

## LACTASE PERSISTENCE: EVIDENCE FOR SELECTION

### INTRODUCTION

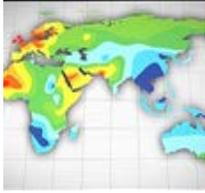
The ability of some human adults to digest lactose—the sugar in milk—is evidence of recent human evolution. All mammalian babies can digest lactose, using an enzyme called lactase. By adulthood, however, most mammals stop producing this enzyme. One exception is a minority of human adults who retain an active lactase enzyme. These “lactase-persistent” individuals have a mutation in their DNA that keeps the lactase gene turned on into adulthood, and they are therefore able to digest lactose. Evidence from different fields suggests that these lactase-persistence mutations arose in the last 10,000 years in different populations and increased in frequency by natural selection. In this activity, you will explore some of this evidence by watching three short video segments and answering questions about the scientific data presented in three figures.

### PROCEDURE

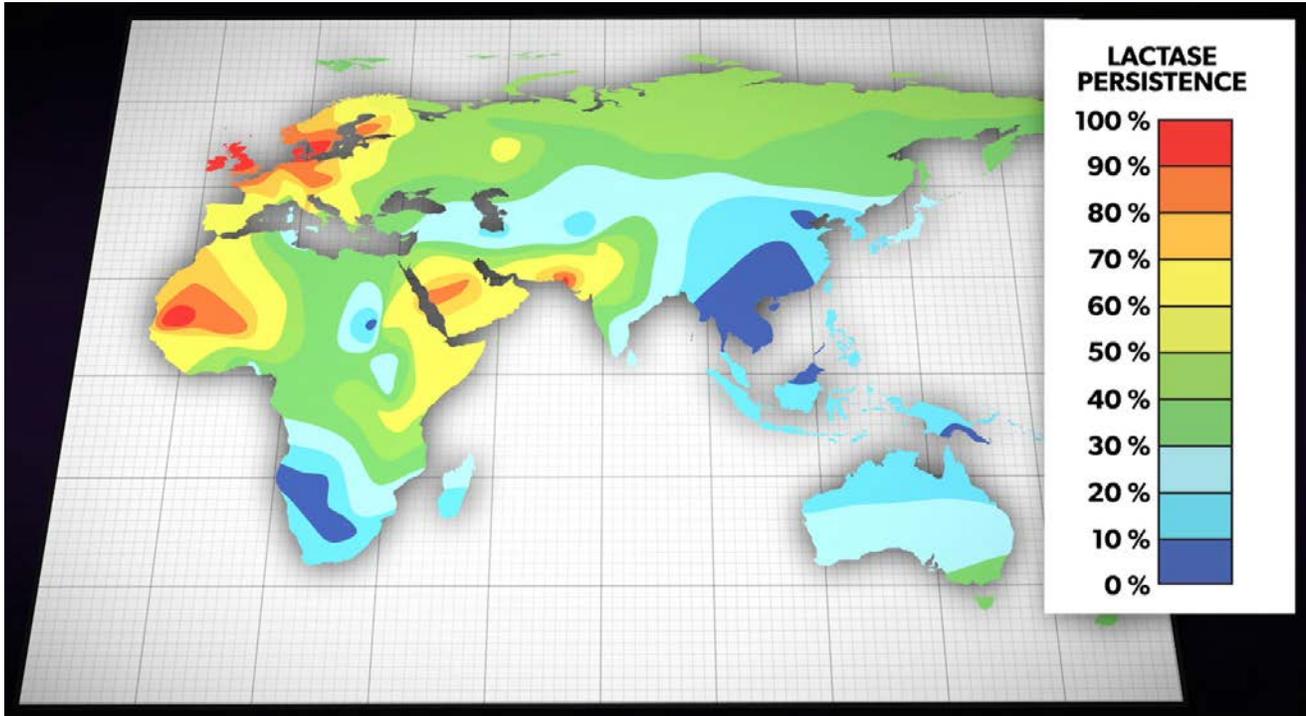
#### PART 1: What Is Lactase Persistence?

One of the mutations giving rise to lactase persistence first arose about 7,500 years ago in a population in what is now Hungary. This mutation consisted of a single nucleotide change from a cytosine to a thymine in a genomic region that controls the expression of the lactase gene. The mutation increased in frequency throughout some parts of Europe. Other “hot spots” of lactase persistence include parts of Asia and east and west Africa. Here, the responsible mutations arose more recently than the European mutation did. In all these populations, the ability to digest milk as adults likely provided a survival advantage to individuals with the lactase-persistence allele.

*A **mutation** is a change in a sequence of DNA. When a measurable proportion of individuals has that particular change, it is referred to as a **genetic variant** or **genetic polymorphism**. **Functional variants** often change the section of DNA that determines the amino acid sequence of the protein produced or affect how the gene is turned on or off. One version of a DNA sequence is referred to as an **allele**. So individuals who are lactase persistent have one particular allele or variant and individuals who are not lactase persistent have a different allele or variant.*



# The Making of the Fittest: Got Lactase? The Co-evolution of Genes and Culture

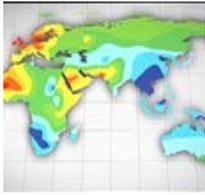


**Figure 1. Global Distribution of Lactase Persistence.** Worldwide, only about 35 percent of adults can digest lactose, and most are concentrated in particular geographic regions or “hot spots”: northern Europe, parts of east and west Africa, the Middle East, and South Asia. (Source: Adapted from Curry, Andrew. “The Milk Revolution.” *Nature* 500 (2013): 20–22. doi:10.1038/500020a. For an animated version of the map, see the HHMI film [Got Lactase? The Co-evolution of Genes and Culture](http://www.hhmi.org/biointeractive/making-fittest-got-lactase-co-evolution-genes-and-culture), <http://www.hhmi.org/biointeractive/making-fittest-got-lactase-co-evolution-genes-and-culture>, from time stamp 4:12 minutes to 4:26 minutes.)

### Interpreting the Figure

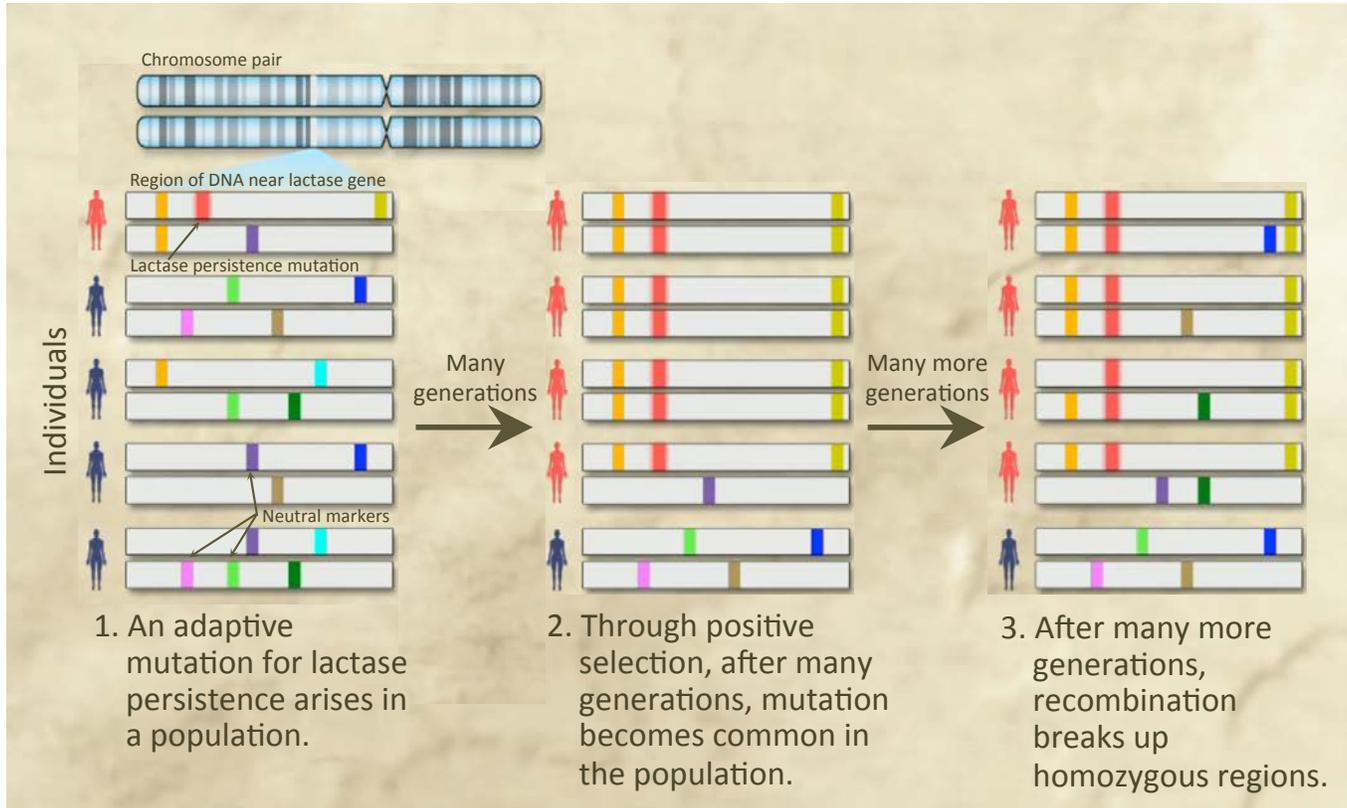
1. Why would a mutation leading to lactase persistence become common in a population?
  
  
  
  
  
  
  
  
  
  
2. Use the map in Figure 1 to predict where you might find early evidence of dairying (i.e., using animal milk).





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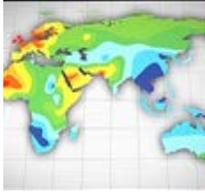
## PART 2: Evidence of Selection



**Figure 2. Evidence of a Selective Sweep for Lactase Persistence.** Each individual has two copies of each chromosome, including the region around the lactase-persistence gene, shown as the white rectangles next to each individual. Lactase-persistent individuals have red silhouettes; lactase-nonpersistent individuals are blue. Comparing DNA sequences around the lactase gene in different individuals has revealed several neutral variations, or markers, which are denoted by different colored bands. In the first column, the red band indicates a genetic variant or mutation associated with lactase persistence—the lactase-persistence allele. When natural selection favors a beneficial allele, such as the lactase-persistence allele (red band), that allele is more likely to be passed on from one generation to the next. Over many generations, the beneficial allele increases in frequency. The frequencies of the nearby neutral markers (orange and yellow bands) also increase. These markers do not provide any selective advantage but are “swept” along with the beneficial allele. Column 2 shows evidence of this process as a reduction in genetic diversity in this particular region of chromosome 2. Over time, the association between the beneficial allele and neutral markers breaks down as a result of recombination, and the evidence for a selective sweep eventually disappears. (Source: Adapted from Tishkoff, Sarah A., [Lecture 2 – Genetics of Human Origins and Adaptation](http://media.hhmi.org/hl/11Lect2.html?start=50:42&end=51:47), 2011 Holiday Lectures on Science series Bones, Stones, and Genes: The Origin of Modern Humans. <http://media.hhmi.org/hl/11Lect2.html?start=50:42&end=51:47>.)

### Interpreting the Figure

1. In column 1, the red band represents the lactase-persistence mutation. Why is it more prevalent in column 2, which shows the same DNA region in the same population after many generations?

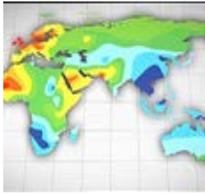


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2. In column 2, why do the orange and yellow bands always border the red band? What do the orange and yellow bands represent?
3. How many individuals in column 2 are homozygous for the lactase-persistence allele? How many are homozygous for the surrounding region (i.e., the white rectangle)?
4. Why would scientists want to identify regions in the genome that are homozygous in many individuals in a population (i.e., regions of homozygosity, or reduced diversity)?
5. How many individuals in column 3 are homozygous for the lactase-persistence allele? How many are homozygous for the whole region?
6. How do you explain the differences between columns 2 and 3?

**ADDITIONAL DISCUSSION QUESTIONS**

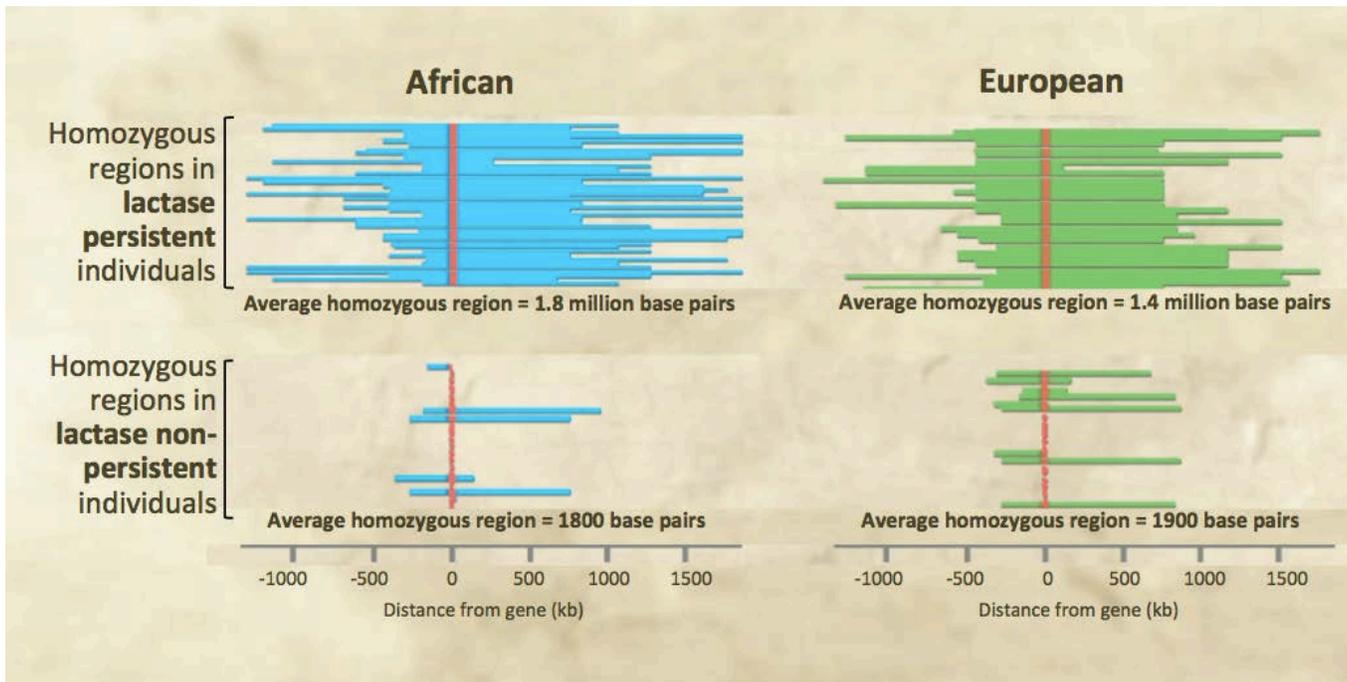
1. Is lactase persistence a dominant or recessive trait? Use Figure 2 to explain your answer.
2. What does the length of the region of homozygosity around an allele reveal about its evolutionary history?



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## PART 3: Lactase Persistence in East Africa

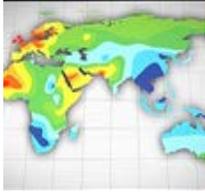
Dr. Sarah Tishkoff and colleagues investigated lactase persistence in East Africa. The mutation leading to lactase persistence in this population is different from the one found in lactase-persistent individuals from Europe. Both genetic changes occur in the regulatory region of the lactase gene.



**Figure 3. Evidence of Selection for Lactase Persistence in African and European Populations.** Lactase-persistent individuals in African and European populations have large regions of homozygosity around the lactase-persistence alleles. Each blue and green bar represents a region of homozygosity in one individual; the lengths of these regions are shown at the bottom of the figure. Large areas of homozygosity indicate strong, recent selection. (Source: Adapted from Tishkoff, Sarah A., [Lecture 2 – Genetics of Human Origins and Adaptation](#). 2011 Holiday Lectures on Science series Bones, Stones, and Genes: The Origin of Modern Humans. <http://media.hhmi.org/hl/11Lect2.html?start=50:42&end=51:47>; and Figure 6 in Tishkoff, Sarah A., et al. "Convergent Adaptation of Human Lactase Persistence in Africa and Europe." *Nature Genetics* 39 (2007): 31--40. doi:10.1038/ng1946.2007.)

### Interpreting the Figure

1. In the African population, why do lactase-persistent individuals have large areas of homozygosity compared to individuals who are not lactase persistent?



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2. Use evidence to explain whether either the African or European population shows evidence of strong, recent selection in the genome.
3. The African and European populations have different lactase-persistence alleles. Use data from Figure 3 to formulate a hypothesis about which allele originated more recently.
4. What additional evidence might support this hypothesis?

**PART 4: Summary Discussion**

1. What is evolution?
2. Do the data on lactase persistence support the idea that humans are evolving? Use data to support your answer.
3. Does lactase persistence provide an example of a selective sweep? Use data to support your answer.