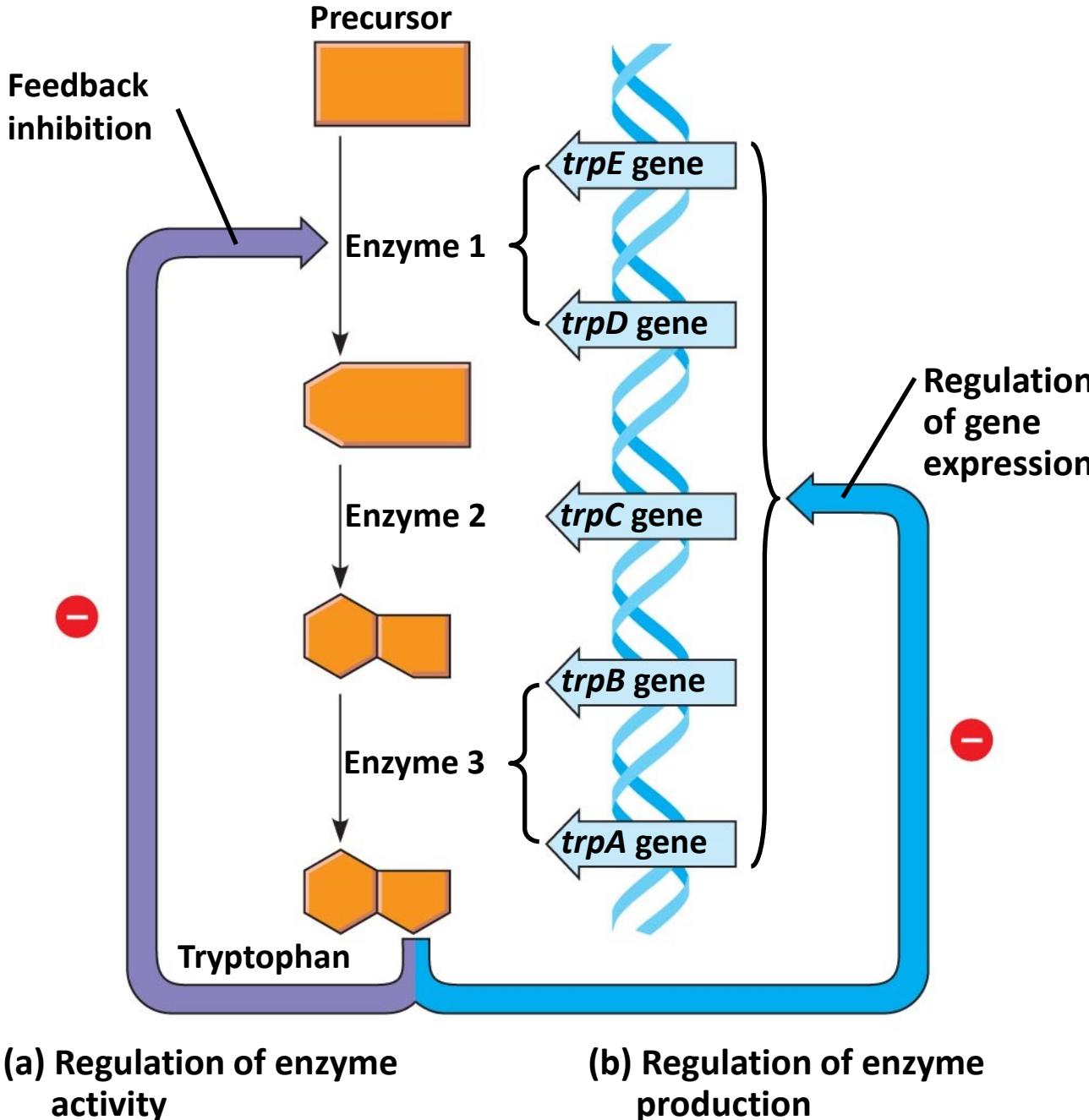


Regulacija genske ekspresije kod eukariota

Pregled - prokarioti

- Prokarioti i eukarioti mijenjaju ekspresiju gena obzirom na promjene u okolišu
- Genska ekspresija kod prokariota se kontrolira preko operon modela
- Stanice mogu regulirati produkciju enzima preko povratne sprege ili preko regulacije gena

Fig. 18-2

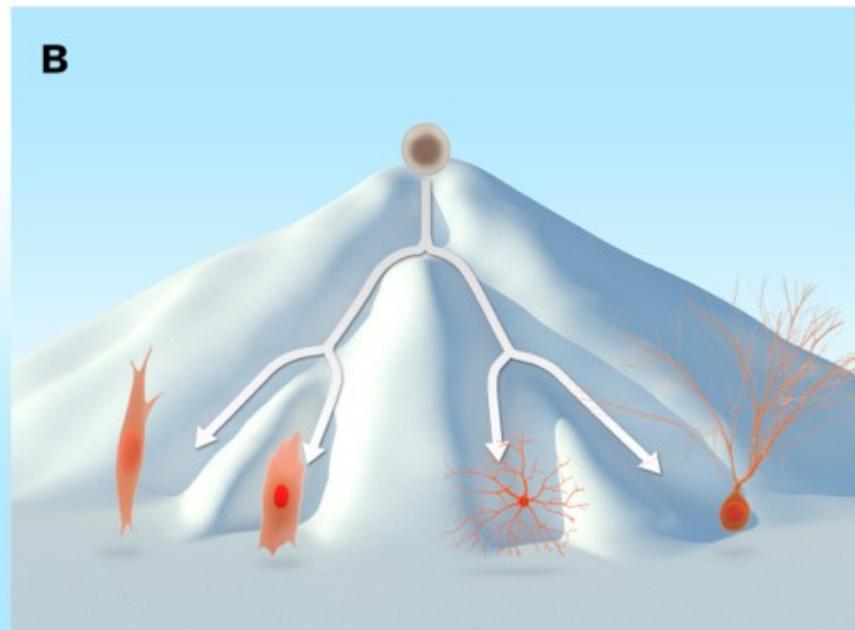
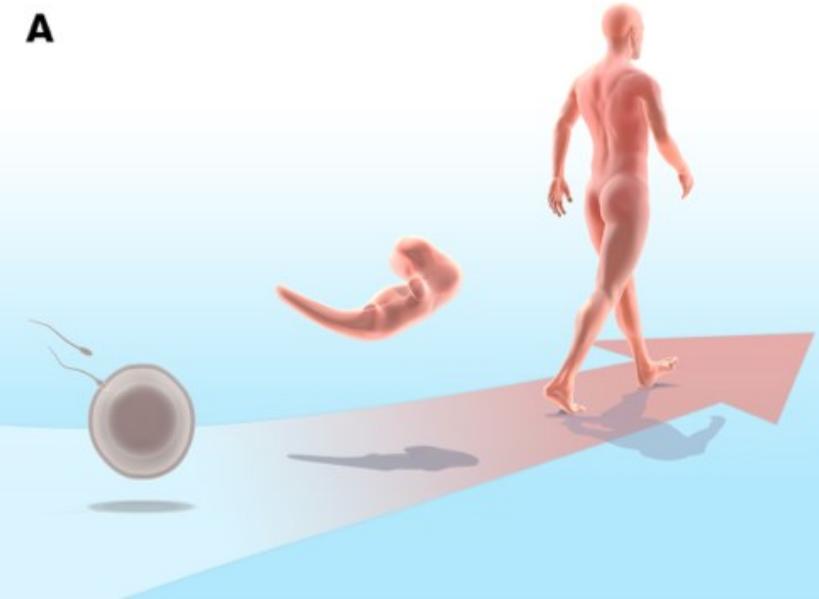


(a) Regulation of enzyme activity

(b) Regulation of enzyme production

Eukarioti

- Svi organizmi moraju regulirati ekspresiju gena jako precizno – vrijeme, mjesto i kao odgovor na promjene u okolišu
- Kod višestaničnih organizama regulacija ekspresije gena je neophodna za specijalizaciju stanica



Diferencijalna ekspresija gena u organizmu



Fig. 18-6

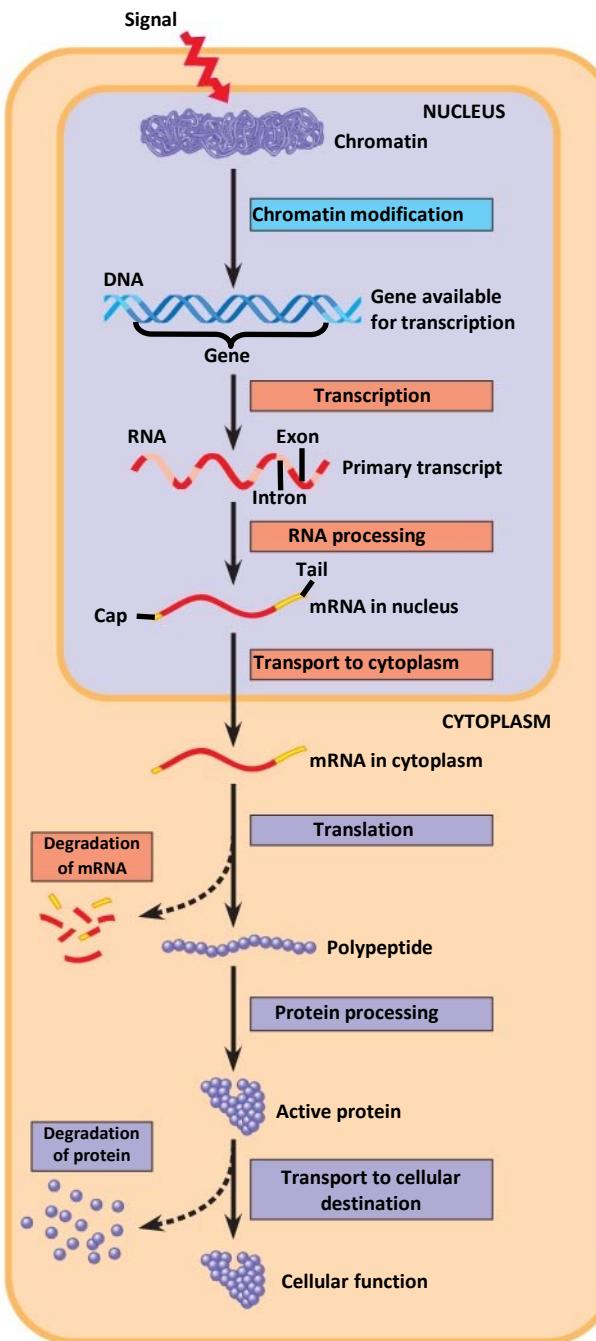
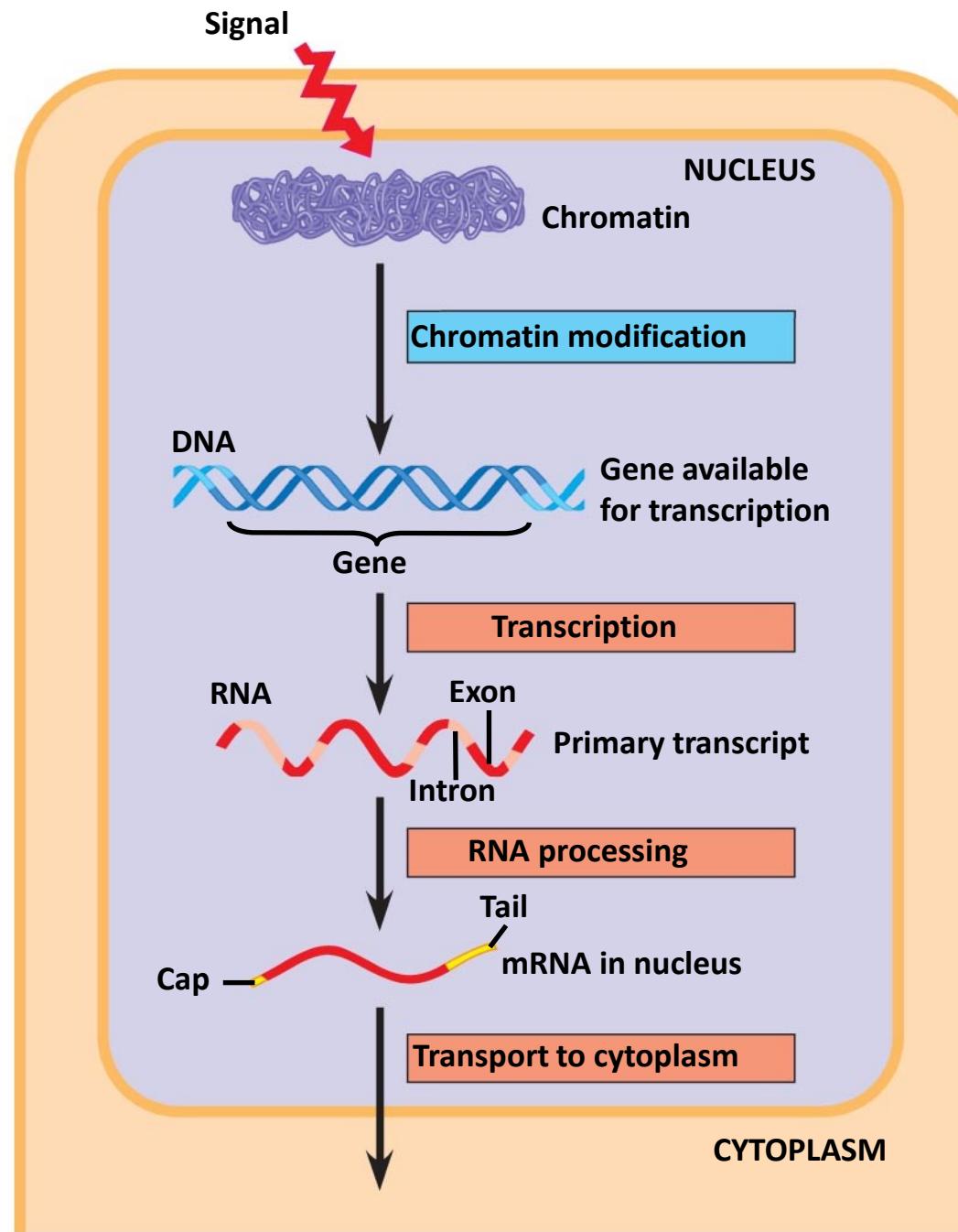
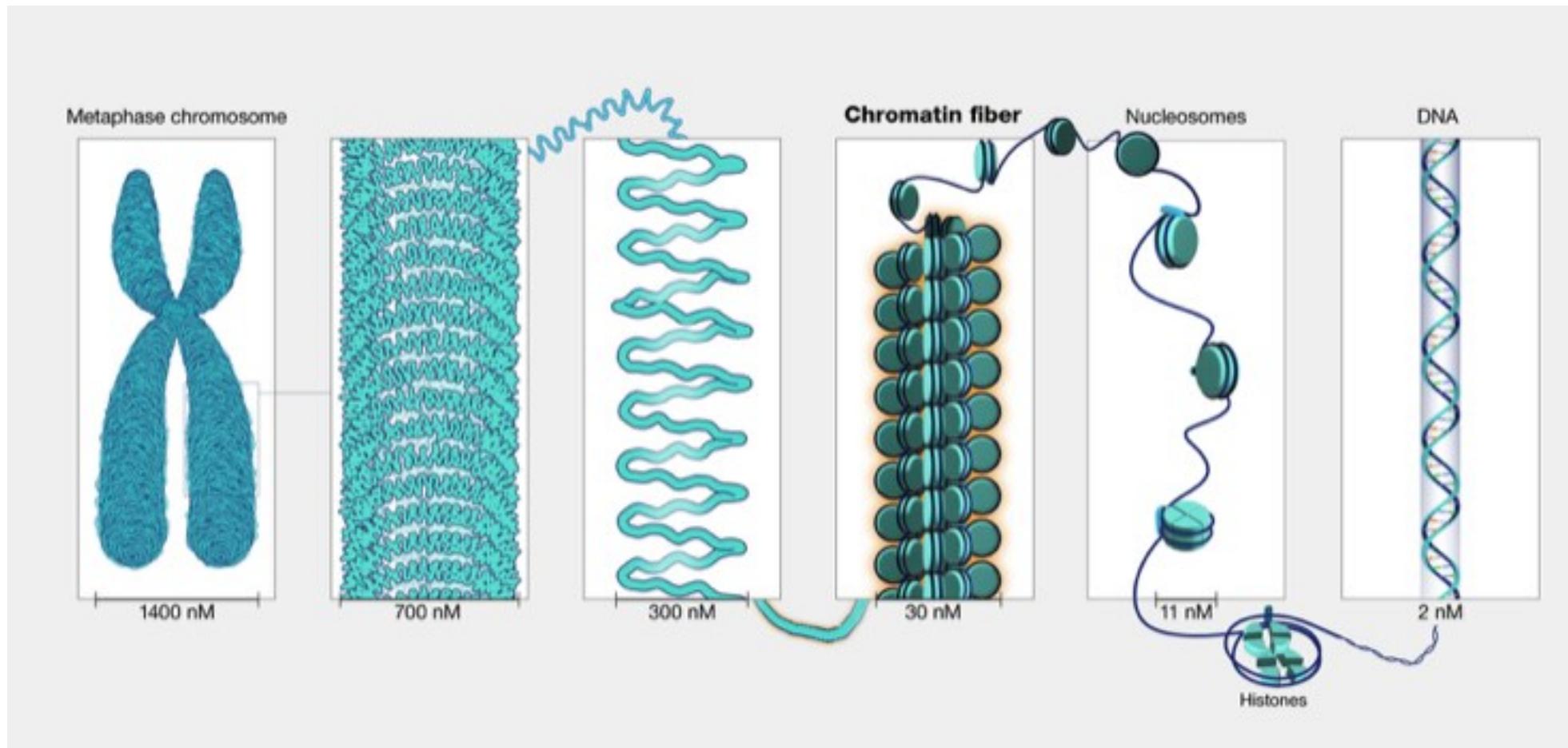
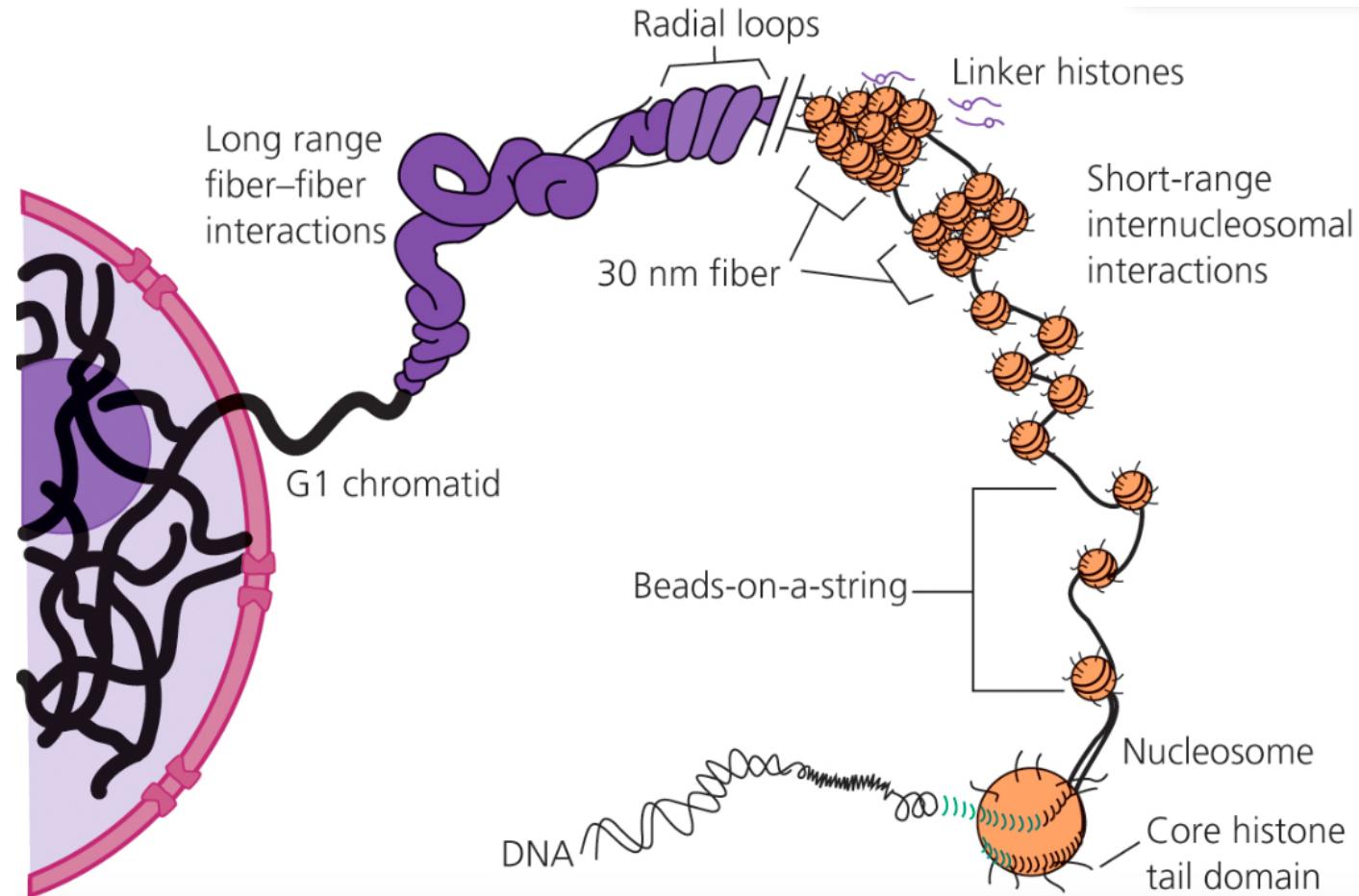


Fig. 18-6a



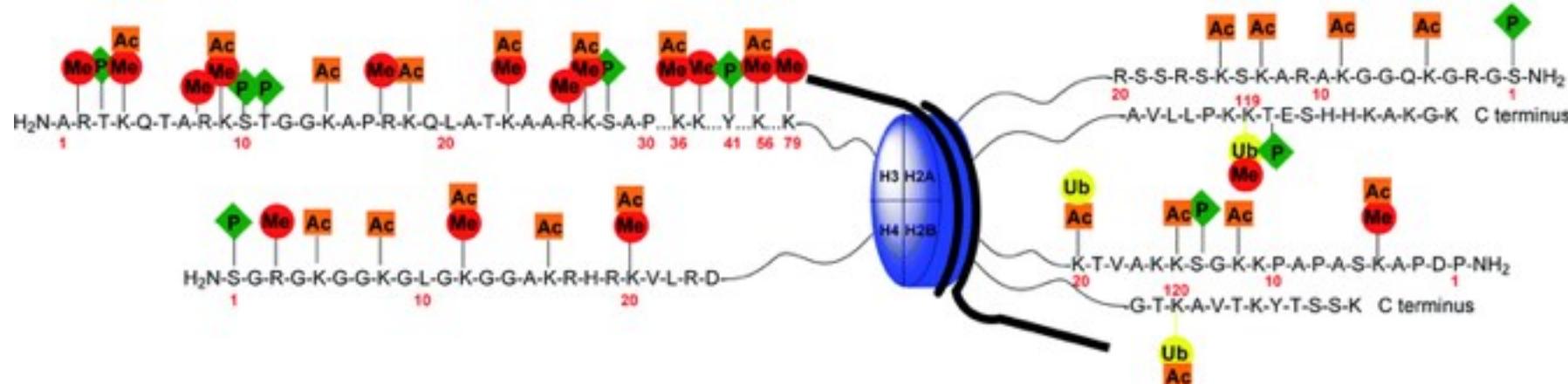


Struktura kromatina

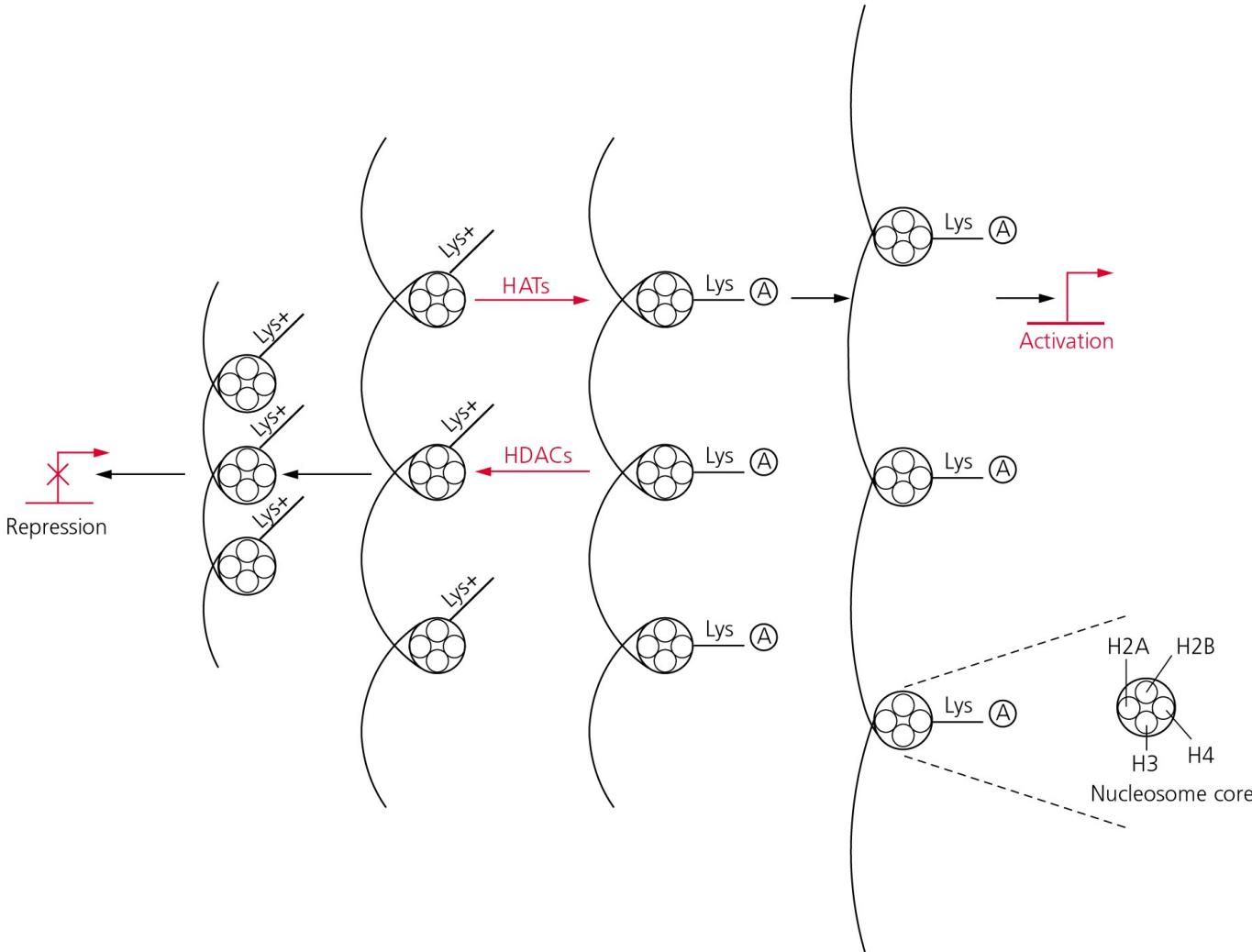


Modifikacije histona

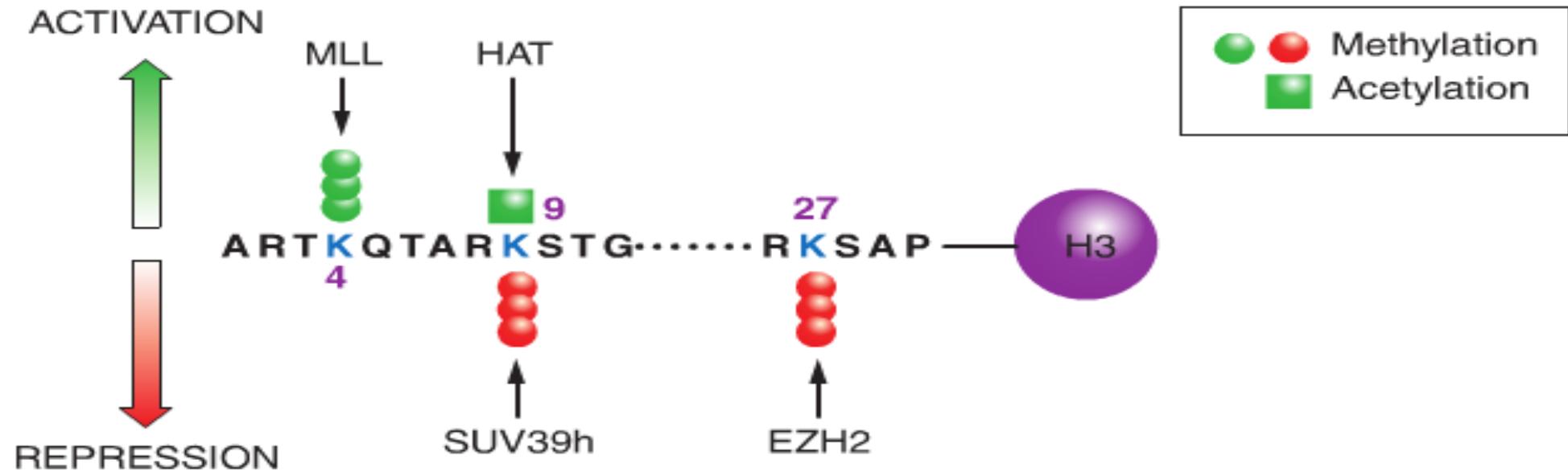
- Acetilacija
- Metilacija
- Fosforilacija
- Ubikvitinacija



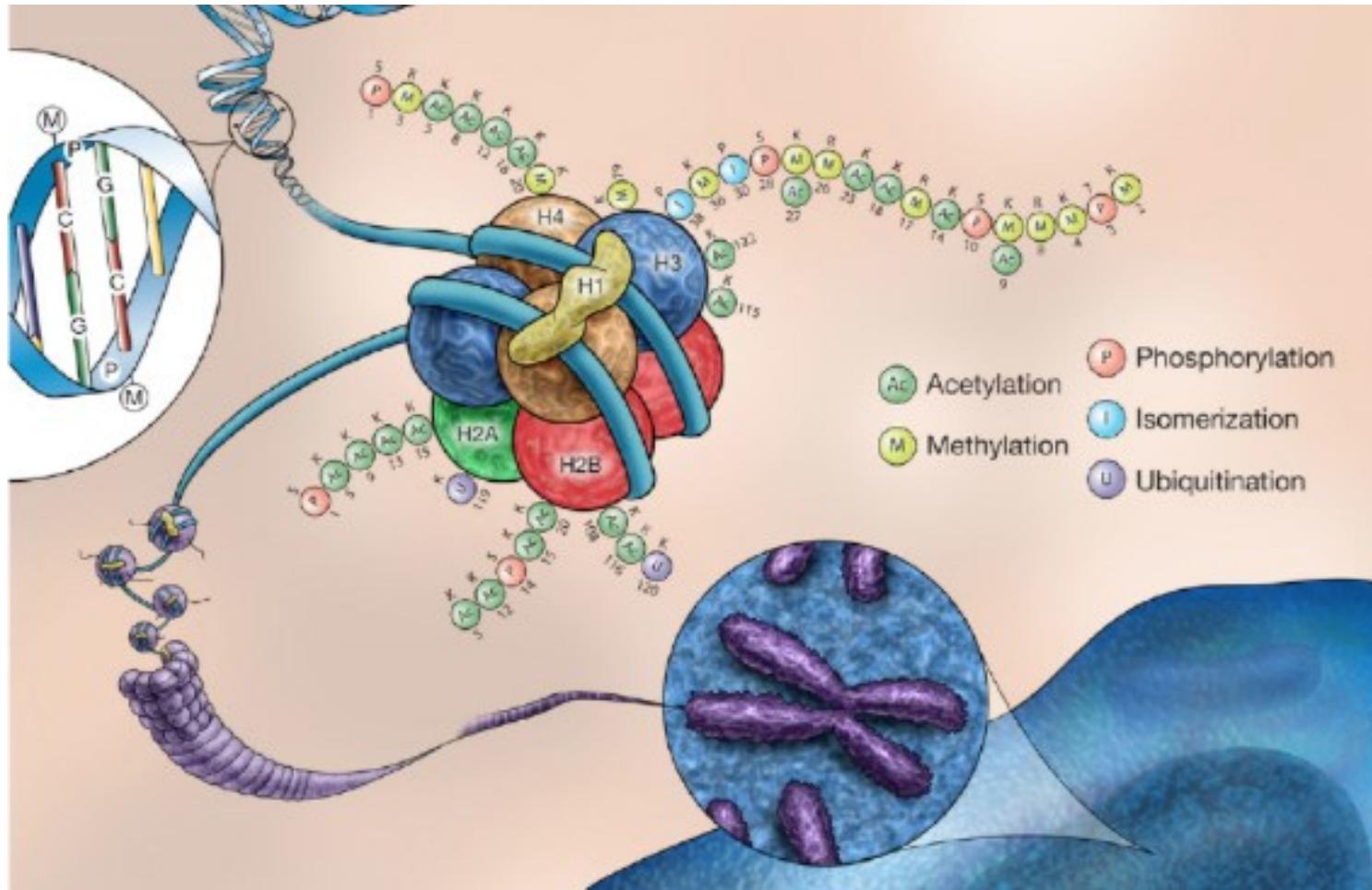
Acetilacija histona



Acetilacija i metilacija histona H3

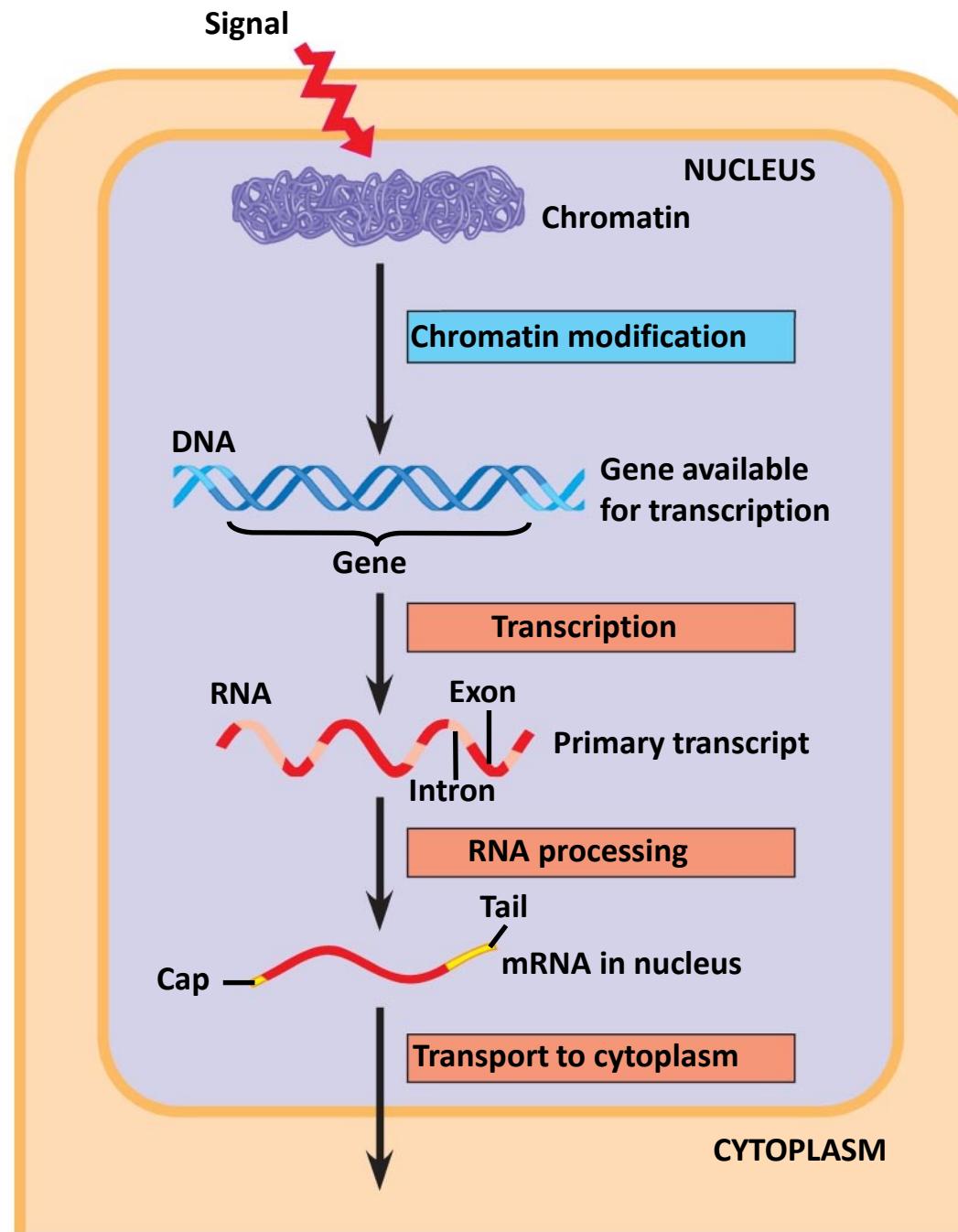


Modifikacije kromatina



- <https://www.youtube.com/watch?v=XelGO582s4U>

Fig. 18-6a



Organizacija tipičnog eukariotskog gena

- Regulatorna i kodirajuća regija
- Kontrolni elementi se vežu na nekodirajuću regiju i reguliraju transkripciju preko proteina koji se vežu na njih

Fig. 18-8-1

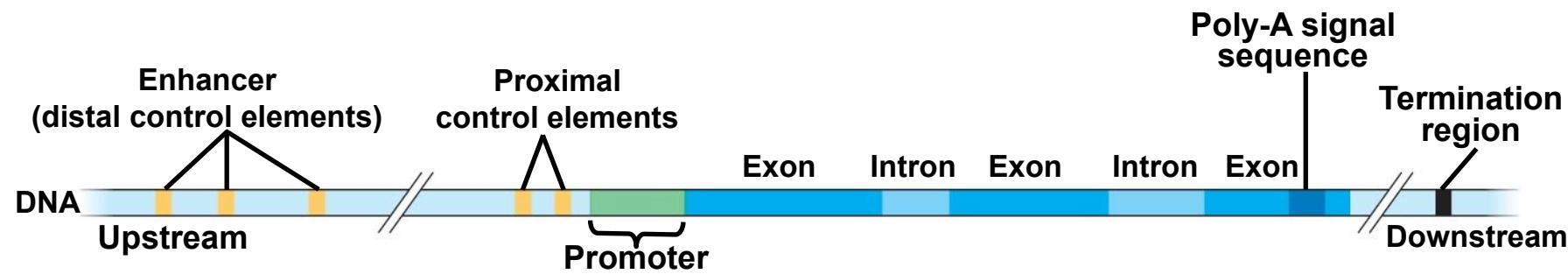


Fig. 18-8-2

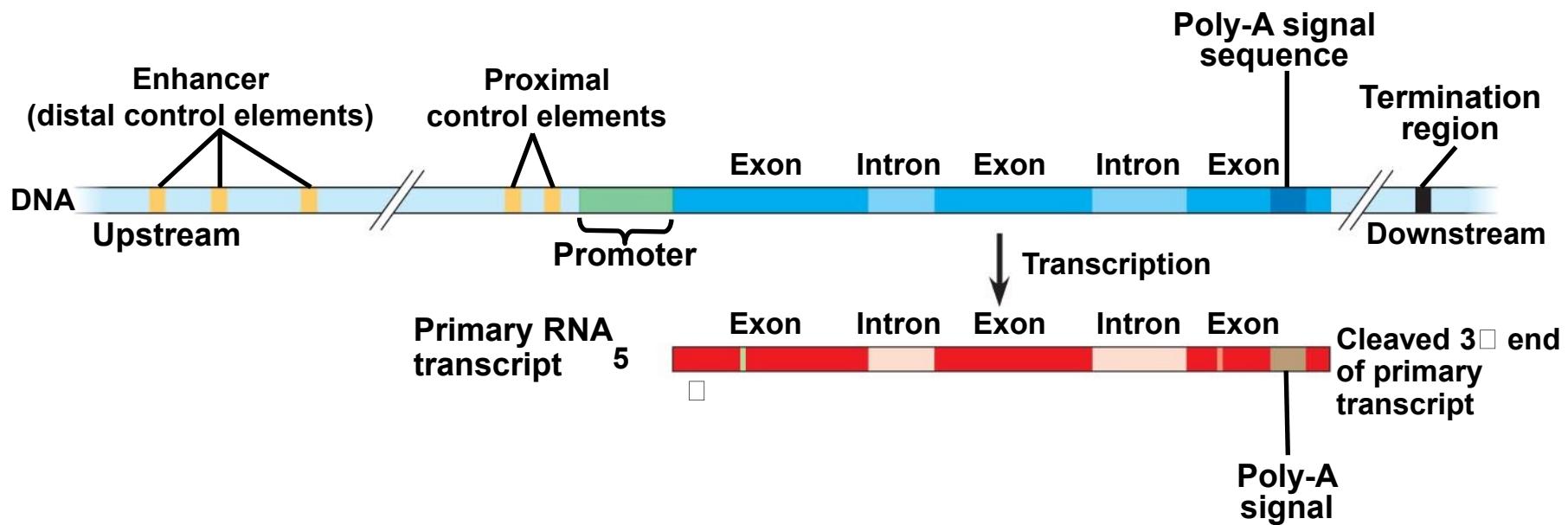
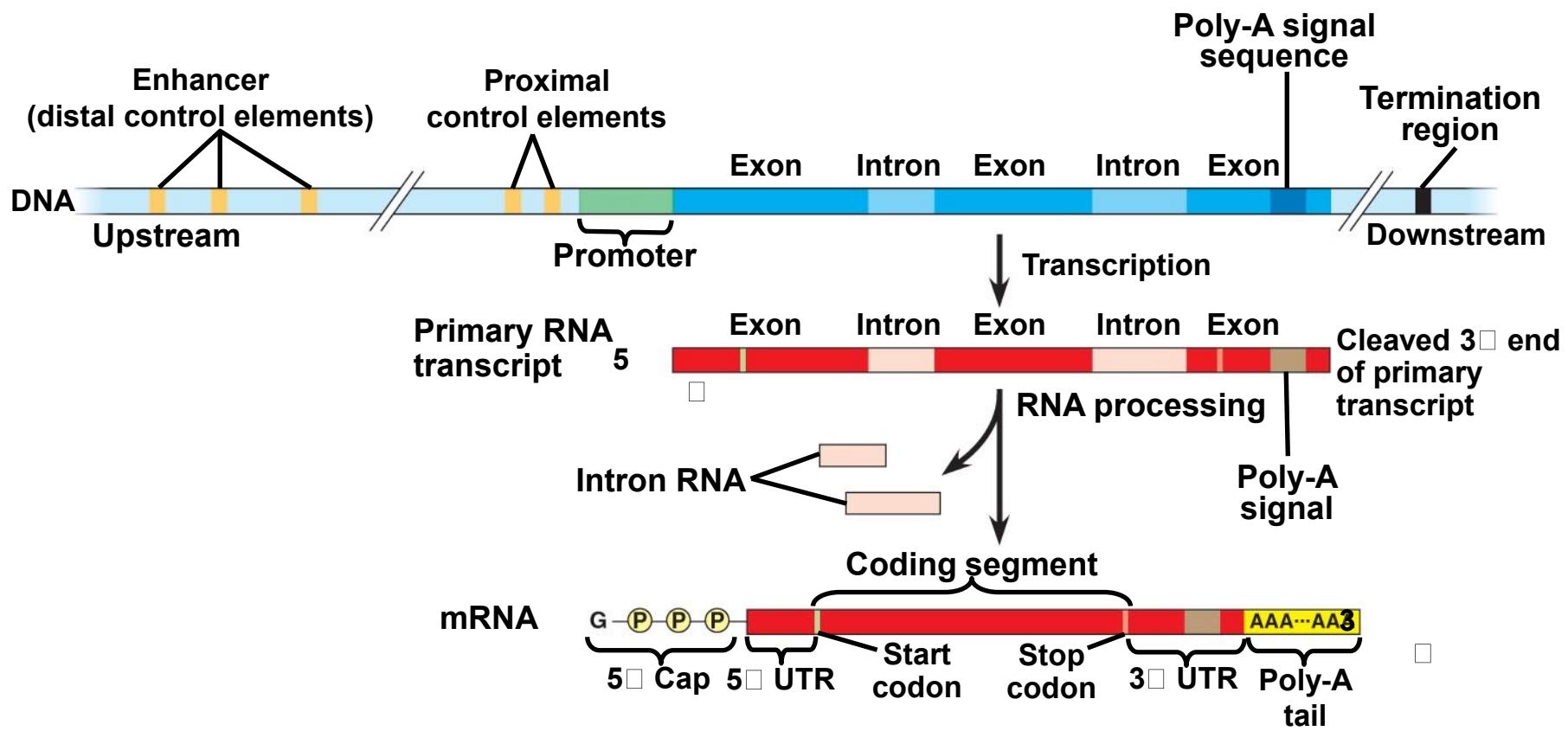


Fig. 18-8-3



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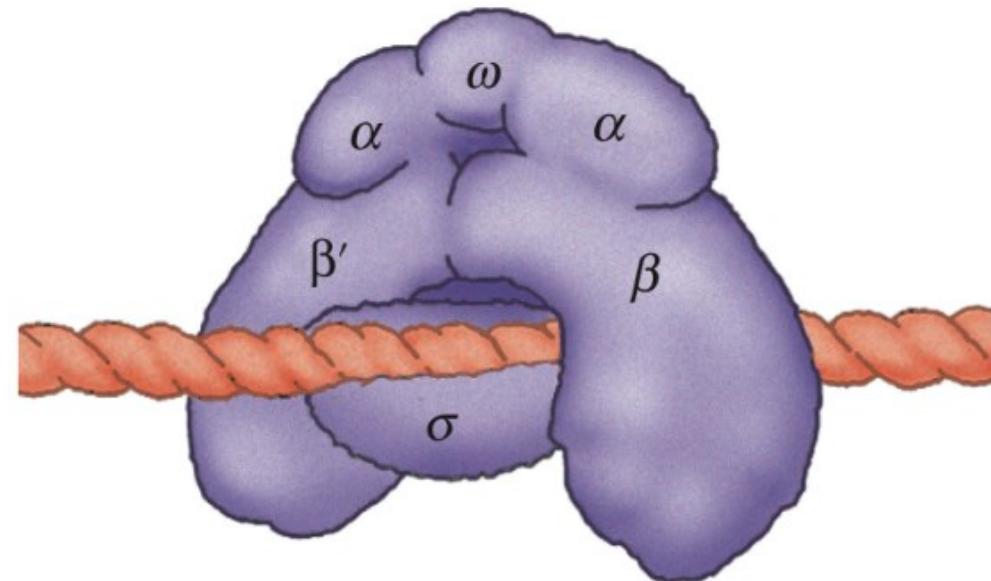
RNA polimeraza kod prokariota

Sinteza RNA na DNA kalupu
samo u 5' – 3' smjeru

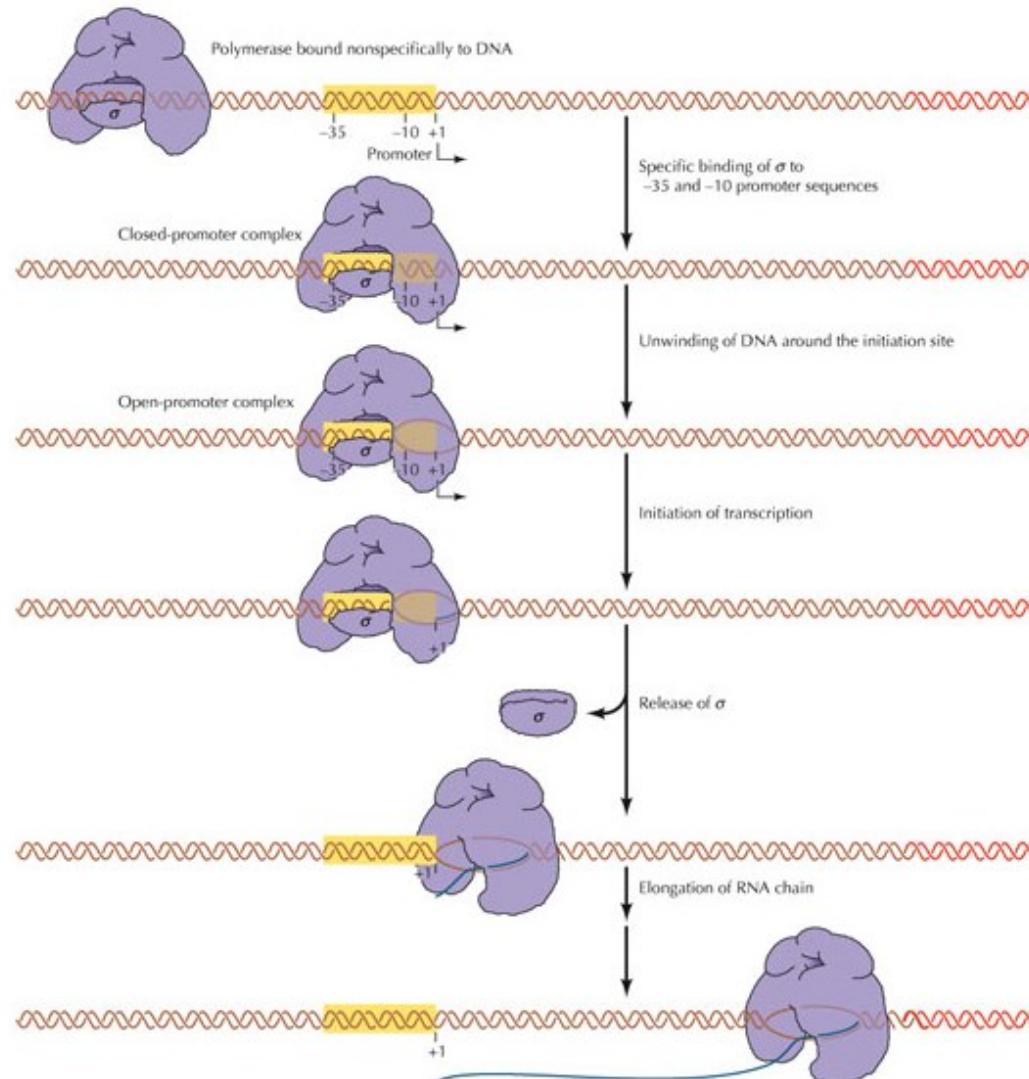
Nije potrebna početnica

Sadrži 5 podjedinica

Veže se na promotore gena



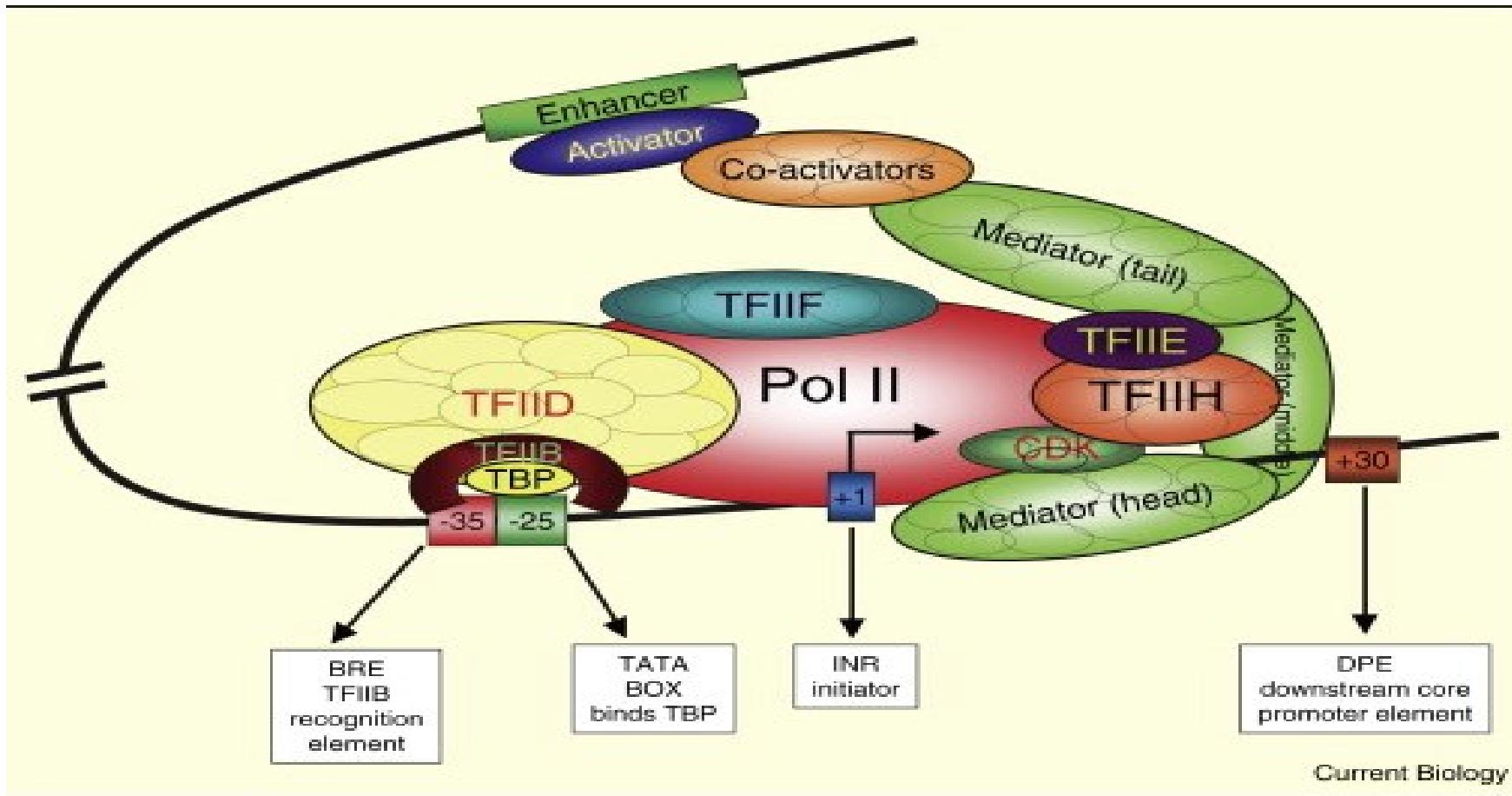
Sinteza RNA



Transkripcija u eukariotima

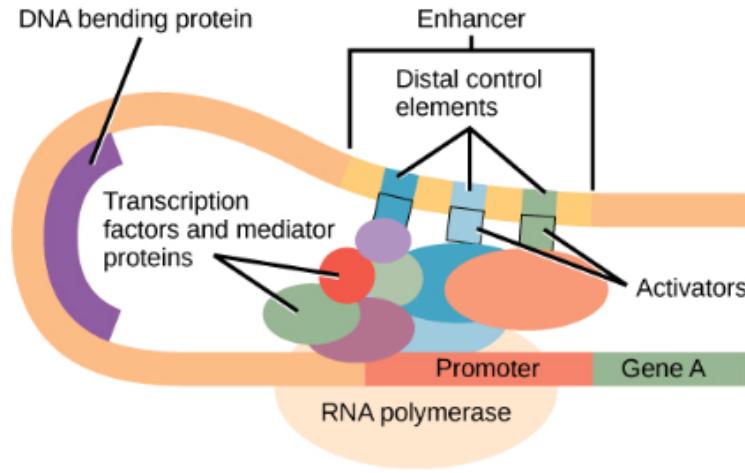
- Znatno složeniji proces s tri bitne razlike:
 - 1. više RNA polimeraza (I, II i III)
 - 2. potrebni interakcijski partneri za vezanje na promotore (TF)
 - 3. transkripcija se odvija na kromatinu te je potrebna regulacija kromatinske strukture

RNA polimeraza II



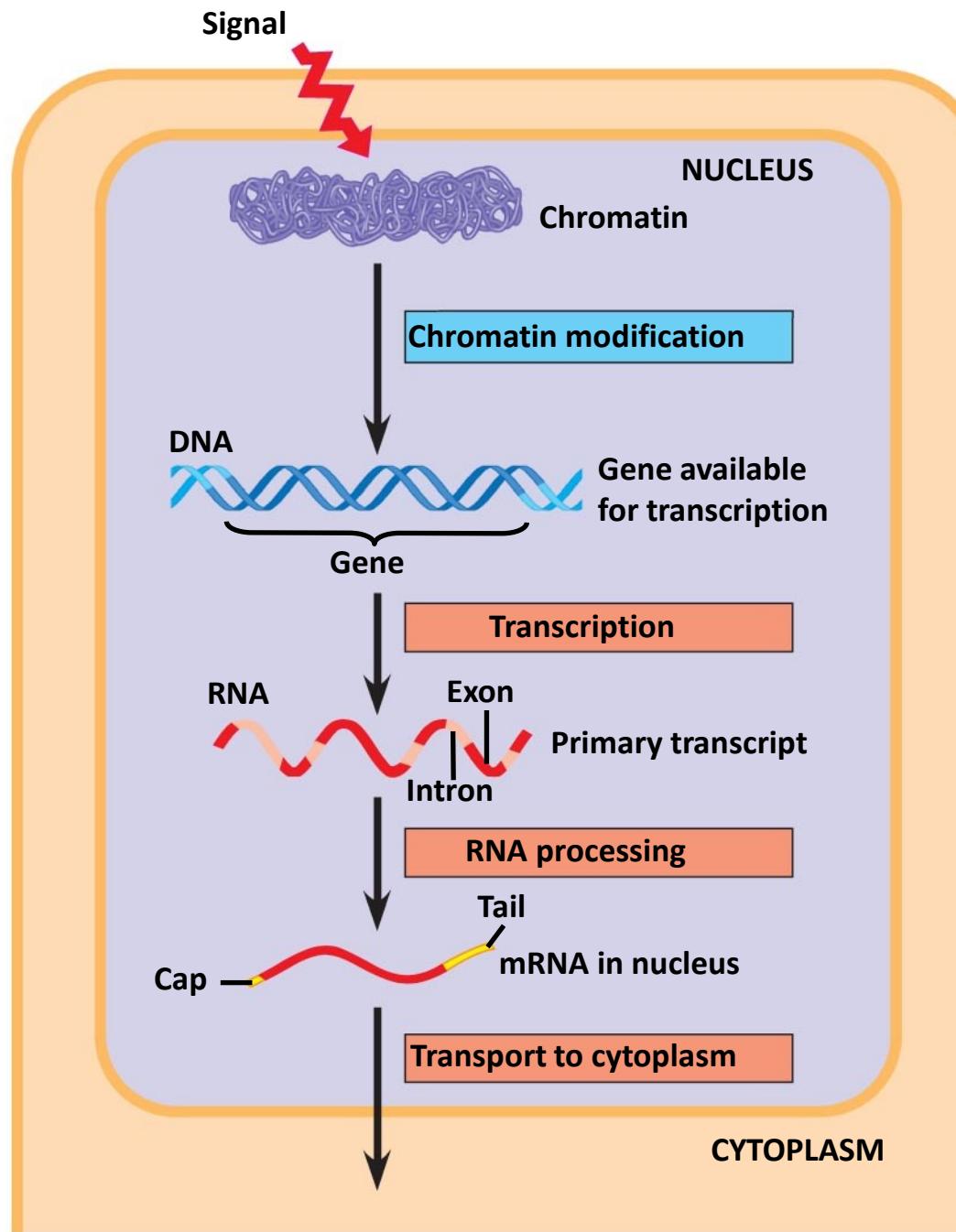
Regulacija ekspresije u eukariotskim stanicama

- Pojačivači i utišavači
 - Transkripcijski faktori
-
- Transkripcijski aktivatori
 - Transkripcijski represori

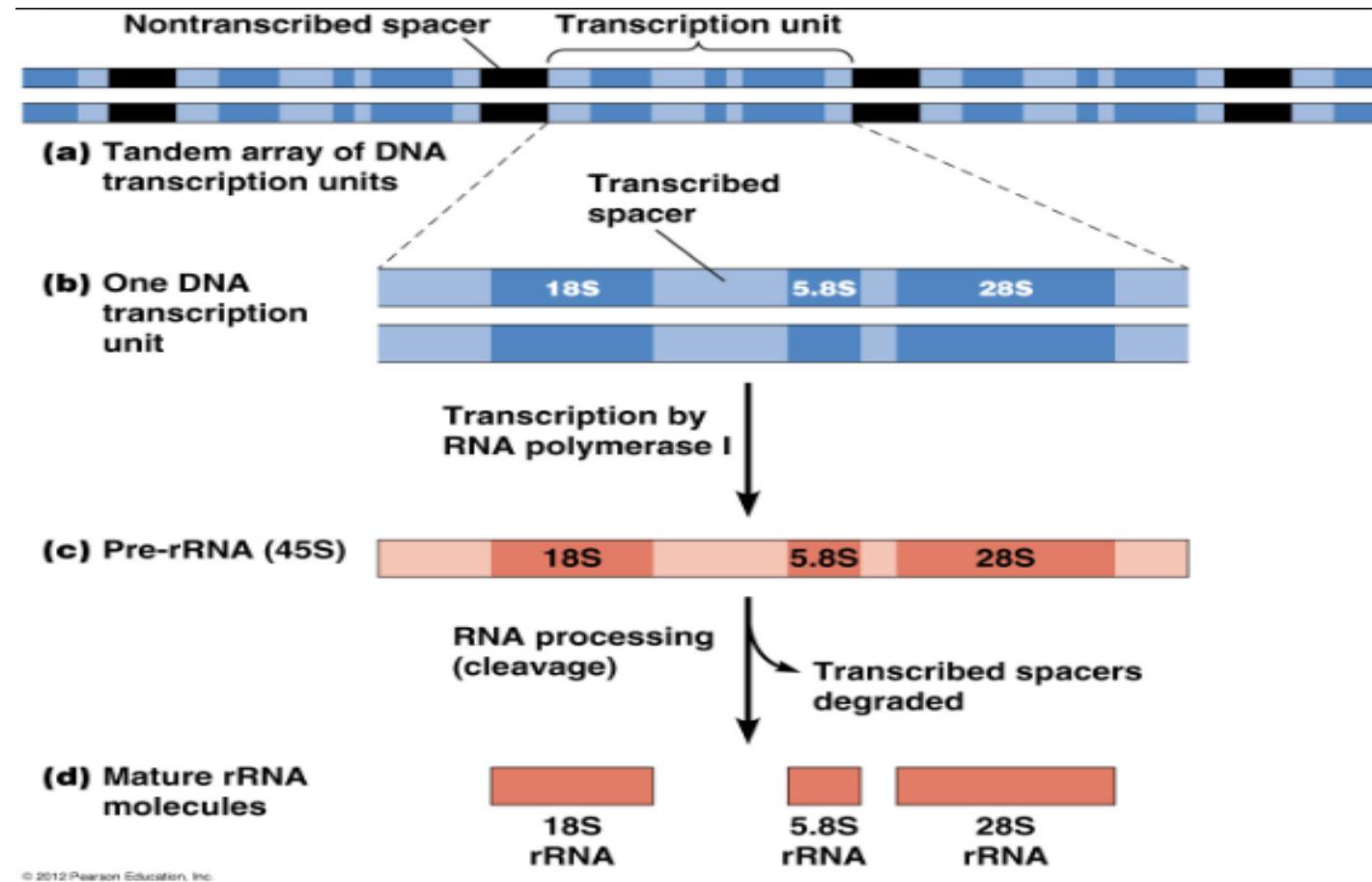


- Interakcija s transkripcijskim sustavom
- Modifikacija kromatinske strukture

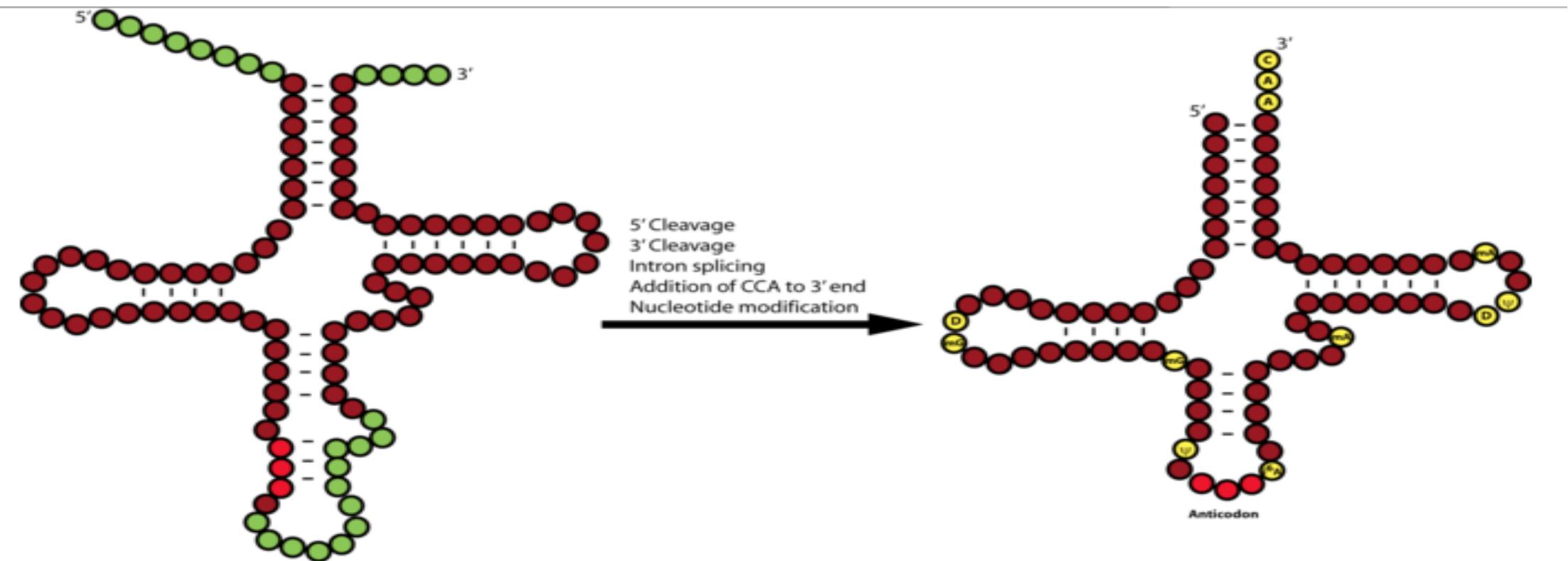
Fig. 18-6a



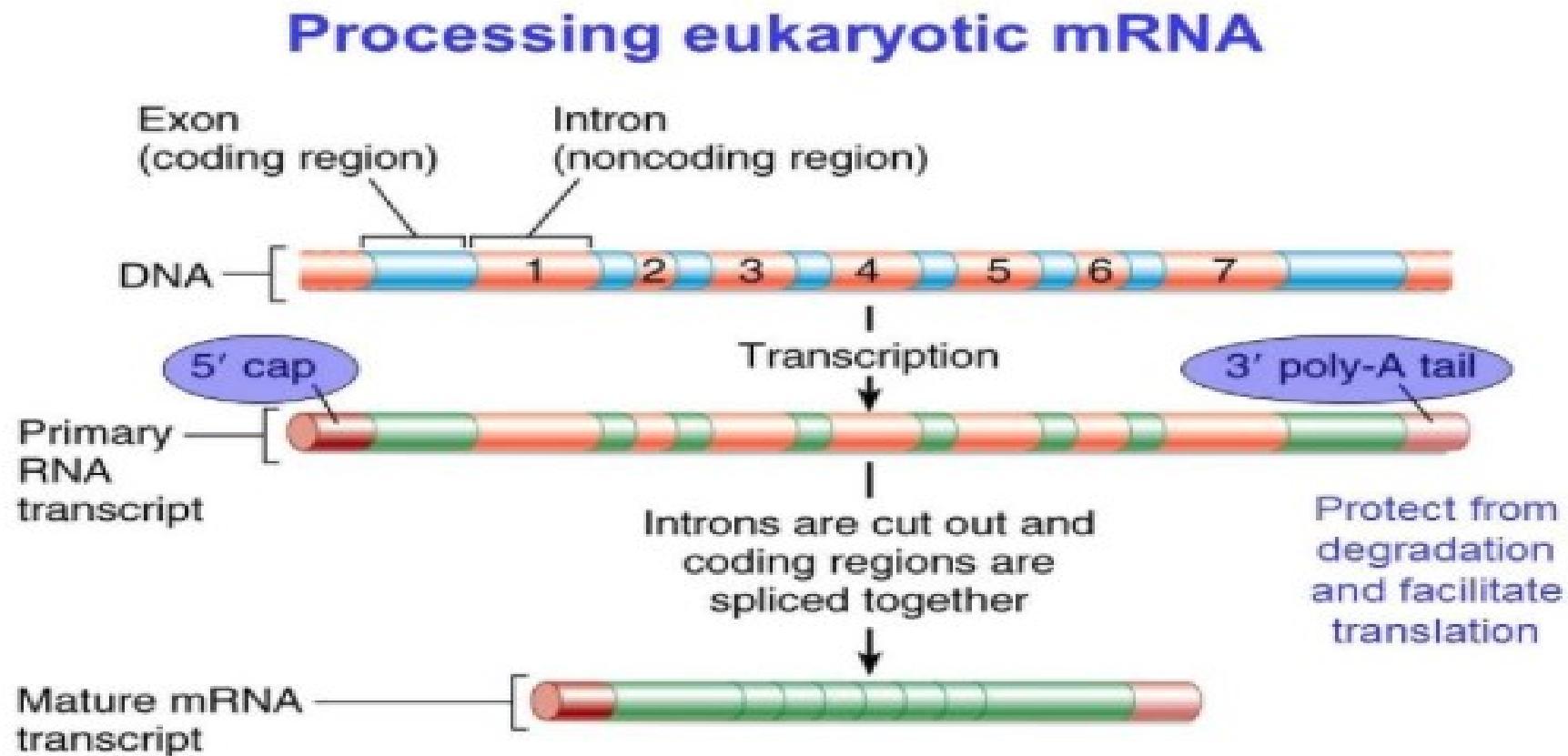
Doradba i promet rRNA



Doradba i promet tRNA



Doradba i promet mRNA



- <https://www.youtube.com/watch?v=aVgwr0QpYNE>

Fig. 18-11

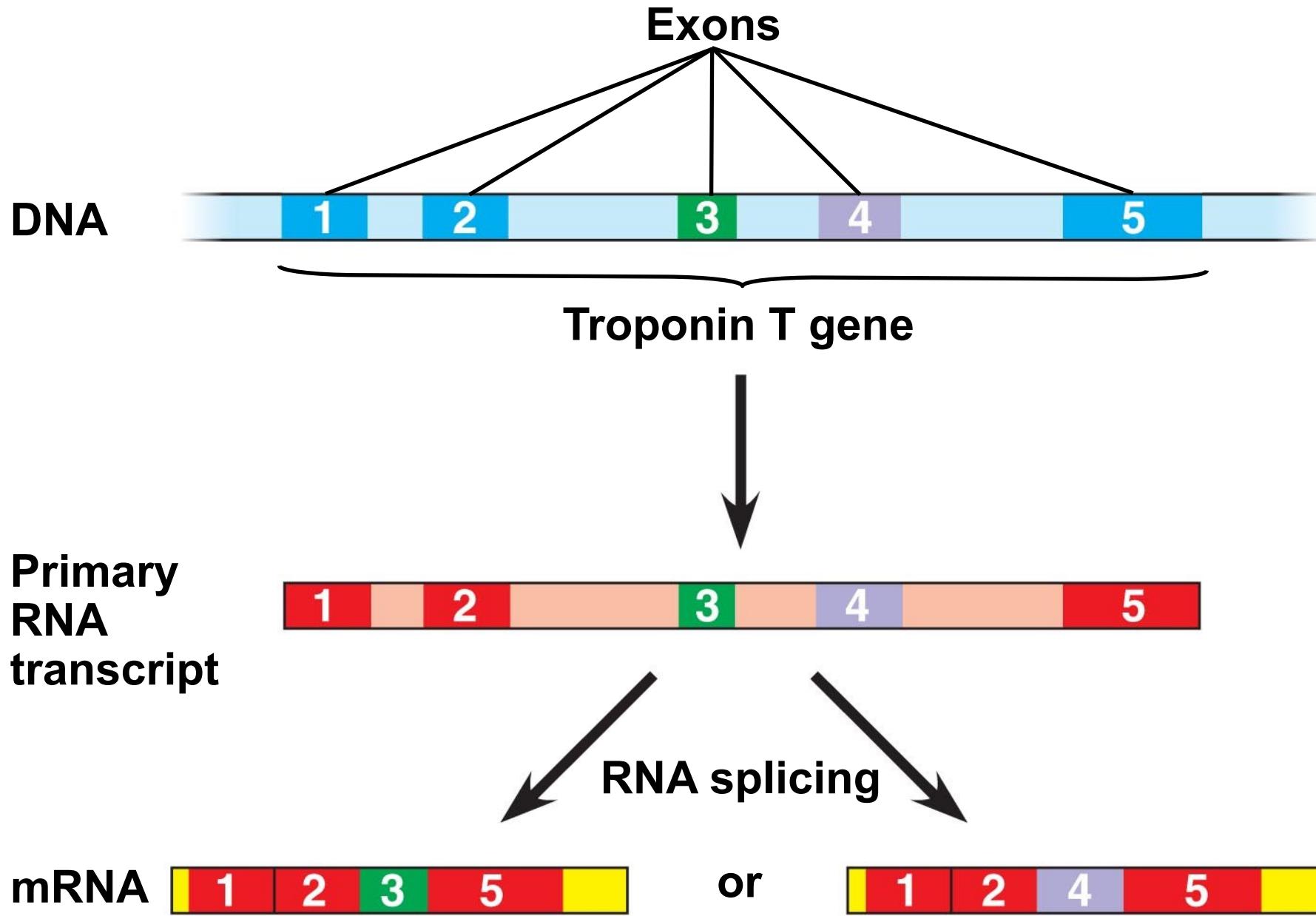


Fig. 18-6a

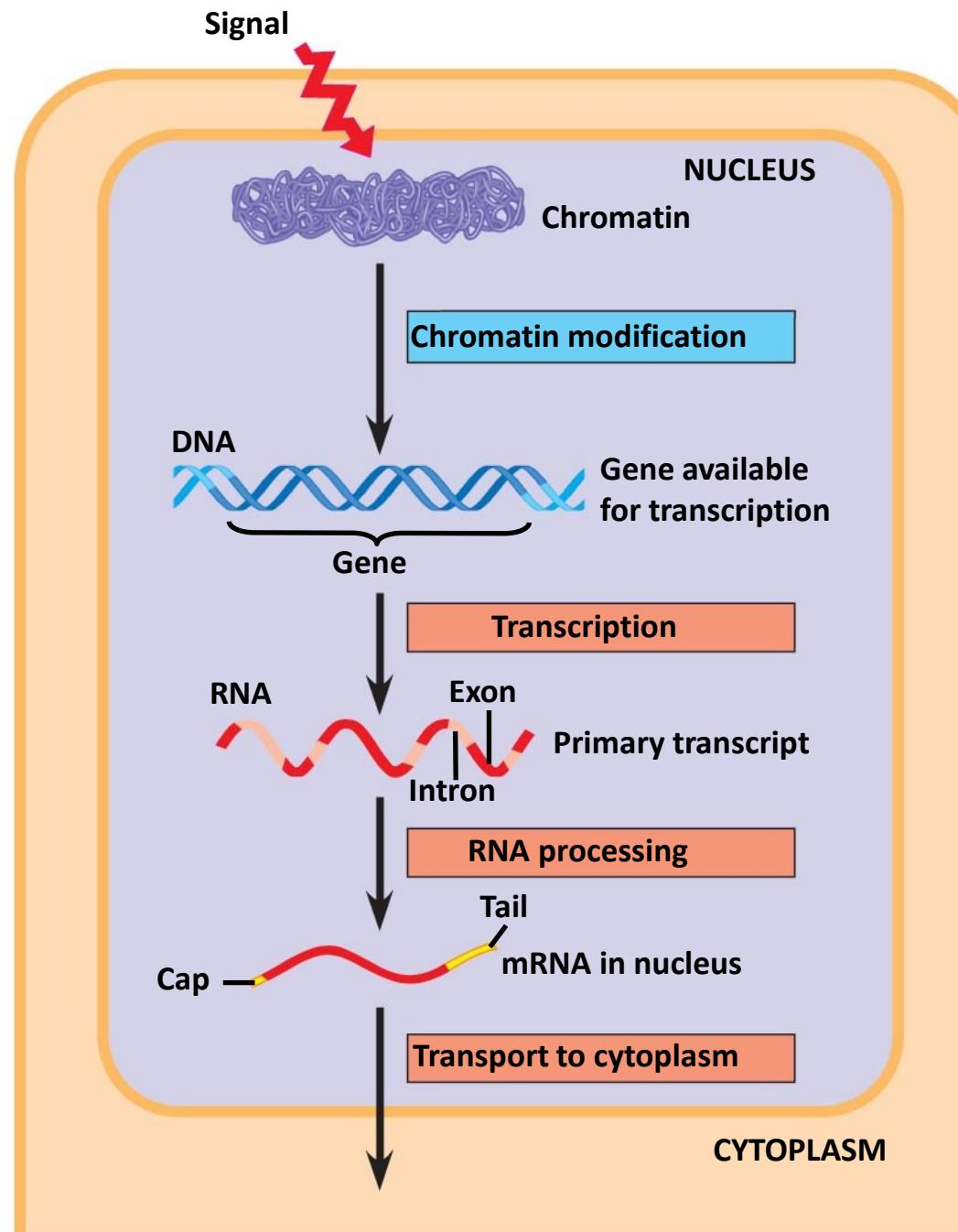
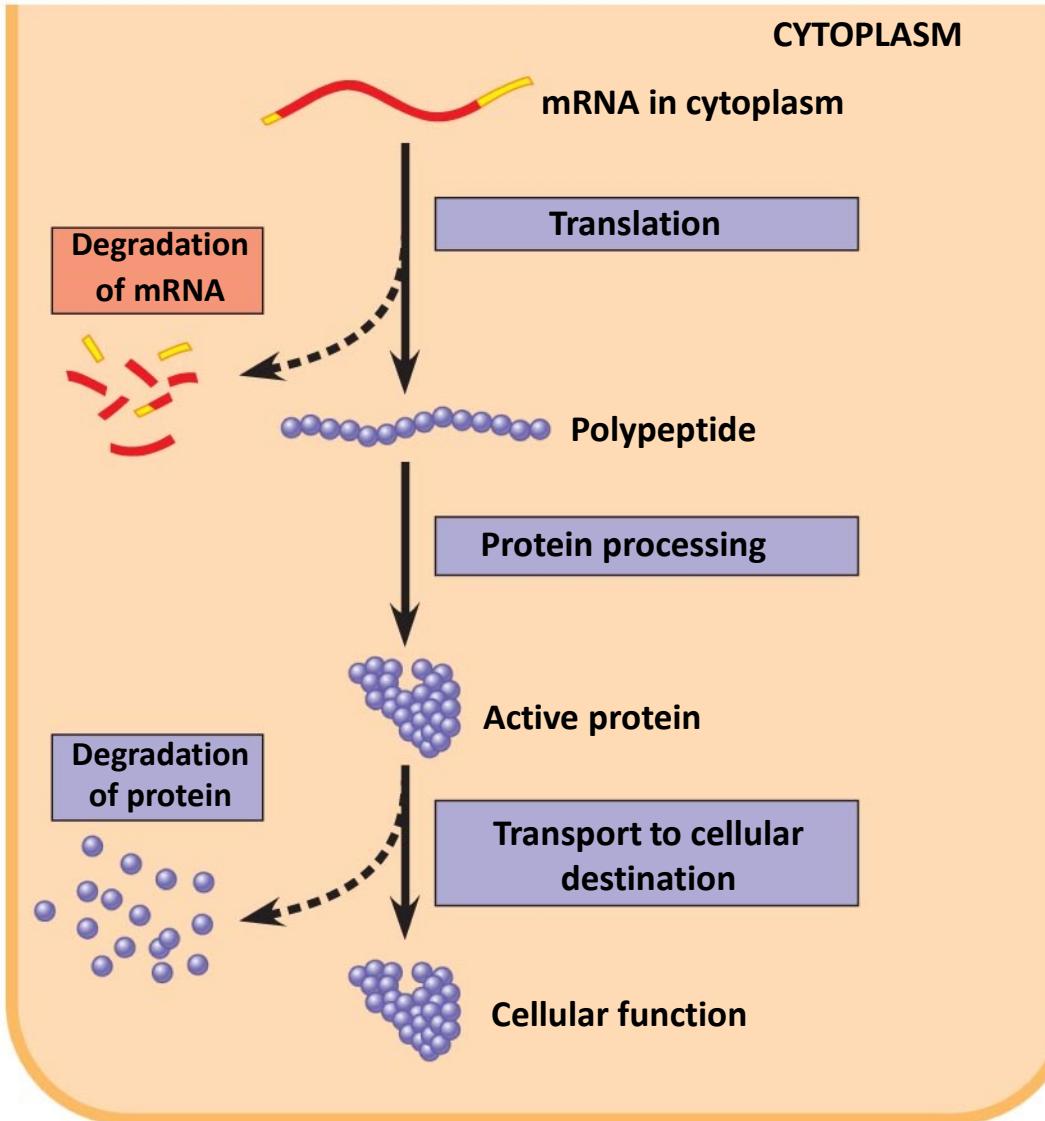
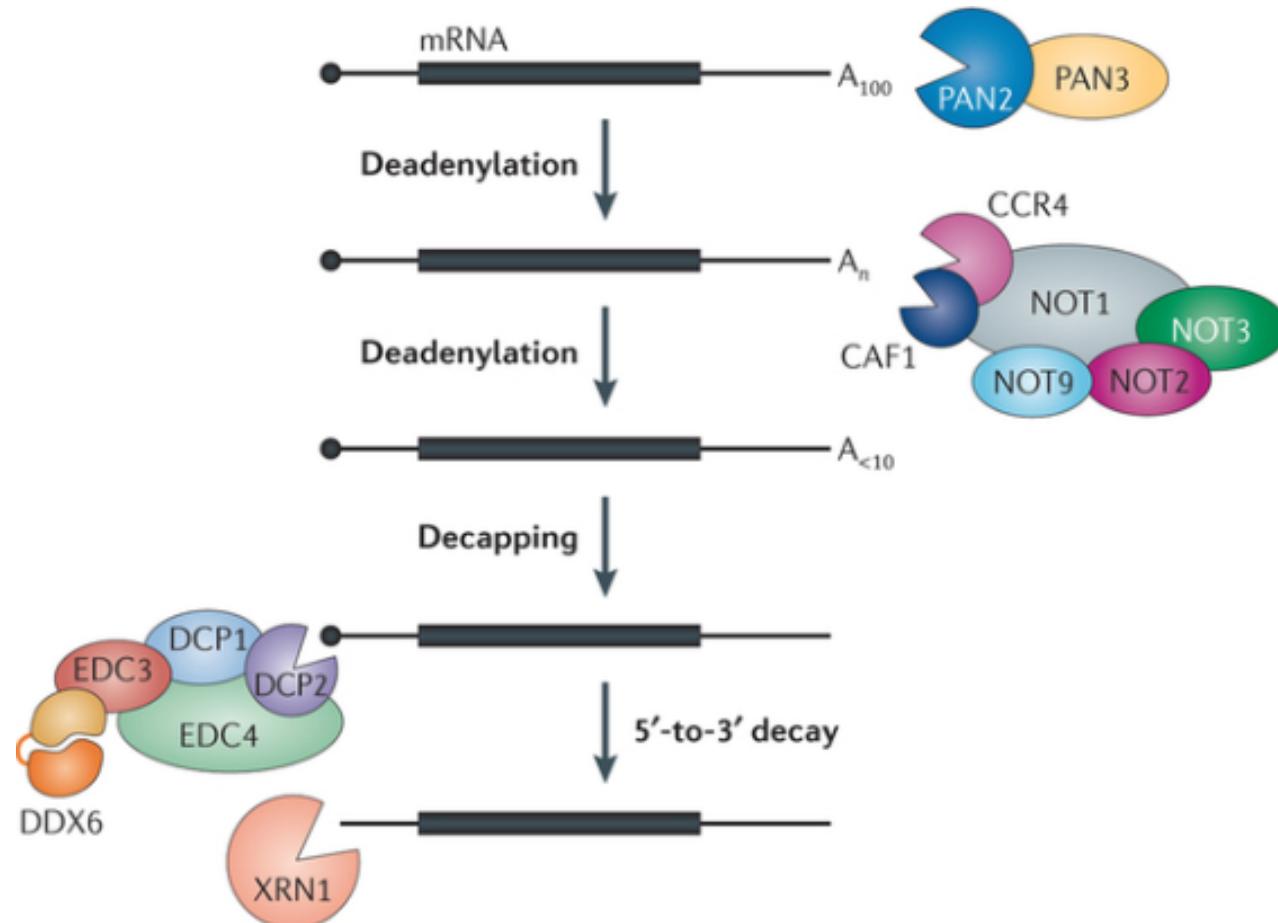


Fig. 18-6b

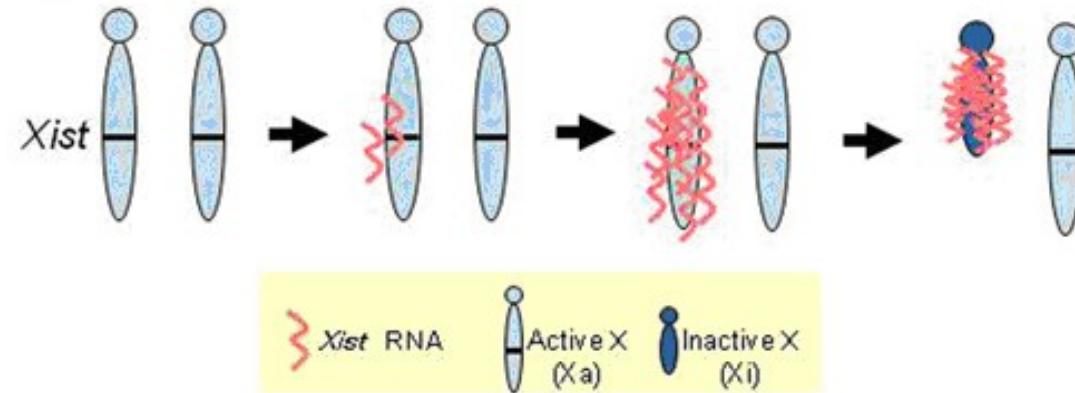


Razgradnja RNA kao mehanizam kontrole ekspresije gena



Nekodirajuće RNA igraju ulogu u kontroli genske ekspresije

- Samo mali udio DNA kodira za proteine i strukturne RNA
- Veliki udio se transkribira u nekodirajuće RNA
- Nekodirajuće RNA reguliraju ekspresiju gena na razini translacije i konfiguracije kromatina



RNA svijet

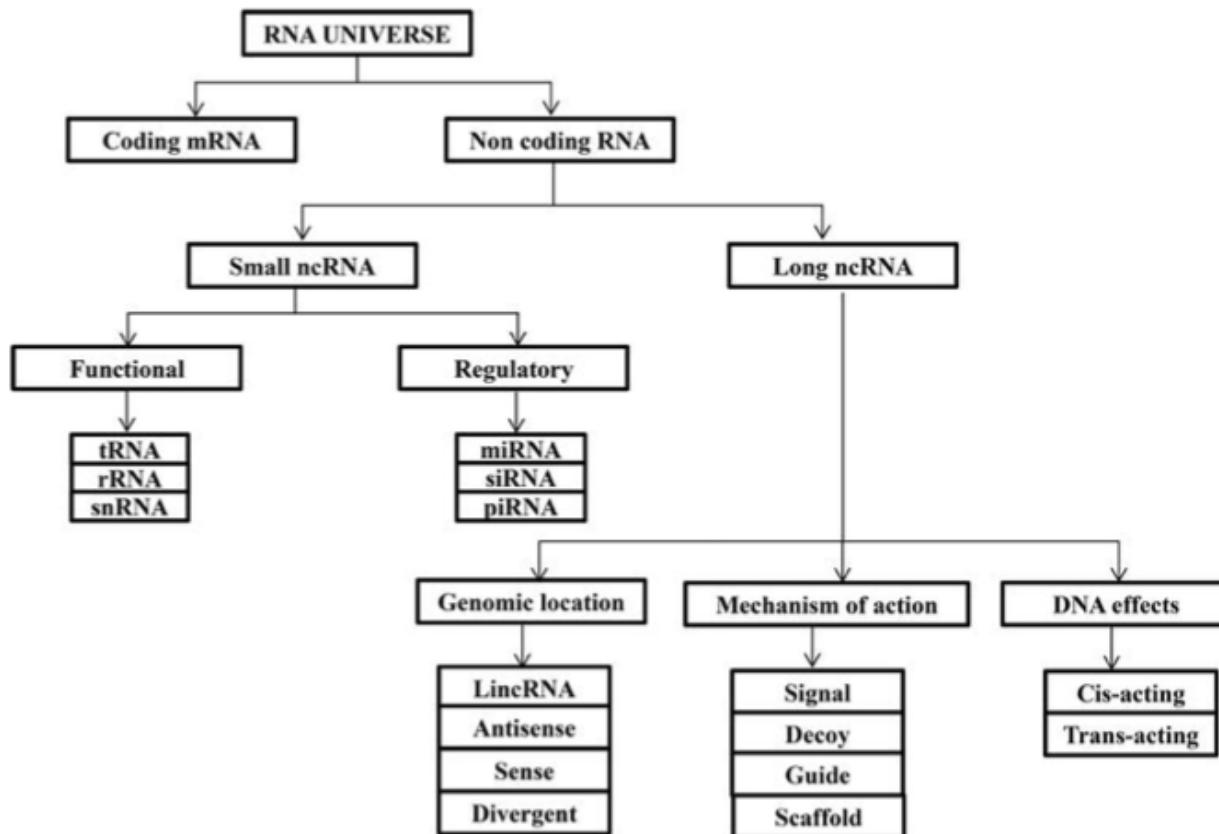
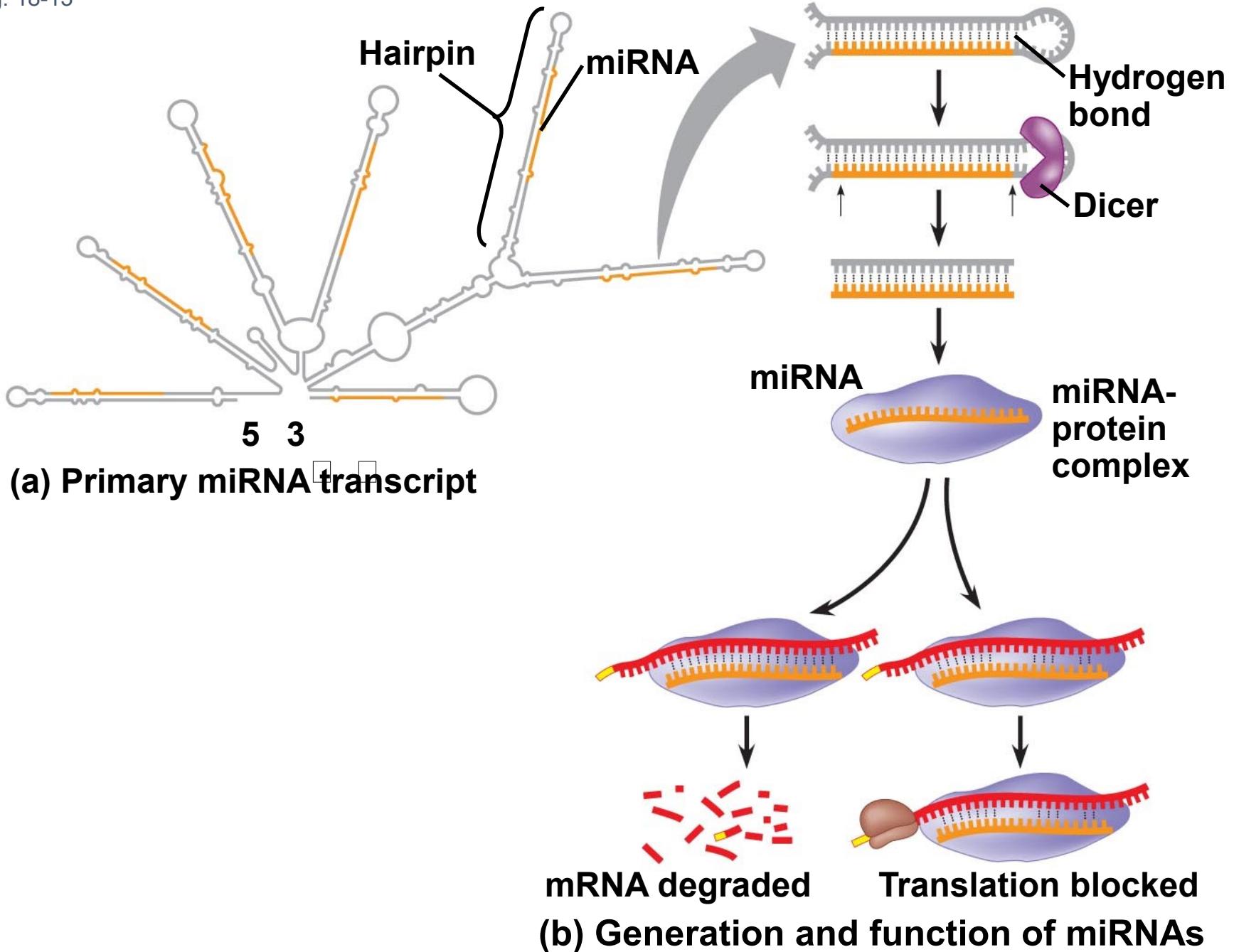
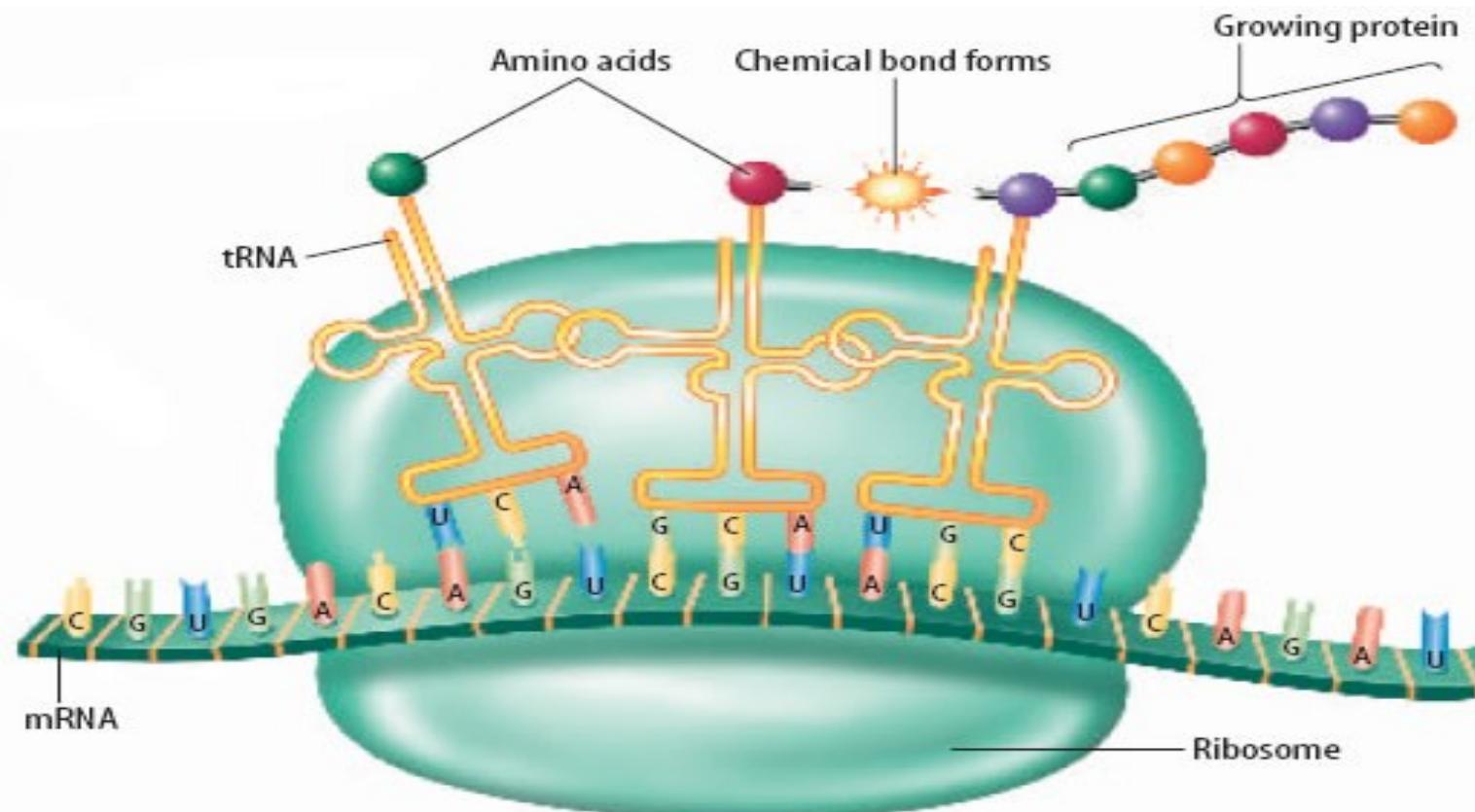


Fig. 18-13

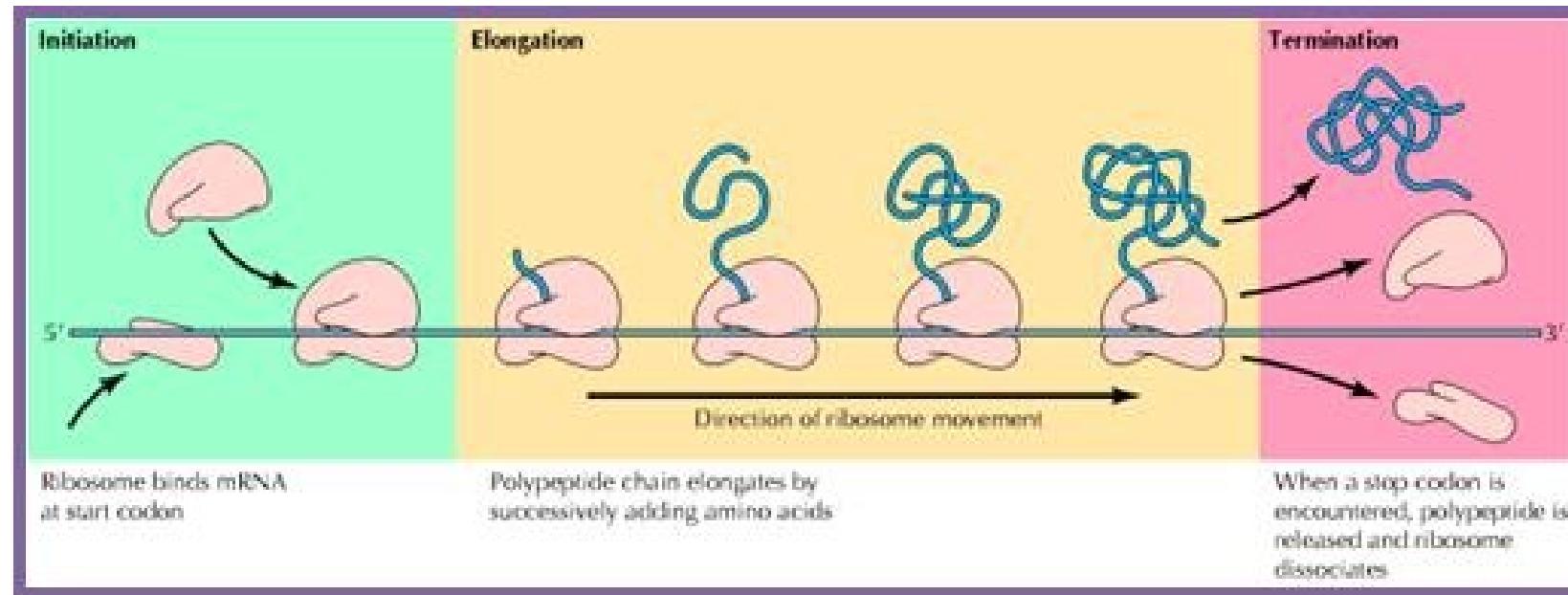


Sinteza, doradba i regulacija proteina



At the ribosome, the RNA's message
is translated into a specific protein.

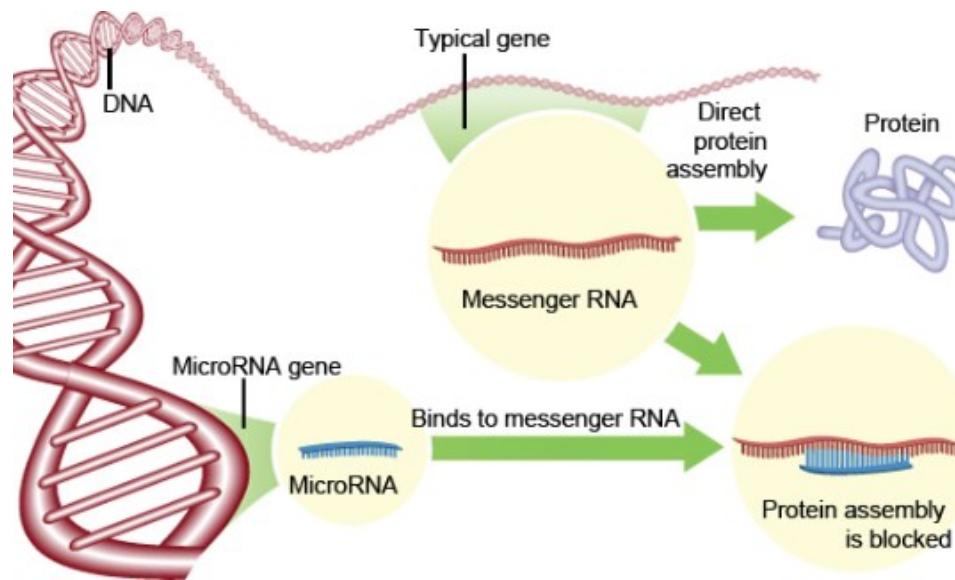
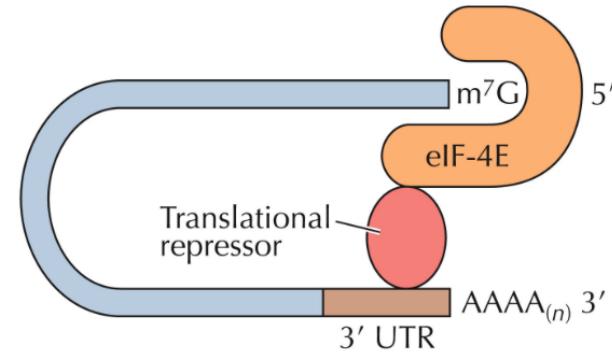
Inicijacija, elongacija i terminacija



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

Regulacija translacije

- Represori translacije
- Nekodirajuće mikroRNA



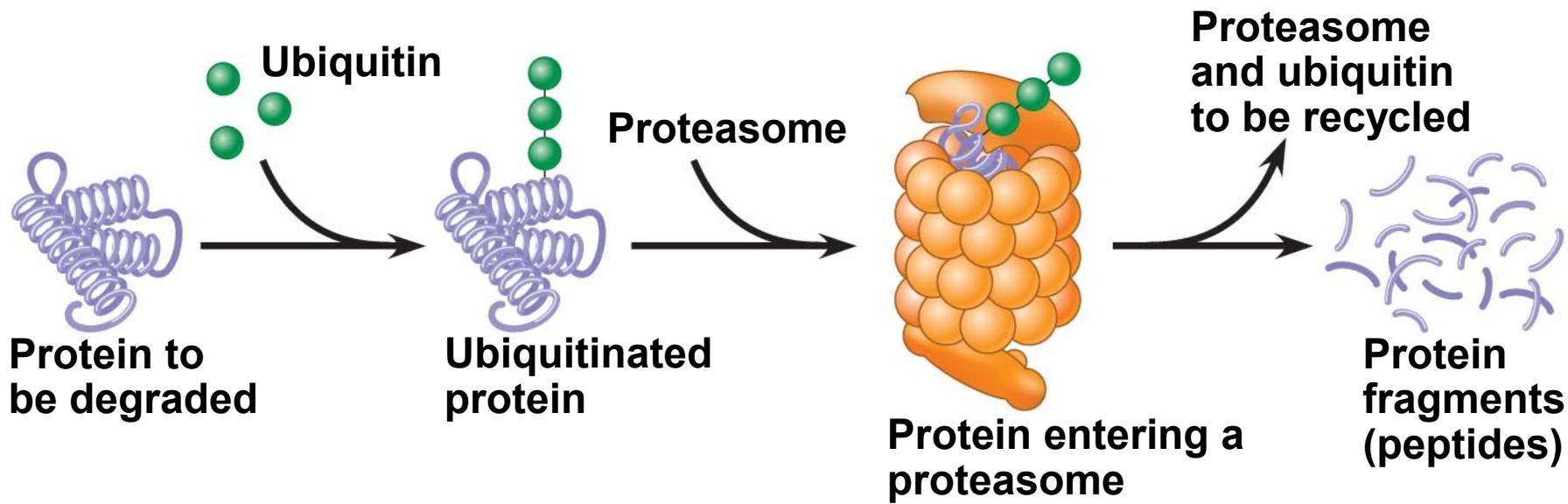
Smatanje i doradba proteina

- Pravilno smatanje - šaperoni
- Udruživanje u komplekse – interakcijske domene
- Modifikacije (vezanje ugljikohidrata i lipida, kidanje kovalentnih veza)

Razgradnja proteina

- Razgradnja u proteasomu nakon ubikvitinacije
- Lizosomska proteoliza

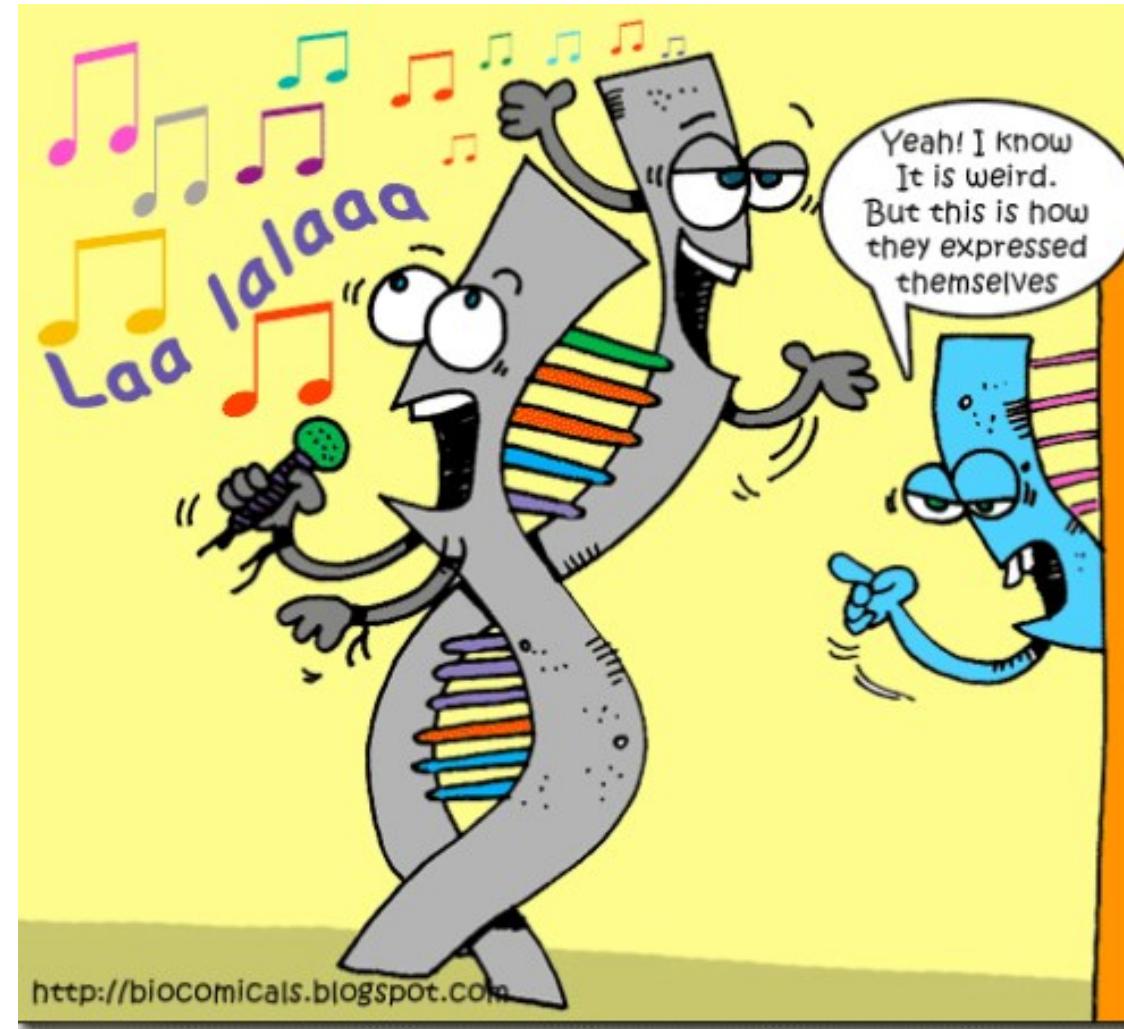
Fig. 18-12



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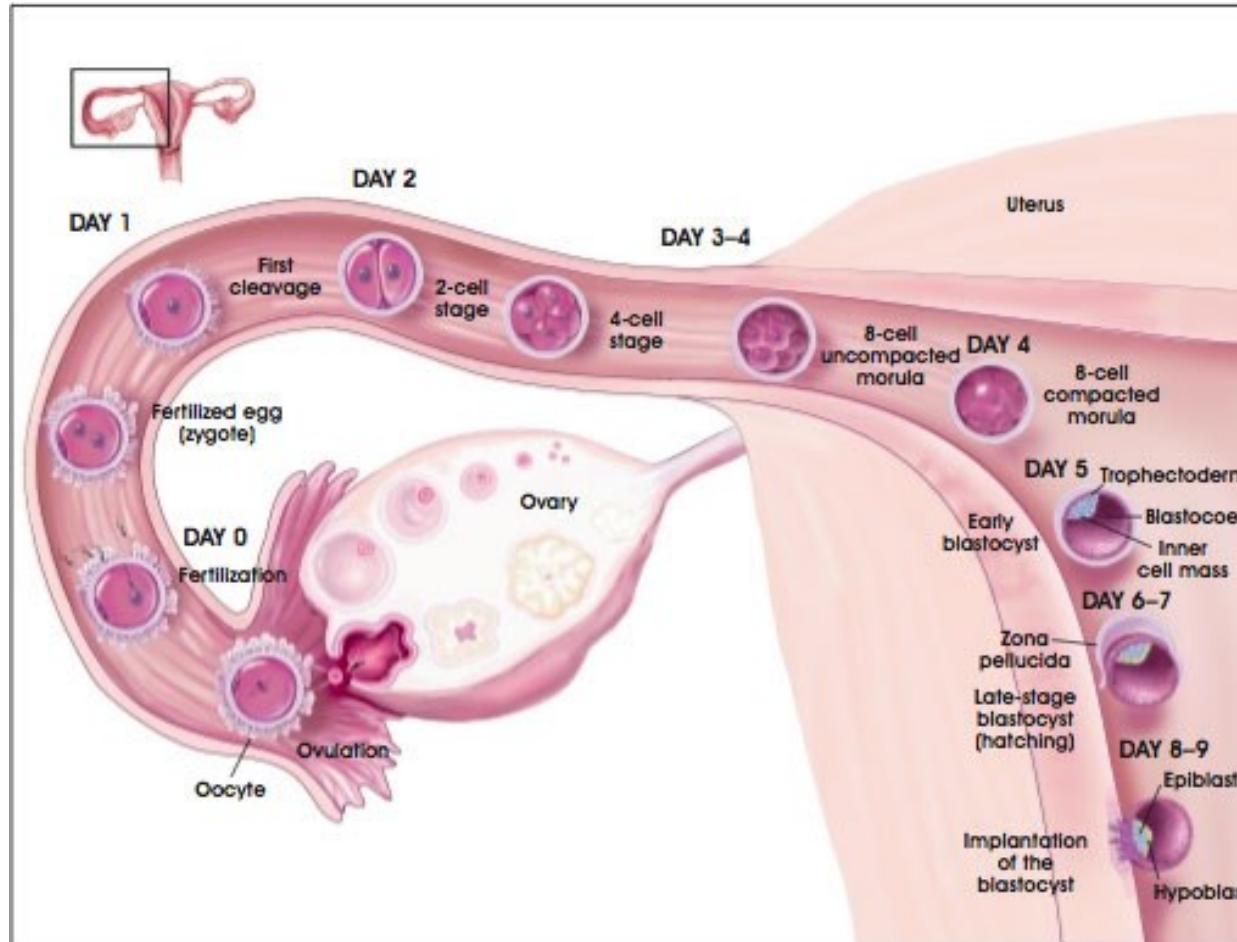
Sažetak

- Regulacija genske ekspresije odvija se na nivou transkripcije, translacije, doradbe i degradacije
- Sinteza RNA:
 - Prepisivanje u RNA (aktivatori, represori, pojačivači, utišavači)
 - Struktura kromatina (metilacija DNA, modifikacije histona)
- Doradba RNA
 - Izrezivanje introna, degradacija
- Sinteza proteina
 - Represori translacije, mikroRNA
- Doradba proteina
 - Smatanje, modifikacije, degradacija

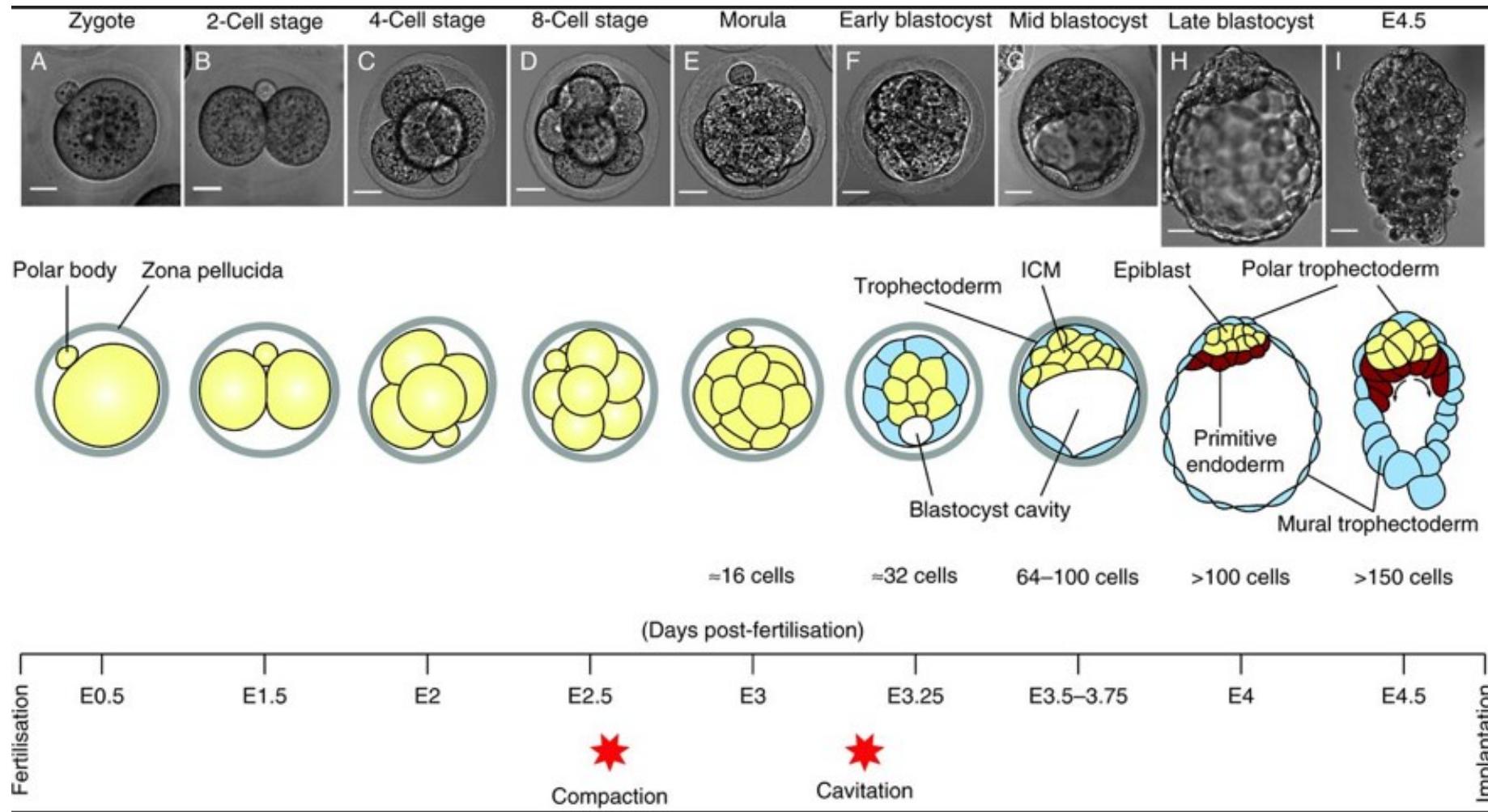


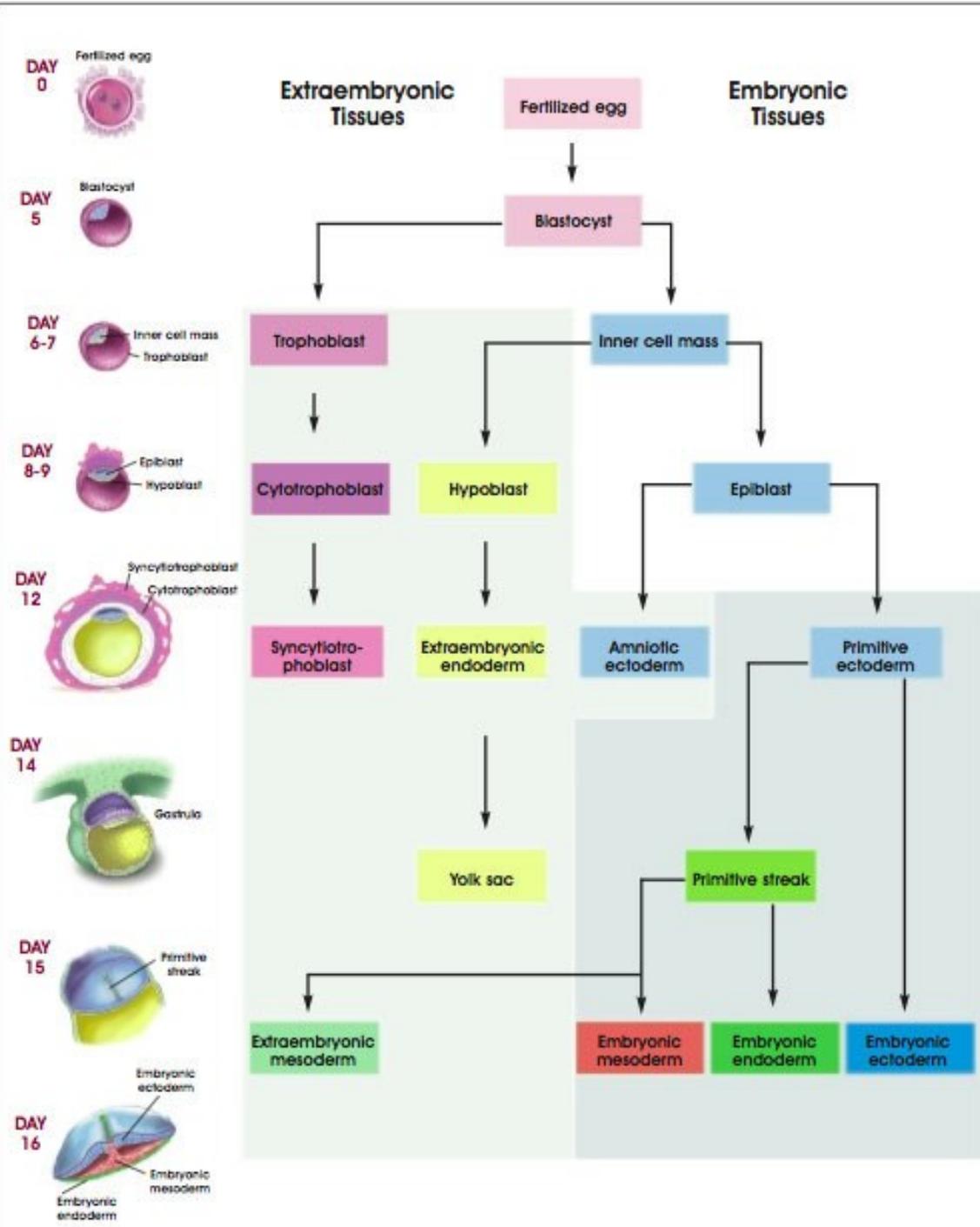
Fertilization

<https://www.youtube.com/watch?v=UgT5rUQ9EmQ>

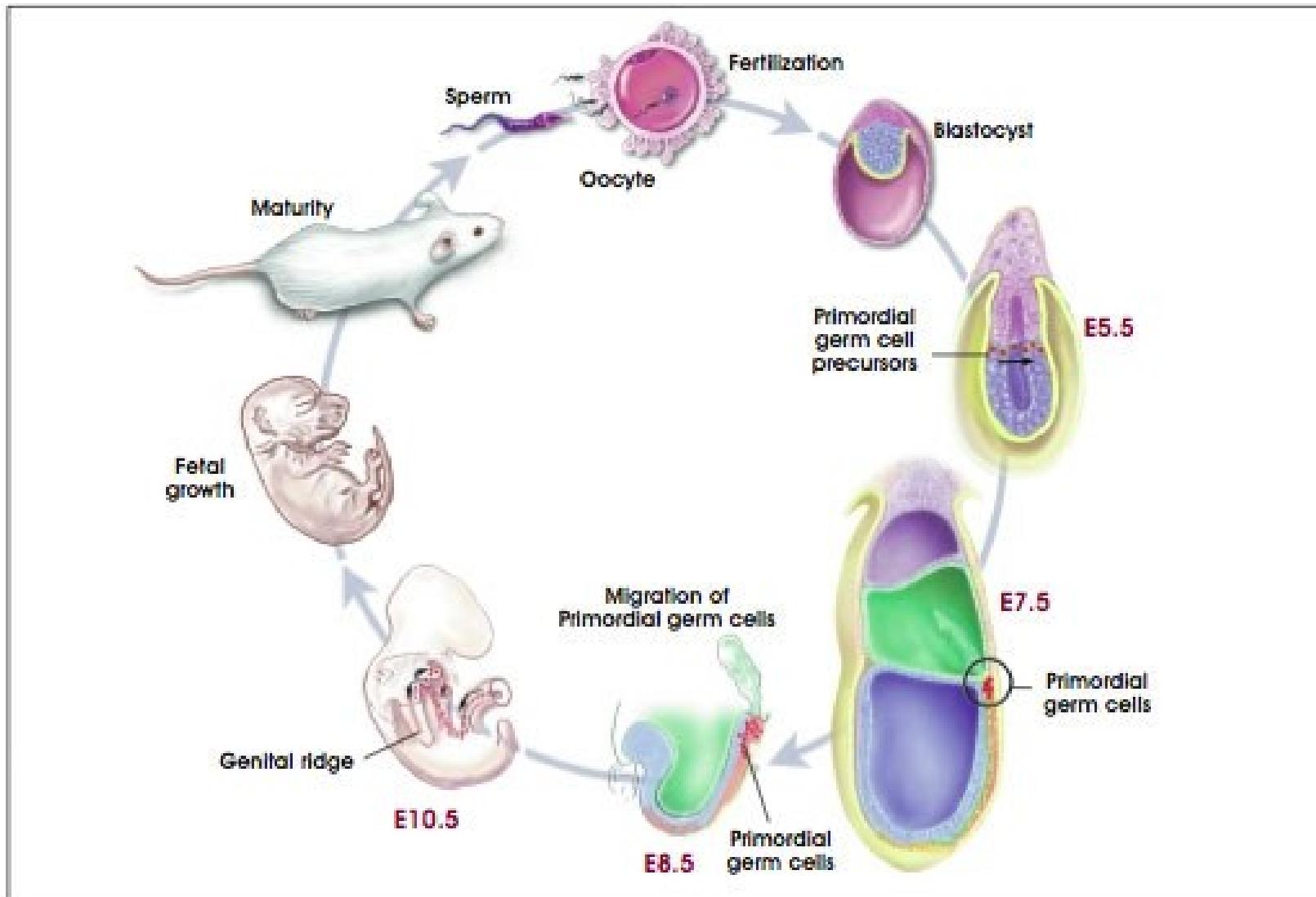


Preimplantation development

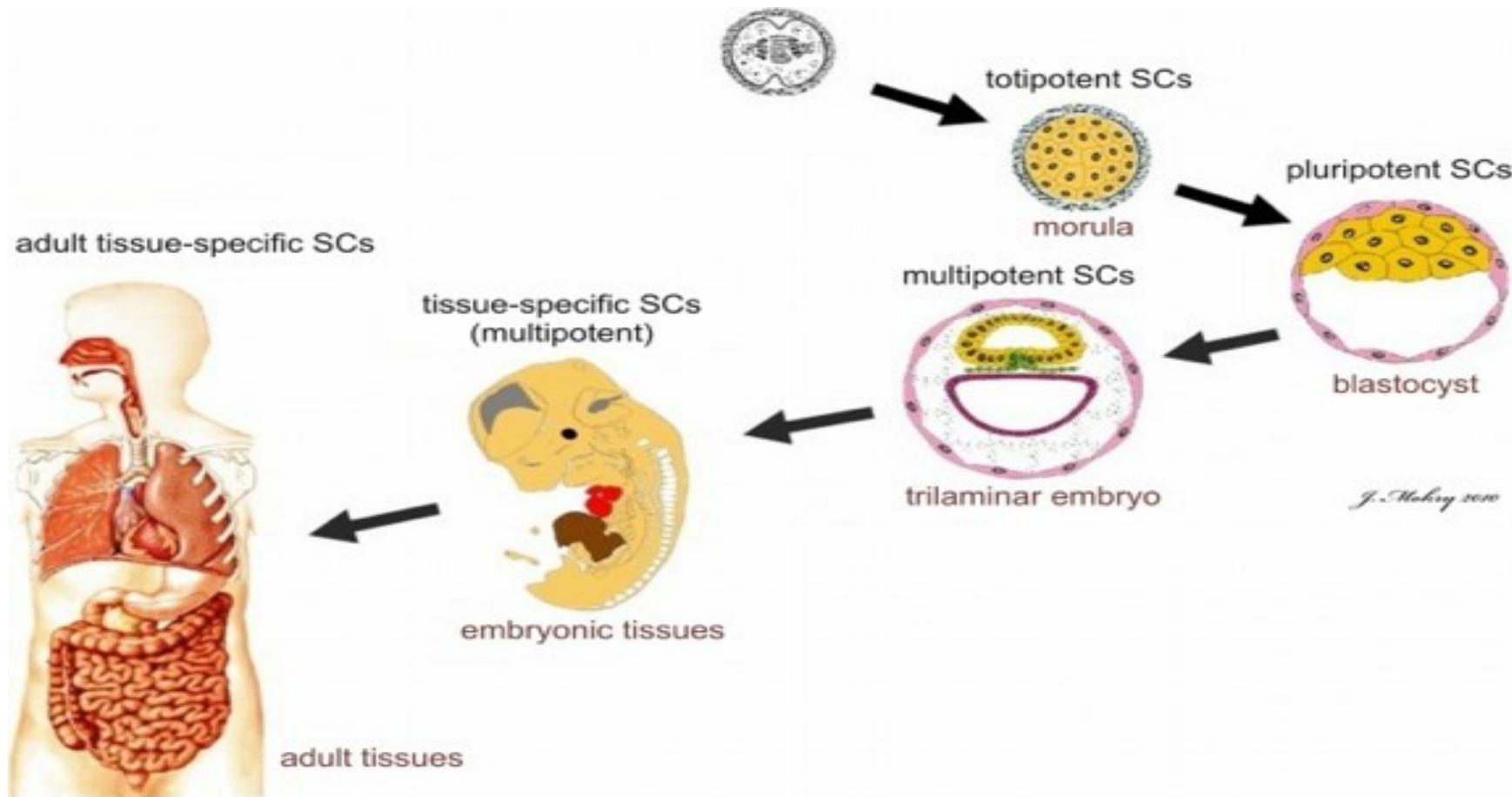




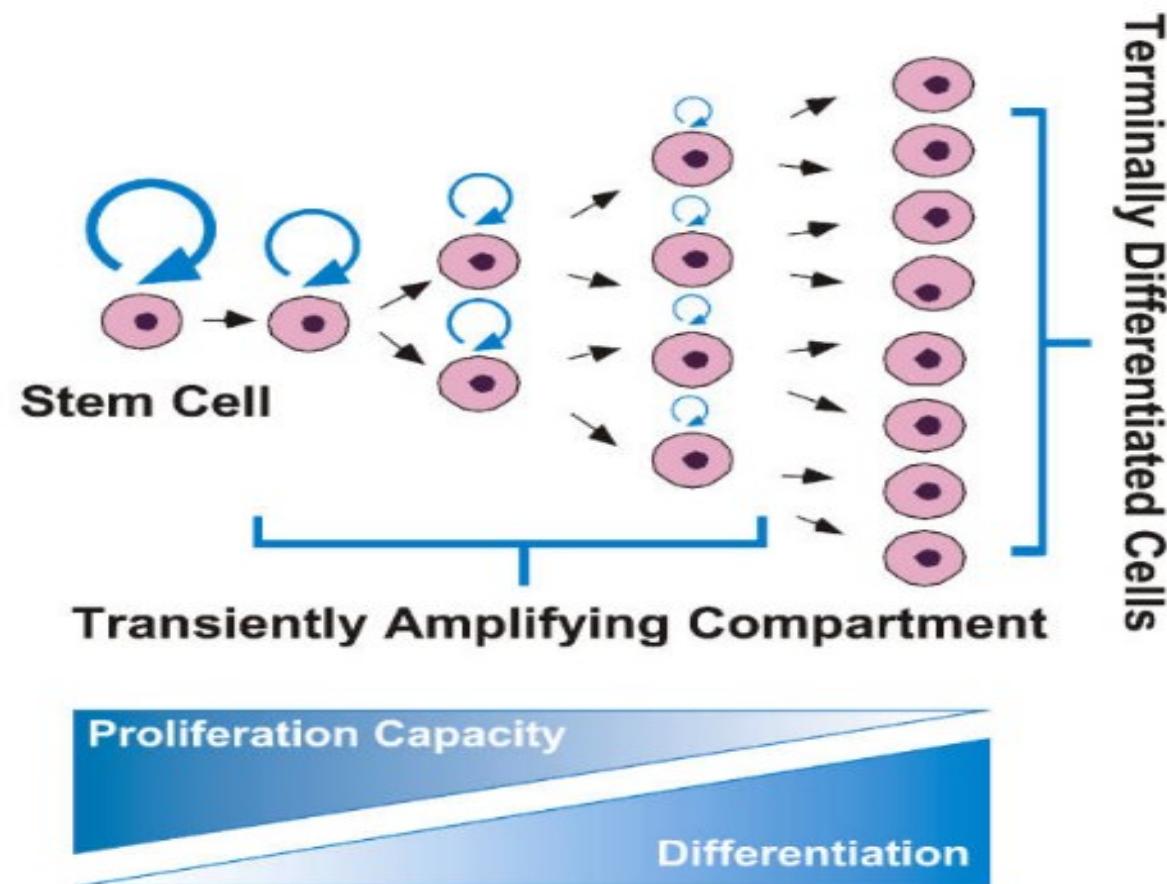
Primordial germ cells



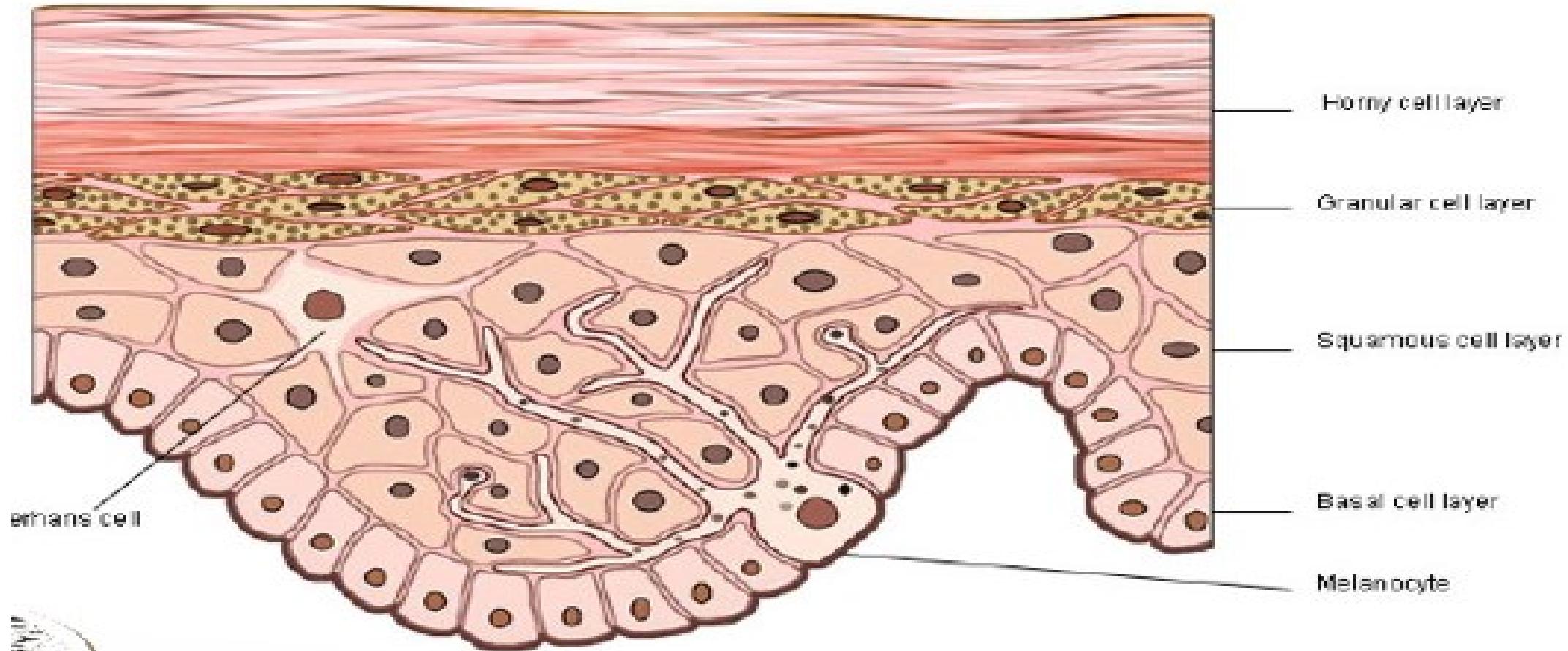
Stem cells during development



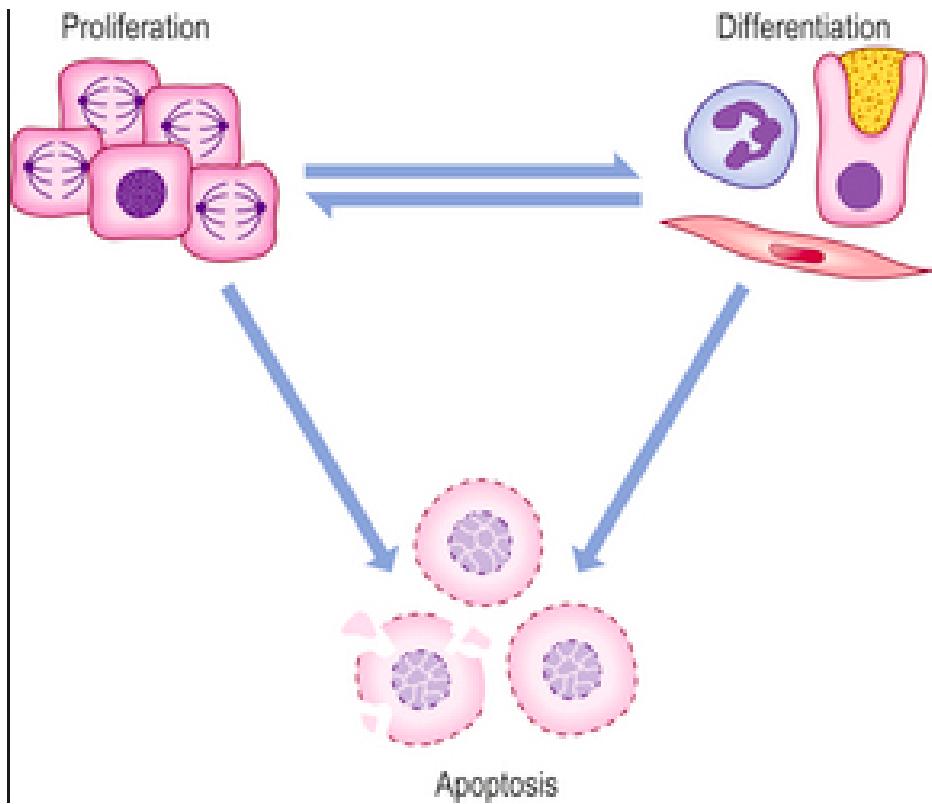
Tissue compartment



Primjer pločastog epitela

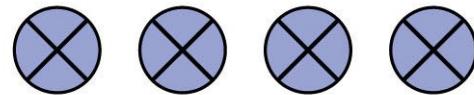


Sudbina stanice u tkivu

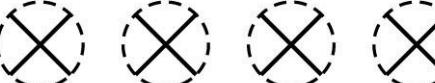
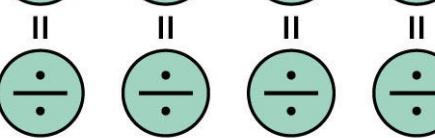


Proliferacija, diferencijacija i apoptoza

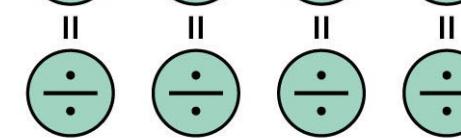
(a)

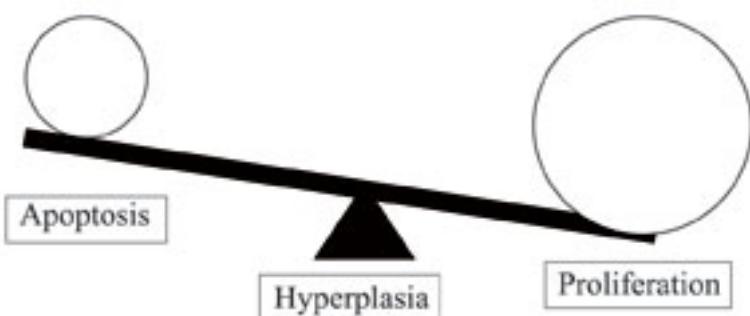
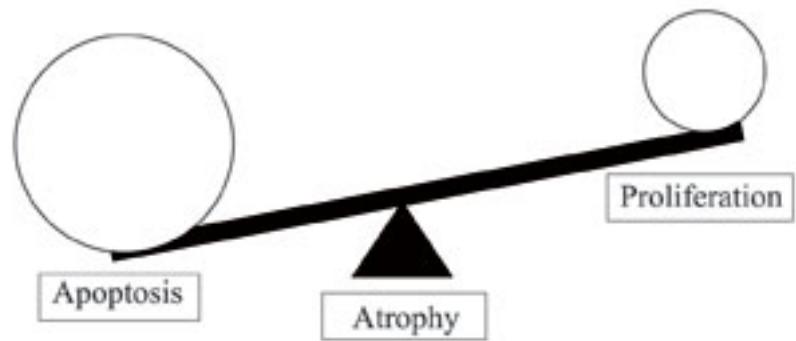
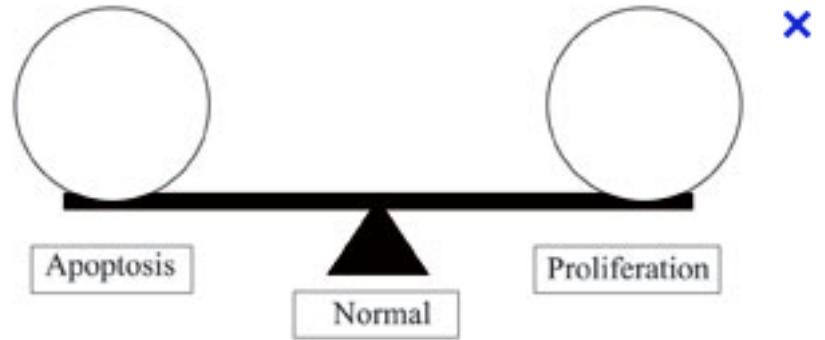


(b)



(c)





Pozitivni i negativni regulatori

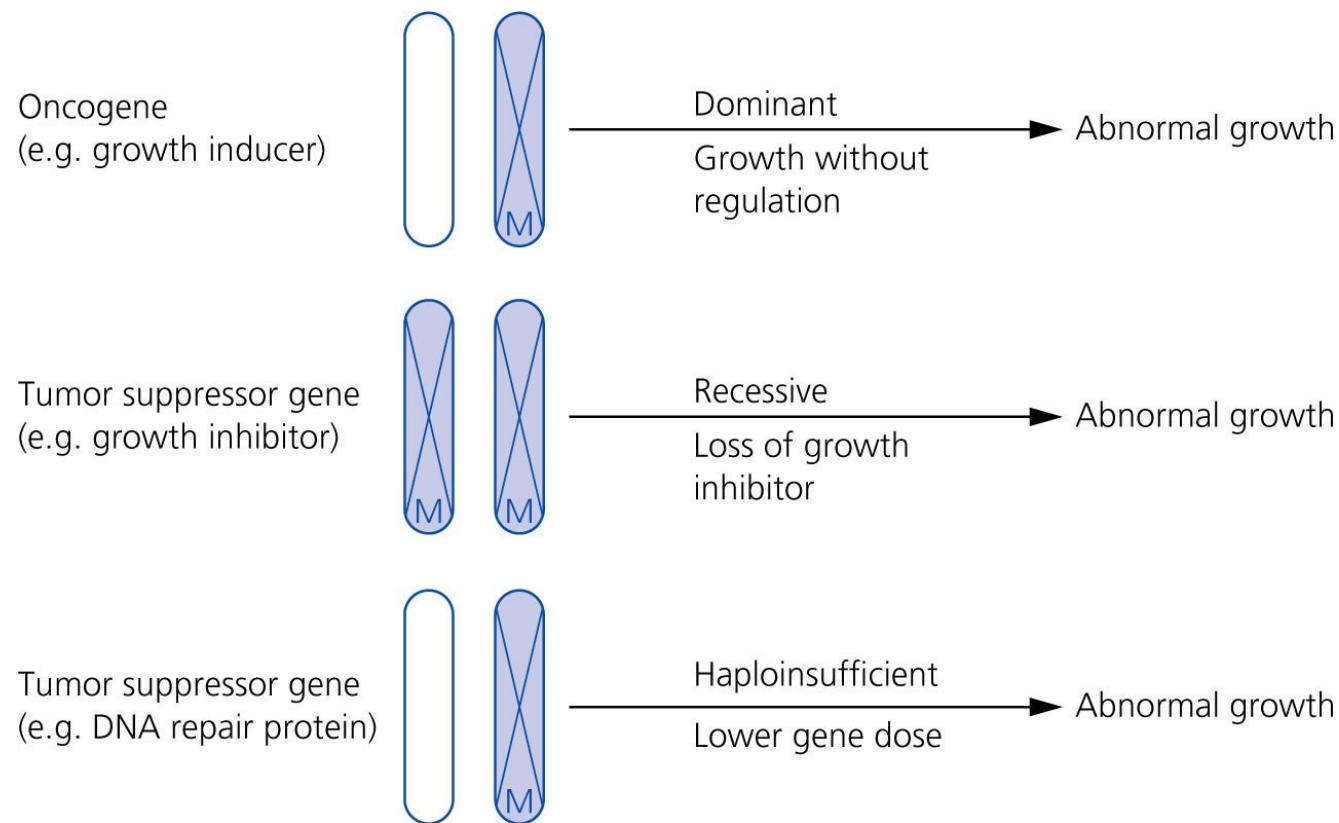


Fig. 18-21a

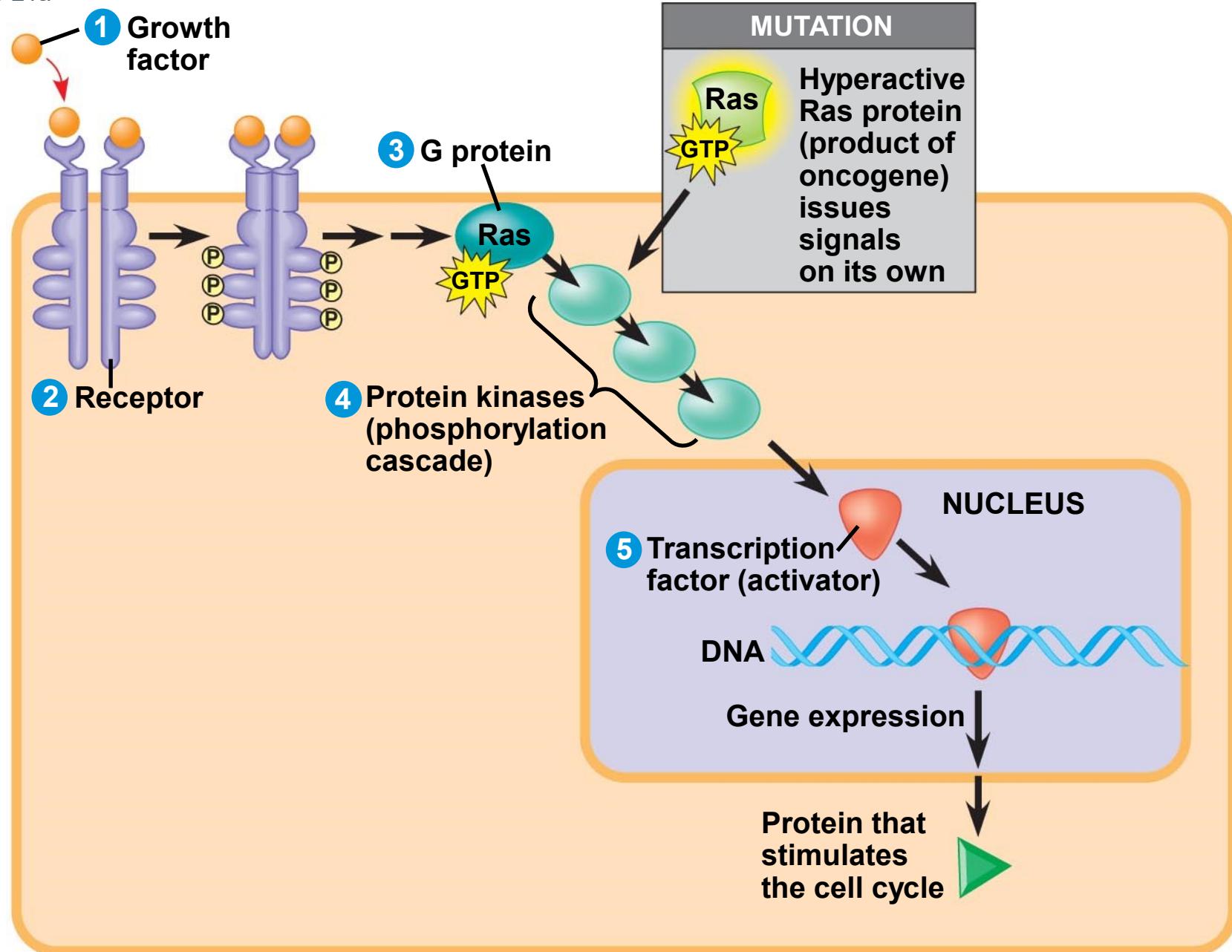
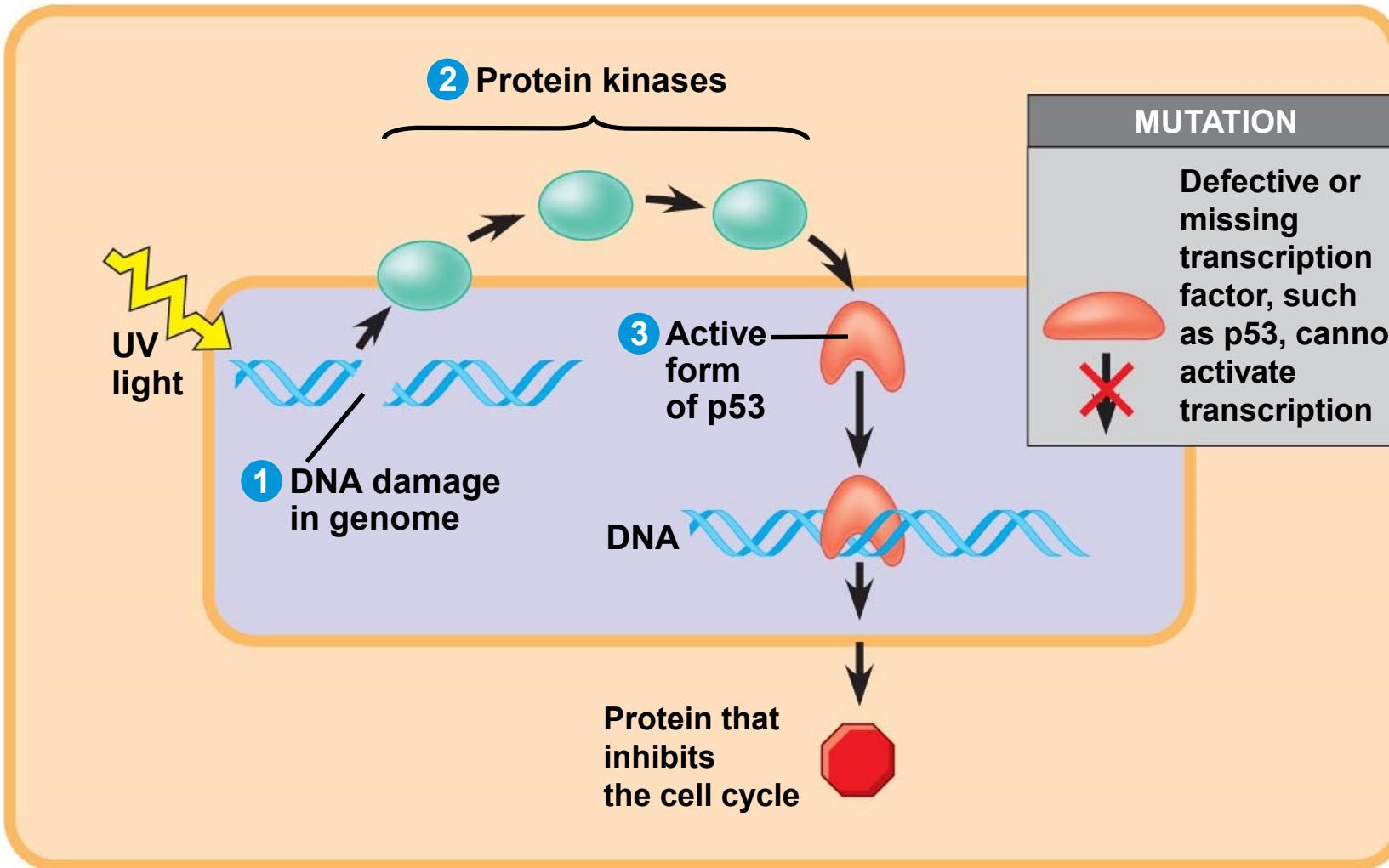


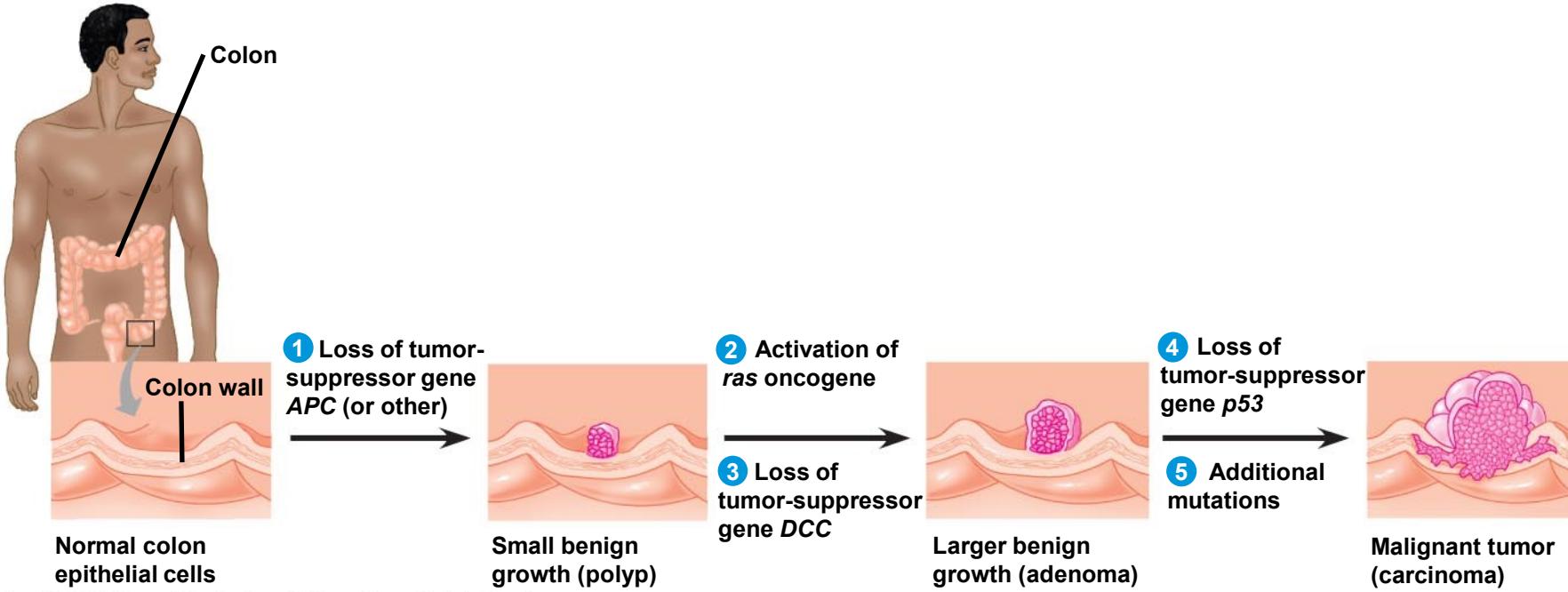
Fig. 18-21b



(b) Cell cycle-inhibiting pathway

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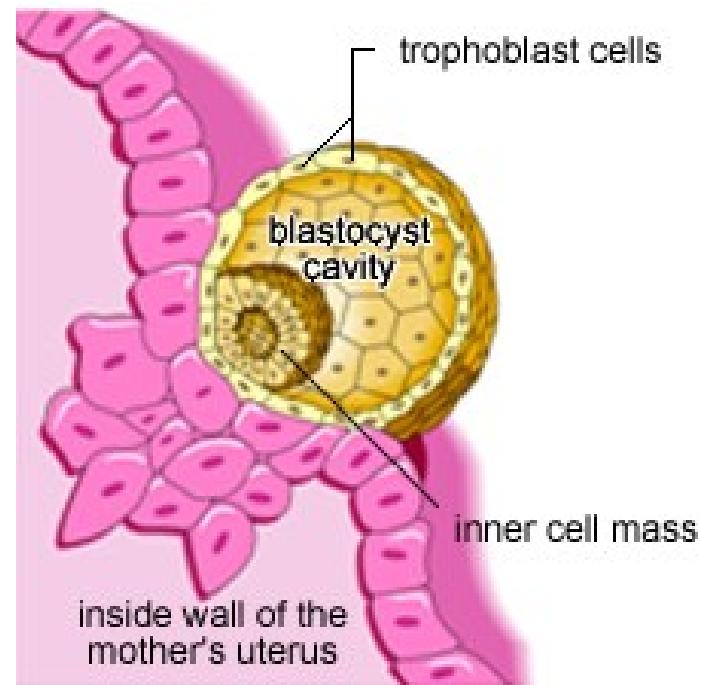
Fig. 18-22



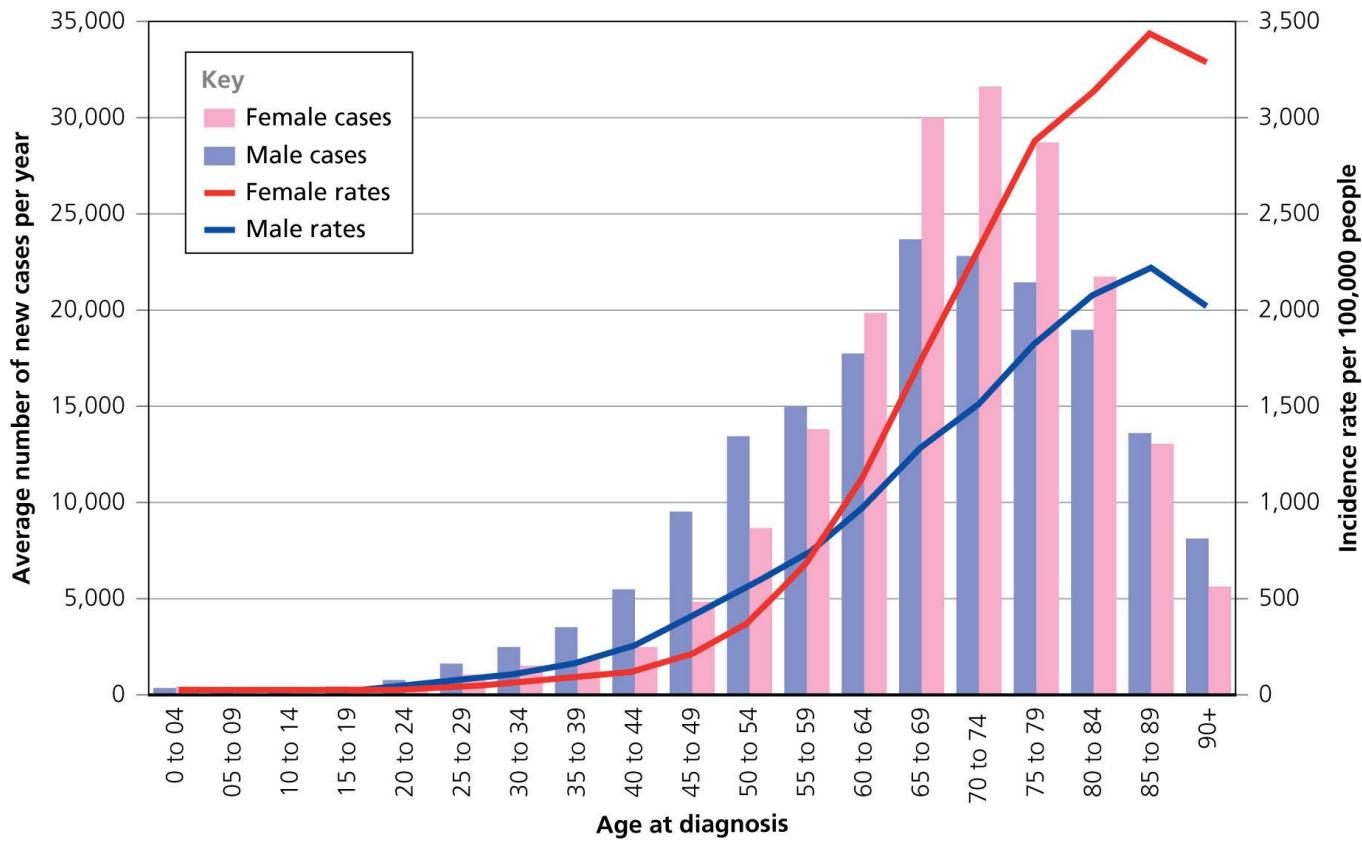
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Osobine višestaničnih organizama koje stanice raka koriste:

- Stanična invazivnost
- Stanična mobilnost
- Veliki broj stanica
- Veliki kompleksni genom
- Dugi životni vijek



Rak – bolest starenja



Prikaz broja novooboljelih na 100000 ljudi ovisno o starosti
u UK za period 2015-2017

Životni vijek

