

A Discovery that Reframes the Whole of Global Healthcare in the 21st Century: The Importance of the Imprintome

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Abstract

Within the genome exists a specific subset of genes whose expression is controlled by epigenetic marks. These tags can be modified by lifestyle factors including diet, behavior, environment and social interactions. Differences in genetic expression, despite identical genes, is explained in part through metastable epialleles—alleles that, while genetically indistinguishable, are variably expressed as a function of epigenetic modification. As a group, these metastable epialleles have been given a unique descriptive name: the imprintome. This breakthrough in understanding genetic expression has led to a wider recognition that our genes are fundamentally controlled at two levels. One is the hardware of the genetic code, which is modified slowly by natural selection through mutational changes in the genome over centuries of time. The other is the software that controls the expression of our genetic code, converting nucleotide sequences into

phenotype in response to the imprinting of our epigenome. Acting as a rapid translator for real time changes, the imprintome responds to environmental and lifestyle inputs by genomic methylation and histone modifications that affect promoter accessibility and transcription factor activity. In application, this understanding of the plasticity of the imprintome necessitates a rethinking of both health and disease states. It's a concept that cuts across all forms of healthcare: physical, metabolic, and cognitive-behavioral interventions. But at the same time, it is an aggregating concept—one that brings disciplines together to collaborate on the personalization of health and the delivery of truly individualized care. This article reviews the development of the concept of the imprintome, as well as clinical studies supporting its importance as a potential driver of change in global health care.

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Throughout the 20th century, the education and training of healthcare providers was heavily influenced by two 19th century scientists: Charles Darwin and Gregor Mendel. Darwin, of course, elucidated the frameshifting concept of natural selection, while Mendel's work on recessive and dominant traits became the cornerstone of the field of genetics. For many decades, these principles were accepted as guiding truths that came with little flexibility: when the genes of the sperm of a biological father met the genes of the egg of a biological mother, the future of the offspring was written. This belief system ultimately came to shape not only biological "rules," but also cultural ones. Genetic inheritance became the basis

for describing why some people develop certain illnesses, why some people are more talented and successful than others, and why some people have a physical advantage that predisposes them to increased resilience and longevity. In the 1930s, the emergence of the eugenics movement was a decidedly dark chapter in the history of the concept.

As we entered the 21st century, genetics research was accelerating at an extraordinary pace as a result of new discoveries and technology. Yet even today, genes are used to categorize people in medicine. Because society has been trained to believe that the nature of our genome is deterministic and there is little we can do to alter its course, many health researchers and providers have focused their attention on "fixing" bad things that lurk in a person's genes and cause disease. Imperfect genes have been linked to heart disease, diabetes, arthritis, dementia, and cancer. Historically, it has been assumed that when a certain disease has made frequent appearances in a family, it must be a consequence of a genetic issue. But studies, in fact, are revealing that most of the common diseases that physicians and other providers treat have a very weak connection to genetics. What we are beginning to understand is that members of families not only share genes, but lifestyles, environments, diets, and behavior patterns. We now know that these factors can alter the way