Conference Report:
Gut feelings - what can we learn from recent research on gut microbiota?

Centre for Nutrition & Food Science, University of Queensland, Australia
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ILSI SEAR Australasia in association with the ARC Centre of Excellence in Plant Cell Walls, held this symposium with prominent scientists in the field to discuss this emerging research area of the human gut microbiota.

Professor Peter Gibson, Professor & Director of gastroenterology at Monash University and Alfred Health emphasised the importance of the microbiota as an ‘organ’ - being no less significant than the role of the liver in human health. Prof. Gibson noted the influence of gut microbiota on all aspects of wellbeing makes dysbiosis an important marker for clinicians. He discussed advances in methodology to classify microbes, their genes, and functions. A ‘fishing expedition’ to define abnormalities in microbiota across many disease states exists, in order to uncover pathogenic secrets and lead to therapeutic strategies to correct dysbiosis. Current therapeutic intervention to clinically manipulate microbiota includes biotic therapy, which is the introduction of ‘foreign’ substances i.e. antibiotics, probiotics, prebiotics, synbiotics and faecal microbiota transfer (faecal transplant). Prof Gibson envisioned a clinical setting capable of biotic therapy based on metagenomics showing functional deficiencies leading to a diagnosis. Currently this is available at significant cost to the patient. However, his professional concern was that it is still speculative science, and the interpretations and recommendations are not evidence based. In his opinion, our knowledge is still too limited to answer the questions: what is a ‘normal’ microbiota, what specific alterations from ‘normal’ mean, and how to correct for these alterations and prevent disease?

Professor Patricia Conway, Professorial Fellow at the University of NSW discussed the importance of laying down foundations of a beneficial microbiota from birth. Microbiota describes the community of the gut as a whole, while Prof Conway expressed the view that the genetic potential or microbiome is the real “crux” of the field. The digestive tract is sterile at birth and is populated from a range of sources, most notably the maternal gut, placenta, mode of delivery and breast milk. Post-birth, the infant receives passive immunity from the mother but there is a critical window of sensitivity between 4 - 6 months of age, where the infant is exposed to environmental and dietary challenges. These trigger the immune responses and memory, plus influence components of the emerging complex microbiome. Differing distributions of Gram-negative and Gram-positive bacteria in African and European infant populations reflect differences in the two most represented phyla, Bacteroidetes and Firmicutes. The emerging pandemic of non-communicable diseases (NCD) in first world countries may reflect alteration of the gut microbiota. Well-documented probiotic strains can promote infant growth and development, and potentially assist in reversing the NCD pandemic. However, we need apply caution as probiotics are both strain and dose specific. Prof Conway described future research in the field as requiring a range of multidisciplinary perspectives to begin ‘re-programming’ the microbiota.

Dr Jane Muir, Research Dietitian at Monash University discussed the ‘best’ dietary pattern for maintaining optimal gut health. Optimal gut health is defined by good bowel habit, prevention of common inflammatory and functional gut disorders and long term protection against colorectal cancer. Maintaining gut health is dependent on a varied diet including soluble, fermentable and indigestible dietary fibre which are all important ‘food stuffs’ for our colonic bacteria. The main dietary fibre groups are polysaccharides and oligosaccharides, which are largely undigested in the small intestine and pass through to the large intestine for fermentation by colonic bacteria. Dr Muir reiterated that dietary fibre is a complex mixture of different types of fibre that determines the production of beneficial fermentation end products. To date, focus is on investigating isolated dietary fibre specialist ingredients but Dr Muir noted no single type of dietary fibre supplement performs all these physiological functions. Her research looked at mixing wheat bran with resistant starch (RS) to assist in
transport to the large intestine as a preventative measure for colorectal cancer. Results suggest that a wheat bran and RS composite could improve the gut environment and may have beneficial therapeutic applications. She recommended -15-20 g/day of RS for physiological benefits and -4-15 g/day of fructo-oligosaccharides (FOS), inulin, galacto-oligosaccharides (GOS) for selective growth of microbiota species. People who limit their intake of cereal and grains, or follow prescribed diets i.e. gluten-free, Paleo, low FODMAPs diets, may not be getting sufficient prebiotic fibre. Dr Muir also stressed that the current AOAC methods for total dietary fibre analysis need to be revised, as they do not accurately capture all individual fibre types.

**Professor Mike Gidley**, Director of the Centre for Nutrition & Food Sciences, University of Queensland continued on the topic of the impact of food structure on gut fermentation. He discussed which dietary components get to the large intestine; what happens when they reach there; and the health implications. All food particles and secreta that are not absorbed in the stomach or small intestine make it to the large intestine. To predict these macronutrients and ‘co-passenger’ micronutrients reaching the large intestine relies on calibration against data from ileostomy patients. However, results are limited by the absence of large intestinal feedback mechanisms. Animal models are more reproducible, but he questioned how representative this is of human responses? The complexities of in vivo passage rate are enormous; “kinetics is everything in this game, and rate and site of fermentation”, are important. For example, the amount of RS entering the large intestine depends on the extent of salivary and pancreatic amylase hydrolysis, chewing, levels of enzymes secreted and the extent of mixing in the small intestine. With the exception of non-starch polysaccharides (NSP) and lignin, all other major food components (i.e. starch, protein and lipids) have the potential to be digested and absorbed by the end of the small intestine. However, it is also clear that at least some dietary protein and starch enter the large intestine and these act as energy sources for the resident microbiota. Prof Gidley gave examples of ‘inside-out’ vs ‘outside-in’ fermentation concepts: smaller wheat particles are fermented more rapidly, in contrast to multi-cellular carrot particles which have a faster rate of fermentation compared to single carrot cells and fragments. Prof Gidley explained that carrot has a more ‘open’ structure where the microbes can enter to attack but wheat has a denser structure, which is potentially inaccessible. Prof Gidley predicts that self-measured faecal and other biomarkers will become important future tools for assessing the impacts of dietary choices/changes.

**Associate Professor Andy Holmes**, School of Molecular Bioscience & Charles Perkins Centre, University of Sydney presented on the topic of defining gut microbiome targets for management of obesity and metabolic disease. Our gut microbiota has more cells than our own body, and all humans are distinct - common mechanisms can lead to different outcomes in terms of diagnostic approaches. We differ because of our own genome, lifestyle and environment plus unique differences in our ‘other genome’, the microbiome. A/Prof Holmes noted: “Our birthday is indeed our inoculation date”. Diet and lifestyle are major causal factors of gut microbiota shifts, and it is possible that gut microbiota may be associated with the increase in obesity rates. A/Prof Holmes suggests two opportunities for improving healthcare; using the microbiome as a metric to improve diagnosis and; targeting the microbiome for therapeutic intervention. He discussed recent links between the microbiome and diet-induced metabolic disease. His research compared a Western versus a Korean diet, noting that diets of different macronutrient distribution may induce microbiome change but do not necessarily drive the same microbiota outcomes in individuals. For example, although calorie intake was vastly dissimilar, weight loss outcomes were comparable. The correlation between energy intake, adiposity and metabolic disease is not uniform, and dietary patterns drive different relationships between obesity and disease. A/Prof Holmes also stressed that successful dietary weight loss strongly correlates with successful microbiota community change. He also spoke about rational engineering of the microbiome as part of diet intervention strategies, and a need to identify people with unique genetic or microbiome signatures to define obesity subtypes that require distinct intervention.

**Dr Meera Esvaran**, microbiologist & immunology researcher, University of New South Wales spoke about the role of probiotics in immune function. Immune disorders are on the rise and this high rate can be linked to lower incidences of infectious disease, overuse of antibiotics, diet and metabolic disorders. Patients with irritable bowel syndrome have lower diversity in their gut microbial community. Dr Esvaran acknowledges that the gastrointestinal microbiota is vital in the maintenance of homeostasis in the gut and immune function. We know the microbiota plays a pivotal role in health and immune function from experiments conducted using germ free mice where sterile guts led to underdeveloped tissue and a decrease in subsets of immune cells, important in differing disease states. Clinical trials have demonstrated that the gut microbiota constitutes an ecosystem regulating inflammation beyond the GI tract and shows potential for vaccine adjuvants.

**Professor Yuan Kun Lee**, Department of Microbiology, Yong Loo Lin School of Medicine, National University of Singapore addressed: “Diet or Gene determines human intestinal microbiota?” presenting
research investigating the gut microbiome of young Asian children. Prof Lee described that individuals have their greatest exposure to a developing microbiota during infancy and this changes with age, and diet playing a direct role. He described a collaborative Asian Microbiome project consisting of 10 cities across 5 countries, representing both rural and metropolitan city locations. In this Phase 1 study, gut microbiota could be differentiated into two major cluster types wherePrevotellaceae was prevalent in cities of Thailand and Indonesia, andBifidobacteriaceae andBacteriodaceae were dominant in China, Japan and Taiwan. Prof Lee explained that high meat consumption in Chinese and Japanese diets is not a good indication of this microbial enterotype distribution as seasonal dietary patterns within 3-5 months could alter the resident microbiota community. A Mongolian study illustrated how changes in dietary patterns from a high meat diet during winter months to dairy products in summer changed the microbial community between seasons. Prof Lee emphasised that staple carbohydrates and specifically, the type of rice consumed, reflects the gut bacterial distribution; Japonica or ‘sticky’ rice, typically consumed in Japan, China and Taiwan is high in amylopectin as compared to Indica or ‘loose’ rice that is consumed in Thailand and Indonesia. Clusters of geographical influence have a strong association with dietary habits, and possibly are related to genetic disposition too. Prof Lee added that a Phase 2 study involving mothers, infants, adults and the elderly, from cities of Korea, Mongolia, Malaysia and Singapore is currently in progress.

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