# Regulation of Gene Expression

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# Regulation of Gene Expression

- Regulation of transcription or gene expression is achieved by the functions of various operons which is a functioning unit of DNA containing a cluster of genes under the control of a single promoter.
- Presence of Operon allows protein synthesis to be controlled coordinately in response to the needs of the cells.
- There are two types of operon in prokaryotes, which are:

  - ✓ **Lac operon**
  - ✓ **Trp Operon**

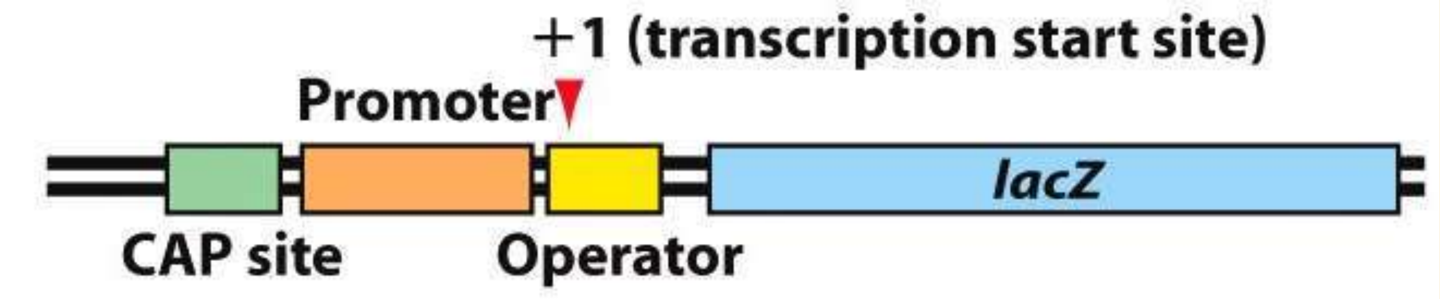
- Another mode of regulation of gene expression is:

  - ✓ **Gln regulation by NTRC –** Enhancer function

# Regulation of Gene Expression – *lac* operon

## ***E. coli lac* Operon**

- It encodes 3 genes (*lac ZYA*) involved in lactose metabolism.
- In this model, a specific repressor protein (*lac* repressor) inhibits transcription from the *lac* promoter by binding to an adjacent DNA sequence known as the *lac* operator in the absence of lactose.
- A general activator protein known as catabolite activator protein (CAP) binds to a site immediately upstream of the promoter, stimulating transcription. However the binding of CAP to its site requires the co-activator, cAMP, the concentration of which is low in glucose-containing medium.

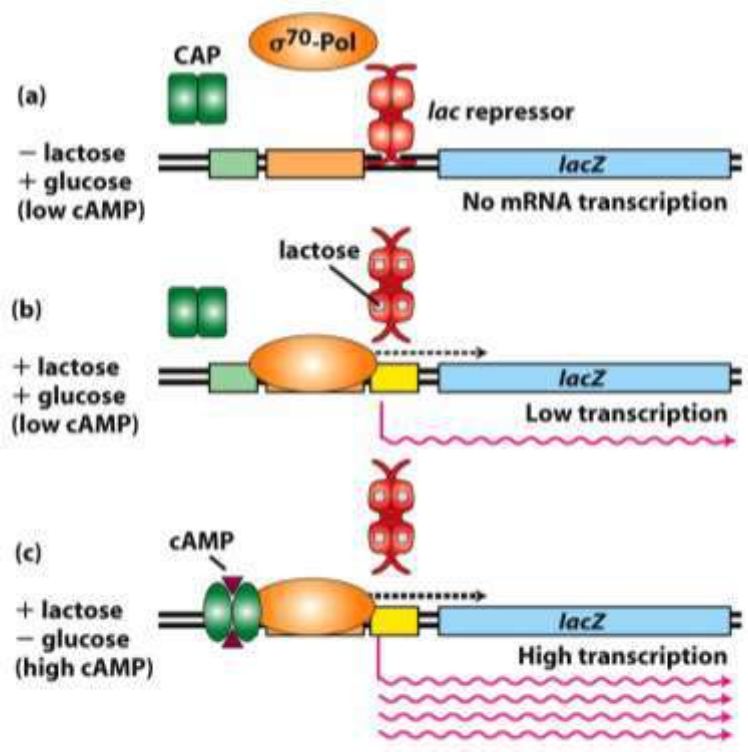



*E. coli* lac transcription-control regions

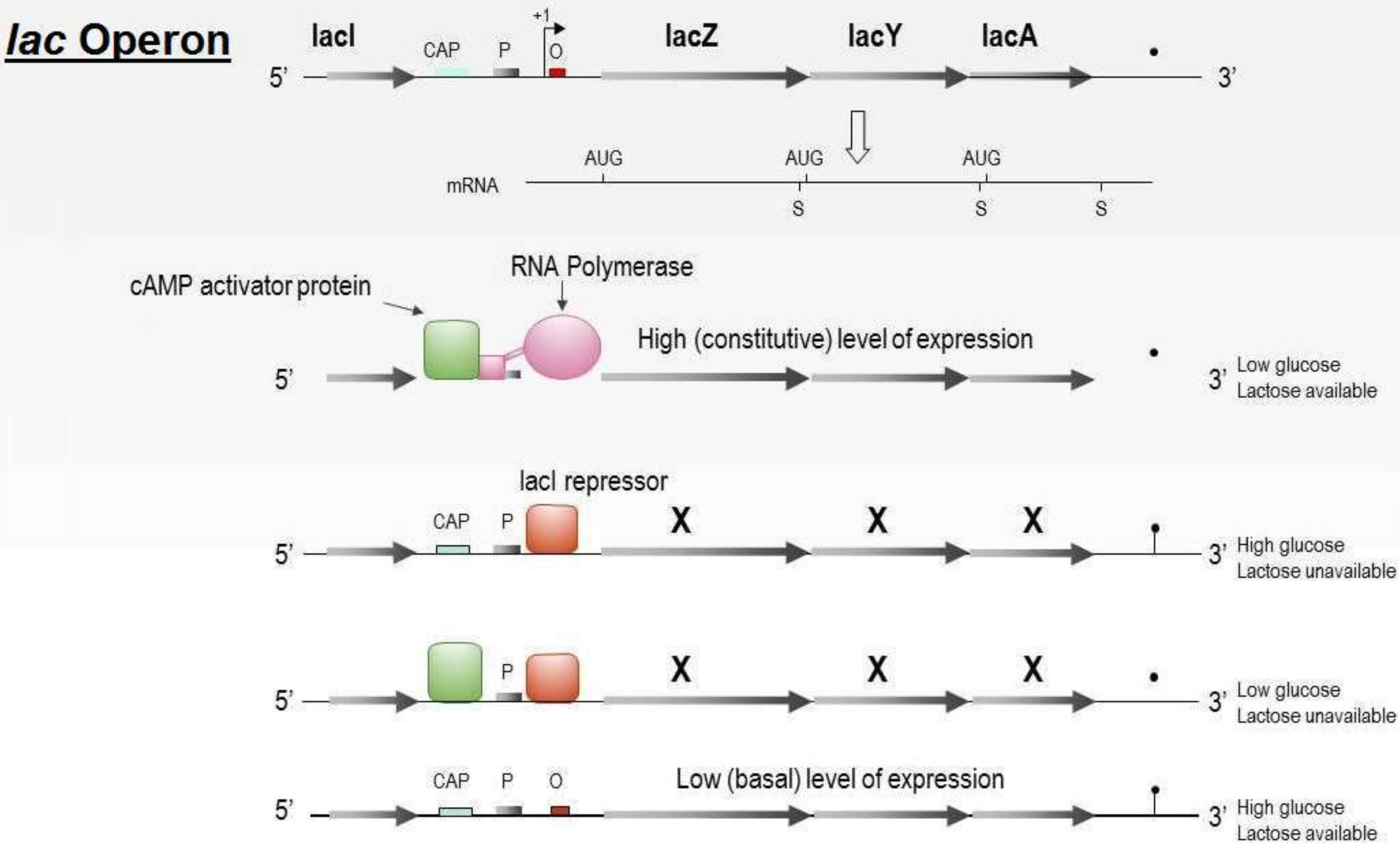
# Regulation of Gene Expression – *lac* operon

## ***E. coli lac*** **Operon**

- In the presence of glucose and absence of lactose, the transcription of the *lac* operon is repressed. The lac repressor is bound to the *lac* operator, while CAP is not bound to its control site due to low level of cAMP.
- The addition of inducer 'lactose' to media and its binding to the *lac* repressor causes it to dissociate from the *lac* operator sequence.
- Then if glucose is still in medium, CAP can't bind to its site and transcription is relatively low.
- If glucose is absent, in the presence of lactose, cAMP level becomes high, binds to CAP to form a complex which then binds to the control site strongly activating transcription by RNA polymerase.
- The lac promoter reuires σ70 out of 7 sigma factors of RNA pol.



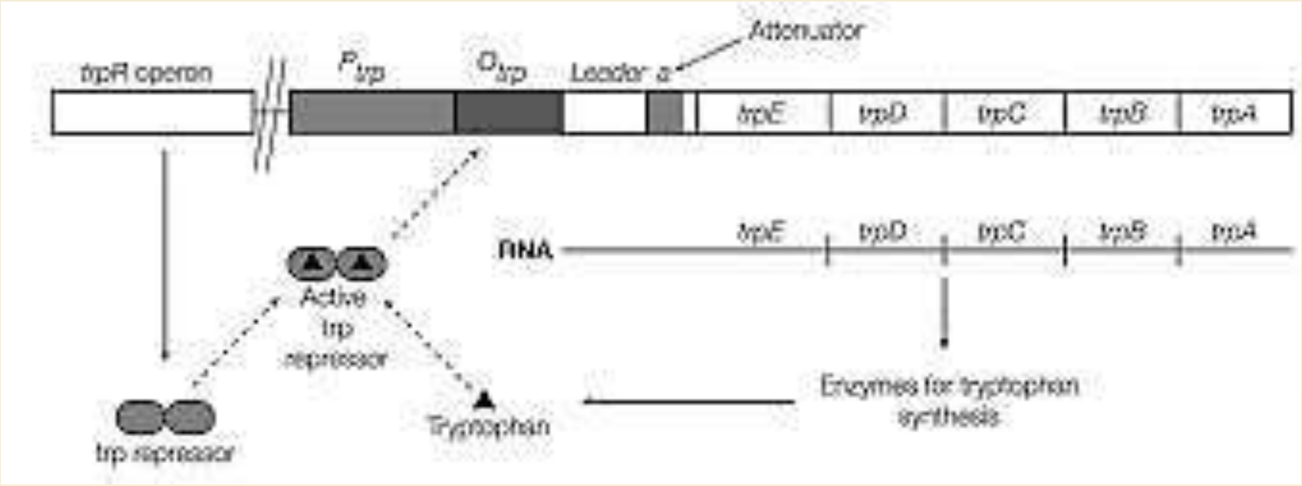
# Regulation of Gene Expression – *lac* operon



# Regulation of Gene Expression – *trp* operon

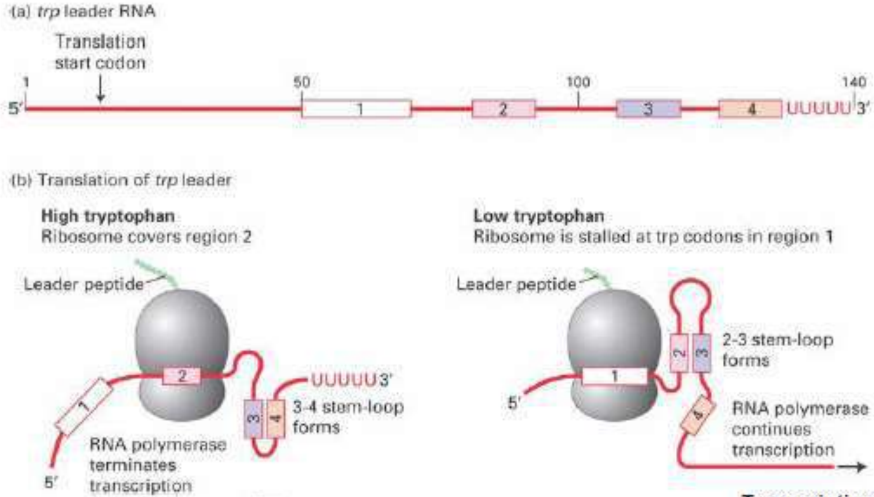
***The trp* Operon**

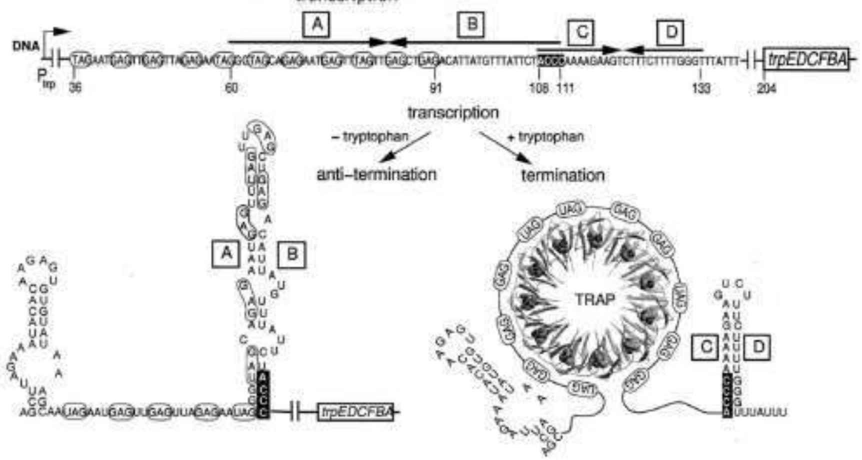
- It includes 5 genes encoding enzymes needed for tryptophan biosynthesis, along with a promoter (RNA pol binding site) and an operator (repressor protein binding site).
- The *trp* operon is considered a repressive operon and its genes are transcribed as a single mRNA.
- It is regulated by the amount of tryptophan present.
- Here tryptophan acts as a repressor.



# Regulation of Gene Expression – *trp* operon

***trp* operon**



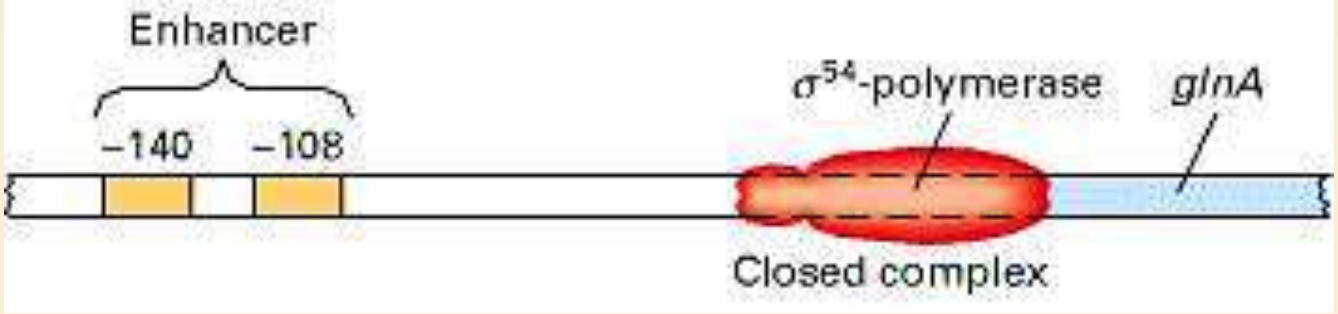

Transcription attenuation model of the *trp* operon. When tryptophan is limiting ( tryptophan) TRAP is not activated. During transcription, antiterminator formation (A and B) prevents formation of the terminator (C and D), which results in transcription of the *trp* operon structural genes. When tryptophan is in excess (+tryptophan) TRAP is activated. Tryptophan-activated TRAP can bind to the (G/U)AG repeats and promote termination by preventing antiterminator formation. The overlap between the antiterminator and terminator structures is shown. Numbering is from the start of transcription.

Babitzke and Gollnick, J. Bacteriology, 2001

# Regulation of Gene Expression – NtrC/NtrB

## ***The gln regulation by NtrC/NtrB***

- It is involved in the regulation of gene expression of proteins involved in nitrogen metabolism.
- At low nitrogen levels, NtrC binds to DNA and activates transcription.
- In case of glnA gene, NtrC regulates the transition from a closed to open transcription complex, an example of allostery. NtrC interacts with a specialized sigma factor (sigma 54) which directs the RNA polymerase to a specific set of genes containing variations in the consensus promoter sequence.
- NtrC has separate activating and DNA-binding domains, and binds DNA when the nitrogen levels are low.
- The phosphorylated by a kinase NtrB, NtrC change the structure and display the activator domain.



# Regulation of Gene Expression – NtrC/NtrB

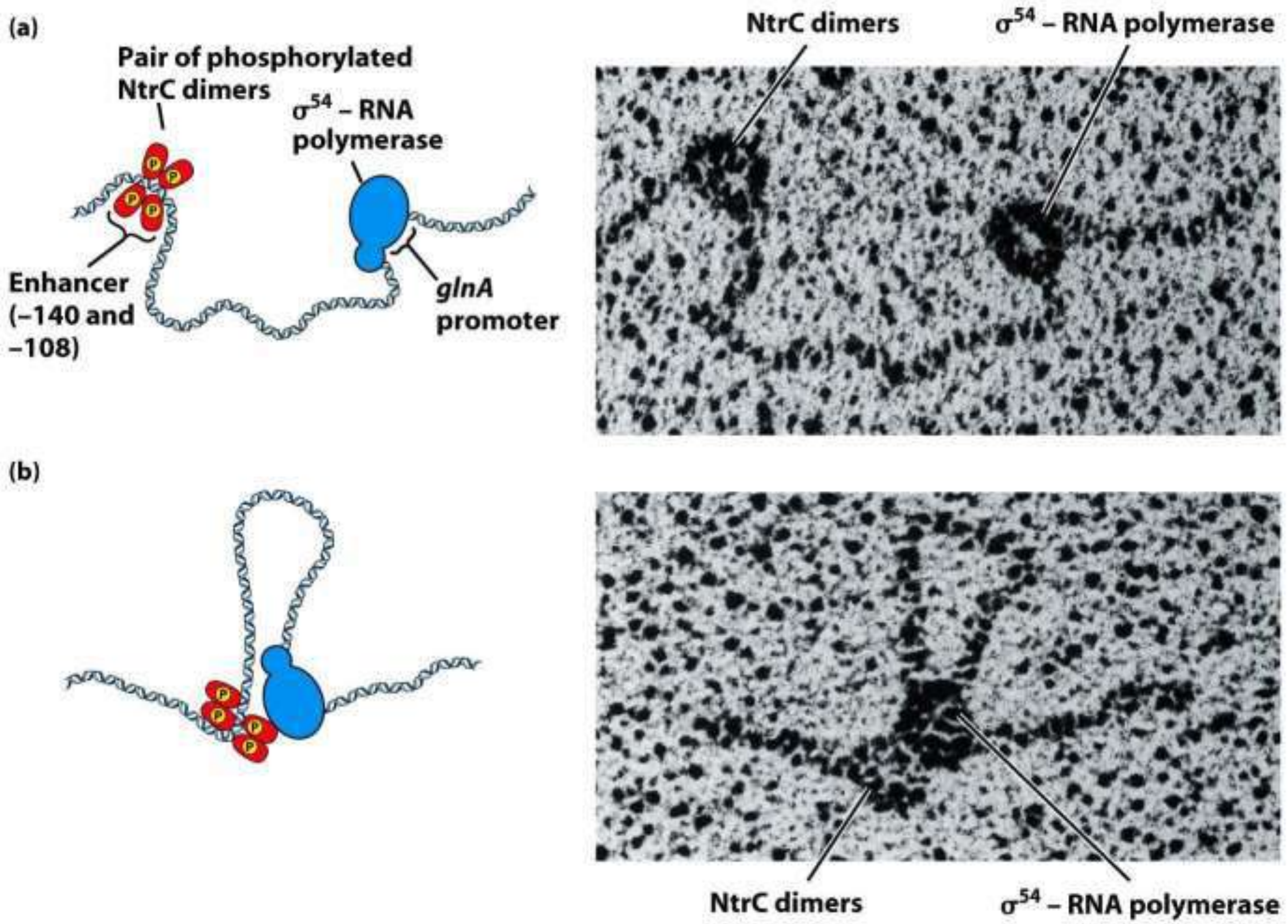



Figure 7-4
*Molecular Cell Biology, Sixth Edition*


**Lodish7thedition, Fig. 7.4**

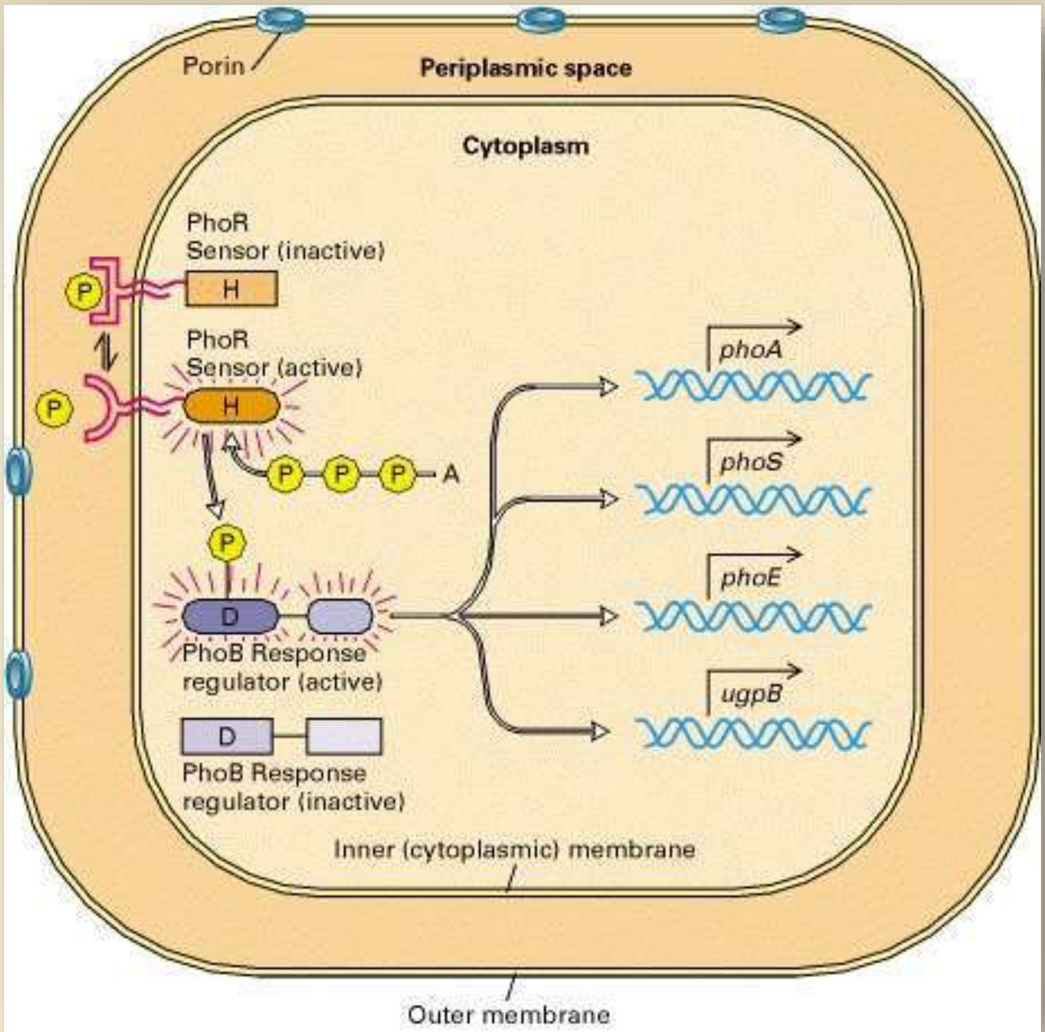
# Regulation of Gene Expression – PhoR/PhoB

***The free phosphate regulation by PhoR/PhoB***

- PhoR is a transmembrane protein, located in the inner membrane, whose periplasmic domain binds phosphate with moderate affinity and whose cytosolic domain has protein kinase activity.
- PhoB is a cytosolic protein.
- When the phosphate concentration in the environment falls, it also falls in the periplasmic space, causing phosphate to sissociate from the PhoR periplasmic domain.
- Dissociation of phosphate form PhoR causes a conformational change in the PhoR cytoplasmic domain, that activates its protein kinase activity.
- The activated PhoR initially transfers a γ-phosphate from ATP to a histidine side chain in the PhoR kinase domain itself.
- The same phosphate is then transferred to a specific aspartic acid side chain in PhoB, converting PhoB from an inactive to an active transcriptional activator.
- The phosphorylated, active PhoB induces transcription of several genes that help to cope with low phosphate conditions.

# Regulation of Gene Expression – PhoR/PhoB

**PhoR/PhoB gene regulation mechainsm**



# Further reading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- Krebs J.E., Goldstein E.S., Kilpatrick S.T. 2017. Lewin's Genes XII. Jones and Bartlett Publishers, Inc., Burlington, MA, USA
- Snyder L.R., Peters J.E., Henkin T.M., Champness W. 2013. Molecular Genetics of Bacteria, 2nd ed., ASM Press, Washington DC, USA, 2003.
- Graumann P.L. Chromosome architecture and segregation in prokaryotic cells. Microbial Physiology 24(5-6).
- Regulation of gene expression in prokaryotes: Negative regulation and positive regulation, Transcriptional activator, transcriptional repressor, lac operon and trp operon
https://www.ncbi.nlm.nih.gov/books/NBK26872/
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