Chapter 21
Regulation of Gene Expression

I. Gene Regulation in Prokaryotes

A. **some genes not regulated**

1. **constitutive genes** = genes that are always active
   - -genes that are always "turned on"
   - -genes are always needed
   - -eg: genes that code for enzymes of glycolytic pathway

B. **some genes are regulated**
   - -some genes only needed under certain conditions
   - -**transcription can be "turned on or off"**
   - -enzymes produced from these genes vary greatly in cytoplasmic concentration

C. **strategies of prokaryotic gene regulation**

1. enzymes for catabolic pathways **regulated differently** than enzymes from anabolic pathways
2. all enzymes of a given pathway **regulated together**
3. two basic types of regulation

a. **induction is associated with catabolic pathways**
   - -enzymes for a given catabolic pathway synthesized only when needed
   - -**eg: catabolism of lactose**
   - -lactose is not always present in the growth media
     - -when lactose **is not present** in growth media
       - -bacteria do not make beta-galactosidase
       - -bacteria do not make permease
     - -when lactose **is present** in growth media
       - -both galactosidase and permease are synthesized by cell
       - -**galactosidase and permease regulated together**
       - -see beta-galactosidase reaction
       - -see function of galactoside permease
       - -enzyme synthesis "turned on" in presence lactose
       - -**substrate induction** = turning on enzyme synthesis (transcription + translation) in the presence of the substrate
       - -**inducible enzymes** = enzymes whose synthesis requires the presence of an inducer (usually a substrate)
       - -**MOST catabolic pathways in bacteria are subject to substrate induction**

b. **repression is associated with anabolic pathways**
   - -focus on the **"end products"** of anabolic pathways
   - -opposite of catabolic pathways
   - -amount enzyme varies inversely with amount end-product in cell
   - -**eg: tryptophan synthesis in cell**
     - -low tryptophan in cell
       - -enzymes required to synthesize trp are turned on
       - -see the pathway
     - -high tryptophan in cell
       - -enzymes required to synthesize trp are turned off
     - -**regulated by tryptophan repression**
       - -high [trp] represses (turns off) genes for pathway
       - -low [trp] => no repression so genes are turned on
     - -**MOST anabolic pathways in bacteria are regulated by end-product repression**
     - -**repression** = reduction in the expression of a gene or group of genes
       - -repression deals with protein (enzyme) synthesis starting with DNA

c. **effector molecules**
   - -**effector molecules** = small molecules that trigger the activation or deactivation of a gene or group of genes
   - -substrate induction uses effector molecules
     - -**effector molecules of catabolic pathways**
       - -usually **substrates**
       - -act as **inducers**
     - -eg: lactose (the substrate) is the small molecule that **"turns on"** the genes coding for the enzymes of the pathway
   - -end-product repression uses effector molecules

-**effector molecules of anabolic pathways**
-usually **end-products**
-act as **repressors**
-eg: tryptophan is the
small molecule that **"turns off"** the genes
coding for the enzymes of the pathway

4. **Inducible Operons**
   a. catabolic pathways have inducible operons
   b. pathways turned **ON** by the presence of starting materials
   c. eg: ***lac* operon in *E. coli***
   -key paper by Francois Jacob and Jacques Monod (1961)
   -discovered two types of genes associated with lactose catabolism
   -**structural genes** = genes that code for proteins involved with uptake and metabolism of a given molecule
   -eg: beta-galactosidase
   -eg: galactoside permease
   -eg: transacetylase
   -**regulatory genes** = genes that code for proteins that regulate the activity of the structural genes
   -eg: repressor protein
   -Jacob and Monod discovered 3 things:
   (1) that the **structural** genes were only **expressed in the presence of an inducer** molecule (eg: lactose)
   (2) that the **structural genes were all immediately adjacent to each other**
   (3) that the **regulatory** genes were **elsewhere** in the genone
   -Jacob and Monod proposed the Operon Model for gene regulation
   -based on the lactose catabolism system
   -proposed that the three structural genes were part of an **"operon"**
   -operon = a cluster of related genes that are turned off/on together
   -proposed that lac repressor protein is an allosteric protein
   -has binding site for lactose chime
   -has a **binding site for DNA**
   -represser + lactose => no DNA binding
   -repressor only => binds DNA chime
   -proposed that the repressor specifically binds to operator of the lac operon and blocks RNA polymerase from binding and transcribing the mRNA
   -proposed that **when lactose is present,** the lactose binds to the repressor protein and PREVENTS repressor from binding DNA => polymerase CAN bind and start making mRNA
   -new mRNA codes for beta-galactosidase permease & transacetylase
   -enzymes are synthesized and lactose is metabolized
   -**What happens when the lactose is fully metabolized?**

5. **Repressible Operons**
   a. biosynthetic pathways have repressible operons
   b. pathways turned **OFF** by products of pathways
   c. **eg: trp operon in *E. coli***
   d. has a regulatory gene and an operon
   -**regulatory gene codes for a protein (the repressor) that is INACTIVE**
   -inactive repressor is activated by trp
   -in absence of trp, repressor is inactive and RNA polymerase transcribes the structural genes
   -**structural genes code for enzymes that synthesize trp**
   -[trp] in cytoplasm rise
   -at a triggering [trp], trp binds to inactive repressor, making it an ACTIVE repressor
   -active repressor binds to trp operon operator and prevents RNA polymerase binding and transcription
   -levels of trp operon enzymes fall
   -[trp] in cytoplasm fall
   -repressor returns to inactive form, etc, etc, etc

6. **Negative Control of Transcription**
   a. both the lac operon and trp operon are examples of negative control
   b. repressor turns OFF transcription under certain circumstances

7. **Positive Control of Transcription**
   a. some operon's are positively controlled
   b. regulatory protein turns ON transcription
   c. **eg: catabolite repression**
      (1) presence of glucose inhibits the ability of metabolites (eg: lactose) to induce transcription
      (2) enzymes for glucose metabolism are constituitive
      (3) prokaryotic cells prefer to metabolize glucose
      (4) don't make enzymes needed for lactose metabolism if glucose is available
         (a) eg: grow bacteria on media containing glucose and lactose
            -bacteria metabolize only glucose until all glucose is gone
            -glucose gone => bacteria induce enzymes lactose metabolism
            -start metabolizing lactose
      (5) mechanism of catabolite repression
         (a) cells have **cyclic AMP Receptor Protein (CRP)** chime
         (b) **cAMP allosterically activates CRP**
         (c) **activated CRP binds** to a specific DNA sequence (C) just upstream from the lac promoter (Plac)
         (d) bound CRP greatly facilitates RNA polymerase binding and transcription
         (e) What about glucose?
            -When **[glucose] is high** in cytoplasm
               -glucose inhibits **adenyl cyclase**
               -adenyl cyclase catalyzes:
                  ATP <=> cAMP + P-O-P
               -high glucose => low [cAMP]
               - low [cAMP] => inactive CRP
               -inactive CRP => no DNA binding
               -no DNA binding => little induction of the lac operon
               -SO: in presence of glucose, the cell doesn't make the enzymes needed to metabolize lactose
            -When **[glucose] is low**
               -low glucose => high [cAMP]
               -high [cAMP] => active CRP
               -active CRP => CRP binds to DNA
               -CRP binding to DNA => increased RNA polymerase binding
               -enzymes of lac operon are synthesized
               -lactose is metabolized

8. Dual Control of Inducible Operons
   A. **inducible operons often under dual control**
      (1) eg: lac operon
         a. lac operon **subject to negative control** by a repressor
            -allows the presence of lactose to "turn on" the system
         b. but, lac operon also **subject to positive control** by CRP
            -allows the "turn on" to only occur under appropriate conditions

9. **Sigma Factors**
   A. bacterial RNA polymerase uses a sigma factor
      (1) recall from **chap 19**: sigma factors help control initiation of transcription
         -**sigma factor binds to RNA polymerase**
         -sigma factor helps RNA polymerase find the promoter
         -bacterial cells have **different types sigma factor specific for sets of genes**
            -**sigma factor 70** (MW = 70 kDa) is most common form
               -initiates transcription at most promoters
            -**sigma factor 32** (MW = 32 kDa) is produced after heat shock
               -initiates transcription at promoters of genes needed for responding to heat
            -**sigma factor 54** turns on genes for nitrogen utilization
            -**bacteriophage produces a powerful sigma factor** that preferentially transcribes the phage DNA instead of the bacterial DNA

skip attentuation (only found in prokaryotes)

II. Skip Comparison of Gene Regulation in Pro and Eukaryotes for 2005
    A. differences in genome expression

III. Skip Eukaryotic Gene Regulation for 2005
    A. Genomic Control
    B. Transcriptional Control
    C. Posttranscriptional Control