Chapter 6

Regulation of Gene Expression in Eukaryotes

【教学目的】

本章要求学生掌握真核生物基因表达调控的基本概念和理论，包括真核生物基因表达调控的多个层次，顺式作用元件、反式作用因子及其相互关系，以及真核基因不同水平的表达调控机制等。

【重点与难点】

1. 染色质重塑
2. 顺式作用元件、反式作用因子及其相互作用机制
3. 组蛋白密码
4. RNA干扰机制

【教学方法】

讲述式、多媒体教学、English Animation

【课时安排】

6-8课时

6.3 Transcriptional Regulation

1. Cis-Acting Element

(1) What is cis-acting element?

----- DNA sequences close to a gene that are required for gene expression.

(2) Features of Cis-Acting Elements

- contain short consensus sequences
- not fixed in location but usually within 200 bp
- usually upstream of the transcription start site
- a single element is usually sufficient for regulation
- many of them could bind specific proteins

Examples

TATA box

GC box

CAAT box

Promoter

Enhancer

Silencer

Insulator

……

(3) Types

Cis-acting elements may be divided into two types:

- positve control elements

  → acivate transcription

- negaitve control elements

  → repress transcription

2. Major Types of Cis-Acting Element

(1) Promoter

--In genetics, a promoter is a region of DNA that facilitates the transcription of a particular gene.

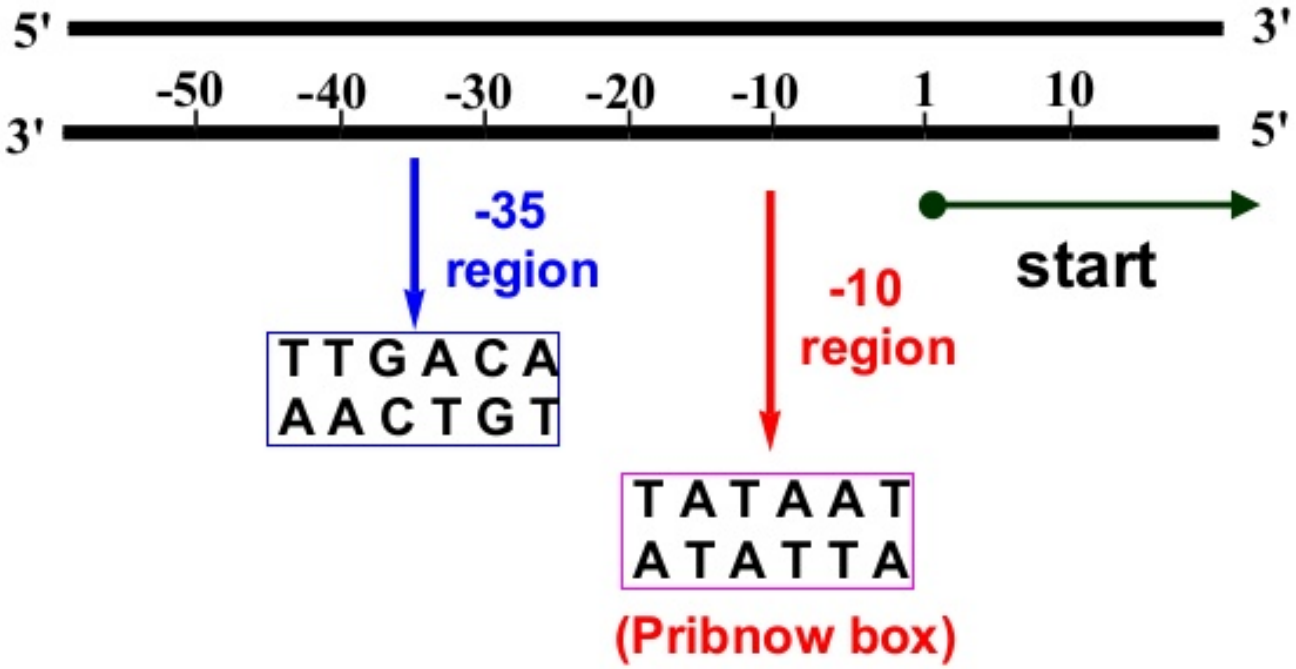
- **Core promoter**
  - in eukaryote: TATA-box, Initiator (Inr)
  - in prokaryote: -10 region, Inr

- **Proximal elements of promoter**
  - **in prokaryote: -35 region**
  - **in eukaryote: CAAT-box, GC-box**

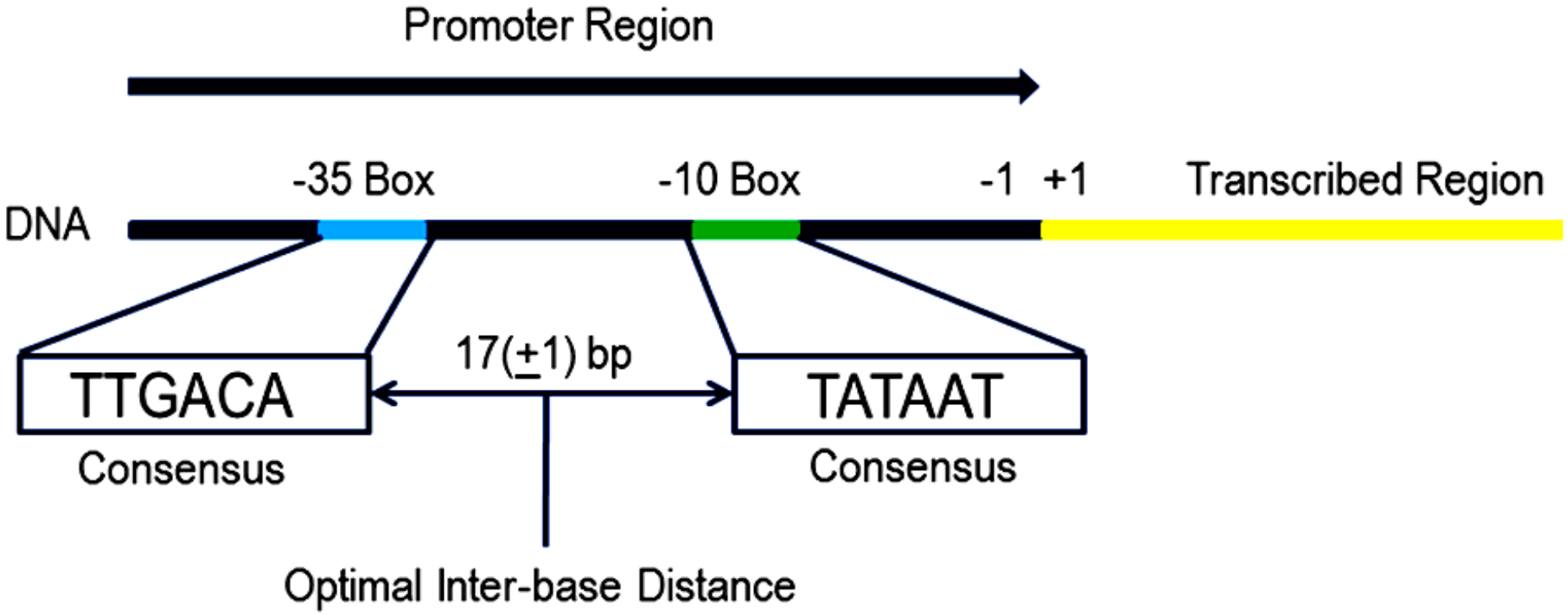
    UPE: upstream promoter element

    UAS: upstream activating sequence

Prokaryotic promoter



Consensus sequence


Promoter Region
-35 Box
-10 Box
-1 +1
Transcribed Region
DNA
17(±1) bp
TTGACA
TATAAT
Consensus
Consensus
Optimal Inter-base Distance

Eukaryotic Promoter

Site where other regulatory proteins bind to enhance transcription

A site where regulatory proteins can bind to enhance transcription

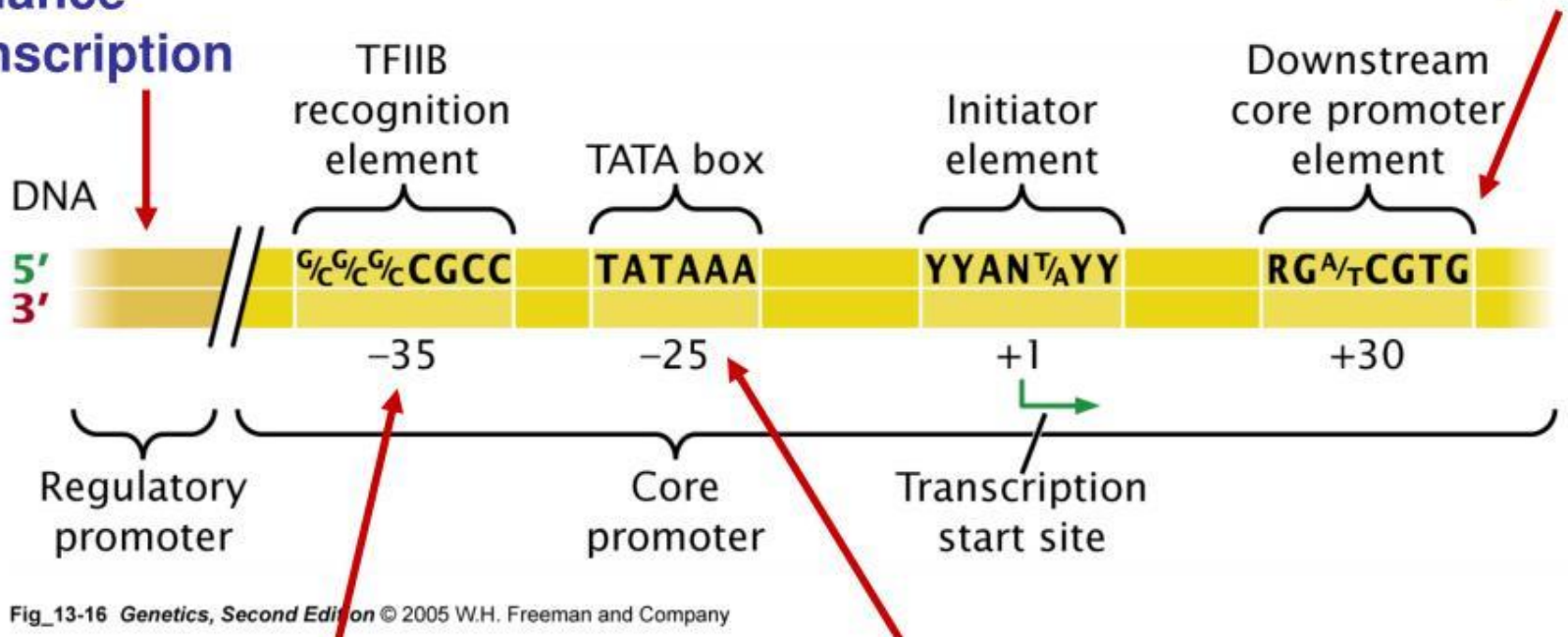
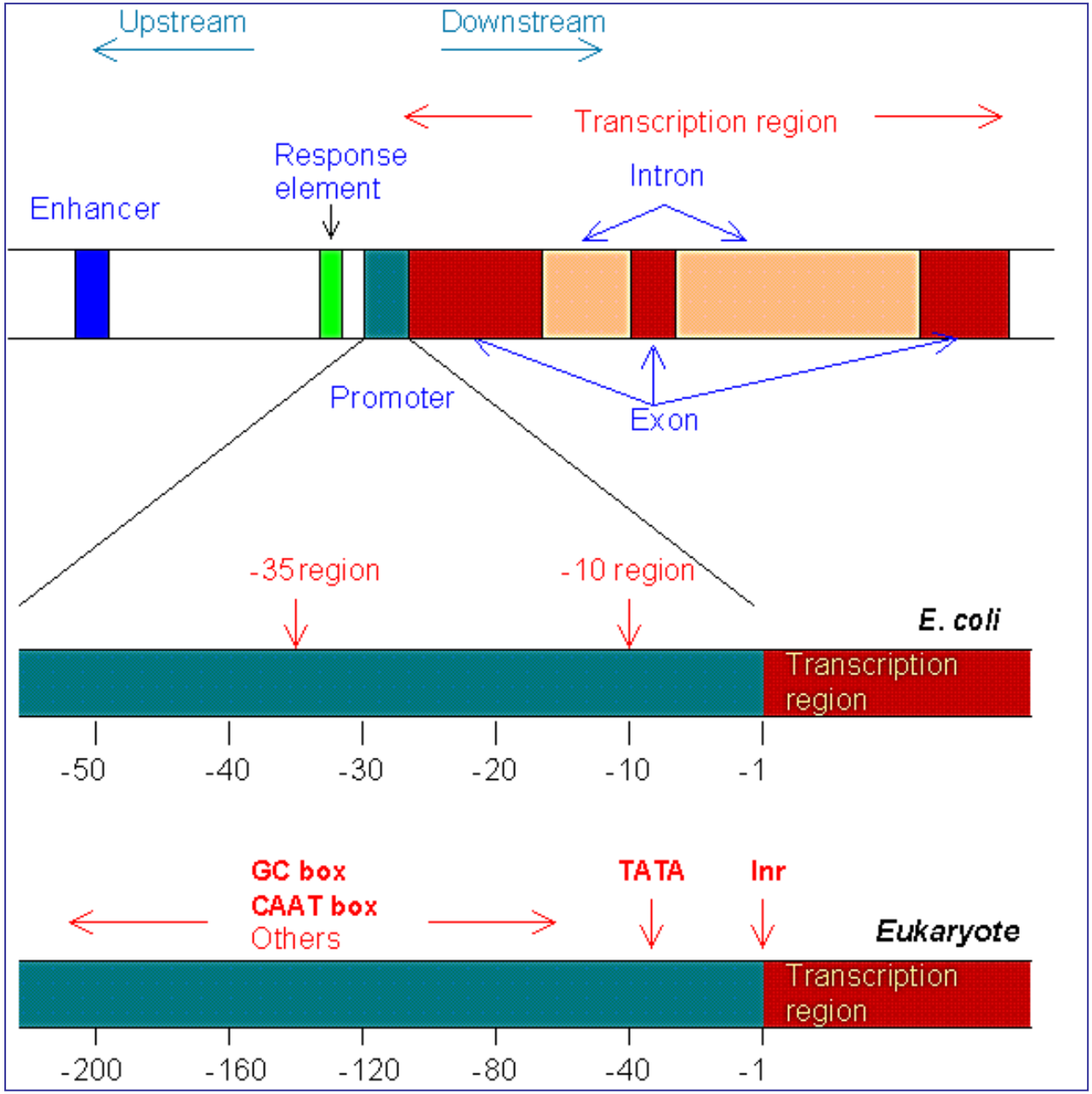


Fig_13-16 *Genetics, Second Edition* © 2005 W.H. Freeman and Company

Sequence recognized by a transcription factor

Sequence where DNA is denatured determining where transcription starts


Upstream
Downstream
Transcription region
Response element
Intron
Enhancer
Promoter
Exon
-35 region
-10 region
E. coli
Transcription region
-50
-40
-30
-20
-10
-1
GC box
CAAT box
Others
TATA
Inr
Eukaryote
Transcription region
-200
-160
-120
-80
-40
-1

Question

Every promoter of eukaryotic gene must have a TATA box?

A True

B False

TATA-less promoter ！

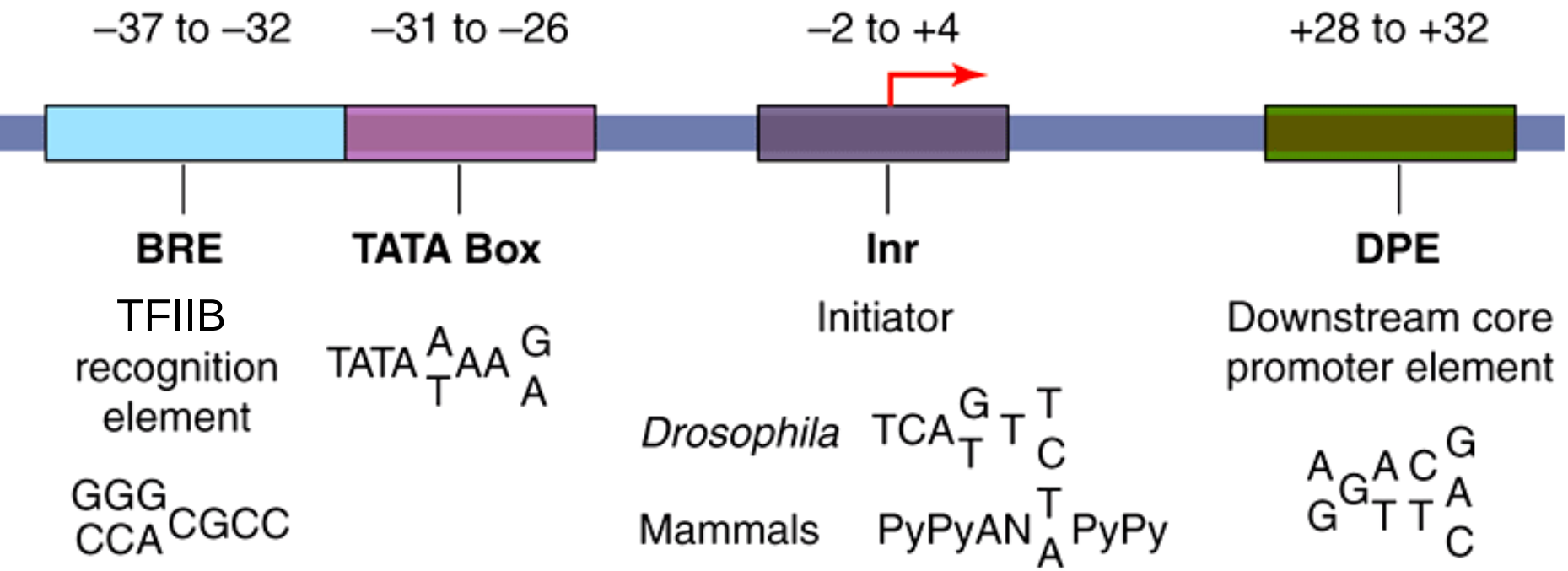
- **The downstream promoter element (DPE) is a common component of RNA polymerase II promoters that do not contain a TATA box (TATA-less promoters).**
- **A core promoter for RNA polymerase II includes the Inr and, commonly, either a TATA box or a DPE.**

  – 10 region = Pribnow box

  – 35 region = Sexfama box

  TATA box = Hogness box

Core promoter Elements



BRE: TFIIB recognition element;
DPE: downstreamcore promoter element;
Inr: initiator region

RESEARCH ARTICLE

Structural insights into preinitiation complex assembly on core promoters

Xizi Chen[1,†], Yilun Qi[1,†], Zihan Wu[1,†], Xinxin Wang[1,†], Jiabei Li[1,†], Dan Zhao[1,†], Hai...

+ See all authors and affiliations

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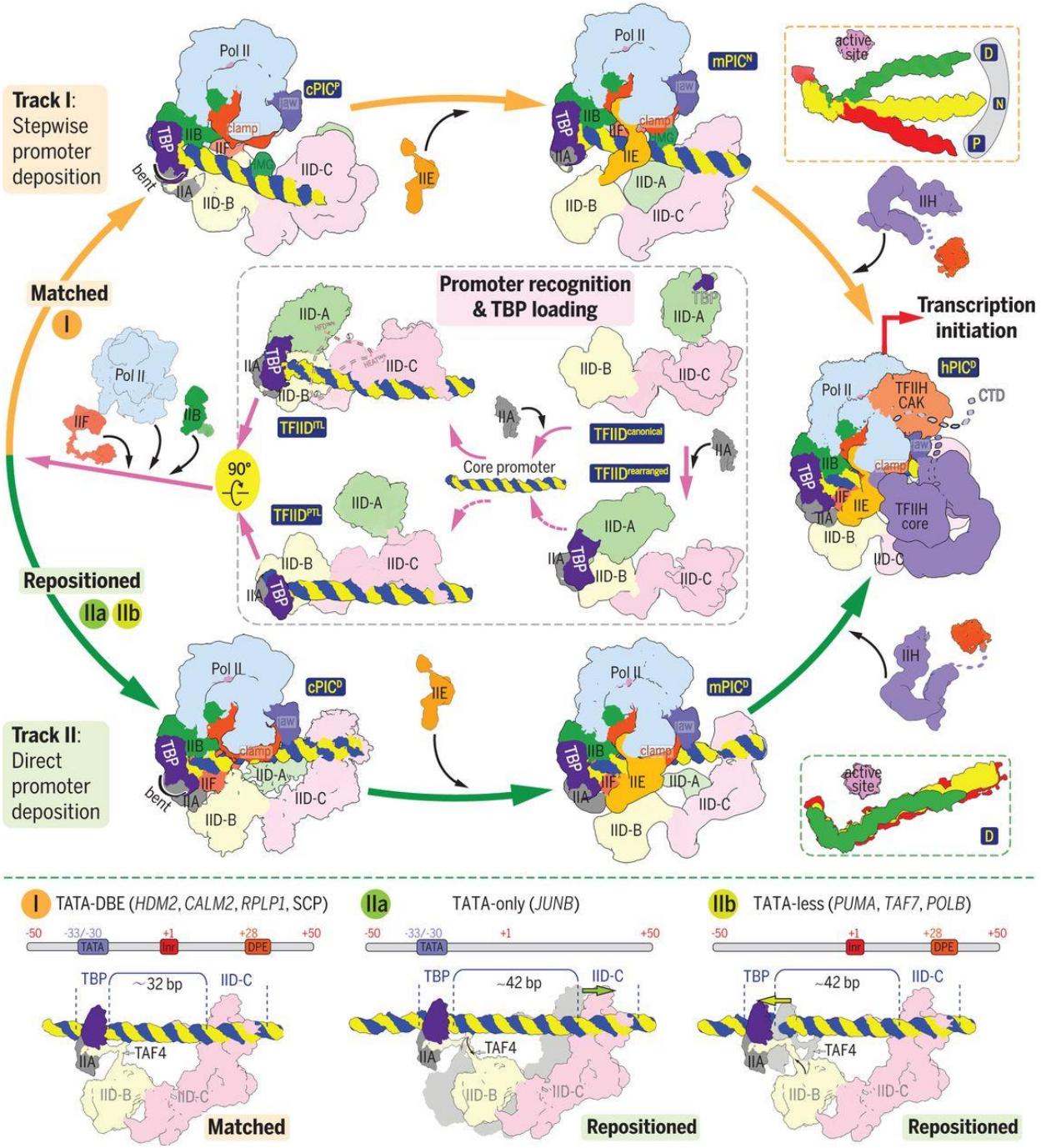

Track I: Stepwise promoter deposition
Track II: Direct promoter deposition
Matched
I
Repositioned
IIa IIb
Promoter recognition & TBP loading
Transcription initiation
Pol II
cPIC^D
mPIC^N
mPIC^D
hPIC^D
TFIIH CAK
TFIIH core
CTD
IIH
IIE
IIF
IIB
IIA
TBP
clamp
HMG
IID-A
IID-B
IID-C
bent
active site
D
N
P
90°
Core promoter
TFIID^ITL
TFIID^PTL
TFIID^canonical
TFIID^rearranged
I TATA-DBE (HDM2, CALM2, RPLP1, SCP)
IIa TATA-only (JUNB)
IIb TATA-less (PUMA, TAF7, POLB)
-50
-33/-30
+1
+28
+50
TATA
Inr
DPE
~32 bp
~42 bp
TAF4
Matched
Repositioned
Repositioned

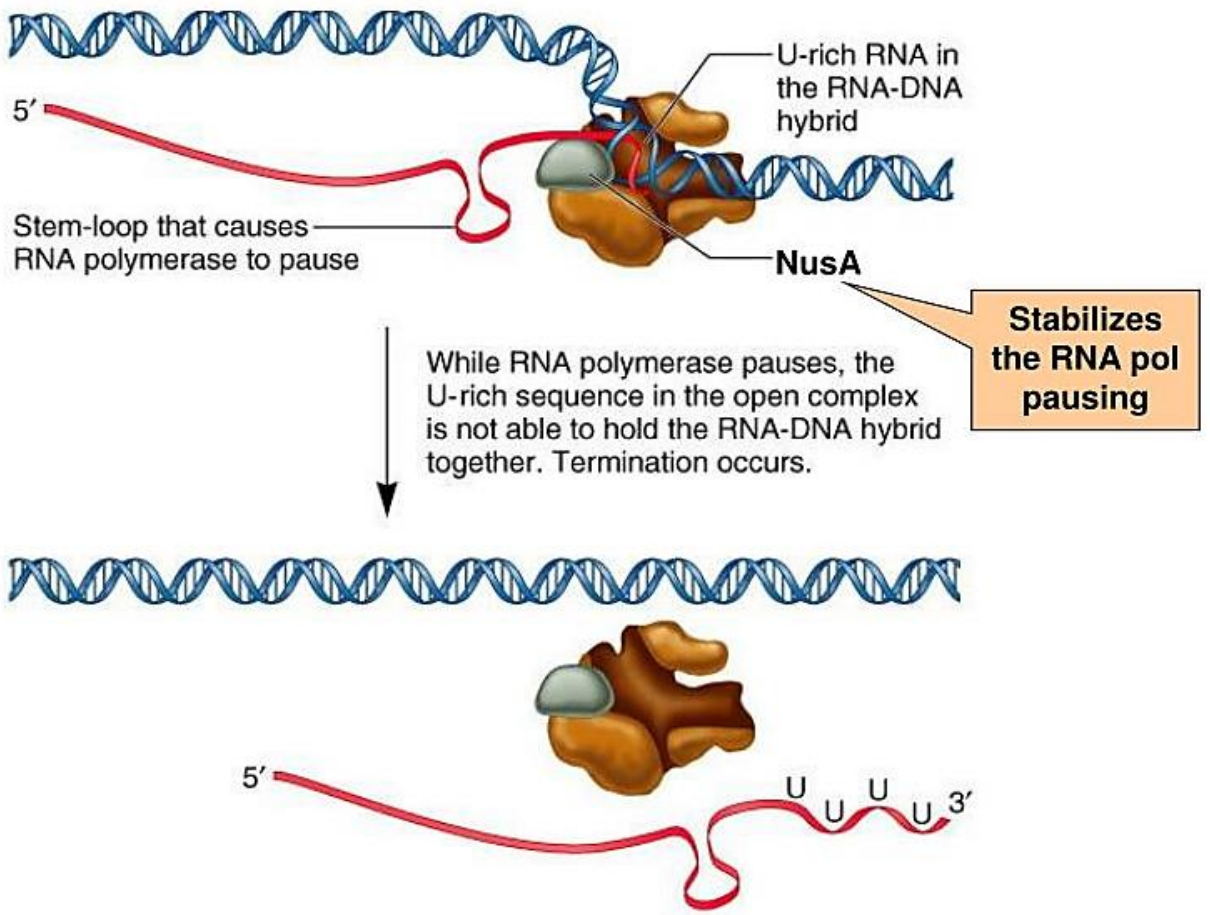
(2) Terminator

A DNA sequence just downstream of the coding segment of a gene, which is recognized by RNA polymerase as a signal to stop transcription.

In prokaryotes, two types of transcription termination:

- **ρ-dependent termination (weak)**
- **ρ-independent termination (strong)**

ρ-independent termination requires two sequences in the RNA
– A stem-loop structure upstream of 7-9 U residues



In eukaryotes, transcription termination occurs in a reaction coupled to RNA 3′-end processing.

Most eukaryotic mRNA precursors are cleaved in a site-specific manner in the 3′-untranslated region, followed by polyadenylation of the upstream cleavage product.

The exact mechanism of coupling between 3′-end processing and transcription termination remains unclear.

Termination is accompanied by dephosphorylation of the pol II CTD, but the precise timing of pol II dephosphorylation is also unclear.

(3) Enhancer

① Concept

A regulatory DNA sequence that greatly enhances the transcription of a gene.

enhancer-binding protein ---- activator

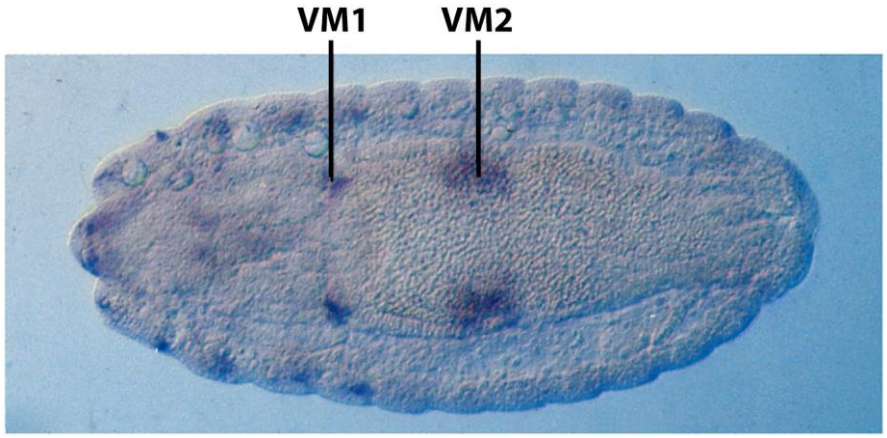
② Functional Features of Enhancer

- greatly increase transcriptional rate
- can be upstream or downstream of promoter
- close to promoter or far away from promoter
- no direction requirment (di-direction)
- no gene-specific regulation

……

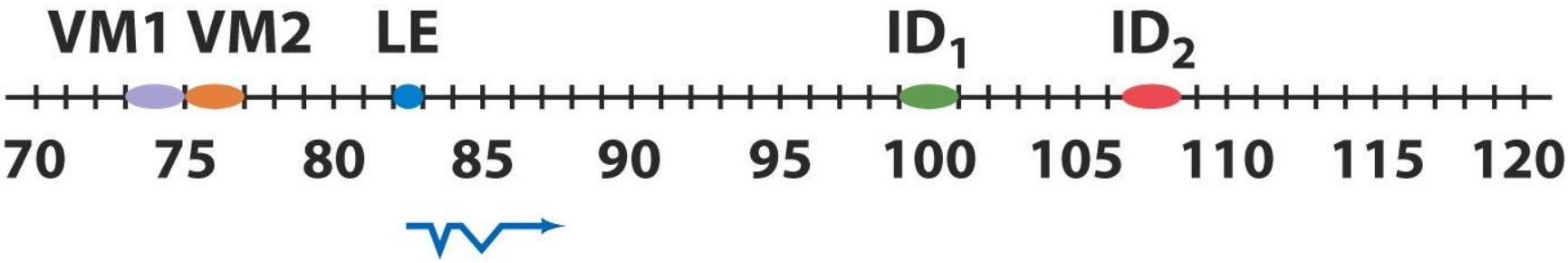
LE enhancer: lateral ectoderm

VM enhancers



ID enhancer: imaginal disc

VM1: anterior visceral mesoderm
VM2: posterior visceral mesoderm



(4) Silencer

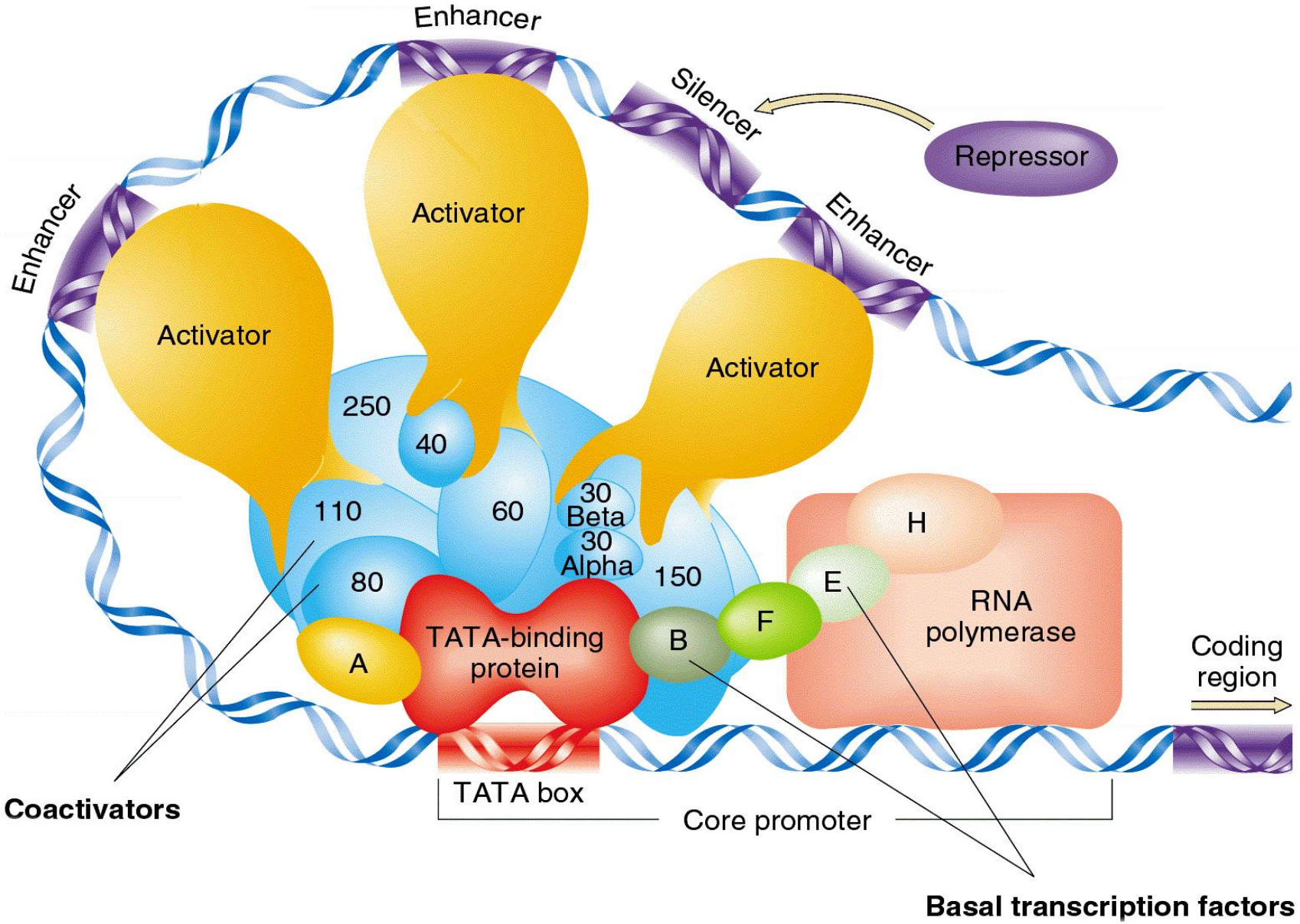
① Concept

A DNA sequence that helps to reduce or shut off the expression of a nearby gene.

Silencer-binding protein ---- repressor

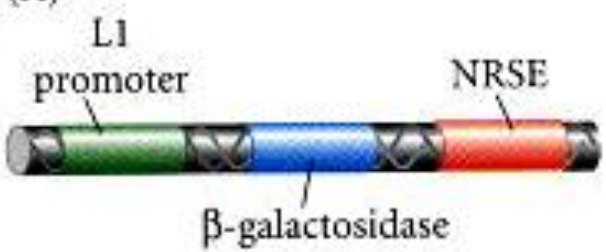
② Functional Features of Silencer

- **bind to the repressor**
- **represse or block transcription**
- **negative control element**

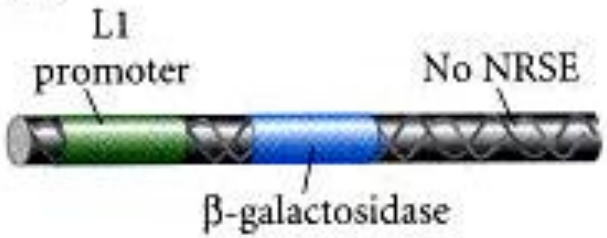


Animation: Enhancer & Silencer

(A)


L1
promoter
NRSE
β-galactosidase

(B)


L1
promoter
No NRSE
β-galactosidase

Question

TBP is a component that is required for each type of RNA polymerase to bind its promoter.

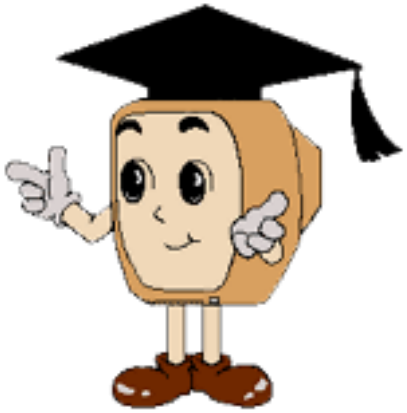
A True

B False

Question

Enhancers can turn on promoters of genes located thousands of base pairs away.

What is to prevent an enhancer from inappropriately binding to the promoter and activating the gene transcription?



(5) Insulator

① Concept

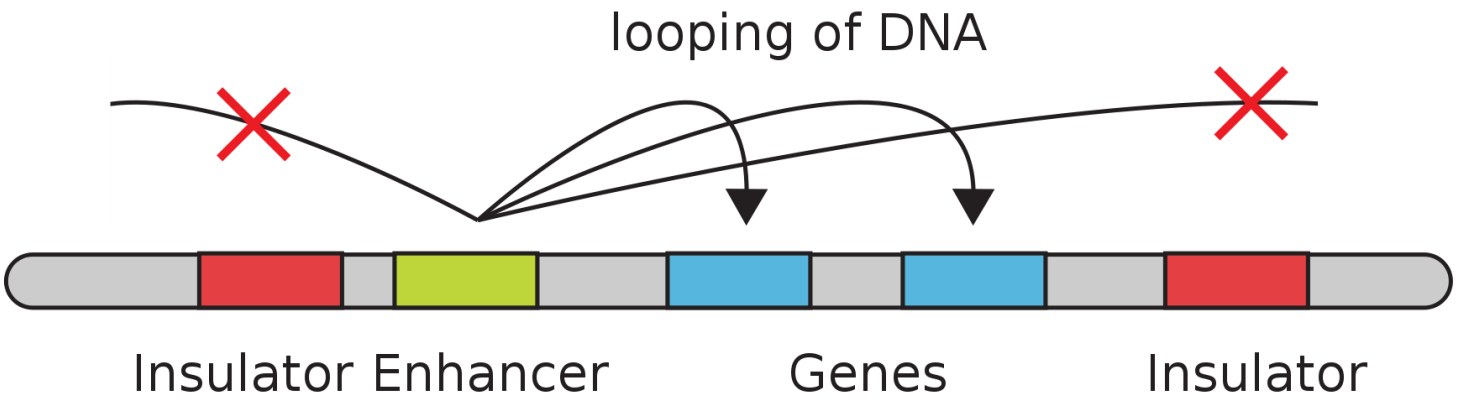
Insulators are DNA sequence elements that help to prevent inappropriate interactions between adjacent regions of the genome.

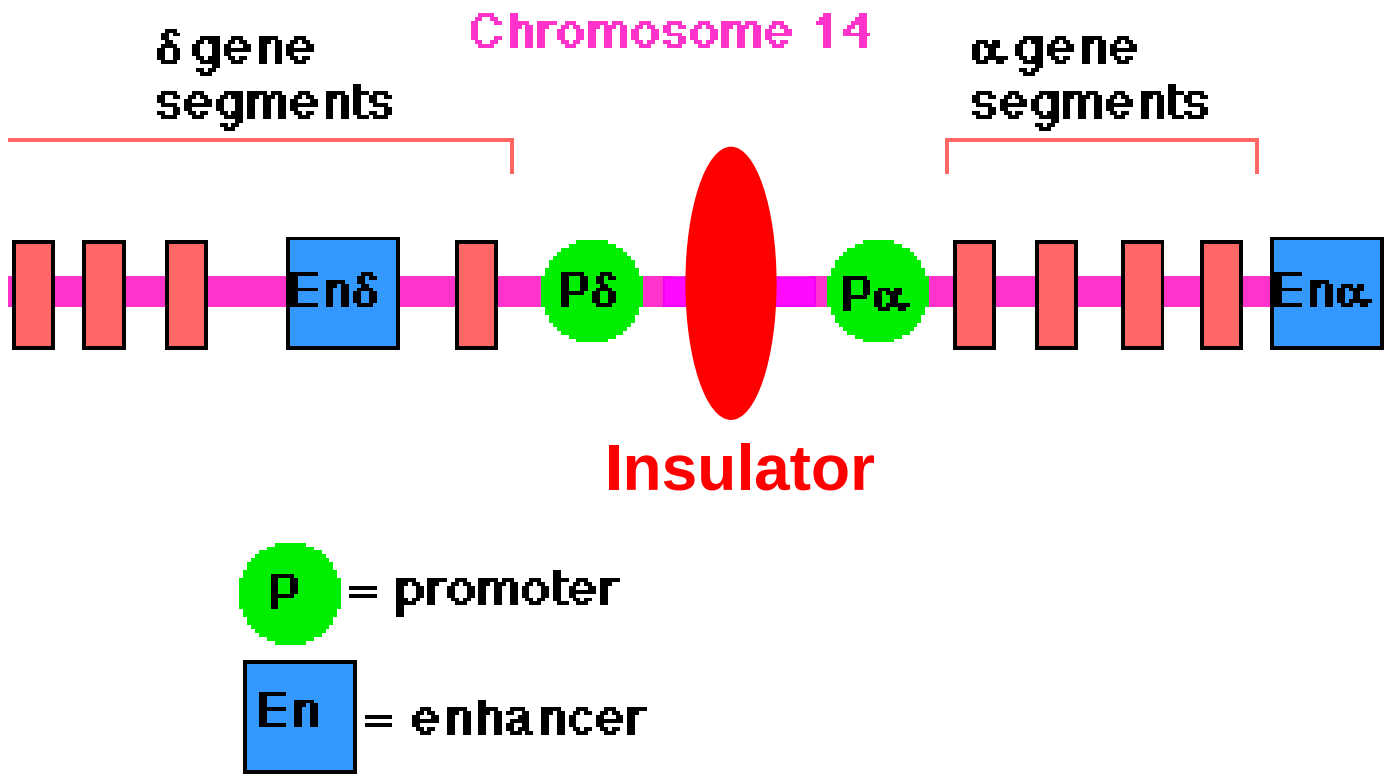
(enhancer and promoter or silencer and promoter)

② Functional Features of Insulator

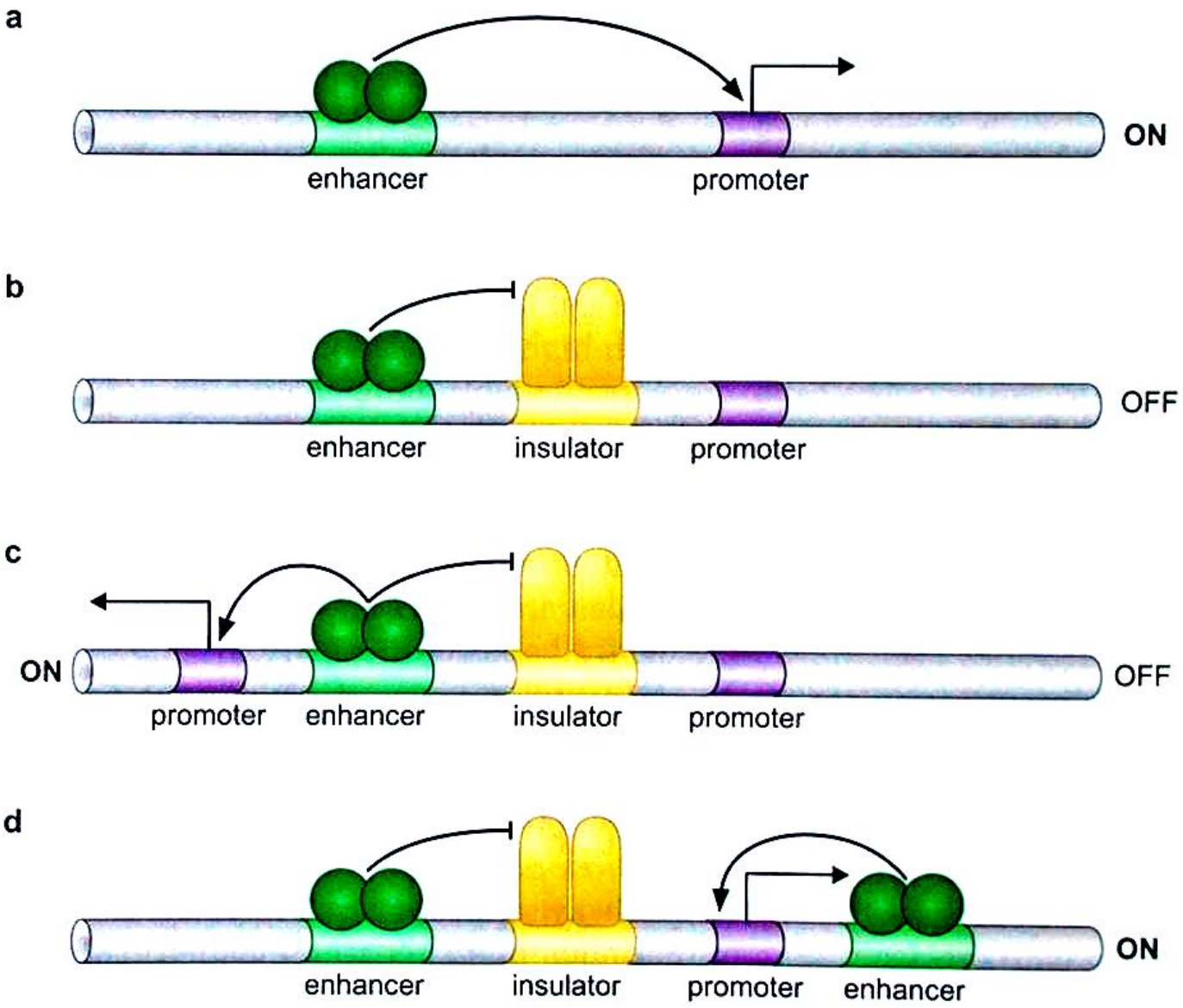
- **one that is involved in enhancer-blocking activity**
- **the other that provides a barrier to the spread of heterochromatin**

Insulator function is to prevent a gene from being influenced by the activation (or repression) of its neighbors.

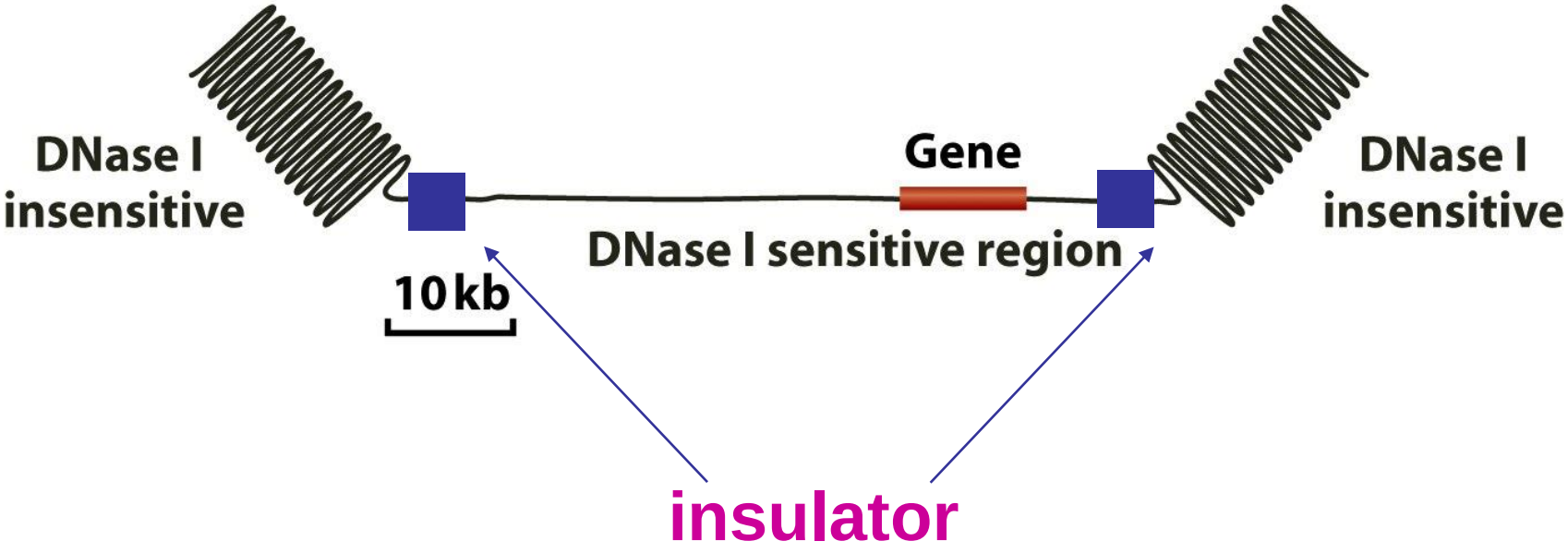




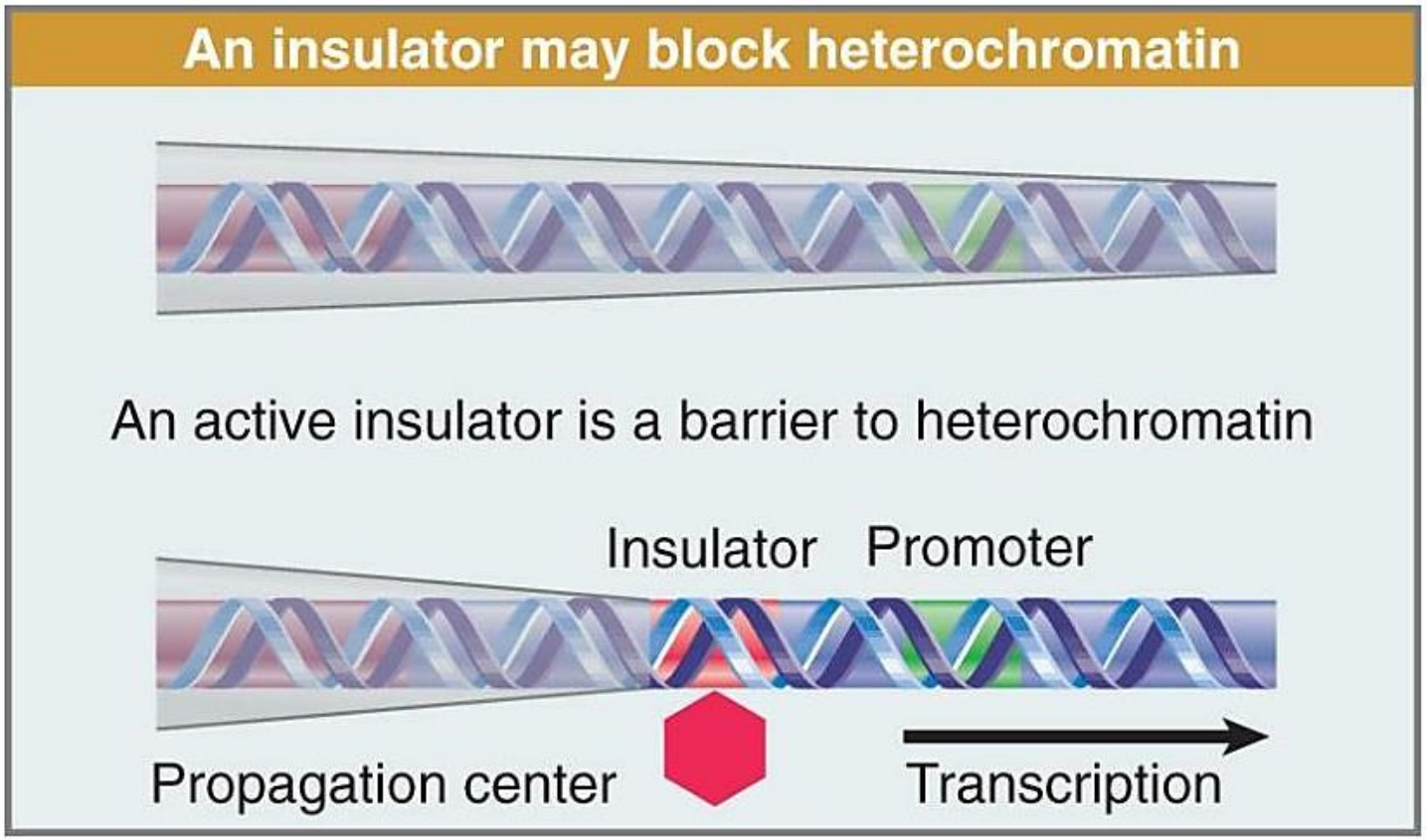
There is an insulator between the α gene promoter and the δ gene promoter of the α/δ T-cell receptor (TCR) that ensures that activation of one does not spread over to the other.

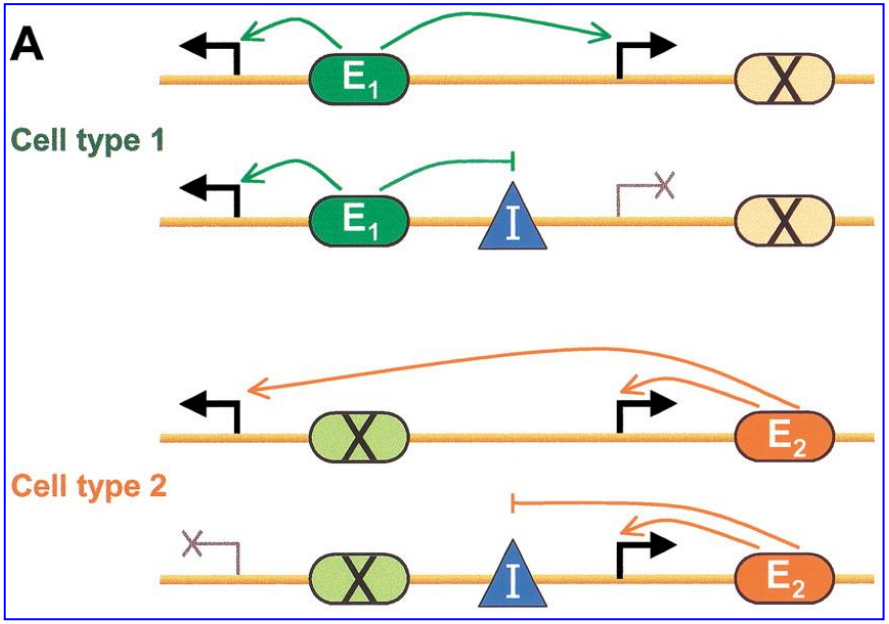

a
ON
enhancer
promoter
b
OFF
enhancer
insulator
promoter
c
ON
OFF
promoter
enhancer
insulator
promoter
d
ON
enhancer
insulator
promoter
enhancer

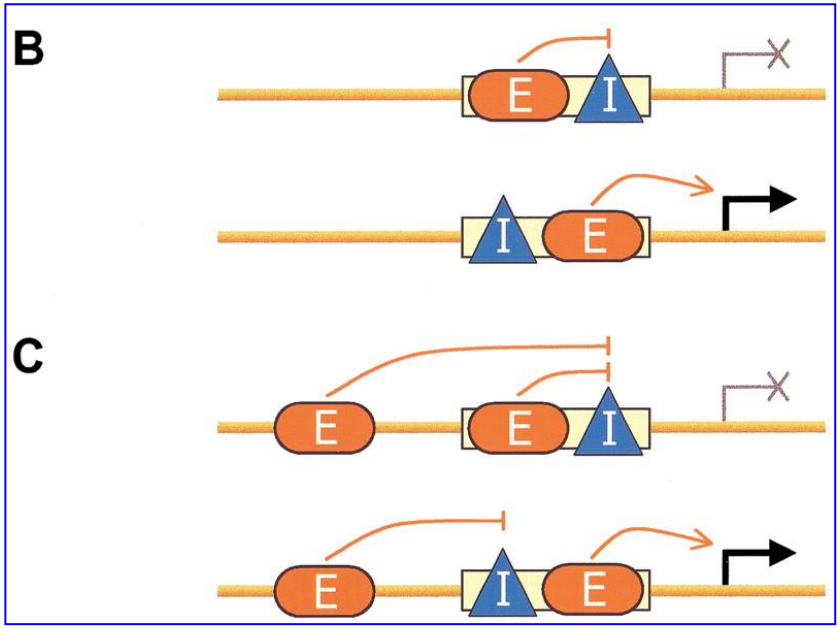
Insulators block the spread of heterochromatin

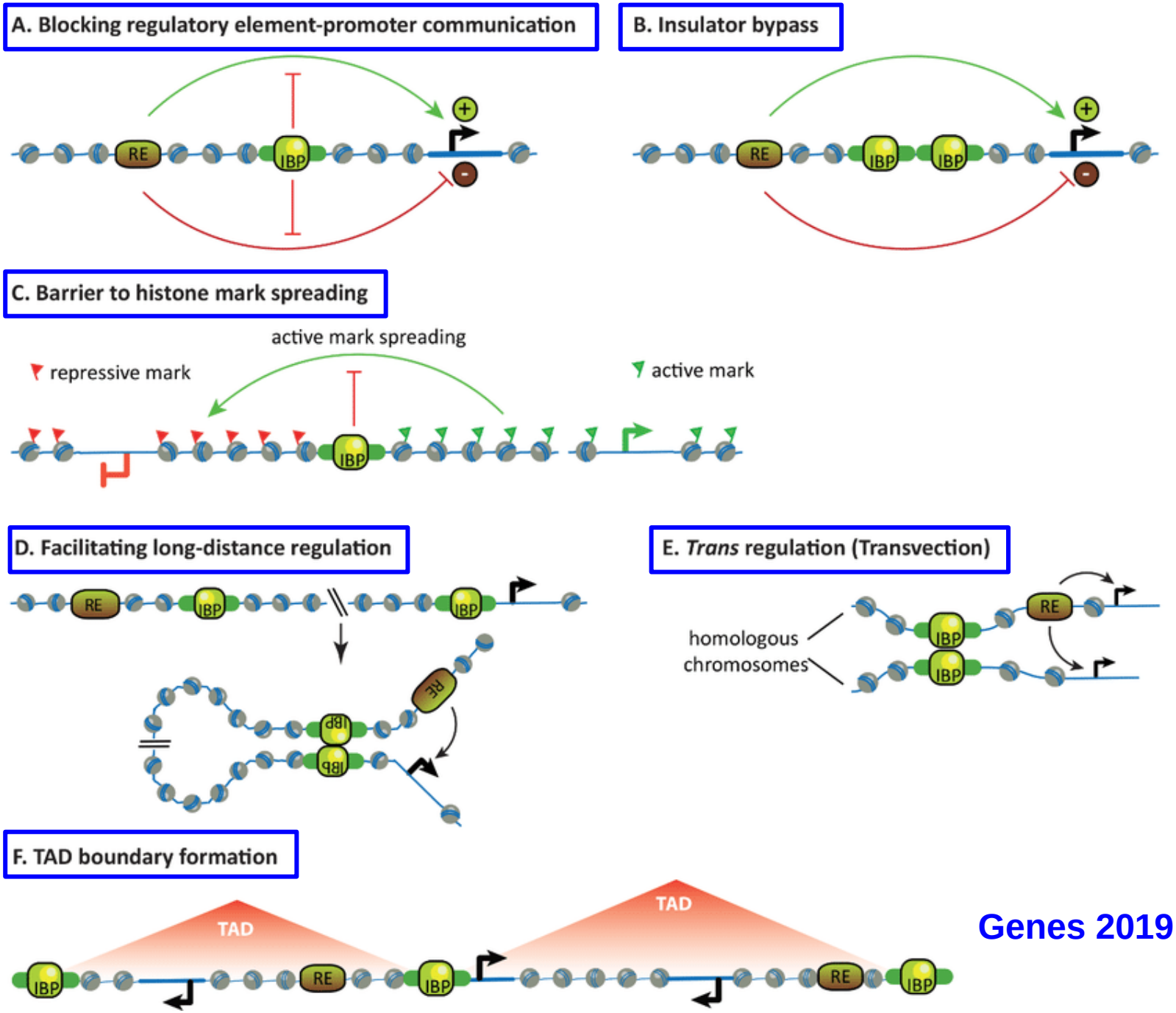


Insulators may provide barriers against the spread of heterochromatin.




A
Cell type 1
E1
E1
I
X
X
E2
Cell type 2
X
I
E2


B
E
I
I
E
C
E
E
I
E
I
E



Genes 2019, 10, 767

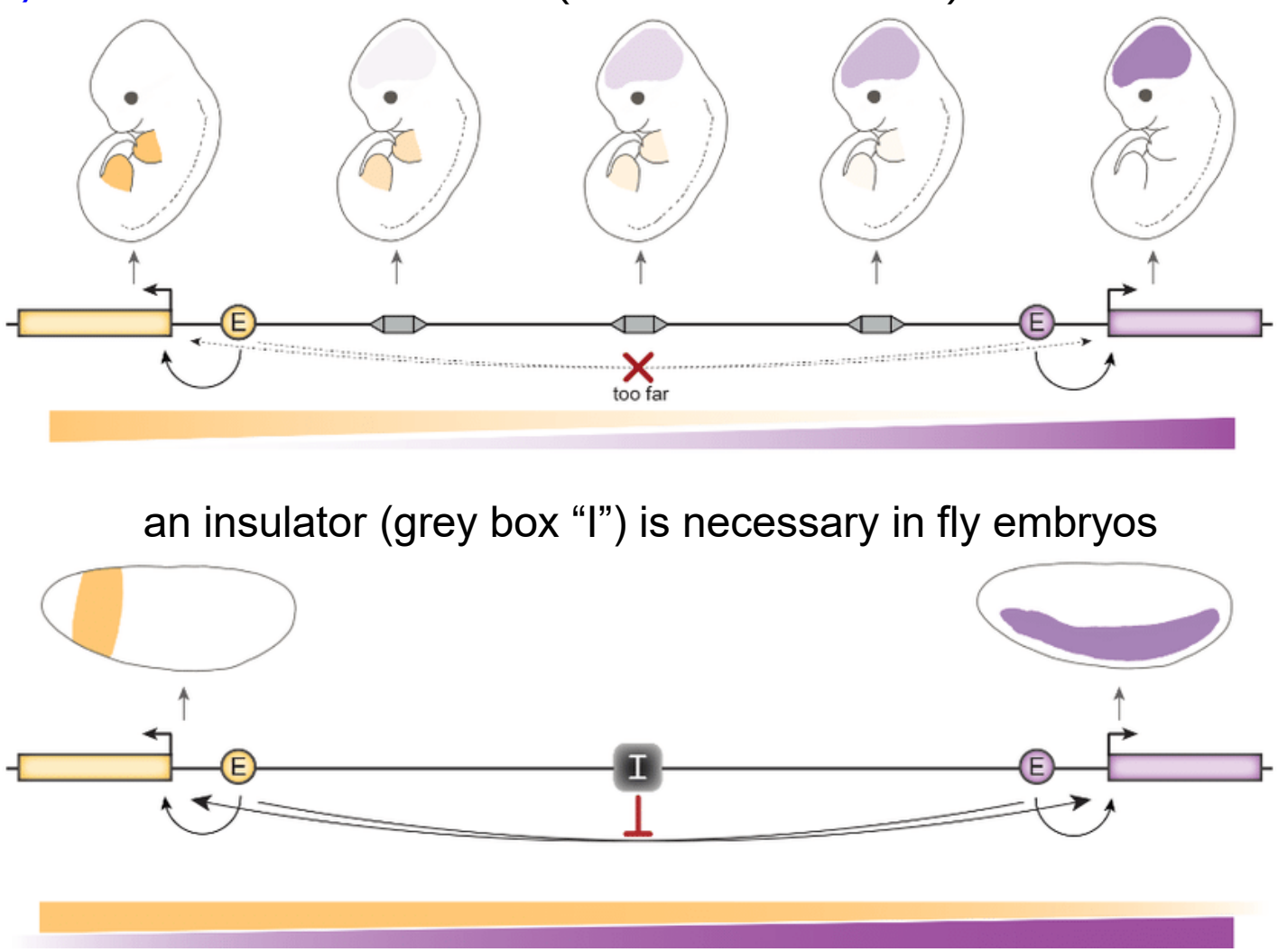


Figure 4. An important difference between mammals and flies is the greater distances between developmental genes and their regulatory elements in mammals, whereas the fly genome is more compact. This may result in a greater need for insulation in flies.