Replacing Red Meat with Dairy Could Lower the Risk for Type 2 Diabetes

- Red meat consumption is associated with an increased risk of developing type 2 diabetes (T2DM).
- A prospective study of nearly 150,000 participants found that replacing one daily serving of red meat with low-fat dairy reduced the risk of developing T2DM in the following four years by 18%.
- The whey proteins in dairy foods may have a protective effect on glucose metabolism and insulin sensitivity.

From eating clean to eating like a caveman, there is no shortage of fad diets promising weight loss and improved health. But what is trendy might not always be effective. Although dietary regimes that eschew carbohydrates and focus on proteins seem ideal for keeping blood sugars in check, not all proteins have the same effect on insulin sensitivity and glucose metabolism, and some can even increase the risk for developing type 2 diabetes mellitus (T2DM) [1, 2]. For people wanting to maintain a high protein diet, a new study [1] offers some helpful guidance—replacing red meat consumption with other protein sources, including dairy, lowers the risk of developing T2DM.

It’s a Sensitive Topic

Cells in the human body use glucose (the sugars from the food we eat) for energy. And, insulin, produced by the pancreas, is the protein responsible for moving glucose from the bloodstream into cells (or into the liver, where it is stored to be used for energy at a later date). Being sensitive to insulin is a good thing—when insulin signals to cells that it has glucose to use for energy, the cells respond. But as sensitivity to insulin decreases, the pancreas needs to make more insulin to get a response. At some point, the pancreas cannot make enough insulin to signal a cellular response; this is insulin resistance, or T2DM. Even in the blood, sugar can be sticky; if glucose remains in the bloodstream it can stick to fats and proteins and damage the blood vessels. If left unchecked, this can result in serious conditions such as heart disease, vision problems, kidney disease, and stroke.

How Risky is Your Diet?

Dietary proteins, and the amino acids that these proteins are composed of, are biologically active and can influence the way the body uses and moves glucose into cells. Several prospective studies (i.e., studies that follow people for long periods of time, collect a lot of data on their lifestyle, and look for the development of diseases) indicate that red meat has a negative effect on insulin sensitivity, whereas soy protein, seafood, and dairy have a protective effect [1-3].

The most recent prospective study to tackle this topic [1] investigated how decreasing red meat consumption and simultaneously increasing consumption of other protein sources influenced the risk of developing T2DM. The researchers included three large prospective cohorts for a total of 148,853 participants and over 2,000,000 person-years of follow-up. Diet and several factors that would indicate an individual had T2DM were assessed at baseline (1986 for two cohorts and 1991 for the third) and every four years after using a food frequency questionnaire. Because of the four-year nature of data collection, the study specifically assessed how dietary changes over a given four-year period were associated with
the development of T2DM over the next four-year period.

Decreasing red meat intake and replacing it with poultry, seafood, nuts, eggs, legumes, and dairy (both low- and high-fat) was associated with a lower risk of T2DM in the following four-year period. More specifically, a one daily serving decrease in red meat with a concomitant increase in high-fat dairy lowered the risk of developing T2DM in the following four-year study period by 10%, and low-fat dairy lowered the risk by 18%, which was equivalent to the effect of replacement with seafood and poultry [1].

**Daily Dairy?**

The effect of replacing red meat with dairy foods on T2DM risk is likely the result of several properties that could directly impact glucose metabolism and insulin sensitivity. For starters, dairy products are associated with a small rise in blood sugar after consumption. This means less insulin is required to move that glucose out of the blood stream and into cells [4]. Additionally, whey proteins, which are unique to dairy foods, have been demonstrated to stimulate the pancreas to produce insulin. When those whey proteins are broken down into peptides during digestion, they can influence the movement of glucose from the bloodstream into cells, again pointing at the need for less insulin to move glucose into cells or the liver [4]. Calcium and beneficial bacteria found in fermented dairy foods, such as yogurt, cheese, and kefir, may also be involved, having favorable impacts on overall inflammation in the body, which can interfere with insulin production and delivery [1, 4].

Dietary and other lifestyle changes can be very effective in reducing the incidence of T2DM, a disease that currently affects over 30 million Americans. A major dietary overhaul can be a hard sell for physicians to their patients, but the overall takeaway from prospective studies suggests that small daily changes make a difference—no fad diet required.


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**The Promise and Challenges of Producing Human Milk in the Lab**

- Multiple startup companies are attempting to produce human milk from lab-grown cells to better replicate breast milk.
- Their efforts are still at an early stage and lab-produced human milk still has a lot of limitations, including the lack of important breast milk components such as immune cells and lipids.
- Lab-produced human milk is unlikely to replace breastfeeding, but it may have the potential to eventually serve as an alternative to formula.
- Additionally, studying how such lab-grown cells lactate could help researchers better understand lactation issues in humans and in the dairy industry.

Breastfeeding is known to be both nutritious and beneficial to the health of infants, including improving their immunity and helping to protect them from infections. However, not everyone is able to breastfeed, and many mothers have to rely on donor milk or formula instead.
Current formula is generally derived from cow’s milk and still lacks many important human milk components, including certain sugars, fats, and immune cells. “The aspiration for formula has always been to make it closer to human milk,” says Monique Rijnkels, Research Associate Professor at Texas A&M University. “And cow’s milk is not human milk and there’s differences with it,” she says.

Recently, multiple startup companies—including Biomilq of North Carolina and TurtleTree Labs of Singapore—have been attempting to produce human milk from lab-grown cells in order to better replicate breast milk. The specific approaches of the companies vary, and they’re all still at an early stage.

Biomilq grew mammary cells in a bioreactor—a vessel for growing cells under controlled conditions—and successfully produced two major milk components, lactose and casein [1]. At the moment, the mammary cells are derived from commercially available cell lines. “The Biomilq people are currently using just off-the-shelf mammary epithelial cells,” says Rijnkels. “They’re interested in pursuing making their own cell line or things like that eventually, but I think they just want to do a proof-of-concept with what they have right now,” she says.

TurtleTree Labs uses a different approach, extracting stem cells from donor human milk and differentiating them into mammary cells that can produce human milk [2]. Other startups are using food science approaches that don’t require mammary cells at all, such as New York-based Helaina’s yeast-centric approach [3].

Details about these startups’ methods are scarce, as each uses proprietary technology in its efforts to produce human milk. Regardless of the method used, they’re all far from having a commercially available product that’s received regulatory approval. They are also likely to face many challenges in getting closer to replicating human milk, or even formula, which is manufactured to be consistent in composition and is closely monitored for quality. However, these cell-based approaches may eventually present an intriguing alternative to formula.

“If this enables us to produce a formula or some kind of baby food milk that is closer to human milk compared to what’s on the market, that’s probably good,” says Rijnkels. “I would like to see the price proposition that’s related to that, but if this is a cost-effective proposition then there might be a niche for it,” she says. “It’s not going to take over the formula market in the next couple of years, but if they pull it off there will be a market for it,” she says.

So far, none of these companies is close to reproducing all the constituents of human milk. “I think these companies also admit that they’re never going to totally replace breast milk, because it’s just virtually impossible,” says Rijnkels. “It’s not like these cells need to make this one particular protein or a small group of proteins,” she says. “It’s very complex matter that is made and that’s why it’s so fascinating,” says Rijnkels.

“There’s so much that is sourced directly from the mother that’s not produced in the cells, and we’re not even talking about whether we’ll ever get the cells to actually produce at the levels that they do in the body,” says Rijnkels. “I’m still somewhat skeptical, but I’m excited that people are trying this, and it will be an advancement for the field if they can actually pull it off by producing in cells at high enough levels something that resembles human milk to a good degree,” she says.

A complex mix of components

There’s still a lot researchers don’t know about the composition of human milk. But it’s clear that it’s a complex mix of ingredients, containing variable levels of immune molecules, proteins, lipids, sugars, hormones, vitamins, and other nutrients and microbes. Many of these components interact in ways that
can affect immunity [4-7].

In addition, human milk is customized to the baby. Human milk varies from mother to mother, and its nutritional contents change throughout the day and over the course of weeks to meet a baby’s needs (8). It can also vary based on environmental factors, the mother’s food choices, and exposure to infections. An infection in the mother can lead to her passing on antibodies to that infection in her milk, which can help her newborn fight off infections [9,10].

"It’s all custom made for the baby and that’s one of the advantages of breastfeeding,” says Rijnkels. “If that’s not an option, there needs to be other good options that are as close as we can get,” she says. “Of course, we can also discuss what better support for breastfeeding could add to the picture,” says Rijnkels.

Many breast milk components would not be produced by mammary cells in culture, and lab-produced milk would thus need supplementation. “Milk has a lot of components that are passed through the mammary cells rather than being made in the cells,” says Rijnkels. “So a number of those either would have to be added or won’t be in there,” she says. These include immune components such as immunoglobulins and hormones such as serotonin.

What about the milk components actually produced by mammary cells? “In principle everything that is made in a mammary cell could be made in cell culture, given the right signals,” says Rijnkels. “I’m not quite sure if we’re clear on what the right signals are for all of those ingredients, however, and how efficient the process is going to be; that’s kind of the challenge that I see” she says. The stage of the cells could also matter. Studies on milk-derived mammary epithelial cells from dairy animals showed that lactation stage can significantly affect milk composition [11].

Rijnkels says Biomilq’s ability to get cells to produce lactose and casein is just a start. “It’s a good start if we can make that, but the question is, can we make the other things that are in milk at acceptable levels to the right ratios,” she says.

While researchers have been studying the major milk protein genes for a long time, they still have a lot to learn about other components, such as lipids. “We’re learning more about how the lipids are formed and in a large part that can still be a challenge in the culture systems,” says Rijnkels. Previous work has shown that production of milk lipids, and especially their secretion in complex structures known as milk fat globules, varies based on the body’s metabolic and hormone signals, lactation stage, and nutrition [12-16].

The lab-grown cells will also need to produce all the milk ingredients at sufficiently high levels. It’s unclear whether mammary cells in culture would include sufficient quantities of vitamins E and K, minerals such as iodine and iron, and omega-3 fatty acids. Current infant formulas are generally fortified with such components.

“A mammary cell in the body will turn out milk ingredients at such high levels, and I have yet to see a cell in culture do that,” says Rijnkels. “That’s kind of where my fascination is with the systems they are setting up and maybe it doesn’t need to be at those levels because they can concentrate things a little bit afterwards,” she says.

**Culturing mammary cells**

Growing mammary cells in a lab isn’t a novel idea. Researchers such as Rijnkels have long been doing this in order to study such cells. So far, they’ve learned a little bit about how complex the process of lactation is, and why it might be hard to replicate outside the body.

“I’m totally fascinated, because I’m a mammary gland biologist and I know the challenges of trying to replicate what the mammary gland does outside of the body,” says Rijnkels. She points out that the
companies appear to use various proprietary bioreactor systems quite different from the cell culture systems researchers use in the labs. “If with their culture systems they can replicate that closer than most of the cell culture systems that we have right now, that’s fantastic, and I want to know how they do it,” she says.

How the cells are cultured can make a big difference. “They definitely like to be in the right environments having the right interactions with the matrix and with each other,” says Rijnkels. “In a lab culture, it would be easy if we could just place them on a plastic dish and have them do what a mammary gland epithelial cell does in the body, but that’s just not happening,” she says.

Researchers have tried to replicate the signals that the cells receive within the body. “People have done a lot of work and established that they need some kind of matrix and they need the right signals,” says Rijnkels. “There are different signals that will signal the making and the secreting of milk, and we know most of that, but I’m pretty sure we don’t know everything about it,” she says.

Lactation is also a metabolically demanding activity for the cells. “One of the challenges of keeping lactation persistence is to keep those cells healthy and alive,” says Rijnkels. “In a mammary gland in the body, there’s such a demand on those cells for bioactive production that it’s really hard to keep them around for a long time, and they need to renew and there’s processes in the glands to support that,” she says. “So I think that’s going to be a challenge too, to keep the cells healthy and productive,” says Rijnkels.

Researchers could benefit from companies’ successful efforts to produce human milk from lab-grown cells. “We know that there are absolutely challenges in culturing cells and making them work as they work in the actual mammary glands,” says Rijnkels. “People in the field would benefit from the ability to use these companies’ approaches for our research, and I think it will help mammary gland biologists and scientists helping moms that have issues with lactation and studying lactation in the dairy setting as well,” she says. “If this works well, it’s fantastic and I would love to learn more details.”

The Environmental and Nutritional Impact of Removing Dairy Cattle

- The United States dairy industry is a major contributor to the US food supply and also contributes roughly 1.58 percent of the total US greenhouse gas emissions.
- One suggested approach to reducing greenhouse gas emissions has been to reduce or eliminate animal production in favor of plant production.
- A new study set out to examine the nutritional and environmental impacts associated with removing dairy production.
- The study finds a tradeoff between nutrient production and environmental impact, with scenarios that most reduce greenhouse gas emissions also majorly reducing essential nutrient production.

The United States dairy industry is a major contributor to the US food and nutrient supply. Dairy products are a major source of protein, calcium, and many essential vitamins not just in the US but all over the world [1-3]. The US dairy industry also accounts for 16 percent of the greenhouse gas emissions from all of US agriculture, and contributes roughly 1.58 percent of the total US greenhouse gas emissions [4,5].

One suggested approach to reducing greenhouse gas emissions has been to reduce or eliminate animal production in favor of plant production [6,7]. A new study set out to examine the nutritional and environmental impacts associated with removing dairy production [8].

“The project is actually a continuation of some work that we put out in 2017 where we evaluated what would happen if we removed all animals from US agriculture,” says assistant professor Robin White of Virginia Tech. The 2017 study revealed an increase in micronutrient deficiencies despite greater food availability in a simulated system without farmed animals for food production [4]. “This work is a specific follow-up to look individually at the dairy industry, which has some unique trade-offs in terms of provision of human edible nutrients and environmental impact,” says White. Dairy products contain a mix of unique nutrients required by humans, while milk production from dairy cattle has a lower environmental impact than meat production or production of some plant products, such as lettuce [9-11].

White and her colleagues set out to determine the current contributions of dairy products to the nutrient supply in the US. The new study also considered the mechanics of how land use within the agricultural system might adapt to reduced consumption of animal products. Previous studies found that when non-livestock animals move into areas previously used by livestock, there is a significant effect on greenhouse gas emission [12].

The researchers also took into account the effects of different approaches to dairy depopulation. “We have two different types of scenarios, one focusing on the question of practicality, if we are to reduce the size of the dairy industry, how would we go about doing that, and the second question focusing on how we might use agricultural land that would be liberated when we reduce the size of the dairy industry,” says White.

The researchers considered three scenarios of dairy removal—depopulation, current management (export dairy), and retirement. In the depopulation scenario, all dairy animals are removed, whereas in the
current management (export dairy) scenario, animals are kept under current management and dairy products are not consumed in the US. Finally, in the retirement scenario dairy animals are retired to a pasture-based system.

“We have three scenarios or three levels, one of which is kind of the extreme scenario where we actually go through and do a one-time depopulation of all dairy cattle,” says White. “That is effectively a mass slaughter of dairy cows, so that we no longer have them contributing to environmental impact,” she says. “In all likelihood that’s something that would be really socially unacceptable,” says White.

“Our results suggest that depopulation probably is a scenario where we get a big environmental benefit and highlights that there are some trade-offs there,” she says. Under this scenario, greenhouse gas emissions from agriculture declined 7.2% compared with emissions from the current production system, although supplies of several essential nutrients declined as well.

The researchers also considered a second scenario, the current management (export dairy) scenario, where people may stop consuming dairy products, but the dairy industry largely remains unaffected because they sell dairy products for other purposes and use those products as an export instead of selling them to US consumers. “That’s kind of the extreme scenario in terms of if we were only economically motivated,” says White. Greenhouse gas emissions were unchanged in this current management (export dairy) scenario, with a decrease in nutrient supplies compared with current diets or the depopulation scenario.

The researchers also considered a retirement scenario, where dairy animals are retired to pastures. “Then there’s a third scenario that probably reflects what the average consumer would expect to see when we talk about reducing the size of the industry, and that’s a scenario where effectively dairy cattle are just retired out of the milk production sector and animals are allowed to maintain their semi-feral existence on available pastures and such,” says White. She notes that this scenario doesn’t address how one would actually achieve population control for those animals, which is an issue for other feral populations in the US such as feral horses and feral cats. The retirement scenario showed an 11.97% decline in total agricultural greenhouse gas emissions compared with current emissions, likely because of the greatly reduced population of cows sustainable on available pastureland. However, available supplies of all nutrients decreased in this scenario.

The researchers estimate that retiring dairy would translate to a 72.6%, 56.7%, and 53.9% decrease in domestically produced supplies of calcium, vitamin B12, and vitamin D, respectively, relative to the current contributions of dairy to the US agricultural system. “The sheer quantity of nutrients that are contributed to from the dairy industry was pretty staggering,” says White.

The study’s investigation into the impacts of removing dairy cows from US production agriculture suggests that the greenhouse gas changes would be relatively minor, equivalent to 0.7% of the total US emission. The researchers found that removal scenarios that did not reduce micronutrient availability also did not improve greenhouse gas emission relative to the current production system. They suggest that nutrient production and meeting of essential nutrient requirements should be considered when evaluating the impact of removing any animal production system.

“The primary takeaway is that there are tradeoffs within the food production system between the production of high quality human edible nutrients and the environmental impact of the food production system,” says White. “Of the numerous scenarios we evaluated there wasn’t a single one that was better in both of those categories than our current agricultural system,” she says. “The current agricultural system does present some sort of optimum there, and in evaluating different strategies to try and influence some of the negative aspects of that system—the environmental impact being an example—we need to be considering the collateral impacts of those choices on the other aspects of the system,” says White.

In follow-up experiments, White and her colleagues plan to work toward similar assessments at a global
scale. Such assessments may help policy makers consider the pros and cons of various scenarios. “From the standpoint of deriving policy, I think that this highlights the importance of looking at the different policy options with as wide a lens as possible,” says White.

“That includes the biological feasibility, the potential impact on the environment, the potential impact on climate change, the impact on the economics both at a micro and a macro scale, and the social aspects, because really agriculture exists at the intersection of all of those,” White says.

**Post-script: A note about methane’s role in greenhouse gas emissions**

Methane is a potent greenhouse gas that is 25-28 times stronger than CO2 over a 100-year period. However, there is some evidence, including from a recent white paper, that carbon dioxide (CO2) and methane differ in the way they contribute to global warming, particularly depending on the source of methane. Whereas the burning of fossil methane—such as from natural gas—gives rise to CO2 that can remain in the atmosphere for centuries, methane emitted by cows is relatively short-lived and is broken down after 12 years in the atmosphere.


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**Primate Milk Microbiome Reveals Shared and Unique Features**

- Milk has its own set of bacterial communities, or microbiome, that could provide health benefits to infants.
- A new study investigated milk microbiome structure across nine primate species, including humans, to look for features that were shared across all primates and those that were unique to individual species.
- There is a core primate milk microbiome of seven bacteria taxa, five of which come from genera identified from other mammal milks.
- Humans and other primate species had unique milk microbiome signatures.
- More studies are needed to understand how milk bacteria influence human and nonhuman primate infant health.

Mammalian milk was once thought to be free of bacteria, but it is now well understood that milk has its own microbiome, or community of bacteria. Although only recently “discovered,” microbes were likely one of milk’s original ingredients and have an evolutionarily ancient relationship with their mammal hosts. Many bacterial species are likely common to all mammalian milks. But because some bacterial strains could potentially benefit infant health by promoting the growth of beneficial bacteria in the gut or enhancing infant immunity [1-4], there may have been numerous opportunities for the evolution of
species-specific milk bacterial communities. Does each mammal, including humans, pass on its own unique mix of bacterial strains in milk or is there a more general milk microbiome shared across mammals?

A new study [4] on the milk microbiome of humans and eight other primate species provides a unique opportunity to address milk bacterial communities from an evolutionary perspective. Muletz-Wolz and colleagues took advantage of archived primate milk samples that had corresponding nutritional composition data [4]. In addition to not having to collect any new milk samples, they were able to investigate how milk components, such as protein and fat, might influence microbiome structure. Nonhuman primate milk samples came from five ape species (chimpanzees, bonobos, western lowland gorillas, Bornean orangutans, and Sumatran orangutans), one Old World monkey species (rhesus macaques), and two New World monkey species (owl monkeys and mantled howler monkeys). All nonhuman primates were captive living except for the mantled howler monkeys. Human milk samples came from human mothers living in the Philippines and the United States.

The study identified a core primate milk microbiome of seven operational taxonomic units (OTUs), which are clusters made from similar gene sequences meant to represent a species or genus of bacteria [4]. These seven OTUs were present in >80% of the samples across the nine primate species. Five of these OTUs came from bacterial genera (Acinetobacter, Staphylococcus, Streptococcus) that have been reported from other mammalian lineages. This is exciting as it suggests a more ancient evolutionary relationship between these strains and their mammalian hosts and the possibility of a core microbiome [4].

Across the nine primates, researchers found species-specific patterns in microbiome structure [4]. Western lowland gorilla milk samples came from different facilities and even from different time points in lactation, and yet had microbiome profiles more similar to each other than other primate milks. The same was true for human milk, despite the fact that mothers were from both rural and urban populations in the Philippines and the United States. This finding is particularly interesting when considering that human gut microbiomes, which are believed to be one source for milk microbes, vary between geographic regions. This suggests that bacterial taxa are selectively, rather than passively, transported from the mother’s gut to the mammary gland [2-4], and that these pathways are conserved across human populations [4].

Some other highlights of the study results include the potential relationship between milk nutrient content and milk microbiome structure. Milk from rhesus macaques and mantled howlers were the most dissimilar in fat and protein, and were also the most dissimilar in microbiome structure, suggesting that higher fat or protein milks may favor the growth of particular bacteria [4]. The study also identified longitudinal changes in milk bacterial communities in western lowland gorillas and Sumatran orangutans. The nutrient content of milk remained stable, but milk bacterial communities were dynamic over the course of lactation [4]. These changes over time may map onto changing requirements for infant digestion or immunity as older infants engage with more non-milk foods and become more socially active.

One finding that might not be particularly surprising—but is nonetheless interesting from an evolutionary perspective—is that the human milk microbiome was the least rich, in terms of bacterial species diversity, across the primates [4]. This could be the result of cultural practices (e.g., hand washing, food washing) that reduce human interactions with particular types of microbes. However, the only wild living primate sampled (mantled howler monkeys) also had low milk OTU richness, meaning the lack of diversity in human milk microbiomes could potentially be an ancestral feature unrelated to recent cultural shifts. That captive living primate milks (mostly from zoo populations) were more rich than human milk in bacterial diversity further suggests that factors other than the maternal environment influence the types and quantities of bacteria in milk.

There are more than 300 species of primate, but this study of nine species demonstrates both conserved
and recently evolved patterns in milk microbiome structure. It is exciting to think about the bacterial taxa that are shared across all mammals as having a very ancient origin within the mammalian lineage. Equally interesting are the more recently evolved bacterial signatures that distinguish one primate species from another. Both the unique and shared features across primate milk microbiomes deserve further examination to determine how these bacterial species may influence infant health.