Symposium
“Fungi – the forgotten component of metaorganisms”

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Hotel Maritim, Kiel

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Welcome!

to our symposium on "Fungi – the forgotten component of metaorganisms"! Hosted by the **CRC 1182, Kiel Life Science, Kiel Plant Center, CIFAR** and **SymbNET** at the Maritim Hotel in Kiel, "Fungi – the forgotten component of metaorganisms" is designed to be a small and focused meeting including experts and colleagues from different disciplines of research including medical mycology, plant pathology, and fungal genetics. The aim of this symposium, jointly **organised by Prof. Eva Stukenbrock and Prof. Thomas Bosch**, is to share our experiences and knowledge across discipline boundaries and discuss how together we can better explore the role of fungi in animal and plant metaorganisms systems. We are very much looking forward to lively discussions and new insights that will move us all forward in this fascinating field of research!

Contents

Scientific Organisers

Eva Stukenbrock is professor at Kiel University and the Max Planck Institute of Evolutionary Biology in Plön. Following an initial interest in the population genetics of arbuscular mycorrhizal fungi, since her PhD at the ETH Zurich Stukenbrock has focused on plant pathogenic fungi. In particular she is interested in the how fungi adapt to their environment, as well as understanding which evolutionary forces fuel adaptive evolution and how new species emerge. Current work within her group aims to characterize plant-associated microbiota, including bacteria, fungi and oomyctes that colonize the pyllosphere of wild and cultivated wheat species. Stukenbrock is the spokesperson of the Kiel Plant Center which aims to connect plant scientists working throughout the Kiel Region and raise the visibility of plant research being done within the Center. Since 2019 she is a fellow of the Canadian Institute of Advanced Research (CIFAR); in 2022 she was appointed a member of the French Académie des Sciences for her research on the evolutionary relationships between plants and microorganisms, and future applications in sustainable plant protection.

Thomas Bosch studied Biology at the University of Munich and Swansea University College in the UK from 1976 to 1983. He earned his doctorate from the University of Munich in 1986. From 1986 to 1988, Bosch held a postdoctoral position at the University of California, Irvine, USA. After a position as research associate at the University of Munich, he was appointed to professorship for Zoology at the Friedrich Schiller University of Jena in 1997. Since 2000 Bosch is Professor of General Zoology at Kiel University. Bosch is Senior Fellow of the Canadian Institute of Advanced Research (CIFAR). From 2010 to 2013 he served as Vice-President of Kiel University and was responsible for Kiel University's institutional strategy and international relations. Since November 2013 Bosch heads the interdisciplinary research center "Kiel Life Science" (KLS) at Kiel University. Since 2016 Bosch is also spokesperson of the DFG funded Collaborative Research Center (CRC/SFB 1182) "Origin and Function of Metaorganisms" which addresses the recognized role of multi-organismic interactions for health and disease.

Local Organising Committee

Andrea Quatfasel-Arndt

Dorine Boumans

Rosemary Wilson

Schedule

Day 1 **March 1**

Time	Schedule
9:00-9:30	Arrival / Registration / Coffee
9:30 – 10:00	Welcome and Introduction – Organisers Eva Stukenbrock and Thomas Bosch
Session 1 Chair: Petra Bacher, Kiel University	
10:00 – 10:40	**Joseph Heitman**, Duke University Medical Center Fungi on the skin: Malassezia and beyond
10:40 – 11:00	**Hassan Salem**, Max Planck Institute for Biology, Tübingen Quid pro quo: Leaf beetle propagates a phytopathogen in exchange for pupal protection
11:00 - 11:20	*Coffee Break*
11:20 – 12:00	**Marie-Claire Arrieta**, University of Calgary Early-life gut mycobiome in child immune and metabolic development
12:00 – 12:20	**Florian Weinberger**, GEOMAR, Kiel A yeast (*Papiliotrema fonsecae*) amplifies the virulence of a Labyrinthulomycete (*Labyrinthula zosterae*) towards eelgrass (*Zostera marina*)
12:20 – 13:30	*Light Lunch*
Session 2 Chair: Remco Stam, Kiel University	
13:30 – 14:10	**Bart Thomma**, University of Cologne Plant pathogens manipulate host microbiota to promote disease development
14:10 – 14:30	**Carolina Sardinha Francisco**, Kiel University Apoplastic space of two wheat cultivars provides a highly different environment for pathogen colonization: Insights from proteome and microbiome profiling
14:30 – 15:30	Moderated Discussion Session
15:30 – 16:00	*Coffee break*
16:00 – 16:40	**Alga Zuccaro**, University of Cologne Disentangling programmed cell death (PCD) in plant microbe interactions.
16:40 – 17:40	Poster session

17:40 – 18:30	Walk to Zoological Museum
18:30 – 21:00	Reception in the Zoological Museum

Day 2 **March 2**

Time	**Schedule**
Session 3 Chair: Jinru He, Kiel University	
9:00 – 9:40	**Stephan Rosshart**, Friedrich-Alexander-University Erlangen-Nürnberg Born to be Wild - Wildlings a novel translational research model acknowledging the mammalian metaorganism
9:40 – 10:00	**Marjan Ghotbi**, GEOMAR, Kiel Fungal-Bacterial Interactions Shape Amphibian Gut Microbiomes
10:00 – 10:40	**Ingrid Richter**, Leibniz-HKI Jena Chemical communication in a plant-pathogenic fungal-bacterial symbiosis
10:40 – 11:00	*Coffee break*
11:00 – 11:20	**Caroline Saft**, Kiel University Malassezia-Host interaction in head-neck-shoulder atopic dermatitis
11:20 – 11:40	**Frank Kempken**, Kiel University A novel model consisting of *Neurospora crassa* and *Brachypodium distachyon* enables investigation of fungal auxin production in plant-fungus interaction
12:00 – 13:00	*Light Lunch*
Session 4 Chair: Eva Stukenbrock, Kiel University	
13:00 – 13:40	**Petra Bacher**, UKSH, Kiel Anti-fungal immunity in humans: at the intersection of protection and inflammatory disease.
13:40 – 14:20	**Deniz Tasdemir**, GEOMAR, Kiel Marine Fungi: A treasure trove for natural product drug discovery
14:20 – 15:00	Wrap up: New perspectives, new directions

Keynote talks are highlighted in green, selected talks in yellow

Keynote Speakers

Joseph Heitman did his undergraduate at the University of Chicago before doing his PhD at Cornell and Rockefeller Universities, studying how restriction enzymes recognize specific DNA sequences and how bacteria respond to and repair DNA breaks and nicks. He later moved as an EMBO long-term fellow to the Biocenter in Basel Switzerland, where he pioneered the use of yeast as a model for studies of immunosuppressive drug action. Since 1992 Joseph is a member of the Department of Molecular Genetics and Microbiology at Duke University School of Medicine, where his studies focus on microorganisms addressing fundamental biological questions and unmet medical needs.

Marie-Claire Arrieta is an Associate Professor in the departments of Physiology, Pharmacology and Pediatrics of the University of Calgary. Her research examines the interactions between the early-life gut microbiome and the infant's immune and metabolic development. She has developed a research program leading to important discoveries in the gut microbiome field. Her contributions as first or senior author have been published in leading journals such as Gut, Science Translational Medicine, Cell Host and Microbe and Nature Communications. She was awarded the CIHR-Sick Kids New Investigator Award, which is given to a select group of Canadian young investigators with outstanding contributions to children's health. She has also received the Killam Emerging Research Leader and the Peter Lougheed Research awards, given to top researchers at UCalgary, as well being named one of Calgary's top 40 under 40 in 2017, and a UCalgary Peak Scholar in 2018. Dr. Arrieta is co-author of the best-selling public book, ”Let Them Eat Dirt”, and is involved in several science communication initiatives, including public talks, a second book and a documentary film project.

Petra Bacher holds an assistant professorship for Immunology and Immunogenetics at Kiel University, Germany, a position she holds since 2018. She studied biology in Cologne where she also wrote her diploma thesis in pharmacology. After a doctoral thesis at the company Miltenyi Biotec, she received her PhD in Immunology from the University Jena in 2014 and returned to basic research with a postdoc at the Charité in Berlin. The Bacher lab in Kiel has a strong background in human antigen-specific CD4+ T cell analyses and aims to understand the failure of tolerance mechanisms in the human immune system during chronic inflammatory diseases. Specifically the group investigate the role of microbiota-reactive CD4+ T cells in immune-mediated diseases using novel direct analyses of antigen-specific T cells. Recent work demonstrated that TCR cross-reactivity plays an important role in modulating human T-cell responses, including induction of pathogenic Th17 cells by the intestinal microbiota

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and modulation of the response to newly encountered antigens, which particularly affects the elderly. Bacher and her group have also made important contributions to the understanding of the role of microbiota-specific T cell responses in chronic inflammatory bowel and airway diseases.

Stephan Rosshart studied biology and medicine at the Albert-Ludwigs-University Freiburg, Germany. In 2010 he obtained his doctorate in basic immunological research from the University of Freiburg. After his postgraduate training in clinical internal medicine at the Medical Center – University of Freiburg, he joined the National Institutes of Health in Bethesda, USA for a 6-year postdoctoral fellowship in basic immunological research. During this time, he conceived the "natural microbiota theory" and created mouse models for translational research – such as wildlings – that better predict human immune responses. In 2019 he became Emmy Noether group leader of the translational microbiome research laboratory and head of the gnotobiotic mouse facility at the Department of Medicine II, Medical Center – University of Freiburg. In 2023 he took a position as Full Professor and Head of the Department of Microbiome Research at the Friedrich-Alexander-University Erlangen-Nürnberg, Germany. His work focuses on mammalian microbiota and their impact on health and disease. He utilizes natural microbiota- and pathogen-based mouse models – such as wildlings – and a bench-to-bedside approach to (I) discover disease-relevant mechanisms and potential treatments for a wide range of human diseases of global relevance including transplant rejection, GvHD, cancer, infectious diseases, allergies, autoimmune and inflammatory diseases, neurological disorders as well as cardiovascular diseases, (II) improve modelling of immune responses of humans in preclinical studies, and (III) support drug development in collaboration with the pharmaceutical industry.

Alga Zuccaro completed her PhD at the Technical University of Braunschweig. After a postdoctoral training, she took on group leader positions at the Justus Liebig University Giessen and Max Planck Institute for Terrestrial Microbiology in Marburg. Since 2014 she is at the University of Cologne where she is now professor of ecological genetics of microbes, and vice dean of research at the faculty of mathematics and natural sciences. Her research interests focus on plant-microbe interactions, plant immunity and metabolism and cell death.

Bart Thomma studied Plant Pathology at Wageningen University in The Netherlands before going on to receive a PhD from the Katholieke Universiteit Leuven in Belgium. His thesis, on immune signalling pathways in *Arabidopsis,* described that, besides salicylic acid, jasmonate and ethylene also play major roles in defence against pathogens. From 2003 onwards he has established a career at Wageningen University, The Netherlands, starting as postdoc, then assistant and associate professor, before becoming full professor and head of department in 2013. This is where he started to develop his work on the vascular wilt pathogen *Verticillium dahliae*. In 2020, Bart Thomma was awarded a Humboldt professorship to become professor of Evolutionary Microbiology at the University of Cologne in Germany and at the "Centre of Excellence on Plant Science" (CEPLAS), where he moved his research group. Bart Thomma received the first RKS Wood Prize, awarded by the British Society for Plant Pathology, and acts as section editor for the journal PLoS Pathogens and as co-editor-in-chief of FEMS Microbiology Reviews.

Ingrid Richter studied biology at the Friedrich Schiller University Jena, Germany. She obtained her Masters in Molecular Ecology under the guidance of Prof. Craig Cary at the University of Waikato, Hamilton, New Zealand (2011) and did her PhD in Chemical Ecology and Biotechnology at Victoria University Wellington and the Cawthron Institute Nelson, New Zealand (2011 – 2015). She then moved to the University of Constance, Germany, for a postdoc in Environmental Toxicology under Prof. Daniel Dietrich (2015 – 2016). Since 2017 she is a postdoc in in the laboratory of Prof. Christian Hertweck at the Leibniz Institute for Natural Product Research and Infection Biology Jena, which was funded by a Marie Sklodowska-Curie Individual Fellowship (2018 – 2020).

Abstracts – Day 1

Joseph Heitman
Duke University Medical Center

Fungi on the skin: Malassezia and beyond

Hassan Salem
Max Planck Research Group on Mutualisms, Max Planck Institute for Biology, Tübingen, Germany

Quid pro quo: Leaf beetle propagates a phytopathogen in exchange for pupal protection

Many insects rely on microbial protection early in development. However, in contrast to symbiont-mediated defense of eggs and young instars, the role of microbes in safeguarding pupae remains relatively unexplored, despite the susceptibility of the immobile stage to antagonistic challenges. Here, we outline the importance of symbiosis in ensuring pupal protection by describing a mutualistic partnership between the ascomycete Fusarium oxysporum and *Chelymorpha alternans*, a leaf beetle. The symbiont rapidly proliferates at the onset of pupation, extensively and conspicuously coating *C. alternans* during metamorphosis. The fungus confers defense against predation as symbiont elimination results in reduced pupal survivorship. In exchange, eclosing beetles vector Fusarium to their host plants, resulting in a systemic infection. By causing wilt disease, the fungus retained its phytopathogenic capacity in light of its symbiosis with *C. alternans*. Despite possessing a relatively reduced genome, Fusarium encodes metabolic pathways that reflect its dual lifestyle as a plant pathogen and a defensive insect symbiont. These include virulence factors underlying plant colonization, along with mycotoxins that upgrade the defensive biochemistry of the insect host. Collectively, our findings shed light on a mutualism predicated on pupal protection of an herbivorous beetle in exchange for symbiont dissemination and propagation.

Marie Claire Arrieta
Cumming School of Medicine, University of Calgary, Canada

Early-life gut mycobiome in child immune and metabolic development

Substantial evidence supports an early window in life, during which changes to our gut microbiome has long-lasting effects on host development and subsequent risk of non-infectious, chronic diseases, such as asthma and obesity. Much of what is known about this has only included bacteria, ignoring the multi-kingdom diversity of this microbial community. Fungi are ubiquitous members of this ecosystem, elicit distinct host immune responses known to be involved chronic inflammation, and respond to the same factors known to increase disease risk through microbiome alterations, such as antibiotic use during infancy and birth by Caesarean section. However, little is known about the role of host-associated fungi. Our research group has been studying this by applying a 'bedside-to-bench' approach, in which findings from pediatric clinical studies linking the mycobiome with disease risk are scrutinized in experimental disease models in order to address causality and specific mechanisms. Our findings show that gut fungi are influential but overlooked gut microbes that help dictate the trajectory towards early-life health or disease.

Florian Weinberger
Experimental Ecology- Benthic Ecology, Marine Ecology Research Division, GEOMAR, Kiel, Germany

A yeast (Papiliotrema fonsecae) amplifies the virulence of a Labyrinthulomycete (Labyrinthula zosterae) towards eelgrass (Zostera marina)

This study highlights the role of the yeast *Papiliotrema fonsecae* as a facilitator of eelgrass wasting disease outbreaks, which cannot be predicted from distribution patterns of the causative agent *Labyrinthula zosterae* alone. Two different strains of *P. fonsecae* originating from eelgrass in South Portugal and from North Sea water had very similar effects on the virulence of *L. zosterae*, in contrast to five other yeast species that were isolated from eelgrass. Such facilitation may explain the only sporadic occurrence of severe wasting disease outbreaks despite frequent presence of *L. zosterae* in eelgrass stands.

Bart Thomma
Cluster of Excellence on Plant Sciences (CEPLAS), Institute for Plant Sciences, University of Cologne, Germany

Plant pathogens manipulate host microbiota to promote disease development

Beneficial plant-associated microbes are found in and on all organs of the plant and help to mitigate (a)biotic stresses. Moreover, plants are able to shape their microbiota and specifically attract beneficial microbes to suppress pathogen attack. Hence, the plant's microbiome can be considered an inherent, exogenous layer that complements its endogenous innate immune system.

Microbes typically secrete a plethora of molecules into their environment to promote niche colonization. Especially soil-dwelling microbes are well-known producers of antimicrobials that are exploited to outcompete microbial co-inhabitants in the soil. Plant pathogenic microbes similarly secrete a diversity of molecules into their environment for niche establishment.

Upon plant colonization, microbial pathogens secrete so-called effector proteins that promote disease development. While such effectors are typically considered to exclusively act through direct host manipulation, for instance through the suppression of host immune responses, increasing evidence demonstrates that pathogenic fungi exploit effector proteins with selective antimicrobial properties to promote host colonization through the manipulation of beneficial host microbiota. Given that effector-mediated microbiota manipulation may have evolved in fungal ancestors that encountered microbial competition before symbiosis with land plants evolved, we propose that effector-mediated microbiota manipulation is fundamental to fungal biology.

Carolina Sardinha Francisco
Botanical Institute, Kiel University, Germany

Apoplastic space of two wheat cultivars provides a highly different environment for pathogen colonization: Insights from proteome and microbiome profiling

The apoplast comprises the intercellular space between cell membranes. During plant colonization by microbes, the apoplast is a space where the intruder lives for most of its lifetime within host. *Z. tritici* is a hemibiotrophic fungal pathogen that colonized the apoplast of wheat plants. Here, we used *Z. tritici* to unveil cultivar-specific microbiota and protein profiling changes during pathogen infection. We validated the apoplastic fluids as a proxy to understand the warfare between plants and microbes. Using proteomic analysis, we show that *Z. tritici* diminishes the photosynthetic functionality in a susceptible cultivar. Next, we determined the tolerance of apoplastic microbes to plant-produced antimicrobial compounds. We also found several bacterial isolates negatively affecting the growth of *Z. tritici*. Finally, we found secondary metabolite biosynthetic gene clusters in the genomes of antagonistic bacteria. Overall, our findings highlight the potential of a multi-omics approach targeting the outcomes of complex plant-defense-associated and microbial-microbial interactions in the apoplastic fluids.

Alga Zuccaro
Institute of Plant Sciences, University of Cologne, Germany

Disentangling programmed cell death (PCD) in plant microbe interactions

Programmed cell death (PCD) in plants is a fundamental cellular process that can be triggered during developmental programs and by biotic and abiotic stresses. An active cell death process is an essential component of *Arabidopsis thaliana* root cap differentiation. The acquisition of cell death competence depends on the root cap-specific transcription factor ANAC033/SOMBRERO (SMB3). Cell death is followed by cell-autonomous corpse clearing, which involves the senescence-associated nuclease BFN1. Based on the observation that the beneficial root endophyte *Serendipita indica* down-regulates BFN1 at the onset of the cell death-associated colonization phase, we investigated the role of SMB3 and BFN1 in fungal accommodation. Due to the lack of a functional plant nuclease, knock-out mutation of *bfn1* or *smb3* leads to accumulation of host cell corpses and enhanced intra- and extra-radical fungal colonization. These results highlight the importance of root cap differentiation in plant-microbe interactions and lead to the proposition of a mechanism by which *S. indica* manipulates developmental programmed cell death (dPCD) in Arabidopsis roots by down-regulating the nuclease BFN1 to promote fungal colonization through an excess of nutrients in the form of uncleared host cell corpses.

Abstracts - Day 2

Stephan P. Rosshart
Department of Microbiome Research, Department of Medicine 1, Friedrich-Alexander-University Erlangen-Nürnberg, 91054 Erlangen, Germany

Born to be Wild - Wildlings a novel translational research model acknowledging the mammalian metaorganism

Mouse models are paramount for research. However, they suffer from major shortcomings like irreproducible results rooted in divergent microbiota and the fact that the transition from studies in mice to bedside practice in humans routinely fails. Paradigm-shifting work has shown that ultra-clean lab mice are too far removed from natural conditions to faithfully mirror the physiology of humans. This distorts how the immune system of lab mice develops and functions, leading to false assumptions of how the human immune system works. To tackle these shortcomings, we implanted embryos of lab mice into wild mice to create "wildlings". Indeed, in preclinical trials, where even non-human primate models failed to predict the human response, wildlings phenocopied humans and could have prevented these tragically failed human trials. Further, the microbiome of wildlings was stable and highly resilient, thereby providing an excellent model for reproducible experimentation. In summary, such models may open up a promising window of opportunity and (I) improve the reproducibility of studies, (II) increase the safety and success of bench-to-bedside efforts, (III) acknowledge the 3R principles, and (IV) ultimately reduce costs while accelerating the development of novel disease treatments for the benefit of human health.

Lluvia Vargas- Gastélum, Alexander S. Romer, N. Reed Alexander, **Marjan Ghotbi**, Kylie C. Moe, Kerry L. McPhail, George F. Neuhaus, Leila Shadmani, Joseph Spatafora, Jason E. Stajich, Javier F. Tabima, Donald M. Walker
Ocean EcoSystems Biology Group**,** Research Division 3: Marine Ecology, GEOMAR, Kiel

Fungal-Bacterial Interactions Shape Amphibian Gut Microbiomes

Interactions between bacteria and filamentous fungi in various environments are increasingly becoming the focus of research. However, they have rarely been incorporated into animal gut microbiome studies. The herptile gut microbiome can provide a natural system for understanding filamentous fungal-bacterial interactions due to cooccurrence of this type of fungi specifically, genus Basidiobolus, and gut bacteria. Preliminary results suggest interactions between Basidiobolus and the bacterial classes Verrucomicrobiae, Bacteroidiae and Clostridia. Here we discuss fungal and bacterial communities of herptile microbiomes, the potential of co-structuring between Basidiobolus and bacteria in the gut microbiome, and diversity of Basidiobolus across herptile hosts and geography.

Ingrid Richter
Biomolecular Chemistry, Leibniz Institute for Natural Product Research and Infection Biology Hans Knöll Institute, Jena, Germany

Chemical Communication in a plant-pathogenic fungal bacterial symbiosis

Mediators in a plant pathogenic fungal-bacterial symbiosis Fungal-bacterial interactions (BFIs) are critically important in agriculture, biotechnology, and medicine. An important feature of BFIs is the ability of bacteria to control and exploit their eukaryotic hosts. The association of the phytopathogenic fungus *Rhizopus microsporus* with the endosymbiont *Mycetohabitans rhizoxinica* exemplifies a remarkable example of bacteria influencing their host's physiology. We have identified various strategies and effectors used by endosymbiotic bacteria to control their fungal host. For example, bacteria invade the fungal host by secreting effector proteins via the type-2 secretion system (T2SS), while transcription activator-like effectors are required for the formation of a stable symbiosis.

Caroline Saft, Heidland T, Wulf I, Kamps AK, Kniemeyer O, Weidinger S, Bacher P, Suhrkamp I, Bang C, Heine G
Faculty of Medicine, Kiel University, Germany

Malassezia-Host interaction in head-neck-shoulder atopic dermatitis

The commensal Malassezia furfur (MF) is discussed to play a critical role in the head-neck-shoulder dominated subtype of atopic dermatitis (HNS). We investigated the Malassezia-Host interaction by examining patients with HNS and healthy individuals using immunologic, biochemical and molecular genetic methods. Only in HNS, MF-specific IgE was functionally activating basophils and specific Th2 cells were observed. The sensitization to MF was different and isotype specific in each individual in HNS using SDS-PAGE, western blot and ELISA. The correlation of HNS severity and Malassezia spp. colonization of the skin is under investigation using qPCR as well as the interaction with the mycobiome determined by ITS2-sequencing.

Krisztina Kollath-Leiß1, Ursa Repnik[2], Hannes Winter[1], Anna Freund[1], Samuel Johannssen[1], Heinrich Winkelmann[1], **Frank Kempken[1]**

[1]Botanical Institute, Kiel University; [2]Central Microscopy Unit, Kiel University, Germany

A novel model consisting of Neurospora crassa and Brachypodium distachyon enables investigation of fungal auxin production in plant-fungus interaction

In most fungi, auxin is produced as a plant growth hormone [1]. The physiological mode of action of phytohormones in fungi is still elusive, but it is known to play a crucial role in both beneficial and pathogenic plant-fungal interactions [2]. *Neurospora crassa* is used as a model ascomycete since it provides a wide range of molecular tools. In this fungus the main physiologically active form of auxin is indole acetic acid (IAA) [3]. We identified three active tryptophan-dependent IAA biosynthetic pathways with the corresponding enzymes in *N. crassa* [4]. Phenotypical investigations on diverse IAA biosynthetic knock out strains show moderate effects of auxin on conidiation and conidiospore germination. Unlike the general concept, we have shown that auxin secretion but not the biosynthesis of auxin is strictly dependent on external tryptophan sources. *N. crassa* is known as a saprophytic fungus. Its involvement in plant interactions remains elusive, as we could not establish an interaction of *N. crassa* with pine trees, as it had been described earlier [5]. Using light and electron microscopy, we have recently demonstrated that *B. distachyon can form a stable interaction system with N. crassa, suggesting that N. crassa plays an instrumental role* in plant-fungal interaction. This interaction is currently being investigated in relation to auxin.

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5. Kuo HC, Hui S, Choi J, Asiegbu FO, Valkonen JPT, Lee YH. Secret lifestyles of *Neurospora crassa*. Sci Rep. 2015 May;4(1):5135.

Petra Bacher
Institute of Immunology, University Hospital Schleswig-Holstein, Kiel, Germany

Anti-fungal immunity in humans: at the intersection of protection and inflammatory disease

The human body is constantly exposed to a variety of different fungal microbes. How host-fungal interactions are controlled by the human immune system is poorly understood. CD4+ T cells play a central role in controlling the interaction with fungi. Differences in fungal species, as well as interactions at different body sites likely have a major impact on the types of homeostatic T cell reactions. Inappropriate T cell responses against fungi are in turn associated with inflammatory diseases. We aim at understanding how homeostatic interaction with fungal microbes is mediated by the immune system and how alterations of these parameters contribute to fungus-mediated diseases.

We identified ubiquitous aeroantigens, like plant pollen, house dust mite and surprisingly also airborne fungal spores as major targets of human regulatory T cells (Tregs) and that the specificity of the aeroantigen-specific Tregs plays a decisive role in the control of the allergic immune pathology. We further showed that within a panel of 30 fungal species, the intestinal commensal *C. albicans* was the only driver of Th17 cell responses in healthy humans. Some of the Th17 cells also cross-recognize other fungi, such as the airborne fungus *Aspergillus fumigatus.* These cross-reactive Th17 cells are selectively activated and expanded in patients with airway inflammation. Thus, TCR cross-reactivity plays an important role in modulating human T cell responses, including induction of pathogenic Th17 cells by the intestinal mycobiota. Recently we investigated the role of fungal microbes as drivers of pathogenic CD4+ T cell reactions in patients with cystic fibrosis and inflammatory bowel diseases. Our results highlight that fungi play a central role in shaping the human immune system in healthy individuals and identify alterations of fungus-reactive CD4+ T cell responses as critical drivers of immunopathology in different chronic inflammatory disorders.

Deniz Tasdemir[1,2]
[1]GEOMAR Centre for Marine Biotechnology, Research Unit Marine Natural Products Chemistry, GEOMAR Helmholtz Centre for Ocean Research Kiel, [2] Faculty of Mathematics and Natural Sciences, Kiel University, Germany

Marine Fungi: A treasure trove for natural product drug discovery

Marine habitats account for 70% of the surface of the earth and have been shown to harbour diverse fungal communities from the air-surface interface to the very deep seafloor. Although very little portion of marine fungi have been studied so far, vital functions similar to those of terrestrial fungi (as decomposer, symbionts or pathogenic/parasitic) have been attributed to fungi in marine ecosystems. On the other hand, culture-based studies indicate enormous biosynthetic potential of marine fungi to deliver secondary metabolites with application potential in many different areas, ranging from agriculture to pharmaceuticals. A historical example is cephalosporins, the second-generation antibiotics, that have their origin in marine environment. Another prominent example is plinabulin, a synthetic derivative of the seaweed-derived fungal diketopiperazine halimide, which is undergoing phase III clinical trials against lung cancer. Inspired by the halimide story, our group has been searching for new bioactive molecules from cultivable marine fungi against human diseases such as cancer. This presentation will mainly outline our efforts in isolation, innovative cultivation, computational tandem mass spectrometry-based chemical profiling, followed by targeted purification and structure elucidation of marine fungal metabolites with anticancer activity.

Abstracts - Posters

1

Ana E. Bergues Pupo, Elisha Thynne, Eva H. Stukenbrock
Botanical Institute, Kiel University, Germany

Exploring the role in virulence of cytokinin biosynthetic genes of a fungal pathogen of wheat

Plant pathogens manipulate the host hormonal network as a mechanism to promote virulence and disease. To do so, pathogens can secrete molecules, such as proteins or metabolites (also known as effectors); although, their mode of action on hormonal signaling components is not fully understood. Our research focuses on the fungus *Zymoseptoria tritici*, a devastating pathogen in wheat, responsible for Septoria tritici blotch disease (STB), which has been largely associated with severe economic losses. We investigate whether *Z. tritici* manipulates wheat defenses by producing metabolites that interfere with plant hormonal signaling. Here, we explore the role of putative biosynthetic genes related to cytokinin production using phylogenetic analyses, gene expression at different stages of fungal infection in wheat, and reverse genetic approaches. We propose that *Z. tritici* can produce cytokinins through a de novo pathway led by three clustered genes (*Ztipt*, *Ztlog1*, and *Ztfmo*). Transient overexpression of the *Ztipt* gene promoted localized necrosis in leaves of the model *Nicotiana benthamiana*. Ongoing research involves the generation of mutant strains lacking the *Ztipt* gene, which will help to elucidate the contribution of this gene to cytokinin production and virulence of *Z. tritici* in wheat.

2

Ann-Kristin Kamps
Institute of Immunology, University Hospital Schleswig-Holstein, Kiel, Germany

Th17 cells are important for protective immunity against extracellular bacteria and fungi at barrier sites like the skin and intestinal surface, but they can also contribute to immune pathologies. Previous work from our group has shown, that the fungal commensal Candida albicans is one of the strongest inducers of a Th17 response in humans. Besides IL17A, *C. albicans* specific T cells also produce the Th1 cytokine INFÉ£. However, bot cytokines are not co-produced and the TCR repertoire of IL17A and INFÉ£ producing *C. albicans* specific T cells are distinct. Here we are using *C. albicans* as a model to better understand the mechanisms of Th17 vs Th1 induction in humans.

3

Celina Prosch

Research Center Borstel - Leibniz Lung Center, Germany

Microbiota alterations in mice treated with different regimens of antibiotics, antifungals and experimental probiotics C. G. Prosch, U. E. Schaible, M. Hauptmann In microbiome research, resilience describes the microbiota's capacity to overcome disruption and regain previous biodiversity. To study resilience, we rendered mice dysbiotic by antibiotic and/or antifungal treatment. We were able to induce partial recovery by intranasal applications of four bacterial species originally isolated from wild mouse lungs (Muribacter, Corynebacterium, Ligilactobacillus and Staphylococcus). High degree of inter-experimental variation for both, induction of dysbiosis and restoration, entailed a metanalysis of the entire 16S rRNA dataset to determine factors that contribute to microbiota stability and resilience.

4

Clara Igelmann, Michael Habig, Carolina Sardinha Francisco and Eva Holtgrewe Stukenbrock
Botanical Institute, Kiel University, Germany

Inhibition of Bacteria Isolated from Wheat by the Fungal Phytopathogen Zymoseptoria tritici in Vitro

The phytopathogenic ascomycete *Zymoseptoria tritici* shares the wheat leaf with a wide range of other microbiota. Whether *Z. tritici* directly inhibits some of the wheat associated bacteria is currently unknown, although some bacteria were shown to inhibit *Z. tritici*. Here we investigated the inhibition of bacteria from the wheat apoplast by *Z. tritici*. 32 of 69 tested bacteria isolates showed inhibited growth in the vicinity of *Z. tritici* in vitro. This inhibitory effect appeared to be the result of an organic acid produced by *Z. tritici*, that is affecting the pH and thereby the growth of a number of bacteria.

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The human fungal pathogen Aspergillus fumigatus holds a core bacteriome

Fungi are globally ubiquitous and kill more than 2 million people annually worldwide. In particular, invasive aspergillosis comprises a diversity of diseases caused by *Aspergillus* spp. with clinical outcomes ranging from colonization (*e.g.,* lungs) to systemic infections. The most vulnerable population, immunocompromised patients of all ages, continues to grow. Other groups at risk include those suffering from chronic obstructive pulmonary disease, asthma, and cystic fibrosis. The burden associated with fungal diseases on healthcare systems is predicted to rise in the near future.

There are many examples of partnerships of fungi with other organisms with the most emblematic being with algae to form lichens. Recently, a diverse array of bacteria has been found in association with diverse fungal hosts otherwise axenic. *A. fumigatus* usually exhibit extensive genomic and phenotypic heterogeneity in their virulence and drug-resistance profiles, questioning if the bacteriome influences the observed phenotypic heterogeneity.

In this study we focus our attention on the bacteriome of *A. fumigatus* clinical isolates to dissect how the bacterial partners influence fungal growth, infection capacity and drug susceptibility. *Aspergillus fumigatus* strains grown in media containing an antibiotic lost some of the most abundant bacterial partners. To eliminate additional ephemeral bacteria partners (able to subsist the antibiotic treatment) and reduce inter-spore variability, the spores were submitted to a high-temperature shock, then single-conidium cultures were generated. These strains showed great genotypic and phenotypic variability (colony growth rate, antifungal-susceptibility profiles, and *in vivo* infection capacity in *Galleria mellonella*). The bacteriome (region V4 and full length 16S rRNA gene) of strains having distinct phenotypic characteristics is being analysed. The data collected to date suggest that the analysed *A. fumigatus* cultures, otherwise axenic, harbour a complex core bacteriome but each has specific bacterial partners. Further studies are required to better understand how the assembly of a fungal-bacteria partnership influences the *A. fumigatus* phenotype.

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Eva Tanneau
Botanical Institute, Kiel University, Germany

Microorganisms forming the plant microbiome are mainly studied for their impact on host fitness and survival either as pathogens or beneficial mutualists. So far, the functional relevance and diversity of commensal microorganisms is less well understood. Moreover, the dynamic of microbiomes in natural plant populations is poorly described beyond studies in the model plant *Arabidopsis thaliana*. Through the study of the grass species *Agrostis capillaris* at Mols Bjerge national park in Denmark, we aim to characterise fungal and bacterial communities associated with leaves and roots, as well as in the soil where the plants are growing. The microbiome data will allow us to identify keystone species in the *A. capillaris* microbiome and through experimental assays we will investigate the relevance of these to plant health and microbial interactions. We will compare microbiota composition across three different years and address the impact of different management treatments on their composition and functions.

7

Gabriela Rios Martini

Institute of Clinical Molecular Biology, Kiel University, Germany

Dysregulated CD4+ T cell reactions against intestinal antigens are considered to be a causal or driving factor for IBD. The relevant target microbes remain still largely unknown. Using antigen-reactive T cell enrichment (ARTE), we characterized reactive CD4+ T cells against a panel of different microbes in healthy individuals and IBD patients. We found increased T cell reactions to Candida species in Crohns disease (CD) but not Ulcerative Colitis patients. Despite dominant Th17 responses in healthy donors, Candida-reactive T cells displayed increased IFNg production. These Th1 cells display a cytotoxic phenotype and their magnitude correlated with the formation of ASCA-antibodies.

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Guido Heine
UKSH Universitätsklinikum Schleswig-Holstein

9

Laura Rathjens

Institute of Immunology, University Hospital Schleswig-Holstein, Kiel, Germany

The skin microbiota plays an important role in immunity and local inflammatory responses. Alterations in these microbial communities are observed in the context of chronic inflammatory skin diseases, including bullous pemphigoid (BP), atopic dermatitis and psoriasis. CD4+ T cells are central orchestrators of immune reactions against bacteria and fungi. By using innovative tools to analyze microbe-reactive T cells we identified altered reactivity against distinct microbial species in BP patients, surprisingly including the common commensal fungus C. albicans. Our data highlight a role of fungi in shaping human immunity in chronic skin inflammation which will help to develop new treatment strategies.

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Marco Alexandre Guerreiro

Botanical Institute, Kiel University /Max Planck Institute for Evolutionary Biology

Fungi are ubiquitous and inhabit every known terrestrial habitat. Pathogenic fungi are highly diverse, and reports of new pathogens on crops, animals and humans are increasing. We aimed to determine genomic signatures associated with lifestyle transitions. We used comparative analyses of genomes among saprotrophic and reported opportunistic human pathogens. We find evidence for an evolutionary scenario where habitats select for optimal translation of genes involved in proliferation in the respective habitat. We predict that lifestyles are not strictly defined by gene repertoires, but rather by their ability to readily evolve and adapt to new environments through adaptive translation.

11

Pankaj Kumar

Polish Academy of Sciences Institute of Plant Genetics, Poznan, Poland

The plant immune system is made up of a complex response network that involves several lines of defense to fight invading pathogens. On the other hand, fugal plant pathogens have evolved a range of ways to infect their host. The interaction between Ascochyta pisi and pea genotypes was explored to investigate the progression of ascochyta blight (AB) in pea. In this study, we developed an Agrobacterium tumefaciens-mediated transformation system for A. pisi by constructing a new binary vector, pBIF-DsRed and pBIF-EGFP, for the constitutive expression of the red fluorescent protein (DsRed) and green fluorescent protein (EGFP). DsRed and EGFP were chosen as a highly efficient fluorescent markers to study the developmental changes in A. pisi during AB disease progression on the susceptible and resistant pea accessions. Overall, the use of fluorescent proteins in plant pathogenic fungi together with confocal laser scanning microscopy, provide a valuable tool to study the intracellular dynamics, colonization strategy, and infection mechanisms during plant-pathogen interaction.

12

Remco Stam
Institute of Phytopathology, Kiel University, Germany

Phytopathogenic fungi affect the wild tomato phyllosphere microbiome

Agricultural crops are sensitive to climatic variation and crop protection is essential to avoid pathogen epidemics. Natural populations of crop wild relatives have evolved and adapted to withstand biotic and abiotic stresses. Wild tomato species occupy a wide range of habitats, ranging arid coastal deserts to high altitude temperate regions. Yet, all populations maintain quantitative resistance against major tomato pathogens such as Alternaria spp. Dysbiotic (infected) leaves show distinct differences in phyllosphere microbiome composition compared to healthy leaves and loss of plant health-promoting microbial taxa, indicating that plant health might partly be governed by the stability of the phylosphere microbiome.

13

Severin Einspanier
Institute of Phytopathology, Kiel University, Germany

Quantitative disease resistance provides an incomplete, yet broad-range and durable level of resistance of plants against biotic stresses, like fungal pathogens. In contrast to the well-understood R-gene related (qualitative) resistance is quantitative disease resistance against necrotrophic pathogens less understood. During this study, a diverse panel of Soalanaceae and Brassicaceae plants will be examined for disease resistance against pathogens like *Alternaria alternata* and *Sclerotinia sclerotiorum*. Study concept and methods, like a fully automated disease-phenotyping platform will be presented.

Selected Speakers

Carolina Sardinha Francisco completed her PhD in Plant Pathology at the Swiss Federal Institute of Technology (ETH). Currently a postdoc in the group of Eva Stukenbrock at Kiel University, she is interested in the different aspects of plant- and microbe-microbe interactions with the aim of identifying biocontrol agents for sustainable disease control. Her postdoc project includes studies on microbial communities to identify antagonistic microbial interactions, screening of biomolecules with antimicrobial activities, and proteomic analysis of plant apoplast to pinpoint proteome catalogues associated with plant-microbe interactions.

Caroline Saft

Deniz Tasdemir is a pharmacist by training. She obtained her PhD from ETH-Zurich and post-doctoral training on anticancer marine natural products from University of Utah, USA. Following her posts at University of Zurich and London School of Pharmacy, in 2011, she moved to National University of Ireland Galway as full professor of marine biodiscovery. Since 2014, she is full Professor of Marine Natural Products Chemistry at GEOMAR Helmholtz Centre for Ocean Research and Kiel University where she leads the Research Unit Marine Natural Products Chemistry and GEOMAR Centre for Marine Biotechnology (GEOMAR-Biotech). Her research interests include marine metabolomics, drug discovery, chemical ecology and imaging mass spectrometry (DESI-IMS).

Florian Weinberger is a scientist at the GEOMAR Helmholtz Centre for Ocean Research at Kiel, Germany. As a trained botanist and microbiologist, he has been involved in projects on physiological, biochemical and molecular biological aspects of the ecology, aquaculture and utilization of algae and aquatic plants since 1990. His research focuses on seaweed management ecology in natural habitats and aquaculture and covers seaweed biodiversity, the ecological interactions of seaweeds with pathogens, epibionts, consumers and competitors, the ecology of nuisance algae and the eco-evolutionary implications of algal invasions.

Hassan Salem leads the Max Planck Research Group on Mutualisms in Tübingen. Previously he was a Smithsonian Biodiversity Fellow at the National Museum of Natural History in Washington D.C., and Humboldt Postdoctoral Fellow at Emory University in Atlanta. His research is at the intersection of entomology and microbial ecology.

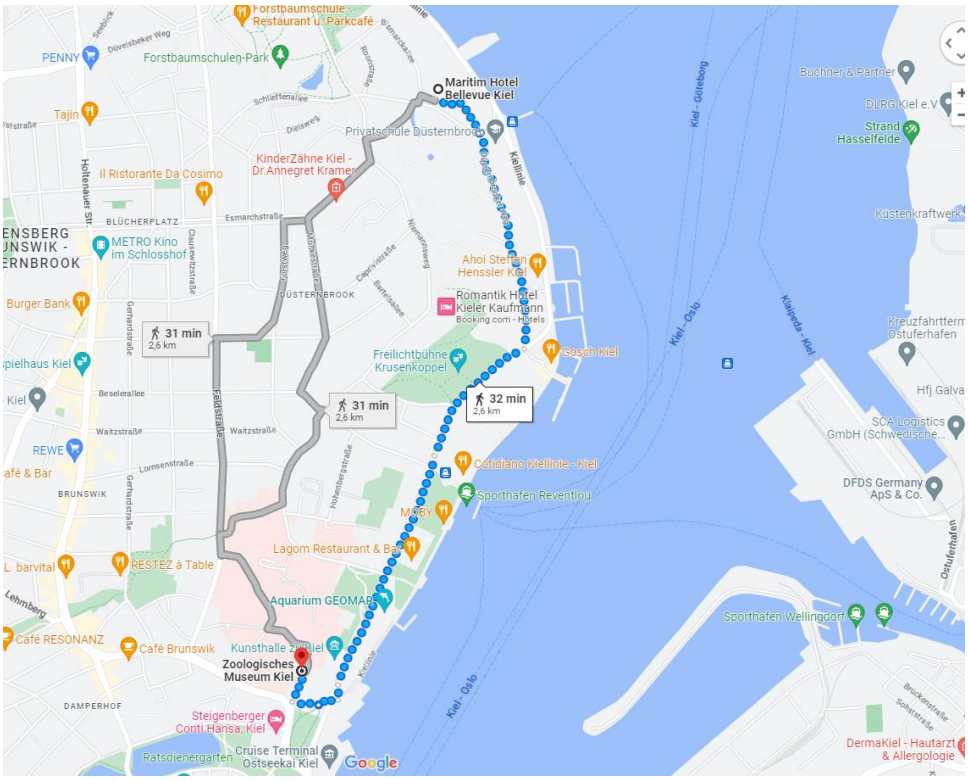
Krisztina Kolláth-Leiß studied biology at ELTE Budapest and CAU Kiel. In 2015, she completed her PhD in the group of Prof. Dr. Frank Kempken with the thesis "Das BEM46 Protein in Neurospora crassa: Eisosomale Lokalisation und Verknüpfung mit der Tryptophan-abhängigen Auxin-Biosynthese". After finishing her studies, she received a lecturer position at the Botanical Institute of the CAU Kiel, and since 2021, has a permanent position as teaching associate at the institute. In her research, which has been repeatedly supported by CAU grants, she investigates principles of polar growth in the model ascomycete Neurospora crassa.

Marjan Ghotbi received her bachelor's and first master's degree in fisheries sciences at IAU, Tehran, Iran. Afterwards she joined a project on biocontrol of *Orobanch aegyptiaca pers* by mean of enhancing pathogenicity of *Fusarium oxysparum* isolates. She did her second Master's degree at CAU/GEOMAR on cultivable gill and gut microbiota of Baltic fish as a new source of marine natural products. Then she joined experimental ecology department of GEOMAR and conducted research on comparing the potential of native vs invasive seaweeds on shaping their microbiomes. At present, she is a PhD candidate at GEOMAR, studying microbe-to-microbe interactions. She is truly fascinated by Fungal-bacterial cross-talks and at the same time collaborates with Herptile Microbiome Project at MTSU.

Important Information

Evening reception at the Zoological Museum on 1 March

After the poster session at the end of day 1, we will walk together to the zoological museum, taking a stroll along the waterfront. See the map for directions and overview.



At the zoological museum we invite you to join us for some finger food and live music.

Zoological Museum
Hegewischstraße 3
24105 Kiel
www.zoologisches-museum.uni-kiel.de

Live music performed by members of the Collegium Musicum, Kiel University:
Constantin Knabbe, Clarinet | Sarah Westphal, Violin | Nadine Waimann, Cello

Program:

Part 1

Wolfgang Amadeus Mozart: Divertimento No. 3 KV. 229

- Allegro
- Adagio
- V. Rondo (Allegro Assai)

Part 2

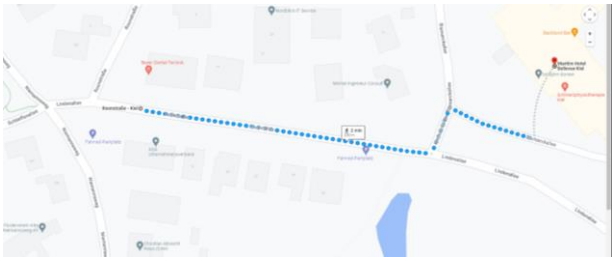
- Wolfgang Amadeus Mozart: Divertimento No. 3 KV. 229, IV. Menuetto
- Paul Desmond: Take Five (Arr.: Jürgen Schmidt)
- Zequinha de Abreu: Tico Tico (Arr.: Roe Goodman)

Symposium venue:

Maritim Hotel Bellevue Kiel
Bismarckallee 2
24105 Kiel
https://www.maritim.de

Travelling to the venue by public transport:

The nearest bus stop to the venue is the busstop “Roonstrasse”. From Kiel train station, take bus number 41 (endstation “Tannenberg”) or 42 (endstation “Suchsdorf”). Travel time ca. 15 minutes, departing from central train station ca. every 10 - 15 minutes. Fare 2.40 Euro. The hotel is a few minutes walk from the bus stop, see map below.



Suggestions for dinner and drinks in Kiel

Forstbaumschule, https://forstbaumschule.de/
Brunswik Café, https://cafe-kiel.de/brunswik/
Cafe Blattgold (vegan), https://cafe-kiel.de/blattgold/
Lanna Thai, https://www.lanna-thai-kiel.de/
Burgerbank, https://www.burgerbank.de/ (Holtenauer str. 113)
Ahoi Steffan Hensler (Kiel Yacht Club), https://www.ahoisteffenhenssler.de/filiale/ahoi-kiel
Cotidiano Kiellinie, https://www.cotidiano.de/kiel-kiellinie
Lagom Restaurant & Bar, https://www.lagom-kiel.de/

Suggestions for sightseeing in Kiel

Kiel Maritime Museum,
https://www.kiel.de/de/kultur_freizeit/museum/schifffahrtsmuseum_fischhalle.php
Aquarium GEOMAR,
https://www.aquarium-geomar.de/
Kiel Art Gallery,
https://www.kunsthalle-kiel.de/en/startseite
Botanical Gardens,
https://www.botanischer-garten.uni-kiel.de/en?set_language=en
Ferry trips from “Reventlou” Pier
Kiellinie 65, Kiel

Hosts and Sponsors

SymbNET – Genomics and Metabolomics in a Host-Microbe Symbiosis Network

https://symbnet.eu/

Origin and Function of Metaorganisms Collaborative Research Centre 1182

https://www.metaorganism-research.com/

Kiel Plant Center - Fostering collaborative plant science in North Germany

www.plant-center.uni-kiel.de/en

Kiel Life Science - Interdisciplinary Centre for Applied Life Sciences at Kiel University

https://www.uni-kiel.de/en/research/priority-research-areas/kiel-life-science

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CIFAR - Canadian Institute of Advanced Research

https://cifar.ca/