Hello everybody, there’s a lot of material to convey here, so I put links to many videos that were helpful to myself and my peers when we took genetics. Please use this resource and the videos as you approach operons!

Remember: the Tutoring Center offers free individual and group tutoring for this Genetics. Our Group Tutoring sessions will be Thursday from 5:15-6:15 PM at the Sid Rich basement, room 75! You can reserve a spot at https://baylor.edu/tutoring. I hope to see you there!

**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 lact operon codes for genes that help lactose enter a cell and be cleaved.
Operon:

$Lac P \rightarrow$ promoter (where RNA-pol binds)
$Lac O \rightarrow$ operator (where the repressor binds)

$Z$-Gene ($\beta$-Galactosidase): aka “$\beta$-Gal”cleaves lactose ($lac Z$) $\rightarrow$ structural gene

$\beta$-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:

$Lac P_I \rightarrow$ regulatory promoter

$Lac I \rightarrow$ 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) $\rightarrow$ lactose can’t enter the cell!

Regulator Gene Mutation:

$Lac I^-$: regulator mutation; can’t bind to operator

$Lac I^+$: superrepressor; no allosteric site $\rightarrow$ cannot be inactivated by inducer

$Lac P^-$: promoter mutation; RNA-pol can’t bind ever $\rightarrow$ 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

All diagrams, tables and figures are the property of Benjamin A. Pierce; Genetics: A Conceptual Approach
**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*

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**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 Coactivators:** 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)

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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

Week 10 Concept Check:

1. What is produced in the presence of lactose of the following operon set?
   
   I’S'O'Z'Y'/I'S'O'Z'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 \textit{in vivo} not seen \textit{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 \textit{Lac Operon}: P,l+ & PO'ZY. What is produced when [glucose] is low, but lactose is present?
   
   a. \textit{β}-Gal will be produced and both convert [to allolactose] or cleave lactose

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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 \(trp \rightarrow \text{corepressor}\)) will make the active site ready to bind substrates, activating an enzyme. An inhibitor (ex \(lac \rightarrow \text{inducer}\)) 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! Again, group tutoring will be every Thursday from 5:15-6:30 PM. You can reserve a spot at https://baylor.edu/tutoring. I hope to see you there!

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