



SPLASH!® milk science update December 2016 Issue



This month's issue features how the antimicrobial cathelicidins in Tasmanian devil milk may combat human superbugs, how milk offers the best relief from the heat of chili peppers, how human milk sugar may prevent intestinal infection and inflammation, and how research reveals racial disparities in clinical support for breastfeeding mothers.

Tasmanian Devil Milk Provides Powerful Antibacterial Proteins

- **Cathelicidins are a family of antimicrobial proteins found in all mammals.**
- **Marsupials, including the Tasmanian devil, have more genes for cathelicidin proteins than do placental mammals, possibly because of the greater pathogen exposure in the pouch compared with the uterus.**
- **Researchers recently identified six cathelicidin proteins in the milk, pouch, and mouth of Tasmanian devil mothers, two of which killed antibiotic-resistant human pathogens.**
- **Cathelicidins from the Tasmanian devil and other marsupials offer promise as potential drugs to combat the growing number of human superbugs.**

The Tasmanian devil is best known for being a swirling, growling, trouble-making cartoon character. But the marsupial mammal's reputation is about to get a complete makeover, thanks to new research on the function of proteins secreted in their milk and their skin [1]. These proteins, called cathelicidins, are found in all mammals, and are known to have antimicrobial properties. However, a team of Australian researchers found that those secreted by Tasmanian devil mothers pack an extra strong punch. In addition to fighting pathogens present in the environment of the developing pups, Tasmanian devil cathelicidins also killed strains of drug-resistant human pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA). If these unique proteins can be utilized in the fight against human superbugs, the Tasmanian devil could transform from cartoon villain to public health superhero.

Milk's ancient ingredients

All mammals, from the egg-laying monotremes to the marine-living whales, produce milk for their offspring, suggesting that this evolutionary adaptation has very ancient roots. Olav Oftedal, a leading expert on mammalian milks, believes that milk first evolved in mammalian ancestors (called "mammal-like reptiles" or synapsids) over 200 million years ago [2]. These earliest "milk" secretions



came from maternal skin glands that would later evolve into the mammary gland and would have served two functions: (1) to provide moisture to the developing egg and (2) to provide antimicrobials to protect the egg from pathogens [2]. Thus, immune factors are some of milk's most ancient ingredients, predating the nutritional components that milk is best known for.

Cathelicidins may be one these very early ingredients. This family of proteins has antimicrobial properties and is part of the innate immune system of all living mammals [1], indicating they were inherited from a pre-mammal ancestor. Cathelicidins kill bacteria, parasites, and fungi directly and also indirectly, by influencing the actions of other immune functions that kill pathogens (such as the inflammatory response) [1].

Because they are part of the innate immune system, they are not pathogen-specific. Although this may mean that they do not create memory cells like B cells or T cells (both part of the acquired arm of the immune system), cathelicidins have the ability to take down a broad spectrum of pathogens at first sight. This attribute makes them especially beneficial to neonatal and infant mammals, which have naïve immune systems and little to no acquired immunity.

Growing up marsupial

While all mammals have DNA that codes for cathelicidin proteins, the number of cathelicidin genes varies widely across species. Compared with placental mammals, marsupials (a group that includes koalas, kangaroos, and Tasmanian devils) have a greater number of cathelicidin genes. For example, one species of opossum (*Monodelphis domestica*) has 12 cathelicidin genes, whereas humans and mice have just one. Why would marsupials differ so much from other mammals?

Researchers hypothesize that the unique pattern of growth and development of marsupials favored selection on an increased number of genes associated with these germ-fighting proteins [1]. Marsupials give birth to extremely underdeveloped offspring that are immediately transferred to a pouch to continue their "fetal" development, nourished through maternal milk. Unlike the uterus,

the pouch is not sterile; young are regularly exposed to pathogens in their environment. Thus, marsupial neonates and infants are extremely underdeveloped immunologically and at a higher risk for pathogen exposure than their placental mammal cousins [1].

The devil is in the details

It turns out that marsupials do not just make more genes for cathelicidin proteins, they also make more potent ones. Two cathelicidin proteins from the tammar wallaby (*Macropus eugenii*) were able to kill two different antibiotic-resistant bacteria (*Klebsiella pneumoniae* and *Pseudomonas aeruginosa*) [1].

A team of Australian researchers argued the Tasmanian devils may have an even greater need than wallabies for strong, broad-spectrum antimicrobials [1]. Offspring are born after only 30 days of gestation and weigh only 0.3 grams [1]. To get an idea of just how small this is, a paper clip weighs around 1 gram. Add to this highly altricial start the observation that Tasmanian devils lead a very aggressive lifestyle (they are not called devils for nothing), resulting in cuts and bites that require pathogen protection. If the calm tammar wallaby makes such potent proteins, what about the truculent Tasmanian devil?

To address this question, researchers Emma Peel and her colleagues began by searching the Tasmanian devil genome for genes associated with cathelicidin proteins. They found six, all on chromosome two. Interestingly, two of the genes (named Saha-CATH1 and 2) have very strong sequence similarities to cathelicidin genes from other marsupials and are believed to have originated over least 70 million years ago. In contrast, three others (named Saha-CATH3, 5, and 6) appear to be species-specific and the result of gene-duplication events during the evolution of the Tasmanian devil. Thus, there is a mix of shared marsupial proteins and those that are unique to the Tasmanian devil, supporting the idea that devils might have unique immunological priorities compared to other marsupial mammals.

The next step was figuring out just where these genes were expressed (that is, which types of cells actually made the proteins that the genes code for). Not surprising for proteins involved in immunity, gene expression was found in the blood, spleen and lymph nodes. But in support of the researchers' hypothesis regarding protection of naïve offspring, cathelicidin genes were also expressed in the uterus, maternal pouch, milk, skin, and mouth mucosa of Tasmanian devils [1].

The final, and most important step, was figuring out protein function. The team made synthetic proteins representing each of the six devil cathelicidins (named Saha-CATH1–6) and applied them to pathogen strains (both bacterial and fungal) from several species of mammals, including humans. Three cathelicidins (CATH1, 2, and 4) did not have antimicrobial activity. However, the fact that the genes associated with these proteins are expressed in cells throughout the body suggests that they may be indirectly involved in immunity, influencing the actions of other immune factors [1]. In contrast, CATH3, 5 and 6 were direct pathogen killers.

Devil or angel?

Fortunately for Tasmanian devil joeys, Saha-CATH1, 2, 4, 5, and 6 are expressed in the milk, the pouch, and the mouth (transferred when mothers lick joeys), providing both direct and indirect immune protection. As it turns out, humans may be quite fortunate, too. Not only did Peel and colleagues find that CATH5 and 6 kill bacteria found in the pouch and skin of the Tasmanian devil, both killed antibiotic-resistant bacteria species that infect humans, including vancomycin-resistant *Enterococcus faecalis* (VREF) and MRSA. Indeed, CATH5 appears to have diverse antibacterial activity, killing both Gram negative- and Gram-positive bacteria as well as species from the genus *Candida*, a fungus common in skin infections.

Why are the Tasmanian devil milk proteins so effective against human pathogens? Exactly how these proteins kill the pathogens is still being worked out, but their effect on human pathogens probably has nothing to do with their methods. Indeed, researchers suspect they work the same way as cathelicidins from placental mammals [1]. Their effectiveness is because of their novelty.

The human immune system and human pathogens are in an evolutionary arms race, constantly changing to try and keep up with the other side. In humans, a mutation may be favored because it allows for more effective identification of a particular pathogen; for pathogens, a random mutation that makes them look less like invaders and more like human cells turns the advantage to their side. Technology, in the form of antibiotics (and antifungals, antivirals, etc.), gave humans the edge but only for a short time. Resistant pathogens, nicknamed superbugs, are an inevitable evolutionary outcome, and a major public health concern, leaving scientists scrambling to find effective alternatives.

Human pathogens have never encountered cathelicidins from marsupials, many of which are species-specific, which means the arms race has yet to begin. Could Tasmanian devil cathelicidins be our secret weapon? The findings of Peel et al. [1] suggest they could. Not only were they able to kill the superbugs MRSA and VREF, they did so at concentrations that kept them from being toxic to healthy human red blood cells (compared with human cathelicidins, which kill pathogens but also kill other types of mammalian cells).

Evolutionary prescription

Although prescriptions for Tasmanian devil milk proteins might not happen right away, these antibiotic alternatives offer great

promise as potential drug candidates. The same is true for cathelicidin proteins from other marsupials; researchers have tested only two species' proteins thus far, and both have demonstrated the ability to kill drug-resistant strains [1].

The study also provides an important reminder of the importance of an evolutionary perspective to medicine. The number of infectious diseases is growing, and it is critical that we think about pathogens and our own immune reactions as products of the evolutionary process if we are to identify treatments that work in both the short and long term.

1. Peel E, Cheng Y, Djordjevic JT, Fox S, Sorrell TC, Belov K. 2016. *Cathelicidins* in the Tasmanian devil (*Sarcophilus harrisii*). *Scientific Reports* 6: 35019.
2. Oftedal OT. 2013. Origin and evolution of the major constituents of milk. In: *Advanced Dairy Chemistry, Volume 1A: Proteins: Basic Aspects*, 4th Edition, McSweeney PLH, Fox PF, editors.

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Milk Beats Olive Oil at Cooling Hot Chili

- **Hot chili sauce causes a burning sensation in your mouth because it contains a substance called capsaicin that activates TRPV1 receptors that surround the taste buds.**
- **Capsaicin's ability to do this hinges on the fact that it is a nonpolar molecule, which is why scientists thought a substance full of nonpolar molecules—olive oil—should be the best option for removing it from TRPV1 receptors.**
- **In a recent experiment, milk and ice cream were shown to outperform olive oil and reduce the burning sensation caused by capsaicin.**
- **The researchers who conducted the experiment suggest this may be because emulsions are better able to travel around the saliva-filled mouth, and reach more TRPV1 receptors than oil.**

Hot chili peppers have been grown as a domestic crop in some parts of South America for between 5,000 and 7,000 years. Today, they can be found in almost every corner of the world. But their biology—and how it interacts with our biology—can still be a source of surprises. Few people realize, for example, that chili fruits are actually berries, and that the substance that makes them hot, capsaicin, isn't present in the seeds at all but is concentrated in the white pithy part [1]. Recently, Mexican researchers investigating a local hot sauce reported another surprise: that the palate-relieving properties of ice cream and milk beat those of olive oil [2]. Initially, this didn't make sense, given capsaicin's chemistry.

When you put hot sauce in your mouth, the capsaicin in the sauce binds a kind of receptor that surrounds your taste buds called transient receptor potential vanilloid-1 (TRPV1) [3]. Capsaicin is able to form a temporary bond with TRPV1 receptors because it is a nonpolar molecule—in other words, because positive and negative charge is spread evenly over its chemical structure. This temporary bond causes part of a TRPV1 receptor to separate, allowing calcium ions to flood into the sensory neuron to which it is connected. That's why your brain gets the message you just ate hot sauce.

Stopping the message requires releasing capsaicin from TRPV1 receptors, such that the part of the receptors that was separated falls



back into place, stopping more calcium ions from entering sensory neurons. Basic chemistry suggests that other nonpolar molecules are needed for that task. Fats are nonpolar molecules, but water is strongly polar. So, for this reason, Mónica Avendaño-Rodríguez and her colleagues from the Monterrey Institute of Technology and Higher Education, in Cuernavaca, Mexico, began their investigations into hot sauce by positing that the more fat and the less water a foodstuff contains, the better it will be at relieving hot sauce-induced burning sensations. Milk contains a little fat and a lot of water. Thus a pure fat like olive oil should be better at removing capsaicin from TRPV1 receptors.

The team's experiment had two parts. First, they had to evaluate the spice-tolerance of the study participants. Spice tolerance is not merely related to experience eating spicy food but also how many TRPV1

receptors you happen to have been born with. Over five days of repeated testing, the courageous volunteers were asked to rate the spiciness of their local hot sauce on a scale from 0 (not hot) to 10 (extremely hot). This enabled Avendaño-Rodríguez and her team to separate the volunteers into three groups of low, medium and high tolerance.

The second part of the experiment tested the effectiveness of different foodstuffs at cooling the burn. Again, the participants showed up for five days in a row, each time receiving a portion of hot sauce. This time they rated the sensation of hotness that they experienced after consuming a second item—one of either olive oil, water, milk, ice cream or a soft drink. Over the course of five days, every participant tested the cooling abilities of all of these liquids. The sequence of the cooling liquids was also randomized, to account for participants potentially building up a tolerance to the hot sauce during the experiment.

The surprise came at the end of this second test: no matter the participants' original spice-tolerance level, ice cream and milk always outperformed olive oil at cooling their mouths. In fact, olive oil provided no more spice-relief than water. The soft drink consistently performed worst.

Why might dairy have beaten a pure fat? One answer points to a fault with the experimental design. While the courageous participants had mentally prepared themselves to eat hot sauce, they weren't, for some reason, willing to consume more than a tablespoon (15 ml) of oil—while they merrily guzzled 100 ml of milk and ice cream.

A second answer points to chemistry. Although olive oil might be good at removing capsaicin from TRPV1 receptors, it probably isn't good at getting to all of the mouth's TRPV1 receptors. This is because it doesn't mix well with watery saliva; instead, it forms large blobs that probably hit only patches of TRPV1 receptors as a taster swallows it. But dairy products are emulsions: they consist of microscopic globules of fat floating around in water. Therefore, when mixed with saliva, milky products have nonpolar parts that are able to move freely into all of the tiny crevasses of the mouth. This might be why milk and ice cream appear to have ripped more of the capsaicin delivered in Mexican hot sauce away from TRPV1 receptors than did the olive oil.

This study offers advice for lovers of spicy food, even if they aren't particularly partial to Mexican cuisine. Capsaicin isn't just what makes Mexican food hot. It is found in paprika—traditionally, a spice typical of Hungary [4]—and packs the heat into many Thai delicacies like tom yum soup. When these other cuisines have undergone tests similar to the one carried out by Avendaño-Rodríguez and her team, milk has consistently been shown to be a highly effective oral fire retardant [5]. So next time you head out for a hot Indian curry, remember to ignore the water and sip mango lassi instead.

1. Mortensen J. M. and Mortensen J. E. 2009. The Power of Capsaicin. *Journal of Continuing Education Topics and Issues* 11(1): 8-12.
2. Avendaño-Rodríguez M., Juárez-Castro M., Rodríguez-Caspeta D., Zavaleta-Vega G. and Cano-Ruiz M. E. 2016. The effectiveness of different palate relievers against a hot chili pepper sauce. *Journal of Emerging Investigators* June 11, 2016: 1–5.
3. Simon S. A. and de Araujo I. E. 2005. The salty and burning taste of capsaicin. *Journal of General Physiology* 125(6): 531–534.
4. Menicagli R, Duca M. and Rancoita P. M. V. 2016. Traditional food habits and their possible relationship in diseases of the mouth. *Merit Research Journal of Medicine and Medical Sciences* 4(1): 1-7.
5. Kitsawad K. and Nguyen T. T. 2014. Determination of suitable palate cleanser for spicy tom yum soup. *Agro FOOD Industry Hi Tech* 25(3): 28–30.

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A Human Milk Oligosaccharide Protects Against Intestinal Infection and Inflammation

- ***Campylobacter jejuni* is a major cause of intestinal inflammation and diarrhea worldwide.**
- **Sugars found in human milk, called human milk oligosaccharides (HMOs), have been shown to protect against intestinal infections.**
- **Studies have found that an HMO called 2'-fucosyllactose (2'-FL) can inhibit *C. jejuni* binding to intestinal cells.**
- **A new study finds that 2'-FL inhibits *C. jejuni* infection and associated inflammation *in vitro* in human cells and *in vivo* in a mouse model.**
- **2'-FL was protective when given to mice before *C. jejuni* infection, which suggests that it also acts as a prebiotic to restore healthy gut microbiota.**
- **Once the results are replicated in clinical trials, 2'-FL could potentially be used to prevent or treat *C. jejuni* and other intestinal infections in humans.**

Sugars found in human milk, called human milk oligosaccharides (HMOs), have various protective effects against intestinal infections [1–4]. A new study finds that the HMO 2'-fucosyllactose (2'-FL) protects against infection and inflammation caused by the pathogen *Campylobacter jejuni* [5].

“*Campylobacter* is a major cause of infant diarrhea in many parts of the world, and that was what got us interested early on,” says David Newburg, who conducted the new study at Boston College. “We wanted to be able to help young children globally,” he says.

Previous work showed that breast milk with higher levels of 2'-FL was associated with a lower risk of *C. jejuni*-caused diarrhea in infants [6, 7]. “What we found was that pure 2'-FL was sufficient to fight this disease,” says Newburg. “It seems as though this molecule found in human milk is very well designed to protect infants from disease,” he says.

Newburg has long been interested in studying the protective effects of HMOs against *Campylobacter*. “Back in 1985, when we were investigating the effects of the HMOs in terms of any protective potential, *Campylobacter* was one of the pathogens that was inhibited by HMOs, and we localized that effect to 2'-FL,” he says.

But Newburg ran into a problem when trying to test the effects of purified 2'-FL. “At the time we didn't have enough 2'-FL to do any more than *in vitro* tests,” he says. “It was only when we got enough 2'-FL to be able to feed to animals that we were able to test its actual effects *in vivo* in an animal model,” says Newburg. “This was not economically feasible until Glycosyn, our company, put together a method to have bacteria make 2'-FL, and to do that in such amounts that it became possible to do these experiments

with mice,” he says.

Before Newburg could test the purified 2'-FL in mice, he and his team first developed a suitable mouse model for human *C. jejuni* infection. “Usually mice cannot be effectively infected by human *Campylobacter*,” he says. “To get a human clinical strain to attack the mice and colonize it in a meaningful way, we treated with antibiotics ahead of time, and that caused the mice to have disrupted gut microbiota, and made the gut much more vulnerable to growth by the human pathogen,” he says.



When the researchers treated human cells with 2'-FL, it greatly reduced *C. jejuni* invasion and associated inflammation. Similarly, when mice ingested 2'-FL, they experienced less *C. jejuni* colonization and reduced intestinal inflammation. When the researchers gave 2'-FL to mice three days before *C. jejuni* infection, they found that it was protective against inflammation and intestinal damage.

C. jejuni needs to bind to host sugars to infect intestinal cells, and previous work found that HMOs, and particularly 2'-FL, can block this binding [4,8,9]. Newburg and his team found that 2'-FL also had a couple of additional tricks up its sleeve. Not only did 2'-FL block *C. jejuni* binding and infection in intestinal cells, but it also inhibited the release of pro-inflammatory signals, and acted as a prebiotic to help restore normal

healthy gut microbiota. “It’s fascinating that this one molecule can have these three very different effects,” says Newburg.

The results suggest that adding 2'-FL to food could help protect against intestinal infections. “It could be formula, it could be a supplement for a mother who’s breast feeding, it could be a supplement for a kid, or it could be added to the diet for a child who’s weaned, in all cases it looks like 2'-FL will protect against *Campylobacter*,” says Newburg.

But there is more work to be done before 2'-FL can be used therapeutically in humans. “I think there are two directions to go in; one is to move towards clinical trials, and the other is to do further research on mechanisms of this protection,” says Newburg.

By including other HMOs besides 2'-FL, the researchers could eventually target a broader range of pathogens. “We’re hoping that with a cocktail of HMOs we’ll have something that’s more universal,” says Newburg. “I think it’s very, very hopeful.”

1. Newburg DS, Walker WA. Protection of the neonate by the innate immune system of developing gut and of human milk. *Pediatr Res* 2007;61:2–8.
2. Morrow AL, Rangel JM. Human milk protection against infectious diarrhea: implications for prevention and clinical care. *Semin Pediatr Infect Dis* 2004;15:221–8.
3. Newburg DS, Ruiz-Palacios GM, Morrow AL. Human milk glycans protect infants against enteric pathogens. *Annu Rev Nutr* 2005;25:37–58.
4. Morrow AL, Ruiz-Palacios GM, Jiang X, Newburg DS. Human-milk glycans that inhibit pathogen binding protect breast-feeding infants against infectious diarrhea. *J Nutr* 2005;135:1304–7.
5. Yu ZT, Nanthakumar NN, Newburg DS. The human milk oligosaccharide 2'-fucosyllactose quenches *Campylobacter jejuni*-induced inflammation in human epithelial cells HEp-2 and HT-29 and in mouse intestinal mucosa. *J Nutr*. 2016;146:1980-1990.
6. Newburg DS, Ruiz-Palacios GM, Altaye M, Chaturvedi P, Meinzen-Derr J, Guerrero Mde L, Morrow AL. Innate protection conferred by fucosylated oligosaccharides of human milk against diarrhea in breast-fed infants. *Glycobiology* 2004;14:253–63.
7. Morrow AL, Ruiz-Palacios GM, Altaye M, Jiang X, Guerrero ML, Meinzen-Derr JK, Farkas T, Chaturvedi P, Pickering LK, Newburg DS. Human milk oligosaccharides are associated with protection against diarrhea in breast-fed infants. *J Pediatr* 2004;145:297–303.
8. Day CJ, Tiralongo J, Hartnell RD, Logue CA, Wilson JC, von Itzstein M, Korolik V. Differential carbohydrate recognition by *Campylobacter jejuni* strain 11168: influences of temperature and growth conditions. *PLoS One* 2009;4:e4927.
9. Ruiz-Palacios GM, Cervantes LE, Ramos P, Chavez-Munguia B, Newburg DS. *Campylobacter jejuni* binds intestinal H(O) antigen (Fuc alpha 1, 2Gal beta 1, 4GlcNAc), and fucosyloligosaccharides of human milk inhibit its binding and infection. *J Biol Chem* 2003;278:14112–20.

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From Bench to Bedside: Translating Milk Science at the Clinician-Patient Interface

- **Breastfeeding is examined through a social science lens.**
- **Racial disparities exist in clinical support for breastfeeding.**
- **Research reveals the need for improving clinical care in consideration of racial disparities.**

Emerging empirical research from chemistry, microbiology, animal science, nutrition, pediatrics, and evolutionary anthropology is accelerating our understanding of the magic of milk. Translating the findings about milk, however, for the end-user (babies) and end-producers (moms), requires shining a light on emerging social science and public health research tackling breastfeeding initiation and support. Moreover, understanding the context and experiences of mothers of different races highlights the persistence of health care deficits that perpetuate breastfeeding disparities.

Demographics and epidemiology

In 2014, Dr. Lind and colleagues evaluated the maternity and perinatal practices at 2,227 hospitals and birth centers in the United States in conjunction with the racial demographics of the area these health care providers served [1]. Combining data from the CDC's 2011 Maternity Practices in Infant Nutrition and Care survey [2] with census data on racial demographics in the same Zip Code as the surveyed health facilities, the authors discovered failures of health care delivery in communities with higher proportions of Black residents. Early initiation of breastfeeding within the first hour of an uncomplicated vaginal birth, rooming-in, and post-discharge patient support were all less likely to be standard practice in Zip Codes in which Black residents were >12.2% of the population. Facilities serving these communities were also less likely to limit the use of breastfeeding supplements. These are four of the ten important steps toward optimal support for breastfeeding and mother and infant bonding. Together these practices underlie the Baby-Friendly Hospital Initiative and have been demonstrated to improve breastfeeding initiation and success, including among Black women [3].



More recent research by Dr. McKinney and colleagues investigated differences among white, Hispanic, and Black mothers in breastfeeding initiation and duration [4]. Using a large sample (N = 1636) of mothers from the Community and Child Health Network, a multi-community project of the National Institutes of Health, McKinney replicated previously-demonstrated patterns of disparity between white and Black mothers, 78% vs. 61% initiation, respectively. Hispanic mothers had the highest initiation with more than 90% initiating breastfeeding. The disparity between white and Black mothers was explained by poverty, college education, and marital status as white mothers were wealthier, more likely to be college educated, and more likely to have a spouse. Although Hispanic and Black mothers had similar socioeconomic and demographic backgrounds, the higher initiation among Hispanic women reflected a family history of breastfeeding [4].

For the mothers who initiated breastfeeding, however, these socioeconomic and demographic factors could not alone explain differences in breastfeeding duration among these groups [4]. Hispanic mothers breastfed 10 and 17 weeks (English-speaking and Spanish-speaking, respectively), while white mothers breastfed on average 16.5 weeks and Black mothers breastfed only 6.4 weeks. The introduction of formula feeding during the hospital stay was a significant predictor for the disparity between white and Black mothers in breastfeeding duration. The

authors concluded that “if only hospital formula introduction were eliminated, the Black/white gap in breastfeeding duration could be reduced by ~1.8 weeks or 20% of the overall difference.”

Taking a closer look

The above quantitative analyses are importantly complemented by qualitative, ethnographic approaches to understanding the socio-cultural context of infant-feeding decisions. In August 2016, Dr. Ifeyinwa Asiodou and colleagues published the results from a “critical ethnographic” approach to infant feeding among first-time African-American mothers [5]. Critical ethnography moves beyond earlier forms of cultural description to specifically capture the complex factors and their intersections that contribute to observed societal disparities. This research method provided rich detail that informs “culturally inclusive messaging” in public health and clinical practice.

Over the course of many interviews, mothers and members of their support networks described the factors related to breastfeeding initiation and success. Consistent with the quantitative work of McKinney et al. [4], Asiodou and colleagues found that a family history of breastfeeding among African-American women was rare but if present improved breastfeeding initiation. Moreover, a mother's broader social networks, and the support or lack of support therein, could improve or diminish breastfeeding practices. Motherhood as a critical aspect of self-identity was also a motivating factor in breastfeeding and infant nurturing. Lastly, access to community public health programs that provided support and information, and facilitated new mothers connecting with other new mothers also contributed importantly to breastfeeding practices and attitudes [5].

Understanding the importance and cultural context of female social networks for shaping breastfeeding practices contributes to adopting best practices in the clinical setting, namely implementing peer-mentor programs. Dr. Paula Meier and colleagues at the Rush University Medical Center (RUMC) in Chicago have established the Rush Mothers' Milk Club in the NICU that provides a road map for building partnerships among many stakeholders to promote breastfeeding [6]. From the clinical staff, to the families and patients, to the broader community members in the neighborhood surrounding the RUMC, the core principle of the program is “sharing the science of human milk and lactation with NICU families so that the families could serve as active participants in their infants' feeding decisions and management plans” [6].

Within a year of launching this integrative program, breastfeeding initiation rates for mothers with babies in the NICU went from 17% to 95% as mothers decided to breastfeed after hearing about “milk as medicine for their baby” [6]. The mothers most likely to change their infant-feeding decision from formula feeding to breastmilk feeding were low-income, African-American mothers who

had particularly vulnerable small, pre-term infants and who had few, if any, breastfeeding models within their existing social support networks [6]. Informal mother-to-mother peer counseling was an emergent dynamic during weekly Rush Mother’s Milk Club meetings and inspired a peer-mentoring network. Breastfeeding peer counselors, who had themselves had a baby in the NICU, became valuable role models and sources of information for mothers whose existing social support network had little information about breastfeeding—especially small, premature infants, particularly for African-American mothers [6].

Moving forward

These studies at the social science/life science/clinical practice interface reveal key gaps, but they also provide solutions for addressing persistent health care disparities. Life scientists are prioritizing understanding how early life organization can exert life-long consequences [7, 8], a field known as the Developmental Origins of Health and Disease [8]. At the same time, researchers in the social sciences are investigating how babies born in nearby zip codes can have 20–30 year differences in their life expectancy because of deficits in the quality of care and disparities of life experiences [9]. Due to inadequate breastfeeding support and therefore breastfeeding initiation and success, more Black mothers and babies are likely to accrue compounding health impacts throughout the lifetime and across generations [9]. Indeed, epidemiological models published by Dr. Melissa Bartick, Dr. Alison Steube, and colleagues reveal that the racial breastfeeding gap is associated with poorer health for non-Hispanic Blacks than non-Hispanic whites [10]. Non-Hispanic Blacks experienced over 3x greater incidence of necrotizing enterocolitis (NEC) and over 2x higher infant mortality attributable to reduced breastfeeding rates [10]. Earaches and other gastrointestinal disorders were also more common as a result of breastfeeding disparities for non-Hispanic Blacks than non-Hispanic whites [10]. These higher incidences of illness were associated with greater medical costs but are likely to also contribute to missed work days and lost income, compounding the impacts of breastfeeding disparities [10]. As evidenced by the articles cited here, the development and adoption of emergent and evidence-based approaches, tools, and interventions within health delivery settings, for both clinicians and patients, require more frequent collaboration among life and social scientists to recognize and resolve race-based disparities.

1. Lind, J. N., C. G. Perrine, R. Li, K. S. Scanlon, J. M. Grummer-Strawn. Racial disparities in access to maternity care practices that support breastfeeding—United States, 2011. *Morbidity and Mortality Weekly Report* 63, no. 33 (2014): 725-728.
2. CDC. Maternity Practices in Infant Nutrition and Care (mPINC) survey. Atlanta, GA: US Department of Health and Human Services, CDC; (2013). Available at <http://www.cdc.gov/breastfeeding/data/mpinc>.
3. Philipp, B. L., A. Merewood, L. W. Miller, N. Chawla, M. M. Murphy-Smith, J. S. Gomes, S. Cimo, J. T. Cook. Baby-friendly hospital initiative improves breastfeeding initiation rates in a US hospital setting. *Pediatrics* 108, no. 3 (2001): 677-681.
4. McKinney, C. O., J. Hahn-Holbrook, P. L. Chase-Lansdale, S. L. Ramey, J. Krohn, M. Reed-Vance, T. NK Raju, M. U. Shalowitz. Racial and ethnic differences in breastfeeding. *Pediatrics* 138, no. 2 (2016): e20152388.
5. Asiodu, I. V., C. M. Waters, D. E. Dailey, A. Lyndon. Infant feeding decision-making and the influences of social support persons among first-time African American mothers. *Maternal and Child Health Journal* (2016): 1-10.
6. Meier, P. P., J. L. Engstrom, B. Rossman. Breastfeeding peer counselors as direct lactation care providers in the neonatal intensive care unit. *Journal of Human Lactation* 29, no. 8 (2013): 313-322.
7. Thayer, Z. M., Kuzawa, C. W. Early origins of health disparities: material deprivation predicts maternal evening cortisol in pregnancy and offspring cortisol reactivity in the first few weeks of life. *American Journal of Human Biology* 26, no. 6 (2014): 723-730.
8. Rubin, L. P. Maternal and pediatric health and disease: integrating biopsychosocial models and epigenetics. *Pediatric Research* 79, no. 1-2 (2015): 127-135.
9. Graham, G. N. Why your ZIP code matters more than your genetic code: promoting healthy outcomes from mother to child.” *Breastfeeding Medicine* 11, no. 8 (2016): 396-397.
10. Bartick, M. C., B. J. Jegier, B. D. Green, E. B. Schwarz, A. G. Reinhold, and A. M. Stuebe. Disparities in Breastfeeding: Impact on Maternal and Child Health Outcomes and Costs. *The Journal of Pediatrics* (2016) Nov 10. pii: S0022-3476(16)31096-4. doi: 10.1016/j.jpeds.2016.10.028. [Epub ahead of print]

Note: Terms for race designations, such as “Black” and “African-American,” came directly from the articles cited. These terms were capitalized in accordance with recommendations from Halley, J., Eshleman, A., and Vijaya, R. M. (2011). *Seeing white: An introduction to white privilege and race*. Rowman & Littlefield Publishers.

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