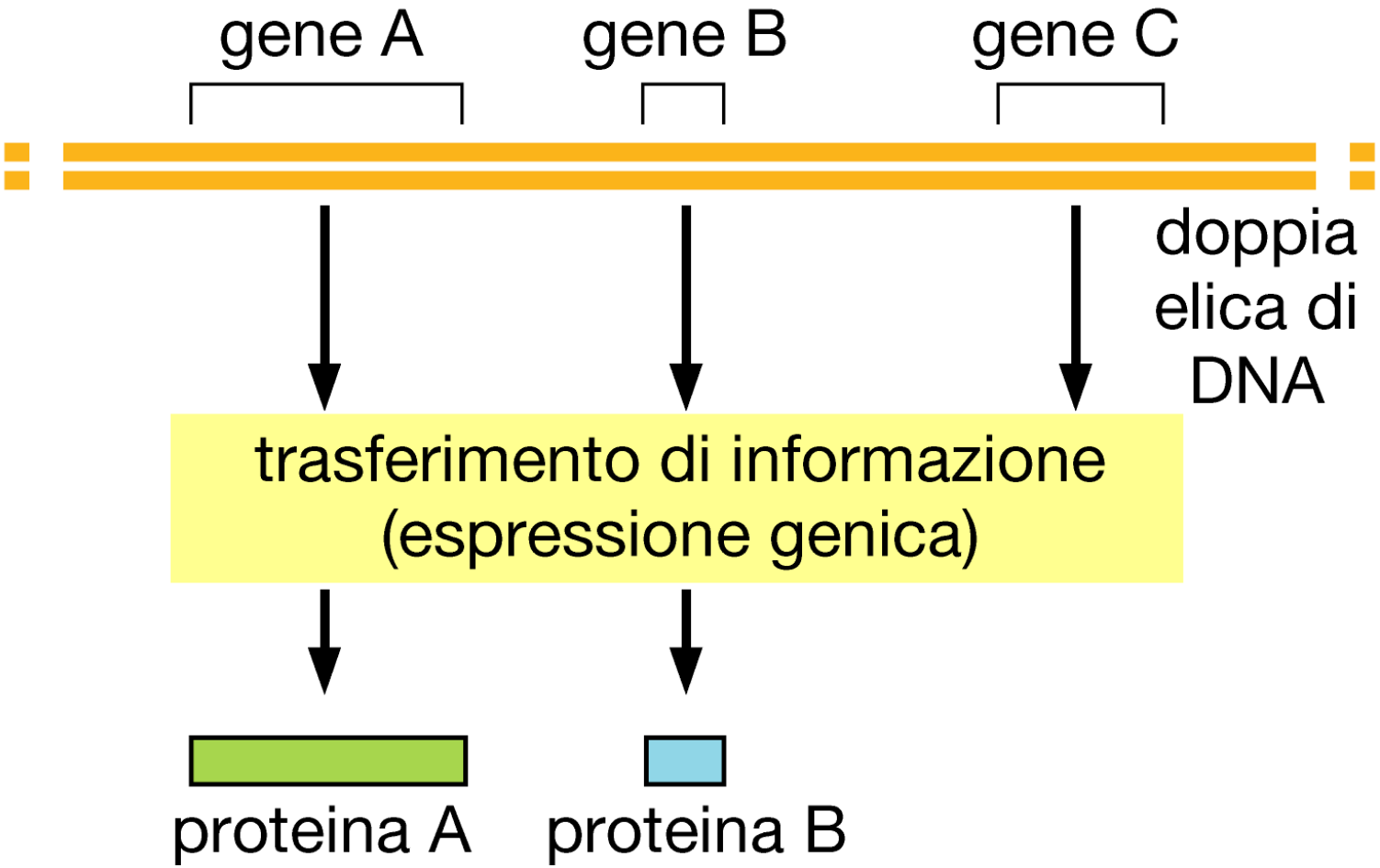
Biologia generale

Parte 4

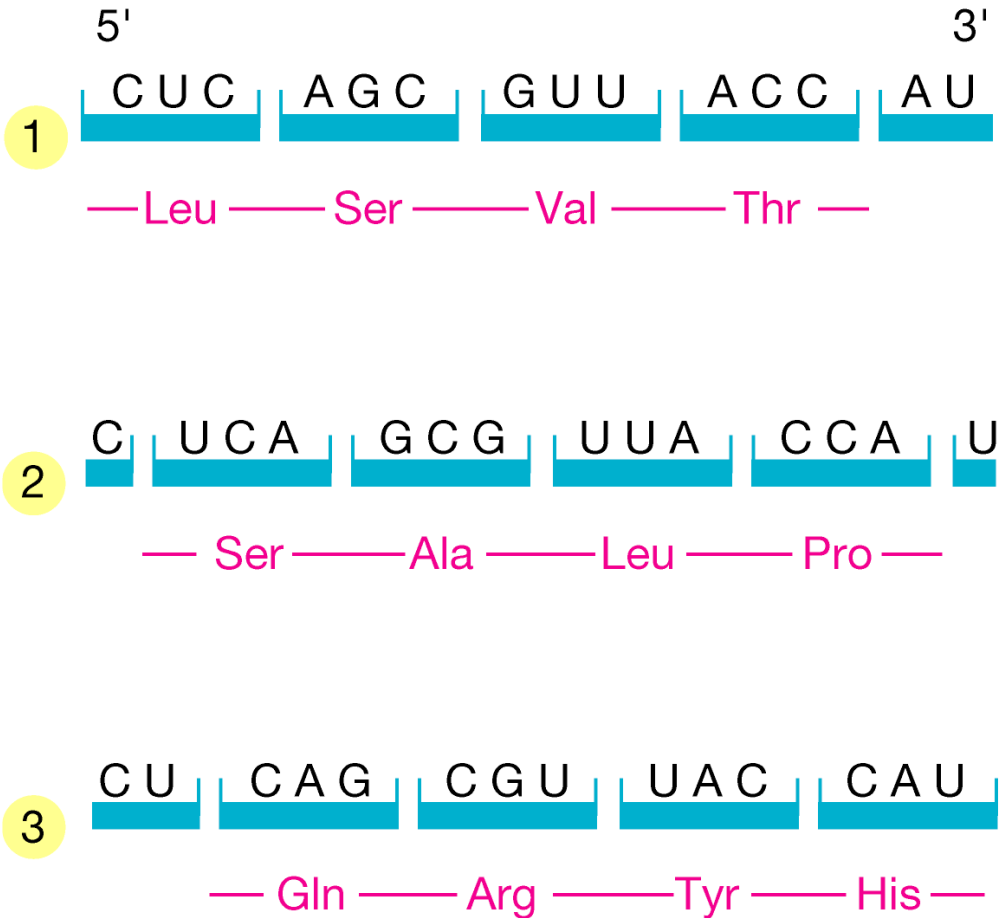
L'espressione genica: il processo di traduzione

LINK A VIDEO DIDATTICI - SINTESI PROTEICA
https://www.youtube.com/watch?v=G8RYhV569xg

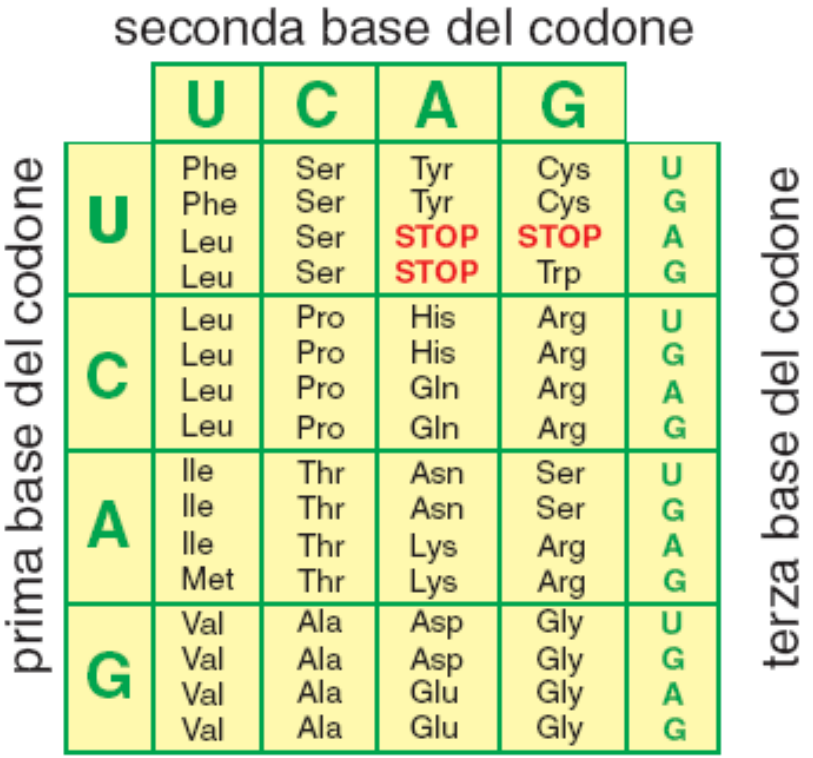
L'informazione contenuta nei geni può essere tradotta in proteine



Il DNA codifica l'informazione per la sintesi di polipeptidi nella sequenza di nucleotidi: con "parole" di 3 lettere (triplette) che specificano gli aminoacidi, scritte con un alfabeto di 4 lettere (GUAC)



La traduzione: codice genetico a triplette univoco e ridondante

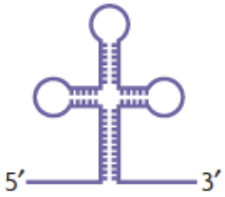


prima base del codone	U	C	A	G	terza base del codone
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	G
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	G
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	G
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	G
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

UNIVOCO: ciascuna tripletta specifica solo 1 aminoacido
Gli **aminoacidi sono in tutto 20**: 64 combinazioni di 3 lettere sono **RIDONDANTI**

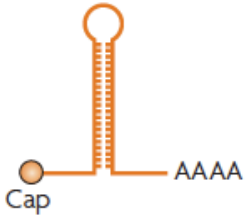
La regione codificante del mRNA (ORF) inizia con un AUG (metionina) e termina con un segnale di STOP.

Le classi di RNA coinvolte nella traduzione



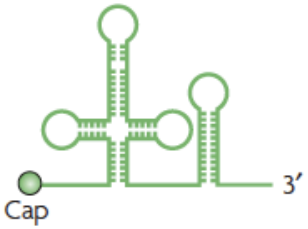
tRNA

adattatori tra mRNA e aminoacidi nella sintesi proteica



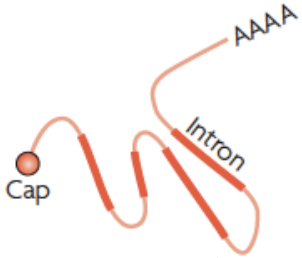
microRNA

regolazione dell'espressione di altri RNA



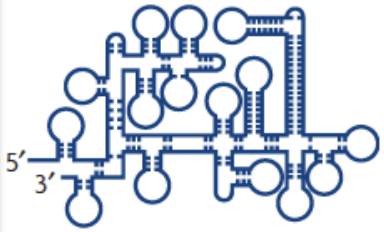
snRNA

splicing dei pre-mRNA, …



mRNA

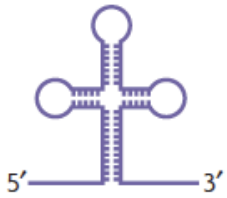
codificano per proteine



rRNA

struttura dei ribosomi e catalisi nella sintesi proteica

Le classi di RNA coinvolte nella traduzione



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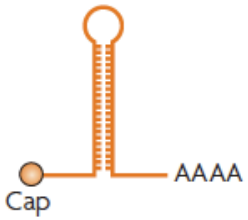

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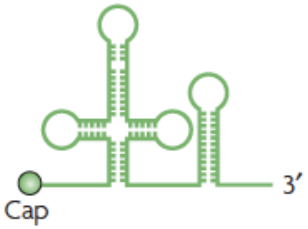

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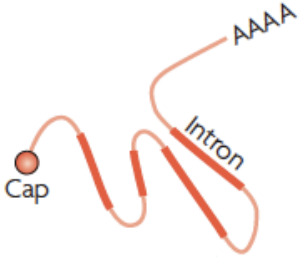

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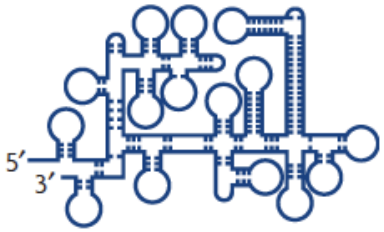
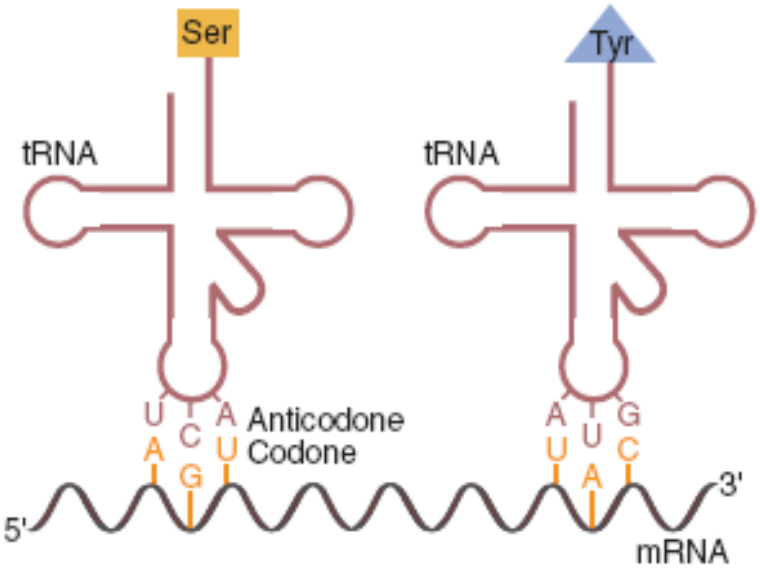
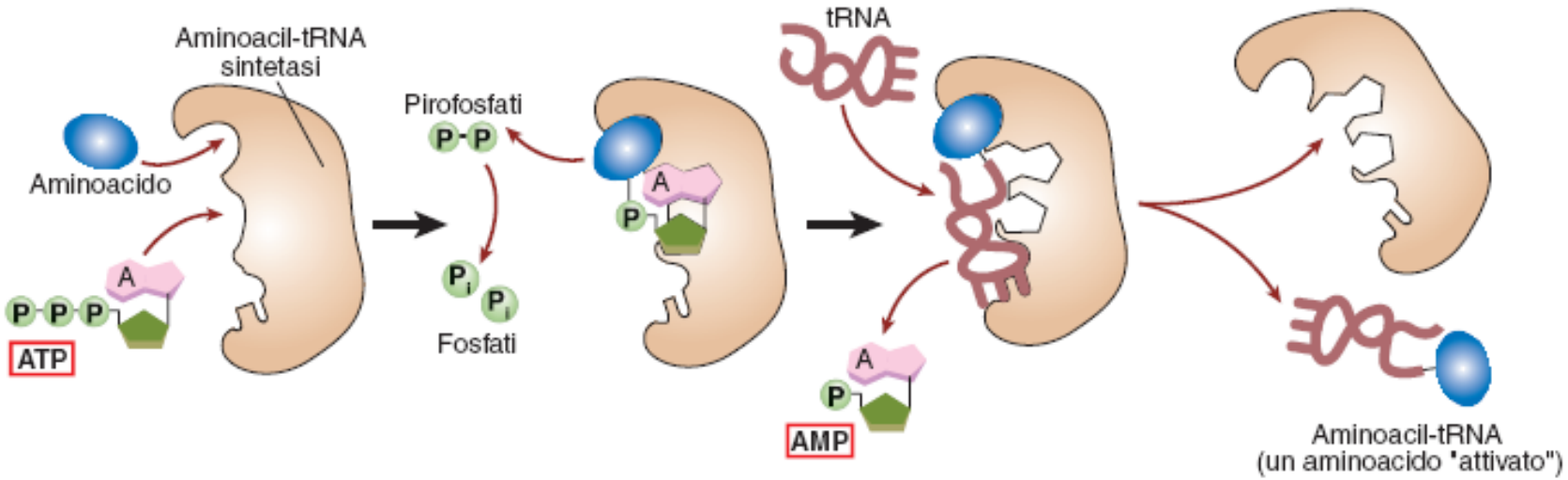


rRNA

struttura dei ribosomi e catalisi nella sintesi proteica

La decifrazione del codice genetico avviene grazie agli RNA transfer





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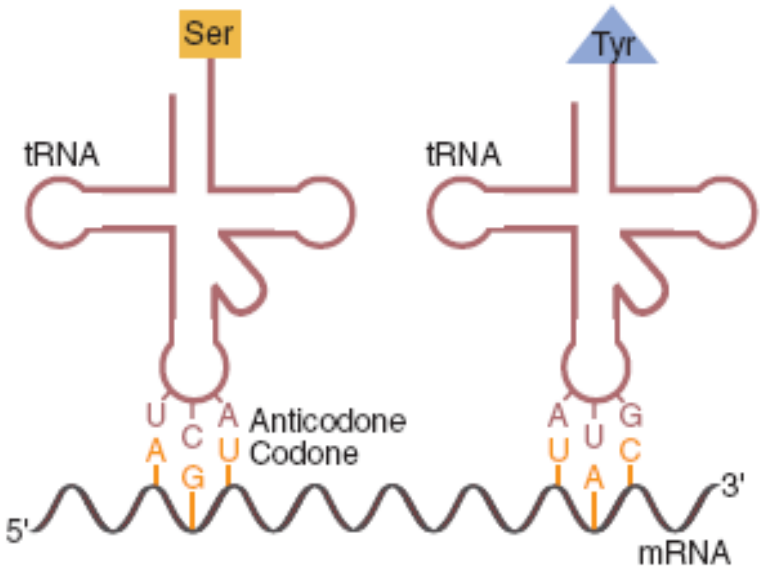

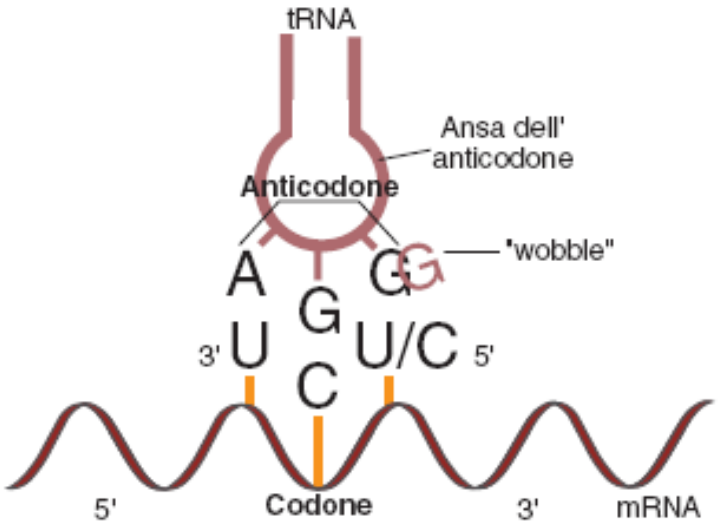

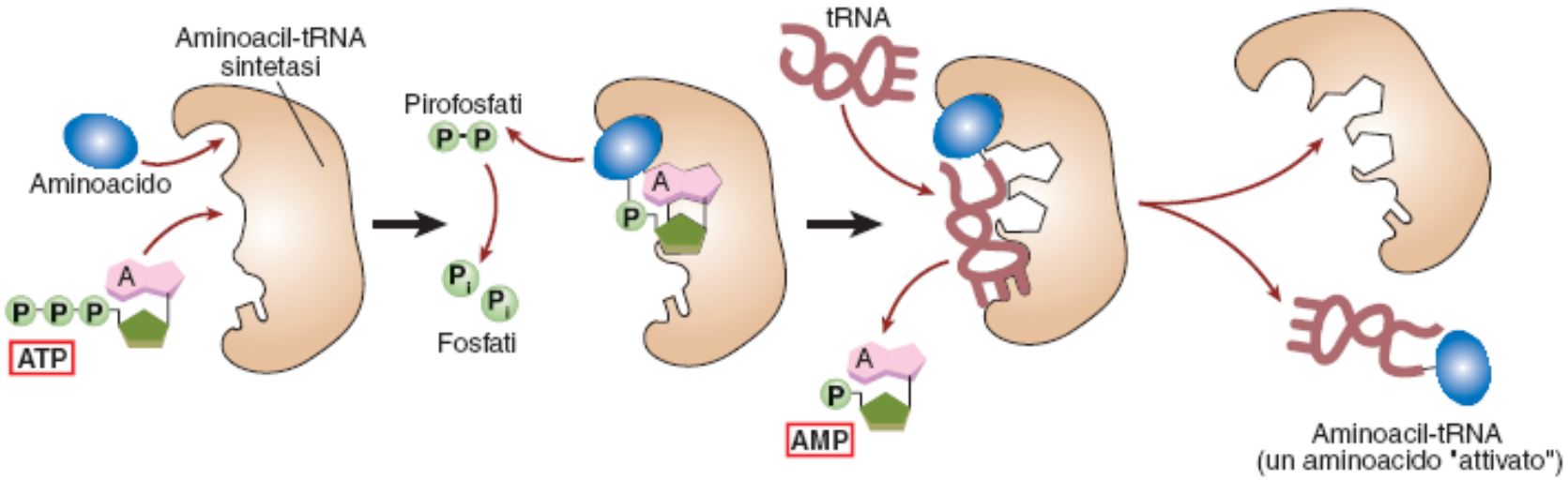

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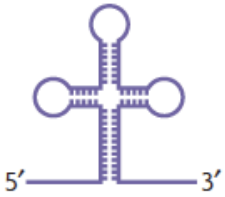

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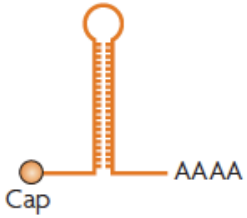

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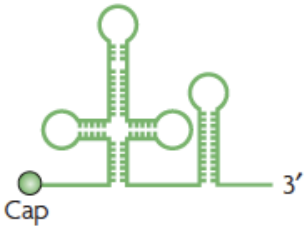

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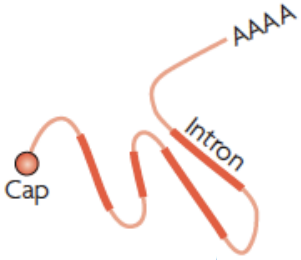

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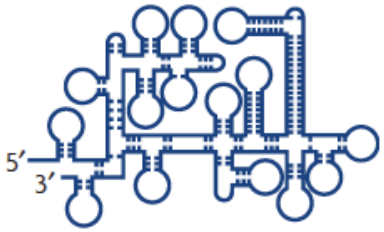
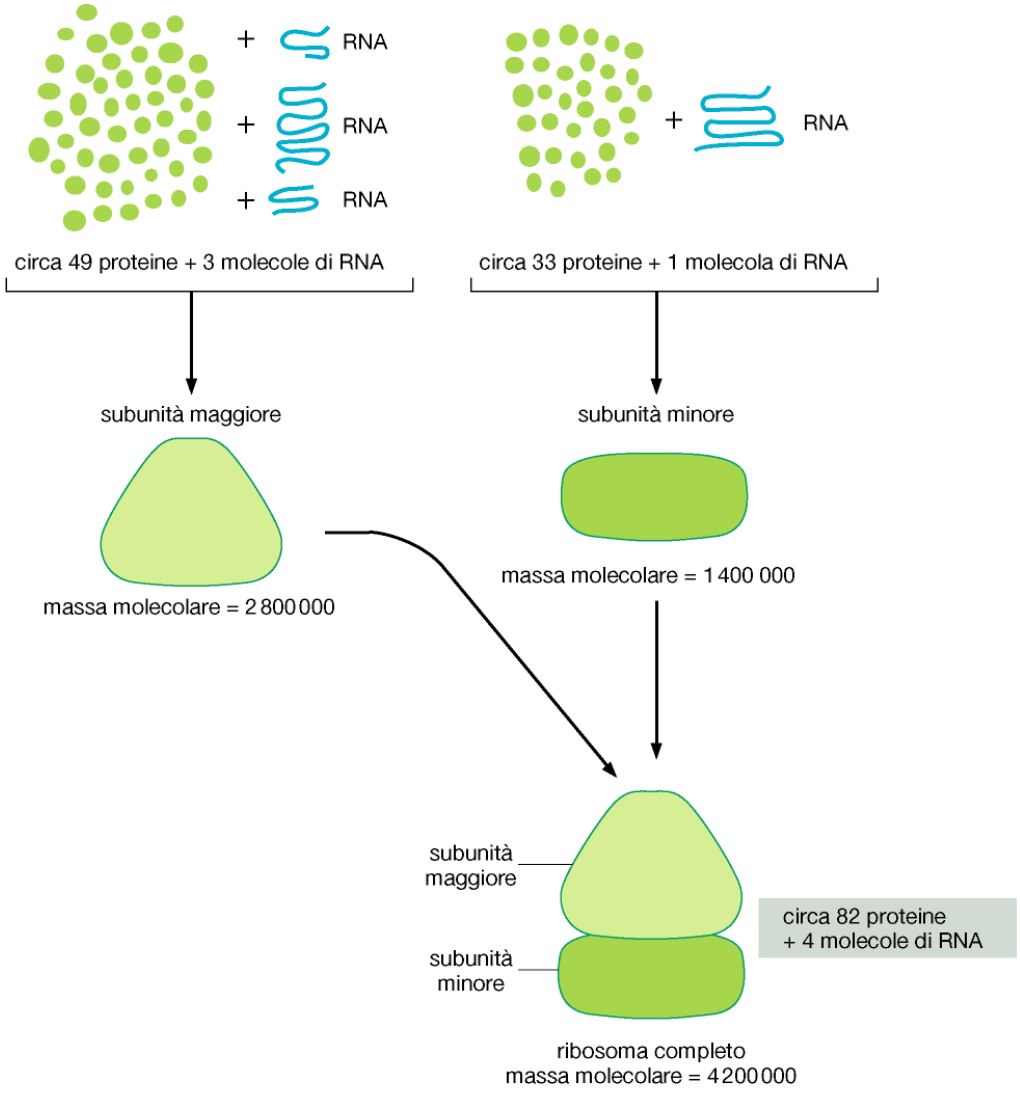


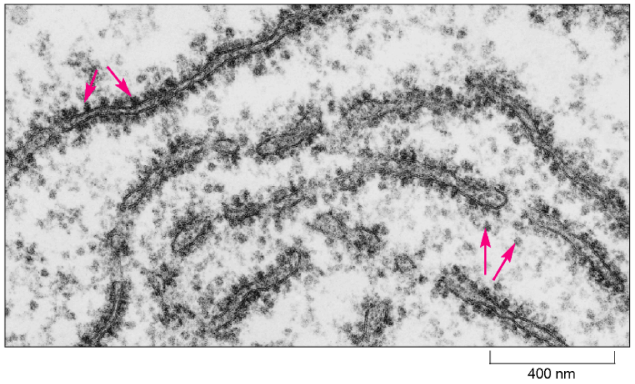
rRNA

struttura dei ribosomi e catalisi nella sintesi proteica

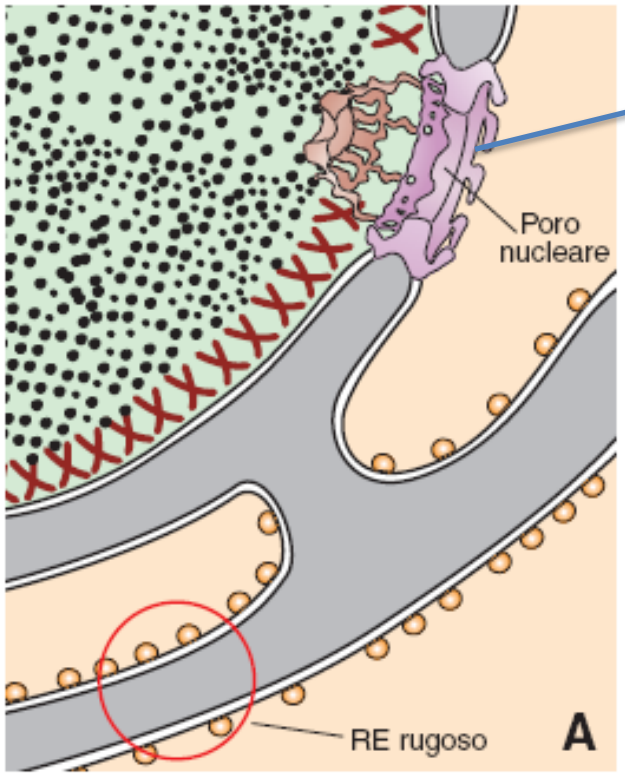
I ribosomi sono la sede della traduzione



Ribosomi:
liberi nel citoplasma o presenti sul Reticolo endoplasmatico rugoso

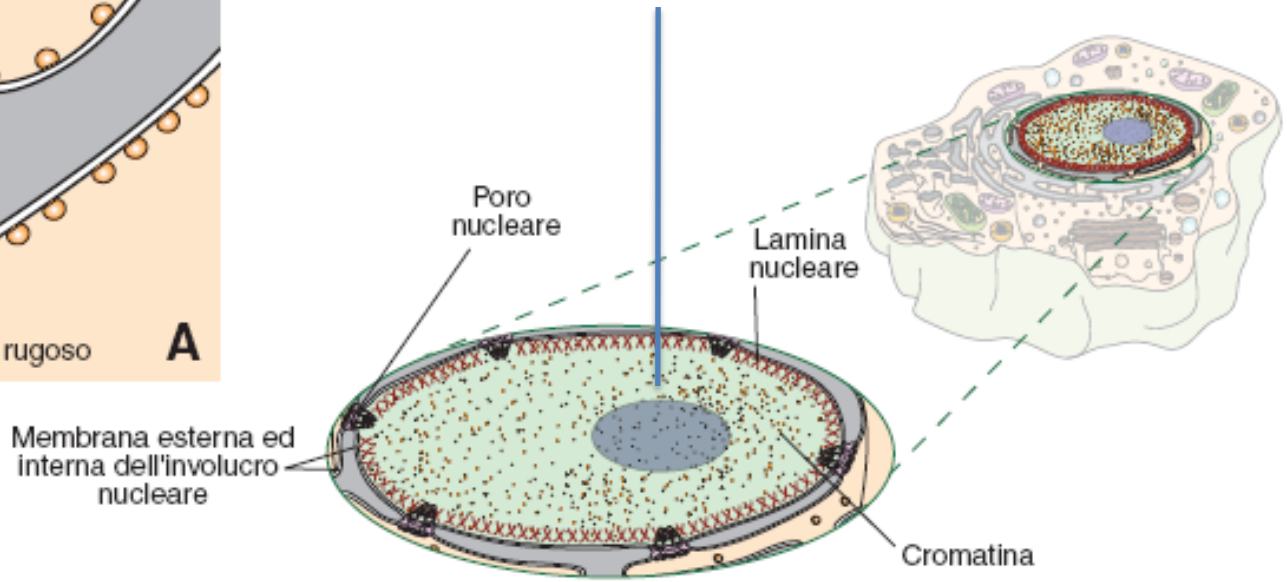


I ribosomi sono prodotti nel nucleo

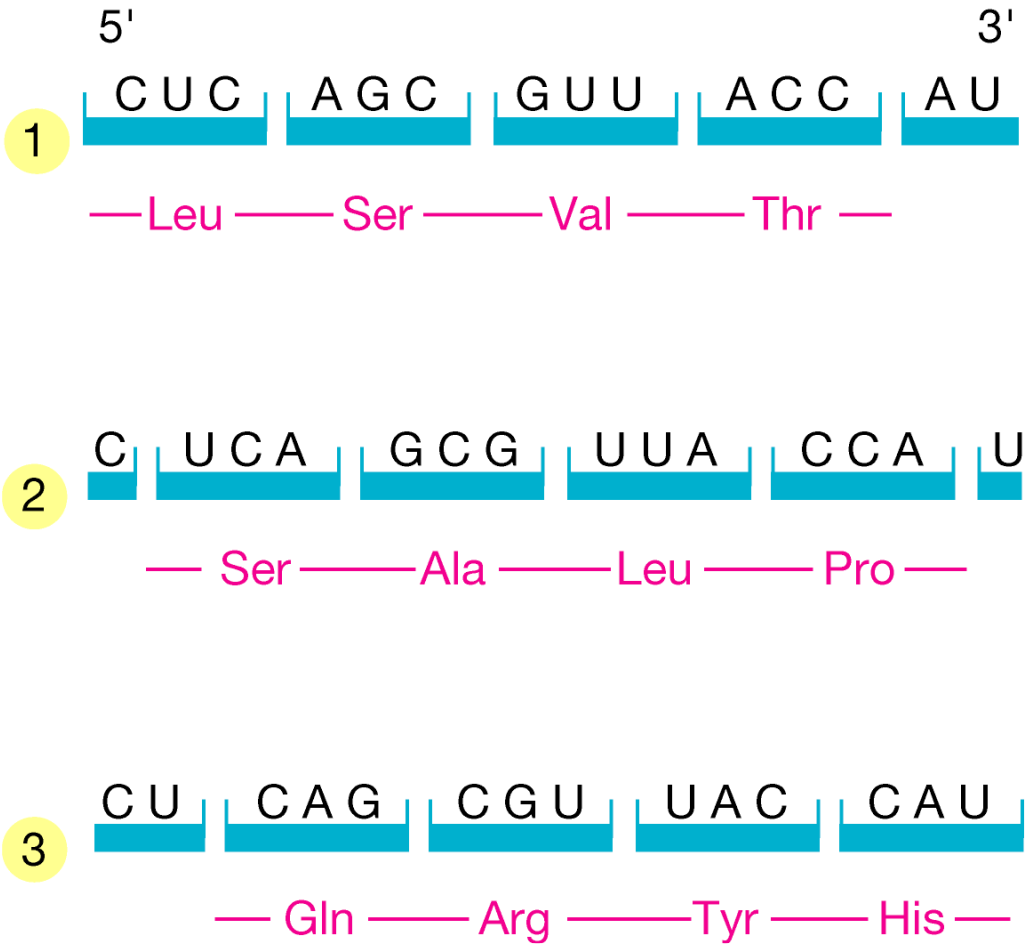


Complessi ribonucleoproteici e subunità ribosomali vengono esportate attraverso i pori nucleari

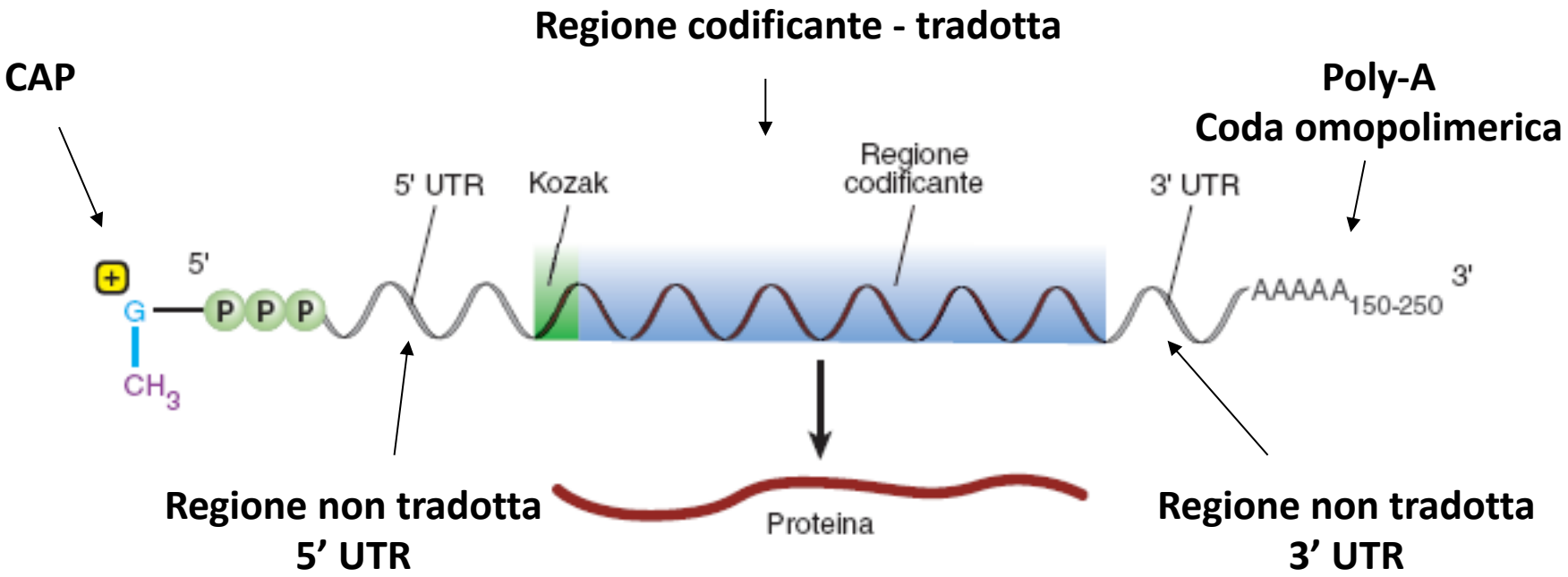
NUCLEOLO: contiene i geni per rRNA
È la sede della sintesi degli rRNA e dell'assemblaggio delle subunità ribosomali



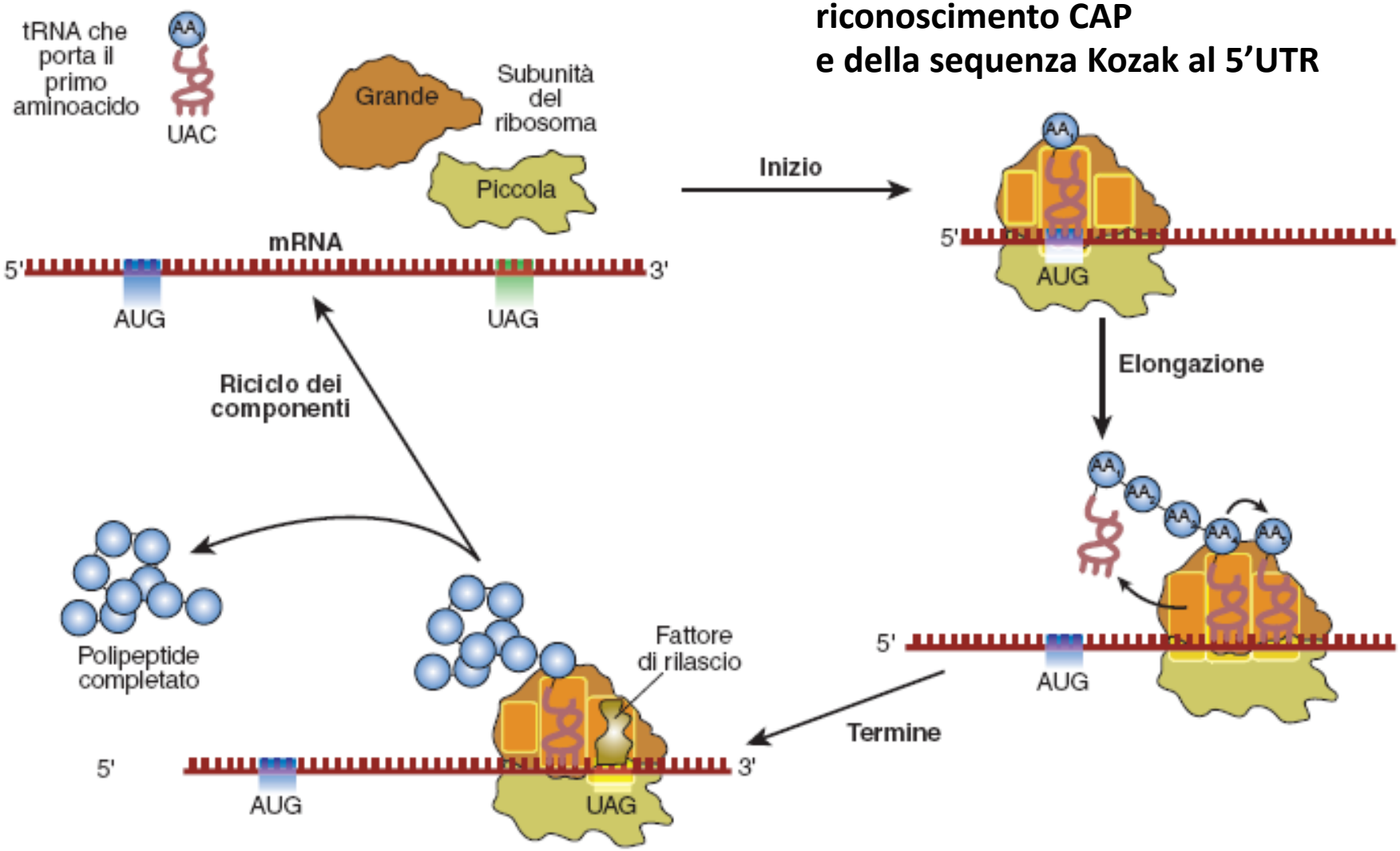
La cornice di lettura



Struttura del mRNA eucariotico

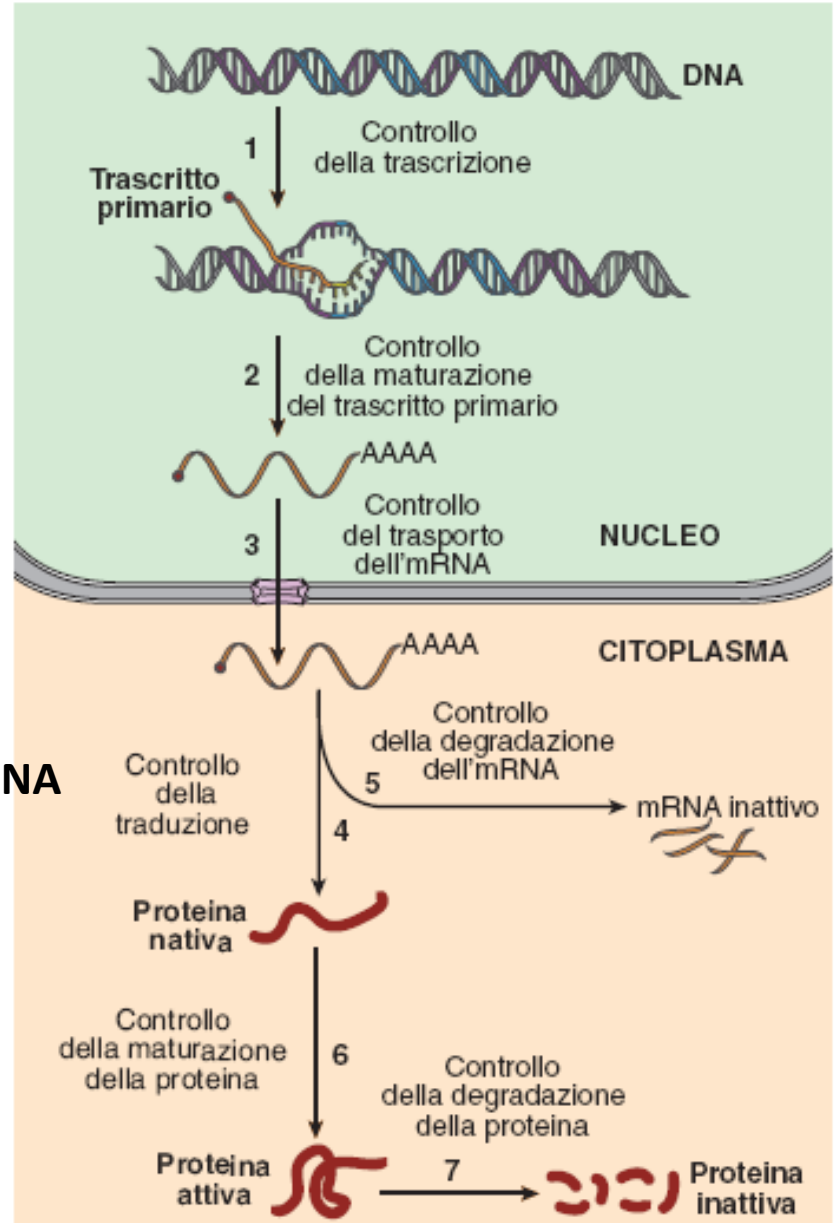


Fasi della sintesi proteica

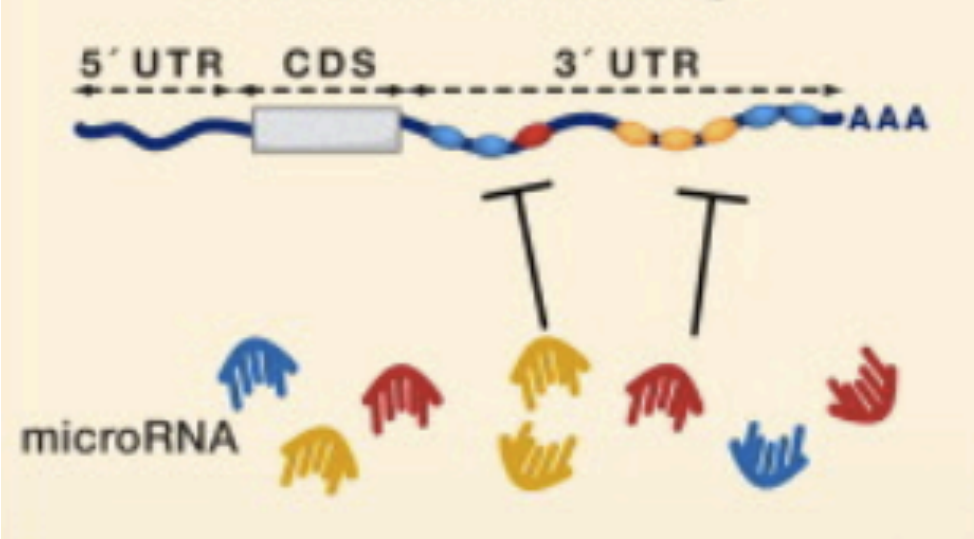


Livelli di controllo dell'espressione genica eucariotica

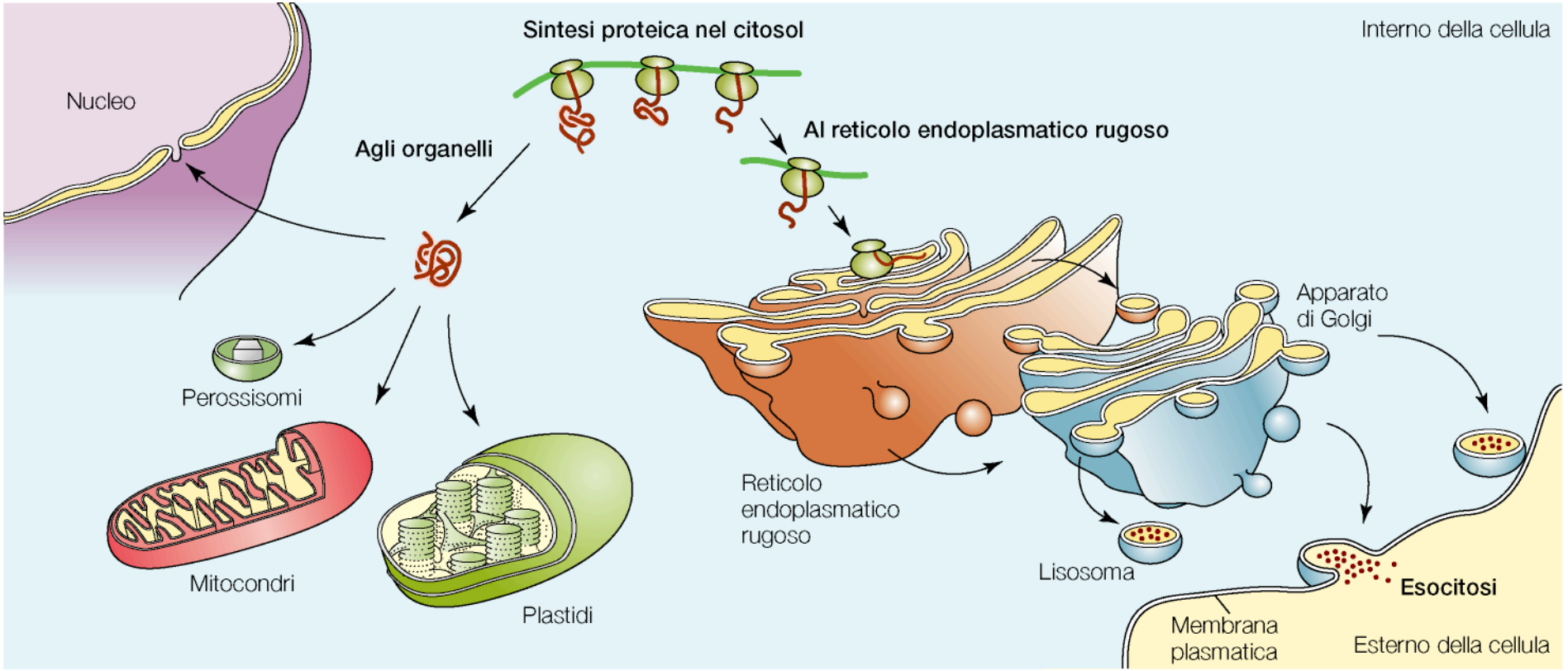
microRNA



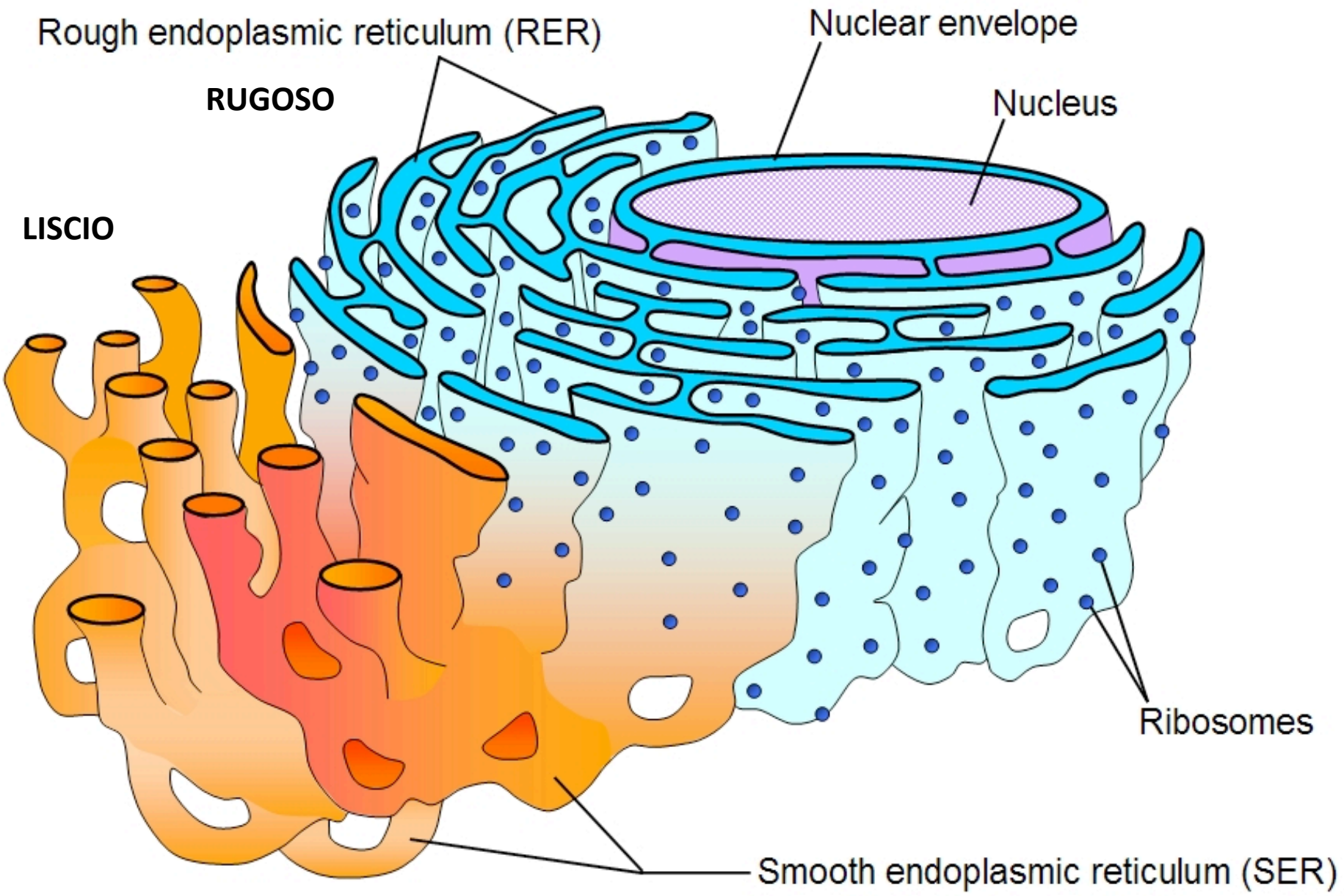
Ruolo dei microRNA nella regolazione dell'espressione genica



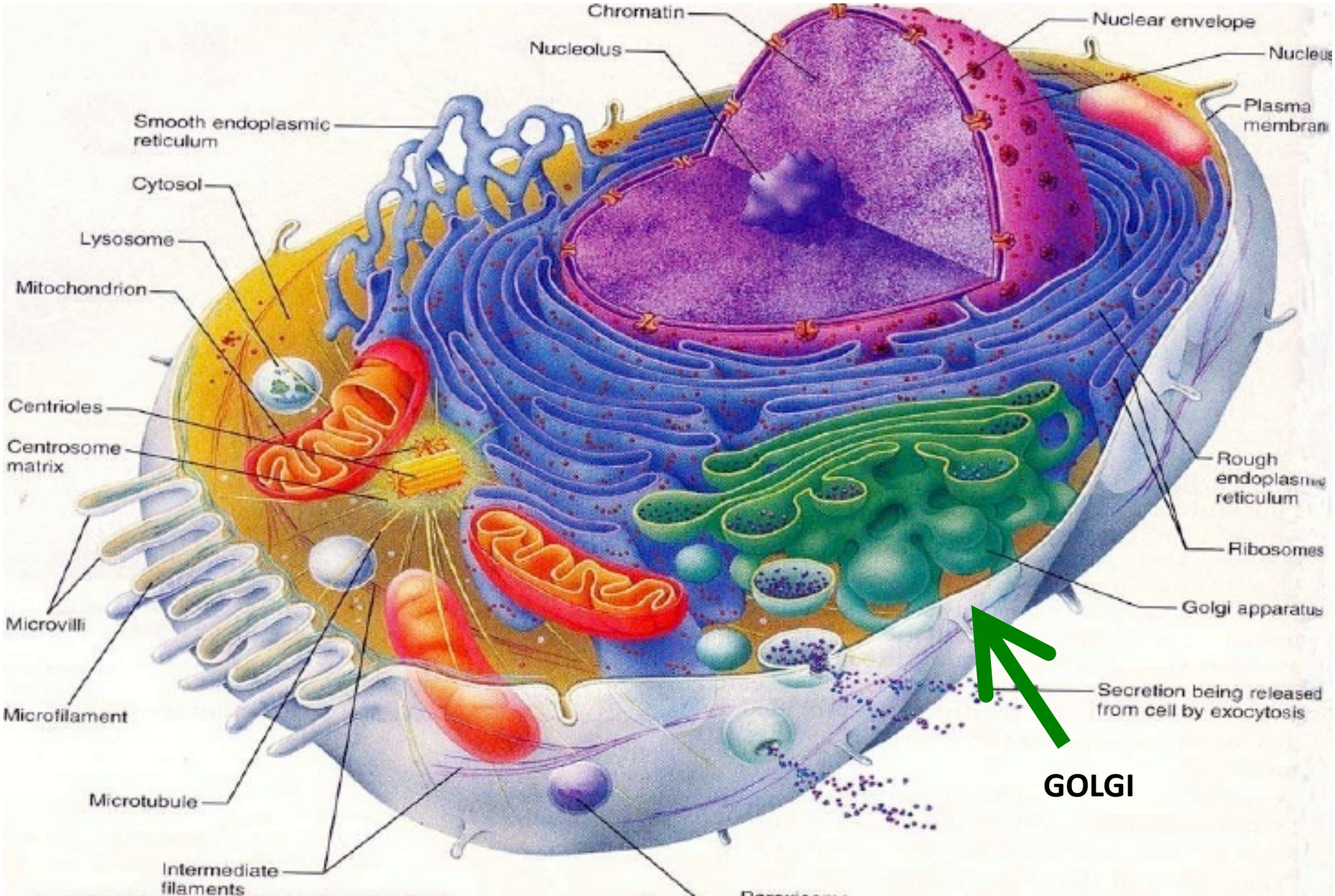
La sintesi proteica avviene nel citosol e nel RER



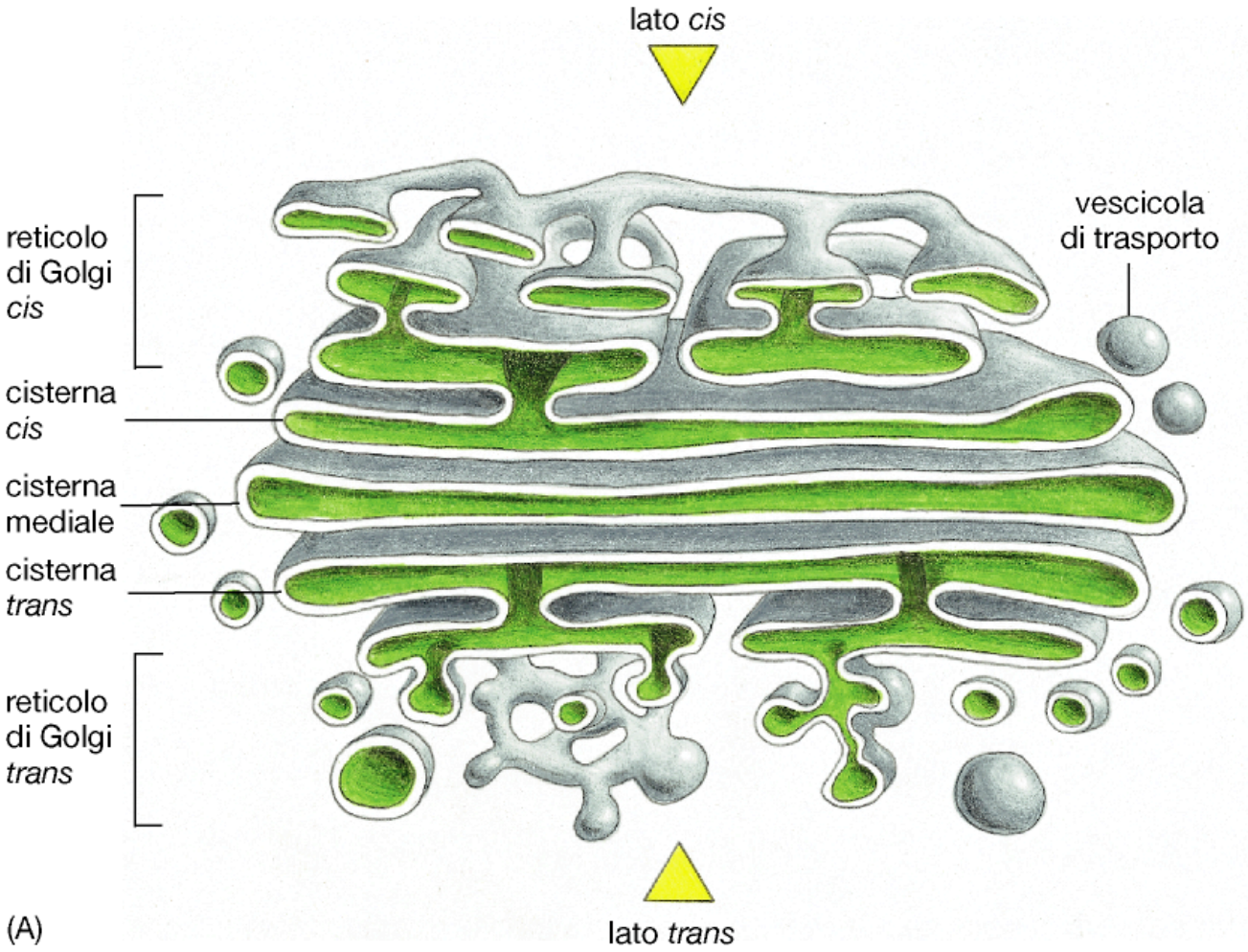
Il reticolo endoplasmatico



Apparato di Golgi



L' apparato di Golgi nella glicosilazione di proteine e nel metabolismo di lipidi e polisaccaridi e nel loro smistamento



Apparato di Golgi

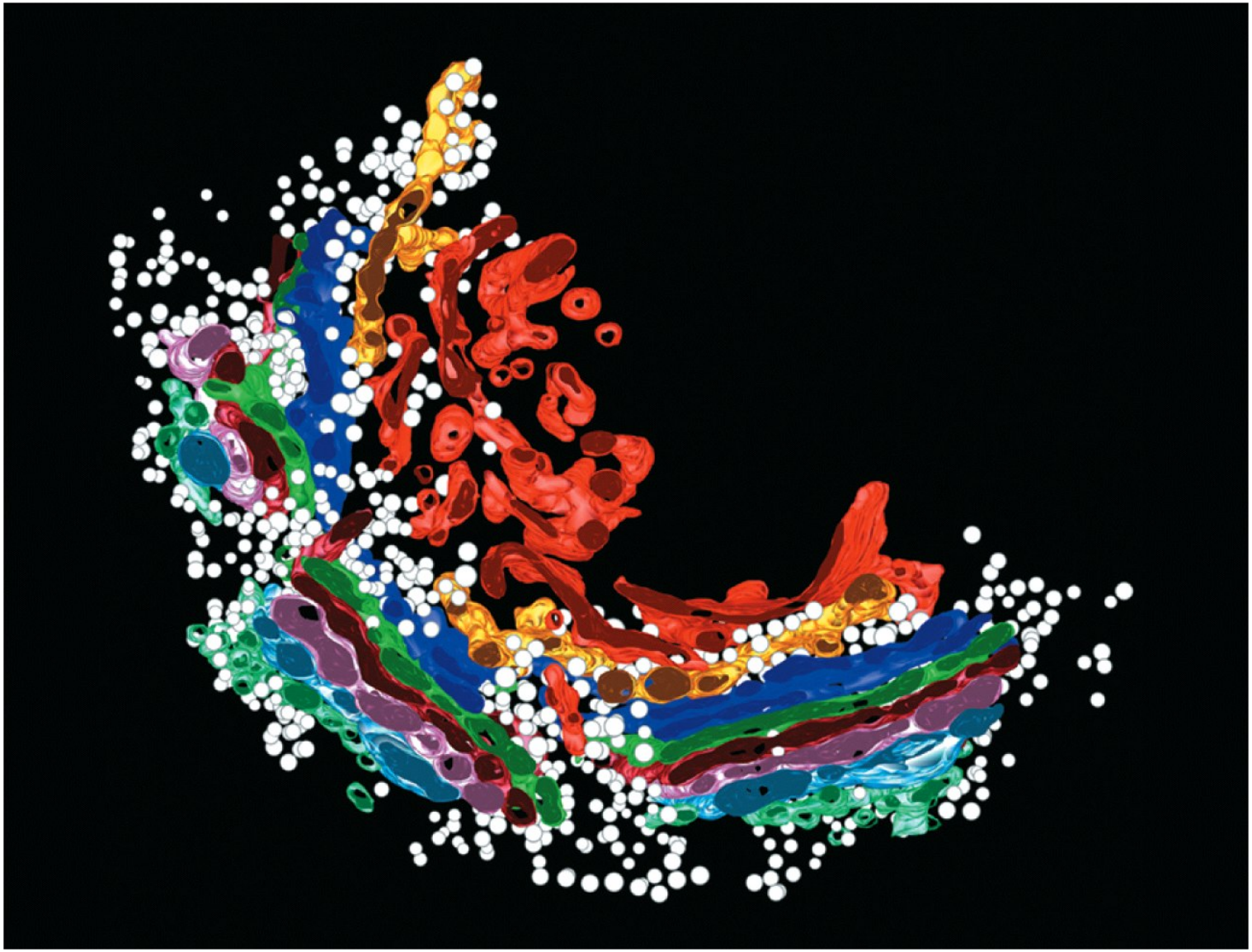
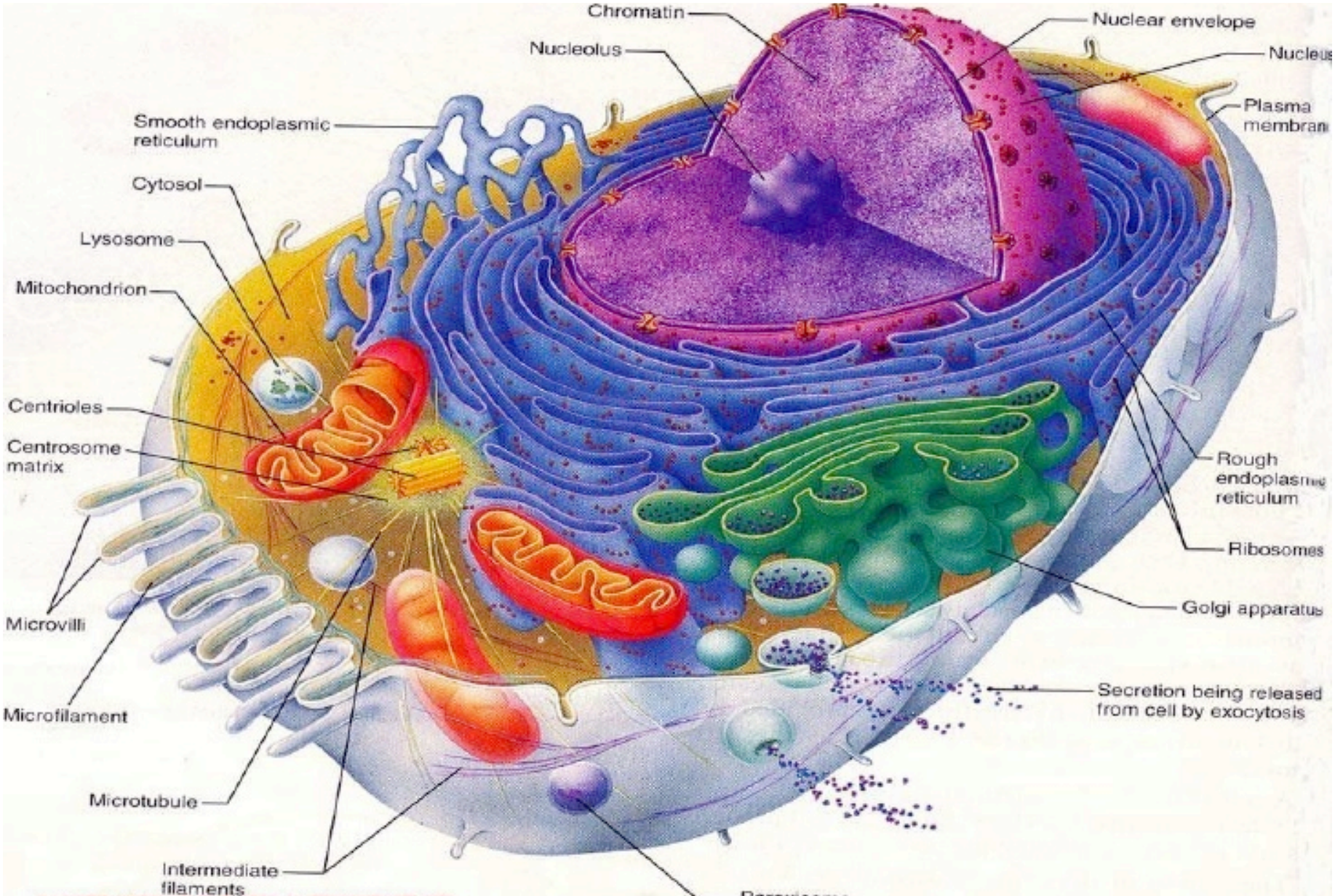
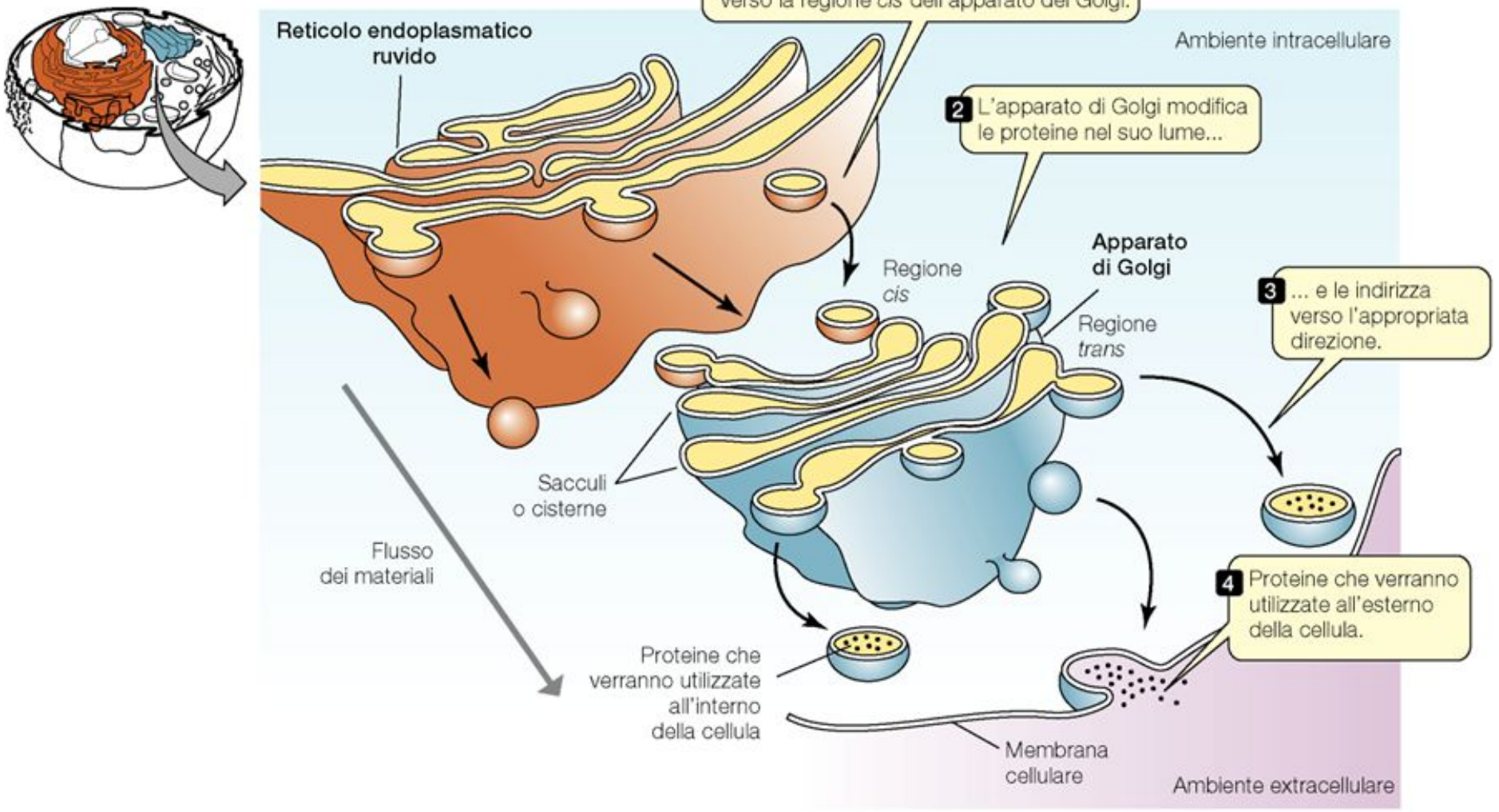


Figure 9-6
Molecular Cell Biology, Sixth Edition

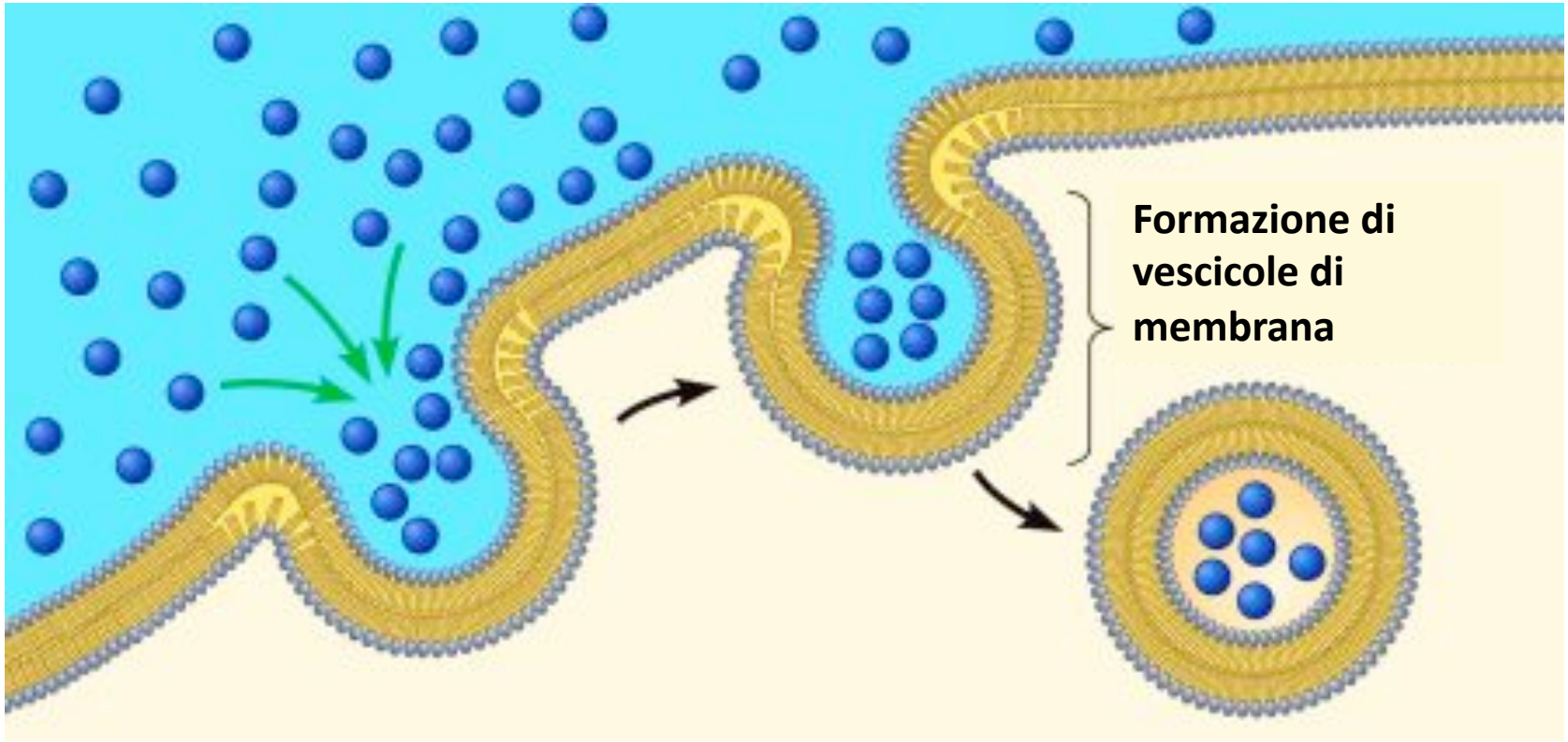
Continuità delle membrane



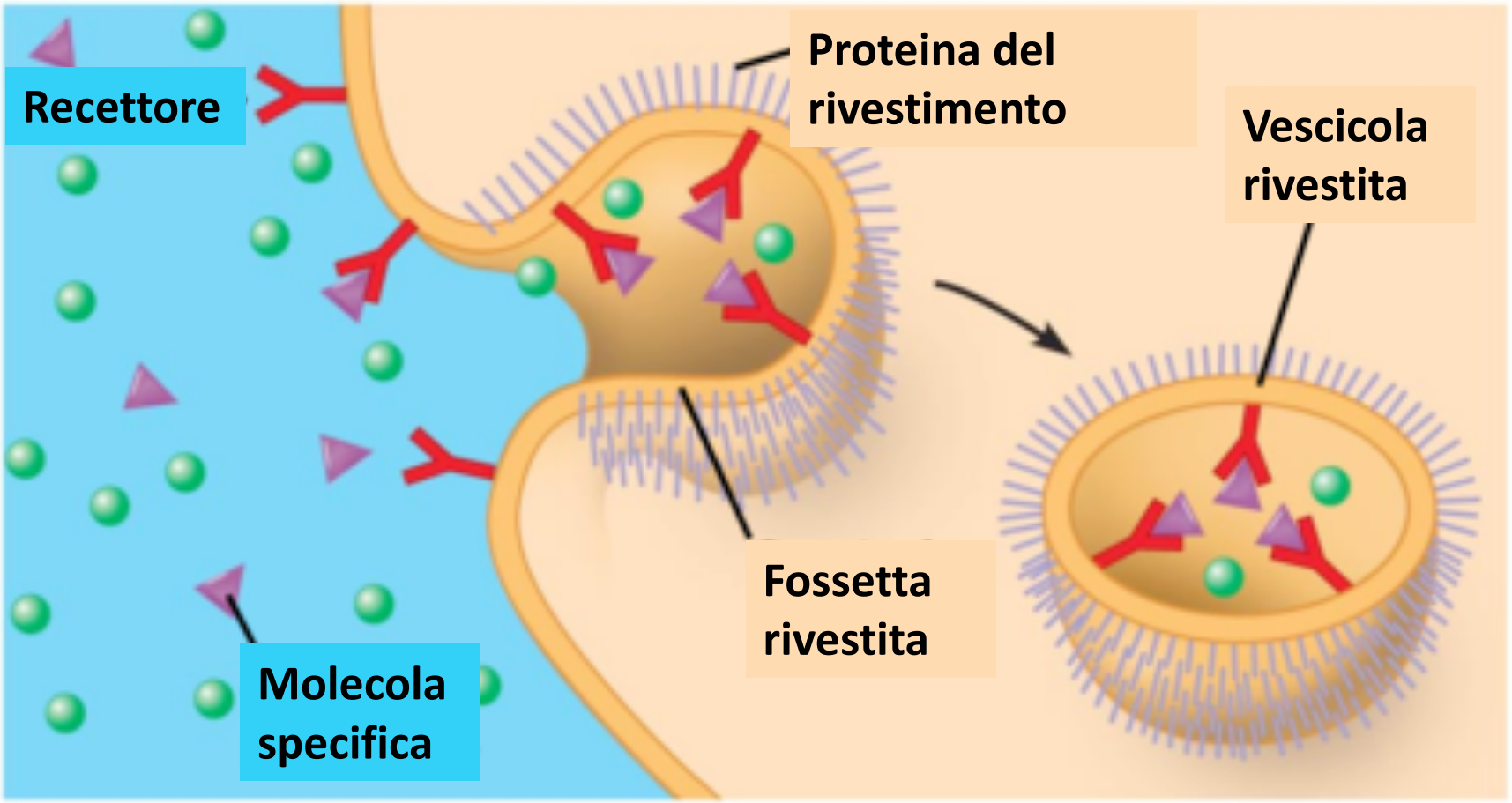
Il traffico vescicolare: la via secretoria



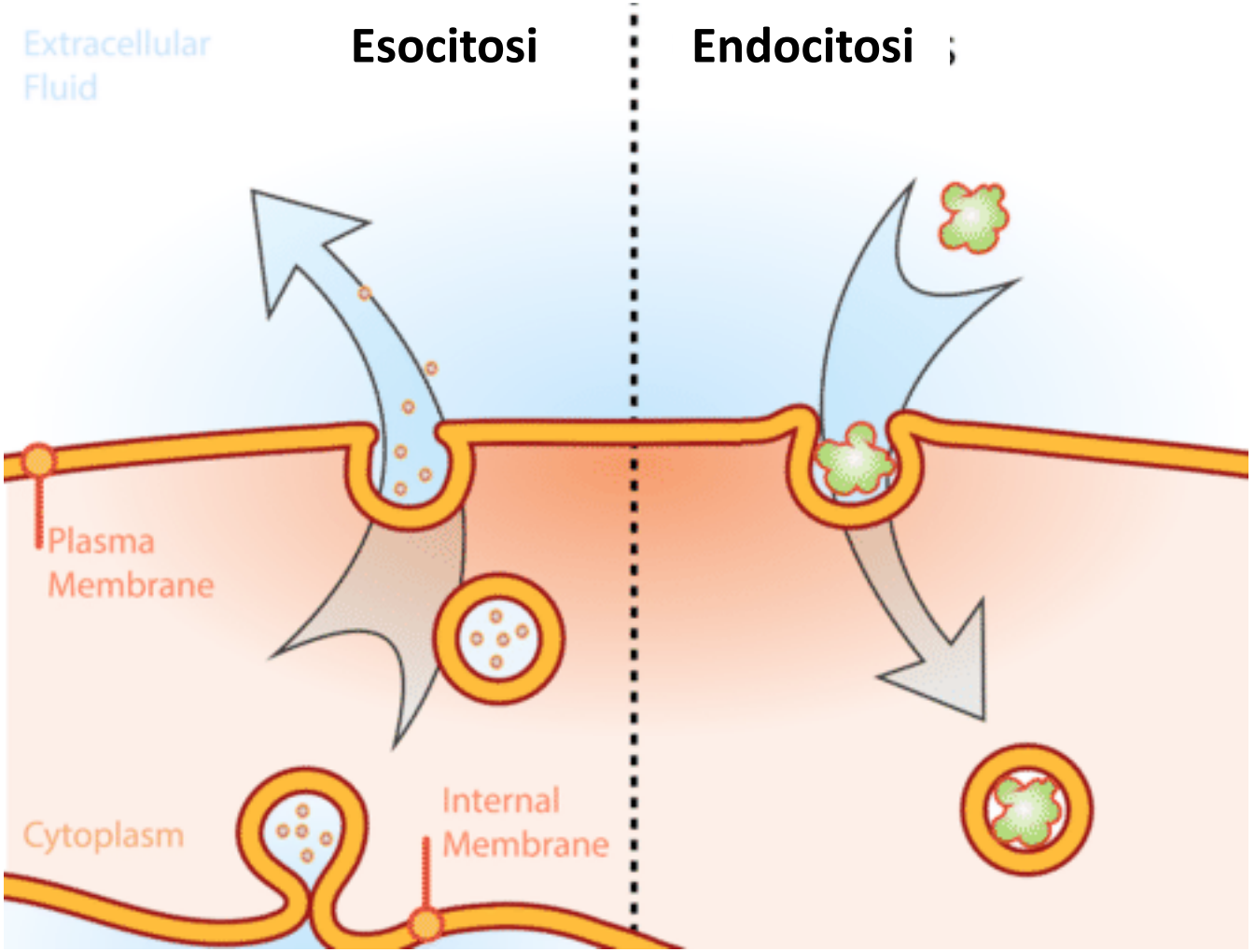
Endocitosi

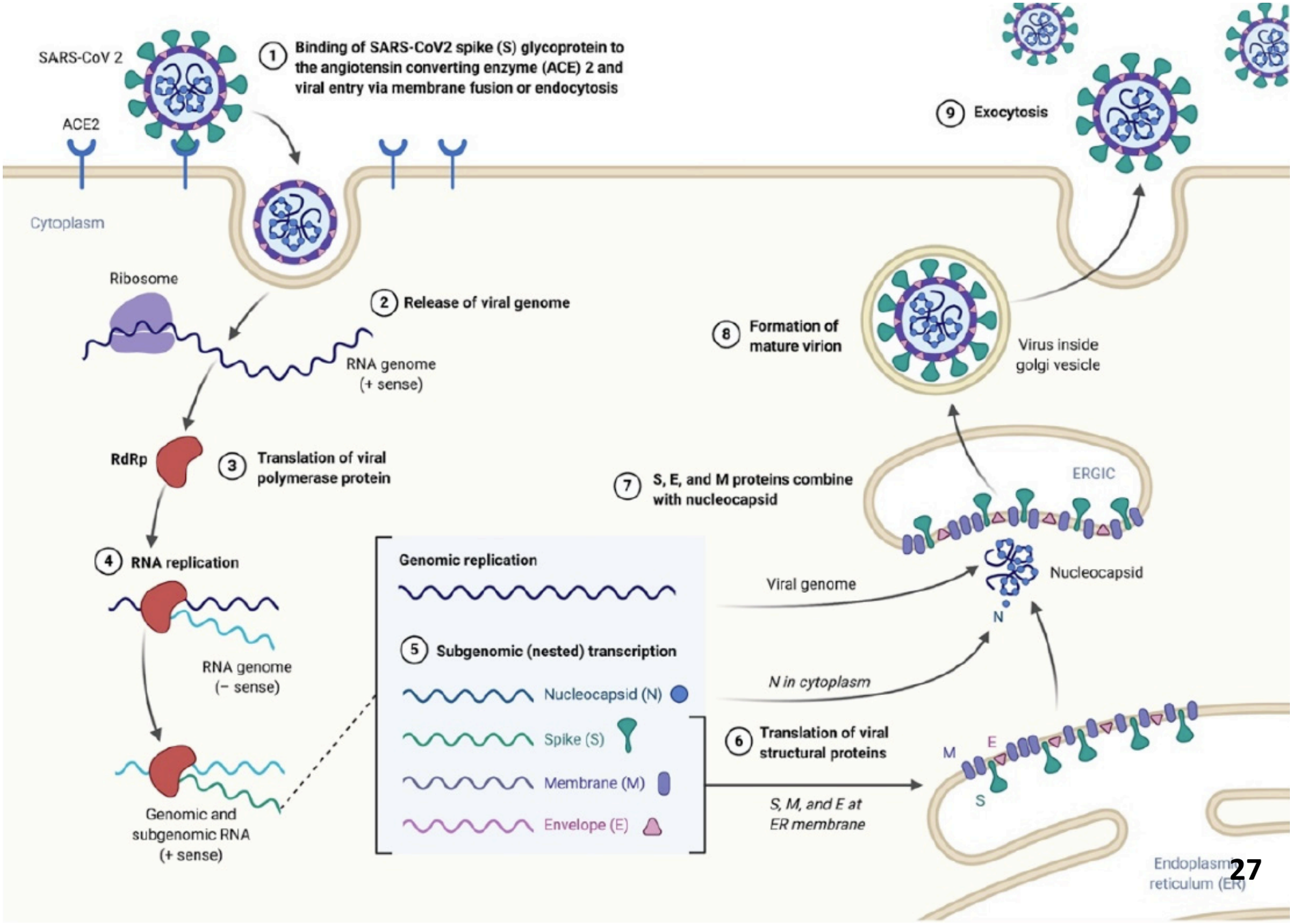


Endocitosi mediata da recettore

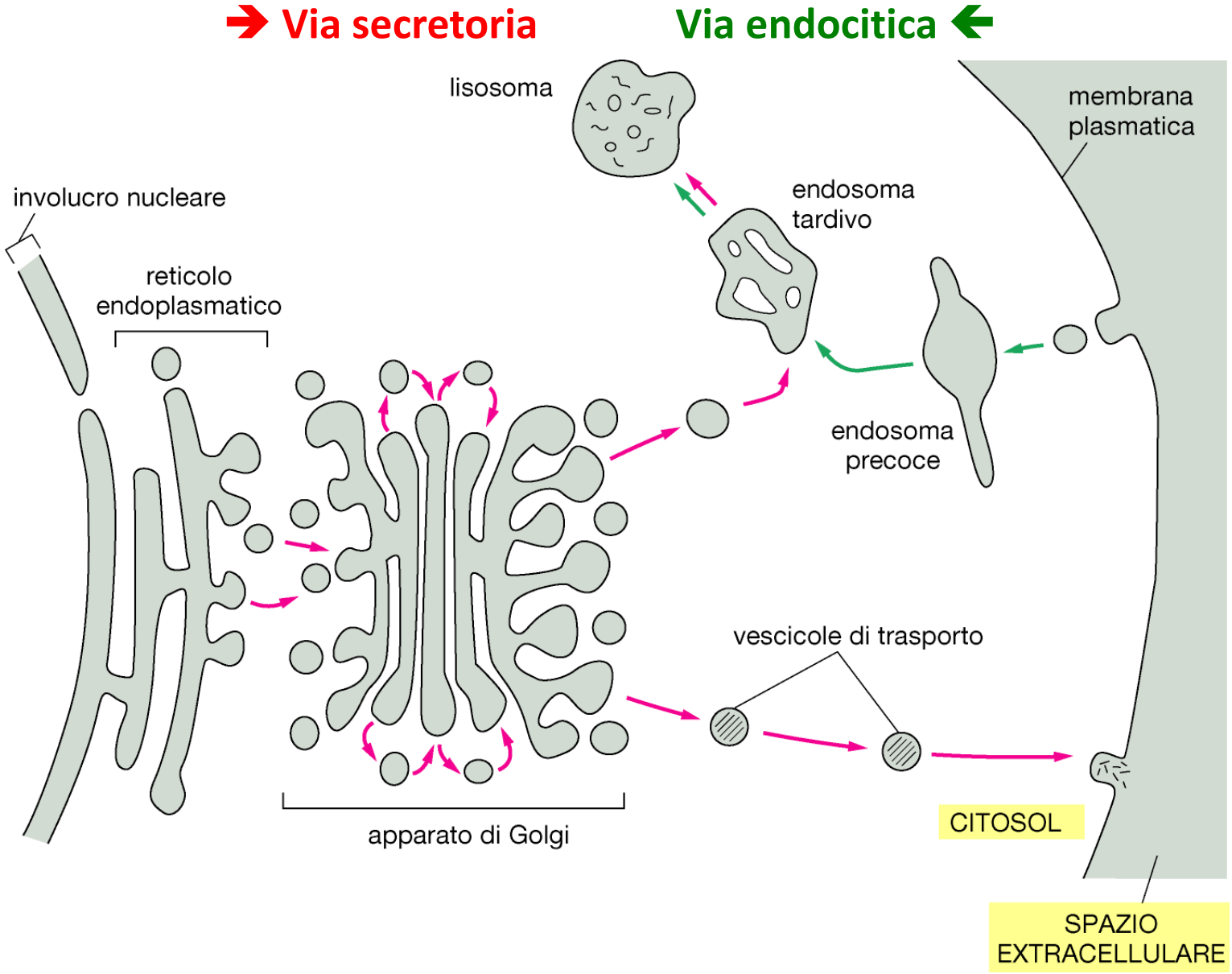


https://www.youtube.com/watch?v=OejK9KAfFCY

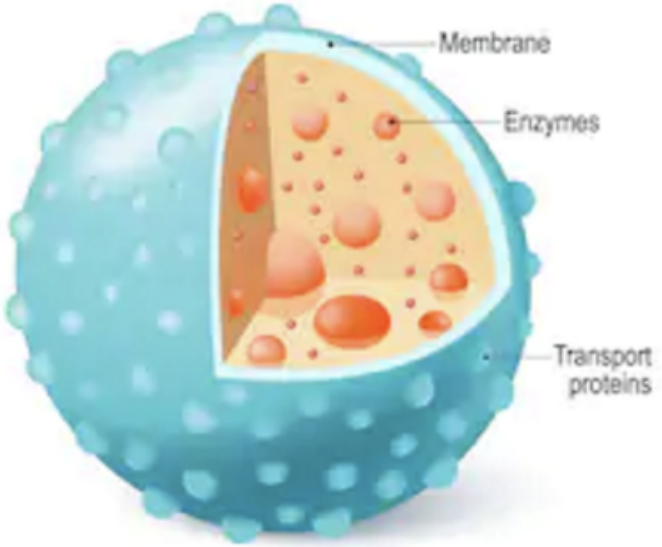

Extracellular Fluid
Esocitosi
Endocitosi
Plasma Membrane
Cytoplasm
Internal Membrane


SARS-CoV 2
ACE2
Cytoplasm
1 Binding of SARS-CoV2 spike (S) glycoprotein to the angiotensin converting enzyme (ACE) 2 and viral entry via membrane fusion or endocytosis
Ribosome
2 Release of viral genome
RNA genome (+ sense)
RdRp
3 Translation of viral polymerase protein
4 RNA replication
RNA genome (− sense)
Genomic and subgenomic RNA (+ sense)
Genomic replication
5 Subgenomic (nested) transcription
Nucleocapsid (N)
Spike (S)
Membrane (M)
Envelope (E)
6 Translation of viral structural proteins
S, M, and E at ER membrane
M
E
S
Endoplasmic reticulum (ER)
7 S, E, and M proteins combine with nucleocapsid
ERGIC
Viral genome
N in cytoplasm
N
Nucleocapsid
8 Formation of mature virion
Virus inside golgi vesicle
9 Exocytosis

Il trasporto vescicolare



I lisosomi: sede della digestione intracellulare



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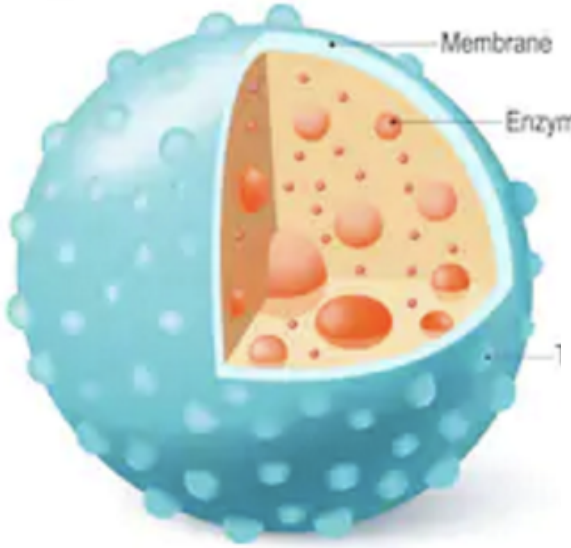
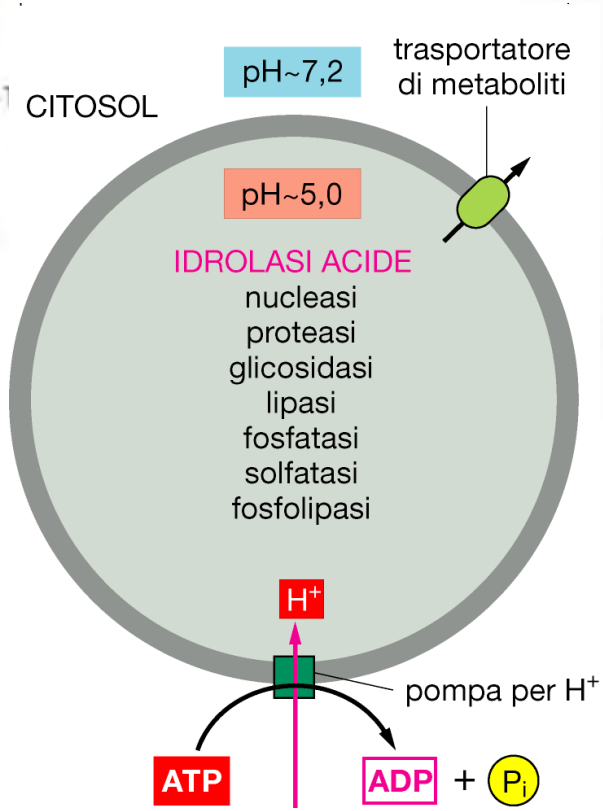
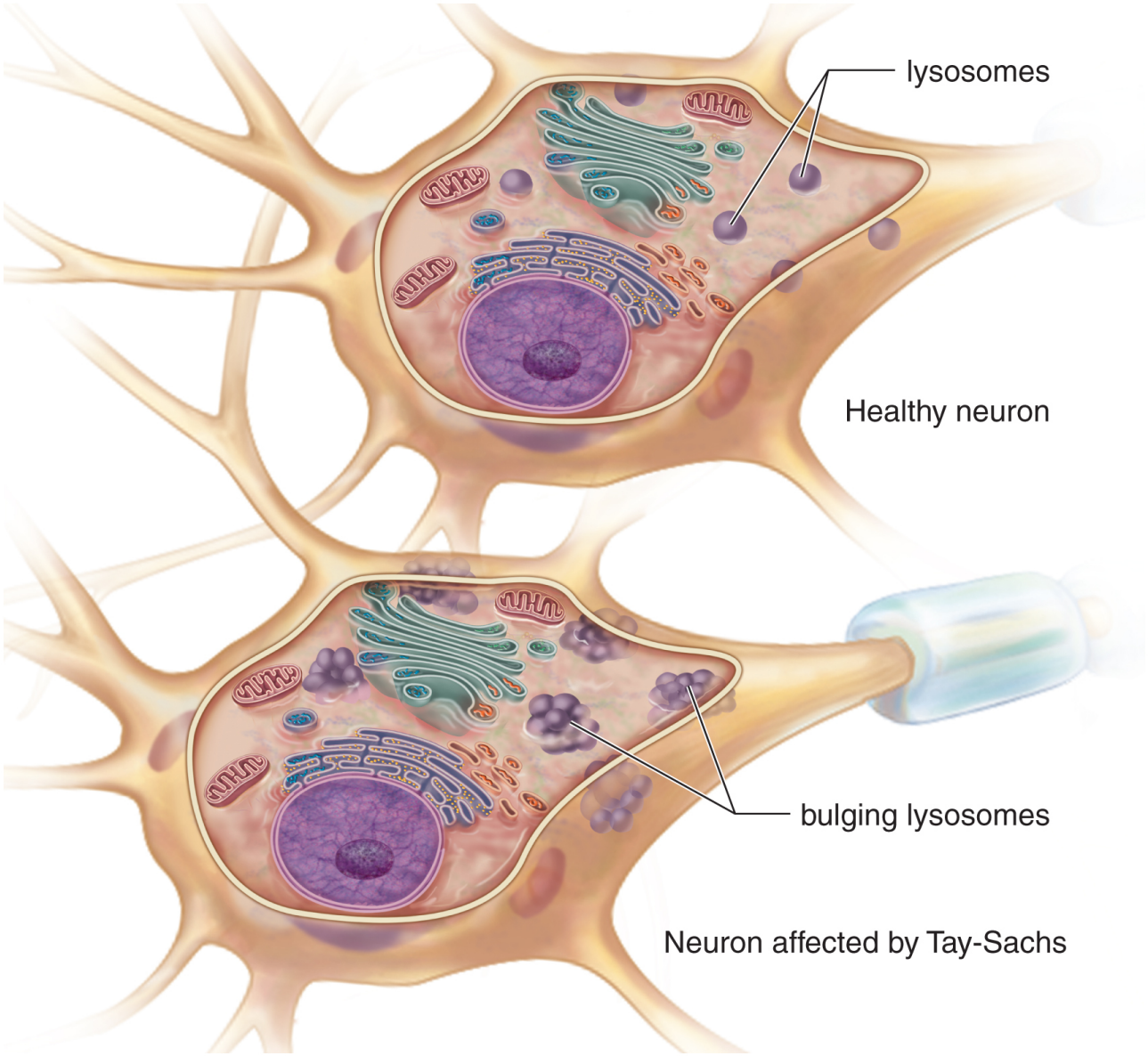




Lysosomal storage disorders = malattie genetiche causate da mutazioni di enzimi lisosomiali



PRIMEVIEW

LYSOSOMAL STORAGE DISORDERS

nature REVIEWS DISEASE PRIMERS

For the Primer, visit doi:10.1038/s41572-018-0031-6

Lysosomal storage disorders (LSDs) are a group of inherited metabolic disorders that are characterized by the accumulation of macromolecules inside lysosomes. Lysosomes engulf and break down macromolecules, including nucleic acids, proteins, carbohydrates and lipids, inside cells. LSDs are multi-system diseases that frequently involve pathology in the brain.

EPIDEMIOLOGY

Collectively, LSDs are relatively common disorders (1: 5,000 live births), although individual disorders are rare and have an incidence between 1 in 50,000 and 1 in 250,000 live births. The most common disorders are Gaucher disease and the neuronal ceroid lipofuscinoses.

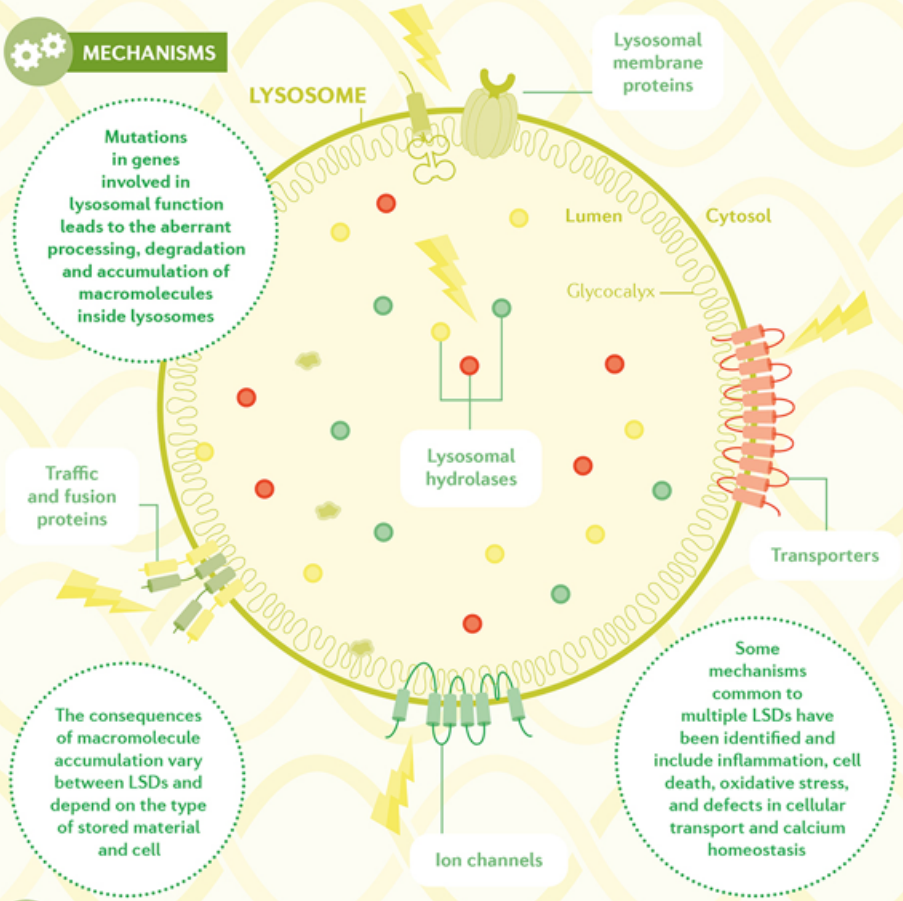
The incidence of some LSDs can be higher in specific populations owing to a genetic founder effect, such as Tay–Sachs disease in the Ashkenazi Jewish population

SCREENING

In the United States, carrier screening for Tay–Sachs disease in the Ashkenazi Jewish community has reduced the incidence of this disorder by 90% in this population. However, universal newborn screening for LSDs is only available in a few countries worldwide.

Preimplantation genetic diagnosis can be offered to couples who have a child with an LSD and for whom the disease-causing mutation has been ascertained

MECHANISMS



Mutations in genes involved in lysosomal function leads to the aberrant processing, degradation and accumulation of macromolecules inside lysosomes

The consequences of macromolecule accumulation vary between LSDs and depend on the type of stored material and cell

Some mechanisms common to multiple LSDs have been identified and include inflammation, cell death, oxidative stress, and defects in cellular transport and calcium homeostasis

OUTLOOK

Most LSDs do not have an approved therapy, and supportive therapy is the only option. However, many new therapies are being evaluated pre-clinically and in clinical trials, including proteostasis modifiers, anti-inflammatory therapies and gene therapy. Indeed, several gene therapies that use viral vectors to deliver normal lysosomal genes are being trialled in patients.

DIAGNOSIS

LSDs can be sub-classified as, for example, enzyme deficiency disorders, post-translational modification defects, integral membrane protein disorders, and lysosome-related organelle disorders. In general, diagnosis is based on clinical presentation and results from laboratory tests. For example, enzyme assays can be carried out to diagnose lysosomal enzyme deficiency disorders, followed by genetic testing to identify the specific disease-causing mutation(s). Some LSDs can only be diagnosed by mutation analysis.

In general, most LSDs present during infancy or childhood, although adult-onset forms do occur. Symptoms affect multiple organ systems, and depend on the genetic defect and the resulting stored macromolecules.

MANAGEMENT

Approved therapies are available for some LSDs, although their efficacy is variable. Approved therapies include replacing the defective enzyme (enzyme-replacement therapy), reducing the accumulation of macromolecules (substrate reduction therapy) or improving the function of the defective enzyme (chaperone therapy). For LSDs without an approved therapy, supportive care is available and depends on the patient's clinical manifestations.

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Written by Louise Adams; designed by Laura Marshall

Quesiti di autovalutazione

In quali compartimenti cellulari avviene la sintesi proteica nelle cellule eucariotiche?

Quali sono le principali classi di RNA coinvolte nella sintesi proteica e quali ruoli svolgono?

Come fa il tRNA a riconoscere l'aminoacido giusto da aggiungere alla catena polipeptidica in crescita sul ribosoma?

Qual è il destino delle proteine tradotte da ribosomi liberi nel citosol e di quelle tradotte da ribosomi associati al reticolo endoplasmatico rugoso?

Spiegare cos'è la via secretoria e quali sono gli organelli coinvolti.