



CONVERGENCE

News, Links, and Insights
by JEFFREY BLAND, PHD



February 2019 - Mid-Month Bonus

Thank you for subscribing to Dr. Jeffrey Bland's newsletter. Enjoy and share this information, which is for educational purposes only. Always consult with a qualified healthcare professional when you are in need of medical advice, diagnosis, or treatment.

In this issue: The Vantage Point: Personalized Lifestyle Medicine Center Grand Opening; Human Vitality Likes a Challenge, and Humanin Chimes in for Mitochondria; Classic FMU: Jeffrey Mechanick, MD

The Vantage Point: What's Been Happening in Dr. Bland's World?

Do you want to track Dr. Jeff Bland's activities and see photos from his travels? Follow his [Instagram page](#) to stay connected!



Exciting News Close to Home

It's a great year to start new projects! On January 24th, Dr. Jeff Bland was honored to attend the opening of the Personalized Lifestyle Medical Center in Gig Harbor, WA. Much will be learned about applying the N-of-1 concept to patient care at this state-of-the-art facility. Congratulations are in order for Brent Eck, CEO of Metagenics, Dr. Joseph Lamb, Dr. Michael Stone, and many others who are involved in this effort. To learn more about the PLMC and a groundbreaking research program called LIFE-HOUSE (Lifestyle Intervention and Functional Evaluation - a Health Outcomes Survey), read the [press release](#).

Human Vitality Likes a Challenge, and Humanin Chimes in for Mitochondria

Research into how human function is affected by genetics



and environmental interactions helps us understand: there is a certain threshold below which stress helps an organism maintain vitality and adaptivity, but above which it contributes to biological aging. Rather than existing as a discrete set point, however, this threshold likely represents a dynamic range in which various challenges are encountered, decoded, and answered, constantly exercising an organism's responsivity rather than conferring any kind of static optimum. Because energy creation (whether under normal circumstances,

disease, injury, or perceived stress) tends to be the main source of metabolic and oxidative stress, and because mitochondria are the primary location for this event, mitochondria are often the vanguard indicating when 'healthy' stress crosses the line to cumulative damage.

Genomics is beginning to explore mitochondrial DNA (mtDNA, which is quite separate from human DNA), and a few 'spokes-molecules' are emerging to help translate the mitochondrial dialect. One of these has been named "humanin," despite being purely mitochondrial and thus not strictly human, perhaps to denote its somewhat emissarial role. This peptide is considered a 'mitokine' (a cytokine analogue), and is released into the blood during mitochondrial distress, where it may serve as a hormetic signal for vital organs. While an early study indicated that its circulating levels may decrease with age, more stringent recent research has found that plasma [levels of humanin gradually increase](#) in an age-dependent fashion, which is consistent with the idea of mitochondrial dysfunction being integral to progressive biological aging.

Humanin is [highly expressed in cardiomyocytes](#), reflecting the high energy demands of cardiovascular function. Humanin levels are significantly [lower in pre-diabetic individuals](#) compared to normal controls, and researchers cite evidence that, in animal models of diabetes, administering humanin can improve insulin sensitivity. Though humanin signals mitochondrial energy stress, it has also been shown to inhibit neurotoxic effects of amyloid beta, and a [mitochondrial genetic variant](#) (the rs2854128 G-to-A polymorphism in the mitochondrial genome) that results in lower humanin levels has been linked to faster cognitive aging. This study also found that African Americans (AA) have lower circulating levels of humanin compared to Caucasian Americans (CA) and experience more marked effects from this gene variant, though it is much more common among CAs.

It may seem paradoxical that a mitokine indicating metabolic stress shows beneficial effects on glucose regulation and brain function, but this reminds us that cytokines and mitokines are signaling molecules. They are neither "bad guys" nor medicines, but instead serve as qualitative and quantitative communications that trigger a corrective response—with humanin particularly eloquent regarding the welfare of mitochondria. Humanin tends to [promote cellular survival](#) during challenge, and, interestingly, its levels correlate inversely with those of [insulin-like growth factor-1](#) (IGF1), which furnishes further clues about its roles. Minimizing stimulation of IGF1 is a key therapeutic focus during the modified fasting periods of the Fasting-Mimicking Diet, and appears to be instrumental in recruiting stem cells to rejuvenate tissues.

Humanin may function through [activating the chief energy regulator AMPK](#) and increasing expression of the cellular protection and longevity factors Nrf2 and PGC1 α —'paths less taken' in modern lives characterized by plentiful calorie-dense food and relative ease but employed to improve metabolic flexibility by caloric restriction, intense exercise, and dietary calorie restriction mimetics like resveratrol. It is possible that when metabolic stress more widely engages AMPK (adenosine monophosphate-activated protein kinase) to launch the process of deciding which cells and organelles can survive and which are slated for recycling, humanin levels may help indicate mitochondrial viability. The interplay among humanin, AMPK, and IGF1 reinforce the notion of essential links between mitochondria and energy/glucose metabolism—which plays out in cognitive, cardiovascular, and immunometabolic functions, especially as we age.



Diabetes as Cultural Mosaic

An interview with:
Jeffrey Mechanick, MD

February 2013

Remember when diabetes used to be one disease with one standard treatment approach? Now we understand that, far beyond the type 2 designation, there are genomic and proteomic subtypes that respond differently to treatment and have different co-morbidities and prognoses. Because feeding behaviors underpin many mechanisms of diabetes, behavioral nutrition is one of the few factors that links every subtype. However, each subpopulation presents unique cultural, economic, social, and logistic challenges, and applying a “one-diet-fits-all” philosophy cannot serve everyone’s needs. [In this classic FMU talk](#), endocrinologist and Mt. Sinai School of Medicine professor Jeffrey Mechanick, MD and Dr. Bland discuss a transcultural approach to diabetes and how to create versatile nutritional protocols that can be finely tailored to suit the needs of many while allowing care givers to develop individualized yet evidence-based plans. By considering endocrine influences on metabolism, well-conceived dietary guidelines may begin to address all stages of metabolic dysregulation as well as prevention. This attention is exemplified by the American Association of Clinical Endocrinologists’ and American College of Endocrinology’s 2015 comprehensive diabetes care guidelines to which Dr. Mechanick contributed, available at:

<http://journals.aace.com/doi/pdf/10.4158/EP15672.GL>

Classic FMU Top Ten Clinical Pearls: Jeffrey Mechanick, MD

1. Obesity, metabolic syndrome, and diabetes constitute a preventable progression
2. Prevention is the only way to keep up with chronic disease
3. Diabetes treatment must encompass psychosocial, economic, cultural issues
4. Chronic inflammation involves pituitary-bone interactions and vitamin D
5. “Gut talks to bone and bone talks to beta cells”
6. Chronic conditions require evaluating broader signaling network inputs
7. Medicine constitutes an ongoing education about individuals’ functioning
8. Solid understanding of nutrition principles enables adaptation in different situations
9. With proper clinical support, bariatric surgery can cause remission of diabetes
10. Environmental pollution is associated with autoimmune disease

Interview Links:

<http://jeffreybland.com/knowledgebase/february-2013-issue-jeffrey-mechanick-md/>

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