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Genes and the Environment: The Science of Epigenetics

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At one time scientists believed our DNA held the key to preventing and reversing disease. But we now know that our environment—not our genes—is the primary driver of health and longevity. The science of epigenetics is turning what we've long held true about biological destiny upside down. Although it remains true that our DNA—our genetic code—provides the blueprint for our physiological makeup, researchers have discovered that there's something extra controlling our genes—and food and herbs may in fact be the most important factors in our genetic well-being. That extra "something" controlling our genes is the epigenome, the cellular material that sits on top of the genome (the complete set of genetic material present in a cell or organism). While epigenomes do not alter the genetic code, they direct genes to switch on (becoming active) or off (becoming dormant) through a variety of biological mechanisms. This intriguing finding means that your genetic heritage is not the primary determinant of your health, disease risk, or longevity.

In other words, whether or not you develop a disease is determined by how your genome is being directed to express itself. The abnormal gene (genotype) isn't necessarily a player in forming the phenotype (the characteristics of an individual resulting from the interaction of the genotype with the environment). These changes in gene activity do not involve alterations to the genetic code, but are in great part determined by the choices we make. For example, increased chronic activation of the sympathetic nervous system can cause the β-adrenergic receptors to promote the metastatic phenotype in breast cancer and other cancers. So here we have a strong link between high stress behavior, and specifically lack of vagus nerve activity (the most important nerve of the parasympathetic nervous system that extends throughout the body and calms us down), determining gene expression.1

Most of these factors influencing the genome are pretty straightforward—diet, lifestyle, exercise, sleep habits, environmental factors, stress, and social relationships have all been shown to influence the expression of your genetic inheritance. Other factors, including aging, cause chemical modifications that switch genes on and off. And certain diseases, such as cancer, initiate changes that cause genes to deviate from their normal, healthy state. We now know that genes account for about 10 percent of human disease. So if our genes aren't driving disease, what is?

The Exposome as the Primary Driver of Health and Disease: The "exposome" is a concept that was originally proposed by Christopher Wild in 2005. It refers to the sum of all non-genetic exposures in an individual lifetime, starting from the moment of conception. It encompasses everything from the food we eat, to the water we drink, to the air we breathe, to the social interactions we have, to the lifestyle choices we make, to the health of our parents at the time of our conception. In short, it's the word scientists are using to describe the full range of environmental exposures that influence our health. The exposome has been broken down into the following three categories:

1. **Specific External Environment:** This includes diet, physical activity, water, consumer and personal care products, lifestyle choices like smoking, infectious agents, chemical pollutants, etc. It also includes our environment at the earliest stages of our life, including our mother and father's health at the time of our conception and gestation, the method of our birth, whether we were breastfed or not, and our early life bond with our mother and other social and psychological influences.

2. **General External Environment:** This includes climate; urban vs. rural setting; traffic; our wider economic, social, and psychological influences including social status, education, financial status, and stress.

3. **Internal Environment:** This includes internal biological factors such as metabolism, the microbiome, inflammation, hormones, and oxidative stress.

The reason the exposome is important as a concept is that we now know it is the primary driver of human health and disease. If genes cause less than 10 percent of disease, it follows that the exposome—our diet, lifestyle, and environment—drive the remaining 90 percent. The emerging field of epigenetics holds great promise for complex diseases including cancer, Alzheimer's, cardiovascular disease, and autoimmune, reproductive, and neurobehavioral illnesses. Through the process of epigenetic reprograming, using whole foods and botanicals rich in a diversity of molecular health-promoting compounds, it is possible to rewrite the instructions to your cells, activating desirable genes while deactivating undesirable genes. As an herbalist, I'm particularly intrigued by traditional herbs and spices that exhibit

epigenetic influence through protection and repair—as well as the miraculous ability to identify unrepairable cellular damage and to induce cell death through apoptosis.

Epigenetics and Cancer: Epigenetic modifications play a critical role in many cellular processes, including DNA methylation, histone modification (acetylation, methylation, and phosphorylation), and microRNA expression. Massive deregulation of all components of the epigenetic machinery is a hallmark of cancer. These alterations affect normal gene regulation and impede normal cellular processes including cell cycle, DNA repair, cell growth, differentiation and apoptosis.2 Because epigenetic alterations appear early in cancer development and represent potentially initiating events during carcinogenesis, they are promising targets for anticancer interventions by chemopreventive and chemotherapeutic strategies using epigenetically active agents. Like gene mutations, epigenetic lesions that disrupt gene expression probably occur in both driver and passenger forms—many lesions won't contribute to tumor formation while a critical few will promote carcinogenesis. Epigenetic lesions can result from gene mutations, but environmental exposures can also cause epigenetic aberrations.3

The Quality Control Theory of Aging and The ETMS: The quality control (QC) theory of aging is based on the concept that aging is the result of a reduction in QC of cellular systems designed to maintain lifelong homeostasis. Four QC systems associated with aging are 1) inadequate protein processing in a distressed endoplasmic reticulum (ER); 2) histone deacetylase (HDAC) processing of genomic histones and gene silencing; 3) suppressed AMPK nutrient sensing with inefficient energy utilization and excessive fat accumulation; and 4) beta-adrenergic receptor (BAR) signaling and environmental and emotional stress. Reprogramming these systems to maintain efficiency and prevent aging would be a rational strategy for increased lifespan and improved health.4 The "Quality Control Theory of Disease & Aging" represents the need for a comprehensive botanical and nutritional plan, such as I recommend in the Eclectic Triphasic Medical System (ETMS).

Botanicals and Epigenetic Modification: Epigenetic modifications include DNA methylation, histone modification, and other patterns. These processes are associated with carcinogenesis and cancer progression. Thus, epigenetic modification-related enzymes, such as DNA methyltransferases (DNMTs), histone methyltransferases (HMTs), histone demethylases (HDMTs), histone acetyltransferases (HATs), and histone deacetylases (HDACs), as well as some related proteins, including methyl-CpG binding proteins (MBPs) and DNMT1-associated protein (DMAP 1), are considered potential targets for cancer prevention and therapy. Many natural compounds derived from medicinal herbs (ranging from polyphenols and flavonoids to mineral salts), inhibit the growth and development of various cancers by targeting multiple genetic and epigenetic alterations.

Plant-derived epigenetic modulators are like jazz musicians, who improvise according to harmonic structure, melody, rhythm, tempo, and the "feel" of a song, all the while listening to everything going on within and around which is in constant flux. The bandleader of botanical epigenetic modulators is the "Life Force," and their mission is to normalize and aid in innate auto-regulation. Plant-derived epigenetic modulators have numerous intracellular targets, including the cellular processes of proliferation, differentiation, cell death, inflammation, angiogenesis and invasion; the targets also include the mechanisms of inflammation and carcinogenesis. These pleiotropic effects may be the reason why botanical epigenetic modulators are efficient at killing tumor cells presenting multiple alterations of their regulatory mechanisms, but have limited toxicity on normal cells.5

Studies show that plant-derived phenolic compounds with antioxidant and anti-inflammatory activities improve mitochondrial biogenesis and modulate the AMPK/ mTOR pathway (a central regulator of cell metabolism, growth, proliferation and survival) and traditional culinary herbs and species rich in phytonutrients aid in epigenetic modification and expression.6

Biography

Tito N. Habib is the head of molecular genetics' Lab., Zoology department, Faculty of Science, Sohag University, since 2015 till 2018, and a professor of genetics and molecular Biology. He got his PhD from Texas A& M University, in 1999 as visiting scholar in the department of wildlife and fisheries, Bryan-College Station, Texas, USA, in the field of Molecular Genetics. He followed his promotion as assistant professor of molecular Genetics, Zoology department, Faculty of Science, Sohag University, Egypt, (2007-2011), and Head of Biology Department, Faculty of Science, Balgurashi, Albaha University, KSA (2011-2015). He served as HEEPF project council member (B-035-P1) for the development of Genetics' courses, Faculty of Science, Sohag University, Egypt. He was a main advisor for 2 PhD, and 2 Master Thesis in Medical Genetics topics, Faculty of Medicine, Sohag University. He became a head of Sohag- Syndicate of Scientific professions in Sohag-Branch from December, 2017 till February, 2020. He works as a reviewer for journal of Clinical Pathology and Forensic Medicine, Chronicle Journal of Cancer Science. He got an invitation from 7th International Conference on Biomedical Engineering and Biotechnology (ICBEB 2018) which will be hold in October 17th - 20th, 2018, Nanjing, China.

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