

## FUNCTIONAL MEDICINE UPDATE

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### **Developmental Epigenomics and Increasing Risk to Certain Diseases**

Dr. Bland begins this issue with a philosophical discussion of how nutrition, lifestyle, and environment can influence epigenomics, the topic of this month's interview with Dr. Randy Jirtle. Can disease prevalence change very rapidly, and can diseases cluster in populations? Are the dramatic changes that have taken place in the prevalence of diseases such as autism, attention hyperactivity disorders, or atopy leading to asthma related to such epigenetic changes? These are issues Dr. Bland addresses in his opening commentary.

### **Applying the Concept of Epigenetics to Metabolic Disorders**

By 2020 the number of patients with diabetes is expected to increase to 350 million worldwide. Excess weight affects between 30% and 80% of adults in the WHO European Region, and up to one-third of children. Women with diabetes have a higher risk for spontaneous abortions and congenital malformations. All of these statements are taken from an article titled "Nutritional Developmental Epigenomics: Immediate and Long-lasting Effects" that was published in the *Proceedings of the Nutrition Society* in 2010. In this article authors Attig et al. write: "Depending on the nature and intensity of the environmental insult, the critical spatiotemporal windows and developmental or lifelong processes involved, epigenetic alterations can lead to permanent changes in tissue and organ structure and function or to phenotypic changes that can (or cannot) be reversed using appropriate epigenetic tools." They also state: "There is compelling evidence that specific ontogenetic stages such as prenatal development and early childhood are in an obesogenic environment particularly sensitive to programming of metabolic disorders, predisposing to diseases of MetS later in life." Dr. Bland discusses this article at length, particularly the issue of reversibility and the role methylation patterns play in epigenetically regulating the expression of function in the adult. REF #1-3

### **Correlating Altered States of Methylation with Health Outcomes**

As more information and data continue to emerge from scientific evaluation of the epigenome, Dr. Bland expresses his opinion that the belief that disease causation is locked in the genes is both rigid and presumptuous. Studies today are focusing on the promoterregions of genes and histone acetylation in genomes. Dr. Bland states: "Rather than being black or white, we're most often in some degree of gray, and that gray can vary in shades depending upon the environment." REF #4-5

### **Is there Historical Context for Today's Research on Epigenetics?**

Are epigenetic marks transmissible to future generations? This is a question many researchers are studying. The concept of transmissibility reminded Dr. Bland of the work of Dr. Lucille Healy from the early 1980s. Dr. Hurley, of the University of California at

Davis, conducted research in animals on the effects of zinc deprivation. In an article titled “Gestational Zinc Deprivation in Mice: Persistence of Immunodeficiency for Three Generations,” Dr. Hurley described her experiments which showed depressed immune function could persist into the second and third generations in a mouse model. REF #6

### **Could Vitamin D Insufficiency During Pregnancy Influence the Epigenome of Offspring?**

Before his interview with Dr. Jirtle, Dr. Bland again turns to philosophical discussion. Vitamin D, because of its complexity, is a topic often discussed in *Functional Medicine Update*. Vitamin D influences nuclear orphan receptor effects and the expression of genes. Exposure to the sun, as Dr. Bland reminds us, is an environmental factor. He explores several ideas related to the possibility that vitamin D insufficiency can produce epigenetic effects. REF #7

### **Researcher of the Month**

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Dr. Jirtle was first interviewed for *Functional Medicine Update* in September 2008. He is Director of the Laboratory of Epigenetics and Imprinting at Duke University, and also a professor of oncology at the school’s medical center. With his colleague, Robert Waterland, Dr. Jirtle conducted groundbreaking research with agouti mice, which revealed that a mother’s diet during pregnancy can influence gene expression in her offspring by altering the epigenome.

In January 2010, Dr. Jirtle’s work was featured in an article in *Time* titled “Why Your DNA, Isn’t Your Destiny.” Most recently, Dr. Jirtle has co-authored an article that appears in *Birth Defects and Research in Clinical Teratology*. The piece is titled “Epigenomic Disruption: The Effects of Early Developmental Exposures,” and Dr. Bland reads the following quote: “Through DNA methylation, histone modifications, and small regulatory RNAs the epigenome systematically controls gene expression during development, both in utero and throughout life. The epigenome is also a very reactive system; its labile nature allows it to sense and respond to environmental perturbations to ensure survival during fetal growth. This pliability can lead to aberrant epigenetic modifications that persist into later life and induce numerous disease states.”

Dr. Bland asks Dr. Jirtle about developments in his research since his last interview. They have a lengthy discussion that at times focuses on the subjects of epigenetics and cancer, and also on transgenerational transmission of epigenetic messages. They discuss the work

now being done by other researchers in the fast-moving field of epigenetics, including Dr. Michael Skinner at Washington State University (interviewed for the December 2008 issue of FMU), and also a group at McGill University. Dr. Jirtle shares his thoughts about future directions—and challenges—for the field. REF #9-14

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