Name:_____ Date:_____ Per:_____

Distance Learning Unit 4 Genomics Packet

Note: If you are completing this packet by hand and you run out of space, please write answers to questions on a separate sheet of looseleaf paper.

Unit Opener: Diabetes and Cancer Incidence[1] Data
Unit EQ:: *Why are some people diagnosed with diabetes and cancer while others are not?*

Directions: Please look at the following data, in the form of maps and graphs, and use the images to make observations and generate questions about the data. As you look through this data, please keep in mind that the issue of disease disparities is complex. The information in these pages is meant to increase your awareness of these issues in your life and your community as well as empower and improve our collective ability to prevent, detect, and cure these diseases.

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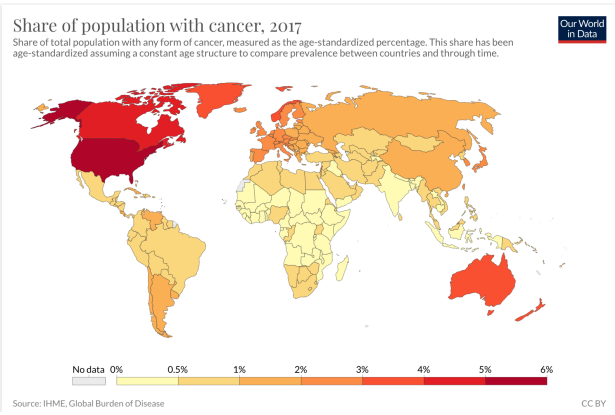
<td> 
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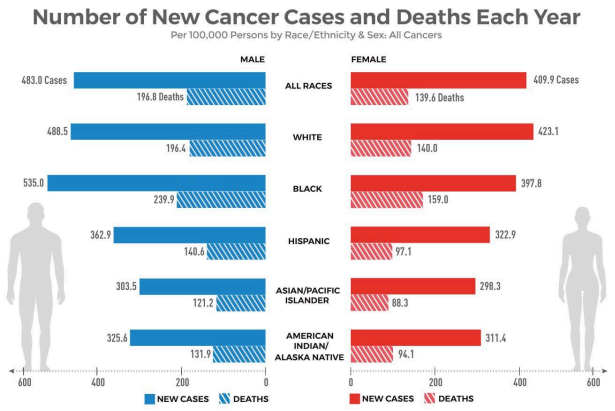
<td> 
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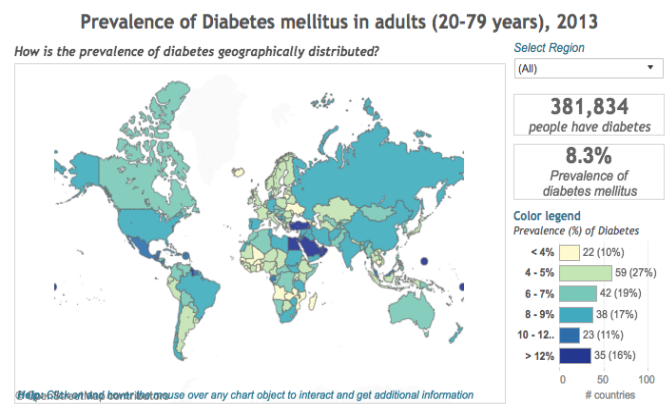
<td> 
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<td>What do you notice?

What do you wonder?</td>
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[1] Incidence - the occurrence, rate, or frequency of a disease, crime, or something else undesirable.

Explore and Explain: Family Health History Pedigree Project

***EQ:** How are traits passed through generations?*

1. The value of a family health history

What is a family health history? A family health history is information about diseases that run in your family, as well as the eating habits, activities, and environments that your family shares. Knowing about the diseases that run in your family can help you make healthy choices. Your family's health is one part of the history of your family. While collecting your family health history, pay attention to events, stories, and experiences as well. Gathering your family history helps you share your family stories and health information with your family members and children.*[2]

2. Data Collection

Who to collect information on: yourself, your parents, your brothers and sisters. Then move on to aunts, uncles, cousins, nieces, nephews, and grandparents. If you do not have access to your family, are adopted, or do not live with your birth parents, you can collect information for the family you live with, or a friend's family, or create fictional characters.

Fill out the table below by collecting some basic age information,then ask about their health. **Examples of diseases or conditions you could ask about:** *diabetes, stroke, allergies, asthma, heart disease, high blood pressure, any type of cancer, deafness (at a young age), learning disorders, high cholesterol, vision loss or blindness, stroke, or substance abuse*. Single-gene disorders such as *sickle cell anemia, cystic fibrosis, hemophilia, or Huntington's Disease* are also useful to track.

Note: You might run into dead ends while interviewing your family. Ask plenty of specific questions but it is okay to not know everything about everyone.

Use initials or codes for identifying your family members (no names!!) and the conditions you are tracking in your pedigree.

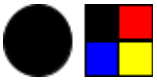
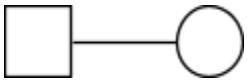
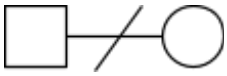
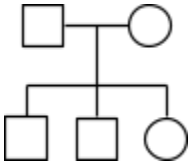
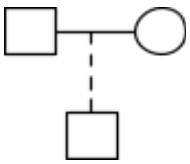
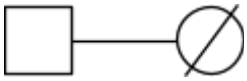
DO NOT TURN THIS TABLE IN ! Keep this page private.

Initials or Code	Age or Year of birth / age at death	Medical Conditions (Code) & Age @ Diagnosis	Risk factors or ancestral home or ancestry, as relevant to medical conditions	Other information, as relevant to medical conditions
Example: E	Died in 1994 @ age 45	Skin cancer (S), 41	Lots of sun exposure, pale skin, Irish ancestry	UVA/UVB sunscreen didn't exist when this person was a child
Example: D	born 12/3/76	Type 2 Diabetes (D), 27	obesity, eats lots fast food -no exercise	
If you need more rows for this table, use an additional sheet of plain paper or notebook paper.				

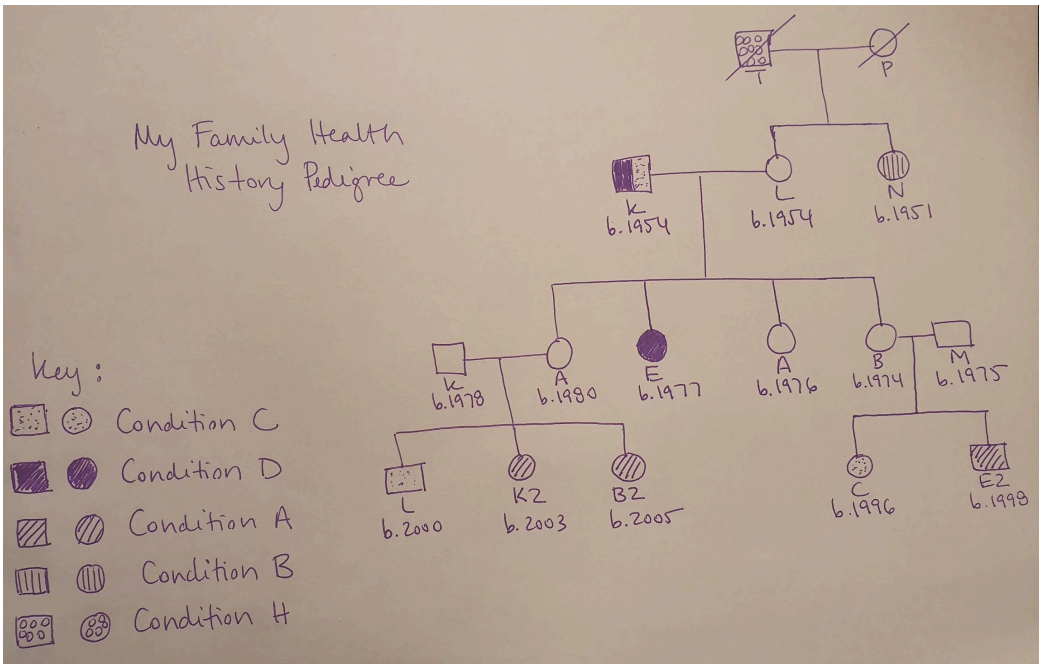
[2] *Excerpts from "Guide to Family Health History" by the Genetic Alliance.* https://drive.google.com/file/d/0Bzk10H0vgVIEVWp1WFgybE9RdEE/view

3. Build a Pedigree

Using the following symbols draw a pedigree that connects everyone in your family. Then color or shade in the squares and circles to represent diseases or conditions. Make sure to include a legend for the conditions.

 Squares represent males. Circles represent females. Diamonds represent non-binary, or unknown gender for a pregnancy.	 Shading indicates that the person has a health condition. Multiple conditions can be represented using different quadrants and different colors.
 A line connecting a male and female indicates a couple.	 A slash through the horizontal line indicates a relationship that isn't current (divorce, separation).
 A vertical line and a bracket connect parents to children.  An adopted child is connected to parents by a dotted line.	 A slash through a circle or square indicates that the individual is deceased.

Example of a pedigree:



Questions to reflect on after completing the pedigree:

1. What determines whether or not you will develop a disease or medical condition?

2. Why is it advantageous to create a Family Health History Pedigree?

Explore and Explain: Meiosis

EQ: *How Does Genetic Variation Arise?*

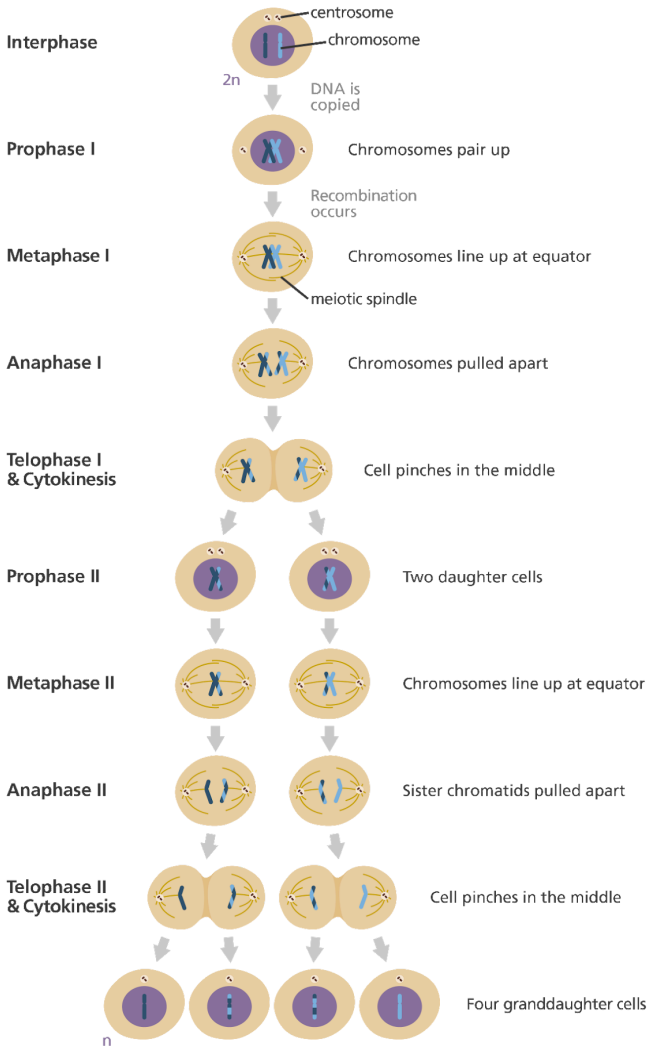
Directions: Read about the process of meiosis and answer the comprehension questions.

Introduction to Meiosis

Sexual reproduction combines gametes from two parents. *Gametes* are reproductive cells, such as sperm and egg. As gametes are produced, the number of chromosomes must be reduced by half. Why? In sexually reproducing organisms, the zygote contains equal amounts of genetic information from both the mother and the father. In other words, when egg and sperm come together at fertilization, half of the zygote's genetic information comes from the mother and the other half from the father.

Gametes (eggs and sperm) are produced by a special type of cell division known as meiosis.This process reduces the number of chromosomes by half, creating eggs and sperm that have the right amount of DNA.

Human cells have 23 pairs of chromosomes, and each chromosome within a pair is called a homologous chromosome. For each of the 23 chromosome pairs, you received one chromosome from your father and one chromosome from your mother. Alleles are alternate forms of genes found on chromosomes. Homologous chromosomes have the same genes, though they may have different alleles. So, though homologous chromosomes are very similar, they are not identical. The homologous chromosomes are separated when during meiosis, resulting in human gametes with only 23 chromosomes, not 23 pairs.[3]



Overview of Meiosis: Meiosis (**Figure** at left) is divided into two divisions: Meiosis I and Meiosis II. Each division can be divided into the same phases: prophase, metaphase, anaphase, and telophase. Cytokinesis follows telophase.

Process of Meiosis

- During meiosis I, the pairs of homologous chromosomes exchange genetic material in a process called crossing over during prophase I.
- The newly recombinant chromosomes line up in their homologous pairs during metaphase I, and are separated during anaphase I and telophase I. Since the lineup of chromosomes is random during meiosis I (independent assortment), each time this process occurs, there are different combinations of chromosomes in each gamete.
- With 23 pairs of chromosomes, there is a possibility of over 8 million (2^{23}) different lineups of chromosomes in a human gamete.
- During meiosis II, the sister chromatids are separated and the gametes are generated.The chromosomes are separated during anaphase I and telophase, in a manner similar to mitosis in body cells. After cytokinesis, each cell has divided twice.
- Meiosis results in four haploid genetically unique daughter cells, each with half the DNA of the parent cell, and genetically unique. In human cells, the parent cell has 46 chromosomes (23 pairs), so the cells produced by meiosis have 23 chromosomes. These cells will become gametes.

[3] Image retrieved from Wellcome Genome Campus https://www.yourgenome.org/facts/what-is-meiosis, credited to Genome Research Limited

Genetic Variation

Sexual reproduction results in infinite possibilities of genetic variation. In other words, sexual reproduction results in offspring that are genetically unique: they differ from both parents and also from each other. This occurs for a number of reasons (listed on next page):

- When homologous chromosomes form pairs during prophase I of meiosis I, crossing-over can occur. **Crossing-over** is the exchange of genetic material between homologous chromosomes. It results in new combinations of genes on each chromosome.
- When cells divide during meiosis, homologous chromosomes are randomly distributed to daughter cells, and different chromosomes segregate independently of each other. This is called **independent assortment**. It results in gametes that have unique combinations of chromosomes.
- In sexual reproduction, two gametes unite to produce an offspring. But which two of the millions of possible gametes will it be? This is likely to be a matter of chance. It is obviously another source of genetic variation in offspring. This is known as **random fertilization.**

All of these mechanisms working together result in an amazing amount of potential variation. Each human couple, for example, has the potential to produce more than 64 trillion genetically unique children. No wonder we are all different!

1. What kinds of cells are produced in meiosis? _____ What kinds of cells are NOT produced by this type of cell division? _____

2. Something happens in Prophase I that causes the chromosomes to change. What is it called? _____ How does this process change the chromosomes?

3. Look closely at the diagram. Are any combinations of chromosomes identical across the 4 gametes?

4. What is the outcome of meiosis?

5. Why do cells made in meiosis have less genetic material than other cells?

6. How does meiosis enhance genetic diversity and account for the incredible variation of traits we see in populations, including the human population?

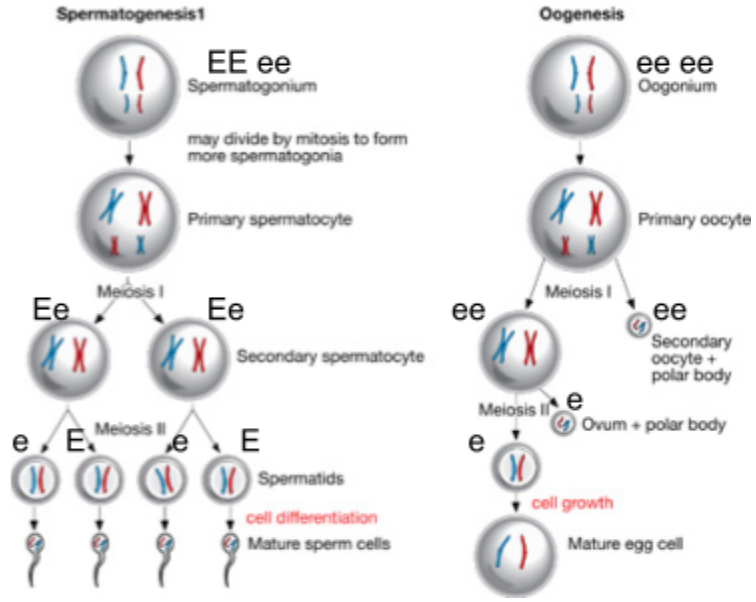
Explore and Explain: Patterns of Inheritance

EQ: *How can we model simple inheritance patterns?*

Phenomenon: Simple inheritance models break down when it comes to more complex traits, such as skin color. We modify these models to account for traits that are controlled by multiple genes.

In the genetic cross shown below, only one pair of chromosomes out of the 23 pairs found in a human nucleus are shown. The E or e shown next to each chromosome represents a particular **allele** (pronounced uh-LEEL) for a **gene** which determines whether your earlobes are attached (ee) or unattached (EE or Ee). A **gene** is a segment of DNA that codes for a certain trait and an **allele** are the different versions of that trait. For example, we all carry *genes* that determine our blood type and the *alleles* for human blood type are A, B, AB, and O.

Heterozygous means that the individual carries two different versions of the gene (1 dominant and 1 recessive). **Homozygous** means that the individual carries two of the same versions of the gene (2 dominant, called homozygous dominant or 2 recessive, called homozygous recessive). Note that the male below is *heterozygous* for unattached earlobes *(Ee).* The female happens to be *homozygous recessive* and has attached earlobes *(ee)*.



In the testis, the male would contain sperm that contained the _____ or _____ allele. In ovaries, the female would only form eggs with the _____ allele.

Punnett Squares are tools used to determine the probability and possibilities of what an offspring could inherit from their parents for a specific trait. A Punnett Square is filled in for you on the next page to determine the probabilities of these parents passing on attached or unattached earlobes.

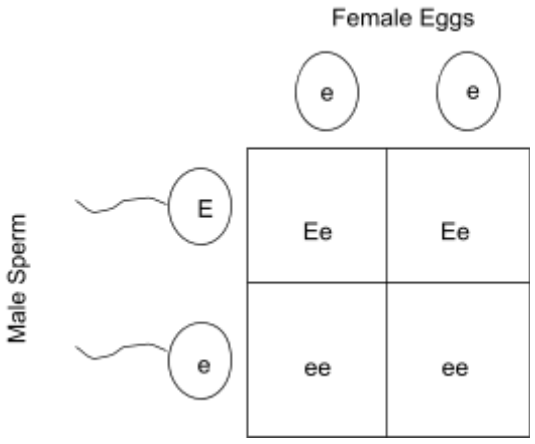
Use this example to complete the Punnett Square problems.

Example: Ee (male) x ee (female)

<u>0</u> out of <u>4</u> possibilities will be EE (unattached)

<u>2</u> out of <u>4</u> possibilities will be Ee (unattached)

<u>2</u> out of <u>4</u> possibilities will be ee (attached)



What is the **probability** (% chance) that one of their children will have <u>attached</u> earlobes? **2 / 4 x 100 = 50%**

What is the **probability** (% chance) that one of their children will have <u>unattached</u> earlobes? **2 / 4 x 100 = 50%**

Punnett Square Practice Problems

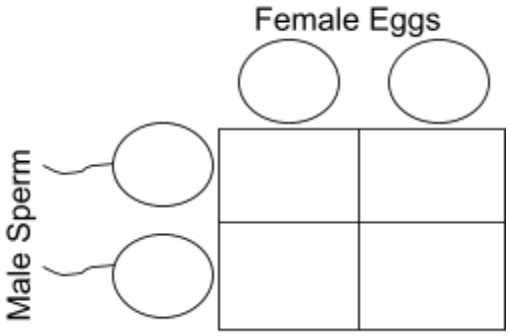
Genotype is the set of genes that a person carries for a trait. The possible genotypes for the earlobe example are EE, Ee, and ee. **Phenotype** is the expressed version of a trait, such as attached earlobes or unattached earlobes. It is what we "see", even though we can't "see" all of our phenotypes (being lactose intolerant, for example).

COMPLETE DOMINANCE - Monohybrid Crosses

1. Freckles (F) is a dominant trait in humans while not having freckles (f) is recessive. If a female that is **homozygous dominant** for freckles has a child with a man who **does not have freckles**, what will their children look like?

a. What are the genotypes and phenotypes of the parents?

	Genotype	Phenotype
Homozygous dominant		
Homozygous recessive		



b. Set up a Punnett square.

c. Analyze the cross by filling in the possible genotypes that lead to having freckles or not having freckles.

_____ out of _____ possibilities will be FF (freckles)	_____ out of _____ possibilities will be Ff (freckles)
_____ out of _____ possibilities will be ff (no freckles)	d. What is the probability that one of the offspring will have freckles? _____

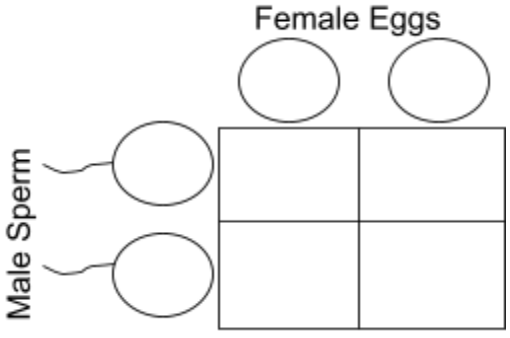
SEX-LINKED TRAITS: Duchenne Muscular Dystrophy (DMD)

2. DMD is inherited as an **X-linked recessive disorder** (X^m), just like color-blindness, and occurs because the mutated gene fails to produce virtually any functional dystrophin that prevents the early death of muscle cells.

a. Make a cross representing a **man with DMD** having a child with a woman with no family history of DMD.

b. List the possible genotypes, phenotypes, and probability that a child of these parents would have each one.

	Genotype	Phenotype	% chance



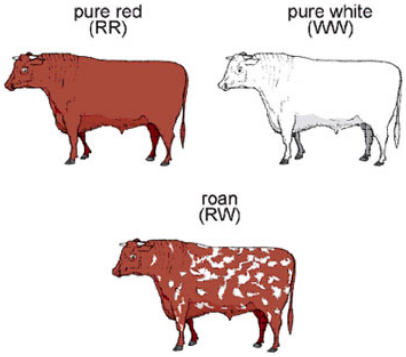
c. What is the chance that a male child would have DMD? _____	d. What is the chance that a female child would have DMD? _____

A **carrier** is an individual who carries the gene for the recessive form of the trait but does not have the trait (so they are heterozygous). In this example, their genotype would be X^MX^m.

e. What is the chance that a female child would be a **carrier**? _____

CODOMINANCE: Horse & Cow Coat Color

3. In horses and cows that have roan coat color, it is due to codominance, where both traits appear together in the organism's phenotype.

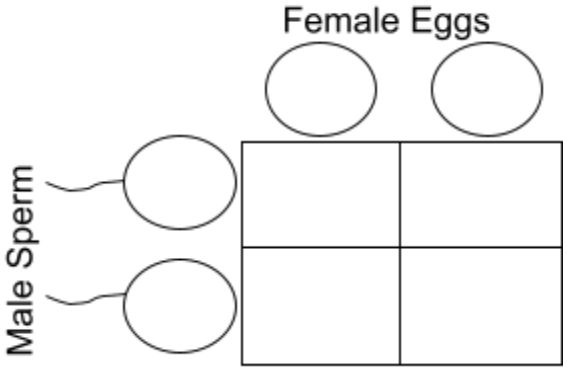


a. Set up a Punnett square for a **red cow** and a **red and white spotted** bull.

b. What is the probability that one of the offspring would be red? _____

c. What is the probability that one of the offspring would be white? _____

d. What is the probability that one of the offspring would be red and white spotted? _____



MULTIPLE ALLELES & CODOMINANCE: Blood Type

4. Blood Type is determined by 3 different alleles A, B and O. A and B are codominant, while O is recessive. Possible blood types are A, B, AB and O. A man with O type blood marries a woman with AB type blood. What are the possible blood types of their offspring?

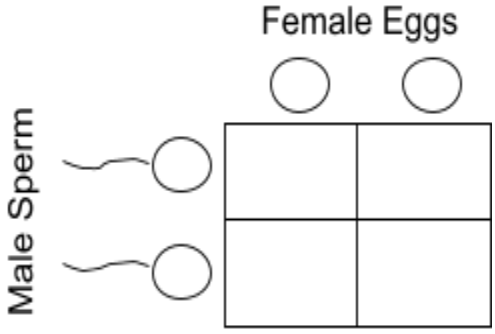
a. Set up a Punnett square for an O and AB blood type.

b. What is the probability that the offspring will have O blood? _____

c. What is the probability that the offspring will have A blood? _____

d. What is the probability that the offspring will have B blood? _____

e. What is the probability that the offspring will have AB blood? _____



Summary

1. What are the **similarities** and **differences** among the different patterns of inheritance?

Similarities	Differences

2. Draw a picture or write a paragraph that helps you to clarify the similarities and differences.

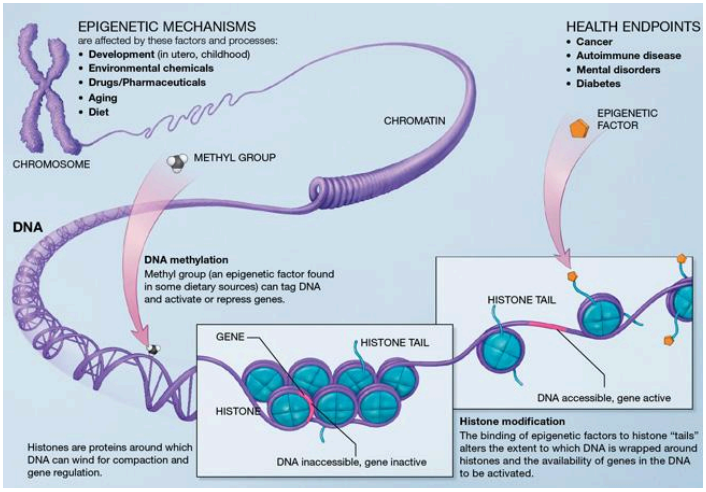
Explore & Explain: Epigenetics

***EQ:** How are genes turned on and turned off, and why does this matter?*

Directions: Read about epigenetics and answer the comprehension questions that follow.

Epigenetics

Did you know that your DNA can undergo changes that aren't genetic mutations? You know that a cell's DNA is in its nucleus. As you can see in the image at right, this DNA is wrapped around proteins called histones, making chromatin. This chromatin not only contains an organism's genome, or all its genetic information, but it also includes the epigenome: chemical modifications to the chromatin that regulates how genes are expressed. Epigenetic regulation works by making certain genes active or inactive throughout an organism's life.



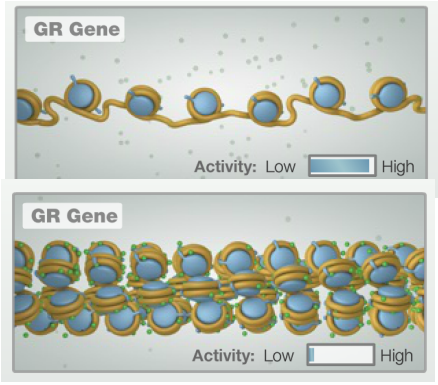
Studies suggest that differences in epigenetic regulation may be responsible for subtle variations in appearance and behavior of identical twins. Identical twins are more epigenetically similar early in life but show remarkable differences along their epigenome with age. Many factors have been identified to influence the epigenome, such as environment (ex. exposure to pollutants) or lifestyle choices (ex. diet and exercise). These factors can change the way DNA is expressed throughout an individual's life.

Methylation

Epigenetic pathways, such as DNA methylation, interact with each other to regulate expression of genes. DNA methylation occurs when an enzyme (methyltransferase) covalently attaches a methyl ($-CH_3$) group to the DNA strand. (Note: These CH_3 molecules are represented by tiny dots in the images below.) Genes that are essential for a cell's function are not methylated. In contrast, inactive genes are usually methylated to suppress their expression - think of methylated genes like a book whose pages are glued together.

Nature vs. Nurture: Licking Rat Pups

A study conducted in 2003[4] demonstrated that rat pups that are nurtured by their mothers tend to be calm as adults, and rats that are not as nurtured grow up to be more anxious. It was found that the differences in behavior are due to a change in a glucocorticoid receptor (GR) gene during development. At birth, the gene is highly methylated and inactive. If a rat mother is attentive towards her pups (an example of an environmental factor), the pups' GR gene gradually demethylates, making it more active (upper image at right). These pups will be more relaxed in response to stress. Those that were not given attention, and do not express the GR gene (lower image at right), respond poorly to stress and are more prone to disease.



1. What is the epigenome? How does it compare to the genome?

2. What is epigenetic regulation? How does methylation work to regulate the epigenome?

3. How could epigenetic changes function to cause differences in the DNA of identical twins?

4. Compare and contrast the GR gene in relaxed versus stressed rat pups.

[4] Weaver, I., Cervoni, N., Champagne, F. *et al.* Epigenetic programming by maternal behavior. *Nat Neurosci* 7, 847–854 (2004). https://doi.org/10.1038/nn1276

Explore and Explain: Breast Cancer

***EQ:** Why are some people diagnosed with breast cancer and others are not?*

Phenomenon: Some groups of people have higher incidence rates of breast cancer than others.

Breast cancer is the leading cause of cancer death for women in the United States (American Cancer Society,http://www.cancer.org). At the present time, the overall lifetime risk for a woman in the United States to develop breast cancer is one in eight (this means that approximately 13% of women in the U.S. will develop breast cancer in their lifetime). It is thus important for us to understand some of the risk factors for breast cancer, as well as some of the screening tests for breast cancer.

During this activity you are going to learn about some risk factors for breast cancer, evaluate the medical histories of a woman with respect to her breast cancer risk, then make some recommendations for how she might reduce her risk.

In order to be prepared to evaluate the medical histories, please read the following excerpts from the American Cancer Society (ACS). Complete the table below as you read.

Breast Cancer (BC) Lifestyle Risks that You <u>Can</u> Change

1. Drinking alcohol is clearly linked to an increased risk of breast cancer. The risk increases with the amount of alcohol consumed. Women who have 1 alcoholic drink a day have a small (about 7% to 10%) increase in risk compared with non-drinkers, while women who have 2 to 3 drinks a day have about a 20% higher risk than non-drinkers. Alcohol is linked to an increased risk of other types of cancer, too.The ACS recommends that women who drink have no more than 1 drink a day.

2. Being overweight or obese after menopause increases breast cancer risk. Before menopause your ovaries make most of your estrogen, and fat tissue makes only a small part of the total amount. After menopause (when the ovaries stop making estrogen), most of a woman's estrogen comes from fat tissue. Having more fat tissue after menopause can raise estrogen levels and increase your chance of getting BC. Also, women who are overweight tend to have higher blood insulin levels. Higher insulin levels have been linked to some cancers, including BC.

Still, the link between weight and BC risk is complex. For instance, the risk of BC after menopause is higher for women who gained weight as an adult, but the risk before menopause is actually *lower* in women who are obese. The reasons for this aren't exactly clear. The ACS recommends you stay at a healthy weight throughout your life and avoid excess weight gain by balancing your food intake with physical activity.

3. Not being physically active. Evidence is growing that regular physical activity reduces BC risk, especially in women past menopause. The main question is how much activity is needed. Some studies have found that even as little as a couple of hours a week might be helpful, although more seems to be better. Exactly how physical activity might reduce BC risk isn't clear, but it may be due to its effects on body weight, inflammation, hormones, and energy balance. The ACS recommends that adults get at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity activity each week (or a combination of these), preferably spread throughout the week.

4. Not having children and Not breastfeeding. Women who have not had children or who had their first child after age 30 have a slightly higher BC risk overall. Having many pregnancies and becoming pregnant at an early age reduces BC risk. Still, the effect of pregnancy on BC risk is complex. For example, the risk of BC is higher for about the first decade after having a child, particularly for hormone receptor-negative BC (including the less common triple-negative BC). The risk then becomes lower over time. Most studies suggest that breastfeeding may slightly lower BC risk, especially if it's continued for a year or more. But this has been hard to study, especially in countries like the United States, where breastfeeding for this long is uncommon. The explanation for this possible effect may be that breastfeeding reduces a woman's total number of lifetime menstrual cycles (the same as starting menstrual periods at a later age or going through early menopause).

5. Birth control. Some birth control methods use hormones, which might increase BC risk. **Oral contraceptives:** Most studies have found that women using oral contraceptives (birth control pills) have a slightly higher risk of BC than women who have never used them. Once the pills are stopped, this risk seems to go back to normal within about 10 years. **Birth control shot:** Depo-Provera is an injectable form of progesterone that's given once every 3 months for

birth control. Some studies have found that women currently using birth-control shots seem to have an increase in BC risk, but other studies have not found an increased risk. **Birth control implants, intrauterine devices (IUDs), skin patches, vaginal rings:** These forms of birth control also use hormones, which in theory could fuel BC growth. Some studies have shown a link between use of hormone-releasing IUDs and BC risk, but few studies have looked at the use of birth control implants, patches, and rings and BC risk.

6. Hormone therapy with estrogen after menopause (often combined with progesterone) has been used for many years to help relieve symptoms of menopause and help prevent osteoporosis (thinning of the bones). This treatment goes by many names, such as post-menopausal hormone therapy (PHT), hormone replacement therapy (HRT), and menopausal hormone therapy (MHT). The increased risk from combined HT appears to apply mainly to current and recent users. A woman's BC risk seems to go back down within 5 years of stopping treatment.

7. Breast implants have not been linked with an increased risk of the most common types of BC. However, they have been linked to a rare type of non-Hodgkin lymphoma called breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), which can form in the scar tissue around the implant. This lymphoma appears to happen more often in implants with textured (rough) surfaces rather than smooth surfaces. If BIA-ALCL does occur after an implant, it can show up as a lump, a collection of fluid, swelling, or pain near the implant, or as a change in a breast's size or shape.

Breast Cancer (BC) Risk Factors You <u>Cannot</u> Change

1. Being born female. This is the main risk factor for BC. Men can get BC, too, but this disease is much more common in women than in men.

2. Getting older As you get older, your risk of BC goes up. Most BCs are found in women age 55 and older.

3. Inheriting certain gene changes. About 5% to 10% of BC cases are thought to be hereditary, meaning that they result directly from gene changes (mutations) passed on from a parent. The most common cause of hereditary BC is an inherited mutation in the *BRCA1* or *BRCA2* genes. In normal cells, these genes help make proteins that repair damaged DNA. Mutated versions of these genes can lead to abnormal cell growth, which can lead to cancer.

- If you've inherited a mutated copy of either gene from a parent, you have a higher risk of BC.
- On average, a woman with a *BRCA1* or *BRCA2* gene mutation has up to a 7 in 10 chance of getting BC by age 80. This risk is also affected by how many other family members have had BC. (It goes up if more family members are affected.)
- Women with one of these mutations are more likely to be diagnosed with BC at a younger age, as well as to have cancer in both breasts.
- Women with one of these gene changes also have a higher risk of developing ovarian cancer and some other cancers. (Men who inherit one of these gene changes also have a higher risk of BC, as well as prostate and some other cancers.)
- In the United States, *BRCA* mutations are more common in Jewish people of Ashkenazi (Eastern Europe) origin than in other racial and ethnic groups, but anyone can have them.

Other genes: Other gene mutations can also lead to inherited BCs. These gene mutations are much less common, and most of them do not increase the risk of BC as much as the *BRCA* genes.

4. Having a family history of breast cancer. It's important to note that most women who get BC *do not* have a family history of the disease. But women who have close blood relatives with BC have a higher risk. Overall, about 15% of women with BC have a family member with this disease.

- Having a first-degree relative (mother, sister, or daughter) with BC almost doubles a woman's risk. Having 2 first-degree relatives increases her risk about 3-fold.
- Women with a father or brother who has had BC also have a higher risk of BC.

5. Having a personal history of breast cancer. A woman with cancer in one breast has a higher risk of developing a new cancer in the other breast or in another part of the same breast. (This is different from a recurrence or return of the first cancer.) Although this risk is low overall, it's even higher for younger women with BC.

6. Race and ethnicity. Overall, white women are slightly more likely to develop BC than African-American women,

although the gap between them has been closing in recent years. In women under age 45, BC is more common in African-American women. African-American women are also more likely to die from BC at any age. Asian, Hispanic, and Native American women have a lower risk of developing and dying from BC.

Risk in different groups also varies by type of BC. For example, African-American women are more likely to have the less common triple-negative BC.

7. Being taller. Many studies have found that taller women have a higher risk of BC than shorter women. The reasons for this aren't exactly clear, but it may have something to do with factors that affect early growth, such as nutrition early in life, as well as hormonal or genetic factors.

8. Having dense breast tissue. Breasts are made up of fatty tissue, fibrous tissue, and glandular tissue. Breasts appear denser on a mammogram when they have more glandular and fibrous tissue and less fatty tissue. Women with dense breasts on mammograms have a risk of BC that is about 1 1/2 to 2 times that of women with average breast density. Unfortunately, dense breast tissue can also make it harder to see cancers on mammograms.

9. Having certain benign breast conditions. Women diagnosed with certain benign (non-cancer) breast conditions may have a higher risk of BC. Some of these are more closely linked to BC risk than others. BC risk is about 4 to 5 times higher than normal in women with these changes. If a woman also has a family history of BC and either hyperplasia or atypical hyperplasia, she has an even higher risk of BC.

10. Starting menstrual periods early. Women who have had more menstrual cycles because they started menstruating early (especially before age 12) have a slightly higher risk of BC. The increase in risk may be due to a longer lifetime exposure to the hormones estrogen and progesterone.

Risk Factors for Breast Cancer			
Lifestyle Risks We <u>Can</u> Change		**Risk Factors We <u>Cannot</u> Change**	
Risk	**Notes on this risk**	**Risk**	**Notes on this risk**
ex.: drinking alcohol	*1 drink / day, small risk* *2-3 drinks / day: risk ↑ by ~20%*		

Profile

Read Ana's profile and determine whether each aspect of her medical history increases, decreases or has no impact on the patient's risk for breast cancer.[5]

Example: Ana *circle either* ↑ *(increases risk)* ↓ *(decreases risk)* or *no impact*

- Ana is a 64-year-old woman.(↑ / ↓ / no impact)
- She is generally in good health. (↑ / ↓ / no impact)
- She had her first child when she was 20. (↑ / ↓ / no impact)
- She nursed her child for 2 years. (↑ / ↓ / no impact)
- She entered menopause at the age of 58. (↑ / ↓ / no impact)
- She has been on combined hormone replacement therapy since entering menopause (for the past 6 years). (↑ / ↓ / no impact)
- She has gained some weight since menopause, having a BMI classified as "overweight". (↑ / ↓ / no impact)
- Her mother had breast cancer diagnosed at age 37. (↑ / ↓ / no impact)

Claim, Evidence, Reasoning Task

Write a Claim, Evidence Reasoning paragraph that addresses Ana's risk of developing breast cancer. You will also make recommendations about what you think the patient could (or should) do to inform herself or to reduce her risk. Please complete this task on a separate piece of paper, and if you wish, you may use the sentence frames below.

Claim: Make a claim about Ana's risk of developing breast cancer (low, average, slightly above average, high), as compared to the general population. If you think your patient might have a risk of another type of cancer, you can also note that.

- _____ *is most/least likely to* _____ *I believe that* _____ *has a* _____ *chance of...*
- _____ *has a* _____ *possibility of…*

Evidence: Cite specific evidence from Ana's patient facts in the case study that support your claim.

- _____ *supports my claim because…*
- *The evidence suggests that…*
- *In multiple sources/studies, experts consistently state …*

Reasoning: Cite statistics/facts from the fact sheets and other readings that link your patient's evidence to your claim about their risk level.

- *According to* _____, _____ *increases/decreases* _____ *because…*
- *In research about* _____, *experts agree that…*
- *As stated by* _____, *there is little doubt that...*

Recommendations: Make one or more recommendations for Ana about one or more of the following:

- how she could change her lifestyle to reduce her risk
- steps she could take to improve her preventive care
- ways she could increase her level of understanding about her risk

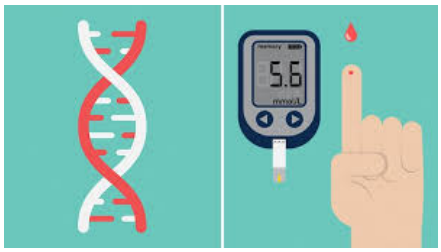
Make sure to explain how following through on each recommendation would decrease Ana's risk.

- _____ *should consider* _____ *since…* *It would be a good idea for* _____ *to* _____ *so that…*
- *A recommendation for* _____ *might be to* _____ *because...*

[5]Modified from: *Shuster, Michele and Karen Peterson. Breast Cancer Risk: Using Real Medical Histories to Rank Genetic and Environmental Influences. American Cancer Society.*

Explore and Explain: Diabetes

EQ:*Why are some people diagnosed with diabetes and others are not?*
Phenomenon: *There are disparities in who acquires, gets diagnosed with, receives treatment for, and dies from diabetes.*
Directions: Read the excerpts from the "Biotech Basics: Diabetes" article and answer the questions that follow.



Biotech Basics: Diabetes

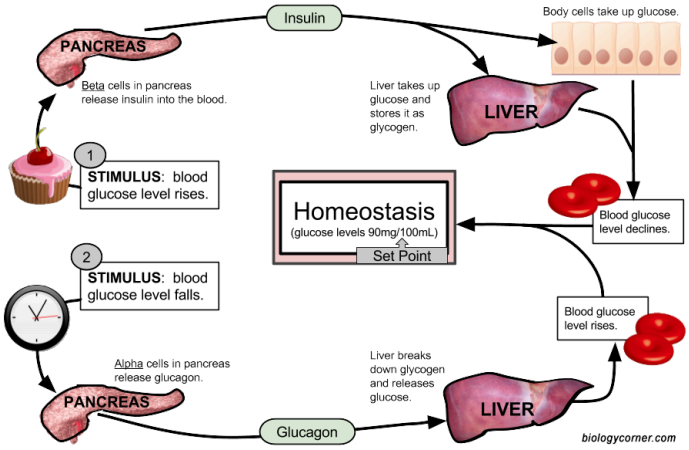
By Dr. Neil Lamb and Victoria Cumbow

Introduction to Diabetes

Diabetes is a disorder of metabolism, affecting the way the body uses food for energy. There are several types of diabetes with different causes, treatments and outcomes, but each type of diabetes is characterized by high blood glucose, or high blood sugar. These include type 1, type 2, type 1.5 or latent autoimmune diabetes of adults, gestational diabetes and MODY (maturity-onset diabetes of the young). There is no cure for diabetes, though some forms can be managed through diet and exercise, oral medication or insulin injections.

Understanding Glucose Metabolism

The body's glucose levels, or blood sugar levels, rise naturally from eating and the body's beta cells in the pancreas release insulin which stabilizes those blood sugar levels. Insulin "opens" the receptor molecules on cells so glucose enters and is converted into energy. In the liver, glucose units are assembled into glycogen. A variety of things cause a person's glucose levels to drop including exercise or minor illnesses. When glucose concentrations fall below a specific level, another type of pancreatic cells release the hormone glucagon. Glucagon causes liver cells to break up glycogen which produces multiple glucose units that enter the bloodstream and are passed to other body cells for energy.



Types of Diabetes

Type 1

Type 1 diabetes, also known as juvenile diabetes, is an auto-immune disease. The body attacks and kills the insulin-producing beta cells so no insulin is produced. The immune system is constantly balancing between attacking what it perceives to be foreign invaders and suppressing those attacks. Too much suppression risks allowing infectious agents unrestricted access to the body or allowing cancer cells to escape detection. In contrast, constant attacking can destroy the body's own cells, as occurs in an auto-immune disease like type 1 diabetes. In the past, type 1 diabetes was more commonly diagnosed in children, but it can be diagnosed at any age. This form of diabetes is not something a person can outgrow, and it cannot be managed with diet alone.

Type 2

Type 2 diabetes, or adult onset diabetes, is the most common form of diabetes. When a person develops type 2 diabetes, cells become resistant to the effect of insulin. The pancreas produces more insulin to compensate and ultimately, the pancreas stops making insulin altogether, causing blood glucose levels to rise and complications to appear. Sometimes, improvements in diet and exercise can achieve good results in the first few years after a type 2 diabetes diagnosis. In some cases, weight loss and exercise reduce insulin resistance. Diet plus exercise can often reduce the progression from prediabetes to diabetes. A prescription drug is often required to help stabilize blood sugar levels. There is no cure for type 2 diabetes, but in cases where weight management and dietary modifications stabilize a person's blood sugar levels, the symptoms of type 2 diabetes will return if a person regains lost weight or reverts back to unhealthy eating habits. Like type 1 diabetes, the disease requires constant attention and management.

Treatments

There is a link between type 2 diabetes and obesity, but not all type 2 diabetics are overweight. In cases where a person's lifestyle contributes to type 2 diabetes, a change in activity and diet can help a person manage blood sugar levels. In other cases, a change in lifestyle as well as oral medication is required. For type 1 diabetics, insulin is required through multiple daily injections or through an external insulin pump. All diabetics must test blood sugar levels through multiple daily finger pricks using a small blood glucose monitor. It's important for diabetics to keep an eye on blood pressure and lipid levels as well as look for other signs of complications.

Genetics and Environmental Risks

Until recently, the genetic basis underlying most forms of diabetes was unknown. Mutations in a few genes had been identified in rare forms of diabetes, but the genetic contributions for types 1 and 2 remained a mystery. It is likely that both forms of diabetes are caused by a combination of multiple small genetic changes that lead to disease only in the presence of risk-increasing environments. Thanks to high-throughput [6]approaches like genome-wide association studies, the genetic players are beginning to surface. More than 50 genes have been linked to type 1 diabetes. Not surprisingly, most are associated with the development and maintenance of the immune system. Clinicians are beginning to combine this genetic information with other risk factors, such as the presence of autoantibodies[7], to identify individuals who are at the greatest risk of developing type 1 diabetes. As prevention and treatment options continue to emerge, this class of individuals is the first group to target. Several genetic risk factors have also been identified for type 2 diabetes. Early indications suggest that many of these are associated with the declining function of the beta cells in response to increased insulin sensitivity. The genes identified to date represent only a small percentage of the expected overall genetic contribution. This points to the presence of a number of yet-unidentified genes - each contributing only modestly to overall disease risk. The advent of whole genome and/or whole exome sequencing is expected to speed the discovery of this large group of risk factors. Scientists are also researching environmental risks and what roles they play in developing diabetes. Preliminary evidence has highlighted viral infections, stress, exposure to pets and other allergens, and maternal weight gain around pregnancy for type 1 diabetes. Obesity and the presence of specific intestinal bacteria have been implicated in type 2 diabetes. These do not represent the full total of all risk factors and none of the risks is, by itself, sufficient to develop diabetes. Diabetes requires continual monitoring, across multiple aspects of daily life. Affected individuals must read food labels and know what ingredients are in the foods they consume. They must track their activities and pay particular attention to the signals being sent by their bodies. Even so, with proper care and treatment, individuals impacted by diabetes live full and productive lives.

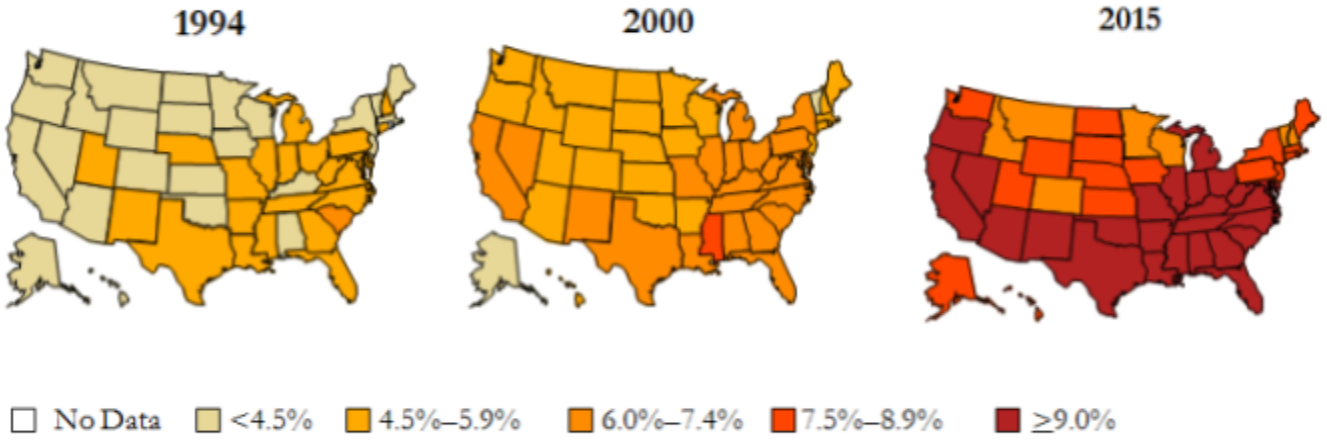


Figure 1: Incidence of Diabetes in the US

(CDC's Division of Diabetes Translation. United States Surveillance System Available at http:// cdc.gov/diabetes/data)

[6] High throughput research can be defined as the automation of experiments such that large scale repetition becomes feasible. https://www.jvir.org/article/S1051-0443(09)00353-4/fulltext

[7] Autoantibodies are antibodies (immune proteins) that mistakenly target and react with a person's own tissues or organs. One or more autoantibodies may be produced by a person's immune system when it fails to distinguish between "self" and "non-self." https://labtestsonline.org/tests/autoantibodies

Article Questions

1. What characteristic is common to **all** types of diabetes?

2. Is the regulation of blood glucose levels an example of **positive** or **negative** feedback? What role does insulin play in this regulation process?

3. Based on the reading, how would you describe an "auto-immune disease"? Which type of diabetes is this associated with?

4. What are two things a person with type 2 diabetes can do to potentially reduce insulin resistance?

5. Most of the more than 50 genes that have been linked to type 1 diabetes are associated with the development and maintenance of which body system?

6. List 2 risk environmental risk factors for type 1 and type 2 diabetes.

7. Look at the data showing the incidence of diabetes in the US from 1994 to 2015. What are two things you **notice**? What are two things you **wonder**?

8. Why do **you** think people with diabetes (I and II) are at a higher risk of having serious complications (and even death) if they contract COVID-19? (Make sure to identify your sources if you get information from somewhere else.)

Explore and Explain: CRISPR

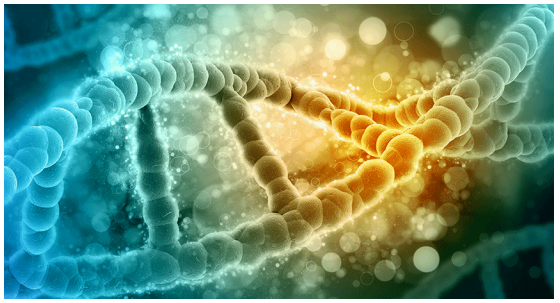
EQ: *What are the pros and cons of using CRISPR technology to make changes to the genomes of plants and animals?*

Phenomenon: CRISPR is a gene editing technique that has the potential to fix genetic diseases.

Directions: Read the following article about CRISPR and answer the questions that follow.

Explainer: How CRISPR works

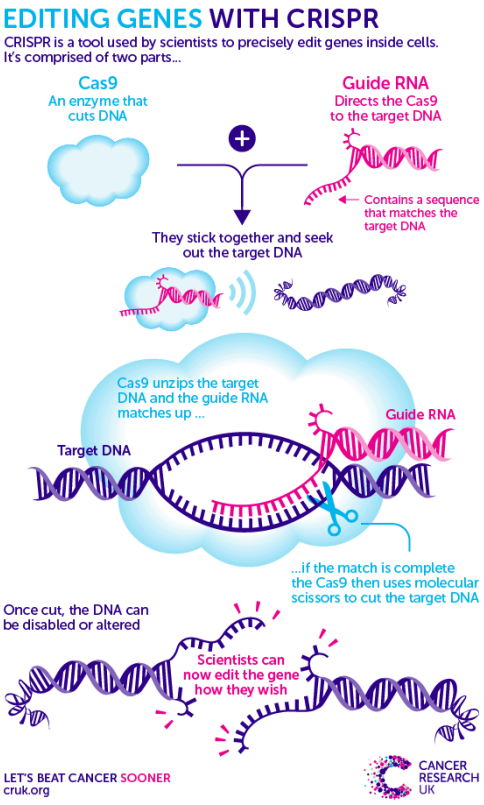
This technique lets scientists edit DNA in plants and animals By Tina Hesman Saey 7/31/2017



Scientists usually shy away from using the word *miracle*. Unless they're talking about the gene-editing tool called CRISPR, that is. "You can do anything with CRISPR," some say. Others just call it amazing.

CRISPR stands for "clustered regularly interspaced short *palindromic* repeats." Those repeats are found in bacteria's DNA. They are actually copies of small pieces of viruses. Bacteria use them like collections of mug shots to identify bad viruses. Cas9 is an *enzyme* that can cut apart DNA. Bacteria fight off viruses by sending the Cas9 enzyme to chop up viruses that have a mug shot in the collection. Scientists recently figured out how bacteria do this. Now, in the lab, researchers use a similar approach to turn the microbe's virus-fighting system into the hottest new lab tool.

This CRISPR/Cas9 tool was first described in 2012 and 2013. Science labs around the world soon started using it to alter an organism's genome — the entire set of its DNA instructions. This tool can quickly and efficiently tweak almost any gene in any plant or animal. Researchers already have used it to fix genetic diseases in animals, to combat viruses and to sterilize mosquitoes. They have also used it to prepare pig organs for human transplants and to beef up the muscles in beagles.



So far CRISPR's biggest impact has been felt in basic biology labs. This low-cost gene editor is easy to use. That has made it possible for researchers to delve into the basic mysteries of life. And they can do it in ways that used to be difficult if not impossible. Robert Reed is a developmental biologist at Cornell University in Ithaca, N.Y. He likens CRISPR to a computer mouse. "You can just point it at a place in the genome and you can do anything you want at that spot." At first, that meant anything that involved cutting DNA. CRISPR/Cas9 in its original form is a homing device (the CRISPR part) that guides molecular scissors (the Cas9 enzyme) to a target section of DNA. Together, they work as a genetic-engineering cruise missile that disables or repairs a gene, or inserts something new where the Cas9 scissors has made some cuts. Newer versions of CRISPR are called "base editors." These can edit genetic material one base at a time, without cutting. They're more like a pencil than like scissors.

Here's how it works

Scientists start with RNA. That's a molecule that can read the genetic information in DNA. The RNA finds the spot in the *nucleus* of a cell where some editing activity should take place. (The nucleus is a compartment in a cell where most of the genetic material is stored.) This guide RNA shepherds Cas9 to the precise spot on DNA where a cut is called for. Cas9 then locks onto the double-stranded DNA and unzips it. This allows the guide RNA to pair up with some region of the DNA it has targeted. Cas9 snips the DNA at this spot. This creates a break

in both strands of the DNA molecule. The cell, sensing a problem, repairs the break. Fixing the break might disable a gene (the easiest thing to do). Alternatively, this repair might fix a mistake or even insert a new gene (a much more difficult process). Cells usually repair a break in their DNA by gluing the loose ends back together. That's a sloppy process. It often results in a mistake that disables some gene. That may not sound useful — but sometimes it is.

Scientists cut DNA with CRISPR/Cas9 to make gene changes, or *mutations*. By comparing cells with and without the mutation, scientists can sometimes figure out what a protein's normal role is. Or a new mutation may help them understand genetic diseases. CRISPR/Cas9 also can be useful in human cells by disabling certain genes — ones, for instance, that play a role in inherited diseases. "The original Cas9 is like a Swiss army knife with only one application: It's a knife," says Gene Yeo. He is an RNA biologist at the University of California, San Diego. But Yeo and others have bolted other proteins and chemicals to the dulled blades. That has transformed that knife into a multifunctional tool.

CRISPR/Cas9 and related tools can now be used in new ways, such as changing a single nucleotide base — a single letter in the genetic code — or adding a fluorescent protein to tag a spot in the DNA that scientists want to track. Scientists also can use this genetic cut-and-paste technology to turn genes on or off. This explosion of new ways to use CRISPR hasn't ended. Feng Zhang is a molecular biologist at the Massachusetts Institute of Technology in Cambridge. He was one of the first scientists to wield the Cas9 scissors. "The field is advancing so rapidly," he says. "Just looking at how far we have come…I think what we'll see coming in the next few years will just be amazing."

Article Questions

1. What type of macromolecule is *Cas9* and how do bacteria use this molecule to fight off viruses?

2. List 3 **specific** examples from the article of how scientists have used CRISPR to make changes to the genome of organisms.

3. Briefly explain how newer versions of CRISPR are considered "more like a pencil than like scissors".

4. What role does RNA play in the CRISPR process?

5. How can this tool be used to prevent the expression of inherited diseases?

6. What excites you about this technology? What concerns do you have?

7. CRISPR has the potential to allow scientists to select or alter certain genes in humans to create "designer babies". Do you think this is an ethical use of this technology? Why or why not?

8. How do you think CRISPR could be used to fight SARS-CoV-2 (coronavirus)?

ANSWER KEY

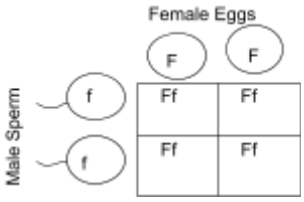
Unit Opener: Diabetes and Cancer Incidence Data
Answers will vary.

Explore and Explain: Family Health History Pedigree Project

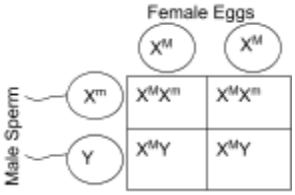
Answers will vary.

Explore and Explain: Meiosis
1. Gametes, Body cells **2.** a. Crossing over b. homologous chromosomes pair up and exchange genetic information, which results in new combinations of genes on each chromosome. **3.** No, the combinations of chromosomes are not identical, they have different combinations of genes (represented by the shading and line differences). **4.** The outcome of meiosis is four haploid genetically unique daughter cells. **5.** Cell made during meiosis go through a reduction division to form gametes. Gametes, sperm and egg, contain half of the genetic information. When a zygote is formed during fertilization, half of the genetic information comes from the sperm and the other half comes from the egg. **6.** Meiosis enhances genetic diversity through three processes: crossing over, independent assortment, and random fertilization. Crossing over allows for genetic recombination during prophase I of meiosis I. Independent assortment occurs when homologous chromosomes randomly distribute to daughter cells and segregate independently of one another, creating unique combinations of genetic material. Random fertilization refers to the process of a unique sperm combining with a unique egg during sexual reproduction.

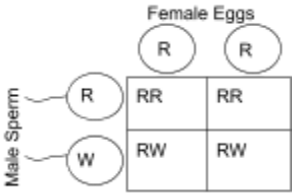
Explore and Explain: Inheritance Patterns
COMPLETE DOMINANCE - Monohybrid Crosses:
a. homozygous dominant: FF genotype, freckles phenotype
homozygous recessive: ff genotype, no freckles phenotype
b. See punnett square to the right
c. 0 out of 4 possibilities will be FF (freckles)
4 out of 4 possibilities will be Ff (freckles)
0 out of 4 possibilities will be ff (no freckles)
d. 100%



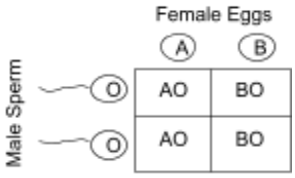
SEX-LINKED TRAITS: Duchenne Muscular Dystrophy
a. See punnett square to the right
b. 50% X^MX^m; 50% X^MY, 100% no DMD
c. 0%
d. 0%
e. 100%



CODOMINANCE:
a. See Punnett square to the right
b. 50%
c. 0%
d. 50%



MULTIPLE ALLELES:
a. See Punnett square to the right
b. 0%
c. 50%
d. 50%
e. 0%



Summary:
1. T-chart: answers will vary
2. Summary: *Sometimes traits are inherited in pretty straightforward patterns. For example, if the trait is completely dominant, the offspring either display the recessive or dominant trait so there are only two phenotypes. However, if the trait is incompletely dominant, there can be more than two phenotypes. In either situation, though, the offspring can have a phenotype different from either parent. For example, if both parents carry the dominant trait but their offspring inherits two copies of the recessive trait, they will have a phenotype different from their parents. This is because one or both parents can carry a recessive trait. In sex-linked traits, the inheritance patterns vary depending on whether the offspring is male or female. Males are more likely to inherit sex-linked traits because they only have one copy of the X chromosome. This means that since they inherit only one copy of a trait, they will have the phenotype associated with that allele. They don't have another allele to mask, or cover up, the recessive allele if it's present.*

Explore and Explain: Epigenetics

1. The genome is all of an organism's genetic information. The epigenome is an organism's genome including chemical modifications to the chromatin that regulate how genes are expressed. **2.** Epigenetic regulation works through making certain genes active or inactive throughout an organism's life. Methylation is a type of epigenetic regulation that occurs when methyl groups are attached to a DNA strand, which causes those genes to suppress gene expression. **3.** Identical twins can accumulate changes to their epigenome throughout their lives. Environmental factors, such as exposure to pollutants, as well as lifestyle choices, such as diet and exercise, can change the way DNA is expressed throughout their lives. **4.** In stressed rat pups, the GR gene is highly methylated and inactive. In relaxed rat pups, the GR gene is demethylated allowing it to be more active and expressed.

Exemplar CER for Breast Cancer Case Study: Ana

Ana has a slightly above average possibility of breast cancer. Ana is 64, which naturally increases her susceptibility to breast cancer according to the American Cancer Society. This can be explained on the basis that cells in her body have gone through mitosis more and bodily functions slow down as we age. The American Cancer Society also noted in “What Are the Genetic Risk Factors for Breast Cancer?” that women who enter menopause after the age of 55 have a slightly higher risk of breast cancer. Ana entered hers at 58. Therefore, she has a slightly increased risk of breast cancer because she has been exposed to estrogen for a longer period of time. To deal with menopause symptoms, she has been on hormone replacement therapy for the last 6 years. According to a study published in 2007 called the Women’s Health Initiative, they found that women who take estrogen and progestin to treat menopause have a higher risk of breast cancer as well. Ana is overweight. According to research by the American Cancer Society, women who are overweight after menopause increases their risk of breast cancer because their fat tissue is increasing their estrogen levels. Ana’s mother was diagnosed with breast cancer at the age of 37. Having first-degree female relatives with breast cancer doubles one’s risk of developing breast cancer, says breastcancer.org. However, there are factors that decrease Ana’s risk of breast cancer. First of all, she is generally in good health. That means she has made relatively good choices throughout her life, which means her epigenomics have adapted to a healthy lifestyle and her body is more likely to detect errors in DNA replication and protein production than if she had poor health. She had her first child when she was 20. Dana-Farber Cancer Institute found that giving birth to a child early decreases a woman’s risk of breast cancer because of hormonal changes that allow mature breast cells to protect against breast cancer. Ana breastfed her child for two years. A study done by the University of Texas found that during breastfeeding, women shed breast tissue and hormonal changes during lactation delays their menstrual periods. This decreases the risk of breast cancer because a woman is being exposed to less estrogen in her lifetime.The evidence above shows that Ana has a slightly above average chance of developing breast cancer. There are ways for Ana to decrease the risk. She should exercise regularly. This will help balance out her weight as well as keep her organs strong. She should get enough sleep because this is when the body does most of its self-repairing. Last but not least, she should avoid hot flash triggers like coffee, tea and alcohol. That way she can manage her menopause symptoms and stop depending so strongly on hormone replacement therapy.

Diabetes Article Questions

1. High blood sugar (glucose) **2.** a. Negative feedback b. Insulin LOWERS glucose levels by opening the receptor molecules on cells so glucose enters and is converted into energy. **3.** a. The body’s own immune system attacks and kills the insulin-producing beta cells so no insulin is produced. b. Type 1 diabetes **4.** Maintain a healthy diet and exercise **5.** Immune system **6**. a. Type 1 environmental risk factors include: viral infections, stress, exposure to pets and other allergens, and maternal weight gain around pregnancy b. Type 2 environmental risk factors include: obesity and the presence of specific intestinal bacteria **7.** Student answers will vary, but should include at least 2 noticings and 2 wonders **8.** If a PWD (person with diabetes) gets a virus: a. their blood glucose level will rise which will cause inflammation of the respiratory tract; inflammation in the body lowers the body’s immune response to new threats b. When glucose levels go up and down or remain heightened, the body’s immune response is decreased c. They have a greater chance of diabetic ketoacidosis, which stops the body’s response to sepsis (bacterial infection in blood) which is a major reason people with COVID-19 die.

CRISPR Article Questions

1. a. enzyme (protein) b. Bacteria fight off viruses by sending the Cas9 enzyme to chop up viruses. **2.** 3 of the following examples: Fix genetic diseases in animals, Combat viruses, Sterilize mosquitoes, Prepare pig organs for human transplants, and Beef up the muscles in beagles. **3.** Newer versions of CRISPR can edit genetic material one base at a time, without cutting. **4.** RNA finds the spot in the nucleus of a cell where some editing activity should take place. This guide RNA shepherds Cas9 (enzyme) to the precise spot on DNA where a cut is called for. **5.** Newer versions of CRISPR can edit genetic material one base at a time, without cutting. **6.** Student answers will vary. **7.** Student answers will vary. **8.** Student answers will vary.