Hello everybody, here is a final review! This is an overview of major topics covered this fall.

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:** Final Review

**Section 1:** Review of Conceptual Genetics (Weeks 3 & 4)

**Chromosomes:** chromosomes are bundles of DNA wrapped around proteins
- **Sister Chromatid:** 1 chromosome composed of 2 DNA strands joined at the centromere by cohesin proteins
- **Locus:** the specific point on a chromosome where a gene is located

**Eukaryotes vs. Prokaryotes:**
https://www.youtube.com/watch?v=RQ-SMCmWB1s

**Cell Cycle:** the cycle of cellular growth and division
- **Interphase:** the part of the cell cycle dedicated to growth/repair, metabolism, and DNA replication
- **M-Phase:** division of the nucleus
- **Mitosis:** the division of a parent cell into two identical daughter cells

(2n → 2n) → Equational division

**Meiosis:** The 2 divisions of a single diploid parent cell to 4 genetically different haploid daughters (2n→n)

**Sources of Variation:**
- **Random Alignment** of homologs in metaphase 1

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**Crossing Over** of homologs in prophase 1 (*chiatisma*)

**Meiosis 1**: reductional division → separates homologous pairs (2n → n)

**Shugoshin** prevents separase from lysing cohesins in sister chromatids

**Meiosis 2**: equational division → divides chromatids as in mitosis (n → n)

**Mendelian Inheritance**: the general pattern of heredity discovered by Gregor Mendel

**Law of Segregation**: each individual has 2 copies of an allele which code for a trait; these two alleles are separated (*Anaphase 1*) of gamete formation

**Law of Independent Assortment**: in a cross involving more than two genes, the alleles segregate independently of each other (*unless they are linked*)

**Chromosomal Sex Determination**: generally, most studied organisms display the X-Y system for sex determination, though several others exist

**Sex Linked Gene**: a gene located on a sex chromosome

- **X-Linked**: mother to child **or** father to child (dominant or recessive)
- **Y-Linked**: father to son only

**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.

**Lyon Hypothesis**: in all individuals with more than 1 X-chromosome, all but 1 will be inactivated (at random) → **Barr Body**: the remnant of an inactivated X chromosome

*note: some sex determining genes are not inactivated, so the ‘feminizing’ effect depends on X-chromosome dosage and whether or not there is an SRY gene

**Chapter 6: Pedigrees** (covered in the week 4 resource; watch this short video!)

https://www.youtube.com/watch?v=Gd09V2AkZv4

**Section 2**: Review of Mathematical Genetics (Weeks 3, 4, 13)

**Crosses**: do you best to memorize the *common patterns* in all Mendelian crosses

- **Monohybrid Cross**: a cross at a single locus (*Law of Segregation*)
- **Dihybrid Cross**: a cross at two loci (*Law of Independent Assortment*)
- **Testcross**: a cross between a homozygous recessive and and an unknown genotype

**Addition Rules**: rules for *adding* probabilities (Keyword “OR”)

**Multiplication Rules**: rules for *multiplying* probabilities (Keyword “AND”)

**Conditional Probability**: the probability of an event happening *depending* on another

**Binomial Expansion**: the probability (P) that an event (x) with a probability p will occur s times and the alternate event (y) with probability q will happen t times: 

\[ P = \frac{n!}{s!t!}(p^s \times q^t) \]

*n* is the number of times an event occurs and “!” is the factorial, and is typed on the calculator as [value]!

**Chi Square (X²)**: a statistical test which assess if difference between observed and expected values is significant

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\[ X^2 = \sum \frac{(\text{Observed} - \text{Expected})^2}{\text{Expected}} \]

*note: degrees of freedom (DF) is n-1 (number of samples -1)

**Null Hypothesis (H₀):** states that the difference between O and E is due to chance alone
**α-Value = 0.05:** states that you are 95% (1.0 - 0.05 = 0.95) confident in your significance

**Critical Value:** value on \( X^2 \) table that matches with the p value at a given DF

**Rule of thumb:** if \( X^2 > CV, p < 0.05 \) → significant difference; reject H₀
if \( X^2 < CV, p > 0.05 \) → insignificant difference; FAIL TO REJECT H₀

**Linked Genes:** genes which do not follow mendel’s second law of inheritance (in that they do not segregate independently of one another) because the cross over together

**Crossing Over:** exchange of material between adjacent arms on homologous chromosomes in prophase I of gamete formation

**Recombination:** the formation of novel allelic combinations not present in the parents

\[ f_R = \frac{\text{number of recombinant progeny}}{\text{total progeny}} \times 100\% \]

\( f_R \) represents the likelihood that crossing over produces recombinant offspring at two incompletely linked loci

The **recombination frequency** between two completely linked loci would be 50% if a crossover event happened in every meiosis. This is because at a single crossover, half of the gametes will be recombinant and the other half will be non-recombinant.

**Frequency of recombinant gametes:** the likelihood of the creation of each gamete, so frequency of recombinant gametes = \( \frac{1}{2} f_R \)

**Testcross:** an individual with hetero- or homozygous dominant expression of a gene is crossed with an individual who is recessive at both loci

*Generally we use a double heterozygote crossed with a homozygous recessive

What is the expected genotypic ratio of a AaBb x aabb cross? 1:1:1:1; If genes are linked, the number will deviate from this

**Gene Configuration:** the conformation of homologous chromosomes with respect to where the how the dominant and recessive alleles are aligned at each locus coupling (cis) \( (\frac{A}{a} \frac{B}{b}, \text{same side}) \text{ or repulsion (trans)} \ (\frac{A}{a} \frac{b}{B}, \text{opposite sides}) \)

**Three-Point Testcross:** a single testcross used to show a double crossover

**Why:** use a gene in between 2 loci of crossovers

\[
\begin{array}{ccc}
A & B & C \\
\text{a} & B & c \\
\text{a} & \text{B} & \text{C} \\
\text{a} & \text{b} & \text{c} \\
\text{a} & \text{b} & \text{c} \\
\text{A} & \text{b} & \text{C} \\
\text{A} & \text{b} & \text{C} \\
\text{A} & \text{b} & \text{C} \\
\text{A} & \text{b} & \text{C} \\
\text{A} & \text{b} & \text{C} \\
\text{A} & \text{b} & \text{C} \\
\end{array}
\]

**OR**

\[
\begin{array}{ccc}
A & B & C \\
a & b & c \\
a & B & a \\
b & c & a \\
b & c & a \\
c & a & b \\
\end{array}
\]

**Gametes:** ^nonrecombinant \hspace{1cm} ^single crossover^ \hspace{1cm} ^double crossover^

**How:** follow the following steps to solve the position of genes and
1. Write out genotypes or phenotypes of offspring and categorize them by crossover (on noncrossover) pairs
   a. The double crossover (DCO) will be the smallest number of progeny
   b. The non-recombinant group will be the largest number of progeny
2. Locate find the middle gene by comparing the DCO with the nonrecombinant
   a. Where? the middle gene is the place where the DCO is different than the non-recombinant
3. Rewrite the genotypes in proper order (ie with middle gene between the outside genes)
4. Calculate the recombination frequency \( f_R \) for each crossover
5. Calculate coefficient of coincidence and interference

**Coefficient of Coincidence:** the frequency of DCO’s relative to total crossovers
\[
cc = \frac{\text{observed DCO}}{\text{expected DCO}} = \frac{DCO}{(A\!-\!dc)*(C\!=\!Dc) \cdot \text{total progeny}}
\]

**Interference:** the presence of one crossover event tends to inhibit the occurrence of another
*larger values of I means greater interference between crossovers*
\[
I = 1.0 - cc = 0.228
\]

**Heritability:** the proportion of phenotypic variance which can be explained by genetic variance

**Phenotypic Variance** \( (V_P) \): \( V_P = V_G + V_E + V_{GE} \)

**Genetic variance** \( (V_G) \): \( V_G = V_D + V_A + V_I \)
*thus, \( V_P = (V_D + V_A + V_I) + V_E + V_{GE} \)*

**Broad-Sense Heritability** \( (H^2) \): \( H^2 = \frac{V_G}{V_P} \)

**Narrow-Sense Heritability** \( (h^2) \): \( h^2 = \frac{V_A}{V_P} \)

**Response to Selection:** the extent of selected character change in a generation \( (R) \rightarrow R = h^2 \times S \)

**Selection Differential:** the difference between the selected populations’ mean and that of the total population for the characteristic

**Population Genetics:** the study of microevolution (changes in the allelic frequencies within a population of individuals) that can lead to speciation (the creation of a new species)

**Gene Flow:** the transmission of genetic information between two groups of a species; cutoff of gene flow between populations considered speciation.

**Allelic Frequency → NOTE:** 2N is the total number of alleles present

**Dominant Allelic Frequency:** the frequency of a dominant allele (ex. A)
\[
f(A) = p = \frac{2n(AA) + n(Aa)}{2N}
\]

**Multiple Alleles:** when there is more than one allele (ex A1, A2, …)
\[
f(A^3) = p = \frac{2n(A3A3) + n(A3A1) + n(A3A2)}{2N}
\]

**Recessive Allelic Frequency:** the frequency of a recessive allele (ex. a)
\[
f(a) = q = \frac{2n(aa) + n(Aa)}{2N}
\]

**Sex-Linked (X-Linked) Genes:** slight variation, were the number of males and females is considered as \( m \) and \( f \), respectively
\[
f(X) = \frac{2n(X1X1) + n(X1X2) + n(X1Y)}{2Nf + 2Nm}
\]

**Hardy-Weinberg Equilibrium:** what about a non-evolving population? Hardy-Weinburg equilibrium describes when a population can be at “rest,” ie. not evolving:

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Ben Fitch

**Large population, Random mating, No mutations, No natural selection, No migration**

**Hardy-Weinberg Equation:**

\[ p^2 + 2pq + q^2 = 1 \]
\[ p + q = 1 \]

- \( p \): dominant allelic frequency
- \( q \): recessive allelic frequency
- \( p^2 \): frequency of homozygous dominant
- \( q^2 \): frequency of homozygous recessive
- \( 2pq \): frequency of heterozygotes

**Section 3: DNA and Chromosomal Structure and Discovery (Week 6)**

**Deoxyribonucleic Acid:** DNA

**Ribonucleic Acid:** RNA

**Nucleic Acid Structure** → **Chargaff’s Rules:** the proportion of A&T and G&C are **equivalent** in DNA and the total proportions add up to 100%

**Griffith’s Experiment:**

Transforming Principle: some “transforming substance” had to have caused the change from the non-virulent to virulent *S. pneumoniae*…

we now know this is DNA

**Avery, MacLeod and McCarty Experiment:** proved that DNA is the “transforming substance”; Used a modified version of Griffith’s experiment where digestive enzymes were applied to transformed bacteria

**Watson and Crick’s Discovery of DNA’s 3D Structure:** Watson, Crick and Franklin discovered DNA’s structure in 1953

**Chromosomal Structure:**

**Chromatin:** the complex of DNA and proteins

**DNase Hypersensitive Site:** sites where DNA is less tightly bound

**Histones:** proteins which associate with DNA (only in eukaryotes and some archaea)

**Five Types:** H1, H2A, H2B, H2, H4

**Nucleosome:** A DNA-histone complex which DNA wraps around (~146bp)

**Core Nucleosome:** an octamer (2 sets of) H2A, H2B, H3, H4

**H1 + Linker DNA:** H1 holds the DNA in place on the nucleosome and linker DNA (~50 bp) joins adjacent nucleosomes

**Histones** generally tend to express (+) charged residues (Lys, Arg) to attract the (-) charged phosphate backbone of DNA → adding methyl or acetyl groups decreases affinity of DNA for a histone

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Section 4: The Central Dogma (Weeks 7, 9, and 10)

Meselson-Stahl Experiment: Proved DNA replication is semiconservative

Stages of Replication:
- Initiation
- Unwinding
- Elongation

Enzymes:

<table>
<thead>
<tr>
<th>Eukaryotic</th>
<th>Prokaryotic</th>
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<tbody>
<tr>
<td><strong>DNA-pol α</strong>: has primase activity; creates RNA primer followed by a short stretch of DNA; <strong>DNA-pol δ</strong>: completes replication of the lagging strand; <strong>DNA-pol ε</strong>: replicates the leading strand; <strong>DNA ligase</strong>: joins the Okazaki fragments</td>
<td><strong>DNA primase</strong> binds to helicase and forms RNA primers; <strong>DNA-pol I</strong> replaces RNA with DNA nucleotides (special exonuclease 5’--→3’); <strong>DNA-pol III</strong> catalyzes the addition of dNTPs to the growing strands of new DNA</td>
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</tbody>
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Transcription (DNA → RNA)

Initiation
1. Promoter Recognition:
   a. The core enzyme of **RNA-pol** binds to the σ factor to form the RNA-pol holoenzyme. This allows the polymerase to bind
2. Formation of transcription bubble: **RNA-pol holoenzyme** begins to unravel DNA
3. Synthesize first bonds between rNTPs (note: the first nucleotide keeps all 3 phosphates)
4. Escape of Transcription apparatus from promoter: **RNA-polymerase** undergoes a change in shape that causes it to release σ and ‘escape’ the promoter to move downstream

Elongation

**RNA-pol** acts as a helicase to unwind downstream DNA and rewind upstream DNA; it also adds rNTPs complementary to the template/non-coding strand 5’ → 3’

Termination (once **RNA-pol** reaches the terminator)
- **Rho-Dependent Termination**: a protein (rho) causes termination
- **Rho-Independent Termination**: inverted repeats and/or poly-uracil stretches

RNA Processing:
- prevents degradation of mRNA and aids in
- **Addition of 5’ Cap**
- **3’-Cleavage and Polyadenylation**

Splicing: see diagram (right) snRNPs = 1 snRNA + proteins → 5 snRNPs make up a spliceosome

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Note: RNA processing may occur in Euk’s or Prok’s, but spliceosomal processing will only occur in eukaryotes.

**Translation** (RNA → Protein)

**Translation:** RNA is copied in the 5’ → 3’ direction to a protein in the N_term → C_term direction

**Codons:** units of 3 nucleotides (5’→3’) which complimentary bind to a tRNA molecule corresponding to an amino acid (Review wobble rules (ch 15/week 9))

Section 5: Gene Regulation (Week 10)

Operons

**Negative Inducible:** the regulator protein is translated in an inactive form, and then is allosterically activated

**Inducer:** molecule that binds to the allosteric site of the repressor, rendering it unable to bind to the operator [allosteric inhibition] (ex. lactose: *Lac operon*)

**Negative 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] (ex. tryptophan: *Trp operon*)

*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. [Watch Video](https://www.youtube.com/watch?v=EjRXz1xAdow)

**Chromatin Remodeling:** Pushing histones out of the way in order to allow transcription machinery to bind or chemical modification → **EUKARYOTES**
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 or induce transcription (Methyltransferase: add/Demethylase: remove)

DNA Methylation: DNA methylation represses transcription because it attracts deacetylase enzymes (DNA to wraps more tightly) CpG islands: consensus sequences for methylation near promoters (cytosines are methylated)

Eukaryotic Initiation: rate is highly regulated by the interaction between TAPs and repressor proteins which act like a foot on and off the accelerator for the rate of basal transcription apparatus (BTA aka holoenzyme) assembly at the Core Promoter.

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

Epigenetics: phenotypic differences transmitted without genetic variation due to structural variation of chromatin (environmental impact on gene expression) see ch. 17 and 21!

Section 6: Mutation and Cancer (Weeks 5 and 13)

Chromosomal Mutation: changes that vary the number and/or structure of chromosomes within an individual

Aneuploidy: change in the number of individual chromosomes (Robertsonian Translocations or Nondisjunction)

Down Syndrome: trisomy 21; developmental and physical delays: https://www.youtube.com/watch?v=eruPJS_guNE

Primary: caused by nondisjunction in Anaphase II (2n+1 = 47)

Familial: caused by a robertsonian translocation between chromosomes 14 and 21 (2n = 46)

Cancer: cells unable to respond to normal controls to cell division which proliferate (divide) indefinitely

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.

https://www.youtube.com/watch?v=UopUxkeC4Ls
Section 7: Other Topics in Genetics (Weeks 11, 12, 13, 15)

Gel Electrophoresis (GE): Separation of DNA due to its mass (ie molecular weight)
DNA moves down an electrophoresis gel due to its net negatively charged backbone

Gel: highly porous agarose gel allows DNA to pass through. The largest pieces will travel the furthest and the smallest pieces will travel the furthest and the largest fragments will travel the least far. DNA is dyed to visualize under UV light (above, right)

Cathode (-): the negatively charged pole will repel the DNA towards the anode
Anode (+): the negatively charged DNA will be attracted to the positive charge

Polymerase Chain Reaction (PCR): DNA amplification using thermocycling (cycles of changing temperatures)

‘Raw Materials’: buffer solution (KCl or MgCl₂), Taq Polymerase, dNTPs, Template DNA, forward and reverse primer (ie free 3’-OH group)

Reaction: a process repeated ~20-40 times to amplify DNA exponentially

Denaturation (~2min @95°C): separates (denatures) DNA strands at high heat
Annealing (~1min @60°C): primers bind (anneal) to the ssDNA templates
Elongation (~1min @72°C): Taq Pol. adds dNTPs to ssDNA template

DNA Sequencing: determining the primary (nucleic acid) sequence of a DNA molecule

Sanger ‘Di-deoxy’ Sequencing: reaction is similar to PCR, but uses 4 separate containers with one of the four types of di-deoxy nucleoside triphosphates (ddNTPs) in addition to dNTPs. This gives the sequence complementary to each DNA strand

These lack a 3’-OH group, so they terminate DNA replication

Each of the four reactions (ddATP, ddGTP, ddTTP, and ddCTP) are placed into separate gels and run in electrophoresis → each ddNTPs has a fluorescent tag

The shortest molecules travel the furthest, so the DNA sequence can be determined by looking at band position from the bottom up [to the wells].

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:

<table>
<thead>
<tr>
<th>Prezygotic barriers</th>
<th>Postzygotic barriers</th>
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<tbody>
<tr>
<td>Habitat isolation</td>
<td>Reduced hybrid viability</td>
</tr>
<tr>
<td>Temporal isolation</td>
<td>Reduced hybrid fertility</td>
</tr>
<tr>
<td>Behavioral isolation</td>
<td>Hybrid breakdown</td>
</tr>
<tr>
<td>Mechanical isolation</td>
<td></td>
</tr>
<tr>
<td>Gametic isolation</td>
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Individuals of different species
Practice Questions From the Whole Course:

1. Click this link to view the practice problems:
   https://docs.google.com/document/d/13vQZ0q78hm8ORjilg22ZpWfVuq8dSWo6kEbq9aGfMCK/edit?usp=sharing

CONGRATS; You made it to the end of this COURSE! The tutoring center will be closing early on the last day of classes (05/05/22), so the last group tutoring session will be held 04/28/22. However, please feel free to come meet with me in the tutoring center with any questions over content or practice material!

Tuesday: 11:00am-12:30pm
Wednesday: 11:30am-1:30pm
Thursday: 11:00am-12:30pm

(by appointment only for the first 30 minutes of each shift)