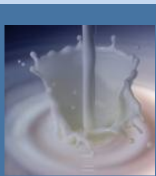
SPLASH! milk science update: June 2015 Issue



SPLASH! milk science update
June 2015 Issue

This month's issue explores how a mother's DNA alters the gut microbiome of her baby, lower vitamin D in children who avoid cow's milk, the economics of breast milk banking, and predictions of a dairy cow's performance using DNA.

Mother's DNA Alters Baby's Gut Microbes

- **About 20% of mothers in the US have an inactive version of a gene that modifies sugars in breast milk.**
- **A new study finds that the gene, FUT2, affects the amount and type of bifidobacteria present in the intestines of breastfed infants.**
- **Bifidobacteria were established earlier and in greater amounts in infants whose mothers had an active copy of the FUT2 gene.**
- **The study provides insights into how breast milk sugars affect populations of specific bacteria in infants.**
- **Bifidobacteria are known to have several beneficial effects, and the results could lead to ways to enrich beneficial bacteria in at-risk populations, such as premature infants.**

A mother's genes determine a lot of things about her newborn, and it turns out that their effects extend even to the bacteria that colonize the baby's gut. The establishment of a baby's gut microbial community is an important event in a newborn's life. A new study, conducted by microbial ecologist Zachary Lewis, finds that the gut microbiome of breastfed infants is influenced by the types of sugars present in breast milk [1, 2]. Specifically, a particular gene in mothers that modifies sugars in breast milk influences infants' gut microbiome.

"This is one of the first in vivo tests to see how the composition of breast milk sugars can affect the gut microbiome," says Lewis, a postdoctoral fellow in the laboratory of David Mills at the University of California at Davis. The researchers studied a gene called fucosyltransferase 2 (FUT2), which modifies sugars in breast milk. About 20% of mothers in the United States have a natural mutation in FUT2 that renders the gene inactive, and the researchers examined how mothers' FUT2 status affected babies' gut microbial communities [3].

Lewis and his colleagues examined breast milk samples from 44 women and analyzed fecal samples from their babies. Twelve of the 44 women had the mutated inactive version of the FUT2 gene, while 32 had the active version. "Between mothers who have an active copy of the gene, and mothers who don't, there are differences in their babies' microbiome," says Lewis.

In particular, the researchers looked at how the presence of an active copy of FUT2 affected bifidobacteria, which are some of the first bacteria to colonize breastfed infants. "There are differences in the amount of bifidobacteria, and the types of bifidobacteria," says Lewis. Bifidobacteria were established earlier and in greater amounts in infants whose mothers had an active copy of the FUT2 gene, compared to those with an inactive copy of the gene. The study thus provides insights into what types of breast milk sugars are most likely to lead to high bifidobacteria populations in healthy infants.

Different species of Bifidobacterium have varying preferences for the FUT2-modified sugars. "Some species of bifidobacteria really like those sugars, and others don't need them as much," says Lewis. Infants whose mothers had the active form of FUT2 were enriched for bifidobacterial species that liked FUT2-modified sugars, whereas such species were less abundant in infants whose mothers had inactive FUT2.

Bifidobacteria have previously been shown to have various beneficial effects in infants, and are often used as probiotics. "They seem to do a number of things that are good," says Lewis. This includes reducing inflammation and gut permeability, providing protection from pathogens, and improving immune response to vaccines [4-10].

Although the current study did not look at the health effects of the FUT2-related changes in gut microbes, that's something the researchers plan to look at in the future. One of the ways they're addressing this question is by looking in premature babies. "We've known for a while that premature babies who receive some of their mother's milk seem to have lower incidences of diarrheal diseases," Lewis says. He notes that this effect could potentially be explained by breast milk's influence on gut microbes, especially given that babies who ingest more bifidobacteria seem to be more resistant to gastrointestinal diseases. “Eating more bifidobacteria seems to be protective, and breast milk helps to get more bifidobacteria,” says Lewis.

Lewis emphasizes that regardless of whether the FUT2 gene is active or inactive, “breast milk still seems to be a very good thing for infants.” Breast milk seems to play an important role in establishing the baby’s microbiome, and by understanding this role, researchers could promote the presence of protective and beneficial species of bacteria in at-risk populations, such as premature infants, Lewis says. Although more testing and validation will be needed before the study’s results can be applied, “now that we know that this effect exists, we can look and try to figure out how to do this,” he says.

1. Scholtens PAMJ, Oozeer R, Martin R, Amor Ben K, Knol J. The early settlers: intestinal microbiology in early life. Annu Rev Food Sci Technol. 2012;3:425–47.
2. Lewis ZT, Totten SM, Smilowitz JT, Popovic M, Parker E, Lemay DG, Van Tassell ML, Miller MJ, Jin YS, German JB, Lebrilla CB, Mills DA. Maternal fucosyltransferase 2 status affects the gut bifidobacterial communities of breastfed infants. Microbiome. 2015;3:13
3. Castanys-Muñoz E, Martin MJ, Prieto PA. 2′-Fucosyllactose: an abundant, genetically determined soluble glycan present in human milk. Nutr Rev. 2013;71:773–86
4. Fukuda S, Toh H, Hase K, Oshima K, Nakanishi Y, Yoshimura K, et al. Bifidobacteria can protect from enteropathogenic infection through production of acetate. Nature. 2011;469:543–7.
5. Liévin V, Peiffer I, Hudault S, Rochat F, Brassart D, Neeser JR, et al. Bifidobacterium strains from resident infant human gastrointestinal microflora exert antimicrobial activity. Gut. 2000;47:646–52.
6. Huda MN, Lewis ZT, Kalanetra KM, Rashid M, Ahmad SM, Raqib R, et al. Stool microbiota and vaccine responses of infants. Pediatrics. 2014;134:e362–72.
7. Chichlowski M, De Lartigue G, German JB, Raybould HE, Mills D. Bifidobacteria isolated from infants and cultured on human milk oligosaccharides affect intestinal epithelial function. J Pediatr Gastroenterol Nutr. 2012;55:321–7.
8. Sheil B, MacSharry J, O’Callaghan L, O’Riordan A, Waters A, Morgan J, et al. Role of interleukin (IL-10) in probiotic-mediated immune modulation: an assessment in wild-type and IL-10 knock-out mice. Clin Exp Immunol. 2006;144:273–80.
9. Tanabe S, Kinuta Y, Saito Y. Bifidobacterium infantis suppresses proinflammatory interleukin-17 production in murine splenocytes and dextran sodium sulfate-induced intestinal inflammation. Int J Mol Med. 2008;22:181–5.
10. Preising J, Philippe D, Gleinser M, Wei H, Blum S, Eikmanns BJ, et al. Selection of bifidobacteria based on adhesion and anti-inflammatory capacity in vitro for amelioration of murine colitis. Appl Environ Microbiol. 2010;76:3048–51.

Contributed by
Dr. Sandeep Ravindran
Freelance Science Writer
Sandeepr.com

Children Who Avoid Cow’s Milk May Fall Short of Vitamin D

- **Vitamin D deficiency in children is associated with bone demineralization and other potentially long-term effects on bone health and immune function.**
- **Very few foods naturally contain vitamin D, making fortified cow’s milk one of the best dietary sources of this essential nutrient, particularly for young children.**
- **Children who avoid cow’s milk as a result of allergy, intolerance, or dietary preference are at a greater risk for vitamin D deficiency.**
- **Because of the growing public interest in non-cow’s milk beverages (e.g., soy, almond milk), there is a need for better education about the potential nutritional shortcomings of these milk alternatives.**

Rickets and vitamin D deficiency do not sound like 21st century issues. Yet nearly 100 years since the connection between the two was first identified, the U.S., Canada, and numerous other countries are facing a potential epidemic of vitamin D deficiency among children (1). The reasons for the resurgence are much the same as they were in the past: limited sunlight exposure and poor dietary intake of this essential nutrient. Vitamin D-fortified milk helped bring an end to the rickets epidemic in the early 1900s, and it remains the best dietary source of vitamin D for children today. However, a growing number of children do not drink cow’s milk. A handful of studies in the U.S. and Canada have found that children who avoid cow’s milk due to allergy, intolerance, or dietary preference for alternative milk beverages are at a greater risk for vitamin D deficiency (2-4). When coupled with medical advice to avoid the sun, these findings could help explain the increasing prevalence of vitamin D deficiency in otherwise healthy children. While scurvy may have gone the way of the pirate, rickets is still a modern concern.

The sunshine vitamin

Vitamin D is a term for a set of steroid hormones that help the intestines absorb calcium and phosphorus. Without sufficient levels of vitamin D, only 10-15% of dietary calcium and only 60% of dietary phosphorus are absorbed (5).

Because calcium and phosphorus make up the mineral content of bone, a deficiency in vitamin D influences bone mass, and can ultimately result in rickets (bone demineralization) in infants and children. Vitamin D is important for many physiological functions beyond bone health, playing a role in innate immunity and prevention of several chronic conditions including cancer, diabetes, and cardiovascular disease (3, 5).

Vitamin D is unique among vitamins because it is available both from the diet and from ultra-violet (UV) light. Vitamin D is not metabolically active when ingested or absorbed in the skin; it must be converted to its metabolically active form, 25-hydroxyvitamin D (25 OHD), by the liver. Serum levels of 25 OHD are used to determine vitamin D status, with levels below 50 nmol/L considered indicative of deficiency, and levels above 75 nmol/L considered optimal for obtaining peak bone mass in children (1, 2, 5, 6).

Vitamin D deficiency among children has resurfaced as a major health concern. The reasons for this are two-fold. Firstly, health professionals recommend avoiding the best source of vitamin D—sunlight—because of the potential risks of skin cancer. Protective clothing and sunscreen can help prevent the formation of cancerous cells in the skin by blocking out UVB radiation, but this is the very thing that converts a chemical in the epidermis (called 7-Dehydrocholestrol) into vitamin D. Secondly, there are very few dietary sources of vitamin D. For growing children, the current dietary recommendation in the U.S. and Canada is at least 400 IU (international units) per day (recommendations for pregnant, lactating, and older adults can range anywhere from 400–1000 IU)(6). Fatty fish, such as salmon and tuna, are the best source, having between 500 – 1000 IU of vitamin D in a 3.5-ounce serving. Egg yolks and mushrooms also contain vitamin D, but larger portions are required to meet the daily-recommended values. For example, in order to get 400 IU of vitamin D, you would need to consume 10 eggs or around 5 1/2 cups of shiitake mushrooms (1). While fortified cow's milk falls short of fatty fish (an 8-ounce cup of fortified cow's milk in the U.S. contains 100 IU), it is the most common dietary source of vitamin D for children. In addition to its vitamin D content, cow's milk also contains numerous other nutrients and bioactive components that play a role in bone growth, including calcium, phosphorus, whey proteins, and lactose.

What's in your grocery cart?

But what about children who do not consume cow's milk, either due to allergy, lactose intolerance, taste preference, or dietary practices (e.g., veganism)? With so few dietary options for vitamin D, it is not surprising that North American children who avoid drinking cow's milk have been found to have lower serum 25 OHD levels than their cow's milk-drinking peers (2-4).

Gordon and colleagues (3) analyzed serum samples collected from urban Boston infants and toddlers (8–24 months old) at well check visits (3). Of the 380 otherwise healthy participants, 40% were found to have 25 OHD levels below that optimal threshold of 75 nmol/L and over 12% were deficient (<50 nmol/L). The most important predictor for vitamin D deficiency among infants was breastfeeding without vitamin D supplementation and, among weaned toddlers, it was lower cow's milk intake. With each additional 8-ounce cup of cow's milk consumed per day (determined by dietary data provided by parents), serum 25 OHD increased 7.2 nmol/L.

Maguire et al. also identified an almost identical protective effect of cow's milk consumption in their study of over 1300 healthy 2–5 year olds living in Toronto (2). For every 8-ounce cup of fortified cow's milk consumed, serum 25 OHD levels increased by 5 nmol/L. They conclude that for children with lighter skin pigmentation, approximately 2 cups of fortified cow's milk per day was sufficient to maintain serum 25 OHD levels above the 75 nmol/L threshold. Because of the interaction with skin pigmentation and vitamin D absorption (darker skin reflects more light and thus blocks out more UVB), children with darker pigmentation who were not taking vitamin D supplements would require about twice as much cow's milk to maintain the same levels, especially in winter months in this high latitude location.

Taking it one step further, Lee et al. (4) were specifically interested in vitamin D status of children who avoid cow's milk, and instead consume alternative beverages such as goat, soy, rice, or almond milk (which they refer to collectively as non-cow's milks). Although many of these non-cow's milks are fortified with vitamin D, it is not required, and therefore the levels can vary because they are not regulated. From 2008 to 2013, they collected dietary data and serum samples (as well as information on sun exposure and vitamin supplementation) from nearly 3000 healthy children between the ages of 1 and 6 years of age living in the Toronto area. All else being equal, children who consumed only non-cow's milk were at a higher risk of having 25 OHD levels below 50 nmol/L than those who drank only cow's milk (11% vs. 4%). They also identified a dose-dependent effect of non-cow's milk consumption; every additional cup consumed was associated with a 3.1% decrease in serum 25 OHD. Around 18% of their study population consumed both types of milks, allowing them to test for a potential trade-off between the two types of milks. Consumption of non-cow's milk did indeed appear to modify consumption of cow's milk, with a 4.2 nmol/L drop in 25 OHD with each additional 8-ounce cup of non-cow's milk consumption reported for children who also consumed cow's milk.

One major limitation acknowledged by each of these studies is that they are cross-sectional in design and therefore cannot establish causality. However, that they all converge on the same finding—a protective effect of cow's milk on vitamin D status—is strong support for a relationship between the two variables. Another potential limitation is that results may only be applicable to North American populations living at higher latitudes, like Boston or Toronto, where availability of vitamin D from the sun would be more seasonal than at locations closer to the equator. Vitamin D deficiency is, unfortunately, a global problem (6), suggesting latitude is not the most important predisposing factor.

Putting the D into diet

There is strong evidence to suggest that avoiding cow's milk negatively affects vitamin D status among North American children. Many families may select cow's milk alternatives such as soy, almond, or rice because of perceived nutritional benefits or taste preference, while others do so because of allergies or intolerance to cow's milk. Regardless, education from health care providers about the potential nutritional differences and the need for supplementation is clearly needed. But because compliance with supplementation can be challenging, and with a growing public interest in cow's milk alternatives, Lee et al. (4) suggest that both the U.S. and Canada consider mandatory vitamin D fortification of these milk alternatives. With so many different manufacturers and variation in how these milks are produced, this is not as simple of a solution as it may sound. But with something as critical as childhood bone health hanging in the balance, it seems well worth the effort.

1. Holick MF. 2006. Resurrection of vitamin D deficiency and rickets. The Journal of Clinical Investigation 116:2062-2072. doi:10.1172/JCI29449.
2. Maguire JL, Lebovic G, Kandasamy S, Khovratovich M, Mamdani M, Birken CS, Parkin PC. 2013. The relationship between cow's milk and stores of vitamin D and iron in early childhood. Pediatrics, 131: e144-e151.
3. Gordon CM, Feldman HA, Sinclair L, Williams AL, Kleinman PK, Perez-Rossello J, Cox JE. 2008. Prevalence of vitamin D deficiency among healthy infants and toddlers. Archives of Pediatrics & Adolescent Medicine 162: 505-512.
4. Lee GJ, Birken CS, Parkin PC, Lebovic G, Chen Y, L'Abbé MR, Maguire JL. 2014. Consumption of non–cow's milk beverages and serum vitamin D levels in early childhood. Canadian Medical Association Journal 186: 1287-1293.
5. Holick MF. 2007. Vitamin D deficiency. New England Journal of Medicine, 357.3: 266-281.
6. Wagner CL, Greer FR. 2008. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics 122: 1142-1152.

Contributed by
Dr. Lauren Milligan
Research Associate
Smithsonian Institute

Milk Banking in the 21st Century

- **The Internet has facilitated many new arrangements in breast milk sharing.**
- **Without sterilization or pasteurization, breast milk can pass pathogens to infants, particularly if there is an opportunity for bacteria to grow during shipping.**
- **Modern human milk banks include both non-profit organizations and for-profit strategies.**
- **For-profit companies may increase the overall supply of human milk, but some argue that they create new problems.**

When historians look back on the past 15 years, they will undoubtedly characterize the period through reference to widespread use of its defining technology: the Internet. Among its many benefits, the Internet is a perfect tool for aggregating many small scale and widely dispersed suppliers, and enabling buyers and sellers of obscure products to locate one another. It has therefore facilitated the exchange of human milk. From Craigslist postings to Facebook groups, individual altruism to cooperatives with exclusive sales agreements with private companies, the online exchange of milk now takes many forms.

Elena Medo is the CEO of Medolac, one of the new for-profit human milk companies. She also founded (and left) the other main player, called Prolacta, and in doing so launched what she says was the first human milk website, where would-be donors could apply online, and those who passed initial screening then received house-calls for blood testing. Medolac sources all of its milk from a cooperative, but elsewhere in the tentacles of the Internet, it is perfectly possible for mothers to receive direct payment for milk based on peer-to-peer online exchange. This, of course, carries at least the potential risk of pathogen transfer, or that unscrupulous sellers might add cows milk or some other product to increase sales volumes.

Some people, however—including the CEO of HMBANA (the Human Milk Banking Association of North America), John Honaman—are entirely against moneymaking out of breast milk, in part because it sets up these kinds of perverse incentives. “With so much need in the environment in and outside the hospital, we believe that the best way to meet it is to be nonprofit,” emphasizes Honaman. In more precise terms, HMBANA estimates that 60,000 milk donor-mothers would be required to meet the needs of all of the infants in NICU’s across North America and the young outpatients with doctor’s prescriptions for human milk, yet at present HMBANA only has 4,000 donors signed up.

Tellingly, the entry of for-profit companies into the space has not reduced HMBANA’s overall donated milk volume, which has in fact recently shown year-on-year increases. This implies that some women, who otherwise wouldn’t give their milk away for free, are starting to provide it because they are motivated by the promise of payment. Given the substantial and unmet need, is paying mothers for breast milk the way forward?

One simple argument in favor of payment is the simple fact that milk pumping takes time and effort, and therefore lumbers women with opportunity costs. Rachel Ellen, of the much newer company, Mammalia Breast Milk, puts it succinctly, “We believe paying for breast milk empowers women by giving them the opportunity to make money from home, take more time off work, and spend more time with their baby.” A simple argument against payment is the concern that poor women might reduce the amount of breast milk that they feed to their own infant, and instead sell it. This is certainly possible, admits Medo, although the cooperative from which Medolac sources its milk has instigated various precautions, such as only accepting milk from women who have been breastfeeding for three months or more.

Honaman’s complaints are not purely based on the ideology of maintaining a culture of altruism around breast milk. He thinks that some mothers are being misled. “For-profit entities use sophisticated marketing to emulate the spirit of what we do,” he complains. “They have created front organizations that interface with mothers. These entities carry names that can be easily confused with those of the HMBANA non-profit milk banks.” Certainly, Prolacta has been accused of not making it clear to mothers that they were providing milk to a for-profit in the past, most recently in a New York Times article[1]. Prolacta did not respond to multiple requests for an interview for this article.

Some profit-seeking companies are beginning to carve different kinds of middle-of-the-road solutions, however. Mammalia Breast Milk pays according to a donor’s socioeconomic needs, for example, as well as the volume and amount of time a donor has been with the company. Medolac processes for free and gives away whatever amount of milk mothers opt to not receive payment for. When the company first introduced its ‘pay-if-forward’ scheme, as it calls this, about one in a thousand mothers volunteered, says Medo. But since it started automatically slipping an extra bag for donations into shipper packs, most of the mothers have at some point sent it back with milk. About 5% to 6% of Medolac’s total processed volume now falls under this category, Medo estimates.

This is roughly in line with the 9.1% that is processed and given away to needy mothers by the International Milk Bank, another for-profit run out of Reno, Nevada. Glenn Snow, a former real estate broker who is the company’s CEO, is intent on keeping prices down. Compared to Prolacta, whose flagship product for NICU babies sells for about $180 per ounce, he says, “We’re instead trying to bring a lot more milk at an affordable price point to the market. We’re really focused on being a high-volume supplier and making it so that every baby that needs [human] milk has access to it.”

Snow argues that his for-profit model provides the financial resources needed to screen and process milk in far more appropriate ways than non-profit milk banks currently manage. Not all milk banks use methods that kill *Bacillus cereus*, he says, and some don’t thoroughly test for drug use by mothers. (Although Honaman defends HMBANA’s banks against this critique.) On this point, little is known about the hazards of milk in direct peer-to-peer online exchange, but one study led by Sarah Keim of Nationwide Children’s Hospital in Columbus, Ohio, has found higher levels of Staphylococcus bacteria in peer-provided milk compared with unpasteurized samples sent to milk banks[2]. Due to these concerns, the FDA has recommended “against feeding your baby breast milk acquired directly from individuals or through the Internet,” as reported by Katie Hinde. Worryingly, one study found that even though recipients in these exchanges were largely aware of the potential for pathogen transfer, less than half of them considered the potential for other kinds of contamination, such as drugs.

The size of this online community is not clearly characterized. The most thorough attempt comes from nutritional scientist Maryanne Perrin, of North Carolina State University in Raleigh[3], who monitored three Facebook milk-sharing communities in the Eastern US, three in the Centre of the country, and three in the Western states. Perrin found that the central region had the most milk sharing compared to the number of births in the region, and that the median offer of milk was 90 ounces—which is interesting because it is less than the typical per-mom minimum that formal outfits require. In only three months of monitoring, she also observed 532 individuals offering milk on the nine web pages in her study. This suggests that the online community may rival, if not surpass, HMBANA’s total number of donors.

Perrin has an alternative solution for increasing the volume of human milk available than simply offering mothers cash. She says that the majority of milk banks in the U.S. stop accepting milk from mothers when their most recent offspring reaches 12 months old. If her findings—which are not yet published—provide evidence of little or no change in nutrient content and function, they might contribute to extending the donation or sales period per mom.

Such an extension, like the evolution of online sharing platforms, better education for potential donors, and the incentive of an income, is likely to increase the overall supply of available human milk. And that is a good thing because in spite of well known health benefits to very young infants, some of the most recent surveys report that a minority—22% to 42%—of maternity hospitals in the United States use donor milk in their advanced care units [4-6]. An increased supply also brings the potential for new products based on human milk. In next month's newsletter, SPLASH! will report on what those are.

1. Pollack, A. Breast Milk Becomes a Commodity, With Mothers Caught Up in Debate. New York Times, 20 March 2015.
2. Keim, S. A. et al (2013) Microbial Contamination of Human Milk Purchased Via the Internet. Pediatrics 132(5), e1227-e1235.
3. Perrin M. T. et al. (2014) A mixed-methods observational study of human milk sharing communities on Facebook. Breastfeeding Medicine 9(3), 128-134.
4. Perrine C.G. & Scanlon K. S. (2013) Prevalence of use of human milk in US advanced care neonatal units. Pediatrics 131, 1066-1072.
5. Parker M.C.K., Barrero-Castillero A., Corwin B.K. et al. (2013) Pasteurized human donor milk use among US level 3 neonatal intensive care units. J. Hum. Lact. 29, 381-389.
6. Colaizy TT. (2015) Donor human milk for very low birth weights: patterns of usage, outcomes, and unanswered questions. Curr Opin Pediatr. Apr;27(2):172-6. doi:10.1097/MOP.0000000000000201. PubMed PMID: 25689453; PubMed Central PMCID:PMC4414040.

Anna Petherick
Professional science writer & editor
www.annapetherick.com

Predicting Performance in Dairy Cows of the Future

- **Modern genomic tools can be used to predict how much milk dairy cows will produce.**
- **Scientists are working hard on maximizing the accuracy of these predictions while minimizing the cost.**
- **This study used markers that identify large sections of DNA to simplify analysis.**
- **The approach improved prediction accuracy.**
- **Soon these methods will be applied to predict milk production in the herds of the future.**

Selective breeding of dairy cows is a major part of modern dairy farming. Farmers can select the bulls they want to use to produce animals for their herd. One bull may sire thousands of daughter cows via highly developed systems for artificial insemination. The availability of lots of stored semen from bulls that have been shown to produce cows with excellent production and health traits has been a backbone of improving efficiency and production in dairy farms for several decades. There has been a continuous effort to build on the methods and procedures that contribute to selective breeding, most recently with the advent of genomic tools.

Genomic tools are based on detailed information arising from the Bovine Genome Sequencing Project. Since its first release, the bovine genome assembly has fuelled an enormous increase in activity to find the regions in the bovine genome where there are differences between individuals (referred to as genetic polymorphisms) that contribute to the capacity of cows to produce milk. Genome technologies have advanced to a stage where many individuals have had their entire genome sequenced, but when comparing cattle, the polymorphisms are a tiny percentage of the whole. Scientists are able to focus just on these parts to do calculations that predict how individual cows, and future generations of cows will perform in milk production.

The most common forms of genetic variation are called SNPs—single nucleotide polymorphisms. As the name suggests, these are single "letter" changes in the DNA sequence. Some are found within genes, but the majority are spread throughout the DNA sequence between the gene coding regions. In the case where a gene contains a SNP that alters a trait, it then is referred to as a causal SNP. However, because the genome is organized in blocks or haplotypes, knowing the position of SNPs that are close to the causal SNP allows scientists to do calculations based on the assumption that these SNPs track the cause. This assumption is how the science has progressed to-date, and the major effort has gone into increasing the number of SNPs analyzed, from 50,000 SNPs, to more recent tools that can identify over 770,000 SNPs.

Armed with this additional level of detail, geneticists have been evaluating how it can be used most effectively in genomic prediction. Surprisingly, the additional data does not translate into an equivalent increase in prediction accuracy. Mogens Lund and his colleagues from Aarhus University have been studying this issue in Nordic cattle and, for comparison, in French Holsteins with Didier Boichard from Institut National de la Recherche Agronomique (INRA). Their recent publications explored the improvement to prediction by using either haplotype-based methods [1], or including information from sequence data analysis [2].

The first study was based on the knowledge that, because they represent a block of DNA sequence, a haplotype contains more information than an individual SNP, and therefore are more likely to result in improved accuracy. The study began by defining haplotypes based on all the information drawn from 770,000 SNPs in each individual from a large number of cattle. When they used the haplotype approach for their genomic prediction calculations, they found a small but significant (3.1%) gain in accuracy for prediction of milk protein yield. In addition to the increase in accuracy, the method also allows a simplification of the number of SNPs required to capture the information, and would therefore translate into a reduced cost if the method was adopted.

The second study used data from previous analyses that identified some key DNA sequence information for dairy traits. This allowed the researchers to add SNPs from regions that had a known link to dairy traits. Again, the researchers were mindful of keeping the complexity of any direct measurements on cattle DNA to a minimum, with a view to producing a cost-effective method for potential industry applications. They looked at the capacity of this new set of markers to improve predictions of 17 dairy traits—ranging from body shape to milk production. The analysis showed an improvement in accuracy of up to 4% for production traits when the calculation put more emphasis on the added SNPs from the sequence data.

These studies are indicative of what is emerging in the field of dairy genetics globally: drawing together highly detailed data on dairy cattle genomes, reducing the complexity of the information that it contains to minimize the difficulty of calculations and the cost of potential applications, and gradually improving the accuracy of predictions. With such a flurry of research activity and the palpable excitement of what will result, we are very close to having accurate predictions of the best genetic composition of future generations of dairy cows.

1. Cuyabano BC, Su G, Lund MS (2014) Genomic prediction of genetic merit using LD-based haplotypes in the Nordic Holstein population. BMC Genomics 15: 1171.
2. Brøndum RF, Su G, Janss L, Sahana G, Guldbrandtsen B, Boichard D, Lund MS (2015) Quantitative trait loci markers derived from whole genome sequence data increases the reliability of genomic prediction. Journal of Dairy Science 98: 4107-4116.

Contributed by
Professor Peter Williamson
Associate Professor, Physiology and Genomics
University of Sydney, Australia

Funding provided by California Dairy Research Foundation and the International Milk Genomics Consortium.