16TH SEEON CONFERENCE

MICROBIOTA, PROBIOTICS AND HOST

MIKROBIOTA, PROBIOTIKA UND WIRT

JUNE 27TH – 29TH 2024

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KLOSTER SEEON KULTUR & BILDUNGS ZENTRUM

16TH SEEON CONFERENCE

MICROBIOTA, PROBIOTICS AND HOST

MIKROBIOTA, PROBIOTIKA UND WIRT

June 27th – 29th 2024

SHUTTLE SERVICE DETAILS (BOOKING REQUIRED)

Train station shuttle ~ 30 min
Airport shuttle ~ 1,5 h

Wednesday 26th to Seeon Monastery (1 day before conference/ first day of Summer School)

12:00 - 13:30 shuttle from Munich Airport (only for airplane travelers)

12:50 - 13:20 shuttle from Bad Endorf train station

Thursday 27th (1st day of conference) to Seeon Monastery

13:30 - 15:00 shuttle from Munich Airport (only for airplane travelers)

14:00 - 14:30 shuttle from Bad Endorf train station

Thursday 27th leaving from Seeon Monastery

13:30 Shuttle departure to airport and Bad Endorf train station

Saturday 29th (last day of conference) leaving from Seeon Monastery

12:30 Shuttle departure to airport and Bad Endorf train station

CONFERENCE CENTER

Kloster Seeon (Monastery Seeon/ Chiemsee)

Kultur- und Bildungszentrum des Bezirks Oberbayern

Klosterweg 1, 83370 Seeon

www.kloster-seeon.de

NAVIGATING THE DIGITAL ABSTRACT BAND

In the agenda/ program: The titles of the talks hyperlink to the abstracts. The date in the abstract header hyperlinks to the corresponding day in the agenda/ program. [This feature does not apply to the "AGENDA AT A GLANCE" section.]

The poster titles in "Poster session overview" hyperlink to the poster abstracts of each presenter.
You can jump back to the poster overview by following the hyperlinked header "POSTER" on the upper left-hand corner of each abstract.

Dear Participants,

We warmly welcome you at Kloster Seeon for the 16th Conference on Microbiota-Host interactions.
This meeting is organized annually by the German Society for Hygiene and Microbiology **(DGHM) section "Microbiota, Probiotics and Host"**. Since the first meeting in 2008, the "Seeon Conference" has become a forum to unite various disciplines in basic and clinical sciences with the aim to understand the human microbiome and its role in health and disease. Past activities around this conference have substantially contributed to the creation of the **DFG-funded Priority Program "MICROBIOTA – a Microbial Ecosystem at the Edge between Immune Homeostasis and Inflammation"** (SPP 1656), which gathered >30 research groups between 2013-2019. Since then, microbiome research has continued to blossom in Germany: established in 2015, the **Collaborative Research Center CRC1182 "Metaorganisms"** in Kiel studies how resident microbes influence fitness of their plant and animal hosts to form a holobiont. In 2018, the **Cluster of Excellence CMFI - Controlling Microbes to Fight Infections** in Tübingen was funded to elucidate the mechanisms of interaction between beneficial and harmful bacteria to make them useful for targeted therapeutic interventions. Since 2019, **CRC1371 "Microbiome Signatures"** in Munich, which aims to determine the precise functional relevance of microbiome signatures in disease-specific contexts, and **CRC1382 "Gut-liver axis"** in Aachen, which dissects microbiome-derived mediators involved in organ-crosstalk, further expanded this fruitful research landscape around the microbiome. Last but not least, a **new Priority Program** (SPP2474) has been launched to elucidate gene functions in the human gut microbiome. Researchers from these consortia all meet in Seeon to discuss latest advances in their field. Seeon is a scientific event that particularly encourages the participation of young scientists. Besides the conference, the **Seeon Summer School on "Microbiome in Health and Disease"** was launched in 2018, with the aim of creating a sustainable platform to train and promote young scientists across various disciplines, including gastroenterology, nutritional medicine, immunology, infection research, microbial ecology, synthetic biology, animal science, and computational biology in the area of basic and applied microbiome research.
Again this year, we have a fantastic line-up of speakers and selected talks. We are looking forward to fruitful discussions and good science; let's have a great time together in Seeon!

Prof. Thomas Clavel,
on behalf of the Steering Committee:
ProfIN Maria Vehreschild, University Hospital Frankfurt am Main, Germany
Prof. Till Strowig, Helmholtz Center for Infection Research, Braunschweig, Germany

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Thursday, 27th June 2024		
Rooms Check-In after 15:00		
13:30	15:00	Shuttle transfer from Munich Airport
14:00	14:30	Shuttle transfer from Bad Endorf train station
14:00	**16:00**	**Registration** & Coffee
16:00	16:15	Welcoming
16:15	17:00	**KEYNOTE LECTURE** How Bugs Stay Together – Cooperation And Competition For Place In Communities **Kiran R. Patil** Chair: Joel Selkrig
17:00	18:00	SESSION 1: FUNCTIONAL DIVERSITY OF MICROBES ❖ **Ning Qu:** Identification Of Secreted Serine Proteases In *Phocaeicola Vulgatus* ❖ **Lina Michel:** Insights Into *Phocaeicola Vulgatus* Bacteriophage Diversity ❖ **Ylenia Heinrich Sanchez:** Ecophysiology Of Trimethylamine-Producing Bacterial Communities Of Human Gut Microbiota Chair: Joel Selkrig
18:00	19:30	Dinner
19:45	21:15	POSTER PITCH (2 minutes/ slides) Chair: Maja Magel
21:30		Bowling & Socializing

Friday, 28th June 2024		
9:00	9:45	**KEYNOTE LECTURE** Effects of the Diet-Microbiota Axis on Immunity and Tumour Therapies **Nicola Gagliani** Chair: Till Strowig
9:45	10:45	SESSION 2: COMMENSAL-PATHOGEN BATTLEFIELD ❖ **Éva de Hoog-Almási**: *Klebsiella Oxytoca* Facilitates Post-Antibiotic Microbiome Recovery And Restores Colonization Resistance In A Diet-Dependent Manner ❖ **Shreeya Tavkari:** Distinct Colonisation Patterns And Immune Interactions Delineate Commensal And Pathogenic Strains *Of Staphylococcus Epidermidis* ❖ **Simon Graspeuntner:** Vaginal Microbial Dynamics Are Linked To Reduced Colonization Resistance To Chlamydial Infection Chair: Till Strowig
10:45	11:15	Coffee break/ **Poster at first glance**
11:15	12:00	**KEYNOTE LECTURE** Keystone Gut Bacteria Promotes Microbiota Recovery And Pathobiont Clearance **Karina B. Xavier** Chair: Bärbel Stecher
12:00	12:25	**HOT TOPIC** Anti-Fungal Immunity In Humans: At The Intersection Of Protection And Inflammatory Disease **Petra Bacher** Chair: Bärbel Stecher
12:25	13:55	**Lunch**

13:55	14:20	**HOT TOPIC** Targeting The Gut Microbiota In Inflammatory Bowel Diseases: Where Are We? **Tobias Schwerd** Chair: Thomas Clavel
14:20	14:45	**HOT TOPIC** Host Microbiome Interactions In The Context Of Recent Human Evolution **Mathilde Poyet** Chair: Thomas Clavel
14:45	15:45	SESSION 3: MICROBES, HOST, AND DRUGS ❖ **Rémy Villette**: Multi-Omics Analysis Of Gut Microbiota Unveils Microbial Functions Alterations Associated To Parkinson's Disease ❖ **Annika Hausmann:** Deep Visual Proteomics Reveals In Vivo-Like Functionality In Orthotopically Transplanted Human Colon Organoids ❖ **Jan Homolak:** Impact of Antidepressants on Human Gut Microbiota Chair: Thomas Clavel
15:45	16:15	**Coffee break**
16:15	16:45	**DGHM Fachgruppenmeeting for members**
16:15		Free time for others
18:30	19:30	Dinner
19:30	21:00	**Poster session**
21:00		Bowling & Socializing

Saturday, 29th June 2024		
Room Check-Out before 11:00		
9:00	9:45	**KEYNOTE LECTURE** Host microbial interactions: Faecal microbiota transplantation to tackle antimicrobial resistance from poo to policy **Lindsey A. Edwards** Chair: Maria Vehreschild
9:45	10:45	SESSION 4: CLINICAL MICROBIOME RESEARCH ❖ **Anastasia Tsakmaklis:** FMT Donor Screening Experience in Germany ❖ **Benjamin Auch:** Precision Metagenomics Reveals Dynamic Changes In Plasmid And Phage Interaction Networks Following Fecal Microbiota Transplantation ❖ **Márcia S. Pereira:** Fasting Suppresses A Pathogenic Th17 Cell-Inducing Gut Pathobiont In RA Patients Chair: Maria Vehreschild
10:45	11:05	Coffee break
11:05	12:05	SESSION 5: MICROBIAL AND HOST MEDIATORS ❖ **Marlène Birk:** Secreted Gut Microbiota Proteins As Mediators Of Organ Cross-Talk ❖ **Lena Amend:** PUL-Dependent Cross-Feeding Mechanisms Between The Gut Commensal *Bacteroides Thetaiotaomicron* And The Enteric Pathogen *Salmonella Typhimurium* ❖ **Sarah E. Woodward:** Could Off-Target Binding Of Pathogen-Induced Antibodies To Commensal Bacteria Enhance Vaccine Efficacy? Chair: Thomas Clavel
12:05	12:15	Awards & Farewell
12:15	12:25	Lunch to Go
12:30	13:00	Shuttle departure from Kloster Seeon

THURSDAY, JUNE 27TH 2024

14:00 - 16:00 Registration & Coffee

16:00 - 16:15 WELCOMING

By Thomas Clavel, *Functional Microbiome Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Germany*

16:15 – 17:00 KEYNOTE LECTURE

HOW BUGS STAY TOGETHER – COOPERATION AND COMPETITION FOR PLACE IN COMMUNITIES

Kiran R. Patil, *MRC Toxicology Unit and Department of Biochemistry, University of Cambridge, UK*

Chaired by Joel Selkrig*, Host-Microbe Interactomics Group, Institute of Medical Microbiology, University Hospital of Aachen, Germany*

17:00 – 18:00 SESSION 1 – FUNCTIONAL DIVERSITY OF MICROBES

Identification Of Secreted Serine Proteases In *Phocaeicola Vulgatus*

Ning Qu, *Institute of Medical Microbiology, RWTH Aachen University Hospital, Aachen, Germany*

Insights Into *Phocaeicola Vulgatus* Bacteriophage Diversity

Lina Michel, *Max von Pettenkofer Institute of Hygiene and Medical Microbiology, Faculty of Medicine, LMU Munich, Germany*

Ecophysiology Of Trimethylamine-Producing Bacterial Communities Of Human Gut Microbiota

Ylenia Heinrich Sanchez, *Medical Microbiology and Hospital Epidemiology, Hannover Medical School (MHH), Hannover, Lower Saxony, Germany*

Chaired by Joel Selkrig*, Host-Microbe Interactomics Group, Institute of Medical Microbiology, University Hospital of Aachen, Germany*

18:00 - 19:30 Dinner

19:45 - 21:15 POSTER PITCH (2 MIN/ 2 SLIDES)

Chaired by Maja Magel, *Functional Microbiome Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Aachen, Germany*

21:30 Bowling & Socializing

FRIDAY, 28TH JUNE 2024

9:00 - 9:45 KEYNOTE LECTURE

EFFECTS OF THE DIET-MICROBIOTA AXIS ON IMMUNITY AND TUMOUR THERAPIES

Nicola Gagliani, *Department of Medicine and Department of General, Visceral and Thoracic Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*

Chaired by Till Strowig, *Microbial Immune Regulation, Helmholtz Centre for Infection Research, Braunschweig, Germany*

9:45 - 10:45 SESSION 2: COMMENSAL-PATHOGEN BATTLEFIELD

Klebsiella Oxytoca Facilitates Post-Antibiotic Microbiome Recovery And Restores Colonization Resistance In A Diet-Dependent Manner

Éva de Hoog-Almási, *Department of Microbial Immune Regulation, Helmholtz Centre for Infection Research (HZI), Braunschweig, Germany*

Distinct Colonisation Patterns And Immune Interactions Delineate Commensal And Pathogenic Strains Of *Staphylococcus Epidermidis*

Shreeya Tavkari, *Würzburg Institute of Systems Immunology, Max Planck Research Group, University of Würzburg, Germany*

Vaginal Microbial Dynamics Are Linked To Reduced Colonization Resistance To Chlamydial Infection

Simon Graspeuntner, *Department of Infectious Diseases and Microbiology, University of Lübeck, Germany*

Chaired by Till Strowig, *Microbial Immune Regulation, Helmholtz Centre for Infection Research, Braunschweig, Germany*

10:45 - 11:15 Coffee break/ POSTER AT FIRST GLANCE

11:15 - 12:00 KEYNOTE LECTURE

KEYSTONE GUT BACTERIA PROMOTES MICROBIOTA RECOVERY AND PATHOBIONT CLEARANCE

Karina B. Xavier, *Instituto Gulbenkian Ciência, Oeiras, Portugal*

Chaired by Bärbel Stecher, *Microbiota & Infections, Max von Pettekofer-Institute, LMU Munich, Germany*

12:00 - 12:20 HOT TOPIC

ANTI-FUNGAL IMMUNITY IN HUMANS: AT THE INTERSECTION OF PROTECTION AND INFLAMMATORY DISEASE

Petra Bacher, *Institute of Immunology & Institute of Clinical Molecular Biology, Christian-Albrecht-University of Kiel, University Medical Center Schleswig-Holstein, Kiel, Germany*

Chaired by Bärbel Stecher, *Microbiota & Infections, Max von Pettekofer-Institute, LMU Munich, Germany*

12:25 - 13:55 Lunch

13:55 - 14:20 HOT TOPIC

TARGETING THE GUT MICROBIOTA IN INFLAMMATORY BOWEL DISEASES: WHERE ARE WE?

Tobias Schwerd, *Department of Pediatrics, Dr. von Hauner Children's Hospital, University Hospital, LMU Munich, Germany*

Chaired by Thomas Clavel, *Functional Microbiome Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Germany*

14:20 - 14:45 HOT TOPIC

HOST-MICROBIOME INTERACTIONS IN THE CONTEXT OF RECENT HUMAN EVOLUTION

Mathilde Poyet, *Institute of Experimental Medicine, University of Kiel, Germany*

Chaired by Thomas Clavel**,** *Functional Microbiome Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Germany*

14:45 - 15:45 SESSION 3 – MICROBES, HOST AND DRUGS

Multi-Omics Analysis Of Gut Microbiota Unveils Microbial Functions Alterations Associated To Parkinson's Disease.
Rémy Villette, *Luxembourg Center of Systems Biomedicine, University of Luxembourg, Belval, Luxembourg*

Deep Visual Proteomics Reveals In Vivo-Like Functionality In Orthotopically Transplanted Human Colon Organoids
Annika Hausmann, *reNEW – NNF Center for Stem Cell Medicine, Denmark*

Impact of Antidepressants on Human Gut Microbiota
Jan Homolak, *M3 Research Center, Interfaculty Institute of Microbiology & Infection Medicine Tübingen (IMIT), Eberhard Karls University & University Hospital Tübingen, Germany*

Chaired by Thomas Clavel, Functional *Microbiome Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Germany*

15:45 – 16:15 Coffee break

16:15 - 16:45 DGHM FACHGRUPPENMEETING FOR MEMBERS

(FREE TIME FOR OTHERS)

18:30 - 19:30 Dinner

19:30 – 21:00 POSTER SESSION

21:00 Bowling & Socializing

SATURDAY, 29TH JUNE 2024

9:00 - 9:45 KEYNOTE LECTURE

HOST MICROBIAL INTERACTIONS: FAECAL MICROBIOTA TRANSPLANTATION TO TACKLE ANTIMICROBIAL RESISTANCE FROM POO TO POLICY

Lindsey Ann Edwards, *Institute of Liver Studies, King's College London, Department of Inflammation Biology, School of Immunology and Microbial Sciences, Faculty of Life Sciences and Medicine, London, United Kingdom*

***Chaired by Maria Vehreschild**, Infectiology, Medical Clinic II, University Hospital Frankfurt, Germany*

9:45 - 10:45 SESSION 4 – CLINICAL MICROBIOME RESEARCH

FMT Donor Screening Experience in Germany

Anastasia Tsakmaklis, *Department I of Internal Medicine, University Hospital Cologne, University of Cologne, German Center for Infection Research (DZIF), Cologne-Bonn & Department of Internal Medicine, Infectious Diseases, University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt, Germany Germany*

Precision Metagenomics Reveals Dynamic Changes In Plasmid And Phage Interaction Networks Following Fecal Microbiota Transplantation

Benjamin Auch, *Phase Genomics, Inc, Seattle, WA, USA & University of Minnesota, Minneapolis, MN, USA*

Fasting Suppresses A Pathogenic Th17 Cell-Inducing Gut Pathobiont In RA Patients

Márcia S. Pereira, *Institute of Musculoskeletal Medicine, University of Münster, Germany*

***Chaired by Maria Vehreschild,** Infectiology, Medical Clinic II, University Hospital Frankfurt, Germany*

10:45 - 11:05 Coffee break

11:05 - 12:05 SESSION 5 – MICROBIAL AND HOST MEDIATORS

Secreted Gut Microbiota Proteins As Mediators Of Organ Cross-Talk
Marlène Birk, *Host-Microbe Interactomics Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Germany*

PUL-Dependent Cross-Feeding Mechanisms Between The Gut Commensal Bacteroides Thetaiotaomicron And The Enteric Pathogen Salmonella Typhimurium
Lena Amend, *Department of Microbiology, Biocentre, University of Würzburg & Helmholtz Institute for RNA-based Infection Research (HIRI), Helmholtz Center for Infection Research (HZI), Würzburg, Germany*

Could Off-Target Binding Of Pathogen-Induced Antibodies To Commensal Bacteria Enhance Vaccine Efficacy?
Sarah E. Woodward, *Sir William Dunn School of Pathology, University of Oxford, Oxford, England*

Chaired by Thomas Clavel, *Functional Microbiome Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Germany*

12:05 - 12:15 AWARDS & FAREWELL

Chaired by Thomas Clavel, *Functional Microbiome Research Group, Institute of Medical Microbiology, University Hospital of RWTH Aachen, Germany*

12:15 - 12:25 Lunch to Go

12:30 SHUTTLE DEPARTURE FROM SEEON TO AIRPORT AND TRAIN STATION

POSTER SESSION OVERVIEW

#1	**Anne Rosier**	Cd14-Deficient Macrophages Show Compromised Tolerance Induction After Repeated Antigen Stimulation And Promote Intestinal Inflammation In An Acute Mouse Colitis Model
#2	**Bei Zhao**	The Role Of The Gut Microbiota For The Mammalian Immune System: Using Inborn Errors Of Immunity As A Window Into Co-Development And Complexity
#3	**Berkay Berk**	Influence Of Ph On The Pathogenicity Of *Staphylococcus Aureus* In Atopic Dermatitis
#4	**Eva-Magdalena Schorr**	A Phenotypic Landscape Of Key Bacteroides Species
#5	**Ivan Liachko**	Building The World's Largest Plasmid-Host And Phage-Host Interaction Atlas Using Proximity Ligation Sequencing
#6	**Jana Brickem**	A Deep-Dive Into Virulence Of The *Klebsiella Oxytoca* Species Complex
#7	**Johanna Saalfrank**	Detecting Microbial Eukaryotes In Human Stool Samples From Rural Madagascar Using 18S rDNA Sequencing
#8	**Johannes Masson**	Ecology Of Secreted Bacterial Proteases In The Human Gut
#9	**Julia Koepsell**	Biomarkers For The Differentiation Of Asymptomatic Bacteriuria In Urinary Tract Infections Requiring Treatment Or In Colonization (Metabio Study)
#10	**Kora Schulze**	Characterization Of Secondary Bile Acid Producing Gut Microbiota
#11	**Kun Huang**	Establishment Of A Non-Westernized Gut Microbiota In Men-Who-Have-Sex-With-Men Is Associated With Sexual Practices
#12	**Lea Eisenhard**	*Klebsiella Oxytoca* Facilitates Microbiome Recovery Via B-Lactam Degradation
#13	**Lucía Huertas Díaz**	Consumption Of Fermented Dairy Enhances Valerate Levels Due To Megasphaera Activity
#14	**Maja Magel**	NFDI4Microbiota: Towards A FAIR Landscape Of Comprehensive (Meta)Data In Microbiome Research
#15	**Michaela Herz**	Intestinal Fungi: Dead Or Alive?
#16	**Nataliia Solntseva**	Metabolic Capabilities Of Widespread Gut Bacteria Of The Family *Sutterellaceae*
#17	**Philipp Rausch**	First Insights Into Microbial Changes Within An Inflammatory Bowel Disease Family Cohort Study
#18	**Svenja Schorlemmer, Mariia Lupatsii**	Deciphering Hormone-Microbiome Interplay In The Context Of Assisted Reproduction Treatment
#19	**Sylvio Redanz**	Identification Of SLE-Derived Human Translocating Microbiota – A Humanized Mouse Model
#20	**Toni Sempert**	The Stratification By Age Is Critical For Microbiome Analyses Of Children With Juvenile Idiopathic Arthritis
#21	**Stefany Ayala Montaño**	A Colonizer Or A Threat? Colonization Dynamics Of Early-Life Microbiomes In A Neonatal Intensive Care Unit

ABSTRACT COLLECTION

HOW BUGS STAY TOGETHER – COOPERATION AND COMPETITION FOR PLACE IN COMMUNITIES

Kiran R. Patil[1,2], Patil lab members[1]

[1]MRC Toxicology Unit and [2]Department of Biochemistry, University of Cambridge, UK

The phylogenetic and metabolic diversity of the gut microbiota is fundamental to the beneficial impact on host through its emergent properties, including resilience to biotic and abiotic perturbations. While factors like diet are correlated with diversity, mechanistic insights remain obscure due to limited understanding of inter-species interactions. This is highlighted by a striking discrepancy between growth fitness of a species in monoculture and its relative abundance in the gut microbiota. I will present results from assembly studies under controlled nutrient conditions showing how species survival is jointly determined by supplied resources and community metabolism. Over 95% of the tested gut bacterial species show markedly improved or diminished performance relative to monoculture, including numerous cases of emergent survival, i.e., species incapable of surviving on their own but thriving in a community. With these and other examples, I will discuss the role of communal metabolic dividend as a key biotic force promoting emergent survival and diversity in microbiomes and its implications for precision probiotics.

IDENTIFICATION OF SECRETED SERINE PROTEASES IN *PHOCAEICOLA VULGATUS*

Ning Qu[1], Kemal Bandu, Christian Preissinger[2], Marléne Birk, Joel Selkrig

[1]*Institute of Medical Microbiology, RWTH Aachen University Hospital, Aachen 52074, Germany*
[2]*IZKF Proteomics Core Facility, RWTH Aachen University Hospital, Aachen 52074, Germany*

Phocaeicola vulgatus, a highly abundant anaerobic bacterium in the human gut microbiome, plays a crucial role in maintaining intestinal health. However, certain strains have been linked to greater disease severity in ulcerative colitis (UC) patients. Accumulating evidence suggests that proteases, especially serine proteases, may contribute to the pathogenesis of UC by degrading the intestinal barrier, leading to intestinal inflammation. However, it remains unclear which serine proteases *P. vulgatus* secretes and their function. To elucidate which serine proteases *P. vulgatus* secretes, the fluorophosphate (FP) chemical warhead conjugated to fluorescent TAMRA (TAMRA-FP) was used to selectively and covalently react with the active site of intra- and extra-cellular serine proteases from *P. vulgatus*. Three serine protease candidates were selected based on molecular weight, putative proteolytic activity, and abundance, *i.e.*, BVU_2253, BVU_2252, and BVU_1991. The serine hydrolase activity of these candidates was verified in mutants overexpressing these genes or knockout strains. Our result suggests that the most abundant and active serine protease secreted by *P. vulgatus* is BVU_2253 (dipeptidyl-peptidase 11). Furthermore, we show that BVU_2253 over-expression protects *P. vulgatus* against extracellular attack from serine proteases, *e.g.,* trypsin and proteinase K. Taken together, our work identifies the major serine protease secreted by *P. vulgatus* (ATCC 8482) and suggests it may play a role in mediating protection against attack by hydrolytic enzymes within the gastrointestinal lumen. Future work will focus on exploring the impact of BVU_2253 on intestinal barrier erosion.

INSIGHTS INTO *PHOCAEICOLA VULGATUS* BACTERIOPHAGE DIVERSITY

Lina Michel[1,2], Alexandra von Strempel[1], Monica Steffi Matchado[1], Bärbel Stecher[1,3]

[1] Max von Pettenkofer Institute of Hygiene and Medical Microbiology, Faculty of Medicine, LMU Munich, Munich, Germany
[2] European Molecular Biology Laboratory, Genome Biology Unit, Heidelberg, Germany
[3] German Center for Infection Research (DZIF), partner site LMU Munich, Munich, Germany

Phocaeicola vulgatus is a prevalent member of the core microbiota in the mammalian intestinal system. Strains of *P. vulgatus* have been associated with human health but have also been described in the context of chronic intestinal inflammation; the species possesses thus a broad range of strain diversity with different pathogenic potential. Bacteriophages (phages) are highly abundant in microbial communities in various environments. They are important effectors and indicators of human health and disease by managing bacterial population structures and by targeting community functions, yet gut-resident phages and their interactions with the bacterial hosts remain poorly understood. Employing a *P. vulgatus* strain collection comprising isolates from different gut environments, 18 strain-specific *Siphoviridae* phages were isolated from sewage water. The *P. vulgatus* phages exhibited diverse plaque morphologies and a range of lysis kinetics on their host strains. Plaque assays showed very narrow host ranges, almost exclusively restricted to the respective host strains, while growth in liquid culture revealed eight out of 18 phages to inhibit the growth of several strains. Testing the *P. vulgatus* phages for their efficacy as potential therapeutic phage cocktails, no increase in virulence was observed compared to single phage infections. Lastly, the *P. vulgatus* phages were shown to facilitate directed strain replacement in batch culture of two competing strains, providing a proof-of-concept for potential strain replacement therapies targeting *P. vulgatus*. Taken together, this study established a collection of *P. vulgatus* isolates with a corresponding collection of strain-specific phages, expanding the knowledge on gut-resident phages and laying a base for further studies on the use of phages as tools for targeted microbiota manipulation.

ECOPHYSIOLOGY OF TRIMETHYLAMINE-PRODUCING BACTERIAL COMMUNITIES OF HUMAN GUT MICROBIOTA

Ylenia Heinrich Sanchez [1], Sabrina Woltemate [1], Katharina Rox [2 3], Mark Brönstrup [2], Madeline Bartsch [4 5], Henrike-Anne Freke [1], Torben Schweer [6], Marius Vital [1]

[1] Medical Microbiology and Hospital Epidemiology, Hannover Medical School (MHH), Hannover, Lower Saxony, Germany
[2] Chemical Biology, Helmholtz Center for Infection Research (HZI), Braunschweig, Lower Saxony, Germany
[3] German Center for Infection Research (DZIF), Partner Site Hannover-Braunschweig, Braunschweig, Lower Saxony, Germany
[4] Institute of Food Science and Human Nutrition, Leibniz University Hannover, Hannover, Lower Saxony, Germany
[5] Nutrition Lab- Faculty of Agricultural Sciences and Landscape Architecture, Osnabrueck University of Applied Sciences, Osnabrueck , Lower Saxony, Germany
[6] Nephrology and Dialysis, Klinikum Peine, Peine, Lower Saxony, Germany

The gut microbiota (GM)-derived metabolite trimethylamine (TMA) is converted by host enzymes to trimethylamine-N-oxide, which is involved in the promotion of cardiovascular diseases and kidney function impairment. Of most importance are bacteria harbouring the cut gene cluster that produce TMA from the dietary precursor choline. Currently, a comprehensive analysis of cut gene carriers, as well as information on their ecophysiology are largely lacking, which is indispensable to develop therapeutic strategies to restrict their growth and reduce TMA production. Here, we verified TMA production of predicted cut gene carriers and characterized their nutritional niche. We first applied in silico screening approaches to identify potential TMA producers and assessed their abundance and prevalence using publicly available metagenomic datasets. Main contributors are members of the Proteobacteria and Firmicutes that are ubiquitously present at low abundances. For the poorly described Firmicutes their ability to produce TMA was verified in vitro under anaerobic growth conditions via LC-MS/MS. Pure culture experiments revealed a broad substrate spectrum involving many simple sugars. Contrarily, we observed only a limited capacity for polysaccharide degradation with Inulin as the only substrate stimulating growth; transcriptomics analyses elucidating the involved enzymes are currently performed. Additionally, ex vivo experiments based on human stool with selected polysaccharides verified that TMA-producers benefit from Inulin as well as its monomers during competitive growth with other gut bacteria. Lastly, we are currently analysing a cohort of chronic kidney disease patients, where TMA(O) excretion is blocked, to investigate major factors (diet and gut microbiota functioning) that govern TMAO concentration in vivo. Our work identified major TMA-producing Firmicutes and adds crucial information on their ecophysiology specifying their nutritional niches. In combination with investigations on TMA-synthesis dynamics in vivo it represents an important step towards the development of personalised nutritional strategies limiting production of the hazardous compound TMA(O).

EFFECTS OF THE DIET-MICROBIOTA AXIS ON IMMUNITY AND TUMOR THERAPIES

Nicola Gagliani

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As the result of a team effort, we recently contributed to the discovery that not only can the type of diet impact the immune response, but also the length of exposure to that particular diet. In the first study, we found that sudden and short-term changes between a diet rich in fiber and one poor in fiber significantly impact the immune response. Specifically, a sudden withdrawal of fiber leads to a drop in the amount of microbiota-derived short-chain fatty acids, which in turn leads to mucosal and systemic immune depression in mice. Consequently, the mice become more susceptible to infections. Mechanistically, this is due to the inability of T cells to meet the energetic rearrangement needed to secrete both type 1 and type 3 cytokines. This effect is reproducible in volunteers undergoing a switch in their diet for just five days (Siracusa N. et al., Nature Immunology, 2023). Next, we investigated the impact of a short dietary intervention characterized by a diet rich in tryptophan on the efficacy of chemotherapy in pancreatic ductal adenocarcinoma (PDAC). We found that a microbiota-derived tryptophan metabolite, indole-3-acetic acid (3-IAA), boosts the response to chemotherapy in a preclinical mouse model of pancreatic cancer. The mechanism behind this enhancement is that MPO, which might be released by neutrophils infiltrating the tumors, leads to the oxidation of 3-IAA into 3-methylene-2-oxindole (MOI). In parallel to the accumulation of MOI, the autophagy activity in tumor cells, a key evasion mechanism of pancreatic cancer cells, was reduced. We found that once autophagy is reduced, the tumor cells are more susceptible to chemotherapy. Finally, we observed a correlation between the concentration of 3-IAA and the survival of PDAC patients in two independent cohorts (Tintelnot J. et al., Nature, 2023). Overall, our data illustrate that the type of diet as well as the length of exposure to certain macro and micronutrients can significantly impact the immune system and even cancer therapy outcomes. This research provides scientific evidence to increase awareness of the impact our daily food choices have on our health. Additionally, these findings open the door to potential nutritional interventions and, if it becomes too late to change dietary habits, using specific metabolites as integral components of many therapies in the near future.

Disclosure: Similar abstracts have been published at the Keystone Meeting, USA and at the Annual Meeting of SAI, Argentina.

KLEBSIELLA OXYTOCA FACILITATES POST-ANTIBIOTIC MICROBIOME RECOVERY AND RESTORES COLONIZATION RESISTANCE IN A DIET-DEPENDENT MANNER

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Competition among bacteria for carbohydrates is pivotal for colonization resistance (CR). However, the impact of Western-style diets on CR remains unclear. Here, we show how the competition between *Klebsiella oxytoca* and *Klebsiella pneumoniae* is in an animal modulated by consuming one of three Western-style diets characterized by either high-starch, high-sucrose, or high-fat/high-sucrose content. *In vivo* competition experiments in ampicillin-treated mice reveal that *K. oxytoca* promotes *K. pneumoniae* decolonization on all dietary backgrounds. However, mice on the high-fat/high-sucrose diet show reduced pathogen clearance. Microbiome analysis reveals that the combination of Western-style diets and ampicillin treatment synergize in microbiome impairment, particularly noticeable in the presence of high dietary fat content. Furthermore, we identify diet-specific expansions of bacteria with pathogenic potential such as Enterococcaceae and Staphylococcaceae, which *K. oxytoca* prevents. Our findings provide insights into how diet modulates functional microbiome recovery and *K. oxytoca*-mediated pathogen elimination from the gut.

DISTINCT COLONISATION PATTERNS AND IMMUNE INTERACTIONS DELINEATE COMMENSAL AND PATHOGENIC STRAINS *OF STAPHYLOCOCCUS EPIDERMIDIS*.

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Staphylococcus epidermidis is a pioneer and a beneficial coloniser of the mammalian skin. However, it has recently emerged *as* an important opportunistic pathogen. *S. epidermidis* ranks as a major causative agent of sepsis, particularly in preterm infants and immunocompromised patients. The persistent and ubiquitous colonisation of the skin, rather than presence of the virulent determinants, defines the “accidental” nature of *S. epidermidis* infections. However, the multidrug resistance and the biofilm formation of strains causing nosocomial infections make treatment extremely difficult. Previous studies based on genome-wide approaches and in vitro research have failed to identify the determinants that distinguish pathogenic and commensal *S. epidermidis* strains, delaying the implementation of therapeutic strategies to eradicate the pathogens. A high-resolution strain-functional analysis of the skin-colonising *S. epidermidis* community revealed a genomic signature driven by environmental pressure and host colonisation. However, this analysis was unable to discriminate between host biofilm-forming and commensal strains, as the genomic determinants for both lifestyles are shared. Since host interactions define the genomic signature of skin colonisers, we reconstructed the early-life colonisation dynamics using human 3D-epidermal and gnotobiotic mouse models exposed to very low biomass bacteria to highlight the unique features employed by commensal and pathogenic strains. Commensal strains rapidly seed and colonised the skin. They housed in deep layers of the stratum corneum and transiently enhanced tissue resident immune cells. In contrast, pathogenic strains failed to expand on the skin, but aggregated in silent biofilms on the surface. However, their long-term habitat on the skin triggered tissue inflammation, as evidenced by inflammatory cytokine production, Langerhans cell activation and neutrophil infiltration. Additionally, in the event of bacteremia, pathogenic strains escaped the liver firewall and spread systemically. Furthermore, these pathogens efficiently colonised and expanded in the gut, as previously observed in infants with necrotic enterocolitis. Taken together, our data reveal unique features that distinguish commensal from pathogenic strains of *S. epidermidis,* which will be further delineated to develop targeted therapeutic strategies that eradicate pathogens while preserving the commensal community.

VAGINAL MICROBIAL DYNAMICS ARE LINKED TO REDUCED COLONIZATION RESISTANCE TO CHLAMYDIAL INFECTION

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Chlamydia trachomatis is the most common bacterial sexually transmitted infection worldwide. The infection is frequently asymptomatic and, hence, left untreated in many infected individuals. These untreated infections can cause ascension of the pathogen, leading to severe sequels such as pelvic inflammatory disease, ectopic pregnancies, or infertility in women. Together with other sexually transmitted infections (STIs) such as *Neisseria gonorrhoeae*, genital tract infections are responsible for a high burden of childless couples in industrialized countries. With women younger than 25 years being of increased risk for exposure to the pathogens, recent data indicate that vaginal microbiota directly influence the susceptibility and course of STIs. However, no longitudinal data linking microbial dynamics with STIs exist and experimental approaches on microbiome-pathogen interactions are scarce. Little is, thus, known about the microbiome-induced colonization resistance to STIs and by what mechanisms the colonization resistance to STIs is perturbed by dysbiosis microbial communities.

We are targeting this question in a multidimensional approach consisting of observational studies in humans and a variety of experimental models to functionally uncover mechanisms of microbial interactions and their contribution to the course of the infection. We are currently disentangling microbial dynamics and co-occurrence networks in the vagina of healthy young women aged between 18 and 22 years. We have recently identified particular microbial structures consisting of a network of *Ureaplasma parvum* and several *Gardnerella vaginalis* strains which likely provide functional shifts via bacterial interactions and are linked to increased susceptibility to genital tract infection by STIs. The complex interplay between the infection, the immune response, and, in particular, the role of the vaginal microbiota, we are further dissecting in mouse experiments and adjacent in vitro models. We show that hormone-induced disbalance of the microbiota induces loss of colonization resistance in vaginal chlamydial infection. Moreover, we could identify that a secreted microbial factor is present which targets the intracellular life stages of the chlamydial life cycle. In particular, the homotypic fusion of chlamydial inclusion is being inhibited, which in turn leads to reduced infectious progeny. The details of the underlying mechanisms in the interplay between the microbiome and the pathogen are yet to be understood but our data already now offer ideas about translational approaches to increase the population-wide colonization resistance to STIs.

KEYSTONE GUT BACTERIA PROMOTES MICROBIOTA RECOVERY AND PATHOBIONT CLEARANCE

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The mammalian gut microbiota plays a pivotal role in various aspects of host health, ranging from nutrition, immune system maturation, and protection against intestinal pathogens. Many environmental factors can influence the composition and function of the gut microbiota. Notably, antibiotic treatments can inadvertently perturb the gut microbiota, rendering the host more susceptible to infections and chronic inflammation. While studying mechanisms underlying microbiota recovery after the cessation of antibiotic treatment, we identified a non-pathogenic *Klebsiella* gut microbe capable of restoring colonization resistance against Enterobacteriaceae following antibiotic treatment. This particular non-pneumonia *Klebsiella* species represents a keystone member of the mammalian gut microbiota found in both mice and humans. In wild-type mice, our studies demonstrated that this bacterium was sufficient for providing colonization resistance against *Escherichia coli* K-12 and delayed the colonization of *Salmonella* Typhimurium through a mechanism of nutritional competition (as detailed in Oliveira et al., Nature Microbiology, 2020). Building on this foundation, we are now expanding our research to explore the potential use of this *Klebsiella* strain as a next-generation probiotic. Our latest findings show that in a mouse model of inflammatory bowel disease, this keystone *Klebsiella* accelerates the clearance of Adherent and Invasive (AIEC) *E. coli*. It achieves this by promoting the recovery of butyrate-producing bacteria and preventing inflammation. These results underscore the importance of identifying microbes with critical microbiota functions and their potential use in developing strategies to facilitate microbiota recovery following antibiotic treatments.

ANTI-FUNGAL IMMUNITY IN HUMANS: AT THE INTERSECTION OF PROTECTION AND INFLAMMATORY DISEASE

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Aberrant CD4+ T cell reactivity against intestinal microbes is considered to drive mucosal inflammation in inflammatory bowel diseases (IBD). The disease-relevant microbial species and the corresponding microbe-specific pathogenic T cell phenotypes remain largely unknown. By using sensitive and specific technologies to study microbe-reactive CD4+ T cells in human samples, we identify common fungal microbes as direct activators of altered CD4+ T cell reactions in patients with Crohn´s disease (CD). Fungus-responsive CD4+ T cells in CD display a cytotoxic Th1 phenotype and show selective expansion of T cell clones that are highly cross-reactive to several fungal species. This indicates cross-reactive T cell selection by repeated encounter with conserved fungal antigens in the context of chronic intestinal disease. Our results highlight a role of fungi as drivers of aberrant CD4+ T cell reactivity in patients with CD and suggest that repeated encounter with conserved antigens present in different fungal species may lead to the expansion and chronic activation of cross-reactive CD4+ T cells. This could reveal a general mechanism how selection of cross-reactive T cells may allow adaptive immunity to cope with the enormous diversity of microbial antigens which, if not properly regulated, could come at expense of fostering chronicity and contribution to therapy resistance in IBD due to persistent antigen activation.

TARGETING THE GUT MICROBIOTA IN INFLAMMATORY BOWEL DISEASES: WHERE ARE WE?

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Microbiome-targeting therapies, such as fecal microbiota transfer (FMT), are being studied as a treatment for a wide range of diseases. FMT involves the transfer of a complex, screened healthy donor microbiota into a recipient in order to improve a clinical condition, that is driven or influenced by the intestinal microbiota. Whereas FMT cures 90% of recurrent *Clostridioides difficile* infections and is now part of clinical care pathways, the role of FMT in inflammatory bowel diseases (IBD) remains uncertain. In patients with ulcerative colitis (UC), FMT has shown the potential to induce remission (disease quiescence) in about 30% of participants in several small clinical trials. In contrast, the use of FMT for the treatment of Crohn's Disease (CD) is poorly studied. There is no controlled trial of FMT for induction of remission in patients with active CD. Interestingly, one trial shows some benefit of FMT for maintenance of remission after steroid induction therapy. However, identification of key success criteria for FMT remains difficult due to substantial heterogeneity between studies in FMT administration (e.g. variable dose, frequency, route of administration and duration of therapy), stool preparation (e.g. aerobic vs anaerobic; frozen vs fresh), timing (induction vs maintenance), FMT preconditioning or concomitant therapies. Furthermore, emerging evidence suggests that factors associated with proper donor-recipient pairing are important to promote engraftment which is often directly associated with clinical improvement. Most likely, engraftment potential is dependent on unoccupied ecological niches in the recipient microbiota pre-FMT. I will describe the lessons learned from past studies, recent advances in clinical trials as well as challenges of the integration of microbiota therapeutics in the treatment of IBD.

HOST-MICROBIOME INTERACTIONS IN THE CONTEXT OF RECENT HUMAN EVOLUTION

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Concurrent with urbanization and industrialization of lifestyles, the human gut microbiome dramatically shifts in composition and diversity. However, to what extent lifestyles transition impacts host-microbiome interactions and host physiology is unknown. In 2016, we founded the Global Microbiome Conservancy a non-profit initiative to 1) preserve the biodiversity of the human gut microbiome, 2) characterize its evolution across populations and host lifestyles and 3) investigate its interactions with the human host. We generated gut microbiome multiomics data coupled with host DNA and physiology data from dozens of populations worldwide, ranging from gatherers to fully industrialized groups. Leveraging these resources, we show that intestinal inflammation, humoral immune response, and patterns of horizontal gene transfers (HGT) between bacteria strongly associate with the host lifestyle. We reveal that gut microbiomes of industrialized individuals associate with elevated secretion of intestinal immunoglobulin A, despite lower levels of parasitic incidence. Furthermore, populations with 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 of lifestyles perturbs our gut ecosystem and homeostasis on many levels, which could contribute to chronic inflammation diseases.

MULTI-OMICS ANALYSIS OF GUT MICROBIOTA UNVEILS MICROBIAL FUNCTIONS ALTERATIONS ASSOCIATED TO PARKINSON'S DISEASE.

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Objective:

Microbiome composition has been associated with Parkinson's disease (PD) at multiple stages. However, these associations are mainly studied using genomics technologies where the functional capacities of microbes are not fully investigated. In this study, we aim at describing the microbiome functions associated with PD using multi-omics technologies.

Methods:

Using integrated multi-omics analysis, we performed deep phenotyping of the gut microbiome in a cross-sectional cohort of 49 healthy control (HC), 28 iRBD and 46 PD patients. Stool samples were phenotyped using shotgun metagenomics (MG), metatranscriptomics (MT), metaproteomics (MP) and metabolomics (MB).

Results:

The gut microbiome showed no clear differences between groups both in alpha and beta-diversity for MG and MT taxonomic composition but differences in MT functions and MB. *Roseburia, Blautia* and *Eubacterium* were however reduced in PD for MT taxonomy. We observed a decrease in glycerol which correlated with *Roseburia* abundance and an increase beta-glutamate for PD patients that was correlated with *Akkermansia* and *Methanobrevibacter* abundance. We observed an increase and a decrease in diversity of gene expression in PD patients for *Methanobrevibacter* and *Roseburia*, respectively. Interestingly, we found important changes in gene expression that were related to glutamate transformation, chemotaxis-flagellin assembly and methane metabolism. Finally, we witnessed a decrease in functional diversity for *Roseburia*, *Eubacterium* and *Blautia*, while *Methanobrevibacter* gained functional diversity.

Conclusions:

MT and MB represented the most powerful omics to differentiate the gut microbiome from HC and PD patients. Microbial functions appeared to be altered in PD context, especially for *Roseburia* and *Methanobrevibacter* that seemed to have contrary links to PD.

DEEP VISUAL PROTEOMICS REVEALS IN VIVO-LIKE FUNCTIONALITY IN ORTHOTOPICALLY TRANSPLANTED HUMAN COLON ORGANOIDS

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The intestinal epithelium plays a central role in human health and disease, and several chronic inflammatory disorders associate with a weakened epithelial barrier. The organoid model allows the cultivation, expansion and analysis of non-immortalized intestinal epithelial cells and has been instrumental in studying epithelial behavior in homeostasis and disease. Recent advances in human organoid transplantation into mouse and human lay the base for models to study human epithelial cell behavior within the intestinal tissue context, and promise novel therapeutic approaches for diseases such as short bowel syndrome and inflammatory bowel disease. It remained unclear how organoid transplantation into the colon would affect epithelial phenotypes and protein expression, which is key to assess the suitability of this model to study human epithelial cells *in situ* and as a therapeutic approach. To address this, we employed Deep Visual Proteomics, which utilizes AI-guided cell classification on high-resolution images, microdissection, and high-sensitivity proteomics, on human colonic epithelial stem and differentiated cells *in vivo*, upon transplantation *in situ,* and organoids cultured *in vitro.* We find that organoids transplanted into the murine colon closely resemble human intestinal epithelial cells *in vivo* compared to organoids grown *in vitro*, indicating that organoid culture induces a transient shift in epithelial phenotypes, which is reversible upon reintroduction into the mucosa. Phenotypic differences between epithelial cells *in vitro* and *in situ*/*in vivo* were largely driven by hallmarks of high proliferation and lower functional differentiation in organoids due to culture conditions. Taken together, we demonstrate that transplanted epithelial cells *in situ* represent a physiological, relevant model for studying functional aspects of mature colonocytes, e.g. in the context of epithelial repair and host-microbe interaction.

IMPACT OF ANTIDEPRESSANTS ON HUMAN GUT MICROBIOTA

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Previous studies have demonstrated that human-targeted non-antibiotic medications significantly impact the growth characteristics of various human gut bacteria. Notably, psychotropic drugs, especially antidepressants and antipsychotics, exhibit discernible effects on specific gut bacteria that extend beyond their chemical characteristics. The antimicrobial properties of these drugs suggest their potential to reshape the composition and functional attributes of gut microbial communities in patients using them, although the biological significance and mechanisms driving these changes remain incompletely understood. One possible implication of these effects is that the alteration of the microbiome by psychotropic drugs might contribute to side effects and tachyphylaxis, yet it's also conceivable that such microbial shifts play a role in the therapeutic outcomes of these drugs. Our aim was to assess how the presence of antidepressants impacts the structure and function of human gut microbial communities. To achieve this, we investigated the effects of commonly prescribed antidepressants on structural and functional aspects of bacterial communities by analyzing metagenomic and growth dynamics in both monocultures and synthetic and complex human-derived communities. To emulate the chronic administration of these drugs, which typically requires several weeks for clinical effects to manifest, we subjected bacterial communities to repeated exposure to predicted colon concentrations of common selective serotonin reuptake inhibitors (SSRIs) over a four-week period. Additionally, we examined the growth of bacteria persistently exposed to SSRIs under different conditions of drug exposure and nutrient availability to better understand the consequences of long-term exposure. In the acute setting, commonly prescribed antidepressants were found to inhibit the growth of commensal bacteria in the human gut, as well as overall growth in synthetic and human-derived communities. Interindividual differences in growth dynamics among human-derived communities indicate that changes in microbial composition might be associated with individual differences in response to psychotropic medication. Chronic exposure experiments indicated that SSRIs with distinct acute effects may lead to similar restructuring of human gut microbial communities after repeated exposure, suggesting that long-term effects of these drugs could be associated with specific changes in the gut microbiome of patients. Moving forward, we aim to assess whether the observed effects in vitro correspond to biological processes in vivo. This will involve studying community dynamics in gnotobiotic mice repeatedly exposed to clinically relevant doses of SSRIs and evaluating structural and functional changes in microbial communities from patients undergoing treatment at various stages.

HOST MICROBIAL INTERACTIONS: FAECAL MICROBIOTA TRANSPLANTATION TO TACKLE ANTIMICROBIAL RESISTANCE FROM POO TO POLICY.

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Background and Aims: The World Health Organization States Antimicrobial Resistance (AMR) is "the biggest threat to global health". Patients with cirrhosis are at high risk for AMR because of frequent antimicrobials, regular invasive procedures such as large-volume paracentesis, and recurrent hospitalisations. Gastrointestinal tract carriage of Antibiotic Resistance Genes (ARGs) increases with advancing cirrhosis and is associated with increased hospitalisation and mortality. Microbiota perturbations, intestinal inflammation, and barrier damage boost ARG carriage and susceptibility to infection. Translocation of bacteria and their products across the gut-epithelial-barrier induces cirrhosis-associated immune dysfunction. We hypothesised that faecal microbiota transplant (FMT) may reduce Gastrointestinal tract ARG carriage and enhance intestinal barrier function and mucosal immunity.

Method: 32-patient prospective, randomised, single-blinded, placebo-controlled trial evaluating jejunely-transplanted FMT [50g] against placebo [PROFIT Trial: NCT02862249] in patients with advanced stable cirrhosis (MELD 10-16). We assessed the impact of FMT/placebo 7, 30 and 90-days post-intervention on enteric pathogen and ARG carriage. Plasma and faecal cytokines, gut barrier integrity markers (electrochemiluminescence/ELISA), metabonomics (1H-NMR), and faecal proteomics were performed. Phase-Genomics-ProxiMeta™-Metagenome-Deconvolution was undertaken to capture co-located-DNA enabling strain-level assignment of phages/ARGs within microbes, not previously possible.

Results: FMT reduced intestinal barrier damage and modified mucosal and systemic inflammation. 20% of participants were colonised with Multi-Drug-Resistant-Organisms including vancomycin-resistant *Enterococci*. FMT virtually eradicated carriage of *Enterococcus faecalis*, Enteropathogenic *Escherichia coli* (EPEC) and ARG [*e.g.*, vanD contributing to vancomycin resistance in *E. faecalis*]. A healthy phagosome, *via* bacterial lysis, drives

microbial diversity and stabilizes microbial populations. We observed bacteriophage network remodelling post-FMT such as the presence of beneficial phages from the family *Oscillospiraceae* which includes *Faecalibacterium prausnitzii*. This contrasted with loss of phages from *E. faecalis*, EPEC and *Klebsiella*. Faecal proteomics quantified 301 proteins modified post-FMT, including enzymes involved in host/microbial immuno-metabolism alongside reduced proteins involved in bacterial virulence and AMR.

Conclusion: FMT increased gut microbial richness, reduced carriage of enteric pathogens, and reduced vancomycin-associated ARGs. This was associated with favourable phage network remodelling. FMT reduced intestinal barrier damage and systemic inflammation. Findings support continued evaluation of FMT as a treatment to reduce AMR in cirrhosis and other systemic inflammatory diseases driven by intestinal barrier damage.

FMT DONOR SCREENING EXPERIENCE IN GERMANY

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The potential of Fecal Microbiota Transfer (FMT) to restore a disrupted microbiota is increasingly recognized, not only as a treatment for recurrent *Clostridioides difficile* infection (rCDI) but also in the context of other indications. FMT products are manufactured using feces from carefully selected healthy individuals who undergo an extensive screening procedure, to decrease the risk of transferring potential pathogens or diseases to the recipients.

Between January 2021 and November 2023, 299 individuals registered interest in becoming a feces donor at the Cologne Microbiota Bank (CMB). Of these, 131 (43.8%) completed a written questionnaire, while the remaining 168 (56.2%) did not respond. 70 out of 131 (53.4%) individuals proceeded to the laboratory testing, while findings in the questionnaire led to an exclusion of 61 out of 131 (46.6%) individuals. Out of the 70 individuals without any critical findings in the questionnaire, 61 proceeded to the laboratory testing, while 9 were lost to follow-up. Among the 61 individuals who provided stool samples for screening, 34 (55.7%) were excluded due to one or more detected pathogens. The most frequent pathogens were *Blastocystis hominis* (12/34, 35.3%), *Dientamoeba fragilis* (11/34, 32.4%), pathogenic *Escherichia coli* (8/34, 23.5%), ESBL-producing bacteria (7/34, 20.6%), *Helicobacter pylori* (2/34, 5.9%). 27 out of the 61 (44.3%) screened subjects showed no detectable pathogens in their stool samples analyzed, making them eligible for subsequent blood screening. One of the 27 subjects was lost to follow-up and 26 subjects provided a blood sample. Among these, 3 (11.5%) were excluded due to an acute Hepatitis E Virus (HEV) infection, 1 (3.9%) due to a positive syphilis titer, and 22 (84.6%) completed the screening without critical findings. In total, 22 out of 299 (7.4%) individuals successfully completed the entire screening process, constituting 7.4% of those initially registered (n=299) and 36.1% of those undergoing sample analysis (n=61).

Currently, data on safety and efficacy of the FMTs derived from the feces donations of these donors are under analysis and will be available by the time of the conference.

In conclusion, the rigorous screening at the CMB highlights the importance of meticulous donor selection in ensuring the safety of FMT products.

PRECISION METAGENOMICS REVEALS DYNAMIC CHANGES IN PLASMID AND PHAGE INTERACTION NETWORKS FOLLOWING FECAL MICROBIOTA TRANSPLANTATION

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Fecal microbiota transplantation (FMT) has proven effective for recurrent Clostridioides difficile infection (rCDI). However, the analysis of microbiome response has been hindered by limitations in 16S and metagenomic shotgun sequencing, particularly in associating mobile elements (plasmids and phages) with their microbial hosts. Studies using bacteria-free filtrates from fecal suspensions have shown comparable efficacy to whole fecal material in rCDI treatment, suggesting the involvement of phages and plasmids in gut remodeling.

Proximity ligation sequencing (Hi-C) is an approach that crosslinks genomic material within cells, capturing physical interactions between the host microbial genome and mobile elements. In addition to recovering highly complete microbial genomes, proximity ligation approaches allow for the recovery of the phage-host and plasmid-host interactome.

We employed this approach with a cohort of 48 patients receiving FMT from a single donor, sampling over several weeks following FMT delivered using oral capsules. Our analysis reveals unique, patient-specific patterns of engraftment, a significant increase in prokaryotic genome diversity, temporal changes in the biosynthetic capacity of the gut, and a re-configuration reminiscent of the donor. Phage-bacteria interactions also exhibit patient-specific patterns. The observed increase in phage diversity post-FMT aligns with that seen in the microbial populations, and is linked to multiple sources, including a donor-derived influx and baseline-derived persistent phages. In some cases, engrafting phages locate new hosts, a poorly understood phenomenon standing in contrast to a canonical “one phage, one host” model. Finally, we show that a failure in initial engraftment of phages may be predictive of FMT failure.

FASTING SUPPRESSES A PATHOGENIC TH17 CELL-INDUCING GUT PATHOBIONT IN RA PATIENTS

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Background: The mucosal origins hypothesis suggests rheumatoid arthritis (RA) is triggered at mucosal sites in genetically predisposed hosts. Mucosal sites can be modulated by dietary interventions. A 7-day fasting intervention on RA patients was shown to clinically improve disease severity, but the mechanisms are unknown. Here, we explore host-microbiota interactions involved in fasting of RA patients.

Methods: Patients fasting (n=10) and under an anti-inflammatory diet (n=8) were characterized for fecal microbiomes (16S rDNA sequencing and qPCR), circulating cytokines, and metabolomes. A heat-killed candidate bacterium was co-cultured with PBMCs from healthy individuals to determine human Th17 induction *in vitro* (n=8). Wilcoxon and Whitney tests were used to compare baseline *vs* intervention and dietary groups. Linear mixed models were used to evaluate differences in IL17 levels over time between two groups.

Results: Fasting RA patients showed reduced circulating lymphocyte counts (p=0.008) while increased ketone bodies (p= 0.008). The gut microbiome was also differentially modulated to control patients. *Bifidobacterium adolescentis* (BA) was the most reduced species under fasting compared with the control diet (p= 0.014; LDA score=5.51) and to baseline (p=0.031). BA+ RA patients, independently of the dietary regimens, displayed higher serum levels of IL-17 than patients not colonized with this species (p=0.037). *In vitro* studies with human PBMCs revealed that BA induces IL-17+IFNg+ pathogenic Th17 cells (p=0.008).

Conclusions: Our data demonstrates that a 7-day fasting intervention in RA patients alters the gut microbiota and suppresses BA, which can induce human IL-17+IFNg+ pathogenic Th17 cells *in vitro*. This bacterium was previously shown to be ketone-sensitive, to induce intestinal Th17 in mice (Ang et. al., Cell, 2020), to exacerbate experimental arthritis (Tan et. al. PNAS, 2016) and to disrupt epithelial barrier function (Bootz-Maoz et. al. Cell Rep, 2022). Altogether, our results put forth a diet-sensitive candidate pathobiont in human RA. They also delineate a host-microbiota interaction that may partly explain the rapid, beneficial effects of fasting in patients with RA.

SECRETED GUT MICROBIOTA PROTEINS AS MEDIATORS OF ORGAN CROSS-TALK

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The gut microbiome impacts critical aspects of human health such as development and activation of the immune system, defense against pathogens or nutrient liberation. Proteins produced by bacteria in the gut have been found to translocate to the liver, heart, kidney, spleen, and brain. Yet the full diversity of these mobile proteins, their tropism for specific organs and their function in target organs remains to be resolved. To identify bacterial proteins amidst the complex mix of host and other microbial proteins in tissue, we have adapted an innovative Click-chemistry based labelling approach. By mutating a bacterium of interest to incorporate a non-canonical amino acid (ncAA) with an azide or alkyne group, newly synthesized bacterial proteins can be labeled (in situ). Bacterial proteins containing ncAA‘s can then be selectively retrieved and identified by mass spectrometry or visualized by coupling to fluorophores. The integration of a non-canonical amino acid with azide or alkyne attachment into wild-type bacterial strains without genetic mutation further broadens the applicability of this technique, enabling comprehensive exploration of in vitro experiments without the need for genetic engineering. For this project we aim to establish general and cell specific ncAA labeling in the abundant gut commensals *P. vulgatus* and *B. uniformis*, track which bacterial proteins migrate to which organ systems using proteomics and tissue imaging, and identify target cell types and the functional impact of secreted gut bacterial proteins on distant organs.

PUL-DEPENDENT CROSS-FEEDING MECHANISMS BETWEEN THE GUT COMMENSAL BACTEROIDES THETAIOTAOMICRON AND THE ENTERIC PATHOGEN SALMONELLA TYPHIMURIUM

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The gut microbiota provides colonization resistance against pathogenic invaders. However, recent findings suggest that the indigenous microbiota can also provide nutritional resources to intestinal pathogens, creating a metabolic niche that supports pathogen outgrowth. For example, metabolites released during breakdown of complex glycans by *Bacteroides*—the dominant genus in the human intestine—are hypothesized to serve as nutrients for pathogens, facilitating their establishment in the gut. Consequently, targeting polysaccharide degradation in *Bacteroides* constitutes a promising therapeutic approach to actively intervene with pathogen invasion and combat intestinal infections.

Here, we dissect metabolic cross-feeding mechanisms between the representative gut commensal *Bacteroides thetaiotaomicron* (*B. theta*) and model enteropathogen *Salmonella* Typhimurium (*S.* Tm). We examined the *in vitro* growth of *B. theta* and gene expression of polysaccharide utilization loci (PULs) during cultivation in defined medium supplemented with diverse dietary- or host-derived glycans. In contrast to *B. theta*, *S.* Tm was unable to thrive on the majority of dietary glycans when provided as sole carbon source. Strikingly however, combining co-culture with spent media assays revealed the pre-degradation of these glycans by *B. theta* to support pathogen outgrowth. Using gene deletion mutants of *B. theta*, we could pinpoint specific PUL genes responsible for the cross-feeding process *in vitro*. In addition, targeted metabolomics enabled us to identify PUL-derived metabolites that constitute substrates for *S.* Tm. Together, our data suggest a metabolic interplay, in which *B. theta* facilitates the utilization of dietary and host-derived carbon sources by *S.* Tm.

COULD OFF-TARGET BINDING OF PATHOGEN-INDUCED ANTIBODIES TO COMMENSAL BACTERIA ENHANCE VACCINE EFFICACY?

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Oral vaccine-induced IgA has been shown to protect against invasive bacterial disease caused by *Salmonella* and *Shigella*. IgA typically targets bacterial surface-glycans, complex molecules that vary in their building blocks, sugar-sugar linkages and non-stoichiometric modifications. Despite glycan diversity, some apparently unrelated bacteria share glycan structures or structural sub-motifs, potentially resulting in antibody cross-reactivity. We found that oral vaccination of mice with peracetic acid-killed *Shigella sonnei* induced O-antigen-specific serum IgG responses. However, we also observed intrinsic IgM targeting of the pathogen, even in naïve vehicle-vaccinated mice, suggesting some cross-specificity exists in commensal and pathogen antibody targeting. To further investigate cross-specificity of pathogen-induced antibodies, we screened a monoclonal IgA antibody (STA5) targeting the O-antigen of related pathogen *Salmonella* Typhimurium for cross-reactivity using a microarray of 300+ known glycan structures from opportunistic and pathogen species. We identified several binding events, including targeting of opportunist *Proteus mirabilis*, which is often present in the gut as a commensal species in mice and humans, and is important for the competitive exclusion of enteric pathogens. Importantly, we also found evidence of cross-binding to commensal species within the host gut. Not only did we observe a significant population of gut commensal microbes in mouse feces of unvaccinated mice that are bound by monoclonal STA5, but we found that oral vaccination against *Salmonella* increased IgA binding of commensal species. We further isolated and confirmed antibody binding of gut commensal *E. coli* species by *Shigella*-vaccination-induced serum IgG1, IgG2b, and IgM, as well as secretory IgA within the intestine. Going forward, we hope to understand the functional importance of IgA target mimicry between intestinal bacteria on antibody-mediated protection, and on off-target effects on microbiota composition.

CD14-DEFICIENT MACROPHAGES SHOW COMPROMISED TOLERANCE INDUCTION AFTER REPEATED ANTIGEN STIMULATION AND PROMOTE INTESTINAL INFLAMMATION IN AN ACUTE MOUSE COLITIS MODEL

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Inflammatory bowel disease (IBD) is a group of chronical intestinal disorders. Although the exact pathomechanisms of IBD remain unknown, there is evidence that the intestinal inflammation is triggered by disruption of epithelial integrity and dysregulated macrophages. The “cluster of differentiation 14” (CD14) is a well-established pattern-recognition-receptor, involved in inflammatory and anti-inflammatory processes in a cell-type dependent manner. We previously identified CD14 as a protective factor in experimental IBD (BUCHHEISTER, 2017). Since it was shown that CD14 ameliorates chronic inflammation through induction of tolerance mechanisms (SAHAY 2009), CD14-dependent anti-inflammatory signaling in intestinal macrophages might be an interesting target for IBD treatment.
Therefore we aim to characterize the protective CD14-dependent effects on macrophages after repeated antigen stimulation and during acute intestinal inflammation in the Dextran-Sulfate-Sodium- (DSS) model.

The cytokine expression of Bone Marrow derived Macrophages from wildtyp (wt) mice and CD14 deficient (*Cd14*$^{-/-}$) mice were analysed after repeated Lipopolysaccharide (LPS) stimulation. Intestinal inflammation was induced by DSS and disease phenotypes were compared between wt and *Cd14*$^{-/-}$ mice after depletion of intestinal macrophages by intraperitoneal injections of Clodronate-Liposomes.

After LPS exposure there was a strong upregulation of pro-inflammatory cytokines, independent of CD14. Re-exposure to LPS hardly induced a proinflammatory response in wt-controls, whereas *Cd14*$^{-/-}$-macrophages showed increased TNFα expression.

As expected, *Cd14*$^{-/-}$ mice developed more severe intestinal inflammation after DSS treatment compared to wt-controls. Remarkably, macrophage depletion reduced the severity of disease development in both genotypes and prevented the detrimental effects of *Cd14*-deficiency during an acute colitis.
These findings demonstrate that *Cd14*-deficiency compromises tolerance induction after repeated antigen stimulation and promotes intestinal inflammation in the acute DSS colitis model likely through dysregulated macrophages. Therefore, CD14-dependent anti-inflammatory signaling in intestinal macrophages might be an interesting therapeutic target for IBD treatment.

THE ROLE OF THE GUT MICROBIOTA FOR THE MAMMALIAN IMMUNE SYSTEM: USING INBORN ERRORS OF IMMUNITY AS A WINDOW INTO CO-DEVELOPMENT AND COMPLEXITY

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Cytotoxic T lymphocyte antigen 4 (CTLA-4) insufficiency is an inborn error of immunity (IEI) characterized by patients carrying heterozygous pathogenic mutations in *CTLA4*. Disrupted T- and B-cell homeostasis due to lack of the activation-dampening signal following T cell activation through the TCR and CD28, leads to a spectrum of auto-inflammatory phenotypes, including cytopenias, inflammatory bowel disease, type 1 diabetes, eczema, and/or granulomatous lung disease. However, the penetrance, expressivity, and severity of CTLA-4 insufficiency vary even among patients carrying the same mutation, and the modifiers determining disease penetrance have remained elusive.

The microbiome plays a crucial role in maintaining host immunity, particularly in patients with a defective immune system. We therefore hypothesize that the gastrointestinal microbiome is a key determinant of phenotypic differences between affected and unaffected *CTLA4* mutation carriers. To address this hypothesis, we conducted 16S rRNA sequencing using the stool samples and correlated the microbial composition with their disease penetrance. The results revealed a significant decrease in microbial diversity among affected CTLA-4 insufficient patients compared to unaffected individuals and healthy controls. Additionally, the relative abundance of Proteobacteria is significantly higher than in healthy controls. Notably, *Campylobacter concisus*, associated with inflammatory bowel diseases (IBD), was enriched in patients experiencing enteropathy.

Our next objective is to assess whether microbial dysregulation and immunopathology improve with CTLA4-Fc (abatacept) treatment. Furthermore, employing disease models in *CTLA4*$^{+/-}$ heterozygous mice will aid in understanding the causal relationships between the observed phenotype and the microbiome. We expect that unravelling the interaction between the microbiota and the immune system in CTLA-4 insufficient patients will enhance the development of individualized therapeutic interventions, benefiting not only CTLA4-insufficient patients but also individuals suffering from anti-CTLA4-antibody treatment derived Immune-Related Adverse Events (irAEs).

INFLUENCE OF PH ON THE PATHOGENICITY OF *STAPHYLOCOCCUS AUREUS* IN ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a common inflammatory skin disease with a complex pathogenesis including imbalanced immune system signaling and impaired skin barrier. The skin pH is an integral part of the skin barrier and has been shown to be increased in AD compared to healthy controls, especially in lesional skin. Furthermore, disease flares are associated with high *Staphylococcus aureus* abundance. The *S. aureus* derived virulence factors play important roles in AD and are mostly regulated by quorum sensing (QS). QS allows bacteria to sense the bacterial density and to respond with genetic adaptation. In *S. aureus*, QS is mainly driven by the accessory gene regulator (agr) system which is influenceable by the pH. Therefore, the pH of the skin has a major impact on *S. aureus* and its pathogenicity. However, the interplay between microbe-host-microenvironment in AD is not yet fully understood. This hypothesis-based project will address the influence of the pH on the pathogenicity of *S. aureus*. Neutral pH is expected to enhance pathogenicity and growth of *S. aureus* isolates from AD patients and healthy controls in vitro and in vivo. Experiments already showed that growth of *S. aureus* isolates from AD patients and healthy controls is highly pH dependent. In addition, metabolic shifts decelerating growth occurred with varying durations depending on the pH. The slowest growth was observed at an acidic pH. Taking also the increased pH in AD into account, acidification of the skin via emollients might hamper *S. aureus* growth. This was tested in vivo with a placebo-controlled study, where first results show an effective pH reduction by an emollient in AD patients with elevated skin pH. For this study, microbiome samples, skin physiology measurements and metadata are available for further analysis. In the last step, the in vitro results need to be verified by stimulating keratinocytes/skin models with collected bacterial isolates and its supernatants at different pH.

This project will broaden our understanding about the influence of the microenvironment on the pathogenicity of *S. aureus* in the context of AD and help to improve the treatment of this skin disease.

A PHENOTYPIC LANDSCAPE OF KEY BACTEROIDES SPECIES

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Most of our knowledge on bacterial gene function stems from few model species that do not represent the large genetic diversity of the gut microbiota. Consequently, about half of all bacterial genes in the human intestinal microbiome remain poorly characterized. The goal of my project is to systematically discover the function of this so called “genetic dark matter” in two core species of the human gut microbiome, *Bacteroides uniformis* and *Phocaeicola vulgatus*.

We will use barcoded transposon mutant libraries and massively paralleled barcode sequencing to determine mutant fitness across hundreds of biological, chemical and physical conditions. For both species barcoded transposon libraries will be profiled to up to 200 conditions (biological, chemical and physical stresses), to determine by sequencing the fitness of each mutant. This enables us to link genes to phenotypes. Genes with similar phenotypes across many conditions are likely functionally related, and together with other types of information (physical complexes, structural predictions, genomic context) will give insights into gene function and organization.

A key function of gut bacteria is the degradation of dietary polysaccharides that are resistant to human ingestion. Specialized enzymes are required to break down these polysaccharides encoded on multiple Polysaccharide utilization loci (PUL). *Bacteroidetes* encode the highest number and the broadest spectrum of PULs relevant for this task. However, not all genes relevant have been discovered. A preliminary screen with 20 different Carbon sources, resulted in potentially linking 4 new PULs to their respective substrate. In the latter half of this year, I intend to shift my focus from primarily expanding the conditions for the chemical genetics screen to validating the hits generated and delving into the mechanism underlying the identified phenotype, that led to their classification as hits.

BUILDING THE WORLD'S LARGEST PLASMID-HOST AND PHAGE-HOST INTERACTION ATLAS USING PROXIMITY LIGATION SEQUENCING

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Plasmids are mediators of horizontal gene transfer (HGT) and serve as both a reservoir and vector for the spread of antimicrobial resistance (AMR) and virulence genes. Phages also shape the global ecosystem through their impacts on community composition and HGT. However, linking mobile elements to their microbial hosts has proven challenging without culture-based experiments. These experiments inherently require that all microbial hosts are culturable, typically restricting the diversity that can be surveyed and limiting our understanding of valuable mobilome relationships.

Metagenomic proximity ligation sequencing is a powerful method for associating viruses and plasmids with their hosts directly in native microbial communities. It captures, in vivo, physical interactions between microbial genomes and the genetic material lytic and lysogenic phages, plasmids, and AMR genes. Like culturing experiments, these linkages offer direct evidence that mobile elements are present within a host cell, thereby establishing a mobile element-host pair. However, unlike culturing experiments, this approach does not require the isolation of living bacterial cells. In addition to binning microbial genomes, this technology allows us to simultaneously deconvolve viral and plasmid genomes, directly from metagenomes, and reconstruct interactions without culturing.

Using large-scale application of this technology to samples in healthcare settings, wastewater, agricultural, and environmental contexts, we have generated the world's largest repository of genomic data for phages, plasmid, and resistance elements connected with their host microbes. We will discuss both published and unpublished work on the application of this technology to microbial modulation in healthcare settings, and effort to address the global AMR crisis.

A DEEP-DIVE INTO VIRULENCE OF THE KLEBSIELLA OXYTOCA SPECIES COMPLEX

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The human gut hosts intricate microbial communities that possess extensive functional capabilities. Disruption of this microbiome by environmental factors, diet, or medications changes its composition, eliminating bacteria and their metabolite capacities. This alteration can render the host to be more susceptible to infections by providing colonization niches for pathogens.

The *Klebsiella* genus encompasses a number of species that are frequently found colonizing humans, including the human gut. These species can be broadly split into the *Klebsiella pneumoniae* and the *Klebsiella oxytoca* species complex. Mainly, *K. pneumoniae* constitutes a significant threat to the global healthcare system due to their emerging hypervirulent and extensively drug-resistant phenotypes, contributing to more severe infections as well as outbreaks in hospitals. Therefore, numerous studies have been conducted on the virulence properties and dissemination possibilities of *K. pneumoniae* in the host. However, the presence of these factors within the *Klebsiella oxytoca* species complex remains largely unknown. Notably, at least nine species belong to the KoSC, most prominently *K. oxytoca*, *K. michiganensis*, and *K. grimontii*, primarily residing in and interacting with the gut as commensals, yet they may exhibit pathogenic behavior under specific circumstances.

To obtain a more precise pathogenic profile of the KoSC, we used various *in vivo* and *in vitro* assays to assess different commensal and patient-derived strains for their virulence patterns. This included, for instance, the indirect assessment of toxin production, the determination of siderophore secretion, biofilm formation, resistance to host factors, and mucoid phenotype. These properties were compared to a strain panel including hypervirulent-associated or commensal *K. pneumoniae*, *E. coli* laboratory reference strains and the probiotic strain *E. coli* Nissle. Notably, we identified a reduction in mucoviscosity for KoSC compared to hypervirulent *K. pneumoniae* strains, suggesting that the complex does not exhibit the hypermucoviscosity phenotype observed in certain hypervirulent *K. pneumoniae* strains. KoSC strains displayed a high serum resistance compared to the non-pathogenic laboratory strains. In the future, we plan to assess the ability of strains to acquire and retain plasmids, which confer fitness advantages such as antibiotic resistance genes, as well as to cause infection-related mortality in vivo, i.e., in the *Galleria mellonella* infection model.

Together, the use of phenotypic assays for detecting pathogenic potential enables a finer characterization even within a bacterial species, resulting in a more comprehensive trait profile of both individual strains and the entire species complexes.

DETECTING MICROBIAL EUKARYOTES IN HUMAN STOOL SAMPLES FROM RURAL MADAGASCAR USING 18S RDNA SEQUENCING

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Majority of world's population is affected by intestinal helminths, often leading to life-threatening diseases. Despite potential benefits of eukaryotic intestinal parasites, they are often neglected in hostmicrobiome studies. Identifying parasites in human samples is crucial to understand host-parasite interactions. In Madagascar, the prevalence of schistosomiasis is 52% and thus, available in human stool samples from this area were used to specifically detect *Schistosoma mansoni*, one causative agent for this neglected disease to obtain further insights into host-parasite interactions.

We established a Metabarcoding Next Generation Sequencing method, targeting eukaryotic 18S rDNA and investigated 1024 human stool samples from rural Malagasy communities. The workflow included DNA amplification with the 616*F/1132R primer pair, paired-end MiSeq® Illumina sequencing, and data analysis including DADA2 pipeline, concatenation of reads and annotations to PR^2 database. Additionally, the bacterial microbiota was investigated using 16S V3V4 rDNA sequencing.

Besides *Schistosoma*, additional intestinal helminths and various fungi were found. Significant differences in eukaryotic microbiota composition were observed, based on region of sample collection and participant's gender. Similarly, bacterial microbiota composition showed significant differences related to gender and location, but surprisingly not concerning *S. mansoni* infection. In addition, diagnosis of schistosomiasis in stool samples was comparable to results of specific PCR from human plasma and more sensitive than the use of a rapid POC-CCA test.

The established 18S rRNA NGS-method exhibited comparable diagnostic results to specific PCR tests. Identifying various helminths and fungi within one sample and could thus be used for high-throughput diagnostics on those samples on site in the future.

ECOLOGY OF SECRETED BACTERIAL PROTEASES IN THE HUMAN GUT

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Proteases are long known for being virulence factors produced by pathogenic bacteria . In recent years it has also been observed that commensal members of the gut microbiome secrete proteases that both alter the microbial community, and may impact host health. While a few proteases have been studied in detail, it is still unclear how common the secretion of proteases is within the human gut and how it effects the ecology of the bacteria. In addition to providing access to additional nutrients, proteases may be used to reduce agglutination by secreted IgA (SIgA). SIgA is secreted into the gut lumen by the host, leading to agglutination of bacterial cells, causing their removal from the gut. Pathogens have been observed to degrade SIgA using secreted proteases to reduce their removal and enhance their chance of survival. However, it has been observed that many commensal bacteria are also bound by SIgA, yet the ability to commensal strains to degrade SIgA, reducing their own removal from the gut, has yet to be assessed.

From the “Human intestinal Bacterial Collection” (HiBC) recently established in the Clavel lab (www.hibc.rwth-aachen.de), we selected 100 representative species to screen for proteolytic activity and found that 30% secreted proteases. All protease-secreting strains were from the phyla *Actinomycetota, Bacteroidota,* and *Bacillota* while none of the four *Pseudomonadota* strains tested were protease-secreting. Noticeably the ability to secrete proteases was conserved between close related species in the phyla Actinomycetota and *Bacillota* (e.g. all tested *Bifidobacteria* and *Blautia* species secreted proteases), while in the phylum *Bacteroidota* the ability to secrete proteases was spread inconsistently between genera (e.g. some species of *Phocaeicola* secreted proteases, while others did not). To assess if protease secreting bacteria were targeted by human SIgA, we incubated each strain with 50µg/ml SIgA for 1 hour and then observed agglutination via FACs, which was confirmed using microscopy. Only a small fraction of the tested strains were agglutinated by SIgA under these conditions. Interestingly two of these strains (*Streptococcus salivarius* and *Thomasclavelia ramosa*) were able to reverse the agglutination over time, potential via proteolytic degradation of the SIgA.

BIOMARKERS FOR THE DIFFERENTIATION OF ASYMPTOMATIC BACTERIURIA INTO URINARY TRACT INFECTIONS REQUIRING TREATMENT OR COLONISATIONS (METABIO STUDY)

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Instead of an abstract, I would like to present an ongoing study of our research group. We have no results yet, but we are confident that the 16th Seeon Conference will provide important insights and knowledge for the conduct of this study as well as for all our research efforts in the field of host-microbiome-pathogen interaction and the pursuit of new therapeutic strategies.

Project outline

Urinary tract infections (UTIs) are among the most common bacterial infections, both nosocomial and in the outpatient setting. The diagnosis of urinary tract infections is currently based on the detection of a relevant quantity of bacteria in the urine in combination with the appropriate clinical symptoms (e.g. alguria, pollakiuria). Particularly in patients with permanent catheterization or those who are unable to adequately express or perceive their symptoms due to dementia or sedation these diagnostic criteria can only be applied in part. Consequently, a diagnosis must then be made solely based on evidence of bacteria in the urine. This situation arises daily in everyday clinical practice and contributes to the fact that UTIs are a very frequent indication for the repeated and often unnecessary administration of antibiotic contributing significantly to the global increase of infections with multidrug-resistant bacteria worldwide.

Metabolome analysis, especially of urine, has recently become an important field for non-invasive biomarkers with which subtle metabolic deviations can be detected as a reaction to a specific disease. In the current guideline on asymptomatic bacteriuria, the IDSA (Infectious Disease Society of America) makes the clear recommendation that the focus of UTI research should be on the evaluation of potential biomarkers to differentiate between symptomatic and asymptomatic urinary tract infections.

The exploratory pilot study presented here uses an untargeted metabolome analysis to examine whether biomarkers / biomarker compositions in urine (e.g. local inflammation markers) can objectively identify patients with urinary tract infections, initially in comparison with healthy test subjects. For this purpose, the urine of 50 premenopausal women with an acute symptomatic urinary tract infection, who fulfil all diagnostic criteria of an uncomplicated urinary tract infection (gold standard), will be analyzed via metabolome analysis and then compared to the metabolomics of a healthy cohort in order to discover specific metabolome signatures of UTIs. This will be preceded by a pre-study of 10 healthy probands to determine the optimal pre-analytical protocol for urine metabolome studies in the clinical setting.

The exploratory trial will be followed by a confirmatory study to validate the biomarkers / biomarker combinations found in patients with bacteriuria without the possibility of recording possible UTI symptoms (e.g. in patients with bladder catheters, neurogenic bladder emptying disorders, dementia or under sedation).

CHARACTERIZATION OF SECONDARY BILE ACID PRODUCING GUT MICROBIOTA

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The role of gut microbiota in the modification of primary bile acids has received increasing attention in the previous years. The deconjugation of primary bile acids is already well described in many species, however, bacteria involved in the synthesis of secondary bile acids (SBAs) remain largely unknown due to difficulties in their cultivation. Based on different *in vitro* as well as *ex vivo* approaches, we try to gain insights into the ecophysiology of members of gut microbiota involved in this process, the impact of the bile acid pool composition on overall gut microbial structure and its relation to disease.

Results indicate that hypothesized SBA-producing bacteria are indeed functionally active and show distinct affinities towards varying energy sources with highest affinities for specific complex carbohydrates when grown in *ex vivo* communities. In healthy individuals, the relative abundance of SBA-producing bacteria showed high inter-individual variability but remained relatively stable over time within a person. Subsequent analyses will reveal whether these associations correlate with the respective bile acid concentrations in stool. Additional experiments in pouchitis patients receiving fecal microbiota transplants showed that the microbial SBA-producing capacity can be transferred from donor to recipient, however, their stable colonization was not achieved in all patients.

Within the Hereditary Intrahepatic Cholestasis (HiChol) Network, we collected fecal samples in a longitudinal manner from pediatric patients diagnosed with familiar intrahepatic cholestasis and determined absolute bacterial compositions based on metagenomics including SBA-producing species. Patients were treated with an inhibitor of the ileal bile acid transporter protein (IBAT) preventing the reabsorption of bile acids from the intestine that results in high bile acid concentrations reaching colonic microbiota. Control groups encompassed treatment naïve children as well as those receiving liver transplantation along with age-matched healthy controls. Based on this approach we aim to reveal the relation between bile acid availability and gut microbiota functioning, with a specific focus on SBA-producing bacteria, in the context of cholestatic diseases. In general, our longitudinal approach will enable us to determine the role of gut microbiota for bile acid composition and its impact on child development. This will facilitate the development of precision treatment strategies targeting SBA producers and, consequently, the composition of the bile acid pool.

ESTABLISHMENT OF A NON-WESTERNIZED GUT MICROBIOTA IN MEN-WHO-HAVE-SEX-WITH-MEN IS ASSOCIATED WITH SEXUAL PRACTICES

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The human gut microbiota is influenced by various factors, including health status and environmental conditions, yet, considerable inter-individual differences remain unexplained. Previous studies identified that the gut microbiota of men-who-have-sex-with-men (MSM) is distinct from that of non-MSM. Here, we reveal through species-level microbiota analysis using shotgun metagenomics that the gut microbiota of many MSM with Western origin resembles gut microbial communities of non-Westernized populations. Specifically, MSM gut microbiomes are frequently dominated by members of the Prevotellaceae family, including co-colonization of species from the *Segatella copri* complex and unknown Prevotellaceae members. Questionnaire-based analysis exploring inter-individual differences in MSM links specific sexual practices to microbiota composition. Moreover, machine learning identifies microbial features associated with sexual activities in MSM. Together, this study shows associations of sexual activities with gut microbiome alterations in MSM, which may have a large impact on population-based microbiota studies.

KLEBSIELLA OXYTOCA FACILITATES MICROBIOME RECOVERY VIA B-LACTAM DEGRADATION

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The gastrointestinal microbiota plays a crucial role in protecting the host from invading pathogens, referred to as colonization resistance (CR). Factors such as secondary metabolite secretion, competition for electron acceptors, and nutrient availability contribute to CR. However, medical interventions like antibiotics or chemotherapy can disrupt CR, leading to pathogen proliferation. As antibiotic residues persist in the intestinal contents after the end of antibiotic administration, commensal growth may be inhibited for a prolonged period due to the gradual excretion and degradation process of the antibiotics.

Here, we investigate whether β-lactamase production by *Klebsiella oxytoca* may indirectly aid in microbiome recovery following antibiotic treatment, in the context of the previously described competition between *Klebsiella oxytoca* and *Klebsiella pneumoniae,* in animals fed one of three different Western style diets: high-starch, high-sugar or high-fat/high-sugar diets. Therefore, we examined the caecal contents of ampicillin-treated mice, both with and without prior colonization by *Klebsiella oxytoca*, for β-lactamase activity using the calorimetric nitrocefin assay. Additionally, we assessed the inhibitory potential of ampicillin residues in the gut on the growth rates of sensitive commensal bacteria, and quantified ampicillin loads in caecal contents using LC-MS measurements.

Overall, we show that residual ampicillin levels are lower in the guts of *Klebsiella oxytoca* pre-colonized mice with detectable β-lactamase activity in isolated caecal contents. This reduces the burden of ampicillin on the commensal microbiome, which is associated with faster commensal outgrowth during post-ampicillin recovery, ultimately improving gut clearance of pathogens.

CONSUMPTION OF FERMENTED DAIRY ENHANCES VALERATE LEVELS DUE TO MEGASPHAERA ACTIVITY

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Fermented dairy products are popular due to high nutritional value, palatability and preservation. Their consumption has been inversely associated with the occurrence of immune and cardiovascular diseases, and metabolic disorders. Their potential health benefits were linked to the presence of certain biomolecules and/or interactions with the gut microbiota. For example, lactose found in fermented dairy can be metabolized to lactate, which can be transformed to propionate or butyrate through fermentative cross-feeding. The aim of this study was to investigate the fermented dairy product consumption on fecal microbiota composition and activity with a focus on the microbial lactose utilization potential.

Fecal samples were collected from a cohort of 49 overweight/ obese women that consumed either a breakfast containing drained yogurt (skyr) (n= 21, high protein, HP group) or a low protein diet (n = 28, low protein, LP group) as a control group. Fecal samples were collected at 0, 6 and 12 weeks and the microbial community and the fermentation metabolite profiles were examined.

The one-meal dietary intervention increased ($p<0.05$) richness of the HP group. Beta diversity was significantly different between diets at week 6 (p=0.002) and week 12 (p=0.018). *Streptococcaceae* relative abundance increased ($p<0.05$) in feces of the HP group possibly due to transfer of the starter culture. Levels of lactate and valerate, which can be produced from propionate through chain elongation with ethanol, were higher ($p<0.05$) in feces of the HP group at 6 weeks. qPCR targeting *Megasphaera*, a valerate producer, was performed to evaluate its relationship with the presence of valerate. When levels of *Megasphaera* were above 7 log/cells in feces of HP group, valerate levels were also higher than feces with low abundance. In batch fermentations initiated fecal slurries, valerate concentration was higher after lactose addition if *Megasphaera* was present in the microbiota.

Valerate has been previously observed in fecal samples, but its origin has not been fully elucidated. In this study we linked availability of lactose to valerate production when *Megasphaera* was present.

NFDI4MICROBIOTA: TOWARDS A FAIR LANDSCAPE OF COMPREHENSIVE (META)DATA IN MICROBIOME RESEARCH

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The NFDI4Microbiota consortium (www.nfdi4microbiota.de), a part of the German National research Data Infrastructure (NFDI), aims to support microbiological research by providing a comprehensive platform for data management, analysis, and collaboration. With a strong focus on the FAIR (findable, accessible, interoperable and re-usable) data principles, open science, and reproducible research, the consortium strives to boost the cultural shift required to enable sustainable microbiome research.

To create FAIR research and to prevent underutilization of data, standardization plays a crucial role. By standardizing data processing, analysis, and metadata collection, the consortium increases the value of data, making it more accessible and interpretable. The promotion and utilization of controlled vocabularies and ontologies enable the creation of machine and human-readable datasets and metadata information, facilitating data integration and interoperability. NFDI4Microbiota will provide an accessible and user-friendly data infrastructure with high-quality tools, workflows, and databases, which will lead to sustainable scientific advancements in microbiome research both nationally and through international efforts.

These efforts are complemented by contributions from the research community. With diverse Use Cases, the consortium is in the process of implementing perspectives and recommendations on topics like multi-omics, data provenance, metadata databases, microbial strain mappings, and benchmarking workflows. In summary, NFDI4Microbiota will serve as a central hub in Germany to support the microbiology community with data access, analysis services, data/metadata standards, and dedicated training opportunities to increase the reuse and (machine) interoperability of research data.

INTESTINAL FUNGI: DEAD OR ALIVE?

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Introduction: The presence of DNA from consumed food in fecal samples raises important questions regarding the origin of fungal DNA within these samples. Considering fungi's widespread presence in the human diet, it is essential to determine whether the detected fungal DNA in fecal samples originates from the gut flora or from dead cells ingested through dietary intake.

Objective: This study aimed to differentiate between living and dead fungi in fecal samples from healthy individuals.

Methods: Fresh fecal samples were collected from ten healthy participants and treated with propidium monoazide to inhibit amplification of DNA from dead cells whereas untreated samples were kept as controls. The microbial composition was analyzed by sequencing of the ITS and 16S rRNA regions, comparing treated samples with their untreated controls to identify DNA from living versus dead cells.

Results: We observed significant differences in fungal abundances between treated and untreated samples. Notably, Saccharomyces cerevisiae showed a significant decrease in abundance after treatment with propidium monoazide, along with other food-associated fungi in individual samples.

Conclusions: Not all fungi detected in microbiome studies may be active members of the gut flora; some could merely be DNA remnants from food. Distinction of living versus dead fungi can therefore improve interpretation of mycobiome research and increase our understanding of the fungal flora.

METABOLIC CAPABILITIES OF WIDESPREAD GUT BACTERIA OF THE FAMILY SUTTERELLACEAE

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Members of the family *Sutterellaceae* (Pseudomonadota) are ubiquitous in the intestinal tract. The genera *Sutterella* and *Parasutterella* are core taxa of the human gut microbiome, but also present in the gut of various animals, including mice, dogs, pigs, and birds. They are associated with different health, disease or lifestyle states, yet, reports on the relationship of *Sutterellaceae* with diseases such as irritable bowel syndrome, autoimmune and neurological disorders are conflicting. Despite wide distribution and associations with various health conditions, their specific metabolic niches and functions in the gut are poorly characterized. *Sutterellaceae* type strains are asaccharolytic, some are capable of nitrate reduction and microaerophilic growth. *Sutterellaceae* members also encode a wide variety of respiratory-type reductases. Here, we studied the physiology of selected gut-derived strains of the genus *Sutterella*. We performed various growth tests, metabolite analyses, single-cell mass measurements, and comparative genomics and transcriptomics. All strains encode a putative octaheme cytochrome c sulfite reductase (MccA), a periplasmic nitrate reductase (NapAB), and a fumarate reductase complex (FrdABC) which suggests they anaerobically reduce sulfite, nitrate, and fumarate. Addition of 1 mM sulfite to the media previously depleted of other electron acceptors stimulated growth and led to production of up to 0.1 mM H_2S, which indicated sulfite reduction. Addition of 5-50 mM fumarate or the fumarate precursor aspartate in combination with formate as electron donor caused the most significant increase in growth of *S. wadsworthensis*, *S. parvirubra,* and *S. megalosphaeroides* and led to a proportional production of succinate. Moreover, the addition of fumarate and formate, but not formate alone, caused significant increase in single cell buoyant mass of *S. wadsworthensis* in the exponential phase, while its cell size remained the same. This suggested a higher density within the cells, presumably caused by a higher nucleic acid content. That finding was supported by transcriptomic data: genes involved in nucleic acid metabolism were significantly upregulated in the fumarate-format treated cells. Moreover, both treated and untreated cells of *S. wadsworthensis* and *S. parvirubra* expressed high levels of *frdA*, *fumarase*, and *aspA* (aspartate ammonia-lyase). This suggests these bacteria heavily rely on fumarate reduction, with protein degradation likely being a major source of fumarate through aspartate. Our work shows fundamental physiological capabilities of members of the ubiquitous gut family *Sutterellaceae* that may support their metabolic niche in the gut and contribute to protection against enteropathogens.

FIRST INSIGHTS INTO MICROBIAL CHANGES WITHIN AN INFLAMMATORY BOWEL DISEASE FAMILY COHORT STUDY

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The prospective Inflammatory Bowel Disease (IBD) Kiel Family Cohort study (KINDRED cohort) was initiated in 2013 to systematically and extensively collate data on relatives of IBD patients, to construct a high-risk population for IBD occurrence, with continuous follow-ups to capture disease development. By combining taxonomic and functional microbial data over successive time points with extensive anthropometric, medical, nutritional, and social information, this study aimed to characterize factors influencing the microbiota in health and disease via detailed ecological analyses. Using two dysbiosis metrics (MD index, GMHI) trained on the German KINDRED cohort, we could identify strong and generalizable gradients within and across different IBD cohorts, which correspond strongly with the IBD pathologies, physiological manifestations of inflammation (*e.g.* Bristol stool score, calprotectin, anti-ASCA IgA/IgG), genetic risk for IBD and general risk of disease onset. Anthropometric and medical factors influencing transit time strongly modify bacterial communities. Strong patterns of overabundance and importance of various *Enterobacteriaceae* (*e.g. Klebsiella sp.*) and opportunistic *Clostridia* pathogens (*e.g. C. XIVa clostridioforme*) further characterize the IBD specific communities, similarly to highly consistent patterns of ectopic colonization with oral *Veillonella sp.*, *C. saccharibacter*, *F. nucleatum*, and others, which also influence physiological signs of inflammation but show little heritability/intra-family transmission. Functionally, pathways involved in amino acid metabolism and flagellar assembly are beneficial and highly heritable, while mucolytic functions associate to IBD. Broad scale ecological patterns associated to tipping-point dynamics (critical slowing down, community variability) indicate drastic state transitions of communities into characteristically chaotic communities in IBD.

DECIPHERING HORMONE-MICROBIOME INTERPLAY IN THE CONTEXT OF ASSISTED REPRODUCTION TREATMENT

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Infertility is a health condition affecting up to 17 % of the adult population (1) leading to severe economic and long-lasting psychological burden even after successful pregnancy outcome (2). Infertility has a multifactorial etiology among which a hormonal imbalance and the microbiome play a crucial role (3) (4). However, current knowledge on the bacterial interplay with hormone metabolism and impact of sex hormones on the female microbiome remains sparse.

This is why the presented study focused on a cohort of women undergoing in-vitro fertilization or assisted reproductive treatment with intracytoplasmic sperm injection. Both treatment strategies involve administration of a combination of estrogen and progesterone with or without subsequent administration of follicular stimulating and luteinizing hormones. Stool, plasma, saliva and vaginal samples are collected across three timepoints before, during and after treatment and analyzed using a combination of different multi-omics approaches.

We compiled a list of more than 50 enzymes involved in hormonal metabolism to bioinformatically screen for potential bacterial homologs involved in hormone-microbiome interactions. Further, analysis of the first set of samples also indicates an impact of hormone administration on growth patterns of selected bacterial strains, including essential gut and reproductive tract commensal microbes such as Lactobacillus species. Shifts in growth patterns were also observed in the microbial communities derived from the patient samples. Overall, our study helps to broaden our understanding of hormone-microbiome interactions in female health and may enable identification of novel factors associated with successful outcomes of assisted reproduction treatment.

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IDENTIFICATION OF SLE-DERIVED HUMAN TRANSLOCATING MICROBIOTA – A HUMANIZED MOUSE MODEL

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Background: Systemic lupus erythematosus (SLE) is a severe multifactorial autoimmune disease, which is potentially life-threatening. Besides genetic polymorphisms and environmental triggers, a variety of bacterial species had been identified to contribute to the onset of this disease. Amongst them are pathobionts, which originate from the gut, translocate through the gut barrier and colonize secondary lymphoid organs and the liver, where they initiate autoimmune reactions.

Objectives: To identify gut barrier breaching bacterial species (and strains) of human origin, we developed an in-vivo system to colonize mice (specific pathogen free (SPF) and germ free (GF)) with human SLE patient-derived microbiota.

Methods: Human stool is preserved and processed for long-time storage under anaerobic conditions. SPF mice are treated with an antibiotic mixture to reduce murine microbiota before colonization. After the colonization procedure, a subgroup of mice is treated with imiquimod (IMQ) to induce a TLR7-driven immune response, which mediates an SLE-like phenotype. After euthanasia, organs (Peyer`s patches, mesenteric lymph nodes (MLN), liver, spleen, and kidney) are specifically homogenized and cultivated under selected conditions to maximize species detection.

Results: We were able to culture various translocating microbiota of murine origin in multiple organs including lupus pathobionts (e.g. *Enterococcus gallinarum* and *Limosilactobacillus reuteri*). Besides gut-associated organs (MLN and liver), we detected translocation to systemic sites such as the spleen and kidney, the latter being a target organ in SLE. Furthermore, we identified human microbiota in mouse tissues (e.g. *Bacteroides thetaiotaomicron*), indicating stabile colonization of SPF mice.

Conclusions: Besides a relatively high extraintestinal colonization rate of murine microbiota in the SPF setting, the current approach represents a powerful tool to identify translocation of potentially SLE-inducing bacteria down to strain levels. The systematic culture-based approach is an obvious advantage over assays relying on comparative sequence analysis only. In addition, this procedure enables deeper and extended downstream analysis of translocation bacteria such as full genome analysis, directed and transposon-based mutagenesis or co-culture experiments with immune competent cells as well as translocation and interaction assays with human organoids.

THE STRATIFICATION BY AGE IS CRITICAL FOR MICROBIOME ANALYSES OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Juvenile idiopathic arthritis (JIA) is the most common autoimmune disease affecting the joints in children and teenagers. The etiology of JIA is unclear, but genetic and environmental factors, such as the intestinal microbiome, have been implicated. We have analyzed the intestinal microbiota from JIA patients and sex- and age-matched healthy individuals using single-cell analysis by multi-parameter microbiota flow cytometry and 16S rRNA gene amplicon sequencing. For microbiota flow cytometry, we assess coating of bacteria with different host immunoglobulin isotypes and the expression of specific sugar moieties on the bacterial surface. We then use a self-organizing map algorithm for dimensionality reduction and clustering combined with machine-learning to identify disease-specific microbial phenotypic signatures. We can show that overall the JIA microbiome significantly differs from that of healthy controls on the taxonomic level. For the identification of a JIA-specific microbial phenotypic signature by flow cytometry, a further stratification of the JIA patients according to age was critical. This suggests that age-dependent, perhaps physiological, alterations additionally shape the JIA microbiota. The stratification by age also revealed that different bacterial taxa were decisively differentially abundant in the microbiomes of JIA patients and healthy donors. Thus, our data indicate that a stratification by age could be particularly important for the specific identification of alterations of the microbiome in JIA and in chronic inflammatory diseases affecting children in general.

A COLONIZER OR A THREAT? COLONIZATION DYNAMICS OF EARLY-LIFE MICROBIOMES IN A NEONATAL INTENSIVE CARE UNIT

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Background

Metagenomics stands as a promising field for hospital epidemiological surveillance. While most analyses rely on short-read sequencing, long-read sequencing may provide finer resolution to identify lineages within species. This study conducted surveillance of neonates admitted to the neonatal intensive care unit over a twelve-month period with a focus on Enterobacterales.

Methods

Sample collection occurred weekly of nasal and rectal swabs, which underwent enrichment prior to a lysis protocol for human DNA depletion and extraction of microbial DNA. Free PCR library preparation was carried out, encompassing swab and water-negative controls for a standard 72-hour sequencing run using GridION. Open-source software were part of an in-house bioinformatics pipeline for downstream analyses.

Results

When patients were grouped by the relative week to birth and regardless of the source (anus or nose), the composition of the microbiome between the consecutive relative weeks showed the highest similarities, clustering with the same or the consecutive week. *Staphylococcus epidermidis* and *S. aureus* stand as the most abundant species shared between both sources. However, the colonization by Enterobacterales caused an overall heterogeneity reduction in the microbiome that shifted towards these dominant microorganisms. In this study, the use of metagenomics allowed us to track with high resolution the transmission events, where *Klebsiella pneumoniae*, *Escherichia coli, Klebsiella oxytoca* and *Enterobacter cloacae* complex were the most relevant. At the same time, we could followed the changes in the microbiome as the colonization occurred for patients staying longer on the ward, and we also detected patients having a second sequence type from the same species.

Conclusions

Long-read sequencing demonstrated significant potential for real-time tracking of colonization dynamics. Human DNA depletion protocols in the lab and within the bioinformatics pipeline are key to obtain a better resolution. We highlight the importance of the alteration in the microbiota composition caused by opportunistic microorganisms, which can be further explored in the context of infection prevention and control measures within the neonatal intensive care unit.

SPEAKERS – KEYNOTE LECTURES & HOT TOPICS

KEYNOTE LECTURES

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