Evolution of Lactase Persistence

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ABSTRACT: Though humans are known to lose lactase ability post-weaning, some people maintain lactase production into adulthood, a condition known as lactase persistence. Global distribution patterns of lactase persistency are inconsistent; the condition is much more prevalent in some populations than others. Using results across independent studies, the existence of such a phenomenon can be attributed to positive selection on ancestral pastoralist populations. Two different hypotheses explain this positive selection: milk-independent economies, and colonic bacteria adaption.

KEYWORDS: Evolution, lactase persistence, lactose (in)tolerance, human genetics

This essay is part of a continuing series of student class work completed in a second-year biology course at The University of Western Ontario, introduced [here](#). The essay illustrates one or more principles of evolution on a topic of the student's own choice.

Lactase non-persistence, the decrease in lactase production post-weaning, results in lactose intolerance, a condition in which the ability to break down lactose (a common disaccharide found in milk) to glucose and galactose is lost (Figure 1). Lactase persistence is a fairly recent and unique phenotype in humans where individuals retain the ability to produce lactase into adulthood. Currently, lactase persistence is unevenly distributed among ethnic cultures. European, African, and Middle Eastern populations show high lactase persistence frequencies, but this phenotype is very rare elsewhere in the world (Figure 2) (1). How and why this uneven global distribution exists are questions that attract further investigation.

Figure 1. Lactose digestion in humans (2). In the small intestine, lactose is broken down to glucose and galactose (left) when lactase is present or persists. In lactose intolerant individuals (right), lactose is not broken down and gastro-intestinal discomfort may result.

Lactase non-persistence is the ancestral trait of all mammals, including humans (1). Although

lactase activity is high at birth, it declines in post-weaning stages, when lactose is no longer an essential part of the diet. The decline in lactase activity is regulated transcriptionally; polymorphisms that confer human lactase persistence affect the LCT promoter or DNA-protein interaction (3,4,5).

Figure 2. Distribution of lactase persistence. Map colours correspond to frequencies ranging from 0 to 1.00 (4).

In early Neolithic era, lactase persistence was a rare phenotype among central Europeans (1). Today, the lactase persistence phenotype has high geographical prevalence, where the trait exists at frequencies over 0.9 in some European populations (Figure 2) (4). The most common single nucleotide polymorphism (SNP) in lactase-persistent Europeans is the dominant mutation, 13910^*T (1), a transition mutation from a cysteine to thymine. Tracing the history of -13910^*T helps to elucidate the evolutionary mechanism responsible for the high prevalence of lactase persistence in Europe. Over the past 7,500 years, 13910^*T allele frequency has continued to increase throughout Europe (1). The

increase coincides with a period of expansion in cattle pastoralism (the practice of raising cattle); farmers began to raise increasing numbers of cattle compared with other livestock, possibly due to its economic benefits (resourcefully using each part of the cow and taking advantage of the nutritional value in milk (6).) Given the preponderance in both cattle pastoralism and lactase persistence, it is likely that pastoralism contributed to a selective pressure on European populations that ultimately led to the positive selection of the lactase persistence phenotype. The growth of pastoralism suggests that the associated practices would also be increasingly adopted, including dairying. This practice may have facilitated a gradual transition towards an economy more dependent on milk. Under this type of economy, the lactase persistence adaptation allows weaned individuals to continue deriving energy from milk, increasing chances of survival during periods of food insecurity. The final effect of this advantage is the increase in lactase persistence allele frequencies over time. Today, average lactase persistence frequency is higher than 80% in traditionally pastoralist populations, such as Finland, but falls below 5% in non-pastoralist populations (1).

Although, natural selection gives reason to the increasing prevalence of lactase persistence, a migratory demographics model must be adopted to understand how the trait disseminated globally. The pervasiveness of lactase persistence in Europe is consistent with the idea that dairying tradition moved with earlier farmers when they migrated across Europe. Compared with non-dairying farmers, dairying farmers have historically been more mobile, sporadically migrating to greater extents (1). As dairy farmers settled in new areas, they acted not only as vessels for gene flow, but also introduced dairying practice and the subsequent selective pressure of milk-dependence. A migratory demographics model indicates that ubiquity in lactase persistence was not a product of simple gene flow, but a complex interaction with the dissemination of selective pressures.

Though lactase persistence is common in some populations, such as Europe and Africa, lactase non-persistence is still the most common global phenotype. The high prevalence of lactase non-persistence can be explained by a reduction in selective pressure. Central Asian populations have historically practised pastoralism, but show lactase persistence frequencies of 40.2% and 40.8% in the Kazakh and Tajiko-Uzbek populations, respectively (7). Both of these frequencies fall short compared with the average frequency for pastoralist

populations (above 80%). Given the great difference between frequencies, it is likely that Central Asian populations faced a reduced selective pressure from milk dependence, possibly because their economies remained milk-independent.

A model suggesting a milk-independent economy as the sole driver of lactase non-persistence can hold true only if one assumes that populations with low prevalence of lactase persistence never practised pastoralism. However, considering that milk has become an essential part of the diet globally, it is hard to believe that this is truly the case. Colonic bacteria adaptation provides an explanation around this limitation by arguing that the same selective pressure could be reduced by the symbiotic relationship between humans and colonic bacteria. Colonic bacteria have demonstrated increased ability to ferment lactose during long-term lactose feeding (8). Furthermore, prolonged lactose feeding in lactase non-persistent individuals can lead to a reduction in the flatus passage—a symptom of lactose indigestion—frequency (8). This alternate route supports the possibility of conferring a lactose tolerant phenotype in lactase non-persistent individuals, thus suggesting that lactose intolerant individuals can still consume milk. Colonic bacteria adaptation provides a plausible explanation for how dairying practice can still lead to widespread lactase non-persistence. An explanation combining milk-independent economies and colonic bacteria adaptation is also within the realm of possibility, but more research is required to clearly establish the relationship.

In conclusion, the uneven global distribution of lactase persistence is the product of many different mechanisms. Populations of high lactase persistence could have been shaped through positive (gene) selection on previous pastoralist generations, a mechanism enhanced by the effects of migration. Populations with high frequencies of lactase non-persistence could have descended from generations that faced a reduced selective pressure of milk dependence. Two different hypotheses explain how a reduced selective pressure came about: milk-independent economies, and colonic bacteria adaption. The positive selection on lactase persistence is suspected to still be in action today; patterns of genomic variation on the *LCT* gene have shown signatures of very recent positive selection (9).

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