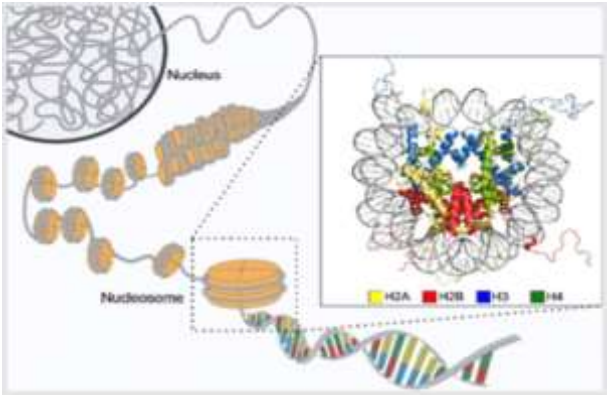
THE SCIENCE OF EPIGENETICS AND NUTRIGENOMICS



Why is it important and what can it tell us?

Abstract

While the science of epigenetics has emerged over the last few decades, the profound implications of these findings have only recently been applied to the assessment of human health. Diet and nutrition have profound effects on the functioning units that control expression of the human genome and maintain health and wellness. Epigenetic changes, which occur across a genome-wide landscape in every cell, every second, provide an avenue for real-time assessment of our nutritional health, assessed through advanced bio-resonance mapping technologies. Employing these technologies for assessment and monitoring of nutritional status can allow individual optimization of nutrient intake for better health and disease prevention.

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Dr. Timothy Van Meter has over 20 years of academic medical and diagnostic industry experience in the areas of molecular diagnostics, neurobiology, cancer, and epigenetics. Dr. Van Meter received his doctorate in Neuropathology and Masters in Neuroscience from the University of London and was a Postdoctoral Research Fellow in Neuro-oncology at Virginia Commonwealth University. He has researched and taught neuroscience, genetics and epigenetics in medical, graduate, and undergraduate settings at four different universities, and has been particularly focused on the science of epigenetics as related to human health and chronic disease states. Dr. Van Meter has served as Chief Consultant and Head of R&D for several innovative genetics and neuroscience companies. He has co-authored two books, received two patents, presented his work at over fifty scientific and medical conferences, and contributed to thirty-seven peer-reviewed scientific/medical publications. Dr. Van Meter serves as a scientific advisor to Regenr8™, a company focused on the utilization of epigenetics and custom nutrition, providing guidance in the development of custom analytics for epigenetics changes influenced by nutritional states.

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As owner and operator of BodyLogicMD of Philadelphia, Kenneth Varano, D.O. dedicates his practice to anti-aging and preventive medicine, where he also serves as Chairman of the Franchise Group of one of the largest functional medicine groups in the country, BodyLogicMD. In 2016, Dr. Varano became one of the first physicians nationwide to receive Board Certification in Integrative Medicine by the American Board of Integrative Medicine, is Board Certified in Family Practice by the American Osteopathic Association (AOA), is a member of the American Academy for Anti-Aging and Regenerative Medicine, and holds extensive training in Anti-Aging provide by the Fellowship in Anti-Aging and Regenerative Medicine. Kenneth Varano, D.O. received his undergraduate from New York University in 1989 and graduated from the University of Health Sciences, College of Osteopathic Medicine in 1994.

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Dr Kevin Hall is a Board Certified physician in Integrative, Functional and Integrative Medicine. He received his Doctor of Medicine from the Uniformed Services University, where he also served as Class President for three years. Dr. Hall has received a Joint Commendation Medal from the Department of Defense, an Air Force Commendation Medal and Meritorious Service Medal from the United States Air Force for his work serving as Chairman of the Joint Healthcare Delivery in Theater Working Group (all four military services) as well as Chief of Modernization and Healthcare Informatics for the US Air Force. Dr Hall received numerous Outstanding Resident Researcher and Outstanding Resident Teacher awards while teaching at the University of Arizona. He has 21 published articles in scientific journals, and has delivered over 50 scientific and clinical presentations at peer conferences. He has also been successful in business endeavors, serving as CEO/Founder/Owner of Advanced Metabolic Medicine (Ridgewood NJ), Do Well Be Well Integrated Medical Center (Haskell NJ), and CapitolMed (Haskell NJ). CapitolMed is Dr. Hall's primary current initiative, focusing on consulting for application of innovative medical technology in emerging markets.

1. Introduction
Setting the stage for proactive human health analysis

Epigenetics is the science of the complete genomic machinery, including not only the DNA backbone that is considered the blueprint of the human body, but also all protein machinery that encrusts the DNA and dynamically changes over time. Epigenetics, literally "what occurs above the DNA", refers to all of the factors that affect the functional expression of genes in the genome, and the inheritance patterns of the entire genome as genetic information is passed on to offspring. The dynamic nature of these processes is affected by levels of key nutrients from diet which have been shown to be determinants of gene function and expression. This naturally influences susceptibility to disease as well as general human health. The functional analysis of our epigenome, that is the active landscape of events happening across the genome of our cells, can be accomplished using known and novel methods to provide a comprehensive profile of our "epigenetic health". The dynamic nature of this landscape and the direct impact on human health are the subject of this review.

Nutrition and Epigenetics

Nutrition provides energy to our bodies in the form of simple carbohydrates such as glucose, as well as cofactors needed by the machinery of the body to operate properly and for optimum performance. The functional components of our synthetic cellular machinery require the proper balance of nutritional components to perform normal metabolic and catabolic processes, and to perform them optimally. These are the critical pieces of the human health and wellness puzzle. Understanding what we need and what to avoid in our diets have been a subject of inquiry since the very beginning of human culture. New tools that harness the expanding knowledge of our human biology can aid us in the quest for healthy habits and optimized nutrition. So, what do we know about epigenetics and human health? What about epigenetics and nutrition? These questions are fundamental to understanding overall genomic health as indicated by genetic expression. Knowing an individual's nutritional status is vital information and can help to modulate the optimal performance of the functional genomic machinery over an individual lifetime. This is especially true when an individual's health status is monitored over time with specific tests.

2. Structure and operation of the human genome.

DNA nucleotides, or bases, form the building blocks of our genetic blueprint, known collectively as the genome. DNA structure and it's accessibility to other essential proteins in cells, determine when the blueprint becomes active. The ability of our cells to express that blueprint (by translating the genetic code to RNA and then in turn proteins) is modified by addition of methyl groups to cytosine bases in DNA. Addition or maintenance of methyl groups leads to more tightly wound DNA coiled around proteins known as histones. These histones, act like spools around which the DNA helix is wound, and are also modified with methyl and acetyl additions, which influences when and where other cellular factors bind to the DNA/protein complex. These modifications to the proteins that encrust our genomic DNA are the basis for the dynamic changes that regulate our genome. Epigenetics, literally the events that occur on top of or above the genes, refers to the process of modification that regulates the active genome, the pattern of which is different in any given cell type.

Nutrition and DNA Methylation.

DNA methylation is also nutrition-responsive, as noted above, and can functionally impact the patterns and quantities of genes expressed in our cells. The degree and pattern of "silenced" DNA (though chromatin condensation), compared with non-silenced, or "open" DNA structure, can be studied throughout the lifespan. Modern epigenomic technologies can rapidly map areas that change across time in individuals pre- and postnatally. Such studies have elucidated the role of these modifications to our DNA in several ways:

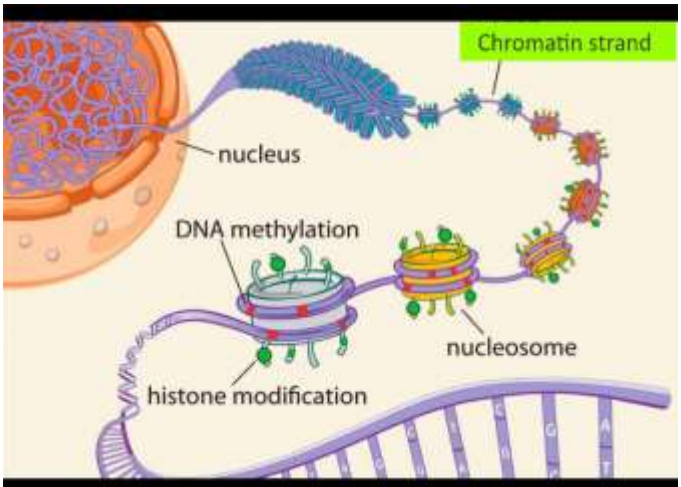


Figure 1. DNA methylation and histone modification are the elements of the active genome, the epigenetic machinery. Understanding the patterns of activity throughout the genome and how the bioavailability of essential cofactors in this process affect human health, are the specific focus of nutritional epigenetics.

1) DNA methylation patterns are established before birth in the growing fetus, establishing patterns that are maintained by the epigenetic machinery of the cell throughout the lifespan of an individual.

2) Different proteins and cofactors within our cells are responsible for establishing versus maintaining methylation patterns.

3) A complex web of modifying enzymes and related proteins provide control over how and when our genes are expressed in any given cell type, which rely on specific nutritional elements for proper function.

4) Changes to the epigenetic landscape at any point across our genome happen in real-time, over milliseconds, in a dynamic and constant balance that is specific to a particular tissue, region, and cellular microenvironment.

5) Maintaining optimal health and lowering our risk of disease relies on the proper balance of nutrition that differs for each individual.

DNA methylation is one example where widespread effects on our cells and tissues can be monitored by specific tests, developed to provide actionable information about human health. There are a large number of other cofactors and enzymes that play a role in the constant dynamic maintenance of our epigenetic state. Understanding the complexity of how these many cofactors interact in any one tissue is an emerging science.

The fundamental process of regulating the active programs of gene repertoires is known to be affected by essential cofactors that can be included in dietary supplements. This has been shown. For example, alpha-ketoglutarate (AKG), which has widespread impacts on epigenetic health (Shenoy, 2017). AKG is a critical nutrient for synthesis of amino acids for protein maintenance and helps to maintain gut health, energy metabolism through the tricyclic acid cycle (TCA, generating ATP), and bone mineralization (He, 2015). But AKG is also a specific and necessary cofactor for enzymes such as TET1 that demethylate DNA and thereby activate gene expression. AKG is a rate-limiting cofactor in this process, which also requires ascorbic acid (vitamin C), iron (Fe^{2+}), and oxygen. The bioavailability of any of these cofactors would impact the efficiency of DNA demethylation and therefore the healthy function of any given cell (Blaschke, 2013).

What to do with epigenetic profile information: The goal of optimum nutrition

Molecular analysis of human specimens has become more efficient, more accurate, and provides a great deal more information than in the past. We now live in an era where molecular testing can be achieved with very little biological material, as examples nanograms of DNA, protein and metabolites, a library of information from a single cell, and readout of the entire symphony of the immune system. Methods have been devised to "read" this detailed information from many different tissue types and biofluids, including saliva, urine and even sweat. The ease of obtaining hair bulb cells is one example where a great deal of information can be gleaned from very little cellular material. In one or a few hair shafts, the attached bulb cells and shaft contents can be used to obtain a full report of the nutritional state and resulting nutritional and epigenetic landscape of an individual.

Since the hair is a reservoir of vitamin and mineral deposition at any given time, this information can be analyzed by a number of techniques that identify the composition of elements in each sample. Traditional hair analysis was developed for forensic purposes as a biosample analysis method for profiling nutrient content, historically used mainly for assessment of mineral content. But the information available within the hair sample and bulb together can allow for much more comprehensive analysis, using state of the art next generation methodologies such as Bioresonance signature mapping.

Regenr8™ is changing the paradigm with Bioresonance Signature Mapping™ that detects the epigenetic signals that influence gene expression so that changes to diet, nutrition specifically Vitamins, Minerals, Amino Acids, Fatty Acids and Antioxidants along with lifestyle can be adopted to support optimal physiology and performance.
The Bio-informational Processor produces a scalar wave that senses the changes that occur when the hair roots are placed on the spectrum coil within the processor.
Informational signals, also known as a signature wave, are emitted from the hair root bulb found in the hair follicle.

The hair root bulb is used as an informational source, since the hair follicle is a part of the sensory system of the body and captures many environmental influences over time. The Bioresonance of the measured hair follicle signature wave then disturbs the scalar wave of the Bio-informational Processor, and the software converts the information into a digital record.

The information is then sent via a secure connection to our high-speed server technology that use bioinformatics to cross correlate the specific results with an extensive database of known optimal resonance ranges of vital nutrients (vitamins, minerals, amino acids, fatty acids, and antioxidants). Out of range conditions are identified as nutrient deficiencies, and the resulting Epigenetic information is presented in a comprehensive report which is returned to the healthcare provider. The Report is relevant for a period of 90-days as the Epigenetic influences are constantly changing.

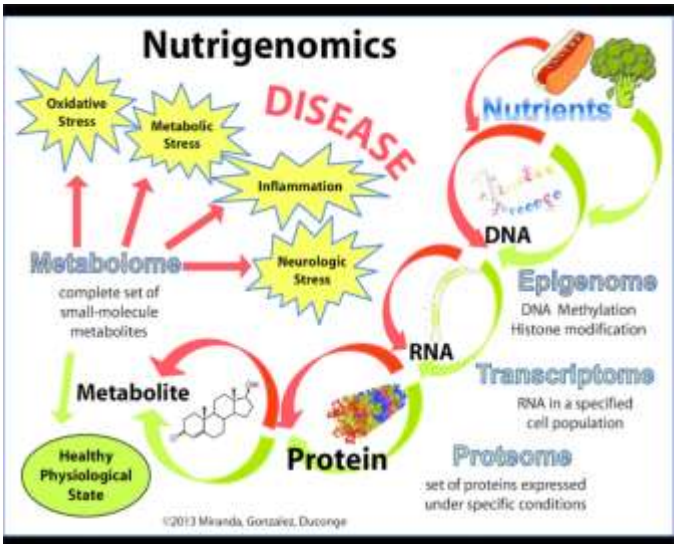
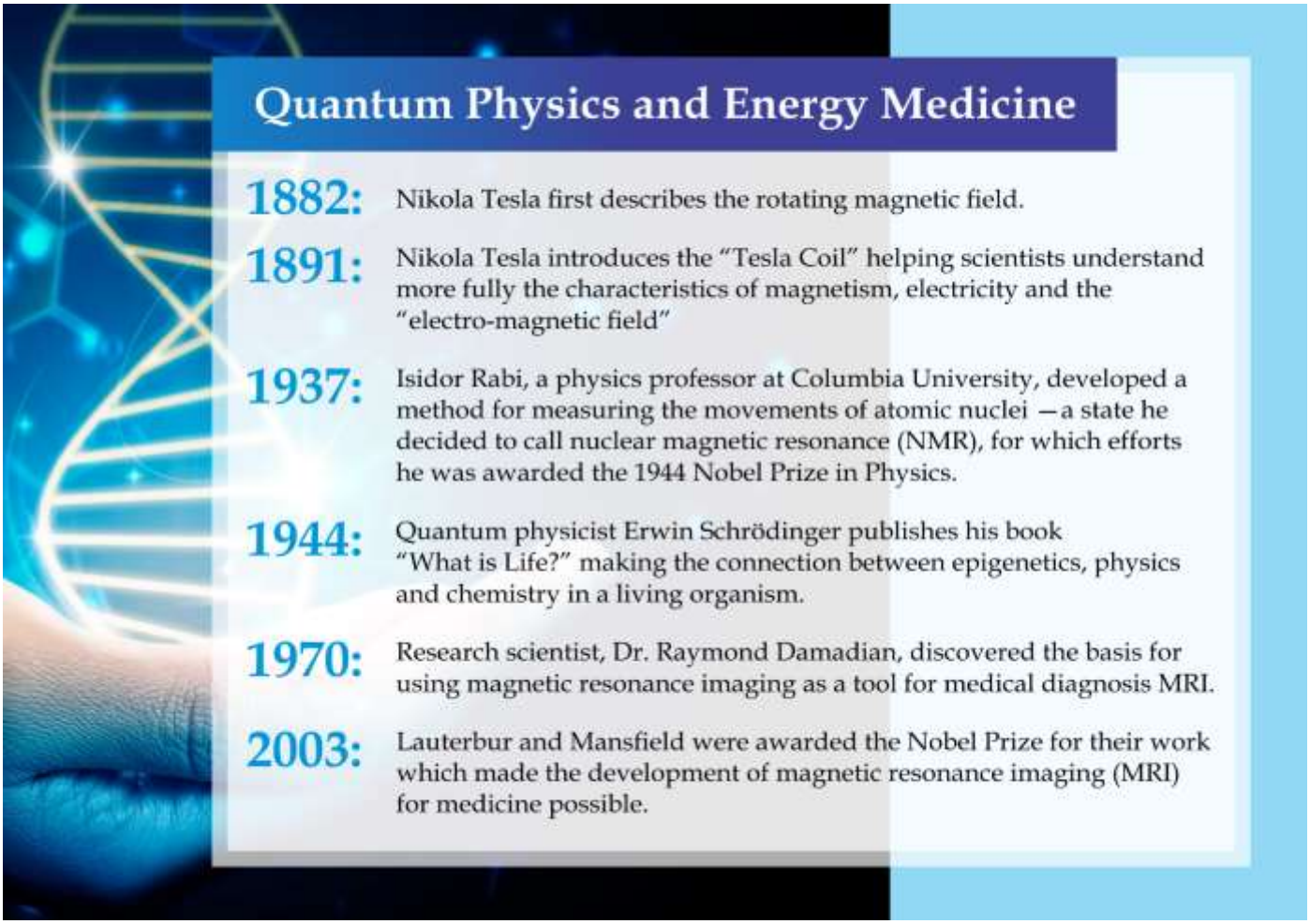


FIGURE 2. NUTRIGENOMICS IS THE SYNTHESIS OF SEVERAL INTERACTING SYSTEMS.

"Regenr8™ is pioneering next generation analytics to monitor nutritional needs which are addressed through custom formulations for optimum health and well being."

Timothy E. Van Meter, PhD



Three questions often arise:

1.) What is a Scalar Wave?
2.) What is Bioresonance?
3.) Why do you use hair?

The Scalar wave is a longitudinal energy way that is capable of carrying a large information set. In his search of a energy source that could travel wirelessly, Tesla developed his now famous coil in 1900. His work was not uniformly understood until the dependence on vortices was proven in 1990 and finally the acceptance of magnetic monopoles in 2009. It was then that the scalar wave, a static wave emanating from one point, began to be understood. The vortex enhanced the compression of information such that a great deal of information could be exchanged between cells even over long distances.

Electromagnetic waves are transverse waves and are better suited for voice transmission, but they decay over long distances. The longitudinally oriented scalar wave does not lose power over long distances.
NASA soon recognized this ability for quantum communication and measurement and to this day explores this technology.

Furthermore, DNA propagates such a longitudinal wave along the vector of its magnetic field. The coding regions of DNA make up only a small proportion of its entirety. What once thought of as "junk" DNA is now known to be "introns" and is the control of what is expressed by the "exons", the essence of epigenetics. This information is carried and transmitted by these waves. This message may be resonant or not and it is this message, whether the same or different, that is communicated back to the reader. It is the presence of the vortices that allows quantum scanning of the information contained in the

the scalar wave to be exchanged between a "reader" and a "writer", be it a cell or man-made coil.

Bioresonance is simply the fact that the biology is filled with frequencies. These frequencies are how one cell, or its nucleus, communicates with another. And if a resonant frequency is absent, or of a higher or lower power this is sensed. The scalar wave is necessary for the "reader" and "writer" to be assured of equal calibration without signal loss. In one experiment colonies of yeast were exposed to either clotrimazole (an antifungal), scalar waves "informed" by clotrimazole or just to scalar waves. The scalar waves informed with the antifungal were effective in killing the yeast without exposing the colonies to the drug itself. The Bioresonance of the drug was successfully transmitted without the physical drug.

We use hair because it contains a record of exposure, recorded in 5-7 days and lasting about 90 days. It is easily accessible, easy to preserve prior to testing and used frequently in other bioassays, so it is familiar to patients.

The hair scanner is a biofeedback device utilizing technology based on the patents and technologies of experimental physicist Nikola Tesla. Using these technologies, morphogenetic energy fields of the DNA sample are scanned, determining where the stressors are. This information then recommends a remedy that communicates and stimulates the patient's metabolism to self-balance.

Biofeedback is traditionally a mind-body technique that helps teach patients how to influence the autonomic nervous systems - the part of the body that controls involuntary physical functions such as blood pressure, heart rate, muscle tension and brainwave frequency. This epigenetic scan extends the ability of a person to monitor his or her internal responses and develop a sense of how to move them in positive ways. Epigenetic mapping can detect internal bodily functions with sensitivity and precision and allow involuntary physical functions to be translated in ways that can be understood.

Why is it that we humans - despite continual improvements in diet and medical care and a more comfortable lifestyle - are forced to battle against ever more illnesses and degenerative conditions? We are constantly being told that our bodies are "weak", and that we should strengthen it with commercially available products etc. In our experience, the DNA is affected, primarily as it directs the inflammatory and immune system response, when time after time it is exposed to electromagnetic fields, magnetic fields, chemicals, pesticides/herbicides, hormones, geopathic stress, radiation or other negative environmental influences. The human's metabolism becomes like a blindfolded boxer: strong, but blind!

The scanner detects, in the hair, entities that are off-balance for that individual at that time. Using this data, remedies are suggested to optimize functional performance.

The Science of Measuring An Energy Signature

Since the foundational building blocks of matter (atoms) contain a unique charge, when combined into molecules, proteins, fats, sugars, cells and subsequently organs, each structure contains a unique energy signature. By identifying the unique signature of each anatomical structure, the MRI is able to visualize the inner body using an electromagnetic field.

Similarly, the epigenetic region of each person's DNA is populated with chemical compounds and proteins which are used by the body to regulate expression of the underlying gene. In essence, the epigenome defines the modifiable phenotype of the individual. These epigenetic regions also contain unique, identifiable energy signatures. By using new quantum physics technology, and utilizing Nikola Tesla's electromagnetic field, we now have a way to analyze a person's epigenetic signature and what varieties of bioactive foods positively and negatively influence the epigenetic activity of an individual.

Modern Application of Energy Signature Mapping

A November 2018 review article published in the International Journal of Molecular Sciences discussed the new science of "Environmental Epigenetics". Powerful evidence has recently been found showing the impact of the environment on epigenetic expression. Of all the possible influencers, the most powerful factor is the use of bioactive food. The authors state "Deciphering the epigenetic signatures triggered by bioactive food components might pave the way for personalized nutritional interventions and aid our understanding of how our bodies respond to specific diets or nutrients." (Tiffon, 2018)

Regenr8™ has made these interventions a reality with the use of Bioresonance Signature Mapping™ and the creation of the Optim8 Bioactive Food Therapy!

Self-renewal, regenerative fasting, and stem cell activation

Regenerative fasting is a practice whereby an individual can activate lipid metabolism, gluconeogenesis, and even stimulate activation of latent stem cells to aid in tissue repair and renewal (Blashke, 2013). Most tissues in the body maintain a reservoir of stem cells that can become activate during normal turnover, such as in epithelial tissues like basal skin cells and cuboidal epithelial cells that line the gut. These tissues are externally exposed- our world facing surfaces, whether covering the outside of our bodies or exposed to all that we ingest along the digestive tract. As such, they are subject to significant insults from our environment, diet and habits of ingestion. There is a natural turnover of these cell types and the hematopoietic cells that give rise to the red and white blood cells, supporting oxygenation of our tissues and forming the basis of our immune system, respectively. In recent decades, we have also elucidated the location and role of stem and stem-like cells in specific areas of the brain, a complex structure once thought to be unable to regenerate cells. The reservoir of stem cells in the brain is a repository that can aid in maintenance and repair of areas of decline and damage, in a limited and tightly regulated fashion. The regulatory program of these stem cells is in fact epigenetically controlled, as with the fate and phenotype of any cell in the body. The program in these cells can be influenced by diet and behavior, as many studies have shown (Niculescu and Lupu, 2011). And the stem cell reservoir is also present in muscle tissue, as well breast and virtually all other tissues. The capacity for these cells to stay in an immature or stem-like state is tightly controlled by epigenetic mechanisms, with the patterns of active and restricted genes controlled by methylation and associated factors. Activation of repair and renewal programs in these latent replacement cells have been shown to be directly inducible by nutritional factors including well-studied examples such as fatty acids, vitamins and soy isoflavones, as well as compounds in citrus, medicines and many other dietary factors (Burdge and Lillycrop, 2010).

Regenerative fasting can engage the cellular programs by which stem cells become activated and engaged in tissue repair. This practice also leads to cell programs where alternative energy sources are utilized and residual fat stores become activated. Stored toxins (many are lipophilic and end up in our fat reserves) can then be released and eliminated in the process. Therefore, regenerative fasting is a simple, easily implemented method to cleanse the body and reset it nutritionally. It is a natural, simple and effective way to engage the body in more efficient self-renewal process. This sets the stage for optimizing nutrition through addressing deficiencies identified in the initial personalized nutrition analysis, and custom formulated blend of supplements. As a simple food additive, the epigenetic status of many health related facets of genomic activity can be more optimally maintained, with easily repeatable analytical results that can show the impact of the program. This can be followed up by periodic monitoring of the individual's spectrum of nutrition at regular intervals, to assess the ongoing benefit and to maintain individual engagement with personal health.

Summary of information presented: Your Epigenome, Your Future!

The information reviewed here is meant to illuminate the specific link between dietary habits and health effects related to nutritional deficiencies. There are many well-documented studies focused on the effects of nutrition and nutritional supplementation on the epigenetic status of individual health related genes (reviewed in part in Niculescu and Lupu, 2011; Tiffon, 2018). The effects of nutrition on maternal and on fetal health and postnatal outcomes are also well presented in the scientific literature. This information is important to understand, as are studies relating epigenetic states to specific health conditions such as dementia and cancer, but these are beyond the scope of this review.

The continuing development and refinement of comprehensive testing modalities, and especially tests that can assess in real-time the status of nutrition as it related to the epigenome and cellular programs related to health, will lead to better outcomes and greater awareness of health and general wellness. Such advances have the potential to non-invasively monitor and optimize personal health and will engage patients and the general public in their own personalized health interventions that can be largely nutritionally based. This approach removes much of the guess work from the personal nutrition assessments, and is complementary to the many wearable health technologies that are emerging and becoming integrated into our daily lives.

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