Why Can Some Digest Dairy and Others Cannot?

hhmi | BioInteractive

Activity
Student Handout

INTRODUCTION

In this activity, you will investigate the phenomenon of lactase persistence by making sense of a series of data sets. After watching a short film clip that introduces the phenomenon, you will analyze authentic scientific data on the frequency of lactase persistence, then use the data to construct explanations about the geographic distribution and origins of lactase persistence. During this investigation, you will also connect biological concepts and data analysis to world geography and culture.

This activity focuses on understanding and engaging in **science practices** that scientists use to figure out problems and phenomena they observe — in particular, the essential practices of analyzing and interpreting data. This includes using multiple lines of evidence, such as data tables and diagrams, to create arguments and ultimately construct an explanation.

MATERIALS

- calculator

PART 1: Asking Questions

Most infant mammals can digest milk by using the enzyme **lactase** to break down **lactose**, the main sugar in milk. Watch this film clip to learn what happens when mammals grow up.

1. What questions do you have about this phenomenon?

2. The clip states that only a third of people worldwide continue to produce lactase as adults. Why do you think only some people have this ability?

3. How could the ability to digest milk and dairy products (such as some cheeses and butter) help people survive, both in the past and today?

PART 2: Analyzing and Interpreting Phenotype Data

Table 1 shows lactase persistence phenotype data collected from different human population samples. Individuals were tested for lactase persistence using tests that measured their ability to digest lactose.

4. Calculate the frequency of lactase persistence ("LP frequency") in each population sample in Table 1. This frequency is calculated by dividing the number of people who tested positive for lactase persistence ("# people positive for LP") by the total number of people sampled ("# people sampled"). The first row has been done for you.

Table 1. Data on the lactase persistence (LP) phenotype in different human population samples. Source: Global Lactase Persistence Association Database.

Row	Continent/ Region	Country	Population sampled	# people sampled	# people positive for LP	LP frequency (%)
A	Africa	Ethiopia	Somali	90	22	24%
B	Africa	Kenya	Maasai	26	23	
C	Africa	Kenya	Sengwer	12	2	
D	Africa	Senegal	Wolof	53	27	
E	Africa	South Africa	Xhosa	17	3	
F	Africa	Sudan	Beni Amer	40	35	
G	Africa	Sudan	Dinka	208	52	
H	Africa	Sudan	Jaali	113	60	
I	Africa	Uganda	Baganda	17	1	
J	Africa	Tanzania	Burunge	16	6	
K	Africa	Tanzania	Maasai	15	10	
L	Asia	Afghanistan	Tadjik	79	14	
M	Asia	India	Indian	100	36	
N	Asia	Japan	Japanese	40	11	
O	Asia	Russia	Udmurt	30	18	
P	Asia	China	Han	248	20	
Q	Asia	China	Mongol	198	24	
R	Asia	Kazakhstan	Kazakh	159	33	
S	Europe	England	British	150	143	
T	Europe	Finland	Finn	638	530	
U	Europe	France	French	102	78	
V	Europe	Greece	Greek	600	330	

W	Europe	Hungary	Hungarian	535	337	
X	Europe	Italy	Northern Italian	208	102	
Y	Europe	Italy	Sardinian	53	6	
Z	Near/ Middle East	Jordan	Jordanian	148	37	
AA	Near/ Middle East	Turkey	Anatolian Turk	122	32	
BB	Near/ Middle East	Saudi Arabia	Bedouin	21	17	
CC	Near/ Middle East	Saudi Arabia	Arab	109	47	

5. Based on the frequencies you calculated in Table 1, determine whether there are patterns across each continent/region and what those patterns may mean. Record your responses in Table 2.

Table 2. Patterns observed in the lactase-persistence frequencies in Table 1.

Continent/ Region	**What patterns do you observe?**	**What do you think these patterns mean?**
Africa		
Asia		
Europe		
Near/Middle East		

6. What questions emerged when you completed Table 2?

7. What can you infer from the patterns as you compare population samples from one continent/region to another?

8. What other information could be helpful for figuring out why these patterns exist?

PART 3: Arguing from Evidence

Watch this next film clip, which discusses lactase persistence in some specific human populations.

9. What did the Maasai and European populations have in common that might explain why they independently evolved the trait of lactase persistence over many generations?

10. How does the cultural practice of pastoralism relate to your answer to the previous question?

11. How might raising animals for milk increase the chances of survival for these populations over time?

12. Why do you think lactase persistence became prevalent in some populations but not others?

13. Choose one of the following claims that can be supported by the data you have so far. Be prepared to share your chosen claim with your group/class during a discussion.
    A) People became lactase persistent because they were drinking milk, so they continued to produce the lactase enzyme that breaks down lactose in milk.
    B) People became lactase persistent because they had mutations that allowed them to continue producing the lactase enzyme that breaks down lactose in milk.
    C) People became lactase persistent because they needed to drink milk to survive.

14. After discussing with your group/class, did your chosen claim change? Explain why or why not.

15. What type of data could help us better understand the variations for lactase persistence within and between populations?

PART 4: Constructing an Explanation for Lactase Persistence

As described in the film clip you watched in Part 1, most adult mammals don't drink milk and will often stop making the lactase enzyme. Whether an individual stops or continues making lactase depends on a segment of DNA called a **regulatory region**. If the sequence of the regulatory region changes, lactase production may be switched on or off.

Figure 1 shows the lactase regulatory region and some other components involved in producing lactase.

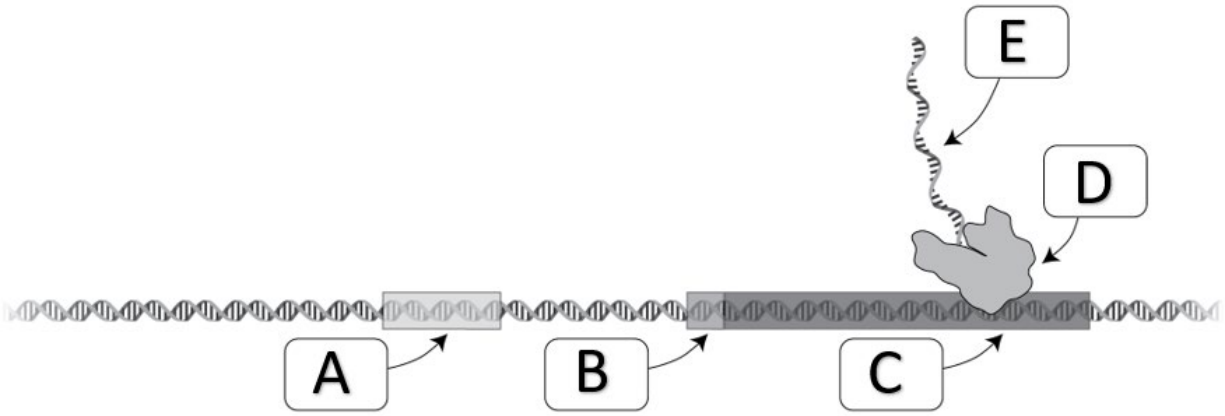

Figure 1. Diagram of components involved in lactase production.

16. Complete the following table by matching each letter in Figure 1 to its corresponding structure.

Structure	Function	Letter in Figure 1
Lactase gene	DNA segment that codes for the lactase enzyme.	
Regulatory region	DNA segment that affects whether lactase production is turned on or off.	
Promoter region	DNA region upstream of the lactase gene where RNA polymerase initially binds to start transcribing.	
RNA polymerase	Enzyme that creates mRNA strands from the original gene sequence in the DNA.	
mRNA	RNA sequence that carries the instructions for how to create a protein (in this case, the lactase enzyme).	

17. How might the position of the promoter region in Figure 1 help us better understand its function?

18. How might a mutation in the regulatory region affect the expression of the lactase gene?

Observe the two DNA sequences in Figure 2.

Sequence from the lactase regulatory region

TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATAC

Sequence from the lactase gene

ATGGAGCTGTCTTGGCATGTAGTCTTTATTGCCCTGCTAAGTTTTTCATGCTGGGGGTCA

Figure 2. *(Top)* A short partial sequence from the lactase regulatory region. *(Bottom)* A short partial sequence from the lactase gene, *LCT*.

19. What do you notice about the two sequences in Figure 2? How are they similar and different?

PART 5: Lactase or No Lactase?

Figure 3 on the next page shows a sequence from the lactase regulatory region of people who are not lactase persistent. These people are usually **lactose intolerant**, meaning that they (like most other mammals) cannot digest lactose as adults.

Figure 4 shows sample sequences from the lactase regulatory region of four different individuals. Your instructor will assign you to one of these four sample sequences. Table 3 provides different **frames** (short sequences of DNA) that may appear in your sample sequence.

Table 3. Frames in the lactase regulatory region that were found in individuals from different countries/regions. Each frame contains a mutation that impacts the regulation of lactase expression, allowing an individual to continue producing lactase as an adult.

Country/Region	Frame containing a mutation
Ethiopia/Sudan	ATGTAGCCCGTG
Europe	TAATGTAGTCCC
Kenya/Tanzania	CCTAAGTTACCA
Saudi Arabia	AAGATAAGGTAG

20. Search for these frames in your assigned sample sequence, identifying any mutations you discover when comparing your sample sequence to the sequence in Figure 3. On your sample sequence in Figure 4:
    - Indicate (for example, highlight or underline) the frame from Table 3 found in your sample sequence.
    - Mark (for example, circle or outline) the mutation within that frame — that is, the nucleotide that differs from the sequence in Figure 3.

TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACGTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAATGTAGCCCCTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Figure 3. A typical sequence from the lactase regulatory region of people who are not lactase persistent.

Sample 1
TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACCTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAATGTAGCCCCTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Sample 2
TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACGTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAAGGTAGCCCCTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Sample 3
TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACGTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAATGTAGTCCCTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Sample 4
TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACGTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAATGTAGCCCGTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Figure 4. Sequences from the lactase regulatory region of four individuals from different populations.

PART 6: Regulating Lactase Enzyme Expression

After you find your frame and associated mutation, share where you found them with your group.

21. Which country/region in Table 3 do you think the individual who provided your sample sequence was from?

22. Does your sequence contain one of the mutations in Table 3 that allows an individual to continue making lactase? (If you answer yes, move on to begin making lactase below.)

The instructions for making lactase are in the *LCT* gene, a small segment of which is shown in Table 4.

23. Complete Table 4 by transcribing and translating the segment of the *LCT* gene shown. The table caption contains more information about each row. For the last row ("AA"), you will need to translate the mRNA codons to the amino acids that make up the resulting protein. Your instructor will provide you with a **"Genetic Code Chart"** for this step.

Table 4. Part of the sequence for the lactase gene, *LCT*. The segment shown is only the first 20 triplets (60 nucleotides), as this gene is over 6,000 nucleotides long. From top to bottom, the rows in the table are: **"DNA,"** the nucleotide sequence for the coding strand; **"cDNA,"** the nucleotide sequence for the complementary DNA or template strand; **"mRNA,"** the nucleotide sequence for the mRNA strand; and **"AA,"** the amino acid sequence for the resulting protein.

	1	2	3	4	5	6	7	8	9	10
DNA	ATG	GAG	CTG	TCT	TGG	CAT	GTA	GTC	TTT	ATT
cDNA	TAC	CTC	GAC							
mRNA	AUG	GAG	CUG							
AA	Met	Glu	Leu							

	11	12	13	14	15	16	17	18	19	20
DNA	GCC	CTG	CTA	AGT	TTT	TCA	TGC	TGG	GGG	TCA
cDNA										
mRNA										
AA										

24. What percentage of nucleotides for the *LCT* gene sequence did you transcribe and translate in Table 4?

25. What allows lactase-persistent adults to transcribe and translate the lactase gene?

26. What does the lactase enzyme allow someone to do?

27. Review the claim you chose in Question 13. Explain how these new data either support your claim or changed your thinking.

PART 7: Using a Model — Structure and Function

Using Figure 5, you will make some observations to explain how lactase affects the lactose found in milk and other dairy products. Think about what the film clip in Part 1 stated about what happens in the digestive system if lactose goes undigested.

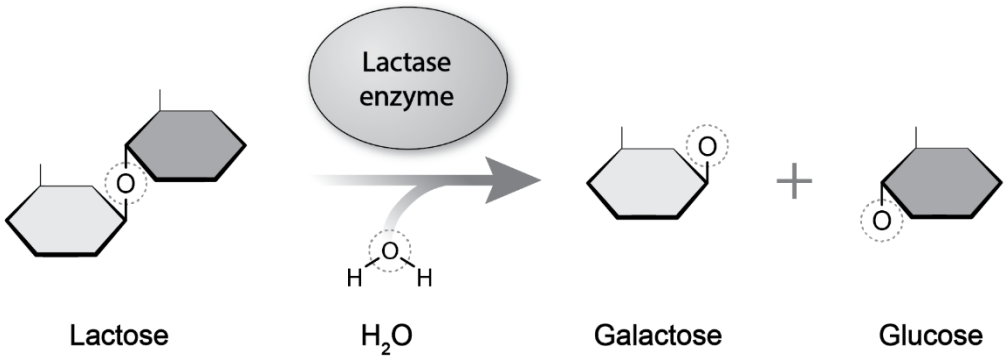

Figure 5. Effect of lactase on the lactose molecule.

28. What do you notice about the diagram in Figure 5? What do you think this means?

29. Based on what you have learned in the previous parts of this activity, explain the role of lactase in Figure 5 and why its function is important. (Consider which of the molecules in the figure would be small enough to cross from the digestive system, through the intestinal wall, into the bloodstream.)

30. If the lactase enzyme is not being made, how would this affect a person?

EXTENSION: Transfer Task with Traditional Agricultural Practices

In many different populations around the world, some people still use traditional agricultural practices to produce food. Some Mongols, people in the country of Mongolia, and some Kazakhs, people in the country of Kazakhstan, engage in the practice of pastoralism (described in the video clip you watched in Part 3).

Make some observations of Figures 6 and 7.

Figure 6. Kazakh herder.

Figure 7. Mongol herders.

1. What do you notice when comparing Figures 6 and 7?

2. Based on what you have figured out throughout the parts of this activity, why do you think the herders pictured are engaged in pastoralism?

3. Revisit your calculations for the Mongol and Kazakh population samples in Table 1 (Rows Q and R). What might you infer about these populations based on your calculations?

People from Mongol and Kazakh populations have traditionally produced fermented dairy products. Dairy fermentation is a common practice around the world that produces many of the foods we eat today, like cheeses and yogurt. It involves adding special bacteria to milk, which perform the process shown in Figure 8.

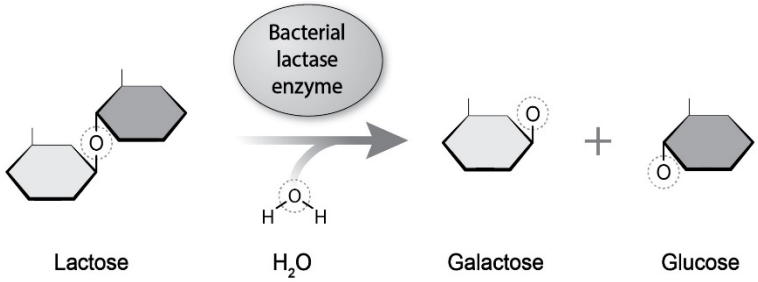

Figure 8. Effect of bacterial lactase on the lactose molecule.

4. How is the process in Figure 8 different from the process in Figure 5?

5. Using information in Figure 8, explain why adding these bacteria to dairy products may have been important to Kazakh and Mongol populations in the past.

As you may already know, milk spoils much faster than cheeses and yogurts, even when refrigerated. This may be why Kazakhs and Mongols traditionally produced cheese and yogurts instead of using milk for regular consumption. Byaslag, a Mongolian cheese, and irimshik, a commonly made cottage cheese in Kazakhstan, are both very nutritious and last longer than milk.

These cheeses (as well as other dairy products like yogurt, butter, and more) are made using "starters," which are small amounts of previous batches. These "starters" change the milk into cheese and other foods from which new "starters" are made, and so on.

6. Based upon what you have figured out so far, what do you think these "starters" contain that enables production of foods like cheese?

Many cheeses, including byaslag and irimshik, as well as yogurt and butter, are all typically lower in lactose than the milk from which they originated.

7. Using all the available evidence you discovered throughout this activity, construct an explanation that answers the following: How can people from the Mongol and Kazakh populations still consume traditional milk-based foods even though their populations are largely lactose intolerant? How could this understanding help people around the world who are lactose intolerant?