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A New Article on Gluten and Gut Permeability

In the June and July issues of *Functional Medicine Update* this year, Dr. Bland presented a two-part series on the pathophysiology of gluten and gut health. The work of Dr. Alessio Fasano, Director of the Mucosal Biology Research Center and Center for Celiac Research at the University of Maryland School of Medicine, was prominently discussed; Dr. Fasano is widely regarded as one of the world's leading experts on celiac disease. In this update, Dr. Bland discusses a new article by Dr. Fasano that appeared in the August 2009 issue of *Scientific American*. Dr. Bland highly recommends the article, titled "Surprises from Celiac Disease," both for the useful clinical information it contains as well as the detailed illustrations that accompany it. REF #1

Metabolic Space and Time

Individual phenotypes differ because individuals are genetically different, but also because of environmental factors. According to a group of Italian and German researchers who authored an article titled "Individual Human Phenotypes in Metabolic Space and Time," which appeared in the Journal of Proteome Research, the metabolic phenotype (or metabotype) is defined as a "multiparametric description of an organism in a given physiological state based on metabolomic data." Using complex analyses, this group performed an analysis of individual phenotypes over a timescale of years. In the article, the researchers state their work supports the idea that the individual metabolic phenotype can be considered a metagenomic entity that is strongly affected by both gut microbiome and host metabolic phenotype (defined by both genetic and environmental contributions). Dr. Bland particularly discusses data related to two study participants who were identical twins. REF #2

Researcher of the Month

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Dr. Marshall is currently a Director of the Autoimmunity Research Foundation and Adjunct Professor of the School of Biological Sciences and Biotechnology at Murdoch University in Western Australia. He is also past Chair of the Engineering in Medicine and Biology Society of the Ventura IEEE (Institute of Electrical and Electronics Engineers). He is Patron of the Australian Autoimmunity Foundation and was the keynote speaker at the 2008 World Gene Congress in Foshan, China.

Dr. Marshall is a translational scientist. While discussing his background with Dr. Bland, he describes his research for his PhD degree, which involved mathematical modeling of insulin and glucose homeostasis in diabetic and healthy individuals. He became interested in biomedicine in the 1980s, and by the end of the 20th century, the sequencing of the human genome created a demand for people who could understand both the biology and also the computer systems involved in analyzing the genome and how proteins move and exist in the environment.

Dr. Marshall's current research is focused on the vitamin D nuclear receptor (VDR) and autoimmune disease. As he writes in a paper titled "Vitamin D: The Alternative Hypothesis" (co-authored by Amy Proal and Paul Albert): "When active, the vitamin D nuclear receptor (VDR) affects transcription of at least 913 genes and impacts processes ranging from calcium metabolism to expression of key antimicrobial peptides. Additionally, recent research on the Human Microbiome shows that bacteria are far more pervasive than previously thought, increasing the possibility that autoimmune disease is bacterial in origin. Emerging molecular evidence suggests that symptomatic improvements among those administered vitamin D is the result of 25-D's ability to temper bacterial-induced inflammation by slowing VDR activity. While this results in short-term palliation, persistent pathogens that may influence disease progression proliferate over the long-term." REF #3

Dr. Marshall's work and a study known as the Marshall Protocol have generated controversy. He and Dr. Bland have a lengthy discussion about the science behind his research, and Dr. Bland synthesizes the details for clinicians who may find the information difficult to interpret due to the complex levels of biochemistry involved. They discuss Dr. Marshall's publications and the work of his foundation. Links to many of his publications and live presentations can be found on Dr. Marshall's website, www.trevormarshall.com. REF #4-11

What Does It All Mean?

The science that underlies Dr. Marshall's theories about the VDR and autoimmune disease is very complex. To demonstrate the relationship to Functional Medicine, one of the tenets of which is to examine underlying biological mechanisms, Dr. Bland describes this research as "a systems biology model of looking at the role that the secosteroid has as a hormonal intercellular modulator, versus looking at it just as a vitamin in a first-order kinetic model."

Dr. Marshall and his colleagues are not the only group pursuing this line of research. Dr. Bland discusses a number of other publications on this subject, including research being

done at the David Geffen School of Medicine at the University of California, Los Angeles. During their discussion, Dr. Bland and Dr. Marshall briefly touched upon the subject how emerging research may be demonstrating a link between obesity and gut flora. Dr. Bland discusses a recently published article titled "The Microbiome and Obesity: Is Obesity Linked to Our Gut Flora?" authored by researchers from the Division of Gastroenterology and Hepatology at the Scripps Clinic in La Jolla, CA. REF #12-16

In Closing: Articles by Dr. John Cannell

John Cannell, MD, is the Executive Director of the Vitamin D Council. Dr. Bland discusses two articles he has written on epidemic influenza and vitamin D. Dr. Bland encourages a visit to Dr. Cannell's website, www.vitamincouncil.org, as it is an excellent resource for both clinicians and the public. REF #17-18

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