Duan Ma, Ph.D. , M.D. **Professor and Deputy Director**

Key Lab of Molecular Medicine, Ministry of Education.

Research Center for Birth Defects.

Chapter XIII

Regulation of Gene Expression in Prokaryotes

原核生物基因表达调控

Why Gene Regulation of Expression?

- Gene expression has temporal specificity and spatial specificity
- Gene expression has physiological specificity and pathological specificity
- Prevention and treatment of diseases are related with gene regulation

François Jacob

Jacques Monod

Andre Lwoff

Mark Ptashne

Walter Gilbert

- 1940-1950: Andre Lwoff, E.coli, Phage, Lysogen, Lysis
- 1961: Jacob and Monod, Operon, Lactose, β-galactosidase
- 1970: Mark Ptashne and Gilbert, Gene Repression.
- 1981: Charles Yanofsky, Trp Operon, Attenuation.

Charles Yanofsky

Regulation Points of Gene Expression

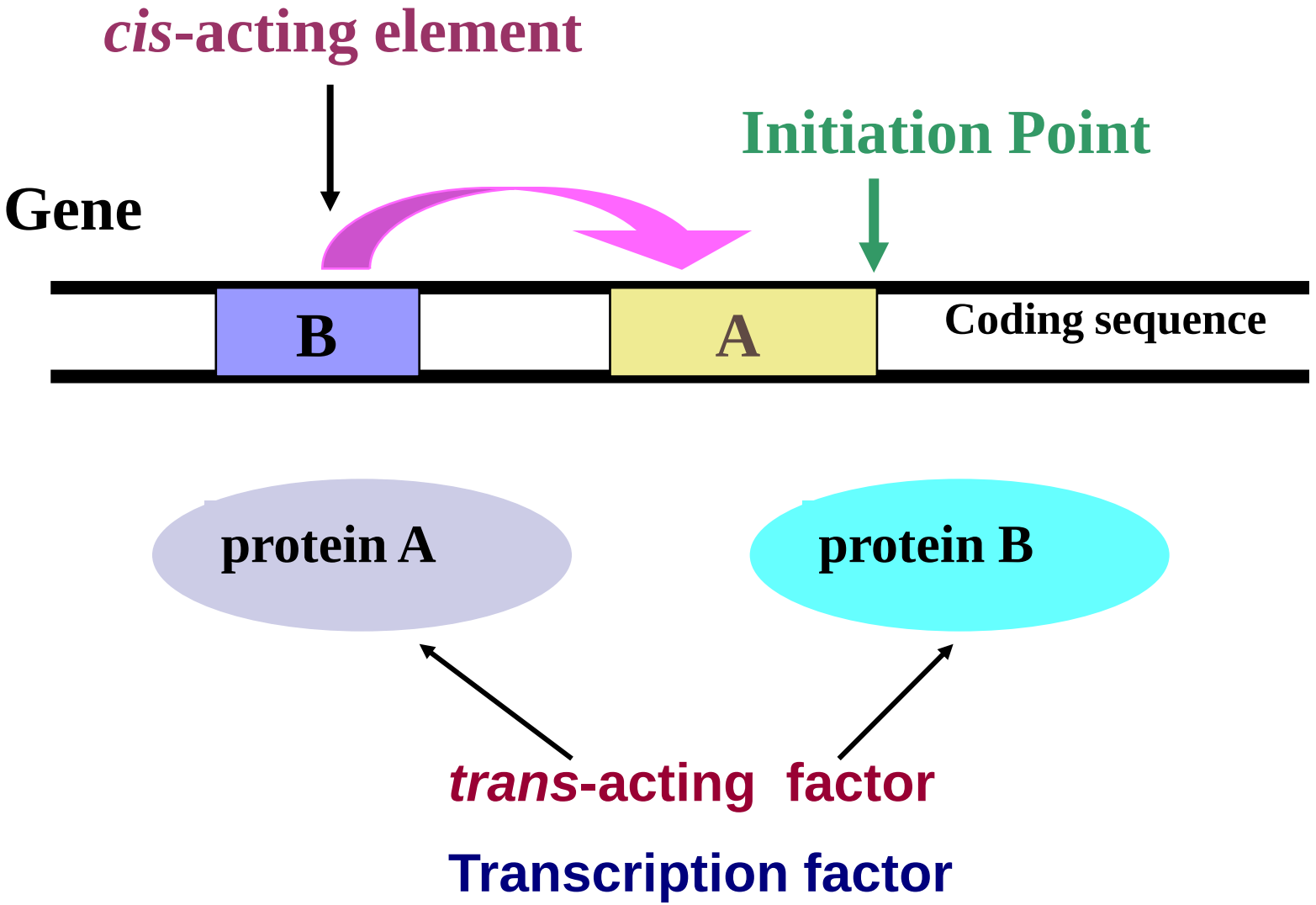
Chromatin activation

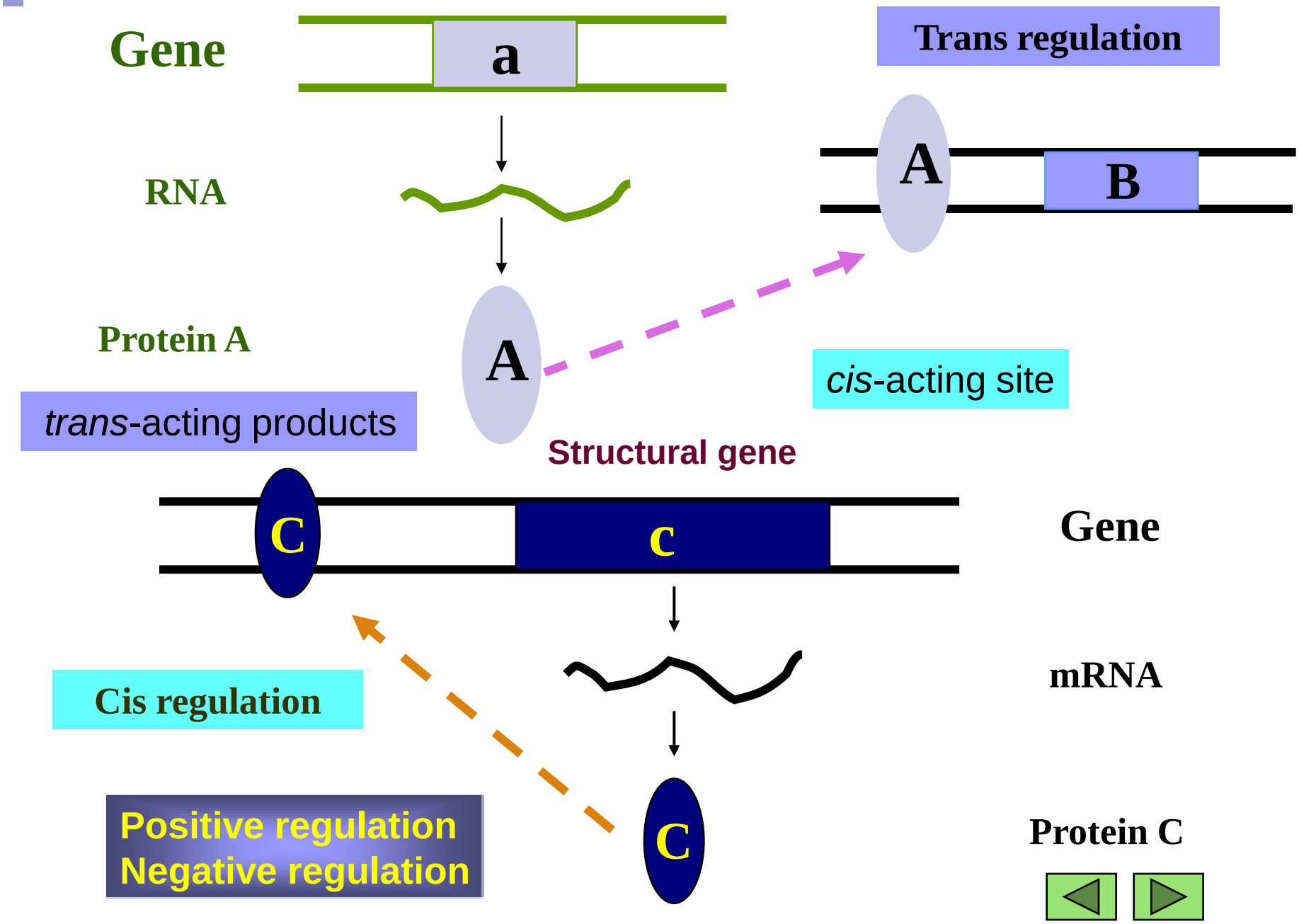
Initiation, elongation and termination of transcription

Initiation is the key point of regulation

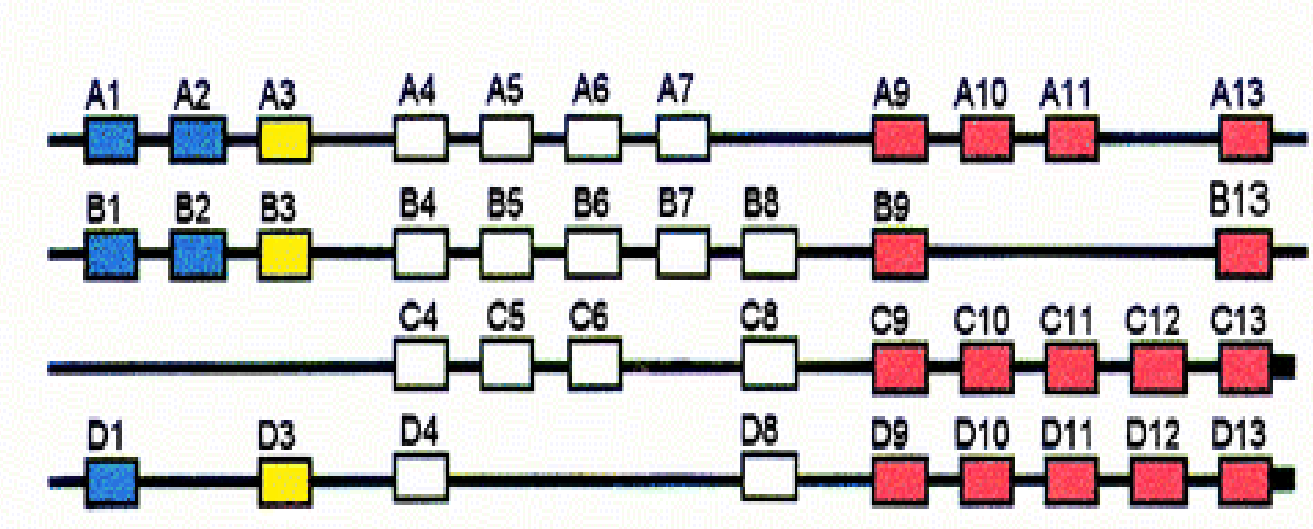
Translation

Processing and Modification of Translation


cis-acting element
Initiation Point
Gene
B
A
Coding sequence
protein A
protein B
trans-acting factor
Transcription factor


Gene
a
Trans regulation
RNA
A
B
Protein A
A
cis-acting site
trans-acting products
Structural gene
C
c
Gene
mRNA
Cis regulation
C
Protein C
Positive regulation
Negative regulation

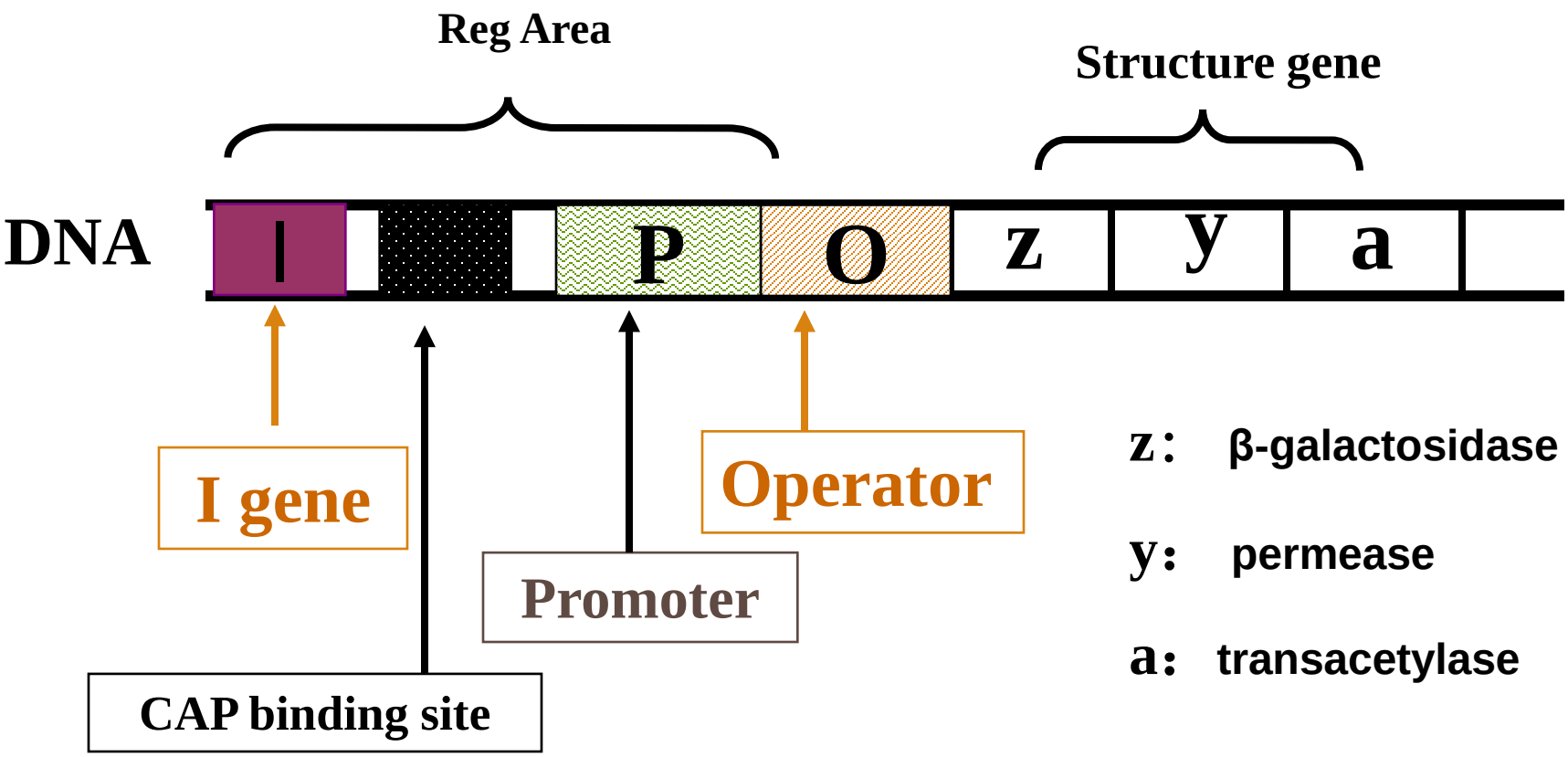
Gene Cluster



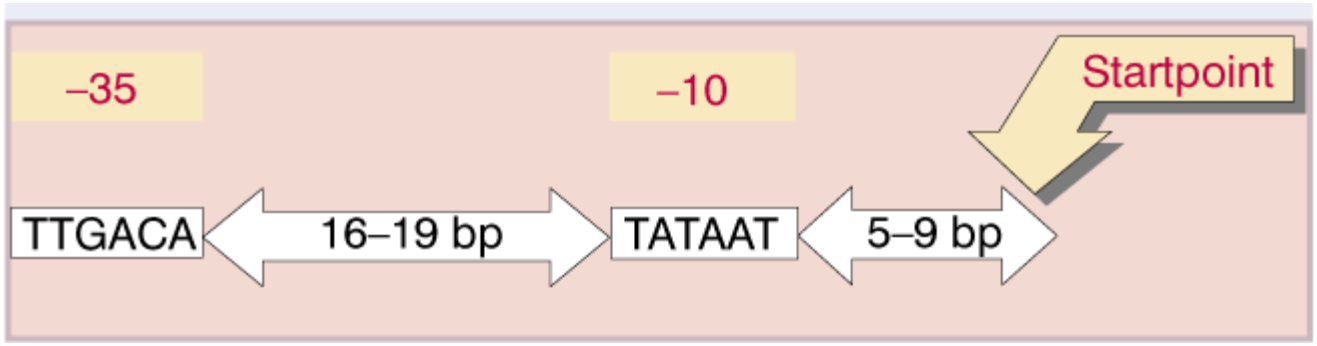
The Operon of Bacteria

细菌操纵子

Structure of Lac Operon



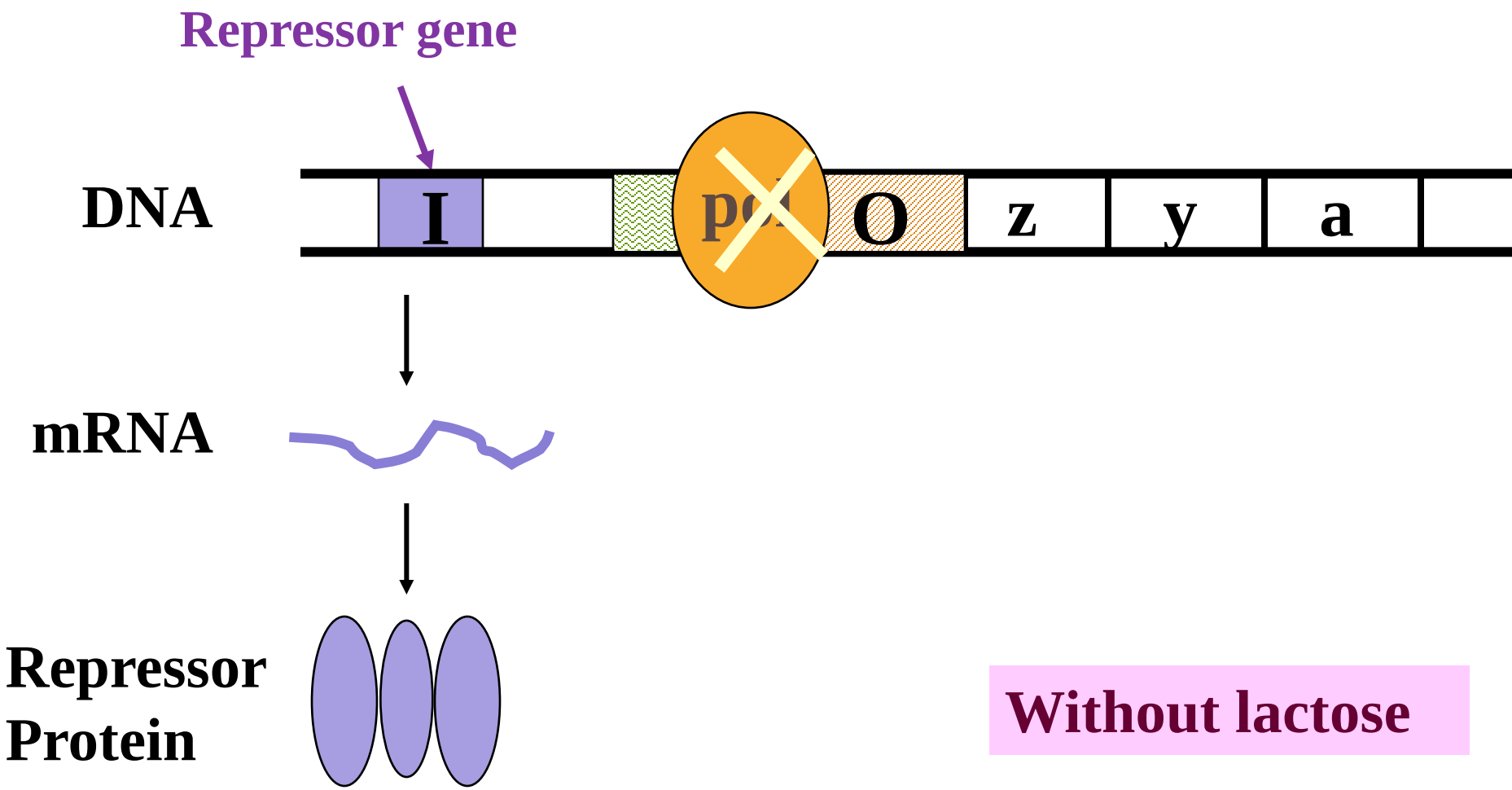
Optimal Promoter



$T_{82}\ T_{84}\ G_{78}\ A_{65}\ C_{54}\ A_{45}$

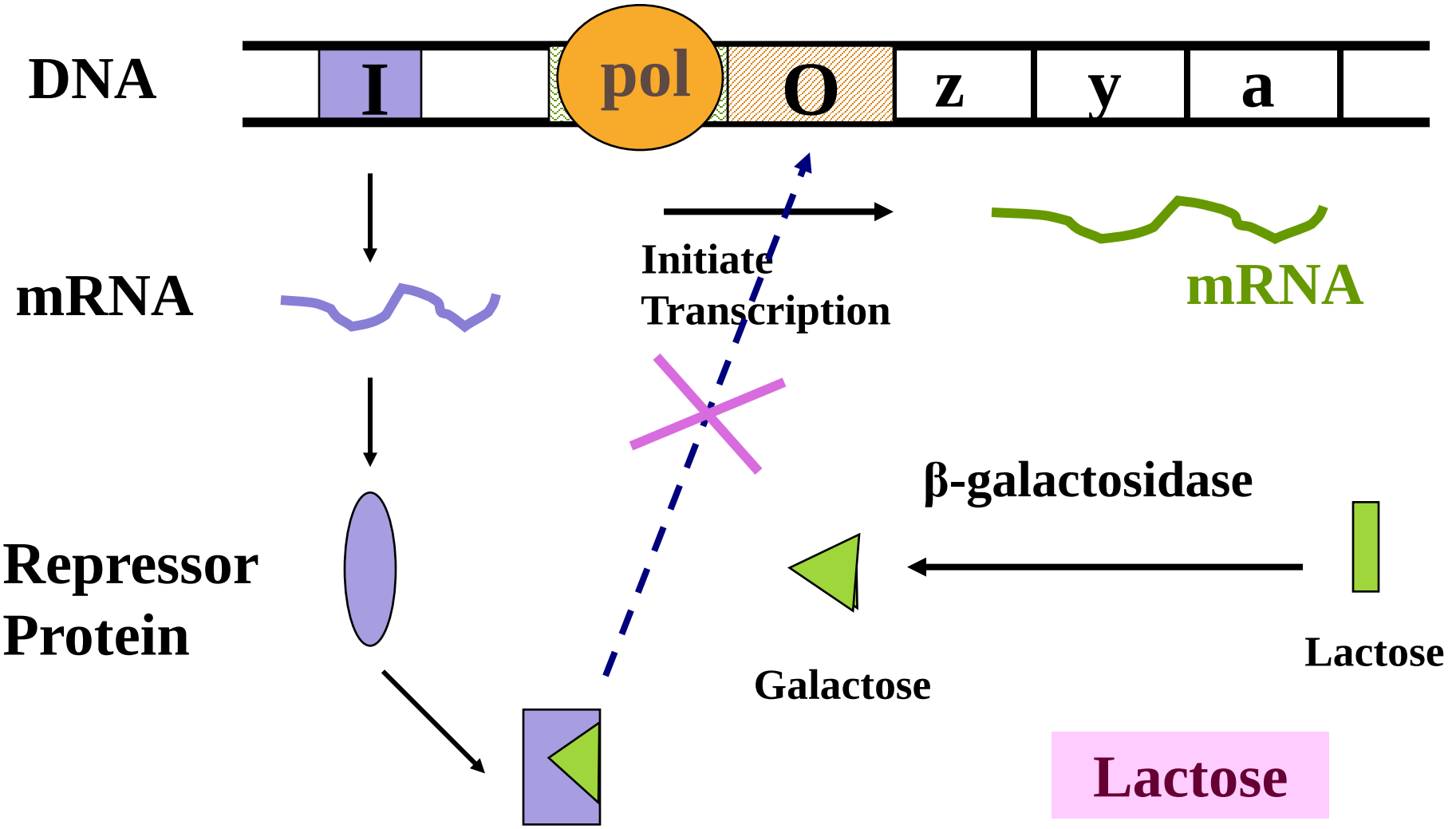
$T_{80}\ A_{95}\ T_{45}\ A_{60}\ A_{50}\ T_{96}$

Lac Operon Is Blocked By Repressor Protein

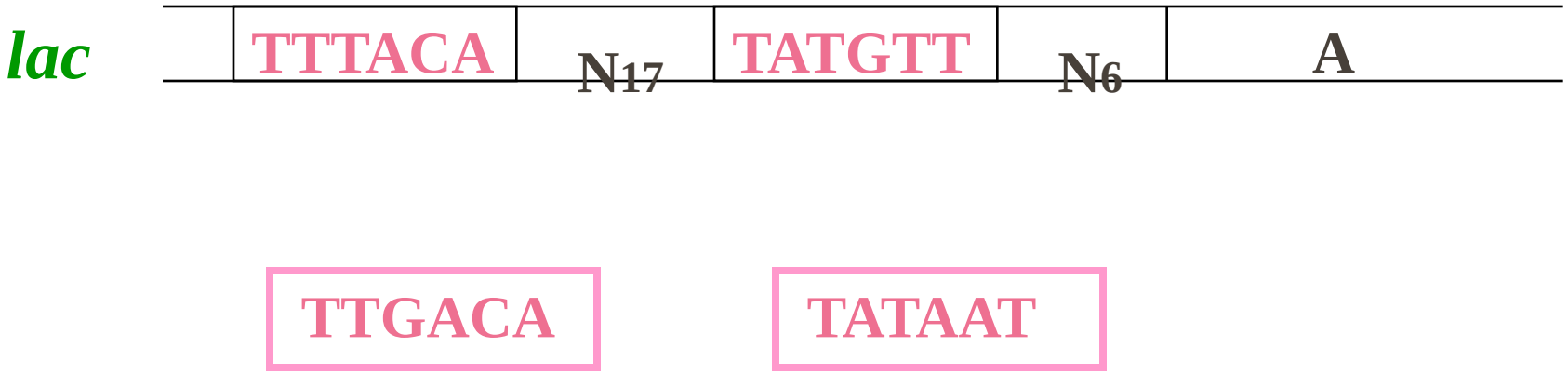


Without lactose

Lactose Operon Opens By Inducer



Lac Operon Is Regulated By cAMP-CAP Positively

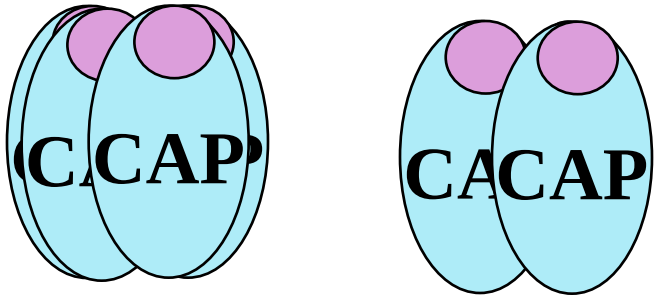


- **Lac operon is weak promoter and activated by AMP-CAP after binding with RNA poly.**

CAP binding site

DNA

+ + + + Transcription

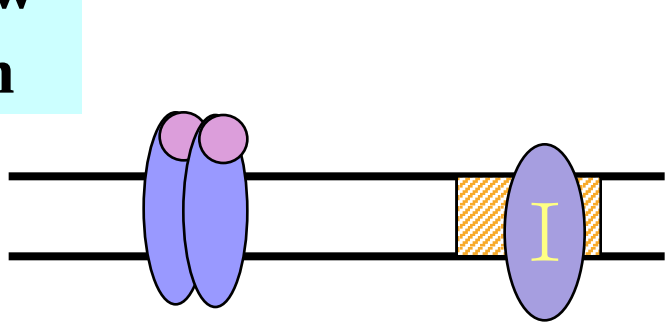


cAMP is high, without glucose

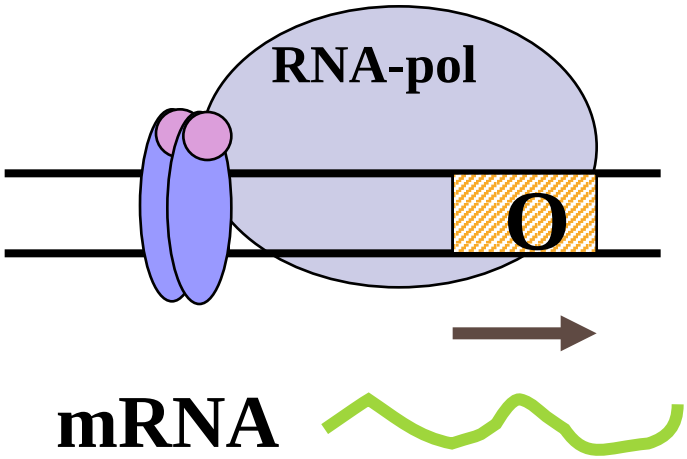
cAMP is low and have glucose

Low galactose | **High galactose**

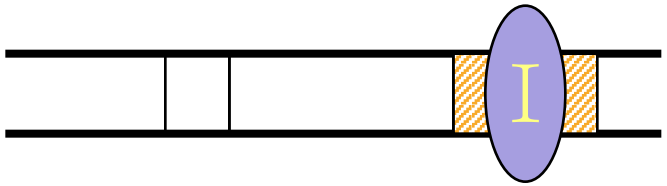
Glucose low
cAMP high



No transcription



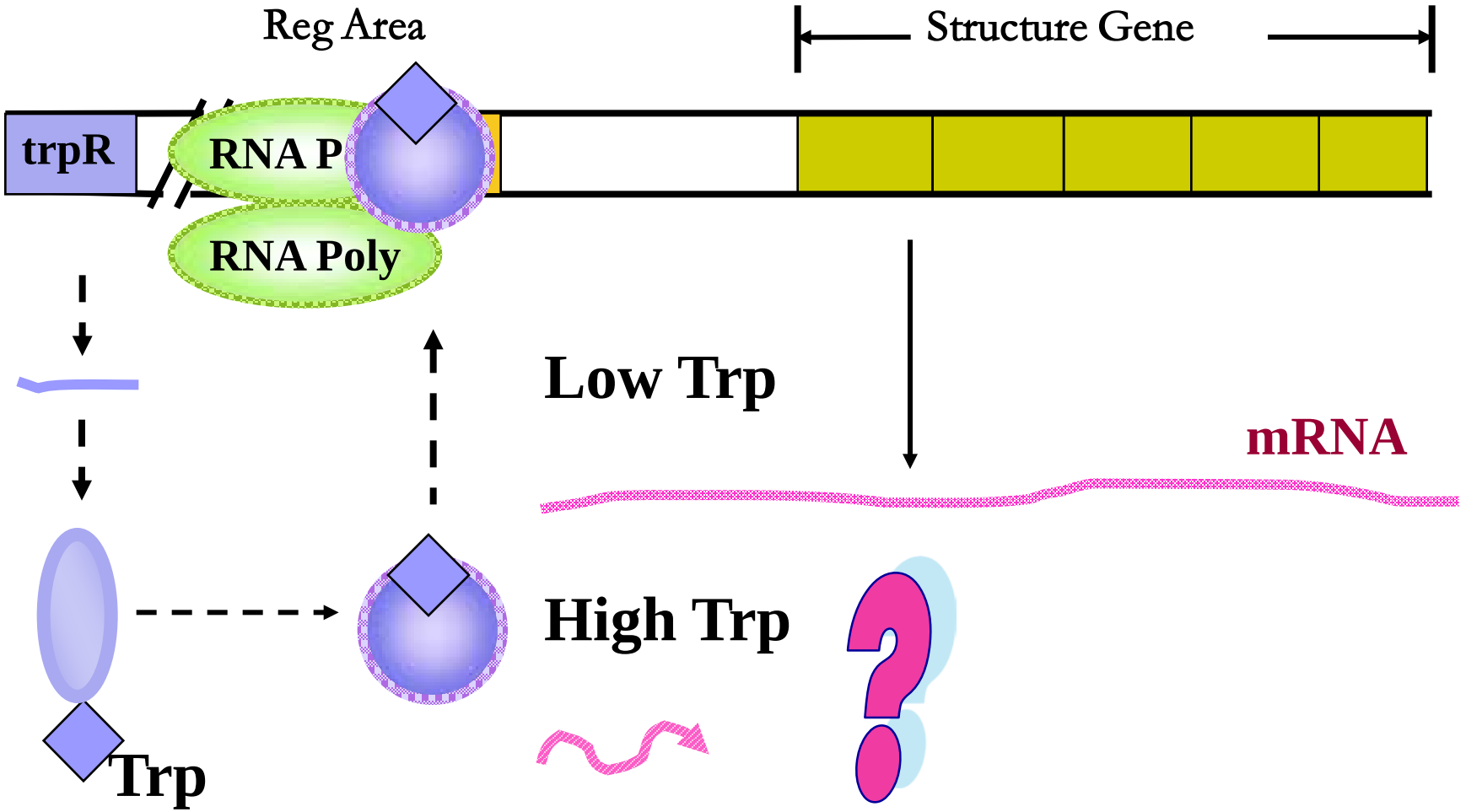
Glucose high
cAMP low



No transcription

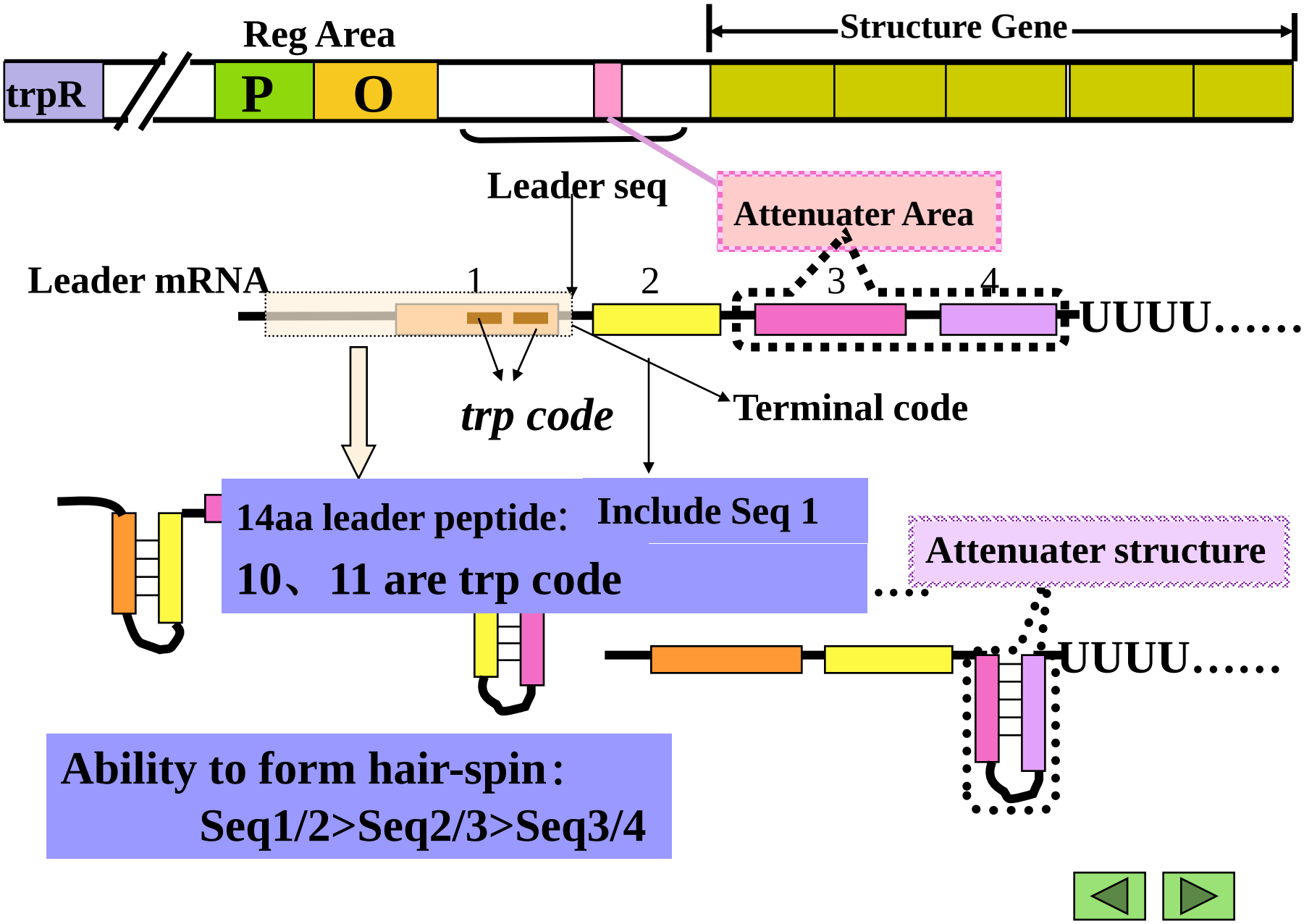
Low transcription

Principal of Trp Operon

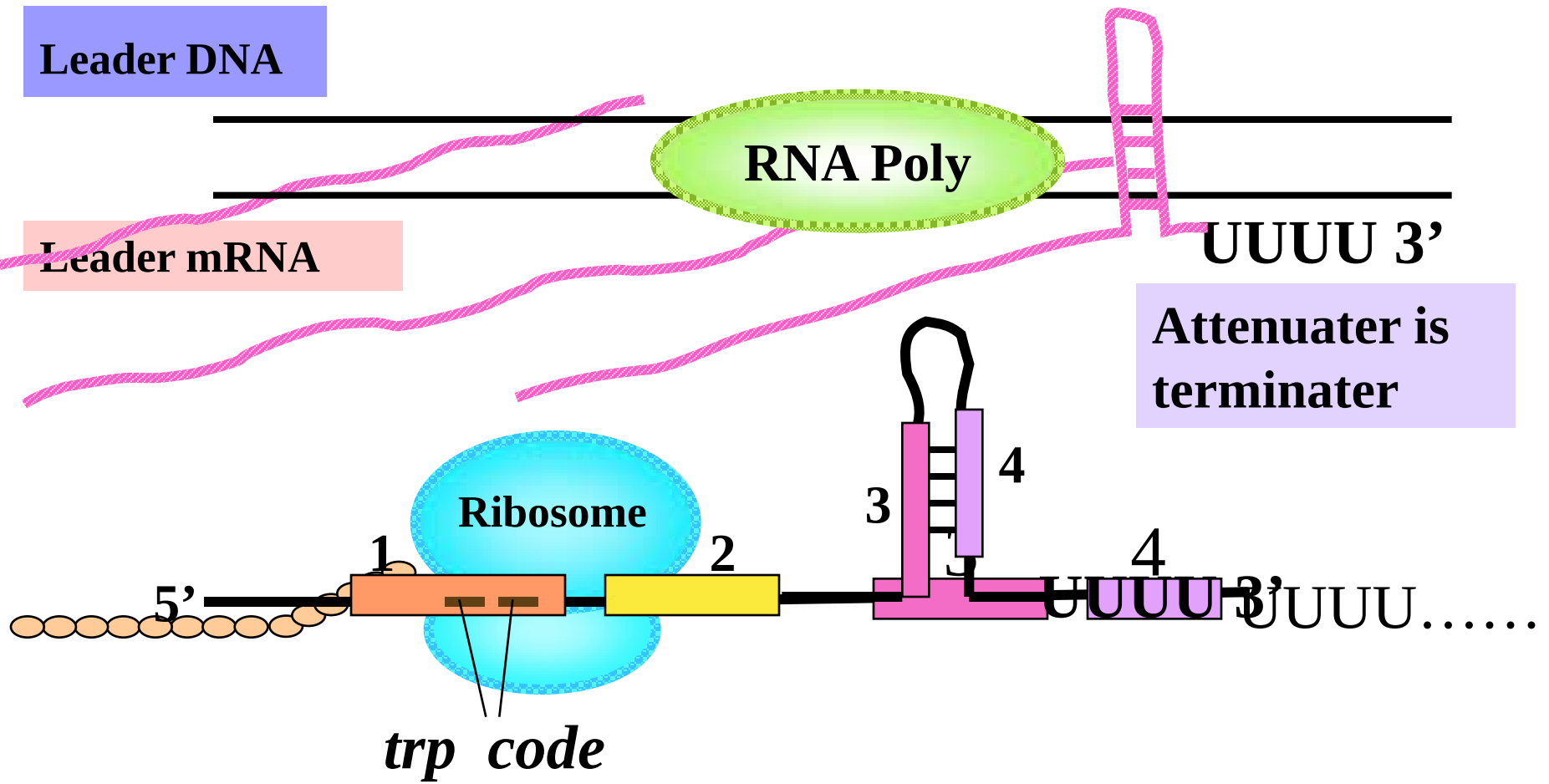


Regulation of translational gene expression in Prokaryotes

原核生物翻译水平的基因表达调控


Reg Area
Structure Gene
trpR
P
O
Leader seq
Attenuater Area
Leader mRNA
1
2
3
4
UUUU……
trp code
Terminal code
14aa leader peptide: Include Seq 1
10、11 are trp code
Attenuater structure
UUUU……
Ability to form hair-spin:
Seq1/2>Seq2/3>Seq3/4

Mechanism of Attenuation



- High Trp

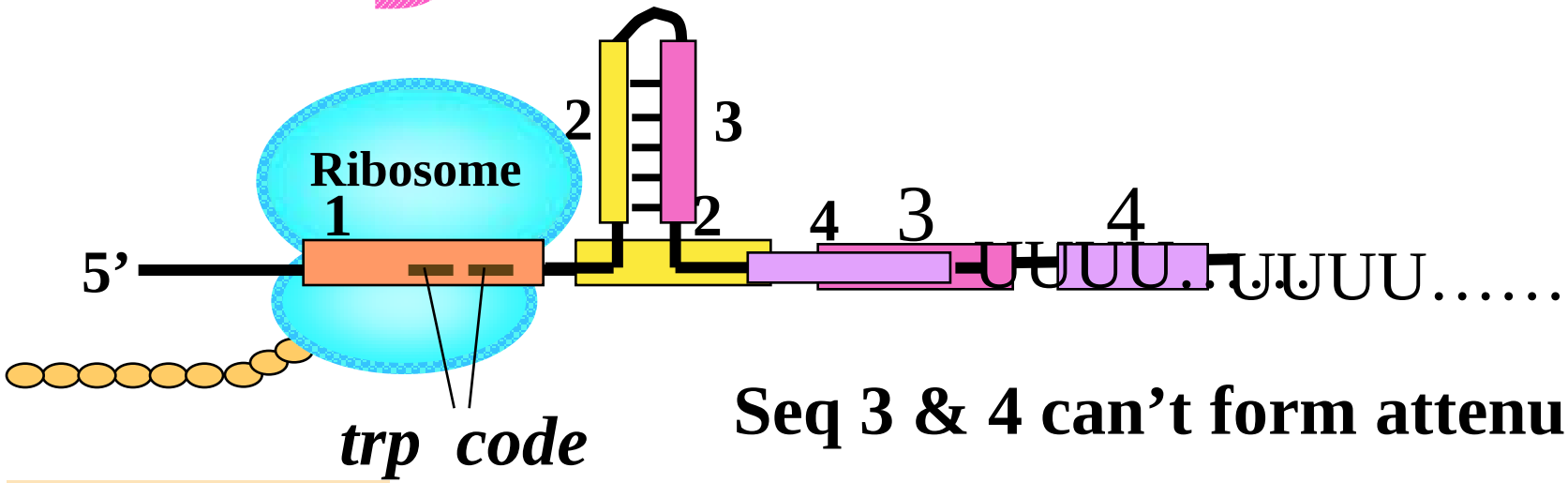
Transcription

Leader DNA

RNA Poly

ucture gene

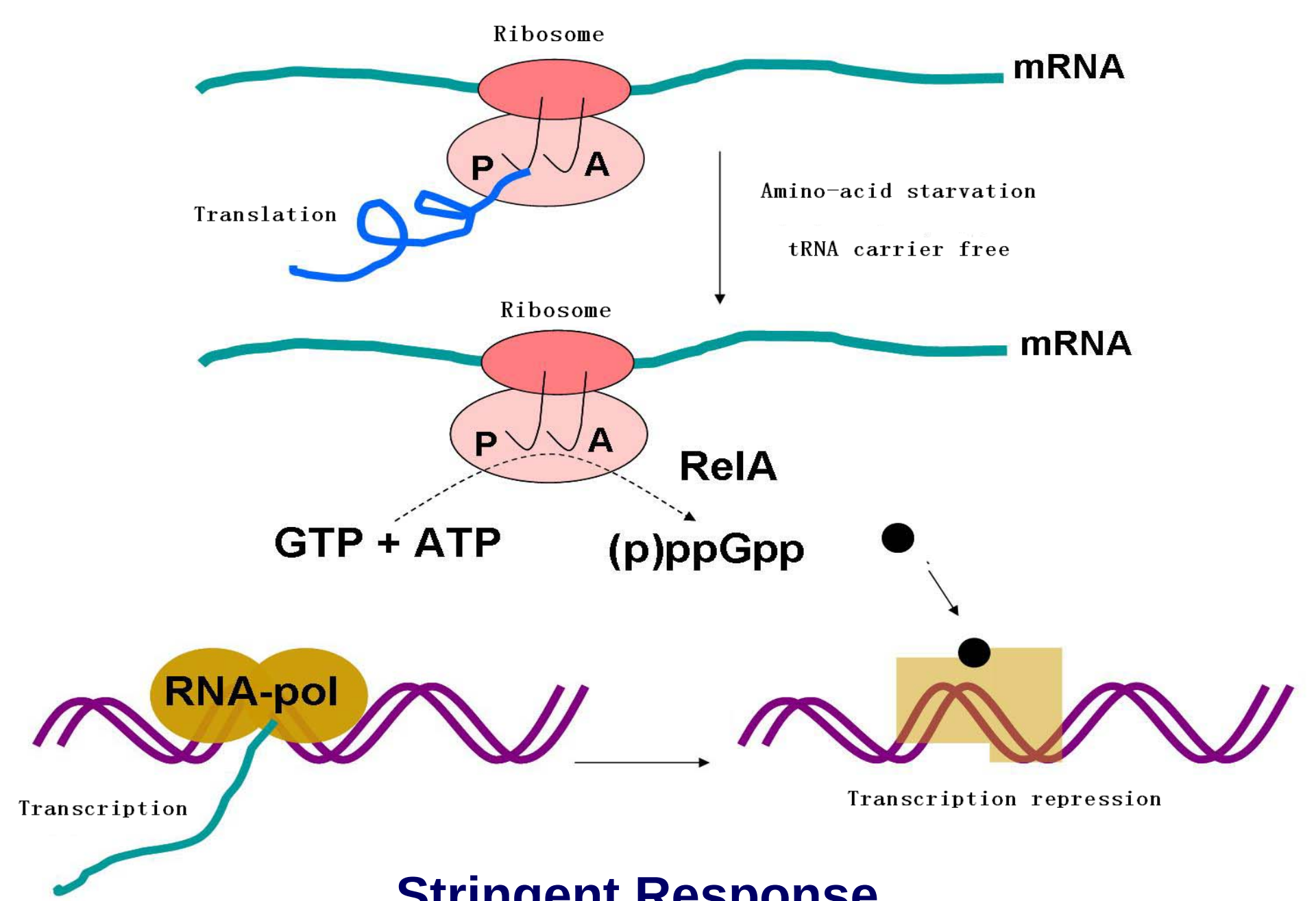
Leader mRNA



Seq 3 & 4 can’t form attenuater

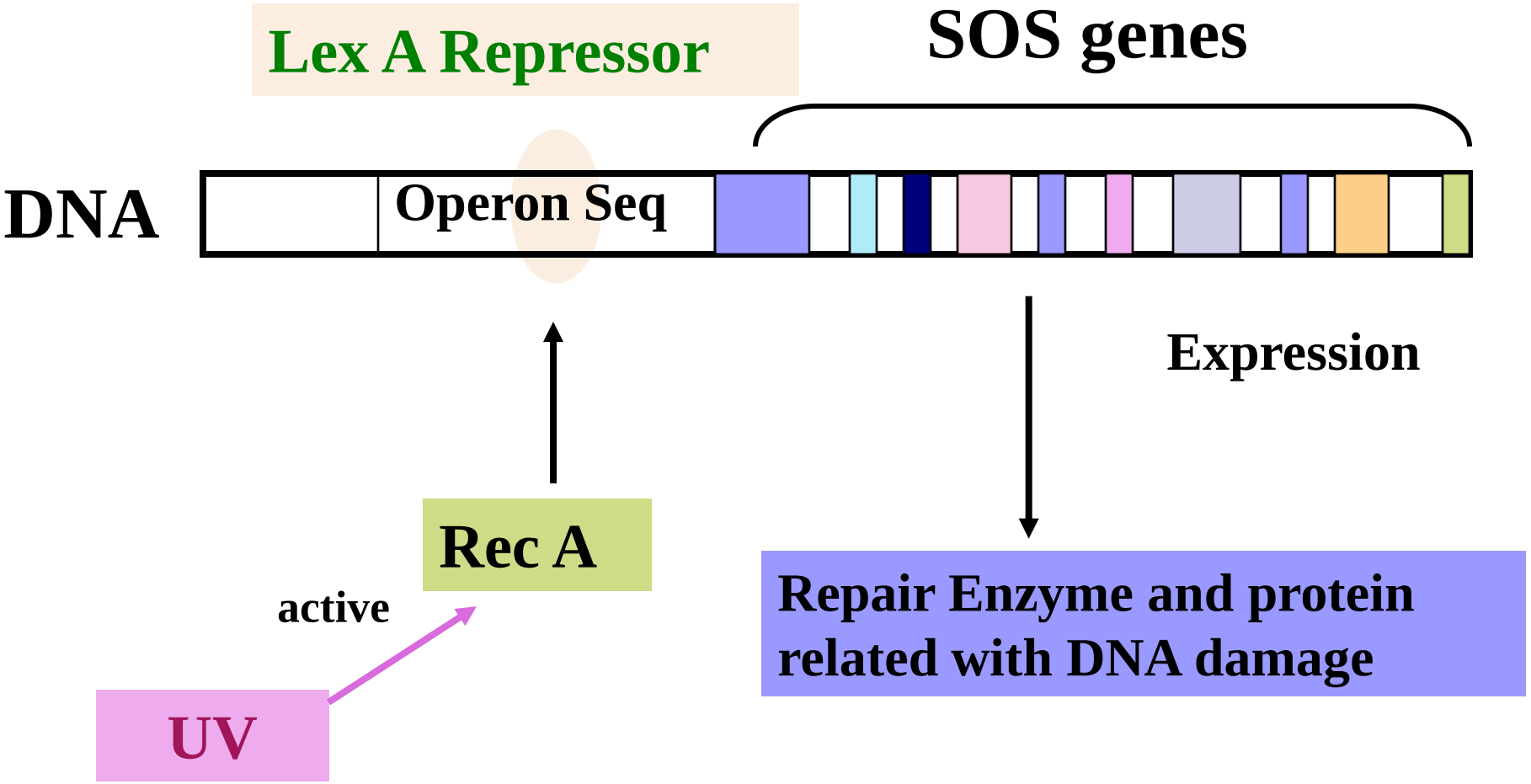
Leader Peptide

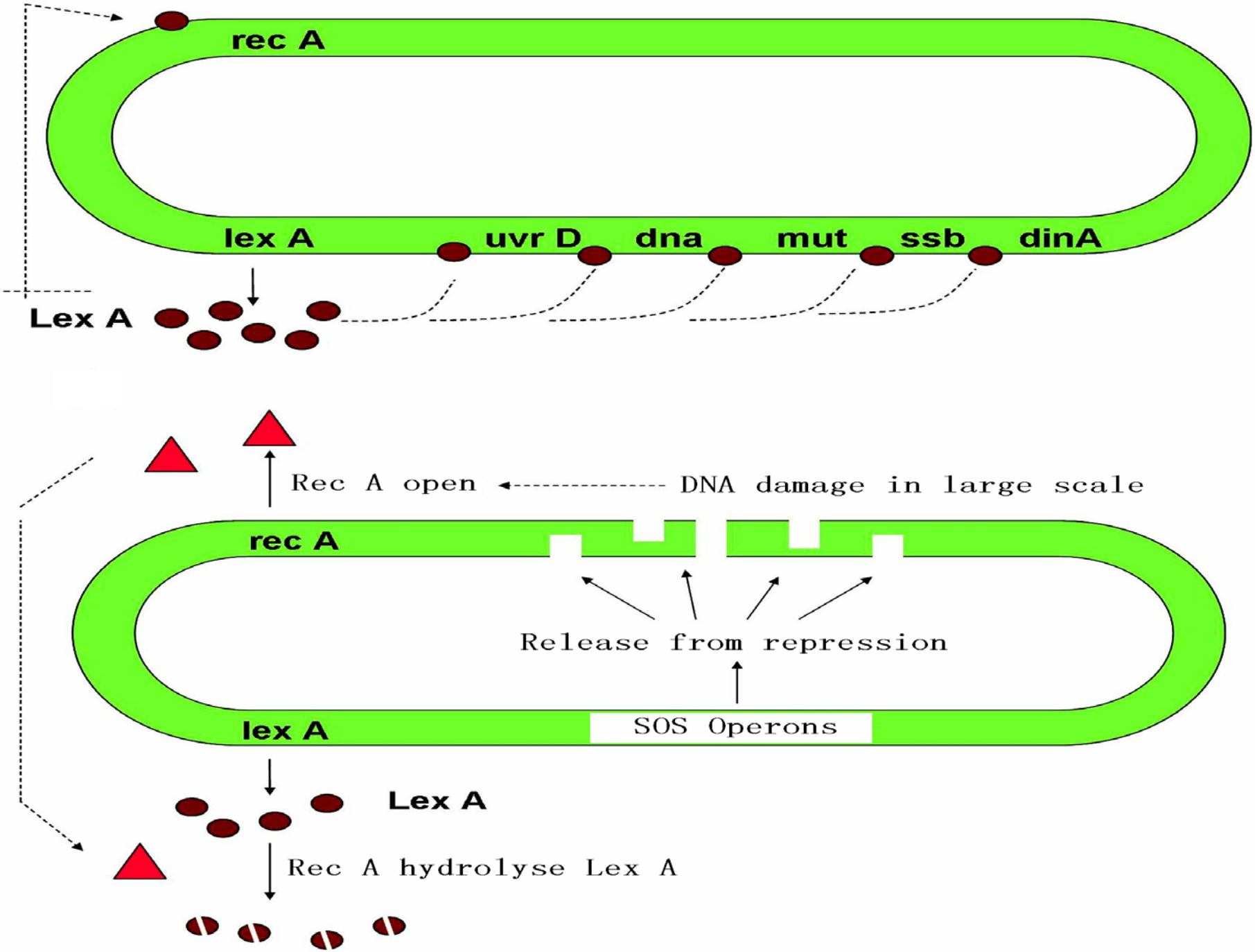
- Low Trp



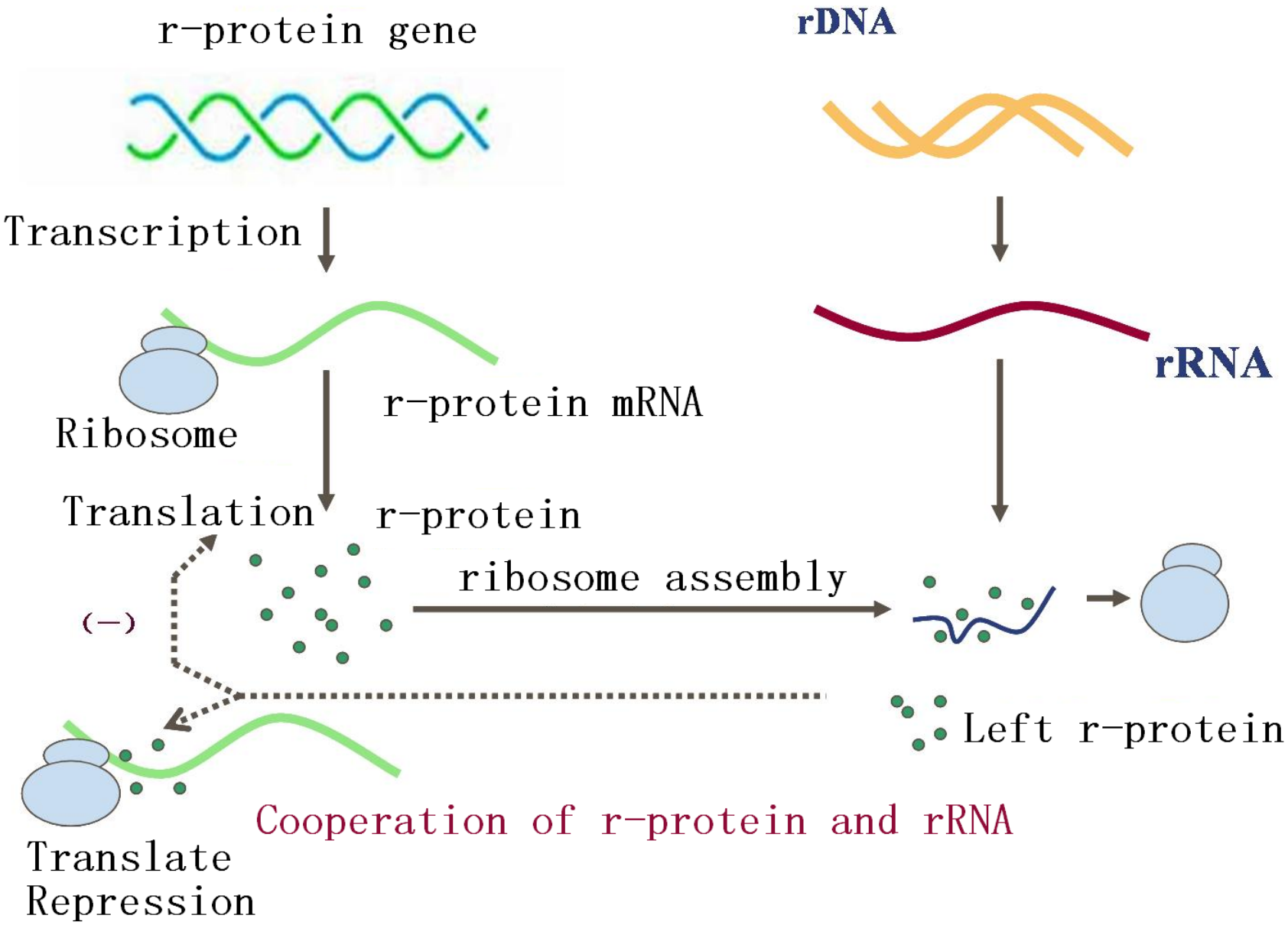
Stringent Response

SOS Regulon


Lex A Repressor
SOS genes
DNA
Operon Seq
Expression
Rec A
active
UV
Repair Enzyme and protein related with DNA damage

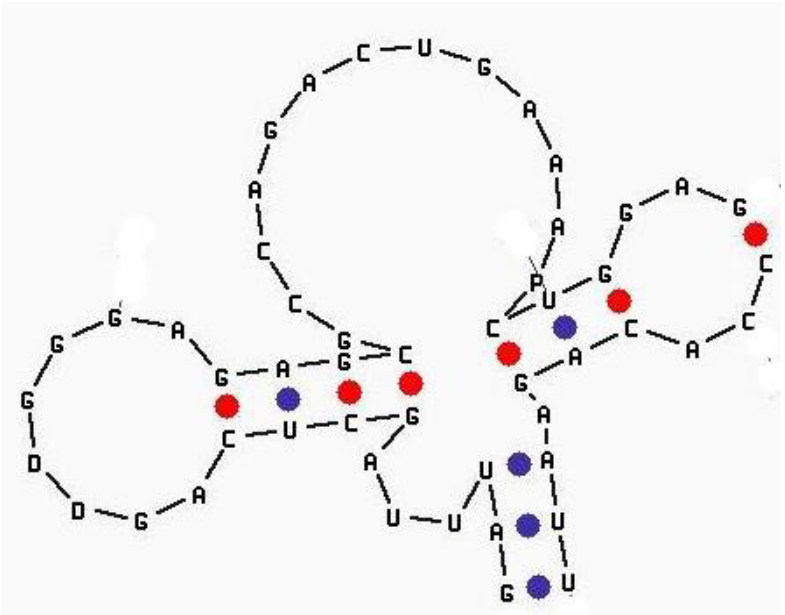

rec A
lex A
uvr D
dna
mut
ssb
dinA
Lex A
Rec A open
DNA damage in large scale
rec A
Release from repression
lex A
SOS Operons
Lex A
Rec A hydrolyse Lex A

Autogenous Control of Ribosome Protein and rRNA

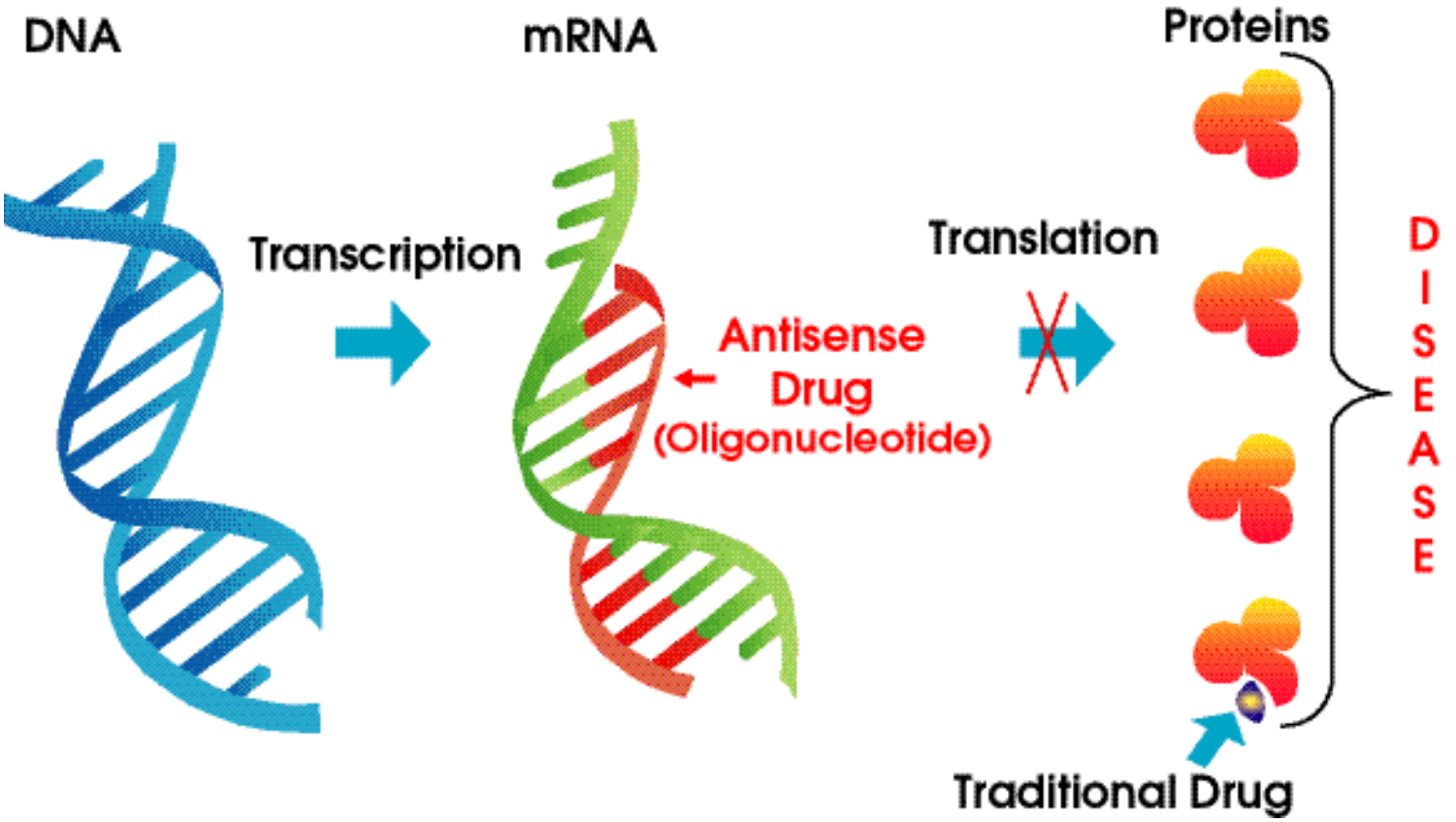


mRNA stability is one type of gene regulation

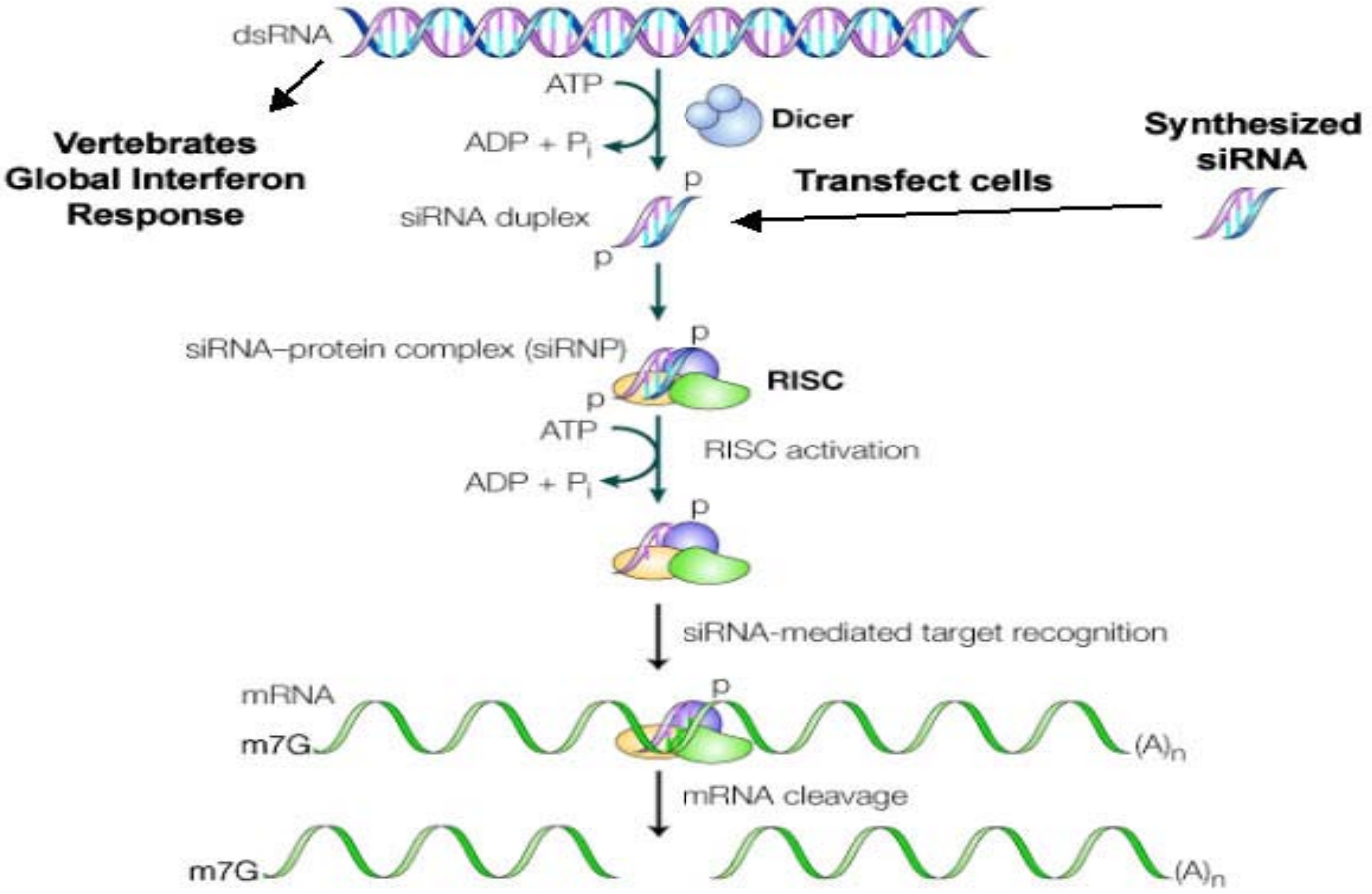
- **Hair-pin of mRNA has anti-RNase ability**
- **Protect proteins bind RNA in cells**
- **Small RNA in vivo and in vitro**



Antisense RNA



Interfering RNA, RNAi



Regulation of gene expression in Lambda phage

Lambda 噬菌体的基因表达调控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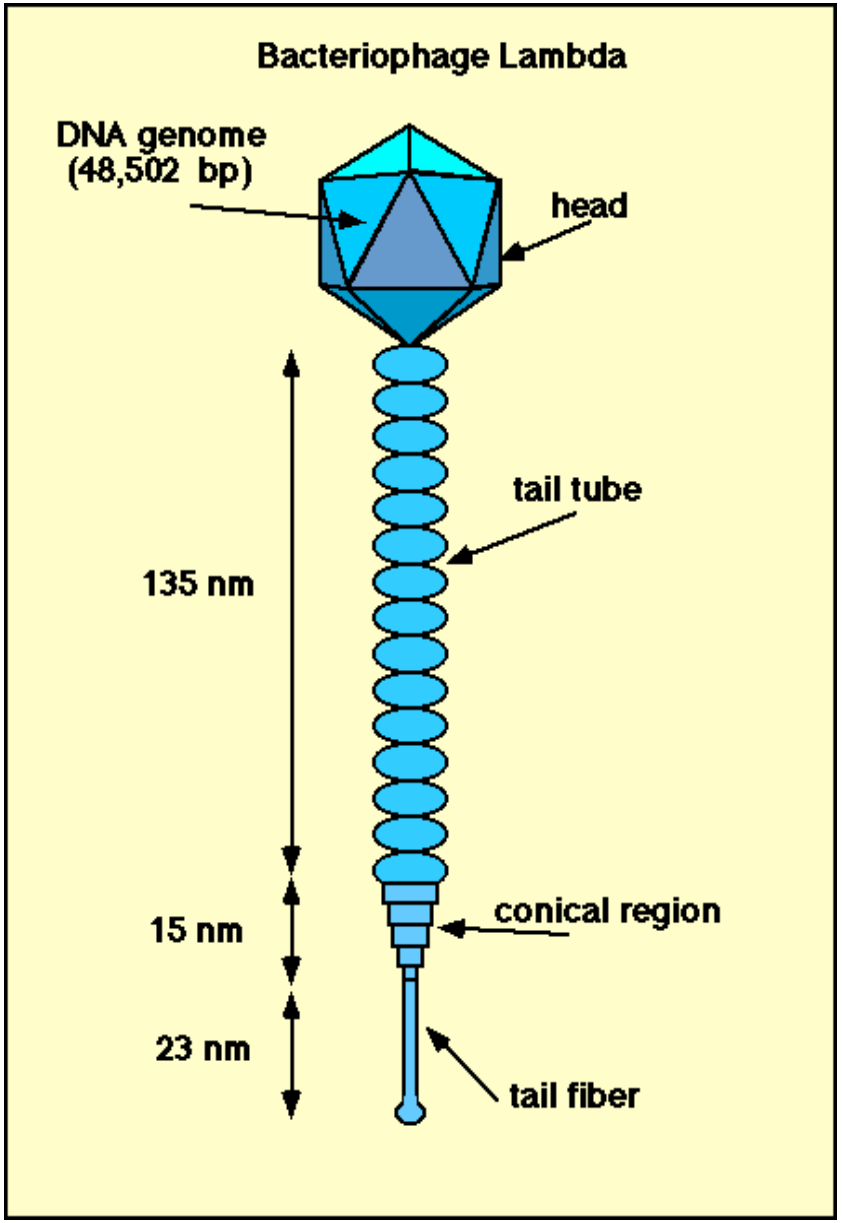
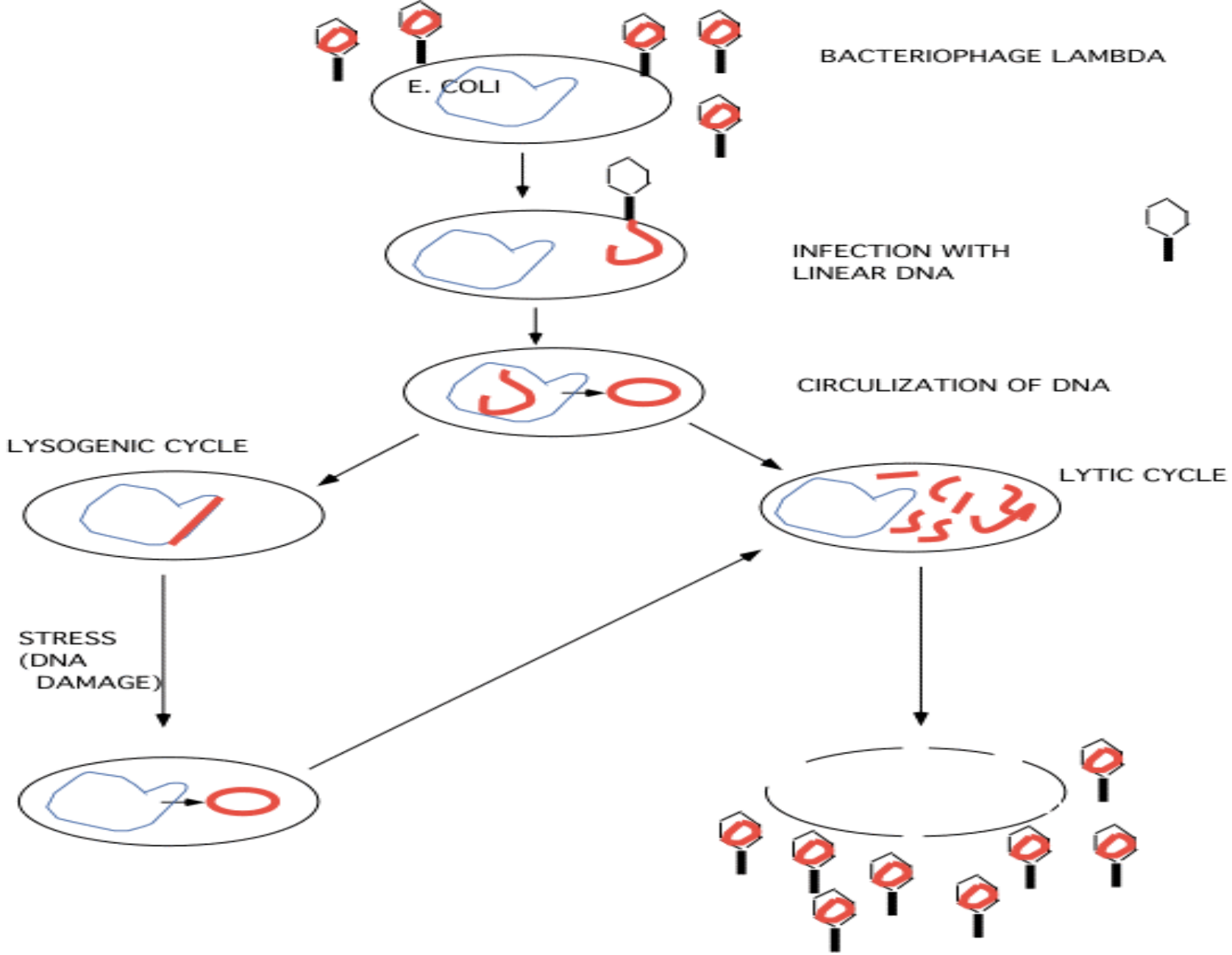
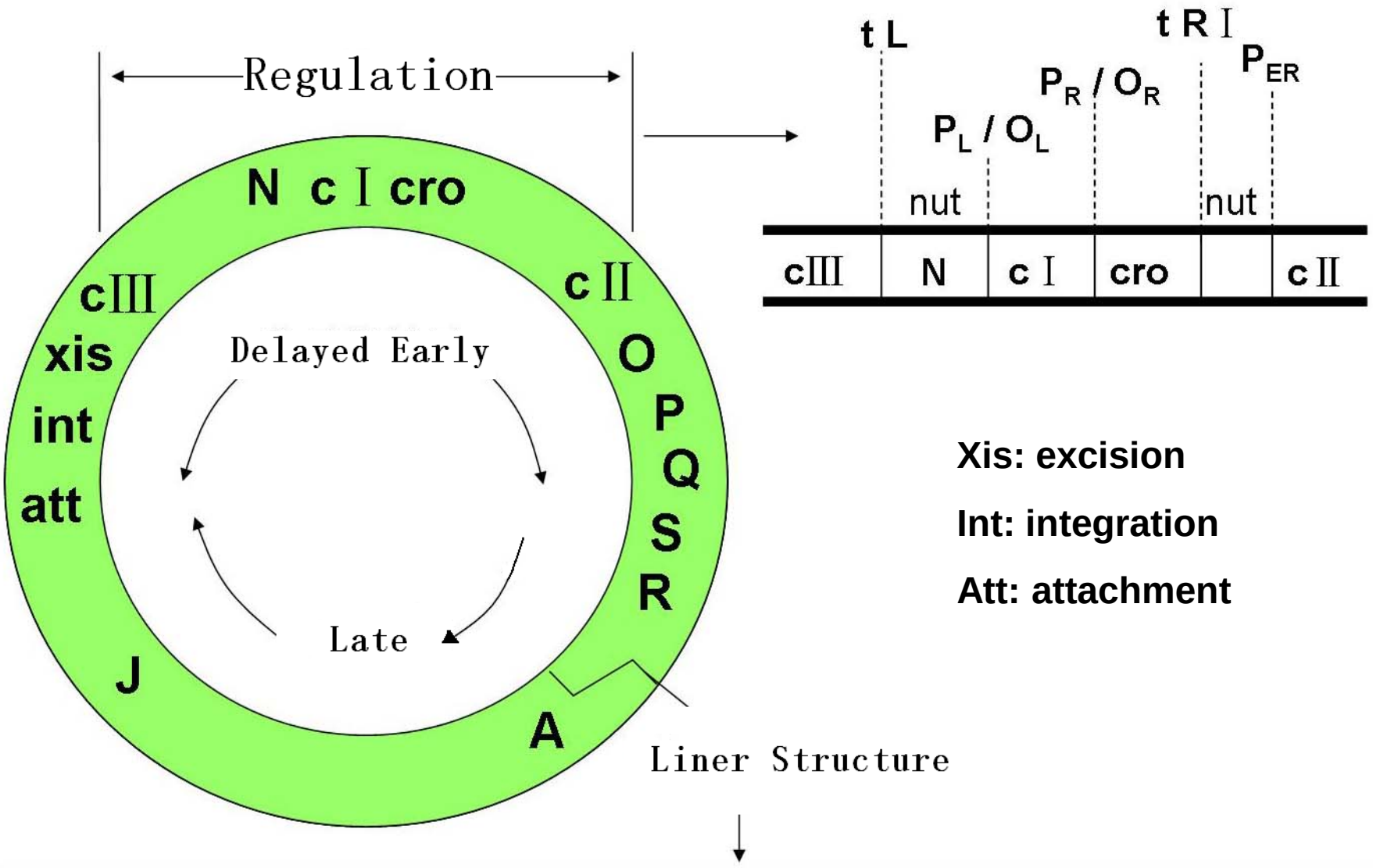
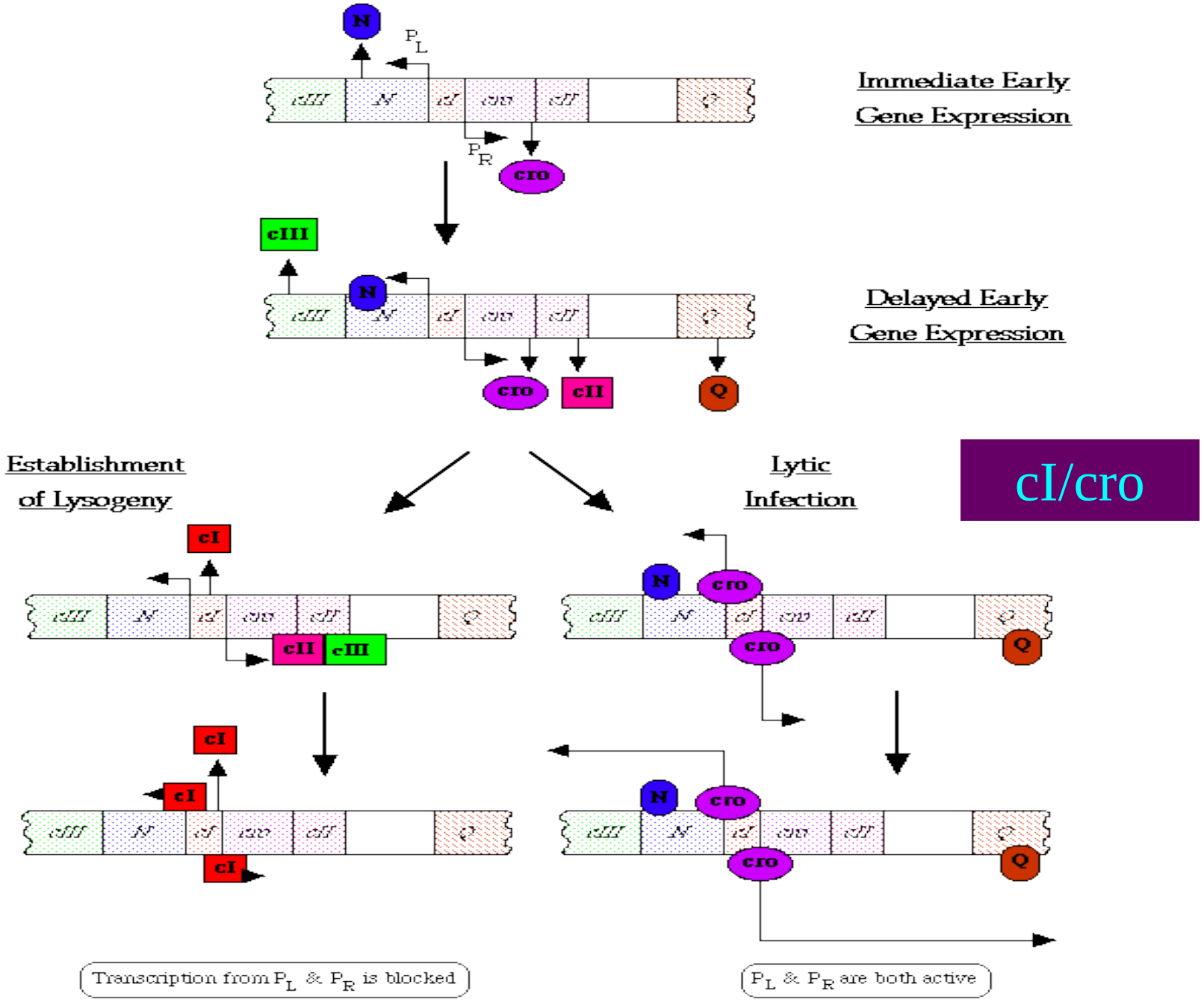
http://www.scripps.edu/mb/goodsell

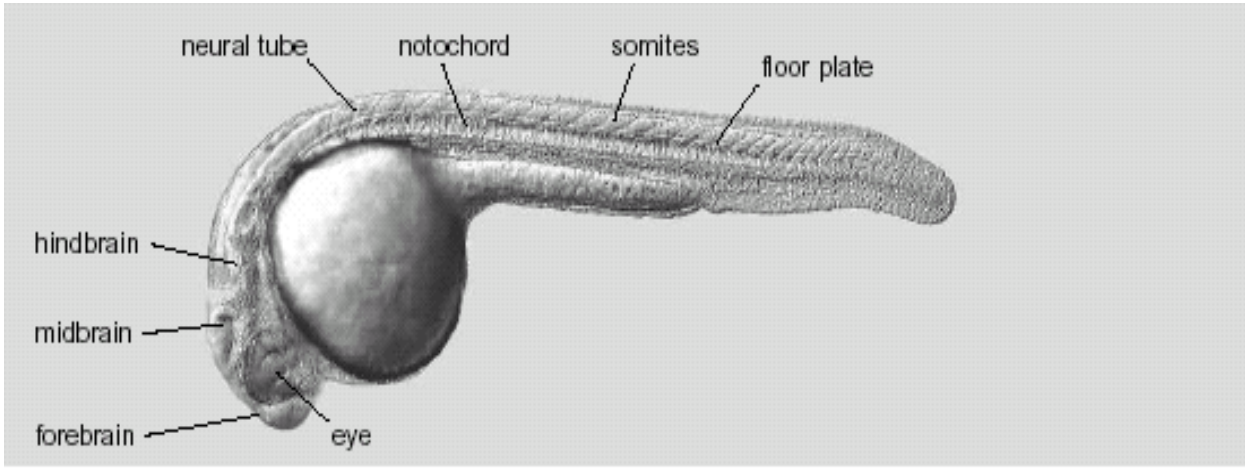

Bacteriophage Lambda
DNA genome
(48,502 bp)
head
tail tube
135 nm
15 nm
conical region
23 nm
tail fiber


BACTERIOPHAGE LAMBDA
E. COLI
INFECTION WITH
LINEAR DNA
CIRCULIZATION OF DNA
LYSOGENIC CYCLE
LYTIC CYCLE
STRESS
(DNA
DAMAGE)

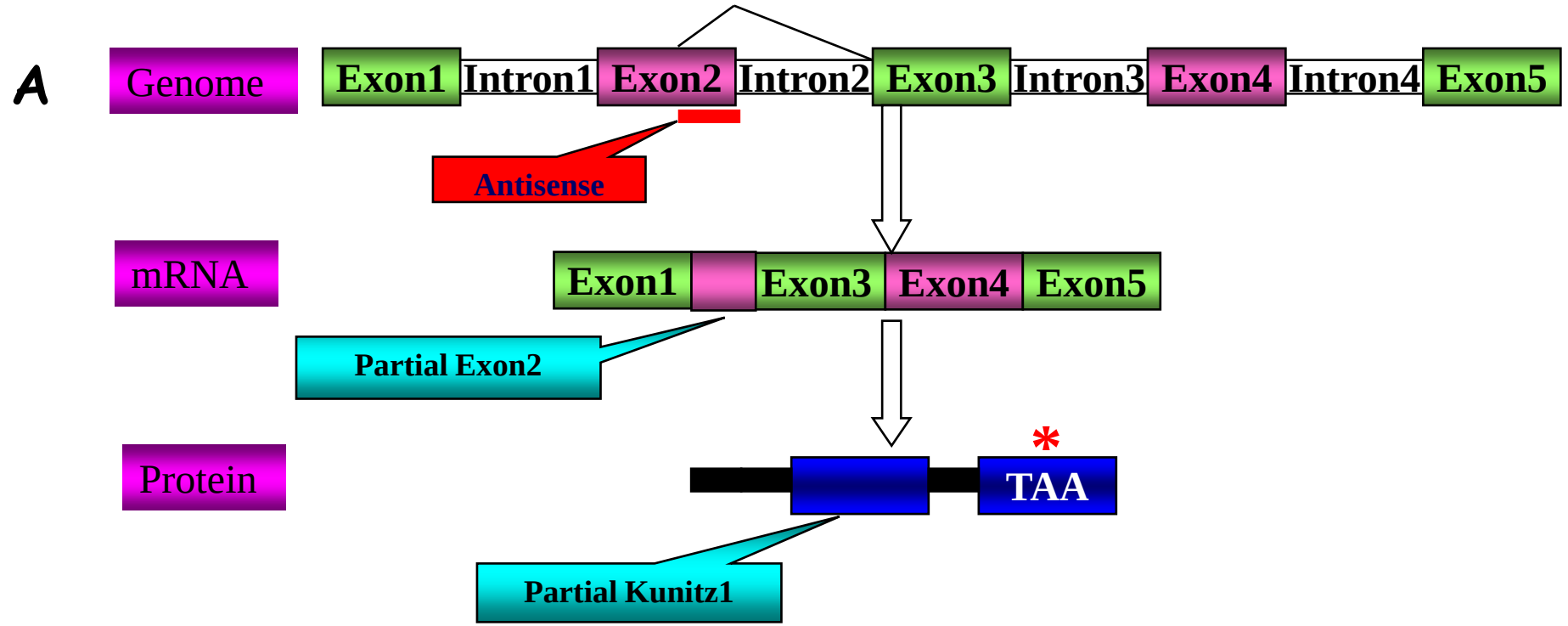

Regulation
N c Ⅰ cro
c Ⅱ
O
P
Q
S
R
A
J
att
int
xis
cⅢ
Delayed Early
Late
t L
t R Ⅰ
P ER
P R / O R
P L / O L
nut
nut
cⅢ
N
c Ⅰ
cro
c Ⅱ
Xis: excision
Int: integration
Att: attachment
Liner Structure
AWBCNuDEFZU VGTHMLKIJ att int xis cⅢ N c Ⅰ cor c Ⅱ O P Q S R
Structure
Recombinant
Regulation
Lysis

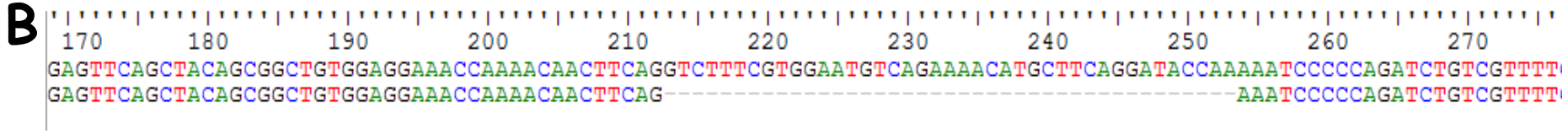

N
P L
P R
cro
Immediate Early
Gene Expression
cIII
N
cro
cII
Q
Delayed Early
Gene Expression
Establishment
of Lysogeny
Lytic
Infection
cI/cro
cI
cII
cIII
cI
cI
cI
N
cro
cro
Q
N
cro
cro
Q
Transcription from P L & P R is blocked
P L & P R are both active

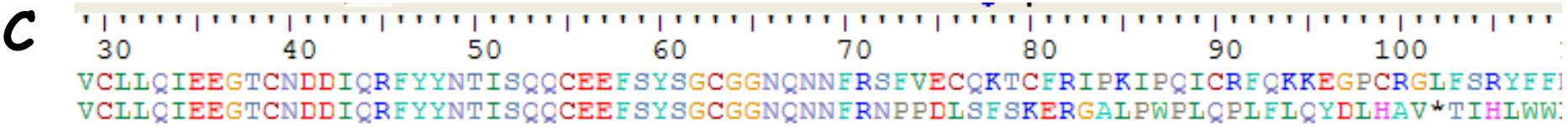

WT

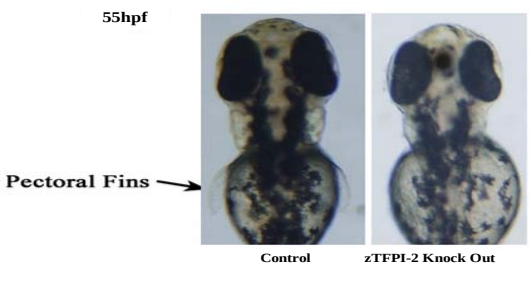

neural tube
notochord
somites
floor plate
hindbrain
midbrain
forebrain
eye

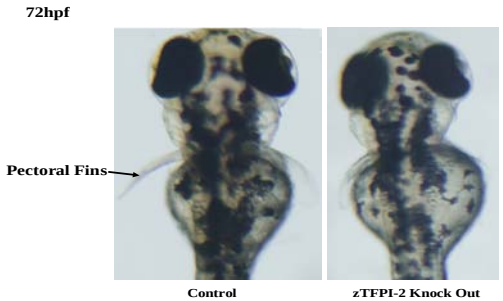

Zebrafish
Human
Mus
Pan
Rat
Bovine
1
61
121
181

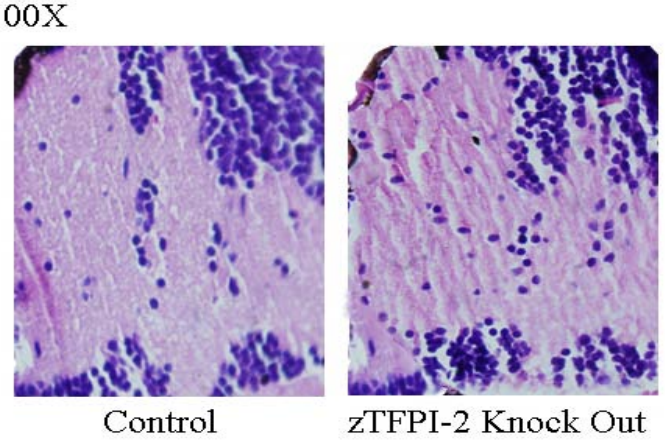

A
Genome
Exon1
Intron1
Exon2
Intron2
Exon3
Intron3
Exon4
Intron4
Exon5
Antisense
mRNA
Exon1
Exon3
Exon4
Exon5
Partial Exon2
Protein
*
TAA
Partial Kunitz1

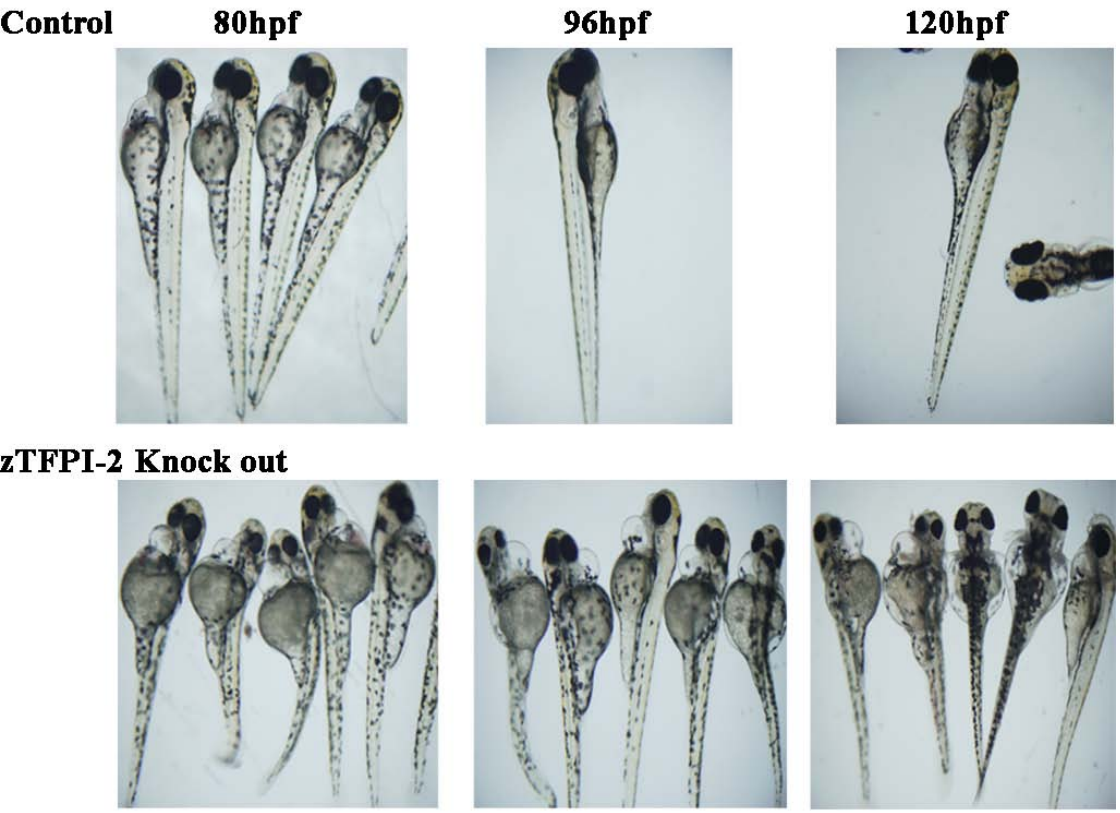

B
170
180
190
200
210
220
230
240
250
260
270
GAGTTCAGCTACAGCGGCTGTGGAGGAAACCAAAACAACTTCAGGTCTTTCGTGGAATGTCAGAAAACATGCTTCAGGATACCAAAAATCCCCCAGATCTGTCGTTTT
GAGTTCAGCTACAGCGGCTGTGGAGGAAACCAAAACAACTTCAG----------AAATCCCCCAGATCTGTCGTTTT

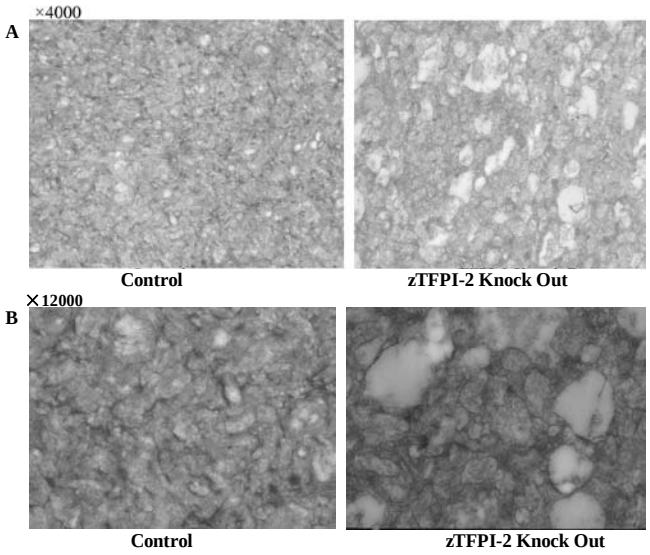

C
30
40
50
60
70
80
90
100
VCLLQIEEGTCNDDIQRFYYNTISQQCEEFSYSGCGGNQNNFRSFVECQKTCFRIPKIPQICRFQKKEGPCRGLFSRYFF
VCLLQIEEGTCNDDIQRFYYNTISQQCEEFSYSGCGGNQNNFRNPPDLSFSKERGALPWPLQPLFLQYDLHAV*TIHLWW

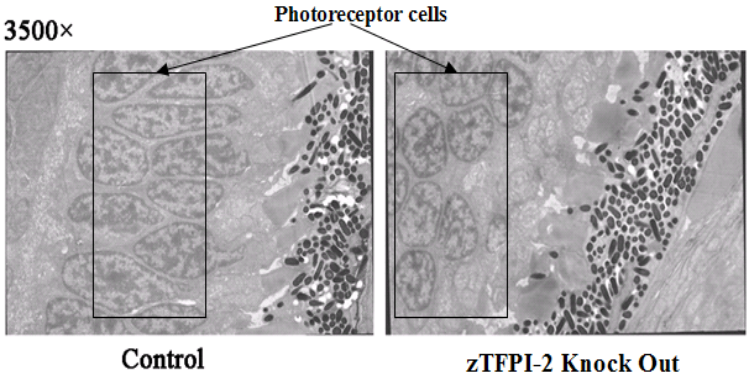

55hpf
Pectoral Fins
Control
zTFPI-2 Knock Out


72hpf
Pectoral Fins
Control
zTFPI-2 Knock Out

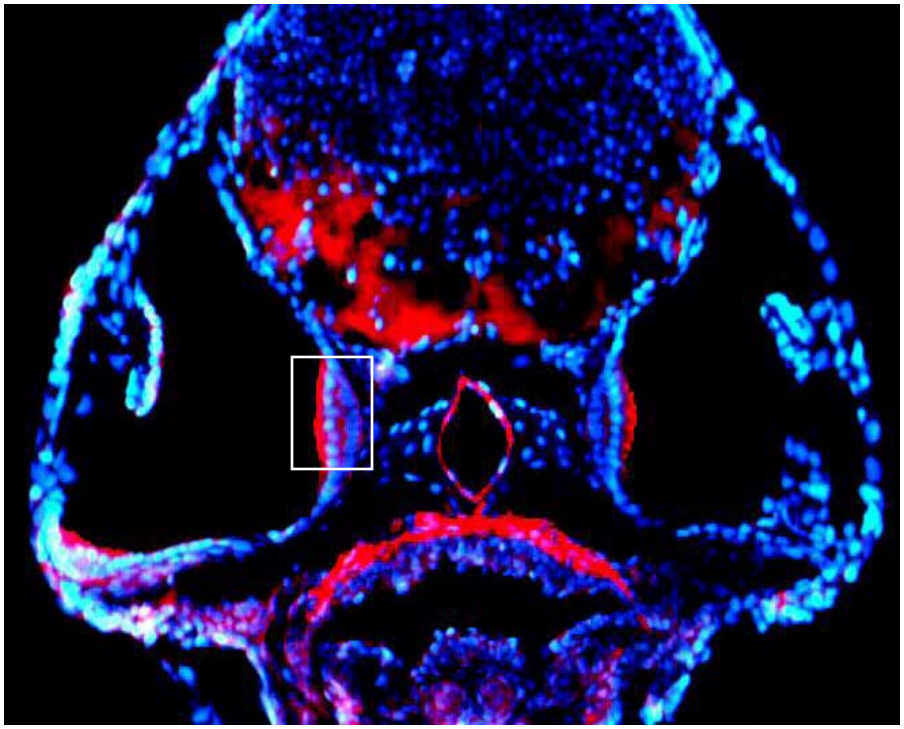

100X
Control
zTFPI-2 Knock Out


Control
80hpf
96hpf
120hpf
zTFPI-2 Knock out

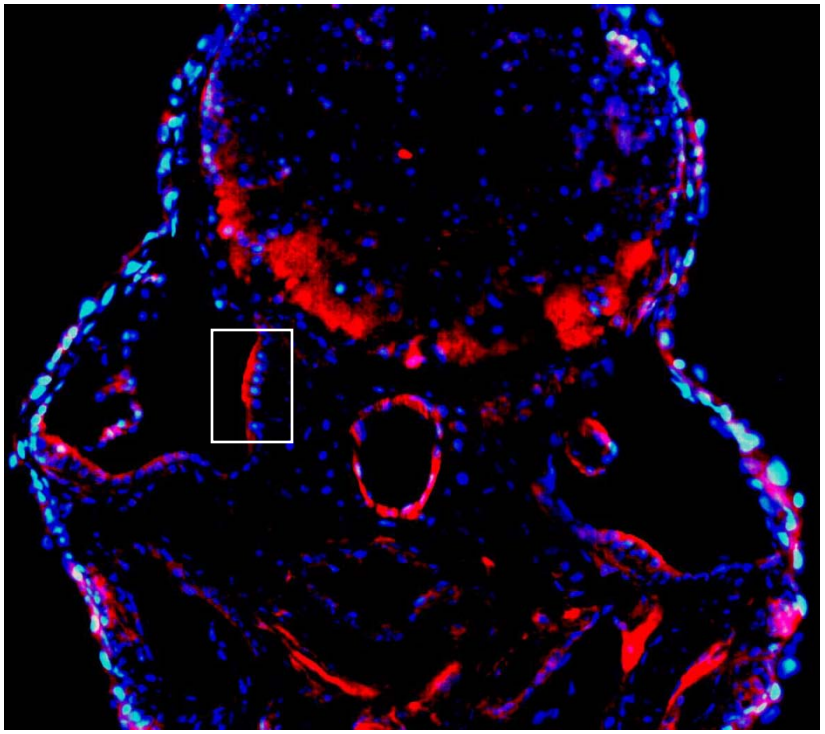

A
×4000
Control
zTFPI-2 Knock Out
B
×12000
Control
zTFPI-2 Knock Out


3500×
Photoreceptor cells
Control
zTFPI-2 Knock Out

Control



zTFPI-2 knock down

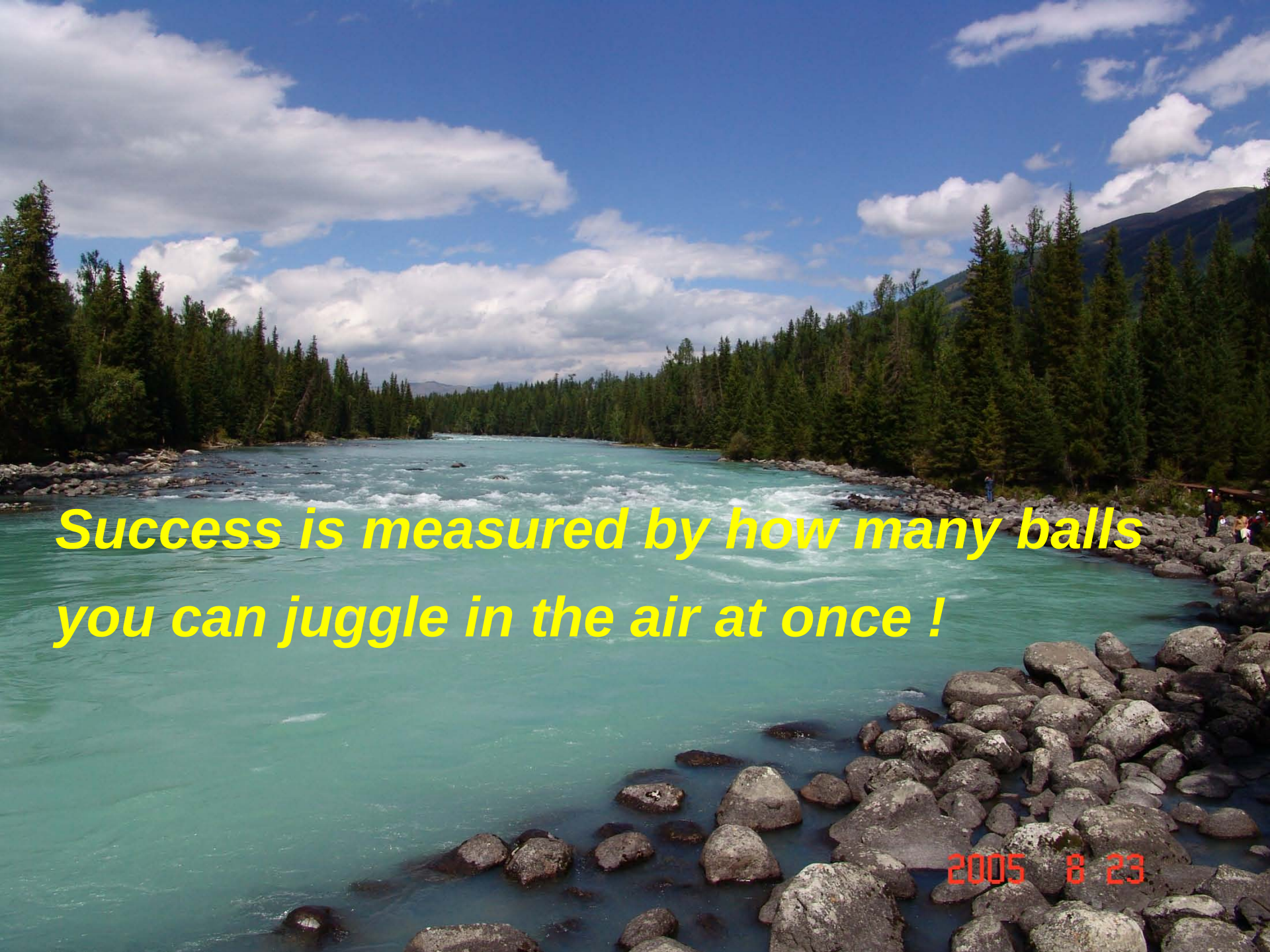


Summary

- Some deffination and basic conception of gene expression in prokaryotes.
- Lac operon
- Trp operon
- miRNA
- Lamda phage

Reference

- **Gene VIII**
- 生物学前沿技术在医学研究中的应用


Success is measured by how many balls you can juggle in the air at once !
2005 8 23