6.4 Gene Regulation

SBI4UP

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Regulating Metabolism

Organisms need to control the amount of protein being made to ensure that it is only being produced in times of need.

Metabolic Control occurs in two ways:

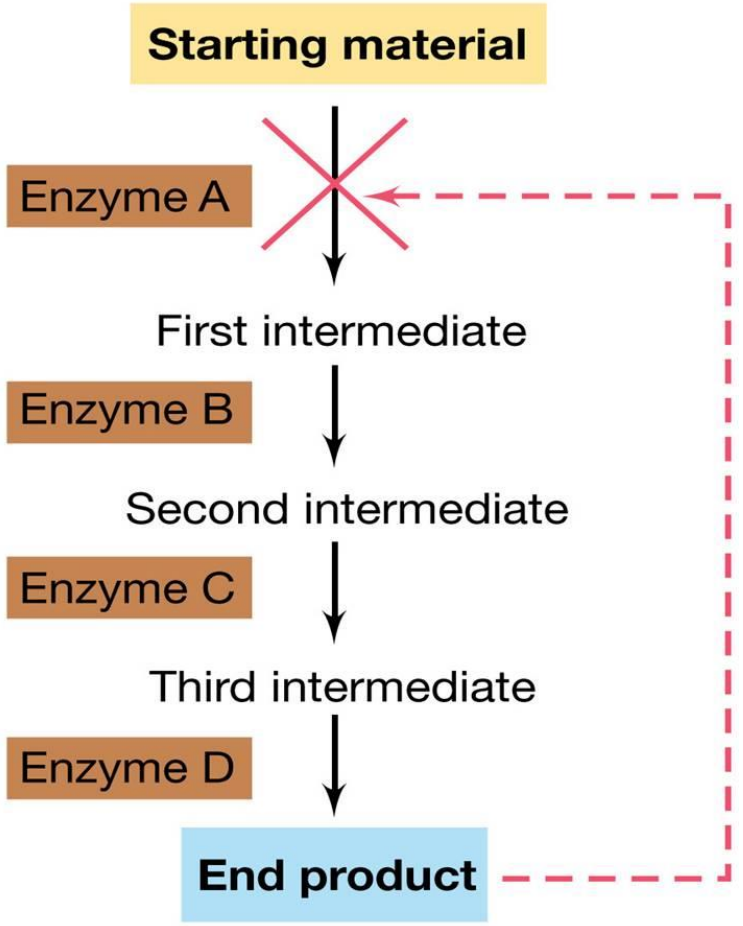
1) Adjusting the activity of the enzyme: feedback inhibition

2) Regulating the expression of genes that encode the enzymes: through transcription

1) Adjusting Enzyme Activity

The activity of the first enzyme in the pathway is inhibited when there is a large production of the final product. This process is known as ***'Feedback Inhibition'.***

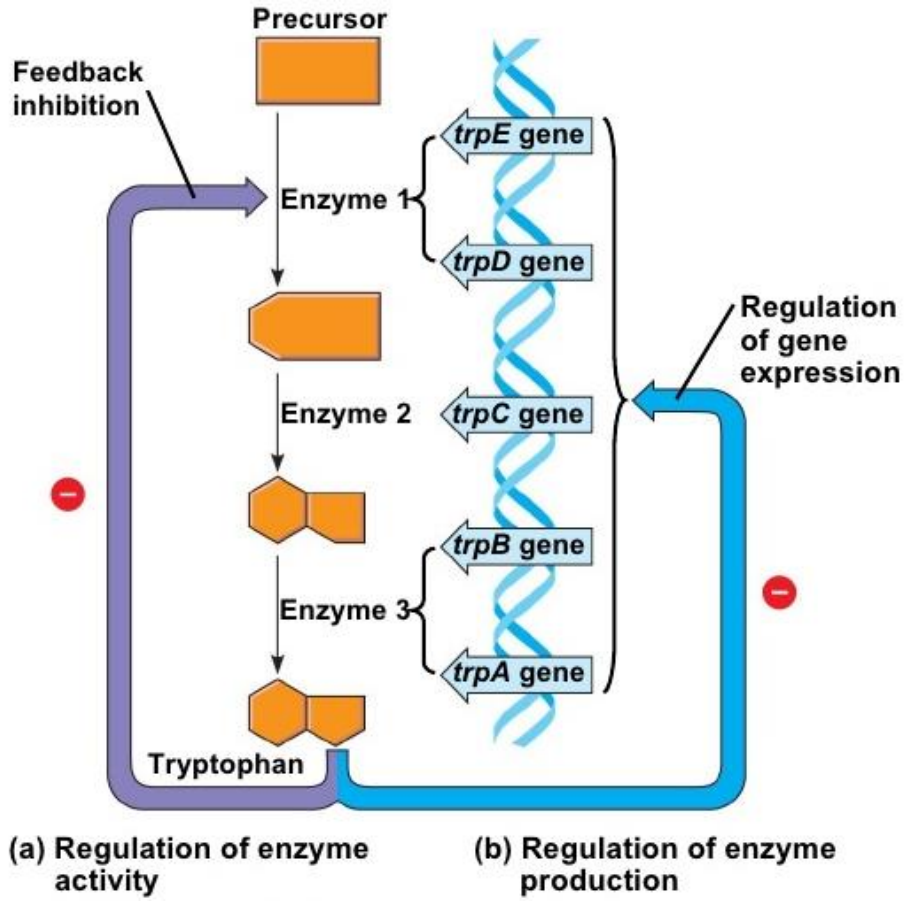
This enables the cell to adapt to short term fluctuations within the cell.



2) Regulating the Expression of Genes

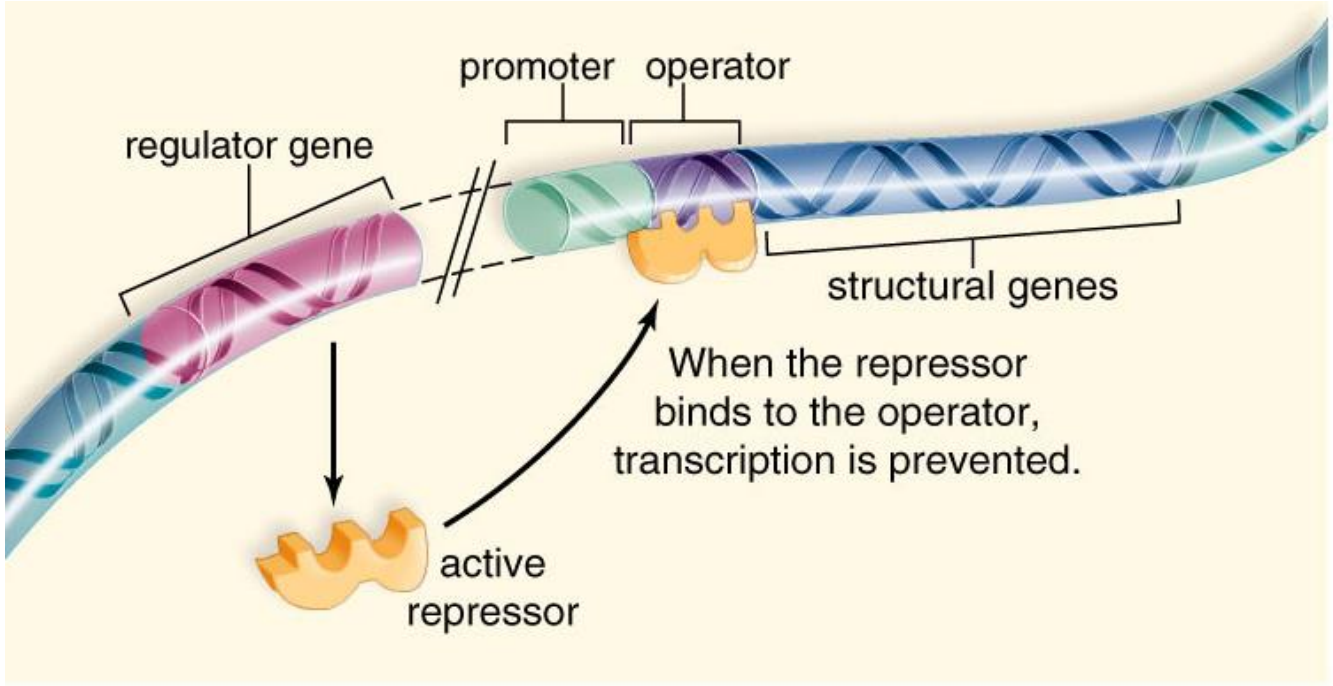
By regulating the transcription of genes into mRNA this can control the amount of proteins/enzymes produced for the metabolic pathway of tryptophan.

If one gene is not transcribed into mRNA, that one enzyme will not be produced, in turn inhibiting the pathway from occurring.



2) Regulating the Expression of Genes

Fracois Jacob and Jacques Monod, discovered how gene transcription could be regulated. The mechanism was known as the 'Operon Model' which is only found in prokaryotic organisms.



Operon: *many genes are under the control of one promoter region*

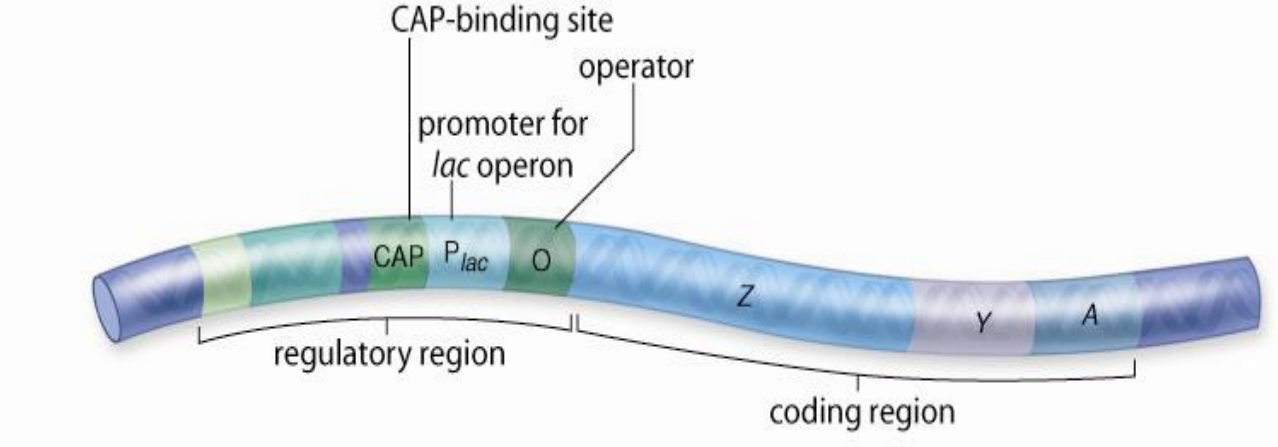
Structural Genes: *genes that encode the enzymes in a pathway*

Regulatory Gene: *codes for a repressor which can inhibit RNA polymerase from undergoing transcription.*

Operator: *region where a repressor binds to inhibit transcription of structural genes.*

The *lac* Operon

E.coli are able to take in a variety of sugars which need to be broken down by different metabolic pathways. The lac operon is involved in the metabolism of the sugar lactose.



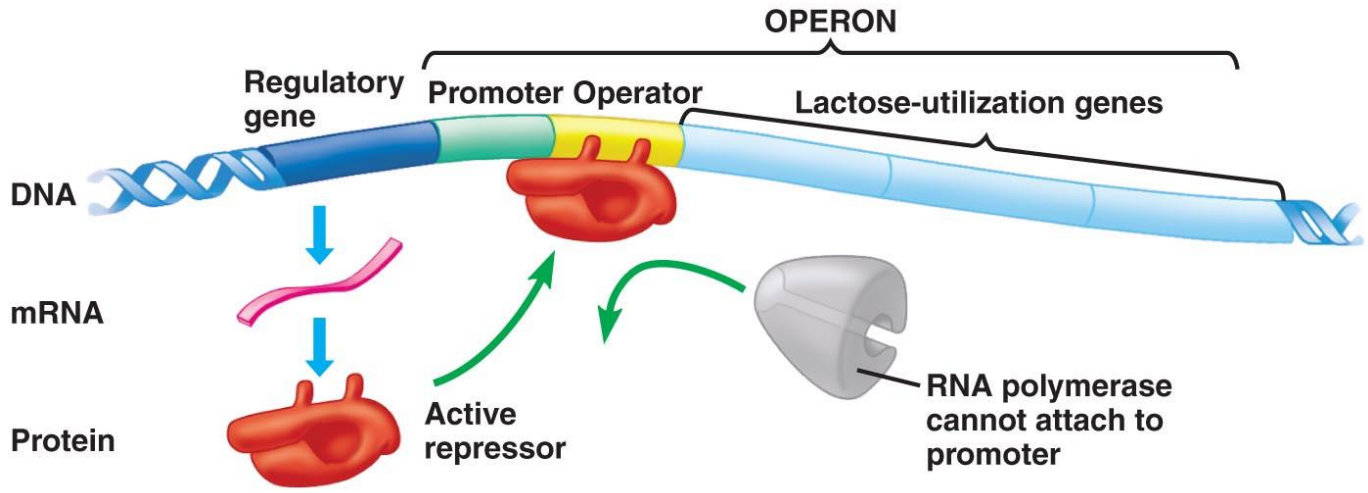
The coding region contains the structural genes that code for the enzymes involved in the pathway for lactose breakdown.

The regulatory region contains a promoter region whereby RNA polymerase will bind.

CAP (catabolite activator protein) binding site is a DNA sequence whereby proteins will bind to increase the rate of transcription.

The *lac* Operon

When lactose is present in the E.coli's environment, a protein must bind to the CAP binding site to increase the production of enzymes, if there is a lack of lactose in the environment transcription o the genes must be inhibited.



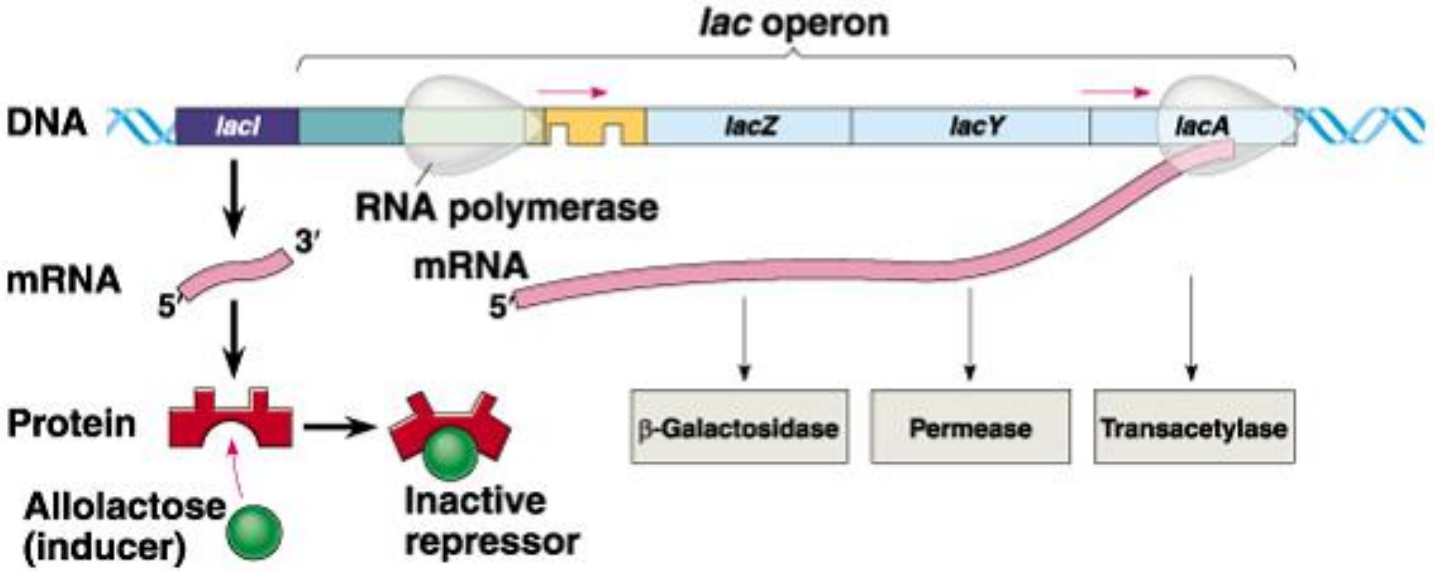
Operon turned off (lactose absent)

The lacI is a regulator gene which codes for a protein that acts as an active repressor. If there is no lactose in the environment transcription of the enzymes must be repressed.

The active repressor binds to the operator and presents the RNA polymerase from moving forward.

The *lac* Operon

Allolactose is an isomer of lactose that is produced in small quantities within the cell. It acts as an inducer that binds to the repressor. This inhibits the repressor from binding to the operator.

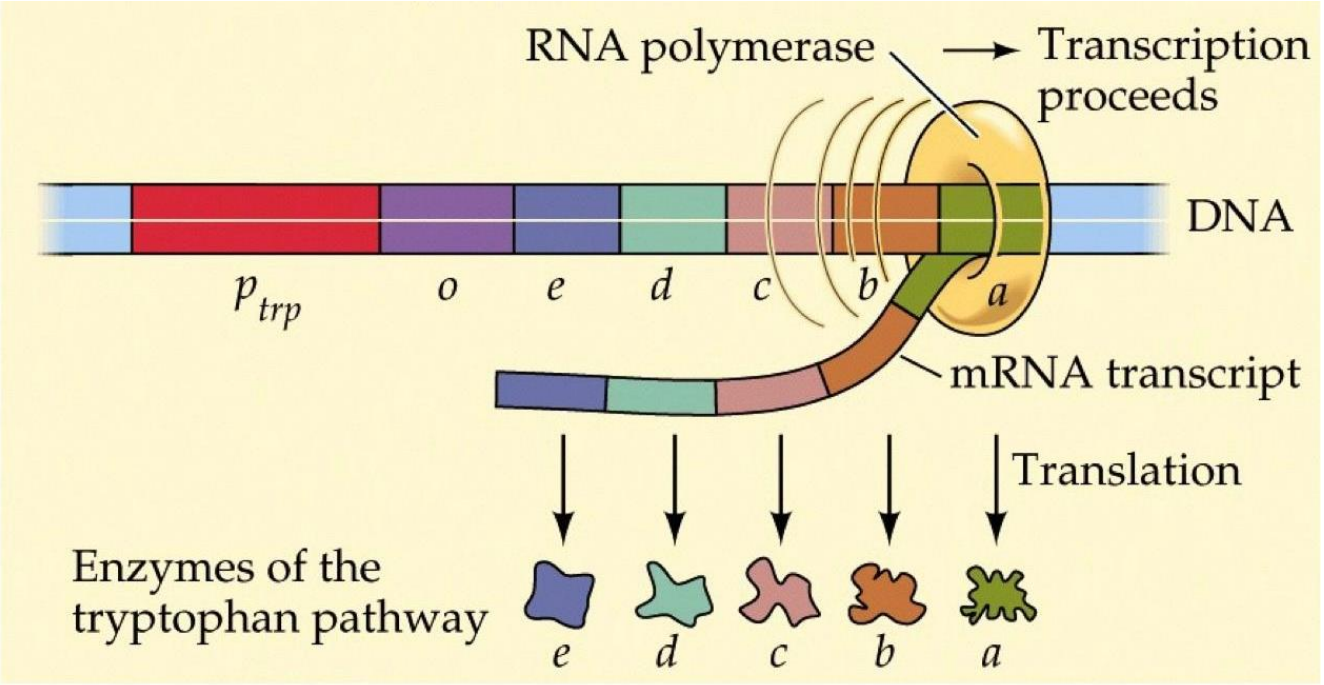


Allolactose can only be produced in the presence of lactose.

The *trp* Operon

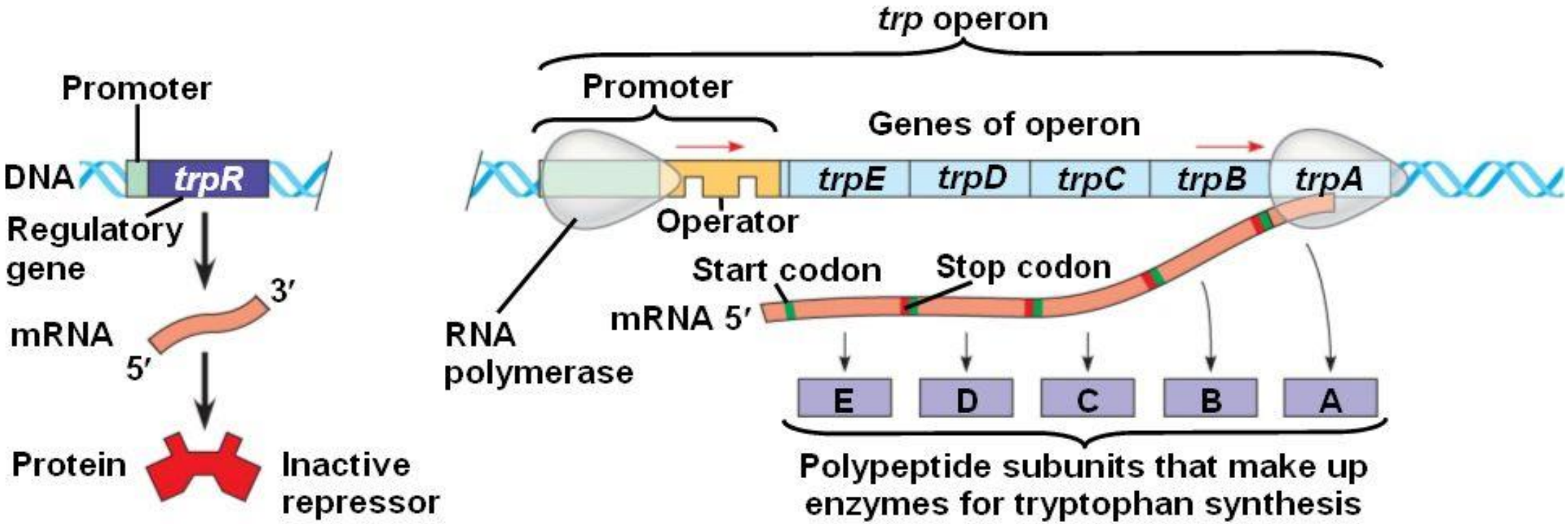
In contrast to the lac Operon, the trp Operon is active on its own and des not require an inducer. In order to shit off the transcription of the genes an active repressor must be made.

Trp Operon is transcribed on its own with the help of RNA polymerase.



The regulatory gene (trpR) codes for a protein that behaves as a repressor. On its own the repressor is not activated and cannot bind to the operator.

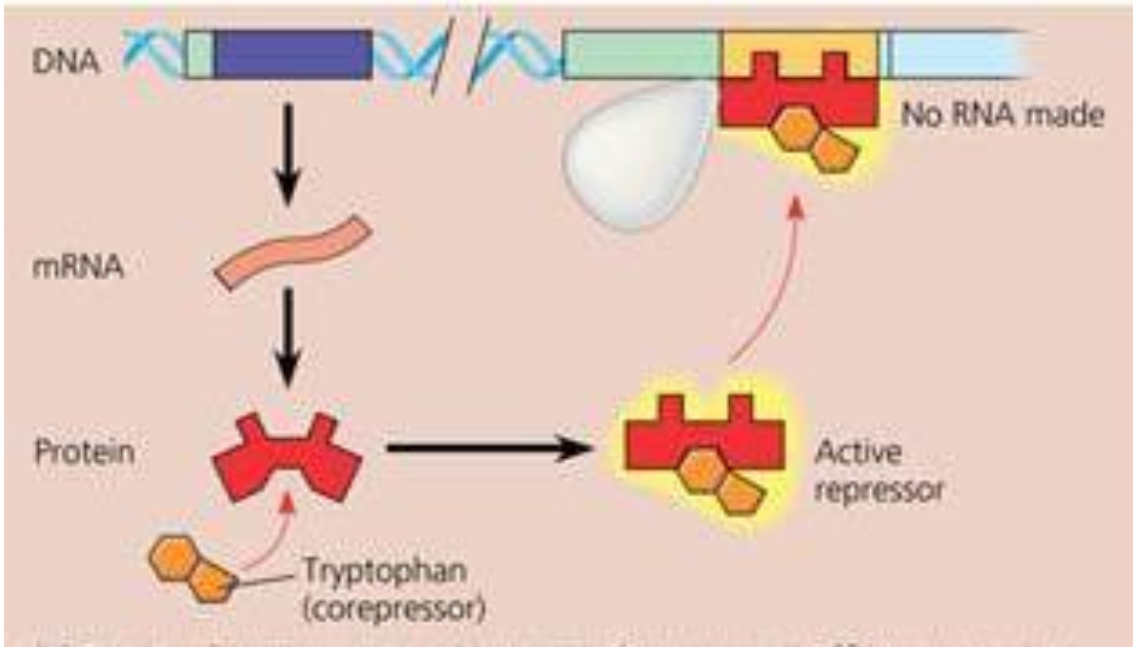
The *trp* Operon



The *trp* Operon

When the cell has produced a large quantity of tryptophan, it no longer needs the pathway to synthesize more. Thus, tryptophan will behave as a co-repressor and bind to the allosteric site of the inactive repressor.

Tryptophan activates the repressor so that it can bind to the operator and prevent RNA polymerase from accessing the promoter region. Thus, no more mRNA is synthesized.

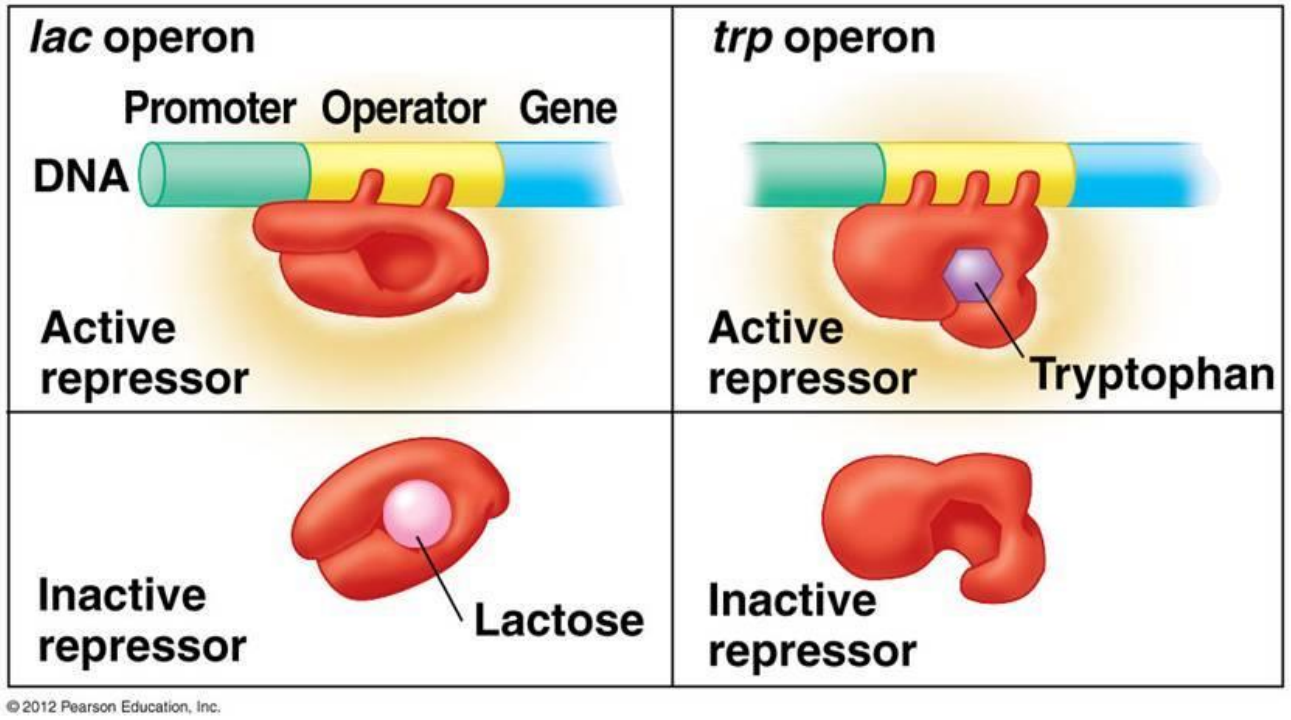


lac vs. *trp* Operon

Lac Operon:

Involved in catabolic pathway (breakdown of lactose)

Allolactose inhibits the repressor and prevents it from binding to the operator.



trp Operon:

Involved in an anabolic pathway (production of tryptophan)

Tryptophan is required to activate the repressor so that it can bind to the operatr.

Without tryptophan, the repressor is inactive.

Regulating Gene Expression - Eukaryotes

Eukaryotic cells use other mechanisms other than operons to control the expression of their genes. The genes can be regulated by targeting different stages of protein formation.

Ways to regulate gene expression in eukaryotes:

1) Target Transcription:

A) Controlling chromatin structure

B) Enhancer regions on the DNA

2) Post-Transcriptional Control:

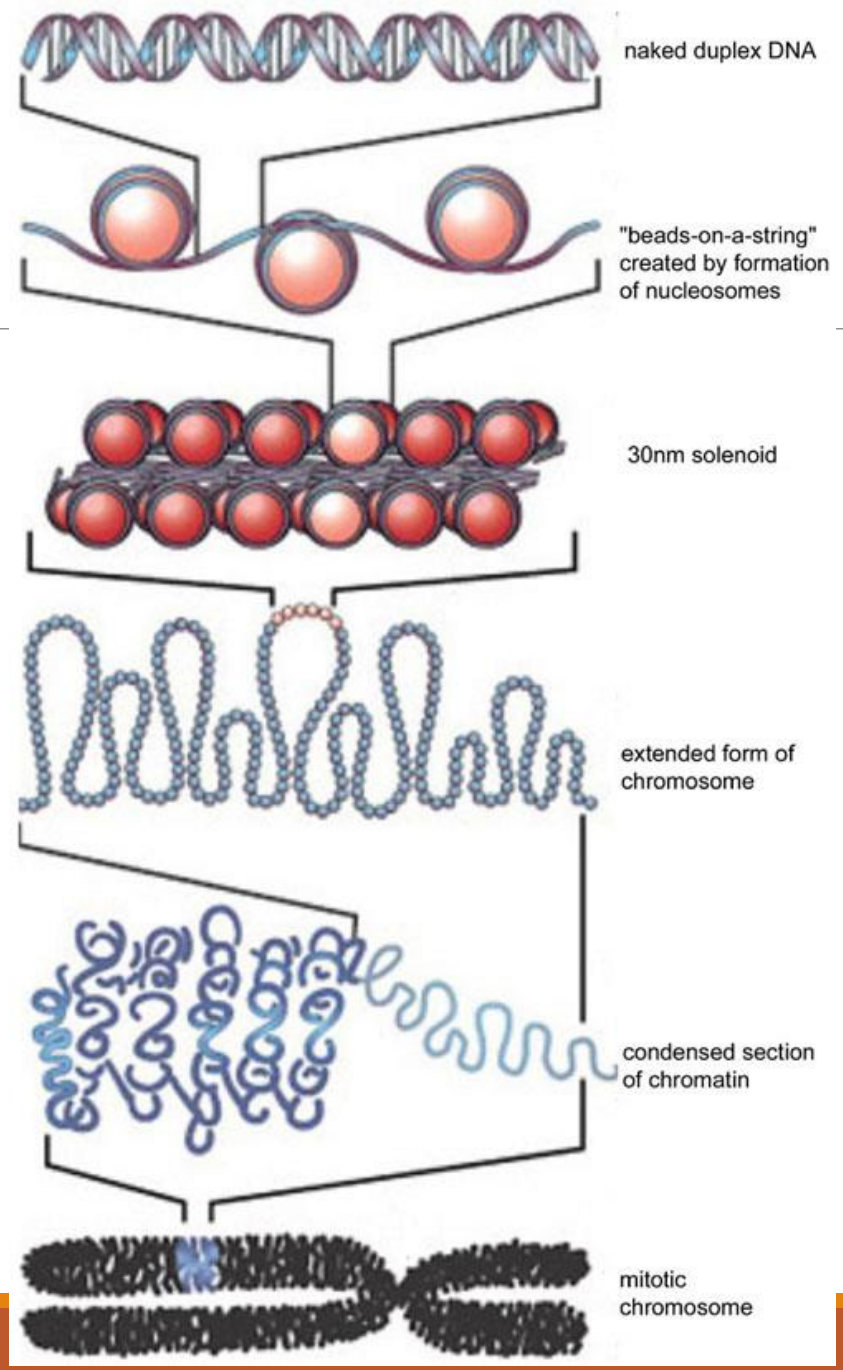
A) Preventing the formation of 5’ cap and poly-A tail

B) RNA interference

Targeting Transcription

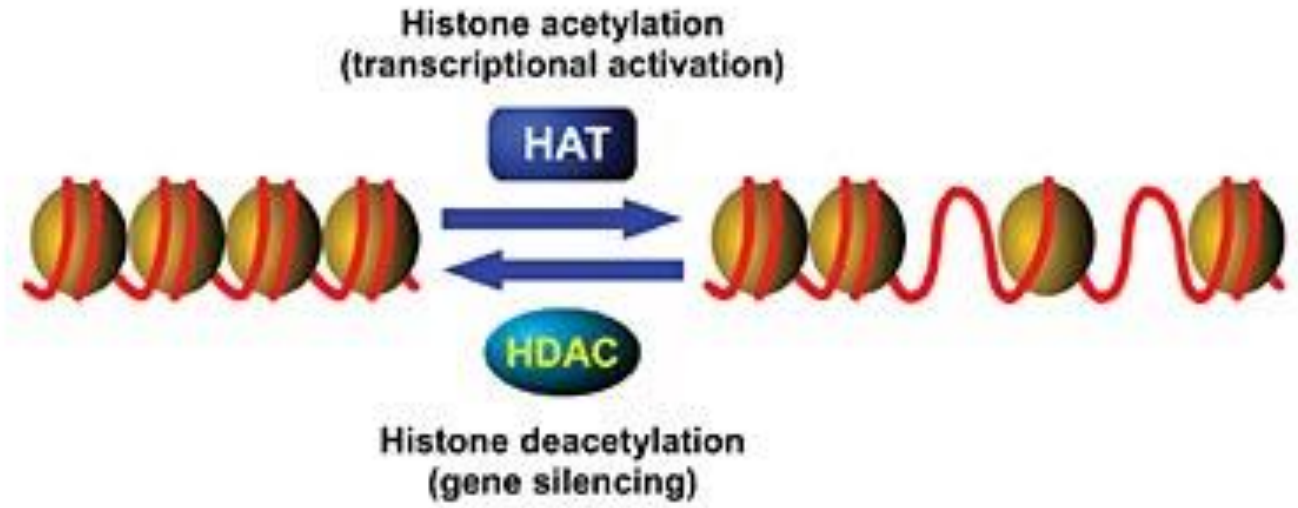
Unlike prokaryotes, eukaryotic cells can regulate gene expression by altering the chromatin structure. When chromatin is highly condensed, the genes cannot be transcribed.

Areas that must be transcribed, require chromatin to uncondense.



Modification of Chromatin

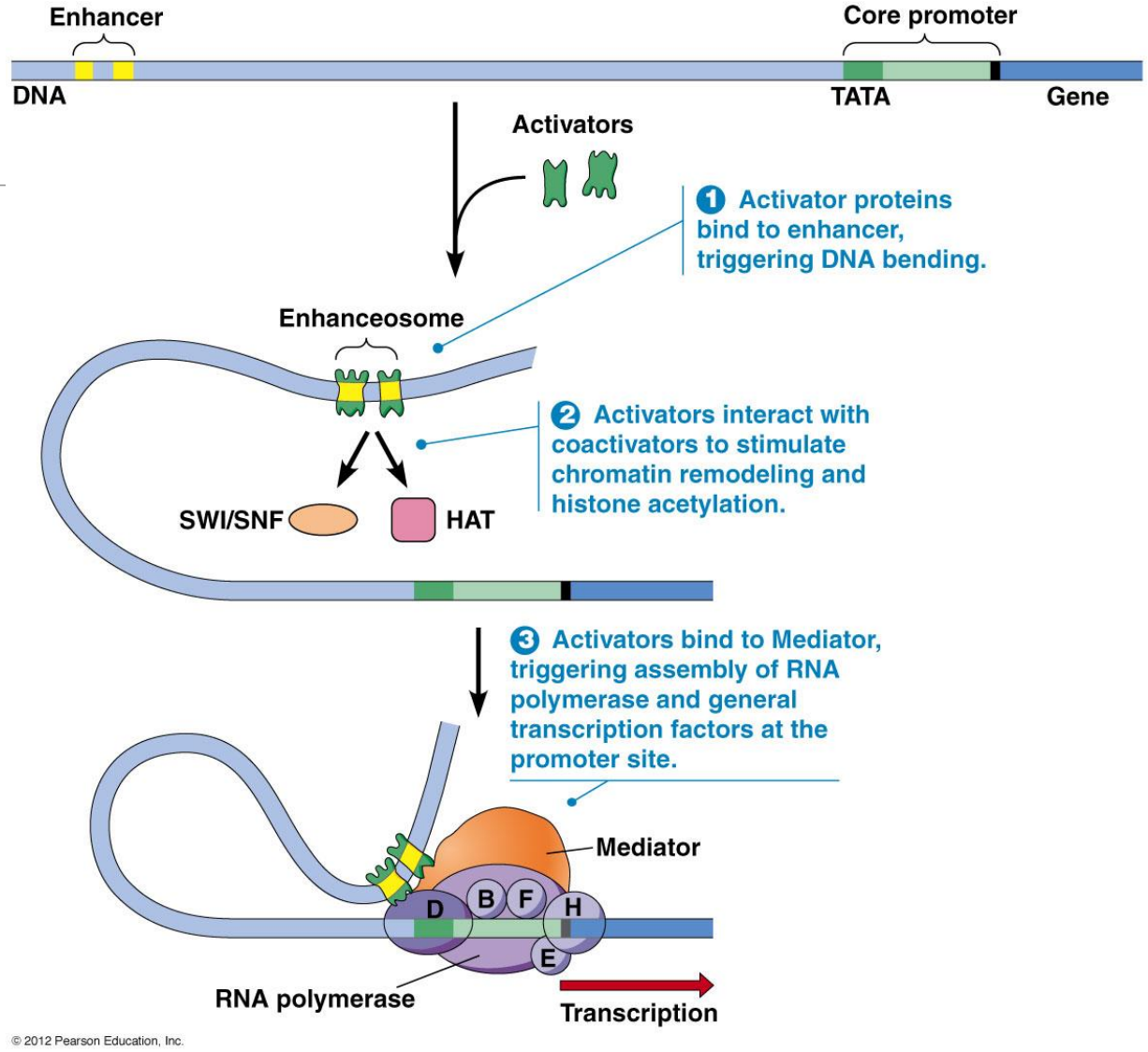
Histone Modification: Each histone has a region that protrudes from the nucleosome. Acetyl groups (-$COCH_3$) are added to this tail region. Histone acetylation prevents the histones from binding to the neighboring nucleosome.



The histones' inability to bind to the other nucleosomes prevent the chromatin from coiling tightly, and exposes the genes required for transcription.

Enhancer Regions

There are a group of enhancers located upstream of the promoter region. The enhancer is a nucleotide sequence whereby activators and repressor bind to control transcription of the genes.



Post-Transcriptional Control

There are two methods the cell will use to control protein production after transcription has occurred:

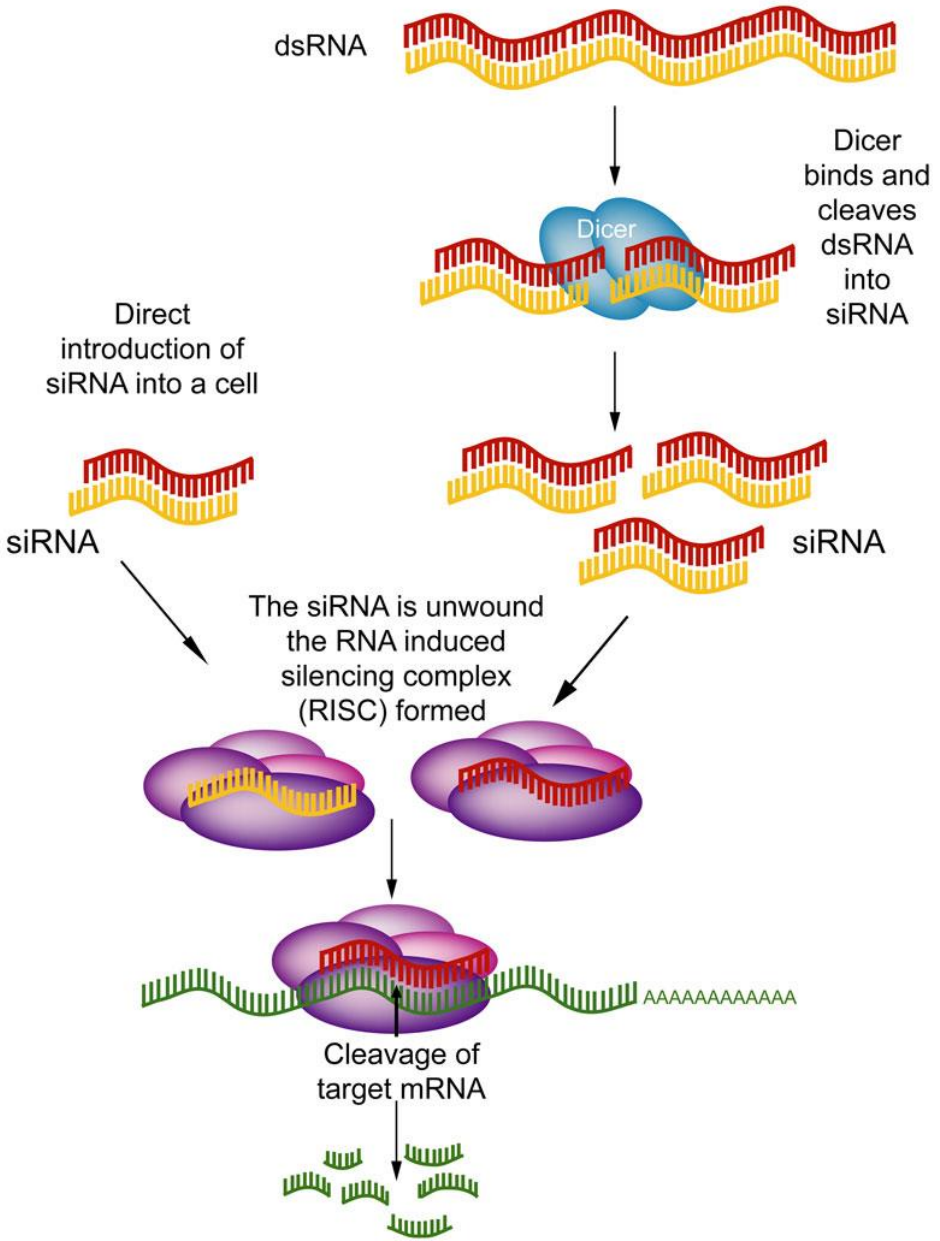
1) 5' cap and 3' poly-A tail are not added to the pre-mRNA

2) RNA interference: the RNA strand degraded so that translation cannot occur.

RNA Interference

During RNA interference small RNAs (siRNA and miRNA) help to degrade the mRNA strand so that it does not get translated.

siRNA, miRNA and additional proteins help to form the RISC complex which cleaves the mRNA into many fragments.



Checking for Understanding

How is transcription directly controlled in eukaryotic cells?

A) through the use of phosphorylation

B) through the use of operons

C) using transcription factors and activators

D) through condensed chromatin, which allows constant gene activation

E) through the addition of a 5’ cap and a 3’ poly-A-tail

Checking for Understanding

What region of DNA do eukaryotic activator proteins interact with?

A) repressors

B) operators

C) coding regions

D) promoters

E) enhancers

Homework

Textbook: pg. 272 # 3 4,6, 7, 8, 9 & 13