

Presentation Abstracts for the 1st Applied HoloGenomics Conference

Session 1: Opening

Title: The extended human hologenome, the next hundred years

Presenter: Prof. Rob Dunn, NC State University, USA

Abstract:

Here, I introduce the term "the extended hologenome" to reflect the set of genes that an organism relies upon including a) host genes, b) symbiont genes and, in addition, c) symbiont genes housed outside of the body. I then consider the evolution of the human extended hologenome over the last million years before by concluding with a discussion of the possible future human extended hologenomes. At the moment, many futures are possible and yet such futures have been little discussed.

Title: Multi-omics techniques applied to investigate the global human microbiome

Presenter: Assistant Professor Mathilde Poyet, University of Kiel, Germany

Abstract:

Biodiversity is disappearing rapidly at a global scale. These widespread losses include a critical but often overlooked ecosystem: the microbial biodiversity of the human gut. A rapidly growing body of literature now shows that this complex microbial community – the gut 'microbiome' – is critical to metabolism, immunity, and health. Imbalances in this community and lack of exposure to beneficial microbes have been linked to diseases like inflammatory bowel disease, autoimmune diseases, and cancer. The human gut microbiome is being profoundly disrupted by the widespread adoption of industrialized diets, lifestyles, and excessive use of antibiotics. As the global population increasingly shifts to urban centers, this critical biodiversity is at risk of experiencing further perturbations and losses. We founded the Global Microbiome Conservancy (GMbC) as an international and collaborative initiative to biobank the global biodiversity of the human microbiome before it is lost to industrialized diets and lifestyles. We aim to develop it as a non-commercial research platform for the scientific community and as a long-term central repository for infinite preservation. So far, we

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biobanked 10,000+ bacterial strains sampled from more than 40 communities of various lifestyles worldwide. Our first investigations expand our understanding of the evolution of human microbiomes in recent human history and illuminate how industrialization perturbs our gut ecosystems.

Session 2: Human Health

Title: Food for thought: hologenomic adaptations to amylose and lactose in the evolving human diet

Presenter: Associate Professor & Team Leader Christina Warinner - Harvard University, USA, MPI, Germany

Abstract:

Human diet has radically changed since the emergence of our genus approximately 2 million years ago. Over that period, gene duplications related to digestion - such as amylase copy number - have vastly expanded, and genetic variants - such as lactase persistence (LP) - are among the genomic features under highest selection in the human genome. Although the evolutionary dynamics behind some of these changes are partly known, their microbial correlates within the human microbiome are less explored. Here we discuss hologenome adaptations to two carbohydrates, amylose and lactose, and show that far from being simple, they involve a complex interplay between the host genome and microbiome. Using direct molecular evidence from the archaeological and paleoanthropological record, we demonstrate that human dietary evolution is best understood at the level of the holobiont, and that only by investigating the host genome and microbiome in tandem can human evolution be fully understood.

Title: Evolution and function of host-microbiome systems

Presenter: Assistant Professor Mathieu Groussin, Kiel University, Germany

Abstract:

Concurrent with industrialization, the human gut microbiome has dramatically decreased in diversity and shifted in composition. However, to what extent transitioning from hunter-gatherer to industrialized lifestyles impacted host-microbiome interactions and host physiology is unknown. Here, we generate gut microbiome multi omics data coupled with host physiology from dozens of populations worldwide, ranging from hunter-gatherers to fully

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industrialized groups, and show that intestinal inflammation, humoral immune response and patterns of horizontal gene transfers (HGT) between bacteria strongly changed with industrialization. We reveal that industrialized gut microbiomes associate with elevated secretion of intestinal immunoglobulin A, despite lower levels of parasitic incidence. Furthermore, populations with hunter-gatherer lifestyles exhibit the lowest levels of intestinal inflammation. Finally, we show that gut bacteria within the microbiome of industrialized individuals exchange genes more frequently than in non-industrialized populations, potentially in response to increased environmental perturbations. Overall, our results suggest that industrialization perturbed our gut. ecosystem and homeostasis on many levels, which could contribute to many chronic inflammation diseases.

Title: The gut microbiota and mental disease – approaching a hologenomics view

Presenter: Prof. Karsten Kristiansen, University of Copenhagen, Denmark, BGI-Shenzhen, China, Qingdao-Europe Advanced Institute for Life Sciences, Qingdao, China

Abstract:

Monogenic diseases offer clear insight into the relation between the genome and diseases, but the importance of the host genome in relation to more complex multifactorial diseases has proven more difficult to establish. During the last decade, it has become well established that the gut microbiota may play an even more important role in relation to metabolism and immune functions, and evidence has been presented that the gut microbiota may also affect behavior. However, the exact molecular mechanisms by which bacteria in the gut exert their actions remain elusive. In this lecture, I will summarize recent work from Copenhagen, Shenzhen, and Qingdao demonstrating how distinct changes in the gut microbiota are associated several multifactorial diseases, focusing on mental disorders, and how integration of different omics-technologies and the use of mouse models allow us to move from association to causality. I will discuss our work combining multi-omics technologies to approach a hologenomics view on the development of multi-factorial disorders, and I will conclude the lecture by discussing possible functional consequences and perspectives of these findings.

Title: Distinctive Streptococcus clades characterize oral niches regardless of industrialization status and oral pathology

Presenter: Dr. Irina M. Velsco, MPI, Germany

Abstract:

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The genus Streptococcus is highly diverse and a common member of human, animal, and fermentation microbiomes. The streptococci are grouped into at least 8 phylogeneticallysupported clades, five of which, Sanguinis, Mitis, Anginosus, Salivarius, and Mutans, are found almost exclusively in the mouth. Within the human mouth, these Streptococcus species occupy, and are often the dominant genus in, distinct oral niches. It is not known whether niche specialization is a characteristic of human biology, whether it is structured by modern, industrialized lifestyles, or the extent to which oral health status influences the clades abundances. We explored the dominant phylogenetic clades in samples from dental plaque, dental calculus, buccal mucosa, and saliva of living industrialized and non-industrialized populations across the globe, as well as in historic dental calculus. We found that clade dominance is conserved across oral sites, regardless of industrialization status, but that each oral site is distinct. Dental plaque and calculus, which represent different developmental stages of a dental biofilm, are dominated by Sanguinis streptococci, yet a minority of plaque are dominated by Mutans streptococci, while a minority of historic dental calculus samples are dominated by Anginosus streptococci. In plaque, Mutans blooms with no change in levels of Sanguinis, while in calculus, Anginosus becomes dominant only when Sanguinis levels drop. No associations between dominant clades and oral pathology were found in either modern or historic plaque or calculus. Saliva and buccal mucosa were both dominated by Mitis group streptococci, yet non-industrialized saliva showed a higher abundance of streptococci that are not known to inhabit humans or animals. In conclusion, neither industrialization status nor oral pathology show associations with the dominant Streptococcus clades of the oral sites we examined. However, Streptococcus profiles of non-industrialized saliva may be shaped by external factors, leading to artificially high estimates of diversity in these populations.

Title: Why are there different microbial community types?

Presenter: Dr. Karoline Faust, KU Leuven, Belgium

Abstract:

The human gut microbiome comes in different community compositions known as enterotypes. Alternative community compositions have also been reported for other human body sites such as the vagina and the oral cavity. Since enterotypes are differentially represented in various diseases, a better understanding of what drives community types also has implications for human health. Here, I will explore different hypotheses that have been proposed to explain alternative community types and how well they are supported by gut microbial data sets, with a particular focus on human gut microbial time series. In addition, I will emphasize the value of mathematical models to explore mechanistic explanations that can then be tested in microbiome data.

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Title: Ancient oral microbiome reveals gradual adaptation of Italian prehistoric communities to Neolithic dietary shifts towards agriculture

Presenter: Research Fellow Andrea Quagliariello, University of Padova, Italy

Abstract:

The human microbiome has become a valuable source of information about host life and health. To date, little is known about how it may have evolved during key phases of human evolution, such as the transition from hunting-gathering to agriculture occurred in the Neolithic period. This event radically changed our history, promoting sedentarism, population growth and leaving selection marks on the human genome.

In this frame, which was the influence of agriculture transition on human-associated microorganisms?

To answer this question, we investigated the evolution of the oral microbiome during this transition, by comparing Palaeolithic hunter-gatherers oral metagenomes with that of Neolithic farmers that populated the same area in Southern Italy. Such geographical region constitutes a perfect case-study to investigate the Neolithic transition as (i) the time when the shift towards agriculture took place is known, (ii) hunter-gatherers' and farmers' societies shared the same environmental background, (iii) bioarchaeological data on population diet and climate condition are available.

Starting from 76 dental calculi, we reconstructed the ancient oral microbiome profiles through shotgun sequencing and identified the embedded plant remains consumed during life. The integration of these results with ancient diet and environmental data allowed us to detect two key shifts in the oral microbial community. The first took place in the early phases of Neolithic and is related to the cultural transition to agriculture; and a second shift characterized by the increase of several oral pathogens occurred in the middle of the Neolithic period, coinciding with a climate shift toward aridity that affected the area. Such dry phase influenced the agricultural practices (plant used and harvest times), and probably affected the microbiome composition as a consequence.

Our findings demonstrate that the introduction of agriculture, along with specific climate conditions, greatly shaped the evolution of the human oral microbiome, ultimately affecting human health.

Session 3: Agriculture, Aquaculture and Food Production

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Title: Research and Innovation for microbiomes

Presenter: Magdalena Gajdzinska, Directorate General for Research and Innovation of the *European* Commission, Brussels

Abstract:

Microbiomes are in, on and all around us, understanding what microbiomes do, what they are, and how they interact is a new scientific frontier made now reachable by rapid advances in genomics. What we know and understand so far is that the microbiome has essential impacts on our health and on the food we produce, on plants and animals and on ecosystems in general. Unravelling their complexity offers huge potential for innovation and will be a major game changer in the way we manage our planet's resources to obtain our food and improve our health. Microbiome research and innovation has the potential to touch upon many areas, from primary production and sustainable agricultural to food production and food science, to human health and waste management. Thereafter the co-benefits spans from reduction of GHGs emissions to increased adaptation options to climate change, from reduction of risk factors for NCDs to protection of biodiversity.

Title: Engineering algal microbiomes for sustainable food and feed production

Presenter: Prof. Lone Gram, DTU BioSustain, Denmark

Abstract:

Microalgae are used as feed for fish larvae, as producers of valuable compounds such as polyunsaturated fatty acids or as part of biological waste water treatment. As all other organisms, algae are colonized by a microbial community establishing a phycosphere equivalent to the plant rhizosphere. The phycosphere may harbor algal pathogenic species, but also bacteria that improve algal growth and productivity, and bacteria that subsequently, when the algae are used as live feed in aquaculture, can suppress fish pathogenic bacteria. Thus the algal microbiome can be used in a biocontrol strategy in aquaculture allowing a reduction in use of antibiotics and, hence, the risk of antibiotic resistance. Our understanding of which microorganisms in the phycosphere that are beneficial to the algae is limited. On a species level, different algal species are hosts to different microbiome. This talk will introduce the phycosphere and discuss challenges in its analyses as well as presenting examples of using algal microbiome engineering as biocontrol strategy in aquaculture.

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Title: Leveraging microbiota services through hologenomic analyses to improve gut health in farmed salmon

Presenter: Dr. Jaelle C. Brealey NTNU, Norway

Abstract:

Atlantic salmon aquaculture is one of the most profitable and technologically advanced fish production industries in the world. However, improved practices are imperative if the industry is to sustainably meet future global production demands. Ongoing industry challenges include frequent disease outbreaks, inefficient feed conversion and losses due to unpredictable variation in fish size at harvest, even in fish from the same genetic broodstock raised in identical environmental conditions. We investigated whether a hologenomic approach could identify novel pathways linking the salmon gut microbiome, gut metabolism, and host genetic variability to the observed phenotypes, focusing on fish size at harvest. Genomes, transcriptomes, epigenomes, metabolomes, and metagenomes were generated from the guts of 460 harvest-aged Norwegian salmon (gutted weights: 0.8–7.8 kg), from the same broodstocks and open-water pens. Consistent with previous studies, the salmon gut microbiota was characterised by low microbial biomass and low alpha diversity, with most individuals dominated by a species of Mycoplasma specific to salmonids. As expected, host genetic variation was low, and a GWAS found only weak evidence for a host genetic link to microbiota composition. However, we identified subtle shifts in the microbiota that were associated with fish size, including increased abundance of Mycoplasma in larger, healthier fish. Multi-omic factor analysis revealed that these fish were also characterised by shifts in gene expression and metabolic profiles, including changes in fatty acid and lipid metabolism, concordant with the higher levels of omega-3 fatty acids observed in the muscle of these larger fish. We also identified links between Mycoplasma genome functions and host gut metabolism, specifically in prenol-associated pathways of both, suggesting host-specific adaptation of Mycoplasma to the salmon gut. Our results demonstrate the value of a hologenomic approach to more fully understand how complex host-microbe interactions shape growth and health performance in farmed salmon.

Title: A hologenomic approach to the management of infectious diseases affecting the American oyster, Crassostrae virginica

Presenter: Prof. Marta Gomez-Chiarri, University of Rhode Island, USA

Abstract:

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Management of infectious diseases affecting aquaculture species requires the use of multidisciplinary approaches able to disentangle the complex relationships between host, pathogens and the environment in which diseases occur. Our collaborative research focuses on the study of microbial – host interactions in the American Crassostrea virginica using experimental manipulations with probiotics and pathogens, lines of oysters with different levels of disease resistance, and integrated functional and -omics approaches targeting the oyster holobiont in a variety of environments. Our research shows that probiont - pathogen interactions are complex, involving processes like antibiosis, quorum quenching, and detoxification. While probionts lead to immune stimulation of the larval host, the bacterial pathogen Vibrio corallilyticus leads to immunosuppression. We have also identified potential members of the oyster microbiota associated with oyster performance and ecosystem function through examination of microbiome composition and function in a variety of environmental conditions. Resequencing analysis of oyster genomes indicates the evolutionary significance of pathogenic pressure and environmental conditions, leading to significant expansions in the number of genes in families involved in regulation of cell death. Transcriptome analysis of lines of oysters with varying levels of resistance to viral, bacterial, and protozoan pathogens identify serine protease inhibitors and genes in cell-death pathways (apoptosis) as potentially important in disease resistance. We are now exploring how to integrate data from both the host and the microbial transcriptomes to identify key processes and members of the holobiont that determine oyster performance. Our research serves to elucidate the complex interactions between members of the oyster holobiont and how these interactions determine health and function of this important seafood species.

Title: Microbiota-mediated protection against Flavobacterium infection in gnotobiotic zebrafish

Presenter: Postdoctoral Researchers Rebecca J. Stevick and David Pérez Pascua, Institute Pasteur, France

Abstract:

Host-associated microbiomes play a key role in protection against infection by pathogenic microorganisms. In the context of intensive aquaculture prone to disease outbreaks, the use of beneficial or probiotic bacteria has recently emerged as a desirable prophylactic alternative to the use of antibiotics. However, the selection of probiotic bacteria is still often empirical and evidence-based identification of probiotics is limited by the complexity of bacteria-host interactions. To improve the evidence-based identification of fish probiotics and their efficacy in disease prevention, the use of germ-free or fully controlled gnotobiotic hosts is a promising strategy. A robust model of infection in larval zebrafish was previously developed by the team using Flavobacterium covae, a common fresh-water fish pathogen. We have observed that F. covae kills germ-free zebrafish but not conventional (non-sterile) fish with their natural

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microbiota. Cultivable bacterial strains were isolated from conventional zebrafish and screened for protection against F. covae. Among them, three potential probiotic strains protect the fish when added individually to germ-free fish: Chryseobacterium sp., Nubsella sp., and Brevundimonas sp. Current efforts focus on how Chryseobacterium sp. protects against infection by analyzing its impact on zebrafish host immune response, colonization in the presence or absence of the pathogen, and screening for transposon mutants unable to protect zebrafish larvae. We have identified a single mutation in a glycosyltransferase codifying gene that leads to loss of protection against F. covae and reduced colonization of the zebrafish. Ongoing characterization of the WT and non-protecting mutant will allow us to decipher the mechanisms involved in microbiota-mediated protection in vivo. This study will inspire novel strategies for engineering next-generation probiotics against F. covae and other pathogens in aquaculture and beyond.

Title: What if the unit of selection in breeding is the holobiont instead of the plant?

Presenter: Assistant Researcher Dr Amaia Nogales, ISA, Universidade de Lisboa, Portugal

Abstract:

Plant breeding aims to produce genotypes with superior traits that are economically profitable to humans. Such traits include higher biomass, yield and quality, nutritional level, disease and pest resistance, abiotic stress tolerance, and easy harvesting and processing.

In conventional plant breeding an elite variety is crossed with a donor that has a desired trait. After subsequent cycles of backcrossing of the offspring to the elite variety, plant phenotyping of the resulting population is performed and a new variety, that combines the elite traits and the new desired trait, is selected. In grapevine, the high intra-varietal diversity present in ancient varieties allows to follow a different approach. The procedure involves the phenotyping of an experimental population composed of individuals that represent a wide genetic variability, and the subsequent selection of the best genotypes based on quantitative genetic methods.

For obtaining easy genetic gains in plant breeding for a particular trait, this should be mainly controlled by genetic factors, with little influence of the environment. However, this is not the case for many traits, especially for complex traits like abiotic stress tolerance or nutrient use efficiency. These are highly influenced by plant symbiotic microbial populations, which play crucial roles in plant nutrition, growth and response to the environment, and may contribute to a substantial part of the observed phenotype. Hence, including them in plant breeding procedures could improve the efficiency of the whole process – i.e. breeding at the holobiont, and not just at the plant level.

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An example on grapevine breeding on enhanced P-use efficiency will be presented, where arbuscular mycorrhizal fungal communities, which contribute to P uptake in their hosts, are considered in the statistical model developed to calculate the genetic gains obtained when selecting the suitable holobionts.

Title: Plant microbes and bacteriophages; the smallest, most abundant entities of plant microbiomes

Presenter: Prof. Lars Hestbjerg Hansen, University of Copenhagen, Denmark

Abstract:

Plant associated microbiomes arguably play a big role in plant resilience. The complexity of the interactions between the environment, the host and the microorganisms, approach astronomical proportions, and traditional microbiomics is often insufficiently detailed to decipher this complexity. Above ground, in the plant phyllosphere, there are abundant, but poorly studied, plant/microbe-microbe interactions occurring. In the presented, I will zoom in on the major biological components of the phyllosphere and rhizosphere of plants. These include at least one set of biological entities, the bacteriophages, that are often neglected as keystone regulatory components in plant associated microbiomes or in holobionts in general. I will present both experimental and bioinformatic data, supporting a key role of bacteriophages in the plant microbiome regulation.

Title: Potential drivers of plasticity and persistence of the gut microbiome

Presenter: Prof. Itzik Mizrahi, Ben-Gurion University of the Negev, Israel

Abstract:

Relationships between gut microbial ecosystems and their vertebrate hosts have been shown in recent years to play an essential role in the well-being and proper function of their hosts. In my lecture, I will discuss some of our recent findings on vertebrate gut microbiome ecosystem stability, development, and interaction with the host.

Title: Copy number variation on ABCC2-DNMBP loci impacts the diversity and functions of the gut microbiota in pigs

Presenter: Yuliaxis Ramayo Caldas, Institute of Agrifood Research and Technology, Spain

Abstract:

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Genetic variation in the pig genome can modulate the composition and function of porcine gut microbial communities. Previous studies have been focused on the association between single nucleotide polymorphisms and gut microbiota composition, but little is known about the relationship between host genome structural variants and gut microbial traits. The main goal of this study was to assess the effect of porcine copy number variants (CNVs) on the diversity and functions of the pig gut microbiota. For this purpose, we used whole-genome sequencing data from 100 healthy 60-day-old Duroc pigs to undertake a comprehensive identification of CNVs followed by a genome-wide association analysis between the estimated CNV and gut bacterial diversity. Among the identified CNVs, one gain (DUP) on ABCC2-DNMBP loci was significantly associated with the richness and the Shannon α -diversity index. Compared to their diploid counterparts, the gut microbiota of DUP pigs exhibits significantly higher α -diversity (p=7.6x10-4) and richness (p=1.4x10-4). After the identification of CNV-breakpoints, the gain of copies on ABCC2-DNMBP loci was confirmed by real-time quantitative PCR (qPCR). The variation of the CNV was positively correlated with α diversity (r=0.44, p value=7.3×10-3) and richness (r=0.54, p value=6.5×10-4). In addition, functional metagenomic predictions indicated that DUP samples had a higher relative abundance of key bacterial enzymes involved in the bile acid metabolism. Altogether, our results suggest the gain of copies on ABCC2-DNMBP loci as a putative host-genetic factor for the modulation of diversity, composition, and functions of the gut microbiota in pigs.

Title: Elucidating host genetic effects on the microbiota using zebrafish and CRISPR/Cas- a hologenomic approach

Presenter: Eiríkur Andri Thormar, University of Copenhagen, Denmark

Abstract:

Host genetic effects on the microbiota are an often overlooked aspect in the context of hostmicrobiota interactions. The field of Applied hologenomics offers a unique framework to address if, how, and to what extent host genetics contribute to the composition of the hostassociated microbiota. Understanding the effects of host genetics on the associated microbiota has great potential to be applied in future biotechnological advancements in the food production industry. One can imagine selective breeding and genetic engineering of livestock to promote a microbiota that enhances a given production trait or feed specifically tailored to be beneficial for the microbiota of a specific host genotype. With the main objective being such beneficial applications, we have, with the help of genetic engineering techniques and the extremely useful zebrafish model, devised an applied hologenomic approach to directly test the effects of host genes on the composition of the host-associated microbiota. Using the CRISPR/Cas system we have created zebrafish knockout mutants for the gene coding for tyrosinase (tyr), a rate-limiting enzyme in melanogenesis, and irf8, a gene responsible for a subset of intestinal macrophages. We then compare the microbiota of the mutant cohort to that of a wild type (WT) cohort, using multi-omic approaches such as metagenomics,

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metatranscriptomics, metabarcoding, and metabolomics. The initial results indicate a difference between the microbiota of a mutant zebrafish cohort and the WT cohort, providing evidence for the effects of a single gene on the host microbiota. With this, we also provide a proof of principle that zebrafish and CRISPR/Cas can be used in an applied hologenomic framework to address the effects of specific host genes on relevant traits associated with the microbiota.

Title: Supplemented diets with quercetin and epicatechin enhance the growth performance of Totoaba macdonaldi related to the improvement of gut microbiota metagenomic analysis and liver transcriptome: a hologenomic approach

Presenter: María Fernanda Barragán-Longoria, Monterrey Institute of Technology and Higher Education (ITESM), Mexico

Abstract:

Totoaba macdonaldi is an endemic, vulnerable, carnivorous fish of the Gulf of California. It is currently being cultivated in Mexico for commercial and conservation purposes. There are key aspects that need to be addressed for its conservation and exploration to be successful. One of the most difficult to overcome is to find a diet supplementation that reaches protein requirements at an acceptable price and does not compromise its overall performance; several have been tested but so far, none has worked on a long term because their side effects on the digestive system. The aim of this study is to apply an hologenomic approach on the Totoabas diet problem, evaluating the effects of supplemented diets with quercetin and epicatechin, at two doses with and without inulin, on gut microbiota and liver expression. Conjoining metagenomic and transcriptomic analysis to understand microbiota composition and liver metabolic processes, provides novel insights into the biological mechanisms involved in its response to different diet strategies, allowing the fish optimal growth for its commercialization, and more importantly, for its successful reintegration into its natural habitat. The flavonoid supplementation (FL and FH) outperformed the Inulin and Control diets; FL and FH diets caused positive changes in the microbiota diversity by reducing the presence of pathogenic species, such as V. anguillarum and E. faecalis, and increasing the presence of beneficial organisms for intestinal health, such as Lactobacillaceae. From the differential expression analysis, FH presented enriched pathways with genes involved in lipid metabolism, these results complement those obtained in the hematological analysis, where the same diet presented a significant decrease in plasma cholesterol and triglycerides levels. From this results, flavonoid supplementation might modulate the bacterial composition of the intestinal microbiota, and microbiota can influence the absorption of these compounds and their interaction on lipid metabolism expression.

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Session 4: Biodiversity and Conservation

Title: Global hologenomics to reveal the impact of wild animal-microbiota interactions on ecological and evolutionary processes

Presenter: Dr. Aoife Leonard, University of Copenhagen, Denmark

Abstract:

Understanding the bi-directional interactions of wild animals and their associated microorganisms represents a key advance in eco-evolutionary studies, but to date our understanding of how such interactions act in nature is limited. A global effort to jointly study the genomic and metagenomics features of a diverse array of species will facilitate a better understanding of these bi-directional animal-microbiota interactions involved in ecological and evolutionary processes in the wild

I will introduce the Earth Hologenome Initiative, which addresses biological, technical, and strategic aspects, to help overcome current limitations in wild animal-microbiota research within an ecosystem framework. By standardising sample collection and processing, and facilitating data sharing, the EHI opens a wide range of research possibilities to improve our understanding of the underlying interactions and evolutionary patterns that explain population, temporal, and geographic variation. Such a framework is key to exploring how hologenomic information can be used to improve conservation measures.

Title: Metagenomic shifts in mucus, tissue and skeleton of the coral Balanophyllia europaea living along a natural CO2 gradient

Presenter: Research Fellow Giorgia Palladino, University of Bologna, Italy

Abstract:

Using the Mediterranean coral Balanophyllia europaea naturally growing along a pH gradient close to Panarea island (Italy) as a model, we explored the role of host-associated microbiomes in coral acclimatization to ocean acidification (OA). Coral samples were collected at three sites along the gradient, mimicking seawater conditions projected for 2100 under different IPCC scenarios, and mucus, soft tissue and skeleton associated microbiomes were characterized by shotgun metagenomics. According to our findings, OA induced functional rearrangements in

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the microbiomes genetic potential that could mitigate the sub-optimal environmental conditions at three levels: i. selection of bacteria genetically equipped with functions related to stress resistance; ii. shifts in microbial carbohydrate metabolism from energy production to maintenance of cell membranes and walls integrity; iii. gain of functions able to respond to variations in nitrogen needs at the holobiont level, such as genes devoted to organic nitrogen mobilization. We hence provided some glimpses on the functional role of the coral associated microbiome in favoring host acclimatation to OA, remarking the importance of considering the crosstalk among all the components of the holobiont to unveil how and to what extent corals will maintain their functionality under forthcoming ocean conditions.

Title: The gut microbiota affects the social network of honeybees

Presenter: Prof. Philipp Engel, University of Lausanne, Switzerland

Abstract:

The gut microbiota influences animal neurophysiology and behavior but has not previously been documented to affect emergent group-level behaviors. Ww combined gut microbiota manipulation with automated behavioral tracking of honeybee sub-colonies to show that the microbiota increases the rate and specialization of social interactions. Microbiota colonization was associated with higher abundances of one third of metabolites detected in the brain, including several amino acids, and a subset of these metabolites were significant predictors of social interactions. Colonization also affected brain transcriptional processes related to amino acid metabolism and epigenetic modification in a brain region involved in sensory perception. These results demonstrate that the gut microbiota modulates the emergent colony social network of honeybees, likely via changes in chromatin accessibility and amino acid biosynthesis.

Title: Host-microbiota responses to a series of perturbations in two case-studies

Presenter: Adam Koziol, University of Copenhagen, Denmark

Abstract:

Continued anthropogenic change is exposing species' to novel environmental and dietary conditions at increasing rates than ever before. A major hurdle that is being met however, is the speed at which environmental conditions are changing which require more labile mechanisms in order to respond at faster time-scales such as the gut microbiome. Moreover, as gut microbiomes responses may be highly host-specific and as such, demonstrate varying levels of plasticity and adaptive potential to different hosts. To address how hosts of different evolutionary and ecological histories may respond to novel environmental conditions we measured the host-microbial dynamics of two species – an insectivorous-specialist – Crocidura

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russula (N = 29) and an omnivorous-generalist – Apodemus sylvaticus (N = 22) to a series of different environmental and dietary perturbations. Using shotgun-sequenced fecal samples collected at the conclusion of each disturbance event we observed that not only did A. sylvaticus harbor a greater diversity of gut microbiota than C. russula, but that there was also significantly more stability with lower species and functional turnover across each perturbation. Interestingly, we observed that host-species plasticity reached functional peaks at different time-points for both species. In the case of C. russula, temperature significantly modulated metabolic processes switching to a community structure which either increased or decreased the metabolic capacity during hot and cold treatments respectively which is consistent with its life-history traits. Inversely, A. sylvaticus was less affected by environmental changes and more sensitive to dietary perturbations, and was able to alter the gut composition to exploit novel food sources. Taken together, our data suggests that environmental perturbations will affect many different species' in different ways. Understanding how different host-associated gut microbiomes will respond under different scenarios will be important in pin-pointing which species' may be under increased threat and offer conservation managers an important resource in their available tool-kit.

Title: Hologenomic analysis of hundreds of herbarium specimens reveals the genomic basis of a plant invasion

Presenter: Dr. Vanessa Bieker, NTNU, Norway

Abstract:

Host genetic effects on the microbiota are an often-overlooked aspect in the context of hostmicrobiota interactions. The field of Applied hologenomics offers a unique framework to address if, how, and to what extent host genetics contribute to the composition of the hostassociated microbiota. Understanding the effects of host genetics on the associated microbiota has great potential to be applied in future biotechnological advancements in the food production industry. One can imagine selective breeding and genetic engineering of livestock to promote a microbiota that enhances a given production trait or feed specifically tailored to be beneficial for the microbiota of a specific host genotype. With the main objective being such beneficial applications, we have, with the help of genetic engineering techniques and the extremely useful zebrafish model, devised an applied hologenomic approach to directly test the effects of host genes on the composition of the host-associated microbiota. Using the CRISPR/Cas system we have created zebrafish knockout mutants for the gene coding for tyrosinase (tyr), a rate-limiting enzyme in melanogenesis, and irf8, a gene responsible for a subset of intestinal macrophages. We then compare the microbiota of the mutant cohort to that of a wild type (WT) cohort, using multi-omic approaches such as metagenomics, metatranscriptomics, metabarcoding, and metabolomics. The initial results indicate a difference between the microbiota of a mutant zebrafish cohort and the WT cohort, providing evidence for the effects of a single gene on the host microbiota. With this, we also provide a

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proof of principle that zebrafish and CRISPR/Cas can be used in an applied hologenomic framework to address the effects of specific host genes on relevant traits associated with the microbiota.

Session 5: Technical and Methodological Perspectives

Title: Network analysis of host-microbiome omics data

Presenter: Prof. Torgeir Hvidsten, NMBU, Norway

Abstract:

Host genetic effects on the microbiota are an often overlooked aspect in the context of hostmicrobiota interactions. The field of Applied hologenomics offers a unique framework to address if, how, and to what extent host genetics contribute to the composition of the hostassociated microbiota. Understanding the effects of host genetics on the associated microbiota has great potential to be applied in future biotechnological advancements in the food production industry. One can imagine selective breeding and genetic engineering of livestock to promote a microbiota that enhances a given production trait or feed specifically tailored to be beneficial for the microbiota of a specific host genotype. With the main objective being such beneficial applications, we have, with the help of genetic engineering techniques and the extremely useful zebrafish model, devised an applied hologenomic approach to directly test the effects of host genes on the composition of the host-associated microbiota. Using the CRISPR/Cas system we have created zebrafish knockout mutants for the gene coding for tyrosinase (tyr), a rate-limiting enzyme in melanogenesis, and irf8, a gene responsible for a subset of intestinal macrophages. We then compare the microbiota of the mutant cohort to that of a wild type (WT) cohort, using multi-omic approaches such as metagenomics, metatranscriptomics, metabarcoding, and metabolomics. The initial results indicate a difference between the microbiota of a mutant zebrafish cohort and the WT cohort, providing evidence for the effects of a single gene on the host microbiota. With this, we also provide a proof of principle that zebrafish and CRISPR/Cas can be used in an applied hologenomic framework to address the effects of specific host genes on relevant traits associated with the microbiota.

Title: Connecting structure and function from organs to molecules in host-microbe interaction

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Presenter: Dr Manuel Liebeke- Max Planck Institute for Marine Microbiology, Germany

Abstract:

Our understanding of metabolic interactions between symbiotic animals and bacteria or parasitic eukaryotes that reside within their bodies is extremely limited. This gap in knowledge originates from a methodological challenge, namely to connect histological changes in host tissues induced by beneficial and parasitic (micro)organisms to the underlying metabolites. We addressed this challenge and developed chemo-histo-tomography (CHEMHIST), a culture-independent approach to connect anatomic structure and metabolic function in millimeter-sized symbiotic animals. CHEMHIST combines chemical imaging of metabolites based on mass spectrometry imaging (MSI) and microanatomy-based micro-computed X-ray tomography (micro-CT) on the same animal.

Title: New data, same challenges: Case study of DNA-methylation associated with tenacibaculosis and microbiome composition in Atlantic Salmon (*salmo salar*)

Presenter: Søren Blikdal Hansen, University of Copenhagen, Denmark

Abstract:

Technological development has enabled the study of host-microbe interactions on a variety of "omic" levels, which allows hologenomic studies to go beyond the study of variation at the genomic level1. Epigenomic variation is an emerging "omic" level having received increasing attention in applied hologenomics due to its manipulability by environmental factors and its heritable potential2,3. However, as a young field, many epigenomic results are presented as "preliminary" and are still to pass the test of time4. Only by understanding the current state of the field and its methodologies, one can fully interpret and integrate new omic levels as epigenomics into hologenomic analyses.

Based on our work with DNA-methylation analyses of HoloFish and HoloFood samples, we will present our current approach for processing large scale whole genome bisulfite sequencing datasets into the most significant variation for hologenomic integration. Focusing on our preliminary, yet significant findings of profound epigenomic variation associated with the ulcerous skin disease tenacibaculosis and microbiome composition in Atlantic salmon, we will present current breakthroughs and hurdles in the three main aspects of epigenomic analyses: i) Exploratory analysis of genome-wide methylation patterns, where the salmon clustered according to disease phenotype and microbiome composition. ii) Identification of specific methylation differences between sample groups including validation of differentially methylated regions using an independent nanopore based method. iii) Functional annotation of the identified differentially methylated regions, where several were located within regulatory regions of genes highly relevant for the disease phenotype.

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Based thereon we discuss our future directions for the best integration of the young imperfect field of epigenomics in the nascent field of hologenomics.

Title: A Microbial Genome Atlas enables novel insights into bacteria-host interactions via functional mapping

Presenter: Arturo Vera-Ponce de León, NMBU, Norway

Abstract:

Our knowledge about the salmon (Salmo salar) gut microbiota is limited, despite the importance of salmonid aquaculture as one of the most expanding food-production sectors worldwide. This hampers the study of functional interactions between host and bacteria, and the development of dietary strategies aimed at the manipulation of the gut microbiota to improve salmon welfare. Furthermore, the lack of salmon gut-derived microbial genome data makes it difficult to interpret the functional omics dataset, as much of the data do not match the available reference bacterial genomes. Combining published and unpublished data, here we present the first version of the Salmon Microbial Genome Atlas (SMGA), originating from fish reared both in fresh water and saltwater. The SMGA consists of 96 high-quality bacterial genomes recovered by both metagenomics (n=18) and culture isolation ("culturomics"; n=78), these last were recovered as complete circular chromosomes, using Illumina and long-reads Nanopore sequencing. Bacterial genomes were taxonomically assigned into 11 different genera. Genomes in the SMGA encode genes for carbohydrate-active enzymes (CAZymes) and short-chain fatty acid production, indicating that some of these bacteria can access glycans derived from both the diet or host gut epithelium and produce beneficial metabolites. When using the SMGA as a database to map three different meta-transcriptomic datasets, we could map 12 % of the reads, demonstrating the SMGA's versatility as a tool to facilitate exploration into active bacterial populations in the salmon gut. These results showcase the SMGA as a useful resource and open new possibilities for functional studies of the salmon gut microbiota.

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Poster abstracts for the 1st Applied HoloGenomics Conference

Poster ID: 1

Title: Improving accessiblity to ancient microbiome data beyond palaeogenomics

Theme Area: Session 5 Technical & Methodological Perspectives

Paper type: Poster

Main Author: James A. Fellows Yates

Co-authors:

Affiliation: Leibniz Institute For Natural Product Research And Infection Biology & Max Planck Institute For Evolutionary Anthropology

Abstract:

Ancient metagenomics is a powerful tool for adding a deep-time dimension to biological projects. Being able to look into the past gives us the ability to trace the long-term evolutionary relationships between microbiomes and their hosts. Therefore, ancient microbiomes represent a rich untapped source of potentially extinct biodiversity. However, to date, the use of ancient metagenomic data has been largely limited to the fields of archaeology, palaeoecology, and biological anthropology.

In this talk I will present two community iniatives from the [SPAAM community](spaamcommunity.github.io) to improve the metadata reporting and findability of ancient hostassociated microbiome data (a database - AncientMetagenomeDir [https://spaamcommunity.github.io/AncientMetagenomeDir], and an aDNA MIxS checklist - MInAS [http://minas.paleogenomics.eu]). I will give an overview on the open-source bioinformatic best-practice pipeline (nf-core/eager [https://nf-co.re/eager]), and demonstrate how it improves the accessibility of reproducible ancient DNA analysis for both host and microbial data. Finally, I will present a case-study on how we are utilising these resources to explore past biodiversity in order to tackle present-day problems, including the identification of new antibiotics.

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Title: Impact of feed additives and host-related factors on bacterial metabolic activity, and immunological traits in the ileum of broilers

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Yada Duangnumsawang

Co-authors: Farshad Goodarzi Boroojeni, Wilfried Vahjen, Joan Tarradas, Enric Esteve-Garcia, Antton Alberdi, Sofia Marcos, Jürgen Zentek

Affiliation: Institut Für Tierernährung/ Freie Universität Berlin

Abstract:

One-day old male and female chicks from Ross (1,440 chicks) and Cobb (1,440 chicks) were randomly assigned to 72 pens. Broilers were offered a wheat-soybean diet without (control) or with a probiotic (Bacillus subtilis and B. amyloliquefaciens) or phytobiotic (grape extract) supplement. One chicken per pen was selected at day (d) 7, 21, 35 of age for ileal sampling. Data were subjected to ANOVA with a 3×3×2×2 (diet, age, breed and sex) factorial arrangement. Spearman's correlation (r) was analyzed between bacterial metabolites and gene expressions. Overall, at d 21, the concentration of short chain fatty acids (SCFAs) reached the peak, while lactate decreased to its lowest level (p < 0.05). Breed affected D-lactate, with a higher concentration in Ross than Cobb (p < 0.05). Expression of all genes including interleukin (IL)-1 β , 2, 4, 6, 8, 10, 12, 17, 18 as well as TNF- α , IFN- γ , TGF- β 2, MUC2 and CLDN5 increased from d 7 to 21 but decreased from d 21 to 35 (p < 0.05). Broilers fed phytobiotic and control diets had higher IL-1 β expression than those fed probiotic diet (p < 0.05). Cobb showed higher expression of IL-4, IL-6 and TNF- α , while Ross showed greater IFN- γ expression (p < 0.05). The influence of sex and interactions between factors on measured variables was obscured (p > 0.05). SCFAs showed negative correlations with pro-inflammatory cytokines at d 7 (r = -0.41 to -0.24) but displayed positive correlations with them at d 21 (r = 0.25 to 0.59). The correlations almost disappeared at d 35. Lactate showed negative correlations with pro-inflammatory cytokines at only d 7 and 35 (r = -0.27 to -0.23). Alterations in the evaluated bacterial metabolites by age may affect gut immune response in the ileum of broilers.

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Title: Impact of feed additives and host-related factors on bacterial metabolic activity, and immunological traits in the caecum of broilers

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Yada Duangnumsawang

Co-authors: Farshad Goodarzi Boroojeni, Wilfried Vahjen, Joan Tarradas, Enric Esteve-Garcia, Antton Alberdi, Sofia Marcos, Jürgen Zentek

Affiliation: Institut Für Tierernährung/ Freie Universität Berlin

Abstract:

A total of 2,880 one-day-old male and female broiler chicks from Ross and Cobb were randomly allocated to 72 pens. Broilers were fed a wheat-soybean diet without (control) or with a probiotic (Bacillus subtilis and B. amyloliquefaciens) or phytobiotic (grape extract) supplement. One chicken per pen was selected at day (d) 7, 21, 35 of age for caecal sampling. Data were subjected to ANOVA with a 3×3×2×2 (diet, age, breed and sex) factorial arrangement. Spearman's correlation (r) was analyzed between bacterial metabolites and gene expressions. Overall, short-chain fatty acids (SCFAs) concentration increased with age (p < 0.05). L- and D-lactate decreased from d 7 to 21 (p < 0.05) and stayed constant until d 35. Expression of interleukin (IL)-2, 4, 6, 8, 10, 12, 17, 18 as well as IFN- γ and TGF- β 2 increased with age, but IL-1 β and TNF- α increased from d 7 to 21, then declined (p < 0.05). Expression of MUC2 decreased from d 7 to 21, and then increased afterward, while expression of CLDN5 increased from d 21 to 35 (p < 0.05). Cobb showed higher D-lactate concentration and IL-1 β , IL-6, TNF- α and CLDN5 expressions than Ross (p < 0.05). Probiotic diet showed higher IL-10 expression compared to the control (p < 0.05). At d 7 and 21, SCFAs and lactate were negatively correlated with pro-inflammatory cytokines e.g., IL-18 (r = -0.51 to -0.24) and TNF- α (r = -0.37 to -0.24), but these correlations almost disappeared at d 35. Age influenced all variables measured. A few effects of diet and breed on the variables measured showed no systematic biological pattern, while the influence of sex and interactions between factors was obscured. Age-related alterations in bacterial metabolites may affect immunological response in the caecum of broilers.

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Title: Evaluation of computational methods for human microbiome analysis using simulated data

Theme Area: Session 5 Technical & Methodological Perspectives

Paper type: Poster

Main Author: Matthieu J. Miossec

Co-authors: Sandro L. Valenzuela1, Marcos Pérez-Losada, W. Evan Johnson, Keith A. Crandall and Eduardo Castro-Nallar

Affiliation: George Washington University

Abstract:

We compared eight popular taxonomic profiling pipelines (MetaPhlAn2, metaMix, PathoScope 2.0, Sigma, Kraken, ConStrains, Centrifuge and Taxator-tk) against metagenomic datasets modeled after 426 genomes from the Human Oral Microbiome Database. Datasets were designed to simulate multiple experimental conditions by varying read length, sequencing depth, taxa composition and abundance, and presence of unclassified genomes. We measured the sensitivity, specificity and computational time of each pipeline, and also their relative root mean square error and average relative error at estimating microbial abundances. Our simulations generated 144 metagenomic datasets and produced 1,104 discrete results. Pipelines using a marker gene strategy (e.g., MetaPhIAn2 and ConStrains) were overall less sensitive than other pipelines, with the notable exception of Taxator-tk. This difference in sensitivity was largely compensated with significantly faster runtimes than more sensitive pipelines, like PathoScope2.0, that rely on whole-genome alignments. However, pipelines that used strategies to speed-up alignment between genomic references and metagenomic reads (e.g., Kraken and Centrifuge), such as kmerization, were able to combine both high sensitivity and low run time. Absent species genomes in the database mostly led to assignment of reads to the most closely related species available in all pipelines. Our results, therefore, suggest that taxonomic profilers that use kmerization have largely superseded those that use gene markers, coupling low run times with high sensitivity and specificity. Taxonomic profilers using more time-consuming read reassignment, such as PathoScope 2.0, provided the most sensitive profiles under common metagenomic sequencing scenarios. We have created an R Shiny application available at https://github.com/microgenomics/HumanMicrobiomeAnalysis to visualize all results described and discussed in this study. All of our datasets, pipelines and results are also available at the same GitHub repository for future benchmarking.

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Title: Comparative analysis of metagenomics and metataxonomics for the characterization of vermicompost microbiomes

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Keith A. Crandall

Co-authors: Marcos Pérez-Losada, Ignacio Ramos-Tapia, Eduardo Castro-Nallar, Jorge Domínguez

Affiliation: George Washington University

Abstract:

The study of microbial communities or microbiotas in animals and environments is important because of their impact in a broad range of industrial applications, disease, and ecological roles. High throughput sequencing (HTS) is the best strategy to characterize microbial composition and function. Microbial profiles can be obtained either by shotgun sequencing of genomes (metagenomics), or through amplicon sequencing of target genes (e.g., 16S rRNA for bacteria and ITS for fungi) (metataxonomics). Here, we compared both HTS approaches at assessing taxonomic and functional diversity of bacterial and fungal communities during vermicomposting of white grape marc (Vitis vinifera L. cv. Albariño) from wineries in the northwest part of Spain (Galicia). We applied specific HTS workflows to the same twelve microcosms, with and without earthworms, sampled at two distinct phases of the vermicomposting process occurring at 21 and 63 days. Microbial composition and abundance estimated by both HTS approaches agreed reasonably well at the phylum level, but larger discrepancies were observed at lower taxonomic ranks. Shotgun HTS identified ~1.8 times more bacterial genera than 16S rRNA HTS, while ITS HTS identified two times more fungal genera than shotgun HTS. This is mainly a consequence of the difference in resolution and reference richness between amplicon and genome sequencing approaches and databases, respectively. Our study also revealed great differences and even opposite trends in alpha- and beta-diversity between amplicon and shotgun HTS. Interestingly, amplicon PICRUSt2-imputed functional repertoires overlapped ~50% with shotgun Humann2 profiles. Finally, both

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approaches indicated that although bacteria and fungi are the main drivers of biochemical decomposition, earthworms also play a key role in plant vermicomposting.

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Title: A data-driven selection scheme of nutritionally beneficial bacteria for marine aquaculture fish

Theme Area: Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Konstantinos Kormas

Co-authors: Alexandra Meziti

Affiliation: University of Thessaly, Greece

Abstract:

The field of marine aquaculture microbiomes is moving from the observational (which microorganisms are there and what they do) to the interventional phase (manipulate the microbiome towards the host's benefit). To date, most probiotics used in aquaculture have not originated from the specific farmed species, rendering their appropriateness, occasionally, dubious. For this, we propose a user-friendly selection scheme of fish-beneficial bacteria that can be customised according to specific needs. We demonstrate here a relevant case study focusing on gilt head sea bream (Sparus aurata), aiming at investigating the suitability of its gut Bacteria for specific metabolic traits beneficial to their host. S. aurata does not have the complete biosynthetic pathways for the amino acids lysine, arginine, methionine, K1 and K2 vitamins and the vitamins of the B complex. Thus, the supplied aquafeeds are supplemented with these ingredients, which increase production cost. As an alternative, probiotics with such biosynthetic capacities are considered for possible fish microbiome manipulations. At first, we collected from the literature the most well-known S. aurata beneficial microbes (37 bacterial species). Following, we investigated whether these Bacteria bear the complete biosynthetic pathways for the amino acids lysine, arginine, methionine and the vitamins of the B complex and also whether their growth optimal and tolerance range of temperature, pH and salinity are within the range of the respective values for S. aurata farming. Twenty Bacteria were found to be capable of synthesing the three amino acids investigated and one of them was able to synthesize all B vitamins and K2 vitamin. Of these bacteria, only a few have ecological requirements that would allow them to proliferate in the S. aurata gut habitat. Our approach provides a targeted, informative and easy to use approach for selecting potentially hostbeneficial microbes by exploiting the ample and available genomic knowledge of these microorganisms.

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Title: microbetag: a microbial co-occurrence network annotator

Theme Area: Session 5 Technical & Methodological Perspectives

Paper type: Poster

Main Author: Haris Zafeiropoulos

Co-authors: Karoline Faust

Affiliation: Rega Institute, KU Leuven

Abstract:

Microbial interactions play a fundamental role in deciphering the underlying mechanisms that govern

complex host-associated microbial communities. High throughput sequencing enables the taxonomic and functional characterization of such communities. Yet, new approaches are required to analyse sequencing data but also to exploit such information at a meta-study level and integrate it with further channels of knowledge.

Co-occurrence networks have been widely used for inferring microbial associations and/or interactions from metagenomic data. However, spurious associations and tool - dependence are limitations of network inference. The integration of previous evidence or/and knowledge can increase or decrease the confidence level of the retrieved associations. This way, associations can be further investigated and more reliable conclusions can be drawn.

Here we present microbetag, a command line tool that implements data integration techniques to enhance microbial co-occurrence network analysis for amplicon or/and shotgun metagenomics data. More specifically, microbetag retrieves the KEGG modules that have been assigned to each of the species found related. Based on the pathway complementarity concept, pathways found in both taxa of an association are further explored to check whether the processes of each of the two taxa are complementary denoting a positive interaction. Likewise, if the same processes are found to occur in both taxa, a negative interaction will be derived. On top of that, microbetag integrates phenotypic information; a series of environmental variables (pH optima, oxygen tolerance etc.) are assembled in each node of the network. Their comparison in each pair of correlated taxa evaluates their corresponding association further.

In the near future, microbetag will exploit the potentials of constraint-based modelling by

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integrating publicly available genome-scale models. Flux sampling, in the space of paired associations, would highlight potential dependencies of the studied interactions on the environmental composition.

GitHub repository: https://github.com/hariszaf/microbetag

Poster ID: 12

Title: Recovering ancient fermented beverages from trans-Himalayan trade routes along the Tibetan plateau

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Maxime Borry

Co-authors: Mark Aldenderfer, Christina Warinner

Affiliation: Max Planck Institute For Evolutionary Anthropology

Abstract:

Located along a trans-Himalayan trade route more than 4000 m above sea level, the ancient Nepalese site of Samdzong contains some of the best-preserved evidence of fermented beverages in the archaeological record. With traces of occupation dating back to the 5th century AD, this site opens up a window into the past on the technological and cultural practices of alcohol production by plateau peoples prior to the foundation of the Tibetan empire in the 7th century. While this site has been investigated by various bioarchaeological methods since its discovery, the elucidation of the purpose and content of its artefacts remained challenging until now. By leveraging the power of ancient DNA shotgun metagenomics sequencing, we reconstruct the plant and microbial composition of the funerary offerings, and identify the contents of a large copper cauldron as chaang, a fermented barley beer. Using de novo assembly, phylogenomics methods, and functional analysis, we explore the composition and function of this early alcohol ferment and outline a method for better understanding the origins of culinary microbes and their long relationship with human foods and beverages.

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Title: Can shallow shotgun-based profiling of the gut microbiome improve the detection of host genetic effects?

Theme Area: Session 5 Technical & Methodological Perspectives

Paper type: Poster

Main Author: Felipe Morillo Sanz Dias

Co-authors: Amelie Baud

Affiliation: Centre for Genomic Regulation

Abstract:

One of the main questions in hologenomics is to what extend microbiomes affect host phenotypes. Even though strong associations have already been described, demonstrating causality is still difficult due to the presence of many confounders. In order to solve this problem, genetic epidemiology has recently become a promising approach as it uses host genetic variants as anchors to limit reverse causation and confounders in causal inference analyses. However, to this date few variants have been robustly associated with microbiome profiles. We hypothesize this happens for two reasons: firstly, because most studies have focused on taxonomy rather than function, even though we know that microbial functions can be redundant among taxa; secondly, because most studies have relied on 16S data to characterise the microbiome, lacking species and strain level resolution. Although deep shotgun sequencing can provide a direct map of taxa and functional genes, its cost is prohibitive for large samples. Hence, we evaluated shallow shotgun sequencing as an alternative to define taxonomic and functional profiles of ceacal microbiomes from 1,041 outbred genotyped laboratory rats, as its costs are comparable to 16S and it is almost as informative as deep shotgun due to the possibility to use microbial gene catalogues as references. We first compared two different catalogues, one including sequences from a great diversity of habitats (proGenomes) and one built solely from rat stool metagenomes. Then, we quantified aggregate host genetic effects (i.e., heritability), using the mapped microbiome taxa and functional genes (i.e., orthologs) as traits and compared the results to the ones obtained with 16S-based taxonomic profiles. This shed light on the potential of shallow shotgun and functional profiling as new methodological perspectives for detecting host genetic effects and the subsequent dissection of causal relationships between gut microbiomes and host phenotypes.

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Title: Origin and acquisition of rhizosphere microbes in antarctic vascular plants

Theme Area: Session 4 Biodiversity & Conservationand Food Production

Paper type: Poster

Main Author: Eduardo Castro-Nallar

Co-authors: Sergio Guajardo-Leiva; Jaime Alarcón; Jorge Gallardo-Cerda; Marco Molina-Montenegro; Keith A. Crandall; Marcos Pérez-Losada

Affiliation: Universidad de Talca

Abstract:

Rhizosphere microbial communities exert critical roles in plant health, nutrient cycling, and soil fertility. Despite this, the origin and acquisition of the rhizosphere are not entirely clear. We investigated the diversity and potential origin of microbial communities using the only two native Antarctic plants Deschampsia antarctica (Da) and Colobanthus quitensis (Cq). Regarding bacterial communities, the Da rhizosphere showed the lowest richness and diversity compared to Cq and Da.Cq. In contrast, for rhizosphere fungal communities, plant species only influenced diversity, whereas the rhizosphere of Da exhibited higher fungal diversity than the Cq rhizosphere. Also, we found that species turnover between microbial communities was determined by environmental-geographic pressures and, to a lesser extent, biotic factors. Moreover, our analysis shows that the origins of the bacterial communities in the rhizosphere were local soils that contribute to homogenizing the community composition of the different plant species growing in the same sampling site. In contrast, the origins of rhizosphere fungi were local (for Da and Da.Cq) and distant soils (for Cq).

Our study shows that rhizosphere microbial communities differ in their composition and diversity and that these differences are explained mainly by the microbial composition of the soils that harbor them, acting together with plant species-specific effects. Both plant species acquire bacteria from local soils to form part of their rhizosphere. Seemingly, the acquisition process is more complex for fungi, where we identified an important contribution from unknown fungal sources because of stochastic processes and known sources from soils across the Byers Peninsula.

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Title: Microbiome composition and distribution of major endosymbionts in Scaphoideus titanus Ball,1932 across northern Italy.

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Juan Sebastian Enciso

Co-authors: Abdelhameed Moussa, Erika Corretto, Lilyia Serbina & Hannes Schuler

Affiliation: Free University of Bolzano Bozen

Abstract:

The Nearctic leafhopper Scaphoideus titanus Ball, 1932 is the main vector of Flavescence dorée phytoplasma in Europe. The disease is inflicting damage to grapevine across the biggest viticultural areas of Europe including high producing territories in northern Italy. Despite quarantine control and obligatory management, outbreaks of Flavescence dorée are still ongoing in winegrowing communities. Whereas few studies focused on the importance of the microbiome in the modulatory transmission of phytoplasma in leafhopper vectors. On the other hand, it is poorly understood if the host biology and the monophagous habits of sapfeeding hemipterans produce boundaries in the diversity of the microbiome community. Meanwhile, the importance of an unbalanced diet relies in strong host-associated trade-offs. Allowing the feeding specialization and shaping the distribution of highly specialized sapsucking bugs. Therefore, the role of endosymbiotic associations remains crucial for the sustainability of the host. Providing amino acids and vitamins supplements that are lacking in sap-feeding and off-setting physiological pathways. Currently, information about the changes in microbiome composition through different scales of time and space are missing. Consequently, the aim of this work is to characterize the microbiome composition and the relative abundance of the metagenomic microbiota in Scaphoideus titanus across spacetemporal locations in northern Italy. For the present study we conduct a massive sequencing of 16S rRNA from individuals collected in diverse regions from August 2020 to July 2021, using a metabarcoding approach. Our preliminary results suggest a complex diversity and a high prevalence of common microorganisms with subtle differences in distribution across space.

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Title: Paleofeces reveal recent loss of diversity and microbial symbionts in the Western gut microbiome

Theme Area: Session 2 Human Health

Paper type: Poster

Main Author: Alexander Hübner

Co-authors: Courtney Hofman, Irina Velsko, Zandra Fagernäs, Allison E. Mann, Nicole Boenke, Abigail Bouwman, Choongwon Jeong, Tanvi Honap, Richard Hagan, Marsha Wibowo, Aleksandar Kostic, Karl Reinhard, Abolfazl Aali, Cecil M. Lewis, Jr., Thomas Stöllner, Frank Rühli, Krithivasan Sankaranarayanan, Christina Warinner

Affiliation: Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

Abstract:

The human gut microbiome plays a key role in human health by contributing to a wide range of essential biological and physiological functions. A decrease in gut microbiome diversity, mainly driven by diet and lifestyle changes has been associated with both metabolic disorders and chronic inflammatory diseases. Western industrialized diets, in particular, are associated with greatly reduced gut microbiome diversity compared to more traditional forms of subsistence, including foraging, pastoralism, and horticulture. To better understand the systematic decline of gut microbiome diversity in present-day industrialized societies, we studied 39 paleofeces samples from archaeological sites located in present-day Austria (Dürrnberg salt mine, Celtic Iron Age: 500 BCE), Iran (Chehrabad salt mine, Achaemenid Empire: 500 BCE), and Mexico (La Cueva de los Muertos Chiquitos, Loma San Gabriel Culture: 700 CE) along with 19 published paleofeces samples. After confirming the exceptional preservation of the majority of these samples, we found that the gut microbial communities of all three populations more closely resemble those found in traditional, non-industrialized societies today than in Western industrialized populations. This includes the Celtic Iron Age population, who consumed an agricultural diet rich in barley, wheat, beef, and pork. Furthermore, we identified several socalled "missing microbes" (e.g., Treponema spp.) in all three archaeological populations, indicating that although these taxa are today absent in industrialized populations, they were still present, including in European populations, as recently as 2,500 years ago. We conclude that the great reduction in microbial diversity observed in the modern Western industrialized gut microbiome appears to have occurred very recently - within the past 2,500 years - and may help explain the apparent greater susceptibility of industrialized populations to metabolic disorders and chronic inflammatory diseases.

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Title: Specific microbial fingerprints are associated with low levels of LT toxin-carrying enterotoxigenic Escherichia coli in the gut

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Alessandra Tancredi

Co-authors: Evy Goossens, Eric Cox, Filip Van Immerseel

Affiliation: UGENT

Abstract:

Post-weaning diarrhoea is an economically important gastro-intestinal disease affecting piglets, causing growth retardation, diarrhoea, mortality and therefore, represents one of the main problems for the piglet industry. Post-weaning diarrhoea is a multifactorial disease in which enterotoxigenic Escherichia coli (ETEC) strains play a major role. Their pathogenicity is due to the production of enterotoxins and adhesins. However, other factors can contribute to onset of the disease, including host genetics, host immunity, stress factors and/or impaired gut microbiota. Gut microbiota indeed plays important role in porcine health as it affects metabolism, immunity and defense against pathogens. The microbiota composition can influence the host, but host genetics can also shape the microbial community function and structure. Using 16S rDNA sequencing, we characterized the rectal microbiome and the jejunal, ileal and colonic microbiome of 64 piglets across 8 different farms differentially affected by post-weaning diarrhoea, starting from 7 days of birth up to 4 days post-weaning. The microbiota composition was analyzed in relation to ETEC shedding pattern and colonization levels in different intestinal segments. We categorized piglets based on their ETEC levels quantified by qPCR. In particular we focused on the presence of the LT toxin and by using a supervised clustering approach we identified microbiota members associated with low levels of LT colonization post-weaning, in different timepoints pre and post-weaning and different intestinal segments. We also tested the genetic susceptibility of the piglets for ETEC colonization and we observed how it can shape the gut microbial community structure. Our findings contribute into understanding the role of gut microbiota composition and its interaction with the host in the development and resistance against post-weaning diarrhoea. These data can be used for rational development of preventive measures that promote a microbiota composition to reduce ETEC levels in the gut.

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Title: Engineering microbiomes to improve insect production and performance

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Muurmann, A.

Co-authors: Gilbert, T., Rasmussen J., Limborg, M., Tomberlin, J., Bahrndorff, S.

Affiliation: Aalborg University

Abstract:

The need for producing nutritious food and at the same time better utilize different sidestreams is increasing as the global population rise. Insects, especially black soldier fly larvae, have proven effective at converting multiple types of biological waste and by-products into high-quality proteins and fat. As a relatively new player in food production, insect production has great potential to be improved to meet the increasing demands of a growing population. One way to do this, is through better understanding and utilisation of the host-microbiome interactions. Symbiotic microbiomes are known to play a beneficial role for insects, including dietary supplementation, the host immune system, and social interactions. In my PhD project I will study insect-microbiome interactions and utilise this knowledge to manipulate insect microbiomes to improve insect productivity and performance in two insect species, Musca domestica and Hermetia illucens. The insect-microbiome interaction will be investigated with a holo-omics approach analysing both the host genomics and gut transcriptomics as well as the microbiome metagenomics and metatranscriptomics. Using holo-omics should give knowledge about microbes important for substrate conversion and other desired growth characteristics, as well as the host-microbiome interactions in general. With this information, desired microbial strains may be identified and ultimately can be used as probiotics to improve growth performance in industrial insect rearing facilities.

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Title: The Parasite microbiome: a novel resource for therapeutic and diagnostic development

Theme Area: Session 2 Human Health

Paper type: Poster

Main Author: DHEILLY Nolwenn

Co-authors:

Affiliation: Anses UMR Virology

Abstract:

Parasites are ubiquitous. They cause significant burdens to public health and pose a risk to global food security due to their impact on domestic and wildlife animals. The Parasite Microbiome Project was launched in 2019 to apply a hologenomics approach towards the development of innovative solution in the fight against parasites. I will review studies by my group and others showing that cestodes, trematodes and nematode parasites host both bacteria and viruses. Experimental studies showed that the parasite microbiome shapes the parasite phenotype. There is also clear evidence that microbes are often vertically transmitted, but transmission to the host can also occur, modulating the host immune response to infection, and pathogenesis. Our rapidly growing understanding of the composition and functions of bacterial and viral communities inhabiting parasites is exposing opportunities that are being exploited for the development of novel therapeutic and diagnostic strategies.

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Title: Role of the microbiota in alimentary tick-borne encephalitis virus infection

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: DHEILLY Nolwenn

Co-authors: Phillipine Toneatti, Rayane Amaral-Moraes, Maxime Fusade-Boyer, Marine Dumarest, Camille Migné, Sandra Martin-Latil, Gaëlle Gonzalez,

Affiliation: Anses UMR Virology

Abstract:

The expansion of Tick-borne encephalitis virus (TBEV) through Europe increases the risk of infection. Individuals can be exposed to TBEV through tick bites, or through the consumption of fresh dairy products. While this mode of transmission is well documented and seems to be more frequent with goat milk, the factors that lead to TBE foodborne cases are still very poorly understood. Of significance, when infection occurs through the alimentary route, neurological symptoms are more frequent, and the presymptomatic phase is significantly shortened. Our objective is to characterize the factors that influence the clinical outcome of an infected individual following an alimentary infection by TBEV. First we investigated the hypothesis that TBEV physically interacts with microbes in milk or in the host gut and identified bacterial components and bacterial species that modulate the virus infectivity. Now, we are investigating the damages that TBEV inflict to the gastro-intestinal tract and potential for virus translocation causing immune defects that modulate the virus pathogenicity. This body of work opens up new prospects for the prevention and treatment of alimentary borne TBEV inflection.

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Title: Large intestine Caco2-cell adhesion of probiotic microbiota when exposed to spice/herb extracts and Thai curry under in-vitro digestion model

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Jutamat Klinsoda

Co-authors: Kanokwan Yodin, Khemmapas Treesuwan

Affiliation: Institute of Food Research and Product Development, Kasetsart University, Bangkok 10900, Thailand

Abstract:

Hologenomics have become high importance approach that will improve the efficiency of food production systems how gut microbiota and biological data play a role in food consumption. Little information reveals on spice/herb extracts in Thai curry after digestion on host-probiotic microbiota interactions with impact on the quality and property of prebiotic and probiotic products. Present study evaluated the selected probiotics presenting in human and commercial products on large intestine Caco2-cell adhesion when the probiotics exposed to spice/herb extracts and Thai curry using an in-vitrodigestion model. The results showed that most of fifteen spice/herbs (i.e., chili, garlic, galangal, turmeric, shallot, lemon grass, basil, red cotton tree flowers, clove, coriander root, cumin, kaffir lime leaf, curry powder, cinnamon, and finger roo) and eight Thai curry (i.e., Hang-lay curry, Nam Ngeaw curry, Gaeng Aom curry, Red Curry, Green curry, Massaman curry, Yellow curry, and Som curry) had both negative and positive effects on adherence to Caco-2 cells among all selected probiotics (i.e., Lactobacillus acidophilus, Lactobacillus casei, and Bifidobacterium bifidum). L. acidophilus loss the Caco-2 cell adhesion property after exposed in many spice/herb extracts and Thai curry. Interestingly, L. casei and B. bifidum increased adherence to Caco-2 cells. Present study shows a potential knowledge for the diet-host interaction on the consumption of probiotic microbiota and spice/herb extracts and Thai curry after digestion. These enhanced Caco-2 cell attachments of probiotic microbiota may lead to positive effects on human's gut health and immunity.

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Title: Temporal development of the intestinal microbiota and tissue gene expression in broiler chickens

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Sofia Marcos

Co-authors: Ostaizka Aizpurua, Eray Shain, Raphael Eisenhofer, Jorge Langa, Iñaki Odriozola, Antton Alberdi

Affiliation: University of The Basque Country - EHU

Abstract:

Poultry has the best feed-to-food conversion rate and the smallest environmental footprint per kg of meat produced. However, production efficiency is often challenged by bacterial infections that spread throughout the flock, and by high interindividual performance variability, even between siblings. We argue that understanding the so far untraced interactions of rapidly developing chickens and their gut microbial communities is the most optimal strategy to overcome such challenges, for guiding the development of new strategies to improve sustainability of animal production, and animal welfare.

In the multi-partner H2020 project HoloFood we ran three identical experiments with a randomised pen design in which broilers from two genetic lines were grown under three dietary treatments with different feed additives. Chickens were euthanized and sampled at three stages (days 7, 21 and 35). Genome-resolved metagenomic, microbial gene expression and epithelial gene expression data were generated from each individual, along with multiple complementary performance indicators.

The dietary treatments did not exert any significant variation in the development of microbial communities and host gene expression, yet we observed significant functional differences throughout the development of the animals. Although the microbial diversity increased through time, the capacity of the microbial community to degrade complex carbohydrates and produce short chain fatty acids dropped. In parallel, chicken epithelial tissues exhibited an increased expression of genes involved in IgA production and cytokine-cytokine interactions. These observations were associated with animal performance and welfare features to identify candidate mechanisms that could have contributed to shaping them.

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Title: Feed-microbiome-host interactions in Atlantic salmon over life stages

Theme Area: Session 4 Biodiversity & Conservationand Food Production

Paper type: Poster

Main Author: Shashank Gupta

Co-authors: Sabina LeantiLa Rosa, Arturo Vera-Ponce de León, Miyako Kodama, Morten Tømsberg Limborg, Simen R. Sandve, Torgeir R. Hvidsten, Phillip B. Pope

Affiliation: NMBU, Norway

Abstract:

To meet future food demands, more efficient and sustainable animal production systems are needed. Given the crucial importance of the gut microbiota to animal (host) health and nutrition, selective enhancement of beneficial microbes via prebiotics may be a powerful approach for promoting farmed fish welfare and robustness. In this study, we employed three versions of a beta-mannan prebiotic that were fed to Atlantic salmon and explored the combined responses of both gut microbiota and the host from freshwater to seawater life stages. We have used weighted gene co-expression network analysis (WGCNA) of host RNAseq and microbial 16S rRNA amplicon sequencing data to identify biological interactions between the gut ecosystem and the host. We observed several microbial and host modules through WGCNA that were significantly correlated with life stage, but not with diet. Microbial diversity was highest in early life of Atlantic salmon and decreased over time. In particular, Lactobacillus and Paraburkholderia were the dominating genera, and showed the highest correlation with host modules. Our findings demonstrate that salmon-microbiota interactions are mainly influenced by life stage, while further research is required to determine whether supplementation of selected prebiotics to diet can be used to modulate the salmon gut microbiota for improving host health and production sustainability.

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Title: Recovering High-Quality Host Genomes from Gut Metagenomic Data through Genotype Imputation

Theme Area: Session 5 Technical & Methodological Perspectives

Paper type: Poster

Main Author: Melanie Parejo

Co-authors: Sofia Marcos, Andone Estonba, Antton Alberdi

Affiliation: University of The Basque Country - EHU

Abstract:

Metagenomic datasets of host-associated microbial communities often contain host DNA that is usually discarded because the amount of data is too low for accurate host genetic analyses. However, genotype imputation can be employed to reconstruct host genotypes if a reference panel is available. We implemented a two-step strategy to impute genome-wide SNP variants in low-depth host genomic data (\approx 2× coverage) recovered from intestinal samples of two chicken genetic lines. We thereby tested four types of reference panels according to the resources scientists studying microbial metagenomics may have, and evaluated how the panel composition affected imputation performance. First, we estimated imputation accuracy in 12 samples for which both low- and high-depth sequencing data were available, obtaining high overall concordance (>0.90) and precision of heterozygous sites (>0.78) for all tested panels. However, the best imputation performance was achieved when using the combined panel. Second, the impact of the choice of the reference panel on downstream population genetic analyses was assessed by imputing 100 chickens with all four panels yielding comparable results. Our results showcase that the employed approach enables leveraging insofar discarded host DNA to get insights into the genetic structure of host populations. However, the feasibility and application of the presented strategy depends on the proportion of host DNA in metagenomic samples, the genomic diversity of the hosts, and the availability of a reference

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panel. Our pipeline, available on github

(<u>https://github.com/SofiMarcos/recovering host genomes</u>), can therefore aid scientists to conduct hologenomic research through jointly analysing host and microbial genomic data from metagenomic mixtures.

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Title: Experimental warming and cooling shapes host microbiota composition

Theme Area: Session 4 Biodiversity & Conservationand Food Production

Paper type: Poster

Main Author: Jingdi Li

Co-authors: Kieran Bates, Kim Hoang, Tobias Hector, Sarah Knowles, Kayla King

Affiliation: University of Oxford

Abstract:

Global climate change has led to an increase in extreme thermal events. Plants and animals host diverse microbial communities which may be vital for their physiological performance and help them survive and adapt to these stressful environmental conditions. How microbiome communities change in response to warming or cooling may be an important factor predicting host performance under global change. Using a meta-analysis of 462 effect sizes from 43 terrestrial and aquatic host species, we found a decrease in ASV-level microbiome phylogenetic diversity and alteration of microbiome compositions under both experimental warming and cooling. But the microbiome dispersion did not change significantly across the hosts under thermal manipulation. We showed that environmental and experimental factors affect microbiome diversity and composition more than host thermal type. Host microbiome diversity loss increased with longer periods of static warming/cooling, but was attenuated by long-term prior-experimental lab acclimation, and when a ramping warming regime was used. Temperature-associated loss of microbiome diversity was greater among hosts from regions of lower temperature variability. Aquatic hosts have greater decrease in microbiome diversity under cold conditions, compared with terrestrial hosts, which may hinder their ability to persist in colder habitats under global climate change. Further differential analysis on bacterial and functional compositions revealed several potential indicator bacterial taxa for hosts under warming treatment. Overall, our findings suggest that global temperature changes are likely to result in general shifts in animal and plant microbiome structures across a diversity of habitats. The next step will be to link these changes to host measures of performance as well as community functions to determine if microbiomes can buffer some species against a more thermally-variable world.

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Title: Kojī-based fermented foods as a model system for understanding fungal-bacteria interactions and their potential effects on host-associated metabolism

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Tiffany Mak

Co-authors: Nabila Rodriguez, Leonie Jahn, Juan Carlos Arboleya, Pia Sorensen, Morten Sommer

Affiliation: Novo Nordisk Foundation Center for Biosustainability (Dtu Biosustain)

Abstract:

Our food system is an interconnected ecological network of fauna, flora and funga, and their connections are shaped by both the physical interactions and metabolic dependencies mediated by their associated microbial communities. The diversity and interactions of these communities can have profound effects on host metabolism as well as functional phenotypes.

Fermented foods in the recent years have received notable attention for their potential dietary effects on increasing gut microbiome diversity and reducing diseases-associated inflammatory immune response, especially in mammalian hosts. The sensorial and perceptive qualities of fermented foods are great illustrations of how microbial composition and metabolism result in differential substrate utilisation and enzymatic production, and provide a good model system for studying multispecies microbial interactions.

In this study, we have selected kojī-based fermentation, which is a process that involves inoculating sterilised substrates with Aspergillus oryzae (A. oryzae) spores, as our model system of study. This approach provides a genetically tractable system to investigate the dynamics of microbial community formation and evolution. In particular, we are interested in the potential effects genomic variations in the A. oryzae genome can have on the overall microbial composition of the community, as well as the functional relationships between fungi and bacteria under different environmental constraints.

By coupling metagenomic analyses with phenotypic characterisations of microbial community metabolism, the goal is to gain a better understanding of the molecular mechanisms driving fungal-bacterial interactions. Findings from the study can provide insights into the microbial interaction dynamics especially for hologenomes with higher fungal representation, including plants-soil mycorrhizal networks and lichen symbiosis. Furthermore, the metagenome of fermented foods is dependent both on the hologenome of the starting substrate and can

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influence the hologenome of the subsequent hosts when consumed. In other words, fermented foods can act as microbial connectors between various ecological niches and holobionts.

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Title: Exploring the pet gut microbiome within a large-scale investigation of animal gut metagenomes

Theme Area: Session 4 Biodiversity & Conservationand Food Production

Paper type: Poster

Main Author: Anna Cuscó

Co-authors: Anthony Noel Fullam; Pamela Ferretti; Oleksandr Maistrenko; Sebastian Schmidt; Peer Bork; Luis Pedro Coelho

Affiliation: Fudan University

Abstract:

Pets share the environment and have constant interactions with their human owners and other household members, thus sharing some of their microbes. From a One Health perspective, pet-associated microbiome should be monitored since it represents a potential source of beneficial microbes and emerging pathogens.

The first step is to characterize the pet microbiome within a global context aiming to identify bacterial taxa associated with specific animal hosts and also 'universal' gut bacteria. We computed mOTUs on the animal gut metagenome subset of the Global Microbial Gene Catalog (n=5,519) to explore the taxonomic composition, with a focus on dogs and cats as representative of pets (n=312).

Some of the highly prevalent taxa on animals' guts included Bacteroides and Clostridium species. Faecalibacterium, Prevotella, and Blautia are highly prevalent but mostly absent in rodents, birds, and some primates. Insects and marine animals presented very different taxonomic profiles.

Prevotella copri is the most prevalent species in dogs' and cats' guts, and one of the most abundant accounting for a total median relative abundance of 16.6% in dogs and 10.1% in cats. P. copri is also highly prevalent in pigs, primates, and humans. Within Canidae gut samples (dogs and wild canids), a specific mOTU from Fusobacterium is highly prevalent and abundant, accounting for a total median relative abundance of 7.1%, suggesting that this unknown Fusobacterium might present a key role in Canidae guts.

Finally, when screening for potential pathogens, we found: i) Clostridoides difficile in both dogs

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(9% prevalence) and cats (17% prevalence) and; ii) Pasteurella multocida in \sim 4% of the dogs. However, they account for <0.1% of the total composition.

In future steps, we will include larger canine and feline cohorts and use metagenomeassembled genomes to compute pangenomes for bacterial species of interest and identify key bacterial species for a specific animal host. s

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Title: Improving the characterisation of the chicken gut microbiome: a multi-kingdom genomic approach

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Germana Baldi, Varsha Kale

Co-authors: HoloFood Consortium, Lorna Richardson, Robert D. Finn

Affiliation: EMBL-EBI

Abstract:

A major global challenge is sustainable food production to meet the needs of a rising population. Given the importance of gut microbiome in health and disease, the HoloFood project investigates the effects of feeding regimes on the gut microbial composition in critically important farmed animals. A study on chicken production generated shotgun reads of chicken caecum and ileum samples from which species-level metagenomic-assembled genomes were derived. The caecum microbiome provided the greatest genomic diversity, with 261 samples giving rise to 11 870 assembled genomes which were used to produce a catalogue of 825 species-level representatives, of which 570 were novel with respect to the Genome Taxonomy Database. While the ileum demonstrated lower overall genomic diversity, it nonetheless shared a core of 130 species representatives with the caecum, as well as 21 ileum-specific species. Comparison of these datasets to existing publicly available chicken gut catalogues added >400 prokaryotes to the known chicken gut microbiome. Protein and metabolic pathway annotation was performed to understand functional potential encoded in the genomes, with the caecum catalogue alone generating 1.45 million non-redundant protein predictions. Viruses and plasmids were also identified for both sample sites to provide a comprehensive understanding of the microbiome composition of the caecum and ileum, and how the microbiota plays a role in food metabolism, potential antibiotic resistance and other factors that influence chicken production. This extensive catalogue is used within HoloFood to identify patterns in microbial diversity and functional capacity between trials, determining the effectiveness of prebiotic and probiotic feeding regimens.

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Title: A paired metagenomic and metatranscriptomic analysis of the salmon gut microbiome to assess the performance of sustainable feed additives

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Varsha Kale, Germana Baldi

Co-authors: HoloFood Consortium, Lorna Richardson, Robert D. Finn

Affiliation: EMBL-EBI

Abstract:

Ensuring food security in the face of climate change is a major global challenge. Reducing dependence on land production and increasing aquaculture farming offers one solution. Consequently, an objective of the HoloFood project is to investigate the effects of a novel seaweed feed additive and novel blue mussel protein source on the gut microbial composition of salmon. In this study, paired metagenomic and metatranscriptomic data was generated from 359 salmon gut samples. The metagenome was processed to generate a species-level catalogue composed of 9 prokaryotic genomes, with a high abundance of a novel Mycoplasmoidacae species. These findings are consistent with similar publicly available studies. Due to the low diversity, it was important to characterise transcriptional variation in the microbiome between feeding trials. The metatranscriptomic data was assembled into transcripts, and used in conjunction with the metagenome to produce a gene catalogue of >101K proteins. Of these, 100,159 proteins could be annotated with a gene ontology term, 30,602 with a KEGG ortholog, and 14,231 by matching to a protein in the metagenome assembled genomes. Proteins that did not match the genome catalogue were mapped to the Uniref90 database to assign a taxonomic annotation. Differential expression using slimmed gene-ontology terms and kegg orthologs, showed an underexpression of genes related to lipid metabolism in the salmon fed with a blue mussel protein supplement. The methods used to characterise the microbiome and its functional expression profile are effective to assess patterns relating to diet, ultimately influencing aquaculture production practices.

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Title: Berberrubine, a berberine-derived metabolite, is produced by the gut microbiota and improves gut health

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Tessa Dehau

Co-authors: Michiel Van de Vliet, Marc Cherlet, Siska Croubels, Filip van Immerseel, Evy Goossens

Affiliation: Ghent University

Abstract:

Reductions in antimicrobial usage in broiler diets resulted in a search for alternative ways to establish beneficial microbiota in chickens to ensure optimal gut health and performance. Amongst the most popular alternatives are phytogenic products. Berberine, an alkaloid isolated from medicinal plants like Coptis chinensis, is a potential candidate with antiinflammatory effects, although the mechanism of action is still poorly understood. One of the possible mechanisms is related to its transformation in the gut into several berberine-derived bioactive metabolites. The aim of this study was to investigate the extent to which the gut microbiota is involved in the metabolism of berberine and whether the berberine-derived metabolites can influence gut health. Berberine was supplemented to the feed of broiler chickens for 21 days and phase I metabolites were quantified in intestinal content and plasma samples using a validated LC-MS/MS method. Berberrubine was in higher concentration in the caecum than the ileum, and its circulating levels in the plasma were positively correlated with gut morphology parameters and negatively correlated with CD3+ lymphocyte infiltration in the gut tissue. Berberrubine was the most produced metabolite in caecal fermentates in vitro. 16S rRNA sequencing was performed on the metabolically active bacterial community, and several genera commonly described as butyrate producers were found to be associated with berberrubine levels. In addition, berberrubine significantly increased the production of Short-Chain Fatty Acids (SCFAs) in caecal fermentates. Our study showed that berberrubine is an important gut-derived metabolite of berberine that might contribute to gut health-promoting effects in vivo, either by promoting optimal gut morphology and controlling inflammation, or by stimulating the production of SCFAs with known beneficial effects for host cells.

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Title: Hologenomic Adaptation of European Whitefish

Theme Area: Session 4 Biodiversity & Conservationand Food Production

Paper type: Poster

Main Author: Meng Zhao

Co-authors: Juan Antonio Rodríguez Pérez, Tom Gilbert

Affiliation: Center for Evolutionary Hologenomics, Globe Institute, University Of Copenhagen

Abstract:

The European whitefish (Coregonus lavaretus) is a classic example of adaptive radiation, having undergone parallel morphological divergences from single founding morphs, across multiple freshwater lakes. Given the well documented role of gut microbiomes in shaping the lives of their hosts, in this study we explored how the morphological divergence of the fish may have shaped their gut microbiomes. To carry out the investigation, we collected the intestinal contents from 30 whitefish, representing 3 different morphs - densely rakered (DR), large sparsely rakered (LSR) and small sparsely rakered (SSR) – from a Norwegian freshwater lake that was colonized in the Holocene after the retreat of the ice that covered Scandinavia prior to that period. DNA was extracted using Qiagen PowerSoil kit and the libraries were sequenced by BGI Genomics with PE150 bp. Sequence raw data were processed following a standard metagenomic workflow with an extra step of host genome removal; binning, refinement and further visualization were done by using an advanced platform for 'omics data called, Anvi'o. The data contain 14 metagenomic assembled genomes (MAGs), that were then classified taxonomically using GTDB-tk. Our data indicate that while all three morphs share a common bacterium from the family Rhabdochlamydiaceae; only the DR and LSR morphs share a common bacterium from the family Bacillaceae; and only the SSR and LSR share a common bacterium family of Metamycoplasmataceae. Subsequently pangenomic and phylogenomic analysis were combined in order to explore how the potential functions of the bacterial genomes vary by fish morphotype.

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Title: Microbiome of pigs treated with different antimicrobials during an outbreak of postweaning diarrhoea

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Judith Guitart-Matas

Co-authors: Maria Ballester, Lorenzo Fraile, Lourdes Migura-Garcia, Yuliaxis Ramayo-Caldas

Affiliation: Institut De Recerca I Tecnologia Agroalimentàries (IRTA)

Abstract:

Antimicrobials are essential to control diseases and protect animal welfare. This project aimed to determine which of the commonly prescribed antimicrobial treatments of post-weaning diarrhoea (PWD) has a minimum impact on pig gut microbiota diversity and composition. A total of 210 piglets were transferred from a farm with recurrent problems of PWD to an experimental farm and divided into six different treatment groups: trimethoprim and sulfonamide (G1), colistin (G2), oral attenuated vaccine (G3), gentamicin (G4), untreated control with water acidification (G5), and untreated control (G6). An extra group remained at the farm of origin following the implemented routine program (GG). Clinical signs were monitored, and faecal samples were collected at four different timepoints (nursery (V1), three days post-treatment (V2), two weeks post-treatment (V3), and four weeks post-treatment (V4)). A total of 280 samples (10 animals/group/timepoint) were selected, DNA was extracted, and shotgun metagenomics was performed in a NovaSeq 6000. Microbial abundance and diversity index were estimated with the Microeco R package. Preliminary results identified significant decreased microbial diversity three days after treatment in G4 group compared to G1 and G3 groups. At this timepoint, significantly increased diversity was observed for the GG group compared to the groups that were treated at the experimental farm. Four weeks after treatment, this comparison was still significant, but microbial diversity significantly decreased for the group that remained at the farm of origin. Moreover, microbial diversity also decreased significantly at this latter timepoint between G5 group and G1 and G3 groups. Overall, this study applied metagenomic strategies to identify the effect of different antimicrobial treatments on microbial diversity. Further studies will be focused on the characterization and determination of the effect of each treatment on the pig gut resistome including the identification of AMR and virulence genes and the presence of plasmids.

The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: Viromes of Atlantic salmon correlate with gut microbiota and disease infection status – potential for modulating microbiome dysbiosis

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Caroline Sophie Wolters Petersen

Co-authors: Jacob Agerbo Rasmussen, Thomas Sicheritz-Pontén, Guillermo Andres Rangel Piñeros, Ling Deng, Xichuan Zhai, Dennis Sandris Nielsen, Mathias Middelboe, Morten Tønsberg Limborg

Affiliation: University of Copenhagen, Globe Institute

Abstract:

Disease outbreaks are one of the biggest challenges in Atlantic salmon (Salmo salar) aquaculture farming. Recently a study found that a spontaneous infection by the ulcer inducing pathogen Tenacibaculum dicentrarchi caused microbiome dysbiosis in the distal gut of salmon. Studies on human microbiome dysbiosis, have found that the bacteriophage (phage) fraction of the microbiome can play a modulating role in stabilising the microbiota of the gut to regenerate the health status of patients. Thus, suggesting that phage communities offer an alternative therapeutic potential for disease treatment. This study is the first virome characterisation of farmed Atlantic salmon and explores potential use of phages for modulating microbiome dysbiosis. Viromes of 20 sick and 20 healthy Atlantic salmon were sequenced using shotgun metaviromics and de novo assembled resulting in 320 novel salmon specific viral OTUs (vOTUs). The relative abundance showed that salmon viromes are predominantly composed of ssDNA and dsDNA phages belonging to the orders Petitvirales and Caudovirales, respectively. The viral community was investigated in association with the bacterial community and the disease state of the fish. A previous 16s rRNA study on the samples established the microbiota of the fish characterized as healthy, to be comprised mainly of a salmon specific genus of Mycoplasma sp., while fish suffering from large skin ulcers had a microbiome dominated by an unknown Aliivibrio sp. Several vOTUs were positively correlated to the Vibrio fraction of the microbiome of sick fish, and a negative correlation of the sick fish virome-microbiome alpha diversity reinforced the observation of a strong cooccurrence. The evident link between the microbiome dysbiosis and virome composition prompts further research of the intricate interactions that shape the health status of this keystone species and insinuates hitherto unexplored potential of using entire viromes for phage therapy and disease management in Atlantic salmon aquaculture production.

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The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: HOLO-OMICS ELUCIDATE COEVOLUTION OF HOST-MICROBIOTA IN SALMONIDS

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Jacob Agerbo Rasmussen

Co-authors: Karsten Kristiansen, Morten Tønsberg Limborg

Affiliation: University of Copenhagen

Abstract:

The microbial communities that inhabit the vertebrate gastrointestinal tract are tightly connected to many traits displayed by its host 1,2. Recent advances in the acquisition of 'omics data sets have resulted in the ability to recover genomes from unculturable bacteria, leading to a higher functional and taxonomic resolution of the gut microbiota in salmonids 3. Further, application of a holo-omic framework to investigate host-microbe interactions is showing increasing potential to improve growth, health, and sustainable animal production 4. Our recent findings include genome resolved metagenomics of the salmonid related Mycoplasma species using phylogenomics and comparative genomics 3. We have recently published a framework on how to use multi omics, including metagenomics and untargeted metabolomics for high resolution interpretation of host-microbiota interactions in response to administration of feed additives in rainbow trout (Oncorhynchus mykiss) 5 as well as how to investigate host-microbiota interactions under disease challenges in rainbow trout 6.

Ongoing research examines the microbiota from wild foraging populations of Atlantic salmon (Salmo salar) using genome resolved metagenomics to decipher functionality and taxonomy of bacteria in the intestinal environment of Atlantic salmon. Our data point to a clear co-evolution between the highly prevalent Candidatus Mycoplasma salmoninae salar and the Atlantic salmon host.

Overall, our results demonstrate the use of holo-omics to investigate complex hostmicrobiome interactions, which enable us to better evaluate the functional potential of the microbiota in farmed salmonids and decipher the dynamics of salmonid microbiota in wild Atlantic salmon. In addition, such knowledge holds potential for the early detection of pathogenic bacteria with implications for pathogen governance in aquaculture and conservation management.

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The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: Gut-on-a-chip in vitro models for a more accurate understanding of the action of probiotics in human health

Theme Area: Session 2 Human Health

Paper type: Poster

Main Author: Ostaizka Aizpurua

Co-authors: Catharina Blijleven, Urvish Trivedi, Carlotta Pietroni, Antton Alberdi

Affiliation: University of Copenhagen

Abstract:

Recent years have witnessed the rise of the gut microbiota as a major topic of interest in human health due to its role in shaping several key immunological and physiological functions. Therefore, the consumption of probiotics for health purposes has increased tremendously in the past few decades, and yet the efficacy of probiotics in treating or preventing diseases has been equivocal. This is probably because biological, technical and ethical limitations limit our capacity to study the exact mechanism of action of most probiotics. Gut-on-chip in vitro models have the potential to overcome many of the current limitations to study hostmicrobiota interactions that impact human health. These next-generation organoids are multichannel microfluidic cell cultures integrated in a circuit (chip) that simulate the activities, mechanics and physiological response of an entire intestine, which enables many biomolecular processes to be studied with an unparalleled level of detail. To study how probiotic agents interact with healthy and dysbiotic microbial communities and the epithelial tissue, we are creating gut-on-a-chip models from human intestinal epithelial cells that will be colonised with different microbial mixtures with and without pathogenic strains to create contrasting dynamic steady-state microbial communities. Then, we will inoculate probiotic strains to analyse their impact on the standing microbial community and epithelial gene expression at the micro scale. Gut-on-a-chip models will be processed through a combination of high-resolution imaging based on CLASi-FISH technology and micro-scale multi-omics for analysing spatially resolved micro-scale interactions. Uncovering the relationship between commensal microbes, pathogens, probiotics and human cells, will surely contribute to the development of microbiota manipulation therapies to fight against human diseases such as obesity and diabetes in the near future.

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The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: Reference-agnostic estimation of microbial read abundance in holobionts

Theme Area: Session 5 Technical & Methodological Perspectives

Paper type: Poster

Main Author: Raphael Eisenhofer

Co-authors: Antton Alberdi, Ben Woodcroft

Affiliation: University of Copenhagen

Abstract:

As we enter the hologenomic era, the microbial component of holobionts will increasingly be studied using genome-resolved metagenomics. In this approach, metagenomic DNA reads are assembled and grouped (binned) to create metagenome assembled genomes (MAGs), which represent the genomes from microbes within the sample. Current methods for evaluating the success of this approach assume that most of the DNA in a sample is of microbial origin. However, we know that metagenomic samples can contain complex mixtures of DNA comprising host, microbial, and dietary components. A common approach for removing nonmicrobial DNA from metagenomes is negative filtering - i.e. the mapping and exclusion of reads that align to non-microbial genomes expected to be in a sample. Negative filtering requires a priori knowledge of what is in a sample, which is impractical forgenome-resolved metagenomics on samples from increasingly novel hosts and sample types. Additionally, this approach relies on high-quality reference genomes, which are currently lacking for the majority of animal, plant, fungal, and microbial eukaryote diversity. To address this gap, we have developed an approach that uses the highly scalable tool, SingleM, to estimate the bacterial and archaeal fraction of metagenomic samples without reference genomes. This method will allow researchers to evaluate how well they are capturing the bacterial and archaeal components of holobionts — which will be critical as hologenomic research moves towards ever more novel organisms and sample types.

The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: Interactions between the probiont Phaeobacter inhibens S4, the marine pathogen Vibrio corallilyticus RE22, and the holobiont of larval American oysters, Crassostrea virginica

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Jessica Coppersmith

Co-authors: Evelyn Takyi, Kira Bernabe, Jamal Andrews, David R. Nelson, David C. Rowley, Marta Gomez-Chiarri

Affiliation: University of Rhode Island

Abstract:

Disease outbreaks in oyster hatcheries can decimate the stock, delay production, and cause supply chain shortages for the expanding oyster aquaculture industry. The daily addition of the probiotic bacterium Phaeobacter inhibens S4 (S4) to hatchery tanks has been demonstrated to protect American oyster, Crassostrea virginica, larvae against bacterial pathogens like Vibrio corallilyticus RE22 (RE22). Mechanisms of action of S4 against RE22 pathogenicity in oysters are complex, including antibiotic production, formation of thick biofilms, inhibition of virulence by quorum quenching, and oyster host immunomodulation. In order to further understand the interactions between these two bacteria, transcriptomes of competition co-cultures were sequenced. Differential gene analysis showed downregulation of several virulence factors in RE22, including genes encoding for parts of secretion systems I, III, and VI, hemolysin, and motility when RE22 is in competition with S4. The interaction between the probiont S4 and the pathogen RE22 does not happen in a petri dish when administered to protect larvae in a hatchery system, but within the larvae and hatchery tanks both of which have a full complement of their own microbiota. Using 16S rRNA amplicon sequencing, we found that the alpha-diversity of larval oyster microbiomes treated with S4 in multiple hatcheries is not affected, but there are subtle changes in specific taxa due to probiotic treatment. Current research is focused on the interactions between S4, RE22, the oyster, and its microbiome using metatranscriptomic investigations. These results will allow us to further elucidate how S4 is able to protect this vital aquaculture commodity from vibriosis disease and inform the effect of probiotics on host-microbiome-pathogen interactions.

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Title: Temporal dynamics of gut microbial communities in wild chimpanzees (Pan troglodytes verus) from Taï forest

Theme Area: Session 4 Biodiversity & Conservationand Food Production

Paper type: Poster

Main Author: Markus Ulrich

Co-authors: Jan Gogarten, Sébastien Calvignac-Spencer, Roman Wittig, Fabian Leendertz

Affiliation: Robert Koch Institute, Helmholtz Institute for One Health

Abstract:

Within the last decades, communities of wild chimpanzees in Taï National Park, Ivory Coast, have experienced some major changes in group size and composition due to disease outbreaks. We are investigating whether these changes in group structures are reflected in variations of microbial communities, both parasites and symbionts. The access to longitudinal samples and observational data provided us with the unique opportunity to ask questions about the influence of the dynamic social structure of chimpanzees on their gut microbiota composition over time. We analyzed the gut microbiota composition of 180 individuals of three neighboring social groups over a time frame of 16 years.

Since 2001, fecal samples were collected, snap-frozen in liquid nitrogen and stored at -80°C till further analysis. We extracted nucleic acids from ~4500 fecal samples with a bead-based extraction kit and produced amplicon libraries for high throughput sequencing on an Illumina NextSeq to access the microbiota composition of Bacteria (16S-V4), Archaea (16S-V4), and eukaryotic microorganisms (18S-V4 and 18S-V9). We processed the received amplicon sequencing data to obtain amplicon sequence variants (ASVs) and calculate diversity metrics based on the ASVs. We further included dietary (molecular and observation), behavioral (grooming), social (rank) and environmental data (precipitation, temperature, tree phenology) to assess the impact of social and natural environment changes on the microbiota composition next to the influence of group size and group composition.

Here, we present a first analyses of the data set and the effects of the social and natural environment on the gut microbiota community of wild chimpanzees.

The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: Unlocking aggressive animal behaviour using metatranscriptomics

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Luisa Santos-Bay

Co-authors: Luisa Santos-Baya, M. Thomas P. Gilberta, a,b Antton Alberdia, Ostaizka Aizpurua

Affiliation: Center for Evolutionary Hologenomics, Globe Institute, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Abstract:

Aggressive behavior is an evolutionarily conserved and heritable trait that serves a number of adaptive purposes. However, excessive aggressiveness can be detrimental and maladaptive, as well as a serious problem in farm animals. Aggression between individuals often results in stress for the animals that can compromise their reproductive success, growth, and immune system, while injuries can affect carcass quality. A large number of studies has shown that the expression of aggressive behavior depends on the interaction between environmental and genetic factors. However, a surge of investigations on the gut microbiota has revealed that microbes make important contributions to numerous aspects of animal health and physiology, including brain development and function. Increasing evidence supports that the gut microbiota and the animal brain maintain bidirectional communication along a network termed the microbiota-gut-brain axis, which can modulate many behavioral traits. Aiming to understand the link between the gut microbes and aggression we are studying the microbial RNA expression of a specific population of silver foxes that have been bred into two distinct cohorts; one that is aggressive and another that is tame, while being raised in otherwise identical environments. The preliminary results reveal differences in the microbial RNA expression between aggressive and tame foxes, suggesting a role of the gut microbiota in the aggressiveness of the animals. This study has the potential to constitute an important first step towards identifying microbial genes and metabolic pathways that promote aggression in foxes, as we expect that the metatranscriptomic data can identify the differences of microbial RNA expression between the aggressive and tame fox cohorts. Thus, a microbial manipulation could be a possible treatment to reduce aggressive behavior of farm animals in the future. Ultimately, this highlights the relevance of using a hologenomic perspective to untangle the complex architecture of behavior.

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Title: The HoloFood Data Portal

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Alexander Rogers

Co-authors: Varsha Kale, Germana Baldi, Lorna Richardson, Rob Finn (all of them are members from Microbiome Informatics team at EMBL-EBI)

Affiliation: Microbiome Informatics Team at EMBL-EBI

Abstract:

The HoloFood project has generated a wealth of data covering the host–gut interactions of two major food systems: chicken and salmon.

A principal legacy of the project is the deposition of these data into the appropriate publicly accessible data archives, to enable further analysis and future work by the scientific community.

Data will be submitted to the most appropriate archive for their type, including ENA, BioSamples, MGnify, and MetaboLights.

The HoloFood Data Portal will serve as an entry point to these databases, enabling clear visibility of the project's samples and discovery of the URLs and API endpoints to access the data housed in supporting databases.

In addition to providing a hub for accessing the archived data, the HoloFood Data Portal hosts documented analyses covering subsets of the HoloFood data.

Partners and collaborators can upload analysis summaries tagged to HoloFood Samples or Projects, allowing the community to discover these whilst browsing the data. These documents will serve as high-level, multi-sample metadata – containing both

aggregative and comparative analyses.

The HoloFood Data Portal has been implemented using Django, with a technical focus on portability and long-term ease of maintainability.

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See more at <u>www.holofood.eu</u> & <u>appliedhologenomicsconference.eu/</u>



Title: Bidirectional causality between gut microbiota and HLA DQ2 celiac patients: a Twosample Mendelian Randomization approach

Theme Area: Session 2 Human Health

Paper type: Poster

Main Author:

Co-authors: BP. González García1, S. Marí1, A. Cilleros Portet1, A. Hernangomez Laderas1, N. Fernandez Jimenez1, I. García Santisteban1*, and JR. Ramon Bilbao1,2

Affiliation: Department of Genetics, Physical Anthropology and Animal Physiology, University of The Basque Country (UPV/EHU) and Biocruces-Bizkaia Health Research Institute, Leioa, Basque Country, Spain

Abstract:

Background/Objectives: Celiac disease (CeD) is an autoimmune enteropathy triggered by gluten intake in genetically predisposed individuals. The major genetic determinant is the HLA-DQ2 heterodimer present in 90-95% of celiac individuals. In addition, the host's gut microbiota, influenced by environmental and genetic factors, might play a pivotal role in CeD. Observational studies have shown that individuals carrying HLA-DQ2 haplotypes have a distinctive gut microbiota composition. Whether these alterations are cause or consequence of the disease remains unknown.

Methods: To determine the putative causality between CeD and the gut microbiome, we performed a bidirectional Two-Sample Mendelian Randomization analysis. For CeD, we used data from the Immunochip CeD study¹ considering only high-risk celiac population carrying at least one copy of the HLA-DQ2 alleles (2587 cases, 334 controls). For the microbiome, we employed public data from MiBioGen² consortium (n= 18340).

Results: When assessing the effect of gut microbiota over CeD, we identified five main taxon from the Firmicutes phylum, including Ruminococcaceae, as previously reported. When assessing the effect that CeD has over gut microbiota, we identified other bacteria from the Firmicutes, Proteobacteria, and Bacteroidetes phyla. Our main hit was the Pasteurellaceae family, which belongs to the Proteobacteria phylum.

Conclusion: The existing relationship between CeD and gut microbiota is highly complex and bidirectional.

References:

- 1. G. Trynka et al., 43, 1193–1201 (2011).
- 2. A. Kurilshikov et al., 53, 156–165 (2021).

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729

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Poster ID: 58

Title: Dynamics of the Top Biome of cereal leaf beetle (Oulema melanopus) is influenced by the diet and developmental stage.

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Beata Wielkopolan1,

Co-authors: Alicja Beresewicz-Szabelska2, Krzysztof Krawczyk1, Aleksandra Obrepalska-Steplowska1

Affiliation: Institute of Plant Protection - National Research Institute

Abstract:

The cereal leaf beetle (CLB, Oulema melanopus, Coleoptera) is one of the most serious pests of cereals. The most damaging developmental stage for crops is larva and thus it is the target of insecticide treatments. Recently we established the TopBiome - the most abundant genera of bacteria that make up the greater part of the CLB microbiome of this insect (1). It consists among others of Wolbachia, Rickettsia, Lactococcus, Pseudomonas, Serratia, Stenotrophomonas, and Pantoea. Some of the species belonging to the above-mentioned genera were found previously to be associated with other insects and play a role in insecticide detoxification.

Here we analysed various factors influencing TopBiome dynamics depending on the CLB developmental stage and diet as well as various treatments. We make our observations by sampling insect material from various winter and spring cereals. We observed that the differences in the relative abundance of mentioned genera differ depending on the conditions studied. The biggest differences were observed between developmental stages. Additionally, we found out that treatments influence the microbiome content of CLB. Interestingly, the larval stage was associated with increased levels of some bacterial genera known to play a role in detoxification, such as Pseudomonas. Its role in the insecticide development of CLB will require further investigation.

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 Wielkopolan, B., Krawczyk, K., Szabelska-Beręsewicz, A., & Obrępalska-Stęplowska, A. (2021). The structure of the cereal leaf beetle (Oulema melanopus) microbiome depends on the insect's developmental stage, host plant, and origin. Scientific reports, 11(1), 1-19.

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Title: Revisiting in the ecological origins of bacteria in our fermented foods

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Veronica M. Sinotte

Co-authors: Ana Cuesta-Maté, Jonathan Z. Shik, Sandra B. Andersen, Robert R. Dunn

Affiliation: Center for Evolutionary Hologenomics, Globe Institute, University of Copenhagen

Abstract:

Lactic acid bacteria dominate fermented foods across the globe. These acid-producing bacteria are essential to food preservation and the probiotic health benefits associated with fermented foods. Our consumption of fermented foods potentially reaches well beyond modern times, as both humans and great apes recognize bacteria-derived acids and have an affinity towards sour foods. Despite evidence for evolutionary associations between humans with lactic acid bacteria within ferments, the ecological origin of these bacteria remains largely unknown. Spontaneous or wild ferments may best represent early fermentation because they occur when food is inoculated with environmental bacteria rather than a starter. Here we revisit potential environmental reservoirs of lactic acid bacteria, namely plants and insects known to have robust interactions with these microbes. We then compare them to the lactic acid bacteria found in spontaneous ferments such as sauerkraut, kimchi, and sourdough. We identify potential periods of bacterial diversification and functional adaptations across ecological niches that promoted inoculation into our wild ferments. Ultimately, by reviewing the evolutionary ecology of lactic acid bacteria, we shed light on the partnership between humans and wild ferments that inevitably underlies the domestication of many lactic acid bacteria found in modern fermented food.

The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: Saccharomyces cerevisiae on the rise: Domestication of yeast in breadmaking

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Margot Ruffieux

Co-authors: Alexxis Gutierrez, Nathan Brandt, Rob Dunn, Caiti Smukowski Heil

Affiliation: North Carolina State University

Abstract:

In 2021 the baking industry contributed \$478.4 billion USD to the global economy with over 9 billion kilograms of bread consumed, demonstrating the importance of bread to culture, nutrition, and economy worldwide. Despite bread's integral role in societies as a food source and traditional practice for millennia, the intricacies surrounding human influence and interaction with starter microbial communities for leavened bread production are not well understood. One piece of this domestication puzzle rests in the yeast that ferment bread dough. The dominant yeast in baking is Saccharomyces cerevisiae, which plays a significant role in dough rise and the production of desirable aromas and flavors. The broad genetic and phenotypic diversity of S. cerevisiae provides a lens to explore the array of S. cerevisiae genetic factors contributing to important baking phenotypes. We isolated and sequenced the genomes of 46 S. cerevisiae strains from sourdough starters collected as a citizen science project from home-bakers across North America. We combined our sourdough strain sequencing with S. cerevisiae sequences representing a wide variety of fermentation and natural isolation sources to explore evolutionary relationships and characterize population structure. We identified genomic signatures of domestication in breadmaking yeast and paired these population genomic analyses with phenotypic data collected on our sourdough strains and a selection of commercial baking strains, beer, sake, wine, and natural isolates. We quantified dough rise, growth in maltose, and production of metabolites during fermentation that beget pleasant and aversive sensory traits, and currently seek to connect these phenotypes to genetic mechanisms. This advances our understanding of S. cerevisiae domestication and its impact on S. cerevisiae genome evolution, and provides an opportunity to optimize commercial baking strains, thus improving food production globally.

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Title: Social bee microbiomes are the missing link in the origin of human fermented foods

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Ana Cuesta-Maté

Co-authors: Veronica M. Sinotte, Jonathan Z. Shik, Sandra B. Andersen, Rob R. Dunn

Affiliation: Center for Evolutionary Hologenomics, Globe Institute, Copenhagen University, Denmark

Abstract:

Lactic acid bacteria and acetic acid bacteria are generally considered beneficial microbes for humans and used to produce several fermented foods and beverages. Humans have historically domesticated these bacteria to obtain the ferments that we currently consume, but the question remains on how these microbes got there in the first place. These microbes naturally appear in soil, plants, flowers and fruits, but their presence in such habitats is patchy and, seemingly, stochastic. Building on recent studies of the natural habitats of yeasts, we highlight consider whether these bacteria might have a more predictable presence in the bodies social insects; we focus on honeybees. Our work shows that some of these bacteria are found in the honeybee environment, the beehive, royal jelly, bee bread, and nectar of flowers and fruits social bees visit. Lactobacillus, Bacillus and Fructobacillus associated with social bees are closely related to the fermenting food microbes of wine, cheese or buttermilk. Similarly, Acetobacteraceae typically found in the bee environment are closely related to microbes involved in the fermentation of kefir, kombucha or vinegar. Could social bees be responsible for the original inoculation of these microbes into the food substrates that then will transform into the ferments that we consume? Furthermore, for the establishment of spontaneous fermentation of food, the reinoculation of the same microbes is necessary, as the microbiome of social bees is highly conserved. There could be, however, anthropological intervention in the transmission of these microbes into the fermented food. The best example would be mead, or humans may also act as physical vector for these microbes, our interaction with fruits, flowers, bees and ferments could get these microbes into new nutrient rich substrates. In this project, we will compare the genomes from bee-associated and food-associated microbes and explore the possible human and bee routes of transmission.

The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: Molecular mechanisms of microbiota-mediated protection against Flavobacterium infection in gnotobiotic zebrafish

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: David Pérez Pascual

Co-authors: Rebecca Stevick*, Bianca Audrain, Emmanuel E. Adade, Arthur Lenson, Alex Valm, Jean-Marc Ghigo

Affiliation: Institut Pasteur

Abstract:

The protection provided by host commensal microbiota against pathogens is a long-known phenomenon fostering the notion that introducing beneficial bacteria could reduce or prevent infections. However, the mechanistic study of microbiota-pathogen interactions in vivo is limited by complex microbial communities with unknown functions. Gnotobiotic animal models can be used as a tool to control and reproducibly imitate host-associated microbiota systems. Taking advantage of a robust, controlled and tractable gnotobiotic zebrafish model of infection, we showed that three cultivable strains from the zebrafish microbiota are sufficient to individually protect against the fish pathogen Flavobacterium covae upon addition to germfree fish: Chryseobacterium sp., Nubsella sp., and Brevundimonas sp. Genomic comparison of the 3 probiotic strains, compared to non-protecting strains, shows only 6 shared genes as well as approximately 300 genes that are unique to each strain. By screening for transposon mutants in Chryseobacterium sp. unable to protect zebrafish larvae, we have identified a single mutation in a glycosyltransferase codifying gene that leads to loss of protection and reduced colonization of the zebrafish. In order to further explore the bacteria-bacteria interactions that contribute to larval zebrafish protection, we have sequenced transcriptomes from in vitro bacterial co-cultures of the 3 protecting strains and 2 non-protecting strains with and without F. columnare. Ongoing analysis of these data will determine common and unique transcriptional changes of the pathogen and probiotic upon the interaction that leads to in vivo protection. Understanding the mechanisms underlying this microbiota-mediated protection against infection will allow for improved disease treatment and prevention.

The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



The 1st Applied HoloGenomics Conference is part of the HoloFood Innovation Action. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817729



Title: In vitro model to study synbiotic-pathogen-gut microbiota interactions at microscale

Theme Area: Session 3 Agriculture, Aquaculture and Food Production

Paper type: Poster

Main Author: Andi Erega

Co-authors: 3D'omics consortium, Annelies Geirnaert

Affiliation: Laboratory of Food Biotechnology, Department of Health Sciences and Technology, Institute of Food, Nutrition and Health, ETH Zürich

Abstract:

Biofilms are the predominant bacterial lifestyle. Multi-species biofilms can improve the survival of enteric pathogens that are transmitted along gastrointestinal tract and the food chain. Efficient strategies that reduce transmission are needed to prevent or reduce the pathogen spread. Synbiotics represent a strategy to control intestinal infections with several beneficial properties that are essential to maintain gastrointestinal health. In vitro models mimicking interactions between synbiotic, pathogen and host gut microbiota can aid in elucidating the potential synbiotic mode of action.

Here we present an in vitro approach to investigate spatial microbial interactions based on the continuous PolyFermS fermentation model mimicking the conditions of the host gut. Selected pathogen and probiotics are immobilized and cultivated together with host gut microbiota into porous gel beads, which serve as an in vitro model for sessile microbial growth. Moreover, it allows to preserve the 3D structure enabling the generation of spatially referenced multi-omics data. We aim to investigate the growth dynamics and spatial distribution of targeted pathogen and probiotic bacteria during the development of multispecies niches inside of the gel beads by determining CFU, qPCR, and confocal laser scanning microscopy.

We will present first data on a case study with a synbiotic that inhibits the outgrowth of enteropathogens residing in the chicken gut. The gel bead model allowed the growth interaction of the enteropathogen with the probiotic mixture and gut microbiota in close proximity. We observed different distributions of live and dead bacteria in multiple microcolonies inside of the beads, which are currently under investigation.

Our in vitro model can aid in a better understanding of multi-species spatial arrangements and the identification of interacting taxa, which could bring forward novel applications of probiotics.

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