomas

(b) Cell-free protein synthesis; microsomes present



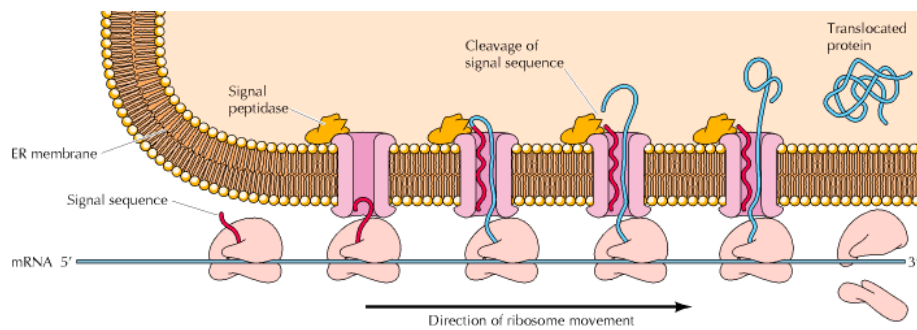
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### The signal sequence of growth hormone

Most signal sequences contain a stretch of hydrophobic amino acids, preceded by basic residues (e.g., arginine).



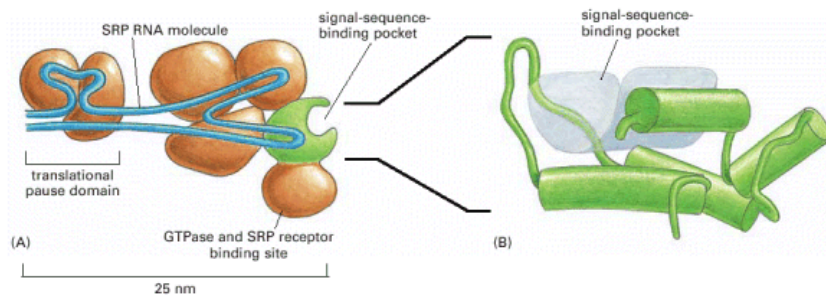
31



**The role of signal sequences in membrane translocation** Signal sequences target the translocation of polypeptide chains across the plasma membrane of bacteria or into the endoplasmic reticulum of eukaryotic cells (shown here). The signal sequence, a stretch of hydrophobic amino acids at the amino terminus of the polypeptide chain, inserts into a membrane channel as it emerges from the ribosome. The rest of the polypeptide is then translocated through the channel and the signal sequence is cleaved by the action of signal peptidase, releasing the mature translocated protein.

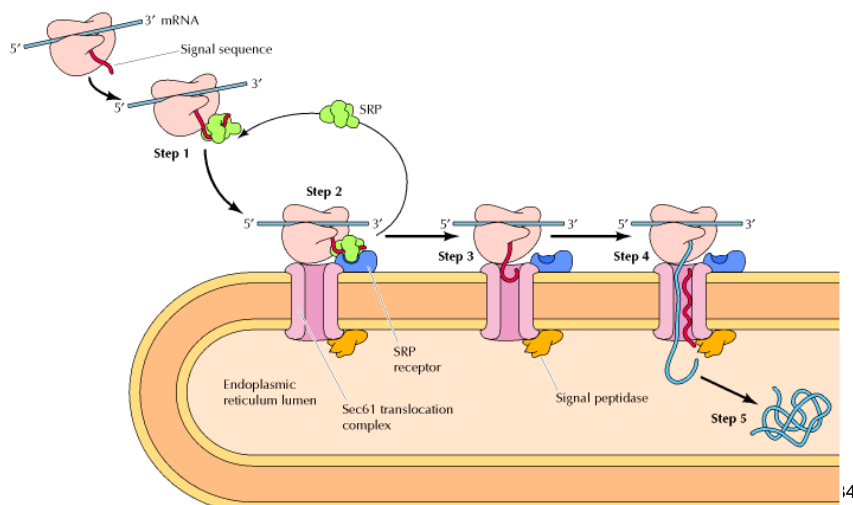


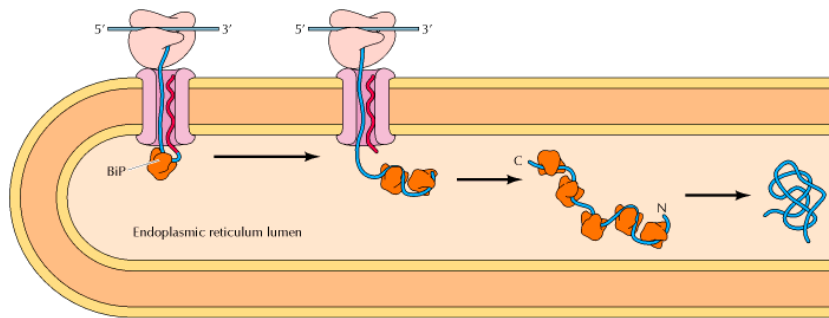
## Estructura de la partícula de reconocimiento de la señal “signal recognition particle” (SRP)



33

**Cotranslational targeting of secretory proteins to the ER** Step 1: As the signal sequence emerges from the ribosome, it is recognized and bound by the signal recognition particle (SRP). Step 2: The SRP escorts the complex to the ER membrane, where it binds to the SRP receptor. Step 3: The SRP is released, the ribosome binds to a membrane translocation complex of Sec61 proteins, and the signal sequence is inserted into a membrane channel. Step 4: Translation resumes, and the growing polypeptide chain is translocated across the membrane. Step 5: Cleavage of the signal sequence by signal peptidase releases the polypeptide into the lumen of the ER.

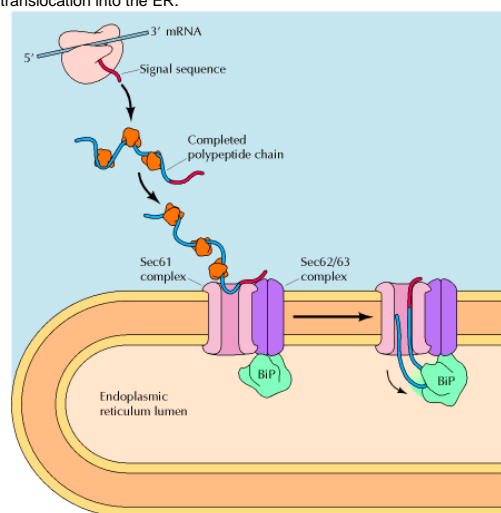




35

#### More unusual pathway for translocation of proteins into the ER

**Figure 9.8. Posttranslational translocation of proteins into the ER** Proteins destined for posttranslational import to the ER are synthesized on free ribosomes and maintained in an unfolded conformation by cytosolic chaperones. Their signal sequences are recognized by the Sec62/63 complex, which is associated with the Sec61 translocation channel in the ER membrane. The Sec63 protein is also associated with a chaperone protein (BiP), which acts as a molecular ratchet to drive protein translocation into the ER.



36

# Chaperones

Protein family	Prokaryotes	Eukaryotes	Cell compartment
Hsp70	DnaK	Hsc73	Cytosol
		BiP	endoplasmic reticulum
		SSC1	mitochondria
		ctHsp70	Chloroplasts
Hsp60	GroEL	TriC	cytosol
		Hsp60	Mitochondria
		Cpn60	chloroplasts
Hsp90	HtpG	Hsp90	Cytosol
		Grp94	endoplasmic reticulum
		Hsc73	Cytosol

37

Espacio extracelular



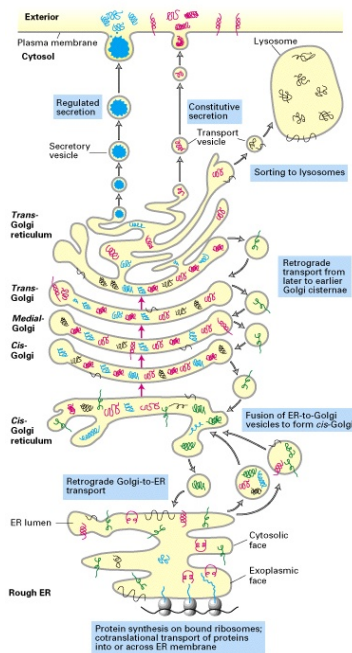
trans Golgi



Cis Golgi



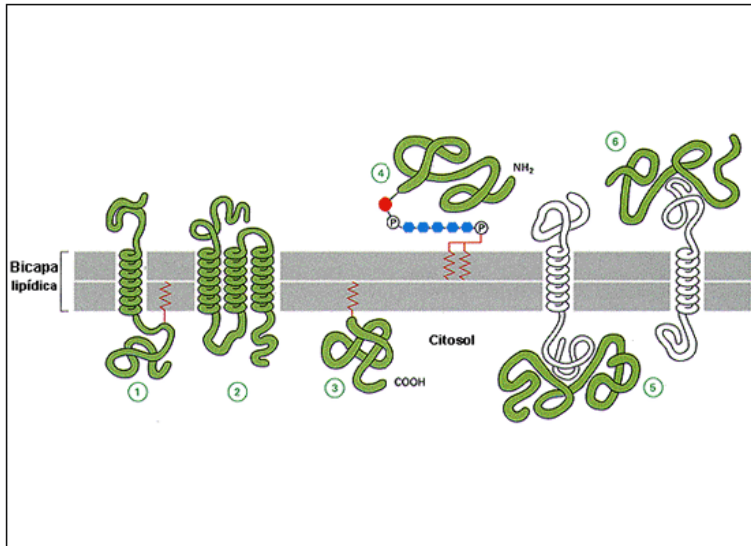
RE rugoso



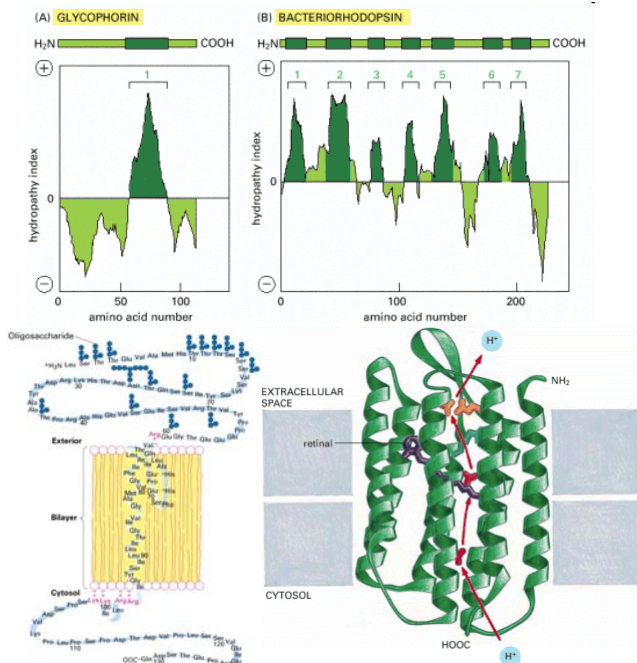
ruta secretoria

38

## proteínas de membrana

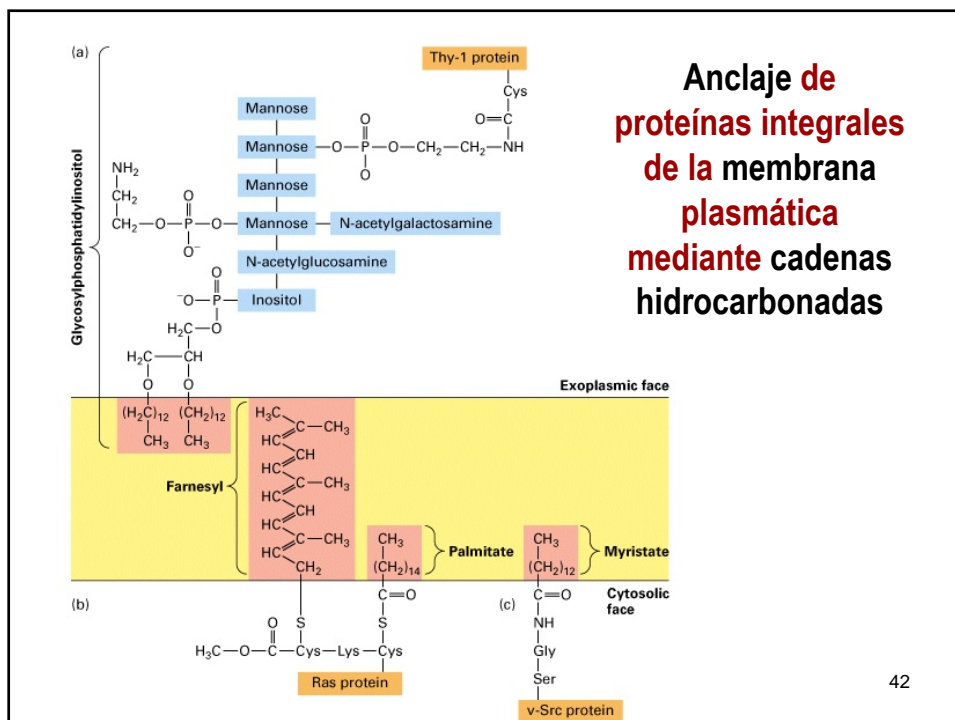
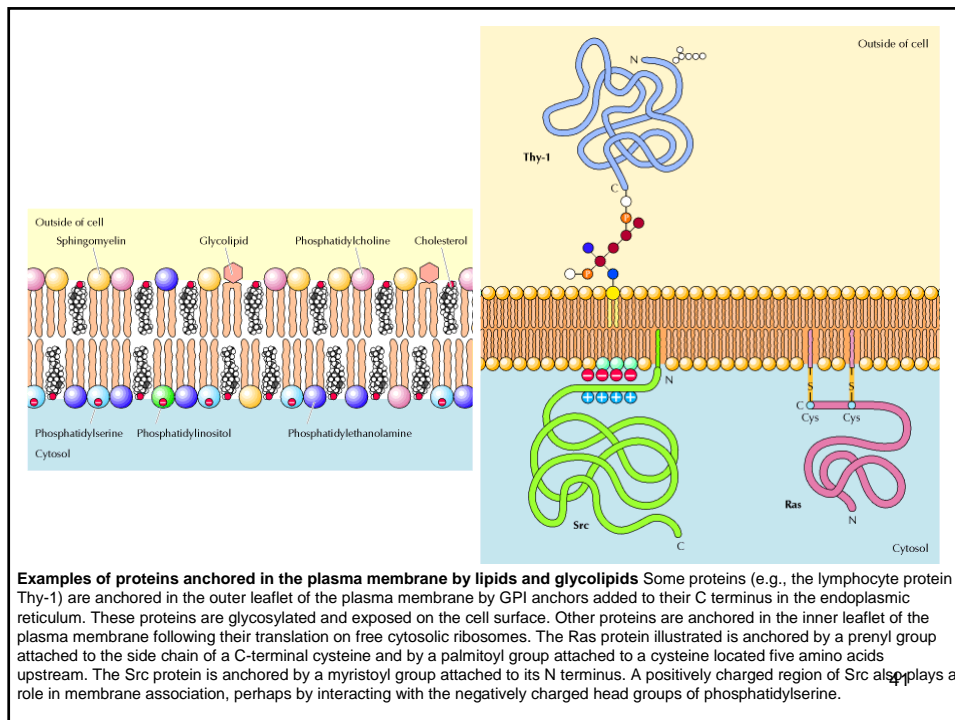


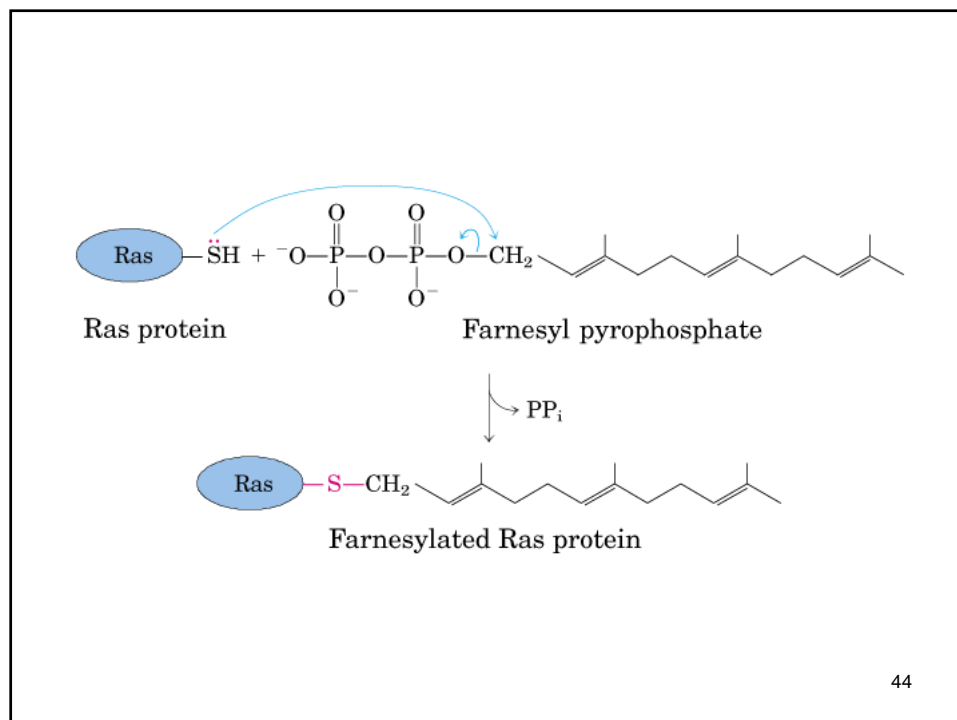
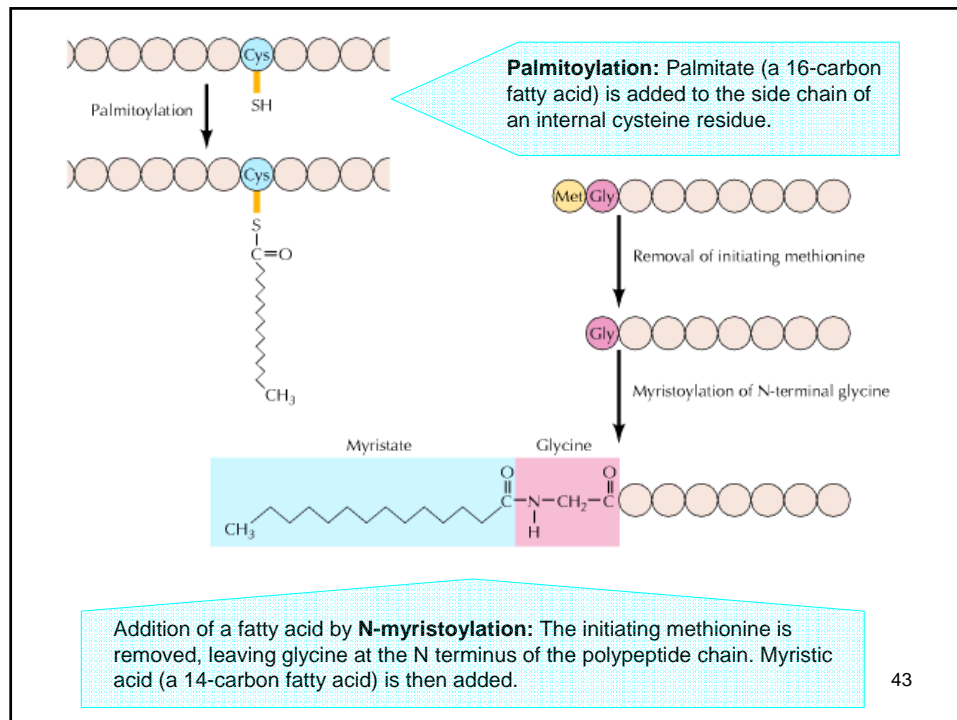
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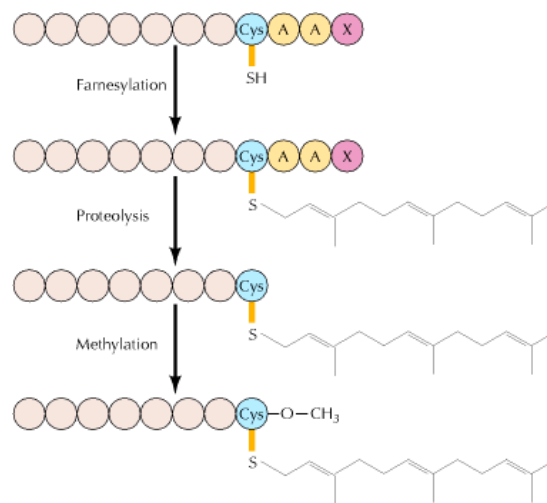


**Figure 10-37. The three-dimensional structure of a bacteriorhodopsin molecule.** The polypeptide chain **crosses the lipid bilayer seven times as  $\alpha$  helices**. The location of the retinal chromophore (*purple*) and the probable pathway taken by protons during the light-activated pumping cycle are shown. The first and key step is the passing of a  $H^+$  from the chromophore to the side chain of aspartic acid 85 (*red*, located next to the chromophore) that occurs upon absorption of a photon by the chromophore. Subsequently, other  $H^+$  transfers—utilizing the hydrophilic amino acid side chains that line a path through the membrane—complete the pumping cycle and return the enzyme to its starting state. Color code: glutamic acid (*orange*), aspartic acid (*red*), arginine (*blue*). (Adapted from H. Luecke et al., *Science* 286:255–260, 1999.) [Alberts 2002](#)

40







**Prenylation of a C-terminal cysteine residue:** The type of prenylation shown affects Ras proteins and proteins of the nuclear envelope (nuclear lamins). These proteins terminate with a cysteine residue (Cys) followed by two aliphatic amino acids (A) and any other amino acid (X) at the C terminus. The first step in their modification is addition of the 15-carbon farnesyl group to the side chain of cysteine (farnesylation). This step is followed by proteolytic removal of the three C-terminal amino acids and methylation of the cysteine, which is now at the C terminus.

After insertion into the ER membrane, some proteins are transferred to a GPI anchor

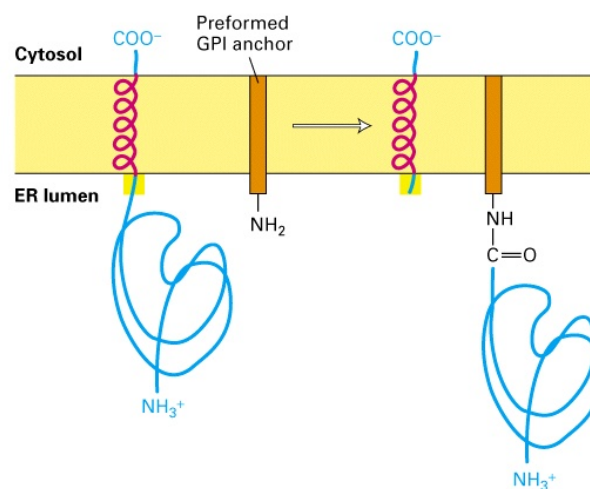
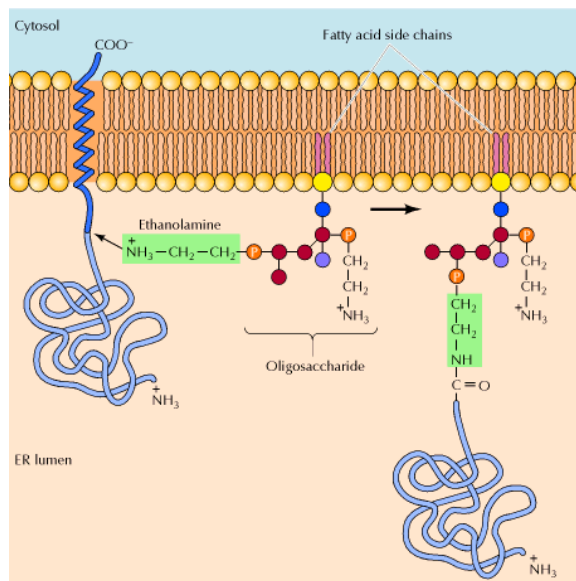


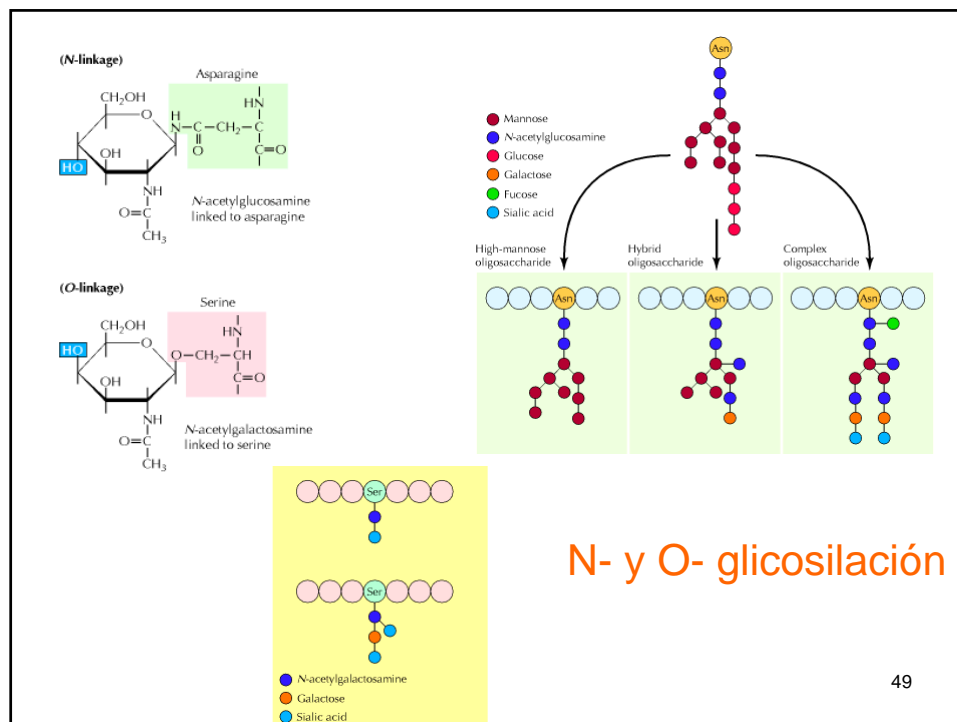
Figure 17-25  
46



**Addition of GPI anchors: Glycosylphosphatidylinositol (GPI)** anchors contain two fatty acid chains, an oligosaccharide portion consisting of inositol and other sugars, and ethanolamine. The GPI anchors are assembled in the ER and added to polypeptides anchored in the membrane by a carboxy-terminal membrane-spanning region. The membranespanning region is cleaved, and the new carboxy terminus is joined to the NH<sub>2</sub> group of ethanolamine immediately after translation is 47 completed, leaving the protein attached to the membrane by the GPI anchor.

glicosilación de proteínas





49

## ABO blood type is determined by two glycosyltransferases

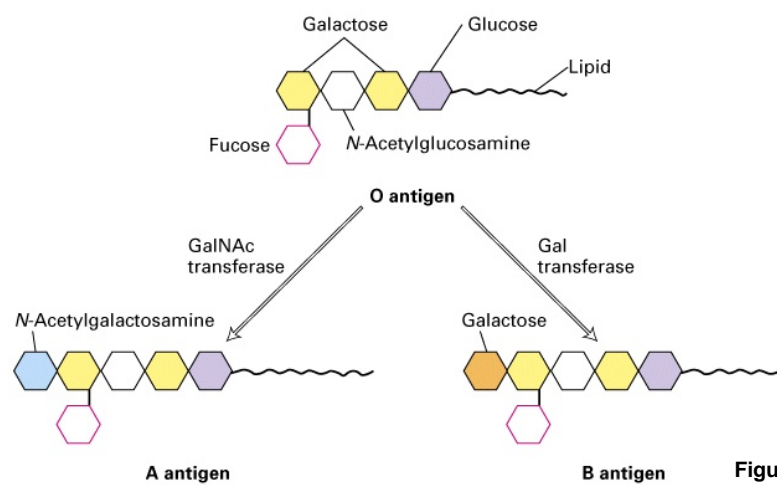
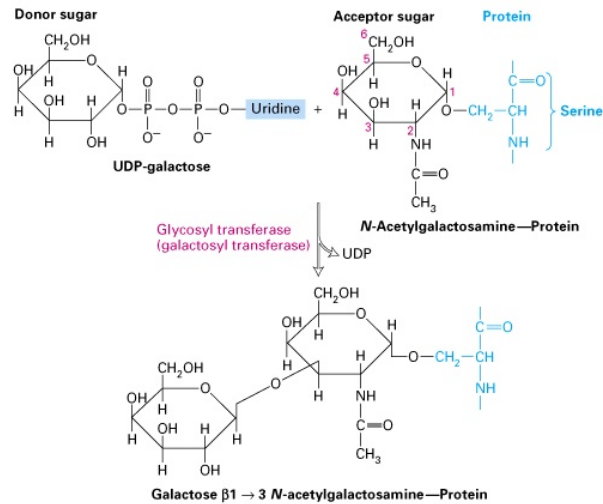
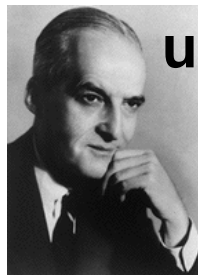


Figure 17-34  
50

Las **glicosiltransferasas** adicionan azúcares en forma específica utilizando **nucleótidos-azúcares** como dadores



51



## uridina-difosfato-glucosa UDPG

Luis Federico Leloir (1906-1987)  
Premio Nobel de Química (1970)



Luis F. Leloir  
Two decades of research  
on the biosynthesis of saccharides

Nobel Lecture, 11 December, 1970



52

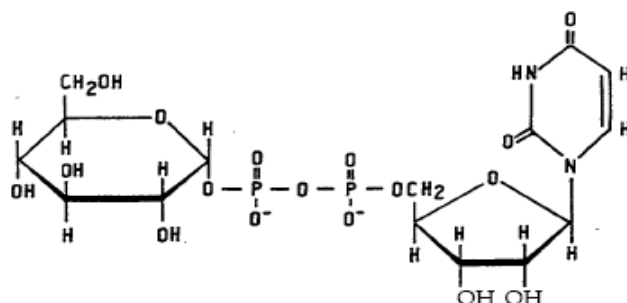
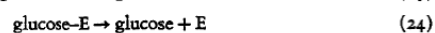
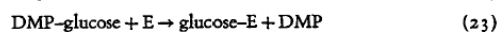
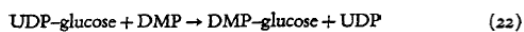
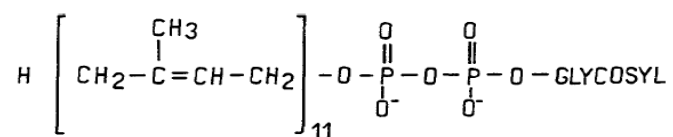
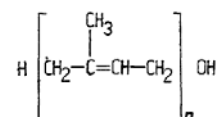


Fig. 1. Uridine diphosphate glucose (UDPG).

10. R.Caputto, L.F.Leloir, R.E.Trucco, C.E.Cardini and A.C.Paladini, *Arch.Biochem.*, 18(1948) 201.  
 9. R.Caputto, L.F.Leloir, C.E.Cardini, and A.C.Paladini, *J.Biol.Chem.*, 184(1950) 333.  
 12. C.E.Cardini, A. C. Paladini, R.Caputto and L.F.Leloir, *Nature*, 165(1950) 191.  
 48. E.Recondo, M.Dankert and L.F.Leloir, *Biochem.Biophys.Res.Comm.*, 12(1963) 204

53

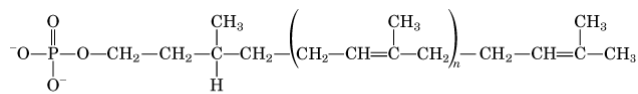
## Lipid Intermediates



In these equations DMP stands for dolichol monophosphate and E for an endogenous acceptor believed to be a protein.

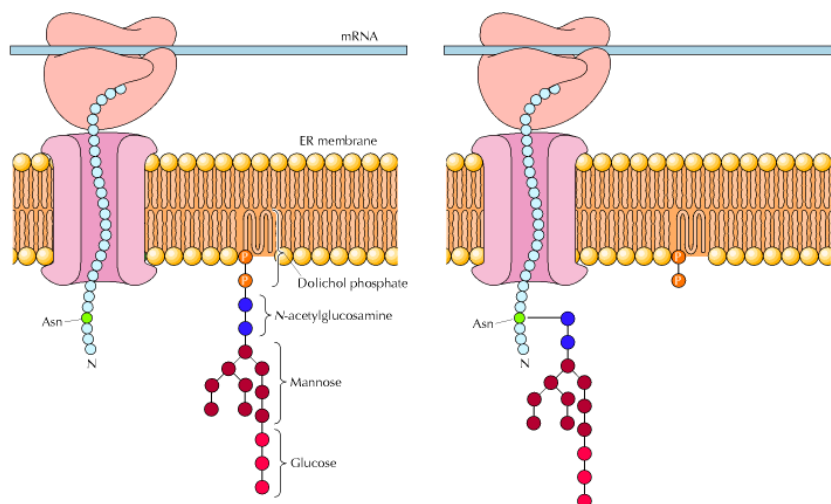
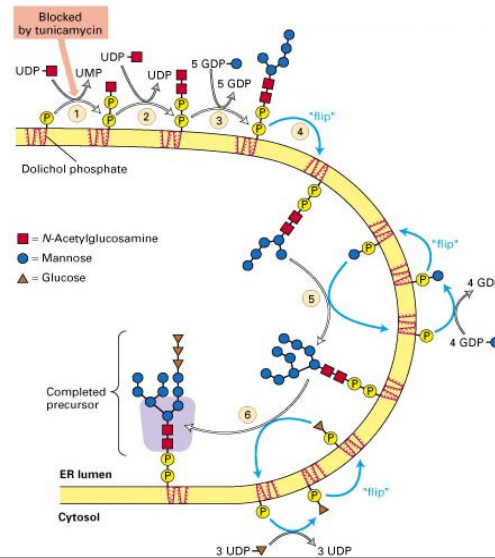
- A.Wright, M.Dankert, P.Fennesey and P.W.Robbins, *Proc.Natl.Acad.Sci.(U.S.)*, 57 (1967) 1798.  
 N. H. Behrens and L. F. Leloir, *Proc. Natl.Acad.Sci. (U.S.)*, 66 (1970) 153.

54

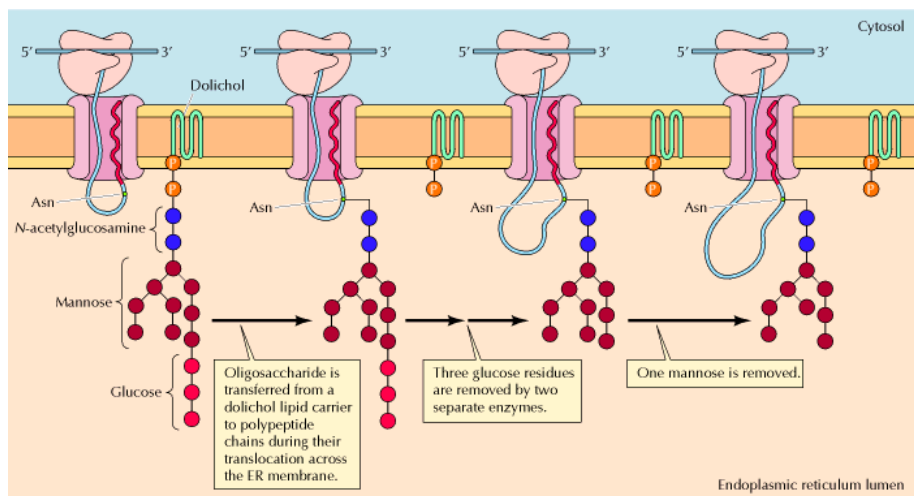


Dolichol phosphate  
( $n = 9-22$ )

A common  
**preformed N-linked  
oligosaccharide**  
is added to many  
proteins  
in the **rough ER**



**Figure 7.26. Synthesis of N-linked glycoproteins** The first step in glycosylation is the addition of an oligosaccharide consisting of 14 sugar residues to a growing polypeptide chain in the endoplasmic reticulum (ER). The oligosaccharide (which consists of two *N*-acetylglucosamine, nine mannose, and three glucose residues) is assembled on a lipid carrier (dolichol phosphate) in the ER. It is then transferred as a unit to an acceptor asparagine residue of the polypeptide.



57

*Science*, **298**, 1790-1793 (2002)

## N-Linked Glycosylation in *Campylobacter jejuni* and Its Functional Transfer into *E. coli*

Michael Wacker,<sup>1\*</sup> Dennis Linton,<sup>2\*</sup> Paul G. Hitchen,<sup>3</sup>  
 Mihai Nita-Lazar,<sup>1</sup> Stuart M. Haslam,<sup>3</sup> Simon J. North,<sup>3</sup>  
 Maria Panico,<sup>3</sup> Howard R. Morris,<sup>3,4</sup> Anne Dell,<sup>3</sup>  
 Brendan W. Wren,<sup>2</sup> Markus Aebi<sup>1†</sup>

N-linked protein glycosylation is the most abundant posttranslation modification of secretory proteins in eukaryotes. A wide range of functions are attributed to glycan structures covalently linked to asparagine residues within the asparagine-X-serine/threonine consensus sequence (Asn-Xaa-Ser/Thr). We found an N-linked glycosylation system in the bacterium *Campylobacter jejuni* and demonstrate that a functional N-linked glycosylation pathway could be transferred into *Escherichia coli*. Although the bacterial N-glycan differs structurally from its eukaryotic counterparts, the cloning of a universal N-linked glycosylation cassette in *E. coli* opens up the possibility of engineering permutations of recombinant glycan structures for research and industrial applications.

58

## Disulfide bonds are formed and rearranged in the ER lumen

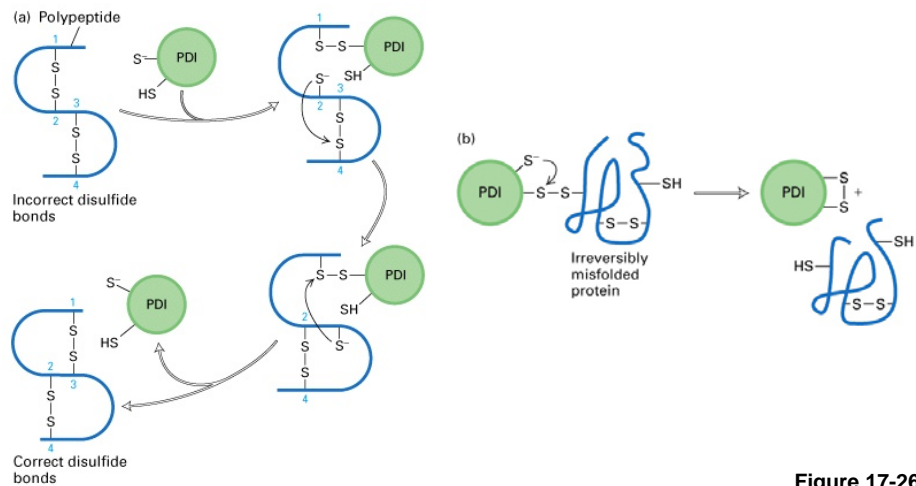
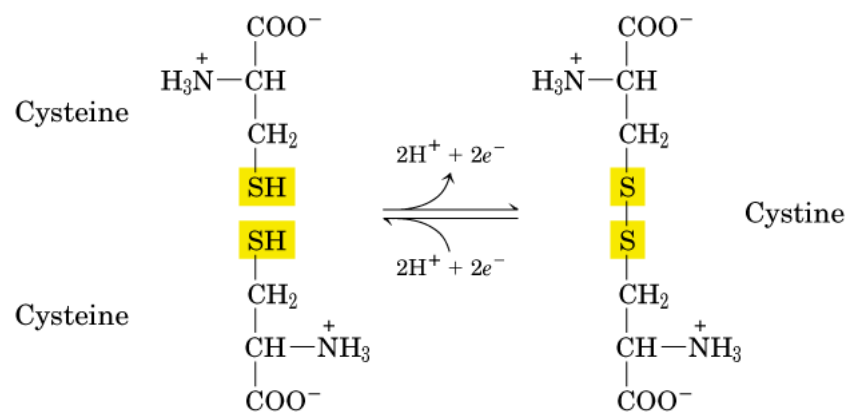
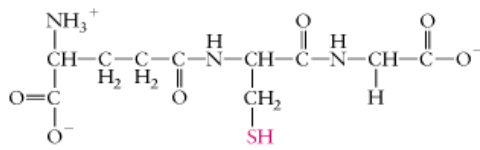


Figure 17-26  
59

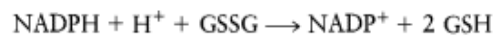




**glutathione (GSH)**

The **GSH:GSSG** ratio is over **50:1** in the **cytosol**; oxidized GSSG in the cytosol is reduced by the enzyme glutathione reductase, using electrons from the potent reducing agent NADPH

Thus, **cytosolic proteins** in bacterial and eukaryotic cells **do not utilize the disulfide bond** as a stabilizing force because the high GSH:GSSG ratio would drive the system in the direction of Cys SH and away from Cys S-S Cys.



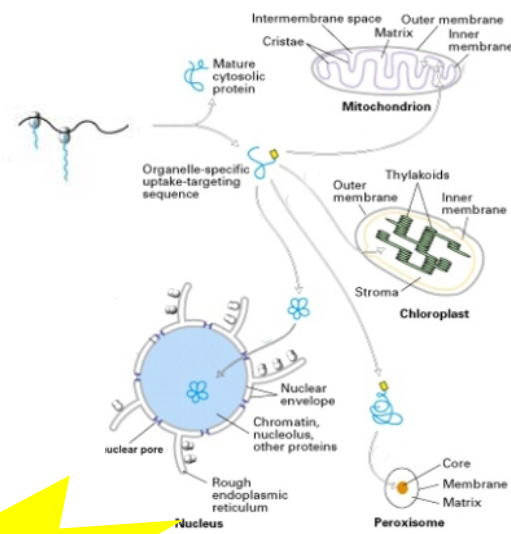
61

## Post-translational modifications and quality control in the rough ER

- Newly synthesized polypeptides in the membrane and lumen of the ER undergo five principal modifications
  - Formation of disulfide bonds
  - Proper folding
  - Addition and processing of carbohydrates
  - Specific proteolytic cleavages
  - Assembly into multimeric proteins

62

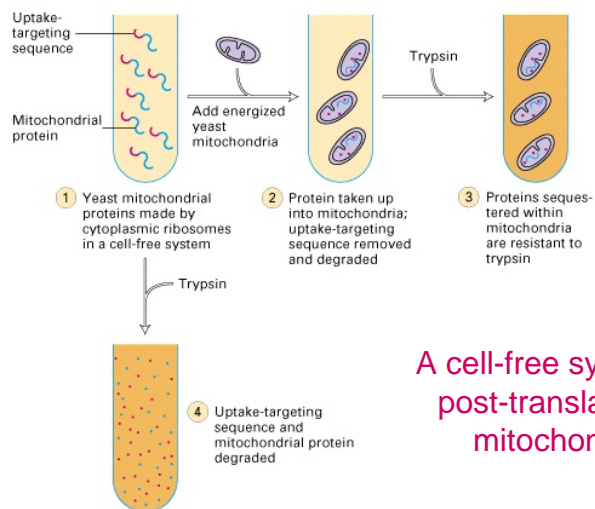
Las proteínas destinadas al **citósol** o a ser incorporadas en el **núcleo**, **mitocondria**, **cloroplasto** o **peroxisoma** son sintetizadas a en ribosomas libres, no asociados a membranas



**Direccionamiento postraducciona**

63

## Direccionamiento postraducciona de proteínas sintetizadas en citósol



A cell-free system for studying post-translational uptake of mitochondrial proteins

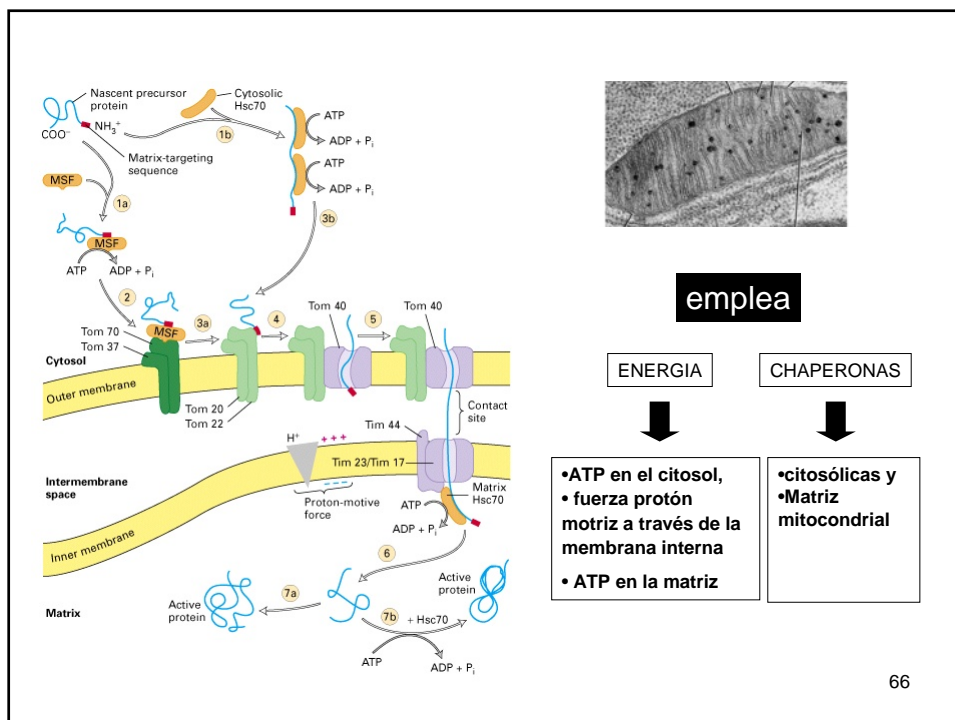
64



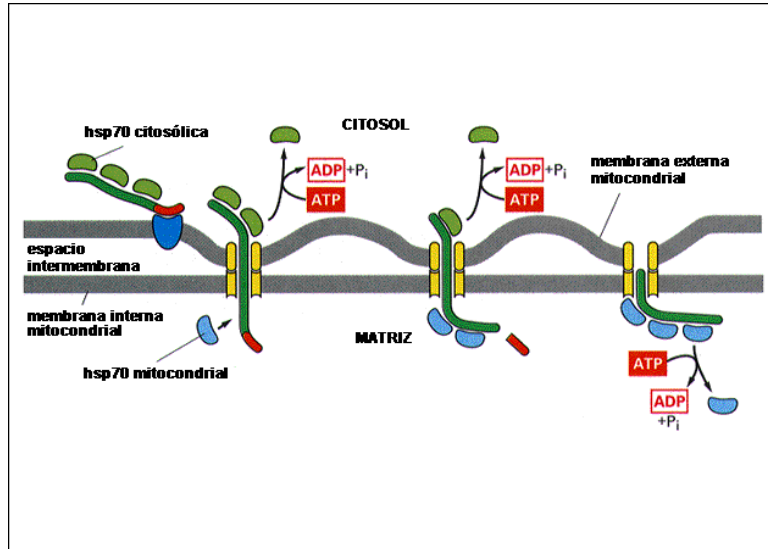
## ¿Qué elementos son requeridos para el direccionamiento mitocondrial?

- Una o más señales en la proteína
- Un receptor que reconozca la señal y direcciona la proteína a la membrana correcta
- Una maquinaria de translocación, un canal
- Energía para abrir la compuerta y translocar la proteína
- **Chaperonas para desplegar la proteína ya sintetizada**

65

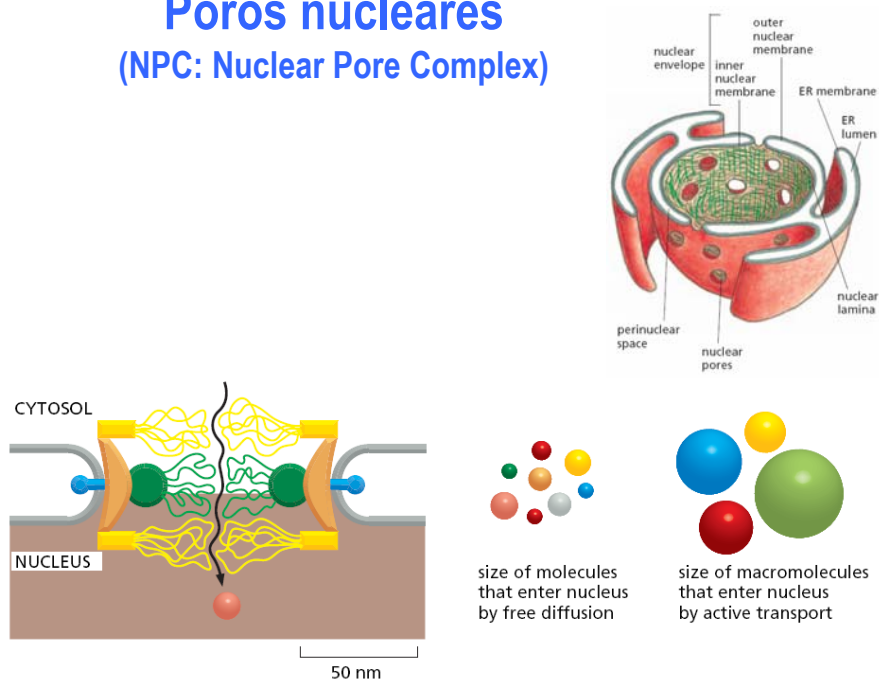


## direccionamiento a mitocondrias

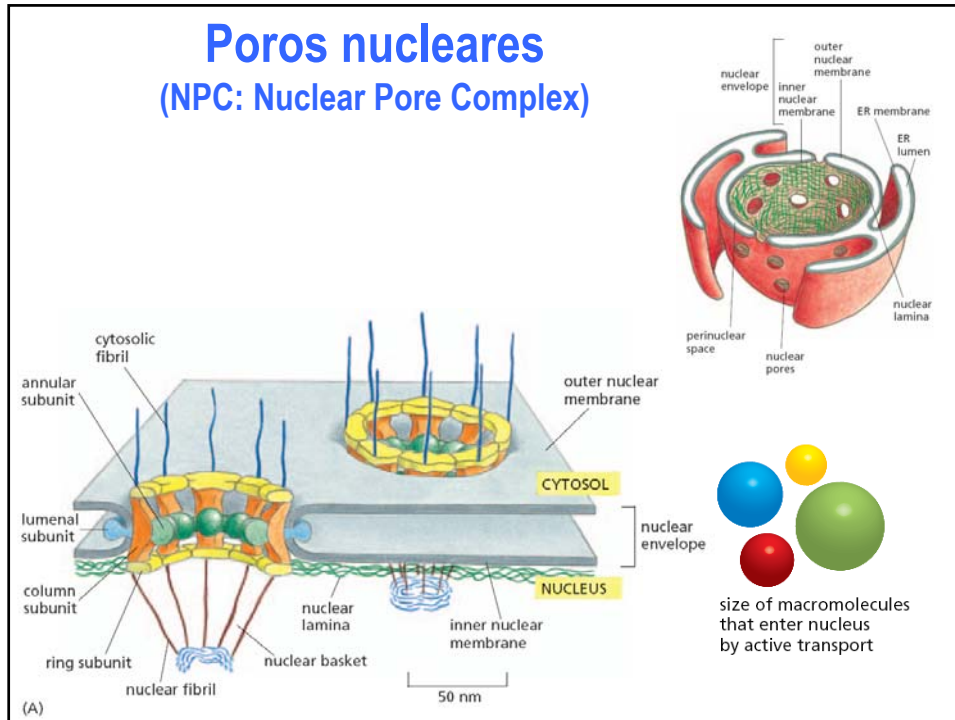


67

## Poros nucleares (NPC: Nuclear Pore Complex)



## Poros nucleares (NPC: Nuclear Pore Complex)

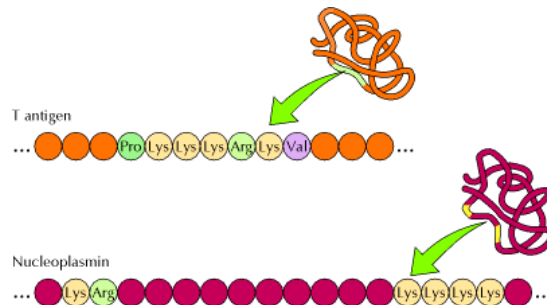


## ¿Qué elementos son requeridos para la entrada al núcleo?

- Una **REGION SEÑAL** en la proteína (no es clivada!!)
- Un receptor que reconozca la señal y direcciona la proteína
- Una maquinaria de translocación, un canal
- Energía para translocar la proteína

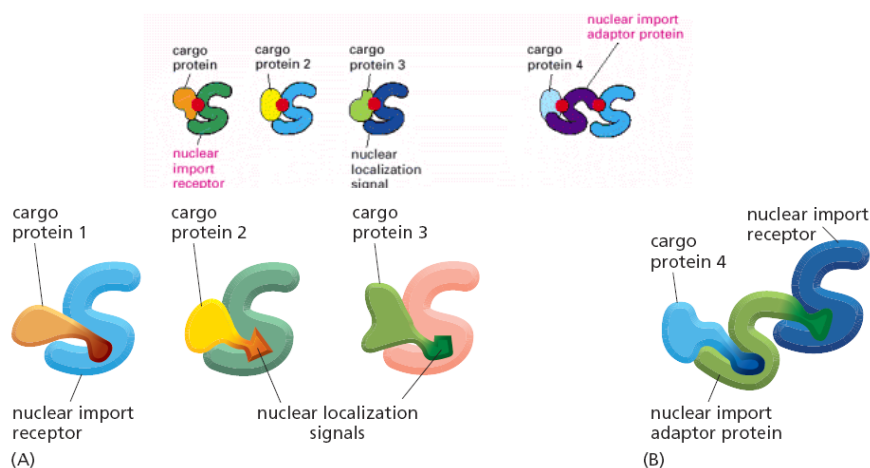
## Importación al núcleo: señal de localización nuclear NLS

(señales con un bloque de varios aminoácidos básicos y señales bipartitas)



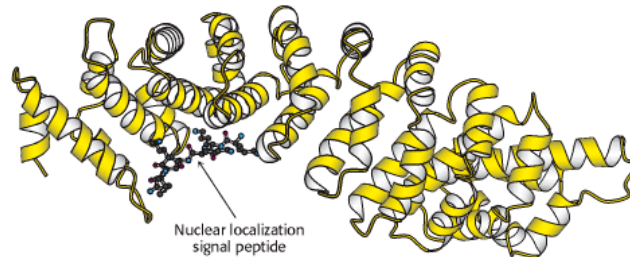
**Nuclear localization signals:** The T antigen nuclear localization signal is a single stretch of amino acids. In contrast, the nuclear localization signal of nucleoplasmin is bipartite, consisting of a Lys-Arg sequence, followed by a Lys-Lys-Lys-Lys sequence located ten amino acids farther downstream

## Proteínas transportadoras: reconocen NLS



**Nuclear import receptors.** (A) Many nuclear import receptors bind both to nucleoporins and to a nuclear localization signal on the cargo proteins they transport. Cargo proteins 1, 2, and 3 in this example contain different nuclear localization signals, which causes each to bind to a different nuclear import receptor. (B) Cargo protein 4 shown here requires an adaptor protein to bind to its nuclear import receptor. The adaptors are structurally related to nuclear import receptors and recognize nuclear localization signals on cargo proteins. They also contain a nuclear localization signal that binds them to an import receptor

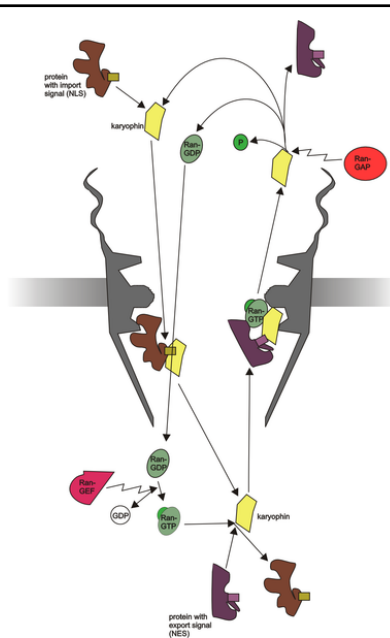
## Transporte de polipéptidos al núcleo: importina



Protein Targeting Signal Recognition. The structure of the nuclear localization signal-binding protein  **$\alpha$ -karyopherin** (also known as  **$\alpha$ -importin**) with a nuclear localization signal peptide bound to its major recognition site.

<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Search&db=books&doptcmdl=GenBookHL&term=nuclear+localization+signal+AND+stryer%5Bbook%5D+AND+215912%5Buid%5D&rid=stryer.figgrp.1705>

73



## Transporte de polipéptidos al núcleo: importina

The entry and exit of large molecules from the cell nucleus is tightly controlled by the nuclear pore complexes (NPCs). Although small molecules can enter the nucleus without regulation, macromolecules such as RNA and proteins require association with karyopherins called importins to enter the nucleus and exportins to exit.

### Karyopherins

#### Importins

Kap95/Kap60  
Kap104  
Kap121  
Kap123  
Kap125  
Nrm5  
Nrm6  
Nrm7  
Nrm8  
Nrm9  
Nrm10  
Nrm11  
Nrm12  
Nrm13  
Nrm14  
Nrm15

#### Exportins

Crm1  
Cse1  
Kap120  
Ltn1  
Mex67-Atb2  
Nrm5  
Nrm6  
Nrm7  
Nrm8  
Nrm9  
Nrm10  
Nrm11  
Nrm12  
Nrm13  
Nrm14  
Nrm15

#### Transportins

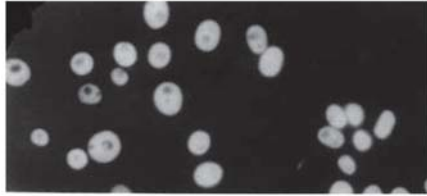
Nrm5



## Importación al núcleo: señal de localización nuclear NLS

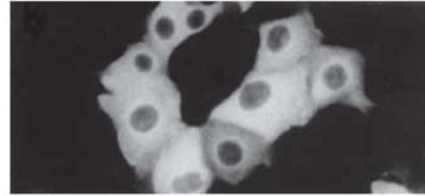
(A) LOCALIZATION OF T-ANTIGEN CONTAINING ITS NORMAL NUCLEAR IMPORT SIGNAL

Pro — Pro — Lys — Lys — Lys — Arg — Lys — Val —



(B) LOCALIZATION OF T-ANTIGEN CONTAINING A MUTATED NUCLEAR IMPORT SIGNAL

Pro — Pro — Lys — Thr — Lys — Arg — Lys — Val —

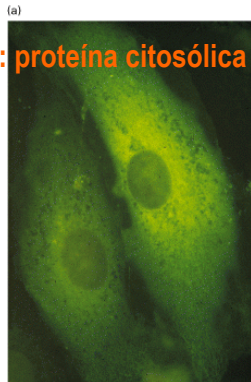


The function of a nuclear localization signal. Immunofluorescence micrographs showing the cellular location of SV40 virus T-antigen containing or lacking a short peptide that serves as a nuclear localization signal. (A) The normal T-antigen protein contains the lysine-rich sequence indicated and is imported to its site of action in the nucleus, as indicated by immunofluorescence staining with antibody against the T-antigen. (B) T-antigen with an altered nuclear localization signal (a threonine replacing a lysine) remains in the cytosol. (From D. Kalderon, B. Roberts, W. Richardson, and A. Smith, *Cell* 39:499–509, 1984. © Elsevier.)

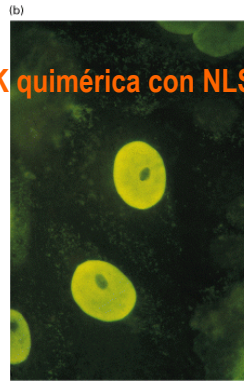
75

## Importación al núcleo: señal de localización nuclear NLS

PyrK: proteína citosólica



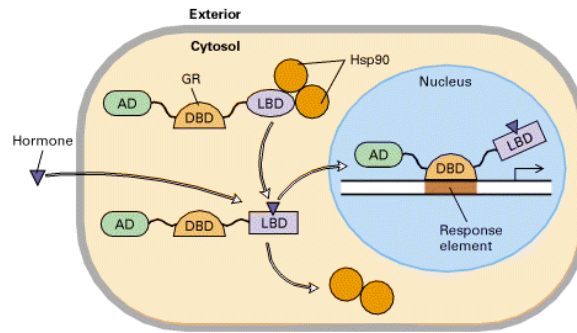
PyrK quimérica con NLS de SV40



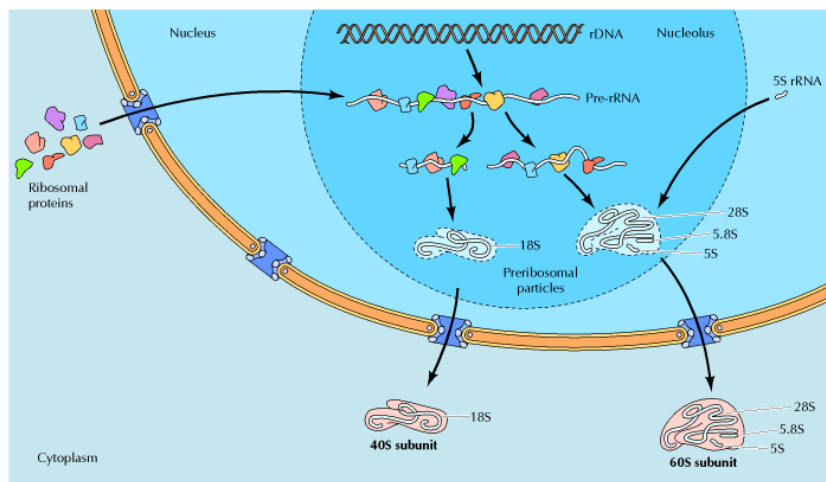
Demonstration that the nuclear-localization signal (NLS) of the SV40 large T-antigen can direct a cytoplasmic protein to the cell nucleus. (a) Normal pyruvate kinase, visualized by immunofluorescence after treating cultured cells with a specific antibody, is localized to the cytoplasm. (b) A chimeric pyruvate kinase protein, containing the SV40 NLS at its N-terminus, is directed to the nucleus. The chimeric protein was expressed from a transfected engineered gene produced by fusing a viral gene fragment encoding the SV40 NLS to the pyruvate kinase gene. [From D. Kalderon et al., 1984, *Cell* 39:499; courtesy Dr. Alan Smith.]

76

## Importación al núcleo: exposición de NLS cambio conformacional por unión a un ligando (traslocación del receptor de glucocorticoides → activación de la transcripción)



Model of hormone-dependent gene activation by the glucocorticoid receptor (GR). In the absence of hormone, GR is bound in a complex with Hsp90 in the cytoplasm via its ligand-binding domain (light purple). When hormone is present, it diffuses through the plasma membrane and binds to the GR ligand-binding domain, causing a conformational change in the ligand-binding domain that releases the receptor from Hsp90. The receptor with bound ligand is then translocated into the nucleus where its DNA-binding domain (orange) binds to response elements, allowing the activation domain (green) to stimulate transcription of target genes



**Ribosome assembly** Ribosomal proteins are imported to the nucleolus from the cytoplasm and begin to assemble on pre-rRNA prior to its cleavage. As the pre-rRNA is processed, additional ribosomal proteins and the 5S rRNA (which is synthesized elsewhere in the nucleus) assemble to form pre-ribosomal particles. The final steps of maturation follow the export of pre-ribosomal particles to the cytoplasm, yielding the 40S and 60S ribosomal subunits.

78

## señales de direccionamiento:

en un bloque o en varias partes

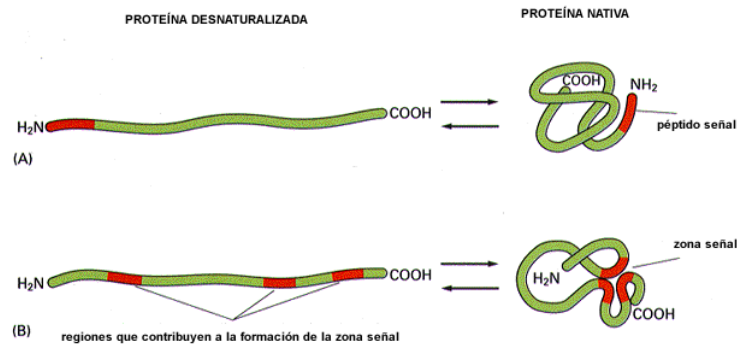


Figure 12-8. Two ways in which a sorting signal can be built into a protein. (A) The signal resides in a single discrete stretch of amino acid sequence, called a signal sequence, that is exposed in the folded protein. Signal sequences often occur at the end of the polypeptide chain (as shown), but they can also be located internally. (B) A signal patch can be formed by the juxtaposition of amino acids from regions that are physically separated before the protein folds (as shown). Alternatively, separate patches on the surface of the folded protein that are spaced a fixed distance apart can form the signal.

## Señales de direccionamiento de proteínas

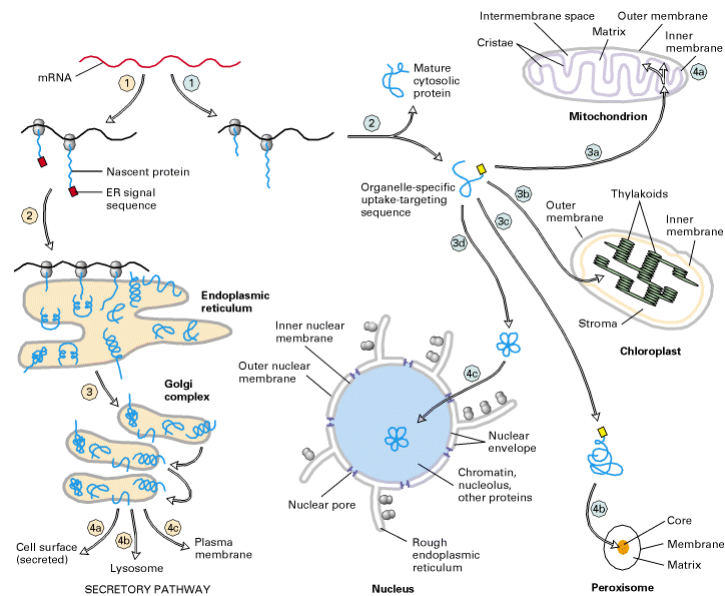
Table 12-3 Some Typical Signal Sequences

FUNCTION OF SIGNAL SEQUENCE	EXAMPLE OF SIGNAL SEQUENCE
Import into nucleus	-Pro-Pro-Lys-Lys-Lys-Arg-Lys-Val-
Export from nucleus	-Leu-Ala-Leu-Lys-Leu-Ala-Gly-Leu-Asp-Ile-
Import into mitochondria	*H <sub>3</sub> N-Met-Leu-Ser-Leu-Arg-Gln-Ser-Ile-Arg-Phe-Phe-Lys-Pro-Ala-Thr-Arg-Thr-Leu-Cys-Ser-Ser-Arg-Tyr-Leu-Leu-
Import into plastid	*H <sub>3</sub> N-Met-Val-Ala-Met-Ala-Met-Ala-Ser-Leu-Gln-Ser-Ser-Met-Ser-Ser-Leu-Ser-Leu-Ser-Ser-Asn-Ser-Phe-Leu-Gly-Gln-Pro-Leu-Ser-Pro-Ile-Thr-Leu-Ser-Pro-Phe-Leu-Gln-Gly-
Import into peroxisomes	-Ser-Lys-Leu-COO <sup>-</sup>
Import into ER	*H <sub>3</sub> N-Met-Met-Ser-Phe-Val-Ser-Leu-Leu-Leu-Val-Gly-Ile-Leu-Phe-Trp-Ala-Thr-Glu-Ala-Glu-Gln-Leu-Thr-Lys-Cys-Glu-Val-Phe-Gln-
Return to ER	-Lys-Asp-Glu-Leu-COO <sup>-</sup>

Some characteristic features of the different classes of signal sequences are highlighted in color. Where they are known to be important for the function of the signal sequence, positively charged amino acids are shown in red and negatively charged amino acids are shown in green. Similarly, important hydrophobic amino acids are shown in white and important hydroxylated amino acids are shown in blue. \*H<sub>3</sub>N indicates the N-terminus of a protein; COO<sup>-</sup> indicates the C-terminus.

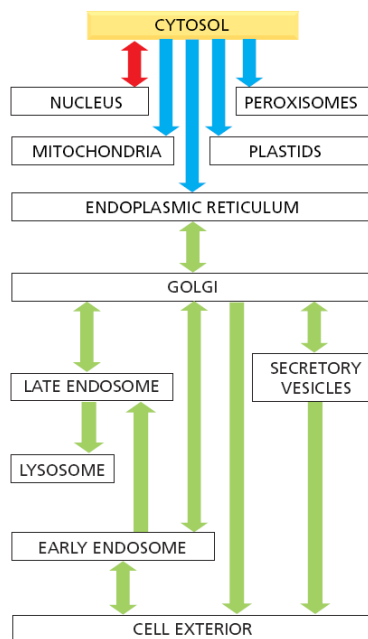


## Direccinamiento de proteínas



81

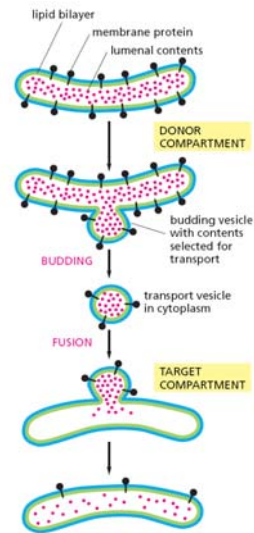
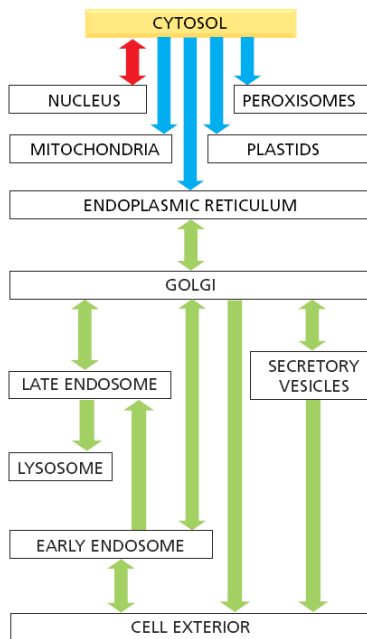
## Direccinamiento de proteínas



KEY:   
█ = gated transport   
█ = transmembrane transport   
█ = vesicular transport

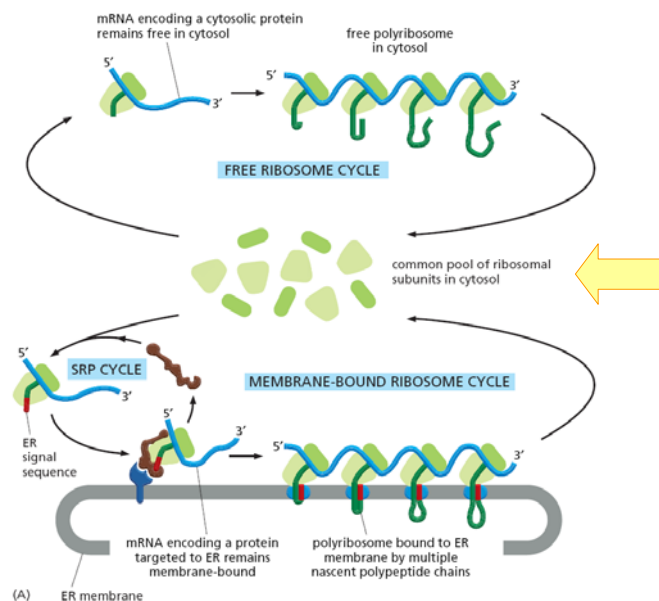
82

## Direcccionamiento de proteínas



83

## pool de subunidades ribosómicas



84