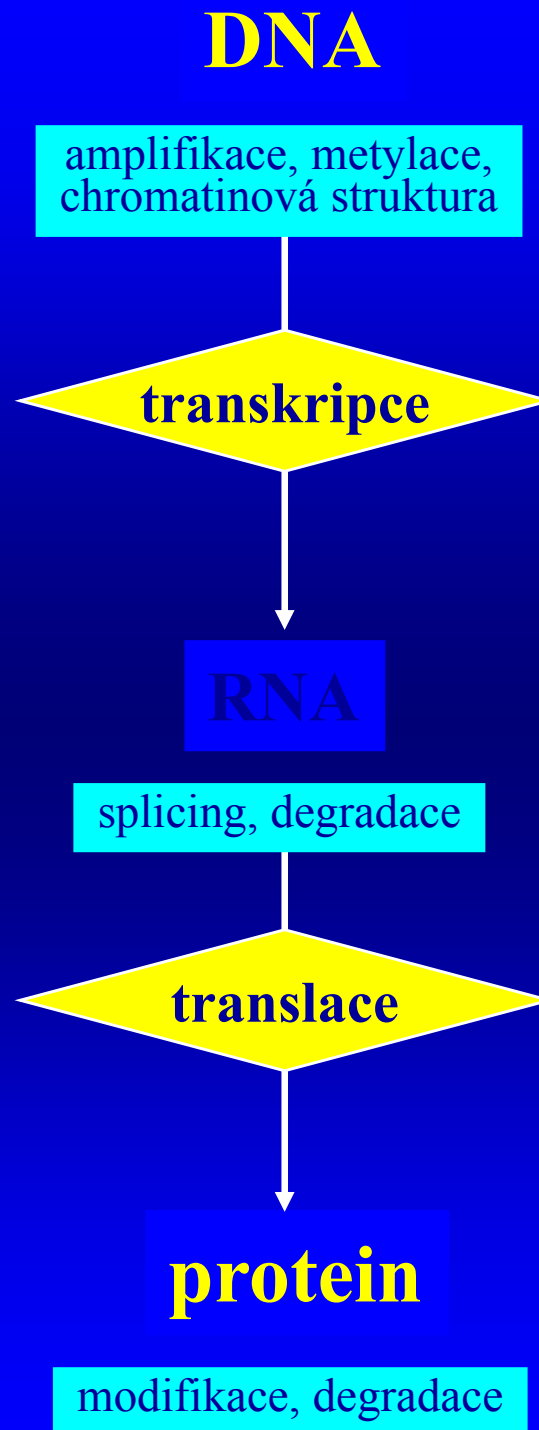
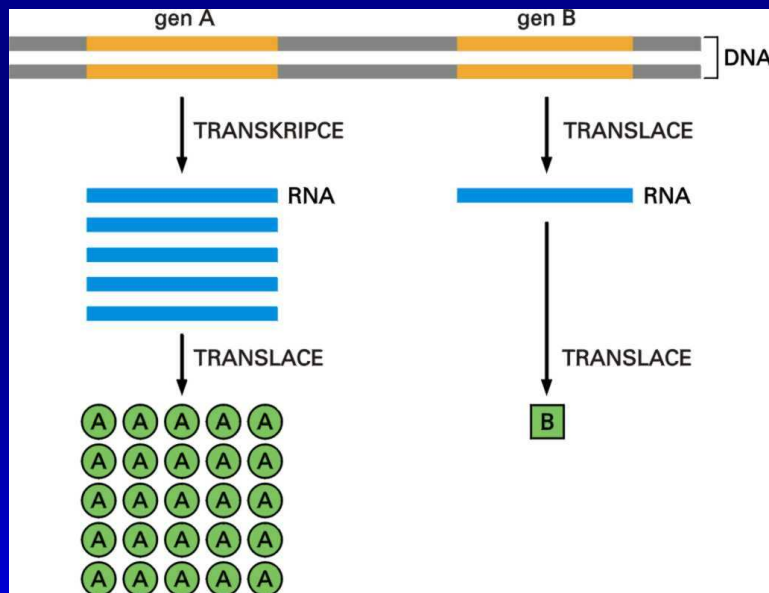
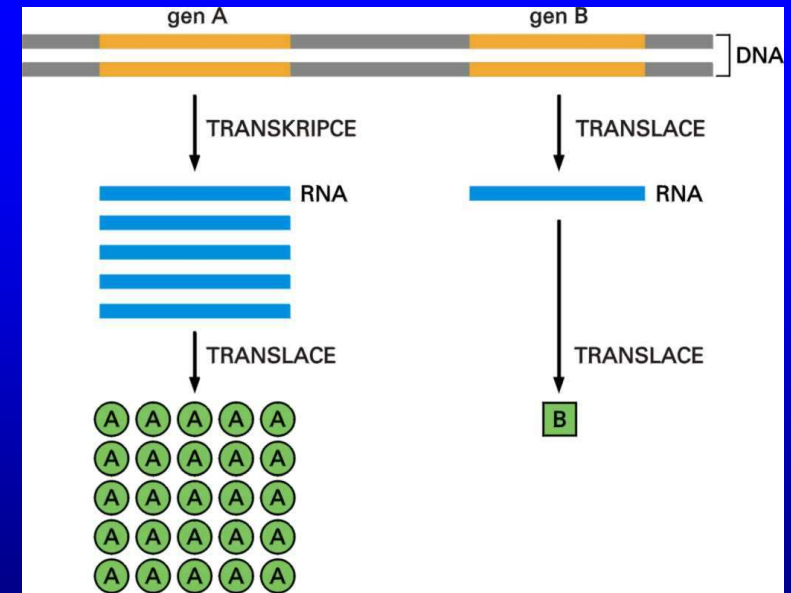


# *Regulace genové exprese*

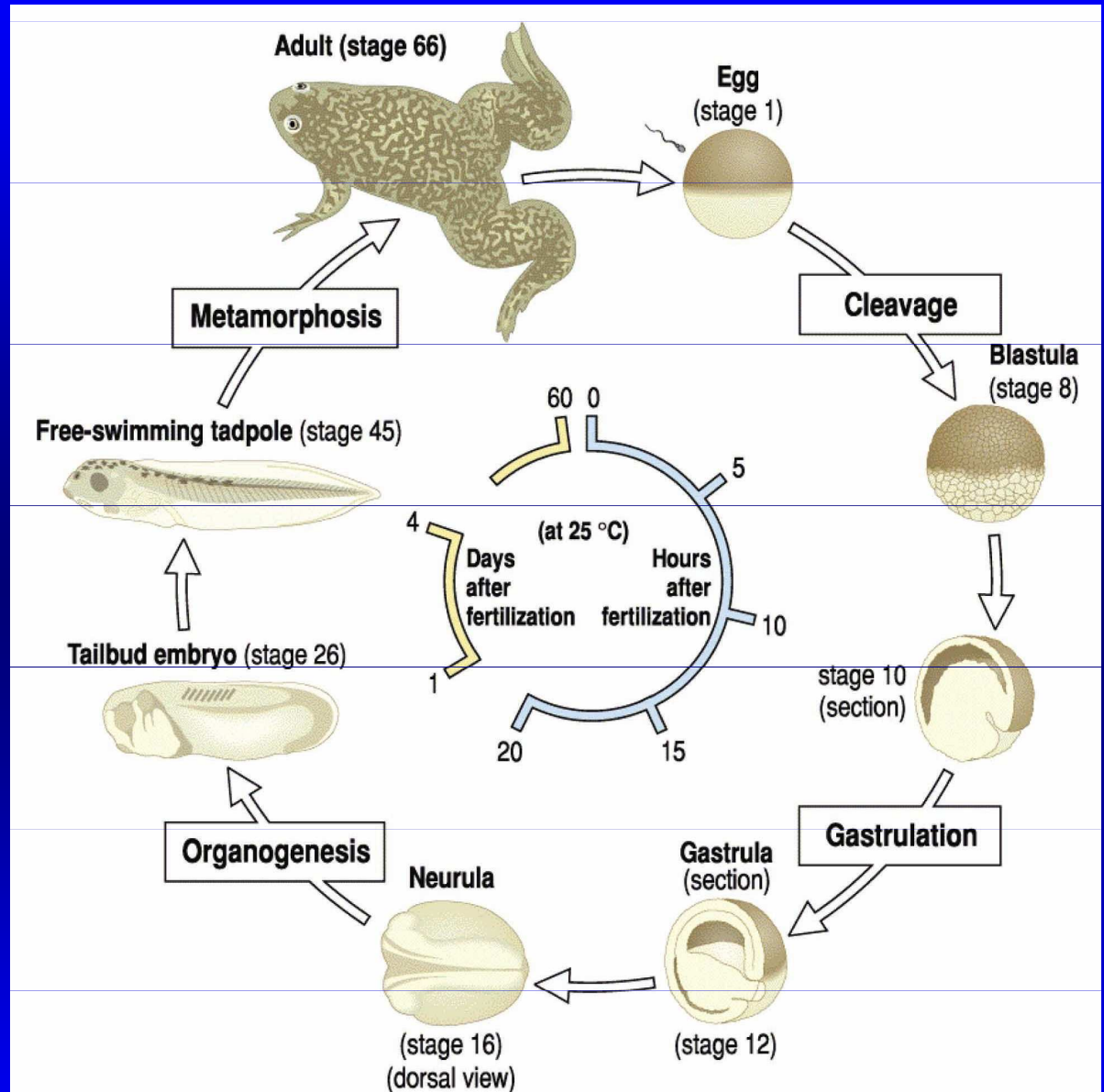


# Regulace genové exprese

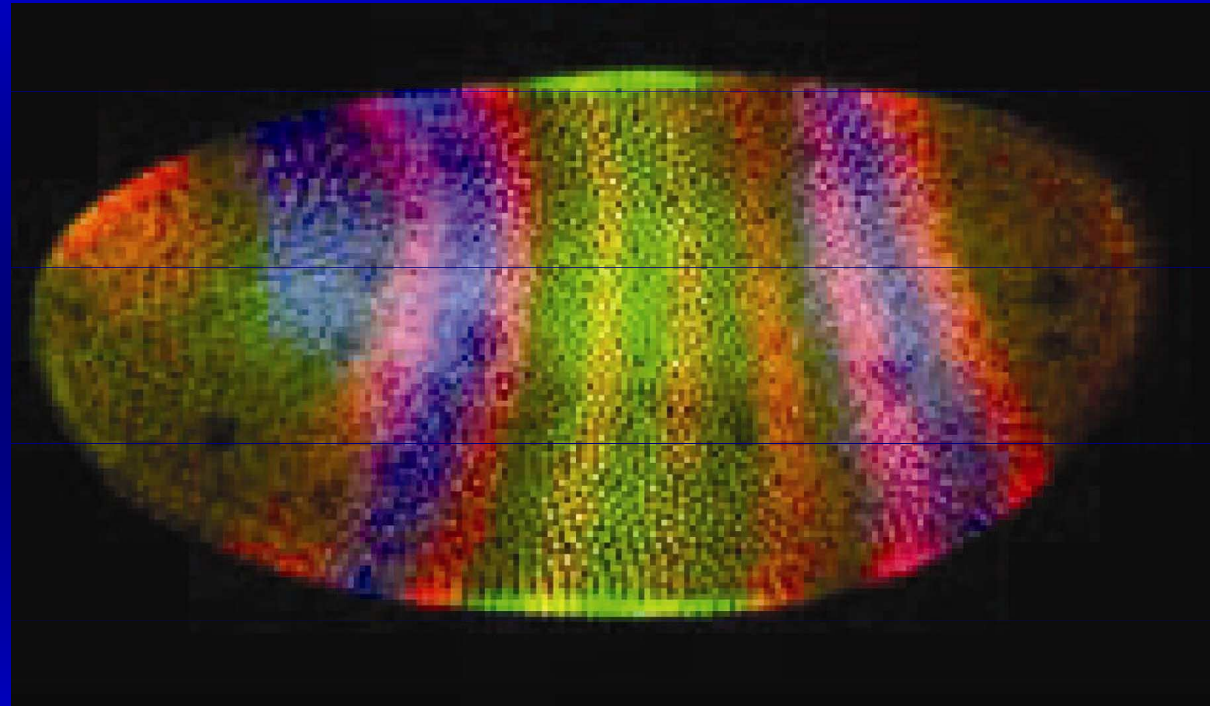
- **Buněčná úroveň**
- **Buněčný cyklus**
- **Patogeny během infekce (*Shigella*, EIEC)**
- **Environmentální podmínky (živiny, toxiny)**
- **Mnohobuněčný organismus**
- **Buněčná diferenciaci**
- **Environmentální podmínky (živiny, toxiny)**
- **Genetické choroby, nádorová onemocnění**

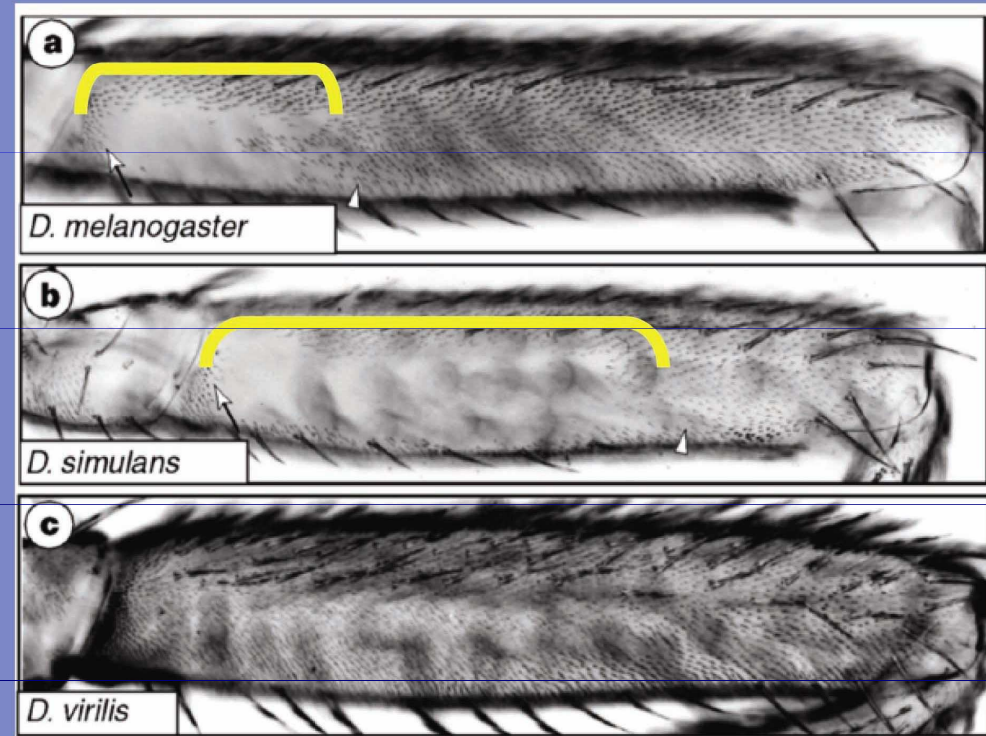
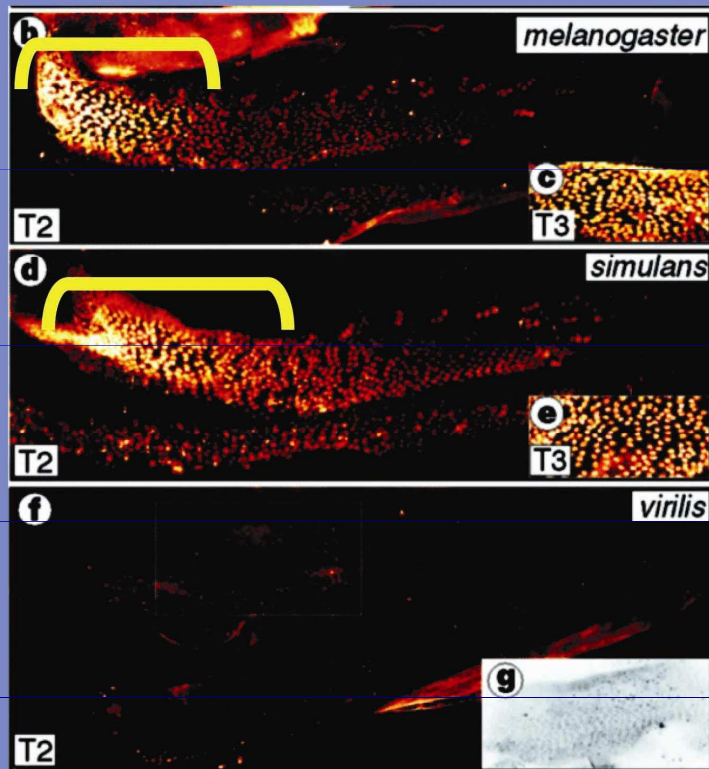


Genová exprese  
musí být regulována  
v čase



Genová exprese  
musí být regulována  
v **prostoru**

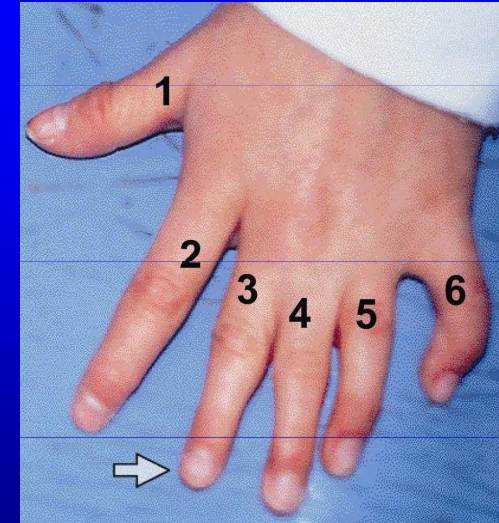
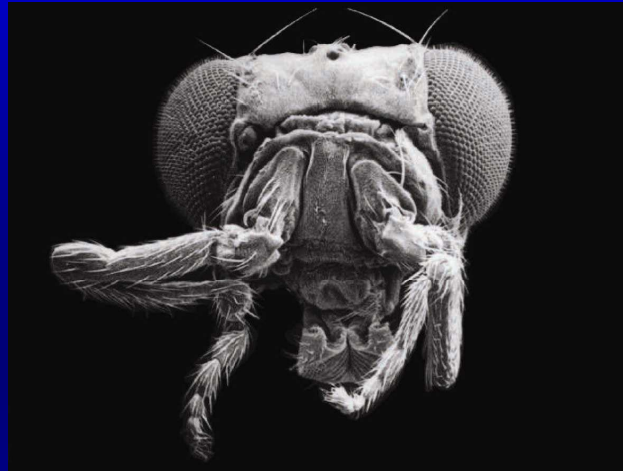
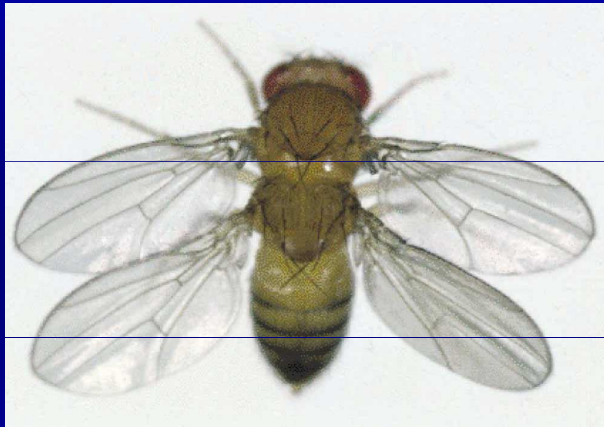




Genová exprese  
 musí být regulována  
 z hlediska množství genového produktu

# Poruchy genové regulace

- Vývojové abnormality



Down  
Syndrome

*Homo sapiens*

**3 miliardy** nt

~ 20.000-25.000 **genů**

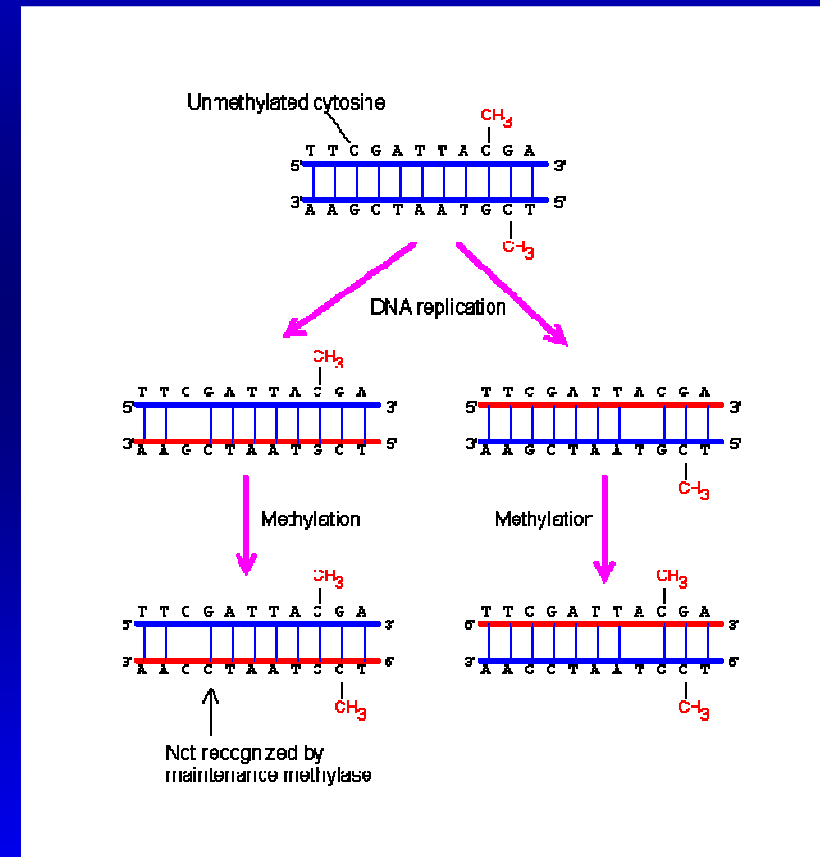
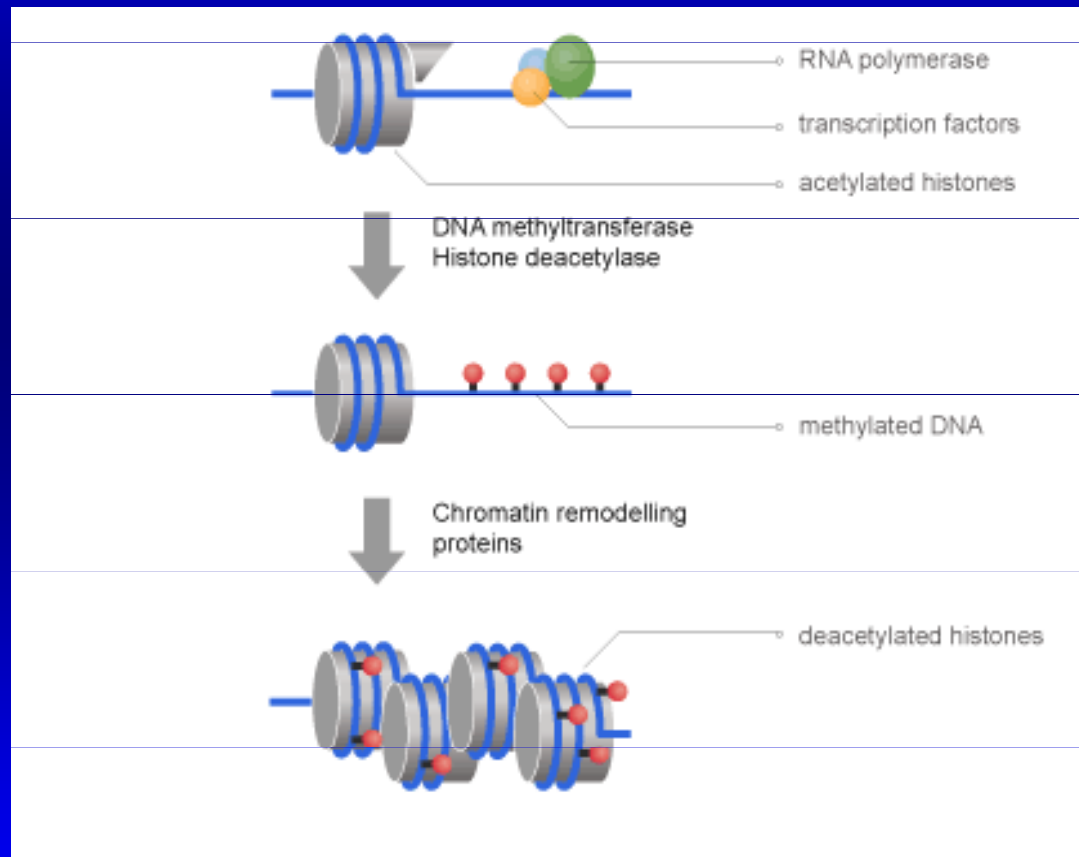
100.000 - 300.000 transkriptů

~ **300 buněčných typů**

## *Regulace genové exprese*

- DNA metylace, epigenetické změny
- **Regulace transkripce**
- MicroRNA (miRNA), stabilita mRNA, RNA processing
- Regulace translace
- Post-translační modifikace

# Epigenetické změny







### Rettův syndrom

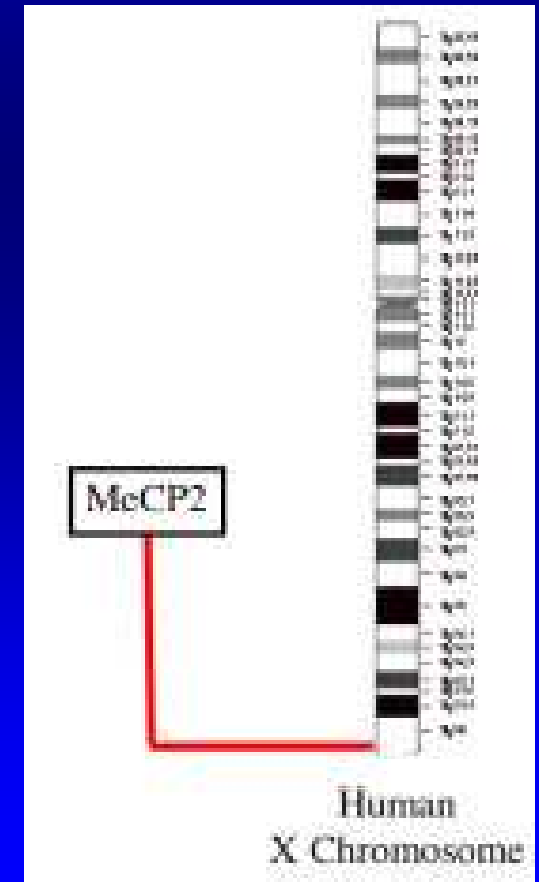
neurologická porucha objevující se téměř výhradně u žen charakterizovaná stereotypními pohyby rukou, narušení chůze a držení těla, zpomalení růstu hlavy.

**Apraxie** - neschopnost programovat tělo k vykonání účelných pohybů

### Mutace v **MeCP2**

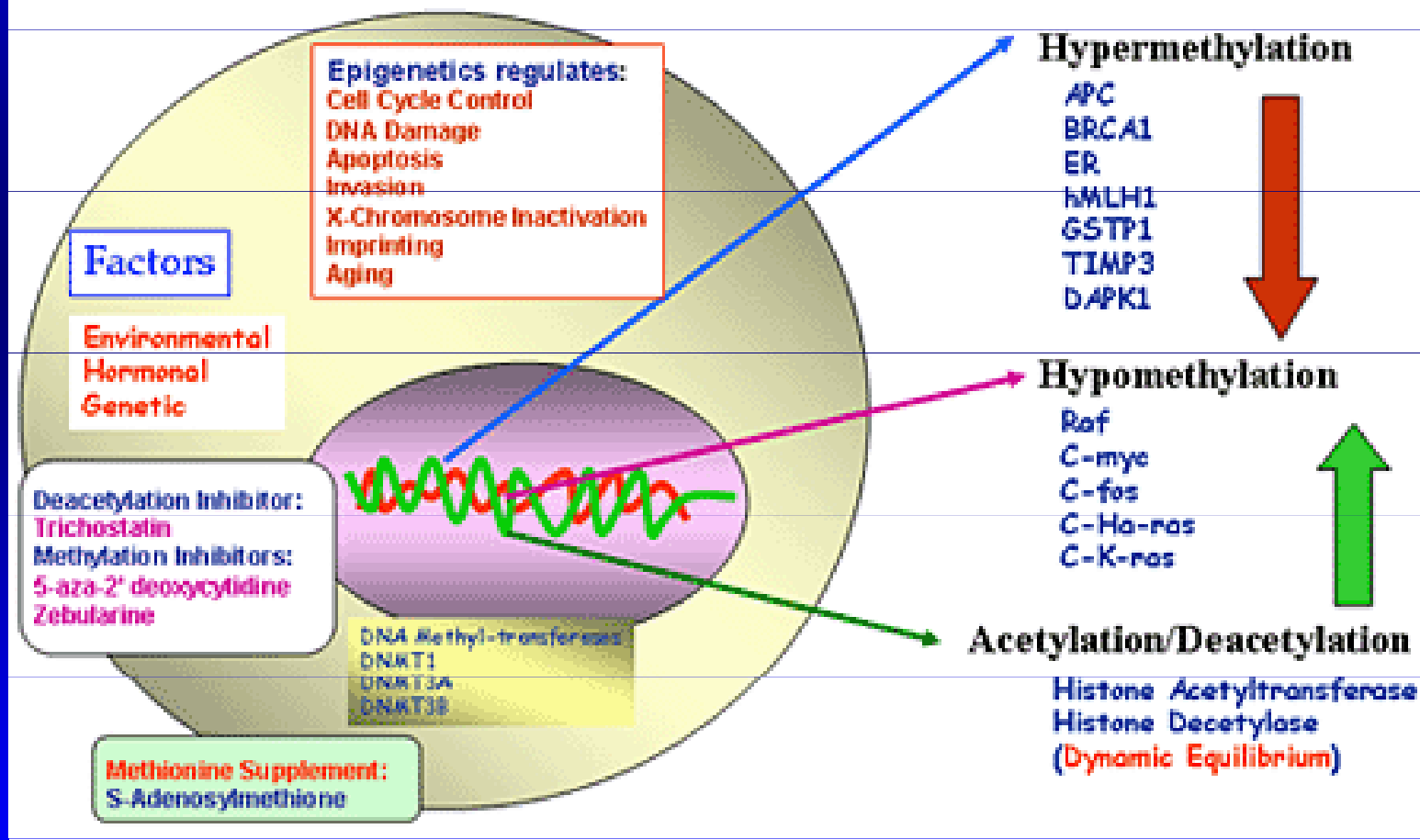
- methyl cytosine binding protein 2

Protein MeCP2 řídí vyjádření dalších genů (**gene silencing**)



# Epigenetická regulace u nádorových onemocnění

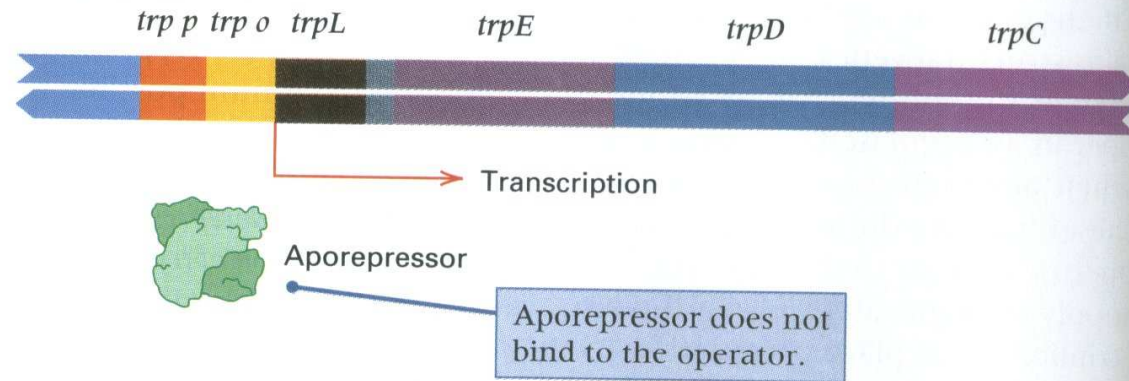
## Epigenetic Targets in Cancer Detection and Risk Assessment



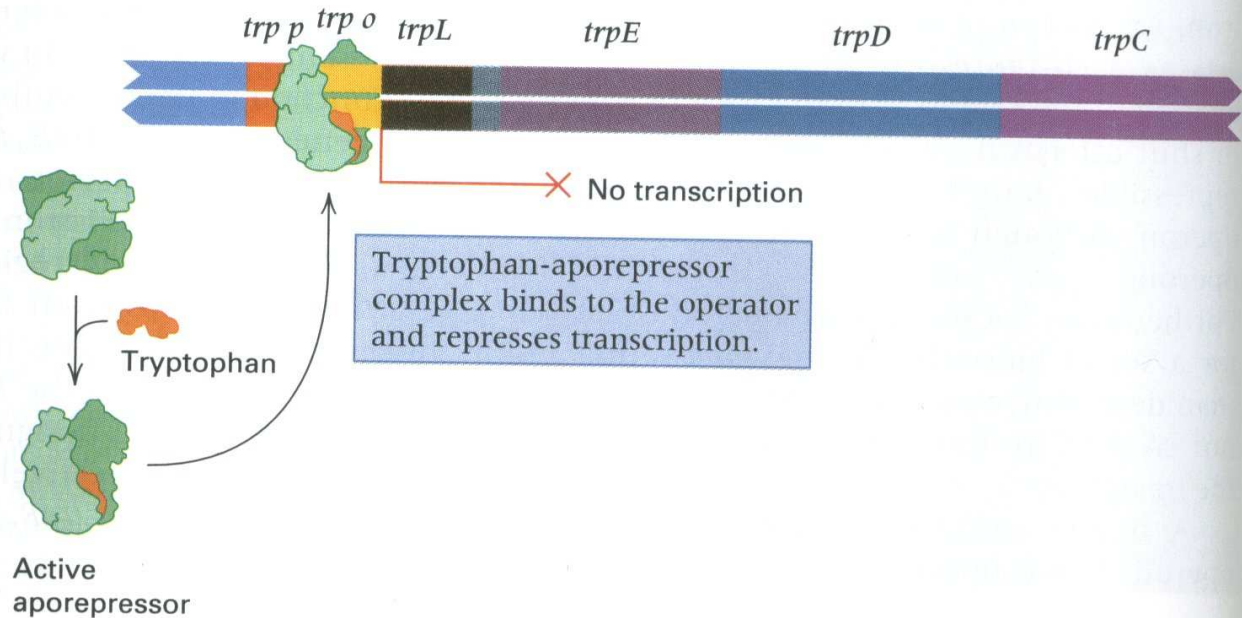
# Regulace transkripce *trp* genů

Nízká hladina tryptofanu –  
transkripce *trp* genů

(A) Transcription occurs



(B) Transcription is repressed



## Expresa *lacZYA* genů:

1. Hladina glukózy – nízká hladina glukózy – vysoká hladina cAMP

2. Hladina laktózy

### transkripce

vysoká hladina glukózy – nízká hladina cAMP  
nízká hladina laktózy

-

Lac operon - 1962

nízká hladina glukózy – vysoká hladina cAMP  
nízká hladina laktózy

-

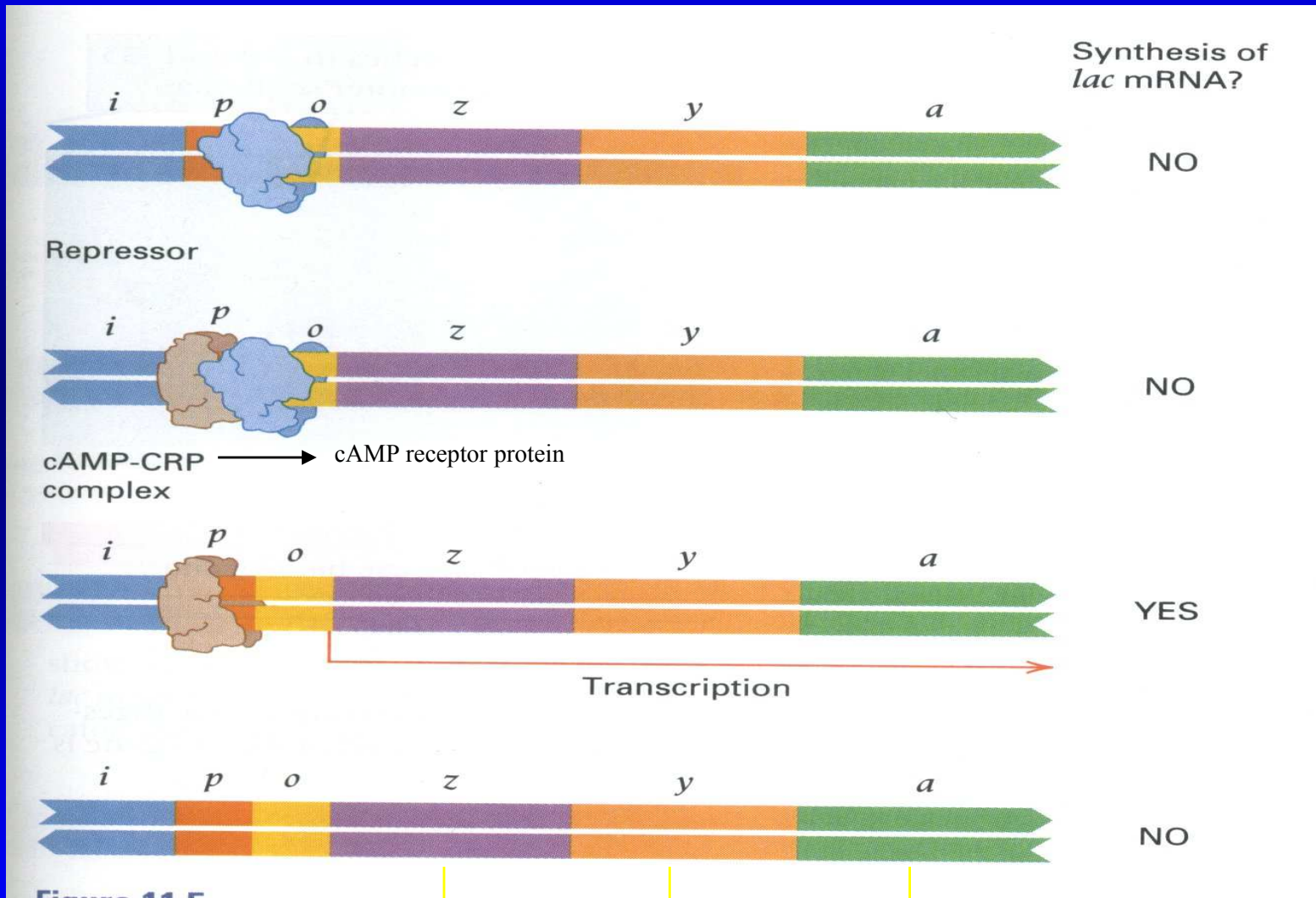
**nízká hladina glukózy – vysoká hladina cAMP**  
**vysoká hladina laktózy**

**+**

vysoká hladina glukózy – nízká hladina cAMP  
vysoká hladina laktózy

-

# Regulate transkripce lac geni



High glucose – low cAMP  
Low lactose

Low glucose – high cAMP  
Low lactose

**Low glucose – high cAMP**  
**High lactose**

High glucose – low cAMP  
High lactose

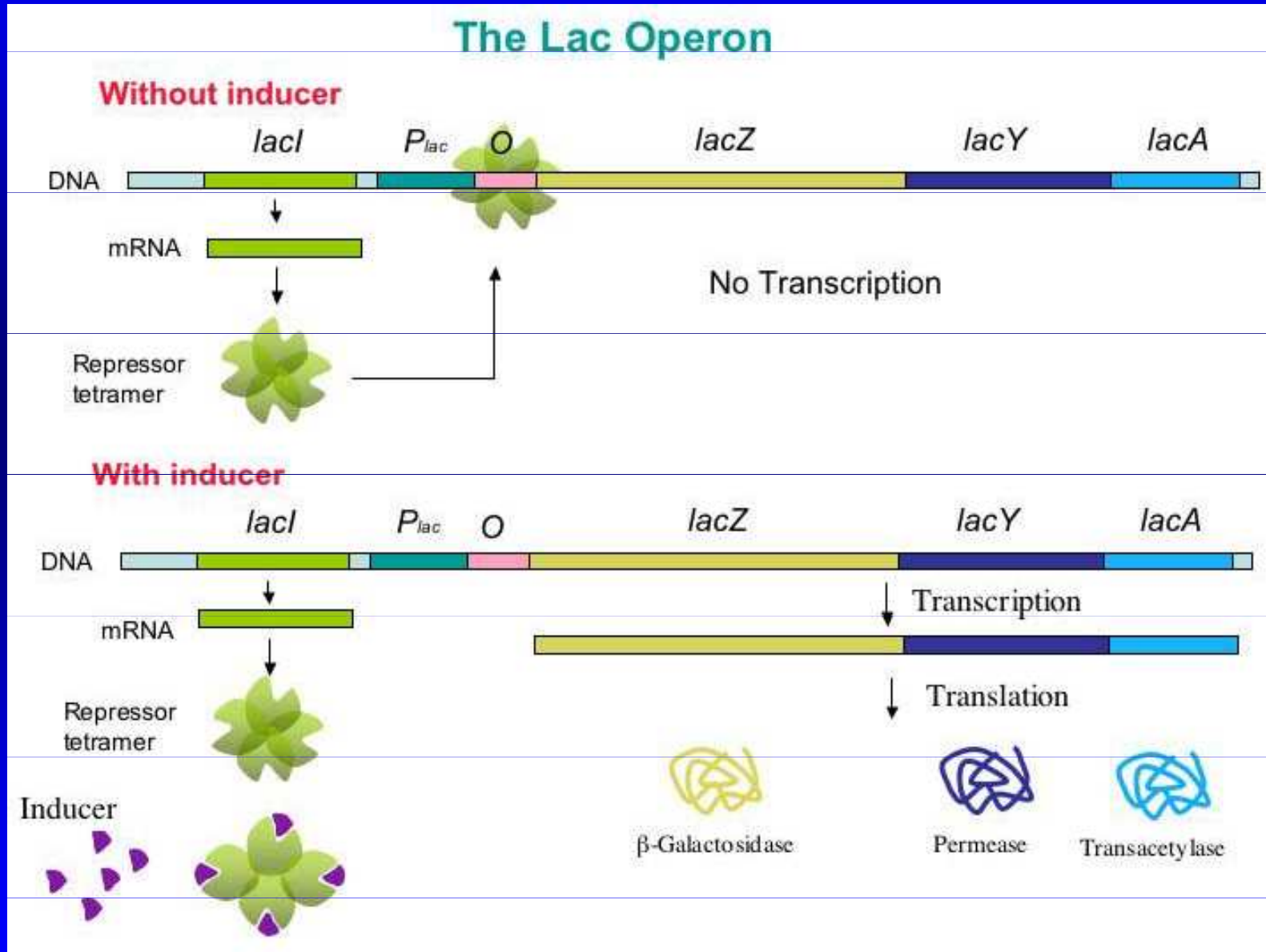
β-galactosidase

permease

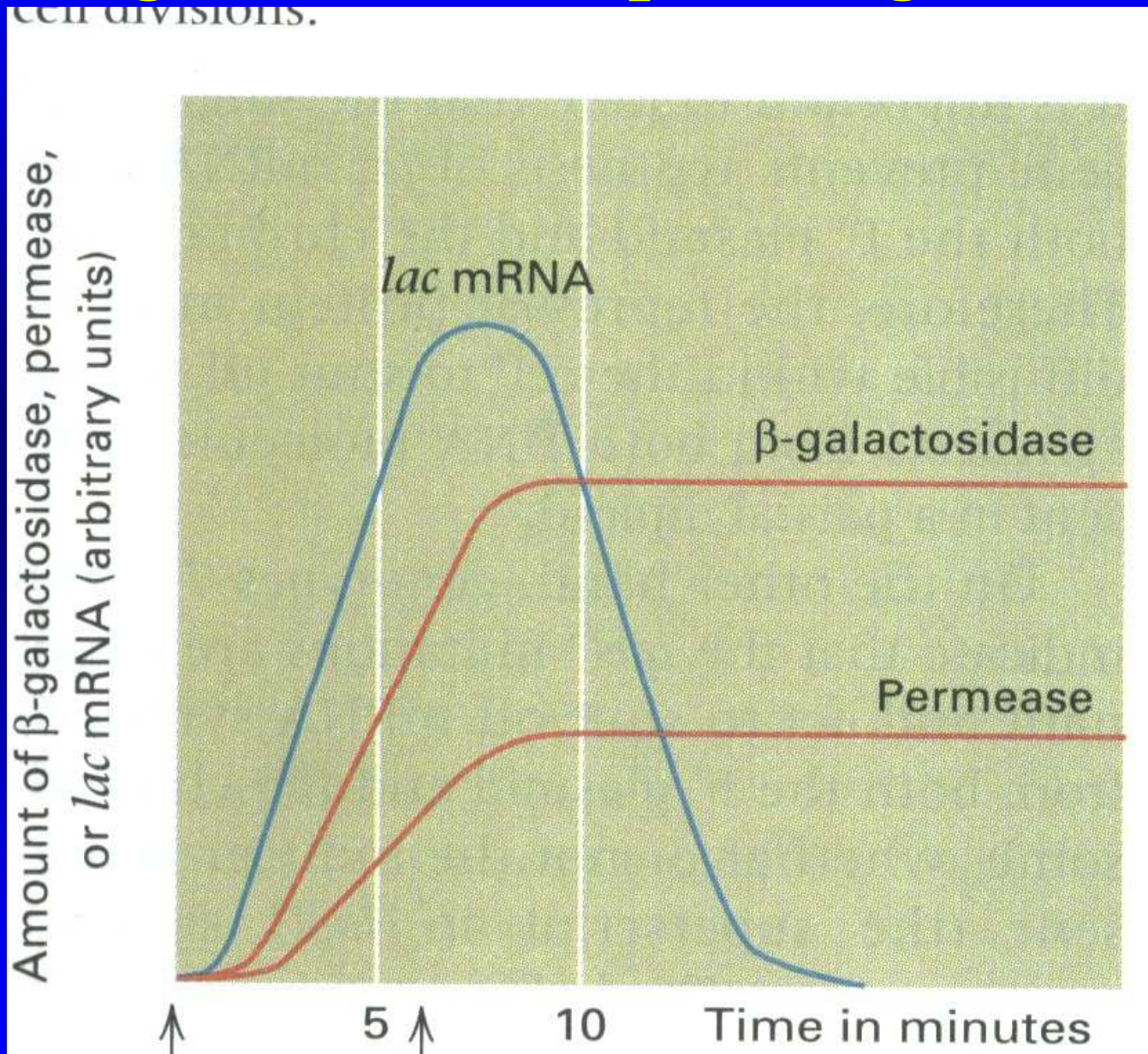
transacetylase

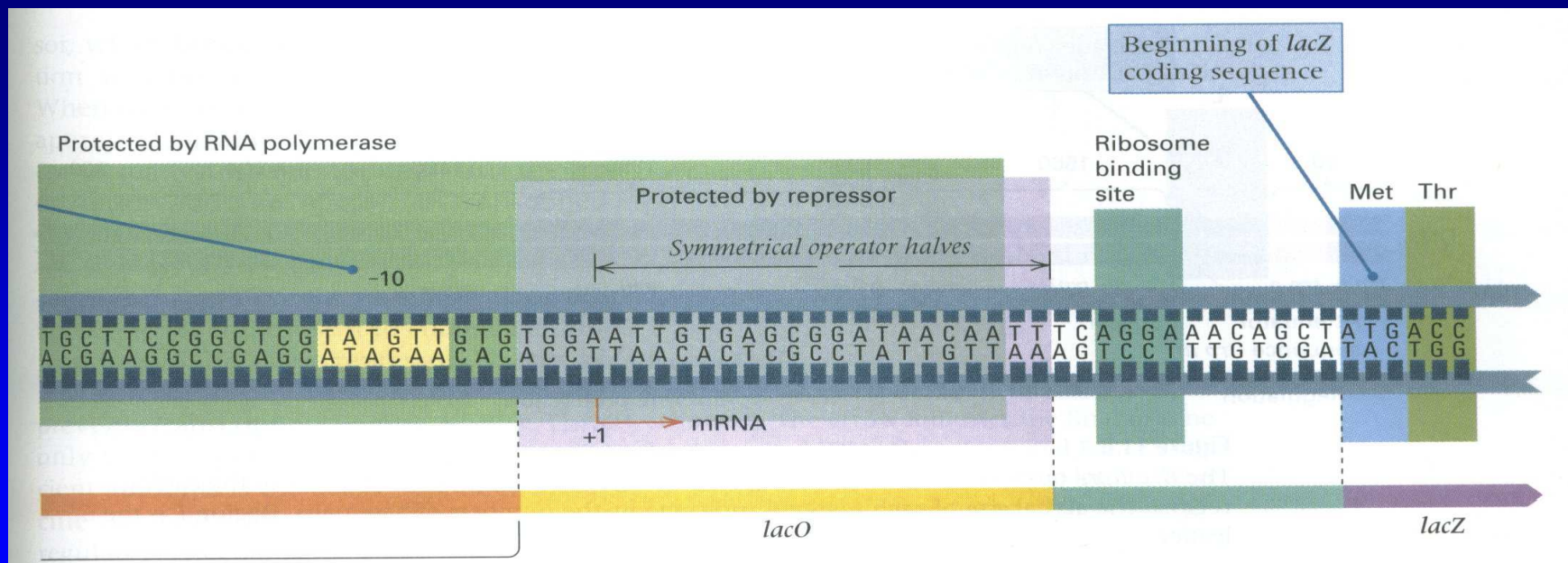
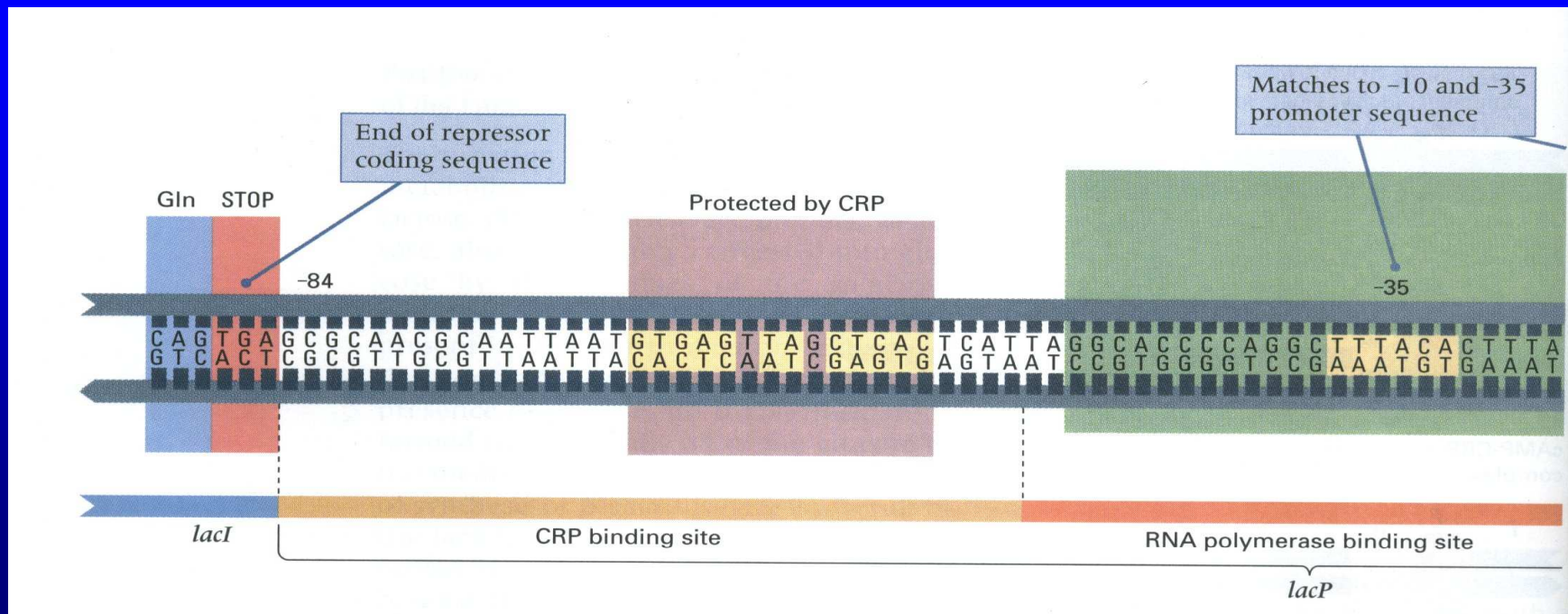
Figure 11.5

# Regulate transkripcije lac gena



# Regulate transkripce lac geni

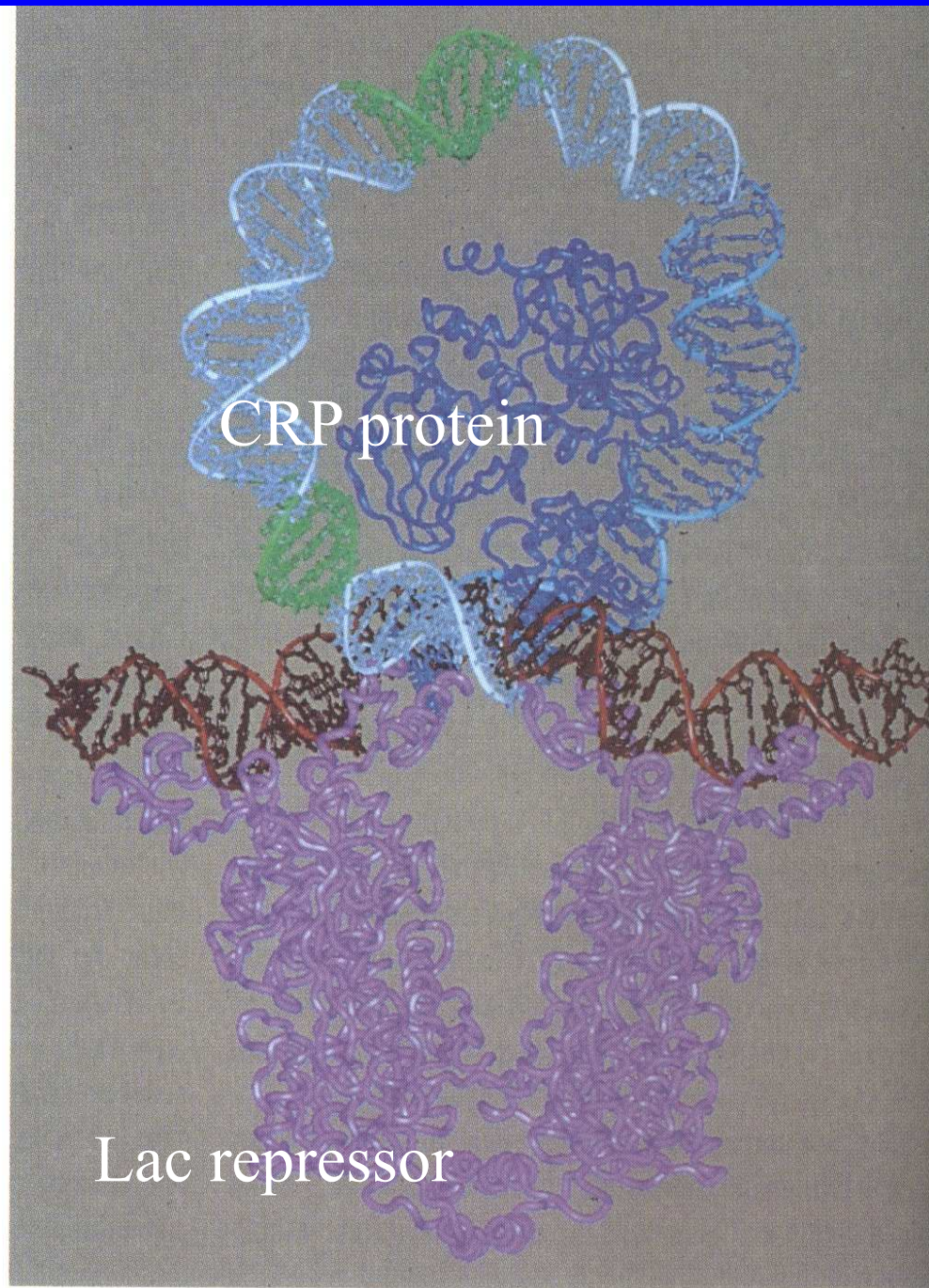




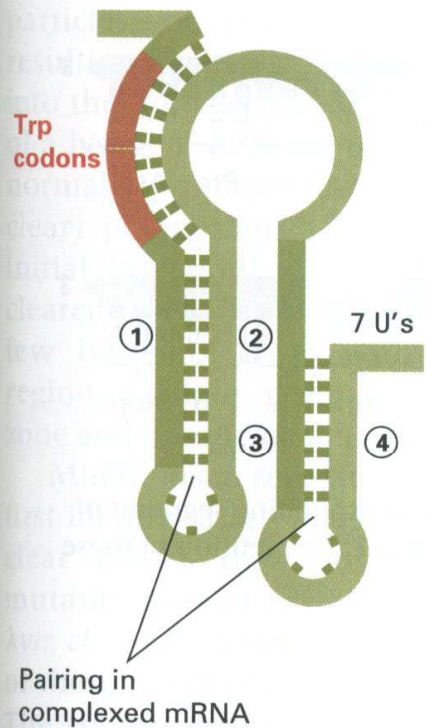


**Figure 11.7**

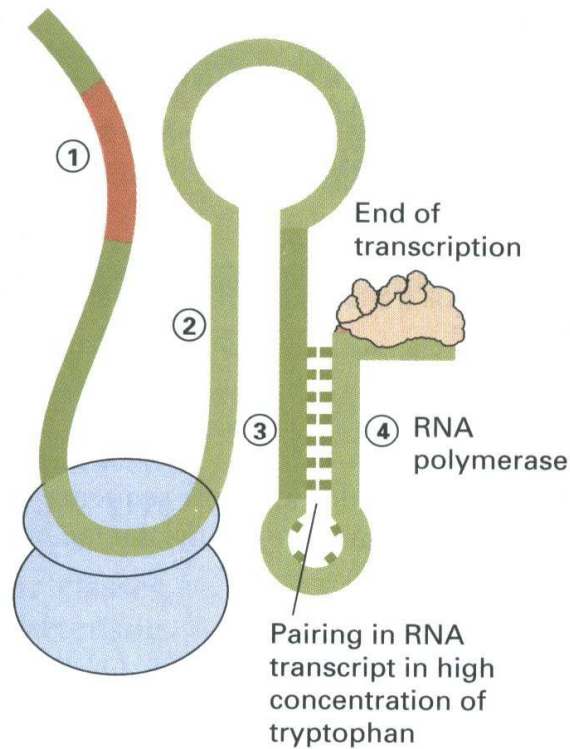
Structure of the *lac* operon repression loop. The *lac* repressor, shown in violet, binds to two DNA regions (red) consisting of the symmetrical operator region indicated in Figure 11.6 and a second region immediately upstream from the CRP binding site. Within the loop is the CRP binding site (medium blue), shown bound with CAP protein (dark blue). The  $-10$  and  $-35$  promoter regions are in green. [Courtesy of Mitchell Lewis; from M. Lewis, G. Chang, N. C. Horton, M. A. Kercher, H. C. Pace, M. A. Schumacher, R. G. Brennan, and P. Lu. 1996. *Science* 271: 1247.]



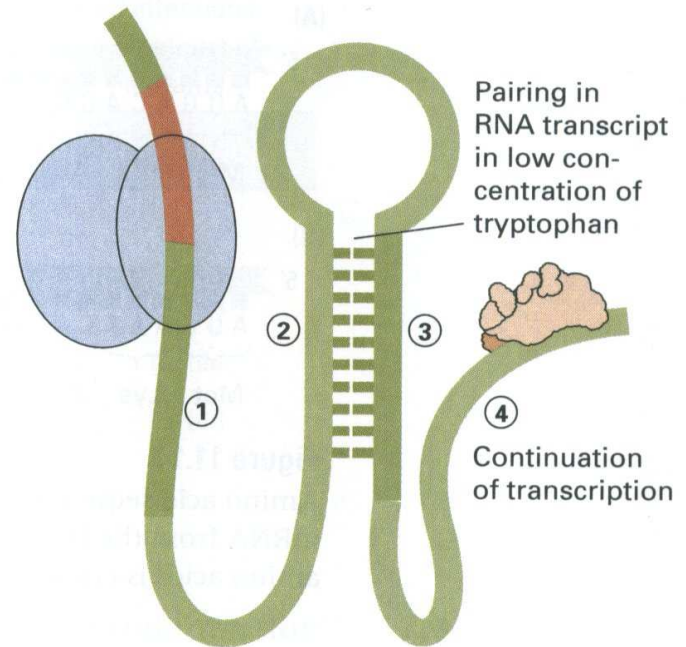
# Attenuation



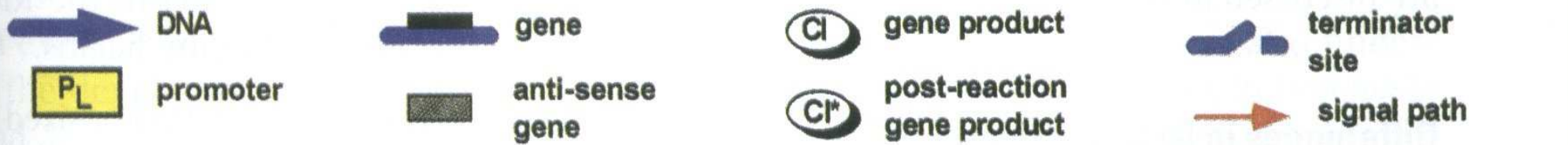
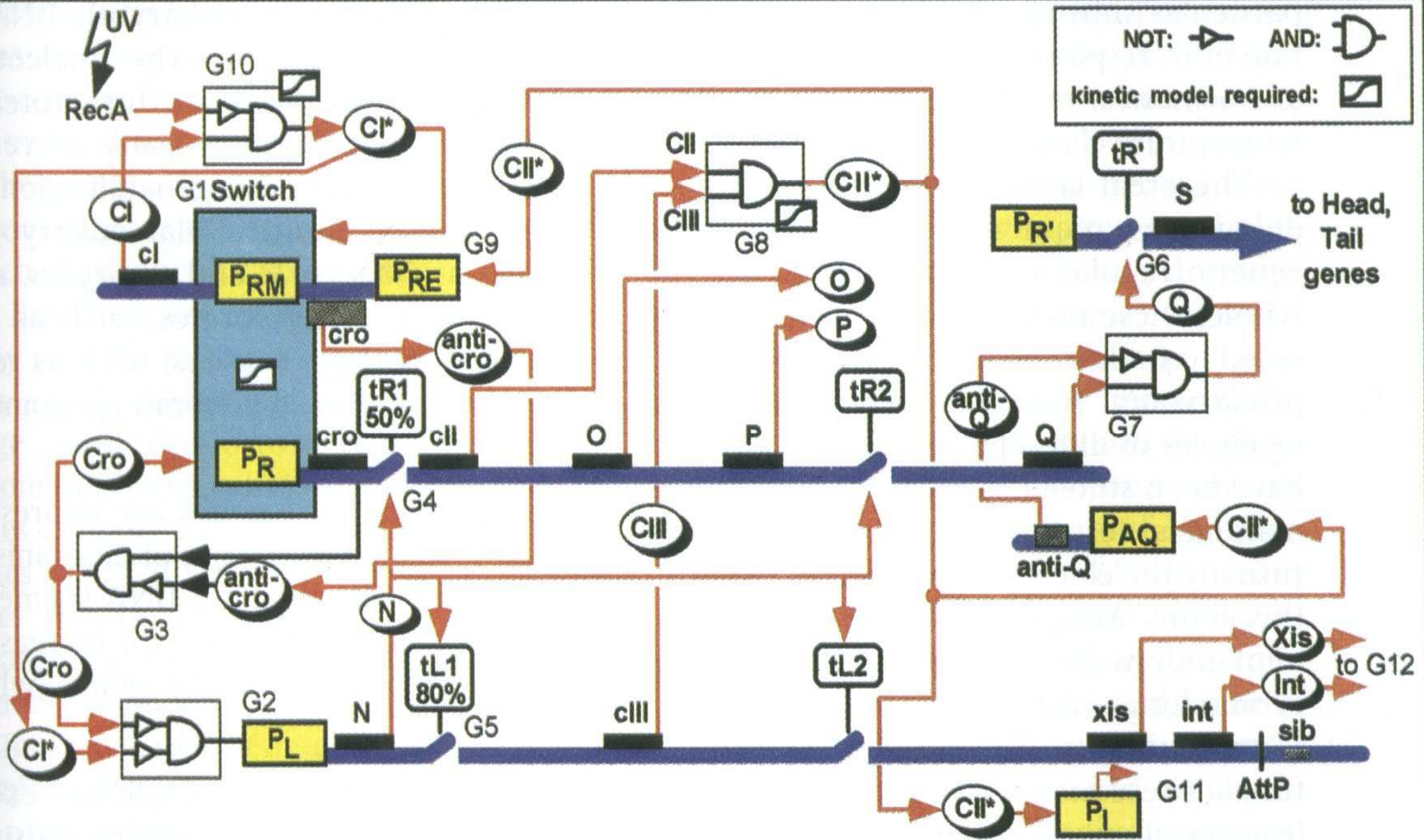
(A) Free mRNA. Base pairs between 1 and 2 and between 3 and 4.

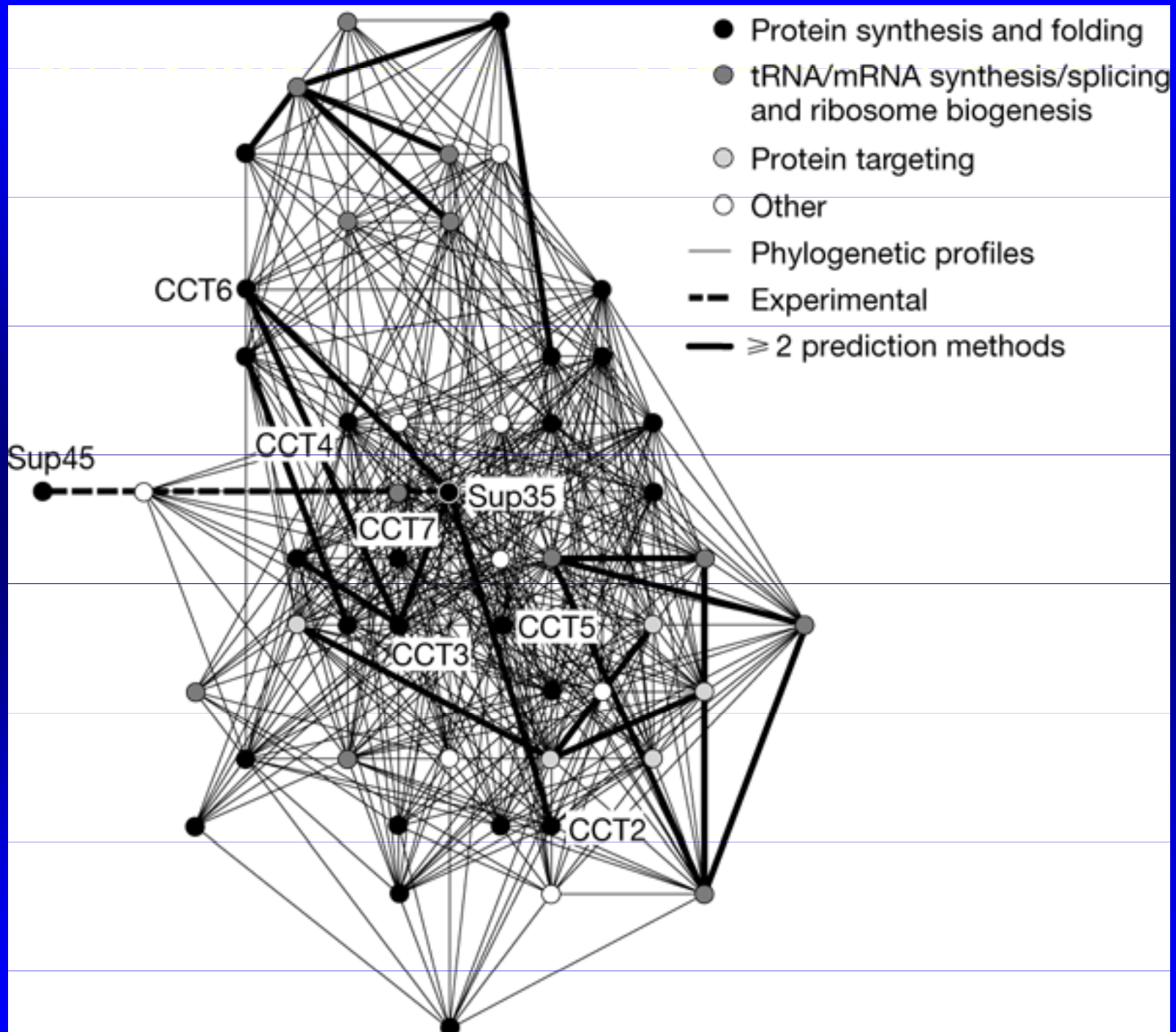


(B) High concentration of tryptophan. Ribosome reaches region 2 and pairing of 3-4 causes termination of transcription.



(C) Low concentration of tryptophan. Ribosome stalled in region 1 at Trp codons permits pairing of 2-3 and transcription is not terminated after region 4.

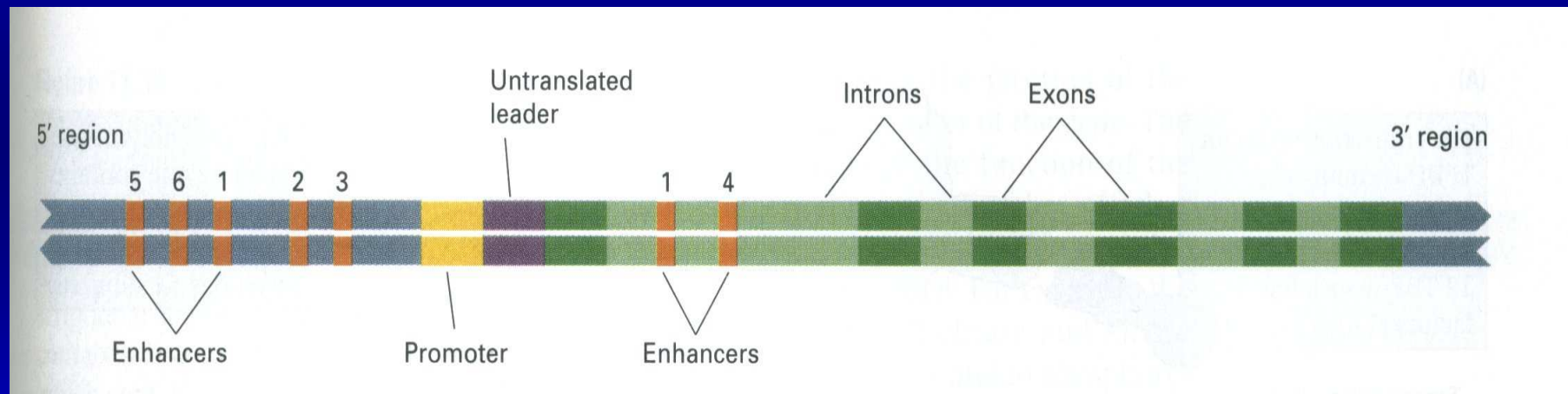




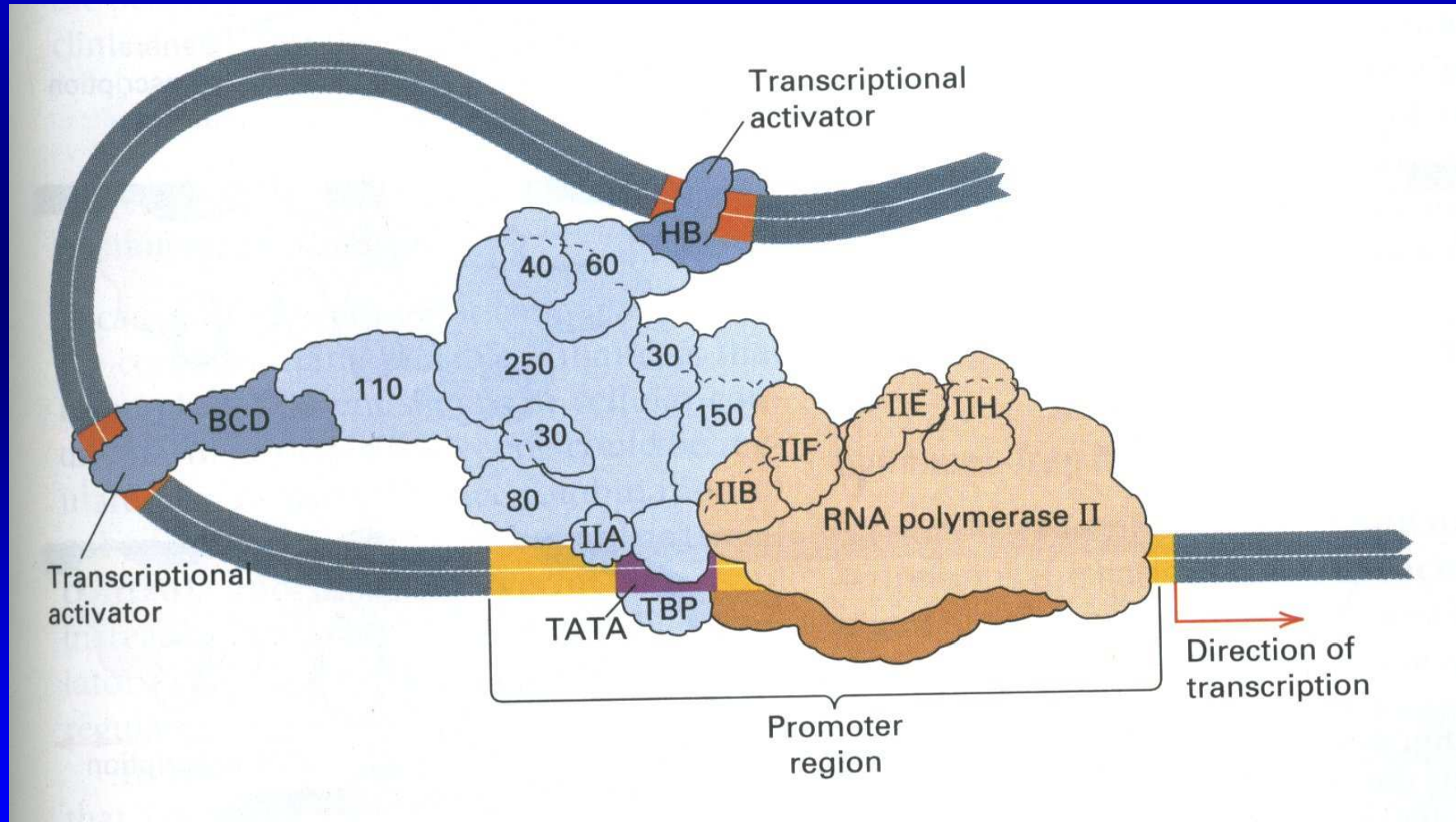
## *Rozdíly mezi prokaryontními a eukaryontními organismy*

- Monocistronická vs. polycistronická mRNA
- DNA BP (histony a jiné proteiny)
- Repetitivní sekvence
- Více než 95% DNA není translatováno
- Přestavby genů (amplifikace genů, Ab, T-cells)
- Exony a introny
- Oddělené jádro (transport mRNA)

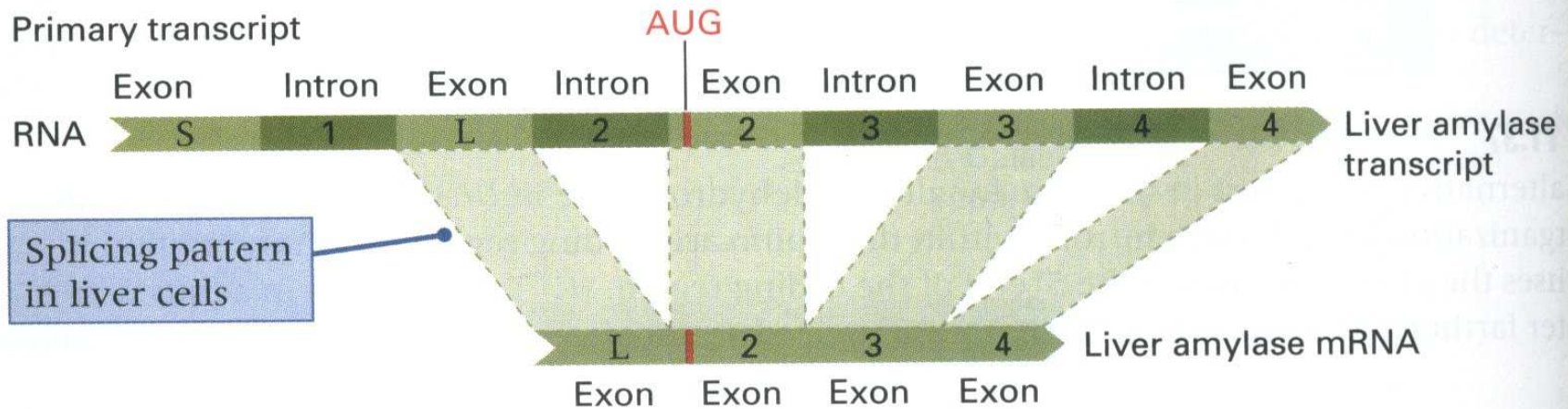
# *Regulace transkripce u eukaryont*



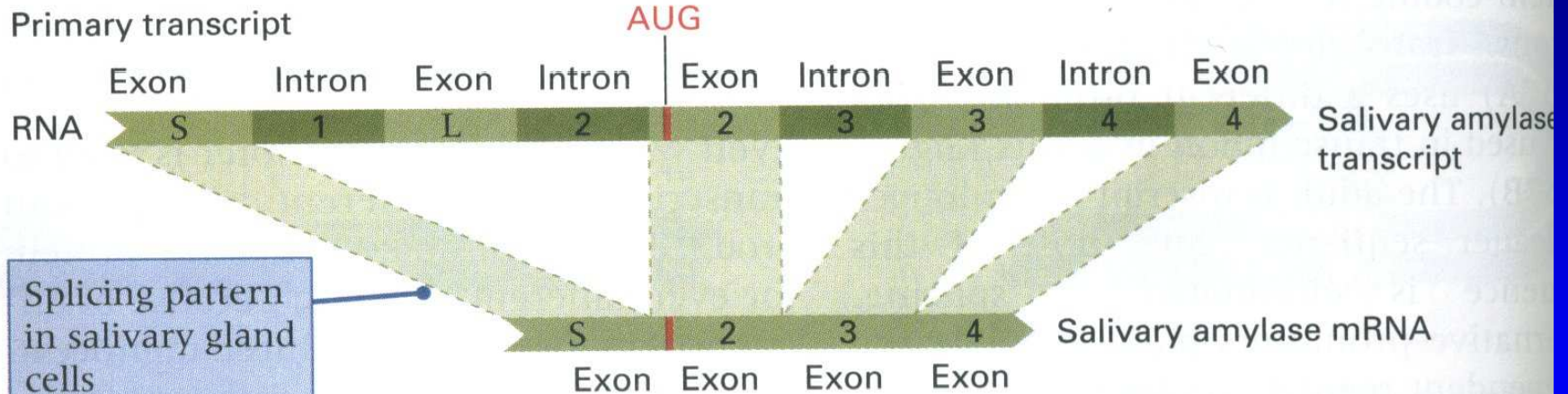
# *Regulace transkripce u eukaryont*



# Regulace transkripce u eukaryont

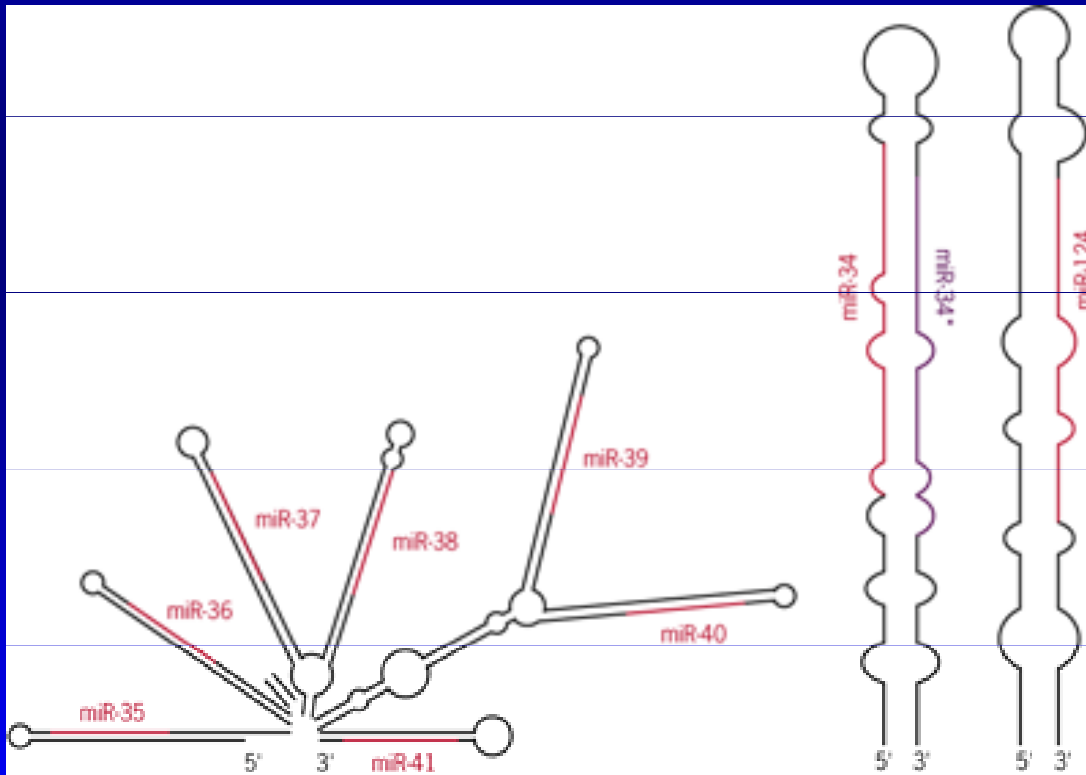


(B)



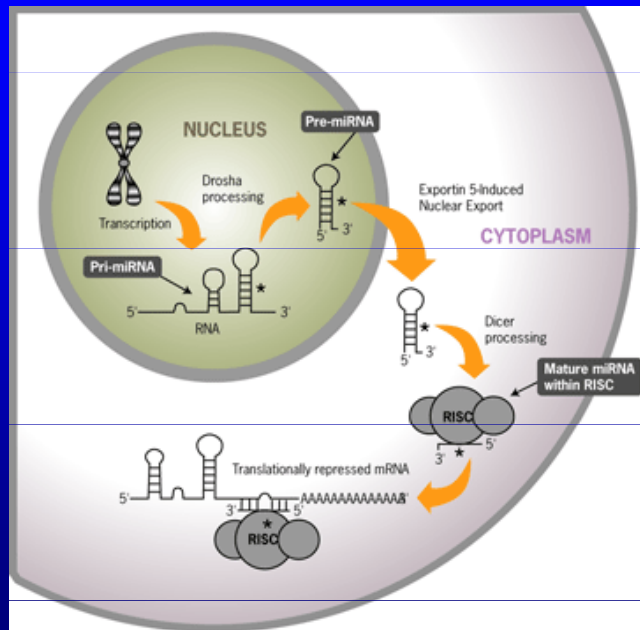


**MicroRNA (miRNAs) jsou krátké molekuly RNA kódované v genomech rostlin a živočichů. Tyto ~21-mery regulují genovou expresi vazbou na 3'-UTR (3'-untranslated regions ) specifické mRNA.**



Transkripce miRNA.

Approximately 60% of miRNAs are expressed independently, 15% of miRNAs are expressed in clusters, and 25% are in introns.



# miRNA processing

## Mechanismy účinku miRNA u rostlin a živočichů

