Introducing Evolution of the Human Lactase Gene using an Online Interactive Activity

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Abstract

Human evolution is a sensitive and controversial topic, which might explain why it is not included in science curricula or textbooks in many countries. We prepared an online student-centered human evolution activity dealing with lactose tolerance. In constructing the activity, we considered the following design principles: a medical issue connected to students' lives, a noncontentious topic of human evolution, and a one-step genetic example that can be demonstrated by basic bioinformatics tools. The activity consists of four units dealing with the activity of the enzyme lactase in our small intestine, the differences in lactose tolerance in people from different origins, the genetic foundation of lactose tolerance, and an extension unit dealing with the control of lactase gene expression. The activity was experienced by a pilot group of approximately 100 students, preservice and in-service teachers who showed great interest in the genetics of a trait that has undergone evolutionary changes. We noted the need for a teacher as mediator while students perform the activity. We suggest using the activity in the context of evolution, genetics, or when teaching about systems of the human body, either all units in succession or as a modular activity.

Key Words: human evolution; lactose tolerance; bioinformatics tools; online student-centered activity; high school.

Introduction

Human evolution is a controversial topic worldwide. Those who accept evolution are willing to do so for both animals and plants. However, theologians claim that the status of humans is different because they have a soul and moral order in their societies; thus, theologians do not accept the notion of an evolutionary process for humans (Webb, 2002). Moreover, a recent study among Israeli science teachers showed that one of the topics that is most unknown to them is human evolution (Siani & Yarden, 2021). These findings, among many others, show us that human evolution is a very sensitive and controversial issue, which might explain why it is not included in the science curricula and textbooks in many countries, including the (Next Generation Science Standards, 2013).

An approach led by Briana Pobiner (Pobiner, 2012, 2016; Pobiner et al., 2018) shows the advantage of dealing with human evolution while taking into consideration the following design principles:

- A medical issue that is connected to nearly every student or his/her family's life
- A noncontentious topic of human evolution that will not raise protests from different sectors of the population
- A human evolution example that occurred in the not too distant past
- An unambiguous genetic frame story that includes a simple, one-step genetic mutation that affects a known trait
- An example that exposes students to basic bioinformatics tools through which students can gain a glimpse of authentic science that deals with genetic evidence of evolution

Educational stakeholders spoke about the need for learning materials that include evidence of evolution as a way of avoiding theological tensions (Siani & Yarden, 2020). Thus we decided to construct an online activity that deals with human evolution while taking into consideration the following design principles:
Activity Description

The activity consists of four units. Here we describe the main items in each unit.

The whole activity is open free of charge at https://petel.weizmann.ac.il/biology/login/signup.php?key=T6518373X&lang=en.

Information regarding the PeTeL (Personalized Teaching and Learning) environment in which this activity is included is at https://stwww1.weizmann.ac.il/petel/home-en.

1. What is the lactase enzyme?

The aim of this unit is to expose students to the normal activity of the enzyme lactase and the consequences when the enzyme does not work. The unit includes:

a. A diagram of lactase activity and a short description of the fact that humanity has undergone changes since the agricultural revolution, when humans started to domesticate plants and animals. It is only with the latter that they began to consume dairy products and the need arose to break down the sugar lactose (found in milk) throughout the individual’s lifetime.

b. A short clip “Lactose - What Is Lactose - What Is Lactose Intolerance” (Whats Up Dude, 2017). Throughout the clip, there are short questions that the students must answer in order to continue with the clip (Figure 1).

c. A diagram of the small and large intestines. By clicking on the purple hot spots, the students can see the process occurring in each part of the digestive system (Figure 2).

An exercise to summarize the knowledge that has been obtained from this unit (Figure 3).

2. Can I drink milk?

The aims of this unit are to reveal the fact that in some populations lactase activity decreases after weaning and to explain the advantage of this trait in some regions of the world.

a. A graph showing the reduction of lactase activity in people who are lactose intolerant in comparison to those who are lactose tolerant. The information is obtained by clicking on the purple hot spots (Figure 4).

b. An interactive Google map that gathers the origin of the students’ families, showing that lactose tolerance is a trait that is connected to one’s origin, as depicted on the map (Figure 5) (Ségurel & Bon, 2017).
c. One of the advantages for lactose tolerance, as a possible explanation for why the trait has been preserved, is that lactose can substitute for calcium absorption (Camara-Martos & Amaro-Lopez, 2002). Substances are fermented by the bacterial flora in the colon, while lactose and other organic acids such as acetate, propionate, and butyrate lower the pH and make the calcium more soluble. The solubility of calcium improves its absorption (Trinidad et al., 1993). Since infants cannot produce vitamin D, we can understand why most mammalian milks contain lactose (Wacker & Holick, 2013). Thus, according to this hypothesis, the ability to tolerate lactose in the gut would enhance calcium absorption and protect against bone malformities in the context of insufficient UVB light to synthesize vitamin D. This would further help explain why some European dairying populations have high frequencies of lactose tolerance and make extensive use of high-lactose dairy products. Students are asked to drag the phrases into the figure according to the information that they have read (Figure 6).

3. The genetic foundation of lactose tolerance

The aim of this unit is to use bioinformatics tools to reveal the positive mutation that has led to lactose tolerance.

a. The students get detailed instructions on using pairwise sequence alignment in the Clustal Omega tool, available at https://www.ebi.ac.uk/Tools/psa/emboss_needle/ (Figure 7).

By using the DNA pairing tool and comparing DNA 1 (in Appendix 1, without the mutation) to DNA 2 (in Appendix 2, with the mutation), the students can see the exact location of the transition point mutation. A few questions summarize this part of the unit. Examples are demonstrated in Figure 8.

b. To search for the location of the lactase mutation in the human genome, the students get instructions on using the tool Nucleotide BLAST (available at https://blast.ncbi.nlm.nih.gov/Blast.cgi). The results show that the mutation does not occur in the lactase gene but rather in the MCM6 gene, where the enhancer region of the lactase gene is situated; both of these genes are on chromosome 2. An activity summarizes the unit (Figure 9).

4. The control of lactase gene expression

The last unit, which is an extension unit, is intended for students who have studied control of gene expression. The aim of the unit is to teach the genetic mechanism governing the
mutated gene's enhancement, as well as to learn more about the site on the MCM6 gene where the mutation occurs.

a. The students are presented with written information along with a scheme depicting the genetic mechanism of lactase gene enhancement due to the mutation (Figure 10).

b. Students are asked to fill in the scheme presented in Figure 11.

c. Since the mutation occurs in the MCM6 gene, why does it not damage the function of the MCM6 gene? The students are referred to the MCM6 gene in the Genome Browser bioinformatics tool (Figure 12; https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg38&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType=default&virtMode=0&monVirtPosition=&position=chr2:135839626-13587436&hgsid=1215176811_3HENOSVE5PalxeQkHAotlhyPoxZf). A few questions, such as the one at the bottom of Figure 12, assist the students to focus on the relevant parts of the information shown in the bioinformatics tool and find out

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**Figure 8.** Exercises to summarize the comparison of DNA with and without the mutation.

**Figure 9.** An activity to summarize Unit 3.

**Figure 10.** A scheme depicting the genetic mechanism of lactase gene enhancement due to the mutation.

**Figure 11.** A scheme summarizing the genetic mechanism of lactase gene enhancement due to the mutation.
that the mutation occurs in the intron. The students discover along the unit that the intron is removed during gene splicing, and there is therefore no damage to MCM6 gene function.

d. An exercise summarizes the unit (Figure 13).
e. A clip that summarizes the whole activity with questions interspersed throughout the clip (HHMI BioInteractive, 2014).

Experiencing the Activity in Schools

The activity has been experienced by approximately 100 Israeli students as well as 10 biology preservice teachers, 11 in-service teachers, and 13 science education researchers. These pilot groups enabled us to improve the activity according to their feedback. So far, most of the students have only completed Units 1 and 2 because they are in the 9th grade and have not yet studied genetics. At the end of Unit 2, they were asked, “What would you like to research and discover about the genetics of the lactase-encoding gene?” The students’ answers reflected a keen interest in the topic, which seems to be relevant to their lives:

- “I wonder if the change in the lactase gene that leads to the tolerance trait is minimal (one nucleotide replacement), completely different, or not different at all. I am interested in knowing the genetic difference between lactose-intolerant adults and intolerant children. Is the change in the same gene?” (L. M.)
- “How does lactose tolerance develop, and will everyone be fully lactose-tolerant in a few years?” (Y. S.)
- “I am interested to know if the gene for lactase has changed during evolution.” (S. Y.)

These quotes and others show the students’ interest in continuing to explore the genetics of this gene. The first two units are therefore a good trigger to continue exploring the genetic change that has occurred.

The preservice teachers completed the whole activity. Their feedback regarding the bioinformatics activity (Units 3 and 4) encouraged us to continue and expose more students to the whole activity:

- “You see the sequences in front of your eyes, and the changes that have taken place. It really illustrates what’s going on. It’s not just theoretical learning.” (O. L.)
- “The use of bioinformatics tools helped me understand how the lactase gene is inherited by understanding where the mutation occurs and that the exchange is between C and T.” (R. Y.)

We also realized the importance of a teacher as mediator in this activity. The preservice teachers performed the activity online with no mediation or support, except for technical support. Maybe that is why we heard this other voice:

- “The activity did not help me so much because I did not understand how to interpret the results I received. I just didn’t understand what I had to do with the information received.” (S. T.)

This response demonstrated the need for a teacher who would help the students grasp the full significance of the bioinformatics results as well as understand the options for application of bioinformatics for evolution research.

Recommendations for Use of the Activity

The activity can be used for teaching not only evolution but also many other topics in the biology syllabus because it deals with a genetic disorder in humans based on enzyme activity. As such, it can be learned as part of the unit on the digestive system dealing with digestion in the small or large intestine, mutations in the field of genetics, or control of gene expression and genetic engineering.

Use of the activity can be modular. The teacher can either use all of the units of the activity in succession or use the first two units to introduce the lactase enzyme and lactose tolerance (Units 1 and 2), and then later on the teacher can familiarize the students with the genetic basis of lactose tolerance (Unit 3); finally, at the appropriate time in the syllabus, the teacher can acquaint the students with control of lactase gene expression (Unit 4). In addition to its modularity, parts of the activity can be performed as either homework or schoolwork, depending on the availability of computers at the school for each student. Whether applied successively or not, the activity is ready for use and handy for the teacher who wishes to diversify his or her teaching tools. However, a teacher must serve as mediator for some parts of the activity, especially when using the bioinformatics tools in Units 3 and 4 and when students are
using these tools for the first time. In addition, since there are a few forum-style questions (Unit 1 Question 2, Unit 2 Question 4, Unit 4 Question 2) in the activity, where the students are asked to express their opinions, the teacher has the option to project the answers in front of the whole class and hold a class debate.

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Appendix 1

GCAATTATGGGTGACTGGATAGGAGCACCTTACGTCCC-GAGTTCCTTGTTAGATTITTAG
TTTGAATATGTTACGTTGATTCCTCTCCTCT-CAAGGAACCTCCGGTCGCCGATGATATGATCAGATCATGGATCACCCAGATTTCTGAAAA

Appendix 2

GCAATTATGGGTGACTGGATAGGAGCACCTTACGTCCC-GAGTTCCTTGTTAGATTITTAG
TTTGAATATGTTACGTTGATTCCTCTCCTCT-CAAGGAACCTCCGGTCGCCGATGATATGATCAGATCATGGATCACCCAGATTTCTGAAAA