Happy Monday!

Have out:
   15.1 Notes (due today)
   Pen or pencil

Upcoming:
   15.1 Quiz on block day
   15.2 Notes due Friday (2/1)
Plan for today

- Check 15.1 Notes
- Go over 15.1
- Practice problems
15.1: Human Chromosomes
Karyotypes

Shows the complete set of diploid chromosomes grouped together in pairs and organized in order of decreasing size.

Used to study a person’s **genome**—their full set of DNA.

A typical human karyotype will have 23 pairs of chromosomes.
What is the largest chromosome?

What is the smallest chromosome?

What biological sex is the person shown in this karyotype?
Autosomal chromosomes are everything BUT sex chromosomes (46-2=44 total)

Sex chromosomes are X and Y in humans

XX=Female (biological sex)

XY=Male (biological sex)
Patterns of Inheritance

**Simple dominance**: each allele is either dominant or recessive. Dominant traits “win” and are expressed over recessive.

**Codominance and Multiple Alleles**: both alleles are expressed, one doesn’t “win” over the other one.
**Sex-linked inheritance:** the genes on X and Y sex chromosomes follow sex-linkage.

Color blindness usually occurs in males! This is because colorblindness is caused by a mutation on the X chromosome.

- **Not colorblind:** XX, XY, XXX
- **Colorblind:** XY, XX (pretty rare)
My favorite!

**X-Chromosome Inactivation**—Females have two X chromosomes, but each cell really only needs one X chromosome to function. Every cell randomly chooses an X chromosome to become inactive.

The inactive X chromosome in a cell is called a **Barr body**.

This is how we get calico cats!
Human Pedigrees

- A **pedigree** shows relationships between family members
  - Can be used to analyze patterns of inheritance for a particular trait
From a pedigree, you can infer genotypes and predict outcomes.

The information gained from pedigree analysis makes it possible to determine the nature of genes and alleles associated with inherited human traits.
Punnett Square Review

Allele: one version of a gene (F or f)

Homozygous: two of the same allele (ff or FF)

Heterozygous: one of each allele (Ff)

Genotype: the alleles on the genes

Phenotype: the expressed trait
Let’s practice

Look at the pedigree in the folder at your table.

What are all of the possible genotypes?

What genotype is person 2?

What genotype is person 1?

Let’s do a punnett square.
15.2: Human Genetic Disorders
Plan for today (1/29)

- Time to work on practice problems from Monday
- Start on research for graphic organizer
- Exit Ticket
Genetic Disorders Graphic Organizer

For each genetic disorder listed in Section 15.2:

- Each table has information about a different genetic disorder
- Each person has a research role (see the slide)
- Be ready to share your information with the rest of the class tomorrow
Roles for research

A: the genetic cause of the disorder

B: common symptoms to look for

C: how and when the disorder appears

D: Long-term impacts of the disorder
Exit-ticket

Red hair is a recessive trait. Harry Potter has dark hair and he marries Ginny Weasley, who has red hair. Lily Potter, Harry’s mom, had dark red hair.

1. What are Harry and Ginny’s genotypes for hair color?
2. Make a punnett square: Is it possible for Harry and Ginny to have a child with red hair?
3. What percentage of their children would you expect to have dark hair?
Chromosomal Disorders

- **Nondisjunction**: an error in meiosis where homologous chromosomes fail to separate, “not coming apart”
- Causes *gametes* to have an abnormal number of chromosomes leading to a disorder of chromosome numbers
- Trisomy: three copies of a chromosome
- Monosomy: one copy of the chromosome
Chromosomal Disorders

- Down syndrome: trisomy 21, three copies of the 21st chromosome
- Turner’s syndrome: only one X chromosome (X,__)
- Klinefelter’s syndrome: two X chromosome in males (X,X,Y)
Molecule to Phenotype

- **Phenotype**: traits that are expressed
- **Genotype**: the inherited genetic information, the genes that code for phenotype
- Changes in a gene’s DNA sequence can change proteins by altering their amino acid sequences, which may directly affect an individual’s phenotype
Disorders caused by individual genes

- **Sickle Cell disease**: caused by a defective allele for beta-globin, which makes hemoglobin a little less soluble
  - Hemoglobin clumps up and distorts the shape of blood cells
- **Cystic fibrosis**: caused by the deletion of three bases in the gene for cystic fibrosis transmembrane conductance regulator (CFTR)
- **Huntington’s disease**: caused by a dominant allele for a protein found in brain cells
Genetic Advantages

- People heterozygous for CF would have been able to fight off the bacteria that cause typhoid
- People heterozygous for sickle cell would be less susceptible to malaria
15.3: Studying the Human Genome
Manipulating DNA

- **Restriction enzymes** cut DNA at specific sites
- By using tools that cut, separate, and copy nucleic acids, scientists can now read DNA base sequences
- Bacteria make restriction enzymes that cut only once they recognize certain sequences of bases
● **Gel electrophoresis** sorts pieces of DNA that have been cut by size
● The smaller the piece of DNA, the farther it can travel
Reading the DNA sequence

- Scientists can attach dyes to each base
- DNA cut with restriction enzymes + bases that are dyed = DNA strands that are dyed
- Do gel electrophoresis again to determine the sequence of bases
Shotgun sequencing: A computer sorts the DNA sequences based on repeating patterns in the bases. The pieces that overlap are lined up and read in order.
The Human Genome

Labs around the world now study:

which regions of DNA are transcribed into RNA,
which bind to proteins,
which are marked with epigenetic tags,
and which vary from one individual to the next.
Functions of Human Genes

Fig. 15.12

• Only about 2% of our entire genome codes for proteins
• We don’t know what most of our DNA does
Comparing individuals

● From person to person, only about 1200 base pairs will be different
● These differences are called “single nucleotide polymorphisms” (SNPs)
● As genetic technology gets better and better, more people are getting their genomes read through companies like 23andMe or AncestryDNA
• Some genes have epigenetic markers that are either going to express or silence a certain gene
• The process of expressing or silencing certain genes with epigenetic markers is called **genomic imprinting**
• **Angelman syndrome** is an example
Case Study: Patient Lee F.

You are all medical students now!
Your patient:

Lee is a 17-year-old male. He came to the hospital with a strange lump on his middle/lower back and after a few tests, you realize he has a tumor growing on his adrenal gland. In order to figure out if the tumor is dangerous, you do a biopsy (take a sample of the tumor cells). Your next step is to take a family history.

Why do you think it is important to take a family history of your patient, Lee?

https://www.hopkinsmedicine.org/healthlibrary/conditions/endocrinology/adrenal_glands_85,p00399
Patient family history

Lee has a sister, Leah (age 10), and a brother, Luke (age 6). Both are healthy. Lee’s mother, Grace, was diagnosed with bilateral breast cancer last year at age 35. Lee’s father, Brian, and Lee’s paternal grandparents have no history of cancer. Grace is the youngest of four children. Her eldest brother, Greg (age 42), and sister, Greta (age 40), have never had any signs or symptoms of cancer. She had a brother, Geoff, who died of leukemia at age 8. He was the third child of Grace’s parents. Greg’s two fraternal twin daughters have no signs or symptoms of cancer. Grace’s father, Roger, died of a soft tissue sarcoma at age 35. Grace’s mother, Renee, is still living and in excellent health. Roger’s mother died of a brain tumor at age 30. Roger was her only child.
Using the family history, create a **pedigree** that shows:

The relationships between family members:

*Lee, Leah, Luke, Grace, Brian, paternal grandparents, Greg, Greta, Geoff, Greg’s daughters, Rodger, and Renee*

Any people in the family that have had cancer
What do you notice about the pedigree that you created?

What does the pedigree tell you about your patient, Lee?

What patterns do you notice in your pedigree?

What other information do you wish you had about Lee’s family to help you diagnose Lee?
Patterns in the pedigree

Some diseases and disorders can be inherited. Using your pedigree, you will now try and figure out if and how Lee’s condition is passed on.

Copy the following chart into your notes and complete the chart using your pedigree. You can also use your textbook and notes to look up definitions of the “modes of inheritance”.

<table>
<thead>
<tr>
<th>Mode of Inheritance</th>
<th>Possible</th>
<th>Possible but Unlikely</th>
<th>Not possible</th>
<th>Brief Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal recessive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autosomal dominant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X-linked recessive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X-linked dominant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y-linked</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What mode of inheritance **best** fits the information that you have?

How did you decide?

As a medical community, do we all agree?

What kind of information do we need next to make a diagnosis for Lee?
Time to do some research

The National Institutes of Health have an online database called “Genetics Home Reference” which can give you information about the genetic variation in humans and lots of different health disorders.

You do a quick search for “autosomal dominant adrenal cancer” and get 5 possible results.
<table>
<thead>
<tr>
<th>Genetic Disorder</th>
<th>OMIM #</th>
<th>Gene(s) involved</th>
<th>Clinical manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple endocrine neoplasia</td>
<td>131100 &amp; others</td>
<td>$MEN, RET$ or $CDKN1B$</td>
<td>Tumors of the parathyroid/pituitary glands and pancreas; kidney stones, hypertension, fatigue, vomiting, nausea.</td>
</tr>
<tr>
<td>Carney complex type I</td>
<td>160980</td>
<td>$PRKAR1A$</td>
<td>Signs/symptoms commonly begin in teens/early adulthood. Changes in skin pigmentation (brown spots), heart tumors, tumors in endocrine tissues (thyroid, testes, ovaries)</td>
</tr>
<tr>
<td>Li Fraumeni syndrome</td>
<td>151623</td>
<td>$TP53$</td>
<td>Breast, bone and soft tissue cancers common. Cancers of blood-forming tissues and adrenocortical carcinomas are possible among others.</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>256700</td>
<td>$KIF1B$ &amp; others</td>
<td>Most often affects children under age 5. Tumor originates in adrenal gland but can also form in nerve tissue of abdomen, chest, and pelvis. Can metastasize to bone, liver, skin. Fatigue, pain, loss of appetite, and more possible.</td>
</tr>
<tr>
<td>Von-Hippel-Lindau syndrome</td>
<td>193300</td>
<td>$VHL$</td>
<td>Tumors (both benign and malignant) and cysts in various locations (kidneys, pancreas, male genital tract, inner ear), non-cancerous blood vessel tumors.</td>
</tr>
</tbody>
</table>
Based off the information from both Lee and his family, what genetic disorder do you think is *most likely* causing Lee’s tumor?

What gene(s) are involved in this genetic disorder?

Another pediatric oncologist is worried about Lee’s siblings, Leah and Luke. Why are they concerned?
What do we do next?

Now that we have an idea about what gene is causing Lee’s tumor, the way that this gene is passed on, and Lee’s family history, what kinds of tests can we do to make sure that we are correct?

Why do we need to double check our diagnosis?

What do we know about genetic testing?

What kinds of tissue samples do we need? Why?
Final recommendations

Unfortunately, Lee’s biopsy results came back and show that Lee does have adrenocortical carcinoma (ACC). The good news is that you caught it early and you are good friends with a renowned researcher and doctor that specializes in gene therapy for adrenal cancers, so you recommend Lee see your friend for treatment.

Based on all of the information you have collected, should Lee’s siblings, Leah and Luke, be tested for the same genetic disorder? Why or why not? Use evidence from the case study, the textbook and your observations to support your recommendation.