**INTRODUCTION** **NAME**

This activity explores the research shown in the short film *Got Lactase? The Co-evolution of Genes and Culture*. This film is about the genetics and evolution of lactase persistence, a trait that affects whether people can digest milk as adults. By watching the film, you'll explore how key biology concepts, like natural selection and gene expression, apply to a real example in humans. You'll also learn how scientists can use different types of evidence to answer questions.

**PROCEDURE**

Answer the following questions based on the information provided and what you learned from the film. You may want to use the film's transcript as a reference.

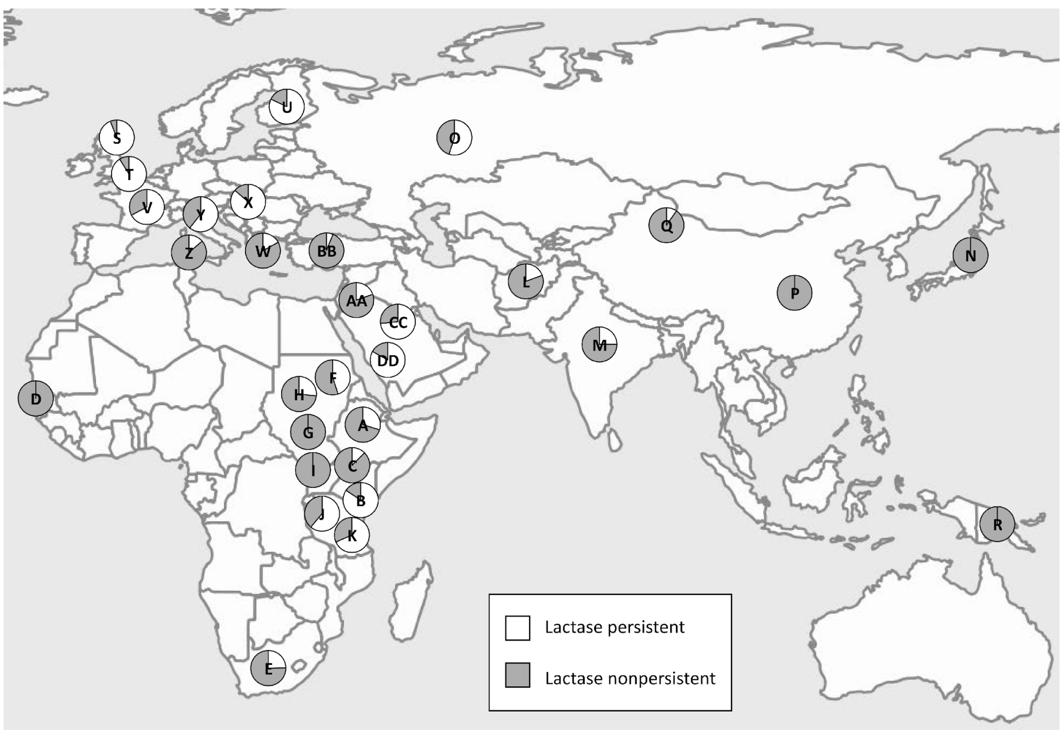
1. When the enzyme lactase breaks down the sugar lactose, which two simpler sugars are formed?
   a. glucose and fructose
   b. galactose and maltose
   c. glucose and galactose
   d. glucose and maltose
2. In the film, geneticists discovered that the difference between lactase-persistent (lactose-tolerant) and lactase-nonpersistent (lactose-intolerant) people was due to a mutation. This mutation was *not* in the part of the lactase gene that encoded the lactase enzyme. In which of the following was the mutation located?
   a. the genetic switch for the lactase gene
   b. an intron of the lactase gene
   c. the gene for glucose production
   d. different genes for different individuals
3. Which statement most accurately describes human evolution?
   a. Humans stopped evolving 200,000 years ago when they became a distinct species (*Homo sapiens*).
   b. Humans stopped evolving after adapting to a pastoralist way of life.
   c. Humans are still evolving and will continue to evolve through natural selection.
   d. Human evolution through natural selection ended with the development of modern medicine.
4. Scientists hypothesize that the use of milk in pastoralist cultures drove evolution of lactase persistence. Which discovery best supports this hypothesis?
   a. The lactase gene is present both in humans and in domesticated animals.
   b. Ancient pots used to hold milk are about the same age as the lactase-persistence mutations.
   c. Most human cultures today drink milk, and most people worldwide are lactase persistent.
   d. Scientists have identified different mutations that cause lactase persistence.
5. As shown in the film, one test for lactose tolerance involves drinking a liter of milk, then measuring your blood glucose levels. Why does this test indicate whether you are able to digest lactose?
   a. When lactose is digested by lactase in the small intestine, different cells in the body start releasing glucose into the bloodstream.
   b. When lactose is digested by lactase, the glucose that is produced enters the bloodstream from the small intestine.
   c. When lactose enters the large intestine, glucose is digested by bacteria and then enters the bloodstream.
   d. The fats and proteins in milk are digested by the body, causing glucose levels in the blood to increase.
6. What could be the effect of a mutation in the coding region of the lactase gene?

7. According to the film, why might milk have provided strong favorable selection for lactase persistence?

In humans, the ***AMY1*** gene produces the enzyme **amylase** in cells of the salivary glands. Amylase breaks down **starch**, which is a type of sugar, into **maltose**, a simpler sugar. People from cultures with diets high in starch are more likely to have a certain mutation in the *AMY1* gene. This mutation causes them to produce more amylase than people from cultures with diets low in starch do.

8. In two or three sentences, explain why this *AMY1* mutation would have become more common in populations with a high-starch diet.

9. Study the partial world map below. Each pie chart represents a unique population. The unshaded part of each pie chart represents the proportion of the modern-day population that is lactase persistent.




a. Identify two trends from the map. Provide evidence to support each trend.

b. Write a hypothesis to explain the global distribution of lactase persistence and lactase nonpersistence. Include the following key terms in your hypothesis: fitness, survival, natural selection.

## The Science

The film *Got Lactase?* follows geneticist Spencer Wells as he unravels one of the most compelling examples of gene-culture co-evolution: the evolution of lactase persistence in humans. The sections in this appendix describe the science in the film in more detail. **Lactose Digestion**

Milk contains complex biomolecules, including fats (50% of milk's calories), proteins (20%), and carbohydrates/sugars (30%). These biomolecules must be digested in multiple steps before they can be used by the body's cells. The proteins are digested in the stomach, whereas the fats and sugars are digested primarily in the small intestine.

The main sugar in milk, the disaccharide **lactose**, is digested by the enzyme **lactase**. Lactase is produced by cells called **enterocytes** that line the small intestine. The membranes of enterocytes have tiny fingerlike projections called **microvilli.** The microvilli increase the surface area of the enterocytes, which makes the digestive process more efficient, and contain molecules of lactase (Figure 1A).

After binding to lactose molecules that enter the small intestine (Figure 1B), lactase cleaves lactose into the monosaccharides **glucose** and **galactose** in a process known as **lactose hydrolysis** (Figures 1C and 1D).

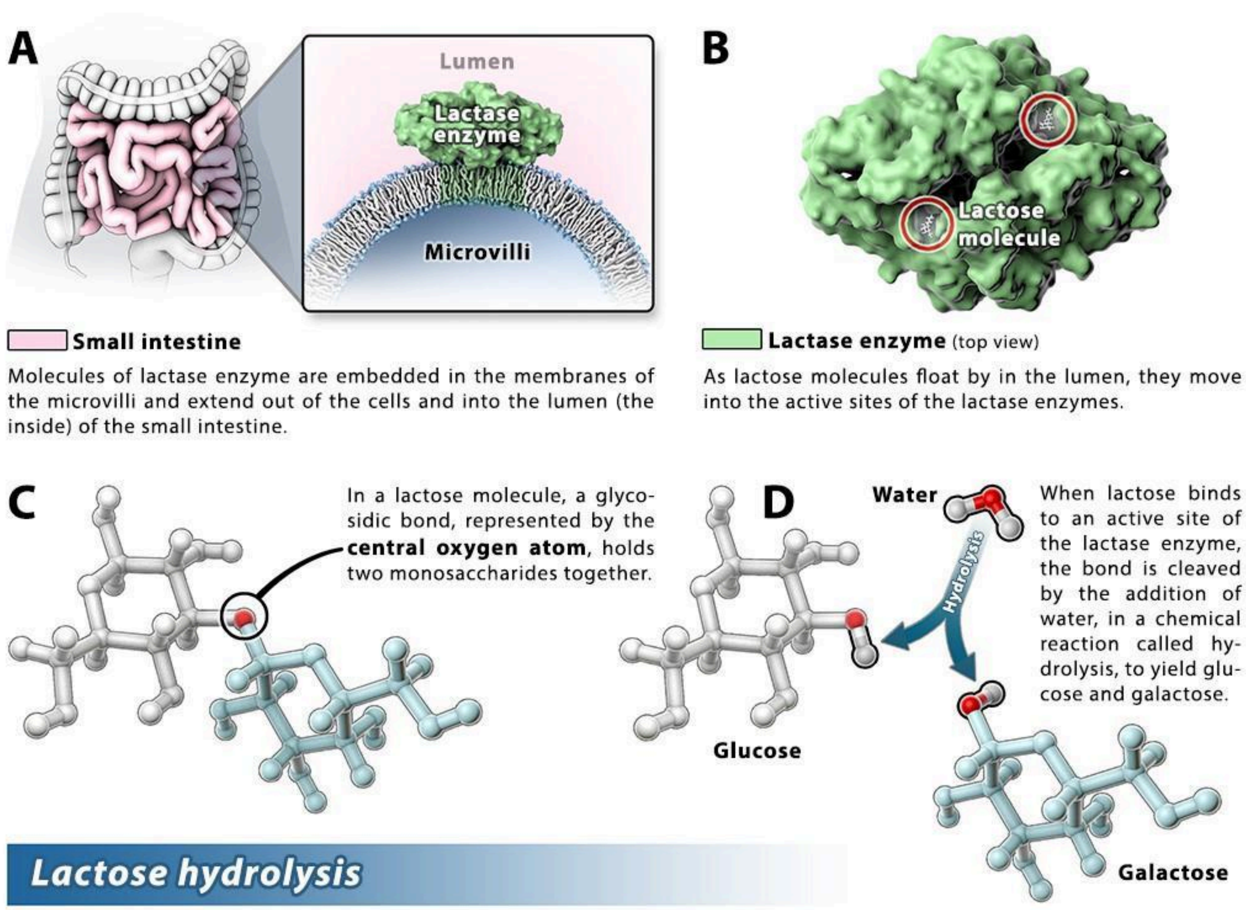


**Figure 1.** A diagram that shows **A)** where lactase is located, **B)** how lactose binds to lactase, and **C/D)** how lactase breaks down lactose through lactose hydrolysis.

Both glucose and galactose diffuse through the intestinal wall, enter the bloodstream, and are delivered to the body's cells, where they are converted to cellular energy. (Galactose is eventually converted to glucose in cells of the intestine.) Glucose is the main energy source for most cells in all organisms. Most of the foods we consume are eventually converted to glucose. **Lactase Production**

All mammal species produce milk, through the process of **lactation**, specifically to be consumed by their infants. From birth to **weaning** (when they become able to eat solid foods), all infant mammals consume milk and produce lactase to help digest it. After weaning, mammals typically stop drinking milk, so continuing to make lactase would be a waste of energy. As a result, the gene for lactase is usually "turned off" so that lactase is no longer produced.

Humans who do not produce lactase as adults are called **lactase nonpersistent** and are typically **lactose intolerant**, meaning that they cannot digest lactose. When a person who is lactose intolerant drinks milk, undigested lactose flows from their small intestine into the large intestine (Figure 2). This can make it difficult for the intestines to reabsorb water, causing diarrhea. The lactose may be partially digested by the microbial community in the large intestines through a process known as **fermentation**. Fermentation produces gases (carbon dioxide, hydrogen, and methane) that can cause abdominal pain, bloating, and flatulence.

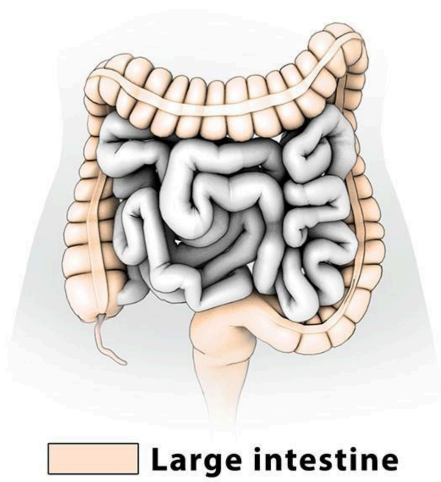



**Figure 2.** A diagram of the intestines with the large intestine highlighted.

#### Lactase Persistence

Some people continue producing lactase even as adults. These individuals are called **lactase persistent** and are typically **lactose tolerant**, meaning that they can digest lactose easily and drink milk without problems.

Five different mutations are known to be associated with lactase persistence. All five mutations occur in a regulatory element, known as a **genetic "switch,"** for the lactase gene on chromosome 2 (Figure 3). The switch is in a neighboring gene called *MCM6*, and all the mutations are within two of the introns of this gene. Individuals need only one copy of a mutation in the switch to be lactase persistent, which makes lactase persistence a dominant trait.

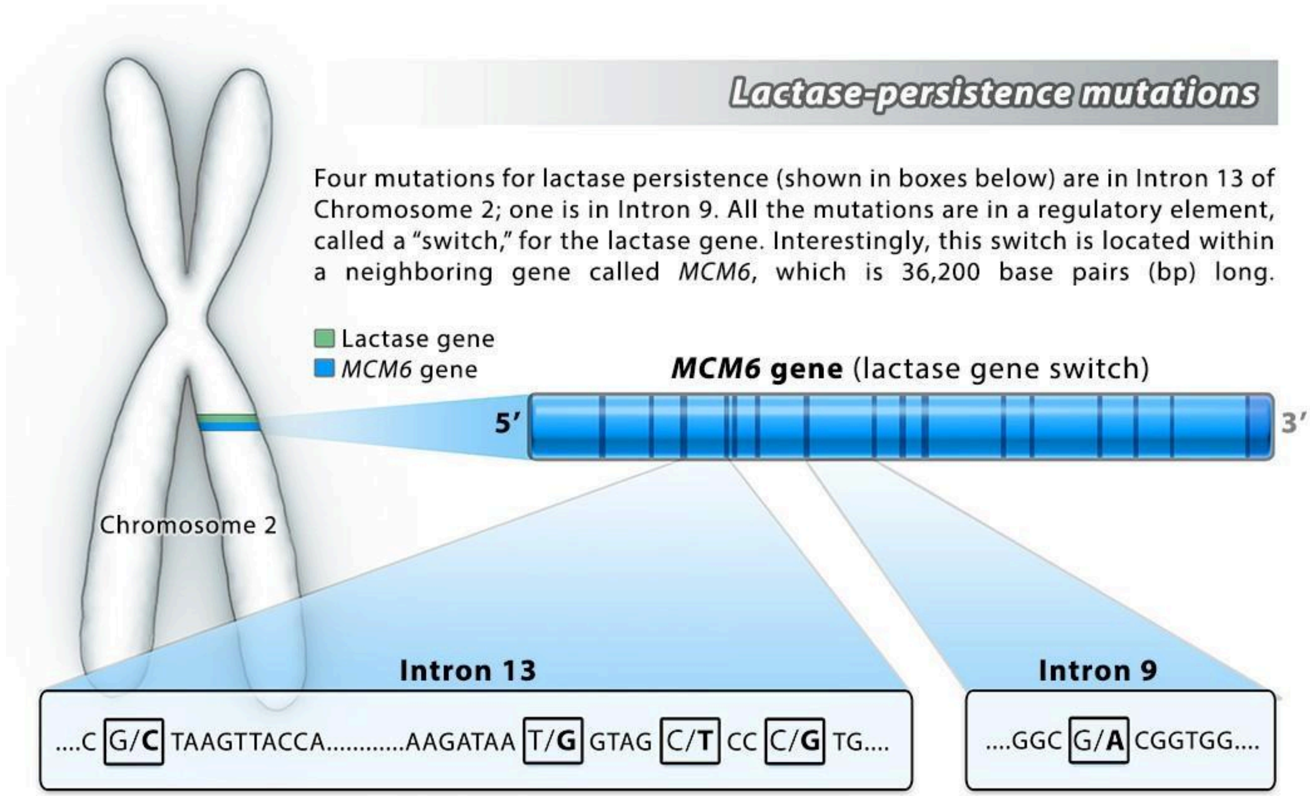



**Figure 3.** A diagram of the five mutations that cause lactase persistence; the prevalence of these mutations varies in different populations. All the mutations occur in *MCM6*, the genetic "switch" for the lactase gene, on Chromosome 2. The introns in *MCM6* are colored light blue, and the exons are colored dark blue.

#### Gene-Culture Co-evolution

Early humans, which evolved around 200,000 years ago, survived primarily by hunting animals and gathering plant-based foods. Between 10,000 and 7,500 years ago, during the Neolithic Period, populations in both Africa and Europe began domesticating other mammals like goats, sheep, and cows. This practice of keeping and using domesticated animals is called **pastoralism**, and it gave these cultures a reliable source of meat, milk, and milk products — such as butter, cheese, and yogurt. A practice like pastoralism is considered **cultural** because it is taught and learned, rather than an instinct dependent on the transmission of genetic variations.

Genetic analyses suggest that the mutations associated with lactase persistence arose less than 10,000 years ago, and that they became more common specifically in populations that practiced pastoralism. In these populations, individuals with the lactase-persistence mutations were more likely to survive, reproduce, and pass on their alleles than were people without the mutations — especially in times of famine, when other food sources were scarce.

Over just a few dozen generations, the frequency of a lactase-persistence mutation may have increased rapidly under intense positive selection. Having more lactase-persistent individuals in a population would mean that more people could depend on milk from domesticated animals, further promoting the culture of pastoralism.

**Fill-in-the-Blank**

1. The enzyme ____________________ is responsible for breaking down lactose in the small intestine.
2. The process by which lactase breaks lactose into glucose and galactose is known as ________________.
3. In mammals, the production of lactase typically stops after ___________________________ when the animal no longer consumes milk.
4. A person who is unable to produce lactase as an adult is referred to as _________________________.
5. Lactase persistence is a _______________________ trait, meaning only one copy of the mutation is required for it to be expressed.

**Multiple Choice**

6. Which of the following biomolecules provides 50% of the calories in milk?
   A) Proteins
   B) Fats
   C) Carbohydrates
   D) Minerals
7. Where is the enzyme lactase primarily located?
   A) Stomach
   B) Large intestine
   C) Small intestine
   D) Liver
8. Which gas is NOT typically produced as a result of fermentation of lactose in lactose-intolerant individuals?
   A) Methane
   B) Hydrogen
   C) Carbon dioxide
   D) Oxygen
9. The five mutations responsible for lactase persistence are found in which gene?
   A) LCT
   B) MCM6
   C) LAC1
   D) MAM1
10. Gene-culture co-evolution refers to:
    A) Evolution influenced by genetic mutations alone.

B) Cultural practices influencing which genetic traits are advantageous.
C) Natural selection only in wild animal populations.
D) Genetic mutations changing cultural practices.

**Short Answer**

11. Explain why lactase production is turned off after weaning in most mammals.

12. How do individuals who are lactase nonpersistent react physically when they consume lactose, and why does this happen?

13. Describe the role of the enterocyte and its microvilli in the digestion of lactose.

14. How does the practice of pastoralism relate to the prevalence of lactase persistence in certain populations?

15. Why might a lactase-persistent individual have a survival advantage in a culture that practices pastoralism?

**Higher-Order Thinking**

16. Explain how lactase persistence is an example of gene-culture co-evolution. Why is this concept significant in understanding human evolution?

17. Compare and contrast lactase persistence and lactase nonpersistence in terms of genetic expression and its effects on the human digestive system.

18. Discuss the environmental pressures that might have influenced the rapid spread of lactase persistence mutations in populations practicing pastoralism. What selective advantages would this mutation provide?

19. Considering the process of natural selection, hypothesize how the frequency of lactase-persistence mutations might change in a future society where dairy products are no longer consumed. Provide reasons for your hypothesis.

20. Analyze the potential benefits and drawbacks of lactase persistence in modern populations with varied diets, and explain how changing dietary habits might impact the evolution of this trait.