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The Structure-Function Continuum
Dr. Bland leads off this issue by describing a theme: Structure versus Function as Connected through Cellular Signaling. His goal is to establish a conceptual framework for this theme using examples from the molecular to the whole organism.

The Clinical Efficacy and Safety of Cruciferous Vegetable Phytochemicals
Epidemiological and prospective clinical studies have shown that populations that consume higher amounts of cruciferous vegetables have lower incidences of cancer and improved biochemical indices. The substantial health benefits of cruciferous vegetables such as broccoli, Brussels sprouts, cabbage, and cauliflower are believed to be imparted by a class of sulfur-containing compounds called glucosinolates. Supplementation with the crucifer-derived phytochemicals indole-3-carbinol (I3C) and 3,3'-diindolylmethane (DIM) has been an area of active interest due to their role in estrogen metabolism. Some researchers have proposed that I3C may serve as a precursor compound for DIM, which is present in the blood of subjects supplemented with I3C. A recently published review authored by Dr. Bland and Dr. Deanna Minich documents the clinical data available on I3C and DIM studies. REF #1

The Role of Acid-Alkaline Balance in Chronic Disease and Detoxification
High-protein diets increase net dietary acid load and acidify the urine pH. Conversely, diets high in fruits and vegetables have been proposed to be associated with a greater degree of alkalinity. From a physiological perspective, the body has compartmentalized organ systems operating within specific pH ranges. In order to maintain acid-alkaline balance throughout the various body systems, one system may be required to support another. However, repeated borrowing of the body's alkaline reserve in response to a consistent increased (dietary) acid load can potentially be detrimental.

Another aspect of the acid-alkaline balance is its role in detoxification, via either the acute removal of a drug or poison due to overdose or a nutritional protocol to support metabolic detoxification and decrease dietary toxins. The method by which urine alkalinization works to enhance toxin elimination is by the medically recognized process of "ion trapping," which is the ability to enhance urinary excretion of weak acids in alkaline urine, preventing the reabsorption of xenobiotics by renal tubules. REF #2

A Study of the Clinical and Biological Activity of Soy Protein Powder Supplementation
Dr. Bland discusses a recently published study that sought to determine if a commonly used soy protein supplement exhibits biological activity *in vivo* and *in vitro* in healthy male volunteers. Although the study authors concluded that soy protein decreases serum testosterone levels in healthy men and acts as an ER-β agonist, the individual data showed inconsistent and highly variable responses when closely analyzed. REF #3

Neuroprotective Effects of Natural Products
The effects of polyphenols may be attributable, at least in part, to the presence of specific binding sites. The findings of a study recently published in *Neurochemistry Research* support the role of polyphenols in the beneficial effects of red wine, tea, fruits, and vegetables in reducing the risk for developing neurological disorders. Data from this study suggest that polyphenols target multiple enzymes/proteins leading to their neuroprotective actions. REF # 4

Metabolic Endotoxemia
Seeking an inflammatory factor causative of the onset of insulin resistance, obesity, and diabetes, a group of researchers from the Institute of Molecular Medicine in Toulouse, France identified bacterial lipopolysaccharide (LPS) as a triggering factor. A 4-week high-fat diet chronically increased plasma LPS concentrations two- to three-times in a mouse model, a threshold this group defined as metabolic endotoxemia. They feel these findings, published in a recent issue of *Diabetes*, demonstrate that metabolic endotoxemia dysregulates the inflammatory tone and triggers body weight gain and diabetes. They suggest that lowering plasma LPS concentration could be a potent strategy for the control of metabolic diseases. REF #5

Can a Carbohydrate-restricted diet Alter Gut Peptides and Adiposity Signals?
One mechanism by which leptin and insulin reduce food intake is through their interactions with short-term satiation signals such as the intestinally derived gut peptide, cholecystokinin (CCK). Researchers at Pennsylvania State University designed a correlational, observational investigation of the effects of a carbohydrate-restricted diet on weight loss and body fat reduction and associated changes in circulating leptin, insulin, ghrelin, and cholecystokinin concentrations in overweight/obese patients with metabolic syndrome. The results of this investigation suggest that in patients with metabolic syndrome, improved adiposity signaling and increased postprandial CCK concentrations may act together as a possible compensatory control mechanism to maintain low intakes and facilitate weight loss, despite an increase in fasting ghrelin concentrations and subjective measures of hunger. REF #6

Prevention of Gliadin Peptide-induced Apoptosis by a Decapeptide from Durum Wheat
Villous atrophy is the main distinctive feature of coeliac small-bowel mucosa. Enterocyte apoptosis is the pivotal mechanism in determining the villous atrophy. Prevention of this event could be a therapeutic approach for treatment of coeliac disease. An Italian research group aimed to test the ability to prevent gliadin-induced enterocyte apoptosis in small-bowel mucosa from coeliac patients. Data from this research, published in a recent issue of the *Scandinavian Journal of Gastroenterology*, show that, *in vitro*, 10mer is able to prevent gliadin peptide-induced apoptosis of enterocytes in coeliac small-bowel mucosa. The research team suggests that identification of nontoxic sequences in the cereals and the overexpression of the genome encoding for these sequences may represent a new therapeutic strategy for coeliac disease. REF #7

Clinician/Researcher of the Month

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Dr. Frank Lipman received his initial medical training in South Africa and worked in both private practice as a general practitioner and in the rural areas of South Africa before emigrating to the United States and settling in New York City. While practicing Western medicine, Dr. Lipman became aware of both the weaknesses and strengths of his training. He began to study acupuncture, Chinese medicine, functional medicine, herbal medicine, meditation, and yoga. He founded the Eleven Eleven Wellness Center in New York City, a practice with an emphasis on preventive heath care and patient education.

Dr. Lipman is the author of *Total Renewal: 7 Key Steps to Resilience, Vitality and Long-Term Health*. He is also very involved with nonprofit work in his native South Africa, applying the skills he has learned to impoverished communities.

Dr. Lipman is a believer in Ubuntu (a Xhosa word) which serves as the spiritual foundation of African societies. It basically translates as "what makes us human is the humanity we show each other."

Dr. Lipman and Dr. Bland discuss the approaches Dr. Lipman uses in his medical practice. They also discuss the published research of Dr. Helene Langevin and colleagues. Dr. Langevin has studied the mechanism of action of acupuncture and her research suggests that needle manipulation transmits a mechanical signal to connective tissue cells via mechanotransduction. REF #8-9

Statin-induced Hepatotoxicity
Coenzyme Q10, or ubiquinone, acts as an antioxidant, has membrane stabilizing effects, and is important for cellular mitochondrial respiration (essential for energy production in organs). The antioxidant activity of CoQ10 depends on its concentration as well as on its redox status.

Statins, beneficial for both primary and secondary prevention of atherosclerotic cardiovascular disease, competitively inhibit the conversion of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) to mevalonate, a precursor for cholesterol. Mevalonate is also a precursor of Coenzyme Q10, and thus treatment with statins could lower its levels. It is suggested that CoQ10 deficiency plays an important role in statin-induced hepatopathy, and that CoQ10 supplementation protects HepG2 cells from this complication. REF #10

References

1. Minich DM, Bland JS. A review of the clinical efficacy and safety of cruciferous vegetable phytochemicals. Nutr Rev. 2007;65(6):259-267.
2. Minich DM, Bland JS. Acid-alkaline balance: role in chronic disease and detoxification. *Alt Therapies*. 2007;13(4):62-65.
3. Goodin S, Shen F, Shih WJ, Dave N, Kane MP, et al. Clinical and biological activity of soy protein powder supplementation in healthy male volunteers. *Cancer Epidemiol Biomarkers Prev*. 2007;16(4):829-833.
4. Bastianetto S, Brouillette J, Quirion R. Neuroprotective effects of natural products: interaction with intracellular kinases, amyloid peptides and a possible role for transthyretin. *Neurochem Res*. 2007;32(10):1720-1725.
5. Cani PA, Amar J, Iglesias MA, Poggi M, Knauf C, et al. Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes*. 2007;56:1761-1771.
6. Hayes MR, Miller CK, Ulbrecht JS, Mauger JL, Parker-Klees L, et al. A carbohydrate-restricted diet alters gut peptides and adiposity signals in men and women with metabolic syndrome. *J Nutr*. 2007;137:1944-1950.
7. Silano M, Leonardi F, Trecca A, Mancini E, Di Benedetto R. Prevention by a decapeptide from durum wheat of in vitro gliadin peptide-induced apoptosis in small-bowel mucosa from coeliac patients. *Scandinavian Journal of Gastroenterology*. 2007;42(6):786-787.
8. Langevin HM, Yandow JA. Relationship of acupuncture points and meridians to connective tissue planes. *The Anatomical Record*. 2002;269:257-265.
9. Langevin HM, Churchill DL, Cipolla MJ. Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture. *FASEB.* 2001;15:2275-2282.
10. Tavintharan S, Ong CN, Jeyaseelan K, Sivakumar M, Lim SC, et al. Reduced mitochondrial coenzyme Q10 levels in HepG2 cells treated with high-dose simvastatin: a possible role in statin-induced hepatotoxicity? *Toxicol Appl Pharmacol*. 2007;223(2):173-179.