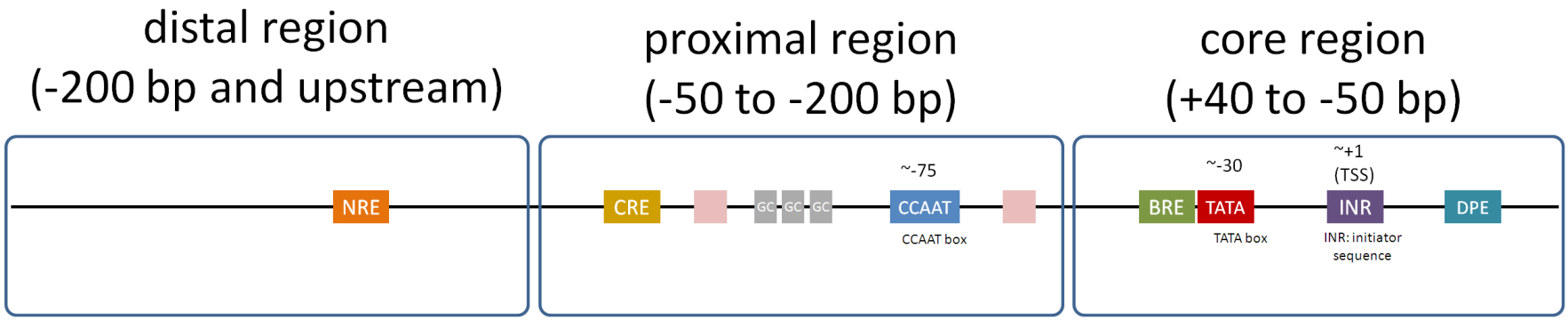
Evkarionti in regulacija izražanja genov

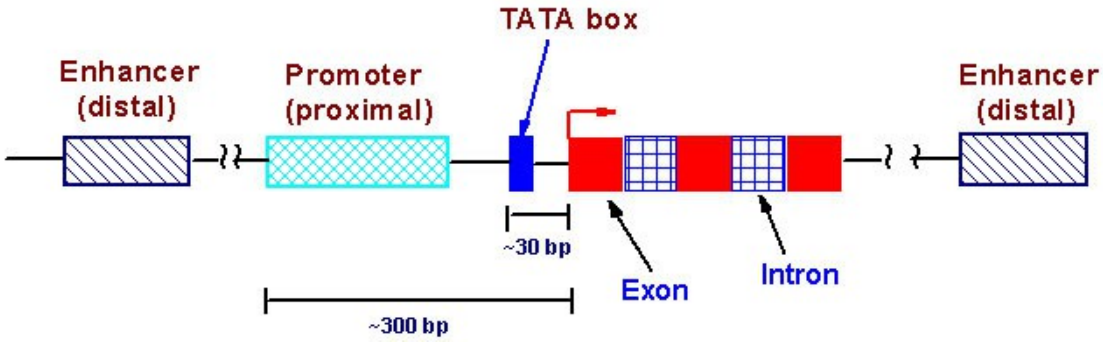
- večji genom, več kromosomov
- razpršenost zapisov za encime iste poti
- različni tipi celic
- celični razdelki
- transkripcija in translacija nista povezani

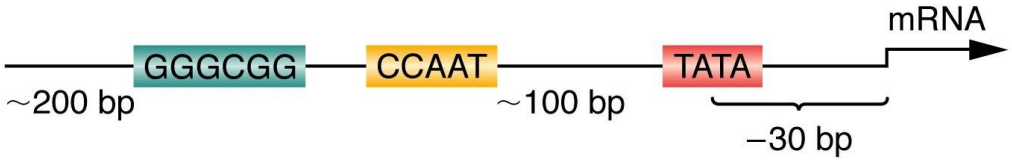


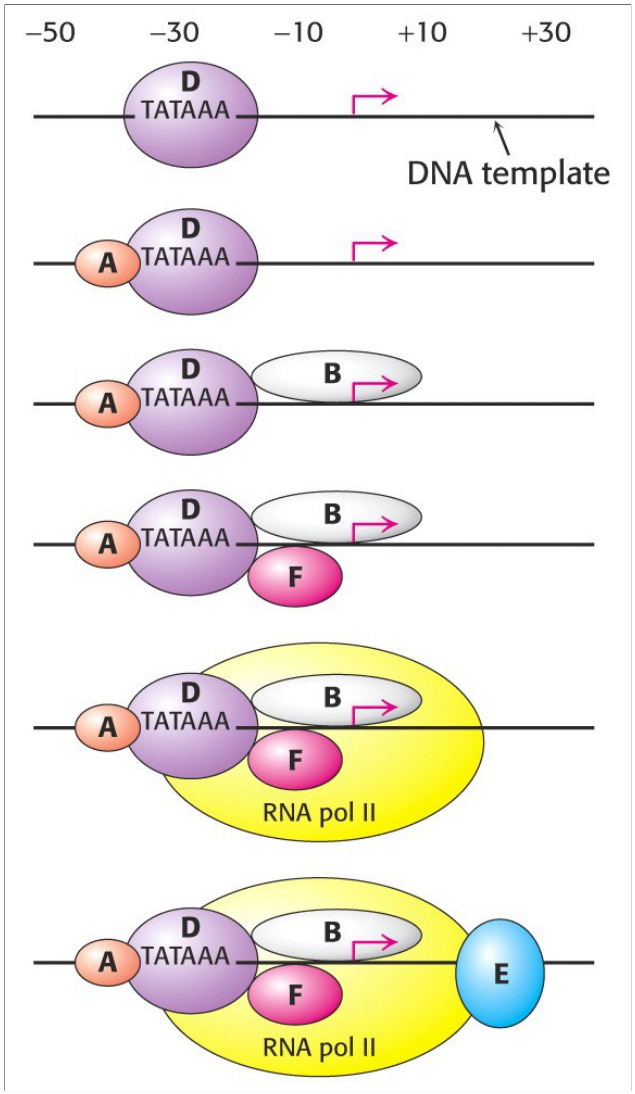
Shematski prikaz promotorja gena za inzulin:

Tipični promotor za RNA-polimerazo II sestavljajo osrednja, bližnja in oddaljena regija

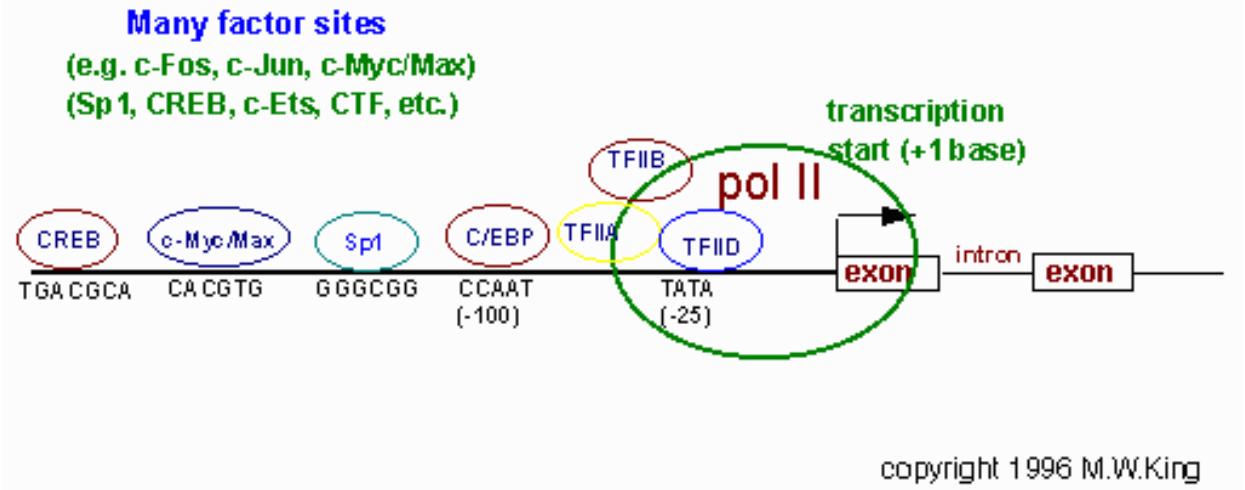
http://genocon.org/assignment-2012/assignment-a/basic-science-a-eukaryotic-promoter/



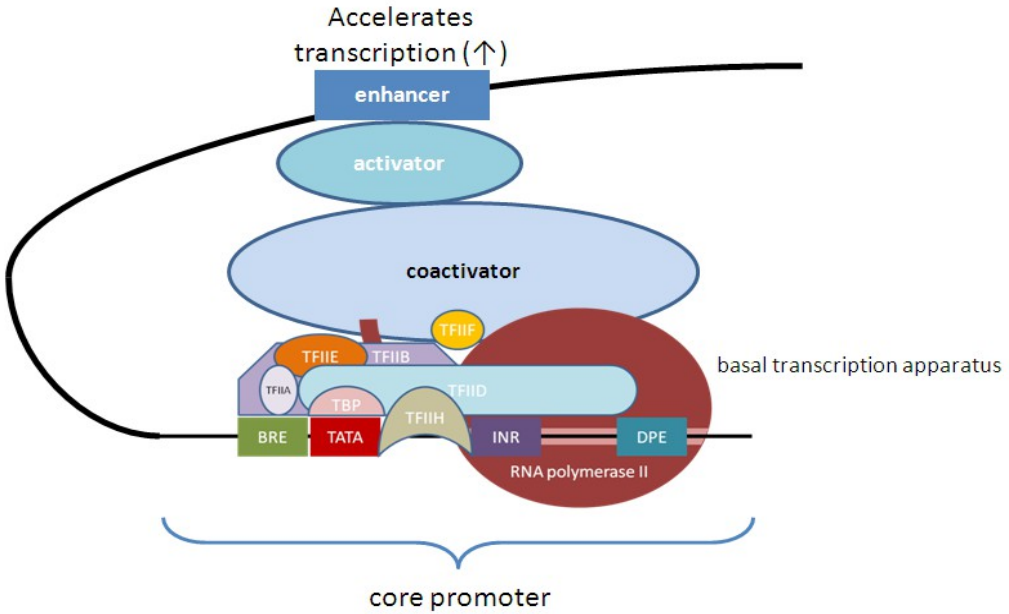


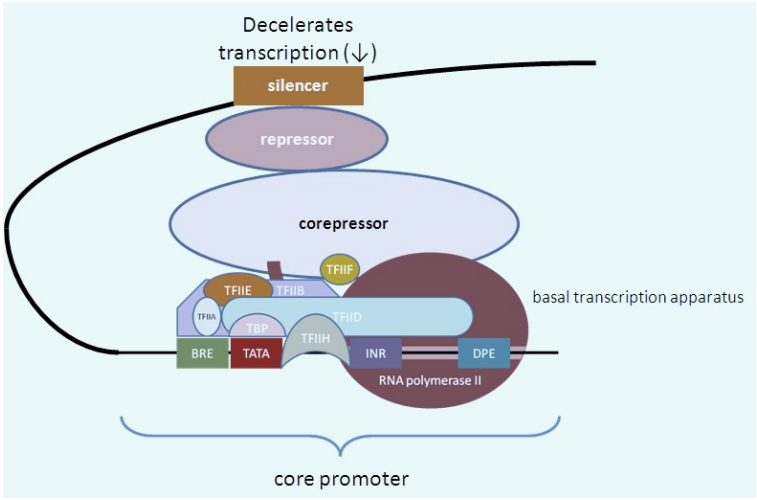


Osrednji promotor predstavljajo vezavna mesta za splošne transkripcijske faktorje



Bližnji promotor predstavljajo vezavna mesta za regulatorne transkripcijske faktorje



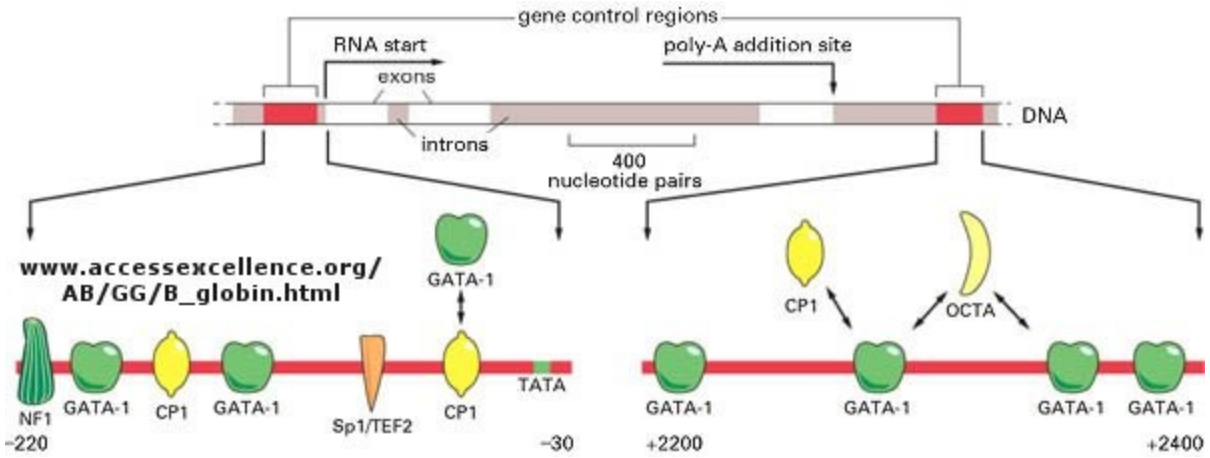


Na oddaljene regije – ojačevalna in utiševalna zaporedja – se vežejo aktivatorji ali represorji.

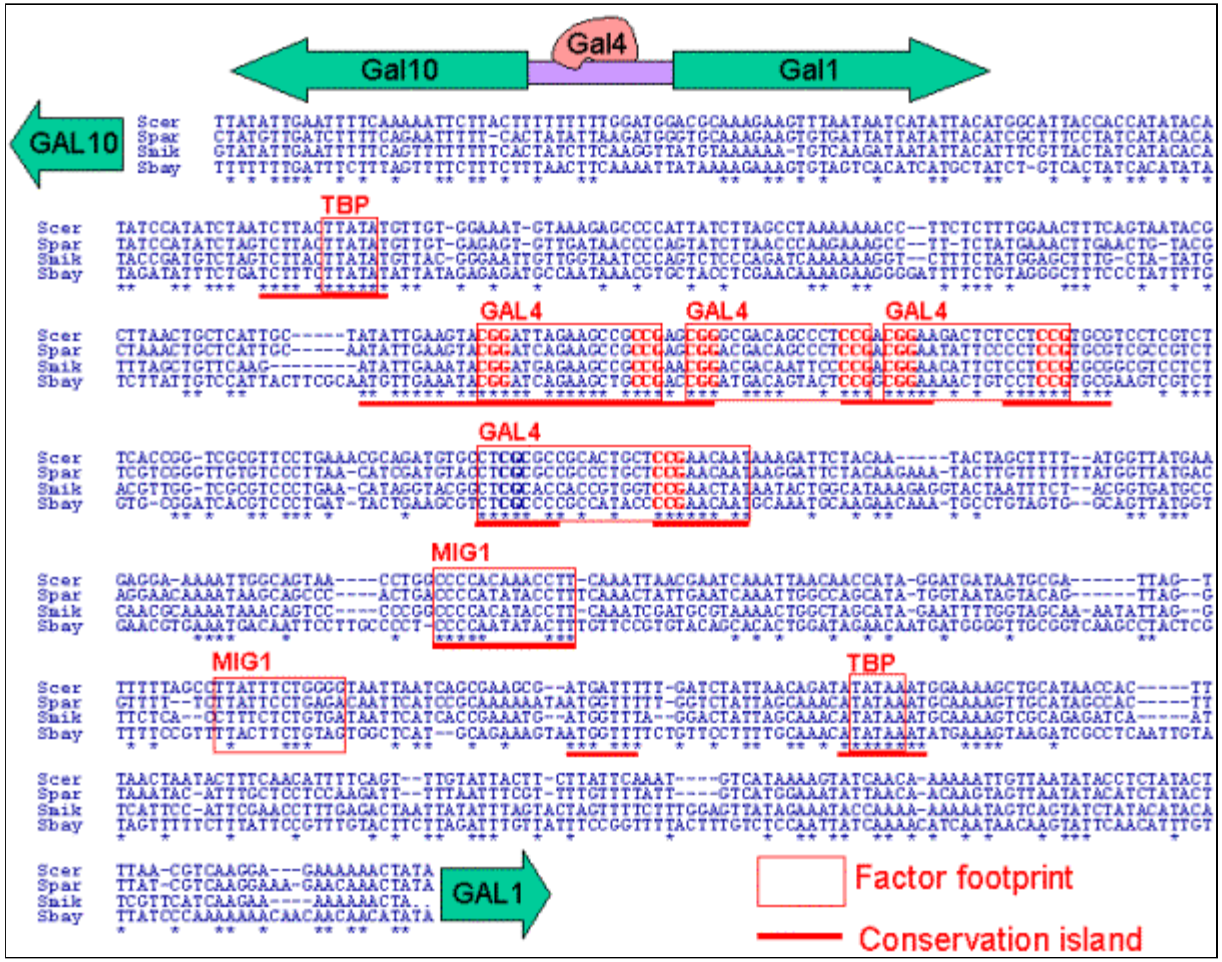
Interakcija z osnovnim transkripcijskim aparatom poteka preko koaktivatorjev oz. korepresorjev.

http://genocon.org/assignment-2012/assignment-a/basic-science-a-eukaryotic-promoter/

Uravnavanje izražanja gena za globin

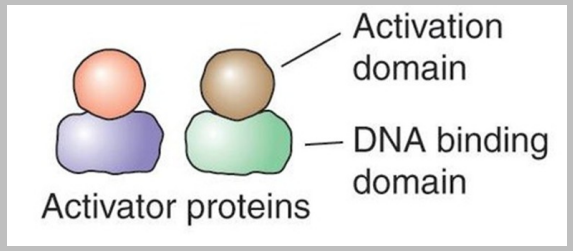


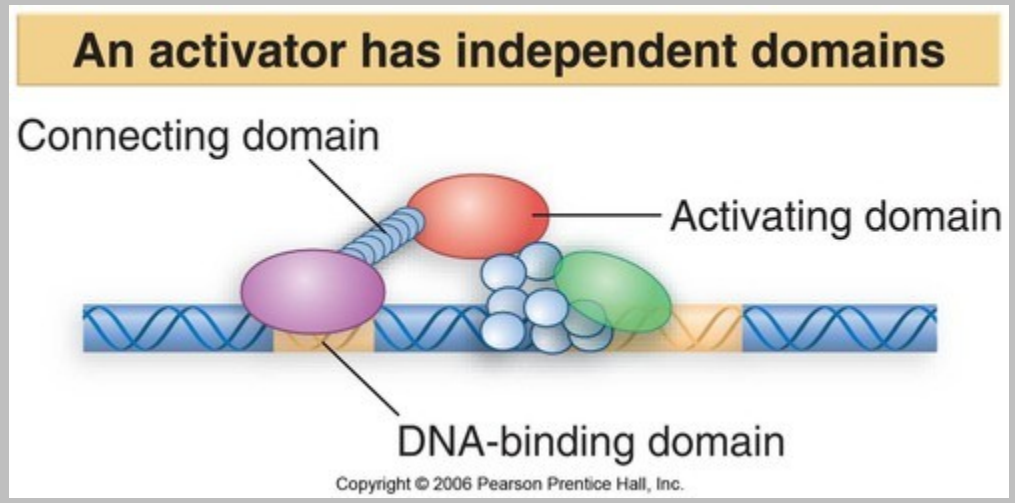
GATA-1: eritroidni transkr. faktor se veže na škatlo GATA
Sp1: specifičnostni protein 1 se veže na škatlo GC
NF1: jedrni faktor 1 se veže na CCAAT
CP1: centromer-vezavni protein 1 se veže na CCAAT

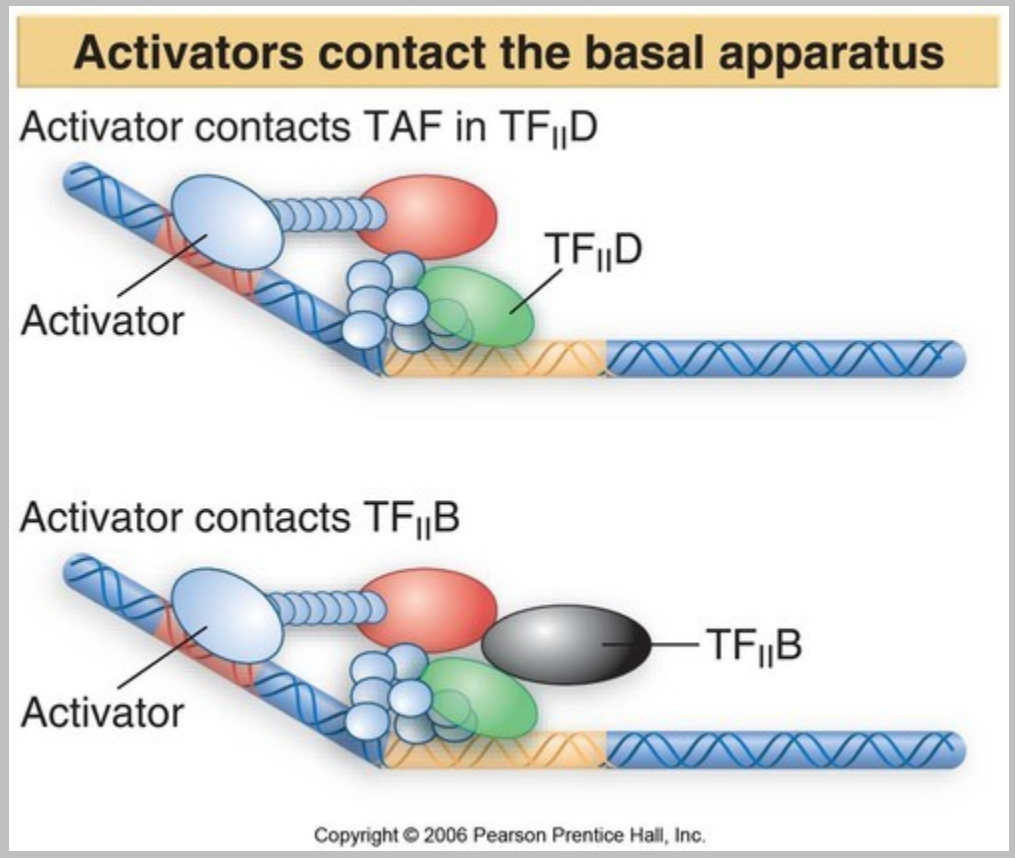


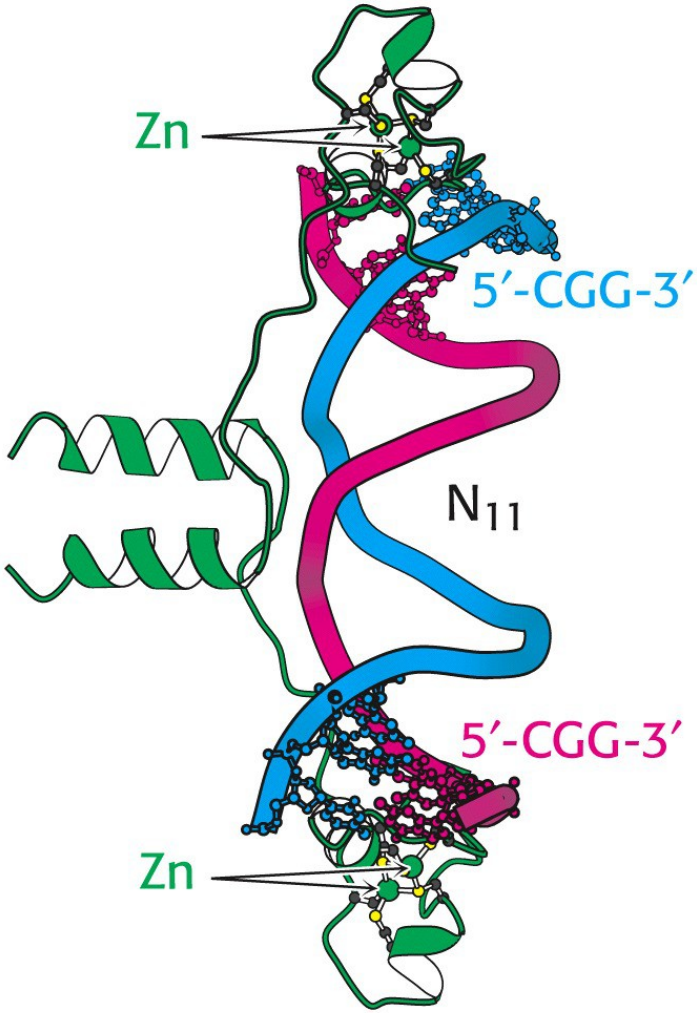
http://web.mit.edu/manoli/www/thesis/Chapter3.html

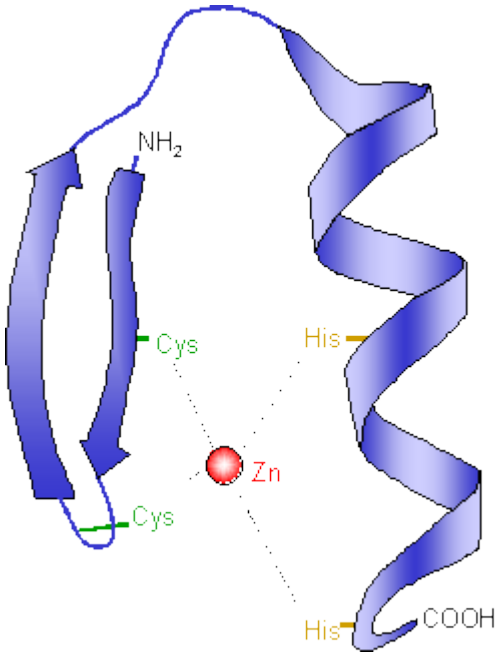
Nukleotidna zaporedja intergenske regije gal10 – gal1 z vezavnimi mesti za regulator Gal4. Zgornja aktivatorska zaporedja pri kvasovkah označujemo z UAS.


Activation domain
DNA binding domain
Activator proteins

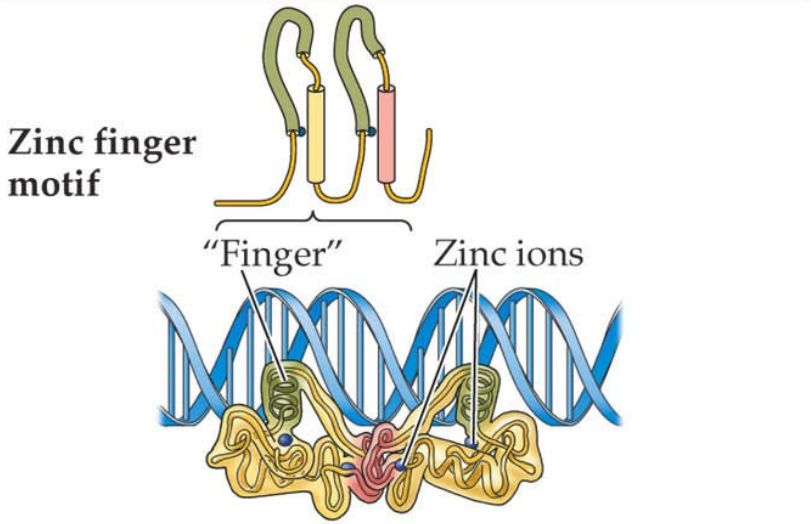

An activator has independent domains
Connecting domain
Activating domain
DNA-binding domain
Copyright © 2006 Pearson Prentice Hall, Inc.


Activators contact the basal apparatus
Activator contacts TAF in TFIID
TFIID
Activator
Activator contacts TFIIB
TFIIB
Activator
Copyright © 2006 Pearson Prentice Hall, Inc.

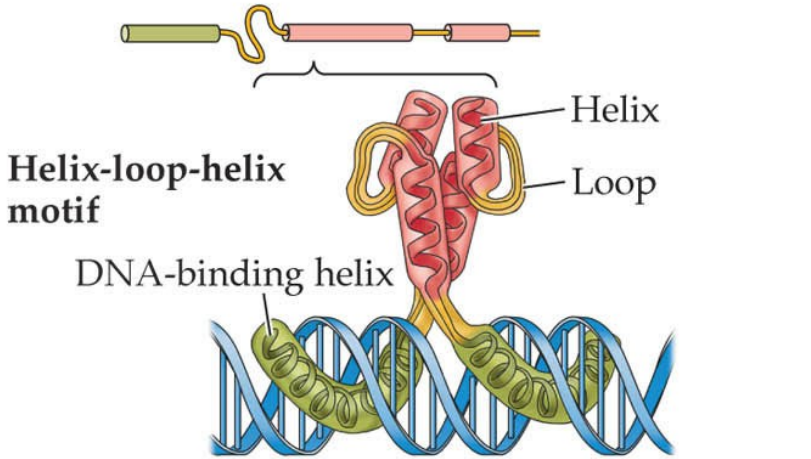




GAL4 („transkripcijski faktor“ pri kvasovkah): veže se na CGG N11 CCG

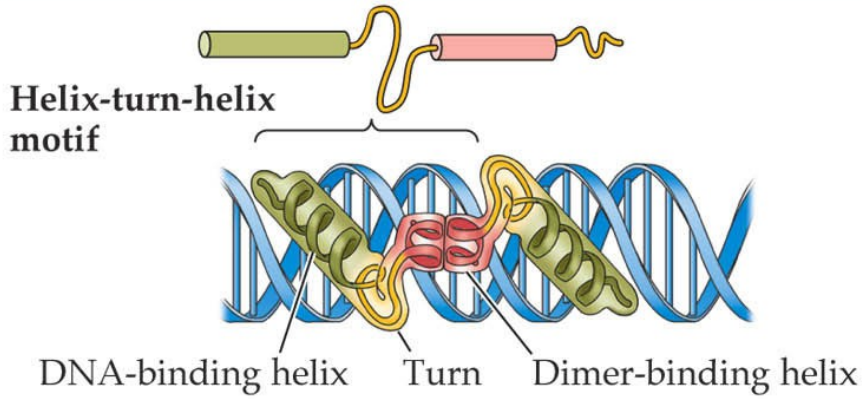


These proteins are steroid hormone receptors.

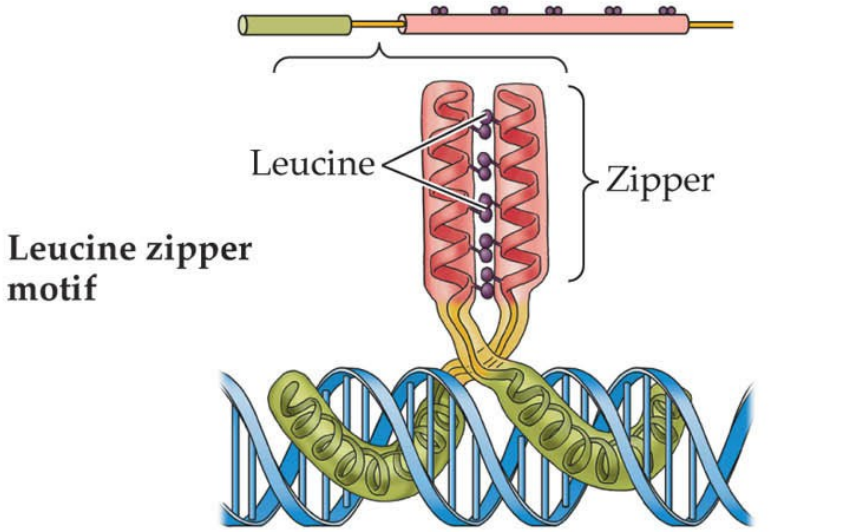


These proteins regulate immune system genes.

LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, **Figure 14.15 Protein-DNA Interactions (Part 2)**

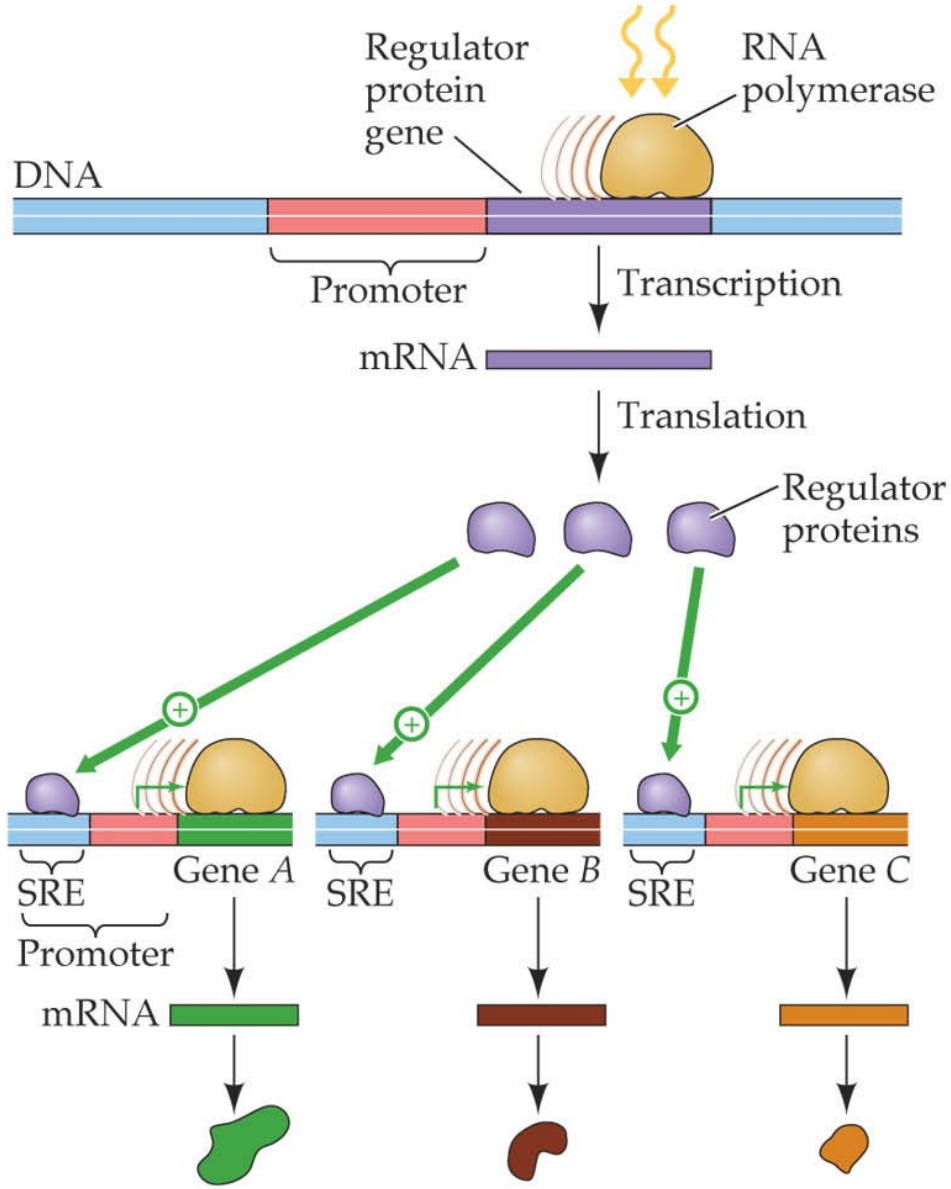


These proteins regulate genes involved in development.

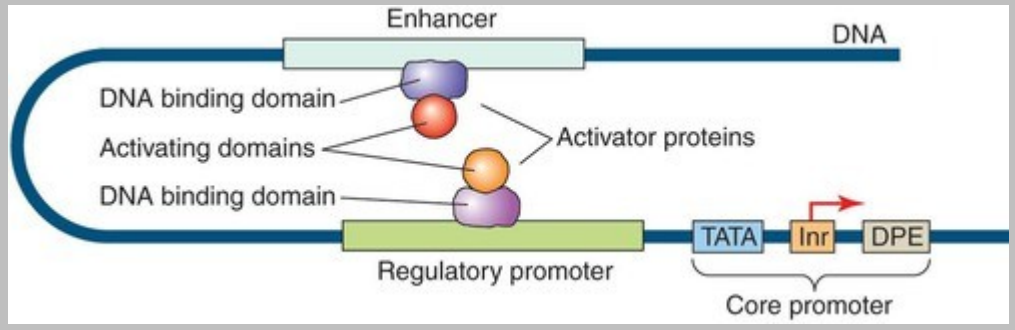


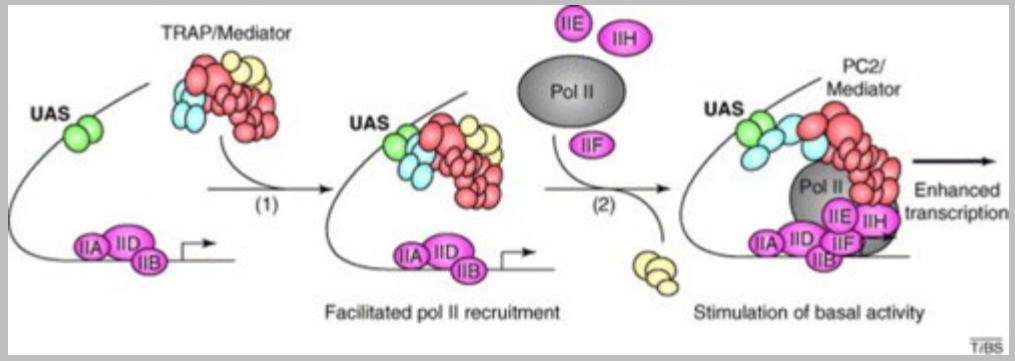
These proteins regulate cell division genes.

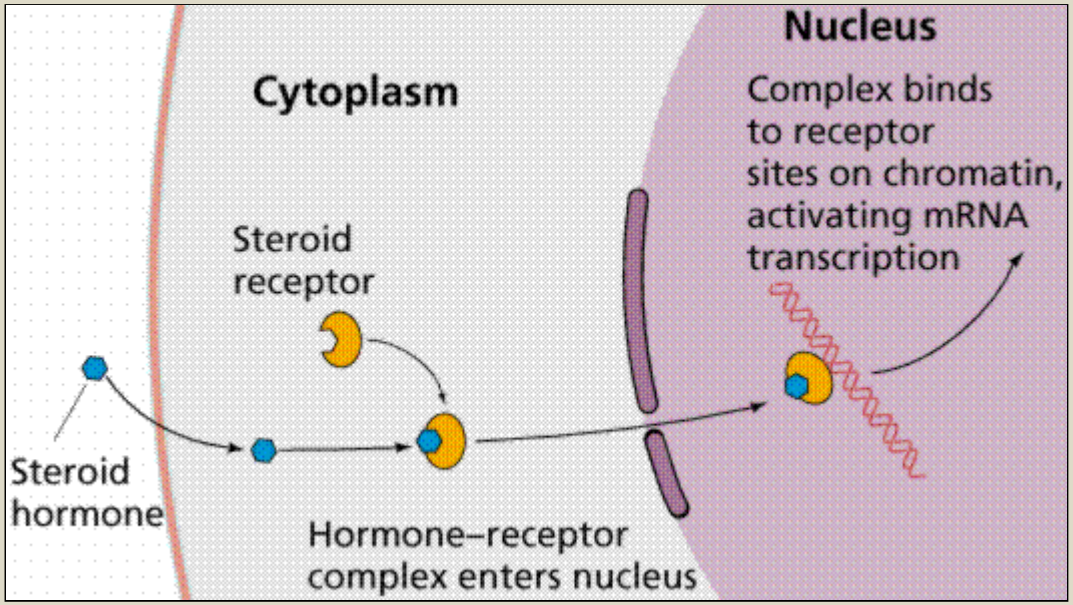
LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 14.15 Protein-DNA Interactions (Part 1)

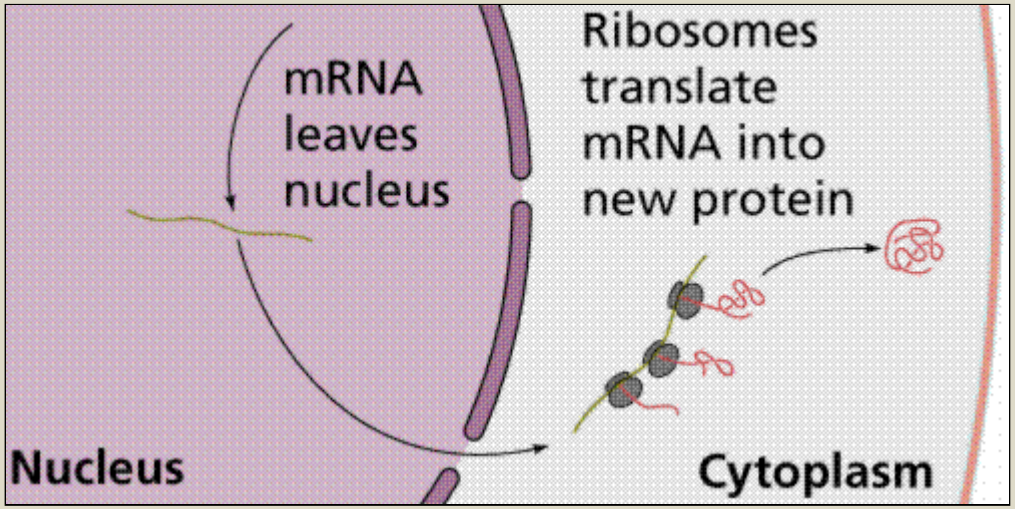


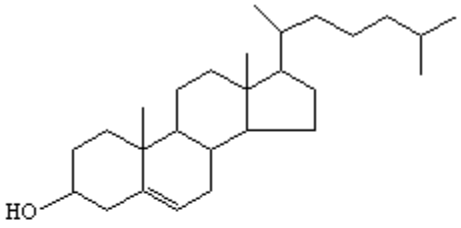
LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, **Figure 14.14 Coordinating Gene Expression**


Enhancer
DNA
DNA binding domain
Activating domains
DNA binding domain
Activator proteins
TATA
Inr
DPE
Regulatory promoter
Core promoter

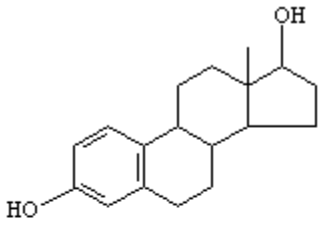

TRAP/Mediator
UAS
IIA
IID
IIB
(1)
IIE
IIH
Pol II
IIF
(2)
PC2/
Mediator
Enhanced
transcription
Facilitated pol II recruitment
Stimulation of basal activity
TiBS


Nucleus
Cytoplasm
Complex binds to receptor sites on chromatin, activating mRNA transcription
Steroid receptor
Steroid hormone
Hormone–receptor complex enters nucleus

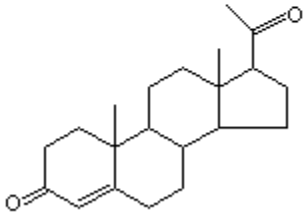

mRNA leaves nucleus
Ribosomes translate mRNA into new protein
Nucleus
Cytoplasm



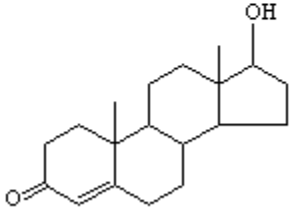
Cholesterol (34)



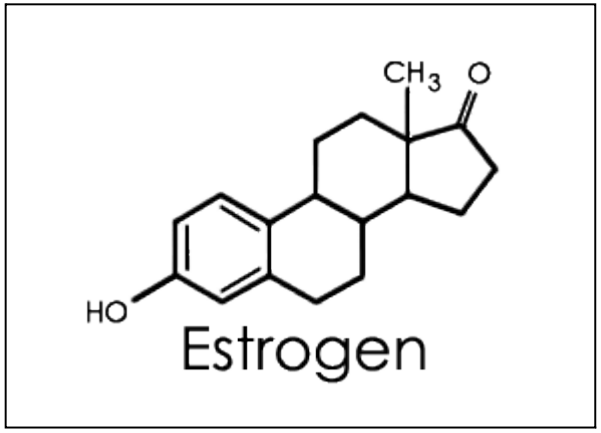
Oestrogen (35)

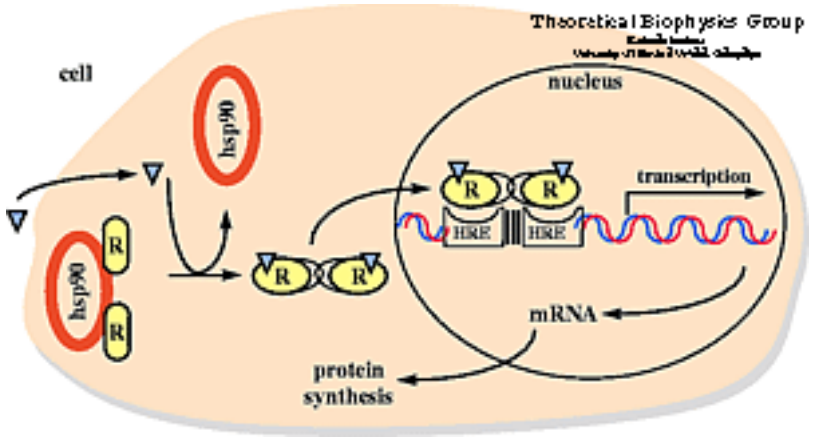


Progesterone (36)

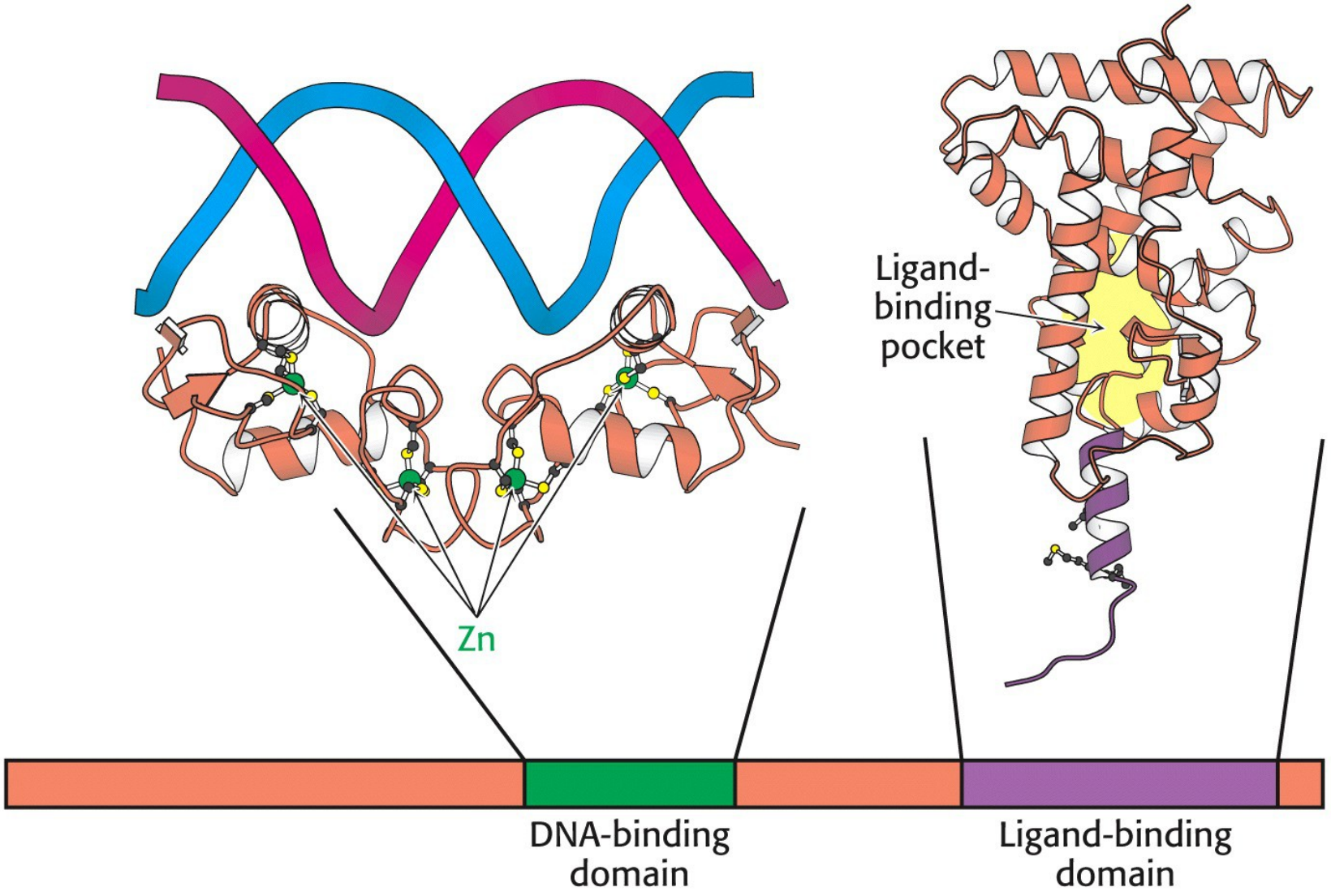


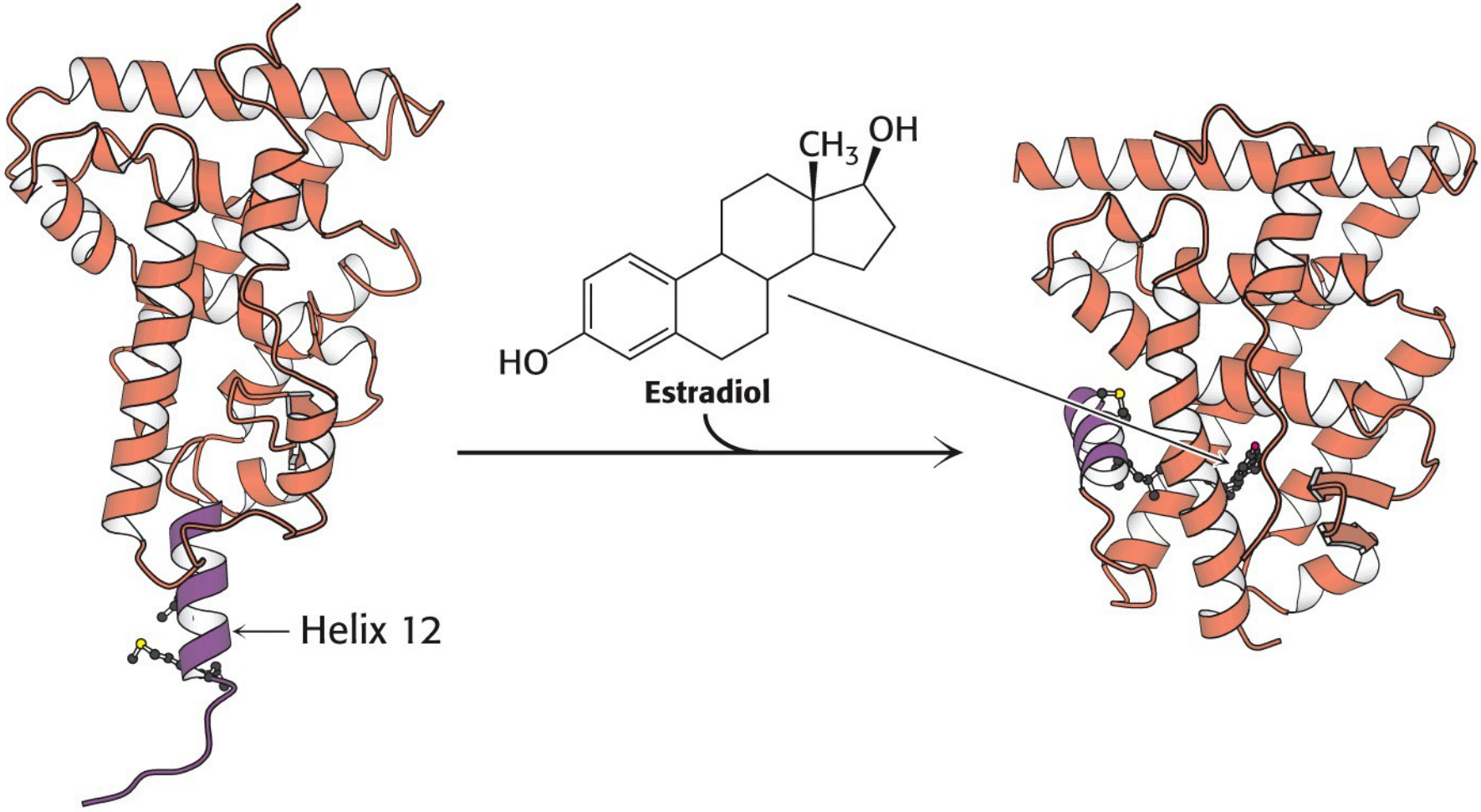
Testosterone (37)

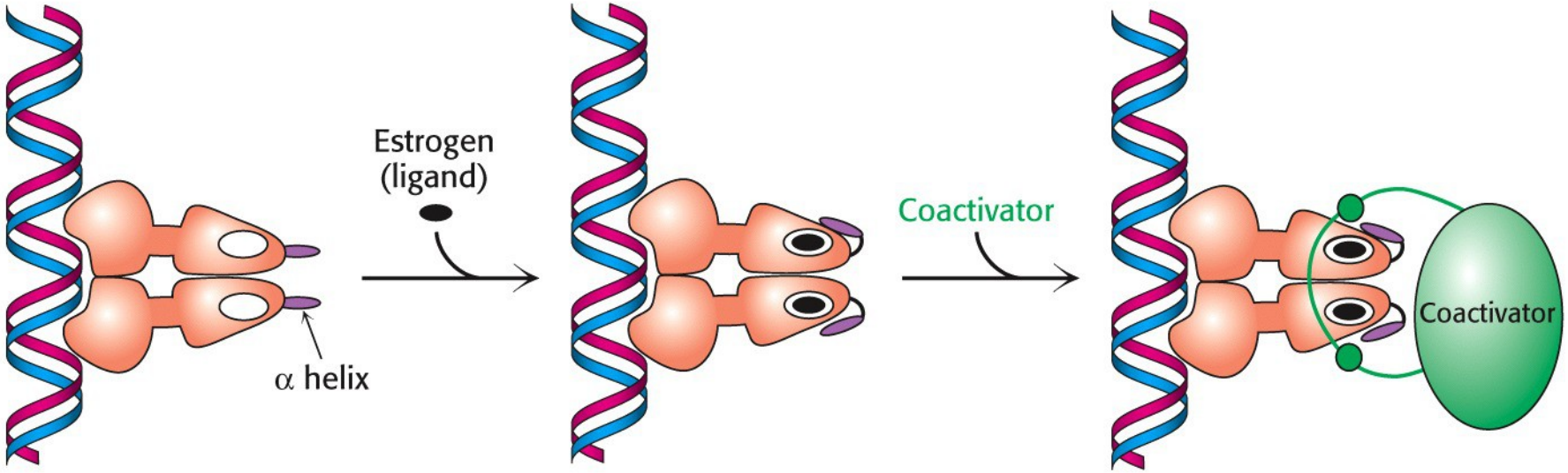


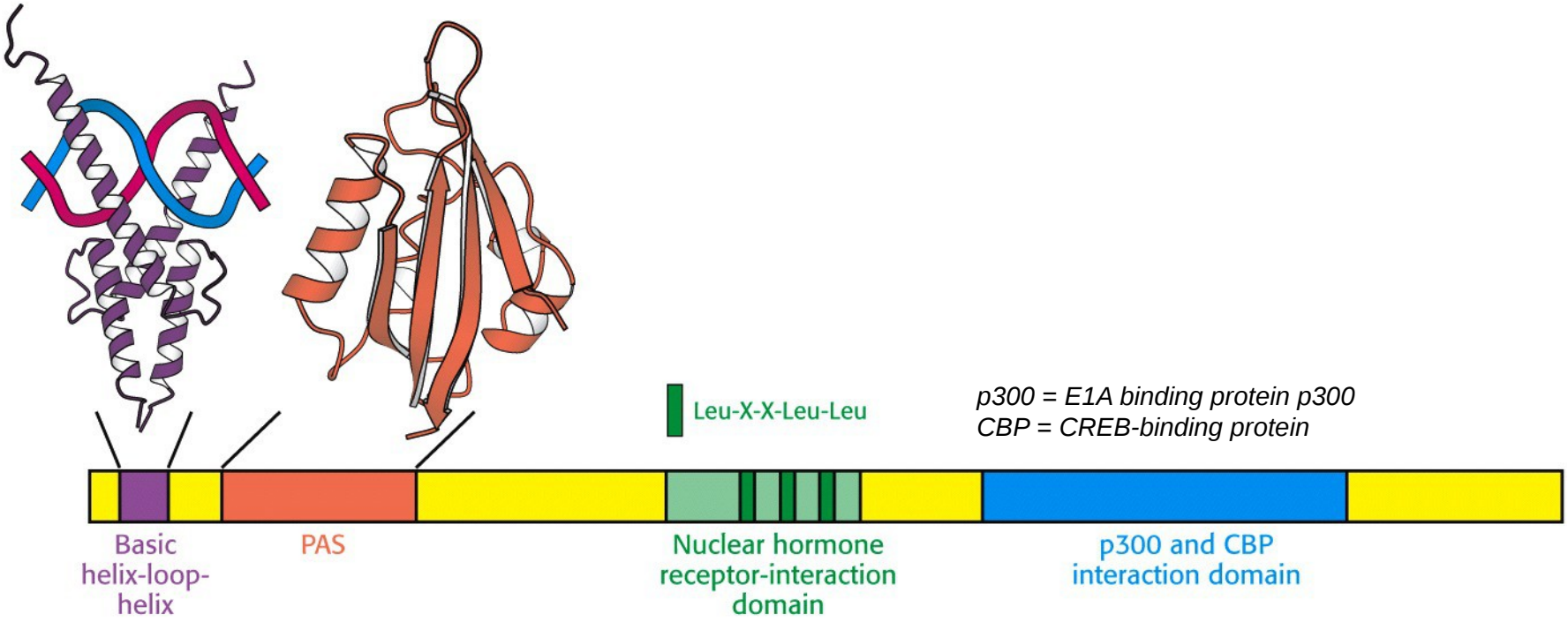


steroidni hormoni

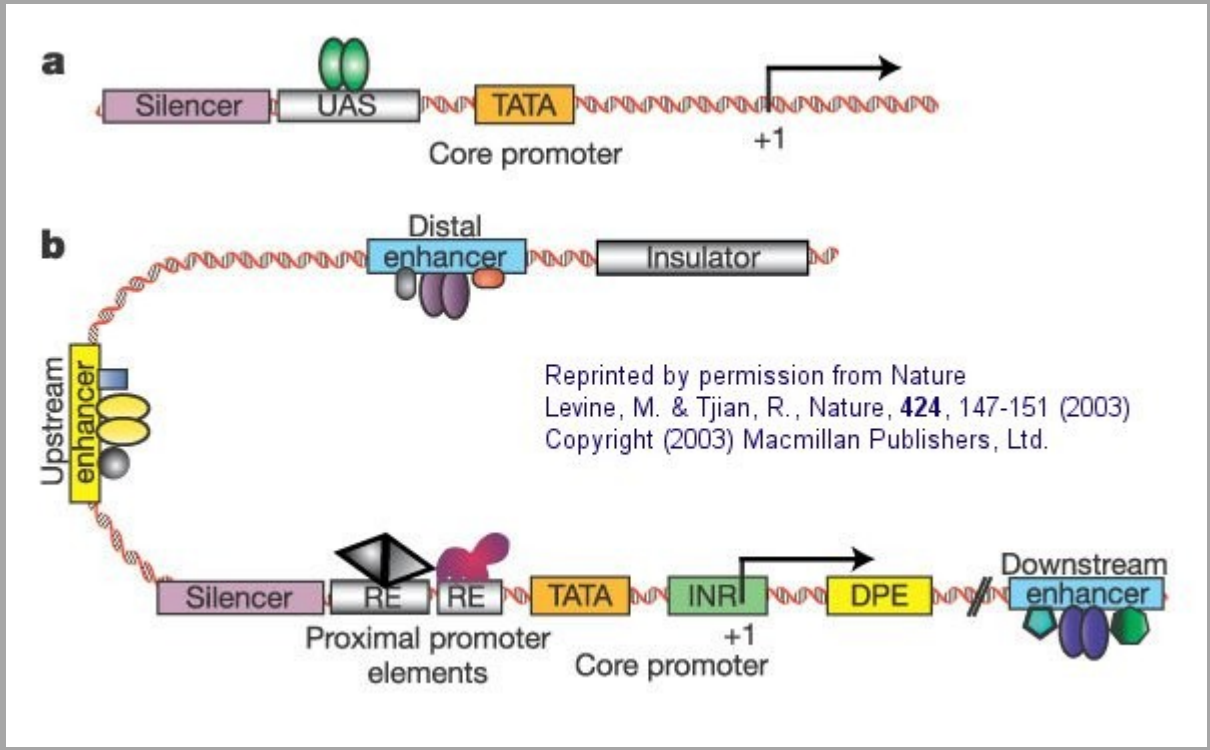

Zn
Ligand-
binding
pocket
DNA-binding
domain
Ligand-binding
domain


Helix 12
CH3
OH
HO
Estradiol

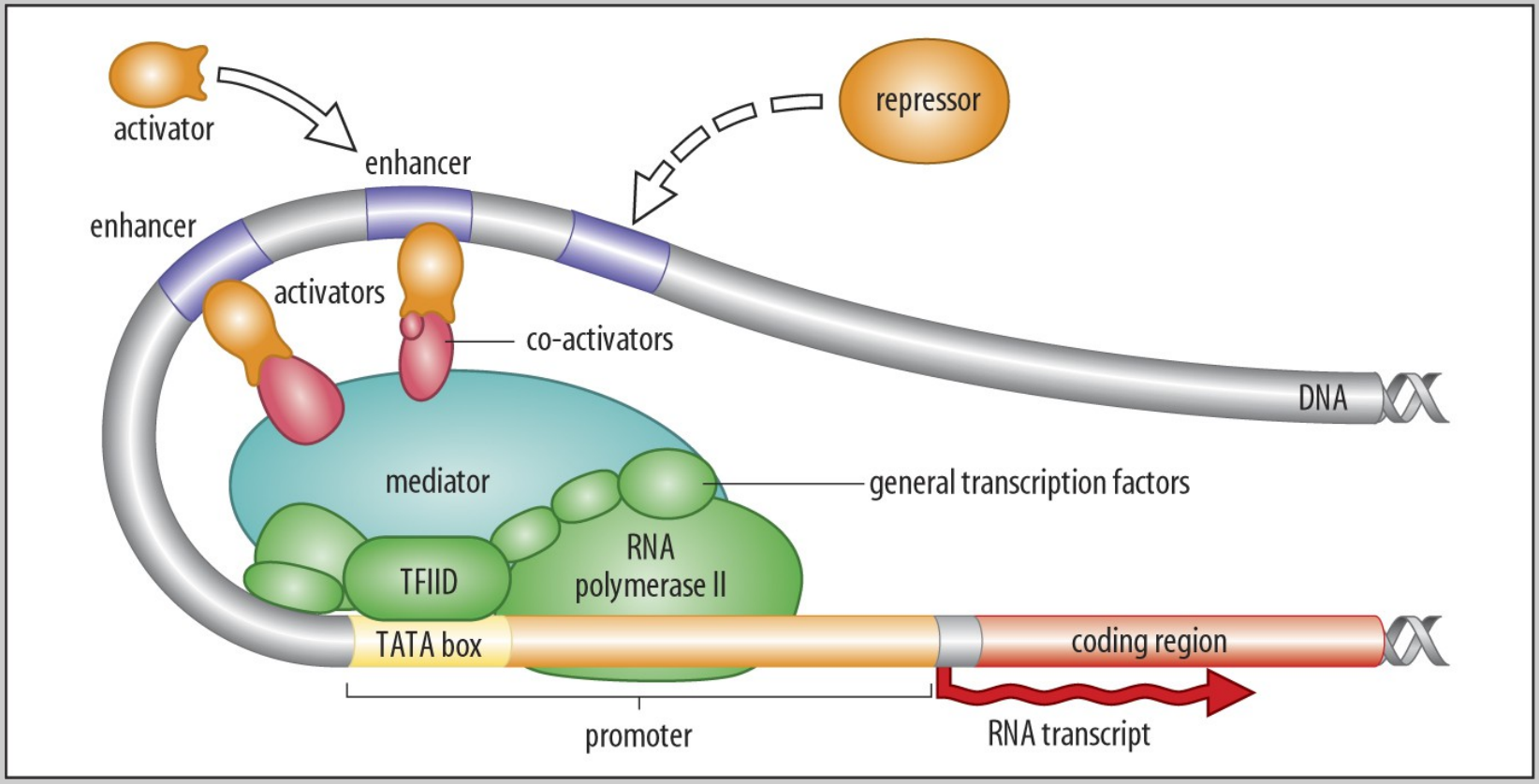

Estrogen
(ligand)
α helix
Coactivator
Coactivator

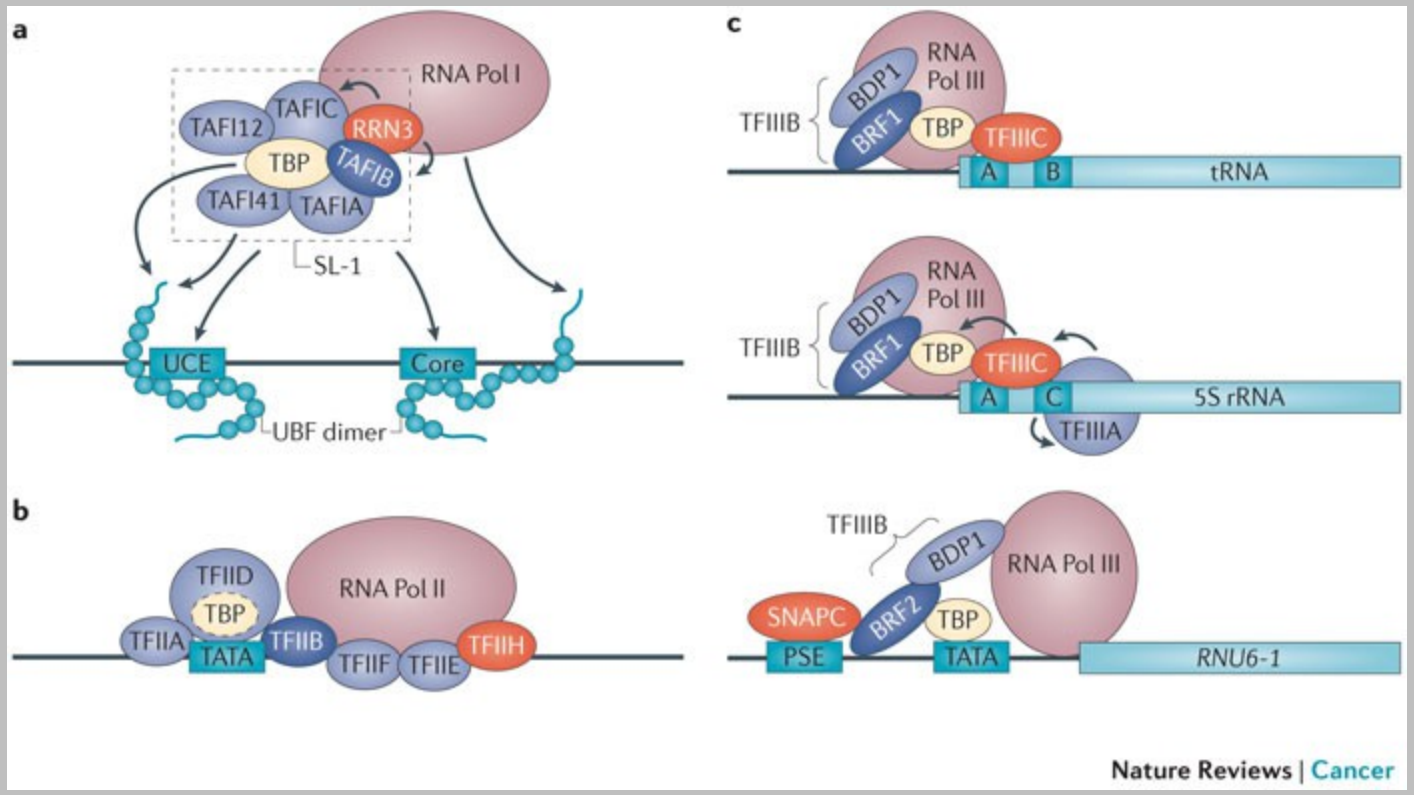


Zgradba koaktivatorjev iz družine p160



Primera preproste (a) in kompleksne transkripcijske enote (b)

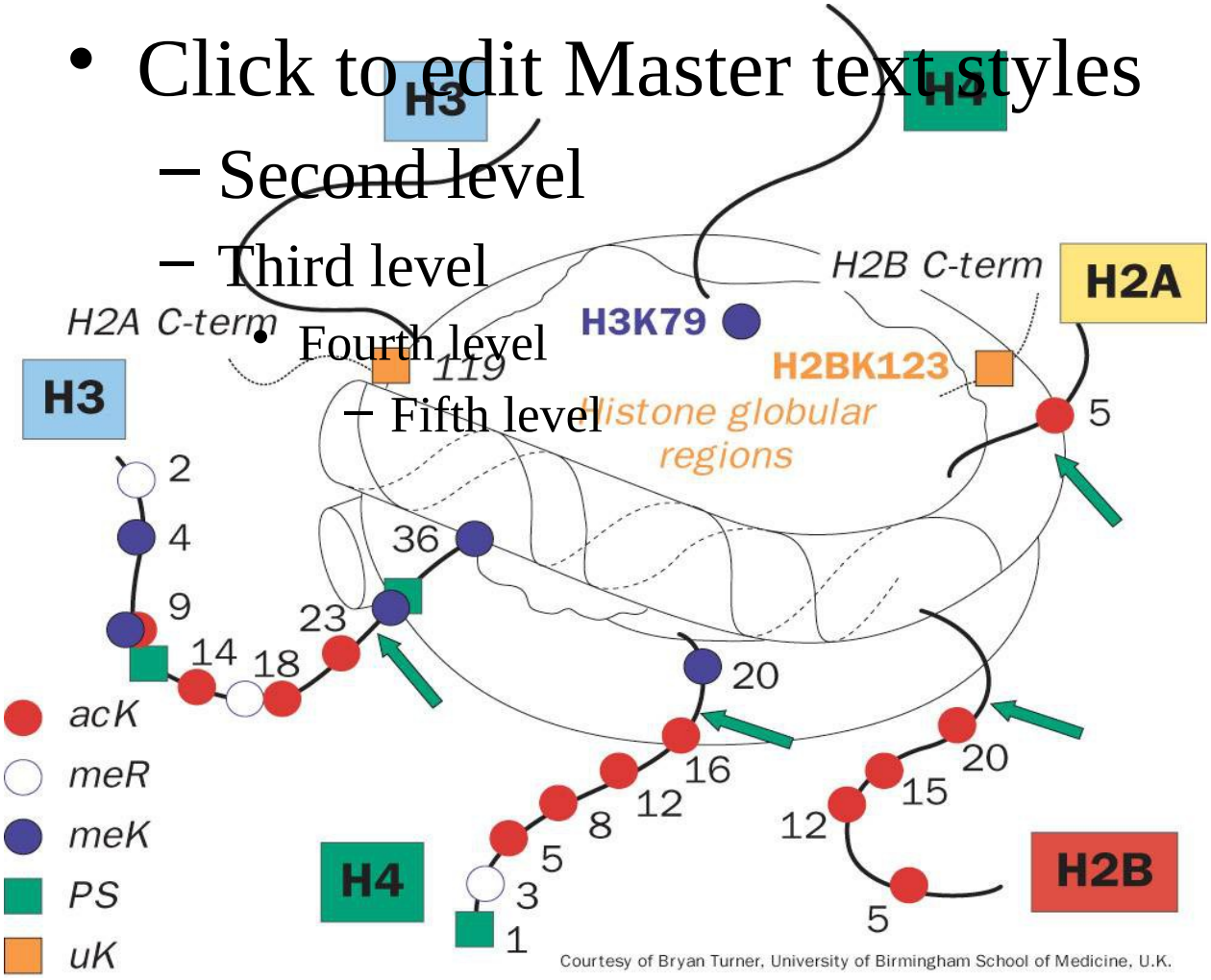

activator
repressor
enhancer
enhancer
activators
co-activators
DNA
mediator
general transcription factors
RNA
polymerase II
TFIID
TATA box
coding region
promoter
RNA transcript



NRC 13, 299-314 (2013)

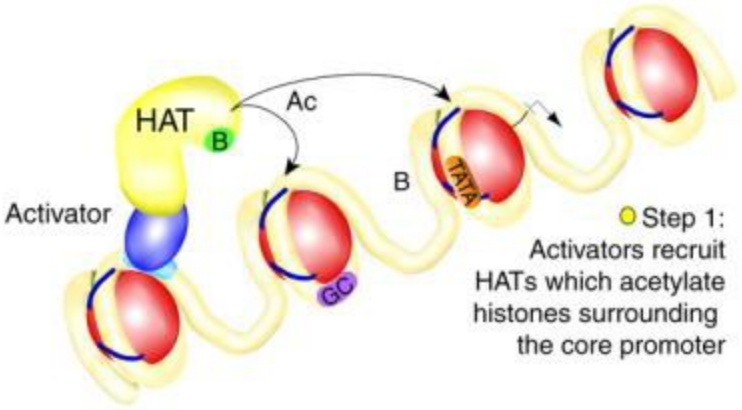
Modifikacije osrednjih histonov

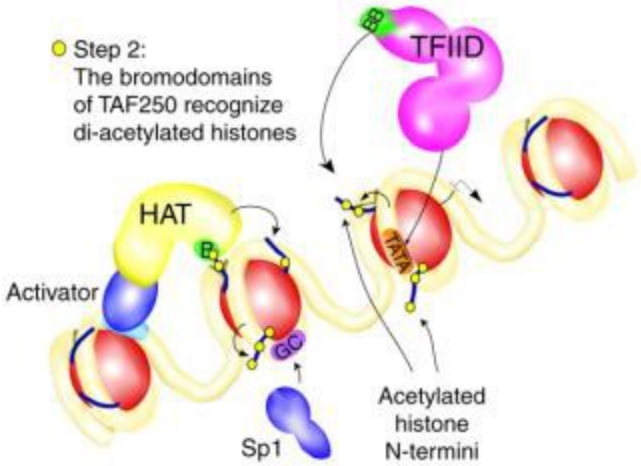
- Click to edit Master text styles
  - Second level
  - Third level
    - Fourth level
      - Fifth level

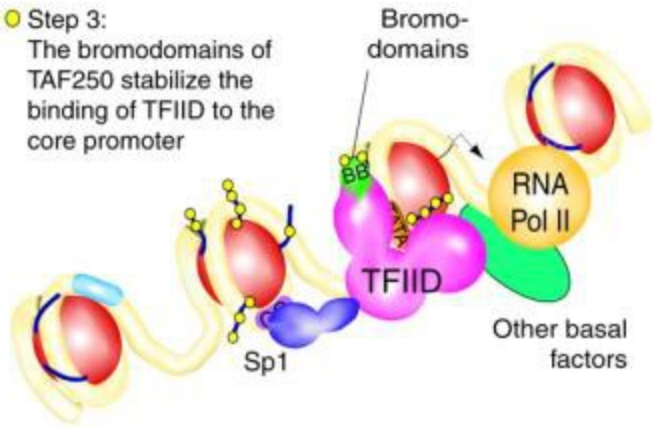


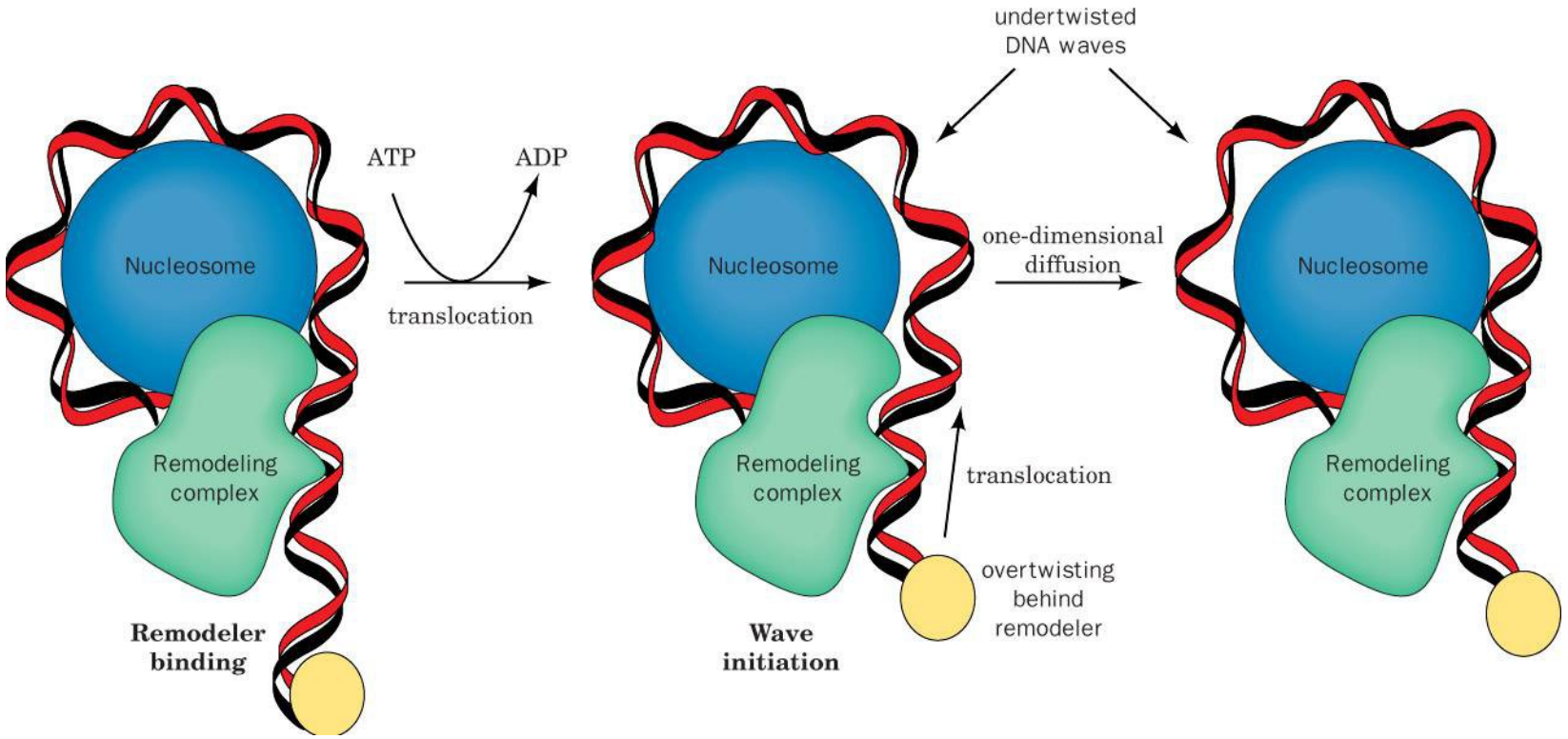
A model for the role of histone acetylation in the stabilization of TFIID to the core promoter

Näär, A.M., Lemon,B.D.and R.Tjian
Transcriptional Coactivator Complexes
Annu. Rev. Biochem. 2001. 70:475-501.



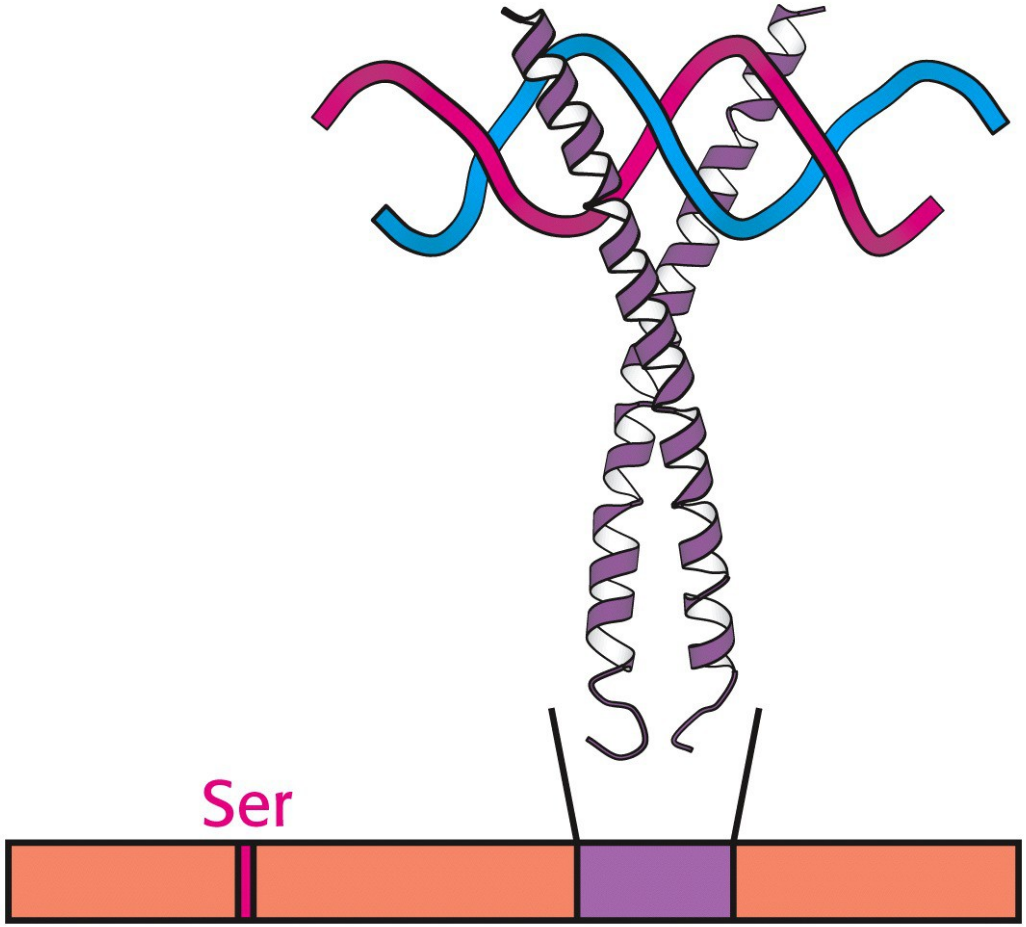


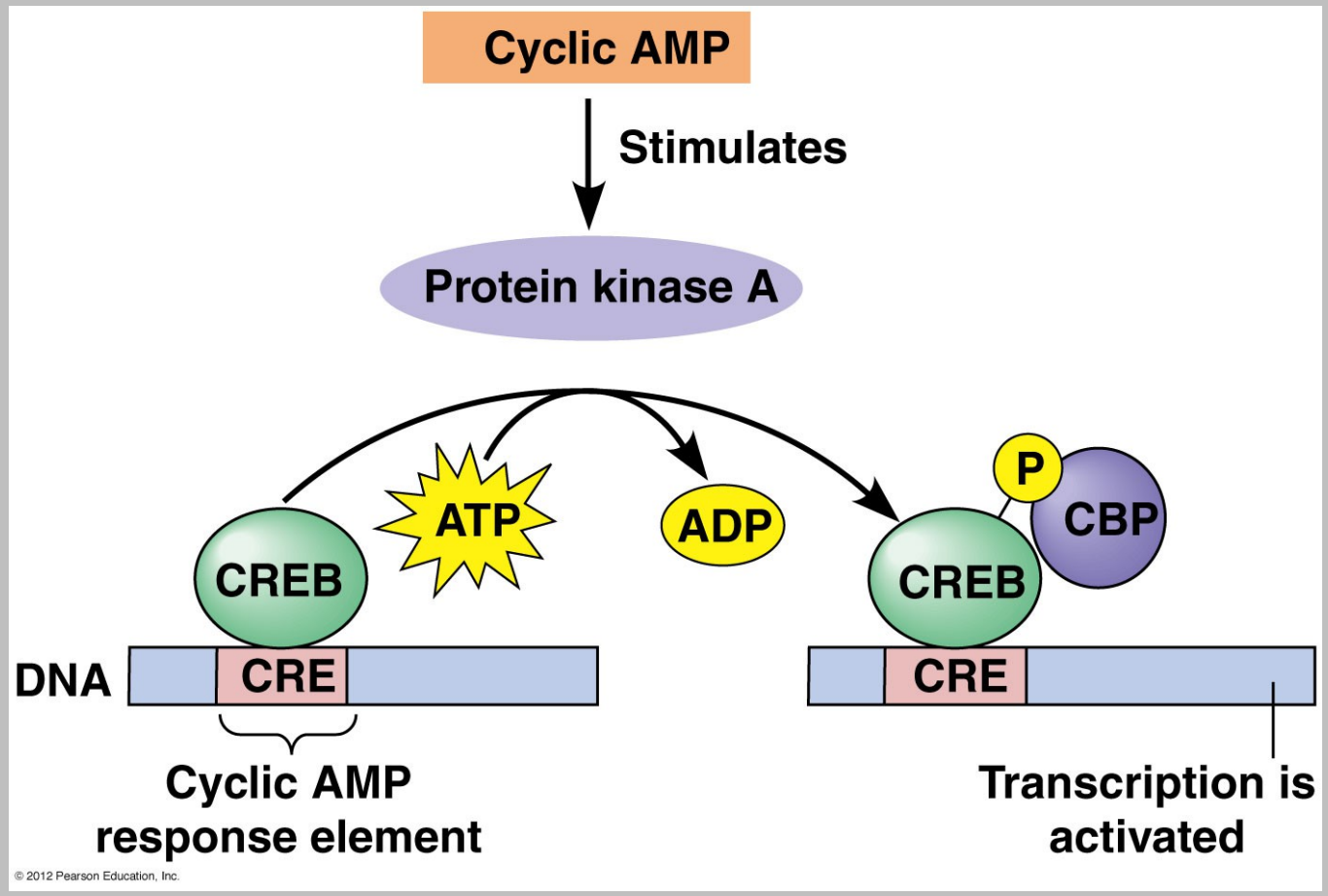




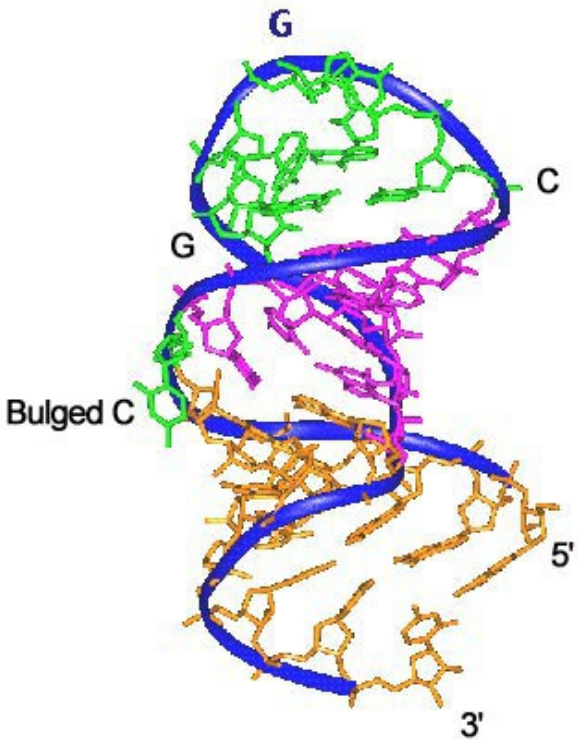
Model preoblikovanja nukleosoma z delovanjem kromatin-preoblikovalnega kompleksa.

Odzivni element za cAMP: vezava CREB

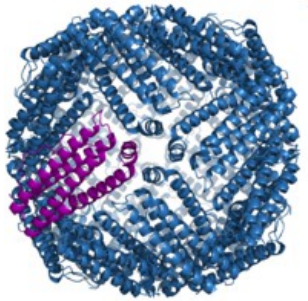


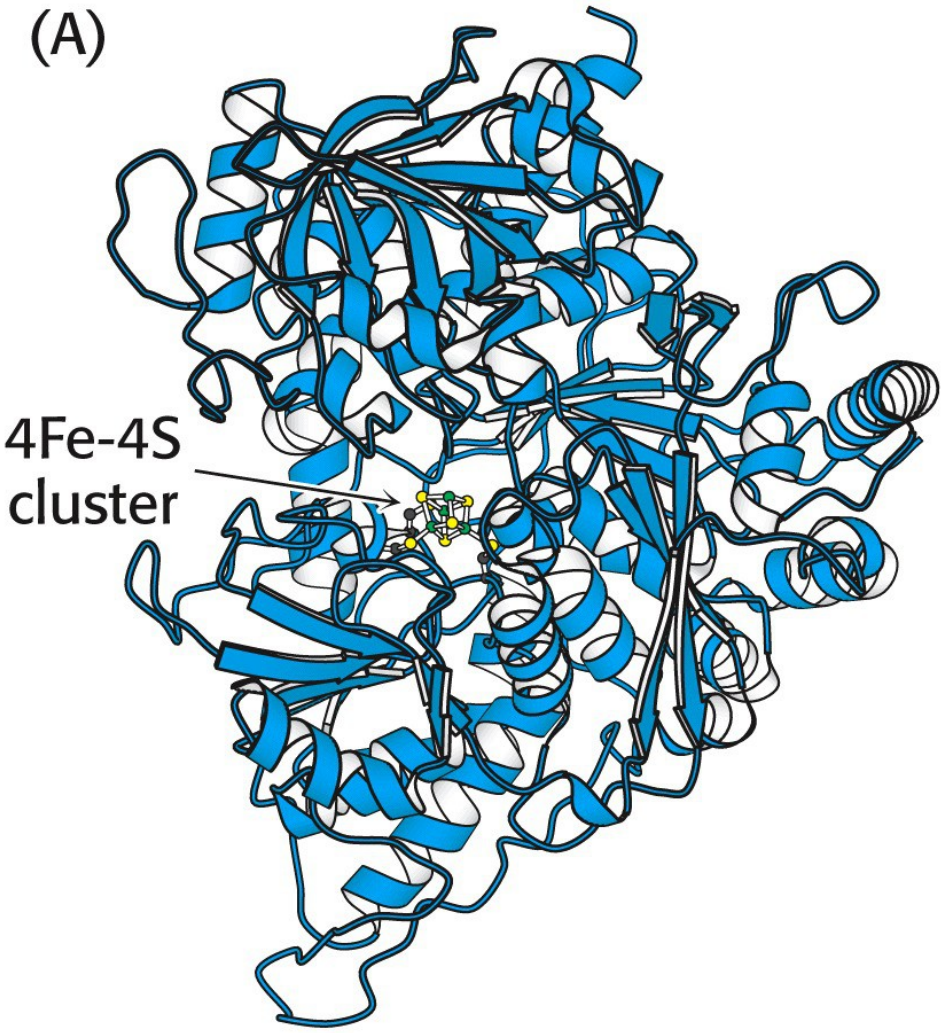

Cyclic AMP
Stimulates
Protein kinase A
ATP
ADP
P
CBP
CREB
CREB
DNA
CRE
CRE
Cyclic AMP
response element
Transcription is
activated
© 2012 Pearson Education, Inc.

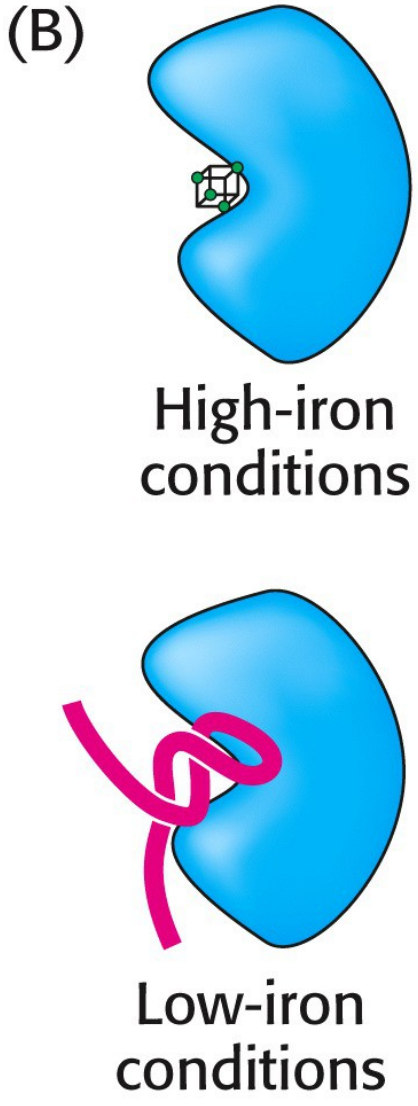
Iron-response element



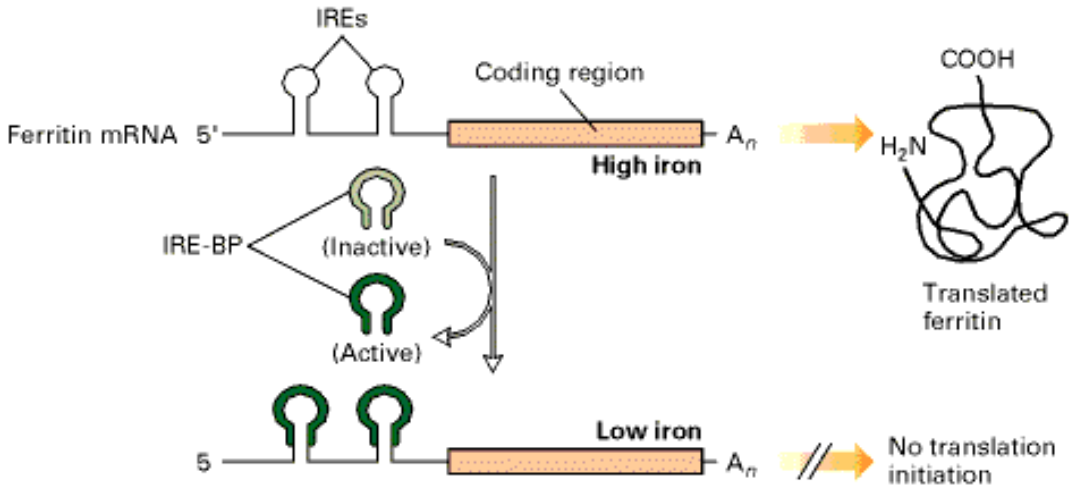
odzivni element za železo →
posttranskripcijska regulacija izražanja feritina

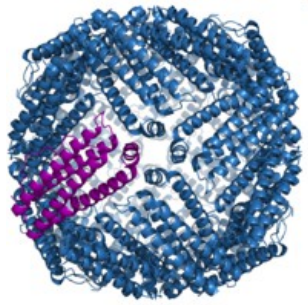




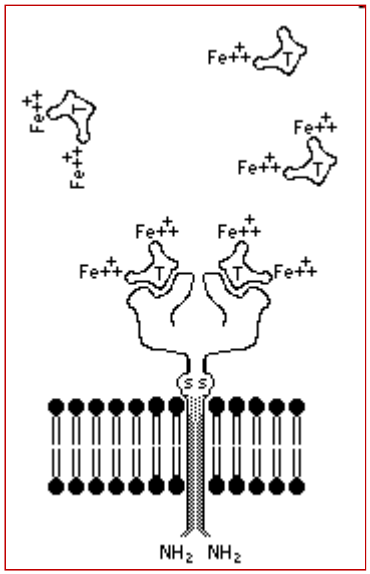


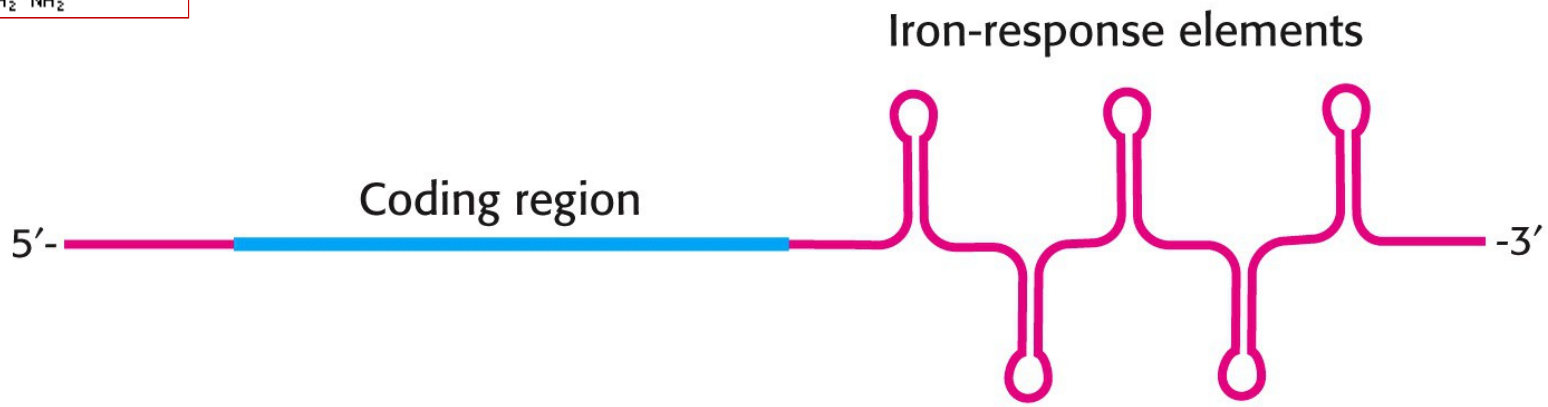
IRE-BP z mestom za vezavo 4Fe-4S



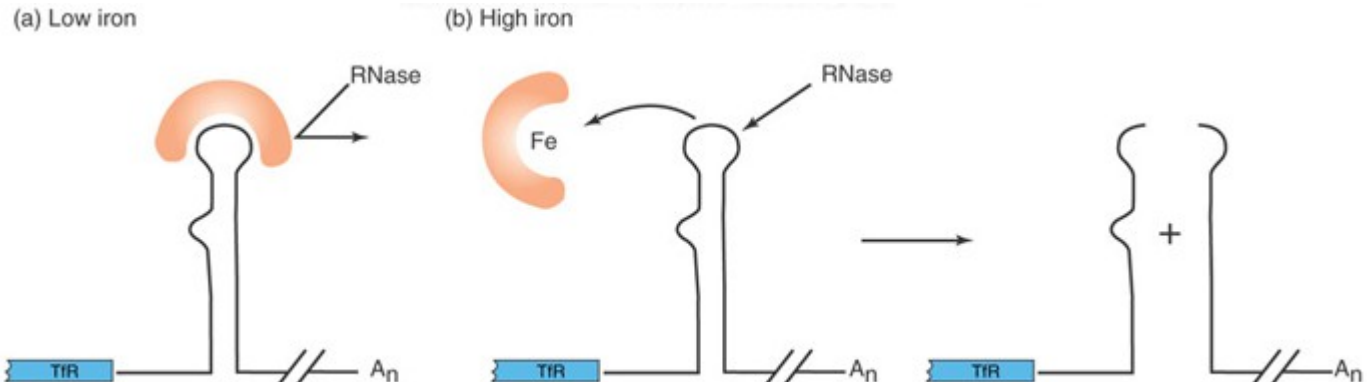


- veliko Fe: Fe se v veže na IRE-BP - nekativen, zato ne pride do atenuacije
- malo Fe: IRE-BP – aktiven – se veže na DNA (IRE) in prepreči translacijo





odzivni elementi za železo → regulacija izražanja transferinskega receptorja



malo Fe → IRE-BP se veže in
stabilizira mRNA za transferinski receptor