The declined activity of the lactase-phlorizin hydrolase (LPH) in intestinal cells after weaning results in adult-type hypolactasia, also known as lactose intolerance. The LCT gene provides instructions for making lactase-phlorizin hydrolase (LPH) which digests lactose, a sugar found in milk and other dairy products. A speciýc DNA sequence within the MCM6 gene called a regulatory element helps control the expression of the LCT gene (MCM6 Gene: MedlinePlus Genetics, n.d.). Since it is unclear how the LCT gene can be dramatically downregulated with age in most individuals, but remain active in some, it is important to investigate the possible causation. In this report, I will introduce past research that investigated LCT and MCM6 genes and epigenetic factors that contributed to lactase persistence and lactase non-persistence among humans and mice.

Carbohydrates, one of the main nutrients that keep us alive, are found in foods and drinks that we consume and come in a variety of forms depending on the source. Of those, lactose, commonly known as milk sugar, is the main carbohydrate found in dairy products such as milk, cheese, yogurt, and some prepared packaged foods such as bread and pancakes. Lactose is made of two sugar molecules called disaccharides. Since our body uses carbohydrates in the simplest form of monosaccharides for energy

There are four di erent forms of lactase enzyme deýciency. Primary lactase enzyme deýciency is the most common type of lactose intolerance across the world ondary lactase deýciency is the most common cause of lactose intoler

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ance among infants and toddlers in the UK (NHS website, 2021), which can be di cult as they primarily rely on breastmilk and formula for nutrition. Developmental lactase deýciency is seen in babies born prematurely before the 37th week of pregnancy. A baby's small intestine creates cells producing lactase at the end of the third trimester of pregnancy. Therefore, babies born early have underdeveloped small intestines and are not able to produce lactase enzyme, though this generally resolves soon after birth (NHS website, 2021). Lastly, congenital lactase deýciency (CLD) is a rarer form of the condition that produces very little or no lactase. The baby will develop this symptom if both parents have mutations in the lactase (LCT) gene, therefore impairing the body's ability to make lactase enzymes. In this case, the baby cannot tolerate breastmilk or regular infant formula, as this will cause excessive diarrhea and dehydra-

ingesting a speciýc dose of lactose. A lactose intolerant patient will have an increased amount of hydrogen gas in their breath after ingesting lactose. This is due to undigested lactose traveling down to the large intestine where it is fermented by bacteria that produce hydrogen. On the other hand, the lactose intolerance test requires patients to drink lactose solution, and their blood samples are taken to measure the amount of blood glucose their blood contains. In this case, patients with lactose intolerance will not experience a rise in blood glucose levels since they are not able to break down lactose into glucose. Clinical testing and a history of symptoms such as bloating, abdominal cramps, and diarrhea after ingesting lactose products are used to diagnose lactose intolerance (NHS website, 2021).

Currently, there is no cure for lactose intolerance; however, most people are able to manage their symptoms by cutting down or avoiding food and drinks containing lactose and replacing them with lactose-free alternatives (NHS website, 2021). Over-the-counter medicine, such as Lactaid, contains lactase enzyme derived from Aspergillus oryzae which can aid in the digestion of lactose. When taken together with dairy products, Lactaid will break down the lactose into glucose and galactose for digestion and patients will not experience side e ects from ingesting dairy products (Dajani, 2004).

The activities of LPH enzymes are maximal at birth when we heavily rely on breast milk for survival. However, the majority world's population experiences a decline in the production of LPH enzymes from the toddler years to young adulthood (Olds, 2003). Why do most individuals become lactase non-persistence (LNP) and others maintain lactase persistence (LP) throughout their life? What a ects the amount of LPH enzymes produced in the small intestine? Two main genes control the production of LPH enzymes: lactase gene (LCT) and minichromosome maintenance complex component 6 (MCM6) gene, however, much of the mechanism remains incompletely understood (OMIM).

Lactose is a disaccharide that is made of two sugar molecules of glucose and galactose held together by glycosidic linkage. LPH enzymes, which lie in the brush border membrane of the small intestine, hydrolyze lactose to produce D-glucose and D-galactose and are actively absorbed to be exported to the liver for metabolism (Kuchay, 2020). The initial polypeptide that forms from this gene is called preprolactase (prepro-LPH) which is

its mature form of LPH enzymes. However, only 60% of the initial pre-

This experiment aims to analyze the relationship between the epigenetic factors of aging and a phenotype-related environmental change, speciýcally a lactose-containing diet. Epigenetic factors such as aging and diet are known to change the expression level of the LCT gene which produces the LHP enzyme responsible for digesting milk products (Oh et al., 2017). The result from the previous study by Oh et al in 2017 concluded that mice that were fed lactose increased LCT mRNA levels in the enterocytes in the small intestine compared to mice without lactose in their diet. Moreover, their study discovered that LCT gene transcription in the small intestine can be suppressed by epigenetic factors such as aging. Therefore, this experiment will further explore how the LCT mRNA expression level changes with age and whether post-adult mice that are fed a lactose-containing diet can maintain their LCT gene expression when they age. In addition, this experiment can also help determine which epigenetic factors (aging vs diet) are more likely to induce the change in LCT gene expression among mice. The result of the proposed experiment may support one of the hypotheses listed below.

H1: The LCT mRNA expression level decrease with age. Age is a stronger epigenetic factor than a diet.

H2: The LCT mRNA expression level increased with age. Diet is a stronger epigenetic factor than age.

H3: The LCT mRNA expression level maintained constant with age.

H0: No di erence in the level of the LCT mRNA expression level between adults and senior mice.

C57BL/6, a common inbred strain of laboratory mice that typically lives up to 26ï30 months, will be housed under di erent conditions. To investigate how diet is associated with epigenetic changes in the LCT gene, two conditions will be used. Under condition 1(LAC++), mice will be supplied with ad libitum sterile food and 2% lactose-containing milk 3 times a day for 60 days. Condition 2 (LAC--) will be used as a ® ɻ ᴀ ɲ ɕ ᴛ ᵐ ᴛ ᴀ ɣ tiou Á ɻ ɻ