Mitochondrial Memory and Maternal Mourning

My Bokbok (maternal great-grandmother) was married for only a brief time before her husband migrated from China to the United States to work on the railroad. One day, his foot got caught in the tracks, and he was killed by an oncoming train. My Bokbok was widowed at the young age of twenty-nine, and my Popo grew up without a father.

My Popo immigrated with her husband and four children to the United States in March 1956. They had "six people and seven dollars" when they arrived. Those first few decades in the United States were marked by extreme poverty. To make ends meet, my Popo and her children, including my mother, worked as farm hands during the day, and my Popo worked at Hunt Wesson cannery at night. Whenever she was home, Popo was in the backyard tending to her vegetable garden—the family's primary food source. To make matters worse, my Popo's arranged marriage was filled with discord. Her husband, my Gonggong, did not take an active role in parenting—except to unleash harsh corporal punishment (what many would call physical abuse) on his children. Thus, my mother grew up without a close relationship to either parent. Nonetheless, as a young adult, she supported my Popo's decision to go against Chinese societal expectations and divorce my Gonggong by promising, along with her siblings, to take care of my Popo, financially and otherwise.

Fortunately, my mother did have one family member who offered her unconditional love and support—her Popo (my Bokbok). In 1963, my Bokbok was finally able to join her children and grandchildren in the United States. As a teenager, my mother had lots of fun with my Bokbok, passing her off as her mother at school open houses, and even teaching her how to do the twist. Bokbok was quick to defend my mother whenever anyone commented on her skinny frame, saying, "What do you want her to be so fat for, anyway?" A decade later, when my mom was studying at UC Berkeley, Bokbok's memory began diminishing; Mom regularly commuted to her hometown, about an hour and a half each way, to visit Bokbok. When Bokbok died, my mother was studying in the student lounge. She knew the exact moment Bokbok died—she was flooded by an overwhelming sadness, and she cradled her head on the table and wept. When she arrived back at her apartment, she immediately called home and learned the news.

For as long as I can remember, my parents have been divorced. My mother, the managing attorney of her office, worked incredibly long hours, often billing 115 hours per week. Like my mother, my closest relationship as a child was with my Popo. She called me her "shleem gohn bahng"—"the core of her heart". Similarly, I've always known she is inextricably embedded inside my being. Our bond made me who I am. While I was in my twenties, Popo started losing her memory to dementia. I was attending Brown on the other side of the country and conducting ethnographic research in Spain, but we Skyped every day I was away. On summer breaks, I drove to her house in the early morning hours and crawled in her bed to spend a few minutes with her before scrubbing in on surgeries at Sutter Medical Center and UC Davis Children's Hospital. Popo's mind was the clearest first thing in the morning, so those minutes every day were my opportunity to encounter all of her.

When my Popo passed away, I, like my mom before me, was studying at UC Berkeley. My mom called me on my cell phone to give me the opportunity to tell my Popo I loved her one last time. Initially, my phone was set to "do not disturb" because I was in a biostatistics exam. Knowing how important it was for me to say goodbye, my mom made repeated calls to me,

again and again, without break, over the course of ten minutes. When I finished the exam and noticed my missed calls, I immediately called my mom back. Fortunately, I was able to briefly say goodbye. Those few minutes were much too short, and I regret not having connected with my mom sooner. At the same time, Popo already knew what I felt in my heart—after all, I am her "shleem gohn bahng."

I went home over the weekend for my Popo's funeral. Over twenty years prior, Popo asked me to sing her favorite hymns—"Blessed Assurance" and "Jesus Loves Me." Not wanting to bring bad luck by directly stating her request, she told me to sing these songs, "the day I am no longer here." I knew what she meant, and I never forgot. Members of my extended family and church community approached me at her funeral, weeping and offering me their hugs and condolences. An older cousin, knowing how close our relationship was, asked me, "How are you keeping your composure?" The pain I felt on that day—and the pain I've been feeling ever since—is not the type of pain one can wear on the outside. That would be unbearable. It's a pain one carries, in every fiber of one's being, every moment of the day, and throughout the night. Some nights, I have moments of relief, because Popo visits me in my dreams. Other nights, she is not where I expect her to be, and I am consumed by despair.

In October 2019, I was attending the Advances in Mitochondrial Medicine Symposium in Dallas, TX when Dr. Heyman explained that all of his patients, individuals who seek out Dr. Heyman's expertise because their complex illnesses are rooted in mitochondrial dysfunction, became ill after being exposed to a tripartite model of risk. All his patients had been exposed to pathogens and environmental toxins, suffered a traumatic brain injury, and experienced emotional trauma approximately two years before the onset of their mitochondrial dysfunction symptoms. Suddenly, I felt singled out—as if he were speaking to all of his physician colleagues about me. I created a timeline in my mind. While completing my masters in epidemiology and PhD in medical anthropology, I struggled through a concussion for six months, from March to September 2015. My Popo's passing was in July 2015. In 2018, when I was at my worst, my lab results were positive for heavy metal poisoning, BPA poisoning, and multiple viral infections. Just as Dr. Heyman indicated, my mitochondrial dysfunction resulted from "the perfect storm"—a trifecta of exposures affecting HPA axis dysfunction and leading to cellular damage. I sat a little longer and reflected on what my body already knew—when my Popo died, it was as if a piece of every cell in my body died with her.

"Mighty" Mitochondria

Dr. Heyman's research unfolds at the forefront of mitochondrial medicine, thus providing innovative insights for clinical application. On the other side of the world, University of Newcastle professor Mary Herbert gave a TEDMED talk that explained some of the biological characteristics of mitochondria. She explained to her TEDMED audience, "Our mitochondria descend from ancient free-living bacteria that, two billion years ago, were engulfed by precursors of our modern-day cells. This has been referred to as the most important meal in history because it turned out the mitochondria could use oxygen to generate energy from the food we eat and store it in the form of ATP. ATP is an energy-carrying molecule that carry the fuel for life in all living things." Up until this point in her talk, her explanations were aligned with conventional understandings of mitochondria.

However, characterizations of mitochondria as "the powerhouses of the cell" are insufficient from a functional medicine perspective. Dr. Edeas emphasized the energy produced by mitochondria affect the entire body, saying, "Mitochondria can be found in all cells and placed strategically to provide energy. When you say energy, it's life. When you say energy, it's everything. It is connection. It is muscle contractions. It is brain behavior." Dr. Martin Picard, neurology researcher at Columbia University, furthermore critiqued the "powerhouse of the cell analogy" on *The Energy Blueprint* when he said, "We actually think it is a bad analogy because it is pretty mechanistic. It's very mechanical, I should say…this powerhouse analogy, which portrays mitochondria as little machines—this powerhouse that takes an input and transforms it into an output, and that is power generation or transformation. Mitochondria actually have this beautiful, complex life where they interact with each other."

Extending the holobiont theory of the body, Dr. Achacoso explained, "Essentially, [mitochondria] became what we call endosymbionts, or things that live inside our cells. So, if we have…100 quadrillion mitochondria inside our bodies, why don't we take care of them?" Mitochondria are in every cell of the human body, yet they are of bacterial origin and, as Dr. Achacoso explained, they continue to behave like bacteria. "They divide. They fuse. They have the ability to move inside the cell. They kill themselves. So, they have all of these particular mechanisms that behave as a bacterium, and, also, they have particular behaviors that are beneficial to the cell."

That is, mitochondria behave as if they are all members of a community, abiding by a certain set of rules, to the benefit of their *huge* society. Dr. Zach Bush, triple certified physician, indicated on *Autoimmune Secrets,* "The mitochondria are abundant. There are an estimated 14 quadrillion mitochondria inside a human body. That is roughly two hundred mitochondria for every human cell. In the neurons, we know that there are two thousand mitochondria per neuron.... So, an amazing density of these bugs living inside of our cells, and we are intrinsically dependent on these organisms to thrive inside of our cells so that we survive."

In addition to their communal behavior, mitochondria are in constant communication with other substances and microorganisms in our bodies. Pointing to other biological substances that interact with mitochondria, Dr. Picard indicated, "What we are finding is that mitochondria can actually respond to different hormones, or to different metabolic signals, and that's fairly well documented." Dr. Picard furthermore argues that, in certain situations, mitochondria act as hormones in the way they signal messages to various parts of the human body.

Focusing on mitochondria-microbiota crosstalk, Dr. Edeas indicated, "Mitochondria and microbiota share the same…structure and…mechanistics. So, we ask the question [of] whether there is a kind of relationship between mitochondria and microbiota." As if responding to this question, Dr. Michael Ash, an osteopath, naturopath, and nutritional therapist with a sub-specialty in immunology, explained the symbiotic relationship between mitochondria and microbiota in humans. During his interview for *The Human Longevity Project,* he indicated, "We have two bacterial components. One is the microbiota, which exists as a large range of different species. And we have the remnants of a bacteria that was subsumed by a cell a billions of years ago. [These] exchange information…. That access between mitochondria and microbiota is predicated in terms of efficacy by developers of nutrients. So, the bacteria require the nutrients to be extracted from the foods in order to make mitochondria become replicable, reparable,

and functional. And, equally, mitochondria release various metabolizers as a result of their activity, which favors a smooth, calm, functioning microbiota." Dr. Bush summed up these ideas when he said, "We see this beautiful communication or cooperation between the microbiome outside the cell and the mitochondrial microbiome within the cells."

Speaking on *The Mitochondrial Summit,* Prall explained how this metabolic relationship between mitochondria and microbiota unfolds: "The microorganisms metabolize…all the foods…and then the metabolites that come from these microorganisms communicate directly to our mitochondria. And those mitochondria pick up the signals about what to do." To give one example, Prall explained, ""Butyrate is one of the most beneficial metabolites that help mitochondria. They make new mitochondria, they repair cell walls. As a signaling molecule, [butyrate] is very important for mitochondria." Butyrate is produced by certain strains of Clostridium, Eubacterium, and Fusobacterium when they metabolize a plant-based diet rich in fiber and resistant starch.

Many functional medicine practitioners affectionately refer to mitochondria as "mighty" mitochondria because they are acutely aware of the determining role mitochondria play in human health. On *The Evolution of Medicine* podcast, Dr. Heyman revealed, "For me and our research group, there has been a revelation around the role the mitochondria play in a variety of chronic illnesses. If you think back to what we all originally learned about the mitochondria, as being, essentially, the power pack of each cell producing ATP. And that's where our knowledge end[ed]…. More recently, because of the research that I've done in chronic-fatiguing illnesses and, in particular, bio talks and exposure, what we've learned is that the mitochondria play an incredibly central role in controlling a number of different cell processes." Dr. Picard extended Dr. Heyman's comments when he asserted, ""The medical and the scientific community has linked mitochondrial dysfunction to every disease that I know of…. There is a very large body of scientific evidence linking the aging process and mitochondria, showing, quite convincingly, I think, that dysfunctional mitochondria can precipitate the accelerated aging process."

As Whitten explained on *The Human Longevity Project*, "mitochondria aren't just these mindless energy generators. They actually have a second role…that is, that they're actually danger sensors. They're actually the first thing that senses when there's some kind of threat, or danger, present in our environment. In response to that danger, whether it be an infection, whether it be psychological stress, whether it be a toxin—any different type of threat to the organism—those mitochondria sense it. Then, their job is to trigger a cascade of different responses in the cell that ultimately are designed to protect the organism from that threat." Like mother's protecting their babes, Whitten described the mitochondria's response as, "seal off the cell…so that toxin or infection can't spread throughout the rest of the body. Seal things off, turn off energy generation in that cell."

What Whitten is describing is "cell danger response"—a physiological process that has been extensively researched by Dr. Naviaux. Dr. Heyman's work unfolds adjacent to Dr. Naviaux' research. Dr. Heyman explained, "We've basically arrived at a similar place through two different modes of inquiry, whether it's metabolomics or genomics, but both of our roads have led to the mitochondria." Dr. Heyman furthermore indicated that Dr. Naviaux' conceptualization of "cell danger response" is extraordinary since it describes, "the pathway through which the cells and the mitochondria become injured and begin to shift their

metabolism." This emerging paradigm redefines existing etiologies since, according to Dr. Naviaux, when a patient is "stuck" in cell danger response mode, this situation gives rise to most of the chronic disease we are observing today. As Dr. Heyman put it, "We've learned the ways in which, when the mitochondria and the cell more broadly gets stuck in a phase, certain diseases arise." While the two doctors are conducting research on opposite coasts of the United States—Dr. Naviaux is at UC San Diego and Dr. Heyman is at George Washington University—their research is very complementary. Dr. Heyman explained, "He has his perspective, we have ours, and I think together, we form a full framework that, to me, represents a new model of medicine."

This reconceptualization of chronic disease etiology challenges our basic understandings of genetic inheritance since, as Whitten explained, "our genes are not actually controlling our biology in the way that's been thought for a long time. They're not the most upstream thing. Actually, the most upstream thing is the environment…. Your environment communicates with your mitochondria and then that, in turn, determines all kinds of genes that get switched on or off, which ultimately…dictate our response to stress and how resistant to disease we are…how much inflammation and oxidative stress we have going on in our bodies, as well as, ultimately, how long we live."

Explaining the link between the biological aging process and the functional integrity of mitochondria, Dr. Bland indicated on *The Human Longevity Project*, "Lifestyle, diet, [and] environment play principle roles. It's not just your genes alone. It's how they're influenced by the living process that gives rise to the integrity of your mitochondrial function." In the same vein, Dr. Chiu stated, "[Mitochondria] are exquisitely sensitive to toxins…. When we have so many toxins in our environment that severely impacts our mitochondria, we suffer from that." Dr. Chiu explained that when he encounters a patient with Alzheimer's, dementia, thyroid disorders, or autoimmunity, "I do the whole workup and I find they have issues with, guess what? Number one, mitochondria. But then, number two, issues with the ability to detoxify these poisons."

While a toxic environment poisons mitochondria and, in turn, harms human health, a clean environment can promote healing. Dr. Chiu explained that time in nature, "heals us at the deep energetic levels of our mitochondria." Sayer Ji, philosopher, curator of scientific literature, and founder of GreenMedInfo, described one particular way mitochondria derive health benefits from nature. Speaking on *The Human Longevity Project,* Ji said, "Chlorophyll has been found to be broken down in the gut into a metabolite, which then is taken up by the mitochondria and then utilized to capture sunlight energy. And so that actually recategorizes us as photoheterotrophic entities." That is, if provided the right food, mitochondria can use sunlight as an additional source of energy.

Environmental effects on mitochondria are important since mitochondria send signals and provide instructions to our human genes. Michael McEvoy, functional diagnostic nutritionist and founder of Metabolic Healing, noted, "There is a lot of crosstalk between our nuclear DNA and our mitochondrial functionality." McEvoy clarified nuclear DNA are the human genes inherited from both mothers and fathers, while mitochondrial DNA are bacterial in origin and are only passed down from mothers. He continued, "[The] crosstalk happening between our DNA and our mitochondrial function…is directly tied to how the cell methylates, how certain methyl groups and methyl reactions are going back and forth, how they're coming in

and out of the mitochondria at a specific rate. These things are really intricate when we get into mitochondrial metabolism and mitochondrial defense mechanisms."

Mitochondrial metabolism is responsible for regulation of innate immunity, calcium homeostasis, programmed cell death, and stem cell regulation, among other roles. Dr. Achacoso explained two of these functions when he said, "It is called a calcium sink, meaning it's where the calcium actually goes and is buffered inside a cell…. It can commit suicide—if there's too much damage to it, it can kill itself. Or, if there is too much damage to the mitochondria as a whole and the cell cannot be sustained, it will send a signal to destroy the cell and mark it for recycling."

Dr. Picard explained other biological pathways by which mitochondria determine what happens throughout the body: "Mitochondria also release other biochemical signals. They may be vibrational, or electrical—like [electromagnetic fields]—or maybe something else. These can be transmitted among mitochondria; between mitochondria and other parts of the cell, including the nucleus, where the nuclear genome rests and waits for signals and information to know what genes to turn on and which genes to turn off through epigenetics; and then ultimately to the rest of the cell and the rest of the body. So, mitochondria can send signals, including their own genome—they can release their DNA into the cell cytoplasm, the internal part of the cell, or even into the bloodstream. Those mitochondria-derived signals can go everywhere in the body. So, now the view that we are starting to develop is one of a communicating collective of mitochondria distributed across different organs and different cells that talk to each other."

Dr. Heyman compared this new paradigm to what he called "old school genetics." Instead of looking to see whether the patient has particular genetic SNPs, Dr. Heyman explained, "Now, we're able to answer the question, 'Well, with the genes you have, what are the genes doing? Are they on? Are they off? Are they responding to inputs appropriately? Are they working against you?' It turns out that the gene sequences in the mitochondria in particular are really the crossroads of all of this activity, and so the therapeutic interventions for us have become very specific, very targeted, and incredibly powerful for getting these patients better."

This last remark of Dr. Heyman's counters existing notions that mitochondrial diseases are present since birth and irreversible later in life. Dr. Heyman continued, "It's a whole new model of care, and one that basically rejects the disease model and really focuses on cell activity and self-healing and cell metabolism. It basically just tears down the conventional medical model of disease-based illness and really gets into the more process and functional and genomic aspects of how our bodies basically behave and respond to threats and stressors. It's an enormous insight, and it's certainly not ours only. There are other research groups that are beginning to target the same ideas, but it's a whole new day, essentially, for clinical medicine from that perspective."

One research group targeting similar ideas is that of Dr. Sinclair. He described how his research at the Paul F. Glenn Center for the Biology of Aging at Harvard Medical School proves it is possible to reverse the aging process in damaged mitochondria. He explained, "Within a week we could make old, dysfunctional mitochondria function and appear exactly like a young animal's mitochondria in the muscle…. We were told that mitochondrial dysfunctions were due to mutations that were largely irreversible…. We could turn a sixty-year-old equivalent mouse

back into a twenty- or thirty-year-old within a week. To me that defied everything we were expecting."

"Mommy and Me"

In her TEDMED presentation, Dr. Herbert explained mitochondria have their own unique DNA. While many of us have been taught our genetic identities are determined by the combination of two sets of DNA—those of our mother and father—mitochondrial DNA represent a third set of DNA. The mother's egg provides mother's DNA and the father's sperm provides father's DNA. Mitochondrial DNA is dispersed through mother's egg; however, this DNA is distinct from the mother's DNA. Father's sperm also contain mitochondria, but these are destroyed after fertilization.

Dr. Bland elaborated on this point during his interview for *The Human Longevity Project* when he said, "Mitochondria are passed down exclusively through our mothers because the mitochondria of sperm are in the tail, which drops off. The ovum, the egg, is really big and it has all sorts of mitochondria." Dr. Achacoso expounded, "During the fertilization process…the sperm [has] mitochondria because it needs to power up to fertilize the egg, but once inside, the fertilized egg actually produces mechanisms by which the paternal mitochondria commit suicide in and of themselves." Thus, while both males and females have mitochondria, they are only passed down from mother to child. Dr. Bland continued, "So our energy level metaphorically comes from our mothers. That's why you have a lot of maternally sex-linked conditions of toxicity associated with mitochondria, because it comes through the mother's genetics."

Through "three parents IVF," Dr. Herbert is working to provide parents with a new solution that helps to ensure the mutations in a mother's affected mitochondrial DNA (mtDNA) isn't passed on to her child. Using in vitro technology, mitochondrial DNA can be obtained from a donor's egg and combined with the human DNA of the intended mother and father. Since mitochondrial DNA do not undergo genetic recombination, simply passing through the maternal line from each generation to the next, Dr. Herbert's 2017 TEDMED talk pushes the limits of our understanding of reproduction and looks toward a future where certain mitochondrial diseases can be eliminated from a family for generations to come.

From the perspective of functional medicine, mitochondrial inheritance is a direct mechanism by which the well-being of our foremothers determines our own health. For example, Prall suggested on *The Mitochondrial Summit* that one's maternal lineage may influence how efficiently one is able to metabolize particular foods. Pointing to a potential mismatch between the language of mitochondrial genes and the language that is being spoken by metabolites from foods, Prall explained, "If I were to eat turmeric, does my mitochondria really even understand [the metabolites that are produced from] turmeric very well? Because from all that I can understand [about] my lineage from my mom's side, my mitochondria probably didn't have a lot of turmeric, wherever we came from…. My hunch is that me as a Northern European white guy, my mitochondria probably doesn't metabolize turmeric as well as someone from Indian…heritage."

Mitochondrial inheritance is woven together with other supra-genomic mechanisms by which mothers' well-being shapes children's biology. As Nakayama explains, "We cannot deny that our children's health is reliant on…particularly the health of the mother going into the

place of conception and pregnancy. There's more and more showing us that connection, whether it's about the microbial environment, or the toxins that mom is exposed to that are passed through the placenta, through the breast milk." According to Nakayama, "illness narratives" like the one I have shared are integral to discovering the appropriate path for healing. She said, "From a functional medicine or functional nutrition perspective, we look very closely at…the antecedents, the triggers, and the mediators. I call this, the client's story. What is their story? ...A huge part of it is the ancestry…. I don't think we can remove the child and their health from the mother and the father, but particularly the mother and her health in her life, and her ancestry."

Dr. Lambert elaborated on the multiple ways a mothers' health and well-being determines the biology of her child. "There's an increasing body of literature that supports the notion that a mother's microbiome can be transferred to her child, and the microbiome is of critical importance for immune health. It's been linked to the development of asthma, allergies, [and] autoimmune diseases." Dr. Gail Cresci is a dietician with over twenty-five years of experience. Her interest in gut microbiome, probiotics, and prebiotics inspired her to obtain a PhD in biochemistry and molecular biology. She explained to *The Human Longevity Project* audiences, "We always thought the fetus was sterile in utero and we're starting to realize now that, no, in fact, there are not only viruses that get transferred to the fetus, but also bacteria. And we started to find, through the umbilical cord, that the first colonization is happening in utero…. We do know that postpartum or during the delivery is [when the majority of the] baby's first colonization occurs."

Dr. O'Bryan explained the underlying mechanism for the microbial transference Dr. Lambert mentioned to *The Human Longevity Project* viewers. "In the last month pf pregnancy, the [vaginal] microbiome changes completely and there's a very high concentration of what's called Prevotella. It's a family of good bacteria…. Baby gets smothered in all of this bacteria as baby's coming down the canal. It gets in its eyes, and its ears, and its nose, and its mouth—just smothered with this bacteria. Why? Because the bacteria are the genetic blueprint for the baby. This says, 'Okay, baby, here's the code of the person who's going to be feeding you, and this is the code of the proteins that you're going to get from Mom's milk….' So, baby's genes get turned on to start producing digestive enzymes to break down Mom's milk. It's a beautiful, beautiful system."

Mother's milk, far from simply serving as a source of calories and macronutrients, also provides an extraordinary amount of indispensable information to the newborn's body. Dr. Cresci explained, "Breast milk is the magical food for an infant. The mom is producing the ideal food for her baby. It's predominantly carbohydrate…. But all those carbohydrates [are] a rich source of what we call oligosaccharides, and these are prebiotics. So, they're the form of polysaccharide that we, the host, don't break down. They feed the gut microbiota so they are able to then increase the abundance and quality of the gut microbiota." Dr. Achacoso clarified this point when he said, "Breast milk actually contains oligosaccharides that are not digestible to the infant. It's actually being produced in order to feed the gut bacteria in the colon of the infant."

Dr. Cresci then elaborated on the probiotic quality of breastmilk, explaining, "The other thing that a lot of people don't realize is there is live bacteria in breast milk. And so, breast milk does contain probiotics. And that's why it's really important to have the breastfeeding because

you have both the probiotic and the prebiotic there…. Formula companies…actually try to mimic breast milk…and even [despite] their best attempts, it still doesn't match the quality of human breast milk."

On the other hand, Dr. Lambert noted mothers whose microbiomes are out of balance will transfer vulnerabilities to their child through vaginal birth and breastfeeding. She explained, "So this is a multigenerational thing that can happen. If grandma took lots of rounds of antibiotics, that vulnerability in the immune system will be transferred down to the mother, which will then be transferred down to their grandchild."

Given that mitochondria are descendants of bacteria, they, too, are affected by antibiotics. Dr. Bland explained on *The Human Longevity Project,* "There are a whole variety of substances in our environment, including some antibiotics and other drugs that are very sensitive in the way that they influence the capabilities of those little mitochondria. For instance, as you think of [mitochondria] as once millions of years ago being bacteria, certain bacteria are killed by certain antibiotics. There are antibiotics we have today that actually are not so good for the mitochondria of our body, which are legacies for microbes from millions of years ago." Dr. Davidson further specified for *Autoimmune Secrets* viewers, "Science is actually now showing that antibiotics damage the mitochondria…. If you are having fatigue, if you are having energy issues…I think antibiotics can be [contraindicated]."

Dr. Bland signaled that his research has also identified other pharmaceuticals that have similar effects—for example, statin drugs. "People who develop what's called the myopathies from statin drugs—some 50% of people on statins have these muscle pains—that's associated with mitochondropathies. It's actually a result of a kind of low-level poisoning of the mitochondria." In essence, when mothers take certain pharmaceuticals—ranging from antibiotics to statin drugs—the damage to their mitochondria can have lasting effects on future generations.

Similarly, the food a mother eats will not only shape and determine her gut microbiome, but as Prall indicated, above, the metabolites produced from the mother's diet provide instructions for her mitochondria. In this vein, Dr. Cresci identified malnutrition as another potential source of microbiome imbalance that can have direct effects on future generations. "That fact that we are transferring bacteria—we're transferring mom's nutrients in utero—is really exciting, but also concerning too, if the mom is not eating properly." When considering the information that is passed to the baby through the mother's diet, it is easy to focus exclusively on the nutrients *inside* the food. However, what is *on* the food is also very important. Roundup, a common pesticide, has also been approved by the FDA as an antibiotic. Dr. Bush clarified, "Just like the microbiome is suffering under the herbicides and pesticides outside of our cells, this mitochondrial microbiome within our cells is also dying under the pressure of all these chemicals. That is, pesticides kill bugs—including tiny bugs like bacteria *and* mitochondria. Thus, taking certain pharmaceuticals, malnutrition, and exposure to pesticides are a few of the many ways in which a mother's microbiome and mitochondria may be damaged.

However, even if the mother is "microbially healthy," the baby may not be properly exposed to the mother's microbiome. Examples include babies who are born via cesarean and are formula-fed. In the case of cesarean section births, Dr. O'Bryan gave a nuanced description: "Sometimes it is [necessary], and you save lives. It's great. Nothing wrong with that. But there's

a deficit. Because baby doesn't come down the canal, baby doesn't get that inoculation, so the bacteria in baby's gut after birth thinks that the bacteria that was in the operating room is the normal bacteria there should be in the gut. So, baby has staph, and strep, and clostridium, and these bacteria that really aren't supposed to be there, that baby's GI tract thinks is normal. That's why the studies show those kids three, four, five years later [have] much higher incidence of allergies and eczema, and asthma." To ameliorate this problem, some obstetricians use a sponge to collect as much of the mother's vaginal bacteria as possible. Dr. O'Bryan continued, "When the baby comes out by C-section, the nurse takes [this] sponge and just smothers baby's face with this bacteria, and [uses] a Q-tip inside the gums and stuff, just to try to inoculate baby with some of these really critical messengers from Mom's reproductive tract."

Dr. Cresci turned to a final mechanism by which mothers' health determine how children will respond to the environment—IgG antibodies passed through the placenta in the last month of pregnancy. "What most people don't realize [is that] breast milk contains…immunoglobulin. So, it does have a lot of immune properties to it." Dr. O'Bryan elaborated by anthropomorphizing the mother's immune system and describing how it whispers to her unborn baby: "Mom's antibodies start going into baby. 'Here's some antibodies to cats. We've got cats at home. They're nice cats. You don't need to freak out when you come home, right?' Or, 'Here's some antibodies to mold. We live in the woods, and the leaves fall, and the leaves decay. There's some mold in the air. Don't worry about it. Here's some antibodies to help prime you so you know they're okay." He also explained the opposite scenario—when the mother has antibodies to her own tissues and to foods. Babies exposed to these latter types of antibodies can be born with sensitivity to foods, and are already primed for autoimmunity.

Dr. Achacoso acknowledged that an increased emphasis on the multiple ways mothers' health affects their children, beyond inheritance of human DNA, can inadvertently place pressure on women. He said, "So the mother is heavily invested in ensuring the survival of the child and she does it by a lot of mechanisms. First, of course, by passing on the healthy mitochondria to the child, and then nurturing the child with nutrients that actually make the child more adapted to the environment that it's in. I know it puts a lot of pressure on mothers to be perfect in a way." Likewise, Nakayama reflected on how emergent scientific discoveries increase the potential of so-called "mom guilt." Nakayama said, "How we get to [the role of mothers' health on children's health] and how we as women don't blame ourselves for our children's health is another thing to contend with."

At times, mothers struggle to weigh their own health recovery against opportunities to give their children the best start—all the while recognizing that mother and child's health are mutually imbricated. These types of moral dilemmas were encapsulated in one concerned husband's post to an online support group: "Wondering if anyone is in the same boat as my wife or can offer advice/support. She has Hashimoto's (7 years) and her hs-CRP results this week were 12.4 mg/L….She is currently breastfeeding our youngest, a 9 month old, and doc says we should consider stopping to get her health back on track. This has upset her more than anything. Would tapering off the feeds assist in lowering her inflammation?"

Transgenerational Trauma

On Day 5 of *Your Best Years Start Now*, Prall pointed to recent research findings to emphasize the unique effect of pregnant mothers' emotions on their developing fetuses. Prall described a study in which mice were conditioned to associate the smell of acetophenone with electric shock. The next generation had a spike in their stress response whenever they smelled acetophenone, even in the absence of a shock (Dias and Ressler 2013). These "energetic memories" can be passed down for at least two generations.

Dr. Bradley Nelson, author of *The Emotion Code*, applied the concept of emotional inheritance to humans when he said, "It's possible to inherit trapped emotional energy…. Usually those trapped emotions are from what the mother is going through because the mother is feeling an intense emotion and her whole being is resonating and vibrating at that frequency and the babies inside her are resonating at that frequency too." Prall pointed to research that has explored trans-generational trauma among the descendants of Holocaust victims. Prall asserted chronic and autoimmune diseases can be caused by lingering trauma, either from "adverse childhood events" (ACEs) or past generations.

Merging the perspectives of multiple colleagues, Dr. Jolene Brighten, naturopathic doctor, explained to *The Human Longevity Project* audience, "If mama's under stress, yes, it's going to change baby's telomeres, but it's also going to make baby run the [mitochondrial] stress response. Baby is going to get the signal the environment is not safe." She went on to explain that babies of "chill mamas" can adapt to multiple stressors, while babies of "stressed out mamas" will react to the same stressors with pain and fear. Over time, these negative emotions cause higher cortisol, HPA dysregulation, rapid cellular aging, and inflammation.

Dr. Picard's research connects emotional and psychological states back to the mitochondria. Problematizing the Cartesian split,[1] he explained, ""Mitochondria psychobiology—this mind-mitochondria link—sort of gets at the whole Descartes mind/body dualism and the fact that, it is very widely accepted of course, the mind has a profound influence on the body…. We know, for example, that childhood trauma can greatly influence risk of disease later on in life." Dr. Picard argued, "The mind/body connection and disassociating [Cartesian dualism] as a little artificial." He continued, "There is the mind, and there is this subjective experience which is very real—whatever we think in our head is very real to the person who experiences it—and then there are these biological changes in the immune system, in the wound, or in the brain. These are very real biological changes. What are connecting these things? How does subjective experience get translated into a language that the biology follows and then responds to?"

Returning to the role of mitochondria, Dr. Picard indicated, "Our guiding hypothesis is that mitochondria, and the flow of energy, is that connection—that interface." Speaking about his collaborative work with Anna Marsland and Brett Hoffman, "If you expose someone to a psychological stress—you ask them to speak in front of a camera, and then they feel stressed, they feel a bit angry and uncomfortable—we found that thirty minutes later, if you take blood and then you look in serum, there is more mitochondrial DNA that is released. That demonstrates that the mitochondria somehow respond to that subjective experience and then respond by releasing the mitochondrial genome."

---

[1] See Chapter 2.

Dr. Picard's research is driven by a few overarching questions: "Does how you feel inform your mitochondria? How you feel, meaning both negative stuff like stress, sadness, and depression, and also positive stuff like feeling inspired, feeling love, closeness, and trust, feeling motivated and uplifted…. Are these things predictive of how well someone's mitochondria will work? Or is it that how well mitochondria work predict how you feel in the future?"

In order to begin answering these questions, Dr. Picard referred to research he conducted with Dr. Elissa Epel at the University of California San Francisco. Describing the study procedures, Dr. Picard explained, "We had women fill out questionnaires. In the morning, it takes about ten minutes, you fill out how stressed you feel right now, how stressful you think the day is going to be, how much love and closeness you are experiencing, and how much sadness and rejection and anger you feel. Then they would do this also in the evening. For a whole week people would do this at home…. We had measures of how positive and how negative people felt in the morning and in the evening for seven days in a row…. On the fourth day, people came into the research lab and gave blood. From the blood we isolated white blood cells, which are cells of the immune system that have mitochondria, and then we measured the mitochondrial health."

Dr. Picard went on to explain the goals of data analysis: "We looked at whether how people felt on Day 1, Day 2, or Day 3—does that predict how well the mitochondria worked on Day 4? So, is it the mood that is predicting the mitochondria? Or is it the mitochondria that is influencing…the mood on Day 5, Day 6 or 7?" Turning to the study results, Dr. Picard indicated, "We found that it was how positive people felt on the day just before the blood draw where the association was the strongest. How people felt the day before they came—how positive, especially, in the evening—was associated with how much energy the mitochondria could generate the next morning. To us, that was mind blowing. The effects were pretty strong…. Ten to fifteen percent of mitochondrial capacity in the immune system is explained by how you feel the night before. That's a lot." There was no association in the opposite direction—mitochondrial function did not predict the emotions people felt. However, he recognizes "there is nothing in biology that is linear" and that more research needs to be done.

Physiological Memoirs: A Multilevel Sense of Self

Dr. Picard's research, combined with those of other mitochondrial experts, illuminates how mothers' psychological and emotional stress may shape the health of future generations. While this research is at the cutting-edge of mitochondrial medicine, its foundational concepts are not new. Thirty years before contemporary observations in functional medicine regarding mitochondria and the multigenerational effects of women's health, medical anthropologist Mariella Pandolfi described how the secret, emotional world of women is fundamentally experienced through the body.[2] In her 1990 article, "Boundaries Inside the Body: Women's Suffering in Southern Peasant Italy," Pandolfi described a symbolic anatomy, pathology, and physiology that bridges inner and outer experiences and distinguishes male and female worlds.

[2] Pandolfi's article emerged two years after Wallace et al.'s landmark paper in *Science* that established a connection between human diseases and mutated mitochondrial DNA. While Wallace pointed to how mitochondrial DNA affects human health, he did not explore broader issues regarding how women's emotional, psychological, and physical experiences affect future generations.

Her work documented how the female body feels and absorbs external events. Women experience a continuum between social catastrophe—wars, earthquakes, emigration, the disintegration of traditional social roles—and bodily catastrophe.

Using ethnographic evidence, Pandolfi argued this process allows the past to become inscribed on future generations of female bodies. The stories she collected during fieldwork clearly linked a multigenerational history to individual women. She wrote, "The ancestral discourse indissolubly links the women in the maternal line of descent by way of a metaphorical string of symptoms and illnesses that petrify any possibility of social redemption or recovery" (264). The "traces" women absorb convert the female body into a physiological memoir, thus opening up new interpretations of distress, illness, and disease. In essence, Pandolfi signals how the experiences of foremothers in one's maternal line produce new identities, characterized by a polysemic and multilevel sense of self, for subsequent generations of women.

I combine recent discoveries in mitochondrial medicine with Pandolfi's perspective of female bodies as physiological memoirs containing a multilevel sense of self. In so doing, I am bridging the discursive gap between what Pandolfi refers to as "symbolic anatomy, pathology, and physiology" and what Dr. Picard identifies as "real biological changes." Harking back to my dismissal of how "psychosomatic" illness is often characterized in biomedicine[3], emotional suffering is symbolically and somatically inscribed on female bodies in intertwining ways. Thus, I propose the concept of "mitochondrial memory" to signal how the symbolic and the somatic are knotted together in women's biologies.

Mitochondrial Memory

When I was in my mid-twenties, my Popo sensed the end was near. She was losing more and more of herself to dementia, and she was increasingly reminding the Lord she was ready to go home, whenever it was His will. During a family get-together over the holidays, she passed out all her jewelry to unmarried grandchildren and great-grandchildren. According to Chinese tradition, she would have gifted these gold pieces to each person on the occasion of their wedding. Knowing she would not live long enough to attend future weddings, she made the decision to distribute wedding gifts while she still could. I guarded Popo's wedding gift for the following years. When I eventually married, I wore the gold pendant my popo gave me with my Chinese chang sahm (a red traditional wedding dress). On my right wrist, I wore my mother's wedding gift—a gold and black coral bracelet that her Popo gave her as her wedding gift.

These pieces of jewelry are much more meaningful to me than the value they possess as material objects. For me, they are a symbolic representation of how my life is inextricably linked to foremothers in my maternal line. Some of the jewelry I have inherited dates back to the early Twentieth Century—and while the years have passed, these objects have stood the test of time, unchanged. When I wear them, I am reminded of how my foremothers' physiologies were unique among the general population, but unchanged from one generation to the next. The bracelets and rings I have inherited are a perfect fit for my size 3.5 ring finger and 5-inch wrists. They were custom made for me, and my mother, and my grandmother, and my great-grandmother….

[3] See Chapter 2.

Our similarities do not stop at our shared bone structure. Over the course of my mother's early thirties, multiple, overlapping chronic diseases started to take hold of her life, causing her severe pain and fatigue. When I was growing up, she didn't share her "private" information with me regarding her health diagnoses. I think she didn't want to burden me, or to cause me worry. Now that I am in my early thirties and have also struggled with chronic disease, she sometimes shares her health woes with me; however, this has tended to be after the worst symptoms have already passed. I will not describe her health issues with the same detail in which I have described my own. Suffice it to say many of the health issues I have struggled with—hypothyroidism, autoimmunity, viral infections, etc.—my mother has also experienced and is continuing to experience. It makes sense we would share similar diagnoses given the influence of genetic inheritance on health. However, I have always sensed our commonalities are rooted in something even more pervasive than the fifty-percent of my genome that I inherited from her.

My mother and I share mitochondrial memories of suffering and loss. Our multi-generational story unfolds continuously, like links in a chain. At least four generations have suffered the effects of truncated marriages, and absent or uninvolved fathers. At the same time, from one generation to the next, the unconditional love of maternal grandmothers has been the sustaining force. And, when maternal grandmothers have passed on, they have been mourned through the body.

Mom and I lost our Popos at the ages of twenty-nine and twenty-seven, respectively. We acknowledge to each other how fortunate we are to have had our Popos for as long as we did—at the same time, the time we had will never be enough. The mitochondria in every cell of my mother's body are exact copies of the mitochondria in her Popo's body. Likewise, the mitochondria in every cell of my body are exact copies of each of my foremothers' mitochondria, and they hold the stories of our maternal line. When our Popos died, it was as if our mitochondria knew that millions of themselves, copies from another link in the chain, had left the world.

Mutual Recognition: A "Spooky Science"

Using the concept of "mitochondrial memory," I am not only suggesting that emotional, psychological, and physical experiences of women are recorded by their mitochondria and passed down to subsequent generations, I am furthermore alluding to mutual recognition among mitochondria from the same maternal origin. The mitochondria of women in the same maternal line can directly influence one another—even when they are located in different bodies and separate by many miles. Since this may be difficult to imagine, I turn to physics and the theory of "quantum entanglement"—the phenomenon Albert Einstein affectionately referred to as "spooky action at a distance."

Einstein, along with Boris Podolsky and Nathan Rosen, first described quantum entanglement in the 1935 paper "Can Quantum-Mechanical Description of Physical Reality Be Considered Complete?" Quantum entanglement occurs when a pair or group of particles interact in such a way the quantum state of each particle cannot be described independently of its pair or group, even when the participles are separated by great distances. Writing for *Live Science,* Tim Childers explains, "Quantum entanglement is the ethereal connection between two or more particles such that any action performed on one instantaneously affects the

others, regardless of how far apart they are."[4] This notion lies at the heart of the disparity between classical and quantum physics since, according to classical physics, particles will respond to their immediate physical surroundings.

I will provide a simple analogy in order to place these concepts into layman's terms. Water, also known as H^2O, is a liquid at room temperature. If exposed to temperatures below zero degrees Celsius (32 degrees Fahrenheit), water will freeze and convert into a solid. Conversely, at temperatures above one hundred degrees Celsius (212 degrees Fahrenheit), water will begin to boil, create steam, and evaporate into the air. In each of these cases, the physical state of water is determined by its immediate surroundings.

However, quantum entanglement defies these general physical principals. In experiments with different types of particles—ranging from photons to molecules as large as buckyballs (Arndt et al. 1999; Nairz, Arndt, and Zeilinger 2003), and even small diamonds (Lee et al. 2011)—scientists have observed phenomena that violate the local realism view of causality. Entangled particles were separated and taken to two separate locations, as far as 746 miles apart.[5] In these experiments, certain features of the entangled particles—for example, polarization or spin—were measured at separate locations. When the particle at the first location was manipulated, this shifted the outcome of the particle at the second location. These studies show that entanglement produces a correlation between the measurements of particles, and that these particles share an instantaneous form of communication or "mutual information."

Recent findings in astrophysics suggest a degree of galactical connectedness that scientists had not formerly anticipated and, thus, share commonalities with quantum discoveries. In 2014, Damien Hutsemékers and his team noted unexplained alignments, stretching across billions of light years, of supermassive black holes at the cores of nineteen quasars[6]. Since black holes are actually ancient ultra-luminous galaxies—galaxies that have metaphorically "died"—these alignments beg the question of how interconnectedness persists, even after death.

Subsequently, a 2019 study by Joon Hyeop Lee et al. examined the rotations of 445 galaxies within 400 million light years of earth. That is, Lee et al. have observed a "mysterious coherence" in galaxy rotation, operating against the predictions of cosmological models, thus suggesting that galaxies are tied together by enormous, invisible structures. Like quantum entangled particles, distant galaxies are moving in unison. These "entangled" galaxies demonstrate interconnectedness across distances that are too great to be explained by the direct interaction of their gravitational fields.

In her article, "There's Growing Evidence that the Universe is Connected by Giant Structures," Becky Ferreira writes, "Galaxies within a few million light years of each other can gravitationally affect each other in predictable ways, but scientists have observed mysterious patterns between distant galaxies that transcend those local interactions. These discoveries hint at the enigmatic influence of so-called 'large-scale structures' which, as the name suggests,

---

[4] https://www.livescience.com/quantum-memory-entangled-far.html

[5] https://www.scientificamerican.com/article/china-shatters-ldquo-spooky-action-at-a-distance-rdquo-record-preps-for-quantum-internet/

[6] https://www.sciencedaily.com/releases/2014/11/141119084506.htm

are the biggest known objects in the universe. These dim structures are made of hydrogen gas and dark matter and take the form of filaments, sheets, and knots that link galaxies in a vast network called a cosmic web."[7]

It may be these findings from quantum- and astro-physics are simply confirming, at much smaller and larger scales, Pandolfi's observations of multilevel identities and functional medicine's application of the holobiont theory of interconnectedness. Stated differently, all these phenomena may, in fact, be one. Different types of scientists are discovering, using their unique tools, skillsets, and perspectives, an astonishing degree of connectedness at different scales, ranging from particles, to individual humans, to ecosystems, to galaxies.

With this in mind, I coin the term "mitochondrial memory," thus combining the theory of entanglement from quantum physics with recent advances in mitochondrial medicine. In so doing, I am embracing the murky waters between the literal and the figurative. As part of their study design, Jian-Wei Pan and colleagues developed "quantum memories"—devices that store quantum information. Using frequency-manipulated photons, these physicists successfully achieved entanglement between different "quantum memories." My interpretation of the term "quantum memories" is twofold—a "memory" references a technological device used to store information, and, at the same time, memories are, in and of themselves, the information being stored—the information that consolidates communicative, entangled bonds.

"Mitochondrial memory" furthermore brings Pandolfi's "physiological memoirs" to bear on functional medicine's understandings of maternal-inherited mitochondria and quantum physics perspectives of "memories" as the loci of entanglement. By pointing to "mitochondrial memory," I argue women experience a multilevel sense of self because their mitochondria are, to use the language of quantum physics, inextricably *entangled*. Since women inherit exact copies of the mitochondria in their maternal line, these mitochondria are *memories that contain memories*. They store the shared history of women linked by maternal lineage and entangled by maternal love. Mitochondrial memories exist in unison with the mitochondrial memories in foremothers' bodies. They carry the pain and suffering individual women never experienced but are inscribed on their bodies nonetheless. That is, when a mitochondrial memory is linked to the mitochondrial memory of a subsequent generation, it provides the code for being, loving, and loss.

Because of my entanglement, when the Lord finally took my Popo home, a piece of every cell in my body died with her. Ever since then, I've struggled to come to terms with how to live and heal in a world where she is not. My mitochondrial memory is searching for its source. It is searching…searching….

[7] https://www.vice.com/en_us/article/zmj7pw/theres-growing-evidence-that-the-universe-is-connected-by-giant-structures