



SPLASH!® milk science update April 2019 Issue



This month's issue features sleep apnea and dairy, livestock genomes, and lactose intolerance.

Can Dairy Foods Help Sleep Apnea?

- **Sleep apnea is associated with increased serum markers of inflammation.**
- **A small study of 104 participants on diet and sleep apnea reported that participants that consumed two servings of dairy per day had less severe sleep apnea.**
- **Dairy's anti-inflammatory properties may reduce the number of obstructive breathing events in individuals with sleep apnea.**

Drinking warm milk at bedtime to help you fall asleep might be a myth, but dairy foods playing a role in improving sleep could be a reality. The warm milk myth likely came from the finding that cow milk contains tryptophan, the same amino acid thought to make people sleepy after eating Thanksgiving Day turkey. Foods with tryptophan have not shown the same sleep-inducing effects as pure tryptophan. But milk has many other ingredients that could potentially influence the symptoms of sleep apnea, a sleep disorder where breathing stops and starts numerous times during sleep due to relaxed throat muscles.



In a newly published report [1], researchers investigated the potential effect of diet on the severity of sleep apnea. Overweight and obesity are considered the largest risk factors for development of sleep apnea [1-3]. However, not all individuals that suffer from this sleep disorder are overweight, an observation that prompted Hynes and colleagues to hypothesize that certain food types could also be risk factors [1].

Over 100 study participants completed four dietary surveys and one sleep study that measured the number of breathing interruptions per hour of sleep (called the Apnea-Hypopnea Index or AHI); an AHI of 5–15 is considered mild disease, 15–30 is moderate, and >30 is considered severe sleep apnea [1]. In addition to identifying foods that are associated with higher AHI scores (e.g., processed meats), Hynes [1] reports that study participants that had two servings of dairy a day had lower AHI scores, and thus less severe sleep apnea.

Why would processed meats make sleep apnea worse whereas dairy foods might lessen the severity? Hynes [1] suggests both relate to inflammation. Several studies have found that, compared with controls, sleep apnea patients have increased serum levels of inflammatory markers such as tumor necrosis factor- α (TNF- α), interleukin 6 (IL-6), and interleukin β (IL- β) [reviewed in 4]. Processed meats are believed to contain inflammatory compounds that can further increase the levels of these inflammatory markers in the body [5, 6], which could in turn influence the severity of sleep apnea.

In contrast, dairy foods contain numerous nutrients and compounds with anti-inflammatory properties, including calcium, vitamin E, polyunsaturated fatty acids, and the amino acid leucine. Several studies support Hynes' finding that simply meeting dietary guidelines for daily dairy intake may have an anti-inflammatory effect. For example, a large prospective study of 3000 Greek adults found that serum markers of inflammation (TNF- α and IL-6) were significantly lower in individuals that consumed >14 servings of dairy per week

compared with those consuming <8 servings [7]. Moreover, an intervention study [8] on overweight and obese adults with metabolic syndrome found that consuming 3.5 servings compared with just 0.5 servings of dairy per day significantly reduced inflammatory stress independent of weight loss. Finally, Hynes [1] highlights research that demonstrates the effect of low-fat dairy on the prevention of gout, presumably by inhibiting the inflammatory response responsible for the creation of urate crystals in the joints.

Hynes does not suggest that dairy intake has the same preventative effect on the development of sleep apnea as it does on gout. However, the finding that dairy intake is associated with a less severe form of sleep apnea (i.e., fewer obstructive events during sleep) certainly warrants more research on how dairy's anti-inflammatory ingredients may influence the etiology of sleep apnea.

Such investigations don't just stand to make some people better rested. Sleep apnea, believed to affect between 3% and 7% of the U.S. population, is considered a risk factor for development of cardiovascular disease, hypertension, and type 2 diabetes [3, 4]. Simply identifying which foods make sleep apnea better or worse could have downstream effects on the development of these deadly chronic diseases.

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Contributed by

Dr. Lauren Milligan Newmark

Researcher, Science Writer

Feeding the Preterm Infant: Fresh or Processed Breastmilk?

- **Preterm birth is the leading cause of death in children younger than 5 years worldwide, with its prevalence worryingly increasing.**
- **Preterm babies are currently fed mother's own milk that has been previously frozen, pasteurized donor milk, and/or formula, depending on what is available.**
- **A new study found significant benefits with lower incidence of NEC and lower morbidity in very preterm babies given one daily feed of fresh mother's own milk complementing frozen milk as feed.**
- **Importantly, 87% of the participating mothers were able to achieve expression of at least one daily feed of fresh breastmilk.**
- **These findings call for revision of the current guidelines to feed fresh breastmilk to the preterm infant, a practice that was now shown to be not only feasible, but also potentially life-saving.**

This is the million-dollar question when it comes to feeding those infants that are born the most vulnerable. Preterm infants are entirely dependent for their survival on the level of medical care offered to them. Amongst the important decisions to be made by health professionals as to how a baby born preterm will survive is how and what this baby will be fed. Currently, the standard practice in the neonatal intensive care unit (NICU) is to feed preterm babies frozen mother's own milk, pasteurized donor milk and/or formula, depending on what is available. However, a ground-breaking study by Sun and colleagues has now challenged

this well-accepted but poorly researched dogma, showing that fresh mother's own milk (non-refrigerated, non-frozen, completely unprocessed) is the most beneficial for the preterm baby, just as it is for the term baby [1].



Preterm birth is not uncommon. In fact, its incidence is worryingly rising worldwide, with more than 1 in 10 babies born preterm (WHO) [2]. Despite the enormous advancements in medicine, patient care and medical research in the last decades, preterm infants still face a number of health complications, many of which ultimately lead to their death or a lifetime of disability [3,4]. The WHO states that more than three quarters of preterm babies can be saved with feasible, cost-effective care, highlighting breastfeeding as one of the few vital interventions that can facilitate these babies' survival [2].

And although breastfeeding would indeed provide the maximal protective, nutritional and developmental benefits to preterm babies, including reducing the incidence of necrotizing enterocolitis (NEC) [5-8], many of them are unable to breastfeed, at least for the first days or weeks of their lives. Therefore, provision of mother's own milk to these babies, or donor human milk, if the former is unavailable, is the next best to feeding on the breast. But, do these babies get from breastmilk fed to them in the NICU what they would normally get if they fed directly at the breast?

The answer is no. And this is because the breastmilk fed to the preterm infant is either frozen or pasteurized, processes that destroy a large part of those bioactive components of breastmilk that have been associated with protective and developmental benefits. Importantly, these breastmilk bioactive components include not only molecules with immuno-protective functions (such as cytokines, immunoglobulins, lactoferrin, oligosaccharides, etc.) but also live cells [9].

Of the cells of breastmilk, different types of immune cells have been described that are not only present in breastmilk under normal conditions, delivering what is called a baseline immunity to the infant, but they also specifically respond to maternal or infant illness to allow transfer of boosted immunity to the infant from the mother, depending on the infant's specific needs [10-12]. This is truly amazing, with potential direct benefits in the NICU.

But, in addition to immune cells, breastmilk contains another, perhaps a little undermined cellular treasure, stem cells! So far, these cells have been mostly studied and discussed in relation to their transfer and integration as well as potential developmental benefits in term offspring [12-15]. It is only now that the medical research community is starting to contemplate how stem cells in breastmilk may play a fundamental role in the maturation of the preterm immune and gastrointestinal systems to the level needed to prevent NEC and other deadly infections in the NICU [12].

The first hint that breastmilk stem cells may be involved in the survival of preterm infants via protection against NEC came from an animal study by Zani and colleagues in 2014, which showed that various types of externally provided stem cells improve survival and increase the repair of damaged tissue in NEC-affected mice [16]. An understated outcome of this study, which likely went largely unnoticed, was that the greatest survival was found in the control group of mice, which was the breastfed group!

Since this study showed actual, measurable differences in the survival of the animal group that received fresh breastmilk, neonatologists have been wondering whether the standard practice in the NICU of feeding frozen or pasteurized breastmilk to preterm babies adversely affects these babies. Can we do better than that?

In an effort to tackle this question, Sun and colleagues performed a pilot study examining approximately 100 very preterm babies in each of two groups: a control group that was provided the usual previously frozen breastmilk (mother's own or donor), and an intervention group that was given fresh mother's own milk once daily in addition to the rest of the usual frozen milk [1]. And although perhaps this study was not powered to detect major differences, surprisingly enough, significant benefits were found in the intervention group.

The intervention group had shorter durations of mechanical ventilation and parenteral nutrition [1]. Significantly lower incidence of NEC, mortality, sepsis, retinopathy of prematurity, and bronchopulmonary dysplasia were also recorded for the intervention group [1]. And all these effects occurred even with only one fresh breastmilk feed a day!

Interestingly, no critical incidents were observed during the study, supporting the safety of feeding the preterm infant, even the very preterm, fresh mother's own milk [1]. This now sets new grounds against the notion that fresh mother's own milk may be a source of bacterial and viral contamination for her child, especially since the baby has already been exposed to the mother's microbiome during pregnancy. Now the emphasis is shifted for mother's own milk from a potential "contaminant" to a potentially important inoculate of a beneficial microbiome necessary for the healthy development of the neonatal gastrointestinal tract [1,19].

Importantly, the provision of mother's own milk to preterm babies has often been discussed in light of the reduced milk production of their mothers or the availability of the mother to provide freshly expressed milk. In the Sun study, 87.5% of mother's in the intervention group were able to express at least one feed of fresh breastmilk a day [1], further supporting not only the safety, but also the feasibility of a fresh milk-centered approach for feeding the preterm infant in the NICU.

These results are indeed noteworthy and should not go unnoticed. Although a randomized multi-center study recruiting many more subjects is currently underway, this first pilot study by Sun and colleagues [1] shakes the well-established dogma of freezing mother's own milk or pasteurizing donor milk prior to provision to the preterm infant. If fresh mother's own milk is safe for the preterm babies, and not simply beneficial but actually lifesaving, if it reduces the prevalence of NEC and sepsis, why do we currently deprive them from this? This is a question for all health professionals and policy makers that needs to be seriously considered and acted upon to improve the outcomes of our most vulnerable infants, and give renewed hope to their families. If death can be prevented and disability avoided simply by providing to these babies what is rightfully theirs, let's do it.

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Contributed by

Prof. Foteini Kakulas (formerly Hassiotou)

Adjunct Research Fellow

University of Western Australia

Dr. Shoo K. Lee

Scientific Director, Canadian Institutes of Health Research

Professor, University of Toronto

Pediatrician-in-Chief, Mount Sinai Hospital, Toronto

Discovery of “Dark Matter” in Livestock Genomes

- **The genomes (DNA) of livestock animals each contain about 20,000 genes that code for proteins.**
- **Livestock genomes additionally contain thousands of genes that do not code for proteins, and when active these genes produce long noncoding RNAs.**
- **Most long noncoding RNAs are specific to a species, however about 50 were identified in all five species studied: human, mouse, cow, pig, and chickens.**
- **Long noncoding RNAs are speculated to regulate the activities of protein-coding genes.**
- **DNA marker-assisted breeding programs aimed at improving livestock production efficiencies, like getting more milk for less feed in dairy cows, could be enhanced by exploiting additional genetic markers directly associated with the controls of gene activity.**

Paradoxes are uncomfortable. They remind us of how little we understand. Worse, it sometimes seems the more we know, the less we understand, and that's a bitter-sweet paradox in itself. Nowhere are paradoxes more apparent than in our understanding of life, and in particular the scientific understanding of the encyclopedia of life—the genome present in every living cell. Many scientists conclude that without understanding these genomic paradoxes, humans cannot fully exploit the amazing potential of genetics to improve human health and enhance the efficiencies of livestock production systems. The latter occurs primarily through DNA marker-assisted selective breeding of livestock [1, 2]. This process exploits the genetic (DNA) variations present in a large population of a livestock species to help select for the high-performing animals that then go into breeding programs. The aim is to improve animal productivity in each generation. It's a little like how a savings account grows with each year of interest.

Genomic Paradoxes Rule!



The genome contains all of the genetic material in a cell, which includes all genes. It is the blueprint for life, and it shouts out that all life is related. The genome contains a huge amount of encrypted information that is only partially deciphered [3]. But many scientists note that there are glaring paradoxes. First, how does the genome direct the form and function of a complex living organism, like a human or dairy cow, when the genome only contains about 21,000 genes that code for proteins, a similar number to that present in a tiny worm

consisting of only a thousand cells [4, 5]? Second, only a minuscule 1.5% of the mammalian genome contains genes that code for proteins [1, 6, 7], the mainstay of cellular functions, and only about 8% of the genome, including these genes, is thought to be functional [8]. Yet, mammals have diligently carried the remaining 92% of their genomes on their respective chromosomal backs for millions of years of evolutionary history. For each mammalian species, the DNA sequence in this big chunk of the genome changed a lot with evolutionary time, but it was always there. Usually, when traveling on a long trek, non-essential baggage gets dumped early. What, if anything, does this 92% of the genome do? Third, the sizes of the genomes of multicellular life forms are unrelated to their biological complexities [9]. Surely, mammals like the dairy cow and in particular humans have some of the largest genomes. Not so. Embarrassingly, the humble single-celled amoeba living the quiet life in a pond has a genome size much larger than that of a cow or human [9]. Adding insult to injury, even toads and onions have genomes slightly larger than those of mammals [9]. The three big paradoxes are likely interrelated and scream the obvious; something is badly amiss in scientists' understanding of genomes.

Discovering the “Dark Matter” in Livestock Genomes

Recently, a team of eleven scientists from the University of California at Davis applied a powerful new technology, called RNA-Seq, to detect tens of thousands of active genes in eight very different tissues taken from the cow, pig, and chicken [10]. The lead author was Colin Kern and the team's intriguing results were published in the journal *BMC Genomics* [10]. In all, the investigators produced a staggering four billion pieces of scientific data! They also discovered more than they bargained for, perhaps much more: the “dark matter” of livestock genomes [11].

What Is an Active Gene?

An active gene is one that produces RNA, the first cousin of DNA. This process is called transcription. Often genes are active in one tissue but not another, or active in very early life but not in mature life (or vice versa). Other genes have mundane but essential house-keeping roles in all cells throughout life. In the transcription process, the coded molecular information in a gene's DNA is transcribed and then processed into an RNA. It is a little like a wayward monk transcribing the bible in the middle ages who leaves out a few chapters and rearranges some verses here and there, but in the end, his finished book is still amazingly coherent. The molecular codes present in most RNAs contain detailed instructions for making specific proteins. Proteins are used to build structures in cells like molecular machines, communication systems, power plants, regulatory systems (traffic lights), repair systems, and transport systems. They even have a testy management group that keeps things on track and takes no nonsense. Multiple teams of scientists in the 1960s first deciphered the protein code in RNA, a milestone of human achievements [12]. Since that time, many scientists became obsessed with protein-coding genes and their transcribed RNAs; they were lured by the intriguing code of molecular order in the seeming chaos of life. But their obsession hid the larger picture.

The RNA World Is Big

Kern and colleagues, as well as many others, demonstrated that there is a great deal more going on in the RNA world than just producing RNAs coding for proteins [1, 2, 10, 13]. The breakthrough in this area of science was due to a new technology, RNA-Seq, that rapidly characterizes tens of thousands of RNAs and their abundances well before a much-anticipated mid-morning espresso the next morning. In the past, this type of measurement was laboriously performed for one specific RNA at a time and, importantly, the RNA had to be already known to exist; the scientists then were oblivious to the bigger RNA world. The new technology measures all RNAs! That's also an enormous challenge for scientists to digest after their morning espresso when they find their computers full of massive quantities of nondescript data and rude complaints from a data manager.

At first, Kern and colleagues identified the active genes that coded for all of the proteins made in eight tissues from the cow, pig, and chicken. This was relatively easy for the investigators as these genes were already well-documented and many produced highly abundant RNAs in the tested tissues from all three species, i.e. there was a lot of experimental data for these genes. The numbers of protein-coding RNAs discovered were about the same for the cow, pig, and chicken tissues. Other scientists point out that most genes that encode proteins are also present in related animal species, and only a minority are unique to a species [14]. Thus, Kern and colleagues indicated that it is unlikely that the protein-coding genes alone could explain the enormous form and function differences of the cow, pig, and chicken. Kern and colleagues then discovered that there were considerable and unexpected complexities associated with how individual genes produce protein-coding RNAs in each species. Complexity starts to rear its head.

Next, the investigators looked very closely at the remaining RNAs, the ones that did not code for proteins [10]. They restricted their analysis to only long noncoding RNAs (the variety of tiny RNAs present in most tissues was not part of their analysis). The surprise for Kern and colleagues was that there were about 10,000 long noncoding RNAs produced in each of the cow, pig, and chicken species, and about half of these RNAs had never been previously detected in any species. The investigators had discovered the "dark matter" of the genome. They explained that these long noncoding RNAs were hidden for a long time because they were hard to find for a variety of reasons; long noncoding RNAs were present in cells in tiny amounts, many were unique to a particular species, and the few that were common to multiple species showed only weak relatedness in their RNA molecular codes.

By adding the long noncoding RNAs discovered in humans and mice to the cow, pig, and chicken RNAs, Kern and colleagues [10] then discovered a very special collection of about 50 long noncoding RNAs common to all five species. The investigators suggested that this small group of RNAs was very important for regulating the physical packing of the genome within chromosomes and by inference the evolutionarily ancient processes that are common to all of these animal species, i.e. helping to regulate the remarkable biological transformation from a fertilized egg to a complex animal. Kern and colleagues also noted the mystery surrounding the functions of most of the huge number of long noncoding RNAs that were uniquely present in each livestock species. They speculated that many of the long noncoding RNAs could regulate the activities of other genes, particularly, when, where, and how much of the protein-coding RNAs are produced. These collective results from Kern and colleagues clearly indicate that a much bigger fraction of the genome than 8% is functional and that there are many new elements of complexity associated with the regulation of gene activity that may underpin the huge variation in the biological complexities of animals.

The three genomic paradoxes are starting to crumble and reveal a new biological order. Kern and colleagues and others suggested that long noncoding RNAs primarily regulate the activities of protein-coding genes [1, 2,

10, 11, 13]. The investigators inferred that since many of these newly discovered RNAs were specific to one species, then they are likely to be important for the unique form and function of each species, and possibly contribute to some of the genetics-based production differences between individuals within a livestock species population. This genetics-based individual variation in a species population is the bread and butter of selective breeding programs widely used in livestock industries. The revelation inferred from the research of Kern and colleagues is that population variation for complex production traits within a livestock population, like milk quantity, feed efficiency, and muscle deposition, could be mostly about how gene activities are regulated rather than the genes themselves.

Implications

The pace of genetic improvement in livestock has markedly accelerated over the last 50 years as producers applied intensive selection pressure in their breeding programs to produce more productive animals. Perhaps the best example is the dairy cow. Scientists at the USDA calculated that from 1980 to 2015, milk production in the USA increased by about 60% and at the same time, the size of the national dairy herd decreased by about 16% [15]. This history of exceptional improvement in dairy industry efficiency also occurred elsewhere in the world and was achieved by better herd management, better nutrition and pastures, improved disease control, and importantly, continued genetic improvement of animals through intensive selective breeding for commercially desirable dairy production traits [16].

More recently, livestock genetic improvement programs have been accelerated by the application of DNA marker-assisted selective breeding of animals [17], i.e. using DNA variations in the genome to help select specific high-performing animals for entry into breeding programs. Some scientists suggest that this approach is limited as the hundreds of thousands of DNA markers used in these DNA marker-assisted breeding programs are largely not positioned in the genomic regions where all the biological action occurs. You always get a better picture closer to the action.

The research undertaken by Kern and colleagues [10], and others [2, 18, 19], hints that the efficiency of DNA marker-assisted selective breeding programs could be further improved if additional DNA markers were included that represented genetic variation in the very special regions of the genome that regulate the complexities of gene activity and include the multitude of newly discovered genes producing long noncoding RNAs [2]. This strategy could allow the livestock industries, especially the dairy industry, to further improve their efficiencies of production. Generating more from less is the name of the game in the livestock and poultry industries and this seeming paradoxical goal now may be even more likely to be achievable.

How wonderful that we have met with a paradox. Now we have some hope of making progress. (Niels Bohr)

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*Contributed by
Dr. Ross Tellam (AM)
Research Scientist
Brisbane, Australia*

Treating Lactose Intolerance and Malabsorption

- **People who struggle to digest lactose should not completely avoid dairy products, instead they should manage their consumption.**
- **Certain dairy products, such as yogurt and kefir, are well-tolerated by lactose-intolerant individuals.**
- **There are various innovations, such as lactase tablets and pre-biotic treatments, that seek to enable lactose-intolerant people to gain the health benefits of consuming dairy, without experiencing the unpleasant symptoms of troublesome digestion.**

The ability to digest lactose is essential for very young humans, for whom the sugar provides approximately one-third of their daily calories. But upon weaning and growing up, to varying extents, human bodies become less proficient at this task. For many people, the change is so evident that they are diagnosed as lactose intolerant, and, as a result, cut dairy completely out of their diets in an effort to avert unpleasant symptoms. Yet the medical consensus advises against this [1]. Several strategies to manage the symptoms of lactose intolerance and malabsorption are instead proposed: careful dietary management, supplementing the missing lactase enzyme, and, most recently, consuming pre-biotics.



The symptoms of lactose intolerance arise because, in the absence of the enzyme lactase, the sugar hangs around in the gut where it alters the osmotic forces. Gut bacteria are left to ferment lactose, leading to the rapid generation of gases. The reason that some people do not produce lactase is genetic. Most people with European ancestry who can digest lactose owe this ability to a single nucleotide mutation known as “T-13910,” which is situated in a “control” region of the genome (specifically, a transcription factor), upstream of the lactase gene. A few other mutations are associated with lactase

persistence into adulthood, as detailed in a [previous issue](#) of *SPLASH!* [2].

Managing lactose intolerance is often difficult because it is misdiagnosed. Self-diagnosis is frequently misguided. One review of 26 studies reported that during testing, both people whose bodies have no trouble absorbing lactose and those whose bodies struggle to digest it frequently report symptoms [3]. Bloating, bellyache and so forth simply have various possible causes, yet lactose intolerance is often assumed because it is a well-known medical term. The standard diagnostic test measures changes in the concentration of hydrogen gas in the breath after consuming a lactose solution. High readings imply that gut bacteria are doing the lactose digestion rather than lactase produced by one's own body. The hydrogen breath test is also used to find out if strategies to manage lactose intolerance are effective.

The most obvious way to manage lactose intolerance or malabsorption is to watch what you eat. Even completely intolerant individuals tend to be unaffected by small amounts of lactose in the region of 12–15 grams of lactose per day. Indeed, some dairy products, such as [yogurt](#), are especially well tolerated by lactose-intolerant individuals because yogurt passes more slowly through the digestive system than does milk, and because the bacteria in live yogurt start to break down lactose inside the gut before resident gut bacteria get the chance [4]. Eating yogurt, or drinking fermented milk beverages such as kefir, or leben, as opposed to other kinds of dairy, therefore enables lactose-intolerant people to get more of the considerable health-promoting benefits of dairy, such as calcium that strengthens the bones, and better protection against [digestive problems](#) and [cardiovascular diseases](#) [5,6]. In particular, dairy foods that contain bacteria that produce beta-D-galactosidase are understood to be especially calming of the symptoms of lactose intolerance [2].

An alternative to avoiding dairy is to find non-dairy substitutes that contain the nutrients and minerals otherwise lacking in one's diet. In recent years, many products have appeared on supermarket shelves, claiming to be fortified with proteins, calcium, and vitamins such as A, D, and B12. But typically there is an important unknown in switching one's diet to these products: that they contain particular components does not automatically imply that the components are easily available to the body for absorption. Whereas the "Digestible Indispensable Amino Acid Score" of cow's milk protein is extremely high—meaning that it contains very high-quality and bioavailable proteins—the protein bioavailability of most fortified plant-based beverages is unknown [2]. The same goes for the vitamins and minerals that are added to these products. [One study](#) of more than 5,000 Canadian children found that children who consumed plant-derived substitutes for dairy, such as soy and almond milk, were on average 0.4 cm shorter in height than those who drank milk [7].

Another strategy for managing lactose intolerance while seeking to avoid the downsides of low dairy consumption is to deliver lactase to one's intestines in gel, capsule, or tablet form, so that the enzyme survives the journey through the acidic environment of the stomach. To date the results of this approach have been encouraging yet patchy—one study analyzing shifts in the hydrogen breath scores of lactase-deficient people given two lactase tablets per day reported significant reductions in breath hydrogen among 18% of participants but no change in the rest [2].

Then there are pre-biotics (foods that induce the growth of "good" gut bacteria). The Food and Drug Administration in the United States recently approved galacto-oligosaccharide for the management of lactose intolerance. This is a prebiotic that has been demonstrated to improve hydrogen breath test scores in randomized double-blind trials. After 30 days of ingesting galacto-oligosaccharide, participants in one of these trials were six times more likely than the participants who received a placebo to report experiencing no problems tolerating lactose after their ate dairy foods [8].

These innovations, and the deepening understanding of contributors to nutrient bioavailability, mean that options for reaping the health benefits of dairy consumption are increasing for lactose-intolerant people. In the day-to-day, it would be far easier, if food labeling were better standardized, to enable consumers to

straightforwardly assess the lactose content of different products. Scientists are calling on governments to introduce legislation that mandates this [2]. Consumers would benefit if they did.

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Contributed by

Anna Petherick

Professional Science Writer & Editor

www.annapetherick.com

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