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Symposium Highlights GI Detoxification: Probiotics, Enzymes, and Complementary Agents

Reno, NV, November 14, 2009 — On November 13th and 14th, the Foundation for Care Management and WorldLink Medical sponsored the Third Annual Symposium on GI Detoxification: Probiotics, Enzymes, and Complementary Agents. The Symposium was organized and supported, in part, by Klaire Labs™, a division of ProThera®, Inc. An international faculty reviewed the important facets of gastrointestinal (GI) detoxification and elucidated current hypotheses and research on the mechanisms of action and use of probiotics, prebiotics, enzymes, and various complementary agents to enhance and promote healthful GI detoxification. The Symposium was moderated by Dr. Lonnie Bristow, a noted California internist, member of the Institute of Medicine, and the first African-American president of the American Medical Association.

Dr. Walter Crinnion, Professor of Environmental Medicine at Southwest College of Naturopathic Medicine, delivered a highly informative overview of GI detoxification and review of phase one and phase two detoxification. He noted that phase one detoxification can actually render toxins more noxious and generate reactive oxygen species and hydroxyl radicals. Dr. Crinnion observed that phase one detoxification relies on an intact cytochrome P450 system and depends on magnesium, copper, vitamin A, thiamine, and riboflavin for proper function. He set forth the essential role played by glutathione in detoxification and outlined nutritional interventions that increase glutathione levels and glutathione S-transferase activity such as intake of curcumin, green tea, rosemary, and sulforaphane-containing vegetables. Dr. Crinnion concluded with dietary interventions which included rice bran fiber, chlorophyll-containing foods, and matcha green tea to promote gut excretion of fat-soluble toxins.

Dr. Sabrina Peterson, Assistant Professor of Foods and Health at the University of Minnesota and authority on phytochemical induction of CYP1A2 and its implications for carcinogenesis, delivered a lucid overview of the biotransformation of various ingested procarcinogens to carcinogens and how this could alter somatic DNA leading to cancer. Dr. Peterson communicated the complexity of the system emphasizing that any one receptor may have multiple ligands, each pathway may be modulated by multiple genes, and each gene may be coregulated by multiple pathways. She presented her clinical research on the effect of cruciferous vegetable intake in subjects with genetic polymorphisms in the cytochrome P450 system. She concluded that diet can both induce

and inhibit biotransformation and while our understanding is very incomplete, diet has great potential for enhancing detoxification and reducing cancer risk.

Dr. Stephanie Cave, a family practitioner in Baton Rouge, Louisiana and internationally recognized authority on the role of heavy metals and vaccinations in autism spectrum disorders and other illnesses, spoke on the role of detoxification in the management of autism. She presented data documenting the growing epidemic of autism and its complex pathogenesis involving the interaction of genetic predilections with environmental toxins such as heavy metals, pesticides, petrochemicals, and food additives. Dr. Cave outlined research documenting that children on the spectrum tend to have lower levels of methionine, S-adenosylmethionine, and total glutathione, have impaired methylation capacity, and are at increased risk of oxidative stress. She reviewed her approach to treating autism through case studies. Her clinical strategy consists of removing offending dietary allergens, elimination of gastrointestinal pathogens, institution of a gluten-free, casein-free diet, and utilization of dietary enzymes and probiotics to restore a normal gut microbiota. She enhances gut repair with the use of soluble fiber, demulcents, omega-3 and -6 fatty acids, and glutamine. She uses a variety of botanicals in her practice to promote healing including curcumin, ginger, and quercetin. When clinically indicated, Dr. Cave prescribes chelating agents for toxic metal detoxification.

Dr. Fandi Ibrahim from the University of Turku, Finland concluded the first day of the Symposium with a presentation of his research on the use of probiotics to facilitate the elimination of lead and cadmium from the body. Dr. Ibrahim presented his current research on probiotics and cadmium. He selected cadmium because it is ubiquitous in food, sometimes in very high concentrations. Cadmium is carcinogenic and nephrotoxic with a disproportionate toxic impact on children and the elderly. Dr. Ibrahim stated his laboratory has screened about 20 probiotic strains for the ability to bind cadmium, lead, and arsenic. He has found the best results with *Lactobacillus rhamnosus* and *Propionibacterium freudenreichii* spp. *shermanii* JS. His research has found that probiotics can bind and sequester cadmium in vitro and that probiotics may have a role in the prevention and treatment of toxicity due to toxic metals.

Dr. Iman Hakim, Professor of Public Health and Dean of the Mel & Enid Zuckerman College of Public Health at the University of Arizona, began the second day of the Symposium by presenting her research on green tea extract and cancer prevention. Dr. Hakim noted green tea is the non-oxidized, non-fermented product of tea leaves containing several polyphenolic components such as epicatechin, epicatechin gallate, epigallocatechin, and epigallocatechin gallate. She reviewed the many health benefits of green tea consumption which include cancer prevention, blood pressure reduction, diminished risk of stroke, maintenance of normal body weight, and enhancement of immunity. The mechanisms for the inhibition of carcinogenesis are modulation of carcinogen-metabolizing enzymes, reduction in abnormal cell proliferation and tumor promotion, reduced angiogenesis and DNA methylation, and induction of apoptosis. Green tea's strong anti-

inflammatory and antioxidant properties may contribute. Dr. Hakim presented the results of her clinical studies using green tea in smokers showing that it reduces the extent of DNA damage. She reviewed the rationale and design of her current clinical trial on the use of green tea to reduce lung cancer risk in former smokers with chronic obstructive lung disease. She is comparing green tea, green tea extract, and placebo in a Phase II randomized, double-blinded trial and assessing a variety of genes thought to be involved in lung carcinogenesis. As a practical point, Dr. Hakim said that green tea should be brewed for 2-3 minutes to ensure maximal benefit.

Mr. Steven Horne, a practicing herbalist and former president of the American Herbalists Guild, presented the scientific rationale for colon cleansing. Mr. Horne offered a clinically relevant approach to colon detoxification. He stated that the focus should be on restoring healthy gastrointestinal function and not on stimulating bowel movements. He recommends generous water and fiber intake, the use of digestive enzymes to promote complete breakdown of food, and the use of bitter herbs such as dandelion root and burdock to stimulate digestive secretions and bile flow. Mr. Horne noted that there is a role for laxatives and prefers anthraquinone glycosides. He also uses anti-inflammatory herbals such as aloe vera and chamomile to promote mucosal healing and highlighted the great value of probiotics to promote a healthy gut microflora.

Dr. Michael Gleib, head of the Department of Nutritional Toxicology at Friedrich-Schiller-University of Jena, Germany, presented his research on the use of prebiotics to reduce the risk of colorectal cancer. He reviewed the epidemiology of colorectal cancer, now the third most common form of cancer. He said there is an inverse relationship between dietary fiber and colorectal cancer risk. Animal studies have shown that the prebiotic inulin can significantly reduce the risk of colon tumors. Inulin is not only a dietary fiber, but its prebiotic effect is primarily to promote the growth of *Bifidobacterium* populations in the distal ileum and colon. This is associated with the induction of apoptosis in colonocytes and attenuation of proliferative responses as well as a reduction in colonic concentrations of carcinogenic enzymes. Dr. Gleib's research shows that prebiotic inulin can block the initiation of colorectal cancer and suppress its progression.

Dr. Stephen Olmstead, Chief Science Officer of Klaire Labs™, ended the Symposium with a review of gastrointestinal biofilm and its role in health and disease. He defined biofilm as a heterogeneous community of attached microorganisms encased in a self-produced matrix. Biofilm is now known to be the preferred mode of existence for microbes and provides them with a protected environment. Biofilm formed by normal commensal microbes can confer health benefits to the host while gut biofilm formed by pathogens can be associated with GI and systemic disease. Dr. Olmstead highlighted *Helicobacter pylori* infections, autism, and chronic fatigue syndrome and diseases associated with pathogenic biofilm. He observed that pathogens within biofilm are highly resistant to antimicrobials and the body's immune system. Strategies to disrupt pathogenic biofilms may have significant clinical impact. Dr. Olmstead reviewed his invention of a

formulation of enzymes shown in laboratory studies to disrupt a wide spectrum of pathogenic biofilms. He presented a clinical approach to disrupting pathogenic biofilm using the enzyme formulation which permits the eradication of pathogens using appropriate antimicrobials. He emphasized the importance of using probiotics and prebiotics to restore and support a healthy GI microbiota.

A set of audio CDs with the accompanying Symposium syllabus are available for order at www.probioticsymposium.com or by calling 1-888-488-2488. Klaire Labs™ will organize and fund the Fourth Annual Probiotic Symposium delving into the role of probiotics, prebiotics and enzymes in the management of pathogenic gastrointestinal biofilm, modulation of immune function, and management of GI and systemic disease. The Fourth Annual Probiotic Symposium is planned for the Fall of 2010.

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