Why Can Some Digest Dairy and Others Cannot?

hhmi | BioInteractive

Activity
Educator Materials

OVERVIEW

In this activity, students investigate the phenomenon of lactase persistence by making sense of a series of data sets. Using science practices, they analyze authentic scientific data to construct explanations about the geographic distribution of lactase persistence and how this phenomenon may have begun.

This investigation provides an interdisciplinary approach to studying lactase persistence by connecting biological concepts and data analysis to world geography and culture. It focuses on understanding and engaging in the science practices that allow researchers to figure out problems and make sense of phenomena they observe.

The activity contains the following parts:

- **Part 1:** Students watch a short film clip that introduces the concept of lactase persistence, then pose questions after making their observations.
- **Part 2:** Students analyze data on lactase persistence in different human populations and identify patterns in lactase-persistence frequencies.
- **Part 3:** Students answer questions related to a new film clip, then choose a claim based on the evidence they have discovered thus far.
- **Part 4:** Students use a model (diagram) to help conceptualize the process of transcription. They also make observations of DNA sequences from the lactase gene and regulatory region.
- **Part 5:** Students analyze sequences from the lactase regulatory region. They search for one of four mutations to determine whether lactase expression is switched on.
- **Part 6:** After determining that lactase expression is "on," students transcribe and translate a segment of the lactase gene.
- **Part 7:** Students use a model (diagram) to determine the role of lactase in lactose digestion.
- **Extension:** Students transfer what they figured out to a new context involving dairy fermentation.

This educator document contains multiple resources for implementing this activity with students, including the following (select links to go directly to each section in the document):

- background information on the science
- teaching tips for implementing the activity and scientific caveats/clarifications
- procedure for each part of the "Student Handout"
- assessment guidance, including sample answers for the questions in the "Student Handout"
- optional extensions involving other BioInteractive resources and data sources

Additional information can be found on this resource's webpage, including suggested audience, estimated time, and curriculum connections.

KEY CONCEPTS

- Humans, like all species, evolve and adapt to their environment. Lactase persistence is an example of a human adaptation.
- Both the physical and cultural environment can affect selective pressures. The cultural practice of dairying provided an environment in which lactase persistence was advantageous.
- Segments of DNA contain the information needed to create or regulate the expression of proteins.

- A DNA molecule has two strands: a coding strand and a template strand. The cell transcribes the template strand into mRNA and then translates the mRNA into amino acids.

STUDENT LEARNING TARGETS

- Make observations about a phenomenon and generate questions about it.
- Calculate the frequency of lactase persistence in different populations around the world.
- Determine how a regulatory region affects the expression of a gene.
- Identify differences between DNA sequences among individuals.
- Based on the sequence of the coding strand of DNA, determine the sequence of the template strand, the mRNA, and the amino acid sequence.

PRIOR KNOWLEDGE

Students should be familiar with:

- calculating percentages
- inheritance (i.e., that offspring inherit DNA from their biological parents)
- basic information regarding transcription and translation (examples are provided for students)
- enzymes as proteins that can have different functions, including those involved in digestion of macromolecules

MATERIALS

- copies of the "Student Handout" (which should be provided one part at a time)
- copies of the "Genetic Code Chart"
- calculator

BACKGROUND

All mammals, including humans, are typically born with the ability to digest the disaccharide **lactose**, the main sugar in milk. This is because they produce the enzyme **lactase**, which breaks lactose into monosaccharides (glucose and galactose) that are small enough to be absorbed into the bloodstream. As adults, most mammals stop drinking milk and no longer produce lactase. However, some humans continue producing lactase even as adults. This trait is known as **lactase persistence**, because the expression of the lactase gene *persists* beyond childhood.

In general, gene expression can be switched on or off when certain proteins (**transcription factors**) bind to specific segments of noncoding DNA (**regulatory regions**, sometimes also called "switches" or "enhancers"). Expression of the lactase gene, *LCT*, is affected by a lactase regulatory region located in the neighboring gene *MCM6*. Scientists have discovered multiple mutations in this lactase regulatory region that allow production of the lactase enzyme to continue through adulthood, resulting in lactase persistence.

Lactase persistence has been studied around the world as an example of human evolution. Different populations around the world have independently evolved this trait, as evidenced through the analysis of genetic sequences. Lactase persistence is particularly frequent in populations that have traditionally engaged in **pastoralism:** the practice of domesticating animals for food (in particular, milk).

More information can be found in the "Educator Materials" for the *Got Lactase?* film activity.

TEACHING TIPS

Implementing the Activity

- This activity may be done individually, in pairs, or in small groups. There are many opportunities for students to engage in discussion, so pairs or small groups where students can collaborate are ideal.
- Students should not watch the *Got Lactase?* short film before doing this activity. They will watch short clips from the film in Parts 1 and 3 to motivate discovery and provide an anchoring event for their learning experience.
- Distribute each part of the "Student Handout" separately. Students should receive the next part only after they have completed each previous part. It is not recommended to give students all parts of the handout at once.
- Allow students to engage in the activity without frontloading too much information. Scaffolding has more impact when done in the moment when students actually need it.
    - For example, don't discuss how to transcribe mRNA from DNA until students need to do this in Part 6. Even if students do not have much experience with transcription and translation, they should be able to discern base pairings from the examples provided to get started.
- The parts of this activity can be done over multiple lessons. It is key that students build on each part in the sequence without adding extraneous information that could derail the conceptual understandings they are building.

Clarifications and Caveats

- Students may be surprised to learn that most people in the world are lactase nonpersistent/lactose intolerant. You may want to clarify that people who are lactose intolerant can often still consume milk and milk products. They might be able to drink small amounts of milk without any (or only mild) symptoms or use lactase-containing supplements like Lactaid. They may also have no problem eating milk products, like cheese and yogurt, because these foods have much less lactose than milk does (as discussed in the "Extension" of the "Student Handout").
- Students may confuse lactose intolerance with milk allergy, a potentially more serious condition involving an inflammatory immune response to proteins in cow's milk (Crittenden and Bennet 2005). Lactose intolerance does not involve the immune response.
- Table 1 in the "Student Handout" provides data from the Global Lactase Persistence Association Database. You may wish to discuss additional information about these data with students.
    - These data were collected using population samples. Consider discussing why population samples are used (e.g., can't measure everyone in the population) and when the characteristics of a sample may or may not be representative of the overall population (e.g., sample size too small, sampling bias, etc.).
    - In Table 1, the lactase-persistence (LP) frequencies represent people who tested positive in tests that measure the ability to digest lactose, such as the blood glucose test or the hydrogen breath test. These tests are not always 100% accurate. For example, the blood glucose test measures an increase in glucose after drinking milk, which may occur due to factors other than lactose digestion.
    - Students may ask why Table 1 does not include populations from North and South America. Not as many studies of lactase persistence were conducted on the American continent, largely because many people are not indigenous to this continent but instead immigrated there relatively recently. Their lactase-persistence genotypes would depend on their ancestry.
    - The "Optional Extensions" section provides more info and questions about the database.

PROCEDURE

PART 1: Asking Questions

Students are introduced to the phenomenon of lactase persistence through a film clip from the *Got Lactase?* short film and generate questions based on their observations. Students may share their questions with members of their group and/or the whole class during a discussion.

PART 2: Analyzing and Interpreting Phenotype Data

Students calculate the frequency of lactase-persistent individuals for each population sample in Table 1. They then determine whether there are patterns in the frequencies across each continent/region and what those patterns may mean.

If students are working in pairs or groups, encourage them to divide up the table and then check each other's results. Some potential ideas for differentiation may include assigning data in sets to different groups. If students struggle with the calculations, consider having them do a few calculations so they can explain the math before moving on.

PART 3: Arguing from Evidence

Students answer questions related to a new film clip from *Got Lactase?* and then choose a claim based on the evidence they have discovered thus far.

After Question 13, lead a class discussion in which different student groups share which claim they chose and why. Alternatively, students can discuss within their groups. After the discussion in groups or with the whole class, students are asked to reconsider the claim they chose and potentially change it based on the new information they encountered during the discussion. It is important that students understand that changing their claim after hearing evidence from others is part of the scientific process and does not mean they were "wrong."

Before going to the next part, it is recommended to discuss student ideas for their responses to Questions 14 and 15. If students are doing the activity in pairs/groups, they could share their ideas with another group and then engage in a class discussion. This might also be a good time for a "sensemaking" check just to make sure students are on the right track.

PART 4: Constructing an Explanation for Lactase Persistence

Students should attempt to identify labels for the diagram in Figure 1, which shows components involved in lactase production, based on any prior knowledge they may have. After students have had the opportunity to decide on their labels, have them share their answers in a group and revise if needed. Before moving on, discuss the different components that make up Figure 1 and what they do, to ensure that students have all the information they need to move on.

Students then observe the DNA sequences in Figure 2. They should recognize that these sequences are composed of the same elements (nucleotides) but differ in the order/sequence of the nucleotides.

PART 5: Lactase or No Lactase?

For this part of the activity, have students form groups of four. **Assign each student in a group one of the four sample sequences (Samples 1–4) from Figure 4**, which are DNA sequences from the lactase regulatory region.

Each sample sequence contains a single-nucleotide mutation (SNP) that affects how lactase expression is regulated, resulting in lactase persistence.

As described in Question 20, students should compare their sample sequences with the sequence from lactase-nonpersistent individuals in Figure 3. They should identify frames (short sequences of DNA) in their sample sequences that correspond to the different human populations in Table 3. The regions/countries listed in Table 3 reflect how they are labeled in the original published research (Ranciaro et al. 2014).

PART 6: Regulating Lactase Enzyme Expression

Students reflect on their results from Part 5. They should determine that all of their sample sequences include a mutation that allows for lactase to be expressed. They then transcribe and translate a segment of the lactase gene. Make sure to **provide students with copies of the "Genetic Code Chart" or a similar resource** for translating mRNA codons into amino acids.

PART 7: Using a Model – Structure and Function

Students observe a diagram of lactase digestion to explain the role of the components that have been discussed in previous parts of this activity.

EXTENSION: Transfer Task with Traditional Agricultural Practices

Using the information they have figured out throughout this activity, students apply their understanding to the idea of using bacteria to ferment dairy products and why this practice was historically important to certain populations.

ASSESSMENT GUIDANCE

PART 1: Asking Questions

1. What questions do you have about this phenomenon?
   Student answers will vary according to the questions they generate from watching the film clip.

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?
   Student answers will vary, as they most likely do not have enough information yet to answer this question fully.

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?
   Student answers will vary, as they most likely do not have enough information yet to answer this question fully.

PART 2: Analyzing and Interpreting Phenotype Data

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.
   Answers are shown in the last column of the following table.

Row	Continent/ Region	Country	Population sampled	# people sampled	# people tested positive for LP	LP frequency (%)
A	Africa	Ethiopia	Somali	90	22	24%
B	Africa	Kenya	Maasai	26	23	***88%***
C	Africa	Kenya	Sengwer	12	2	***17%***
D	Africa	Senegal	Wolof	53	27	***51%***
E	Africa	South Africa	Xhosa	17	3	***18%***
F	Africa	Sudan	Beni Amer	40	35	***88%***
G	Africa	Sudan	Dinka	208	52	***25%***
H	Africa	Sudan	Jaali	113	60	***53%***
I	Africa	Uganda	Baganda	17	1	***6%***
J	Africa	Tanzania	Burunge	16	6	***38%***
K	Africa	Tanzania	Maasai	15	10	***67%***
L	Asia	Afghanistan	Tadjik	79	14	***18%***
M	Asia	India	Indian	100	36	***36%***
N	Asia	Japan	Japanese	40	11	***28%***
O	Asia	Russia	Udmurt	30	18	***60%***
P	Asia	China	Han	248	20	***8%***
Q	Asia	China	Mongol	198	24	***12%***
R	Asia	Kazakhstan	Kazakh	159	33	***21%***
S	Europe	England	British	150	143	***95%***
T	Europe	Finland	Finn	638	530	***83%***
U	Europe	France	French	102	78	***76%***
V	Europe	Greece	Greek	600	330	***55%***
W	Europe	Hungary	Hungarian	535	337	***63%***
X	Europe	Italy	Northern Italian	208	102	***49%***
Y	Europe	Italy	Sardinian	53	6	***11%***
Z	Near/ Middle East	Jordan	Jordanian	148	37	***25%***
AA	Near/ Middle East	Turkey	Anatolian Turk	122	32	***26%***

BB	Near/ Middle East	Saudi Arabia	Bedouin	21	17	***81%***
CC	Near/ Middle East	Saudi Arabia	Arab	109	47	***43%***

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.
   Students should provide data to support their claims about the patterns they observe. Some sample answers are shown in the following table.

Continent/ Region	**What patterns do you observe?**	**What could these patterns mean?**
Africa	***All the population samples in Africa have some individuals who are lactase persistent, and some of the lactase-persistence frequencies are relatively high (e.g., 67%, 88%).***	***Lactase persistence could be high in African populations that produce/consume milk. Populations with less frequent lactase persistence, like the Baganda, may produce/consume less milk.***
Asia	***All the population samples in Asia have some individuals who are lactase persistent, but the lactase-persistence frequencies tend to be lower overall. The highest LP frequency (60%) is in Russia, and the others are significantly lower than that.***	***Many of these Asian populations may have higher frequencies of lactose intolerance, possibly because they do not produce/consume as much milk.***
Europe	***Many of the population samples in Europe have relatively high frequencies of lactase persistence.***	***Many of these European populations may have people who can consume milk, which could suggest that these populations have been producing milk for a long time.***
Near/Middle East	***Most of the population samples in the Near/Middle East have relatively low lactase-persistence frequencies, except for the Bedouin population sample in Saudi Arabia.***	***The Bedouin population may have been producing/consuming milk longer than the other populations in this region.***

6. What questions emerged when you completed Table 2?
   Student questions will vary. You may want to discuss the data in Table 1 with students by asking them leading questions that draw attention to particular populations. More information about Table 1 is provided in the "Clarifications and Caveats" section.

7. What can you infer from the patterns as you compare population samples from one continent/region to another?
   Student responses may include that there are higher lactase-persistence frequencies in some populations within the same continent/region, or when comparing different continents/regions.

8. What other information could be helpful for figuring out why these patterns exist?
   Student responses may include regional diet information or how different populations produce food.

PART 3: Arguing from Evidence

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?
   Both raised animals that produce milk.

10. How does the cultural practice of pastoralism relate to your answer to the previous question?
    Pastoralism is the practice of domesticating animals for food, including raising animals that produce milk. Both the Maasai and European populations were pastoralists.

11. How might raising animals for milk increase the chances of survival for these populations over time?
    This question is meant to have students consider possible claims, and student answers will vary. They may suggest that milk provides a nutritious food source, especially when other food sources like crops are unavailable (such as in times of famine and drought).

12. Why do you think lactase persistence became prevalent in some populations but not others?
    Students may suggest that lactase persistence became more prevalent in populations that raised animals for milk. Lactase-persistent individuals, who could consume the milk and associated dairy products, would be able to access more food sources than lactase-nonpersistent individuals. This may have given lactase-persistent individuals a survival advantage.

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 enzymes that break down lactose in milk.
    B) People became lactase persistent because they had mutations that allowed them to continue producing lactase enzymes that break down lactose in milk.
    C) People became lactase persistent because they needed to drink milk to survive.

    Students can choose any of the claims as long as they can support their choice with evidence. In general, Claim B is the best supported. Claims A and C are rooted in the misconception that organisms change because they "need" to instead of selection acting on variations that already exist within populations.

    Students may choose an "incorrect" claim at this point, but they will have the opportunity to change their claim after discussing with their classmates. They will also review their claim in Question 27 after analyzing more data. As discussed in the Part 3 procedure, emphasize to students that updating their claim based on new evidence from others is part of the scientific process and does not mean they were "wrong."

14. After discussing with your group/class, did your chosen claim change? Explain why or why not.
    Students may indicate that their choice did not change or that it did because of some compelling evidence another group shared.

15. What type of data could help us better understand the variations for lactase persistence within and between populations?
    Though student responses may vary, most will likely indicate that genetics data could help us better

understand why there are variations.

PART 4: Constructing an Explanation for Lactase Persistence

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.	***C***
Regulatory region	DNA segment that affects whether lactase production is turned on or off.	***A***
Promoter region	DNA region upstream of the lactase gene where RNA polymerase initially binds to start transcribing.	***B***
RNA polymerase	Enzyme that creates mRNA strands from the original gene sequence in the DNA.	***D***
mRNA	RNA sequence that carries the instructions for how to create a protein (in this case, the lactase enzyme).	***E***

17. How might the position of the promoter region in Figure 1 help us better understand its function?
Students may indicate that the promoter comes right before the* LCT *gene, which suggests that they are associated. (You may want students to know that promoters do not necessarily need to be close to their gene. This is because DNA can bend back on itself, allowing the promoter to be farther away.)

18. How might a mutation in the regulatory region affect the expression of the lactase gene?
It may turn the gene's expression on or off.

19. What do you notice about two sequences in Figure 2? How are they similar and different?
They are each made of the same letters (nucleotides), but the letters are in a different order.

PART 5: Lactase or No Lactase?

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.

In the following images, the frames are underlined and highlighted yellow. The mutations are boxed and highlighted blue.

Sample 1

TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACCCTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAATGTAGCCCCTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Sample 2

TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACGTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAAGGTAGCCCCTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Sample 3

TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACGTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAATGTAGTCCCTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

Sample 4

TATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGCTCATACGACCATGGA
ATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTTAGACGGAGACGATCACGTCATAGT
TTATAGAGTGCATAAAGACGTAAGTTACCATTTAATACCTTTCATTCAGGAAAAATGTACTTAGACCCT
ACAATGTACTAGTAGGCCTCTGCGCTGGCAATACAGATAAGATAATGTAGCCCGTGGCCTCAAAGGAAC
TCTCCTCCTTAGGTTGCATTTGTATAATGTTTGATTTTTA

PART 6: Regulating Lactase Enzyme Expression

21. Which country/region in Table 3 do you think the individual who provided your sample sequence was from?
    Student answers will vary depending on which sample they were assigned. The samples correspond to the countries/regions as follows:
    - ***Sample 1: Kenya/Tanzania***
    - ***Sample 2: Saudi Arabia***
    - ***Sample 3: Europe***
    - ***Sample 4: Ethiopia/Sudan***

22. Does your sample sequence allow for lactase to be expressed? In other words, does your sequence contain one of the mutations in Table 3 that allows an individual to continue making lactase?
    Each sample sequence contains one of the mutations in Table 3, so students should answer "yes" for any of the sequences.

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.
    Answers are shown in the table below (broken into two sections due to length).

	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	***AGA***	***ACC***	***GTA***	***CAT***	***CAG***	***AAA***	***TAA***
mRNA	AUG	GAG	CUG	***UCU***	***UGG***	***CAU***	***GUA***	***GUC***	***UUU***	***AUU***
AA	Met	Glu	Leu	***Ser***	***Trp***	***His***	***Val***	***Val***	***Phe***	***Ile***

	11	12	13	14	15	16	17	18	19	20
DNA	GCC	CTG	CTA	AGT	TTT	TCA	TGC	TGG	GGG	TCA
cDNA	***CGG***	***GAC***	***GAT***	***TCA***	***AAA***	***AGT***	***ACG***	***ACC***	***CCC***	***AGT***
mRNA	***GCC***	***CUG***	***CUA***	***AGU***	***UUU***	***UCA***	***UGC***	***UGG***	***GGG***	***UCA***
AA	***Ala***	***Leu***	***Leu***	***Ser***	***Phe***	***Ser***	***Cys***	***Trp***	***Gly***	***Ser***

24. What percentage of nucleotides for the *LCT* gene sequence did you transcribe and translate in Table 4?
60/6000 = 1%

25. What allows lactase-persistent adults to transcribe and translate the lactase gene?
A mutation in the lactase regulatory region allows them to keep expressing the gene/continue making the lactase enzyme.

26. What does the lactase enzyme allow someone to do?
Individuals who produce lactase can continue to digest lactose (the main sugar in milk).

27. Review the claim you chose in Question 13. Explain how these new data either support your claim or changed your thinking.
Student responses will vary. Refer to Question 13 for more information.

PART 7: Using a Model — Structure and Function

28. What do you notice about the diagram in Figure 5? What do you think this means?
Students may describe how the figure shows lactose being broken down into galactose and glucose.

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.)
The figure shows that lactase breaks the lactose molecule into two smaller molecules, galactose and glucose. Galactose and glucose are small enough to cross through the intestinal wall and into the bloodstream. Lactose is a larger molecule, so it cannot cross the intestinal wall as easily.

30. If the lactase enzyme is not being made, how would this affect a person?
Without lactase, a person cannot break down/digest lactose. Students can revisit the film clip from Part 1 to remind themselves of what happens in this case. (As described in the film clip, undigested lactose moves through the small intestine to the large intestine. There, bacteria eat the lactose and can cause cramps, gas, and diarrhea.)

EXTENSION: Transfer Task with Traditional Agricultural Practices

1. What do you notice when comparing Figures 6 and 7?
   Students may mention that both figures show the herders riding camels and herding goats or sheep.

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?
   Pastoralism is the practice of domesticating animals for food. The herders may be using these animals to produce food (including milk) for themselves and others in their communities.

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?
   The frequency of lactase persistence in both population samples is relatively low: 12% in the Mongol sample and 21% in the Kazakh sample. Assuming these samples are representative of their overall populations, students may infer that both the Mongol and Kazakh populations are largely lactase nonpersistent/lactose intolerant.

4. How is the process in Figure 8 different from the process in Figure 5?
   The only difference is that Figure 8 includes the bacterial lactase enzyme instead of the human lactase enzyme. The figures show that both human and bacterial lactase break lactose down into galactose and glucose.

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.
   If most of the people in these populations did not produce the lactase enzyme, they were probably unable to break down lactose on their own. By adding bacteria that produce lactase to dairy products, they could use bacterial lactase to break down the lactose instead.

6. Based upon what you have figured out so far, what do you think these "starters" contain that enables production of foods like cheese?
   These starter batches contain the bacteria used in dairy fermentation. These bacteria produce lactase, which would break down the lactose in these foods.

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?
   A sample response is as follows:
   These populations traditionally consumed fermented dairy products (like cheeses and yogurt), which are made using lactase-producing bacteria. The bacterial lactase in these foods breaks the lactose down (just like human lactase does). So people can still eat these foods even if they are lactose intolerant/don't produce their own lactase.

   This can help other people who are lactose intolerant because it means they can still eat dairy products that have been fermented. Or they can use external sources of lactase (e.g., Lactaid) to break down lactose in milk and other milk-based foods.

OPTIONAL EXTENSIONS

The following BioInteractive resources can be used to complement and extend the concepts in this activity:

- The film activity for the *Got Lactase?* film explores the film's concepts in more depth.
- The Data Point "Spread of a Lactase-Persistence Allele" examines a scientific figure from a study that investigated genetic and cultural adaptations to milk consumption, including dairy fermentation. This relates well to the "Extension" of the "Student Handout."
- The data-driven activity "Blood Glucose Data Analysis" can be used to learn more about the types of tests used to obtain the phenotype data in Table 1 of this activity.
- The hands-on lab activity "Milk: How Sweet Is It?" has students measure glucose levels in samples of milk after adding lactase.
- The Click & Learn *Regulation of the Lactase Gene* explores how expression of the lactase gene is regulated.

Table 1 in this activity is based on data from the Global Lactase Persistence Association Database, which students could explore further.

- The database includes genotype data on allele frequencies associated with lactase persistence. Students could compare lactase-persistence frequencies based on genotype data versus phenotype data (as shown in Table 1) and discuss potential differences and similarities.
- The database combines data from multiple studies. You may wish to discuss the benefits and limitations of this approach. Some prompts could include:
  - Why might many different studies be needed to explore the worldwide distribution of lactase persistence?
  - Why might scientists decide to analyze data published in past scientific papers instead of collecting all the data themselves?
  - What might be some advantages or limitations of using data for a population from different studies with different samples?
  - If different studies measured the same trait in different ways, how might this affect the results?

REFERENCES

Anguita-Ruiz, A., C. M. Aguilera, and Á. Gil. 2020. "Genetics of Lactose Intolerance: An Updated Review and Online Interactive World Maps of Phenotype and Genotype Frequencies." *Nutrients* 12, 9: 2689. https://doi.org/10.3390/nu12092689.

Campbell, M. C., and A. Ranciaro. 2021. "Human adaptation, demography and cattle domestication: an overview of the complexity of lactase persistence in Africa." *Human Molecular Genetics* 30, R1: R98–R109. https://doi.org/10.1093/hmg/ddab027.

Crittenden, R. G., and L. E. Bennett. 2005. "Cow's Milk Allergy: A Complex Disorder." *Journal of the American College of Nutrition* 24, 6: 582S–591S. https://doi.org/10.1080/07315724.2005.10719507.

De Luca, P., D. Iaconis, E. Biffali, C. Enza, L. de Magistris, G. Riegler, D. Pappalardo, et al. 2021. "Development of a novel SNP assay to detect lactase persistence associated genetic variants." *Molecular Biology Reports* 48, 11: 7087–7093. https://doi.org/10.1007/s11033-021-06698-y.

Heyer, E., L. Brazier, L. Ségurel, T. Hegay, F. Austerlitz, L. Quintana-Murci, M. Georges, et al. 2011. "Lactase Persistence in Central Asia: Phenotype, Genotype, and Evolution." *Human Biology* 83, 3: 379–392. https://doi.org/10.1353/hub.2011.a445673.

Lewinsky, R. H., T. G. K. Jensen, J. Møller, A. Stensballe, J. Olsen, and J. T. Troelsen. 2005. "T $_{-13910}$ DNA variant associated with lactase persistence interacts with Oct-1 and stimulates lactase promoter activity *in vitro*." *Human Molecular Genetics* 14, 24: 3945–3953. https://doi.org/10.1093/hmg/ddi418.

Ranciaro, A., M. C. Campbell, J. B. Hirbo, W. Ko, A. Froment, P. Anagnostou, M. J. Kotze, et al. 2014. "Genetic origins of lactase persistence and the spread of pastoralism in Africa." *The American Journal of Human Genetics* 94, 4: 496–510. https://doi.org/10.1016/j.ajhg.2014.02.009.

Scott, A., S. Reinhold, T. Hermes, A. A. Kalmykov, A. Belinskiy, A. Buzhilova, N. Berezina, et al. 2022. "Emergence and Intensification of Dairying in the Caucasus and Eurasian Steppes." *Nature Ecology & Evolution* 6, 6: 813–822. https://doi.org/10.1038/s41559-022-01701-6.

Sibley, E., and J. K. Ahn. 2011. "Theodore E. Woodward Award: Lactase persistence SNPs in African populations regulate promoter activity in intestinal cell culture." *Transactions of the American Clinical and Climatological Association* 122: 155–165. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3116366/.

Tishkoff, S., F. A. Reed, A. Ranciaro, B. F. Voight, C. C. Babbitt, J. S. Silverman, K. Powell, et al. 2007. "Convergent adaptation of human lactase persistence in Africa and Europe." *Nature Genetics* 39, 1: 31–40. https://doi.org/10.1038/ng1946.

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