Week 14
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.

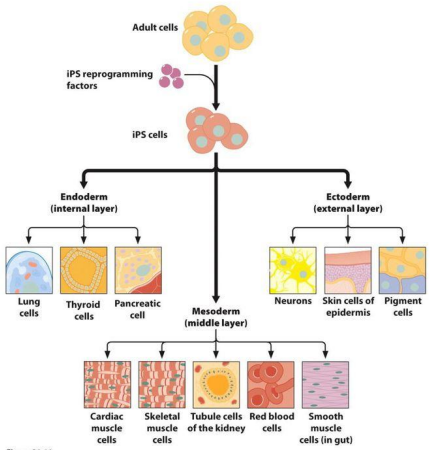
Keywords: Epigenetic, cancer, speciation, evolution

Topic of the Week: ***Epigenetics*** (21.1-3)

Epigenetics: phenotypic differences transmitted without genetic variation due to structural variation of chromatin (**environmental** impact on gene expression)

All cells in an organism have the ***same*** genome, yet express wildly differently; what causes one cell to become a nerve and another to become a muscle cell and so-on is modulated by **epigenetics**.

Additionally, *experiences in life* (both positive and negative) will cause changes to chromatin structure by various mechanisms. This can cause heritable changes to DNA that will influence phenotypes of offspring, again, **without** change to DNA sequence.



Stem Cell: an undifferentiated cell that has the ability to differentiate to any cell type in that organism's body

Pluripotent: the ability of a stem cell to divide into one of many types of cells (**see right**)

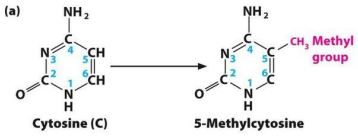
Induced Pluripotency (iPS): stem cells which use 'reprogramming factors' to revert damaged native ("host") cells of an individual into [**induced**] **pluripotent stem cells** (iPS). This permits **stem cell therapy** without ethical concerns such as the use of *embryonic stem cells*.

Mechanisms For Epigenetics:

DNA Methylation: addition of methyl ($-CH_3$) groups to **C**pG islands on DNA [near promoters]; **methyltransferase** adds and **demethylase** removes

How is this 'passed down'? Prior to replication, CpG islands are methylated. When DNA is replicated, each new DNA molecule is *hemi*-methylated (half). *Methyltransferases* are attracted to DNA which complete the methylation of the new strand.

Repression of Transcription: methylated DNA recruits **deacetylases** and **repressor proteins**, while inhibiting the binding of **TFs**.

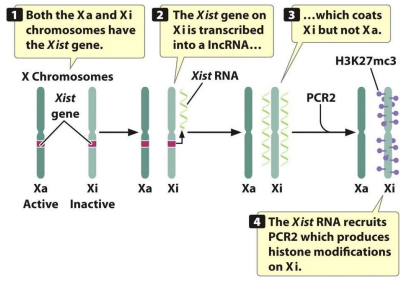


Histone Modification: in general, phosphates, methyl groups, acetyl groups, or ubiquitin may be added to or removed from histones.

Acetylation: adding acetyl groups to histones minimizes charge (from **Arg**$^+$ and **Lys**$^+$); promotes looser binding of DNA to histones ↑ transcription

Methylation: results may vary; may promote/reduce transcription (**it depends!**)

Non-Coding RNA: **lncRNA** (see *X-inactivation*) and **siRNA** direct DNA methylation and histone modification



X-Inactivation: in all normal (**XX**) females (or all with >1 X chromosome), all but one X-chromosome is inactivated to account for **dosage compensation** (see ch. 4).

Xist: a long noncoding lncRNA molecule is synthesized by one X-chromosome (selected at random) that will wrap the coding chromosome and attract additional regulatory molecules. → this structural change causes the chromosome to be inactivated (***barr body***)

Genomic Imprinting: males and females have different patterns of methylation; for certain genes or structural mutations, whether they are inherited from the mother or father will determine the phenotype of the offspring.

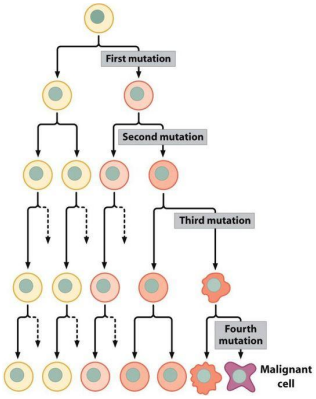
Highlight #1: Cancer and Clonal Evolution (23.1)

Cancer: cells unable to respond to normal controls to cell division which proliferate (divide) indefinitely → organize into **tumors** (masses of cancerous cells) which starve healthy tissue of nutrients, resources and space.

Benign: a localized group of cancer cells which will not invade other tissues

Malignant: cells which invade and damage other tissues through **metastasis** (traveling to other parts of the body to form '*secondary tumors*')

Clonal Evolution: mutations which increase the ability of a tumor to survive and reproduce will be 'selected for' in a growing tumor as it moves towards malignancy.



Alterations: DNA repair pathways, altered chromosomal segregation (creation of aneuploids), structural change to allow *extravasation* (invasion of other tissues during **metastasis**)

Genes vs. Environment: because DNA changes cause cancer, inherited mutations and acquired mutations may cause cancer. Carrying versions

of possible cancer causing (**proto-oncogenes**) may predispose an individual to cancer.

Acquired mutations due to natural DNA damages (ch. 18) or due to mutagenic chemicals or radiation pose further predispositions to cancer development.

Knudson's Multistep Model For Cancer: the mechanism that describes the inheritance of genetically-linked cancers. Also known as the **'Two Hit' Hypothesis** is based on the two mutations [two hits] needed for **retinoblastoma** (a rare pediatric cancer of the eyes)

People **without** the inherited mutation need two mutations to develop mutations in a single eye → this requires two rare, independent events to occur together

People **with** the inherited mutation only need 'one more hit' to develop this cancer, so it only takes the odds of a single mutation for them to develop cancer in both eyes (because they have the *inherited* mutant gene copy in tissue in each eye)

Highlight #2: Evolutionary Genetics (26.1-4)

Biological Evolution: Genetic Change through time

Random mutations arise, causing genetic variation

Increase/decrease in frequencies of genetic variants

Anagenesis: evolution within a single lineage

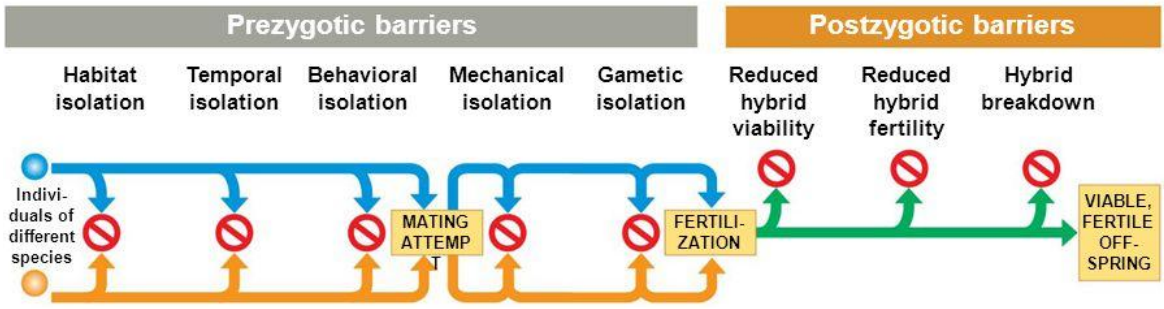
Cladogenesis: the splitting of one lineage into two (form 2 new species)

Neutral Mutation Hypothesis: most variation is *adaptively neutral* (equal fitness)

Balancing Selection: some genetic variation is maintained by natural selection; both alleles at the same locus are maintained because of higher *heterozygote fitness*

Biological species concept: A group of organisms which can interbreed successfully with one another, but are ***reproductively isolated*** by members of other species

Reproductive isolation:



Prezygotic: factors that prevent the formation of a hybrid zygote

Ecological: different niche

Temporal: different time of day/year

Behavioral: different courting rituals

Mechanical: different anatomy

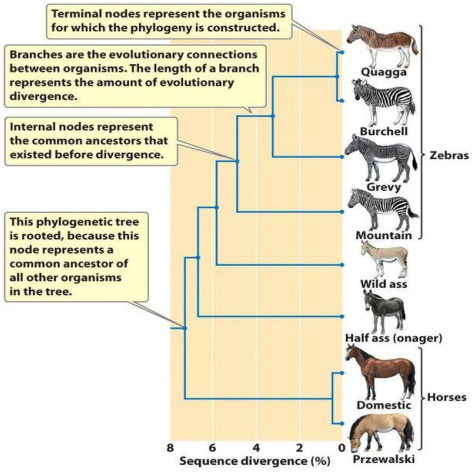
Gametic: mating occurs without gametes fusing

Postzygotic: barriers that prevent the success of a biological hybrid zygote/offspring

Hybrid inviability: no zygote

Hybrid infertility: no offspring
Hybrid breakdown: survive at first but over generations they do not survive

Speciation:
Allopatric Speciation: geographical barrier cuts off gene flow
Sympatric Speciation: speciation without physical barrier
Phylogenetic Trees: depicts evolutionary relationships
Node: common ancestor
Rooted: common ancestor node which is the common ancestor between all organisms
The diagram to the right is an example of a phylogenetic tree of the relationship between zebra and horse families



CHECK YOUR LEARNING

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

1. What is an imprinted gene, and how does the sex of a parent affect the expression of a gene (ie. the phenotype) in the offspring?
    a. A methylated gene; the DNA sequence is different between males and females
    b. A ubiquitinated gene; the charge on DNA is different in male vs female imprinted genes, so the phenotypic expression varies
    c. A methylated gene; methylation is different in males and females so the expression varies without change to sequence
    d. An acetylated histone; patterns are different in males and females
2. Lysine generally has a positive charge when unmodified; methyl and acetyl groups may bind to these to reduce the charge separation between the sugar-phosphate backbone of DNA and the histone. If CpG islands are methylated, what will happen to the modification of a lysine?
    a. Methylation will increase
    b. Histones are deacetylated at lysine residues
    c. Modifications that increase transcription will occur
    d. Acetylases are recruited to histones at lysine residues
3. A supposed proto-oncogenes XZT8Y and XZR7Y control the expression of factor-X a [pretend] protein involved in regulating the production of cyclin in myocytes. If an individual has a family history of this type of cancer, how does this affect their likelihood of developing cancer?
    a. They have a lower likelihood of developing this cancer
    b. They have a higher chance of developing this form of cancer because are more likely to have a proto oncogene copy

   c. They have the same risk of developing this cancer as anyone else
   d. They would have a smaller risk than non-family members if their parents had this cancer
4. A nocturnal owl cannot mate with a diurnal (awake during the day) owl. Which type of reproductive isolation does this represent?
   a. Postzygotic
   b. Mechanical
   c. Behavioral
   d. Temporal
5. In the evolutionary lineage from species A to species D, species B and C branch off. What type of evolution does this illustrate?
   a. Anagenesis
   b. Sympatric Speciation
   c. Cladogenesis
   d. Balancing selection
6. Prader Willi syndrome is due to a deletion on chromosome 15 inherited from the father. Angelman syndrome is a disorder due to a chromosome 15 deletion inherited from the mother. What pattern of genetic inheritance is displayed in this example?
   a. Genomic imprinting
   b. Sex linked genes
   c. Sex limited genes
   d. Multiple alleles
7. Mark is a 27 year old male that develops a rare liver cancer called fibrolamellar carcinoma. Suppose that this is caused by a single dominant mutation in his liver cells. If Mark marries Andrea, a woman without liver cancer. If they have a child, what are the odds that this child will have this same cancer?
   a. 0%
   b. 12.5%
   c. 50%
   d. 100%

THINGS YOU MAY STRUGGLE WITH:

1. With genomic imprinting, please remember that the DNA sequence is the same; the only difference here will be chromatin modification (i.e. methylation)!
2. X inactivation occurs in all cells with **≥2** X chromosomes. Tying together concepts; remember discussing genetic mosaicism back in chapter 4? It was discussed that ~one X-chromosome at random will be inactivated at random, meaning that a heterozygous individual at sex-linked loci could express one phenotype in some areas and its opposite in other areas.

3. Cancer arises from changes to DNA. It can run in families, but it is far more influenced by **environmental factors**. If cancer were inherited like conventional genetic diseases, it could be expected that all cells or even all of a particular tissue-type would express a cancer from an offspring of a parent with cancer (as long as it affected the gametes, of course). Thus we look to models like **Knudson's 'Two-Hit' Hypothesis** to show a more robust model for the inheritance of certain cancers.

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. **C.**
2. **B.**
3. **B.**
    a. This is an extension of the 'Two Hit' Hypothesis
4. **D.**
5. **C.**
6. **A.**
7. **A.**
    a. This cancer is developed within hepatocytes, thus this would not affect his gametes. Because of this, the cancer would not be passed down to his offspring. This would be a *somatic* mutation that turns this proto-oncogene into an oncogene which would not be heritable.