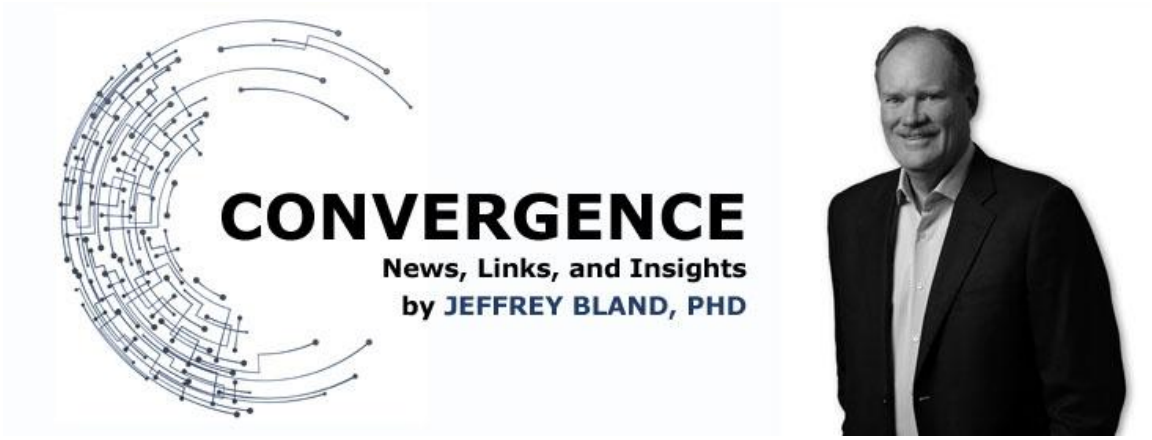

July 2019

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In this issue: Foods Also Have Microbiomes and Exposomes; Eternal Mitochondrial Quandary: Part 2 of 2 on Aging; Sometimes Eyes Appreciate a Little Culture; Announcing Big Bold Health; The Seventh Annual Thought Leaders Consortium

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Foods Also Have Microbiomes and Exposomes

It wasn't so long ago that we established that microbes were part and parcel of what it meant to be human, and even more recently, we've realized that everything we encounter in life—metabolically, cognitively, and otherwise—is recorded in our epigenetic diaries as part of our adaptation to living. Foodomics is the application of -omics sciences to identifying how food affects human health, and it is discovering that, much like ourselves, virtually everything we eat is heavily populated with a broad variety of microbes that interact with its metabolic processes to alter its overall composition, and, prior to their host becoming a foodstuff, these tiny colonists influence the course of its life. Thus, foods have their own microbiomes, and both foods ***and*** their microbiomes have unique metabolomes and exposomes. Plants are already known to cultivate distinct microbiomes on different plant parts, and these distinct microbial communities influence plant growth, health, flavor, nutrition, resilience, and pathogen resistance—some plant metabolites even appear to have close relationships with microbiome members, which may influence plants' evolution and environmental specialization.

The Global FoodOmics Project is tackling the voluminous work of studying foods' entire microbiomes and metabolomes, how food handling alters them, and how these variables affect human health. Its project manager, Dr. Julia Gauglitz, states that "We know about calorie count, and about different food groups, but the whole world of the molecules and the microbes in our food is a black box." The -omics of food encompasses not only nutritional and structural components of plant and animal foods, but also the totality of

microbes colonizing it, the genomes of all those microbes, and the metabolomes of all of the interactions between nutrients used by the food's microbiome in order for it to live and grow. As these microbes and their complex metabolic products are virtually inseparable from foods themselves (much as with humans and our microbiomes), Dr. Gauglitz encourages us to consider them an intrinsic part of foods.

Because foodomics employs sophisticated spectrometric and -omics technologies along with specialized data processing, it can additionally detect and quantify contaminants and non-intrinsic substances in foods, such as antibiotics, other human or animal drugs, growth-promoting substances, specific pathogens, hormones, allergens, acrylamide, and toxins. Food safety, in fact, is one of the most important applications of foodomics, and it can help identify origins and causes of outbreaks of foodborne illness. Food "fingerprinting" is another potential extension of foodomics' broad capabilities; a few examples include:

- distinguishing between organic and conventionally-grown foods (or even between organic and biodynamically-cultivated grapes)
- testing the quality and safety of fermented foods
- distinguishing between safe and toxic algae
- confirming foods' origins
- a more dependable way of grading quality and authenticity of olive oil
- tracing and authenticating specialty foods
- uncovering food fraud
- testing whether or not vegan foods truly are

Foodomics is considered the convergence of food engineering, -omics technologies, and precision medicine. The more we know about foods' complete compositions, biological activities, and influences, the better we can relate these facts to human health and thereby build a robust foundation for personalized nutrition. Foodomics will ultimately identify specific foods that may be helpful or detrimental to a given individual's health condition, and integrating foodomics with individuals' -omics and clinical findings will guide the development of completely personalized diets and tailored medicinal foods.

Julia Gauglitz, PhD

Live Educational Opportunity

Dr. Julia Gauglitz will be a speaker at the 2019 Thought Leaders Consortium in Seattle this fall. This is an event that is organized by the Personalized Lifestyle Medicine Institute and hosted by Dr. Jeffrey Bland. Find useful informational links at the end of this email.

Eternal Mitochondrial Quandary: Accumulation or Spring Cleaning?

Part 2 of 2: Housekeeping and Spring Cleaning

Mitophagy—so critical for successful aging—is enacted by cellular signaling networks indicating stress or damage, such as mediators of inflammation, heat shock proteins, or poly-ADP-ribose polymerases (PARPs) that detect DNA damage. In mitochondria with high ROS/RNS production, repair may be needed on a regular basis, especially if the cellular environment is characterized by low antioxidant concentrations. Whether repair or replacement can occur depends on cells' environmental conditions and availability of necessary resources; energy itself is a crucial limiting factor, and cellular NAD levels decrease with aging. NAD is needed for repair of cellular and mitochondrial DNA as well as mitophagy, and

therefore NAD availability can become a limiting factor in carrying out any of these crucial functions. PARP activation is beneficial in that it instigates DNA repair, but if called upon continuously (as a result of smoking, toxin exposures, overeating, stress, etc.) may leave insufficient NAD for mitophagy. The ketones formed during fasting or a ketogenic diet may help dampen PARP activity and improve mitochondrial efficiency by reducing ROS/RNS production.

These mitochondrial 'housekeeping' processes are mediated by factors that signal between cell nuclei and mitochondria. Chief among these are PGC1α (PPARγ coactivator 1α), which is considered a master regulator of mitochondrial biogenesis and controls nuclear transcription of proteins related to repair functions, and sirtuins, which operate in mitochondrial homeostasis and promote genomic stability by modifying proteins to target their actions. PGC1α and sirtuins receive 'reports' from other factors (such as hypoxia-inducible factor 1α and the forkhead box O proteins, FOXOs) regarding cell life and death cycle, oxidative or hypoxic stress, genomic damage, inflammation, and nutrient status. When cellular circumstances provide sufficient NAD and mitochondrial upkeep is indicated, Sirtuin 1 (Sirt1) will tend to 'vote for' mitochondrial integrity, encouraging mitophagy over cell death and activating PGC1α to order the appropriate functions.

Conditions that help maintain NAD sufficiency include regular exercise, fasting or caloric restriction, and availability of antioxidants that conserve NAD, such as quercetin (found in buckwheat, onions, tea, apple skin, cranberries, and citrus)—particularly important during aging, when PARP tends to be chronically active in correcting DNA damage and may spare less NAD for mitochondrial needs. Under circumstances when both cell nuclei and mitochondria cannot get enough NAD to carry out necessary functions, exhaustion of NAD stores may precipitate cell death. The master overseer directing these interactions is AMPK (adenosine monophosphate-activated protein kinase), which coordinates a broad network of signaling systems to control long- and short-term energy utilization throughout the body. As AMPK is primarily concerned with the body's energy economy, lifestyle factors that allow AMPK to prioritize maintenance of healthy cells and tissues are quite similar to those that aid NAD reserves and include exercise, fasting or caloric restriction, and dietary antioxidants like resveratrol.

While housekeeping is not often considered heroic, within cells and organisms, regular sorting and cleaning of resources increases quality as well as quantity of life and function. In dynamic health, mitochondrial repair and mitophagy are semi-continuous and represent a kind of quality control. As the cell ages, gathers DNA damage, and its genomic stability dips, its energy profile changes—and analogous changes occur within mitochondria, too. One might notice that what appears to be good for NAD sufficiency and activation of Sirt1 and PGC1α is similar to what is good for mitochondria; though NAD is utilized in a variety of body functions (including metabolic detoxification and mental work), they all rely on mitochondria. It is interesting to note that the very best for both are activities that present a slight physiological challenge: mildly stressful endurance exercise, building new brain pathways in problem-solving, a steady low level of oxidative stress, and forcing metabolism to bring out stored energy depots by limiting energy intake. Research increasingly points out that maintaining better mitochondrial function may increase the human healthspan—the period of active, comfortable living during aging. Modest challenges to mitochondrial function actively exercise the normal means by which cells rejuvenate and optimize their function—and so constitute the ideal functional approach to long-term 'clean' energy metabolism.

Hardworking cells like cardiac muscle cells, neurons, and overworked skeletal muscle cells are sensitive to mitochondrial maintenance dynamics and are particularly susceptible to deleterious lifestyle inputs like poor-quality dietary choices, sedentariness, and lack of enjoyable, constructive mental challenges—all of which downregulate our inborn adaptive responses. Mitochondria in many ways reflect how we live—whether we are physical or mentally active (or not), whether maintenance and housekeeping are integrated into our lives (or not), and whether (or not) we are accessing our mental and physical limits. Lifestyle choices that limit mitochondria's and cell's long-term options in resource management also limit the abilities of tissues, organs, and organisms to handle needs and stressors, and provision of 'clean' dietary energy sources and wise use of available energy are ultimately best for the health and comfort of the organism—again, perhaps not so very different from human economies.

Though they may have originated as bacterial gifts that enable heroic human feats of physical endurance and mental marvel, our mitochondria are reflections of ourselves.

Sometimes Eyes Appreciate a Little Culture

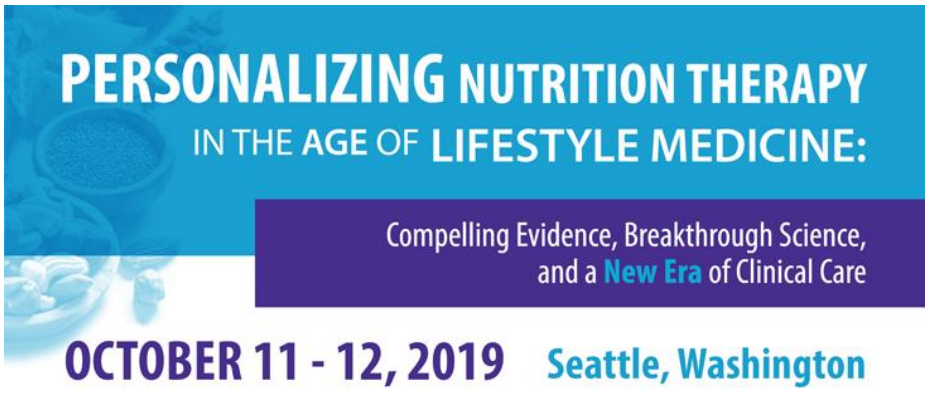
Chronic or excessive exposure to blue light emitted by electronic devices is well-known for irritating eyes and damaging the delicate epithelium nourishing the retina and its color-coding rods and cones. While the rationale for receiving enough of nutrients (like omega-3 fats, lutein/zeaxanthin, B vitamins, anthocyanins, and zinc) that build or protect the eye's specialized structures is easy to grasp, that for supplementation with probiotics is more of a stretch. A recent clinical study in Japan, however, has found that subjects aged 35-45 experiencing a high level of blue light-related eye strain showed significant improvement after receiving *Lactobacillus paracasei* KW3110 daily for 8 weeks compared to subjects receiving placebo. A parallel in vitro study also showed that exposure to this probiotic reduced damage to and extended the survival of human retinal epithelial cells. While this study is considered preliminary and its mechanism of action in relieving eye fatigue is not known, previous research on this probiotic strain discovered antiinflammatory properties that may contribute to these findings.

Big Bold Health is a new project Dr. Jeff Bland announced the launch of last month. Why start a new company? Because Dr. Bland is thinking about future generations. How can you get involved? Visit www.bigboldhealth.com and tell us how you—personally, individually, uniquely—define health. Dr. Bland is collecting responses to that question because he wants to demonstrate that health is a deeply personal and awesomely powerful concept—so much more than the mere absence of disease.

There's more! Dr. Jeff Bland loves a good discussion, so why not launch a new podcast along with that new company? Done and done. The Big Bold Health Podcast is live on YouTube, iTunes, and all of your favorite podcasting platforms. A new episode is published every other week. Watch, listen, subscribe, share, and review!

Be sure to follow Big Bold Health on Facebook, Instagram, and Twitter. We've got a busy

year planned and we don't want you to miss any updates!



THE SEVENTH ANNUAL THOUGHT LEADERS CONSORTIUM

Registration is open and seats are filling quickly! Dr. Jeff Bland is the conference host and facilitator. Join more than 300 attendees from around the world in Seattle this fall.

Click HERE to view the current program schedule.

Click HERE for a conference overview.

Click HERE to visit our 2019 Speaker Gallery.

Click HERE to register for the 2019 Thought Leaders Consortium.

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