



SPLASH!® milk science update

May 2020 Issue



This month's issue features bone health and breast milk, yogurt and mortality, and malaria antigens in breast milk.

Older Adult Bone Health Linked to Breast Milk in Infancy

- **A new study tests the hypothesis that breast milk consumption during infancy is associated with higher bone density in adults 60–75 years old.**
- **Nearly 1000 adults from the Hertfordshire Cohort Study with infant feeding records from their first year of life in the 1930s underwent bone mineral scans between 1998 and 2004.**
- **Males that received only breast milk during their first year of life had higher bone mineral density in their lumbar spine than males that received both breast and cow milk or only cow milk.**
- **Infant nutrition may be a potential mediator for later life bone health in males, whereas hormones and other factors may more heavily influence female bone health.**

Older adults looking to keep their bones strong might turn to a glass of milk with lunch to help meet their daily calcium and vitamin D requirements. New research [1] suggests that older adults interested in healthy bones might also want to find out what they drank for lunch *as an infant*.



Despite the 70-year gap, there are good reasons to believe that infant feeding practices are connected to bone health in later life. Differences in infant feeding practices (i.e. breast milk or formula) have been linked to body length and growth rates both during the first year of life and later in childhood [2, 3]. Early growth rates, in turn, are related to the density of the skeleton when it reaches peak bone mass during the third decade of life [3, 4]. And how strong and dense your bones are at their peak can predict how they will hold up once resorption (or bone loss) exceeds bone formation [4].

But testing these life history connections is tricky, requiring data collected more than a half century apart. A new study took advantage of the unique data set available from the Hertfordshire Cohort Study (HCS), which included almost 1000 males and females born between 1931 and 1939 in Hertfordshire County, Great Britain. All cohort members had health visitor ledgers from their first year of life that included data on birth weight, weight at 1 year, and whether the individual was breast milk fed, breast and bottle milk fed, or bottle fed during the first year and were still living in Hertfordshire County between 1998 and 2004 and available for bone density testing [1]. The data are not ideal, as collections in the 1930s were not performed with any knowledge of how the information would be used decades later. But even without data on age at first solids or age at complete weaning, the HCS still allows researchers to test the hypothesis that infant nutrition is a potential mediator of adult bone health [1].

All participants (498 males and 498 females, who were on average 65 years old) completed questionnaires at the time of their bone scans about potential confounding variables including smoking, exercise, alcohol consumption, diet, and (for females) use of hormone replacement therapy. Dietary information was converted to a prudent diet score as a marker of dietary quality and also used to calculate daily dairy intake. Finally, each participant had his or her lumbar spine and femoral neck scanned for bone mineral content (BMC, or how much bone mineral in grams is in a specific area) and bone mineral density (BMC divided by the area of the bone, or grams/square centimeter) by dual-energy X-ray absorptiometry (DXA). Each participant was separated into either the breast-fed group, meaning no milk other than mother's milk was provided for the first year of life, or bottle-fed, which included those that were bottle fed and those that received both bottles and breast milk. Using historical records, the study authors

determined that bottles were most likely filled with cow's milk preparations rather than commercial infant formula, which was not widely used during the 1930s in Great Britain [1].

Infant feeding was found to be a significant predictor of bone health in later life, but only in males [1]. After controlling for all confounding variables, bottle-fed males had significantly lower lumbar bone mineral density (BMD) measurements than those that were breast fed. But what about females? The study authors propose that for females, factors such as hormones, age at menopause, and postmenopausal lifestyle (weight-bearing exercise, diet) may have a stronger influence on bone density during later life and override any potential effects from infant diet [1].

Normally, this is the part of the article where the results of this study would be discussed in the broader context of research on breast milk during infancy and bone health later in life. Unfortunately, the unique aspects of the HCS population make such discussions challenging. For starters, a review paper on infant milk feeding and bone mass reported that whether or not breast milk and BMD were positively associated depended on the age of study participants [5]. With no other studies on 60 and 70 year olds, the HCS lacks an age-matched population. But equally challenging is the fact that the HCS also lacks a diet-matched population; all other studies on infant diet and bone health examine the influence of breast milk or commercial infant formula, not cow's milk. The suggestion that breastfeeding may potentially provide a protective effect on bone health in males as they age must therefore be interpreted with caution. It is certainly intriguing, however, to think of breast milk conferring health benefits far beyond infancy, even into the twilight years.

1. Carter SA, Parsons CM, Robinson SM, Harvey NC, Ward KA, Cooper C, Dennison EM. 2020. Infant milk feeding and bone health in later life: findings from the Hertfordshire cohort study. *Osteoporosis International* 31(4): 709-714.
2. Fewtrell PA, Cole TJ, Lucas A. 2000. Effects of growth during infancy and childhood on bone mineralization and turnover in preterm children aged 8-12 years. *Acta Paediatrica* 89: 148-153.
3. Martin RM, Smith GD, Mangtani P, Frankel S, Gunnell D. 2002. Association between breastfeeding and growth: the Boyd-Orr cohort study. *Archives of Disease in Childhood, Fetal and Neonatal Edition* 87: F193-F201.
4. Kalkwarf HJ, Khoury JC, Lanphear BP. 2003. Milk intake during childhood and adolescence, adult bone density, and osteoporotic fractures in US women. *American Journal of Clinical Nutrition* 77: 257-265.
5. Muniz LC, Menezes AMB, Buffarini R, Wehrmeister FC, Assuncao MCF. 2015. Effect of breastfeeding on bone mass from childhood to adulthood: a systematic review of the literature. *International Breastfeeding Journal* 10 (1): 31.

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Yogurt Consumption Is Associated with Reduced Mortality in Women

- **Yogurt has many health benefits, but studies looking at its effects on mortality have so far been inconclusive.**
- **A new study of two large prospective US cohorts with long follow-up periods found that regular yogurt consumption was linked to lower mortality risk among women.**
- **The study also found that replacing yogurt with milk or other dairy foods was related to a greater mortality risk in women, suggesting that yogurt may represent a better food choice over other dairy products in women.**

Yogurt isn't just yummy, it's also an excellent source of valuable nutrients—including protein, calcium, magnesium and vitamin B-12—and has been associated with various health benefits (1-9).



Given its beneficial effects on health, it's perhaps not surprising that yogurt has been thought to increase lifespan. "Yogurt and other fermented milk products such as kefir have long been claimed to extend life expectancy by Eastern European countries such as Bulgaria," says Dr. Karin Michels, now at the University of California, Los Angeles. "We were curious whether these claims would be supported by data," she says.

Michels' group has been studying the potential role of the microbiome in mediating the connection between diet and health outcomes. "Fermented foods are the most likely to influence the microbiome so we were curious to see how yogurt might affect longevity," she says.

Previous epidemiologic studies have shown that regular yogurt intake is associated with lower risks of cardiovascular disease, type 2 diabetes, and certain cancers (10-13). However, studies looking at how yogurt consumption relates to mortality have been relatively sparse, and their results have often been inconsistent (14-18).

In a new study, Michels and her colleagues analyzed data from two large ongoing prospective cohorts of US women and men to evaluate whether yogurt consumption is associated with reduced risks of mortality (19). A total of 82,348 women and 40,278 men were included in their analysis, and the researchers used validated questionnaires to assess yogurt consumption. The cohort of women were followed from 1980 to 2012, and the men from 1986 to 2012. "Regular yogurt consumption was associated with longevity among women," says Michels.

In addition, the researchers found that replacing one serving per day of yogurt with nuts or whole grains was associated with reduced mortality risk in women, whereas replacing yogurt with red meat, processed meat, milk, or other dairy foods was related to a greater mortality risk. In men, substituting yogurt with nuts was associated with reduced mortality risk and replacing it with red or processed meat was associated with increased mortality risk. The findings provide important information about healthier or unhealthier food alternatives to yogurt, and suggest that yogurt may represent a better food choice over other dairy products in women.

Follow-up studies will be necessary to elucidate the mechanisms by which yogurt may be influencing mortality risk. Yogurt consumption is correlated with higher intake of calcium, but Michels and her colleagues did not find a major difference in the association between yogurt intake and mortality when they adjusted for calcium intake.

One possibility is that the effects of yogurt consumption on mortality are mediated by changes to the gut microbiome. The human gut microbiota has been previously linked to changes in the immune system, cholesterol, and weight gain (20-26). In addition, studies have suggested that yogurt may modify the intestinal microbiota composition in beneficial ways, and bacteria present in yogurt, such as *Lactobacillus* and *Bifidobacterium*, may have beneficial effects on immune function that could protect against chronic diseases (27, 28). "We are currently conducting feeding studies with yogurt and kefir to more precisely study the impact of these fermented milk products on the microbiome," says Michels.

Michels notes a few limitations of the current study. "We would have liked to be able to differentiate between the types of yogurts to get better insights into the study," she says. "Further, the frequency of consumption in the US is generally lower than in Europe, especially among men, so it is more difficult to evaluate the impact of more frequent consumption and to evaluate a dose-response relation," says Michels.

The study concludes that regular yogurt consumption was related to lower mortality risk among women. "Regular yogurt consumption very likely benefits human health," says Michels. "While we were unable to

differentiate between the types of yogurts, yogurt without added sugar and flavors is likely the most beneficial to health," she says.

1. Webb D., Donovan S.M., Meydani S.N. The role of yogurt in improving the quality of the American diet and meeting dietary guidelines. *Nutr Rev.* 2014 Mar;72(3):180-9.
2. Fernandez M.A., Marette A. Potential health benefits of combining yogurt and fruits based on their probiotic and prebiotic properties. *Adv Nutr.* 2017 Jan 17;8(1):155S-64S.
3. Wang H., Livingston K.A., Fox C.S., Meigs J.B., Jacques P.F. Yogurt consumption is associated with better diet quality and metabolic profile in American men and women. *Nutr Res.* 2013 Jan;33(1):18-26.
4. Kong L.C., Holmes B.A., Cotillard A., Habi-Rachedi F., Brazeilles R., Gougis S., Gausserès N., Cani P.D., Fellahi S., Bastard J.P., Kennedy S.P., Doré J., Ehrlich S.D., Zucker J.D., Rizkalla S.W., Clément K. Dietary patterns differently associate with inflammation and gut microbiota in overweight and obese subjects. *PLoS One.* 2014 Oct 20;9(10):e109434.
5. Cormier H., Thifault É., Garneau V., Tremblay A., Drapeau V., Pérusse L., Vohl M.C. Association between yogurt consumption, dietary patterns, and cardio-metabolic risk factors. *Eur J Nutr.* 2016 Mar;55(2):577-87.
6. Zhu Y., Wang H., Hollis J.H., Jacques P.F. The associations between yogurt consumption, diet quality, and metabolic profiles in children in the USA. *Eur J Nutr.* 2015 Jun;54(4):543-50.
7. Tong X., Dong J.Y., Wu Z.W., Li W., Qin L.Q. Dairy consumption and risk of type 2 diabetes mellitus: a meta-analysis of cohort studies. *Eur J Clin Nutr.* 2011 Sep;65(9):1027-31.
8. Gao D., Ning N., Wang C., Wang Y., Li Q., Meng Z., Liu Y., Li Q. Dairy products consumption and risk of type 2 diabetes: systematic review and dose-response meta-analysis. *PLoS One.* 2013 Sep 27;8(9):e73965.
9. Bonthuis M., Hughes M.C., Ibiebele T.I., Green A.C., van der Pols J.C. Dairy consumption and patterns of mortality of Australian adults. *Eur J Clin Nutr.* 2010 Jun;64(6):569-77.
10. Rice B.H. Dairy and cardiovascular disease: a review of recent observational research. *Curr Nutr Rep.* 2014 Mar 15;3:130-138.
11. Chen M., Sun Q., Giovannucci E., Mozaffarian D., Manson J.E., Willett W.C., Hu F.B. Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *BMC Med.* 2014 Nov 25;12:215.
12. Sapkota A., Hsu C.C., Zaridze D., Shangina O., Szeszenia-Dabrowska N., Mates D., Fabiánová E., Rudnai P., Janout V., Holcatova I., Brennan P., Boffetta P., Hashibe M. Dietary risk factors for squamous cell carcinoma of the upper aerodigestive tract in central and eastern Europe. *Cancer Causes Control.* 2008 Dec;19(10):1161-70.
13. Wu J., Zeng R., Huang J., Li X., Zhang J., Ho J.C., Zheng Y. Dietary protein sources and incidence of breast cancer: a dose-response meta-analysis of prospective studies. *Nutrients.* 2016 Nov 17;8(11). pii: E730.
14. Soedamah-Muthu S.S., Masset G., Verberne L., Geleijnse J.M., Brunner E.J. Consumption of dairy products and associations with incident diabetes, CHD and mortality in the Whitehall II study. *Br J Nutr.* 2013 Feb 28;109(4):718-26.
15. Praagman J., Dalmeijer G.W., van der Schouw Y.T., Soedamah-Muthu S.S., Monique Verschuren W.M., Bas Bueno-de-Mesquita H., Geleijnse J.M., Beulens J.W.J. The relationship between fermented food intake and mortality risk in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *Br J Nutr.* 2015 Feb 14;113(3):498-506.
16. Bonthuis M., Hughes M.C.B., Ibiebele T.I., Green A.C., van der Pols J.C. Dairy consumption and patterns of mortality of Australian adults. *Eur J Clin Nutr.* 2010 Jun;64(6):569-77.
17. Farvid M.S., Malekshah A.F., Pourshams A., Poustchi H., Sepanlou S.G., Sharafkhan M., Khoshnia M., Farvid M., Abnet C.C., Kamangar F., Dawsey S.M., Brennan P., Pharoah P.D., Boffetta P., Willett W.C., Malekzadeh R. Dairy food intake and all-cause, cardiovascular disease, and cancer mortality: The Golestan cohort study. *Am J Epidemiol.* 2017 Apr 15;185(8):697-711.
18. Goldbohm R.A., Chorus A.M., Galindo Garre F., Schouten L.J., van den Brandt P.A. Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands. *Am J Clin Nutr.* 2011 Mar;93(3):615-27.
19. Schmid D., Song M., Zhang X., Willett W.C., Vaidya R., Giovannucci E.L., Michels K.B. Yogurt consumption in relation to mortality from cardiovascular disease, cancer, and all causes: a prospective investigation in 2 cohorts of US women and men. *Am J Clin Nutr.* 2020 Mar 1;111(3):689-697.
20. Filteau M., Matamoros S., Savard P., Roy D. Molecular monitoring of fecal microbiota in healthy adults following probiotic yogurt intake. *PharmaNutrition.* 2013 Oct;1(4):123-9.
21. Kayama H., Takeda K. Regulation of intestinal homeostasis by innate and adaptive immunity. *Int Immunol.* 2012 Nov;24(11):673-80.
22. Kiessling G., Schneider J., Jahreis G. Long-term consumption of fermented dairy products over 6 months increases HDL cholesterol. *Eur J Clin Nutr.* 2002 Sep;56(9):843-9.
23. Agerholm-Larsen L., Bell M.L., Grunwald G.K., Astrup A. The effect of a probiotic milk product on plasma cholesterol: a meta-analysis of short-term intervention studies. *Eur J Clin Nutr.* 2000 Nov;54(11):856-60.
24. Zemel M.B., Richards J., Mathis S., Milstead A., Gebhardt L., Silva E. Dairy augmentation of total and central fat loss in obese subjects. *Int J Obes (Lond).* 2005 Apr;29(4):391-7.
25. Pei R., DiMarco D.M., Putt K.K., Martin D.A., Gu Q., Chitchumroonchokchai C., White H.M., Scarlett C.O., Bruno R.S., Bolling B.W. Low-fat yogurt consumption reduces biomarkers of chronic inflammation and inhibits markers of endotoxin exposure in healthy premenopausal women: a randomised controlled trial. *Br J Nutr.* 2017 Dec;118(12):1043-51.
26. Mozaffarian D., Hao T., Rimm E.B., Willett W.C., Hu F.B. Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med.* 2011 Jun 23;364(25):2392-404.
27. Lisko D.J., Johnston G.P., Johnston C.G. Effects of dietary yogurt on the healthy human gastrointestinal (GI) microbiome. *Microorganisms.* 2017 Feb 15;5(1). pii: E6.
28. Meydani S.N., Ha W.K. Immunologic effects of yogurt. *Am J Clin Nutr.* 2000 Apr;71(4):861-72.

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Malaria Antigens Occur in the Breast Milk of Asymptomatic, Infected Mothers

- A study has shown that an antigen to the malarial parasite, *Plasmodium falciparum*, can pass from a mother's blood to her milk.
- The study tested women in Uganda who were asymptomatic for malaria, yet had been exposed to the parasite at some time.
- It is as yet unclear whether the presence of the antigen in milk offers any protection against malaria infection for infants who consume it.

Malaria still accounts for approximately 435,000 deaths each year, and the substantial majority of these deaths—some 61%—are children under five years of age [1]. Governments of affected countries, international aid organizations and foreign donors put in place various safeguards to reduce the disease rate, including mosquito nets and preventative malaria medicine for children. Yet the World Health Organization bemoans a lack of funding in this space. In 2017, for example, 15.7 million children in the Sahel region in Africa received seasonal malaria prophylaxis, but the paucity of program funding meant that 13.6 million children who could have benefited missed out [1].



Recently, three medical scientists wondered whether human milk from mothers who at some point had been infected with malaria might also contain the antigen. So, they collected data from lactating women in Uganda, and found their suspicions to be correct [2]. It is not yet known whether malaria antibodies in human milk offer protection to infants, and if that is the case, how effective they are compared with other safeguards.

Analogy with other infectious agents suggests that protection is a possibility, though. Viral antigens have been found to pass from a mother's blood into her milk, and some studies suggest that this helps an infant consuming the milk to develop immunity to the viruses in question [3]. Moreover, human milk provides a rich source of immune aids for infants. For the first few months of life, antibodies in milk provide infant immunity at a time of life when the capacity to produce one's own antibodies has not yet fully developed.

The goal of the recent study was to test for the presence of *Plasmodium falciparum* histidine-rich protein-2 in both the blood and breast milk of lactating women. There are several types of malarial parasite, and *Plasmodium falciparum* is the most common type found in Africa. Hence *Plasmodium falciparum* histidine-rich protein-2 is the antigen in response to which the human body produces antibodies. The team—Lieke van den Elsen and Valerie Verhasselt of the University of Western Australia School of Molecular Science in Perth, and Thomas Egwang of Med Biotech Laboratories, based in Kampala—tested women who visited the St Anne Health Center III, in Katakwi District, northeastern Uganda, during both the periods of the year when malaria transmission was high in the area, and when it was low. The idea was to evaluate whether in women who were once infected with *Plasmodium falciparum*, but who showed no symptoms during at least the period of testing, whether antigens in the bloodstream move via the mammary gland into the milk.

The study ran during most of 2018. During that period, 88 lactating women who were asymptomatic for malaria visited the clinic, which ran tests to confirm that their blood samples had detectable levels of the malaria antigen. Of these women, 14 also had the antigen present at detectable levels in their milk. In other words, the results of this small study suggest that about 15 to 16% of lactating women of this group pass on the malaria antigen to breastfeeding infants.

The researchers also ran some preliminary tests to assess whether women with higher levels of malaria antigen in their blood were the most likely to have it pass into their milk. This appears to be the case. Then to double check that they were not for some reason picking up false positives during the laboratory

milk assessments, the team also tested milk samples from 44 women without malaria antigens in their blood. None of these samples contained the antigen.

This study's findings are intriguing, but it would be dangerous to assume that infants who drink human milk laced with malaria antigens are immune to infection. While that would be good news for the infants on the face of things, it could also be pointed to by policymakers who wish to justify the underfunding of some existing malaria prevention measures. The authors of this study are clear that more research is needed. However, the data do add weight to the argument that women should, wherever possible, be encouraged and supported to breastfeed.

1. *World Malaria Report 2018*. World Health Organization, accessed February 13, 2020. <https://www.who.int/malaria/publications/world-malaria-report-2018/en/>
2. van den Elsen L.W.J, Verhasselt V. & Egwang T., *Malaria Antigen Shedding in the Breast Milk of Mothers from a Region with Endemic Malaria*, *JAMA Pediatrics*, Published online January 6, 2020. doi:10.1001/jamapediatrics.2019.5209eprinted
3. Marchant A., Sadarangani M., Garand M., Dauby N., Verhasselt V. & Pereira L. *Maternal Immunisation: Collaborating with Mother Nature*. *Lancet Infectious Disease*. 2017;17(7):e197-e208.

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A Gene that Helps Humans Consume Fermented Dairy

- **Hominids are unique among mammals for possessing a gene called HCA3.**
- **HCA3 appears to be an adaptation to the metabolites produced by bacteria that ferment foodstuffs like cheese and yogurt.**
- **Evidence suggests that HCA3 activation leads to immunological and metabolic responses.**

Humans have many unique attributes, as does the family of species within which humans evolved—the hominids. About 15 years ago, geneticists added to the list of hominid-unique attributes by noting that species within this family have a gene called HCA₃ that other mammals lack. Now a group of researchers from Leipzig, Germany has figured out what this gene does and why it was preserved by natural selection [1]. Their evidence suggests that HCA₃ blessed the hominids with the ability to eat many bacteria-riddled foods without getting sick. These include some foods that played important roles in the story of human evolution, such as fermented milk products.



Frequently, whether the fermented milk product in question is a hard or a soft cheese, a kefir, yogurt or buttermilk, the fermentation is carried out by lactic acid bacteria. These bacteria produce all kinds of metabolites that the hominid body has to handle and, more ideally, harness for some biological purpose. One of the metabolites is called D-phenyllactic acid (D-PLA). It is present at especially high concentrations in foods like sauerkraut, which were fermented by lactic acid bacteria. Another is structurally related to a chemical called 3-hydroxyoctanoate (3HO). When people eat food and drink fermented with lactic acid bacteria, metabolites such as these pass through the wall of the intestines and into the bloodstream.

In the recent paper, which was published in *PLoS Genetics*, researchers led by Anna Peters of Leipzig

University's Faculty of Medicine report that certain metabolites of fermented food trigger white blood cells called primary human monocytes to migrate towards tissues in which the HCA₃ gene is being expressed. Thus, primary human monocytes migrate towards lung cells, skin cells, and fat cells, and other kinds of immune cells.

The team demonstrated monocyte migration in response to fermented food metabolites by measuring metabolite effectiveness at activating HCA₃, relative to two other similar genes that are shared by animals not in the hominid family: HCA₁ and HCA₂. Only HCA₃ was activated by 3HO. HCA₃ was also activated by amino acids known as aromatic D-amino acids, which are secreted by bacteria such as *Bifidobacterium* and *Lactobacillus*—bacteria that are found in fermented milk products. Two aromatic D-amino acids, D-phenylalanine and D-tryptophan, are especially likely to occur in fermented food and beverages at concentrations necessary to activate HCA₃, according to the researchers.

Having demonstrated what substances uniquely turn on the HCA₃ gene, the team assessed the degree of activation of this gene in different tissues by measuring the amount of messenger RNA produced. Among the various tissues, they found that the highest expression of HCA₃ was in immune cells—in neutrophils and in monocytes—and that the pattern of activation in different tissues was distinct from that of HCA₂, from which HCA₃ is thought to have evolved.

But what does the activation of HCA₃ lead to that is of benefit? To some extent, this is still an open question. Certainly, like the similar genes shared by non-hominid animals—HCA₁ and HCA₂—HCA₃ encodes G protein-coupled receptors, which are situated at the top of a biochemical cascade that sends powerful signals within cells. These signals could be doing various things.

There are likely to be immunological and metabolic effects of HCA₃ activation. The research team did not pin down whether HCA₃ activation in monocytes affects these cells' ability to consume and destroy microbes in a process called phagocytosis—or whether it preps these cells to elicit a stronger inflammatory response to bacteria. But such responses would make functional sense, as they would ready the body for the additional bacteria it must grapple with when we eat fermented foodstuffs. It is especially curious that fat cells are among the few tissues to express HCA₃. This very fact suggests that foods and beverages fermented by lactic acid bacteria could exert some sort of influence on fat storage and energy release.

The story of HCA₃ maintenance by natural selection is part of a broader story of hominid adaptation to more diverse ecosystems. Shared across hominids, the gene emerged before fermented milk products appeared in the Balkans and Middle East, perhaps 10,000 years ago, and enabled early humans and other apes to eat various kinds of rotting food [2]. But once established in the genome, a piece of the genetic stage was set for humans to take advantage of fermented milk products. After all, cheese is an awesome source of complex proteins, fats, and minerals that lasts much longer than fresh milk.

1. Peters A., Krumbholz P., Jäger E., Heintz-Buschart A., Volkan Çakir M., Rothmund S., Gaudl A., Ceglarek U., Schöneberg T., Stäubert C. 2019. Metabolites of Lactic Acid Bacteria Present in Fermented Foods are Highly Potent Agonists of Human Hydroxycarboxylic Acid Receptor 3. *PLoS Genetics*, 15(7): e1008283.
2. Tamime A. Y. 2002. Fermented Milks: A Historical Food with Modern Applications—A Review. *European Journal of Clinical Nutrition*, 56, Suppl 4, S2–S15.

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