Week 10
Genetics: BIO-2306

The concepts this resource covers are the topics typically covered during this week of the semester. If you do not see the topics your particular section of class is learning this week, please take a look at other weekly resources listed on our website for additional topics throughout the semester.

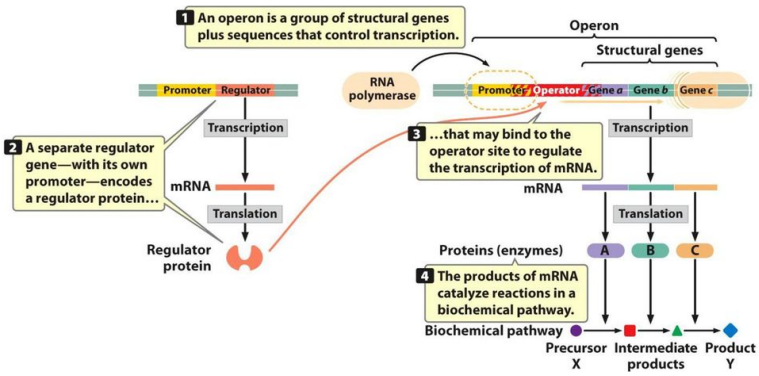
We also invite you to look at the group tutoring chart on our website to see if this course has a group tutoring session offered this semester.

If you have any questions about these study guides, group tutoring sessions, private 30 minute tutoring appointments, the Baylor Tutoring YouTube channel or any tutoring services we offer, please visit our website www.baylor.edu/tutoring or call our drop in center during open business hours. M-Th 9am-8pm on class days 254-710-4135.

Keywords: Regulation, Operon, Repressor, Inducer, Histones

Topic of the Week: ***Operons/Prokaryotic Gene Control*** (16.2-3)

Structural Gene: a gene (or unit of genes controlled by the same ***operon***) which codes for a product (ex. Enzyme, channel, etc.) . **note, though, that the structural genes will interact with the regulator protein**



Operon: the DNA containing the Promoter, the ***Operator***, and the structural gene(s); the structural unit of prokaryotic gene regulation.

Operator: The sequence where a regulatory protein binds (overlaps the promoter and coding region)

Regulatory Gene: a separate gene *upstream* from a promoter that synthesizes a regulatory molecule

Types of Control

- **Positive Control:** the regulator protein is an activator
- **Negative Control:** regulator protein is a repressor
  - **Inducible:** the regulator protein is translated in an inactive form, and then is allosterically activated
    - **Inducer:** molecule that that binds to the allosteric site of the repressor, rendering it unable to bind to the operator [allosteric inhibition]
  - **Repressible:** the regulator protein active, then is allosterically inactivated
    - **Corepressor:** molecule that binds to the allosteric site of the repressor and activates it [allosteric activation]

***Lac* Operons:** negative inducible operon

Prokaryotes need simple sugars to metabolize (create ATP/survive). When **lactose** (the *substrate* of the product of the *lac Z* gene) is cleaved by *β*-Gal, we produce glucose and galactose. The ***lac* operon** codes for genes that help lactose enter a cell and be cleaved https://www.youtube.com/watch?v=EjRXz1xAdow (10:13-end)

Operon:

Lac P → *promoter* (where *RNA-pol* binds)

Lac O → *operator* (where the repressor binds)

Z-Gene (*β-Galactosidase*): aka "*β*-Gal"cleaves lactose (*lac Z*) → structural gene

β-Gal also converts lactose into its isomer **allolactose**.

note: Y-Gene (*permease*) and A-Gene (*Gal-TransAc*) are other genes coded by the operon, but are not particularly focused on in 2306

Regulatory Gene:

***Lac* P_I** → *regulatory promoter*

Lac I → *repressor* [protein] *gene* (binds to operator and inhibits transcription)

When **lactose** (the *substrate* of the product of the *lac Z* gene) is **ABSENT**, the *lac I* repressor protein freely binds and **inhibits** the operon. When **lactose** is **PRESENT**, some **allolactose** is formed; it *allosterically inhibits* the repressor protein, **activating** the operon.

Lac Operon Mutations:

***Lac* Z^-:** B-gal mutation; inactive protein produced (no B-gal)

***Lac* Y^-:** permease mutation (no permease) → lactose can't enter the cell!

Regulator Gene Mutation:

***Lac* I^-:** regulator mutation; can't bind to operator

***Lac* I^S:** superrepressor; no allosteric site → cannot be inactivated by inducer

***Lac* P^-:** promoter mutation; *RNA-pol* can't bind **ever** → no transcription

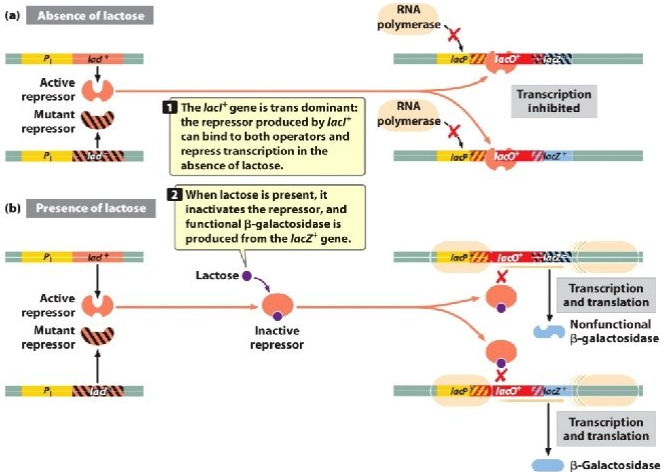
***Lac* O^C:** operator mutation (constitutive); repressor can't bind to the operator

Partial Diploid Mutants: bacteria with **two copies** of the lac operon and lac I gene (*transactive*: works between both copies)

https://www.youtube.com/watch?v=nchc810LfI0 (2:20-end)

Catabolite Repression: bacteria prefer glucose over other sugars for energy, so other sugar-metabolizing genes are inhibited when glucose is present at high supply https://www.youtube.com/watch?v=ERJSYmz-Ovg

Note: max transcription = high levels of lactose & low levels of glucose



Is the *lac Operon* "on" or "off?" Watch this video for a good way to analyze this (***hint hint you will need this if you are in genetics lab and for exam 4***): https://www.youtube.com/watch?v=u5H06cjO91M

***Trp* Operons:** negative repressible operon

The *trp operon* controls biosynthesis of tryptophan in bacteria by regulating the product

Repressor: normally off, but may be activated by a corepressor [tryptophan]

Corepressor: tryptophan is the corepressor, and is the product of the pathway mediated by the *trp operon*

Five structural genes transform **chorismate** into **tryptophan**.

When trp is **low**, the cell wants to make tryptophan, so the pathway is **not inhibited**

When trp is **high**, the trp **corepresses** the inactive protein, making it active and able to bind to the operator and **repress the *trp* operon**

Highlight #1: Gene Regulation in Eukaryotes (17)

Gene Regulation at the Chromatin Level: Tightly wound DNA around histones prevents transcription

***DNase-I* Hypersensitive Sites:** **Tightly** packages area around histones were not broken down by *DNase*, so they could not be easily transcribed

Less tightly compacted regions are more open, more readily transcribed, but are also more readily broken down by *DNase*

Chromatin Remodeling: Pushing histones out of the way in order to allow transcription machinery to bind or chemical modification

Acetylation of Histones: neutralizes positive charge on histone side chains (lys and arg); DNA is less tightly wound

Acetyltransferase: add; induction

Deacetylase: remove; repression

Histone Methylation: can either repress of induce transcription

Methyltransferase: add

Demethylase: remove

DNA Methylation: DNA methylation represses transcription because it attracts deacetylase enzymes (ie causes DNA to wrap more tightly around histones

CpG islands: consensus sequences for methylation near promoters (**cytosines** are methylated)

Gene Regulation at Transcription Initiation:

TAPs and Coctivators: TAPs bind to regulatory promoters and enhancer sites

Enhancers: further upstream from regulatory promoter; wrap around to interact with the BTA

Eukaryotic Repressors: Bind to regulatory promoter or **silencers**

Silencers: repressor equivalent of enhancers

Insulator: Block the action of enhancers when located between enhancers when **IBP** (*insulator binding protein*) binds to the insulator (ie. it blocks the folding of DNA, preventing enhancer and promoter interaction)

Control at the pre-mRNA level: Alternate splicing pathways, degradation of mRNA, and RNAi
RNAi: Transcriptional control/cleavage of RNA by **siRNA**; **miRNA** inhibits translation

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CHECK YOUR LEARNING

Concept Check: *(Answers found on last page)*

1. What is produced in the presence of lactose of the following operon set?
   $I^+S^+O^+Z^+Y^+/I^SS^-O^CZ^+Y^-$
   a. Lac Y
   b. Lac Z
   c. Lac P
   d. Absolutely Nothing
2. A positive repressible operon is discovered in *S. aureus*. When the corepressor is present, what happens to transcription?
   a. Transcription is boosted
   b. Transcription is inhibited
   c. Translation will increase
   d. The inhibitor protein will be translated in an active form
3. A potential drug to treat cancer methylates certain histone proteins in target cells. While this is highly effective in vitro, why might it be deadly in vivo?
   a. It will increase the DNA replication of the user's microbiome in vivo
   b. The drug will cause a reduction in the charge separation between DNA and RNA
   c. The drug may repress transcription necessary/non-cancerous genes in *in vivo* not seen *in vitro*
   d. Due to the negative charge of a methyl group, methylation of histones will create more

(**4 &5**) A certain transcriptional repressor protein binds in a repressor site that blocks a TAP's communication with the core promoter.

4. What part of the BTA should be "communicating" with the TAP?
   a. The insulator
   b. TFII-D
   c. The mediator
   d. Silencer Protein
5. What effect does this have on initiation of eukaryotic transcription?
   a. Increase the rate of elongation, not initiation
   b. Decrease the number of TFs that form the BTA
   c. Reduces the need for an enhancer
   d. Reduces the rate of BTA assembly
6. A prokaryotic cell has the *Lac Operon*: P_II^+ & PO^cZY. What is produced when [glucose] is low, but lactose is present?
   a. *β*-Gal will be produced and both convert [to allolactose] or cleave lactose

b. Lactose will not be transformed due to catabolite repression
c. *β*-Gal will be produced, but will only convert lactose to allolactose
d. Permease, but not *β*-Gal, will be produced

THINGS YOU MAY STRUGGLE WITH:

1. An inducer is normally a reactant or substrate of the pathway moderated by the structural gene products. A corepressor is often the product of a metabolic pathway involving the structural gene.
2. Allosteric interaction is where a molecule binds . An allosteric activator (ex *trp* → **corepressor**) will make the active site ready to bind substrates, **activating** an enzyme. An inhibitor (ex *lac* → **inducer**) will change the active site to prevent substrate binding, **inhibiting** the enzyme.
3. BTA alone gives basal rate of transcription; TAP binding gives normal or higher rates of transcription
4. TAPs *only* affect the rate of initiation (that is, during BTA assembly)

CONGRATS: You made it to the end of the resource! Thanks for checking out these weekly resources! Don't forget to check out our website for group tutoring times, video tutorials and lots of other resources: www.baylor.edu/tutoring!

Answers to check your learning questions are below!

Answers:

1. D; the super-repressor will inhibit the top one; the bottom one has a non-functional promoter so despite the conditional operator it that operon can't be transcribed either.
2. B
3. C
4. C
5. D
6. A