

## Speaker Profiles



### Charles Franz

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Head of Department of Microbiology and Biotechnology, Max Rubner-Institute. Education: B.Sc., B.Sc. Hons & M.Sc. in Microbiology all obtained from the University of the Witwatersrand in Johannesburg, South Africa. 1998 Ph.D. in Food Microbiology from the University of Alberta, Edmonton, Alberta, Canada.

2008 Habilitation in Microbiology at the University of Karlsruhe (now KIT = Karlsruhe Institute for Technology)

Research focus: The microbial biodiversity of complex ecologies such as the human gut or fermented foods, investigations into functionality, physiology and genetics of bacteria associated with the gut or fermented foods and the development of starter cultures for African food fermentations. Publications about 100 in peer reviewed

### Inter-individual trans-resveratrol metabolism by the gut microbiota

*Charles M.A.P. Franz, Melanie Huch, Gyu-Sung Cho, Diana Bunzel and Sabine E. Kulling*

Resveratrol (3,5,4'-trihydroxy-trans-stilbene) is a polyphenol which belongs to the stilbene class of substances. It is a constituent of the skin and seeds of grapes, but also occurs in many other foods such as wine, peanuts and cocoa. A number of health-promoting properties, such as anti-inflammatory, anti-oxidative and anti-carcinogenic properties have been suggested for resveratrol on the basis of various *in vitro* and *in vivo* studies. Our study aimed to determine whether the human gut microbiota plays a role in trans-resveratrol metabolism, which bacteria are involved and which products arise. The metabolism was investigated in 5% feces cultures from seven human volunteers in which 80  $\mu\text{mol/L}$  trans-resveratrol was incubated at 37°C under anaerobic conditions for 48 h. Samples were removed, extracted and characterized using HPLC-UV/Vis and HPLC-MS. Inter-individual trans-resveratrol metabolism could be observed.

Furthermore, three end products of metabolism were identified, i.e. dihydroresveratrol, and the two at that time unknown metabolites 3,4'-dihydroxy-trans-stilbene and lunularin (3,4'-dihydroxybibenzyl).

Bacterial strains representative of the major groups of the gut microbiota were investigated for their trans-resveratrol metabolism *in vitro*. Members of the coriobacteria, specifically *Eggerthella lenta*, *Adlercreutzia equolifaciens* and *Slackia equolifaciens*, could be identified as dihydroresveratrol producers. The genetic basis for dihydroresveratrol production is currently being investigated. However, among 98 intestinal bacterial species tested in pure culture *in vitro*, none could be shown to produce lunularin under the conditions of our study. In an alternative approach, long-term fecal cultures were devised in an attempt to decrease microbial diversity and thus to enable the identification of bacterial lunularin producers. Such cultures were set up at different pH values, or contained inhibitory compounds such as antibiotics or cholic acid. The diversity of the cultures was investigated using an NGS approach with Illumina MiSeq 16S metagenomics. While this investigation highlighted differences in microbial community compositions, it could not clearly point towards specific species associated with lunularin production.



## Maria Carmen Collado

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M. Carmen Collado, PhD (Polytechnic University of Valencia (UPV), Valencia, Spain, 2005); Researcher at Dept. Biotechnology, Institute of Agrochemistry and Food Technology (IATA) of the Spanish National Research Council (CSIC) located in Valencia, Spain. Her research work is multidisciplinary and includes microbiology, food science and nutrition areas. Her interests are focused on probiotics, microbiota and health and nutrition. Her current work includes basic and applied research on molecular analysis and evaluation of health effects of beneficial bacteria and probiotics, the microbial-host interactions, microbiome and its role in human health and diseases and also, the influence of diet and other factors.

### Contribution of maternal microbiota to infant health

Microbiota has become a relevant aspect of human health. The advances in the understanding of the host–microbe interactions suggest that the maternal microbiota plays a crucial role in human health. Microbial colonization runs in parallel with immune system maturation and plays a role in intestinal physiology and regulation. Increasing evidence on early microbial contact suggest that this process begins in utero and later it is modulated by the mode of delivery and by the infant diet. The maternal microbiota forms the first microbial inoculums, and from birth onwards, the microbial diversity increases and converges towards an adult-like microbiota by the end of the first years of life. Taken all information available, delayed microbial colonization, alterations in the microbiota profiles and lower microbial diversity are strong risk factors for the development of life-style diseases such as allergies and obesity. Therefore, an adequate establishment of microbiota during the gestational and early neonatal periods and its maintenance throughout life would reduce the risk of disease in early and late life.



## Sylvia Duncan

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Sylvia Duncan gained her BSc and PhD from University of Aberdeen and is a Research Scientist in the Microbiology group at the Rowett Institute of Nutrition and Health, Aberdeen, UK. She has isolated some of the key bacterial species that degrade fibre, resistant starch and utilise lactate to form acetate, propionate and butyrate in the human colon. Her research interests include anaerobic microbiology and metabolite profiling of gut microbial communities including microbial transformation of plant phenolics. This also includes controlled human dietary intervention studies that have provided unique information on the dynamics of the gut microbiota.

### Predicting the impact of diet composition on the human intestinal microbiota

*Sylvia H Duncan and Harry J Flint*

Changes in the species composition of the human faecal microbiota can be detected within a few days of transferring to a new diet. Certain bacterial phylotypes, identified from 16S rRNA gene sequences, respond to increases in particular dietary non-digestible carbohydrates across many individuals, despite considerable inter-individual variation in microbiota composition. For example, controlled dietary intervention studies have shown that only certain specific groups of Firmicutes are stimulated by resistant starch or inulin, while other representatives of this same phylum are stimulated by complex non-starch polysaccharide (NSP) fibres such as wheat bran. Functional analysis of cultured strains suggests that these Firmicutes bacteria are likely to play a key role in initiating the degradation of these insoluble substrates in the colon. The relationship between dietary intake of fermentable carbohydrates and metabolic outputs of the gut microbiota including the potentially beneficial short chain fatty acids, propionate and butyrate, is of particular interest in terms of human health. This requires understanding of the bacterial groups involved in substrate breakdown, the distribution of metabolic pathways and cross-feeding interactions involved in product formation and how this is driven by the gut environment. Moreover, a deeper comprehension of the complex microbial ecosystem is likely to be gained by theoretical modelling.



## Miguel Gueimonde

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I was born in Asturias (Spain) in 1973. After finishing a MSc in Biological Sciences at the University of Oviedo (1997) I conducted my PhD thesis at the Dairy Research Institute of Asturias (IPLA-CSIC) studying probiotic bacteria and probiotic containing products, as well as the improvement of fermented milks elaboration processes. After my PhD (2002), in order to complete my training in the area of probiotics, I went to Finland for a postdoctoral stay at the Functional Foods Forum of the University of Turku. During this time my work was mainly focused on the study of intestinal microbiota and probiotic bacteria. Since 2006 I am Docent (adjunct professor) of the University of Turku and since 2008 I hold a permanent position as staff scientist at IPLA-CSIC.

### **Microbiota, immunological and nutritional parameters at old-age: opportunities for the development of functional foods for the elderly**

*N. Salazar, L. Valdés, S. González, C. G. de los Reyes-Gavilán, P. Ruas-Madiedo and M. Gueimonde*

The ageing process has been repeatedly reported to affect both the composition of the intestinal microbiota and the immune status of the host. Therefore, the development of functional foods for microbiota and immune modulation in the elderly constitutes an interesting strategy. For such development specific targets in the elderly population, not just in terms of microbiota but also considering immune parameters, should be carefully defined. Previous studies have reported differences in the levels of different bacterial populations in faeces of elderly when compared with those of control subjects. A pro-inflammatory status has been repeatedly indicated as well. These specific senescence-related alterations may be considered targets for modulation and used as criteria for the selection of specific prebiotics and probiotics for elderly. Moreover, specific nutritional deficiencies, as well as specific diet-microbiota-immune system interactions are also present in the elderly population. Thus, the future design of new probiotic and/or prebiotic functional foods for elderly should consider the population specific needs; selected probiotics and prebiotics should be included in nutritionally adequate products formulated to satisfy the particular nutritional needs of elderly. The design of such target-specific foods, in which a multifactorial approach is taken by selecting function-specific probiotics/prebiotics and introducing them in nutritionally optimised products, may constitute an opportunity for improving the functionality and efficacy of probiotic/prebiotic containing functional foods.



## Colin Hill

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Colin Hill has a Ph.D in molecular microbiology and is Professor of Microbial Food Safety in the School of Microbiology at University College Cork, Ireland. His main research interests are defining the mechanisms of virulence of foodborne pathogens. In 2005 Prof. Hill was awarded a D.Sc by the National University of Ireland in recognition of his contributions to research. In 2009 he was elected to the Royal Irish Academy and in 2010 he was a joint recipient of the Metchnikoff Prize in Microbiology and was elected to the American Academy of Microbiology. He has published more than 380 peer reviewed papers and holds 14 patents.

### **Gut microbiota composition correlates with diet and health in the elderly – The ELDERMET story**

Alterations in intestinal microbiota composition are associated with several chronic conditions, including obesity and inflammatory diseases. The microbiota of older people displays greater inter-individual variation than that of younger adults. The faecal microbiota composition from 178 elderly subjects forms groups which correlate with residence location in the community, day-hospital, rehabilitation or in long-term residential care. However, clustering of subjects by diet separated them by the same residence location and microbiota groupings. The separation of microbiota composition significantly correlated with measures of frailty, co-morbidity, nutritional status, markers of inflammation and with metabolites in faecal water. The individual microbiota of people in long-stay care was significantly less diverse than that of community dwellers. Loss of community-associated microbiota correlated with increased frailty. Collectively, the data support a relationship between diet, microbiota and health status, and indicate a role for diet-driven microbiota alterations in varying rates of health decline upon ageing.



## Maria Jenmalm

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My research focuses on childhood immune and allergy development in relation to maternal immunity and microbial exposure. I am an immunologist collaborating with paediatric allergologists, obstetricians, clinical immunologists and microbiologists. Our research is translational, combining advanced laboratory methodology with careful, long-term, clinical follow-up during pregnancy and childhood with excellent compliance rates, also in randomised placebo-controlled intervention studies (see e.g. ClinicalTrials.gov Identifier NCT01542970). In my laboratory at the Division of Inflammation Medicine at Linköping University, Sweden, we analyse systemic and mucosal immune function by ELISA, Luminex, flow cytometry, real time PCR and EILA (epigenetic immune lineage analysis).

### The role of the infant gut microbiota in shaping immune and allergy development during childhood

The increasing allergy prevalence in affluent countries may be caused by reduced intensity and diversity of microbial stimulation, resulting in an abnormal postnatal immune maturation. The gut microbiota is quantitatively the most important source of microbial stimulation and may provide a primary signal for appropriate immune development. While no specific microbes with consistently harmful or allergy protective roles have yet been identified, the gut microbiota differs in composition and diversity during the first months of life in children who later do or do not develop allergic disease. Early establishment of a diverse gut microbiota may be more important than the distribution of specific microbial species in shaping a normal immune maturation. It is also becoming increasingly evident that the maternal microbial environment during pregnancy is important in childhood immune programming. A combined pre- and postnatal supplementation seems to be crucial for the preventive effect of probiotics on infant eczema. Probiotic interventions have so far failed to prevent asthma, however. Further studies on the appropriate timing of interventions and the complex interactions between the infant immune system and the gut microbiota are required to identify preventive strategies to combat the asthma and allergy epidemic.



## Kieran Tuohy

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KIERAN TUOHY received his PhD from the University of Surrey (UK) in 2000. Between 2000 and 2006 he worked as a post doctoral researcher in the Food Microbial Sciences Unit of Professor Glenn Gibson, University of Reading and in 2006, was appointed lecturer in the Department of Food Science and Nutrition, University of Reading. He now leads the Nutrition and Nutrigenomics Group at Fondazione Edmund Mach, Trento, Italy (<http://cri.fmach.eu/Research/Food-Quality-and-Nutrition/Nutrition-and-Nutrigenomics>) which grew out of the Autonomous Province of Trento funded incoming team project TrentinoGUT. His research focuses on the health effects of diet:microbe interactions within the gastrointestinal tract and has expertise in microbial ecology, fermentation technologies, nutrition, functional food design and testing, metabolomics and metagenomics. He has over 79 international, peer reviewed publications in the area of gut microbiology, a H index of 22, and is co-editor of the book "Diet-Microbe Interactions in the Gut", Elsevier.

### Diet : Microbe interactions - ecosystem support

Recent metagenomic studies are confirming what pioneers in gut microbiology have long said, that diet:microbe interactions in the gut impact on human health and disease. The gut microbiota appear to regulate various physiological functions including host energy metabolism, immune homeostasis, and brain development and function. The gut microbiota produces a range of biologically active metabolites, not least, short chain fatty acids, small phenolic compounds derived from polyphenol metabolism, and, immunologically and neurologically active amino acid derivatives such as gamma-aminobutyric acid, serotonin and dopamine. Microbiota activities also control systemic tryptophan metabolism and peripheral concentrations of potentially harmful metabolites derived from choline and carnitine metabolism, notably the cardiotoxicant trimethylamine-N-oxide. The gut microbiota also determines the profile of bile acids returning to the liver through the enterohepatic circulation, important cell signalling molecules involved in various physiological functions, including host energy metabolism and immune function. Diet in large part regulates these important microbiota physiological services and dietary constituents, particularly the relative proportions of fermentable fiber and plant polyphenols on the one hand, and refined sugars, fat and animal protein, on the other, appear to critically determine the flux of either beneficial or potentially harmful metabolites from the gut. This presentation will discuss how diet regulates both the composition and metabolic output of the gut microbiota constituting, in effect, ecosystem support, not just for the gut microbiota, but for the greater human:microbe ecosystem as a whole.



## Anne Salonen

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Anne Salonen is a research scientist at University of Helsinki, Finland. She has multidisciplinary training in biosciences and PhD in microbiology. Several years research experience in molecular microbiology and microbial ecology. Research activities are focused on the composition and activity of the intestinal microbiota in health and disease (MetS, IBS, IBD) with links to nutrition and biomedicine. Main research methodology is phylogenetic microarray (HITChip), also involved in metaproteomic work. Co-organizer of the yearly Finnish Gut Day seminar.

### Dietary Responsiveness of the Human Intestinal Microbiota

There is growing interest to understand how diet affects the intestinal microbiota and how this translates to host health. One of the major challenges in the field is the high individuality of the microbiota composition and its individual-specific dietary responses. Similarly, the high variation of host responses is a challenge in nutritional research and practise. We have recently started to study the microbiological basis of the individual dietary responses by using a deep community-wide microbiota analysis based on phylogenetic microarray before and after dietary interventions. Our proof-of-principle study shows that categorization of the study subjects to dietary responders and non-responders allows identification of microbiota features that are specific to responders, both in terms of the microbiota and most importantly, of the anticipated host parameters (in our case metabolic health markers). If such predictive microbiota signatures can be validated in further studies, they will provide a radically new way to understand and deliberately modulate the gut microbiota to benefit health.



## Jan Knol

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Dr. Jan Knol is the Director of Gut Biology & Microbiology at Danone Nutricia Research - Utrecht, the Netherlands. The Gut Biology and Microbiology platform brings together unique expertises in the area of microbiology and human (gut) physiology to substantiate nutritional concepts and to develop innovative nutrition products. In addition, since April 2012, Jan Knol is Special Professor Intestinal Microbiology of Early Life, at the Laboratory of Microbiology at the Wageningen University. The chair focuses on the early colonization of the intestinal tract of newborn infants linked also to potential health outcomes. Jan studied biology / biochemistry with specialisations in molecular biology and microbiology at the University of Groningen, The Netherlands. He completed his PhD thesis in 1999 at the University of Groningen on sugar transport mechanisms in lactic acid bacteria. Part of this work was performed at the University of Leeds (United Kingdom) and the "Laboratoire J. Maetzi" in Villefranche sur mer (France). After his PhD he started as a scientist at Nutricia Research in Wageningen. After several years as research manager Microbiology he is now leading an expertise group on Gut Biology and Microbiology, with projects focussing on pre- and probiotics, intestinal microbiota, digestion and gut health. The group frequently hosts students from national and international Universities and institutes. Jan Knol published more than 70 peer reviewed papers in the field of microbiology and gut biology, and is inventor on more than 25 patent applications.

### Intestinal Microbiology in Early Life; Nutrition, Health and Disease

Our intestinal microbiota forms an integral part of normal human physiology, and disturbances of the normal gut microbiology have been linked to some important health and disease issues. Newborns are essentially sterile and the microbiota establishes from the very first days of life. These first colonizers may play an important role in the development of the symbiosis and may impact the long-term composition and activity of the microbiota. Considering the importance of the microbiota on the human immune, metabolic, and neurological systems, it is important to understand the dynamics and driving determinants of this development. The development of the human gut microbiota is dependent on many factors, as for example, host genetics, mode of delivery, antibiotic use, etc., but also the diet is clearly an important factor.

Exclusive human milk feeding is widely recommended as the first choice of infant nutrition, not only providing optimal nutrition, but also bioactive components that are crucial for optimal gut development, immune maturation, metabolic development, and even cognitive development. Since breast feeding may not always be possible, human milk substitutes have to provide the best nutrition and functional properties similar to human milk. Based on insights from human milk research and an increasing understanding of the importance of the gut microbiota, a specific mixture of non digestible oligosaccharides for infant formulas has been developed. The impact of these oligosaccharides on the gut eco-physiology in early life will be presented as well as some potential health benefits.

## Gemma Walton

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I have been researching in the field of gut microbiology for 13 years. In 2002 I undertook a BBSRC case PhD studentship at the University of Reading with Prof. Glenn Gibson and Prof. Bob Rastall investigating bowel cancer and the potential impact of prebiotics. I have developed a keen interest in the gut microbiota, how it impacts health and how we can influence its growth. I have worked on in vitro models of the gut and have conducted many human studies on novel prebiotics and looking at impact in atypical populations (including those at risk of metabolic syndrome). My current research role is studying at the impact of specific pharmaceuticals on the gut microbiota and the subsequent impact of the microbiota on the pharmaceuticals.

### The ageing gut microbiota and the impact of prebiotics

Throughout life the gut microbiota develops alongside us influencing our health status. With the advancement of age changes in the gut microbiota are becoming increasingly recognised – these include a decline in bifidobacteria and often the development of a more proteolytic environment within. Furthermore, with ageing changes in the immune system that are frequently termed immunosenescence have been observed, this often involves reduced immune function and increased inflammation. These changes often coincide with increased susceptibility to diseases. Prebiotics are targeted food ingredients that selectively promote the growth of specific members of the gut microbiota. Many prebiotics are selective toward bifidobacteria, as such prebiotic intervention offers the possibility of addressing the alterations of the gut microbiota brought about by the ageing process. Furthermore, as the microbiota are known to interact with the immune system through the gut-associated lymphoid tissue and short chain fatty acid production, the consumption of prebiotics has the potential to impact on the immune function.

## Liping Zhao

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Dr. Liping Zhao is currently a professor for microbiology and the director of Laboratory of Microbial Ecology and Ecogenomics in School of Life Sciences and Biotechnology, Shanghai Jiao Tong University. He is the director of the Laboratory of Nutritional Systems Biology in Shanghai Center for Systems Biomedicine. He is also the director the SJTU-Perfect (China) Joint Research Center on Microbiota and Health. He is a senior editor of the ISME Journal. He was elected the fellowship of American Academy of Microbiology in 2014. His current research focus is the interactions between nutrition and gut microbiota in onset and progression of chronic diseases such as obesity and diabetes, and how traditional Chinese medicine and medicinal foods may modulate this relationship for achieving preventive healthcare. The Science magazine featured a story on how he combines traditional Chinese medicine and gut microbiota study to understand and fight obesity (Science 336: 1248).

### Gut microbiota and metabolic diseases: Hunting down the key players

The gut microbiota has been linked with chronic diseases in humans such as obesity and diabetes. However, the demonstration of causality between constituents of the microbiota and specific diseases remains an important challenge in the field. In this presentation, using Koch's postulates as a conceptual framework, I explore the chain of causation from alterations in the gut microbiota, particularly the endotoxin-producing members, to the development of obesity in both rodents and humans. Three components are essential for identifying the causative agents of obesity in the human microbiota: 1) microbiome-wide association studies; 2) isolation of the putative agents and disease reproduction in gnotobiotic animals; 3) mechanistic analysis of host responses to establish the molecular chain of causation. We employed this strategy in dietary therapy of morbid obesity/diabetes in human clinical trials to show that specific bacterial phylotypes, which are more relevant with MetS, can be identified, isolated and demonstrated in gnotobiotic models to be causatively contributing to MetS development in human. For example, one endotoxin-producing bacterium was isolated from a morbidly obese human's gut and demonstrated to be able to induce obesity and insulin resistance in germfree mice