Leptin Resistance 5E

Unit 3 Evolution of Sick Humans	Biology
Student Name:	

The Role of Leptin Investigation

Research Question:

Introduction: The ability to store fat is an advantageous trait that benefits our survival. However, some people's bodies store excess fat, a condition called obesity. One protein that plays an important role in fat storage is called leptin. Leptin is secreted by fat cells and regulates hunger. In this investigation, you will examine data from two different research studies on fat storage, obesity, and the role of leptin.

Procedure:

Using a jigsaw process, as a group you will engage with two different research excerpts (data sets and brief summaries of scientific articles that include graphs).

1. Starting from a home group you will be assigned to look at one of the article summaries in pairs
2. Using a See-Think-Wonder organizer, work with your partner to generate observations and questions about your assigned study and data set
3. Collaborate with your partner to develop a summary of your assigned study and independently write your summary using the sentence frames given below.
4. Return to your home groups; each pair shares out about their study using the written summary as a guide
5. Each group member takes notes in the space provided below as they listen to each summary
6. Collaboratively decide on high-level observations and questions about the two studies and then independently write your high level observations and questions on them

Written Summary:

The following sentence frames may be helpful:

- The title of study is…
- The researchers in this study wanted to know…
- The researchers found that…
- These findings are interesting and/or connected to… because…
- The study design did/did not provide evidence that as to whether ____ causes ____ because __

Notes on Shared Summaries

Collaborative High-Level Observations and Questions on the Two Studies

See-Think-Wonder Organizer

See *What do you see in the data*	**Think** *What does the data make you think about?*	**Wonder** *What does the data make you wonder about?*
• I see a relationship between ___ and blank ___ • I see that ___ • As ___ increases/decreases ___ increases/ decreases / stays the same	• The data provided is/ is not sufficient to conclude that ____ causes ___ • I would want to collect ____ data before claiming ___ causes _____	

The Role of Leptin Research Excerpts

Study #1: Blood Leptin Levels and Weight in Japanese Women

Researchers were interested in finding out more about factors that might contribute to osteoarthritis. Osteoarthritis is the most common form of arthritis, affecting millions of people worldwide. It occurs when the protective cartilage that cushions the ends of your bones wears down over time. Although osteoarthritis can damage any joint, the disorder most commonly affects joints in your hands, knees, hips and spine. Fifty Japanese women with knee osteoarthritis (age: 50-88 years) were recruited for a study. Radiographs (x-rays) of the knee were taken, leptin levels in the blood were measured, the women were weighed, and their total fat mass was calculated. Some of the results are presented below:

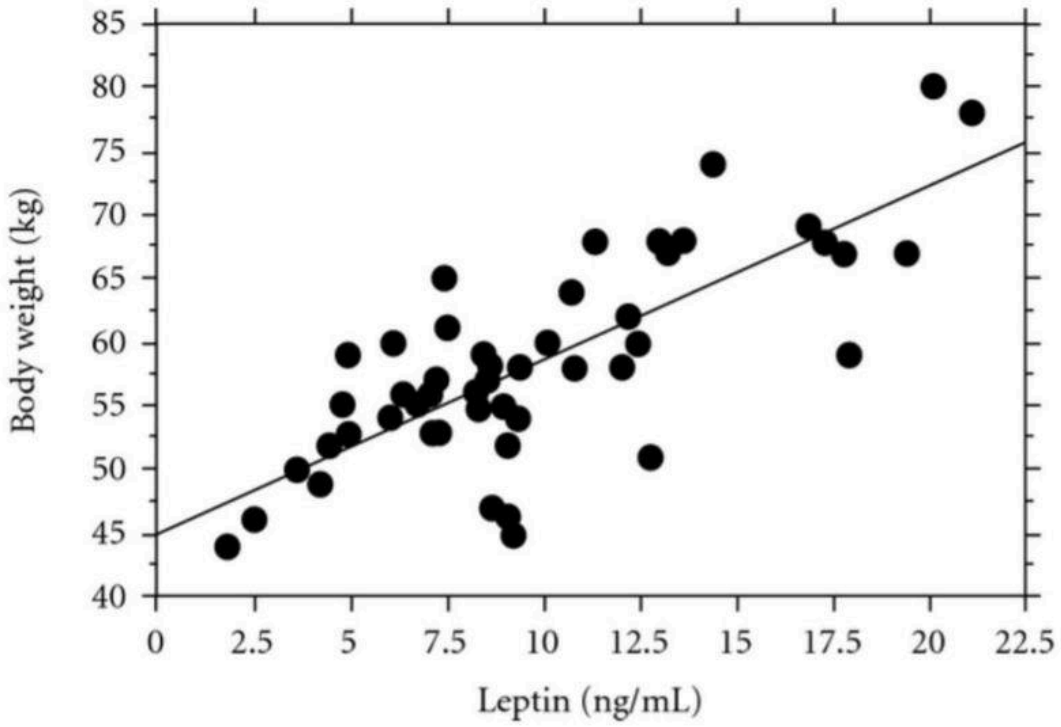


Figure (a) Correlation between serum leptin level and body weight

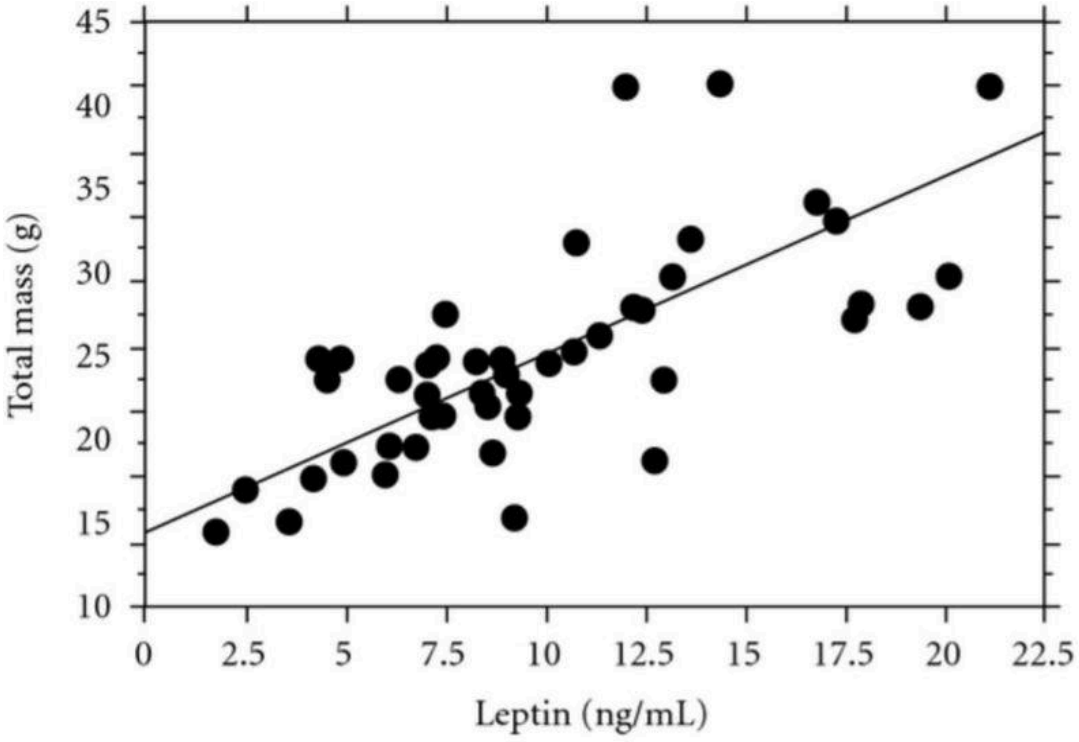


Figure (b) Correlation between serum leptin level and total fat mass

Study #2: The Impact of Dietary Fructose on Obesity

Researchers were interested in finding out if a high-fructose diet (fructose is a sugar) has an impact on how leptin works in the body and on obesity. The researchers designed an experiment with two groups of rats. One group was given a control diet (not high in fructose), and the second group was fed a high-fructose diet for six months. They then tested how well leptin was doing its job in all of the rats. In order to test if leptin was working in their bodies, the rats were given either an injection of saline or of leptin and then recorded how much food each group of rats ate. Food intake was then tracked for 24 hours. Finally, in each group, 50% of those rats were given a diet either high in fat, or they continued on with the respective diet they had been on (either high-fructose or the control diet) for two weeks. Finally, all of the rats were evaluated for weight gain, adiposity (how much fat they stored), and their blood leptin levels. Some of the results are presented below:

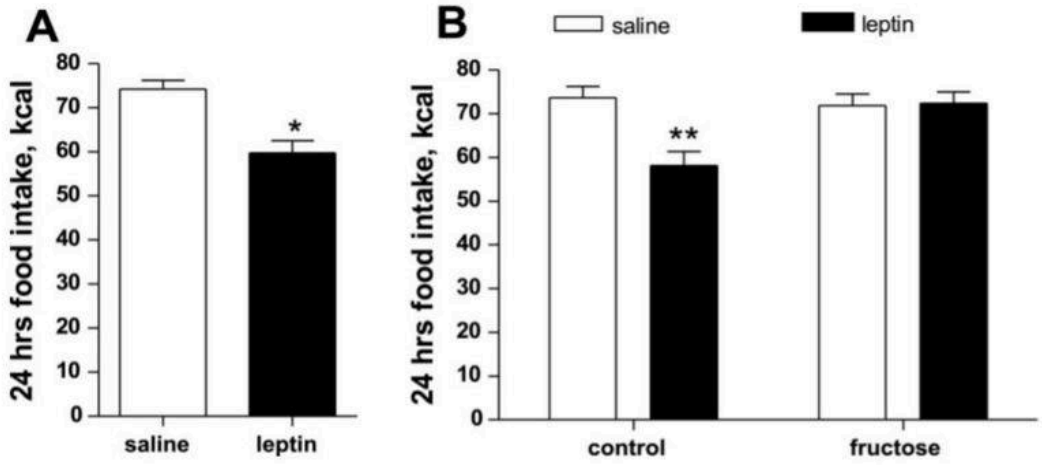


Figure (a) Leptin responsiveness as measured by cumulative food intake 24 h after an injection of either saline or leptin prior to initiating the experimental diets (A) and after 6 months on either the fructose-free control or the high-fructose diet (B). The values used are the mean of each group of rats, and the error bars represent the variation around that mean value.

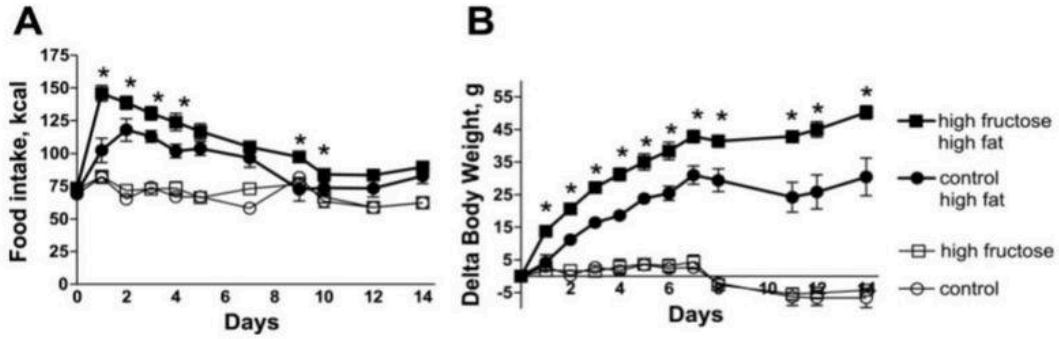


Figure (b) Food intake (A) and change in body weight (B) in rats either maintained on the fructose-free or high-fructose diets or switched from the control to high-fat diet or from high-fructose to high-fat diets. The values used are the mean of each group of rat, and the error bars represent the variation around that mean value.

Table 1. Blood Leptin Levels and Adiposity at the End of the Experiment

	Control Diet	**High Fructose Diet**	**Control + High Fat Diet**	**High-Fructose + High-Fat Diet**
Adiposity (in grams)	129.8	129.1	138.9	143.3
Blood Leptin Levels (ng/dl)	5.4	5.0	10.1	10.4

The Role of Leptin Investigation Rubric

Student Rubric - The Role of Leptin Investigation

How did you do in the investigation?

	Student Self-Score Select one		
I know how this investigation connects to our current unit.	No - I need help.	Almost	Yes
I was able to contribute to the See-Think-Wonder and / or respond to the analysis questions.	No- I need help.	Almost	Yes
I used my time well in this investigation.	No	Mostly	Yes
I plan to come in for extra help to complete parts of the investigation or ask questions.	No		Yes

What other resources could you have used to get more out of this investigation?

- More time
- More resources
- More information
- More help from my partners
- More help from my teacher
- Other:

Partner Rubric - The Role of Leptin Investigation

How did your partners do in the investigation?

Directions: Think back to how your partners participated in the lab. For each of the four categories, write the name(s) of your partner(s) in the appropriate box.

	Unsatisfactory	Pretty Good	Excellent
Contributions	Did not participate.	Did the minimum of what was required.	Provided useful ideas when participating in discussion.
Working with Others	Rarely listened to others. Disrupted or discouraged others' attempts to participate.	Usually listened to, shared with, and supported the efforts of others.	Listened to, shared with, and supported the efforts of others.
Time Management	Procrastinated, did not use school time or schedule provided to get work completed.	Mostly used time well and completed investigation on time.	Used time well to ensure things get done on time.

Protein Synthesis Handout

Guiding Question: How is leptin made in the body?

Introduction

Proteins do all of the work in an organism. Scientists have identified several proteins that impact how we regulate fat storage and may play a role in obesity. One protein we will explore is a hunger regulating protein called leptin. Leptin is a protein-based hormone. Leptin is produced in our fat cells and helps to regulate hunger, thus how much energy we consume. It may be helpful to understand how leptin is created in fat cells so we can investigate the role it may play in obesity.

Directions:

1. **Watch** each of the following animations on silent. Animations: Transcription and Translation (protein synthesis).
2. **Describe** what you see in your own words (don't worry about specific vocabulary at this stage). Write your observations in the left-hand column.
3. **Read** the *Protein Synthesis Text*, and **summarize** the key ideas in the right-hand column.
4. **Draw** an arrow connecting your description from the left to the summary on the right-hand side.
5. Write a final **summary** of the entire process using the terms: DNA, chromosome, gene, protein, codes, instructions, form, function

Description from animation	Summary from text
Transcription: Translation:	

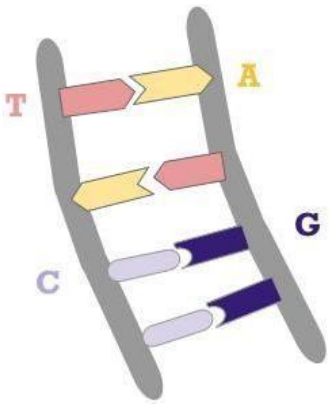
Summary:

Protein Synthesis Text

How are proteins created?

Protein synthesis is the process by which cells make proteins. These proteins are used in a variety of biochemical processes and play a role in the presence or absence of the traits of an organism. For example, through protein synthesis, skin cells produce a protein called melanin that is responsible for determining skin color. The information detailing the production of a specific protein is usually contained in one section of DNA, called a **gene**. However, sometimes multiple genes provide the information to produce a single protein or trait, or one gene can influence multiple proteins and traits. Some stretches of DNA do not code for proteins at all but instead serve regulatory functions. Additionally, there are some stretches of DNA that as of yet, have no known function.

In **eukaryotes**, the first step of protein synthesis (called **transcription**) begins in the **nucleus** of the cell. An enzyme unwinds the needed section of DNA and using complementary **base-pairing**, creates a complementary single strand of RNA. In base-pairing, the original DNA strand is used as a template, and an enzyme matches up the corresponding RNA nucleotides (base). Base pairing works by matching up complementary bases in the DNA. For example, adenosine (A) always matches up with thymine (T).



This single RNA strand is called **messenger RNA** (mRNA) and since it is smaller than a DNA molecule, it can leave the nucleus through tiny openings called nuclear pores. The DNA itself does not leave the nucleus, therefore the mRNA serves as a copy of the original genetic information found in the DNA.

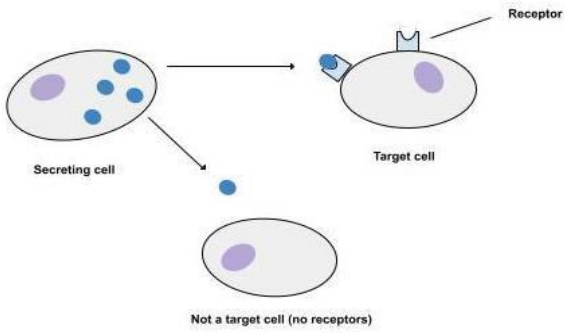
Once the mRNA is in the cytoplasm, it can interact with an organelle called the **ribosome**. Once the mRNA has reached the ribosome, the second phase of protein synthesis, called **translation**, can begin. Within the ribosome, the information coded in the messenger RNA is translated into an amino acid sequence which will form a protein.

The first step in translation is when a transfer molecule approaches the messenger RNA. The transfer molecule is interesting because it is divided up into two parts. On the bottom, it possesses a specific sequence of 3 bases. On the top, it holds a specific **amino acid** that corresponds with those 3 bases.

Within the ribosome, the transfer molecule matches up with a complementary 3-base sequence on the messenger RNA strand. Once it has matched up, or bound, with the mRNA strand, it releases its amino acid. Then, the next transfer molecule that is complementary to the next 3 bases on the mRNA binds with the mRNA and leaves its amino acid. The amino acids bind together to form a specific sequence and eventually a protein. Therefore, the sequence of bases found in the mRNA is *translated* into a set of amino acids that bind to form a protein. Each protein is made up of a unique sequence of amino acids that is formed based on the information originally contained in DNA.

Leptin Resistance Text

Human bodies are designed to store fat. Fat plays many different roles in the body, including energy storage, vitamin storage, insulation, and is essential for reproduction and health. Throughout human history, it has been advantageous to store some body fat. However, we are currently experiencing the problem that too many people are storing too much fat. The storage of too much fat, called obesity, may cause health problems such as diabetes and arthritis.



Leptin resistance has been identified as one contributor to obesity. Leptin is a protein that is produced in fat cells during a meal. The gene for leptin is activated, and through protein synthesis, DNA is transcribed into RNA, and RNA is translated into a specific sequence of amino acids. The sequence of amino acids forms the protein, leptin. When leptin is secreted from fat cells, it travels through the bloodstream and reaches the hypothalamus in the brain. Because leptin is made up of a specific sequence of amino acids, it has a specific shape. The shape of leptin fits into the leptin receptor in the hypothalamus, telling the brain to reduce appetite. Generally, if an individual has more fat cells, they produce more leptin, thus lowering hunger. If a person does not have a lot of fat, less leptin is produced, thus increasing hunger and encouraging food consumption.

If the leptin receptor becomes over-stimulated (used too much) or damaged, the leptin no longer fits inside of the receptor and does not communicate to the hypothalamus to reduce appetite. This is called leptin resistance. Leptin resistance may be, in part, caused by the overconsumption of high-fat and high-sugar food. Other causes of leptin resistance are chronic inflammation, lack of exercise, and the over-consumption of processed foods. Some people have genetic variations that may also impact leptin resistance.

Leptin Resistance Sequence Chart Summary

Documenting the Leptin Resistance Sequence Chart

In the space below, draw, sketch, or insert a picture of the leptin resistance sequence chart.

Individually respond to the prompts below:

1. According to the text and sequence chart, describe one way in which fat cells are specialized to help the body perform an essential function of life

2. How did you use evidence from the texts and research studies to inform the order of causes and effects in your sequence chart?

3. Pretend that a friend of yours is out sick today. In your own words, and using diagrams or drawings to help you communicate clearly, explain how leptin resistance occurs.

Role of Genetics & Environment Investigation

Research Question:

Introduction: The ability to store fat is an advantageous trait that benefits our survival. However, some people store excess fat, called obesity. In the previous investigation, we looked at the role of leptin. However, fat storage and hunger regulation in an individual are complex. In this investigation, you will examine data from two different research studies on fat storage, obesity, and the roles of genetics and environmental factors.

Procedure:

Using a jigsaw process, as a group you will engage with another two different research excerpts (data sets and brief summaries of scientific articles that include graphs).

1. Starting from a home group you will be assigned to look at one of the article summaries in pairs

2. Using a See-Think-Wonder organizer, work with your partner to generate observations and questions about your assigned study or data set

3. Collaborate with your partner to develop a summary of your assigned study and independently write your summary using the sentence frames given below

4. Return to your home groups; each pair shares out about their study using the written summary as a guide

5. Each group member takes notes in the space provided below as they listen to each summary

6. Collaboratively decide on high-level observations and questions about all the four of the studies (the two from your last investigation and the two here) and then independently summarize them below

Written Summary:

The following sentence frames may be helpful:

- The title of study is…
- The researchers in this study wanted to know…
- The researchers found that…
- The study design did/did not provide evidence that as to whether ____ causes ____ because __
- These findings are interesting and/or connected to… because…

Notes on Shared Summaries

Collaborative High-Level Observations and Questions on the Four Studies

Role of Genetics & Environment Research Summaries

Study #3: Genetic Influences on Childhood Eating Behavior

Researchers wanted to understand how genetics influences eating behavior, such as food avoidance or overconsumption of food, and therefore the likelihood of a child storing too much fat (obesity). Questionnaires have been given to parents in order to collect large amounts of data on childhood eating behaviors. To examine this data, two different approaches have been taken:

1) Quantitative genetic studies estimate broadly the extent to which behavior is influenced by genes or environment. Twins are often used in these types of studies because identical twins share 100% of the same genes, while fraternal twins share between 38-61% (or on average 50%) of the same genes just like any two siblings do. Both types of twins share the same environment (same access to food, family culture, etc.) so if there is a greater similarity between identical twins compared to fraternal twins, it suggests that genes influence eating behavior. Heritability is the statistic that is derived from twin studies, and it indicates the extent to which individual differences in the sample are explained by genetic variation. The statistic ranges from 0% (genetic variation does not contribute to individual differences) to 100% (individual differences can be explained entirely by genetic variation).

2) Molecular genetic studies try to identify the specific genes that may influence both eating behaviors and the likelihood of someone storing excess fat. Recent advances in technology and the Human Genome Project have made it possible to explore the impact of millions of genetic variants (variations) on traits such as obesity across the wider population.

Some of the results of these analyses are below:

Table 1: Results from Quantitative Genetic Studies

Indicator	Heritability
General Body Weight	70%
Responsiveness to Food Cues (likely to consume more food)	75%
Satiety Responsiveness (likely to consume less food)	63%
Eating Speed	63%
Enjoyment of Food	53%
Food Responsiveness in Infants	59%

Table 2: Example Genetic Variants found in Molecular Genetics Studies

Gene Variation	Impact	Notes
A set of mutations in genes that regulate leptin production	• Causes severe early on-set obesity • Associated with voracious appetite	• Extremely rare • Does not explain variations in weight across a population
Variations in the FTO gene (fat mass and obesity-associated gene)	• Associated with observational measures of food responsiveness • Associated with satiety responsiveness • People with 2 or more variants in this gene are on average 6.6 pounds heavier than those with no variants	• Nearly half of the population have at least 1 variant in this gene

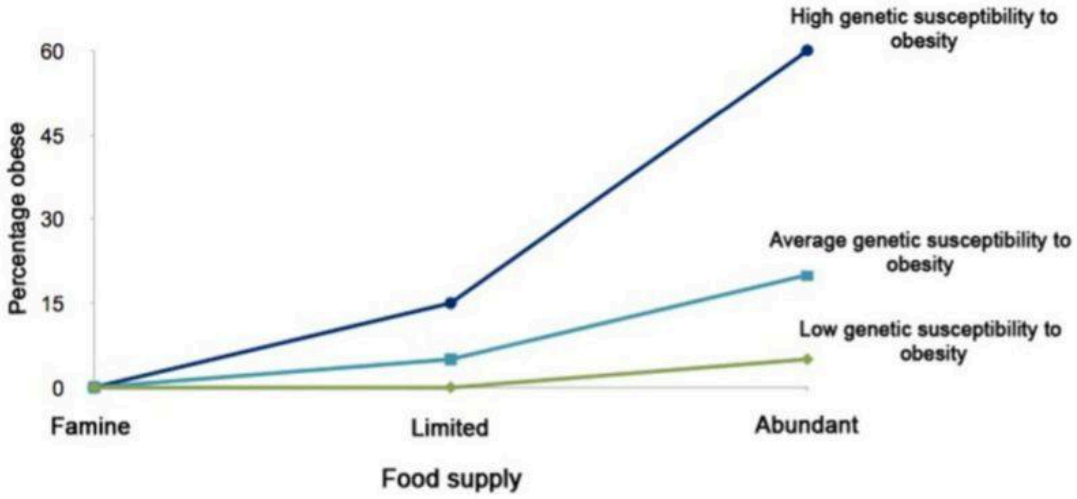


Figure (a) is a hypothetical demonstration of the percentage of children who are obese under three different environmental conditions, according to whether they have a low, average, or high genetic susceptibility to obesity.

Study #4: The global childhood obesity epidemic and the association between socio-economic status and childhood obesity.

Childhood obesity has become a global public health crisis. Researchers wanted to understand the extent of the problem and if there is an association between socioeconomic status and childhood obesity. One important indicator that is used to measure the prevalence of overweight or obsese children is BMI, or body mass index (BMI = weight/height (kg/m2)). The researchers used data from the World Health Organization (WHO) and other similar global organizations to better understand how many children are overweight or obsese across the globe and if there is an association between being overweight and socioeconomic status. Some of the results of these analyses are below:

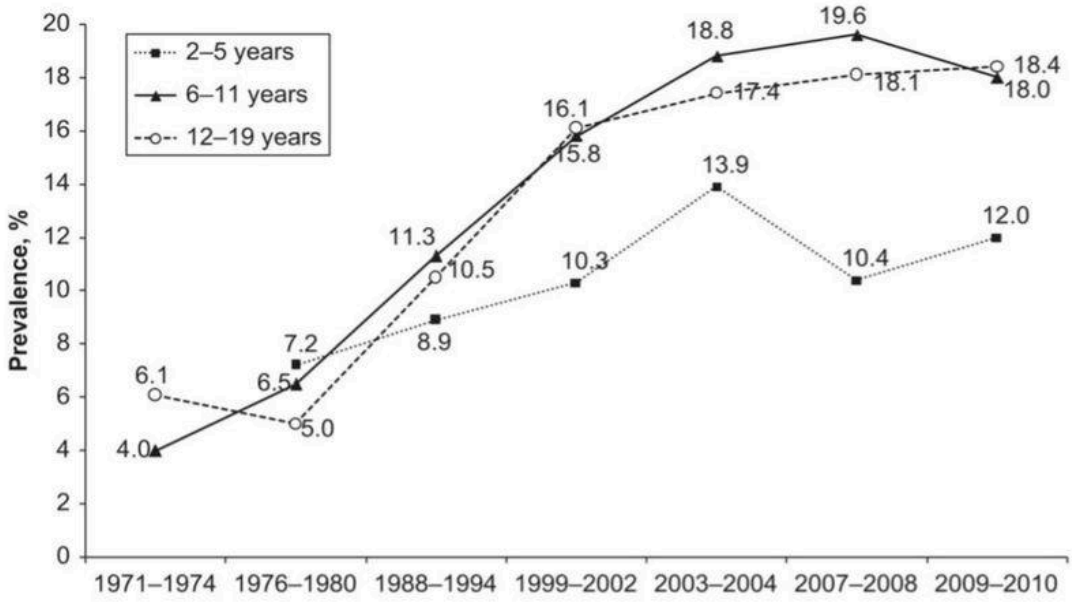


Figure 1. Trends in the prevalence (%) of obesity (BMI ≥ 95th percentile) in US children and adolescents by age: 1971–1974 to 2009–2010.

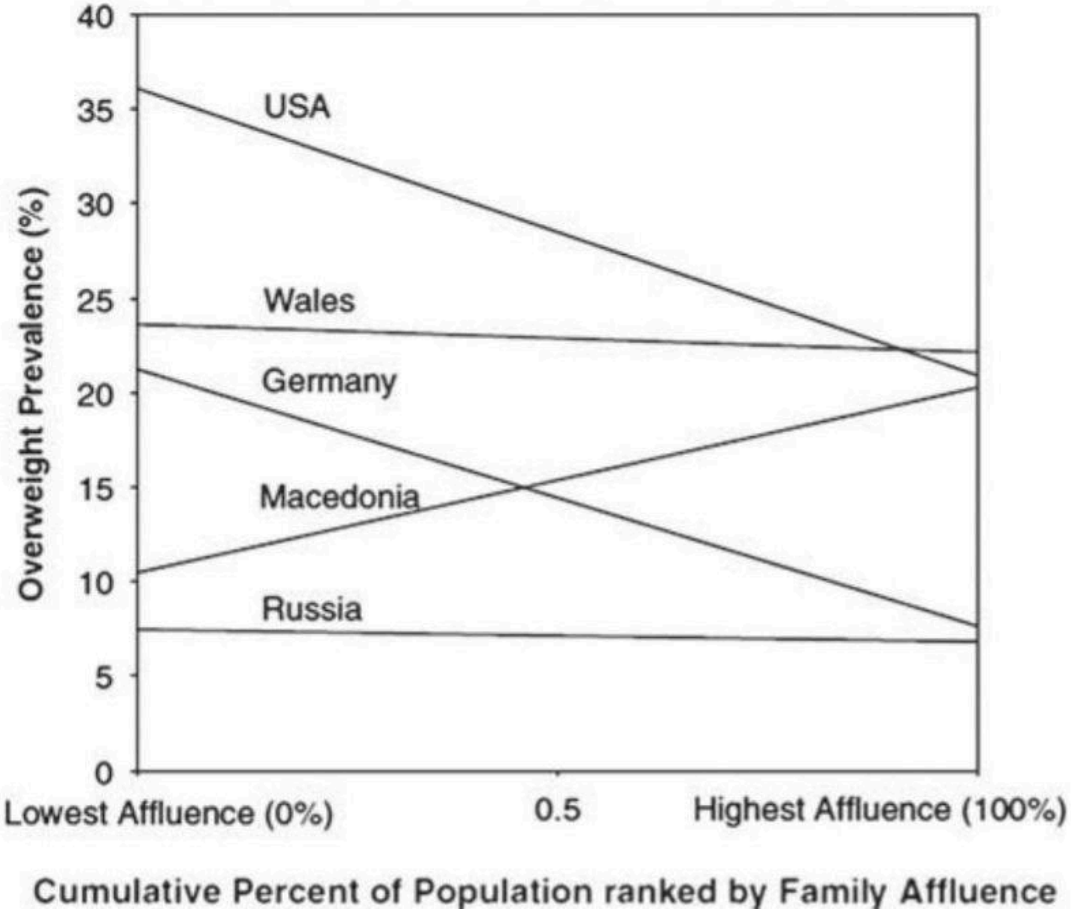


Figure 2. Association between family affluence and obesity in adolescent boys aged 11, 13 and 15 years from five countries. Family affluence was measured as a function of family possessions (e.g. car ownership, number of computers, child had own bedroom) and number of family travels over the past year.

Table 1: Time trends in the combined prevalence (%) of overweight and obesity in preschool-age children aged 0 – 5 years for the years from 1990 to 2010 and projections for 2015 and 2020, by United Nations (UN) region. *Note that the data is from 2012, so 2015 and 2020 are projections based on the data available at that time.

UN Region	1990	1995	2000	2005	2010	2015	2020
Global	4.2%	4.6%	5.1%	5.8%	6.7%	7.8%	9.1%
Africa	4.0%	4.7%	5.7%	6.9%	8.5%	10.4%	12.7%
Asia	3.2%	3.4%	3.7%	4.2%	4.9%	5.7%	6.8%
Latin America & the Caribbean	6.8%	6.8%	6.8%	6.9%	6.9%	7.0%	7.2%
Oceania	2.9%	3.1%	3.2%	3.3%	3.5%	3.6%	3.8%

See-Think-Wonder Organizer

See	Think	Wonder
• I see a relationship between ___ and blank ___ • I see that ___ • As ___ increases/decreases ___ increases/ decreases / stays the same	• The data provided is/ is not sufficient to conclude that ____ causes ___ • I would want to collect ____ data before claiming ___ causes _____	

The Role of Genetics & Environment Investigation Rubric

Student Rubric - The Role of Genetics & Environment Investigation

How did you do in the investigation?

	Student Self-Score Select one		
I know how this investigation connects to our current unit.	No - I need help.	Almost	Yes
I was able to contribute to the See-Think-Wonder and / or respond to the analysis questions.	No- I need help.	Almost	Yes
I used my time well in this investigation.	No	Mostly	Yes
I plan to come in for extra help to complete parts of the investigation or ask questions.	No		Yes

What other resources could you have used to get more out of this investigation?

- More time
- More resources
- More information
- More help from my partners
- More help from my teacher
- Other:

Partner Rubric - The Role of Genetics & Environment Investigation

How did your partners do in the investigation?

Directions: Think back to how your partners participated in the lab. For each of the four categories, write the name(s) of your partner(s) in the appropriate box.

	Unsatisfactory	Pretty Good	Excellent
Contributions	Did not participate.	Did the minimum of what was required.	Provided useful ideas when participating in discussion.
Working with Others	Rarely listened to others. Disrupted or discouraged others' attempts to participate.	Usually listened to, shared with, and supported the efforts of others.	Listened to, shared with, and supported the efforts of others.
Time Management	Procrastinated, did not use school time or schedule provided to get work completed.	Mostly used time well and completed investigation on time.	Used time well to ensure things get done on time.

Think-Talk-Open Exchange + Buzzwords Organizer

1. **Think -** Individually respond to the prompt in the space below.

From an evolutionary perspective, being able to store fat is an advantageous trait. However, the number of people (including children) that are storing excess fat is increasing. Using evidence and scientific reasoning from this learning sequence, construct an explanation for why some populations of people might be experiencing an increase in excess fat storage (obesity). Be sure to use the following words and ideas in your explanation.:

Buzzwords: leptin resistance, gene(s), DNA, protein, cause/causal, empirical evidence.

2. **Talk**: Share with your group one at a time. Record a tally mark (✔✔✔✔) each time you hear a specific buzzword during the share.

	Leptin Resistance	Gene	DNA	Protein	Cause/ Causal	Empirical evidence
Person 1						
Person 2						

3. **Open Exchange:** As a group, discuss the following questions- be sure to use the buzzwords!

- Describe patterns or commonalities between what each group member shared.
- Which buzzwords did you hear the most? Least?

- Are there buzzwords that your group doesn't understand?
- Are there other words you heard a lot? If so, which words?

4. **Reflection -** Individually respond to the prompt below.

What are some new ideas you heard during your discussion with your group?

Summary Task

Today we completed a class consensus discussion. How did it go?

1. One thing that went well in the discussion:

2. One thing we can improve the next time we have a discussion:

3. One person who helped me learn today:

4. What did you learn from this person?

5. One idea that I contributed to my group or my class:

Explain what you know about the following questions based on what we discussed today.

1. Describe where and how leptin is made in the body.

2. Discuss one example of a possible causal relationship discussed in this learning sequence. How did you determine causality and what evidence did you use to differentiate between cause/effect and a correlation relationship?

3. Fat storage is an evolutionarily advantageous trait. Explain how both genetic and environmental influences may lead to excessive fat storage (obesity).

Read-Generate-Sort-Solve Organizer

Insulin is another important protein that serves as a hormone in the body. Insulin is made by a set of specialized cells called the beta cells in the islets of Langerhans portion of the pancreas.

Insulin can also be produced using genetically engineered bacteria. In 1978, scientists successfully inserted the human insulin gene into *E. coli* bacteria. Because the As, Ts, Cs, and Gs of the genetic code are universal, bacterial cells are able to read human genes, and therefore transcribe and translate the gene into insulin protein. The insulin can then be extracted from the bacteria, creating an injectable source of human insulin.

Guiding prompt: Why is injectable insulin a good solution for people with type 1 diabetes, but not insulin resistance?

1. **Watch** the video.

2. **Generate** ideas using evidence from the blurb above, the video, and information from this learning sequence that help explain why injectable insulin is a good solution for people with type 1 diabetes but not insulin resistance.

Name: _____	**Name:** _____	**Name:** _____

3. **Sort -** Discuss each solution or idea and ☆star☆ or highlight the ideas that seem the most useful.

4. **Solve -** Independently respond to the prompt incorporating the most useful ideas from the sorting process! In your response, be sure to
    - Use evidence from the investigation, video, and text blurb and reasoning from the texts to support your claim
    - Describe the difference in causes between type 1 diabetes and type 2 diabetes/insulin resistance
    - Discuss how each condition alters specialized cells and impacts their ability to perform the essential processes of life

Leptin Resistance Engineering Mini-Rubric

Explanation of a mismatch	Identifying a problem:
	● The mismatch problem of leptin resistance is described
	● An accurate explanation of the following science concepts are included:
	  ● How a system of specialized cells create leptin
	  ● The relationship between DNA, genes, and traits
	  ● How resistance is caused by the changing shape of the receptor (due to a combination of genetic and environmental factors) which no longer allows for leptin to bind
		Circle or Highlight One:
		
		Proficient - Includes **all** of the components
		
		Developing - Includes **some** of the components

Engaging with a Design Process	Engaging with the design cycle:
	● An initial description of the design cycle includes:
	  ● Identifying the problem & subproblem(s)
	  ● Brainstorming solutions
	  ● Using science concepts and/or research to inform the initial solution
	  ● Identifying appropriate criteria and constraints
	  ● The lens of cause and effect is used to connect the science concepts and the possible solution(s)
	  ● Includes discussion of evidence needed to make claims about causality
		Circle or Highlight One:
		
		Proficient - Includes **all** of the components
		
		Developing - Includes **some** of the components

Notes, Ideas, and Questions	The open sketch portion of the engineering journal is used to: ● Note down additional ideas ● Initial design sketches ● Develop a representation of a design process ● Additional research ● Additional questions	Circle or Highlight One: Proficient - Includes **all** of the components Developing - Includes **some** of the components
Self-Evaluation	Grow: Glow:	

Teacher / Peer Evaluation	Grow: Glow: