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Summary Report

The Gut, Its Microbes and Health: New Knowledge and Applications in Asia

October 8-9, 2014, Orchard Hotel, Singapore

Advances in technology and bioinformatics have made it possible to examine the influence of the intestinal ecosystem on human health. There is increasing evidence that the nutritional value of food is influenced in part by the structure and operations of a consumer's gut microbial community, and that food in turn shapes the individual's microbiome. Understanding the intestinal microbiome is essential for developing disease prevention strategies and personalized health care regimens.

ILSI Southeast Asia Region held the conference '**The Gut, Its Microbes and Health: New Knowledge and Applications for Asia**' in Singapore from October 8-9, 2014, highlighting current scientific knowledge on the gut microbiome, its interactions with diet and nutrition, and the implications for health and disease, particularly in Asian populations. The conference, organized in collaboration with the Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australia, National University of Singapore, Newcastle University International Singapore and Indonesian Society for Probiotics and Prebiotics, was well attended by over 200 participants from around the region representing academia, government and industry sectors.

The conference, bringing together a panel of leading experts in the field of gut microbiome research, was opened with a Welcome Address from ILSI SEA Region Executive Director Mrs. Boon Yee Yeong and Conference Scientific Chair Professor Yuan Kun Lee, National University of Singapore Yong Loo Lin School of Medicine.

The Intestinal Ecosystem and Core Microbiome

The opening lecture, presented by Professor Liping Zhao, Shanghai Jiao Tong University, China, explored the **basic concepts surrounding the gut microbiota's role in human health**. Prof. Zhao noted that non-digestible and un-digested dietary components together with mucin (a glycoprotein constituent of mucus) and sloughed cells from the colon constitute the nutritional resources to sustain individual gut bacteria. Bio-active substances produced by gut bacteria can have a direct impact on host health, and careful manipulation of the diet can modulate structure and function of the gut microbiota to benefit host health.

Professor Yuan Kun Lee then presented his research findings on **population differences in gut microbiome in relation to diet, environment and the human gene**. Prof. Lee shared the findings of the Asian Human Microbiome Project, a study characterising the gut microbiota in different Asian populations. Phase I consisted of a ten-city study conducted in healthy children aged 7-11 years, and Phase II was conducted in children, adults and seniors in five Asian countries. Data indicated that the variation in gut microbiota of Asian children and adults is clustered into two distinct groups, mirroring

the geographical locations, immigration patterns and agricultural products (diet) of these cities/countries.

Gut Physiology and Intestinal Microbiota throughout the Life Span

The physiology of the colon is inextricably linked to the gut microflora it plays host to, and therefore it is important to first understand human colonic function. Dr. Iain Brownlee, Newcastle University International, Singapore, discussed the **role of the colonic mucus barrier** which provides innate and adaptive immunity. The colonic mucosa is exposed to a spectrum of essential, non-essential and potentially harmful microfloral by-products that must be handled effectively to maintain mucosal integrity, the loss of which is associated with the progression of all major diseases of the colon.

Dr. Patricia Conway, University of New South Wales, Australia, then reviewed the **role and characteristics of the gut microbiota through the life span**. She noted that the initial gut bacteria composition in the infant is affected by the mode of delivery and subsequently by the method of feeding, playing a significant role in the development of the immune system. Successive development and composition of the gut microbiota is influenced by multiple factors including diet, antibiotic exposure, lifestyle and environmental stresses throughout the life span. In the elderly, gut microbiota composition is closely related to where they reside (home or aged-care facility), and a change in major bacteria groups at this life-stage can promote an inflammatory response.

Gut Microbiota in Health and Disease

Dental caries is a public health issue in Southeast Asia, affecting up to 42% of children in Singapore alone. There has been growing interest in the **role for probiotics in caries prevention**, however, no studies to-date have looked at the effect of consumption of probiotic drink products on caries risk. Dr. Stephen Chin-ying Hsu, National University of Singapore, presented research results showing that short-term probiotic drink consumption had cariogenic/harmful effects on low caries-risk participants and cariostatic/beneficial effects in high risk adults. Dr. Hsu emphasised the importance of proper diagnosis and risk assessment by clinicians in the recommendation of probiotic drinks for caries prevention.

Dr. Reuben Kong Min Wong, National University Hospital, Singapore, then described the **role of gut microbiota in Irritable Bowel Disease (IBS),** including the microbial imbalance experienced by IBS patients. Dr. Wong outlined the role that micro-inflammation plays in the pathogenesis of symptoms and presented evidence for the use of probiotics in treating patients with IBS. The direct manipulation of the intestinal microflora through Fecal Microbiota Transplantation (FMT) was described as having therapeutic potential in IBS and Inflammatory Bowel Disease. However, Dr. Wong cautioned that its long-term metabonomic effects are not yet known.

The **influence of the gut microbiome on host physiology** was discussed by Professor Sven Pettersson, Karolinska Institute, Sweden/Nanyang Technological University, Singapore. Prof. Pettersson discussed the Holobiont concept, involving the host organism (human) in interaction with all associated microorganisms as an entity (the holobiont) for evolutionary selection to support the biochemical and biological needs of both the host and its microbes. He then presented data illustrating this concept in the link between the placental microbiome and metabolism in early life.

Recent studies have shown a link between gut microbiota and under nutrition. Dr. G. Balakrish Nair, Translational Health Science and Technology Institute, India, presented research analysing the metagenomes of 20 children with varying nutritional status in rural West Bengal, India. Several **differences were observed in the intestinal microbiota of malnourished children** when compared to healthy children, extending the understanding of the basis of malnutrition beyond nutrition deprivation. Dr. Nair commented that impaired nutritional status is not only due to the abundance of likely pathogenic microbial groups, but also a result of depletion of several commensal genera.

Prof. Liping Zhao then discussed the chain of causation from alterations in the **gut microbiota in the development of metabolic disease**. Prof. Zhao explained that a gut microbiota producing higher amounts of pro-inflammatory metabolic toxins contributes to metabolic deteriorations in genetic obesity. Dietary interventions rich in non-digestible carbohydrates and phytochemicals shift the gut's microbial imbalance to produce lower amounts of toxins and higher levels of beneficial products, alleviating both genetic and simple obesity and related complications. A toxin-producing gut microbiota works as a "molecular checkpoint" for obesity development and can be used as a potential target for effective treatment and prevention.

The **role of fermentable components of dietary fiber such as resistant starch in gut health** was discussed by Dr. Trevor Lockett, CSIRO, Australia. CSIRO, in collaboration with the University of Tokyo and RIKEN, Japan, have demonstrated how short chain fatty acids produced by fermentation can modify important gut functions such as barrier function and T Regulatory cell induction for control of inflammation.

Maintaining Gut Microbiome Stability

Professor Robert Rastall, University of Reading, UK, defined a prebiotic as "a selectively fermented ingredient that results in specific changes, in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health metabolism". Prof. Rastall went on to discuss the key health benefits ascribed to **prebiotic oligosaccharides**, categorising them according to levels of evidence (Groups A, B and C) with Group A, namely inulin and oligofructose, demonstrating good microbiology with state of the art technique, and good human studies showing health benefits. He addressed the position of bifidobacteria as the key mediators of these health benefits, noting that regulators are yet to recognise this link and emphasising the need for more robust human data on Group B & C prebiotics.

The term 'probiotic' was originally defined by the FAO/WHO in 2002. Prof. Seppo Salminen, University of Turku, Finland, reviewed the definition of the term 'probiotic' and outlined the development and conclusions of a recent **International Scientific Association of Probiotics and Prebiotics (ISSAPP) consensus paper** endorsing the definition "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host." Prof. Salminen presented an overall framework for probiotic products including what constitutes sufficient levels of evidence for health benefits.

Prof. Ingrid Surono then discussed recent research conducted on two **novel indigenous probiotics isolated from traditional fermented buffalo milk in Indonesia**. Supplementation with novel probiotics *Lactobacillus plantarum* IS-10506 and

Enterococcus faecium IS-27526 was found to have significant positive effects on humoral mucosal immune response and body weight gain in immuno-compromised (malnourished and HIV positive) pre-school children.

Prof. Kristin Verbeke, KU Leuven, Belgium, presented evidence on the physiological and nutritional effects of microbial metabolites, in particular short chain fatty acids (SCFA), as **biomarkers for the health benefits of prebiotics.** Prof. Verbeke noted that SCFA may have effects on colonic health, host physiology, immunity, lipid protein metabolism and appetite control. At present there is insufficient evidence to use fecal bacterial metabolite concentrations as markers of prebiotic effectiveness, however, integration of results from metabolomics and metagenomics holds some promise for understanding the health implications of prebiotic microbiome modulation.

Environmental Influences on the Gut Microbiota

Recent studies show that commensal gut microflora can act as reservoirs of antibiotic resistance. Dr. Sharmila Mande, TCS Innovation Labs, India, presented results of comprehensive analyses of the **presence of antibiotic resistance genes in the gut microflora** of 275 individuals from eight different nationalities. Results indicated that genes conferring resistance against 53 different antibiotics were found in the human gut microflorsa, with four distinct clusters of individuals (referred to as 'Resistotypes') that exhibited similarities in their antibiotic resistance profiles in their gut microbiota.

Prof. Hideki Ishikawa then presented research on the role of **dietary fiber and *Lactobacillus case*i in colorectal cancer prevention**. A clinical study conducted on 398 men and women free from tumors who had at least two colorectal tumors removed randomly assigned subjects to consume either wheat bran, *Lactobacillus casei* shirota strain, both or neither. No significant difference in the development of new colorectal tumors at 2 and 4 years was observed with administration of either wheat bran or Lactobacillus casei. However, results suggested that the consumption of *Lactobacillus casei* prevented structural abnormality of colorectal tumors.

Foods for Gut Health: Regulatory Challenges

Research findings on the health benefits of probiotics and prebiotics for gut health have led to the introduction of a number of food products in this category. Prof. Seppo Salminen noted that **substantiation of health claims in the area of gut health** has been challenging for probiotics and prebiotics and in the European Union; only one health claim has been approved for use, related to probiotic bacteria in yoghurt with live yoghurt cultures. He noted that the introduction of novel probiotics and prebiotics into the food supply will require a different level of safety assessment.

Ms. Yusra Egayanti, National Agency for Drug and Food Control, Indonesia, outlined **regulatory challenges in the development of foods for gut health**, with a comprehensive review of the pre-market evaluation and post-market control on probiotics in Indonesia. Ms. Egayanti cited examples of common pitfalls in the applications process, including lack of scientific evidence; study population not appropriate for the proposed claim wording; and insufficient data on safety, interaction, and efficacy of multi-strain probiotics. She emphasized that strong collaboration between industry, academia and regulators is needed to support the effective regulation and innovation of foods for optimal gut health. The conference concluded with a panel

discussion **'Gaps, Opportunities and Future Direction for Gut Microbiome Research in Asia'**.

Lastly, a Best Poster Award Ceremony was held. Dr. Wei-Kai Wu, National Taiwan University Hospital, Taiwan, was awarded the best poster award under Group A: Functional Foods and the Gut Microbiota with the poster entitled **Antimicrobial Property of Allicin Reduces the Transformation of L-Carnitine into TMA and TMAO through Gut Microbiota**. While Dr. Boon Tat Chia, Interactive Micro-Organisms Laboratories Pte Ltd, Singapore was awarded the best poster award under Group B: The Gut Microbiota in Health and Disease with his poster entitled **A Microbiome Modulator for Glucose and Cholesterol Control**.