



## 2011 ISAPP Meeting Report October 23-25, 2011 Berkeley, California USA

The International Scientific Association for Probiotics and Prebiotics (ISAPP) convened its 9th meeting October 23-25, 2011 at the Hotel Shattuck Plaza in Berkeley, California. This by-invitation meeting was attended by 115 participants, including 45 scientists from the ISAPP Industry Advisory Committee, 56 invited delegates, 9 members of the ISAPP Board of Directors and 4 Student Fellow Association members. Meeting participants hailed from 21 different countries. The slides presented in all sessions are posted for meeting participants, at a [password-protected site](#).

The scientific program began with a plenary session featuring lectures on the how the adaptive immune system responds to colonizing microbiota, presented by Daniel Peterson, MD, PhD, formerly of the Department of Food Science and Technology Department, University of Nebraska-Lincoln and now with Johns Hopkins University in Maryland. Colin Hill, PhD spoke on bioactive compounds and their potential role in interacting with the microbiota with positive implications for human health. Connie Weaver, PhD, Department of Foods and Nutrition, Purdue University, West Lafayette, Indiana provided perspectives on the limitations of randomized, controlled trials when conducting research on foods. This was followed by a lecture in the developing field of gut/brain signaling. Ted Dinan, PhD, APC Investigator Psychiatry, Cork Ireland highlighted the importance of activities of the gut to brain function, pain perception, and mood disorders, and possible roles of probiotics and prebiotics in modulating some of these activities. Due to a personal emergency, Glenn Gibson was not able to attend the meeting. Therefore his lecture was not delivered. The focus of this lecture was on defining a healthy gut microbiota. Instead, Rob Rastall, PhD, School of Food Biosciences, University of Reading, UK kindly delivered Glenn's talk, and discussed the strength of evidence behind identifying "healthful" members of the gut microbial community. He concluded that a healthy gut microbiota could not be readily defined based on current research. Certain trends emerged suggesting that some members of the microbial community are associated with more healthful metabolic profiles and reduced disease, but the causal nature of the association remains to be defined.

After the plenary lectures, a Late Breaking News session was held. This is a rapid fire session where speakers can present 3 slides in 5 minutes on topics of interest to meeting participants. Lectures aim to be provocative, and highlight new data, new perspectives or new concerns related to the probiotic and prebiotic industries. The 2011 Late Breaking News program is shown in Table 1.

**Table 1. Late Breaking News Program**

Speaker	Title
Dan Peterson	Characterization of the Ileal Microbiota in Rejecting and Non-Rejecting Recipients of Small Bowel Transplants
Inge Tarnow	Is there a better future for probiotics as drugs/medicinal products?
Eric Emond	An Anti-Allergenic Dairy Starter Culture

Nathalie Delzenne	Lactobacilli and host energy homeostasis : a matter of debate
Virginia Robles Alonso	Colonization by <i>Faecalibacterium prausnitzii</i> and maintenance of clinical remission in ulcerative colitis
Trudy Wassenaar	Do probiotics or culture starters contain a genomic signature of safety?
Delphine Saulnier	Unsociable microbes! A pilot study in halitosis patients
Gregor Reid	A cultured response to HIV
Juliet Ansell	You say EFSA, I say FSANZ
Daniel Buijs	Update on Probiotic Natural Health Products in Canada
Francisco Guarner	WGO Practice Guideline: Probiotics and Prebiotics in Gastroenterology - 2011 Update
Arthur Ouwehand	The nutritional value of probiotics; Vitamin K2
Greg Gloor	Ecosystem therapeutics for <i>C. difficile</i>
Jean Macklaim	Caught in the act: A method for meta-transcriptomics in vaginal health and bacterial vaginosis

## **Discussion Groups**

On the second day of the meeting, all meeting participants participated in one of six discussion groups. Discussion group members are listed in Table 2. Key conclusions from these groups follow.

### **Group 1. Bioactives 2.**

Chair: Glenn Gibson (not able to attend); Co-chair: George Fahey

As a follow-up to a discussion of "Bioactives" at ISAPP 2010, a second round of discussions on this same topic occurred at ISAPP 2011. Bacteriocins have application in important areas such as food quality, food safety, veterinary medicine, and human medicine. Bacteriocins can be thought of as "colonising peptides", "killing peptides", and "signalling peptides" that may affect the gut lumen, the large bowel microbiota, the intestinal epithelium, and (or) the intestinal immune cells. Other peptides are found in milk and certain of these have ACE inhibitory activity in probiotic fermented milk. In the area of prebiotics, it was shown that short-chain and long-chain fructooligosaccharides (FOS) have somewhat different potential in reducing intestinal inflammation in HLA-B27 transgenic rats (with the short-chain FOS resulting in a lower histology score and a lower concentration of IL 1-beta). The Bacteroides group, the Bifidobacterium spp. group, and the Clostridium cluster XI group were most impacted by FOS supplementation of these rats. In a human clinical trial, positive outcomes resulted from feeding FOS included the microbiota profile and the production and uptake of butyrate. Isomaltooligosaccharides (IMO) were shown to positively impact beneficial gut microbiota but were poorly metabolized by potential pathogens. Alpha-1,2 glycosidic branching was believed to be important in positively impacting the gut microbiota and the short-chain fatty acids produced as a result of IMO fermentability. Vaccination is the gold standard for evaluating the effect of interventions on immune function. A double-blind, placebo controlled randomized study is underway to determine the effects of prebiotics, probiotics, and synbiotics on the immune response to influenza vaccination and fecal microbiota concentrations in healthy adults. A second study involved use of galactooligosaccharides, five grams per day of which resulted in a 40% reduction in percentage of days with cold and flu for those college students with a healthy body mass index (BMI; 64% of participants had a BMI between 18.5-24.9). Polyphenolics and their metabolites have antioxidant, anti-microbial, anti-inflammatory, and potential prebiotic properties, and research is underway to determine those with the greatest potential. Fibrous

carbohydrates in select fruits also are being evaluated for their ability to modify the colonic ecosystem vis-a-vis the microbiota composition and end-product formation. Finally, the industry scientists in Discussion Group 1 identified several issues important to this general area of science:

- a) Better define "bioactive" as it relates to prebiotics and probiotics (relate "bioactivity" to the mechanism of action of a prebiotic or probiotic).
- b) Better educate and communicate the science of prebiotics and probiotics, especially to health care professionals.
- c) Work on overcoming the conflict in global regulations related to prebiotics and probiotics that is making claims more difficult.
- d) Include more "quality of life" assessments in future human studies of prebiotics and probiotics since consumers are seeking "feel the difference" outcomes.
- e) Identify the specific gut microbial populations associated with health outcomes.
- f) Work towards a complete understanding of the mechanism of butyrate action.

### **Group 2. Guidelines for Safety Evaluations Regarding the Addition of Live Microorganisms in Food.**

**Chair: Jim Heimbach**

Group 2 developed a decision-tree model to provide guidance in meeting regulatory requirements for assuring that probiotics intended for addition to foods or dietary supplements are safe. The model includes recommendations regarding confirmation of the identity of the strain and genomic analysis. Based on the findings of the genomic analysis, history of human exposure to the strain, membership in a species accepted as possessing status of Qualified Presumption of Safety (QPS), presence of potentially transferable antibiotic resistance, and intended use (particularly with regard to target populations), different pathways to safety determination are specified requiring greater or lesser levels of additional research. Additionally, the guidance addresses issues regarding the selection of animal models and the design of human studies that provide evidence of safety as either primary or secondary endpoints. The group intends to further develop this guidance, including a greater level of specification than was possible during a one-day meeting, and incorporation of Bayesian mathematical principles to aid in formalizing and lending a higher degree of objectivity to defining the evidentiary burden on the basis of the level of presumption of safety available a priori. The goal is to publish this guidance in a peer-reviewed scientific journal.

### **Group 3. Culturing the unculturable .**

**Chair: Karen Scott**

The first act of this discussion group was to rename the group to 'Culturing the not-yet cultured'. The discussion then proceeded with some updates on the current knowledge on the microbial composition within the human gastrointestinal tract (GIT), and the changes that occur through life, from infancy through adulthood to old age. Differences between breast-fed and formula-fed babies were recognised, and attributed at least in part to differences in the oligosaccharide content of the milk. The clear succession of colonisation by different bacterial genera can be established through work with gnotobiotic animals. The stability of the microbiota was also debated, with clear evidence that diet-induced changes do occur. Changes that can be associated with the development of disease were also debated, and the difficulties in deciding if the microbial changes are the cause or consequence of the disease.

Despite the fact that new molecular tools have been developed within the last decade that mean that we now know much more about the diversity present within the Human GIT, there have been no similar advances in our ability to culture the obligately anaerobic bacteria that are the most abundant and active residents in the large intestine. In fact it became clear that the most successful methods are still

those that were developed in the 1960's for culturing anaerobic bacteria from the rumen, namely the Hungate technique using a rumen-fluid based medium, with pure CO<sub>2</sub> in tubes, which can be supplemented by the use of anaerobic cabinets. This is at least partly because relatively few labs in the world have the appropriate facilities and know-how, and are actually involved in culturing new anaerobic gut bacteria. However, comparing the prevalence of different bacterial species (assessed using molecular techniques) with the identities of bacteria that have been cultured, there are actually cultured representatives of most of the abundant bacteria, and it is the more diverse, less numerous groups for which cultured isolates are lacking. In fact based on metagenomic and phylogenetic data the Human Microbiome Project have created a list of the '100-most wanted' bacterial isolates, which correspond to sequences frequently encountered in (meta)genomic libraries but for which there are no sequenced, cultured representatives. The merits of using novel new technologies to facilitate culturing these low abundance bacteria were discussed, including encapsulation prior to growth, as well as more traditional options including enrichment cultures. The latter could be helped by utilising metagenome data to identify key growth requirements for some of these hard-to-culture isolates. Other 'omic technologies could also help in identifying important bacterial activities, and metabolic pathways. It is also likely that some pairs of bacterial species live in such close symbiosis, that it will be extremely hard, and may even be impossible, to separate them. The difficulties of getting such bacteria identified as new species were debated. Culturing techniques frequently do not mimic conditions in the large intestine, where there may be little food and bacterial multiplication times are low, and bacteria live as part of microbial communities often in biofilms.

Further discussion points focussed on the bacterial interactions that determine overall bacterial activities in the GIT, and the relative pros and cons of focussing on single strain probiotics, or developing multiple strain ecobiotics (defined bacterial mixtures containing abundant commensal bacterial groups). The latter approach is a more controlled version of faecal transplants, which have had considerable success in treating patients with eg. recurrent *C. difficile* associated diarrhoea. However regulatory issues are currently a problem in this area, and there clearly have to be informed discussions between scientists, clinicians and regulators to reach a satisfactory conclusion.

The main outcome of the discussion was the optimistic message that the group did not believe that gut bacteria were actually unculturable, but rather that we had to try harder to define selective media, and methods to reach the low abundance bacteria, some of which could have important metabolic activities. There was enthusiasm amongst the scientists that it was worth it to try and culture these bacteria, and from industry that any potential novel probiotic bacteria that were isolated could be taken forward to the market place.

10 scientific experts and 5 industry representatives contributed to the lively, interactive discussion of this group.

#### **Group 4. Signaling processes interconnecting microbes and host immune cells**

**Chair: Daniel Peterson; Co-chair: Todd Klaenhammer**

Our discussion section at the ISAPP 2011 annual meeting entitled Signaling Processes Interconnecting Microbes and Host Immune Cells brought together experts in from diverse backgrounds. Some of the recognized outstanding questions in this area that we articulated were: A) What microbial genes, structures and metabolites are altering the immune system? B) Is it specific members of the microbiota or the emergent properties of the whole community that impact the immune system? C) What tools do we need to measure the impact of the gut microbiota on T cell development or other markers of adaptive immunity?

Our first group of speakers discussed microbial and dietary factors that can signal to the innate and adaptive immune system. Federico Rey, presented work in a simplified gnotobiotic model of the gut microbiota, containing *Eubacterium rectale*, a known butyrate producer and *Bacteroides thetaiotaomicron*, a microbe that is known for the diversity of plant and host polysaccharides that it can digest. In combination this pair resulted in significant increased expression of Mcp-1, and importer of butyrate as 500+ host genes (compared to a mere 5-11 when either microbe colonized by themselves). The theme of short chain fatty acid signaling to the host was carried further by Nathalie Delzenne presenting data in the inflammation based model of metabolic disease. In this model, prebiotics directly impact adipocyte size and adiposity through a GPR43 SCFA mediated signaling pathway. Together these results demonstrate that the output of the microbial community is a key influence on the host. Prebiotic approaches indicate that this community behaves in a way that can reflect the impact of selective growth of some organisms, in this case likely *Bifidobacterium*.

Susan Lynch then further described an experiment where the addition of a single organism to the microbiota (in this case *L. rhamnosus*), had a significant impact of the total microbial community, with 361 taxa changing significantly. She introduced the concept of “keystone” species to the discussion, wherein a few microbes, or collection of microbes, can impact the total composition and emergent properties of the community as a whole. To follow up on how *Lactobacillus* may be influencing the microbial community, Maria Marco presented microbial genetic data that has identified a number of *L. plantarum* genes, particularly bacteriocins that could influence the immune system, perhaps directly or indirectly through changing the microbiota.

Wendy Garret presented a model of colitis that happens in the absence of T and B cells when there is Tbet deficiency. Examining the microbiota in these mice identified a number of changes, including an enrichment for Klebsiella and a loss of microbes including *Bifidobacterium*. Interestingly, when these mice are fed a diet with fermented milk containing *B. lactis* and other bifidobacteria and *Lactobacillus* species there is a dramatic improvement in histological colitis scores in these mice. Notably, cecal pH is much lower in these mice, yet the SCFA that are increased were not the lactic acid that you would expect from the milk fermenting microbes, but acetate, propionate and butyrate. This reinforced the concept of keystone microbes, impacting the emergent properties of the microbiota through changing both the composition as well as the output of the community as a whole.

As we moved the discussion towards the adaptive immune system, Keichiro Suzuki, presented work on the follicular dendritic cells (FDC) of Peyer’s patches of the gut, that are strong inducers of IgA class switching and production in the gut through their interaction with B cells. Using a gene-chip approach he discovered that the pathway that creates these specialized IgA inducing cells requires both an innate signal through TLR signaling, but also a dietary factor, vitamin A/ retinoic acid. Together these signals drive the FDC to develop into gut FDC. Likewise, he demonstrated that IgA is also crucial for controlling the microbiota, as he had previously demonstrated that mice without IgA exerted dramatic shifts in the microbiota, specifically with the expansion of SFB (segmented filamentous bacteria).

Ivo Ivanov, demonstrate how the SFB, a single organism, could have a dramatic impact on the immune system, being single handedly responsible for the presence of IL-17 producing CD4 cells in the colon of SFB positive mice. This single organism can provide non-specific protection from pathogens and can promote autoimmunity in both. A true double-edged sword. His dramatic electron micrographs visualized the intimate relationship that exists between host and microbe. It is easy to see how this bacterium poking into the epithelia can have dramatic effects. He reported recent results of genome

sequencing which revealed what appears to be genome reduction, which may be the consequence of moving from the competitive colonic environment into the small intestine or the parasitic relationship it may have evolved to become dependent on host metabolism as has been seen in other organisms like *H. pylori*.

While the specificity of Th17 cells induced by SFB has not been measured, Yingzi Cong provided a great story of cBir1 specific T cells that recognize a common flagellar antigen. An interesting antigen that contains both the T cell epitope, but is also a TLR-5 ligand, that can drive activation of the innate and adaptive immune response. These T cells (cBir1 specific) can induce colitis only when the mice have the correct microbiota present in the GIT. Finally Chyi Hsieh described his new model of examining gut microbe reactive T cells. Using a DNA sequencing approach to identify T cell receptors from the colon (in T regulatory cells), he transferred both specificity to gut microbes to hybridomas in vitro, but also demonstrated that these same T cells when activated and put into mice can induce colitis.

The presentation of Ivanov, Cong, Suzuki and Hsieh, demonstrated that the gut microbiota can have an enormous impact on T cells in both homeostasis and disease. These models show new and innovative ways to address the non-specific signaling and antigen specific adaptive immunity to gut microbes. These presentations demonstrated the change in mucosal immunology over the last 7-8 years moving from anonymous microbes and undefined specificity in the T and B cells, to modern approaches that define both of these through advances in immunology and non-culture based analysis of the gut microbiome.

The discussion in this session focused in part on the exciting questions that now can be addressed, and those that may appear to be too big to tackle even with today's technology. Defining where knowledge stands is a difficult process given the cacophony of results that emerge from the diverse areas that affect mucosal immune signaling; nutrition, microbiology and immunology being 3 of these major fields. Two major questions emerged from the discussion: A) How do we define specific and non-specific immune system responses to diet, probiotic and prebiotic studies, when we don't have the tools to measure specific and non-specific immune cell responses. B) How do we separate the impact of individual microbes that are acting directly or indirectly as "Keystone" species. With these as a guide, we agreed that the future is bright and full of opportunity to pursue these questions.

#### **Group 5. Importance of 'beneficial' microbes in vaginal health.**

**Chair: Gregor Reid; Co-chair: Dilbert Gonders**

Urogenital diseases, especially infection and cancer, are major causes of death and morbidity in females. Yet, millions of women in the developing world have no access to basic urogynecological care, and diagnosis and treatment of widespread aberrant bacterial conditions (bacterial vaginosis (BV) and aerobic vaginitis (AV)) remain sub-optimal the world over. High throughput sequencing is revealing the diversity of bacteria in the vagina and how they fluctuate over time, and switch between healthy and aberrant conditions. Unfortunately, diagnostic methods are inefficient and too often outdated therapies are incorrectly administered. The net result is sub-optimal care and recurrent disease that adversely affects quality of life. This viewpoint outlines a scientific and translational roadmap designed to improve cervico-vaginal health and treatment of disease. This comprises (1) improving education of women and physicians on the vaginal microbiota; (2) having agencies target funding for research to improve diagnosis and test new therapies; and (3) making sure that new approaches are accessible in developing countries, empowering to women, as well as being acceptable and appropriate for different populations.

The conclusions of this discussion group were published:

[Exploring a Road Map to Counter Misconceptions About the Cervicovaginal Microbiome and Disease.](#)

**Macklaim JM, Cohen CR, Donders G, Gloor GB, Hill JE, Parham GP, Ravel J, Spear G, van de Wijgert J, Reid G.** *Reprod Sci.* 2012 May 21. [Epub ahead of print]

### **Group 6. Probiotics and Prebiotics in Neurogastroenterology. Francisco Guarner**

Brain-gut axis allows bi-directional input and thus links emotional and cognitive centers of the brain with peripheral functioning of the bowel, and vice versa, signals arising from the gut can influence brain centers. Recent experimental work suggested that the enteric microbiota may have an impact on the brain-gut axis. Thus, the ability of gut microbiota to communicate with the brain and influence behavior is emerging as an exciting concept.

A group of experts convened by ISAPP discussed around the role of gut bacteria on brain functions and the implications for probiotic and prebiotic science. The experts presented data and discussed topics such as the role of microbia on epithelial cell function, motor bowel function, visceral sensitivity, perception, and behavior. The data suggest interaction of gut microbia not only with the enteric nervous system but also with the central nervous system, either via neural, neuro-endocrine or humoral links. Experimental work indicates that colonization by the gut microbiota impacts mammalian brain development and subsequent adult behavior. In mice, the presence or absence of conventional microbiota influences behavior, and is accompanied by neurochemical changes in the brain (Neufeld et al, 2011). Germ-free mice have increased locomotor activity and reduced anxiety, and this behavioral phenotype is associated with altered expression of critical genes in brain regions implicated in motor control and anxiety-like behavior. It has been shown that some behavioral characteristics of mice are linked to the strain they belong. Interestingly, when germ-free mice are reconstituted with a microbiota from mice belonging to another strain, they display similar behavioral characteristics as the donor mice strain (Bercik et al, 2011). Microbial transfer was also associated with changes in brain chemistry. Thus, experimental work clearly shows that the enteric microbiota can affect brain function.

These findings provide novel insights for a better understanding of the potential role of gut microbial communities on psychiatric disorders, most particularly in the field of psychiatric co-morbidities associated with functional bowel disorders like the irritable bowel syndrome (IBS). Studies with probiotics and prebiotics have already shown promising results for alleviating IBS symptoms. Experts in the meeting concluded that a better knowledge on the gut microbiota structure and function should provide windows of opportunity for interventions (probiotics and prebiotics) in order to produce beneficial effects on brain development, bowel function, abdominal well-being and behaviour, in the future. Translational studies are needed. It was emphasized the common defects of human intervention studies are the lack of definition of phenotypes in sample population in an area with wide heterogeneity, the limitation of current tools (mainly questionnaire-based, lack of biomarkers), and the deficient collection of metadata sets (diet, natural environment, stressors, etc.)

- Neufeld KM, Kang N, Bienenstock J, Foster JA. Reduced anxiety-like behavior and central neurochemical change in germ-free mice. *Neurogastroenterol Motil.* 2011 Mar;23(3):255-64.
- Bercik P, Denou E, Collins J, Jackson W, Lu J, Jury J, Deng Y, Blennerhassett P, Macri J, McCoy KD, Verdu EF, Collins SM. The intestinal microbiota affect central levels of brain-derived neurotropic factor and behavior in mice. *Gastroenterology.* 2011 Aug;141(2):599-609.

### **IAC/BOD meeting. Chair: Arthur Ouwehand**

During the BOD/IAC meeting the following questions were discussed in five groups:

- a) Are faecal bifidobacteria levels a marker for health?

b) Why are faecal bifidobacteria (not) a marker for health?

Three of the groups answered the first question with an unambiguous 'no'. One of the groups argued it might be a marker for 'likelihood of health,' while one group noted that different perspectives exist among different parties. The regulatory views differ among countries (FDA and EFSA 'no', Health Canada 'yes') and the scientific view differs among experts. This group indicated that yes, from a scientific view, bifidobacteria could be considered a biomarker for health, but causality remained to be established. As with all biomarkers, correlation is not 100%.

As for the second question; there was unanimity in the groups that there is not enough evidence on causality. To achieve this, long-term longitudinal studies would be needed.

**Student/Fellow Program**

2011 was the second year the Student/Fellow Program was held along with the ISAPP general meeting. A summary of this event can be found on the SFA website in the [December 2011 newsletter](#).

**Table 2. Discussion group members.**

Last Name	First Name	Affiliation	Country
1. BioActives 2. Chair: Glenn Gibson (absent); Co-chair George Fahey			
Arora	Arti	The Coca-Cola Company	USA
Flambard	Benedicte	Chr. Hansen A/S	Denmark
Möllstam	Bo	BioGaia AB	Sweden
Rastall	Bob	The University of Reading	UK
Langkamp-Henken	Bobbi	University of Florida	USA
Hill	Colin	University College Cork	Ireland
Weaver	Connie	Purdue University, Foods and Nutrition	USA
Hayashi	David	Kraft Foods	USA
Emond	Eric	Nestlé Research Centre	Switzerland
Tzortzis	George	Clasado	UK
Fahey	George	University of Illinois	USA
Pasin	Gonca	CDRF	USA
Leyer	Gregory	Danisco	USA
Kozianowski	Gunhild	BENEO Group	Germany
Knol	Jan	Nutricia (Advanced Medical Nutrition)	Netherlands
O'Donnell	Joseph	California Dairy Research Foundation	USA
Audy	Julie	Agroppur	Canada
Ansell	Juliet	New Zealand Institute of Plant & Food	New Zealand
Dieleman	Leo	University of Alberta	Canada
Sanders	Lisa	Kellogg Company	USA
Fischbach	Michael	UCSF	USA
Ross	Paul	Teagasc Food Research Centre	Ireland
Xin	Wang	Zhejiang Academy of Agricultural Science	P. R. China
2. Guidelines for Safety Evaluations Regarding the Addition of Live Microorganisms in Food. Chair: Jim Heimbach			
Silvia	Bañares	University Abat Oliva in Barcelona	Spain
Daniel	Buijs	Health Canada	Canada

Michael	Cabana	University of California, San Francisco	USA
Eamonn	Connolly	BioGaia AB	Sweden
Charles	Franz	Max Rubner-Institute	Germany
Rajesh	Gupta	Biocodex USA	USA
Jim	Heimbach	JHeimbach LLC	USA
Martin	Kullen	Pfizer Consumer Healthcare	USA
David	Mack	University of Ottawa and Children's	Canada
Ma Maeve	Murphy	General Mills Inc	USA
Dan	O'Sullivan	University of Minnesota	USA
Arthur	Ouwehand	Danisco Health & Nutrition	Finland
Phoukham	Phothirath	Nestlé	Switzerland
Bruno	Pot	Institut Pasteur de Lille	France
Ger	Rijkers	UMC Utrecht and St. Antonius Hospital	Netherlands
Jose	Saavedra	Nestle	USA
Seppo	Salminen	University of Turku	Finland
Mary Ellen	Sanders	Dairy & Food Culture Technologies	USA
Hideyuki	Shibata	Yakult USA Inc.	USA
Daniel	Tancredi	UC Davis	USA
Trudy	Wassenaar	Molecular Microbiology and Genomics	Germany
3. Culturing the unculturable. Chair: Karen Scott, Co-chair: Janet Jansson.			
Ashley	Mueller	Biocodex USA	USA
Emma	Allen-Vercoe	University of Guelph	Canada
Pascal	Molimard	Merck Consumer Healthcare	France
Marion	Leclerc	INRA	France
Pascale	Mosoni	INRA	France
Paul	O'Toole	Alimentary Pharamabiotic Center/Dept.	Ireland
Ariel	Kushmaro	Department of Biotechnology Engineering,	Israel
Jacoline	Gerritsen	Winclove Bio Industries B.V.	Netherlands
Kerstin	Holmgren	Probi AB	Sweden
Sylvia H.	Duncan	Rowett Institute of Nutrition and Health, U	UK
Karen	Scott	Rowett Institute of Nutrition and Health	UK
Janet	Jansson	Lawrence Berkeley National Lab	USA
Pinaki	Panigrahi	University of Nebraska Medical Center	USA
Terence	Whitehead	USDA - Agricultural Research Service	USA
Marcus	Rauch	University of California, San Francisco	USA
Bill	King	DSM	USA
4. Signaling processes interconnecting microbes and host immune cells. Chair: Daniel Peterson. Co-chair, Todd Klaenhammer.			
Harsharn	Gill		Australia
Douwina	Boscher	Cargill - Global Food Research	Belgium
Nathalie	Delzenne	Université Catholique de Louvain	Belgium
Jean Michel	Antoine	Danone Research	France
Keiichiro	Suzuki	Kyoto University	Japan
Margriet	Schoterman	FrieslandCampina Domo	Netherlands
Saskia	van Hemert	Winclove	Netherlands

Niklas	Larsson	Probi AB	Sweden
Chris	Cifelli	Dairy Research Institute	USA
Ravi	Menon	General Mills	USA
Scott	Young	The Dow Chemical Company	USA
Yingzi	Cong	University of Texas Medical Branch	USA
Wendy	Garrett	Harvard School of Public Health	USA
Chyi	Hsieh	Washington University	USA
Ivaylo	Ivanov	Columbia University Medical Center	USA
Susan	Lynch	University of California San Francisco	USA
Maria	Marco	University of California, Davis	USA
Daniel	Peterson	Food Science and Technology Dept,	USA
Federico	Rey	Center for Genome Sciences & Systems	USA
Todd	Klaenhammer	North Carolina State University	USA
Tyler	Cullender	Cornell University	USA
5. Importance of 'beneficial' microbes in vaginal health. Chair: Gregor Reid, Co-chair: Gilbert Donders.			
Gilbert	Donders	University Hospital Leuven Belgium	Belgium
Janet	Hill	University of Saskatchewan	Canada
Gregor	Reid	Lawson Health Research Institute	Canada
Jean	Macklaim	University of Western Ontario	Canada
Inge	Tarnow	Chr. Hansen	Denmark
Janneke	van de Wijkert	Academic Medical Center of the University	Netherlands
JoMay	Chow	Abbott Nutrition	USA
Kathy	Lichtenwald	The Dow Chemical Company	USA
Craig	Cohen	UCSF	USA
Jacques	Ravel	Institute for Genome Sciences, University	USA
Greg	Spear	Rush University Medical Center	USA
Groesbeck	Parham	Cervical Cancer Prevention Program in	Zambia
Clement	Adebamowo	Institute of Human Virology	Nigeria
Greg	Gloor	University of Western Ontario	Canada
6. Probiotics and prebiotics in neurogastroenterology. Chair: Francisco Guarner			
Premysl	Bercik	McMaster University	Canada
Jane	Foster	McMaster University	Canada
Elena	Verdu	McMaster University	Canada
Liisa	Lahteenmaki	Business and Social Sciences, Aarhus	Denmark
Minja	Miettinen	Valio Ltd	Finland
Markus	Rudolph	Merck	Germany
Timothy	Dinan	Department of Psychiatry, University	Ireland
Graham	Waters	Clasado Ltd	Malta
Delphine	Saulnier	NIZO	Netherlands
Pramod	Gopal	FONTERRA RESEARCH CENTRE	New Zealand
Francisco	Guarner	University Hospital Vall d'Hebron	Spain
Virginia	Robles Alonso	University Hospital Vall d'Hebron	Spain
Janine	Barlow	Protexin	UK
Linda	Thomas	Yakult UK Ltd	UK
Steven	Davis	Abbott Nutrition	USA

Artem	Khlebnikov	The Dannon Company	USA
Gail	Hecht	University of Illinois	USA
Mel	Heyman	University of California, San Francisco	USA
Yehuda	Ringel	University of North Carolina	USA
Robert	Shulman	Baylor	USA



**9<sup>th</sup> Meeting of the  
International Scientific Association for Probiotics and Prebiotics  
Berkeley, California  
October 23-25, 2011**

**PROGRAM**

General program starts with lunch on Sunday and concludes with lunch on Tuesday. Special meetings of the ISAPP Board of Directors (BoD) and the Industry Advisory Committee (IAC) are not part of the general program.

<b>Registration desk</b>
<b>Sunday, October 23</b>
<b>Board of Directors (BoD) meeting</b>
<b>Industry Advisory Committee (IAC) meeting</b>
<b>BoD+IAC meeting</b>
<b>Plenary Lecture Session</b> (abstracts below) Chair: Nathalie Delzenne
Late Breaking News + refreshments
<b>Monday, October 24</b>
<b>Discussion Groups</b>
<b>BioActives 2.</b> Chair: Glenn Gibson, Co-chair: George Fahey
<b>Guidelines for Safety Evaluations Regarding the Addition of Live Microorganisms in Food.</b> Chair: Jim Heimbach
<b>Culturing the unculturable.</b> Chair: Karen Scott, Co-chair: Janet Jansson
<b>Signaling processes interconnecting microbes and host immune cells.</b> Chair: Daniel Peterson. Co-chair, Todd Klaenhammer
<b>Importance of 'beneficial' microbes in vaginal health.</b> Chair: Gregor Reid, Co-chair: Gilbert Donders
<b>Probiotics and prebiotics in neurogastroenterology.</b> Chair: Francisco Guarner, Co-chair: Yehuda Ringel
<b>Bus to Gala Dinner</b>
<b>Wine and appetizer reception</b>
<b>Tuesday, October 25</b>
<b>Wrap-Up Session.</b> Chair: Michael Cabana
<b>General meeting adjourned</b>
<b>Industry Advisory Committee-Board of Directors Program.</b> Chair: Arthur Ouwehand
<b>Board of Directors Meeting</b>

## Session Descriptions

### Plenary Session

**1:00-1:15 pm. Welcome. Glenn Gibson**

**1:15-1:45 pm. Seeing the Microbiota through the Eyes of Adaptive Immune System.** Daniel Peterson, MD, PhD, Department of Food Science and Technology Department, University of Nebraska-Lincoln, USA  
Infectious diseases (e.g., malaria, hepatitis and tuberculosis, etc.) are more prevalent in developing countries; however, their decline in industrialized countries is paralleled by the emergence of atopic disease and chronic inflammatory conditions. Several changes in lifestyle are associated with this transition, including diminished exposure to soil and animals, and increased exposure to antibiotics, which all impact the intestinal microbiota. This presentation will focus on potential mechanisms associated with infections, immune responses, possible links to chronic inflammatory conditions or atopic diseases, as well as potential probiotic and prebiotic mechanisms of action.

**1:45-2:15 pm. Bioactive Compounds: Mechanisms and Means to Assess Benefits.** Colin Hill, PhD, Department of Microbial Food Safety, University College Cork, Ireland.  
Bioactive compounds vary widely in chemical structure and function, but are constituents that are found in certain foods, which may modulate health effects in such conditions as hypertension, cardiovascular disease or cancer, etc. In addition, microorganisms may also have the ability to generate bioactive compounds from food components. This presentation will focus on potential mechanisms of bioactives and methods to assess their benefit.

**2:15-2:45 pm. Limitations of RCTs in Functional Food Research.** Connie Weaver, PhD, Department of Foods and Nutrition, Purdue University, West Lafayette, Indiana, USA.  
Systematic, evidence based reviews that prioritize randomized, controlled trials (RCTs) have become the preferred approach for determining public health policies. Related to nutrition, this can mean compromising the rigor of the intervention while opting for strong outcome measures of health. Comparative approaches to setting nutrient requirements will be discussed and extended to bioactive food components, such as prebiotics for bone health as an example.

**2:45 – 3:15 pm. Coffee break**

**3:15-3:45 pm. Gut Brain Signaling.** Ted Dinan, PhD, APC Investigator Psychiatry, Cork Ireland.  
The talk will explore both neuronal and humoral connections between the gut and brain. What role does glutamate play in visceral pain perception? Do gut pro-inflammatory cytokines influence brain activity? Can probiotics influence the stress axis and behaviour? Irritable bowel syndrome will be used as a model of brain-gut axis miscommunication.

**3:45 -4:15 pm. Is there such a thing as a healthy gut flora or is it more realistic that Aberdeen FC will win the Champions League?** Glenn Gibson, PhD, School of Food Biosciences, University of Reading, UK.  
Publications exist suggesting that the microbiota differs in certain clinical states. It is more challenging to unravel what constitutes a healthy gut microbiota, and whether this is even be a realistic objective. Clearly, probiotic and prebiotic science serves to fortify the healthy gut, but what are the targets and why? This presentation will overview a new publication on the concept of a healthy gut. This has included a large literature survey of the microbiota composition in health, different age groups and disorders like IBS, IBD, autism, colorectal cancer, antibiotic associated diarrhoea, NEC and atopic conditions. Some common trends occur and may highlight where dietary interventions could be directed.

## Late Breaking News Session Description

This session is an opportunity for people to give short presentations (3 slides/5 min) on late breaking news topics. These presentations range from 'hot' off-the-bench news from their lab/clinic to controversial or important issues on the science, politics, funding, business or humorous aspects of the field of probiotics or prebiotics. Hosted bar and munchies will be provided in an informal atmosphere. All meeting participants are welcome to present, including students, fellows and industry representatives. ***Extra slides or going over time will not be tolerated.*** To be scheduled for a LBN presentation, please send title and short abstract to George Fahey, [gcfahay@illinois.edu](mailto:gcfahay@illinois.edu). To avoid delays, slides must be submitted prior to the session so they can be preloaded and ready to go. George reserves the right to delete slides if more than 3 are submitted.

## Wrap-Up Session

Presentations (30 min each) provide an overview from each discussion group from chairs of all 6 discussion groups to all meeting participants.

## Industry Advisory Committee-Board of Directors Program

This session is intended as a topical information session for all ISAPP industry partners (IAC members) and the ISAPP Board of Directors. However, any ISAPP meeting participants are welcome to attend, but at their own expense (unless you are an invited content expert for this session).

**1:30 pm – 2:00 pm. Why do products succeed or fail?** What makes a success and what leads to failure with probiotic and prebiotic products? What are consumers looking for? What path will likely lead to success for companies? Liisa Lähteenmäki, Århus University, Denmark

**2:00 pm – 2:30 pm. How can probiotic/prebiotic companies leverage or influence large, longitudinal studies on diet and health? Lessons from ElderMet.** Paul O'Toole, University College, Cork

**2:30 pm – 3:00 pm. Coffee break**

**3:00 – 3:45 pm. The microbiota as a marker for health.** Working session. Divide delegates in 6 groups (one member will function as chair and present at the end of the session) to spend 5 minutes/topic to discuss some questions

**3:45 pm – 4:05 pm. When is a New Dietary Ingredient Notification necessary for dietary supplement ingredients in the US and what special issues exist for probiotic and prebiotic manufacturers?** Mary Ellen Sanders, ISAPP Executive Director