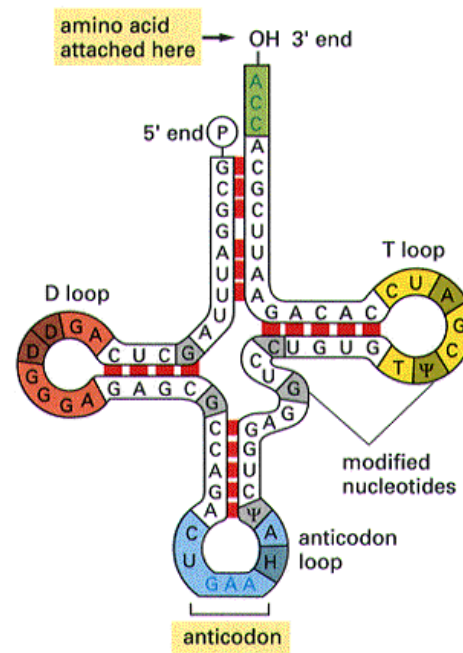


Traduzione e indirizzamento delle proteine

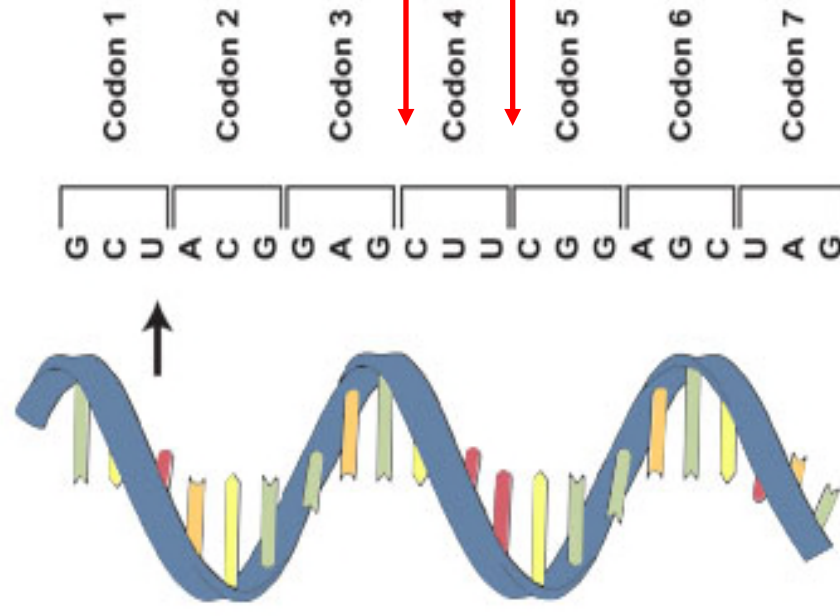
Traduzione



tRNA

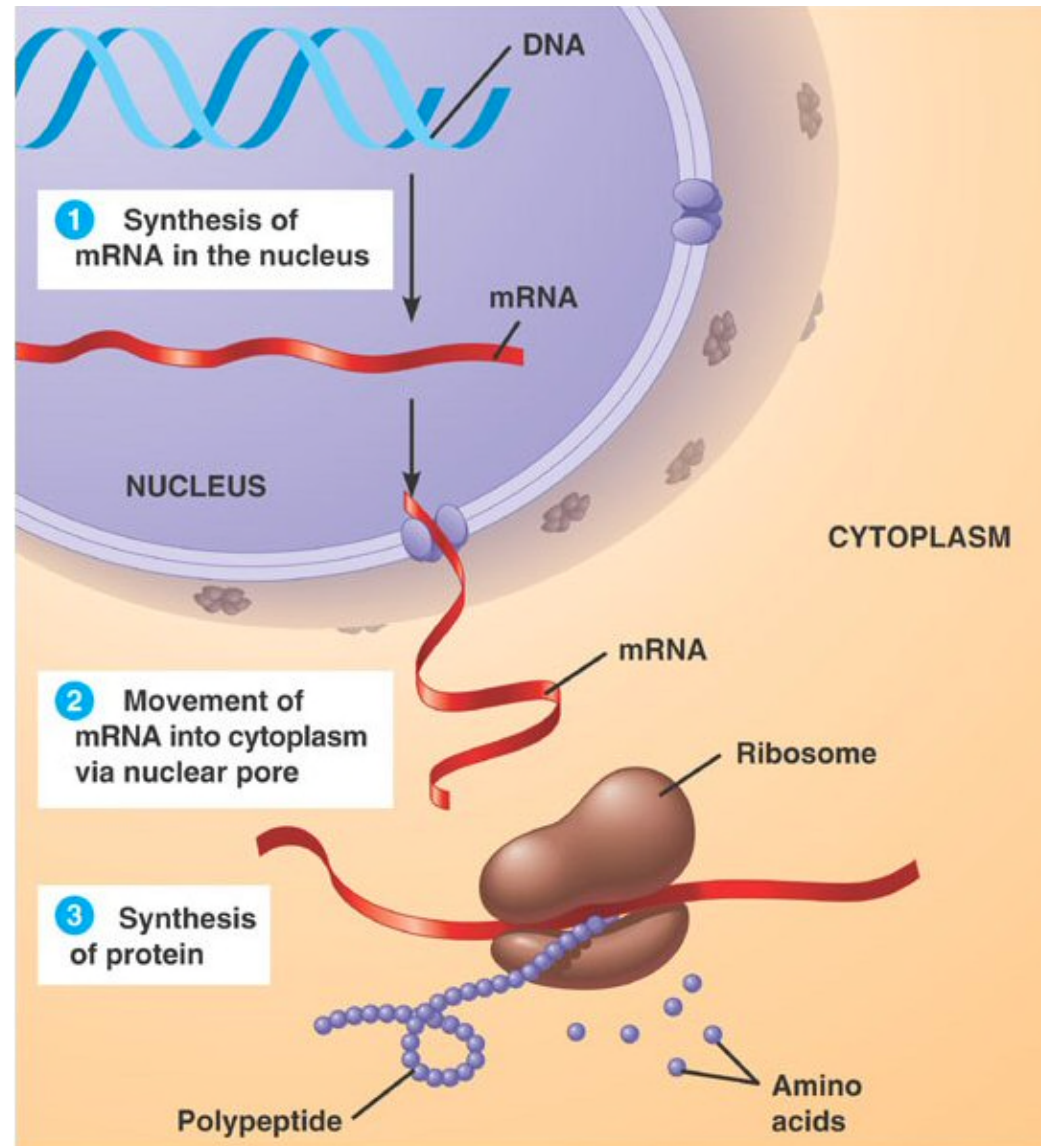


Traduzione:
mRNA -----> proteine



mRNA

Traduzione delle proteine: avviene nel citoplasma





The Nobel Prize in Chemistry 2009

"for studies of the structure and function of the ribosome"



4



Photo: MRC Laboratory
of Molecular Biology

**Venkatraman
Ramakrishnan**

🕒 1/3 of the prize

United Kingdom

MRC Laboratory of
Molecular Biology
Cambridge, United
Kingdom



Credits: Michael
Marsland/Yale University

Thomas A. Steitz

🕒 1/3 of the prize

USA

Yale University
New Haven, CT,
USA; Howard
Hughes Medical
Institute



Credits: Micheline
Pelletier/Corbis

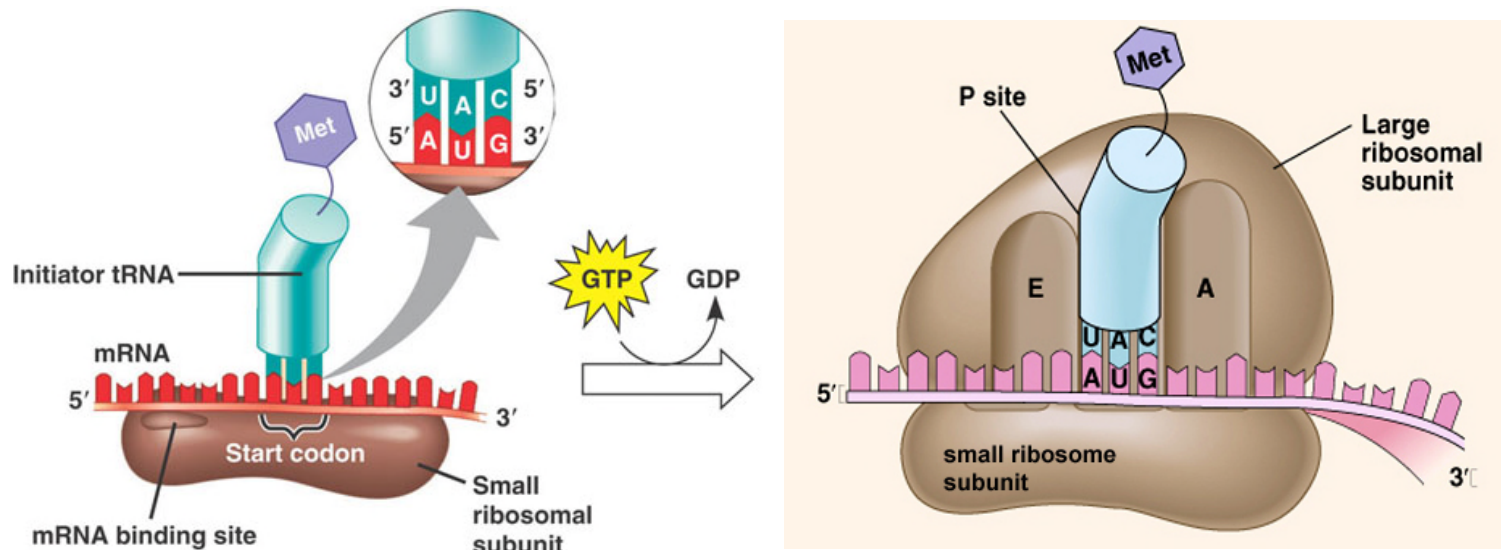
Ada E. Yonath

🕒 1/3 of the prize

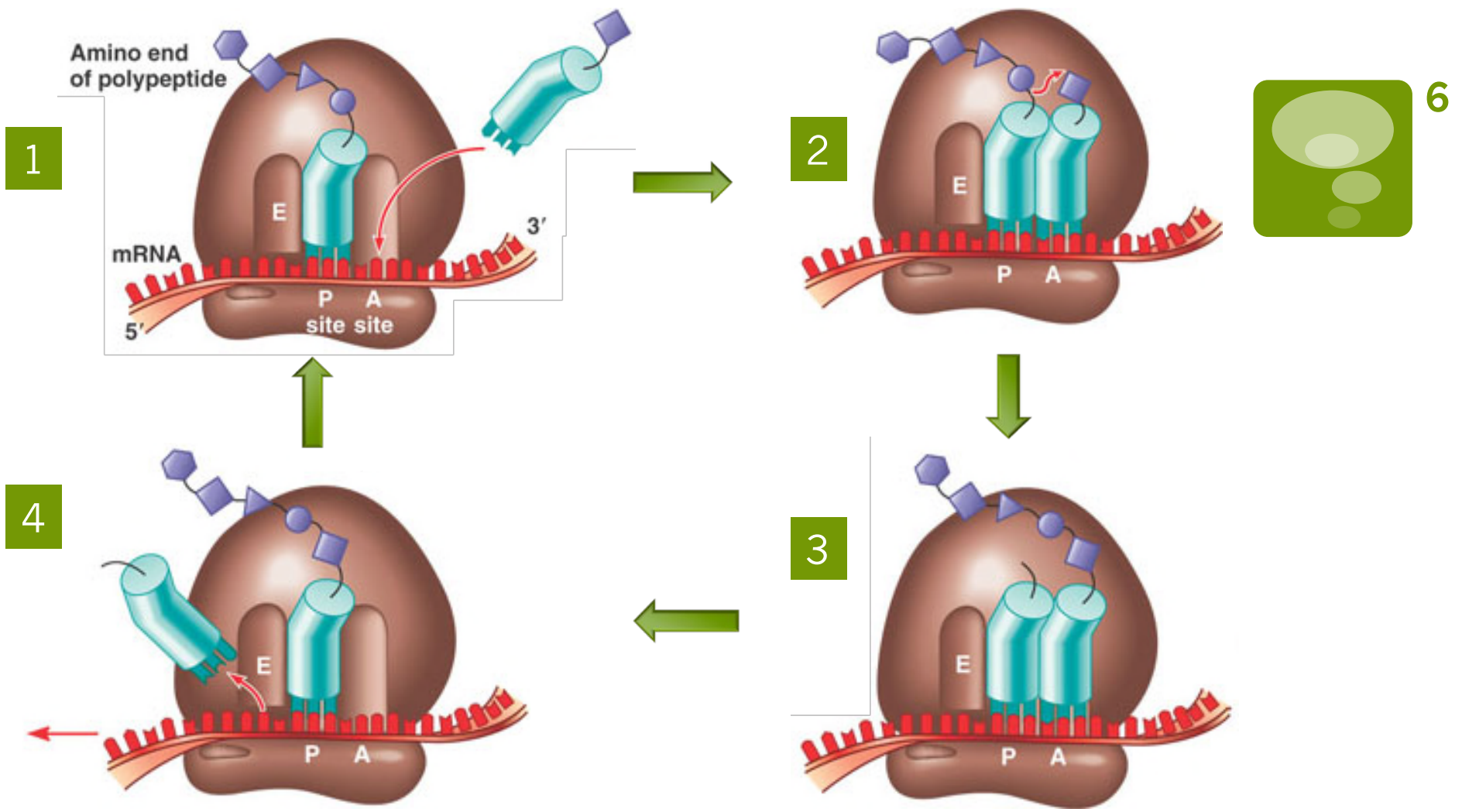
Israel

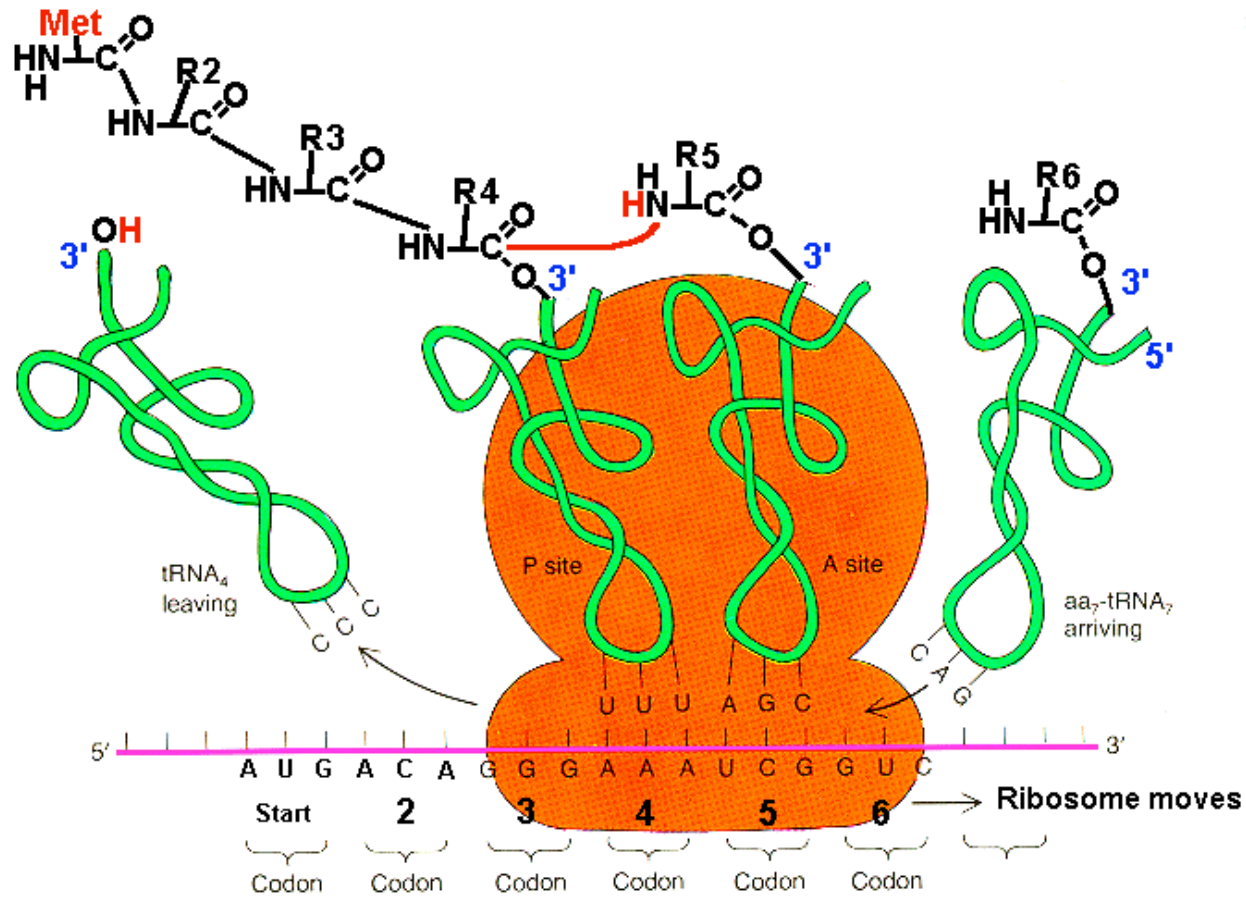
Weizmann Institute
of Science
Rehovot, Israel

Codone di INIZIO all'estremità 5' del mRNA



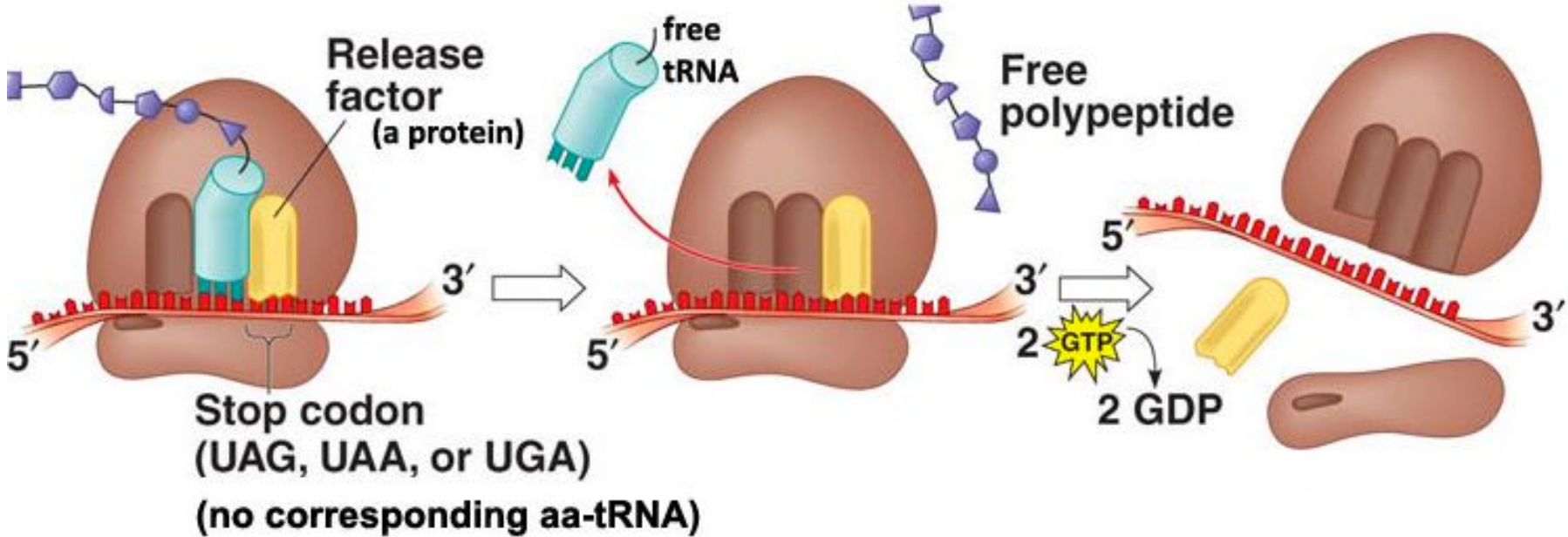
La sintesi proteica inizia nel citoplasma con l'aggancio della piccola subunità ribosomiale all'estremità 5' dell'mRNA. In corrispondenza del codone di inizio "AUG" si aggancia la grande subunità ribosomiale. Il primo a.a. al N-terminale è dunque una metionina (Met) e la sintesi proteica prosegue con la lettura dell'mRNA nella direzione 5'--->3'.





Modified from Griffiths et al., AN INTRODUCTION TO GENETIC ANALYSIS, 6th Ed., W.H. Freeman & Co., 1996.

Codone di STOP



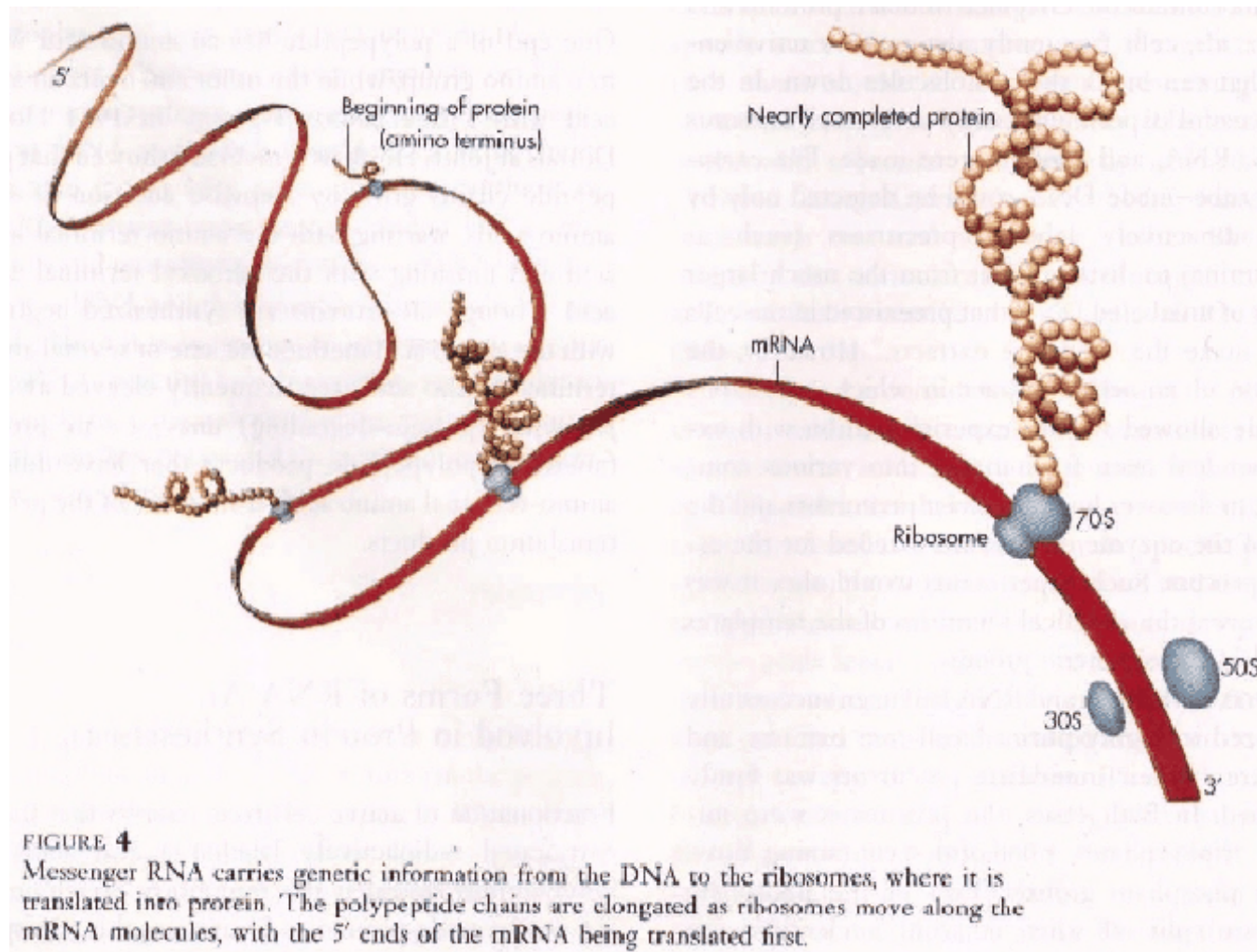
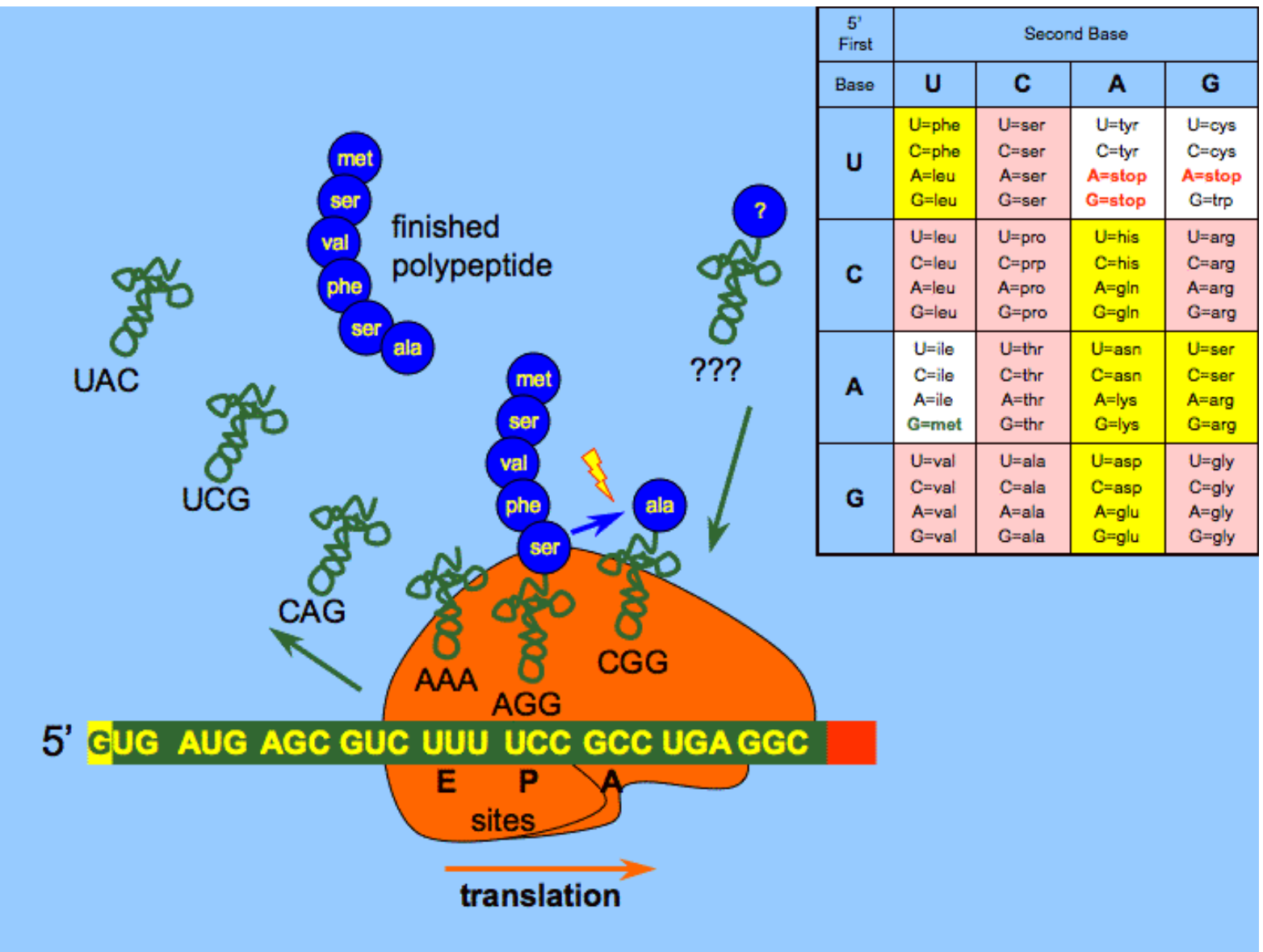


FIGURE 4
Messenger RNA carries genetic information from the DNA to the ribosomes, where it is translated into protein. The polypeptide chains are elongated as ribosomes move along the mRNA molecules, with the 5' ends of the mRNA being translated first.



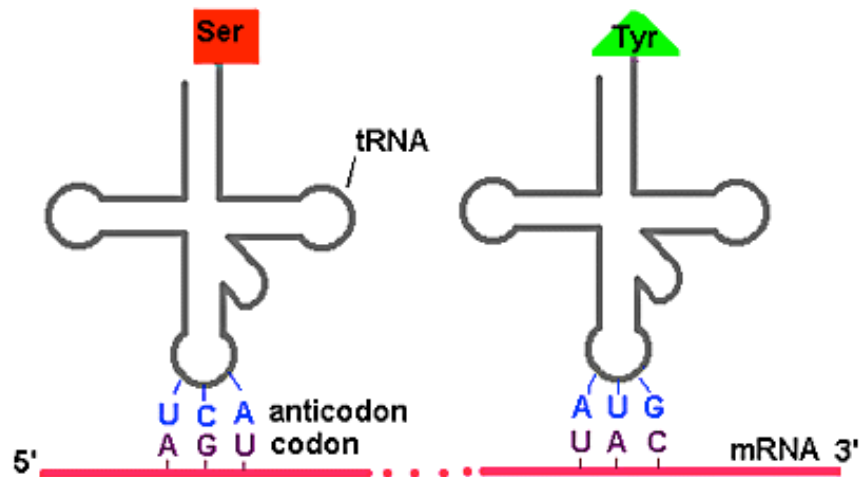


5' First Base	Second Base			
	U	C	A	G
U	U=phe C=phe A=leu G=leu	U=ser C=ser A=ser G=ser	U=tyr C=tyr A=stop G=stop	U=cys C=cys A=stop G=trp
C	U=leu C=leu A=leu G=leu	U=pro C=prp A=pro G=pro	U=his C=his A=gln G=gln	U=arg C=arg A=arg G=arg
A	U=ile C=ile A=ile G=met	U=thr C=thr A=thr G=thr	U=asn C=asn A=lys G=lys	U=ser C=ser A=arg G=arg
G	U=val C=val A=val G=val	U=ala C=ala A=ala G=ala	U=asp C=asp A=glu G=glu	U=gly C=gly A=gly G=gly



10

Codice genetico



		2nd base in codon					
		U	C	A	G		
1st base in codon	U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	3rd base in codon	U
	C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg		U
	A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg		U
	G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly		U
						C	
						A	
						G	

codone di inizio = AUG = Metionina = Met

	T	C	A	G
T	TTT Phe F	TCT Ser S	TAT Tyr Y	TGT Cys C
	TTC Phe F	TCC Ser S	TAC Tyr Y	TGC Cys C
	TTA Leu L	TCA Ser S	TAA stop *	TGA stop *
	TTG Leu L	TCG Ser S	TAG stop *	TGG Trp W
C	CTT Leu L	CCT Pro P	CAT His H	CGT Arg R
	CTC Leu L	CCC Pro P	CAC His H	CGC Arg R
	CTA Leu L	CCA Pro P	CAA Gln Q	CGA Arg R
	CTG Leu L	CCG Pro P	CAG Gln Q	CGG Arg R
A	ATT Ile I	ACT Thr T	AAT Asn N	AGT Ser S
	ATC Ile I	ACC Thr T	AAC Asn N	AGC Ser S
	ATA Ile I	ACA Thr T	AAA Lys K	AGA Arg R
	ATG Met M	ACG Thr T	AAG Lys K	AGG Arg R
G	GTT Val V	GCT Ala A	GAT Asp D	GGT Gly G
	GTC Val V	GCC Ala A	GAC Asp D	GGC Gly G
	GTA Val V	GCA Ala A	GAA Glu E	GGA Gly G
	GTG Val V	GCG Ala A	GAG Glu E	GGG Gly G



GCA	AGA																					
GCC	AGG																					
GCG	CGA																					
GCU	CGG	GAC	AAC	UGC	GAA	CAA	GGA		AUA	UUA				CCA	AGC	ACA				GUA	UAA	
	CGU	GAU	AAU	UGU	GAG	CAG	GGC	CAC	AUC	UUG	AAA		UUC	CCC	UCA	ACC				GUC	UAG	
							GGG	CAU	AUU	CUA	AUG	UUU	CCU	CCG	UCG	ACG	UGG	UAC	GUG	UGA		
							GGU			CUU					UCU	ACU		UAU	GUU			
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	stop		
A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V			

M | A | G | L | T | A |

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Come raggiungere le informazioni contenute nelle banche dati?

GenBank Overview

http://www.ncbi.nlm.nih.gov/Genbank/index.html

BIO ▾ CBUI ▾ Personale ▾ localhost ▾ Ricerca ▾ Biblio ▾ Accademia ▾ Didattica ▾ CampusNet ▾ LMbiologi

GenBank Overview

NCBI **GenBank Overview**

PubMed Entrez BLAST OMIM Books Taxonomy Structure

Search Entrez for Go

NCBI
SITE MAP
Submit to GenBank
Updates
Search GenBank
Entrez Nucleotide
GenBank and RefSeq: a comparison
NCBI Handbook
BLAST

International sequence databases exceed 100 gigabases

In August 2005, the INSDC announced the DNA sequence database exceeded 100 gigabases. GenBank is proud of its contributions toward this milestone. We thank all the scientists who have worked through the submission process at GenBank and made their sequence data available to the world. See the related [press release](#).

Growth of the International Nucleotide Sequence Database Collaboration

Date	GenBank (Billions)	EMBL (Billions)	DDBJ (Billions)	Total (Billions)
Aug-00	~1	~1	~1	~3
Aug-01	~2	~1	~1	~4
Aug-02	~4	~1	~1	~6
Aug-03	~8	~1	~1	~10
Aug-04	~15	~1	~1	~17
Aug-05	~75	~1	~1	~77

Base Pairs contributed by GenBank® EMBL DDBJ




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Nucleotide
Protein
Genome
Structure

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National Institute of Allergy and Infectious Diseases (NIAID) September 24, 2007



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stathmin rat mRNA complete -...

CGCTCAGGATAGGACTTCGCTAGAGATCGGATCCCCGGG...ATTATATAGCTCGATCGATC1
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 CACAGAC...ACGG...CTCAG...CTTAC TAAC CAAT TC GGAGAGGGGCGGCGA TLUUC GC GAG

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All Databases PubMed Nucleotide Protein Genome Structure PMC Taxonomy Books

Search CoreNucleotide for stathmin rat mRNA complete Go Clear Save Search

Limits Preview/Index History Clipboard Details

Found 12 nucleotide sequences. CoreNucleotide [10] EST [1] GSS [1]

Display Summary Show 20 Sort by Send to

All: 10 Bacteria: 0 RefSeq: 0 mRNA: 10

Items 1 - 10 of 10 One page.

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 PUBMED [12477932](#)
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 AUTHORS Director MGC Project.
 TITLE Direct Submission
 JOURNAL Submitted (13-NOV-2003) National Institutes of Health, Mammalian
 Gene Collection (MGC), Cancer Genomics Office, National Cancer
 Institute, 31 Center Drive, Room 11A03, Bethesda, MD 20892-2590,
 USA
 REMARK NIH-MGC Project URL: <http://mgc.nci.nih.gov>
 COMMENT Contact: MGC help desk
 Email: cgapbs-r@mail.nih.gov
 Tissue Procurement: John C. Marshall, M.D., Ph.D
 cDNA Library Preparation: CLONTECH Laboratories, Inc.
 cDNA Library Arrayed by: The I.M.A.G.E. Consortium (LLNL)
 DNA Sequencing by: Genome Sequence Centre,
 BC Cancer Agency, Vancouver, BC, Canada
info@bcgsc.bc.ca
 Steve Jones, Sarah Barber, Mabel Brown-John, Yaron Butterfield,
 Andy Chan, Steve S. Chand, William Chow, Alison Cloutier, Ruth
 Featherstone, Malachi Griffith, Obi Griffith, Ran Guin, Nancy Liao,
 Kim MacDonald, Amara Masson, Mike R. Mayo, Josh Moran, Ryan Morin,
 Teika Olson, Diana Palmquist, Anca Petrescu, Anna Liisa Prahbu,
 Parvaneh Saeedi, JR Santos, Angelique Schnerch, Ursula Skalska,
 Duane Smailus, Jeff Stott, Miranda Tsai, George Yang, Jacquie
 Schein, Asim Siddiqui, Rob Holt, Marco Marra.

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ORIGIN

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CDS 94..543

Codone di inizio: nucleotidi 94-96

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C-term

Capping

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Codone di STOP: nucleotidi 541-543

polyA

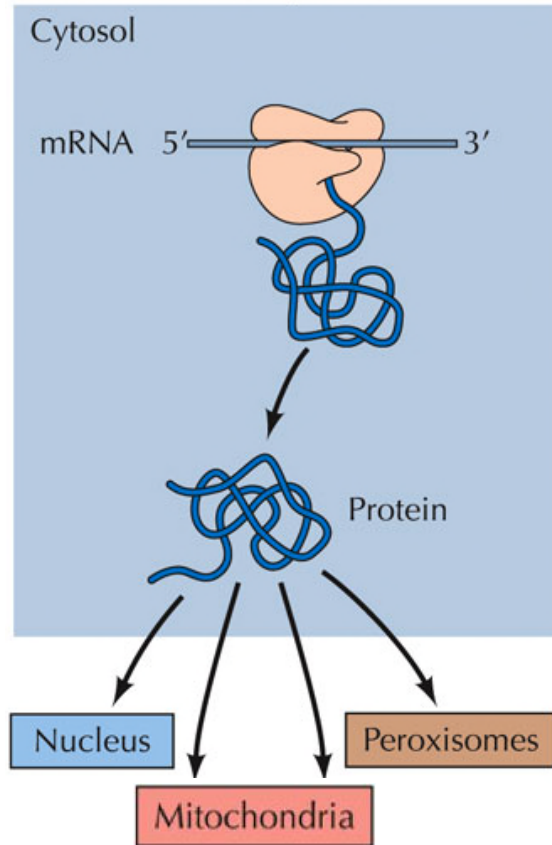
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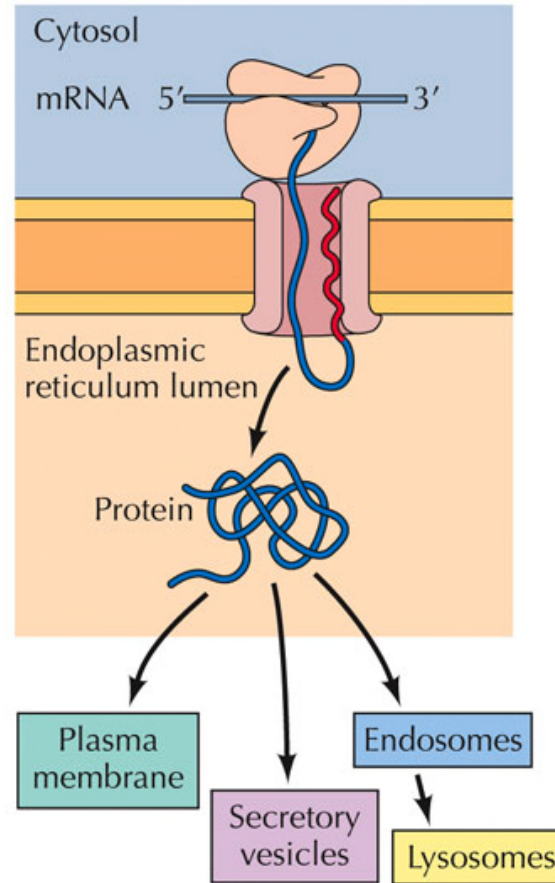
Indirizzamento delle proteine

Ribosomi liberi e ribosomi
associati al RER

Free ribosomes in cytosol



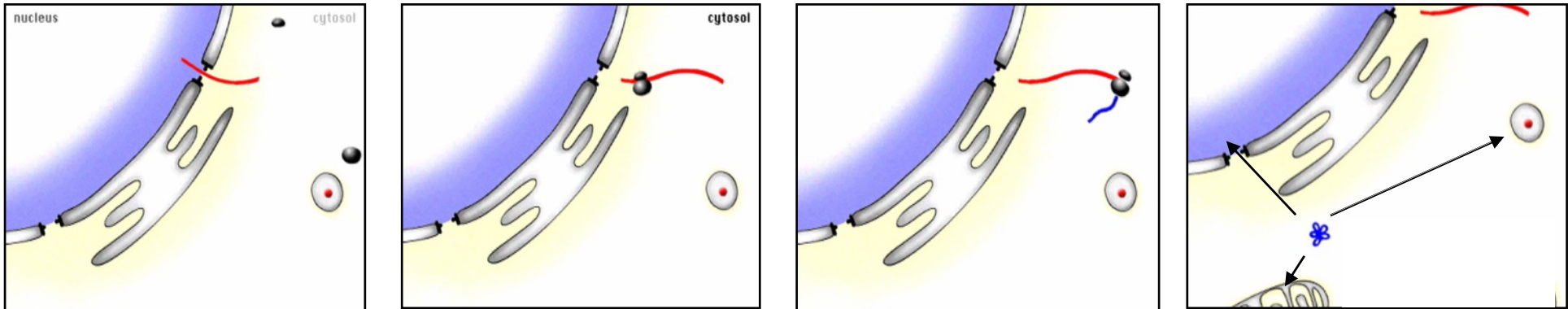
Membrane-bound ribosomes



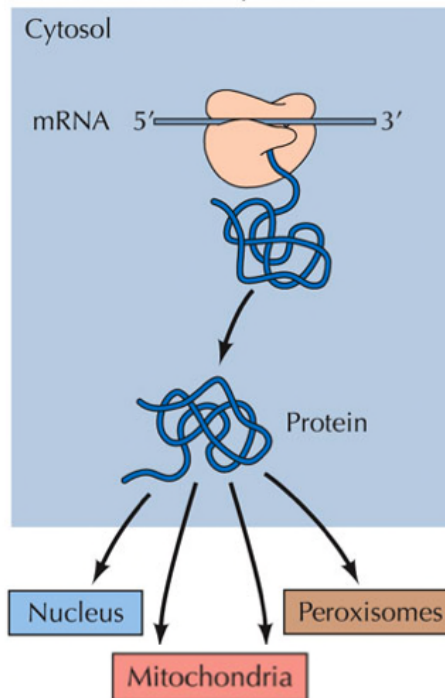
E' la proteina nascente a determinare se il ribosoma che catalizza la sua sintesi deve rimanere libero oppure essere associato alla membrana del RER.

Proteine che hanno destinazione finale nucleo, perossisomi o mitocondria sono sintetizzate da ribosomi liberi mentre proteine che hanno destinazione finale in un compartimento dell'elenco guidano il ribosoma che le traduce verso il RER.

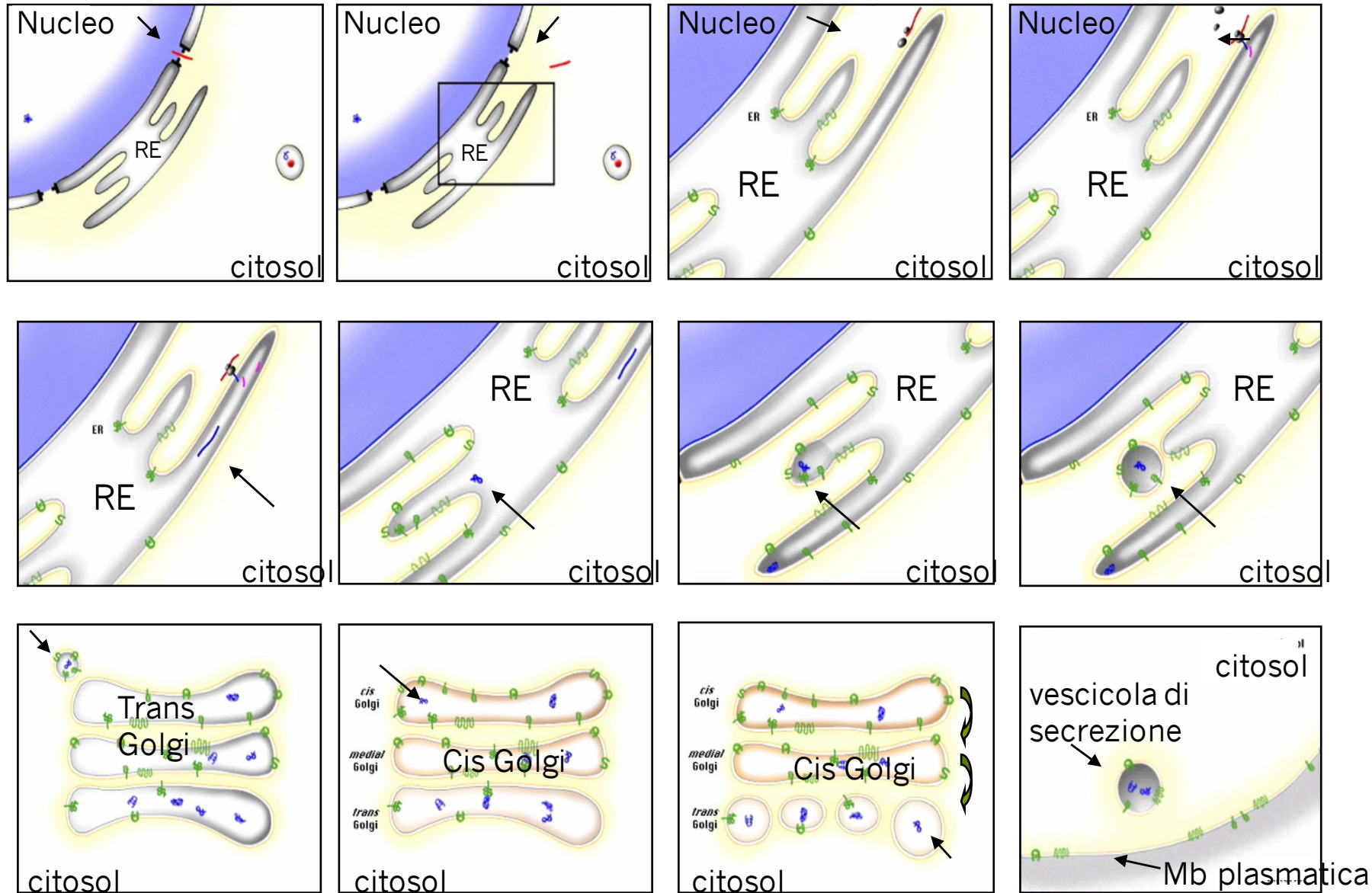
Ribosomi che traducono mRNA che codificano per proteine nucleari, mitocondriali e dei perissosimi rimangono liberi



Free ribosomes in cytosol



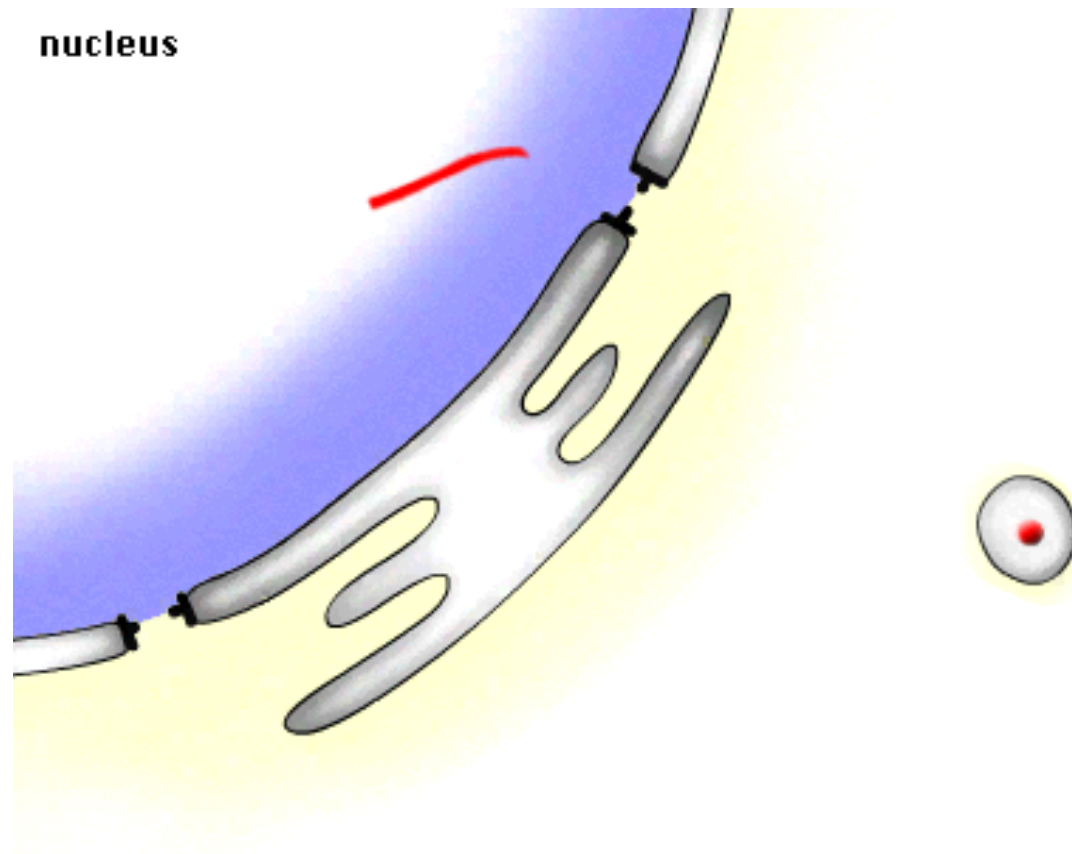
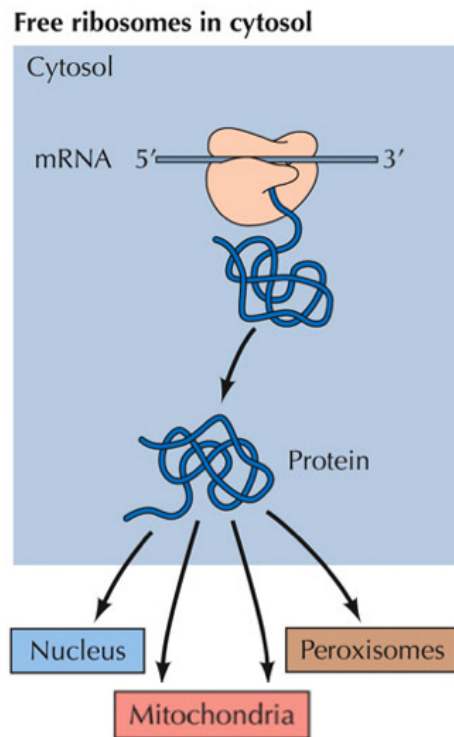
indirizzamento di una proteina di secrezione:
RE --> Golgi --> vescicola di secrezione -->
spazio extracellulare



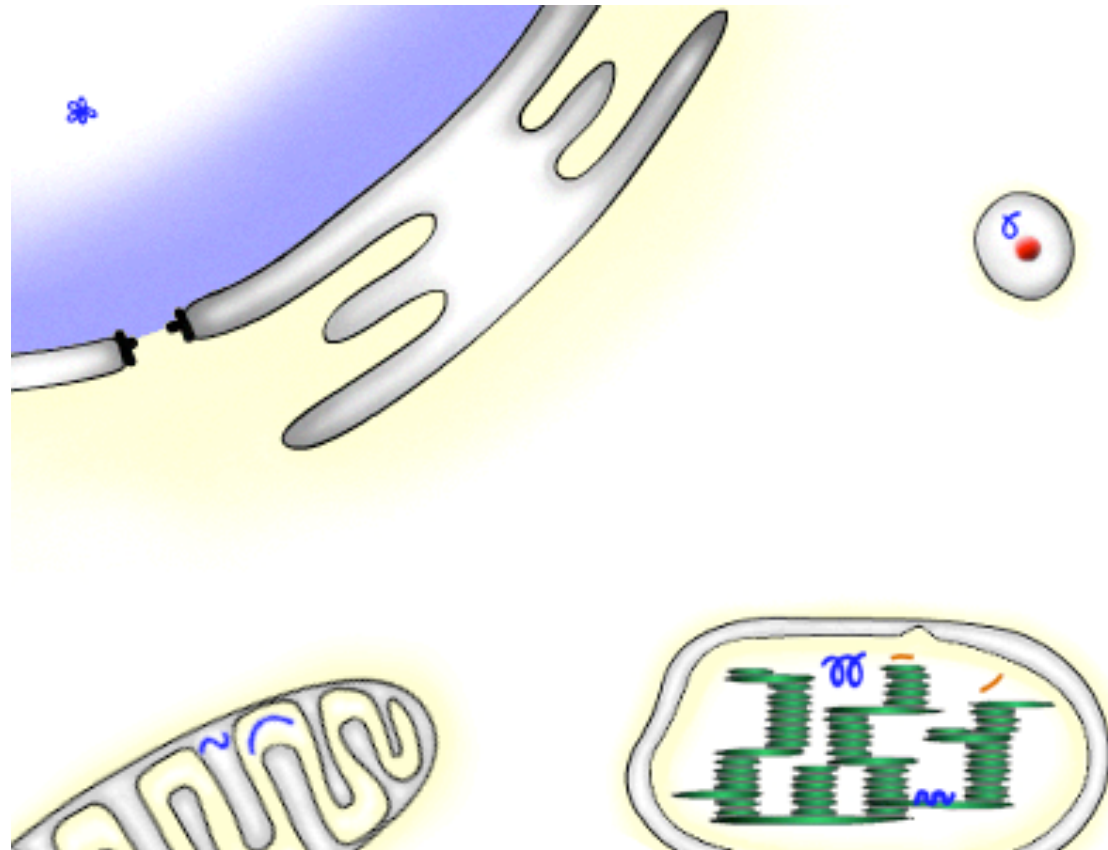
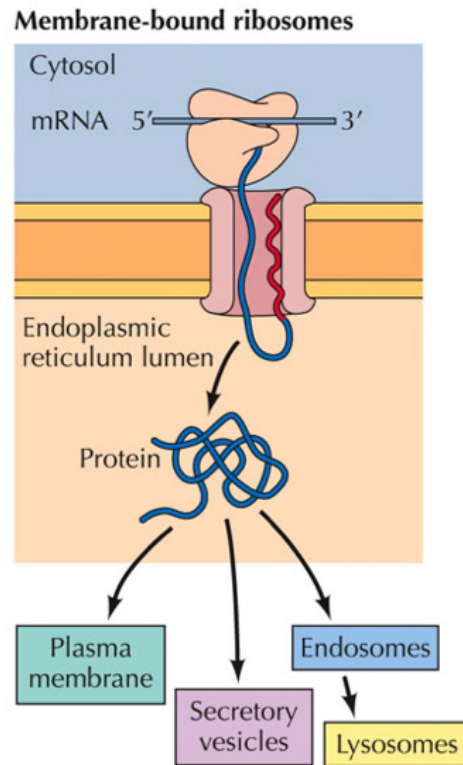
indirizzamento delle proteine nucleari, mitocondriali, dei perossisomi



25



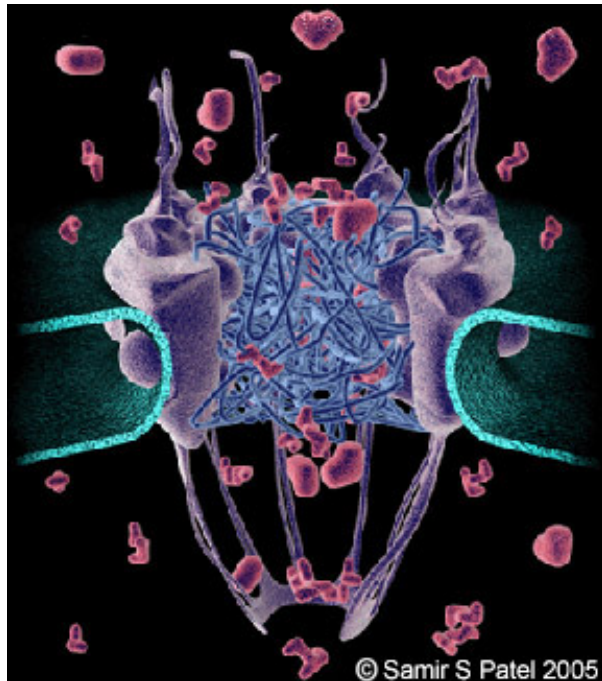
Proteine della via secretoria: RE --> Golgi --> vescicola di secrezione --> spazio extracellulare



Sequenze di localizzazione nucleare (NLS) e di export nucleare (NES)

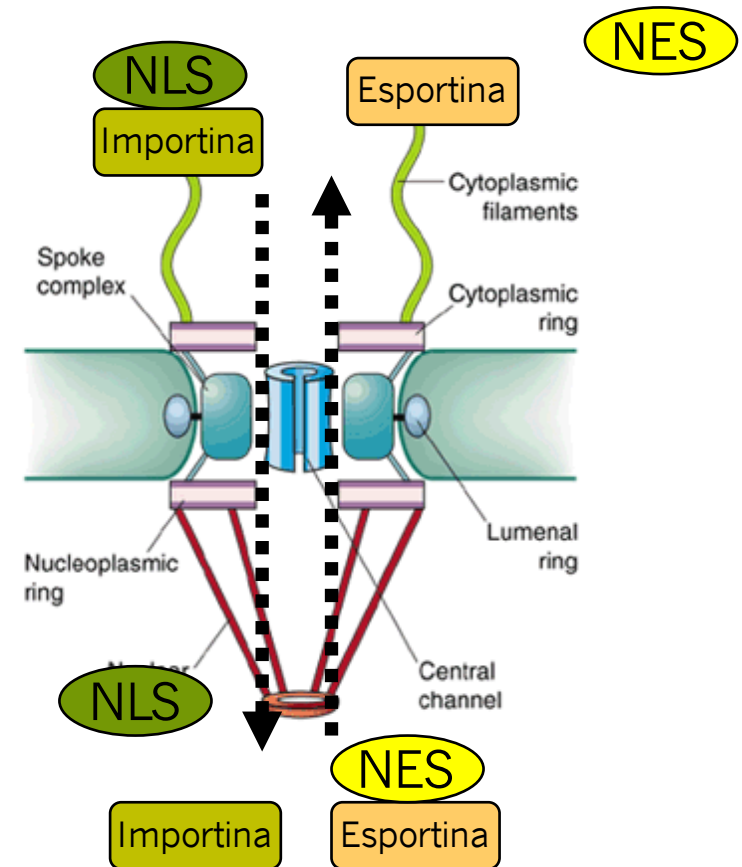


Sequenza di localizzazione nucleare (NLS): Proteine di trasporto tipo "importine" accompagnano le proteine che possiedono una sequenza "NLS" nel passaggio dal citoplasma al nucleoplasma attraverso i pori nucleari.



citosol

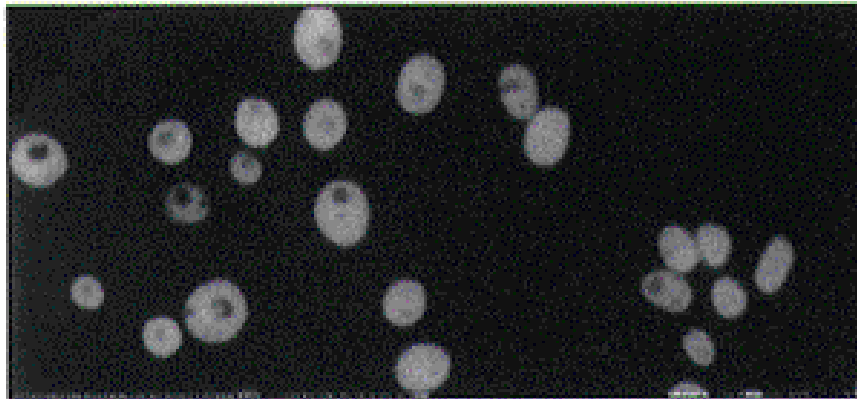
nucleo



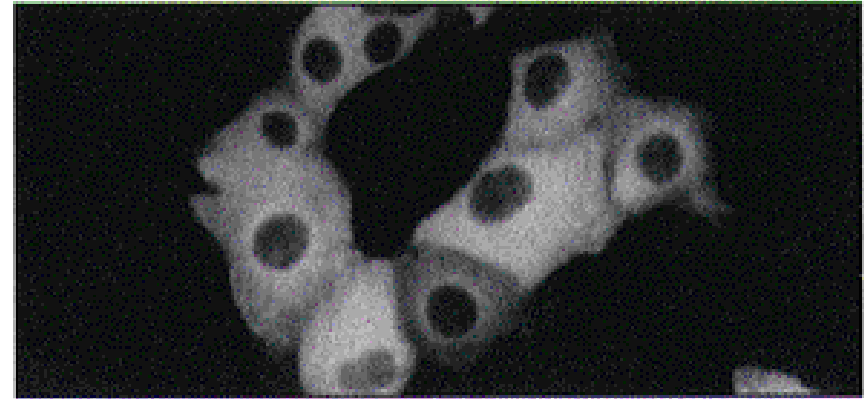
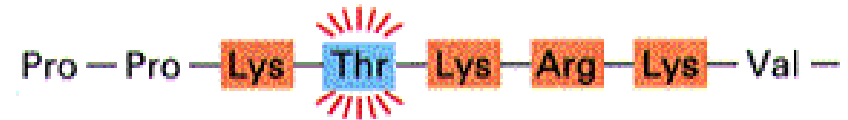
Se la sequenza NLS è mutata, la proteina non viene più trasportata dal citoplasma al nucleoplasma.



(A) LOCALIZATION OF T-ANTIGEN CONTAINING WILD-TYPE NUCLEAR IMPORT SIGNAL



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



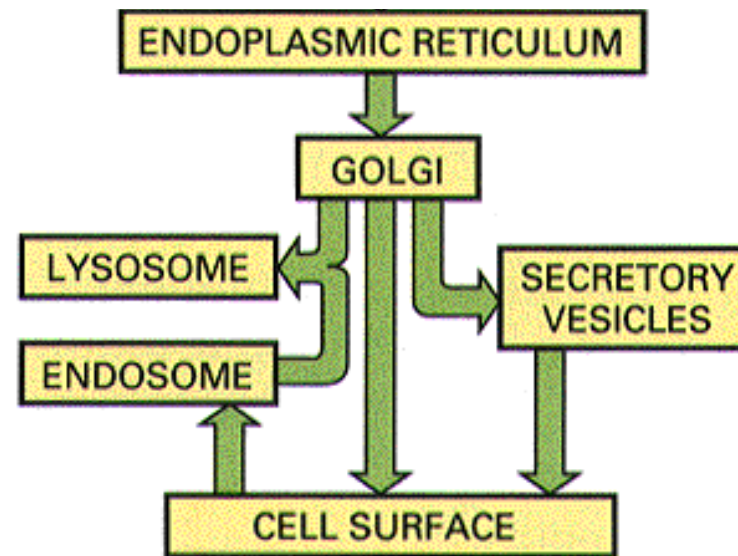
(A): sequenza NLS corretta: la proteina ha una localizzazione nucleare

(B): stessa proteina messa in evidenza in (A) ma con una mutazione puntiforme nella sequenza NLS (a.a. treonina in sostituzione della seconda lisina della sequenza NLS): la localizzazione è chiaramente citoplasmatica e non più nucleare perché la proteina mutata non è più riconosciuta dall'importina.

Indirizzamento delle proteine della via secretoria



Con alcune eccezioni, le sequenze delle proteine della via "secretoria" iniziano con al N-terminale il peptide segnale



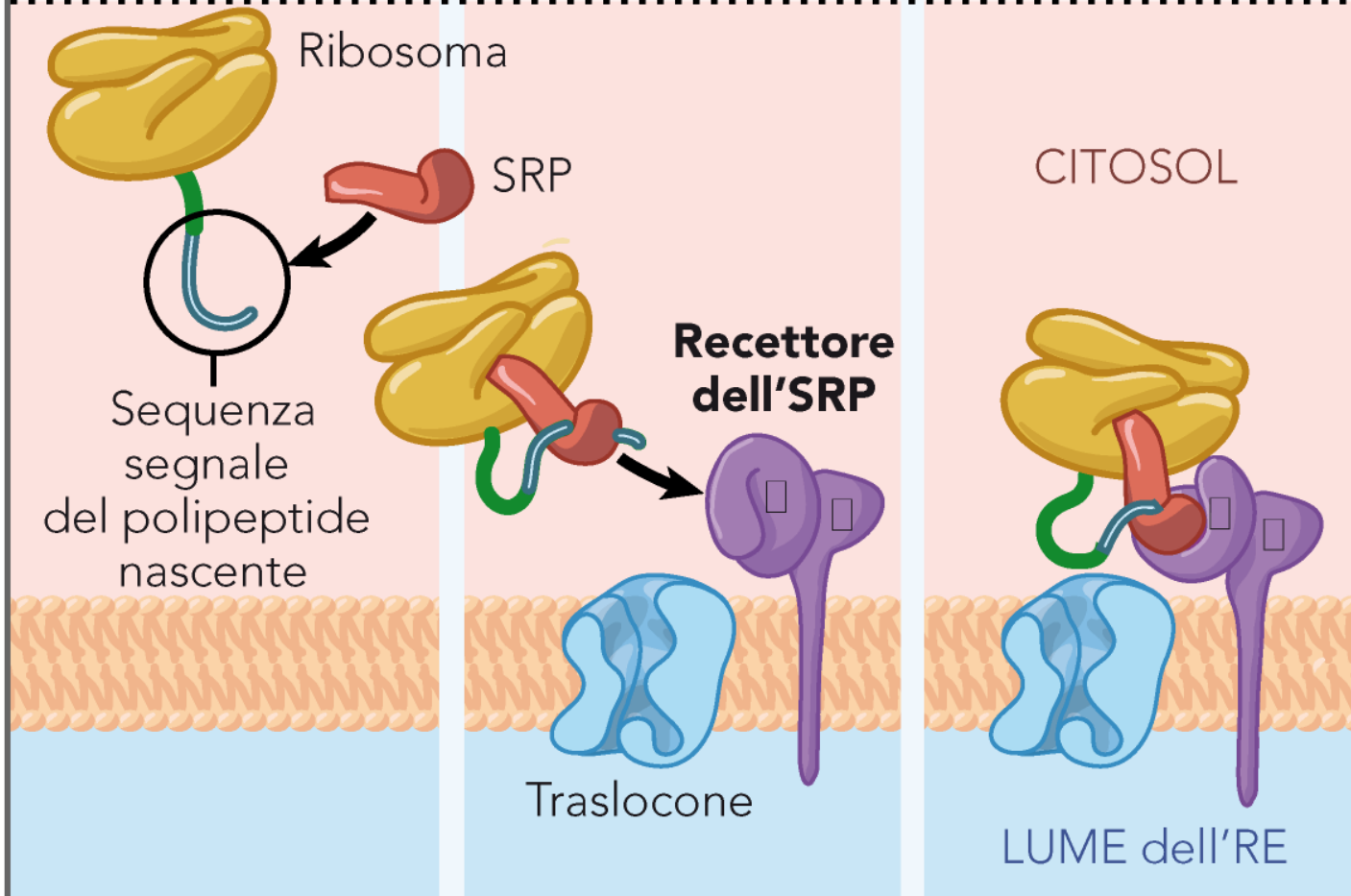
Nota: anche se chiamata genericamente via "secretoria", proteine di questa via possono avere come localizzazione finale uno qualsiasi dei compartimenti elencati ed essere solubili, associate a membrane oppure transmembrana.

Il ruolo dell'SRP

La traduzione espone la sequenza segnale

L'SRP si lega e arresta la traduzione

L'SRP si attacca al complesso ribosoma-proteina nascente sull'RE

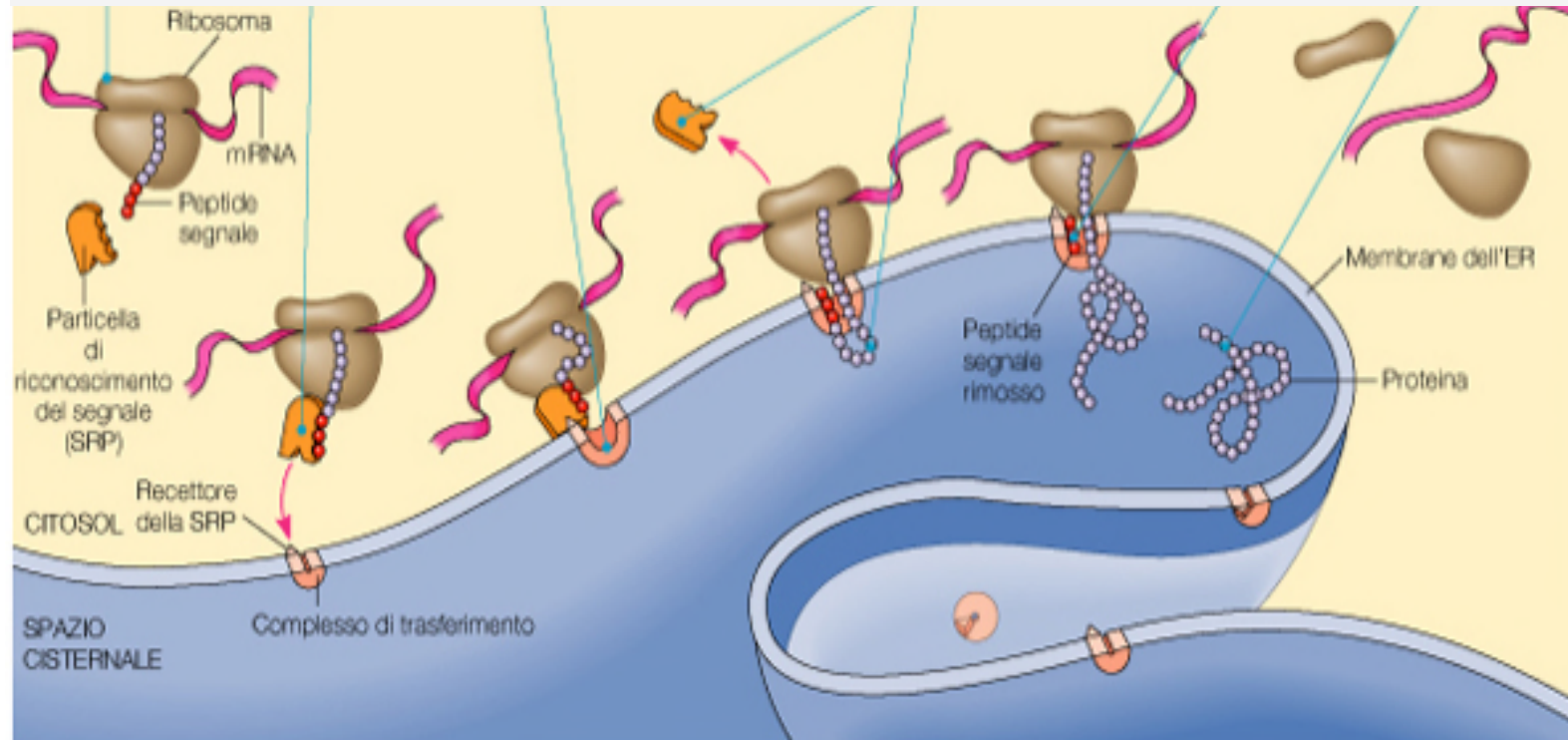


Function of Signal Peptide

Example of Signal Peptide

Import into ER

^+H_3N -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-



1- La sintesi del polipeptide inizia su di un ribosoma libero nel citosol

2- la proteina SRP si lega al peptide segnale e blocca temporaneamente la sintesi proteica

3- SRP si lega ad un recettore posto sulla membrana del RE. Tale recettore fa parte del complesso di trasferimento o traslocone che forma un poro sulla membrana del RE e lega il peptide segnale

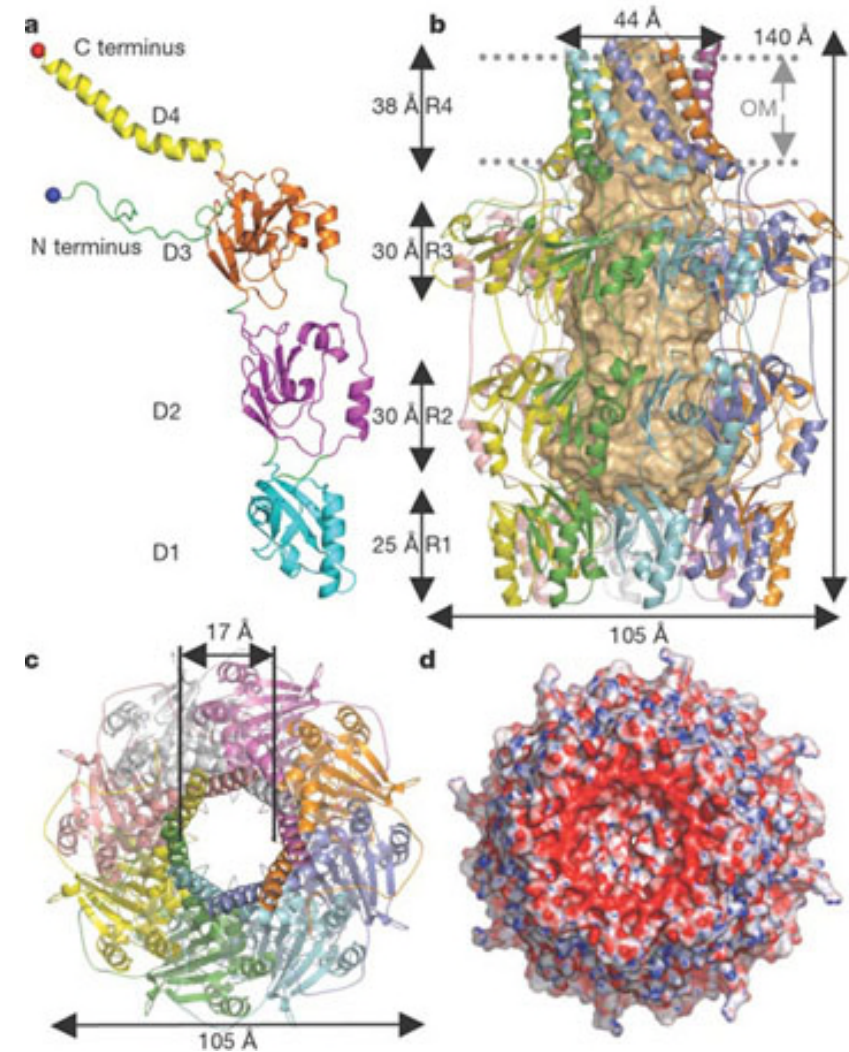
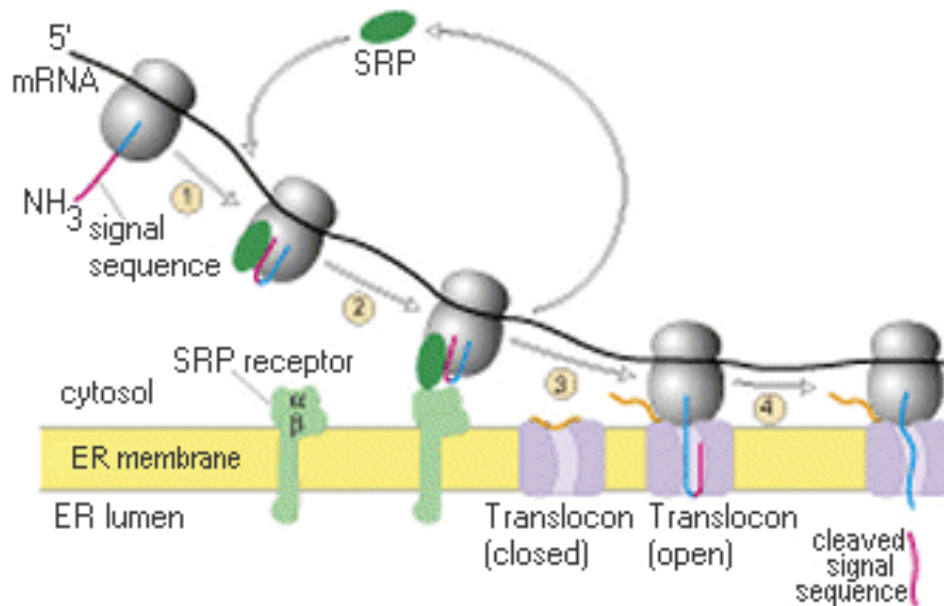
4- SRP abbandona il complesso, la sintesi proteica riprende. La proteina nascente attraversa contemporaneamente

5- un enzima idrolitico rimuove il peptide segnale della proteina

6- In assenza di altro segnale, raggiunto il codone di stop, il ribosoma si sgancia dall'mRNA e la proteina è localizzata nel lume del RER

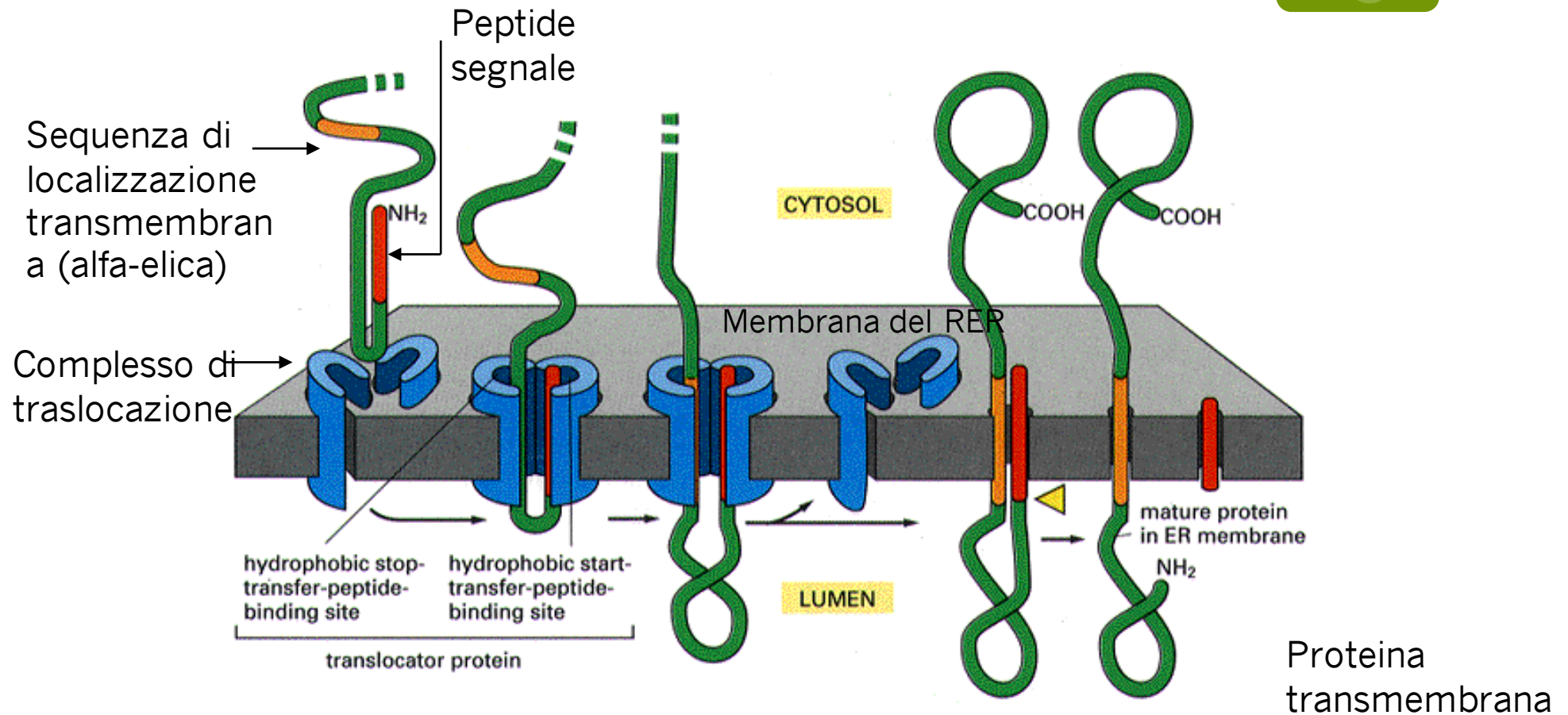
Traslocone: poro proteico

Le proteine SRP sono riciclate

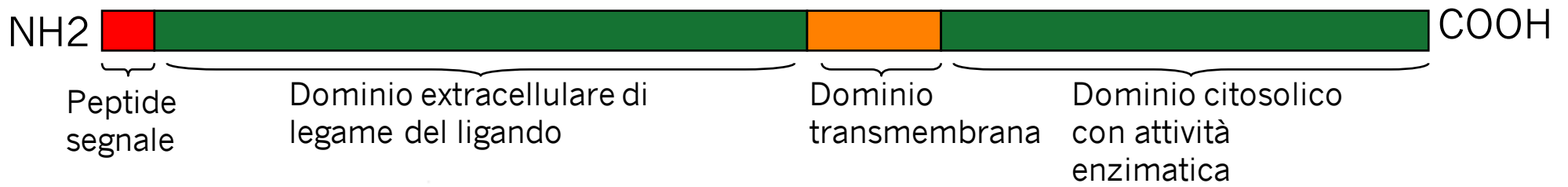


Il traslocone è un poro proteico tappato sul versante del lume del RE che si apre soltanto dopo interazione con un ribosoma.

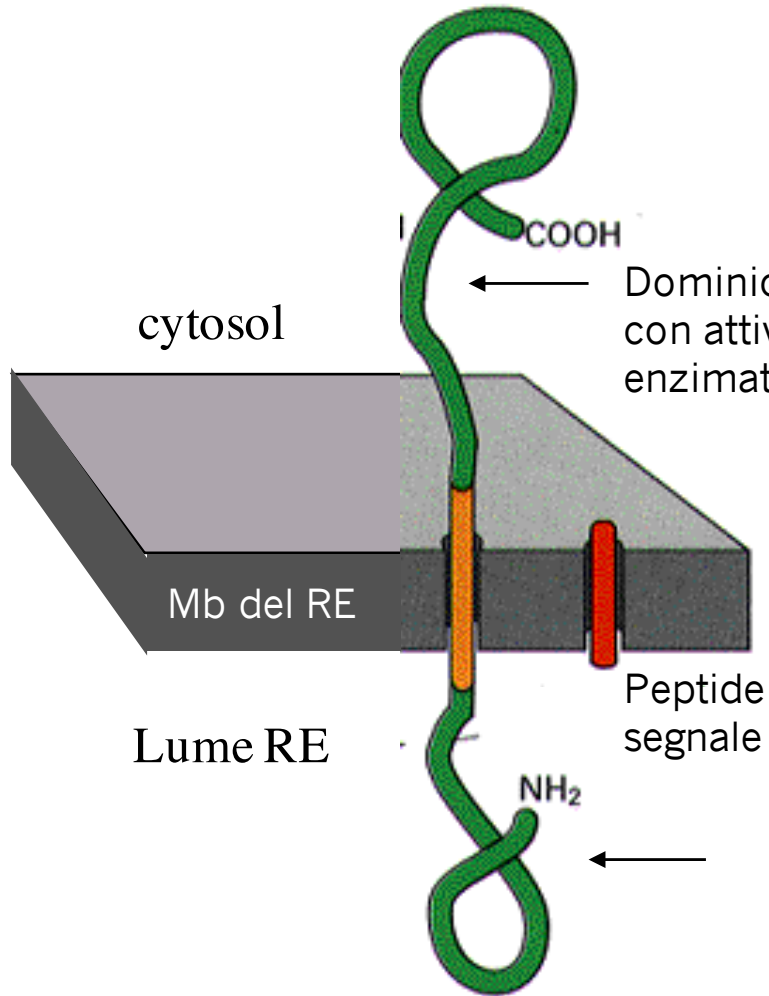
Proteine transmembrana: Inserimento co-traduzionale nel doppio strato fosfolipidico



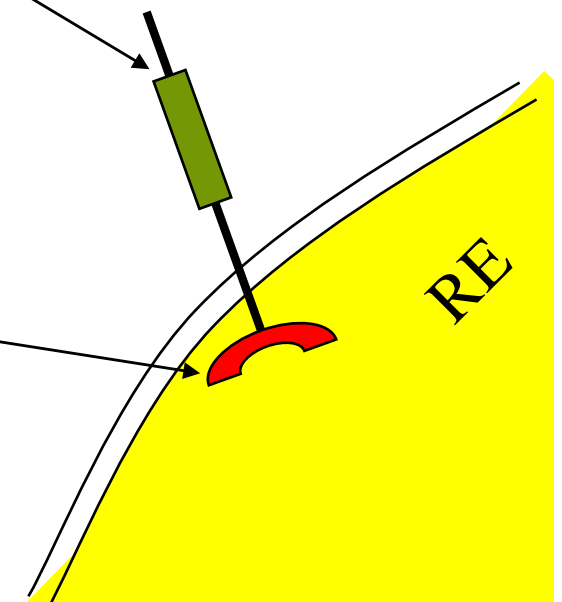
Nota: in questo schema per semplicità non sono più stati rappresentati mRNA e ribosoma.

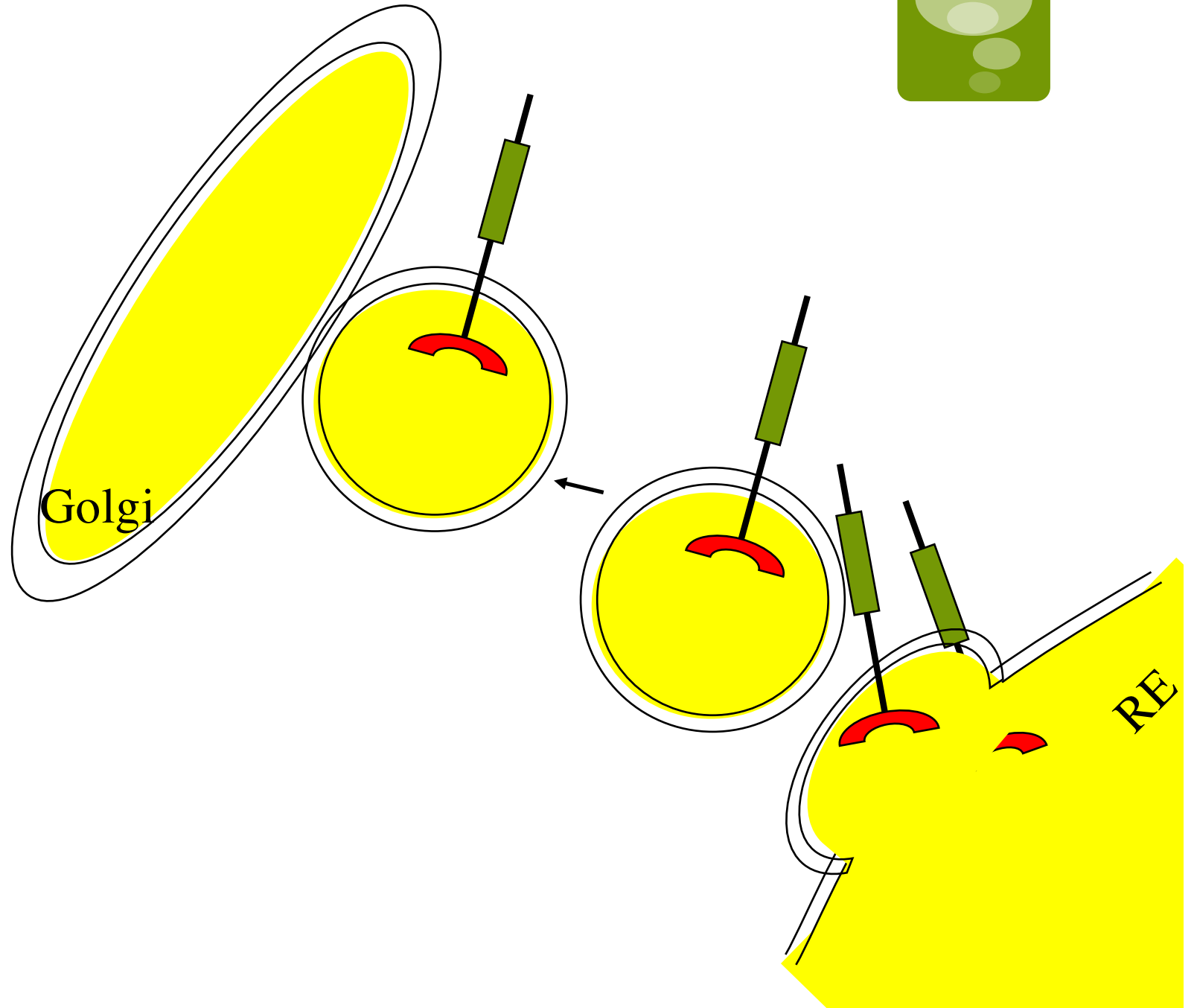


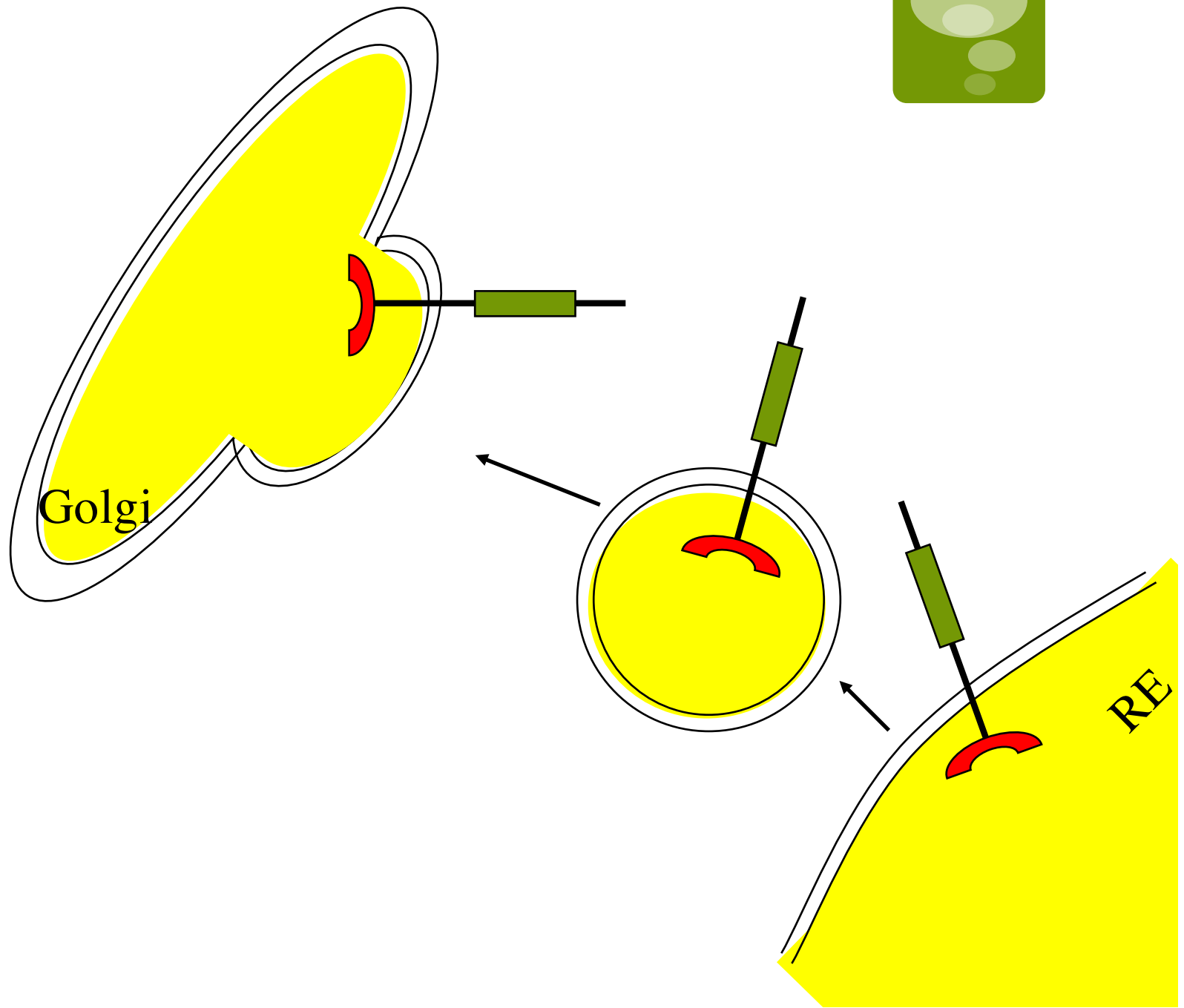
Esempio: sintesi e indirizzamento di un recettore a singolo passo transmembrana la cui localizzazione finale è la membrana plasmatica.

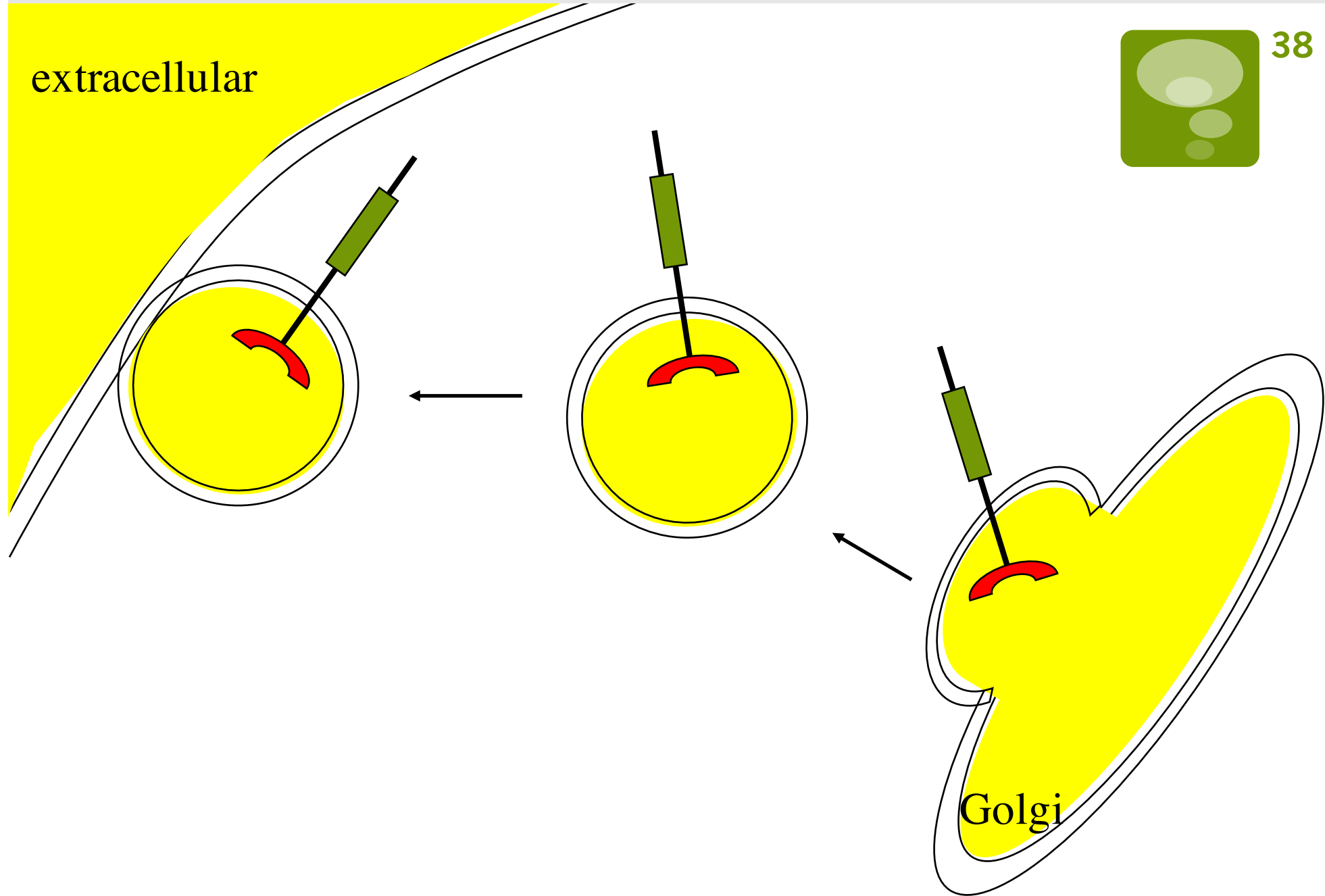


Dominio extracellulare di legame del ligando





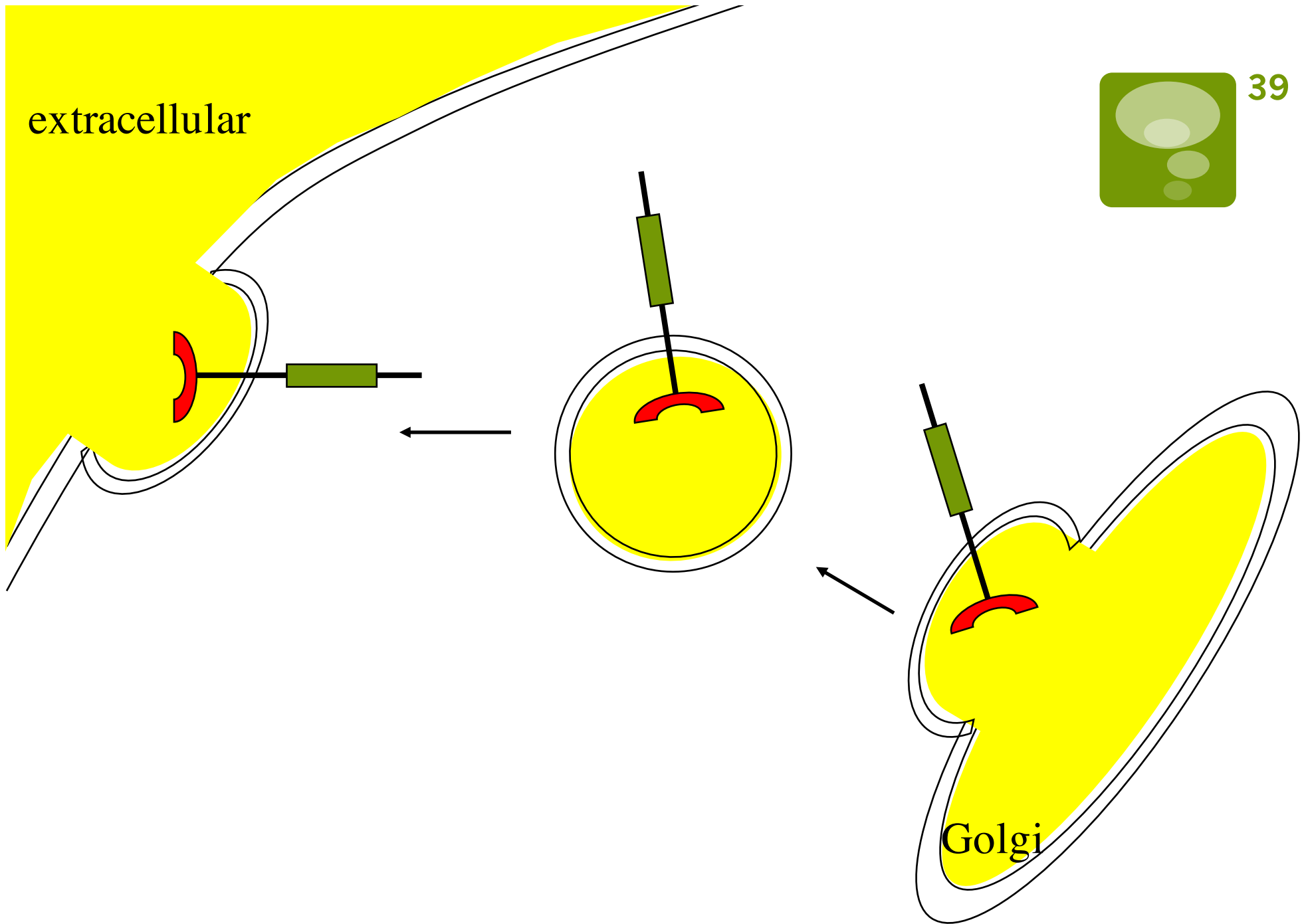




extracellular



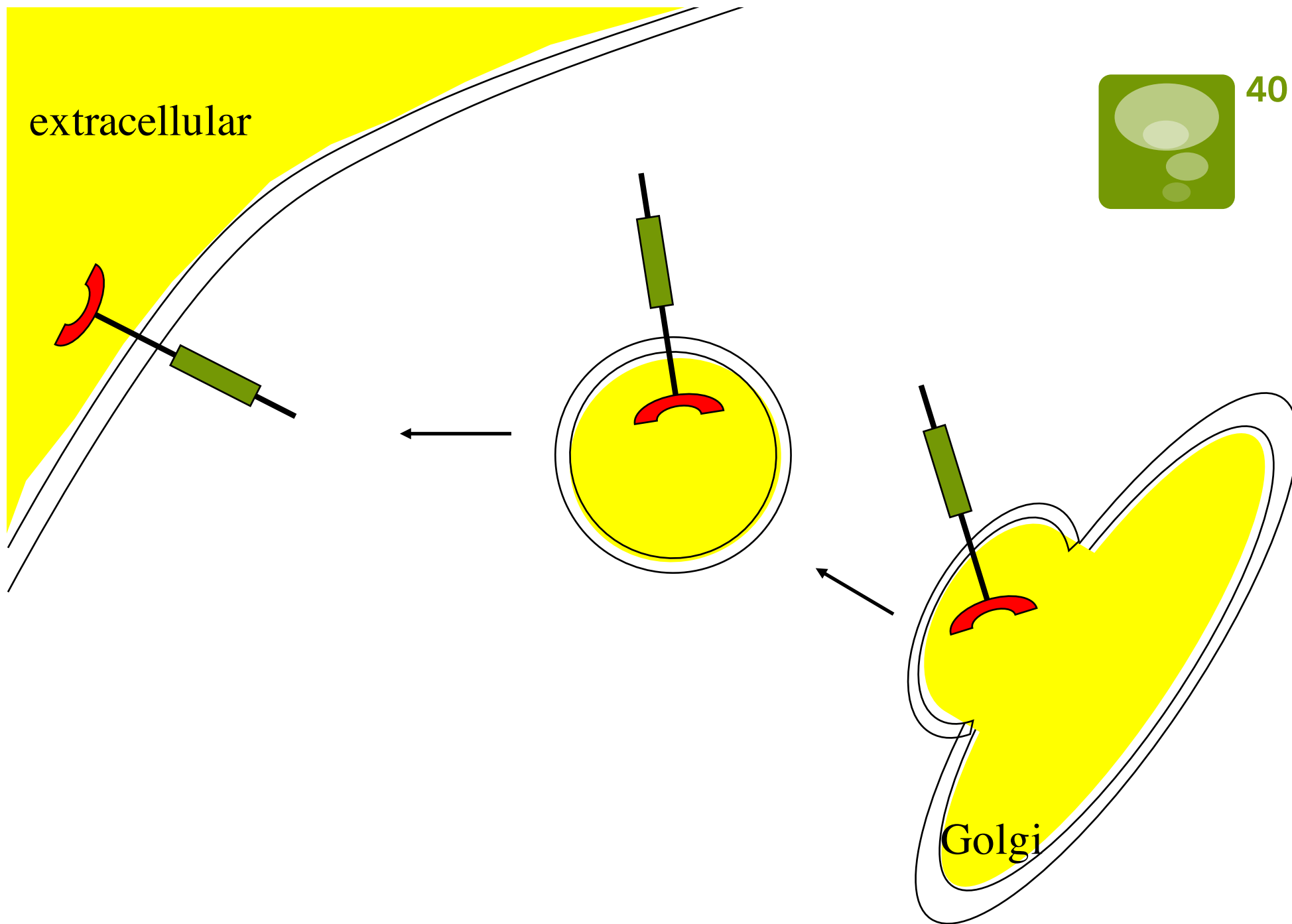
39



extracellular



40



Spiegare la sintesi e lo indirizzamento del recettore metabotropico al glutamato?

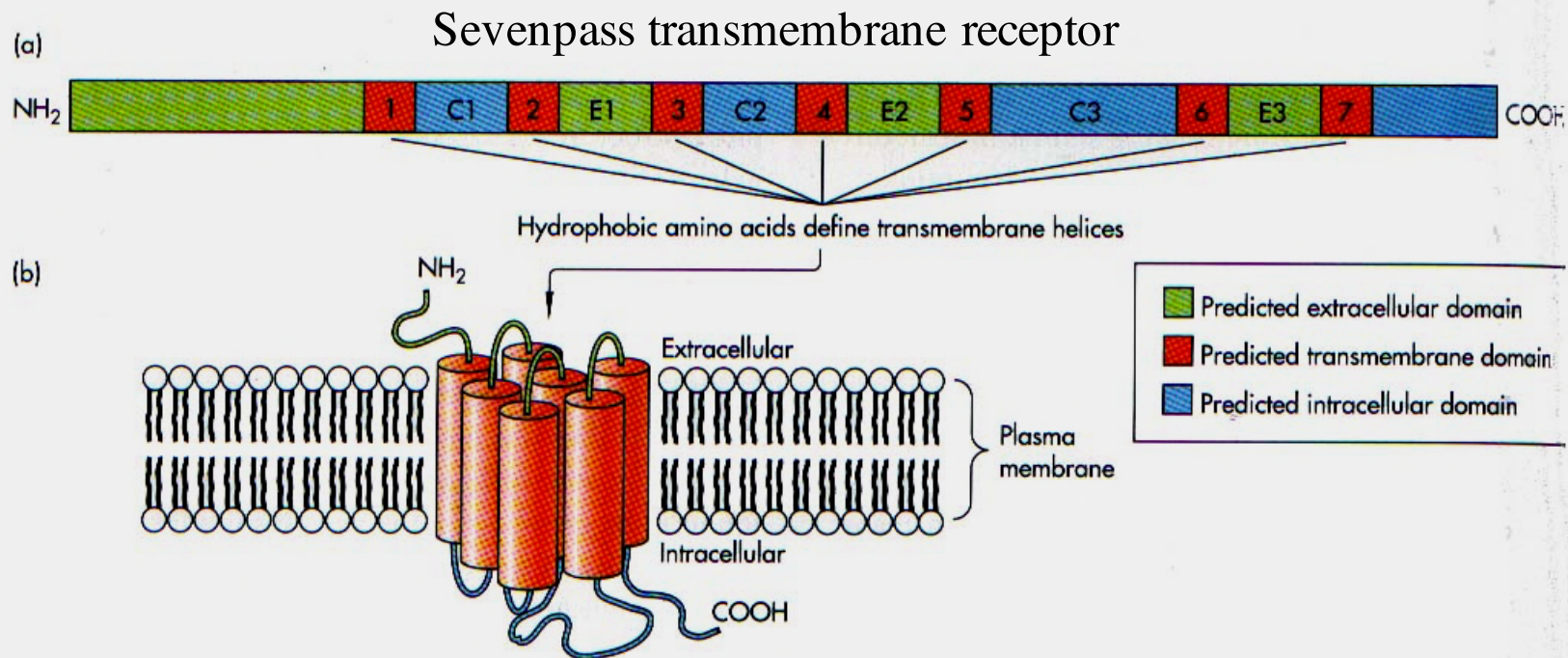


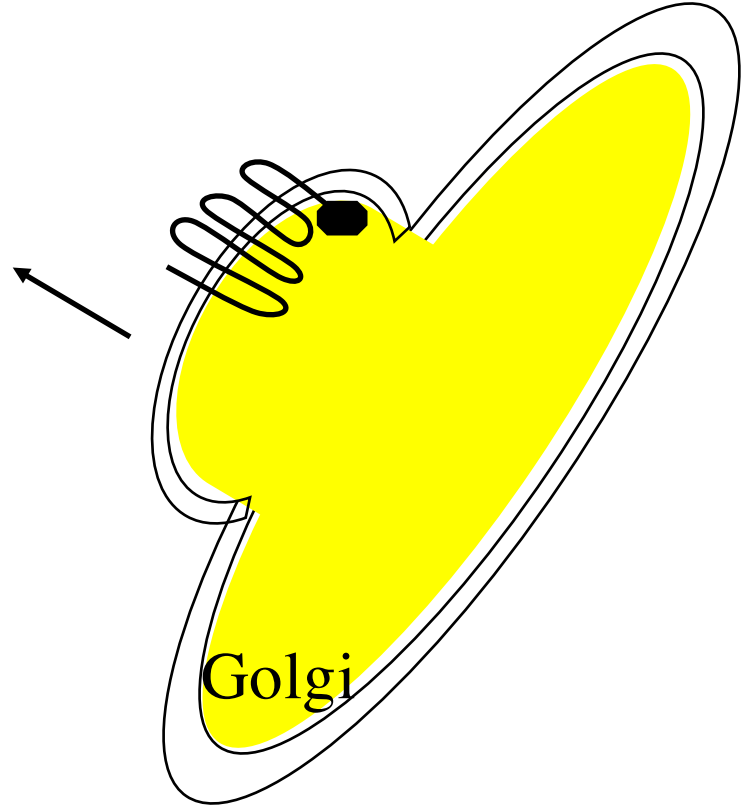
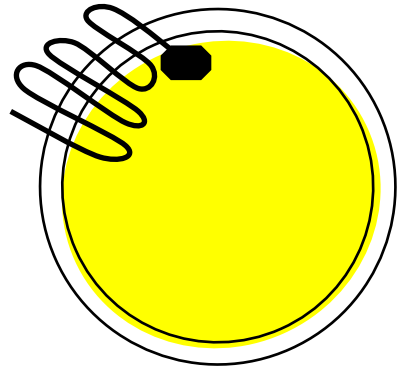
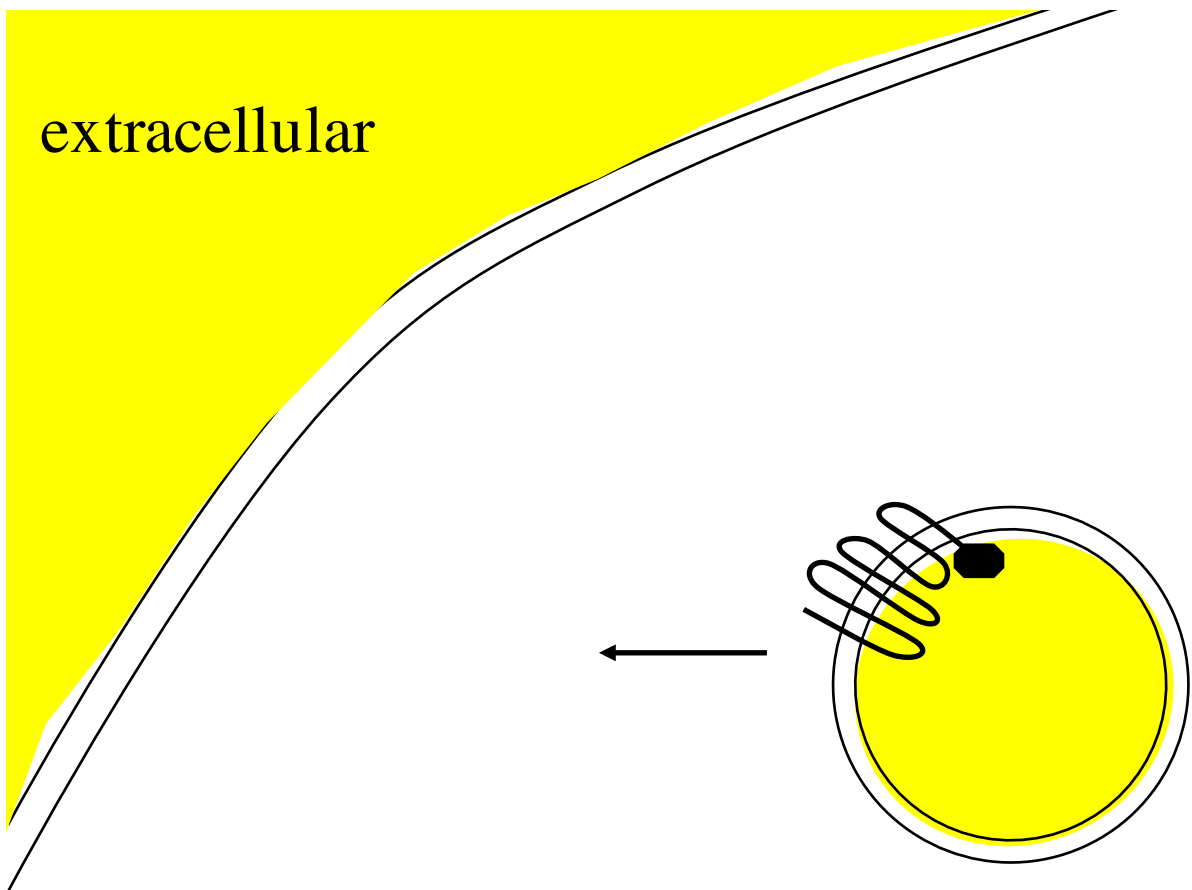
FIGURE 17-3

Structural organization of seven-helix receptors. (a) A linear representation of the receptor structure. Seven blocks of hydrophobic amino acids (1–7) form helices that are predicted to span the membrane. The helices are linked by loops that are alternatively outside (E) or inside (C) the cell. Similarly, the amino-terminal tail is outside, whereas the carboxy-terminal tail is inside. (b) A view of the proposed folded structure of the receptors.

extracellular



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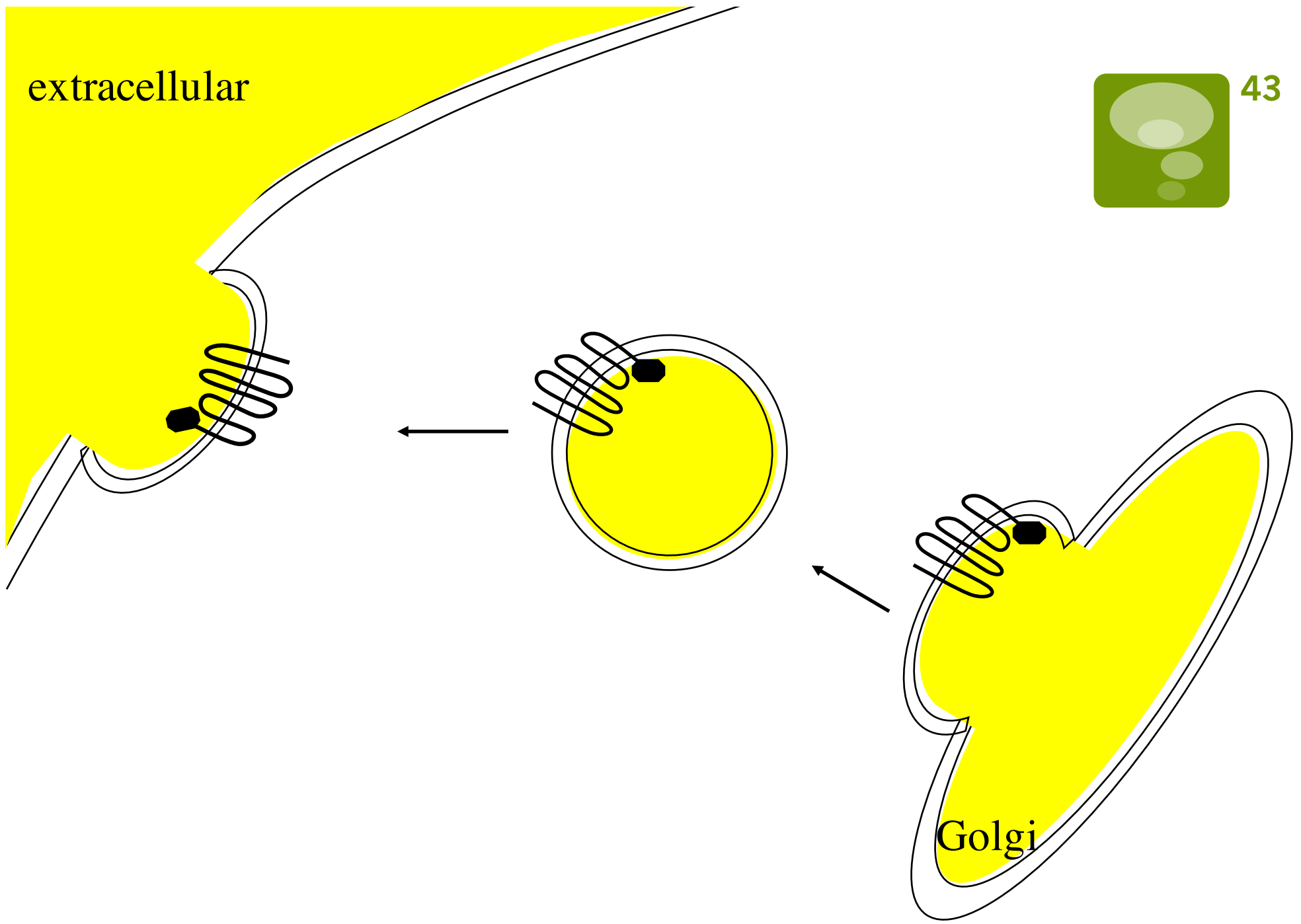


Golgi

extracellular



43



extracellular



44

