



ISAPP

International Scientific Association
for **PROBIOTICS** and **PREBIOTICS**

Report of the 2023 Annual Meeting of the International Scientific Association for Probiotics and Prebiotics



June 26-28th, 2023 | Denver, Colorado, US

EXECUTIVE SUMMARY



ISAPP Interactive Session, The Brown Palace Hotel

ISAPP held its 2023 Annual meeting in Denver, Colorado, USA on June 26-28, bringing together scientists working in the field of biotics to share the latest developments, discuss topical issues and create new connections and collaborations. 151 attendees gathered from 22 countries, comprised of 61 industry scientists from member companies (ISAPP Industry Advisory Committee), 62 invited experts and board members, and 28 students and postdoctoral researchers (ISAPP Students and Fellows Association - SFA).



The meeting included a range of interactive sessions for attendees to discuss and debate current scientific advances and questions of interest, alongside plenary lectures, late breaking news, a poster session and networking events.

- The pre-meeting program for industry members was chaired by Senior Industry Advisory (IAC) representative, Mariya Petrova. ISAPP president Dan Merenstein presented an update on ISAPP initiatives and outputs during 2022-2023, highlighting key activities and metrics of impact, and questions were facilitated from the industry group assembled.
- For industry (IAC) and student (SFA) member scientists, we debuted a new meeting session within the pre-meeting program. A set of interactive, small group innovation workshops connected industry and early career scientists to exchange knowledge and fertilise new perspectives on four key topics for innovation – food and biotics, prebiotic developments, probiotics beyond the gut, and research methodologies.
- The pre-meeting program concluded with an industry-organised plenary session, ‘Microbiome endpoints for clinical trials on biotics’, featuring Jacques Ravel from the University of Maryland, Baltimore and Sean Gibbons from the Institute for Systems Biology, Seattle.
- The main meeting program began with an interactive session, ‘Game-changing insights from recent publications’, where meeting attendees evaluated selected publications within the biotics field, synthesising insights and learnings to illuminate paths forward.
- Plenary lectures from global experts covered a diverse array of topics, including interventions for microbiome maturation in early life as well as resilience in adulthood; vaginal microecology and immune interactions; predictors of interindividual prebiotic response; mechanistic and clinical advances in the gut brain axis field; exploration of microbe:microbe interactions upon probiotic administration, amongst other topics.



*ISAPP Plenary Lecture,
The Brown Palace Hotel*



- Half-day discussion groups were convened around six key questions of current and future relevance in the biotic field. Invited subject matter experts presented relevant data, perspectives, considerations and questions, with discussion amongst the group of attending scientists. Summaries of the group findings were presented back to the larger meeting audience the following day, and peer-reviewed publications will follow for some topics. The six group topics were:
 1. Use of probiotics and prebiotics in agricultural and companion animals. Kelly Swanson and George Fahey, co-chairs
 2. What is the evidence that a biotic intervention can benefit healthy people? Dan Merenstein and Dan Tancredi, co-chairs
 3. Do probiotics improve health by changing the gut microbiome? Maria Marco and Dave Mills, co-chairs
 4. Is there an effective approach to rational design and validation of prebiotics to target members of the microbiota? Bob Hutkins and Bruce Hamaker, co-chairs
 5. How does the development pipeline differ between microbiome-based therapeutics and traditional probiotics for foods/supplements? Sarah Lebeer and Bruno Pot, co-chairs
 6. Can *C. difficile* infections be prevented with bacteriotherapy? Eamonn Quigley and Colleen Kelly, co-chairs
- The poster session featured 36 industry and student posters from around the world. A judging panel composed from the ISAPP board of directors evaluated SFA posters, and awarded the two best poster presentations to Anissa Armet (University of Alberta, Canada) for ‘Immunometabolic effects of physicochemically-distinct dietary fibers in adults with excess body weight: towards precision nutrition strategies’, and Mashaal Aljumaah (North Carolina State University, USA) for ‘The gut microbiome, mild cognitive impairment, and probiotics: a randomized clinical trial in middle-aged and older adults’.



*Poster Session,
The Brown Palace Hotel*



The 2023 Denver meeting marked the retirement of Dr Mary Ellen Sanders, long time Executive Science Officer and the founding president of ISAPP. Mary Ellen's innumerable contributions to the biotics field were celebrated in a special program within the social event held at the History Colorado Center. Her efforts will also be remembered into the future with the 2023 launch of the annual Sanders Award for Advancing Biotic Science. Mary Ellen served as local host from the Denver region for her departing meeting.

Slides and abstracts from the meeting are available to meeting participants (and all IAC members) on the ISAPP website here – meeting attendees and industry members can contact ISAPP for the password via info@isappscience.org.

ISAPP gratefully acknowledges 63 member companies who supported the mission of ISAPP in 2023.

The meeting program was developed and executed by the ISAPP Board of Directors.



Mary Ellen Sanders receives a retirement gift at ISAPP Gala

For more information visit [ISAPPscience.org](https://www.isappscience.org)
or follow us on Twitter [@ISAPPscience](https://twitter.com/ISAPPscience)

Updates from the 2023 meeting can be found
on Twitter by following [#ISAPP2023](https://twitter.com/ISAPP2023)

THE 2022-2023 ISAPP BOARD OF DIRECTORS



ISAPP Board of Directors in 2022-2023: (left to right, top to bottom) Gabriel Vinderola, Karen Scott, Dan Tancredi, Hania Szajewska, Kelly Swanson, Sarah Lebeer, Eamonn Quigley, Maria Marco, Seppo Salminen, Dan Merenstein, Kristin Verbeke, Anisha Wijeyesekera, Marla Cunningham

Missing from photo: Colin Hill



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SUMMARY OF THE INDUSTRY FORUM

MICROBIOME ENDPOINTS FOR CLINICAL TRIALS ON BIOTICS

Mariya Petrova, Chair

Every year ISAPP industry advisory committee (IAC) representatives organize an industry forum during the annual meeting focusing on important topics for IAC members. This year the forum topic was selected based on the increasing interest and questions from industry scientists about microbiome endpoints and microbiome markers associated with biotic clinical trials. The session was titled 'Microbiome endpoints for clinical trials on biotics' with two invited speakers – Jacques Ravel from the University of Maryland, Baltimore and Sean Gibbons from the Institute for Systems Biology, Seattle. The speakers brought the session to light by focusing on the current known and future directions for scientists designing and interpreting clinical studies with microbiome endpoints.

Jacques Ravel discussed the clinical study designed from a live biotherapeutics perspective, with therapeutic indications in mind. He explained that clinical trial design should incorporate appropriate methodologies to capture microbiome data that is relevant to the intended use. While many studies collect microbiome samples from participants before, during, and after biotic administration, Ravel emphasized the benefits of collecting more than one sample at each of these timepoints, to correctly characterize the baseline state and any treatment effects. To provide information on the mechanism of action, advanced techniques such as metagenomics, metatranscriptomics, and metabolomics can be employed to characterize the functional potential and expressed functions of the microbiome, since studying only the taxonomic composition does not reflect the activity of the microbiota. Finally, Ravel explained that evaluating the colonization capacity of live biotherapeutics is challenging due to genomic similarities to endogenous microbes, and applying metagenomic and long read sequencing technology can assist to detect, quantify and differentiate the exogenously administered strain(s) from the indigenous strains.

Sean Gibbons discussed that the response to any (biotic) intervention is a complex interplay between our environment, genome and microbiome. Understanding why some people respond to treatment (responders) while others do not (non-responders) is crucial and may explain why many clinical trials fail. His talk explored deep phenotyping approaches used to investigate a variety of clinical problems, including long COVID risk, poor weight loss response, and heterogeneity in statin medication response.

SUMMARY OF THE INDUSTRY FORUM

MICROBIOME ENDPOINTS FOR CLINICAL TRIALS ON BIOTICS

Mariya Petrova, Chair

Statin medications are the most prescribed medications worldwide to lower cholesterol, and serve as an excellent example of heterogeneity in clinical response, with only some individuals responding to the treatment. Importantly, variations in the gut microbiota composition can explain statin treatment's heterogeneity, as well as predicting the risk of metabolic side effects. This proof-of-concept work showed how gut microbiome composition can be used to stratify patients to inform statin therapy, but in the future, how it might be applied to biotic treatment, with gut microbiome modification and monitoring holding promise for informing treatment optimization. He concluded that the future lies in gaining precision by conducting smaller trials, collecting more data from each trial, embracing heterogeneity, and focusing on identifying and optimizing non-responders.



Networking during break, The Brown Palace Hotel

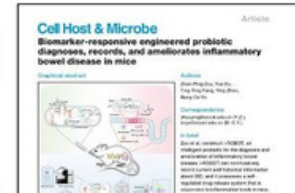
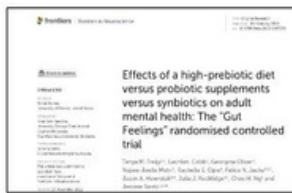
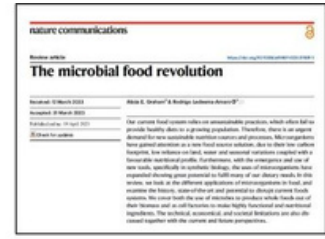
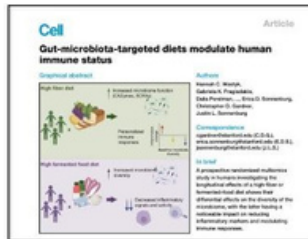
SUMMARY OF THE INTERACTIVE SESSION

GAME-CHANGING INSIGHTS

FROM RECENT PUBLICATIONS

Anisha Wijeyesekera, Chair

ISAPP 2023 opened with the annual interactive session, aiming to engage all meeting participants and to set the stage for networking throughout the meeting. With shades of a journal club, this year's interactive session centered on discussion of recent papers considered by the community to be important – this may be because they moved the field forward, they are controversial, they highlight challenges, or they had a unique methodology. Prior to the meeting, the ISAPP community put forward suggestions of papers. The final list of 12 papers (below) ranged from mechanistic studies to clinical trials, animal as well as human research, and included published work involving a range of different biotic interventions.



SUMMARY OF THE INTERACTIVE SESSION

GAME-CHANGING INSIGHTS FROM RECENT PUBLICATIONS

Anisha Wijeyesekera, Chair



Ten IAC members and two board members kindly volunteered to lead the discussion of these papers, and once groups had gathered participants were given 25 minutes to discuss the highlights and learnings from their papers. With their curated summaries of the papers on the screen, each table facilitator reported back to the main assembly the key points from their group discussions. These included game-changing methods and results, as well as limitations and thoughts on future research directions. At the end of the report outs, the assembly were asked to vote for the paper they considered to be the most interesting. It was extremely close, with the Shalon et al. paper receiving 19% and the Zou et al. paper receiving 18% of the vote. Both of these papers highlighted exciting innovation in analytical approaches to dynamically monitor (and in one case, treat) the gut environment in vivo. Could this be the direction for future biotics research?

Special thanks to our table facilitators: David Obis, Kirstie Canene-Adams, Shalome Bassett, Vimac Nolla, Elaine Vaughan, Seema Mody, Kristin Verbeke, Frederique Respondek, Tami Mackle, Stefan Roos, Charles Budinoff, Seppo Salminen.

DISCUSSION GROUPS

Group 1: Use of probiotics and prebiotics in agricultural and companion animals.

Kelly Swanson and George Fahey, Co-chairs

The primary aims of this Discussion Group were:

- 1) to document successful use of probiotics, prebiotics, and other biotic substances to promote health or treat disease in agricultural and companion animals, and
- 2) to identify opportunities and challenges that may impact the future of this field.

The session was chaired by active and former ISAPP BoD members, Kelly Swanson and George Fahey. They were joined by five academics that were invited speakers and 6 industry members and academics interested in the topic. To begin the session, George Fahey provided the scientific rationale, objectives, and speaker schedule. Nadia Everaert followed by reviewing the importance of microbiota in gut maturation, development of the immune system, how commercial production differs from nature, and how diet and management impact supplementation. Karin Allenspach then presented on the use of probiotics to manage companion animals with acute diarrhea and gastrointestinal disorders as well as chronic gastrointestinal enteropathies. Charlotte Bjornvad finished the first session by giving an overview of prebiotic use to support gastrointestinal health, immune health, and weight management of companion animals.

After a brief break, the presentations then shifted to agricultural animals. Susana Martin-Orue provided evidence of successful probiotic and prebiotic use in the management of growing piglets. In that species, these products may function as antibiotic alternatives, prepare animals for weaning and transition to dry feed, improve nutrient digestibility and growth performance, restore microbiota after challenge, and impact meat quality and food safety. Steven Ricke provided similar evidence for the management of poultry species. Kelly Swanson provided the final presentation that was focused on future needs, opportunities, and challenges pertaining to the biotic field as it pertains to agricultural and companion animals. The primary topics covered included advances in microbiome science, lab assays and tools, and machine learning, strategies for designing next-generation biotics, precision and personalization, non-gut targets and other applications, and translating research to practice.

Group 1: Use of probiotics and prebiotics in agricultural and companion animals.

The group had an active discussion after all presentations were completed. Several topics relevant to animal health and production were discussed, including methods to elucidate mechanisms, proper study designs, study populations, outcome variables, and non-gut targets. A significant part of the conversation also highlighted how biotic use in animals also impacts human health and environmental sustainability. At the end of the discussion, there was general agreement that the topics covered would make for an interesting and valuable review paper. Possible publication targets include Trends in Microbiology, Nature Microbiology, and Frontiers in Microbiology.



Discussion Group 1

DISCUSSION GROUPS

Group 2: What is the evidence that a biotic intervention can benefit healthy people?

Dan Merenstein and Dan Tancredi, Co-chairs

Objective: To explore available evidence and possible research approaches to establishing that a biotic intervention can maintain health or prevent certain diseases.

Secondary Aim: To see if there are sufficient data to propose a review from U.S. Preventive Services Task Force (USPSTF).

Output: Peer-reviewed perspective paper or USPSTF proposal.

The FDA generally requires at least two adequate and well-controlled studies to establish effectiveness. However, that level of evidence seldom exists for most interventions – including biotics – when it comes to keeping healthy people healthy or preventing illness. If two RCTs are not available, the [Bradford-Hill criteria](#) for evidence of a causal relationship are often suggested to be applicable. Regardless, it is inherently difficult to demonstrate that any intervention can keep healthy people healthy, including diet, exercise, sleep, stress reduction, etc.

The U.S. Preventive Services Task Force (USPSTF) makes evidence-based recommendations for clinical preventive services, including screenings, counseling, and preventive medications. Their approaches are worth considering, and one can find their recommendations and grades for evidence [here](#).

As an example, it is widely assumed that diet and exercise have a robust evidence base for preventing adverse cardiovascular conditions. However, the USPSTF gives only a C recommendation for behavioral counseling to improve diet and exercise habits for adults without cardiovascular risk factors. The USPSTF “recommends that clinicians individualize the decision to offer or refer adults without cardiovascular disease risk factors to behavioral counseling interventions to promote a healthy diet and physical activity.” With regard to their assessment of the strength and quality of the evidence, the USPSTF “concludes with moderate certainty that behavioral counseling interventions have a small net benefit on CVD risk in adults without CVD risk factors.”

Group 2: What is the evidence that a biotic intervention can benefit healthy people?

Is there enough existing data in biotics for any preventive outcome to lead to the same or stronger conclusions than those reached in the example above? The focus of our discussion was on endpoints studied in generally healthy populations. We did not discuss use of biotics in disease states or special populations (e.g. ulcerative colitis, rheumatoid arthritis, premature infants at risk of developing necrotizing enterocolitis, etc).

The following questions were addressed:

1. What is the evidence that biotics can prevent disease or help maintain health?
2. Are there data from biotics interventions for one population that are sufficiently robust to enable extrapolation to another population? For example, are there data from a population with a disease that can be extrapolated to a population without that disease? Or are there data that can be extrapolated to a population with substantively different demographics? USPSTF uses an approach that allows a C level recommendation from extrapolated data. The European Food Safety Authority (EFSA) may allow extrapolation of benefits for certain subpopulation and outcomes (e.g. weight loss for obese patients) to the general population, but not for other subpopulations and outcomes (e.g. joint function for patients with arthritis).
3. Are there subpopulations of the generally healthy population for whom biotics may prevent disease or help maintain health? For example, infants born via C-section, travelers at risk of traveler's diarrhea, etc.

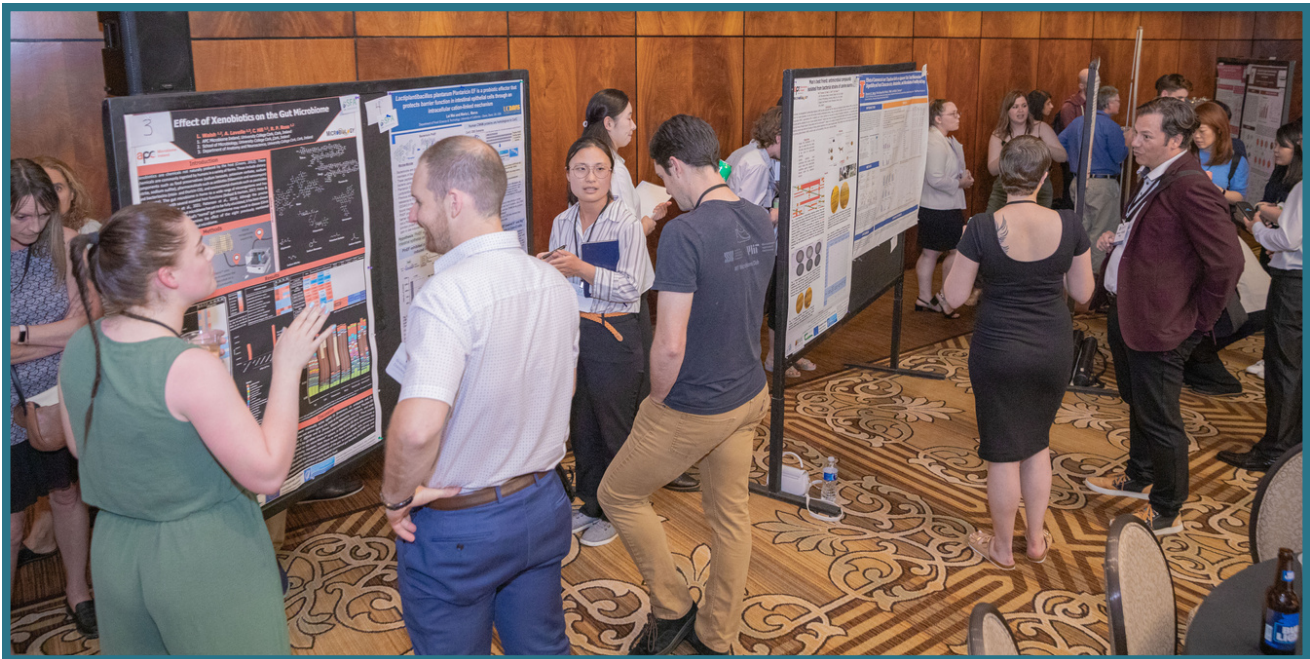
We examined the following topics: Urinary health, Vaginal health, Upper respiratory tract health/reduced antibiotic usage, GI health and Cardiovascular health.



Discussion Group 2

Group 2: What is the evidence that a biotic intervention can benefit healthy people?

Conclusions: The strength of evidence is currently not supportive for the endpoints considered. While there may be some robust data, we very specifically wanted to see if we could make a broad recommendation for all individuals, which is a very different proposition. However, for some indications, building on the current level of evidence with a high quality sufficiently powered study could change this conclusion, most specifically, urinary and vaginal health, and some GI areas. A potential path forward could be to submit to USPSTF to review evidence for the use of specific biotics in the prevention of common infectious diseases (URTI, recurrent BV/URTI) and/or GI illness, however based on existing data it may not be prudent at the current time. We are discussing the best way to present the group's conclusions.



Poster Session, The Brown Palace Hotel

DISCUSSION GROUPS

Group 3: Do probiotics improve health by changing the gut microbiome?

Maria Marco and David Mills, Co-chairs

It is frequently stated that probiotics benefit health by modulating the microbiome. But is this true, or is it even necessary? Our discussion group, including an expert panel and a total of 29 participants, deliberated on this question. The session was organized into two guiding questions: (1) Do probiotics change the gut microbiome? and (2) Do probiotic mechanisms depend on changing the microbiome?

For the first question ‘Do probiotics change the gut microbiome?’, the panel reviewed the literature and presented new research from human studies in which probiotic associated effects on the gut microbiome were measured. The panel concluded that probiotics can have significant effects on the gut microbiota of infants. This capacity is probiotic strain-dependent and there is a large variability in responses. In adults, probiotic effects on gut microbiome composition appear to be minimal. Although most human studies have not been powered to measure for gut microbiome modulation, the resilient community structure of the adult gut microbiota is such that it only has limited capacity for probiotic-mediated effects on those resident microorganisms. Additionally, the ability of an exogenous probiotic to colonize depends on if an open niche is available. Persistence can be augmented by synergistic synbiotic approaches.

For the second question: ‘Do probiotic mechanisms depend on changing the microbiome?’, the panel discussed evidence for direct effects of probiotics on intestinal epithelial, immune, neural cells and on systemic metabolism and immunity. In vitro and preclinical studies show that probiotics and known effector molecules can modulate host cells directly, without an intermediate step modulating the resident microbiota. Thus, for some mechanisms, a change in the gut microbiome is generally not a requirement for conferring a health benefit. However, there may be specific conditions for which modifying the microbiome is the intended health target. Ultimately, interactions between the probiotic-host-microbiome triad will determine the overall effect of probiotics on human health.

Group 3: Do probiotics improve health by changing the gut microbiome?



Discussion Group 3

DISCUSSION GROUPS

Group 4: Is there an effective approach to rational design and validation of prebiotics to target members of the microbiota?

Bob Hutkins and Bruce Hamaker, Co-chairs

The panel approached this question by addressing several related issues. First, the panel noted that while responder and non-responder phenotypes could be described based on taxonomic or metabolic responses, it is far more meaningful to assess responder phenotypes based on health-associated responses. Possible reasons for non-responders were proposed, including interindividual variation in diet, host or microbiome features, the absence of relevant CAzymes and associated genes for a given prebiotic, or simply the wrong outcome being measured. We also considered the possibility that the target function or metabolic pathway was already saturated.

Next, evidence was described showing that fiber and prebiotic structures, and the physical and chemical complexity of these structures, in particular, can have a profound influence on the composition of the microbiota. How microbiomes respond to prebiotic or dietary fiber interventions also depends on which microbes are present or absent. A model was presented which suggested that more complex fiber structures are often more specific in their bacterial utilization, whereas simpler structures are typically more broadly utilized and therefore can produce more variable microbiota responses between individuals. Thus, whether or not individuals will consistently respond to an intervention will ultimately depend on both the complexity of the substrate and the genetic wherewithal of the microbiota to degrade and consume those substrates.

Systems biology approaches were described that could prove useful to provide a framework for translational studies on how interindividual effects of prebiotics could be better understood and harnessed to enhance health benefits in clinical studies. These data-driven frameworks could be used to predict and design microbiomes having functional characteristics and responses relevant to health outcomes.

Group 4: Is there an effective approach to rational design and validation of prebiotics to target members of the microbiota?

Finally, the panel considered machine learning and artificial intelligence approaches to be vital in enhancing responder rates and achieving the goal of personalized medicine. These approaches could be used to stratify individuals based on which fiber or prebiotic they would be expected to respond to, or to design interventions which address multiple types of non-response for enhanced effectiveness within a diverse population.



Discussion Group 4



*Discussion Group 4
(missing from group photo)*

DISCUSSION GROUPS

Group 5: How does the development pipeline differ between microbiome-based therapeutics and traditional probiotics for foods/supplements?

Bruno Pot and Sarah Lebeer, Co-chairs

Increased interest in the microbiome field has boosted the interest in clinical applications of live microorganisms to prevent or treat disease. According to the ISAPP consensus definition, these live microorganisms meet the criteria for probiotics, but there are differences with traditional probiotics for foods and supplements, because the final products with these microorganisms will have to be registered as medicinal products to reach the market in the US and in Europe. The FDA has defined these products as “live biotherapeutic products” (LBP) and is one of the first authorities formulating important guidelines. Since 2019, this category of drug products has also been included in the European Pharmacopoeia. In addition, in other areas around the world, innovative microbiome-based drug products are also being explored and developed.

In this discussion group, we first thoroughly discussed the importance of ‘intended use’ for the regulatory status with great input from Magali Cordaillat-Simmons from the Pharmabiotics Research Institute. We discussed medicinal applications for the gut (fecal microbiota transplantation versus the first recently approved LBPs from Seres and Rebiotix – Sahil Khanna), the vagina (Jacques Ravel & Kingsley Anukam), the ear-nose-throat cavity (Martin Desrosiers), and for infants (Maria Carmen Collado).

The panel discussed that obtaining approved health claims for probiotics, either as drug or food supplement, is not straightforward. The large intra- and inter-individual variation, arising from many confounding factors such as diet, stress, smoking, age, etc., in addition to the lack of validated microbiota-related biomarkers and often multi-mechanistic modes of action, make it difficult to measure significant changes from microbiota-targeted interventions. Also, clearly, the appetite for risk is larger for small biotech start-ups than for large companies. Other aspects that complicate the research and development route are regional differences (biogeography plays a key role in efficacy and this has implications for regulations), a research field that is moving significantly faster than the regulatory field, the lack of causality substantiation for microbiome-related associations and the need for extensive funding to run clinical trials that can really convincingly document efficacy, especially for indications such as IBS, where the “natural” placebo effect is very substantial.

Group 5: How does the development pipeline differ between microbiome-based therapeutics and traditional probiotics for foods/supplements?

Our discussion group also explored how probiotic scientists from academia and/or industry can talk and interact in the best possible way. Together, we can advance the field and work towards probiotics and LBPs that meet patients' needs optimally.



Discussion Group 5

DISCUSSION GROUPS

Group 6: Can *C. difficile* infections be prevented with bacteriotherapy?

Eamonn M Quigley and Colleen Kelly, Co-chairs

Together with *Helicobacter pylori*-related disease, diarrhea and colitis related to infection with *Clostridioides difficile* (formerly *Clostridium difficile*) represent quintessential examples of the how microbiome-host interactions can cause human disease. Indeed, *C. difficile*-related illness/infection (CDI) provides the best-known and one of the few well validated examples of the consequences of disruption of a healthy microbiome. Recent developments in CDI go well beyond a mere name change; thus, the decision to review the status of this common infection.

The epidemiology of CDI has certainly changed with 50% of all infections now being community associated and 9% occurring in the absence of any recent health care exposure. Of late, ribotype 027, previously associated with more severe infections, is decreasing in prevalence but continues to be the most common epidemic strain. Interestingly, no apparent increase in prevalence of hospital-onset CDI was observed in relation to the COVID-19 pandemic.

How you test for *C. difficile* has a major impact on prevalence – PCR testing is highly sensitive but may overdiagnose infection by identifying those who are colonized but not unwell and, for this reason, multi-step testing with the second step being an assay for toxin is now advocated. *C. difficile* is very commonly found in the environment, both in public locations and in food items. In one survey, 30% of retail vegetables were found to harbor *C. difficile* and zoonotic transfer of the bacterium from animals to humans has also been described – one can begin to understand the importance of differentiating infection from asymptomatic carriage.

Much has been learned about the basic molecular biology of *C. difficile* and its interactions with the host – this research, for example, has demonstrated the critical roles of toxins A and B in causing the clinical manifestations of CDI - via injury to epithelial cells, leading to increased permeability and an inflammatory response. An IgG monoclonal antibody to toxin B has been generated, bezlotoxumab, which is now in clinical use and has been shown to reduce recurrence rates.

Group 6: Can *C. difficile* infections be prevented with bacteriotherapy?

A number of targets for primary prevention of CDI can be envisaged, ranging from infection control programs, through antibiotic stewardship, to vaccines and prophylaxis in at-risk individuals through the use of antibiotics or probiotics. Basic research has identified several mechanisms through which probiotics could act, including enhancing mucus production, generating bacteriocins against *C. difficile*, altering the luminal milieu to create an environment less favorable to the bacterium and tilting bile acid metabolism to favor the production of secondary bile acids which are bacteriostatic to *C. difficile*. How well these theoretical benefits translate into clinical results remains a contentious issue with major medical organizations coming to differing conclusions on this issue – conclusions which seem to depend on exactly how one evaluates and aggregates the available data.

For most instances of CDI, antibiotic therapy remains the basis of treatment and should be guided by prevalence of resistance, the severity of the clinical presentation and cost.

The most drastic microbiome-modulating approach to CDI is of course fecal microbiota transplant/transfer (FMT) which has proven highly effective and is now widely employed. While FMT has proven transformative in the management of CDI, its impact in other supposedly microbiome-driven disorders has been far from clear-cut, an interesting contrast. Various modes of delivery have been utilized with somewhat different outcomes, but all appear effective in the right context. Live biotherapeutic products (LBPs) represent a new class of drugs and two have been recently approved for use in CDI; one involves the delivery by enema of fecal microbes (including $>1 \times 10^5$ CFU/ml of *Bacteroides*), the other contains fecal microbiota spores and is taken as a capsule orally. Both have been shown to reduce the recurrence rate of CDI.

Interest has been resurrected in the most universal influencer of the microbiome – diet, and how a diet targeted towards a healthy microbiota may work with these restorative strategies to ensure the long-term normalization of the microbiome and thus minimize the risk of recurrence.

Research on *C. difficile* continues to provide insights into microbe-host interactions and has been at the forefront in leading to new therapeutic options.



Discussion Group 6 (some participants missing from photo)

LATE-BREAKING NEWS

Chaired by Gregor Reid, this session offered participants 5-minute slots to present late-breaking news in an informal, interactive atmosphere.

An end and a beginning. Mary Ellen Sanders, ISAPP Executive Science Officer, Centennial CO, USA

Probiotics in the neonatal intensive care unit: a framework for optimizing product standards. Greg Leyer, Chr Hansens, Milwaukee, WI, USA

Postbiotic polemics: an action to move the field forward. Gabriel Vinderola, UNL-CONICET, Santa Fe, Argentina

Danone North America's qualified health claim petition to the FDA - Yogurt and type 2 diabetes risk reduction. Miguel Freitas, Danone North America, White Plains, NY, USA

Using genomics to track plant intake. Lawrence David, Duke University, Durham, NC, USA

Empowering women through their microbiome. Mariya Petrova, Winclove Probiotics, Amsterdam, the Netherlands

NIH activities and funding opportunities. Gabriela Riscuta, National Institutes of Health/National Cancer Institute, Bethesda, MD, USA

Microbial composition is conserved between paired faecal and rectal biopsy samples from healthy volunteers. Karen Scott, Rowett Institute, University of Aberdeen, UK



Is race relevant to human microbiome/probiotics research? Kingsley Anukam, Nnamdi Azikiwe University, Nnewi, Nigeria

Probiotic-derived EV as therapeutic effectors: biogenesis, host internalization and mechanistic targets. Graciela Lorca, University of Florida, Gainesville, USA

Potential of designed prebiotics for gut-brain axis health: case of Parkinson's disease. Thaisa Cantú-Jungles, Purdue University, West Lafayette, IN USA

Dissecting responses to probiotics with transcriptomics identifies unexpected mechanisms of action. Martin Desrosiers, Université de Montréal, Quebec, Canada

POSTERS

Both Students and Fellows Association members and Industry Advisory Committee members contributed posters at the meeting:

All poster abstracts are found in the [Meeting Guide](#).

SFA Posters

Optimization of the process for the degradation of raw shrimp waste and production of chitinase and chitin oligosaccharides having prebiotic potential. Rahul Warmoota, Panjab University Chandigarh

An examination of the collateral damage caused to the gut microbiome by antimicrobials using an ex vivo distal colon model. Lauren Walsh, School of Microbiology, University College Cork

Lactiplantibacillus plantarum Plantaricin EF is a probiotic effector that protects barrier function in intestinal epithelial cells through an intracellular cation-linked mechanism. Lei Wei, University of California, Davis

Man's best friend: potentially novel antimicrobial compounds isolated from bacterial strains of canine source. Michelle O' Connor, APC Microbiome Ireland, University College Cork

Effects of commercial and traditional kefir on apparent total tract macronutrient digestibility and fecal characteristics, metabolites, and microbiota of healthy adult dogs. Breanna N. Metras, University of Illinois at Urbana-Champaign

Emerging evidence for probiotic-based disease management in honey bees. Brendan Daisley, University of Guelph

A method for the enrichment of bacteriocin-associated genes across the bacterial pangenome. Dave Hourigan, APC Microbiome Ireland

Mining prebiotic active molecules using genetic analysis of plant foods with newly developed aims platform (automated in vitro microbiome screening). Qinnan Yang, University of Nebraska-Lincoln



POSTERS, CONT.

Development of a synergistic synbiotic containing arabinoxylan and *Bifidobacterium longum* using in vivo selection. Evan Jones, University College Cork

In vitro assessment of bacteriocins as microbiome modulators in a simplified human intestinal microbiota. Natalia S. Rios Colombo, APC Microbiome, University College Cork

Endolysins targeting the IBD-associated bacterium *Ruminococcus gnavus*. Ellen Murray, School of Microbiology, University College Cork

Orphan nisin immunity genes are widespread across the Bacillota. Ivan Sugrue, APC Microbiome Ireland, University College Cork

Identification of novel immunomodulatory components in *Lactocaseibacillus rhamnosus* GG. Soyolmaa Jamiyanpurev, Shinshu University

Introducing a CRISPR-Cas9 based prime editing system for precision mutagenesis in lactobacilli. Dieter Vandenheuvel, University of Antwerp

Characterising *Lactobacillus* strains from African women with persistently optimal vaginal microbiota - framework for an African vaginal probiotic product development platform. Anika Chicken, University of Cape Town

Healthy aging: Molecular bases for the development of a bioinnovative food prototype with psychobiotics. Pablo Cataldo, CERELA-CONICET

The gut microbiome, mild cognitive impairment, and probiotics: a randomized clinical trial in middle-aged and older adults. Mashaal R. Aljumaah, University of North Carolina

Protocol for the chemo-gut trial: a double-blind randomized controlled trial investigating the effects of a multi-strain probiotic on gut microbiota, gastrointestinal symptoms, and psychosocial health in cancer survivors. Julie M. Deleemans, University of Calgary Cumming School of Medicine

Investigating the effects of the infant probiotic *Bifidobacterium infantis* and human milk oligosaccharides on the severity of anaphylaxis in a mouse model of peanut allergy. Morgan Cade, University of Nebraska

Identifying novel probiotic candidates to counter kidney stone disease. Gerrit A. Stuivenberg, Western University

Investigating select substrates on a gut microbial community using an ex vivo fermentation model. Cathy Lordan, Teagasc Food Research Centre



POSTERS, CONT.

Immunometabolic effects of physicochemically-distinct dietary fibers in adults with excess body weight: towards precision nutrition strategies. Anissa M. Armet, University of Alberta

In vitro effects of human milk oligosaccharides (HMOs) on gut microbiota in irritable bowel syndrome (IBS). Patricia Sanz Morales, University of Reading

Immunomodulatory effects of galacto-oligosaccharides. Yunan Hu, University of North Carolina

Gut microbiome composition and metabolic capacity differ by FUT2 secretor status. Alexander W. Thorman, University of Cincinnati

Dietary inulin modulates host iron utilization and gut microbiota in high-iron milk formula fed neonatal piglets. Jungjae Park, University of California

Metabolism of human milk oligosaccharides by infant gut microbiota. Simone Renwick, University of California



Poster Session, The Brown Palace Hotel



Industry Posters

A water-soluble tomato extract rich in secondary plant metabolites lowers trimethylamine-n-oxide (TMAO) and modulates gut microbiota in overweight and obese adults. Robert E. Steinert, DSM Nutritional Products, University Hospital Zurich

The microbial metabolites Totipro® PE0401 promoted probiotic bacteria growth and improved intestinal health in humans. Chi-Huei Lin, Glac Biotech Co., Ltd.

Science communication & education on biotics & the gut microbiome: a use-case with virtual reality technology. David Obis, Danone Global Research and Innovation

Bacillus clausii's mechanisms to protect the gut microbiome activity and composition after proton-pump inhibitor treatment, using the *in vitro* SHIME® technology. Peter Justen, Sanofi

A real-world study evaluating use of *Bacillus clausii*, treatment outcomes and patient satisfaction in Italian community pharmacies. Daniel Marquez, Sanofi

A randomized, double-blind, placebo-controlled study to evaluate the effects of chicory inulin on bowel habit and intestinal microbiota in adults with functional constipation. Elaine E. Vaughan, Sensus B.V. (Royal Cosun)

Summary of research studies revealing health-related effects of a specific prebiotic galactooligosaccharides mixture. Ged Baltulionis, Clasado Biosciences

ILSI Europe prebiotic task force: investigating the potential of prebiotics to rebalance and maintain health. Frederique Respondek, CP Kelco, France; The Prebiotic Task Force, ILSI Europe

STUDENTS & FELLOWS ASSOCIATION

The goal of the ISAPP Students and Fellows Association (SFA) is to create an interactive network of graduate students and postdoctoral fellows across the globe working on probiotics, prebiotics, or related fields. A total of 27 participated in the program this year through a competitive abstract selection process. Notably, the innovation workshops co-organized by the SFA and the Industry Advisory Committee allowed participants greater opportunity to interact with industry members than in previous years. Coming from 12 different countries with diverse research backgrounds, those who attended created a dynamic and memorable meeting.

The SFA conference summary, poster abstracts, and competition results are available here: <http://www.isapp-sfa.com/2023-meeting>



ISAPP 2023 Students and Fellows Association members



Program for the 2023 ISAPP Meeting



ISAPP
International Scientific Association
for **PROBIOTICS** and **PREBIOTICS**

June 26-28, 2023 • Denver, Colorado USA

- **Brown Palace** is the main conference hotel. All activities will be held in the Ballroom unless indicated otherwise. **Registration** is in the **Promenade**. **Meals** will be held in the **Central City room**. For those staying at the Brown Palace, breakfast will be provided Monday, Tuesday and Wednesday starting at 6:30. **Posters** will be available to view at all breaks throughout the meeting.
- **Holiday Inn Express** is the hotel and breakfast for the SFA.
- **University Club** will host the **Welcome Reception** and **Discussion Groups** (except SFA). Gala Event will be held at the History Colorado Center.

IAC, Industry Advisory Committee (all industry representatives); SFA, Students and Fellows Association

MONDAY – JUNE 26

7:00-15:30 **Registration Desk**

PRE-MEETING PROGRAM

8:00 -11:00 *Open only to IAC, SFA and Board of Directors*
11:00-13:00 *Open to all*

8:00-8:45 **IAC + Board of Directors meeting.**

Dan Merenstein, Georgetown University School of Medicine, Washington DC, USA
and Mariya Petrova, Winlove Probiotics, Amsterdam, The Netherlands

8:00-8:45 SFA introductions. **Georgetown/Silverplume**

8:45-10:15 **SFA+IAC innovation workshops.** Separate sign-up required. Mariya Petrova
and Brendan Daisley, University of Guelph, Canada

Ballroom, Lodo, Larimer Square, and Georgetown/Silverplume

10:00-12:00 Poster setup

10:15-10:30 Break

10:30-11:00 **Innovation workshops report back.** Mariya Petrova and Brendan Daisley

11:00-12:00 **Industry Forum.** Microbiome endpoints for clinical trials.

Jacques Ravel, University of Maryland School of Medicine, Institute for Genome Sciences,
Baltimore, USA and **Sean Gibbons**, Institute for Systems Biology, Seattle, WA, USA

12:00-13:00 **Lunch**



Program for the 2023 ISAPP Meeting



MONDAY – JUNE 26 (CONTINUED)

13:00 **Welcome.** Dan Merenstein and Marla Cunningham

13:00-14:30 **Interactive Session.** Game-changing insights from recent publications.
Anisha Wijeyesekera, University of Reading, UK

14:30-15:00 The vaginal microecology, immunity and the potential of probiotic interventions.
Jo-Ann Passmore, University of Cape Town, South Africa

15:00-15:30 **Break and poster view**

15:30-16:00 **Design of dietary and bacterial therapeutic interventions to enhance the resilience and health-promoting properties of the human gut microbiome.**
Ophelia Venturelli, University of Wisconsin-Madison, USA

16:00-16:30 How the microbiome converses with the little brain and the big brain.
Premysl Bercik, McMaster University, Hamilton, Ontario, Canada

16:30-16:45 Refreshments.

16:45-17:45 **Late Breaking News.** Gregor Reid, University of Western Ontario, Canada

Walk to the University Club (0.2 miles)

18:00-20:00 **Welcome reception.** Share a drink and gourmet appetizers with old and new friends.
University Club

TUESDAY – JUNE 27

7:00-17:15 Posters available for viewing

6:30-8:00 **Registration**

8:00-13:00 **SFA discussion group** followed by **lunch.** Ballroom, Brown Palace

All but SFA Walk to the University Club (0.2 miles)

8:00-13:00 **Concurrent discussion groups followed by lunch.** University Club

1. *Use of probiotics and prebiotics in agricultural and companion animals.*
Kelly Swanson, University of Illinois – Urbana, USA and George Fahey,
University of Illinois – Urbana, USA [Presidents Room](#)

2. *What is the evidence that a biotic intervention can benefit healthy people?*
Dan Merenstein and Dan Tancredi, University of California – Davis, USA [Lounge](#)



Program for the 2023 ISAPP Meeting



TUESDAY – JUNE 27 (CONTINUED)

3. Do probiotics improve health by changing the gut microbiome?

Maria Marco, University of California – Davis, USA and Dave Mills, University of California – Davis, USA [Directors Room](#)

4. Is there an effective approach to rational design and validation of prebiotics to target members of the microbiota?

Bob Hutkins, University of Nebraska, Lincoln, USA and Bruce Hamaker, Purdue University, W. Lafayette, IN, USA [College Room](#)

5. How does the development pipeline differ between microbiome-based therapeutics and traditional probiotics for foods/supplements?

Sarah Lebeer, University of Antwerp, Belgium and Bruno Pot, Yakult Europe B.V., Almere, The Netherlands [Capitol Room](#)

6. Can C. difficile infections be prevented with bacteriotherapy? Eamonn Quigley, The Methodist Hospital and Weill Cornell School of Medicine, Houston, TX, USA and Colleen Kelly, Brown University, Providence, RI, USA [Library](#)

Walk to Brown Palace (0.2 miles)

13:30-16:30 **Registration**

14:00-14:15 **2023 Glenn Gibson Early Career Researcher Prize winner talk.** Investigating the effects of short-chain fatty acids on the immune system and gut microbiota of healthy humans.

[Paul Gill](#), Monash University, Melbourne, Victoria, Australia

14:15-14:30 **SFA talk.** Immunometabolic effects of physicochemically-distinct dietary fibers in adults with excess body weight: towards precision nutrition strategies. [Anissa Armet](#), University of Alberta, Canada

14:30-14:45 **SFA talk.** Identification of novel immunomodulatory components in *Lacticaseibacillus rhamnosus* GG. [Soyolmaa Jamiyanpurev](#), Shinshu University, Japan

14:45-15:15 Re-imagining the future of healthcare research registries: happening as we speak. [Khurram Nasir](#), The Methodist Hospital and Weill Cornell School of Medicine, Houston, TX, USA

15:15-15:45 Impact and personalized responses to prebiotics by human gut microbiota. [Lawrence David](#), Duke University, Durham, NC, USA

15:45-16:15 Kill to prosper: intra-species competition of a probiotic. [Jan-Peter Van Pijkeren](#), University of Wisconsin-Madison, USA

16:15-17:15 **Poster viewing and SFA poster judging.** Authors will be present for all posters.

17:30 Meet in [Ballroom](#).

Walk to History Colorado Center (0.5 miles)

18.00-21.00 **Gala Social Event.** History Colorado Center



Program for the 2023 ISAPP Meeting



WEDNESDAY – JUNE 28

8:00-10:30 Registration

8:00-8:15 **IAC talk.** Beneficial effects of multispecies probiotics on mood and cognition in clinical studies. [Annemarieke van Opstal](#), Winlove Probiotics, Amsterdam, the Netherlands.

8:15-8:30 **IAC talk.** Inulin-type fructans and 2'fucosyllactose alter microbial composition and alleviate stress-induced mood state in a working population: a randomized, controlled trial. [Jessica Van Harsseelaar](#), BENE0-Institute, BENE0 GmbH, Obrigheim, Germany

8:30-9:00 Microbiome maturation in premature infants. [Marie-Claire Arrieta](#), University of Calgary, Canada

9:00-9:30 Status report on ISAPP projects

Association of live dietary microbes with health outcomes: a brief update. [Bob Hutkins](#)

The role of probiotics in restoring microbiota composition and function following antibiotic-induced perturbation. [Hania Szajewska](#), Medical University of Warsaw, Poland

Prebiotic criteria. [Karen Scott](#), Rowett Institute, University of Aberdeen, UK

9:30-10:00 Use of probiotics and prebiotics to restore microbiome homeostasis and treat GI diseases in companion animals. [Karin Allenspach](#), Iowa State University, Ames, USA

10:00-10:30 Break and poster view

10:30-12:30 **Summary reports from discussion groups.** [Gabriel Vinderola](#), Instituto de Lactología Industrial (CONICET-UNL), Santa Fe, Argentina

12:30 Meeting adjourned.



APPENDIX B: ACKNOWLEDGEMENTS

Thank you to the 63 member companies for their support of ISAPP in 2023.





ISAPP Gala, History Colorado Center