Overview of Biomedical Research and the Causes of Chronic Diseases

This document has been prepared to provide an overview of the findings of the Center for Modeling Optimal Outcomes® relative to the causes of chronic disease that are the result of their 10+ year investigative process.

Three examples of outdated science that have had a catastrophic effect on the ability of biomedical researchers to identify the causes of chronic diseases are provided below. Following these examples, information has been provided that identifies flaws that were created as the result of the lack of adequate technology that started in 1926.

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Substances in the body interact and nitric oxide (a free radical that is the target of antioxidants) is necessary for cellular life!

"Professor Jonathan Stamler's latest findings regarding nitric oxide have the potential to reshape fundamentally the way we think about the respiratory system -- and offer new avenues to save lives. It may be time to rewrite the textbooks.

Scientific dogma has the respiration process involving only two elements -- oxygen and carbon dioxide; specifically, the delivery of oxygen from lungs to tissues, and the removal of the waste product, carbon dioxide, through exhaling.

Recently published online in the journal *Proceedings of the National Academy of Sciences* (*PNAS*), Stamler and colleagues demonstrate that nitric oxide is essential for the delivery of oxygen to the cells and tissues that need it.

Stamler, MD, a Professor of Medicine at Case Western Reserve University School of Medicine and Cardiologist at University Hospitals Case Medical Center, led a team that showed that nitric oxide must accompany hemoglobin to enable blood vessels to open and then supply oxygen to tissues."

Dr. Stamler said, "The simplified textbook view of two gases carried by hemoglobin is missing an essential element -- nitric oxide -- because blood flow to tissues is actually more important in most circumstances than how much oxygen is carried by hemoglobin. So the respiratory cycle is actually a three-gas system." http://www.sciencedaily.com/releases/2015/04/150410095506.htm

Note: The research reported in this study validates two critical issues. First, nitric oxide, a "free radical" targeted by antioxidants, is essential to maintain cellular health and well-being. Without nitric oxide, oxygen alone cannot support cells and they can become cancerous.

Second, substances in the body (e.g. carbon dioxide – nitric oxide and oxygen) interact and, when imbalances occur, the outcome can be diseases.

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The DNA alphabet is incomplete!

"Over the past decade, research in the field of epigenetics has revealed that chemically modified bases are abundant components of the human genome and has forced us to abandon the notion we've had since high school genetics that DNA consists of only four bases.

Now, researchers at Weill Cornell Medical College have made a discovery that once again forces us to rewrite our textbooks. This time, however, the findings pertain to RNA, which like DNA carries information about our genes and how they are expressed. The researchers have identified a novel base modification in RNA which they say will revolutionize our understanding of gene expression." http://www.sciencedaily.com/releases/2012/05/120517131655.htm

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How can plaques accumulate in the brain?

Controversy has existed over the ability of the brain to utilize the mechanism of autophagy to maintain cellular homeostasis. With that being said, studies are finally emerging that elucidate the existence of the process of autophagy as a means of preventing neurodegeneration. http://www.annualreviews.org/doi/abs/10.1146/annurev-neuro-071013-014149

Furthermore, only recently has research linked autophagy to the lymphatic system. http://www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=view&path%5B%5D=2605

Finally, researchers are unraveling the mysteries behind the mechanism of autophagy (a.k.a. the process of "taking out the trash") as the cellular defense that prevents the aggregation of plaques that create Alzheimer's and other forms of dementia.

"Decades of medical theory which considered the brain as different from other organs of the body and without lymphatic drainage system were, well.... simply not correct.

The University of Helsinki has independently published a paper in the Journal of Experimental Medicine which looks amazingly similar to the University of Virginia's paper on lymph vessels published just two weeks ago. Both universities have found:
A dural lymphatic vascular system that drains brain interstitial fluid and macromolecules
http://jem.rupress.org/content/early/2015/06/09/jem.20142290.abstract"
http://ccsviinms.blogspot.com/2015/06/rewrite-textbooks.html

Moving Beyond Outdated Science to Include Flaws

In 2005, while pursuing change inertia and decision-making in the hospital industry, the Center's team inadvertently discovered the fact that brain chemistry (neurohormones) interacted and, at times,

imbalances were created by thought processes that could impact logic and emotions. At that time, these findings were contrary to all existing theories and principles in cognitive neuroscience.

Alerted to the fact that interactions and imbalances occurred at the cellular level, The Center sought input and guidance from a variety of scientists. Using these preliminary findings as a basis, the electrolytes (i.e. sodium-potassium-chloride and calcium-magnesium-chloride) were targeted to determine if imbalances could be responsible for disease states. While tacit knowledge existed relative to the relationship between sodium and potassium, an explicit and scientifically verifiable explanation did not exist. Lacking valid scientific studies to support these hypotheses, The Center was forced to wait several years for peer-reviewed scientific studies to support their assertions. For example, it was not until 2009 that studies identified a mutualistic relationship between sodium and potassium.[1]

The novel nature of these discoveries and the fact that interactions could be verified through existing research prompted The Center to form a separate life sciences group, MCFIP.

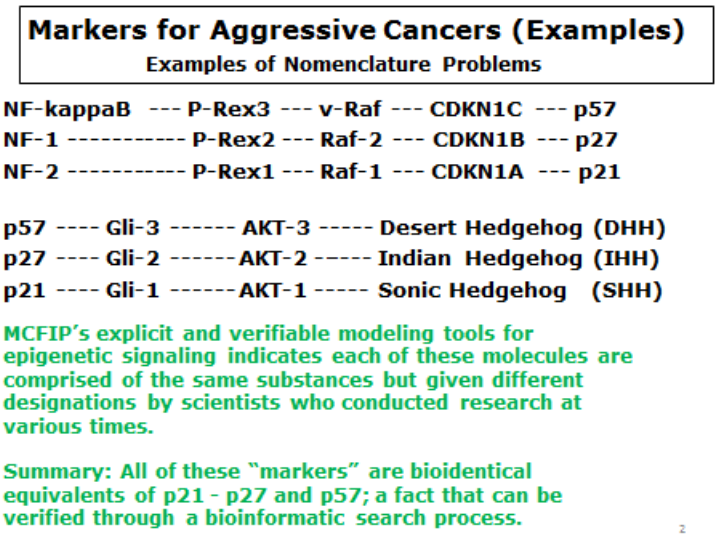
One of the additional early findings of the MCFIP team was the fact that intracellular interactions between the antagonistic elements of calcium and magnesium can result in chronic diseases when imbalances exist in their levels. An explanation of these findings is outlined on the MCFIP website.[2]

As MCFIP's investigative processes associated with cellular level interactions and imbalances progressed, the fact that signaling activities at the cellular level existed in configurations of 3s and 5s became an irrefutable fact.

Following years of investigative work and the input of scientists from a variety of disciplines, MCFIP was able to document an explicit and replicable methodology for the principles of how homeostasis (equilibrium – balance) works in epigenetics and why configurations existed in 3s and 5s.[3] These findings literally convert the tacit knowledge of homeostasis into an explicit and verifiable format; a discovery that has game-changing implications for all aspects of biomedical research and the ability to use the modeling process as a foundation for the evolution of precision (personalized) medicine.

Having developed the ability to identify minerals and elements as constituents of signaling molecules enabled the MCFIP team to establish the fact that enzymes identified as proteins are not configured exclusively from chains of amino acids. Subsequent efforts by the MCFIP team identified that amino acids are, however, an integral part of signaling molecule configurations; i.e. for anabolic activity as well as constituents of isoenzymes. Using its modeling tools to "mine" data from thousands of existing studies enabled MCFIP to identify redundant nomenclature for the same signaling molecules; i.e. alternative designations. An example of these findings is provided below.

[1] http://www.sciencedaily.com/releases/2009/01/090126173839.htm
[2] http://www.mcfip.net/upload/Calcium%20-%20Magnesium%20Imbalances%20-%20Cancers%20-.pdf
[3] http://www.mcfip.net/upload/Homeostasis%20-%20Epigenetics%20Document%20-new.pdf



Looking for What Went Wrong and When

Based on the discovery that key portions of the theories used for biomedical research were be flawed, MCFIP embarked on a multi-year initiative to identify specific verifiable instances of what went wrong and when.

As explained herein, horrendous outcomes have resulted from an erroneous assumption in 1926 due to the lack of adequate technology. At that time, James Sumner used x-ray crystallography to visualize the enzyme urease. He visualized the existence of amino acids. Lacking any frame of reference other than the knowledge that proteins are formed from amino acids, he and other scientists that followed the same process designated enzymes as being proteins.[4] Since that time, the global research community has assumed that all enzymes are proteins.

When atomic force microscopy was utilized in the late 1990s, visualization of cellular level activity was initially perceived to be nanobacteria.[5] These discoveries were subsequently confirmed as being the interactions between minerals and elements; i.e. self-assembly in quantum mechanics based on van der Waals' interactions. Despite these discoveries, due to the lack of data that supported the differences between these highly active signaling molecules (e.g. enzymes), biomedical research has failed to be able to differentiate between such substances except through static visualization using x-ray or NMR imaging.

Epigenome versus Genomic Theory

As outlined previously, apparent misunderstandings relative to the definition of genes, proteins – signaling molecules, DNA alphabet, etc. have created massive confusion in biomedical research. When findings are viewed through the lens of flawed genomic theory; the application of the principles of physical sciences into biology, genomics and epigenetics establishes a foundation from which previous shortcomings and flaws can be rectified. Examples of additional flaws that have been

[4] http://www.chemistryexplained.com/St-Te/Sumner-James.html
[5] http://www.scientificamerican.com/article/the-rise-and-fall-of-nanobacteria/

identified include the existence of "two languages" that exist with regard to DNA[6] and that epigenetics functions to regulate cellular activity without changing DNA.[7]

Several thousand studies support the existence of these epigenetic signaling molecules (albeit erroneously designated as proteins) and the fact that, if mutated in any way, they can be passed from generation to generation. A recent study (using C. elegans) identified epigenetic inheritance as being possible for 25+ generations. http://www.sciencedaily.com/releases/2015/02/150202212449.htm

Having dedicated more than 60,000 hours over an eight year span to the investigation of signaling molecule analytics, in addition to the protein – signaling molecule "glitch," the MCFIP team observed similar confusion with regard to the use of genes to describe cellular activities. In support of the firm's assertions, the global community of geneticists **finally recognized the problem.**

"New definitions of a gene are needed."

Professor Thomas Gingeras, Ph.D., Cold Spring Harbor Laboratory (CSHL), leader of the collaborative effort called ENCODE (Encyclopedia of DNA Elements). This research team was comprised of 441 scientists from 32 institutes in 5 countries and the effort spanned a 5 year period. **http://www.eurekalert.org/pub_releases/2012-09/cshl-img090412.php**

Summary

To avoid confusion relative to various theories that have evolved over the past 90 years, many of the observations and verifiable modeling processes relative to cellular mechanisms that contribute to the causes of chronic diseases have not been addressed in this document. That being said, The Center can share verifiable information with regard to any or all of the following; provided interested parties agree to allocate adequate time to provide linear explanations to prevent terminology problems associated with differences in genomics – epigenetics, organic chemistry – physical chemistry, etc. as well as the application of aspects of quantum mechanics; e.g. interactions pertaining to chromodynamics.

- How biomarkers in isolation (as opposed to being in corollary relationships) are inadequate to determine causal paths for disease states
- The modeling methods used incorporate the principles of physical chemistry as they provide a means of verifying the composition of signaling molecules
- How the spatial alignment of cells (i.e. motility and density) is determined by epigenetic activities created through self-assembly mechanisms
- Three forms of autophagy exist and how they function
- The ability to explain the cellular level roles of gases such as nitric oxide and hydrogen sulfide (i.e. gasotransmitters) for signaling activities
- The ability to explain how cell-surface signaling molecules are formed by autophagy from gasotransmitters into configurations of 3 (trefoils)
- Explanations that support the consequences of disrupting the levels of gasotransmitters such as nitric oxide (designated as being "dangerous" free radicals) by the addition of antioxidants to the food chain; e.g. relative to cardiovascular diseases and cancers

[6] http://phys.org/news/2013-12-scientists-genetic-code.html
[7] http://medicalxpress.com/news/2014-08-dna-epigenetics-large-blood-formation.html

- The specific mechanisms for synaptic activity; i.e. factors that regulate opening and closing of the synaptic cleft.
- The specific details of the flow of processes that comprise endocytosis; i.e. phagocytosis, apoptosis and autophagy. http://www.mcfip.net/upload/Endocytosis%20Unraveled.pdf
  Note: Mechanisms associated with endocytosis have been a mystery until this explicit step-by-step model was developed by the MCFIP team.
- An explanation that vitamins are signaling molecules that includes their specific roles relative to cellular mechanisms
- The consequences of failing to recognize nanoscale and picoscale dynamics relative to toxicology; i.e. the dose determines the poison (Paracelsus 1493 – 1541)