



# CONVERGENCE

News, Links, and Insights  
by JEFFREY BLAND, PHD



## December 2018

Thank you for subscribing to Dr. Jeffrey Bland's newsletter. Enjoy and share this information, which is for educational purposes only and is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always consult with a qualified healthcare professional when you are in need of advice regarding a medical condition.

**In this issue:** Aging and the Fasting-Mimicking Diet; Video Blog: Is Science Under Siege?; Aroma Research and Brain Plasticity; SNIppets: Childhood Asthma; The Link Between Stress and Autophagy; Explore the FMU Knowledgebase: Christoph Westphal, MD, PhD



### FMU KNOWLEDGEBASE

THE AUDIO ARCHIVES OF JEFFREY BLAND, PHD

Name two crucial features linking humans  
and our single-celled ancestors?

Mitochondria and sirtuin enzymes.

Both increase redox capacity, and  
may be functionally induced through  
mental and physical exertion.

AN INTERVIEW WITH:

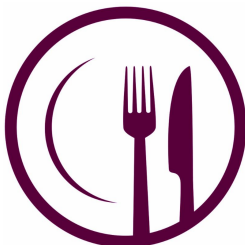
- CHRISTOPH WESTPHAL, MD, PHD  
DECEMBER 2007

FIND A LINK TO THIS ISSUE AT THE END OF THE NEWSLETTER

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## The Premier Way to Address Functional Aging?



We've recently learned that aging is mutable: though functional (biological) aging contributes to disease risk for many, it doesn't have to. Like DNA in somatic cells and mitochondria, stem cells are subject to age-related mutations that augment biological aging and can lead to inflammation, cardiovascular disease, and cancer. However, strategic lifestyle practices (that, incidentally, honor our genetic and epigenetic heritage) can reprogram the way cells utilize resources, limiting processes that cause functional aging as well as age-related dysfunction. Animal study demonstrates that a specialized form of modified fasting can [trigger tissues and cells to 'remodel'](#) their interiors, clearing out

damaged parts that perform inefficiently and activating stem cells to regenerate parts of the immune system, liver, muscles, and brain. Human clinical research has confirmed some of the metabolic and immunologic effects of this controlled, plant-based eating method, called the Fasting-Mimicking Diet (FMD). [In this 2018 article](#), Dr. Bland describes new ways of screening for age-related damage and how period observance of the Fasting-Mimicking Diet may address aspects of suboptimal aging and actively promote cellular rejuvenation.

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## New Video Blog: Is Science Under Siege?

Long before people found connection through social media and online discussion groups, hosted "salons"—gatherings where individuals would come together for a day or evening of discussion and respectful debate—were popular. Although rarer in this modern digital era, salons can (and are) still an effective way to exchange ideas and perspectives. Dr. Bland recently attended a salon hosted by his good friend Ruth Westreich, president of [The Westreich Foundation](#). He shares more about this unique experience and his follow-up thoughts with you in this new video blog.



Video Link: <https://vimeo.com/291992413>

Video is one of Dr. Bland's favorite communication tools. Subscribe to his [YouTube channel](#) to never miss an update, and also find many additional videos on the Personalized Lifestyle Medicine Institute [Vimeo page](#).

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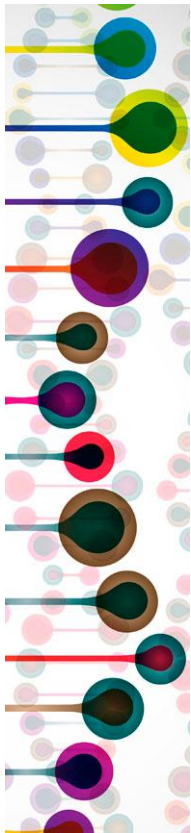
## Aromas May Boost Brain Plasticity Through Methylation



Smells can mean many different things to humans and animals: food, danger or safety, welcome or rejection, changes in weather, preparedness for reproduction, and other key communications. Smells affect neuronal organization and activation of receptors in the central nervous system, and detecting and responding to odors is one crucial means of impacting neuronal plasticity (and the ability to smell is not infrequently blunted in Alzheimer's and Parkinson's diseases). Beyond the mouth and nose, [odorant and taste receptors may be found in body locations](#) like the heart, skeletal muscle, respiratory tract, kidneys, and prostate gland, and in some cases aroma molecules may be 'smelled' solely by the heart, having no receptors elsewhere. After gathering sensory signals, the olfactory nerves communicate directly to the amygdala, hippocampus, and frontal cortex, brain areas critical in attention, emotion, memory, learning, and integrating new information. Some

researchers have even proposed that the olfactory bulb may be the predecessor of the enlarged cortex in mammals.

In one example of how smell relates to experiential learning, traumatic [odor-linked experiences](#) were found to alter genetic expression of odorant receptors in mice and to increase the density of these receptors in their later offspring—a kind of trans-generational warning signal based on epigenetic repatterning. Another example involves the DNMT3A gene, a key regulator of when and why genes are expressed via DNA methylation ‘tagging.’ Mutations in this gene are the main drivers of CHIP (clonal hematopoiesis of indeterminate potential), a preclinical condition that has been linked to biological aging, cardiovascular disease, and certain cancers. Recent animal research suggests that loss of function at the DNMT3A gene could potentially impact learning and memory, as this gene modulates genetic expression of odor receptors involved in neuronal plasticity. In mice [lacking DNMT3A function](#), genes normally activated by particular odorant molecules were found to be significantly undermethylated, leading to changes in genetic transcription and expression of their respective proteins. These alterations reduced neuronal plasticity, thus potentially limiting the ability to respond normally to environmental stimuli and transmit the benefit of these learning experiences to their progeny. Though this specific function of DNMT3A has not yet been confirmed in humans, these findings support the notion that the totality of our exposome, over time, reshapes our cognitive landscape.



## SNiPpets

How significant to health are certain single nucleotide polymorphisms, also known as SNPs? SNiPpets is an ongoing exploration of this topic. This column is produced by Jeffrey Bland, PhD and the Personalized Lifestyle Medicine Institute.

### This SNP Can Impact Childhood Asthma Through Methylation

The risk for childhood asthma is affected by genetic inheritance, and its incidence has increased within the last two generations. It is also strongly related to environmental exposures (like cigarette smoke, pollution, or certain microbes) and can also be influenced by maternal asthma. As it turns out, such alterations in lung and immune function may relate to a child’s epigenetic methylation patterns—or even those of the child’s mother. In humans, DNA methylation usually involves “tagging” the cytosine residue of a cytosine-phosphate-guanine DNA sequence (called a “CpG”) with a methyl group to modify its activity. (Stem cells, interestingly, appear to follow different methylation rules.)

Previous genome-wide association studies (GWAS) have identified specific single-nucleotide polymorphisms (SNPs) linked to asthma, but [a recent epigenome-wide association study](#) (EWAS) has discovered additional strong connections between some of these SNPs and reduced methylation within related genes during childhood. Among affected children aged 4-16, hypomethylation in these genes related to heightened activation of the following immune cell types: eosinophils, T cells, and natural killer cells. Perhaps not surprisingly, the methylation status of eosinophils themselves also affected the propensity to asthma, as they were found in this study to be strongly undermethylated in asthmatic children.

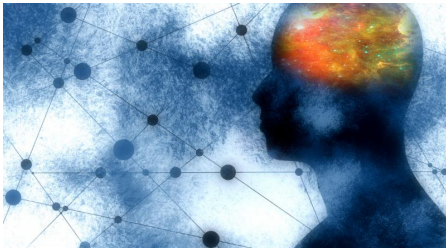
*The gene locations of specific SNPs (gene variant sites within the genome) are indicated by rs numbers, while those of specific CpGs (DNA*

*methylation sites within the epigenome) are called out with cg numbers. This nomenclature will likely become more familiar as medicine evolves in the Age of Personalization.*

In this EWAS, an important association was found for the combination of a G-to-A SNP at the rs9425436 locus of the SERPINC1 gene with hypomethylation at its related **cg01770400** (CpG methylation site) locus. Other undermethylated CpG sites associated with childhood asthma without specific related SNPs include **cg01445399**, cg01901579, cg03131767, cg06483820, **cg08085199**, cg10142874, **cg11456013**, **cg13628444**, cg13835688, **cg15344640**, cg16592897, and **cg19764973**. Among these CpG sites, altered immunoglobulin E (IgE) status in asthma was related to hypomethylation at sites indicated in **bold font**. Parents/guardians of affected children (or mothers with asthma) may wish to consult a Functional Medicine practitioner to consider therapies for improving methylation function and regulation of overactive immune cell populations.

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## Stress is the Doorway to Autophagy



Emerging understanding of how crucial autophagy (cellular repair and renewal) is to long-term health and comfortable function—and the extent to which modern lives tend to disallow this ‘missing half’ of metabolism—undoubtedly marks a turning point in medical science. It’s clear: we need to experience more of the survivable stresses that, throughout human history, have ‘exercised’ our innate

mechanisms of resilience. It can also seem a little intimidating, but, simply put, we exist because ancestral interactions among our genes, environment, and approach to life managed to survive all challenges. Behaviorally honoring this heritage through advantageous lifestyles enhances our own functional health as well as that of our descendants. At an elemental level, these manageable stressors include:

- Regular and periodically intense physical activity
- Limited periods of reduced caloric and protein intake
- Consuming phytonutrients that enable plant survival under metabolic stress

Sourcing food, water, shelter, and tools entailed constant physical effort for our ancestors. This kind of consistent activity is priceless for [triggering renewal at cellular and mitochondrial](#) levels, in turn optimizing energy metabolism and muscular performance. It triggers [the master AMPK metabolic network](#) that controls antioxidant and energetic resources as well as cellular life/death and detoxification functions, which in combination boost cellular efficiency and stress resistance, [especially during aging](#).

Humans evolved under circumstances of periodic food and nutrient scarcity—as did our plant and animal food sources themselves. [Caloric restriction](#) (including [intermittent fasting](#) and fasting-mimicking diet approaches) may be the premier method of [slowing senescence in stem cells](#) and enhancing their innate cellular rejuvenating capacity—again, employing AMPK, our ‘Chief Executive Housekeeper’ of metabolic resources. And by consuming plants that have survived environmental challenges such as drought/flood, excess heat or cold, or insect infestation, we receive the [adaptive hormetic benefits](#) conferred by their phytonutrient constituents. Though many phytonutrients additionally protect against excessive apoptosis (programmed cell death), many are recognized as encouraging autophagy in overstressed cells, and these include [resveratrol](#), [genistein](#), [quercetin](#), curcumin, [formononetin](#) (a phytoestrogen found in bean family members), and [piperlongumine](#) (found in long pepper). Recent research finds that triggering autophagy is another potential mechanism by which [fish oil helps protect](#) immune balance and tissue integrity, and a new study suggests that, in addition to heightening production of lipid mediators in the body, [aspirin \(or salicylate\)](#) may



### Where in the World is Dr. Bland?

Every year, Dr. Jeff Bland speaks in front of audiences around the world.

Will this be the year your paths cross?

[View Appearances Calendar](#)

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## FMU KNOWLEDGEBASE

For more than three decades, Dr. Jeff Bland recorded and self-published a monthly audio journal called Functional Medicine Update (FMU). Although he is no longer recording new issues, an archive of content spanning 1997-2016 is [free to explore](#) on Dr. Bland's website, and this extraordinary collection is now known as the FMU Knowledgebase.

To access the **December 2007** issue, which is featured at the start of this newsletter, click [here](#). That issue features an interview with Christoph Westphal, MD, PhD.

Interview Link:

<http://jeffreybland.com/knowledgebase/december-2007-issue-christoph-westphal-md-phd-sirtris-pharmaceuticals-inc/>

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