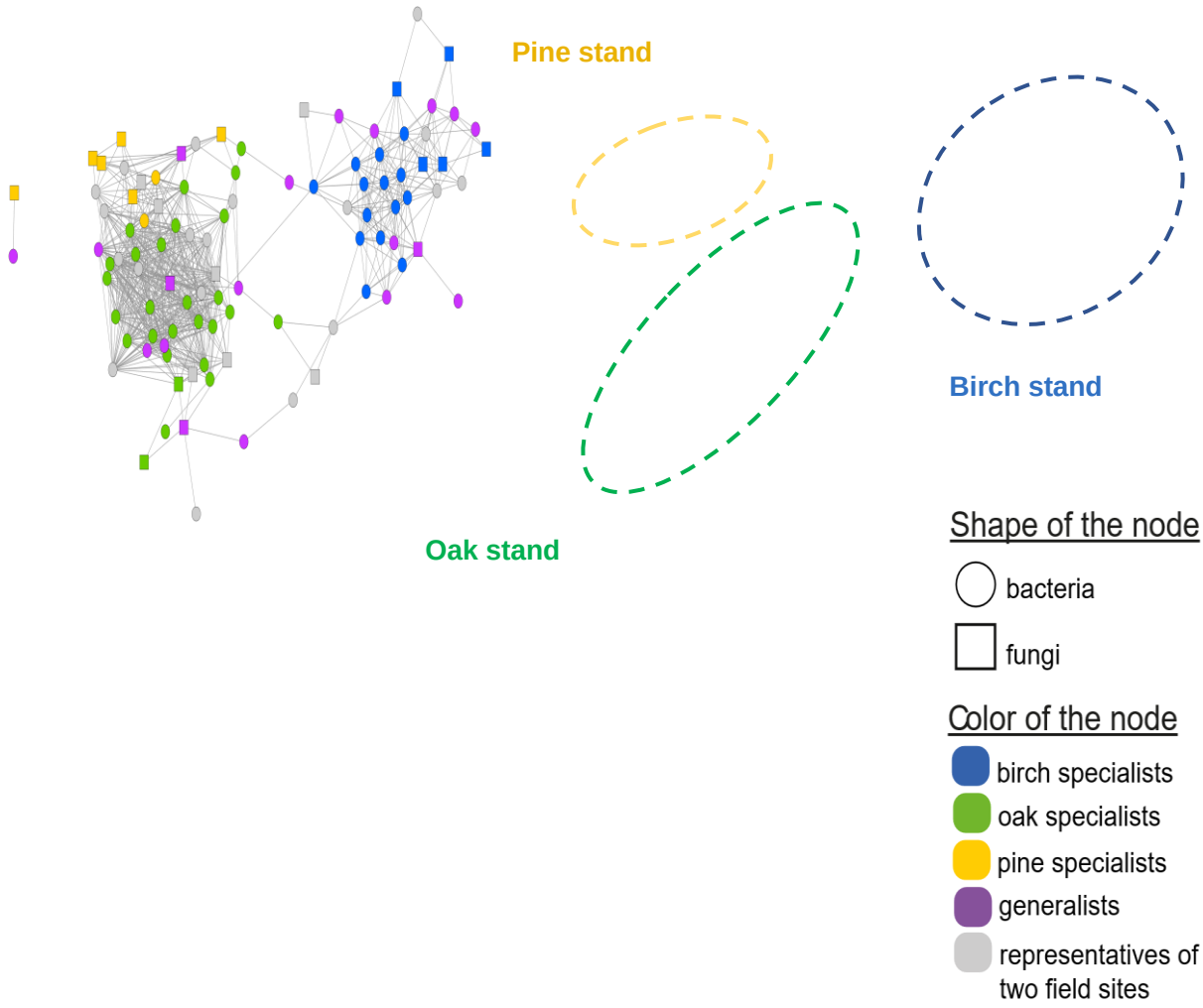
Institut für Mikrobiologie

FRIEDRICH-SCHILLER-
UNIVERSITÄT
JENA

Jahresbericht 2023/2024



Vorwort

Liebe Leserin, lieber Leser,

die Vorbereitung der Antragstellung für eine Verlängerung des Clusters "Balance of the Microverse" hat bereits im Jahr 2023 ihre Schatten vorausgeworfen und das Jahr 2024 dominiert. Die damit einhergehenden Änderungen wie die Übergabe der Sprecherfunktion an Kirsten Küsel oder Neuerungen im Bereich der zugeordneten Graduiertenschule Jena School for Microbial Communication (JSMC) sind nur die von außen am deutlichsten wahrnehmbaren Auswirkungen. Dass ein so guter Antrag mit den Teilbereichen "Signals", "Structures" und "Transitions" erstellt werden konnte, war ein großer und wichtiger Schritt, der das Team nochmals weiter zusammenführen konnte.

Mit Prof. Gianni Panagiotou und der Nachwuchsgruppe von Dr. Amelia Barber steht das im Rahmen des Excellenzclusters vergrößerte Team in der Mikrobiologie. Wir freuen uns, dass sie uns unterstützen und können damit auch die Forschung dieser Gruppen im Bericht des Instituts für Mikrobiologie vorlegen.

Im Umfeld der JSMC konnte nach Auslaufen der Förderung durch die Carl-Zeiss-Stiftung mit Dezember 2024 eine Weiterförderung der JSMC durch Landesmittel sichergestellt werden. Für die Weiterführung - und den Ausbau - des Programms war dies ein sehr wichtiger Schritt, der auch das Institut für Mikrobiologie in der Weiterqualifizierung von Promovierenden und der Unterstützung von Postdocs voranbringt. Insbesondere die Erweiterung des Programms für Postdocs profitiert von der Übergabe der Koordination an Dr. Jasmin Mertens, die diese Aufgabe mit vielen neuen Ideen und einer neuen, verbesserten Struktur unterstützt.

Damit liegt nun der im Zweijahresturnus neu aufgelegte Jahresbericht vor, der das Institut für Mikrobiologie in seiner gesamten Breite vorstellt und damit ein gutes Bild der in Jena möglichen Bandbreite der Forschung in der Mikrobiologie liefert. Ebenfalls Teil dieses Jahresberichts ist wieder die Aufstellung der Lehre, die Studierende an die Forschung früh heranführen und für Mikrobiologie interessieren möchte.

Jena, im Februar 2025

Institut für Mikrobiologie

Fakultät für Biowissenschaften

Friedrich-Schiller-Universität Jena

Mikrobielle Kommunikation (Prof. Erika Kothe)
Nachwuchsgruppe Plant Microbiosis (Dr. Matthew Agler)
Allgemeine Mikrobiologie (Prof. Kai Papenfort)
Nachwuchsgruppe RNA-Biologie der Bakterien (Dr. Kathrin Fröhlich)
Mikrobielle Interaktionen (Prof. Christian Jogler)
Theoretische Mikrobielle Ökologie (Prof. Rosalind Allen)
Microbiome Dynamics (Prof. Dr. Gianni Panagiotou)
Nachwuchsgruppe Fungal Informatics (Dr. Amelia Barber)
Molekulare Mikrobiologie (Prof. Axel Brakhage)
Synthetische Biotechnologie (Prof. Miriam Agler-Rosenbaum)
Angewandte Systembiologie (Prof. Thilo Figge)
Biomolekulare Chemie (Prof. Christian Hertweck)
Mikrobielle Pathogenität (Prof. Bernhard Hube)
Mikrobielle Immunologie (Prof. Ilse Jacobsen)
Infektionsimmunologie (Prof. Christina Zielinkski)
Infektionsbiologie (Sen. Prof. Peter Zipfel)
Jena Microbial Resource Collection JMRC (PD Dr. Kerstin Voigt)
Microbiome Science (Prof. Christina Warinner)
Molekulare Phytopathologie (Prof. Philipp Franken)

Lehrstuhl für Mikrobielle Kommunikation

Prof. Dr. Erika Kothe

1. Research

"Omics" in the basidiomycete Schizophyllum commune

The spread of the white rot fungus *Schizophyllum commune* via spores is tightly linked with its sexual reproduction cycle. Thus, genes of the mating type loci are being researched which encode transcription factors on the one hand, and pheromones and a pheromone receptor system of 7 transmembrane domain family receptors on the other hand. The receptors can discriminate between at least 20 different ligands to control the recognition between self and non-self. In response to a pheromone of a suitable mating partner, intracellular, Ras-dependent signal transduction leads to the induction of dynein-dependent nuclear migration. Beyond the pheromone receptors, four related proteins were attributed to possess functions in filamentous growth and mating. This thesis is supported by the demonstrated localization of the proteins in the hyphal tips, at the septae and non-fused clamp cells. The membrane-located processes were investigated with respect to the involvement of lipid rafts in the fungal membrane.

White rot fungi have great potential for degradation of recalcitrant matter. The white rot fungus *S. commune* thus can be applied for mycoremediation, even in combined (heavy) metal and polycyclic and aromatic hydrocarbon contamination (Traxler et al., 2024). It could be shown to grow even in soil (compare BSc thesis Hory, 2023). Communication with the soil bacteriome thus can be influenced (compare BSc thesis Handschug, 2024), and the

exchange of signals between domains shapes the microbial community in a given spot. A major advantage of mycoremediation is that the hyphal network supports both plants and bacteria in stressful and especially in heterogeneously contaminated sites to build a community and actively participate in the remediation and thus stabilize the site.

The exchange of signals plays a pivotal role in such organismic interactions, and since *S. commune* is genetically tractable, it lends itself as a model to investigate intracellular signal transduction (MSc thesis Orin, 2024). For the hyphal growth important in a structured environment like soil, the cellular membrane features spots of higher complexity at which places the cytoskeleton may be anchored. In such lipid rafts, one of the structural proteins is stomatin, for which a knock-out mutation could be investigated (MSc thesis Jesse, 2023). Although the lipid raft staining showed the structures already known from other filamentous fungi, in the main part ascomycetes. This basidiomycete - like the entire phylum of basidiomycetes - lacks components usually associated with stomatin and lipid rafts, the replacement of conserved functions remains a question of interest.

In an interaction between the dry rot fungus *Serpula lacrymans* with *S. commune* as well as with bacteria such as *Bacillus subtilis* or streptomycetes, specific signaling molecules including volatiles are investigated in the frame of CRC ChemBioSys. The collaborative project with Phamaceutical Microbiology (Prof. Hoffmeister) used specifically designed microscopic slides to show thigmotropic cue decoding by *S. commune* (MSc thesis Petersen, 2023). It turned out that the fungi are specifically responding to surface variation, and already in growth experiments with glass beads, higher biomass is formed as compared to liquid cultivation. It thus seems important to address questions of cell biology and signaling not solely in plate or liquid culture, but to include specifically structured surfaces for the fungi.

Ectomycorrhizal fungi

Colonization strategies and host specificity of ectomycorrhizal fungi are examined. Fungi of the genus *Tricholoma* are capable to form a host-specific, mutually symbiotic relationship with trees. Since only mated, dikaryotic strains are able to grow in axenic culture, the mating types of *T. vaccinum* and its tetrapolar mating system was investigated (MSc thesis Nushrat, 2023). The sequenced genome of *T. vaccinum* and an *Agrobacterium tumefaciens* mediated transformation system enable functional analyses. An aldehyde dehydrogenase and a MATE transporter are induced during the establishment of the symbiosis and in symbiotic tissues. Also, hydrophobins – small, secreted proteins involved in formation of aerial hyphae and mycorrhiza development – were examined in the specific symbiosis of *T. vaccinum* with its host tree spruce (*Picea abies*).

The signal exchange with other soil microorganisms and the host could be linked to sesquiterpenes produced by *T. vaccinum* as a pre-symbiotic exchange that, in turn, influences the phytohormone balance of the host tree (Ezediokpu et al., 2022). Inhibition of fungal sesquiterpene synthases in interaction with the highly compatible host tree *P. abies* and in a low compatibility mycorrhizal interaction with pine (*Pinus sylvestris*). Comparing the experimental variant of volatile exchange only and full contact with morphotype formation, a change in the trees' metabolomes could be associated with a response to rhizosphere beneficial microbes in case of the host compared to PAMP recognition response in the early response followed by symbiotic response in case of the low compatibility host tree (Ezeduokpu, 2023, Ezediokpu et al., 2023).

The mycorrhizosphere microbiome exerts a considerable influence on the communication with the host plant. Simultaneously, the microbial community showed effects on the growth and hyphal branching behavior of *T. vaccinum*. Furthermore, plant root exudates and phytohormones were shown to control and direct the growth of the mycorrhizal fungus. Responses to soil heavy metals was investigated using axenic mycorrhizal co-cultures which identified specific metal responses including glutathione-based detoxification (Östreicher, 2023).

The influence of mycorrhiza on the forest ecosystem is also investigated in heavy metal contaminated habitats analyzing the biodiversity of the ectomycorrhiza and the occurrence of different exploration types in relationship with the environmental pollution (Bogdanova, 2023). Axenic co-culture experiments are performed to elucidate molecular biological background of heavy metal responses.

The production of edible mushrooms has been successful for saprotrophic species. In contrast, the investigation of high-priced ectomycorrhizal fungi such as truffles is difficult. In a field trial, the impact of the ectomycorrhizosphere's microbiome is addressed (BSc thesis Engelhardt, 2023). The effect of soil parameter on growth and cultivation as well as selection of potential mycorrhizal helper bacteria is addressed (MSc theses Jeckstiess, 2023, Nair, 2023).

Bio-Geo Interactions

Streptomycetes from a heavy metal containing site in Eastern Thuringia were used to examine the mechanisms of heavy metal resistance with molecular biological methods. Extreme sites with high metal load like the former uranium mining site near Ronneburg showed adaptations of the microorganisms, for example towards 130 mM nickel. In this context, this *Streptomyces mirabilis* was sequenced, and a transformation system could be established for that strain. That allowed investigation of a metal transporter gene on formation of biomineral formation (Costa, 2023). Both Mg containing struvite and Ni-struvite could be formed with *S. mirabilis*, depending on presence of nickel in the media. The

biosynthesis was accompanied by changes in both, transcriptome and metabolome, allowing to form a hypothesis of mineral formation in a manner influenced by the exudates of the bacteria.
Inoculation of this strain with and without co-inoculation with mycorrhizal fungi at our test field site near Ronneburg was evaluated for the effect on phytostabilization using a short rotation coppice planting with birch, elder and willow on the acidic, metal contaminated soil in addition to application of calcerous soil amendments (Fürst, 2023). The nitrogen fixing bacterial community at the site was investigated as a role in plant growth promotion in low nutrient substrates had been seen (MSc thesis Chen, 2023).
The combined effect of metals and thiopeptide antibiotics was investigated comparing the answers to the model streptomycete *S. coelicolor* (BSc thesis Robel, 2024). This yielded an insight into a link via the orphan thiostrepton binding transcription factor *tipA* between metal and antibiotic responses. The effect of heavy metal exposure on growth and transcriptome was investigated and effect of co-cultivation with thiopeptide producing streptomycetes was evaluated (BSc theses Reichel, 2024, and Markus, 2024).
To evaluate the effect of phages, two newly sequenced streptophages were analyzed (MSc thesis Gloger, 2023). An effect of tals on virulence could be established hinting at specific roles of viruses for microbiome development in metal contaminated areas.

Another focus is the investigation of the microbial diversity in various habitats, also with regard to the geology of the sites, such as extreme sites with high salt loads or radionuclide-containing waters**.** Microbial adaptation and community dynamics were studied again at the former uranium mining and milling site (Harpke, 2023). A protective role of biofilm formation could be predicted from investigation of isolates from the site (Harpke et al., 2023).

With regard to the mycobiome in bio-geo interactions, the investigation of a geological fossil site at Messel, Germany, yielded a high diversity of plant pathogenic fungi that complete the picture of biodiversity in that environment conserved for 42 Mio years. The oil shale preserved leafs were scanned for signs of phytopathogenic fungi and a high diversity of smut and rust fungi could be detected. This confirms, from a mycological aspect, the tropical climate at the time of preservation (Smith et al., 2024).

2. Publications

Bogdanova O, Kothe E, Krause K. 2023. Ectomycorrhizal community shifts at a former uranium mining site. J Fungi 9, 483.

Ezediokpu MN, Halitschke R, Krause K, Boland W, Kothe E. 2023. Pre-symbiotic response of the compatible host spruce and low-compatibility host pine to the ectomycorrhizal fungus *Tricholoma vaccinum.* Front Microbiol 14, 1280485.

Harpke, M and Kothe, E. 2023. Biofilm formation in Gram-positives as an answer to combined salt and metal stress. J Basic Microbiol 63, 888-896

Smith KT, Collinson M, Folie A, Habersetzer J, Hennicke F, Kothe E, Lehmann T, Lenz OK, Mayr G, Micklich N, Rabenstein R, Racicot R, Schaal SFK, Smith T, Tosal A, Uhl D, Wappler T, Wedmann, Wuttke M. 2024. The biodiversity of the eocene Messel pit. Palaeobiodiv Palaeoenviron 104, 859-940.

Traxler L, Krause K, Kothe E. 2024. Basidiomycetes to the rescue: Mycoremediation of metal-organics co-contaminated soils. Adv Appl Microbiol 129, 83-113.

3. Third Party Funding

Projektträger	Vorhaben	Laufzeit	Mittel in 2023
DFG	Sonderforschungsbereich ChemBioSys – Teilprojekt B05	2022-2026	13.000,00 € + 1 Doktorandin
Leibniz Science Campus (LSC) InfectoOptics	Verbundvorhaben "High end" optische Technologien zur Analyse intrazellulärer, membran-beeinflussender Infektionsprozesse – HoT-Aim 2.0	2019 - 2023	41.535,73 €
Carl-Zeiss-Stiftung	JSMC	2019-2023	54.239,28 € (2 Projekte)
DFG	Exzellenz-Cluster "Balance of the Microverse"	2019-2025	37.638,51 €
BMBF	RENA: Biologische Radionuklidentfernung durch Nutzung natürlicher Assoziations-prozesse, Teilprojekt B	2021-2024	264.000,00
Thüringer Aufbaubank	Trüffelanbau in Thüringen	2021 -2023	52.145,60 €
Alexander von Humboldt Stiftung	Forschungsstipendium Prof. Ganiyu Oyetibo Nigeria	2023-2024	8.800,00 €
Projektträger	**Vorhaben**	**Laufzeit**	**Mittel in 2024**
DFG	Sonderforschungsbereich ChemBioSys – Teilprojekt B05	2022-2026	13.500,00 € + 1 Doktorand
Carl-Zeiss-Stiftung	JSMC	2019-2023	141.648,18 €
DFG	Exzellenz-Cluster "Balance of the Microverse"	2019-2025	31.769,88 €
BMBF	RENA: Biologische Radionuklidentfernung durch Nutzung natürlicher Assoziations-prozesse, Teilprojekt B	2021-2024	44.563,16 €
Thüringer Aufbaubank	Trüffelanbau in Thüringen	2021 -2024	12.920,00 €
BMBF	MyKoBEsT. Dendroanalyse, Bildung organische Bodensubstanz, Mykorrhizosphärenprozesse, (kolloidaler) Schwermetall/Radionuklid-Austrag & Drohnenbefliegung	2023 -2026	124.672,00 €

4. Teaching

Angebotene Module der Mikrobiellen Kommunikation

WS 2022/2023 und SS 2023

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
BB029	Terrestrische Mikrobiologie (Praktikum)	10	15
	Terrestrische Mikrobiologie (Theorie)		15
BB028	Terrestrische Mikrobiologie (Theorie)	5	6
BB011	Allgemeine Mikrobiologie (Praktikum)		37
BBio1.5, 011/BEBW4/ BBC2.2, 005(LBio-MBio	Vorlesung Grundlagen der Mikrobiologie, Ringvorlesung Methoden der Mikrobiologie	6+2	177
BB3.MB-WC	Mikrobiologische Methoden und Mikrobiologisches Berufsfeld	6	4
	Vorlesung Vielfalt mikrobieller Lebensformen	3	-
BBGW 1.4/1	Vorlesung Bio-Geo-Interaktionen mit Geländeübung	3	11
BBGW 1.4/2	Seminar Bio-Geo-Interaktionen I/2	3	20
BBGW 4.3	Bio-Geo-Interaktionen II		21
MMB001	Einführung in die Mikrobiologie	6	12 Erstsemester + 36 Mentoring
MMB001	Microbial Communication Colloquium		Ca. 150

MMB003	Praktikum Mikrobielle Kommunikation	10	11
	Seminar Mikrobielle Kommunikation		11
	Vorlesung Mikrobielle Kommunikation		11
MMB007	Praktikum Basidiomyceten (inkl. Exkursion)	10 5	4
	Seminar Basidiomyceten		4
	VL Großpilze/Hausarbeit Zellbiologie und Kommunikation in Basidiomyceten		4+5 BSc Bioinformatik
MMB017	Seminar Mikroben-Pflanze-Interaktionen	5	4
	Übung Mikroben-Pflanze-Interaktionen		4
	Praktikum Mikroben-Pflanze-Interaktionen (Dr. Agler)		4
MBGW1.1	Bio-Geo-Kolloquium	3	20
MBGW 1.3	Vorlesung/Seminar Bioremediation	5	11 9
MBGW 1.4.6	Praktikum Bodenmikrobiologie	6	8
	Seminar Organismische Interaktionen	2	~30

Vertiefungs- und Projektmodule	**ECTS**	**Anzahl Studierende**
Vertiefungspraktikum Mikrobiologie BB3.MB4	10	
Vertiefungsmodul MMB 700	15	7
Projektmodul MMB 800	15	7
Biogeowissenschaftliches Projektmodul BBGW 6.3.1/2	10	2

WS 2023/2024 und SS 2024

Modulnummer	**Veranstaltung**	**ECTS**	**Teilnehmerzahl**
BB029	Terrestrische Mikrobiologie (Praktikum)	10	7
	Terrestrische Mikrobiologie (Theorie)		7
BB028	Terrestrische Mikrobiologie (Theorie)	5	8
BB011	Allgemeine Mikrobiologie (Praktikum)		44
BBio1.5, 011/BEBW4/ BBC2.2, 005(LBio-MBio	Vorlesung Grundlagen der Mikrobiologie, Ringvorlesung Methoden der Mikrobiologie	6+2	176
BB034.MB-WC	Mikrobiologische Methoden und Mikrobiologisches Berufsfeld	6	8
BB1.5/BEBW4	Vorlesung Vielfalt mikrobieller Lebensformen	3	-
BBGW3.6	Praktikum Mikrobiologie für Biogeowissenschaften	3	-
BBGW 1.4/1	Vorlesung Bio-Geo-Interaktionen mit Geländeübung	3	19
BBGW 1.4/2	Seminar Bio-Geo-Interaktionen I/2	3	19
MMB001	Einführung in die Mikrobiologie	6	17 Erstsemester + 10 Mentoring
MMB003	Vorlesung Mikrobielle Kommunikation	10	17
	Praktikum Mikrobielle Kommunikation		17
	Seminar Mikrobielle Kommunikation		17
	Microbial Communication Colloquium		Ca. 150
MMB007	VL Großpilze/Hausarbeit Zellbiologie und Kommunikation in Basidiomyceten	10	2
	Praktikum Basidiomyceten (inkl. Exkursion)		1
	Seminar Basidiomyceten		1
MMB017	Praktikum Mikroben-Pflanze-Interaktionen (Dr. Agler)	5	3
	Seminar Mikroben-Pflanze-Interaktionen		3
	Übung Mikroben-Pflanze-Interaktionen		3
MBGW1.1	Bio-Geo-Kolloquium	3	20
MBGW 1.3	Vorlesung/Seminar Bioremediation	5	5
MBGW 1.4.6	Praktikum Bodenmikrobiologie	6	2
	Seminar Organismische Interaktionen	2	~30

Vertiefungs- und Projektmodule	**ECTS**	**Anzahl Studierende**
Vertiefungspraktikum Mikrobiologie BB3.MB4	10	1
Vertiefungsmodul MMB 700	15	2
Projektmodul MMB 800	15	2
Biogeowissenschaftliches Projektmodul BBGW 6.3.1/2	10	1
Projektmodul BB800	11	3

Abschlussarbeiten

Bachelorarbeiten

Franz Engelhardt. Interaktionen in der Trüffel Ektomykorrhizosphäre (August 2023)

Victoria Hory. Untersuchung des Einflusses verschiedener Kohlenstoffquellen auf das Wachstum von *Schizophyllum commune* in kontaminierten Böden (August 2023)

Anna Lena Windrich. Untersuchung der Aufnahme von Selen *in Phaseolus vulgaris var. nanus* und der Interaktion von Selen mit Wurzelexsudaten (Juni 2024)

Cosima Handschug. „Interaktionen zwischen dem Weißfäulepilz *Schizophyllum commune* und dem Mikrobiomen belasteter Bodensubstrate aus dem Rückbau nuklearer Anlagen (Juli 2024)

Sascha Robel. Thiopeptide antibiotics and their recognition and effect in Streptomyces (Juli 2024)

Emily Reichel. Einfluss von Schwermetallen auf die Genexpression und das Wachstum eines metalltoleranten Streptomyceten (September 2024)

Kyra-Larissa Markus. Untersuchung von Thiopeptidstress und Co-Kultivierung mit Thiopeptid-Produzenten auf Streptomyceten (September 2024)

Zweitbetreuung/Drittgutachten:

Philippa Vestner. Einfluss der Streptomyces-Inokulation auf kolloidale Phasen im Poren- und Grundwasser auf dem Testfeld Gessenwiese (Juli 2024)

Eleanor Frost. Pflanzenökologische und Stressphysiologische Untersuchungen an ausgewählten Standorten der sanierten Abraumhalde Beerwalde mittels Chlorophyl Messungen (August 2024)

Rebecca Ruiter. The degradation of 4MSOB-Isothiocyanat shapes interactions between phytopathogenic *Pseudomonas viridiflava* and commensal Plantibacter (Oktober 2024)

Masterarbeiten

Nayeema Nushrat. Investigation of mating types genes in the basidiomycete *Tricholoma vaccinum* (Januar 2023)

Marla Josephine Jeckstiess. *Tuber aestivum*: Effect of soil parameters and microorganism composition on growth and cultivation (August 2023)

Xinbo Chen. Charakterisierung der stickstofffixierenden Bakterien auf den Flächen eines ehemaligen Uranbergbaugebiets (Oktober 2023)

Robert Jesse. Characterization of stomatin – a lipid raft associated protein – in the basidiomycete *Schizophyllum commune* (November 2023)

Levke Petersen. Growth and degradation capacities of *Schizophyllum commune* (November 2023)

Alexander Gloger. Bioinformatic examination of viruses associated with *Streptomyces* bacteria (November 2023)

Aswathi Gopa Kumar Nair. Micoorganisms associated with Tuber aestivum: Natural and post inoculation soil microbiome in the fields (Dezember 2023)

Leandro Santiago Padilla. Isolation and biochemical characterization of symbiotic yeasts associated with the Erasian spruce bark beetle *Ips typographus* (Januar 2024)

Najmun Naher Orin. *Schizophyllum commune*: Influence of intracellular signal transduction on microbial interaction (November 2024)

Zweitbetreuung/-gutachten:

YoungJun Bae. Optimization of a synthetic carbon fixation cycle using machine learning (Februar 2023) Max-Planck-Institut für terr. Mikrobiologie Marburg

Rhedia Tehrin Proma. Characterization of microbes and microbial consortia from rhizosphere and their impact on plant growth of different Petunia genotypes (2023)

Neetu Neetu. Investigation of beneficial microbe-microbe/plant-interaction in sustainable horticulture (Juli 2023)

Aftab Mahmood Ayas. Elucidation of regulatory metabolites in the cuticle supplementing symbiosis of the grain beetle *Oryzaephilus surinamensis* (September 2023)

Enes Baran Demiray. Specificity and regulation of symbiont transmission in beewolves (Hymenoptera, genus *Philanthus*) (November 2023)

Nicolas Köppner: Untersuchung von Schadstofftransporten in Säulenversuchen mit *Schizophyllum commune* für die Entwicklung von Bioremediationsansätzen radioaktiv kontaminierter Böden (November 2023)

Alicia Maria Göppel. Dendroanalyse verschiedener Baumarten im ehemaligen Uranerzbergbau in Ronneburg (Thüringen) (Dezember 2023)

Inan Sapkota. Clinico-microbiological profile of multi-drug resistant pathogens in high-risk febrile neutropenia and clinical correlation of stool surveillance culture (Januar 2024)

Shivani Kiran Nimbkar. Detoxifiction of spruce phenolic compounds by bark beetle symbiotic fungus *Cylindrobasidium ipidophilum* (Juli 2024)

Karthika Muthuraj. Long-term placenta explant culture: Excluding microbial contamination in toxicity assays (Juli 2024)

Phoebe Chin. The role of *Lichtheimia corymbifera* proteins on the intracellular acidification in human primary monocytes (August 2024)

Felia Knoch „Untersuchung zur Thallusin induzierten Gametogenese in der marinen Makroalge *Ulva* (Chlophyta) (August 2024)

Jan Warthöfer. Stabilisierung organischer Bodensubstanz im ehemaligen Bergbaugebiet Ronneburg durch kalkhaltige und mikrobielle Zusätze (November 2024)

Staatsexamen

Jonas Baumgarten. Effects of *Phocalicola vulgatus* mpk, on epithelial cell damage caused by the human pathogen *Candida albicans* (Februar 2023) – Lehramt Gymnasium

Seminarfacharbeiten

Virginia Meister und Emma Schmidt. Einfluss von verschiedenen Umweltfaktoren auf die Bodenmikroorganismen in Pflanzenkulturen (November 2024)

5. Supporting Early Career Scientists

Promotionsabschlüsse 2023 und 2024

Ezediokpu, Marycolette Ndidi. Terpenes in the ectomycorrhizal association between Norway spruce *(Picea abies*), or Scots pine (*Pinus sylvestris*) and *Tricholoma vaccinum* (Juni 2023)

Murillo-Roos, Mariana. The chemical landscape of leaves as a driver for microbial community structure and metabolic interactions (Juli 2023)

Fürst, David. Einfluß mikrobiologischer Behandlungen auf das Phytoremediationspotential verschiedener Baumarten auf metallbelasteten Böden eines ehemaligen Bergbaustandortes (Oktober 2023)

Silva Costa, Flávio. Biomineralization capabilities of *Streptomyces mirabilis* P16B-1: Insights into struvite and nickel-struvite synthesis and their implications (Oktober 2023)

Harpke, Marie. Microbial adaptation and community dynamics in a former uranium mining and milling site (November 2023)

Östreicher, Manuela. Metal stress response of the ectomycorrhizal basidiomycete *Tricholoma vaccinum* (April 2024)

6. Equal Opportunities, Diversity and Family Support

2023

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
13	7	9
2 PostDocs		3
2 Technische Assistentinnen		

2024

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
11	7	7
2 PostDocs		3
2 Technische Assistentinnen		

7. International Cooperations

ENEA – Casaccia Research Centre – **Italien**
University of Bucharest – **Rumänien**
Babes-Bolyai University of Cluj-Napoca – **Romänien**
Jagiellonian University in Krakow – **Polen**
University of Vienna – **Österreich**
Örebro Universitet – **Schweden**
University of Cagliari – **Italien**
University of Tucumán & PROIMI – **Argentinien**
University of Debrecen – **Hungary**
Instituto Politécnico Nacional CICATA-QRO – **Mexiko**
State Ecological Academy in Kiew – **Ukraine**

7. Administration

Beschäftigungsstruktur

	Personen	Stellenanteile
Beschäftigte im Rahmen von Haushaltsmitteln		
Wissenschaftliche MitarbeiterInnen	5	3,5
Postdoc	2	1,0
Technische Assistenz	2	2,0
Sekretariat	1	1,0
Tutorinnen	2	
Beschäftigte im Rahmen von Drittmitteln		
Wissenschaftliche MitarbeiterInnen	11	5,6
Wissenschaftliche Assistenten	4	
Studentische Assistenten		
Weiteres Personal		
Auszubildende	1	

Vertretung in Selbstverwaltungsgremien (Prof. Kothe)

- Mitglied der Prüfungskommission BSc/MSc Biogeowissenschaften
- Sprecherin der Graduiertenschule Jena School for Microbial Communication
- Mitglied des Rats der Graduiertenakademie der FSU
- Mitglied des Forschungsrats der Universität Hamburg
- Mitglied des Kuratoriums des Helmholtz-Zentrums Dresden-Rossendorf
- Gast im Beirat der Forschungsstelle für gartenbauliche Kulturpflanzen, Erfurt
- Mitglied des Exekutivkommittees der International Max Planck Research School "global Biogeochemcial Cycles"
- Mitglied der International Max Planck Research School "Molecular Ecology ", International Leibniz School "Molecular Microbial Interactions", DFG-SFB "ChemBioSys"; LeibnizCampus InfectoOptics; InfectoGnostics; Abbe Center of Photonics
- Editor-in-Chief: Journal of Basic Microbiology
- Mitglied des Fachausschusses Mathematik und Naturwissenschaften der Akkreditierungsagentur Acquin

8. Team

Leiterin	Univ.-Prof. Dr. Erika Kothe	
Stellvertreterin	Dr. Katrin Krause	
Technische Assistentinnen	Petra Mitscherlich	Peggy Brand-Schön Sylvia Creutzburg
Verwaltung – Sekretärin	Christin Reichmann	
PostDocs	Dr. Lea Traxler	
Promovierende	Nina Carl Flavio Silva Costa Enes Baran Demiry Marycolette Ezediokpu David Fürst Aswathi Gopa Kumar Nair Maximilian Herold Marlene Höller Alex	Evans Iyamu Robert Jesse Kevin Lenk Manuela Östreicher Sebastian Pietschmann Levke Petersen Berit-Frizzy Porsche Johanna Ziethe
Studierende	Xinbo Chen Suiya Begum Marla Jeckstiess Emily Reichel Kyra-Larissa Markus	Najmun Naher Orin Sascha Robel Franziska Vogler Debbar Mossaab

NWG „Plant Microbiosis“

Dr. Matt Agler

A thaliana NG2, isolated from Jena, inoculated in a gnotobiotic system (controlled microbiome) together with a *Janthinobacterium* sp. isolate, recovered from the same wild plant population, and *Sclerotinia sclerotiorum*, a necrotrophic plant pathogen.

1. Research

Plants are constantly exposed to a variety of stressors, including phytopathogenic pathogens. Although plants have their own immune systems, proper microbiota balance is critical to their survival. In fact, interactions between bacteria, fungi and oomycetes are so important, that when certain of these components are missing, plants cannot survive in nature. To better protect plants, we want to understand how and why these important interactions arise.

Microbial Diversity in Natural Plant Populations

Characterizing microbial diversity is an important first step in understanding it. Since establishing methods to more efficiently characterize bacterial and fungal diversity in plant organs like leaves (Mayer et al., 2021), we have been busy looking at what shapes bacterial diversity in natural populations of *Arabidopsis thaliana*. *A. thaliana* populations in Jena are diverse in terms of both their genetic diversity and in the makeup of important secondary metabolites that play roles in defense against herbivores and bacterial and fungal pathogens. By studying bacterial diversity in these populations over several years, we found that a) *A. thaliana* leaf bacterial communities largely overlap with other plants in their environment, but have some microbial “markers” that distinguish them and b) Changing patterns of leaf microbiota recruitment over time are shared between some populations. We have preliminarily published these findings (Mayer et al., 2022) and are working to understand the role of climate in these patterns . Thanks to some of these preliminary findings, we were able to obtain DFG funding (Projekt Nr 458884166) to look at functional diversity in these plant-microbe communities over time using metagenomics, in collaboration with the group of Gianni Panagiotou. In short, we find that abundant modules of leaf bacteria are enriched in functions related to drug resistance. These functions contribute to their survival in niches associated with metabolism of plant specialized metabolites (Unger et al., 2024)

Plant traits and microbial interactions

The habitat of leaf microbes is primarily shaped by the host plant, but can also be strongly influenced by other microbes. We believe that this influence can play a big role.

(1) *A. thaliana* populations around Jena produce diverse glucosinolates that are known to help protect against herbivores or pathogen infestation when they are converted to toxic isothiocyanates (ITCs) upon leaf damage. We found that glucosinolates also help recruit commensal leaf bacteria, who can use them as carbon sources. Some of these microbes can also break down ITCs similar to pathogenic bacteria. We are investigating how these activities shape bacterial recruitment and its importance for plant health, especially its roles in non-host resistance to pathogens.

(2) Plant-derived resources can also play an important role in promoting bacterial diversity and adaptation. We found that the habitat on leaves of different plants can be metabolically very different and that some bacteria on leaves are likely to support each other metabolically through cross-feeding. Since the expression of virulence genes in many bacterial pathogens is dependent on specific metabolites, we are investigating how these metabolic interactions influence virulence.

2. Publications

Unger, K., Raza, A.K., Mayer, T., Reichelt, M., Stuttmann, J., Hielscher, A., Wittstock, A., Gershenzon, J., Agler, M.T. (2024) Beyond Defense: Glucosinolate structural diversity shapes recruitment of a metabolic network of leaf-associated bacteria. *Nature Communications*. doi: https://doi.org/10.1038/s41467-024-52679-7. *For this publication, Kerstin Unger received the 2024 Microverse Publication Prize*

J Jose, E Teutloff, S Naseem, E Barth, R Halitschke, M Marz, MT Agler
Immunity and bacterial recruitment in plant leaves are parallel processes whose link shapes sensitivity to temperature stress. bioRxiv, doi: https://doi.org/10.1101/2024.06.10.598336

Mayer, T., Teutloff, E., Unger, K., Lehenberger, P., Agler, M.T. (2024) Deterministic colonization arises early during the transition of soil bacteria to the phyllosphere and is shaped by plant-microbe interactions. *BioRxiv*. doi: https://doi.org/10.1101/2024.10.24.619992

3. Third Pary Funding

Projektträger	Vorhaben	Laufzeit	Mittel in 2021
Max-Planck-Gesellschaft	International Max Planck Research School "Chemical Communication in Ecological Systems"	01.11.2021-31.10.2024	1 Doktorand
JSMC/Carl Zeiss Stiftung	JSMC / Microverse / Carl Zeiss Stiftung	02.07.2021-31.12.2024	1 Doktorandin + 10.000 €
DFG	Projekt "Mikrobielle Wechselwirkungen auf den Blättern als Treiber für bakterielle Anpassungen"	01.11.2021-31.05.2024	245.182 Personal-/Sachmittel + 162,562 Sequenzierungskosten
DFG	Microverse	01.01.2020-01.06.2023	10.000 € +1 Doktorandin

4. Teaching

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
MMB017	Praktikum Mikroben-Pflanze-Interaktionen (Dr. Agler)	5	18
	Seminar Mikroben-Pflanze-Interaktionen		18
	Übung Mikroben-Pflanze-Interaktionen		18

Vertiefungs- und Projektmodule	ECTS	Anzahl Studierende
Projektmodul MMB800	15	2
Vertiefungsmodul MMB700	15	2

Masterarbeiten

Erik Teutloff. Balance in plant bacterial recruitment affects resilience to fungal invasion of the phyllosphere*. (December 2022)*

Smilla Adler. Cross-feeding as mechanism for pathogen biocontrol*. (October 2023)*

Dissertation

Mariana Murillo-Roos. The chemical landscape of leaves as a driver for microbial community structure and metabolic interactions (July 2023)

5. Equal Opportunities, Diversity and Family Support

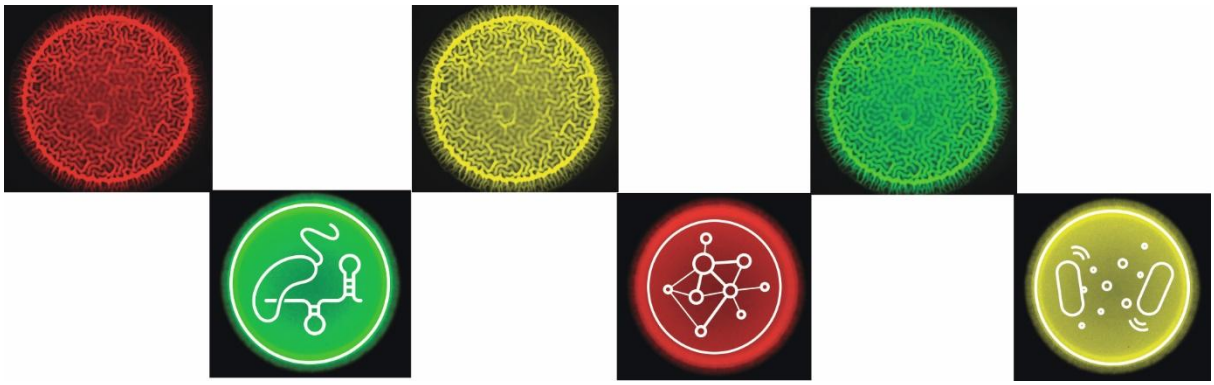
Anteil Frauen	Anteil Männer	Mit Kindern unter 12 Jahren
7	3	2

6. Team

Leiter	Dr. Matthew Agler	
PostDocs	Dr. Shubhangi Sharma	Dr. Mariana Murillo-Roos
Promovierende	Mariana Murillo-Roos Jisna Jose	Kerstin Unger Syed Ali Komail Raza
Studierende	Erik Teutloff Niclas Krauß Smilla Adler (Inst. Técnico, University of Lisbon)	Janek Wunderlich (HiWi) Rebecca Ruiter (HiWi) Simrat Naseem (HiWi)

Lehrstuhl für Allgemeine Mikrobiologie

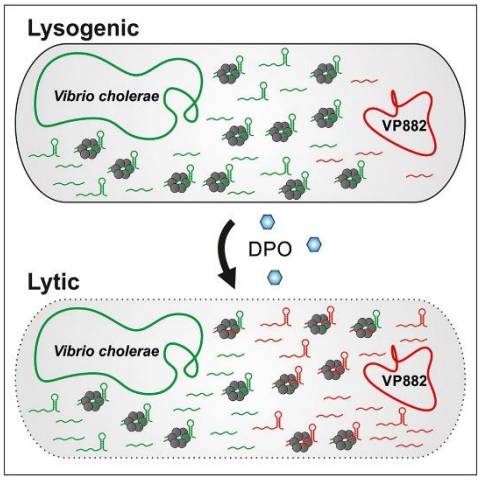
- Prof. Dr. Kai Papenfort -



1. Research

The overall goal of our research is to understand the regulatory mechanisms controlling complex behaviors and stress resistance in pathogenic microorganisms. To this end, we focus mainly on the major human pathogen, *Vibrio cholerae*, which we employ as model to study the following four main areas of research: 1) discovery and characterization of novel functional non-coding regulators; 2) the role of small proteins in microbial physiology; 3) molecular principles of quorum sensing-mediated gene regulatory processes; 4) the interaction of phages with bacterial pathogens.

The influence of regulatory RNAs on host-phage interactions (Sprenger et al, 2024)



Many bacteria, if not all, utilize quorum sensing (QS) as a mechanism to coordinate population-wide behaviors such as biofilm formation, virulence, and motility, based on cell density. Intriguingly, recent discoveries have revealed that bacteriophages (phages) - viruses that infect bacteria - can also engage in QS-like systems. These phages are capable of either producing their own communication molecules or "listening in" on the QS signals of their bacterial hosts to inform critical decisions, such as whether to initiate a lytic cycle (destroying the host) or to enter a lysogenic state (integrating into the host genome and remaining dormant). In this study, we explored the complex interplay between *Vibrio cholerae* and the lysogenic phage VP882, which responds to the host-produced QS molecule DPO (3,5-dimethylpyrazin-2-ol). We demonstrated that activation of VP882 by DPO triggers a shift in the molecular landscape of the host cell: phage transcripts become associated with the host's major RNA chaperone, Hfq. This interaction is not merely passive:

phage RNAs actively compete with and displace host-encoded small RNAs (sRNAs) from Hfq, resulting in downregulation of host regulatory RNA activity.

Remarkably, VP882 does not rely solely on hijacking the host's RNA machinery. It also encodes its own set of sRNAs that bind to Hfq. We identify and characterize one such phage-derived sRNA, named VpdS, which plays a significant role in promoting phage replication. VpdS fine-tunes the expression of both phage and host mRNAs, thereby shaping the intracellular environment in favor of viral propagation. Furthermore, our findings revealed that host-encoded sRNAs are not passive victims in this conflict. Instead, they can act as antagonists to phage development by targeting phage mRNAs for downregulation. This suggests that sRNAs are not only central to bacterial gene regulation but may also constitute a previously underappreciated layer of the bacterial defense system against phage attack. Overall, our findings shed light on the molecular tug-of-war between phage and host and highlights the critical role of RNA-based regulation in shaping infection outcomes.

2. Publications

Three selected publications

Sprenger, M., Siemers, M., Krautwurst, S., and Papenfort, K. (2024) Small RNAs Direct Attack and Defence Mechanisms in a Quorum Sensing Phage and its Host. Cell Host Microbe, https://doi.org/10.1016/j.chom.2024.03.010.

Ghandour, R., Devlitsarov, D., Popp, P., Melamed, S., Huber, M., Siemers, M., Krüger, T., Kniemeyer, O., Klingl, A., Brakhage A. A., Erhardt M , Papenfort K. (2024) ProQ-associated small RNAs control motility in Vibrio cholerae. Nucleic Acids Research doi: 10.1093/nar/gkae1283.

Papenfort K. and Melamed S. (2023) Small RNAs, Large Networks: Posttranscriptional Regulons in Gram-Negative Bacteria. Annual Reviews of Microbiology, 77:23-43.

3. Third Party Funding

Major third party funding:

German Research Foundation (DFG), "Sponge RNA controlled quorum sensing transition in *Vibrio cholerae*", 2020-2024.

Vallee Foundation, Vallee Scholar Award, 2019-2023.

German Research Foundation (DFG), SPP2002, Small Proteins in Prokaryotes, an Unexplored World, 2017-2023.

ERC-CoG, Art-RNA, 2024-2029.

German Research Foundation (DFG), Microverse Cluster, 2020-2024.

German Research Foundation (DFG), SPP2330, "New Concepts in Prokaryotic Virus-host Interactions – From Single Cells to Microbial Communities", 2021-2024; 2024-2027.

German Research Foundation (DFG), SPP2389, "Emergent Functions of Bacterial Multicellularity", 2021-2024.

German Research Foundation (DFG), CRC1127, "Chemical Mediators in Complex Biosystems (ChemBioSys)", 2022-2026.

German Research Foundation (DFG), “Regulatory roles of the global RNA chaperone ProQ in *Vibrio cholerae*”, 2024-2027.

4. Teaching

WS 2023/2024 und SS 2024

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
Wintersemester			
BB031	Bakterielle Genregulation (Praktikum)	10	5
	Bakterielle Genregulation (Theorie)		
BB030	Bakterielle Genregulation (Theorie)	5	8
BBio1.5, 011/BEBW4/ BBC2.2, 005, LBio-MBio	Vorlesung Grundlagen der Mikrobiologie	6+2	176
	Ringvorlesung Methoden der Mikrobiologie		
BBC005, BBC2.2, LBio-MBio	Allgemeine Mikrobiologie (Praktikum)		108
MMB002	Infection biology (Vorlesung)	10	19
	Infection biology (Praktikum)		
	Infection biology (Seminar)		
MMB001	Microbial Communication Colloquium		Ca. 150
	Microorganism Adaption (Seminar)		25
Sommersemester			
BB011, BB1.5	Allgemeine Mikrobiologie (Praktikum)		44
MMB006	Microbial Stress Response (Vorlesung)	10	4
	Microbial Stress Response (Praktikum)		
	Microbial Stress Response (Seminar)		
MMB001	Microbial Communication Colloquium		Ca. 150
	Microorganism Adaption		25

WS 2024/2025

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
Wintersemester			
BB031	Bakterielle Genregulation (Praktikum)	10	8
	Bakterielle Genregulation (Theorie)		
BB030	Bakterielle Genregulation (Theorie)	5	6
BBio1.5, 011/BEBW4/ BBC2.2, 005, LBio-MBio	Vorlesung Grundlagen der Mikrobiologie	6+2	167
	Ringvorlesung Methoden der Mikrobiologie		
BBC005, BBC2.2, LBio-MBio	Allgemeine Mikrobiologie (Praktikum)		104
MMB002	Infection biology (Vorlesung)	10	20
	Infection biology (Praktikum)		
	Infection biology (Seminar)		
MMB001	Microbial Communication Colloquium		Ca. 150
	Microbial Adaption (Seminar)		25

Projekt- und Vertiefungsmodule	ECTS	Anzahl Studierende
Vertiefungsmodul MMB 700	15	3
Projektmodul MMB 800	15	3
Projektmodul BB800	11	1

Bachelorarbeiten
Larissa Ostmeyer, Maxwell Zienecker

Masterarbeiten
Felix Späth, Maria Thamm, Michael Afe, Lloyd Tucker

5. Team

Post-doctoral fellows: Elisabeth Urbauer, Marcel Sprenger, Elke-Martina Jung, Rabea Ghandour, Kerstin Thriene, Sebastian Krautwurst, Federico D'Agostino

PhD students: Hugo Ligthart, Eoghan O'Driscoll, Jose Garcia-Yunge, Liz Maria Luke

Technicians: Kerstin Gluth, Yvonne Greiser

Administration: Sandra Golke-Stiebritz

Student support: Larissa Ostmeier, Christoph Manitz

Master students: Julius Bauer, Ferenc Kanitz

NWG „RNA-Biologie der Bakterien“

Dr. Kathrin Fröhlich

1. Research

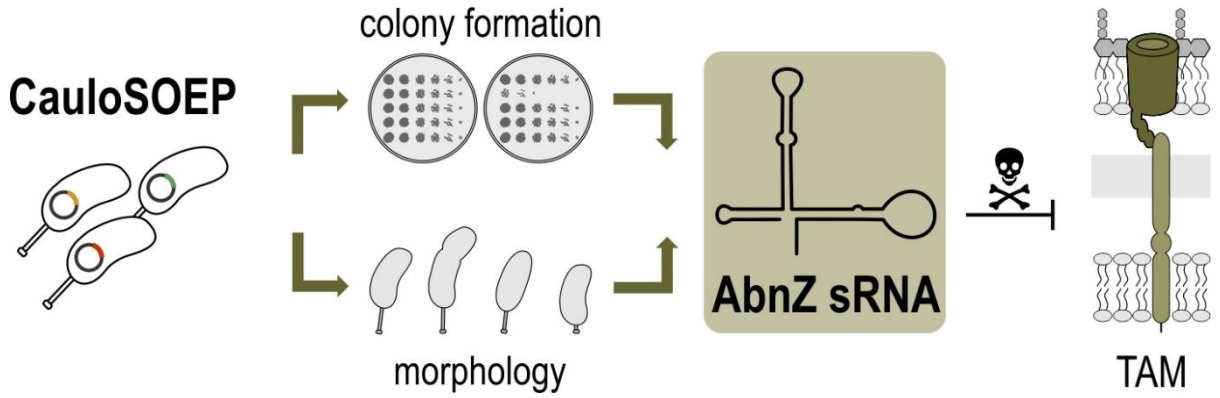
Bakterien sind in der Lage, sich auf ständig ändernde Bedingungen einzustellen und in den verschiedensten Habitaten zu überleben. Diese Anpassungsfähigkeit beruht zum einen auf einer effektiven Wahrnehmung der Umgebung und zum anderen auf der schnellen Regulation der Genexpression. Neben Protein-vermittelten Mechanismen spielt hier die post-transkriptionelle Kontrolle durch regulatorische RNAs eine entscheidende Rolle.

Kleine, regulatorische RNA-Moleküle (engl. *small RNAs*; sRNAs) sind eine heterogene Klasse von Regulatoren die über kurze, meist unvollständige Basenpaarungen mit Zieltranskripten interagieren. RNA-bindende Proteine wie das in vielen Bakterienspezies konservierte RNA-Chaperon Hfq können zur Ausbildung der RNA-RNA-Interaktionen beitragen.

Eines der in der Arbeitsgruppe untersuchten Modellbakterien ist *Caulobacter crescentus*, ein Gram-negativer Mikroorganismus aus der Klasse der Alpha-Proteobakterien. Die charakteristische halbmondförmige (crescentoide) und namensgebende Gestalt des Zellkörpers ist auf das Intermediärfilament-ähnliche Protein Crescentin zurückzuführen, das in polymerisierter Form an der inneren Krümmung der Zelle vorliegt. Die RNA-Biologie in *C. crescentus* ist weitgehend unerforscht und von den ca. 130 sRNAs, die momentan in dieser Spezies annotiert sind, wurden lediglich einige wenige charakterisiert.

Um die Funktion von sRNAs systematisch zu analysieren, ohne dabei auf deren natürliche Expression unter einer gewählten Bedingung oder die Assoziation mit einem RNA-bindenden Protein wie Hfq angewiesen zu sein, eignen sich Überexpressionsplasmide. Für *Caulobacter* wurde die Plasmidbibliothek CauloSOEP (engl. *Caulobacter* sRNA overexpression) erstellt, in der pro Stamm jeweils eine von insgesamt 49 sRNAs unter der Kontrolle eines Vanillat-induzierbaren Promotors synthetisiert werden (Velasco-Gomariz *et al.* 2024 NAR). Im Rahmen der Studie wurde die sRNA AbnZ identifiziert, deren Überexpression mit einer stark veränderten Zellmorphologie und einer deutlich verminderten Fähigkeit zur Koloniebildung einhergeht. Durch Prozessierung wird AbnZ als stabiles 3‘ Ende der polycistronischen *acrABnodT* (*abn*) mRNA freigesetzt. Bei AcrAB-NodT handelt es sich um ein dreiteiliges Sekretionssystem, das den Export von Antibiotika, Toxinen und Detergenzien aus dem Zytoplasma in die Umgebung vermittelt. Damit ist AcrAB-NodT ein wichtiger Faktor bei der Entwicklung von mehrfachen Antibiotikaresistenzen.

Der toxische Phänotyp der AbnZ-Überexpression konnte durch genetische Analysen auf die Repression des Operons *tamAB* zurückgeführt werden, welches für das Translokationsmodul TAM kodiert. Im heterodimeren TAM-Komplex interagieren beide Untereinheiten über im Periplasma lokalisierte Domänen, und sind an der Integration von Transportproteinen und potentiell auch Phospholipiden in die äußere Membran des Bakteriums beteiligt. Unter physiologischen Bedingungen könnte eine kurzzeitige Inhibierung der *tamAB*-Expression durch AbnZ dazu dienen, dass die Insertion des AcrAB-NodT-Komplexes in die Membran des Bakteriums bevorzugt wird.



Charakterisierung der sRNA AbnZ in Caulobacter crescentus.

Eine Überexpression der sRNA AbnZ. über einen induzierbaren Promotor führt zu einer verminderten Fähigkeit zur Koloniebildung und einer Veränderung der Zellmorphologie. AbnZ inhibiert die Expression von TAM, eines für die Zelle essentiellen Membrankomplexes, der am Transport von Membranproteinen und Phospholipiden beteiligt ist.

2. Publications

Velasco-Gomariz, M., Sulzer, J., Faber, F., Fröhlich, K.S. (2024) An sRNA overexpression library reveals AbnZ as a negative regulator of an essential translocation module in *Caulobacter crescentus*. *Nucleic Acids Res*, gkae1139, https://doi.org/10.1093/nar/gkae1139 (online ahead of print)

Bandyra, K.J., Fröhlich, K.S., Vogel, J., Rodnina, M., Goyal, A., Luisi, B.F. (2024) Cooperation of regulatory RNA and the RNA degradosome in transcript surveillance. *Nucleic Acids Res*, 52(15):9161-9173

Vogt, L.N., Panis G., Schäpers, A., Peschek, N., Huber, M., Papenfort, K., Viollier, P., Fröhlich, K.S. (2024) Genome-wide profiling of Hfq-bound RNAs reveals the iron-responsive small RNA RusT in *Caulobacter crescentus mBio*, 15(4):e0315323

Ruhland, E., Siemers, M., Gerst, R., Späth, F., Vogt, L.N., Figge, M.T., Papenfort, K. and Fröhlich, K.S. (2024) The global RNA-RNA interactome of *Klebsiella pneumoniae* unveils a small RNA regulator of cell division *Proc Natl Acad Sci U S A*, 121, e2317322121.

3. Third Party Funding

Projektträger	Vorhaben	Laufzeit
DFG	Einzelantrag “Global Mapping of Hfq-dependent RNA-RNA interactions in *Caulobacter cresentus*”	01.10.2020 - 30.09.2024
DFG	Exzellenz-Cluster “Balance of the Microverse”	01.01.2021 - 31.07.2024
FSU	ProChance career “Global annotation of RNA-RNA interactions in the major human pathogen *Klebsiella pneumoniae*”	01.07.2020 - 30.06.2023

4. Teaching

Modulnummer	Veranstaltung	ECTS
MMB018	Praktikum „RNA Biology“	5
	Seminar „RNA Biology“	
MMB002	Vorlesung „Infection Biology“	10
MMB003	Vorlesung „Cell Biology and Biotechnology”	10
BB011, BBC005, BBC2.2, BB1.5, BEBW4, LBio-Mbio	Ringvorlesung „Methoden der Mikrobiologie“	6+2
	Vorlesung „Grundlagen der Mikrobiologie“	
BB034.MB-WC	Mikrobiologisches Berufsfeld	6
BB800	Projektmodul	11
MMB700	Vertiefungsmodul	15
MMB800	Projektmodul	15

Jena RNA Club

Um die Vielzahl der an oder mit RNA arbeitenden Wissenschaftler*innen in Jena zu vernetzen, organisiert Dr. Kathrin Fröhlich gemeinsam mit Dr. Matt Blango (Leibniz-HKI) und Dr. Holger Bierhoff (Uni Jena) im Rahmen des „Jena RNA Club“ eine monatliche Seminarreihe.

Sowohl 2023 als auch 2024 wurden daneben jeweils eintägige Symposien ausgerichtet, zu denen neben jeweils etwa 50 lokalen Teilnehmern auch Gastsprecher*innen eingeladen waren um im „Haus zur Rosen“ ihre Forschungsarbeiten zu unterschiedlichen Gebieten der RNA-Biologie zu präsentieren.

5. Team

Dr. Kathrin Fröhlich – PI

MSc. Manuel Velasco Gomariz (Promotion)

MSc. Eric Ruhland (Promotion)

MSc. Laura Vogt (Promotion)

BSc. Felix Späth (Abschlussarbeit MSc. Mikrobiologie)

BSc. Maria Thamm (Abschlussarbeit MSc. Mikrobiologie)

BSc. Leonie Giese (Abschlussarbeit MSc. Mikrobiologie)

Pia Kunstmann (Studentische Assistentin)

RNA-Biologie der Bakterien – Sommer 2024

Eric Ruhland, Laura Vogt, Maria Thamm

Manuel Velasco Gomariz, Kathrin Fröhlich

Lehrstuhl für Mikrobielle Interaktionen

Prof. Dr. Christian Jogler

1. Research

Elusive Microbes – cultivating, understanding and applying

The Department of Microbial Interactions aims to bring elusive microbes into axenic culture, to characterize them and to gain a deep understanding of their environmental interactions, their cell biology and their ability to support human health and well-being.

The mission of our laboratory is to push the boundaries of scientific knowledge by exploring the fascinating world of understudied or uncultivated bacteria. We are dedicated to unraveling the mysteries hidden within microbial communities and harnessing their untapped potential for biotechnological applications and the environment. Our research group is driven by a deep curiosity about the vast diversity of uncultivated bacteria that inhabit diverse ecosystems on our planet. We recognize that these microorganisms represent an immense reservoir of biological innovation and possess unique adaptations that can contribute to solving pressing global challenges. Through cutting-edge interdisciplinary research, we aim to understand the ecological roles, evolutionary dynamics, and metabolic capabilities of uncultivated bacteria. By leveraging advanced genomic, metagenomic, and bioinformatic approaches, we strive to decipher the genetic blueprints of these elusive microorganisms and gain insights into their functional attributes.

Our current research topics include:

- Interactions of heterotrophic bacteria and phototrophs
- Bioactive small molecule discovery and development of genetic engineering tools
- Isolation and cultivation of members of the phylum Planctomycetota
- Planctomycetal Cell division without FtsZ
- Magnetotactic bacteria

Interactions of heterotrophic bacteria and phototrophs

Up to 50% of the global CO_2 fixation is achieved by marine microorganisms such as algae. Their mass reproduction frequently occurs as transient events -blooms- that challenge the balance of the ocean's microverse. These large phytoplankton populations are partly consumed by higher trophic orders such as zooplankton and partly degraded by heterotrophic bacteria. Besides re-mineralization and the related CO_2 emission, organic carbon sinks as marine snow to the sea floor, where it is only partly degraded and partly stored in the sediment. However, the role of microbes that determine the ratio between CO_2 storage and CO_2 emission, is hardly studied. This is particularly true as some key players such as members of the phyla *Planctomycetota, Verrucomicrobiota*, *Bacteroidota* and *Gemmatimonadota* are mostly not available as axenic cultures. Thus, many aspects of the allelopathic interaction between algae and bacteria remain elusive.

In our research, we aim at detecting, cultivating and characterizing so far unstudied heterotrophic bacteria that are associated with microalgal blooms in the ocean. Using axenic cultures representing understudied phyla as well as well-studied marine model organisms, co-cultivation experiments are performed with the microalga *Gephyrocapsa huxleyi* (former *Emiliania huxleyi*) to simulate synthetic blooming events and their decay. This will contribute to a functional understanding of niche partitioning within the microalgal microbiota.

Furthermore, the role of members of the phylum *Planctomycetota* in marine communities is investigated. *Planctomycetota* are commonly present in the microbiota of marine phototrophs and can dominate the microbial community of the thalli of seaweeds. Compared to members of the *Roseobacter* group most strains of the phylum *Planctomycetota* are slow-growing, more challenging to cultivate and only little is known about their ecological significance. The isolated strain *Stieleria maiorica* Mal15^T turned out to impact the biofilm formation of *Roseobacter* group members mediated by the production of the small molecule stieleriacine A_1. Both bacterial groups are associated with algae and survive by allelopathic interactions on the surface of marine phototrophs.

The mutual triangular relationship between algae, *Planctomycetota* and *Roseobacter* group members build the centre of a second project on algal-bacterial interactions. The role of the small molecule stieleriacine A_1 in communities as well as its biosynthesis and the spatiotemporal effects during the formation of communities will be examined. The interplay in bi- and tripartite *Planctomycetota-Roseobacter*-phototroph communities will be addressed by visualizing the distribution of mediators in the community and exploring single-cell behavior with other organisms and compounds. The third part of this project aims at an investigation of the impact of *Planctomycetota* on phototroph differentiation and comprises growth assays with axenic *Ulva* sp. cultures and several *Planctomycetota* to identify responsible mediators. The results of the project should contribute to a more holistic understanding of the impact of chemical mediators in complex and vulnerable aquatic ecosystems.

However, the ecological importance of phototrophs does not stop with the transition to land, as they are a main component of biocrusts (BCs). BCs are intriguing communities composed of heterotrophic bacteria and fungi as well as photoautotrophic cyanobacteria, algae, mosses and lichens. Often referred to as the Skin of the Earth, the latest estimates state that they cover about 12% of all terrestrial surface. BCs are found globally where light is available but otherwise harsh conditions make the prevailing growth of higher plants impossible. They dominate arid regions such as the poles, deserts, and high alpine environments, where they are pivotal ecosystem engineers that offer a wide array of ecosystem services stabilizing the soil surface, preventing erosion, fixing carbon and nitrogen, and building up organic soil biomass that enables later plant settlement. Moreover, BCs immobilize heavy metals in contaminated soils, making them promising communities for bioremediation applications.

Despite their long-known ecological importance, many aspects of BC are still poorly understood. While their biogeography and ecology are well researched, detailed studies are confined to few geographical regions, resulting in limited knowledge about both photo- and heterotrophic species composition. Biochemical and molecular processes underlying their ecological functions,

interactions between the many different microorganisms that build a BC, and the role of secondary metabolites in these interactions are, with very few exceptions, still unknown. To investigate these intricate and important communities on a molecular level, model systems consisting of at least two organisms are needed. Such a system, however, so far only exists for cyanobacteria-dominated BCs from temperate North American deserts, which is unsuited to study BCs from other ecoregions like Europe, where BCs are also found in cold climate zones like the Alps or the Arctic. Hence, we strive to develop a model system to investigate microbial interactions in European, green-algal-dominated BCs.

Bioactive small molecule discovery and development of genetic engineering tools

Despite genome- and lifestyle-based evidence, neither the interaction of planctomycetes with bacterial competitors nor their suspected bioactive compound repertoire have been studied on the molecular level so far. As a model system we are currently investigating the interaction of the planctomycete *Stieleria maiorica* with *Phaeobacter inhibens*, a member of the '*Roseobacter* group'. The production of stieleriacines, a class of long-chain *N*-acyl tyrosines, by *S. maiorica* is potentially relevant for altering physicochemical properties of marine biotic surfaces, ultimately leading to active shaping of microbial communities by *S. maiorica*. The discovery of stieleriacines functions as a blueprint for a bioprospection approach targeting the identification of novel bioactive small molecules in characterized and novel members of the phylum. The approach combines agar plate-based bioactivity tests and extraction of liquid cultures with subsequent chromatographic analysis.

As part of the molecular toolbox that is required to investigate the role of secondary metabolite biosynthetic gene clusters and other structural genes, the research also focuses on the development of tools for the targeted modification of planctomycetal genomes as well as for an inducible gene expression. Especially the construction of replicative plasmids and strategies for the marker-free introduction of genomic modifications by two-step homologous recombination are urgently required to push the research field forward.

The large genomes of strains belonging to the class *Planctomycetia* harbour genes encoding uncharacterized biosynthetic gene clusters (BGCs), which are known to produce various bioactive secondary metabolites or small molecules. The project aims on the members of Planctomycetota to produce novel secondary metabolites using different strategies of stimulations and also by developing bioreactors. The project also emphasizes on the cultivation and polyphasic characterisation of novel members belonging to the phylum Planctomycetota. Several doctoral and postdoctoral researchers are associated to the project.

Isolation and cultivation of members of the phylum Planctomycetota

As part of the CRC AquaDiva the project focusses on groundwater microbiomes of the Hainich Critical Zone Exploratory (CZE). The Hainich CZE, located in northwestern Thuringia, covers different land-use types (forests, pasture, and agricultural land) over a hillslope transect of 6 km length. Installed groundwater wells, located all over the transect, enable fast sampling of the deep aquifers, ranging from oxic to anoxic conditions.

The cultivation focusses on the enrichment of planctomycetes as they contribute significantly to the subsurface carbon and nitrogen cycle. Especially "anammox" (anaerobic ammonium oxidation)-performing planctomycetes are abundant regarding metagenomics and have been also proven by the consumption of ammonium and nitrite. Besides the major ecological relevance of anammox-performing planctomycetes, they are also of huge biotechnological interest, especially for wastewater treatment plants. Planctomycetes are potential CPR (Candidate Phyla Radiation) hosts and have significant biotechnological potential, hence, also planctomycetes with an aerobic lifestyle are focused on. In addition to the subsurface, strains from existing collections are re-grown for genome sequencing and several previously explored spots are revisited for sampling.

Planctomycetal Cell division without FtsZ

Since many decades, researchers are focusing intensively on combating harmful bacteria. Most of the well-characterized bacteria, including some of the deadliest pathogens on earth, employ a cell division mechanism called binary fission. Here, a mother cell divides at its cell center giving rise to an identical daughter cell. The proteins required for this process are conserved and essential in all bacterial specimen – loss of function modifications will lead to cell death.

Recently, bacteria with different modes of cell division have attracted cell biologists' attention, like the asymmetrically-dividing *Planctomycetota* – also referred to as budding bacteria. In contrast to almost all other known bacteria today, they seem to lack the canonical and essential proteins for cell division, including the Z ring-forming FtsZ. In addition, it is not known which proteins are involved in the budding machinery. Therefore, we aim to describe the budding process of various planctomycetal specimens including the model organism *Planctopirus limnophila* using light- and electron microscopy. We will furthermore employ comparative genomics, dry-, and wet lab genome mining approaches to yield promising candidates involved in the cell division process. To analyze these candidates, the genetic accessibility of *P. limnophila* will be enhanced by optimized tools for introducing genomic modifications. Using these established systems, candidates will be investigated using molecular cloning techniques, high-resolution fluorescence microscopy, and image analysis.

Magnetotactic bacteria

Bacteria thrive in various complex habitats, which are formed by many different gradients including the earth's magnetic field. Magnetotactic bacteria (MTBs) align to this gradient and navigate effectively along the magnetic lines through these habitats. For this purpose, MTBs form ultra-pure magnetic crystals, the so called magnetosomes, which are nano-sized and membrane-enclosed. These organelles form chain-like structures and therefore function like compass needles aligning the cell to earth's magnetic field. Furthermore, these organelles can be found in various shapes, numbers per cell, and sizes. However, what and how the shape, number, and size of these organelles are regulated, remains undiscovered.

One reason is the scarce number of available axenic cultures of MTBs with different magnetosomes, including the magnetotactic multicellular prokaryote. The poly-phyletic origin of MTBs is the cause for their metabolic diversity and therefore increases the complexity of their cultivation. Despite this complexity and due to their ability to produce ultra-pure magnetite or greigite crystals from environmental available iron, MTBs obtain much attention as potent bioremediators of metal-contaminated soil and as ultra-pure natural iron source for high-end semiconductors.

To understand the formation of magnetosomes, their diversity has to be made accessible in the form of axenic cultures, optimized growth parameters, and analysis of genomic features. Using single cell isolation and single cell genome sequencing techniques, various MTBs will be isolated from environmental sediment samples. Their magnetotaxis and cellular features, focused on their magnetosomes, will be described using light- and electron microscopy potentially leading to accessible model strains for magnetosome research and their application in industry.

2. Publications

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Planctomycetaceae isolated from a red biofilm in the Tyrrhenian Sea close to the volcanic island Panarea. Antonie van Leeuwenhoek, 116(10), 995-1007.

Kumar G, Kallscheuer N, Kashif M, Ahamad S, Jagadeeshwari U, Pannikurungottu S, Haufschild T, Kabuu M, Sasikala C, Ramana, CV (2023). *Gemmata algarum*, a Novel Planctomycete Isolated from an Algal Mat, Displays Antimicrobial Activity. Mar Drugs, 22(1), 10.

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3. Third Party Funding

Funding body	**Project**	**Period**
DFG	CRC 1076 AquaDiva – project A07: "Subsurface Planctomycetes as Sources for Novel Biotechnological Applications"	Since 2021
DFG	CRC 1227 ChemBioSys – project A07: "Planctomycetal Chemical Mediators Shaping Aquatic Phototrophic Communities"	Since 2021
DFG Excellence Cluster "Balance of the Microverse"	Tandem project with Ivo Nischang/Ulrich Schubert: "Developing cryogel-based bioreactors enabling planctomycetal small molecule production"	Since 2022
Carl Zeiss Stiftung/Jena School for Microbial Communication	PhD fellowship "From Microbiome to function: understanding how bacteria support the imbalance of algal blooms and how they restore order to the microverse"	Since 2021
Wissenschaft im Dialog	Mikrobenjäger gesucht! Auf der Pirsch nach Bakterien mit Magnetsinn (Hochschulwettbewerb 2022)	2022-2023

4. Teaching

WS 2022/2023 und SS 2023

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
MMB004	Praktikum Mikrobielle Interaktionen	10	11
	Seminar Mikrobielle Interaktionen		
	Vorlesung Mikrobielle Interaktionen		
MMB008	Praktikum Mikrobielle Gemeinschaften	10	11
	Seminar Mikrobielle Gemeinschaften		
	Übung Mikrobielle Gemeinschaften		
BB031	Teil 2: Mikrobielle Ökologie	10	8

WS 2023/2024 und SS 2024

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
WCM-Mibi.p Molekulare mikrobielle Ökologie	Seminar Molekulare mikrobielle Ökologie	10	4
	Vorlesung Molekulare mikrobielle Ökologie		
	Vorlesung Molekulare mikrobielle Ökologie		
MMB004	Seminar Mikrobielle Interaktionen	10	17
	Vorlesung Mikrobielle Interaktionen		
	Vorlesung Mikrobielle Interaktionen		
MMB008	Praktikum Mikrobielle Gemeinschaften	10	17
	Seminar Mikrobielle Gemeinschaften		
	Übung Mikrobielle Gemeinschaften		

Abschlussarbeiten

BSc theses

Selma Kreiss. Magnetotactic bacteria and where to find them: citizen science and single cell microbiology characterize untapped MTBs (Oktober 2023)

Jordi Schörrig. Differential carbon source usage of three marine isolates representing common bacterial phyla associated with the marine microalgae *Emiliania huxleyi* and comparative cell number determination for a defined mock community (November 2023)

Samuel Schuck. Microscopic and molecular quantification methods for use in bacterial cocultures (September 2023)

MSc theses:

Velemir Lawrinenko. Exploring the Magnetotactic Bacteria: Novel Isolation Techniques and Cultivation Strategies (August 2023)

Moses Maina Kabuu. Functional characterization of novel planctomycetes paves the way to the discovery of bioactive compounds (November 2023)

Carmen E. Wurzbacher. On the Cell Biology of Deep Branching *Planctomycetota* (Januar 2024)

Emanuel Petre. From axenic cultures to a modular algal-bacterial co-cultivation system: Establishing cultivation and monitoring of the cosmopolitan coccolithophore *Emiliania huxleyi* with marine heterotrophic bacteria (Februar 2024)

5. Gender balance and family

2023

Women	Men	Children below 12 years
9	10	5
3 PostDoc m/w		0
1 Technical Assistant		0

2024

Women	Men	Children below 12 years
7	8	5
3 PostDoc m/w		0
1 Technical Assistant		0

6. International Cooperations

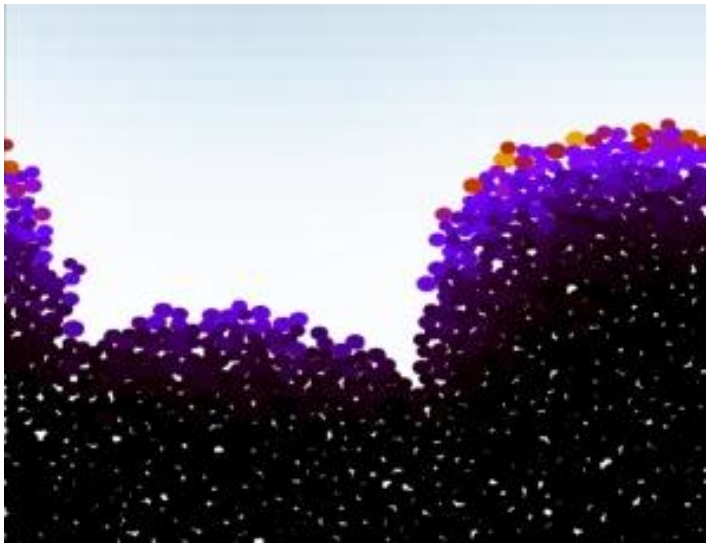
Prof. Olga Lage, Universidade do Porto – Porto, Portugal
Prof. Venkata Ramana Chintalapati, University of Hyderabad – Hyderabad, India
Prof. Lise Øvreås, University of Bergen – Bergen, Norway
Dr. Damien Devos, Institut Pasteur de Lille – Lille, France

7. Team

Head of Department	Prof. Dr. Jogler, Christian
Junior Group Leader	Dr. van Teeseling, Muriel C. F.
Technical Assistance	Wohlfarth, Nicole
Team Assistant	Schein, Sabine
Postdoctoral Researchers	Dr. Hotter, Vivien S.; Dr. Kallscheuer, Nicolai Dr. Kumar, Gaurav
Doctoral Researchers	Hammer, Jonathan; Haufschild, Tom Kündgen, Madeleine; Staack, Myriel Wurzbacher, Carmen E.
Students	Appiah, David; Kabuu, Moses Maina E. Kreiss, Selma; Lawrinenko, Velemir Niegisch, Jana-Sophie; Petre, Emanuel Rabold, Nico; Raupach, Lena Schörrig, Jordi; Schuck, Samuel Siebert, Sebastian; Wurzbacher, Carmen E.

Lehrstuhl Theoretische Mikrobielle Ökologie

Prof. Rosalind Allen

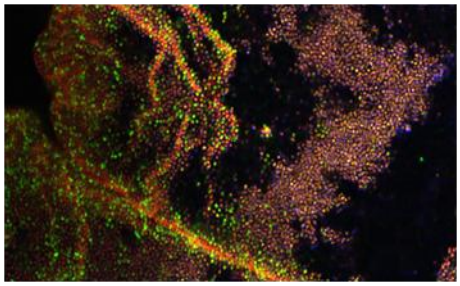


1. Research

The Theoretical Microbial Ecology group combines mathematical modelling with laboratory experiments to probe the mechanistic origins of microbe-environment interactions. We are interested in understanding microbe-environment interactions at the single-cell level, at the level of populations and at the level of microbial communities. The group started in October 2021 with the recruitment of Prof. Rosalind Allen to the Balance of the Microverse Excellence Cluster.

Modelling interspecies microbial interactions

In collaboration with the groups of Stefan Schuster (FSU) and Pierre Stallforth (FSU Jena and Leibniz-HKI), we track the population dynamics of the amoeba *Dictyosteium discoideum* in the presence and absence of toxic and non-toxic bacterial species. We are also developing mathematical models to match our data. Additionally, we are tracking the motion of amoebal cells on agar in the presence and absence of bacteria and developing corresponding individual-based models.



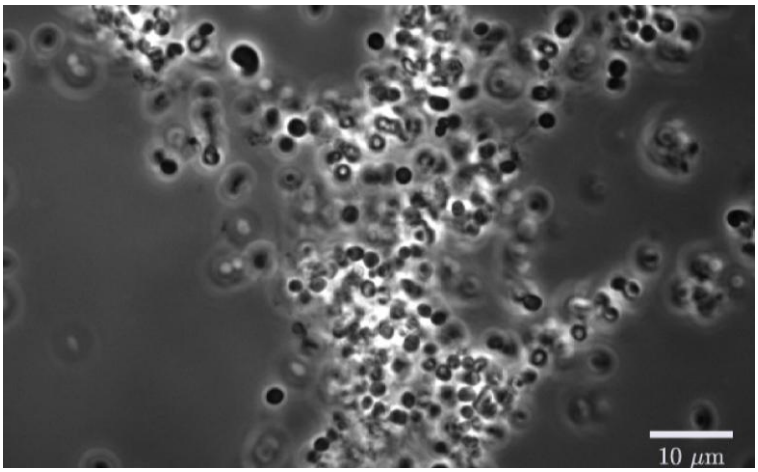
Working with the Agler group, we are developing mathematical models for the interaction between plant leaf pathogens and commensal bacterial species, based on the degradation of plant-produced immune defence chemicals by the pathogen, that can benefit the commensal species under some circumstances.

We are also establishing a new model system in our lab, based on clinical isolates taken from biliary catheter biofilm microbiomes, in which *Klebsiella pneumoniae* supports the growth of *Enterococcal strains* that cannot grow in isolation (see figure).

Microbial ecology of aggregation

Our group is interested in how bacteria form aggregates in liquid suspension, and the ecological consequences of bacterial aggregation. Recently we showed that extremely low doses of cell-wall targeting antibiotic (1/8000 x MIC) can trigger large-scale aggregation in *E. coli* cultures, via a mechanism that involves release of genomic DNA by a small minority of cells that are lysed by the antibiotic (Tavaddod et al, 2024, npj Biofilms & Microbiomes; see figure below).

Supported by a microverse project grant, we are now investigating the microbial ecology of bacterial aggregation within the context of a human host. We are screening a collection of clinical isolates of gut bacteria for their aggregation characteristics in the presence and absence of relevant factors such as bile acids and antibiotics. Our findings reveal that aggregation is prevalent among but bacteria and may be strongly affected by environmental conditions in the gut.

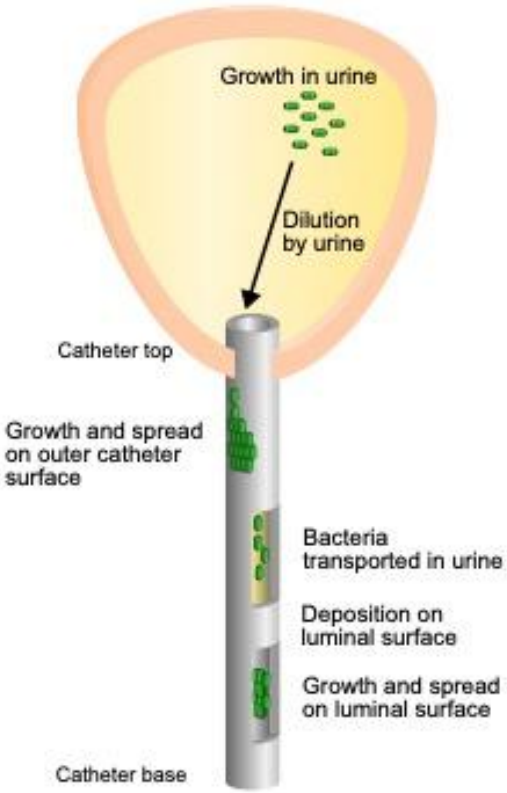


Exposure to very low doses of the antibiotic mecillinam can cause aggregation of *E. coli* cells. Taken from Tavaddod et al (2024) npj Biofilms Microbiomes.

Microbial colonisation of medical implants

We are using experiments and mathematical modelling to understand how bacteria colonise a range of medical implants within the human host. In recent work, we developed a mathematical model for bacterial colonisation of a urinary catheter (Bull et al 2025 Nature Communications). This model revealed a critical transition depending on the urine production rate by the kidneys. If urine is produced rapidly, bacteria are washed out of the system and the patient will not develop bacteriuria (bacteria in the urine). However for slow urine production rates, bacteria proliferate in the bladder and colonise the catheter. Our model also reveals that the catheter length is a key factor controlling the time before bacteriuria is detected. Therefore different clinical interventions, corresponding to different sets of parameters in our model, may be appropriate for long-term versus short-term catheterised patients.

We also have emerging interest in the colonisation of biliary catheters by bacteria, which can lead to life-threating cholangitis infections in patients who have undergone liver transplant surgery. Our work contributed to the development of light-activated antibiotic therapies for such biofilm infections (Eberhardt et al 2024, Int. J. Antimicrob. Ag.). We are now also investigating the factors that control the community composition of biofilm microbiomes on biliary catheters.



Sketch of our mathematical model for bacterial colonisation of a urinary catheter. Taken from Bull et al (2025) Nature Communications.

Modelling antibiotic action and resistance

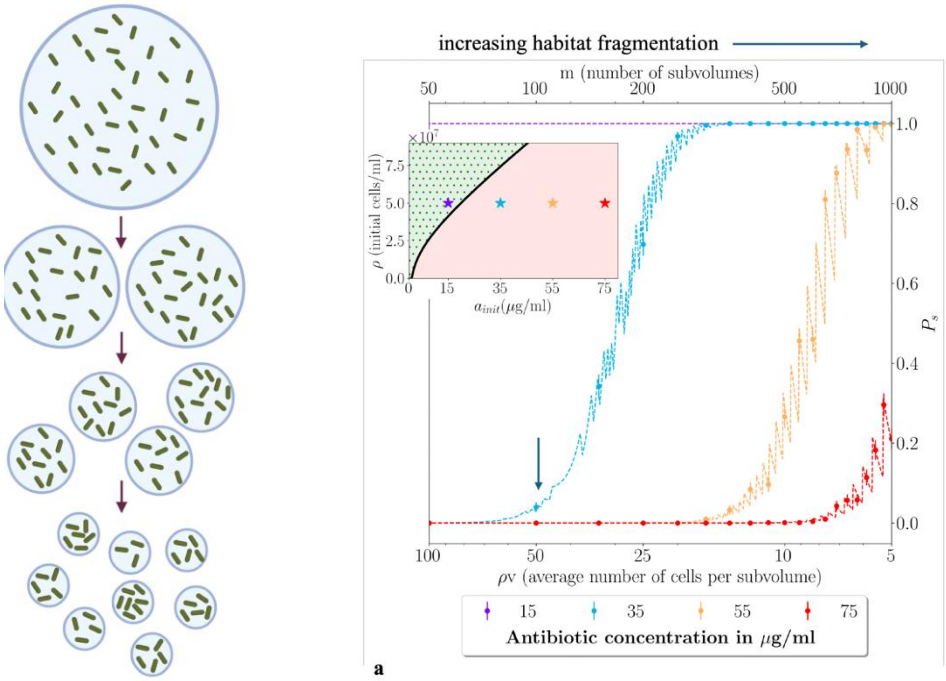
Modern medicine relies heavily on antibiotics to cure or prevent bacterial infections, and the emergence of antibiotic-resistant infections presents an ever-growing threat. Yet the interplay between antibiotic action and the physiology of a growing bacterial cells has been surprisingly little explored.

Biofilm formation and antibiotic efflux pumping are both clinically important mechanisms by which bacteria evade the killing effects of antibiotic treatment. Yet it is not well known how these mechanisms interact (Vareschi, Jaut et al, Trends Microbiol., in press). In a DFG project under the SPP2389 programme “Emergent functions of bacterial multicellularity”, in collaboration with the Schreiber group (BAM, Berlin), we are investigating the interplay between biofilm formation and antibiotic efflux and its role for the emergence of antimicrobial resistance. We have developed mathematical models to explore how efflux of antibiotic can inhibit neighbouring cells within a biofilm, as well as experimental models using colony biofilms of an efflux overexpressing strain.

At the same time, we are developing mathematical and experiments techniques to study the action of antibiotics on small and highly fragmented bacterial populations. Most microbiological assays are performed on very large microbial populations (~10^9 bacteria), but infections can be initiated by only a few individual bacteria, which may be in a confined environment such as a host cell. In theoretical work, we have shown that the fragmentation of a bacterial population into multiple small subpopulations can drastically affect its response to antibiotics (Verdon, Popescu et al 2025 J. R: Soc. Interface, see figure below). At the same time, in a collaboration with the Rosenbaum group (HKI), we have used a multiplexed microfluidic droplet setup to show that the response of small bacterial populations to antibiotics can differ greatly from the response of bulk populations.

We are also developing innovative models for the response of the bacterium *Staphylococcus aureus* to antibiotics. Using methods from mechanical engineering, we have shown how the

pattern of mechanical stress in the *S. aureus* cell wall changes during the cell cycle, and have developed a theory for stress-regulation of the control of cell scission. This model, developed with collaborators at Sheffield University, can explain diverse effects of the antibiotic methicillin, as well as why small cells may tend to show resistance to methicillin.



Habitat fragmentation can promote collective defence against antibiotic. Left: Sketch of our theoretical concept, in which a microbial population becomes systematically more fragmented. Right: theoretical predictions for the survival of a population of beta-lactamase producing bacteria in the presence of a beta-lactam antibiotic, as a function of the degree of habitat fragmentation. More fragmented habitats lead to increased survival hence an increased effective minimal inhibitory concentration. Taken from Verdon, Popescu et al (2025) J. R. Soc. Interface.

2. Publications

Vareschi S, Jaut V, Vijay S, Allen RJ, Schreiber F. 2025. Antimicrobial efflux and biofilms: an interplay leading to emergent resistance evolution. Trends Microbiol. (in press).

Bull F, Tavaddod S, Bommer N, Perry M, Brackley CA, Allen RJ (2025). Different factors control long-term versus short-term outcomes for bacterial colonisation of a urinary catheter. Nature Communications 16, 3940.

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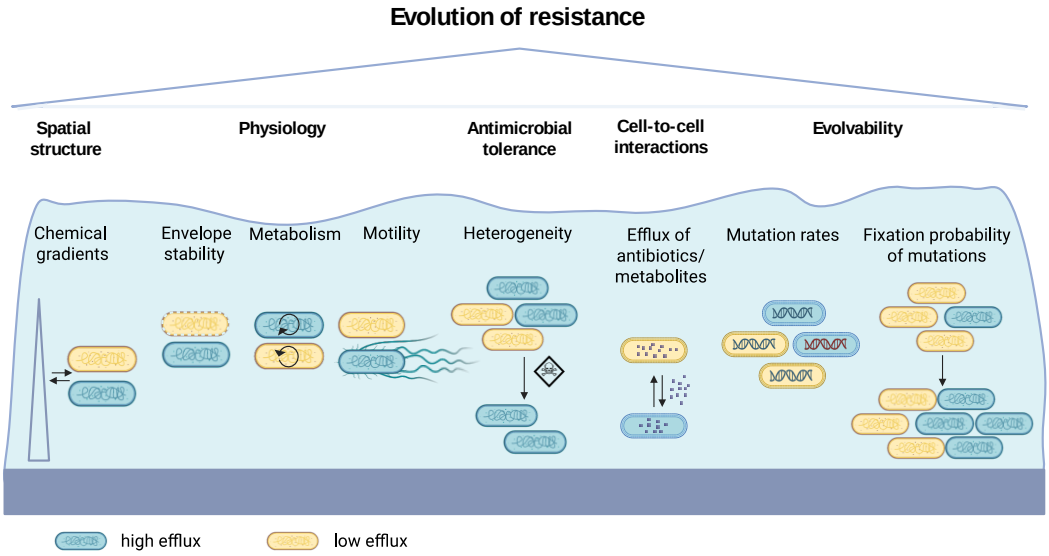
Pastore S … Busch A et al. (2024). NanopoReaTA: Real-Time RNA-Sequencing Analysis for time-efficient Decision-Making. Eur. J. Human. Genet. 32, 1626-1626.
Eberhardt N, Gonzalez Santamarina B, Enghardt ML, Rohland O, Hussain I, Tannert A, Thieme L, Rubio I, Rödel J, Löffler B, Arndt HD, Bauer M, Busch A (2024) The effects of photoactivated ciprofloxacin and bile acids on biofilms on bile duct catheters. International Journal of Antimicrobial Agents 63, 107086.
Busch A et al. (2024) Gut microbiome in atypical depression. Journal of Affective Disorders 349, 277-285



Cover image: individual-based simulation of a growing biofilm. The colours indicate the growth rate of individual bacterial cells; the shading indicates local nutrient concentration close to the biofilm. Taken from Young et al (2023, npj Biofilms & Microbiomes).

3. Third-party funding

Projektträger	Vorhaben	Laufzeit	Mittel pro jahr 2023/4
DFG	Sonderforschungsbereich ChemBioSys – Teilprojekt C07	2018-2022	12.950,00 € + 1 Doktorand
DFG	Sonderforschungsbereich 2389 Emergente Funktionen der bakteriellen Multizellularität	2022-2026	4916,00 € + 1 Doktorandin
DFG	Sonderforschungsbereich ChemBioSys – additional funding	2019-2022	21.000,00 €
DFG	Exzellenz-Cluster “Balance of the Microverse”	2019-2025	70.000,00 € + 4 postdocs + 1 Doktorandin + 1 TA
Wellcome Trust	Discovery grant: Life & death for MRSA	2024-2030	1 postdoc + 8.000,00 €

4. Teaching

WiSe 2022/3 and SoSe 2023

Modulnummer	Veranstaltung
BBio1.5, 011/BEBW4/ BBC2.2, 005(LBio-MBio	Ringvorlesung Grundlagen der Mikrobiologie (Papenfort, contribution Allen)
55380	Optimalitätsprinzipien in der Evolution (Schuster, contribution Allen)
213695	Oberseminar Theoretical Microbial Ecology
MMB001	Praktikum Allgemeine Mikrobiologie (Busch)
MMB019	Introduction to Modelling in Microbiology (Allen, Busch)
206951 (DOSIS)	Molekulare Intensivmedizin (DOSIS) (UKJ, contribution Busch)

WiSe 2023/4 and SoSe 2024

Modulnummer	Veranstaltung
BBio1.5, 011/BEBW4/ BBC2.2, 005(LBio-MBio	Ringvorlesung Grundlagen der Mikrobiologie (Papenfort, contribution Allen)
FMI-B10006	Mathematische Biologie 1 (Schuster, contribution Allen)
213695	Oberseminar Theoretical Microbial Ecology
90366	Praktikum Bachelor Mikrobiologie (Papenfort, contribution Busch)
7237	Grundlagen der Mikrobiologie (Papenfort, contribution Busch)
MMB003	Microbial Communication (Kothe, contribution Allen)
MMB019	Introduction to Modelling in Microbiology (Allen, Busch)
MMB019	Hands on experience handling quantitative data in microbiology (Allen, Busch)
206951 (DOSIS)	Molekulare Intensivmedizin (DOSIS) (UKJ, contribution Busch)
MSc	Infection Biology (Papenfort, contribution Allen)
MMB019	Next Generation Sequencing (Busch)

BSc theses

Lena Rathnow Microbial dynamics of *Enterobacteriaceae* and *Enterococcaceae*: Biofilm formation on surgical catheters in liver transplant patients (September 2024, supervised by Dr. Anne Busch)

MSc theses

Marieluise Enghardt Efflux pumps and nutrient availability: the impact on *Escherichia coli* susceptibility to tetracycline (October 2023, cosupervised by Dr. Vijay Srinivasan)

Abhishek Shaw Influence of nutrient richness and potassium on rifampicin susceptibility of *Escherichia coli* (January 2024, cosupervised by Dr. Vijay Srinivasan)

Gül Duman Investigating biofilm formation and antibiotic resistance profiles of *Enterobacteriaceae* and *Enterococcaceae* strains isolated from bilioenteric catheters of liver transplant patients (September 2024, supervised by Dr. Anne Busch)

Kareena Valecha Influence of bacterial aggregation on the Immune response of THP1 cells (September 2024, supervised by Dr. Stefanie Wagner and Dr. Anne Busch)

5. Research training

Dissertations

Freya Bull. Biophysical modelling of bacterial colonisation of urinary catheters (July 2023; University of Edinburgh)

6. Equality and diversity

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
15	5	5

7. International Collaborations

University of Sheffield – **UK**
University of Edinburgh – **UK**
STFC Hartree Center – **UK**
University of Lyon - **France**
Florida State University – **USA**
Harvard University - **USA**

8. Administration/Finance

Beschäftigungsstruktur

	Personen	Stellenanteile
Beschäftigte im Rahmen von Haushaltsmitteln		
Laborleiterin	1	1,0
Technische Assistenz	1	1,0
Sekretariat	1	0,5
Postdoc	1	1,0
Beschäftigte im Rahmen von Drittmitteln		
PhD students	3	1,95
Postdoc	3	3,0
Technische Assistenz	2	2,0
Wissenschaftliche Assistenten	8	
Computer support	1	0,25

9. Outreach and Science Communication

At the Long Night of Science in Jena (November 2024), Anne Busch, Stefanie Wagner and Andreas Ulmer, presented the fascinating world of microbes at the Zeiss Planetarium Jena as part of the Microverse Cluster science event. Dr. Wagner also gave an introductory science talk at the Microscopy Days in Berlin (April 2025). Dr. Ulmer also participated in the Corporate Run 2025. In November 2024, Berlin Science Week , Silvia Vareschi, Vijay Srinivasan and Rosalind Allen helped present “Bakteriopolis”, a mobile exhibition in a shipping container about the ability of microbes to form spatially organised communities that was developed by the DFG-funded priority program SPP2389.

- Anne Busch sits on the Friedrich Schiller University's Equal Opportunities Advisory Board.
- Anne Busch is also on the committee of the VAAM specialist group "Functional Genomics & Bioinformatics."
- Marco Mauri runs the monthly “Population dynamics” online seminar series with an international audience
- Marco Mauri co-organised the FNEEM mini-symposium “New Frontiers in Modelling Ecology and Evolution of Microbiomes” in October 2023
- Rosalind Allen is a Fellow of the Royal Society of Edinburgh

- Rosalind Allen was on the Royal Society of Edinburgh B1 (Physics) committee member for Fellowship appointments, in 2023
- Rosalind Allen is a member of the Royal Society University Research Fellowships, A(i) Physics panel.
- Rosalind Allen acted as external examiner for 5 PhD theses (2 UK, 1 Netherlands, 1 Denmark, 1 France)

Conference talks and seminars

2024
BEAT-AMR One Health and Antimicrobial Resistance
Imperial College London Ecology and Evolution seminar
UK Microbiology Society Annual Conference
Ecology & Evolution seminar, Freie Universität Berlin
2023
Physics department colloquium, University of Cologne
BSG & Rosetrees Trust Interdisciplinary Workshop on IBD
DPG Fachverband Biologische Physik: Systems Biophysics
Jena Microbiome meeting
Physics Institute Colloquium, University of Bayreuth
Computational Biology seminar, Biozentrum Basel
CECAM - Challenges and opportunities in nonequilibrium soft matter
Systems Biology of Microbial Infection Conference, Jena
ICIAM (online)

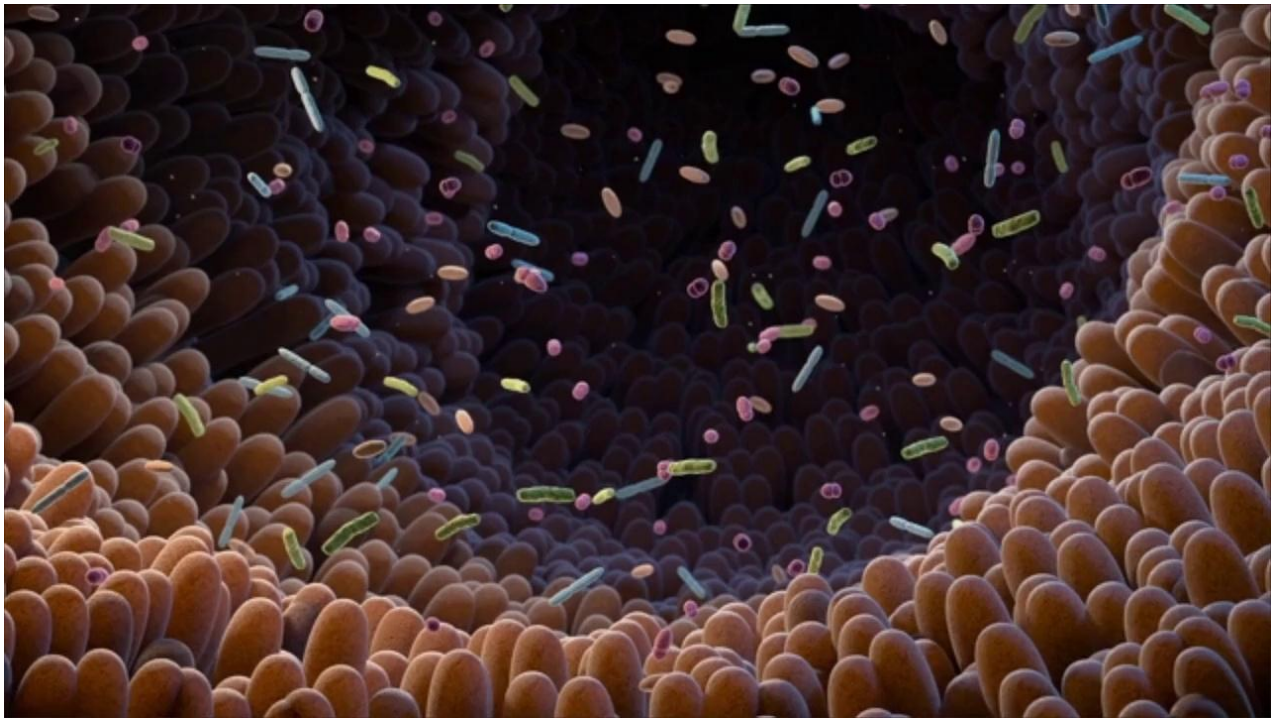
10. Team

Group Leader	Prof. Rosalind Allen	
Lab leader	Dr. Anne Busch	
Technical assistants	Ariane Zander Consuelo Figueroa Zimmermann	Lisa-Marie Karnbach (on maternity leave)
Administrative assistant	Moritz Wiegand	
PostDocs	Dr. Marco Mauri Dr. Stefanie Wagner	Dr. Andreas Ulmer Dr. Elena Tiumina
PhD students	Sheila Hoshyaripour Joel Ching Kuma	Mbanghanih Silvia Vareschi
Masters Students	Sahar Dehkordi Johanna Wallnisch Tia Wünschmann	Anna Baborski Srinath Laka (Ernst-Abbe Hochschule)
Bachelors Students	Lara Heinrichs-Klinzmann	Sarah Schwab

BALANCE OF THE MICROVERSE

Microbiome Dynamics

Prof. Dr. Gianni Panagiotou



1. Research

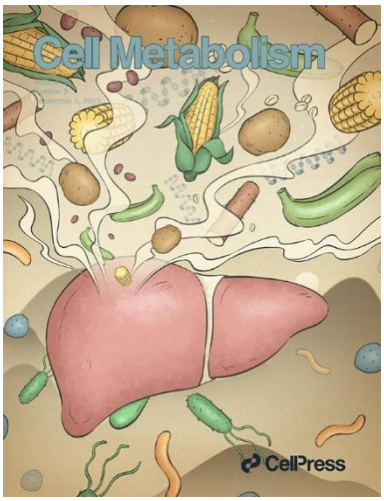
On January, 6, 2023 Gianni Panagiotou head of the Microbiome Dynamics Department at HKI Jena, has been appointed University Professor at the Friedrich Schiller University in Jena and did join the select group of Professors from the cluster of Excellence “Balance of the Microverse”.
The Microbiome Dynamics Group (MBD) takes a highly collaborative approach, combining meta-omics, biochemical and clinical data with emerging technologies in computational biology and bioinformatics to explore the relevance of the human microbiome in health and disease. In particular, our key research activities in 2023 and 2024 revolved around three topics: *i)* the role of the microbiome in infection and sepsis and *ii)* the gut microbiome in non-communicable diseases, and *iii)* the role of the gut microbiome in the success of lifestyle interventions.

Role of the microbiome in infection and sepsis: we explored the interactions between fungal pathogens and the human commensal microbiome and their significance for the onset of infection. We extended our previous study on the genetic diversity of the fungal pathogen *Aspergillus fumigatus* (Barber *et al*, 2021, *Nat Microbiol*) by using metabolic modelling to study the metabolic heterogeneity of different strains of the fungus. Our results suggest that the fungus shapes the lung microbiome to promote its own growth and, in this way, colonize the lung (Mirhakkak *et al*, 2023, *Nat Comm*). In addition, as a result of an international collaboration with European partners, colleagues from the Collaborative Research Center "FungiNet", and the Excellence cluster "Balance of the Microverse", we described the gut microbiome and mycobiome ecology of cancer patients at risk of the fungal infection candidiasis (Seelbinder *et al*, 2023, *Nat Comm*).
Another critical aspect we explored in 2023 was the role of the microbiome in the development and severity of sepsis. In close collaboration with the groups of Prof. Bauer and Prof. Weiss, we conducted a deeply phenotyped study (microbiome, mycobiome, metabolome, lipidome, immunome, and clinical data) of septic and non-septic control patients. This unprecedented characterization helped us find clear associations between sepsis severity and the gut microbiome (Seelbinder *et al., in preparation*). In collaboration with the Jena University Hospital and leading experts on sepsis, we investigated the individual predisposition to develop sepsis in a large cohort of non-infected patients undergoing surgery. Our expertise in transcriptomics analysis and machine learning allowed us to develop highly accurate risk prediction models based on preoperative transcriptomic signatures (Garcia Lopez *et al*, 2024, *Cell Reports Medicine*). Furthermore, in a separate study in collaboration with the group of Sebastian Weis, we applied a multi-omics approach in human cohorts and mice models to characterize the metabolic dysregulation during the onset of sepsis (Xu *et al,* 2025, *Science Advances*).
***The gut microbiome in non-communicable diseases (NCDs)*:** As coordinators of the BMBF research consortium “PerMICCion”, we have been investigating how microbiome-related

features can be used to improve CRC prognosis and diagnosis, particularly in early-onset CRC (EO-CRC). Taking advantage of a deeply characterized CRC cohort, we could identify gut microbiome and mycobiome communities and blood and lipid signatures characteristics of different disease stages (Xu *et al, in preparation*). Furthermore, we identified potential biomarkers (gut bacterial and viral communities) capable of distinguishing CRC patients with early and old disease onset (Zhou *et al, in preparation*).

Another key aspect of our research on NCDs is the study of metabolic diseases, *i.e.*, obesity and non-alcoholic fatty liver disease (NAFLD). In a recently published study, we initiated a clinical trial with leading scientists from China, as part of our previous ITN 'BestTreat', to analyse the effects of resistant starch in obese patients. Our findings suggest that resistant starch facilitates weight loss by reshaping the gut microbiome, promoting the growth of beneficial bacteria (Li *et al*, 2024, *Nat Metab*). In addition, we found robust and highly specific microbiome signatures that can distinguish NAFLD from other co-occurring metabolic diseases and designed synthetic consortia with predicted potential to cooperate against NAFLD development (Nychas *et al*, 2024, *Microbiome*). Furthermore, our results using multi-omics analysis at different stages of the disease indicate the key role of the gut microbiome and its metabolites in fibrosis (Chen et al, *in preparation*) and inflammation (Li *et al*, *in preparation*), two landmarks of NAFLD.

Role of the microbiome in the success of lifestyle interventions: Lifestyle interventions, such as changes in diet or exercise, may have beneficial effects on several disease treatments, presumably by altering the composition of the gut microbiome. Thanks to a large-scale meta-analysis of healthy patients, we were able to predict how resistant an individual's gut microbiome is to change in response to lifestyle interventions (Chen *et al*, 2023, *Microbiome*). Moreover, we showed that the gut microbiome plays a crucial role in the success of a high resistant starch diet in improving NAFLD and obesity, and we demonstrated causality using the emerging technology of fecal microbiota transplantation in mice (Ni *et al*, 2023, *Cell Metab* & Li *et al*, *Nat Metab*, 2024). Furthermore, we are investigating the biosynthetic potential of the gut microbiome to transform the dietary chemical space, with the ultimate goal of designing personalized diets at the micro level. During 2023, we have focused on understanding how the gut microbiome can influence the beneficial effects of a diet with anti-inflammatory properties by conducting extensive experiments in a mouse model of colitis.



Our paper on the role of resistant starch for management of NAFLD made it to the cover of Cell Metabolism (Ni et al, 2023 *Cell Metabolism*).

Finally, in 2023 and 2024 MBD has secured several third-party funds (see section 3 “Drittmittel”): EU funding sources (“MiCCrobioTAckle, coordinator role. "FoodGuard" and “Nutrimmune”, collaborator role), DFG (“M3-NAFLD” as coordinator), and other funding sources (CZS Breakthroughs “Synthera” as collaborators). Furthermore, we have been part of the strategy team preparing and defending the proposal for a 2nd round of funding of the "Balance of the Microverse" which we got on May 22, 2025.

Pre-kick-off meeting MiCCrobioTackle in Berlin on November 13, 2024. MiCCrobioTAckle is a Marie Sklodowska-Curie Action (MSCA) Doctoral Network focused on training doctoral candidates across disciplines and sectors to advance microbiota medicine to combat cancer cachexia.

2. Publications

Bruch A*, Lazarova V*, Berg M, Krueger T, Schaeuble S, Kelani AA, Mertens B, Lehenberger P, Kniemeyer O, Kaiser S, Panagiotou G, Gsaller F, Blango MG (2024) tRNA hypomodification facilitates 5-fluorocytosine resistance via cross-pathway control system activation in Aspergillus fumigatus Nucleic Acids Res , 1-20.

Chen J, Lu RS, Diaz-Canestro C, Song E, Jia X, Liu Y, Wang C, Cheung CKY, Panagiotou G#, Xu A# (2024) Distinct changes in serum metabolites and lipid species in the onset and progression of NAFLD in obese Chinese. Comput Struct Biotechnol J 23(2024), 791-800.

Chen J*, Wang Y*, Xu A, Panagiotou G# (2024) The human gut mycobiome and its potential as a regulator of the host's metabolic health. In: Brakhage AA, Kniemeyer O, Zipfel PF (eds.) The Mycota - Human and Animal Relationships 3. 6, pp. 121-133. Springer, Cham. ISBN: 978-3-031-64852. (Review)

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Garcia Lopez R*, Schaeuble S*, Sae-Ong T, Seelbinder B, Bauer M, Giamarellos-Bourboulis EJ, Singer M, Lukaszewski R, Panagiotou G# (2024) Risk assessment with gene expression markers in sepsis development. Cell Rep Med 5(9), 101712.

Garcia-Morena D, Fernandez-Cantos MV, Lopez Escalera S, Lok J, Iannone V, Cancellieri P, Maathuis W, Panagiotou G, Aranzamendi C, El Aidy S, Kolehmainen M, El-Nezami H, Wellejus A, Kuipers OP (2024) In-vitro influence of specific Bacteroidales strains on gut and liver health related to Metabolic dysfunction-associated fatty liver disease. Probiotics Antimicrob Proteins

Hedin KA, Mirhakkak MH, Vaaben TH, Sands C, Pedersen M, Baker A, Vazquez-Uribe R, Schäuble S, Panagiotou G#, Wellejus A#, Sommer MOA# (2024) Saccharomyces boulardii enhances anti-inflammatory effectors and AhR activation via metabolic interactions in probiotic communities. ISME Journal 18(1), wrae212.

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Li H*, Zhang L*, Li J*, Wu Q*, Qian L, He J, Ni Y, Kovatcheva-Datchary P, Yuan R, Liu S, Shen L, Zhang M, Sheng B, Li P, Kang K, Wu L, Fang Q, Long X, Liu X, Wang X, Li Y, Ye Y, Ye J, Bao Y, Zhao Y, Xu G, Panagiotou G#, Xu A#, and Jia W# (2024) Resistant starch intake facilitates weight loss in humans by reshaping the gut microbiota. Nat Metab 6(3), 578-597.

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McIlroy SE#, Guibert I, Archana A, Chung WYH, Duffy JE, Gotama R, Hui J, Knowlton N, Leray M, Meyer C, Panagiotou G, Paulay G, Russell B, Thompson PD, Baker DM # (2024) Life goes on: Spatial heterogeneity promotes biodiversity in an urbanized coastal marine ecosystem. Glob Chang Biol 30(4), e17248.

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Schruefer S, Pschibul A, Wong SSW, Sae-Ong T, Wolf T, Schäuble S, Panagiotou G, Brakhage AA, Aimanianda V, Kniemeyer O, Ebel F (2023) Distinct transcriptional responses to fludioxonil in Aspergillus fumigatus and its ΔtcsC and Δskn7 mutants reveal a crucial role for Skn7 in the cell wall reorganizations triggered by this antifungal. BMC Genomics 24(1), 684.

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3. Third Party Funding

Nr.	Mittelgeber	Art der Förderung	Titel des geförderten Projekts	Koordinator/in	Beginn	Ende	Fördersumme
1	BMBF	Projektförderung / Zuwendung	PerMiCCion - Ein personalisierter mikrobiom-basierter Ansatz zur Prävention, Diagnose und Behandlung von früh-einsetzendem Darmkrebs - Standort Jena	ja	01.05.2022	30.04.2026	1.202.814,99 €
2	DFG	Projektförderung / Zuwendung - Exzellenzcluster	Metagenomics and Metabolomics Analysis of the Human Microbiome in Critical Illness for Identifying Drivers of Homeostasis Shifts	nein	15.06.2019	14.06.2023	345.000,00 €
3	DFG	Projektförderung / Zuwendung - Exzellenzcluster	Identification of universal mediators of microbiome community structure through large scale cross-habitat comparisons	nein	01.01.2023	31.12.2024	205.000,00 €
4	DFG	Projektförderung / Zuwendung - Exzellenzcluster	Microbiome Dynamics	nein	01.01.2023	31.12.2025	995.000,00 €
5	DFG	Projektförderung / Zuwendung	Mikrobielle Wechselwirkungen auf den Blättern als Treiber für bakterielle Anpassungen	nein	01.08.2021	31.07.2024	176.250,00 €
6	DFG	Projektförderung / Zuwendung - Sonderforschungsbereich	Interaktive Datenbanken und standardisierte Analysen experimenteller Daten	nein	01.07.2021	30.06.2025	491.000,00 €
7	Carl-Zeiss-Stiftung	Projektförderung / Zuwendung "Jena School of Excellence"	Microbiota-driven risk assessment, prevention and clearance of invasive aspergillosis	nein	01.07.2021	31.12.2024	183.000,00 €
8	EU	ERC-Grant	Microbiome applications and technological hubs as solutions to minimize food loss and waste - FOODGUARD	nein	01.01.2024	31.12.2026	325.000,00 €
9	EU	ERC-Grant	Nutrition-responsiveness of the immune system: interplay between infectious diseases and diet-related metabolic diseases and the potential for food-based solutions NUTRIMMUNE	nein	01.09.2024	31.08.2028	470.875,00 €
10	EU	ERC-Grant	Advancing Research at the Intersection Between Gut Microbiota and Cancer Cachexia to Train Europe's Future Leaders in Microbiota Medicine MiCCrobioTAckle	ja	01.11.2024	31.10.2028	794.412,06 €
11	DFG	FSU	Mikrobiombasierte maschinelle Lernmodelle zur besseren Diagnose der nichtalkoholischen Fettlebererkrankung M3-NAFLD	ja	01.08.2024	31.07.2027	416.861,00 €
12	Carl-Zeiss-Stiftung	FSU Konsortium	Syntheric therapeutic microbes for tailored antimicrobial therapies SynThera	ja	01.04.2025	31.03.2030	382.000,00 €

MBD receives a prize for short talk presentation at the Lion Lake Microbiome Conference

Our own Yueqiong (Bernard) Ni was honored with the 2nd prize for best short talk presentation during the Lion Lake International Microbiome Medicine Conference, taking place on October 29-30, 2023 in Qingyuan City in China.

The conference focused on microbiome medicine, an emerging field offering exciting therapeutic opportunities for multiple diseases. During the conference, participants heard about the latest advances in clinical research related to microbiota interventions such as fecal microbiota transplantation, probiotics, prebiotics, and microbial-based drugs.

- Bernard had the opportunity to present his work on prebiotics and non-alcoholic fatty liver, a project recently published in the prestigious Cell Metabolism journal (DOI: 10.1016/j.cmet.2023.08.002).

4. Studium und Lehre

Semester	Modulnummer	Veranstaltung	Lehrperson (Zuständigkeit)	ECTS	Teilnehmerzahl
SS24	228045	Eco-systems Biology of Human Disease (MMB019-10, FMI-BI / Wildcardmodule)	Prof. Panagiotou	10	4

Participation in other FSU courses:

Semester	Modulnummer	Veranstaltung	Lehrperson (Gastreferent)
WS2023/24	SS 2024 228045	MSc Module: Infection Biology	Prof. Panagiotou
WS2023/24	MMB2.11	Molecular and Microbial Infection Biology	Prof. Panagiotou

Participation in external courses:

Datum	Ort	Veranstaltung	Lehrperson
WS2023/24 and SS24	Leibniz-HKI, Jena	Big Data Analysis in Medicine	Prof. Panagiotou (Zuständigkeit)
21.-26.2.2024	UiB, Bergen, Norway	Metabolic modeling workshop	Dr. Schäuble (Gastreferent)
16th, 23rd and 30th of May and 6th of June, 2024	Leibniz-HKI, Jena	The art of scientific presentation	Dr. Depetris-Chauvin (Zuständigkeit)

Masterarbeiten 2023 und 2024

Lin, Weiping. Exploring the Bacteria and Fungi Composition in Young and Old Cases of Colorectal Cancer (June 2023).

5. Supporting Early Career Scientists

Leung, Howell. The Gut Microbiome in NAFLD: Advancing Diagnosis, Understanding Pathogenesis, and Developing Novel Therapies (August 2023)

Loos, Daniel. The Fungal Focus on Broad-Scale Metagenomics (February, 2023)

Lopez Escalera, Silvia. Screening and identification of potential probiotic candidates in pre-clinical models of Non-alcoholic fatty liver disease (October, 2023)

Siliceo, Sara Leal. Humans as holobionts: Systems-level approaches for disease prevention and therapy (July 2023)

6. Equal Opportunities, Diversity and Family

2023

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
7	10	5
1 Professor		
1 Research Coordinator		

5 PostDocs	
9 PhDs	
1 Master student	

2024

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
7	10	5
1 Professor		
1 Research Coordinator		
1 Team assistant		
1 Software Engineer		
5 PostDocs		
8 PhDs		

7. International Collaborations

Title	First name	Last name	University / Institution	City	Country
Prof	Weiping	Jia	Shanghai JiaoTong University	Shanghai	China
Prof	Aimin	Xu	The University of Hong Kong	Hong Kong	China
Prof	Morten	Sommer	DTU	Copenhagen	Denmark
Dr	Bjørn	Nielsen	Clinical Microbiomics	Copenhagen	Denmark
Prof	Mervyn	Singer	University Coll. London	London	UK
Prof	Oscar	Kuipers	University of Groningen	Groningen	The Netherlands
Prof	Max	Nieuwdorp	AUMC	Amsterdam	The Netherlands
Dr	Harriet	Schellekens	University Coll. Cork	Cork	Ireland
Prof	George	Nychas	Agricultural University of Athens	Athens	Greece
Prof	Karine	Clement	Sorbonne University	Paris	France

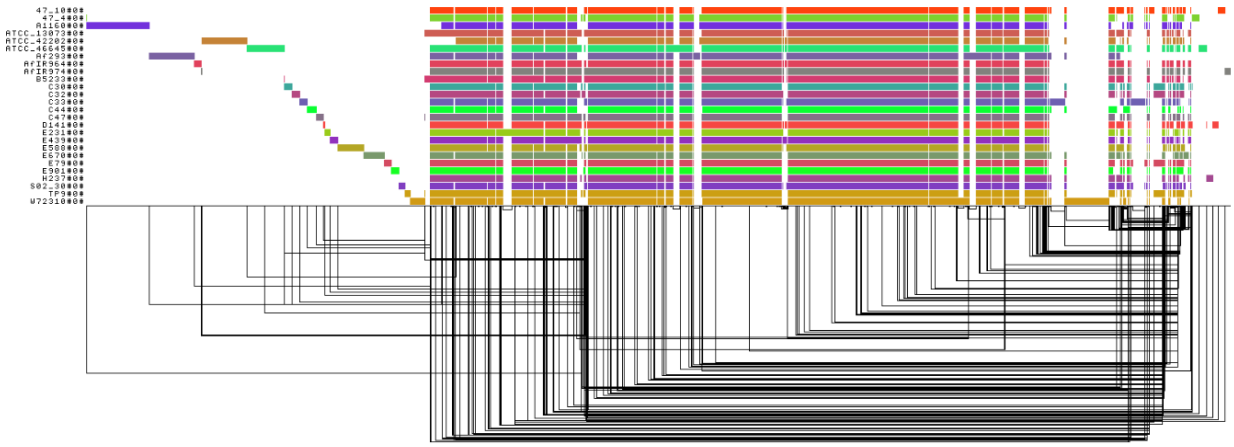
8. Administration/Finances

Beschäftigungsstruktur

	Personen	Stellenanteile
Beschäftigte im Rahmen von Haushaltsmitteln		
Wissenschaftliche MitarbeiterInnen		
Postdoc	2	2,0
Sekretariat	1	1,0
Beschäftigte im Rahmen von Drittmitteln		
Weiteres Personal		
Forschungskoordinator	1	1,0

9. Team

Gruppenleiter	Univ.-Prof. Dr. Gianni Panagiotou
Research Coordination	Dr. Ana Depetris Chauvin
PostDocs	Bastian Seelbinder Sascha Schäuble Mohammad Mirkakkak Esfahani Tongta Sae-Long Yueqiong Ni
Promovierende	Emmanouil Nychas Lin Lin Xu Kexin Li Xiuqiang Chen Le Xu Zhengyuan Zhou Qilian Fan Lu Zhang Andrea Marfil Sanchez Albert Garcia Lopez
Verwaltung – Sekretärin	Anja Faber

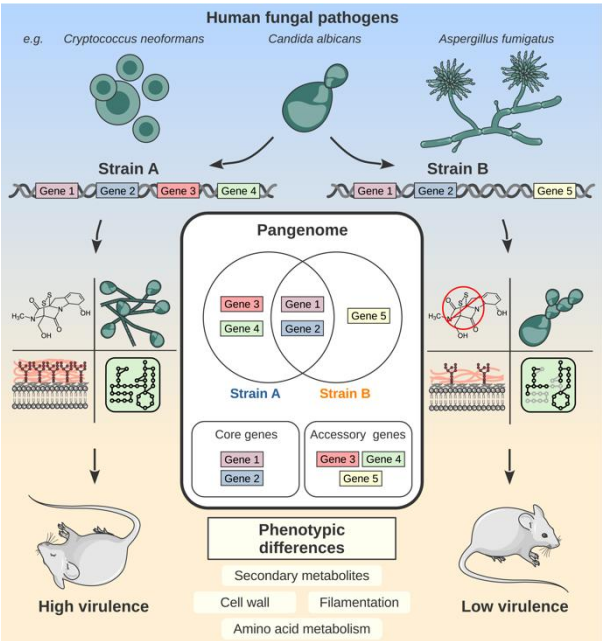


NWG Fungal Informatics

Dr. Amelia E. Barber

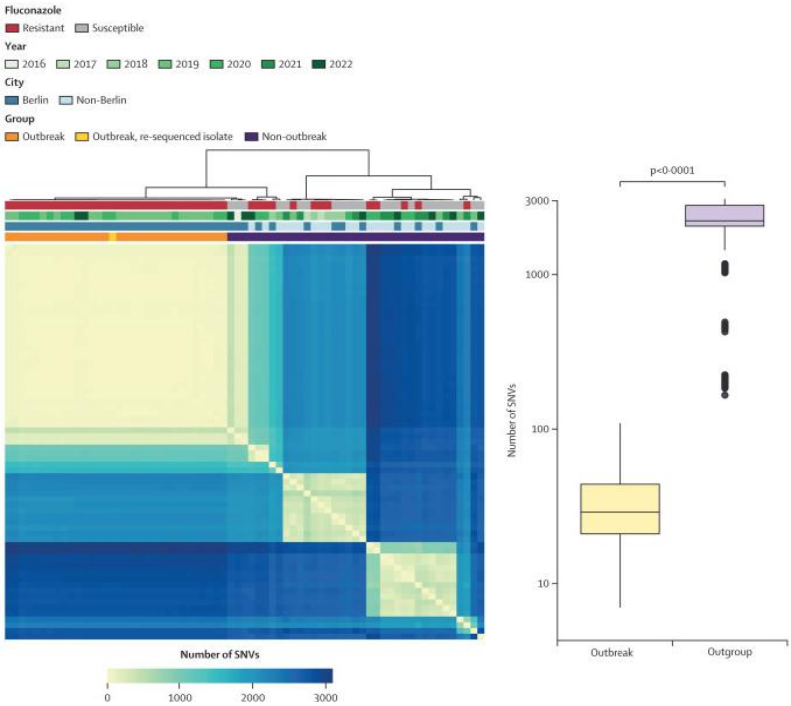
1. Research

Genomics of Human Fungal Pathogens



Fungal pathogens represent a growing and often underappreciated threat to human health, with infections causing significant morbidity and mortality worldwide—particularly among immunocompromised individuals. Among the most prominent of these pathogens is *Aspergillus fumigatus*, an environmental mold responsible for a range of diseases, from allergic reactions to life-threatening invasive aspergillosis and *Candida parapsilosis*, a commensal yeast and opportunistic pathogen. Moreover, multi-kingdom pathogens like *Fusarium* spp. threaten not only human health but also the global food supply. In recent years, genomics

has revolutionized our ability to study the biology and evolution of these organisms. By leveraging high-throughput sequencing and comparative genomics, research in NWG Fungal Informatics is uncovering the genetic basis of fungal virulence, environmental adaptability, and resistance to antifungal drugs.

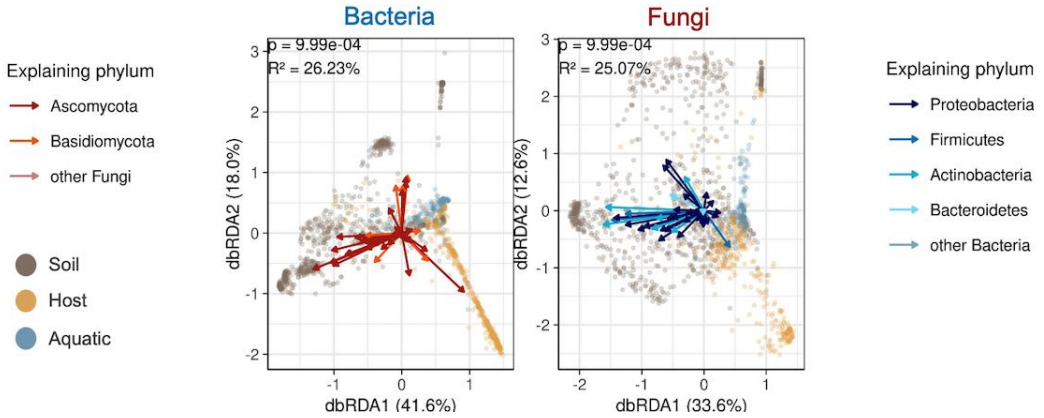


In a recent study led by the group, we investigated a multi-year fungal outbreak in a hospital network in Berlin, Germany, caused by fluconazole-resistant *Candida parapsilosis* (Brassington *et al*., 2024, *The Lancet Microbe*). Using large-scale genomic epidemiology, we reconstructed the dynamics of the outbreak and showed that patient transfers between healthcare facilities were likely responsible for the persistent reimportation of the drug-resistant outbreak clone and subsequent human-to-human transmission. Whole genome sequencing also confirmed the clonal nature of the outbreak strains, which were separated by a small number of pairwise single nucleotide differences (SNVs) compared with non-outbreak samples from elsewhere in Berlin and elsewhere in Germany (top panel). A Y132F substitution in the drug target ERG11 was identified as the dominant resistance mechanism in both the outbreak samples and fluconazole-resistant isolates tested from other sites in Germany. We also introduced a novel multi-locus sequence typing (MLST) scheme tailored to *C. parapsilosis* that allows rapid and cost-effective strain differentiation. This approach, which combines PCR amplification and Sanger sequencing of just four loci, proved effective in distinguishing outbreak strains from unrelated isolates, providing a valuable tool for surveillance and infection control, especially in settings without access to whole-genome sequencing.

Other work in the group is investigating the genomic diversity and pathogenic potential of the *Fusarium solani* species complex (FSSC). This group of closely related fungal species is uniquely capable of causing disease in both plants and humans. Using highly contiguous genome assemblies we generated for clinical isolates of *F. keratoplasticum* and *F. petroliphilum* (n=3 per species), we compared them with other FSSC genomes from plant and animal sources. Interestingly, human pathogenicity appears to be polyphyletic within the FSSC, suggesting multiple evolutionary origins of the underlying virulence traits. Strikingly, pan-genomic analysis revealed significant gene presence-absence variation, with only 41% of genes shared across the FSSC. A closer look at the functional differences resulting from this high level of genetic variation revealed a similarly high degree of presence-absence variation in long non-coding RNAs (lncRNAs) and biosynthetic gene clusters encoding known and novel secondary metabolites. Furthermore, as has been reported for the *Fusarium oxysporum* species complex, we found that that some of the genetic variation is

encoded on discrete accessory chromosomes that could be isolate- or species-specific and even cases where specific accessory chromosomes were incongruent with the whole genome phylogeny. Transcriptomic studies under infection-relevant stress conditions, such as elevated temperature, showed minimal differential gene expression, suggesting that these species are well-adapted to human infection-relevant environments.

Fungal Ecology



An additional research emphasis in the group is fungal ecology through the lens of big data. To this end, in collaboration with the group of the Microbiome Dynamics group of the Institute of Microbiology (Prof. Gianni Panagiotou) we conducted a global survey of public microbiome data from host-, aquatic-, and soil- associated habitats to identify global patterns in bacterial-fungal communities (Loos, Pereira *et al*., 2024, *Cell Reports*). Through this analysis we identified a small number of bacterial and fungal generalists—taxa that were highly prevalent and abundance across divergent habitats, suggesting a high degree of fitness to changing environmental conditions. To identify the properties underpinning this, we used genome mining and found that generalist microbes possess specific genomic features, including an increased number of antimicrobial resistance genes and secondary metabolism genes. Strikingly, while cross-kingdom interactions are often overlooked in microbiome studies, we found that bacterial variation could explain approximately a quarter of the fungal community structure and vice versa (panel above). Moreover, due to their plasticity and ubiquity, bacterial generalists contributed significantly to shaping the mycobiome composition. These findings collectively enhance our understanding of microbial niche breadth and its implications for global biodiversity decline.

2. Publications

Abou-Kandil A, Tröger-Görler S, Pschibul A, Krüger T, Rosin M, Schmidt F, Akbarimoghaddam P, Sakar A, Cseresnyés Z, Shadkchan Y, Heinekamp T, Gräler MH, Barber AE, Figge MT, Brakhage AA, Osherov N, Kniemeyer O. The proteomic response of Aspergillus fumigatus to Amphotericin B (AmB) reveals the involvement of the RTA-like protein RtaA in AmB resistance. microLife. 2024. doi: 10.1093/femsml/uqae024.

Brassington PJT, Klefisch F-R, Graf B, Pfüller R, Kurzai O, Walther G, Barber AE. Genomic reconstruction of an azole-resistant Candida parapsilosis outbreak and the creation of a multilocus sequence typing scheme. The Lancet Microbe. 2024. doi: 10.1016/j.lanmic.2024.07.012

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Loos D[+], Pereira A[+], Dutilh BE, Barber AE, Panagiotou G. A global survey of host, aquatic, and soil microbiomes reveals shared abundance and genomic features between bacterial and fungal generalists. Cell Reports. doi:10.1016/j.celrep.2024.114046. 2024. [+]equal contribution
Bierhoff H, Barber AE, Blango MG. RNA: DNA triplexes: a mechanism for epigenetic communication between hosts and microbes? mBio. 2024. doi:10.1128/mbio.01982-24.
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Barber AE. Breaking the mould: rethinking 'wild type' in fungal pathogens. Nature Reviews Microbiology. 2024. doi:10.1038/s41579-024-01024-2.
Mirhakkak MH, Chen X, Ni Y, Heinekamp T, Sae-Ong T, Xu L-L, Kurzai O, Barber AE, Brakhage AA, Boutin S, Schäuble S, Panagiotou G. Genome-scale metabolic modeling of Aspergillus fumigatus strains reveals growth dependencies on the lung microbiome. Nature Communications. 2023. doi:10.1038/s41467-023-39982-5.
Kelani AA, Bruch A, Rivieccio F, Visser C, Krüger T, Weaver D, Pan X, Schäuble S, Panagiotou G, Kniemeyer O, Bromley MJ, Bowyer P, Barber AE, Brakhage AA, Blango MG. Disruption of the Aspergillus fumigatus RNA interference machinery alters the conidial transcriptome. RNA. 2023. doi:10.1261/rna.079350.122.
Brassington PJT, Fabre ML, Zimmermann A, Perrier M, Martin R, Kurzai O, Barber AE. Comparative pan-genomics reveals divergent adaptations in clinically-relevant members of the Fusarium solani species complex. *bioRxiv*. 2024. doi:10.1101/2024.09.23.614396
Hatmaker AE, Barber AE, Drott MT, Sauters TJC, Alastruey-Izquierdo A, Garcia-Hermoso D, Rokas A. Pathogenicity is associated with population structure in a fungal pathogen of humans. *bioRxiv*. 2024. doi:10.1101/2024.07.05.60224.

3. Third Party Funding

Funder	Description	Duration	Amount in 2023
DFG	Excellence Cluster "Balance of the Microverse"	2022-	264.000 € (NWG Funding)
Freistaat Thüringen / FSU Jena	Postdoc scholarship for Dr. Laura Fabre	2023-2024	13.000 €
FSU Jena	ProChanceCareer	2023-2025	3.333 €
Funder	**Description**	**Duration**	**Amount in 2023**
DFG	Excellence Cluster "Balance of the Microverse"	2022-	264.000 € (NWG Funding)
Leibniz Association	Fungal RNA Tranmsission Impacting Human Epigenome Regulation (FuRTHER)	2024-2027	85.000 €
Freistaat Thüringen / FSU Jena	Postdoc scholarship for Dr. Laura Fabre	2023-2024	11.000 €
FSU Jena	ProChanceCareer	2023-2025	20.000 €

4. Teaching

WS 2022/2023 und SS 2023

Course	ECTS	# Participants
MMB003	Lecture in Microbial Communication Module	11
MMB003	Lecture in Infection Biology Module	11
MMB004	Lectures & Practical Module: Microbial Ecology of Yeasts	11
External	Lecture for MSc. Infection Biology Course at Uppsala University and Swedish University of Agricultural Sciences	Ca. 20

Vertiefungs- und Projektmodule	ECTS	# Participants
Vertiefungsmodul MMB 700	15	1
Projektmodul MMB 800	15	1

WS 2023/2024 und SS 2024

Course	ECTS	# Participants
MMB003	Lecture in Microbial Communication Module	20
MMB003	Lecture in Infection Biology Module	20
MMB004	Lectures & Practical Module: Microbial Ecology of Yeasts	20
BB011	Lecture in Ringvorlesung Methoden der Mikrobiologie	Ca. 40
External	Lecture for MSc. Infection Biology Course at Uppsala University and Swedish University of Agricultural Sciences	Ca. 20

BSc theses
Lea Maria Krämer. Genome Analysis of *Aspergillus oerlinghausenensis* (September 2024)
MSc theses
Hsinyu Lin. Global surveillance of environmental human pathogenic fungi through metabarcoding (September 2023)

Dissertations
Phillip Brassington. Comparative genomics reveals unique features of fungal pathogens (submitted; defense still outstanding)

5. Equal opportunities and family

2023

Number of Women	Number of Men	Children under 12 years
4	2	1

2024

Number of Women	Number of Men	Children under 12 years
3	3	1

6. International Cooperations

University College Dublin – **Ireland**
University of Utah – **USA**
Hebrew University of Jerusalem – **Israel**
University of the Basque Country – **Spain**
Shenzhen Institute of Synthetic Biology – **China**
Vanderbilt University – **USA**
University of Manchester – **UK**

7. Academic Service

- Member of the Aspergillus Genomes Research Policy Committee
- Member of organization team for Myk 2024
- Workshop organizer at FEBS HFP2024
- Poster judge, Joint Conference of the DGHM & VAAM 2023
- Guest editor, PLOS Genetics
- Session chairs at MiCom 2024 and Myk 2024
- Poster judge, Myk2024
- *Ad hoc* peer reviewing and external grant reviewing

8. Team

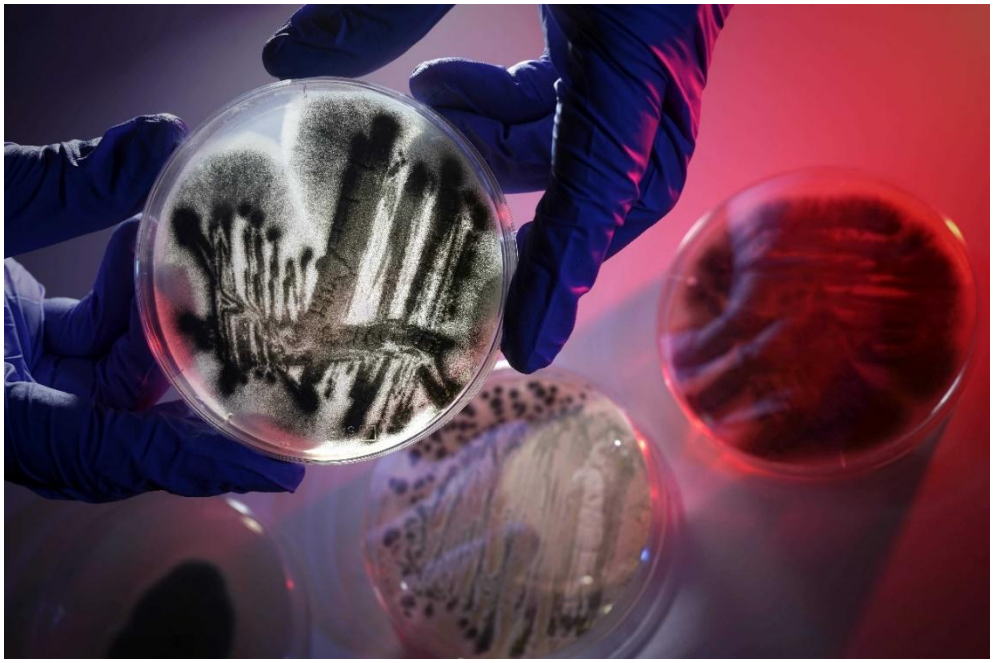
Group Leader	Dr. Amelia Barber
Technicians	Peggy Karanatsiou Martin Herde
Postdoctoral researchers	Dr. Maria Laura Fabre
Doctoral researchers	Phillip Brassington Ailton Pereira Marrion Perrier
Students	Linnea Forslund Hsinyu Lin Lea Maria Krämer
Guest Researchers	John Adeoye *(Hebrew University Jerusalem)* Saioa Cendan *(University of the Basque Country)* Adam Ryan *(University College Dublin)*

Lab Retreat – November 2023

Leibniz Institute
for Natural Product Research
and Infection Biology
Hans Knöll Institute

Lehrstuhl für Mikrobiologie und Molekularbiologie

Prof. Dr. Axel A. Brakhage



1. Research

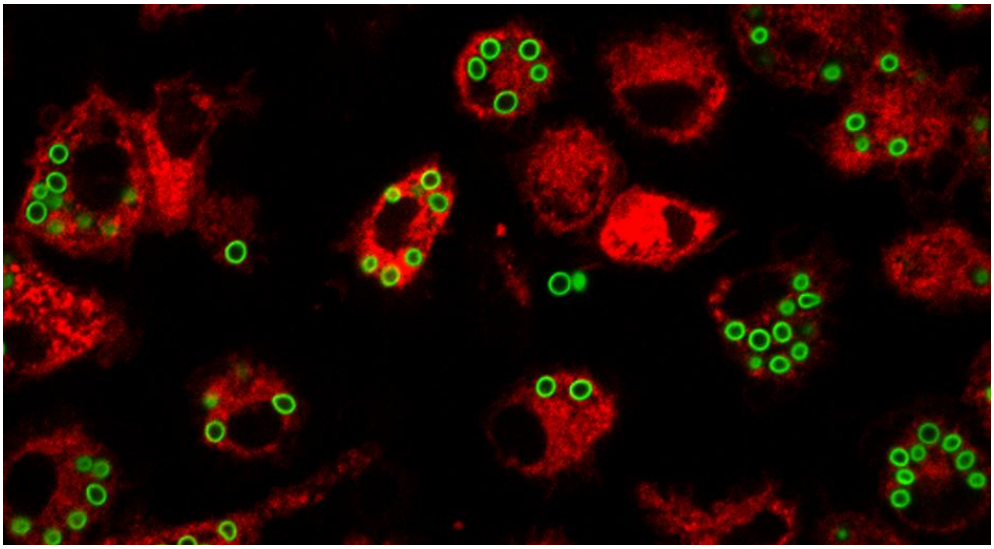
The research of the Department of Molecular and Applied Microbiology (MAM) is dedicated to the pathobiology of the medically important human pathogenic fungi, in particular *Aspergillus fumigatus* and *Lichtheimia corymbifera*. In the field of natural product research, we investigate the role of natural products for microbial communication and how they shape microbial communities.

Host pathogen-interaction

Processing of A. fumigatus conidia in macrophages

The MAM investigates the processing of *A. fumigatus* conidia after uptake by phagocytes such as macrophages or neutrophils. In a study by Jia *et al*. (*Cell Host Microbe*) we discovered that the heat shock protein HscA, which is localized on the surface of swelling and germinating conidia, binds to the p11 protein on human lung epithelial cells or macrophages. This has an impact on the fate of phagocytosed conidia: They preferentially take the route of endosomal recycling and are redirected to the outer cell membrane of host cells, instead of being processed in the deadly environment of a phagolysosome. The

hijacking of p11 increases the fungus' chance of survival and is also of medical relevance. A variant (SNP) of the human *p11* gene is associated with a lower risk of developing invasive aspergillosis in patients after bone marrow transplantation.



The role of extracellular vesicles in host-pathogen interaction

In the field of infection research, we are also interested in exploring the function of extracellular vesicles (EVs) released by host cells during the interaction with *A. fumigatus*. One challenge in the functional analysis of EVs is their small size. To be able to track the EVs during host-pathogen interaction we established a reporter system in alveolar epithelial cells based on the fusion of EV marker proteins (CD 63, CD9, and CD81) with a green fluorescent protein (GFP) and a light-emitting Nanoluciferase. This system allowed us to visualise and quantify EVs and to show that host cell-derived EVs associate with the cell wall of *A. fumigatus* hyphae and co-localise with the fungal cell membrane (*microLife)*.

Factors of A. fumigatus contributing to virulence and drug resistance

In a collaboration with the group of Gustavo Goldman (Brazil) we compared the conidial surface proteome of *A. fumigatus* with two phylogenetically closely related, non-pathogenic *Aspergillus* species and the pathogen *A. lentulus*. The aim was to identify surface proteins with a role in *A. fumigatus* pathogenicity. Altogether, 62 different proteins were exclusively detected on the surface of *A. fumigatus* conidia. Among these proteins was the putative glycosylasparaginase AspA which impacts the secretion of the host proinflammatory cytokine IL-1β. This indicates that *A. fumigatus* attenuates the inflammatory response of immune cell at the initial steps of infection (*Nature Microbiology*). Similarly, the binding of host proteins to the conidial surface enables *A. fumigatus* to modulate the immune response. In collaboration with scientists at the Institute Pasteur we demonstrated that the humoral pattern recognition molecule pentraxin 3 binds to germinating conidia *via* the cell wall polymer galactsoaminogalactan (*Nature Communications*). This PTX3 binding lowers the production of pro-inflammatory cytokines, but leads to an increase in IL-10 production, an anti-inflammatory cytokine.

Another project of the group focussed on the proteomic response of *A. fumigatus* to the antifungal drug amphotericin B (AmB). The membrane protein RtaA, belonging to the RTA-like protein family, showed the highest increase in abundance. Its deletion led to increased sensitivity to AmB and similar polyene drugs, while the overexpression of *rtaA* increased drug tolerance. This suggests that RtaA exhibits a membrane-stabilising function and contributes to polyene resistance (*microLife*). In a collaboration with Mike Bromley, University of Manchester, a functional analysis of 111 *A. fumigatus* kinase null mutants led to the discovery that the absence of the TOR signalling kinase YakA results in hypersensitivity to

antifungal azoles and reduced pathogenicity. Phosphoproteome analyses revealed that YakA regulates blocking of the septal pore during stress conditions. Interestingly, drug-induced blocking of YakA synergised with the antifungal activity of azoles (*Nature Communications*).

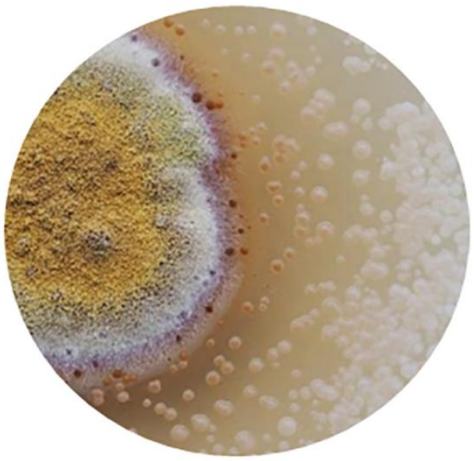
Impact of fungi on the host

In collaboration with the group of Petra Bacher (UKSH Kiel) we found that common gut commensal and food-derived yeast species are direct activators of $CD4^+$ T cells with a cytotoxic T helper cell phenotype in patients with Crohn's disease (CD). This suggests that yeasts of the gut mycobiome and yeast-containing food may contribute to aberrant inflammatory T cell responses in patients with CD (*Nat Med*). Another study with the same group and Carsten Schwarz (Clinic Westbrandenburg) shedded light on the question which types of *A. fumigatus*-specific T-helper cells contributes to protective immunity or inflammation in patients with cystic fibrosis (CF). It turned out that CF patients with allergic bronchopulmonary aspergillosis are characterised by a high frequency of cross-reactive Th2 cells, which recognise different filamentous fungi (*J Clin Invest*). A bioinformatic study in collaboration with the group Microbiome Dynamics constructed 252 strain-specific, genomic-scale metabolic models of *A. fumigatus*. The work shows that around 23% of metabolic reactions of this fungal species are not conserved in all strains. Sputum samples of *A. fumigatus*-infected CF patients suggest that this fungal species shapes the lung microbiome towards a benefical growth environment (*Nat Commun*).

Natural products and microbial communication

Interaction of Aspergillus nidulans with Streptomyces bacteria

The filamentous fungus *Aspergillus nidulans* activates some of its natural product biosynthetic gene clusters only upon interaction with specific soil bacteria of the genus *Streptomyces* (*S. iranensis* and *S. rapamycinicus*). The bacterial natural product azalomycin F that belongs to the newly named arginoketides, was identified as being responsible for this activation. The co-isolation of soil bacteria that produce arginoketide compounds and different fungi that respond to this signal with the production of additional natural products demonstrate that bacterial arginoketide producers are very common in soil. Arginoketides induce a second wave of fungal natural products and most probably contribute to the shaping of microbial soil communities (*Nat Microbiol*).



2. Publications

Abou-Kandil A, Tröger-Görler S, Pschibul A*, Krüger T, Rosin M, Schmidt F, Akbarimoghaddam P, Sarkar A, Cseresnyés Z, Shadkchan Y, Heinekamp T, Gräler MH, Barber AE, Walther G, Figge MT, Brakhage AA, Osherov N, Kniemeyer O (2024) The proteomic response of *Aspergillus fumigatus* to Amphotericin B (AmB) reveals the involvement of the RTA-like protein RtaA in AmB resistance. microLife 6, uqae024.

Behrendt F, Pretzel D, Cseresnyés Z, Kleinsteuber M, Wloka T, Radosa L, Figge MT, Gottschaldt M, Brakhage AA, Schubert US (2023) Hydrophilic cryogels as potential 3D cell culture materials: Synthesis and characterization of 2-(methacrylamido) glucopyranose-based polymer scaffolds. J Polym Sci 61(23), 3039-3054.

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Delbaje E, de Castro PA, Calise DG, Mengyao N, Horta MAC, Akiyama DY, Pontes JG, Fill T, Kniemeyer O, Krüger T, Brakhage AA, Wong KH, Keller NP, Goldman GH (2024) The influence of *Aspergillus fumigatus* fatty acid oxygenases PpoA and PpoC on Caspofungin susceptibility. J Fungi 10(11), 749.

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Ghandour R, Devlitsarov D, Popp P, Melamed S, Huber M, Siemers M, Krüger T, Kniemeyer O, Klingl A, Brakhage AA, Erhardt M, Papenfort K (2024) ProQ-associated small RNAs control motility in *Vibrio cholerae*. Nucleic Acids Res gkae1283, 1-19.

Goldmann M, Schmidt F, Cseresnyés Z, Orasch T, Jahreis S, Hartung S, Figge MT, von Lilienfeld-Toal M, Heinekamp T, Brakhage AA (2023) The lipid raft-associated protein stomatin is required for accumulation of dectin-1 in the phagosomal membrane and for full activity of macrophages against *Aspergillus fumigatus*. mSphere 8(1), e00523-22.

González K, Gangapurwala G, Alex J, Vollrath A, Cseresnyés Z, Weber C, Czaplewska JA, Hoeppener S, Svensson CM, Orasch T, Heinekamp T, Guerrero-Sánchez C, Figge MT, Schubert US, Brakhage AA (2023) Targeting of phagolysosomes containing conidia of the human pathogenic fungus *Aspergillus fumigatus* with polymeric particles. Appl Microbiol Biotechnol 107(2-3), 819-834.

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Jia LJ, Brakhage AA# (2024) Extracellular proteins and their roles in *Aspergillus fumigatus* pathogenesis. In: Brakhage AA, Kniemeyer O, Zipfel PF (eds.) The Mycota - Human and Animal Relationships 3. 6, pp. 67-89. Springer, Cham. ISBN: 978-3-031-64853. (Review)

Jia LJ, González K, Orasch T, Schmidt F, Brakhage AA (2024) Manipulation of host phagocytosis by fungal pathogens and therapeutic opportunities. Nat Microbiol 9(9), 2216-2231. (Review)

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during coinfection with influenza A viruses and *A. fumigatus* in vitro. Front Cell Infect Microbiol 14, 1445428.
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3. Teaching 2023/2024

Module Number	Title	ECTs
MBGW1.4.1	Angewandte Mikrobiologie	
MMB005	Basic Module Microbiology and Molecular Biology	
MMB009	Molecular Biology/Biotechnology/Infection Biology of Lower Eukaryotes	10

BSc theses

First name	Last name	Thesis title	Mentor
Jana-Sophie	Niegisch	Wachstumsphysiologische Untersuchungen zur Eisentoleranz von *Lichtheimia corymbifera* (Mucorales)	Dr. Kerstin Voigt
Lara	Zörner	Charakterisierung der intrazellulären Prozessierung von Virus-bindenden Nanopartikeln in Zellmodellen	Prof. Dr. Axel Brakhage
Marie-Madeleine	Knott	Charakterisierung von extrazellulären Vesikel von Makrophagen und deren Interaktion mit *Aspergillus fumigatus*	Prof. Dr. Axel Brakhage

MSc/diploma theses

First name	Last name	Thesis title	Mentor
Hanan	Alderzy	Investigating the role of the C-type lectin receptor MelLec in the generation of antifungal extracellular vesicles and genetic labelling of extracellular vesicles as a tool for their quantification and visualization *in vitro*	Prof. Dr. Axel Brakhage
Isabel	Heineking	The intracellular processing of *Lichtheimia corymbifera* spores by macorpages	Prof. Dr. Axel Brakhage
Rida	Ali	Evaluation of the intracellular fate of *Lichtheimia corymbifera* in primary monocytes	Dr. Kerstin Voigt
Larissa	Bulmann	Mechanistic basis of the azalomycin F modification	Prof. Dr. Axel Brakhage
Derya	Cömert	Investigations on the role of NADPH oxidase and p11 protein on intracellular processing of *Aspergillus fumigatus*	Prof. Dr. Axel Brakhage
Johanna	Zech	Analysis of Bacterial-Fungal Interactions for the Identification and Characterization of Natural Products	Prof. Dr. Axel Brakhage

Melanie	Händel	Analysis of the regulated cell death in *Aspergillus fumigatus* as basis for the genereation of reporter strain	Prof. Dr. Axel Brakhage
Phoebe	Chin	The role of *Lichtheimia corymbifera* proteins on the intracellular acidification in human primary monocytes	Dr. Kerstin Voigt
Andrew	Zaki	Selective inhibition of eumelanin in Mucorales and its influence in phagocytosis in human primary macrophages	Dr. Kerstin Voigt

4. Young Researchers

Dissertations

First name	Last name	Thesis title	Mentor
Katherine	Gonzalez Rojas	Drug delivery systems for macrophage- and organelle-specific targeting	Prof. Dr. Axel Brakhage
Lukas	Zehner	Transcription factors of *Streptomyces iranensis* regulating secondary metabolites required for activation of silent fungal gene clusters	Prof. Dr. Axel Brakhage
Muhammad	Rafiq	Deciphering Aspergillus fumigatus evasion strategies within immune cell phagolysosomes	Prof. Dr. Axel Brakhage
Dolly E.	Montano	The immune response of human monocytes to *Lichtheimia corymbifera*	Dr. Kerstin Voigt

5. International Cooperations

Aberystwyth University, Wales
Biology Department, Maynooeth University, Ireland
Department of Plant and Environmental Sciences, University of Copenhagen
DOE-Joint Genome Institute, USA
DTU Technical University of Denmark, Denmark
Institute of Animal Physiology and Genetics, Czech Academy of Sciences, Czech Republic
Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Portugal
Medizinische Universität Innsbruck, Austria
Molecular Mycology, Institut Pasteur, Frankce
Tel Aviv University, Israel
Université de Strasbourg, France
University of Bergen, Norway
University of Crete, Greece
University of Gothenburg, Sweden
University of Manchester, UK
University of São Paulo, Brazil
University of Szeged, Hungary
University of Wisconsin-Madison, USA

6. Team

Title	First name	Last name
Prof. Dr.	Axel A.	Brakhage
	Annika	Tittelbach-Helmrich
	Yu	Hu
JMRC, FSU	Yvonne	Schröck
Dr.	Arite	Bigalke
Dr.	Simone	Edenhart

Dr.	Katherine	Gonzalez Rojas
Dr.	Alexander	Gräwe
Dr.	Thorsten	Heinekamp
Dr.	Peter	Hortschansky
Dr.	Olaf	Kniemeyer
Dr.	Thomas	Krüger
Dr.	Muhammad	Rafiq
Dr.	Paula	Reichelt
Dr.	Franziska	Schmidt
Dr.	Volker	Schroeckh
PD Dr.	Kerstin	Voigt
Dr.	Kerren	Volkmar
	Jaime D.	Acosta España
	Melanie	Händel
	Isabel	Heineking
	Nico	Hermsdorf
	Simranpreet	Kaur
	Moemi	Kawashima
	Liubov	Nikitashina
	Muhammad	Rafiq
	Maira	Rosin
	Henrik	Schweder
	Sophie	Tröger
	Corissa	Visser
	Rasha	Zaher
	Lukas	Zehner
	Ann-Kathrin	Zimmermann
	Sylke	Fricke
	Andrea	Hartmann
	Caroline	Semm
	Silke	Steinbach
	Christina	Täumer
	Christiane	Weigel
	Larissa	Bulmann
	Johanna H.	Zech
	Melanie	Händel
	Maximilian	Knott
	Eric	Unger
	Clara	Kraus

Lehrstuhl für Synthetische Biotechnologie (Biotechnikum des Leibniz-HKI)

Prof. Dr. Miriam Agler-Rosenbaum

1. Forschung

Unter dem Slogan „Neue Prozesse für neue Produkte“ bietet das Biotechnikum des Leibniz-HKI multiskalige, ingenieurtechnische Lösungen für biologische Herausforderungen. Wir entwickeln komplette Bioprozessketten für mikrobielle Rein- und Co-Kulturen vom Rohsubstrat bis zum reinen Produkt für Antibiotika, Enzyme, Biotenside, Toxine, Medikamente und Biopolymere bis zum m^3-Maßstab. Dabei liegen die Innovationsschwerpunkte in den Bereichen 1) Online-Monitoring von Kulturen, 2) physikalische Strategien für das Management schwieriger Kulturen (beides realisiert durch die BT-Forschungsteams Bioprozessentwicklung und Bioprozessintensivierung), 3) bioelektrochemische Kontrolle von Kulturen (Forschungsteam Mikrobielle Elektro-physiologie) und 4) Ultra-Hochdurchsatz-Kulturen (Forschungsteam Tropfenmikrofluidik). Unser Portfolio an Forschungsaktivitäten und Technologien ist Grundlage für unsere eigene, international wettbewerbsfähige Forschung, zahlreiche akademische Kooperationen, sowie die translationale Unterstützung bei der Bioprozessentwicklung für KMUs. Das Biotechnikum ist auch Partner in großen Jenaer Forschungsclustern wie dem CoE Balance of the Microverse, dem Leibniz-Wissenschaftscampus InfectoOptics, dem

BMBF-Forschungscampus InfectoGnostics und dem Leibniz-Zentrum für Photonik in den Lebenswissenschaften.

Ausgewählte Ergebniss der Forschungsteams: Das Bioprozessentwicklungsteam hat zahlreiche Bioprozesse für die eigene Forschung, das HKI und externe Partner weitergeführt (insgesamt ca. 100), wobei der Anteil an kontinuierlichen Bioprozessen zunimmt. Wichtige Forschungsergebnisse der kollaborativen Bioprozesse wurden z.B. in Nat Commun 2024 und J Nat Prod 2024 veröffentlicht.

Das Team für Bioprozessintensivierung konzentrierte sich im Jahr 2024 auf drei Hauptaktivitäten:

1) Anwendung von Online-Überwachungs- und Steuerungsinstrumenten für Bioprozesse mit Co-kulturen, einschließlich komplexer Substrate wie Zellulose. Hier haben wir einen unserer neuen zellulosebasierten Bioprozesse patentiert und veröffentlicht (ACS SusChemEng 2024). Seit Ende 2023 wenden wir diese Technologien auch im CoE „Balance of the Microverse“ an, um die Dynamik von semikomplexen Co-Kulturen zu untersuchen.

2) Wir haben unsere neue Druckreaktorkaskade (TAB-Förderung) für die Produktion von Naturstoffen mit biochemisch schwierigen mikrobiellen Systemen eingesetzt (Disc Chem Eng 2024, Micro Biotechnol, 2024). Zudem wurden die ersten anaeroben, CO2-verbrauchenden Bioprozesse publiziert (Eng Life Sci, angenommen).

3) Seit Herbst 2023 wird Lars Regestein (zusammen mit der RWTH) von der Bundesagentur für Sprunginnovationen (SPRIND) gefördert, um ein pilzbasiertes Bioprozesskonzept zur Marktreife zu bringen. BT/HKI stehen kurz vor der Gründung des Spin-offs „Biophelion“.

Das Forschungsteam Mikrobielle Elektrophysiologie verfolgt weiterhin zwei Hauptrichtungen: 1) Im Rahmen des ERC Consolidator Grant eMICROBe erforscht und entwickelt das Team die Integration von extrazellulärem Elektronentransfer und mikrobiellem Energiestoffwechsel (Trends Biotechnol 2024). 2) Zum anderen laufen unsere Arbeiten im DFG-Schwerpunktprogramm 2240 e-Biotech zur Etablierung von Elektro-Bioprozessen mit *C. ljungdahlii* weiter und wir starteten 2024 in die zweite Förderphase. Seit April 2022 koordiniere ich das DFG Schwerpunktprogramm 2240 e-Biotech. Das Tropfenmikrofluidik-Forschungsteam hat sich von der Technologieentwicklung auf die Anwendung von Hochdurchsatzkultivierung und Screening für die fortgeschrittene mikrobiologische Forschung konzentriert. Dabei arbeiten wir weiterhin eng mit externen Partnern zusammen.

Wir haben unsere Kapazitäten für Muliplex-Tropfenexperimente und die Anwendung von Streulicht für den Nachweis von Mikroorganismen mit geringem Gehalt erweitert (zwei Veröffentlichungen in Sens Act B Chem 2024). Mit unserer Arbeit treiben wir das Screening nach seltenen genetischen Varianten in einem hochdiversen Pool mikrobieller Zellen voran, z. B. beim Screening von Mutantenbibliotheken (verschiedene Projekte laufen) und bei der Kultivierung seltener Mikroben aus komplexen Umwelthabitaten, z. B. Grundwassermikroben (ISME Commun 2024). Um mehr Nutzern den Zugang zu unserer Ultrahochdurchsatz-Kultivierungstechnologie zu ermöglichen, haben wir für das Leibniz-Zentrum für Photonik in den Biowissenschaften eine vereinfachte, benutzerfreundliche Version unserer Plattform entwickelt.

Über die Forschung hinaus waren unser Abteilungsretreat in Plothen und die Organisation des HKI Sommerfestes zwei Team-Ereignisse des Jahres 2024, die in Erinnerung bleiben.

2. Publikationen

Boto ST, Bardl B, Harnisch F, Rosenbaum MA (2023) Microbial electrosynthesis with *Clostridium ljungdahlii* benefits from hydrogen electron mediation and permits a greater variety of products. *Green Chem* 25(11), 4375-4386.

Franco A, Chukwubuikem A, Meiners C, Rosenbaum MA (2023) Exploring phenazine electron transfer interaction with elements of the respiratory pathways of *Pseudomonas putida* and *Pseudomonas aeruginosa*. *Bioelectrochemistry* 157, 108636.

Götze S, Vij R, Burow K, Thome N, Urbat L, Schlosser N, Pflanze S, Müller R, Hänsch VG, Schlabach K, Fazlikhani L, Walther G, Dahse HM, Regestein L, Brunke S, Hube B, Hertweck C, Franken P, Stallforth P (2023) Ecological niche-inspired genome mining leads to the discovery of crop-protecting nonribosomal lipopeptides featuring a transient amino acid building block. *J Am Chem Soc* 145(4), 2342-2353.

Munser AS, Trost M, Schröder S, Graf M, Rosenbaum MA, Tünnermann A (2023) Analysis of very low bacterial counts in small sample volumes using angle-resolved light scattering. *Appl Opt* 62(2), 411-418.

Peng CC, Dormanns N, Regestein L, Beemelmanns C (2023) Isolation of sulfonosphingolipids from the rosette-inducing bacterium *Zobellia uliginosa* and evaluation of their rosette-inducing activity. *RSC Adv* 13(39), 27520-27524.

Pflanze S, Mukherji R, Ibrahim A, Günther M, Götze S, Chowdhury S, Reimer L, Regestein L, Stallforth P (2023) Nonribosomal peptides protect *Pseudomonas nunensis* 4A2e from amoebal and nematodal predation. *Chem Sci* 14(41), 11573-11581.
Pourmasoumi F,[*] Hengoju S,[*] Beck K, Stephan P, Klopfleisch L, Hoernke M, Rosenbaum MA, Kries H (2023) Analysing megasynthetase mutants at high throughput using droplet microfluidics. *Chembiochem* 24(24), e202300680.
Schlembach, I, Ott C. (2023) Nicht-invasive Online-Fluoreszenzspektroskopie in Rührkessel-Fermentern zur flexiblen Untersuchung von komplexen Bioprozessen *TechnoPharm* 13(3), 118-123.
Yang Z, Qiao Y, Konakalla NC, Strøbech E, Harris P, Peschel G, Agler-Rosenbaum M, Weber T, Andreasson E, Ding L (2023) Streptomyces alleviate abiotic stress in plant by producing pteridic acids. *Nat Commun* 14(1), 7398.
Harnisch F, Deutzmann JS, Boto ST, Rosenbaum MA (2024) Microbial electrosynthesis: opportunities for microbial pure cultures. *Trends Biotechnol* 42(8), 1035-1047. (Review)
Janevska S[*#], Weiser S[*], Huang Y, Lin J, Hoefgen S, Jojić K, Barber AE, Schäfer T, Fricke J, Hoffmeister D, Regestein L, Valiante V, Kufs JE[#] (2024) Optimized psilocybin production in tryptophan catabolism-repressed fungi. *Microb Biotechnol* 17(11), e70039.
Mahmoud Mohamed MM, Yang Z, Lum KY, Peschel G, Rosenbaum MA, Weber T, Coriani S, Gotfredsen CH, Ding L (2024) Genome-driven discovery of hygrocins in *Streptomyces rapamycinicus*. *J Nat Prod* 87(5), 1321-1329.
Man DKW, Hermans SM, Taubert M, Garcia SL, Hengoju S, Küsel K, Rosenbaum MA (2024) Enrichment of different taxa of the enigmatic candidate phyla radiation bacteria using a novel picolitre droplet technique. *ISME Commun* 4(1), ycae080.
Rosenbaum MA, Graf M (2024) Microfluidics: taking experimentation to the scale and diversity of microorganism. International Microbiology Literacy Initiative (Review)
Samimi A, Hengoju S, Rosenbaum MA (2024) Combinatorial sample preparation platform for droplet-based applications in microbiology. *Sens Actuators B Chem* 417.
Schlembach I, Bardl B, Regestein L, Rosenbaum MA (2024) Nonengineered fungus provides a shortcut from cellulose to bulk *Erythro*-isocitric acid. *ACS Sustainable Chem Eng* 12(9), 3408-3418.
Tiso T, Demling P, Karmainski T, Oraby A, Eiken J, Liu L, Bongartz P, Wessling M, Desmond P, Schmitz S, Weiser S, Emde F, Czech H, Merz J, Zibek S, Blank LM, Regestein L (2024) Foam control in biotechnological processes—challenges and opportunities. *Discov Chem Eng* 4(2), (Review)
Yang Z, Qiao Y, Strøbech E, Morth JP, Walther G, Jørgensen TS, Lum KY, Peschel G, Rosenbaum MA, Previtali V, Clausen MH, Lukassen MV, Gotfredsen CH, Kurzai O, Weber T, Ding L (2024) Alligamycin A, an antifungal β-lactone spiroketal macrolide from *Streptomyces iranensis*. *Nat Commun* 15(1), 9259.

3. Studium und Lehre

Sommersemester
Vorlesung: Mikrobielle Bioelektrochemie/160468 /2SWS
Praktikum: 160469/2 SWS

Wintersemester
Vorlesung: Biotechnologie/Bioverfahrenstechnik/90685/2SWS
Praktikum: 90686/5 SWS

Bachelorarbeiten
Maria Blumentritt. Fermentation und Scale-Up von *Streptomyces coelicolor* mNG und *Trichoderma reesei* mCherry Co-Kulturen auf ZelluloseNährstoffgrundlage

Masterarbeiten

Carolina Casas Mesa. Untersuchung des Einflusses von mikrobiellen Gemeinschaften auf den Celluloseabbau ausgewählter Pilze unter spezieller Berücksichtigung der Glukose-Affinitätskonstante

Riya Kothya. Screening of new anti-Gram negatives in culture isolates from Termite gut and tar contaminated soil samples with a droplet-based microfluidic system

John Oliver Gath. Screening of rylene dyes for cell-staining applications in droplet microfluidics

Jessica Lamber. Respirometric investigations on the influence of white rot fungi on lignocellulose degradation in co-culture

Kareem Gerges. Biosynthesis of ethyl acetate by *Clostridium ljungdahlii* autotrophically using CO_2 and H_2

Menatallah Elsedawy. Generating a reporter strain for the investigation of the mevalonate pathway in *Dictyostelium discoideum* by overexpression of terpene synthase genes

Akbiyik Rengin. The quantification of the energy levels of *Escherichia coli* BL21 cells using a synthetic ATP reporter and fluorescence microscopy

Cole Carlson. Heterologous phenazine production in biotech hosts for bioelectrochemical applications

Oskar Zorc. Exploring physiological stress responses in *Clostridium ljungdahlii*

Kasra Kamali. Droplet-based Microfluidics for High-Throughput Screening of Serine Protease

Philipp Huber. Polyol lipid formation with *Aureobasidium pullulans* in context of circular biomanufacturing

4. Wissenschaftlicher Nachwuchs

Dissertationen

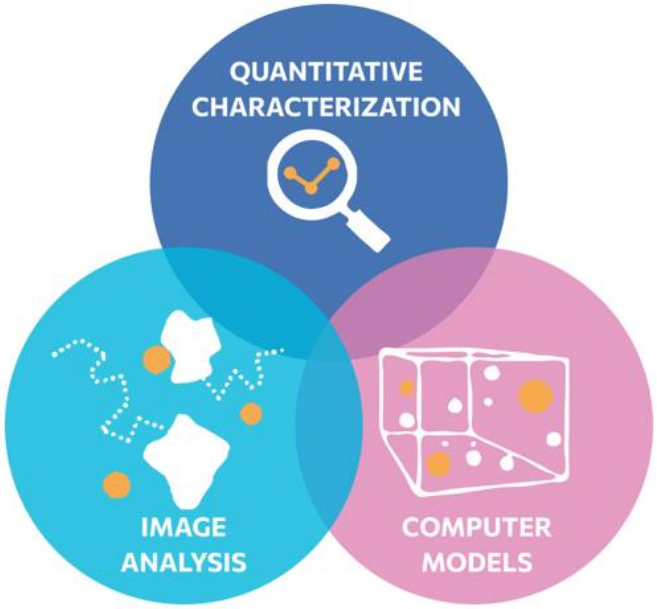
Ana Palacio Barrera. Development of a model co-culture platform with *Trichoderma reesei* RUT C-30 and *Streptomyces coelicolor* A3(2) for natural producttargeted Bioprocesses.

Santiago Boto. Towards product diversification in carbon negative bioprocesses with *Clostridium ljungdahlii.*

Nicolas Schlosser. (Co)-culture processes of *Janthinobacterium agaricidamnosum* for lipopeptide production and novel natural products.

Lehrstuhl für Angewandte Systembiologie

Prof. Dr. Marc Thilo Figge

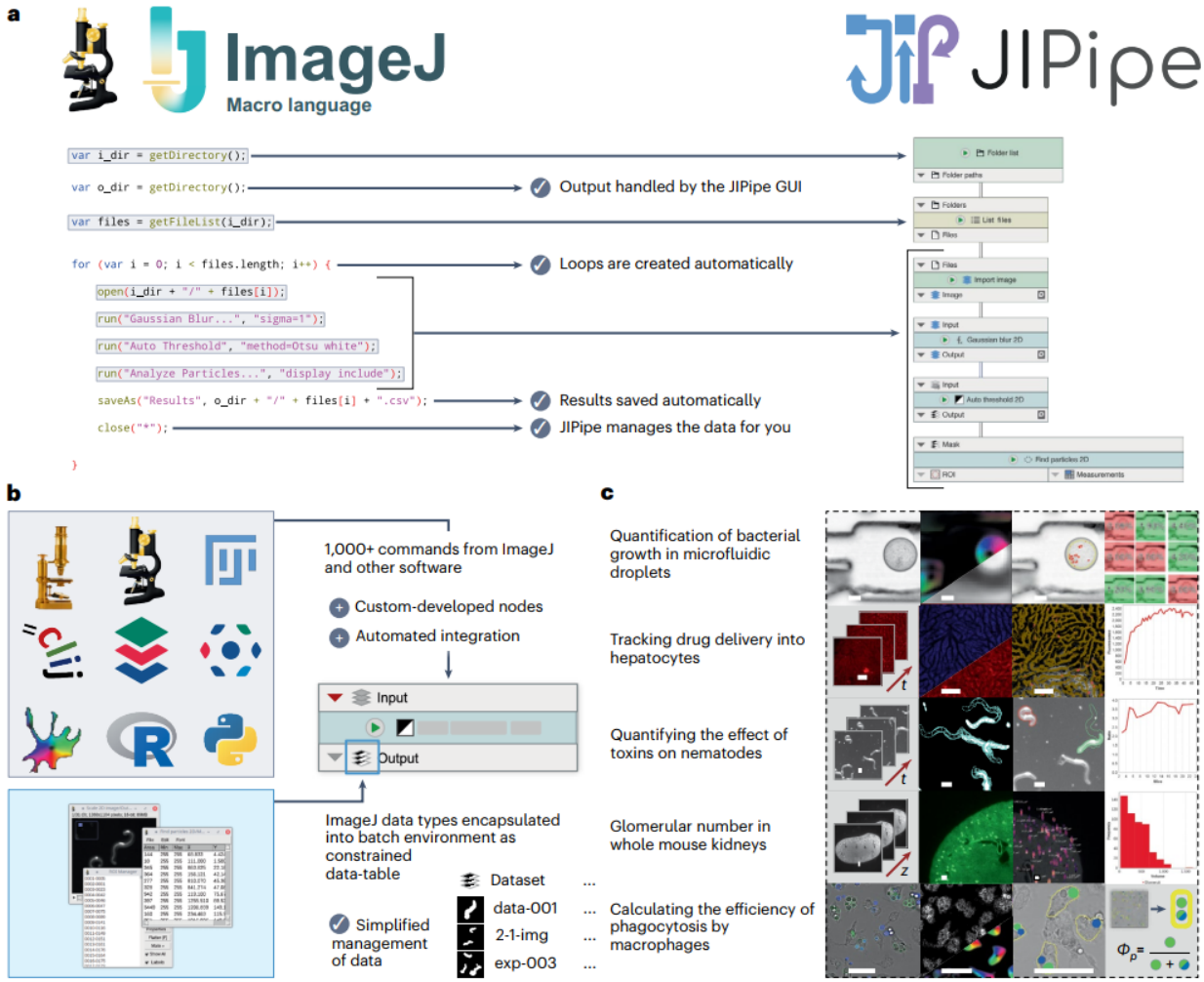


1. Research

Image-based Systems Biology

The Applied Systems Biology (ASB) research group has set itself the task of making biology more quantitative, focusing on the analysis of microscopic and spectroscopic image data. We apply the approach of image-based systems biology (see Figure 1), in which image data is processed in an automated manner with the aim of quantifying biomedical processes in an objective way. Based on the quantification result, we feed the determined parameter values into mathematical models to perform computer simulations in space and time with the aim of developing new hypotheses that can be tested experimentally. We are particularly interested in investigating morphological, functional and dynamic aspects of infection processes as they can be modeled in organ-on-chip models and in vivo mouse experiments. In addition, we contribute to the automation of processes in the context of natural product and antibiotic resistance research by providing algorithms for the online analysis of droplet-based microfluidic approaches with ultra-high throughput.

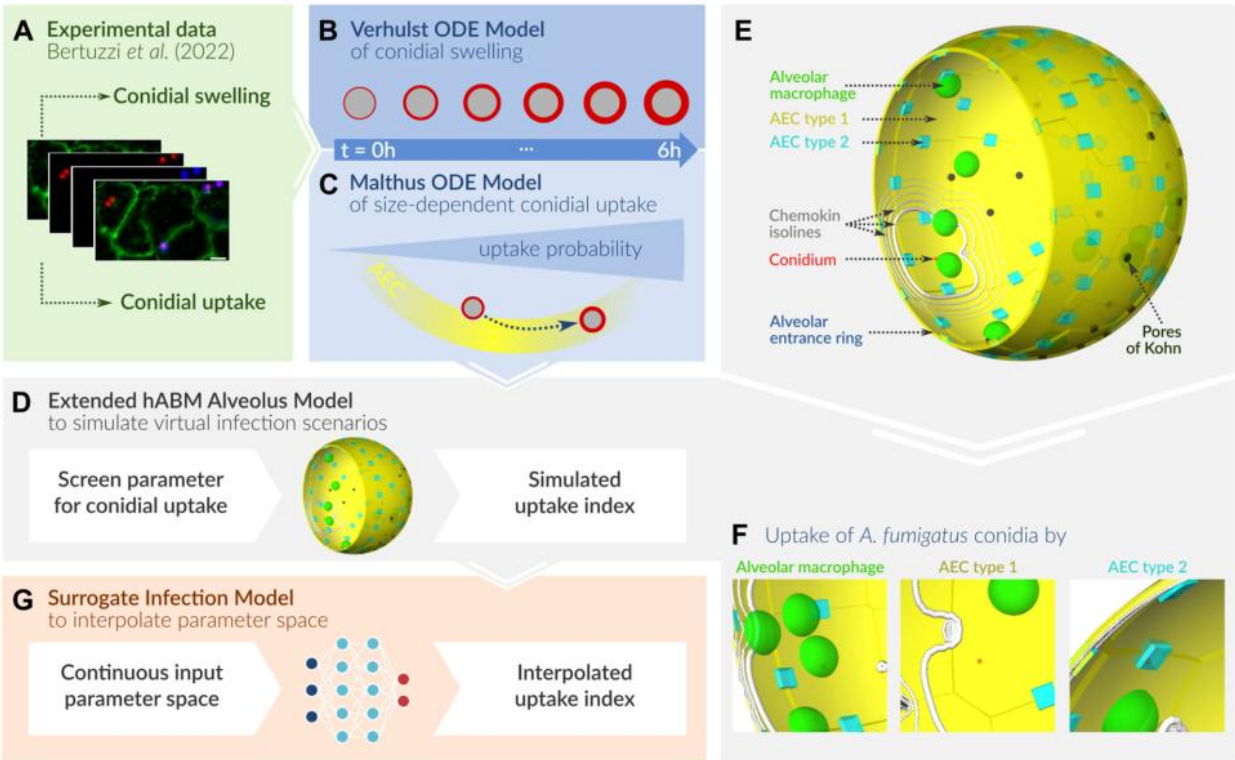
In 2023, the ASB team published or contributed to 19 research articles in renowned journals such as Bioinformatics, Biomaterials, Cell Host & Microbe, Computational and Structural Biotechnology Journal, Nature Methods, Small, Systems Biology and Applications, and various others. The ASB team organized the International Symposium Systems Biology of Microbial Infection (SBMI) for the seventh time in 2023.



Java Image Processing Pipeline (JIPipe). The visual programming language JIPipe allows users to quantify processes observed in image data without the need to code algorithms. In this way the otherwise growing gap between non-programmers and sophisticated image processing techniques, such as artificial intelligence (AI) methods, is being narrowed. *Figure adapted from Gerst et al. (2023) Nature Methods.*

The ASB team's research includes advances in the following areas: (i) Surrogate infection modeling to predict optimal alveolar macrophage number for clearance of Aspergillus fumigatus infections in the human lung, (ii) Quantitative analysis of tracks of intracellular organelles using a Hidden Markov Model to distinguish peroxisome motion under various conditions, (iii) Development of the visual programming language Java Image Processing Pipeline (JIPipe) to enable anyone to perform batch processing (see Figure 2), (iv) Application of tailored approaches from artificial intelligence to evaluate reproducible cryogel preparations based on automated image analysis, to tune the corona-core ratio of polyplex micelles for selective oligonucleotide delivery to hepatocytes or hepatic immune cells, and to realize cost-effective and objective quantification of intramuscular fat in histological sections of muscles.

In 2024, the ASB team published or contributed to 18 research articles in renowned journals such as ACS Synthetic Biology, Biomaterials, Communications Biology, ISME Communication, mBio, Nature Microbiology, PNAS, Small, and various others. The ASB team organized the International Symposium Image-based Systems Biology (IbSB) for the seventh time in 2024.



Bottom-up approach to model the immune response against *A. fumigatus* lung infection. A–C Based on experimental phagocytosis assays between *A. fumigatus* conidia and type 2 alveolar epithelial cells (AECs) (A), we fitted a Verhulst ordinary differential equation (ODE) model to the increase of conidial diameter (B), and an extended Malthus ODE model to uptake indexes resulting in an increasing chance of uptake from non-swelling to swelling conidia. The dotted arrow denotes the transition from a resting to a swelling conidium that is taken up with a higher probability (C). D–F Including the fitted ODEs into a previously developed hybrid agent-based model (hABM) of a human alveolus, we were able to simulate millions of virtual infection scenarios. The hABM comprises one alveolus as a ¾ sphere consisting of type 1 AECs (yellow) and type 2 AECs (light blue). The entrance ring (dark blue) and pores of Kohn (PoK) (black) are the boundaries of the system. The migration of alveolar macrophages (AMs) (green) is directed by the chemokine signal (white isolines) to locate the *A. fumigatus* conidia (red). The conidium can be taken up by AMs, type 1 and type 2 AECs. G By training a surrogate infection model (SIM) on the hABM output, we were able to predict uptake indexes by AMs and AECs for an interpolated parameter space. *Figure adapted from Saffer et al. (2024) Communications Biology.*

The ASB team's research includes advances in the following areas: (i) Spatiotemporal modeling and computer simulations to quantify cellular contributions to uptake of Aspergillus fumigatus in the human lung (see Figure 3), (ii) Modeling microbial growth curves to identify the competitive inhibition and mutualistic growth in co-infections with Staphylococcus aureus and Acinetobacter baumannii, (iii) Organ-on-Chip models for infectious disease re-search: Modeling of intravenous caspofungin administration using an intestine-on-chip reveals altered Candida albicans microcolonies and pathogenicity, (iv) Quantitative investigation of long term stimulation by implanted pacemaker in a human like animal model to reveal the impact of functional electrical stimulation on nerve-damaged muscles using deep learning, and (v) Deep learning-based characterization of neutrophil activation phenotypes in ex vivo human Candida blood infections.

Overall, the ASB team represents a collaborative link between the two profile lines LIGHT and LIFE of the Friedrich Schiller University Jena, which is due to the fact that image-based systems biology is a generic link between experiment and theory in interdisciplinary studies, as microscopic and spectroscopic data are routinely collected in today's experiments. This also explains the role of the ASB team as an active collaborator in a

number of interdisciplinary research initiatives: As part of the Cluster of Excellence "Balance of the Microverse", we are developing our visual programming language JIPipe for image processing in correlative data analysis. As active cooperation partners in the two DFG-funded collaborative research centers FungiNet 124 - "Pathogenic fungi and their human host - networks of interaction" and PolyTarget 1278 - "Polymer-based nanoparticle libraries for targeted anti-inflammatory strategies", we are advancing automated image analysis in the context of fungal infections and the uptake of nanoparticles. Within the DFG-funded Research Training Group 2723 "Materials-Microbe-Microenvironments" the ASB team is responsible for image data analysis. In addition, M.T. Figge is spokesperson for the Leibniz-funded ScienceCampus "InfectoOptics" and coordinates the "PneuThera" project for the treatment of lung infections using a lung-on-chip model. In the "InfectoGnostics" research campus, methods for use in infection diagnostics are being further developed; for example, a microfluidics platform for screening for Staphylococcus aureus in human and veterinary medicine is being developed in the "ADA" project together with Biotechnikum at the Leibniz-HKI. Finally, M.T. Figge co-ordinates the work area "Image Analysis" within the National Research Data Infrastructure "NFDI4Bioimage", where new approaches to FAIR data analysis are being developed. This will be realized as part of the develop-ment of the virtual programming language JIPipe, which enables any user to program ImageJ macros for reproducible analyses and brings modern methods of artificial intelligence within the reach of users who are not experienced programmers.

2. Publications

Battista M, Hoffmann B, Bachelot Y, Zimmermann L, Teuber L, Jost A, Linde S, Westermann M, Müller MM, Slevogt H, Hammerschmidt S, Figge MT, Vilhena C*#, Zipfel PF*# (2023) The role of pneumococcal extracellular vesicles on the pathophysiology of the kidney disease hemolytic uremic syndrome. mSphere 8(4), e0014223.

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Ma F, Kaufmann R, Sedzicki J, Cseresnyés Z, Dehio C, Hoeppener S, Figge MT, Heintzmann R# (2023) Guided-deconvolution for correlative light and electron microscopy. PLOS One 18(3), e0282803.

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Gardey E, Cseresnyés Z, Sobotta FH, Eberhardt J, Haziri D, Grunert PC, Kuchenbrod MT, Gruschwitz FV, Hoeppener S, Schumann M, Gaßler N, Figge MT, Stallmach A#, Brendel JC# (2024) Selective uptake into inflamed human intestinal tissue and immune cell targeting by wormlike polymer micelles. Small 20(21), 2470162.

Günther K, Nischang V, Cseresnyés Z, Krüger T, Sheta D, Abboud Z, Heinekamp T, Werner M, Kniemeyer O, Beilhack A, Figge MT, Brakhage AA, Werz O#, Jordan PM# (2024) *Aspergillus fumigatus*-derived gliotoxin impacts innate immune cell activation through modulating lipid mediator production in macrophages. Immunology 173(4), 748-767.

Jojić K*, Gherlone F*, Cseresnyés Z, Bissell AU, Hoefgen S, Hoffmann S, Huang Y, Janevska S, Figge MT, Valiante V (2024) The spatial organization of sphingofungin biosynthesis in *Aspergillus fumigatus* and its cross-interaction with sphingolipid metabolism. mBio 15(3), e0019524.

Kaden T*, Alonso-Roman R*, Akbarimoghaddam P*, Mosig AS, Graf K, Raasch M, Hoffmann B, Figge MT#, Hube B#, Gresnigt MS# (2024) Modeling of intravenous caspofungin administration using an intestine-on-chip reveals altered *Candida albicans* microcolonies and pathogenicity. Biomaterials 307, 122525.

Liu N, Sonawane M, Sommerfeld O, Svensson CM, Figge MT, Bauer Reinhard, Bischoff SJ, Bauer M, Osuchowski MF, Press AT# (2024) Metamizole outperforms meloxicam in sepsis: insights on analgesics, survival and immunomodulation in the peritoneal contamination and infection sepsis model. Front Immunol 15, 1432307.

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Valentine M*, Rudolph P*, Dietschmann A, Tsavou A, Mogavero S, Lee S, Priest EL, Zhurgenbayeva G, Jablonowski N, Timme S, Eggeling C, Allert S, Dolk E, Naglik JR, Figge MT, Gresnigt MS*#, Hube B*# (2024) Nanobody-mediated neutralization of candidalysin prevents epithelial damage and inflammatory responses that drive vulvovaginal candidiasis pathogenesis. mBio 15(3), e0340923.

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3. Drittmittelprojekte

Projektträger	Vorhaben	Laufzeit	Mittel in 2023 und 2024
DFG	Exzellenz-Cluster "Balance of the Microverse"	2019-2025	1 Doktorandin + 1 Postdoc
DFG	Sonderforschungsbereich FungiNet – Teilprojekt B4	2021-2025	2 Doktoranden
DFG	Sonderforschungsbereich PolyTarget – Teilprojekt Z01	2021-2025	1 Postdoc
DFG	Graduiertenschule MMM – Teilprojekt F	2022-2030	1 Doktorand
DFG	NFDI4Bioimage – Teilprojekt TA4	2023-2028	1 Postdoc
BMBF	InfectoGnotics – Teilprojekt ADA	2021-2024	1 Doktorand
BMBF	Computational Life Sciences	2022-2025	1 Doktorand + 1 Postdoc
BMBF	Leibniz Center for Photonics in Infection Research	2021-2026	2 Postdocs
Leibniz	Leibniz Science Campus (LSC) InfectoOptics – Projekt "PneuThera"	2019-2024	1 Postdoc

4. Studium und Lehre

WS 22/23
Seminar „Systembiologie der Immunologie" (Veranstaltungsnummer 78347)

SS 2023
Vorlesung „Systembiologie der Immunologie" (Veranstaltungsnummer 71799)
Praktikum „Mikroskopie und Bildanalyse" (Veranstaltungsnummer 7251)

WS 23/24
Seminar „Systembiologie der Immunologie" (Veranstaltungsnummer 78347)
Vorlesung „Bildbasierte Systembiologie" (Veranstaltungsnummer 140803)

SS 2024
Praktikum „Mikroskopie und Bildanalyse" (Veranstaltungsnummer 7251)

Bachelorarbeiten
Maurice Falleta. Light microscopy based quantification of the peroxisomal import of matrix proteins (2023)
Lukas Harder. Morphological and temporal investigation of the endosolam nanostructure using labeled cargo proteins (2023)

Masterarbeiten
Mounir Zerdani. Fungal Growth Quantification of *Candida albicans* by Tracking Hyphal Tips in JIPipe (2023)
Ahsanullah Ahsanullah. In vitro Interaction of Human Immune Cells with *Staphylococcus aureus* Biofilms (2023)
Jana Wilms. Machine Learning Surrogate Models for Agent-Based Modeling: Application to Host-Pathogen Interactions in Whole Blood Infections (2024)
Karoline Schied. Stochastic Lung-on-Chip Simulations: Implementing an Agent-based Organ-on-Chip Model in C++ (2024)
Marius Wank**.** From lung-on-chip to virtual alveolus model: Quantitative modeling of *Aspergillus fumigatus* hyphal growth (2024)
Veit Hucke**.** GAN-based image-to-image translation for biomedical image analysis (2024)

5. Wissenschaftlicher Nachwuchs

Dissertationen

Alexander Tille. The human complement system: A mathematical analysis of its regulation (2023)

Philipp Praetorius. From microscopy images to biological insights: Classical image analysis and AI tools for automated quantification (2024)

Kassandra Walluks. Histologische Untersuchung des *M. cricoarytenoideus posterior* von Schafen nach elektrischer Langzeitstimulation (2024)

Christoph Saffer. Mathematical modeling of spatiotemporal host defense mechanisms against pulmonary fungal infections (2024)

6. Gleichstellung und Familie

2023

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
9	15	5

2024

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
10	16	5

7. Internationale Kooperationen

Dr.	Margherita	Bertuzzi	University of Manchester	Manchester	UK
Dr.	Josh	Moore	Divison of Computational Biology, University of Dundee	Dundee	UK

8. Administration/Finanzen

Beschäftigungsstruktur

	Personen	Stellenanteile
Beschäftigte im Rahmen von Haushaltsmitteln		
Wissenschaftliche MitarbeiterInnen	0	0
Postdoc	2	2
Technische Assistenz	0	0
Sekretariat	1	1
Beschäftigte im Rahmen von Drittmitteln		
Wissenschaftliche MitarbeiterInnen	9	9
Wissenschaftliche Assistenten	3	0
Studentische Assistenten	0	0
Weiteres Personal		
Auszubildende	0	0

Vertretung in Selbstverwaltungsgremien

Since 2023	Board Member and Coordinator of Task Area “Bioimage Informatics” in the DFG-funded national research data management initiative NFDI4Bioimage
Since 2023	Board member in DFG-funded Research Training Group 2123 Materials-Microbes-Microenvironments
Since 2023	Board Member of the Beutenberg Campus e.V. “Life Science meets Physics”, Jena
Since 2023	Editor: PLOS Complex Systems
Since 2022	Member of the Faculty Council of the Faculty of Biological Sciences at the Friedrich Schiller University Jena
Since 2022	Coordinator of BMBF-funded Project “Machine Learning Supported Multi-Model Simulator for Infection Research” in funding area Computational Life Sciences
Since 2021	Deputy Coordinator of Excellence Graduate School Jena School for Microbial Communication (JSMC)
Since 2021	PI in the BMBF-funded “Leibniz Center for Photonics in Infection Research”
Since 2020	PI in the of BMBF-funded Research Campus “InfectoGnostics”
Since 2019	Coordinator of Research Area C – Data Synopsis in the DFG-funded Cluster of Excellence EXC 2051 Balance of the Microverse
Since 2019	Member of the Management Board of the Microverse Imaging Center in the DFG-funded Cluster of Excellence EXC 2051 Balance of the Microverse
Since 2019	Speaker of Leibniz ScienceCampus “InfectoOptics”
Since 2019	Editor: Scientific Reports
Since 2017	Ombudsperson at the Leibniz-HKI, Jena
Since 2017	PI in the DFG-funded Collaborative Research Centre 1278 PolyTarget
Since 2017	Editor: Cytometry A
Since 2015	Member of the Jena Center for Soft Matter and the Michael Stifel Center for Data-Driven and Simulation Science, Jena
Since 2014	PI in the DFG-funded Collaborative Research Centre 124 FungiNet
Since 2011	Organizer: yearly international symposia on “Systems Biology of Microbial Infection” (SBMI) and “Image-based Systems Biology” (IbSB)

9. Team

Title	**First name**	**Last name**
Prof. Dr.	Marc Thilo	Figge
Team Assistance	Lisa	Herbich
Dr.	Zoltán	Cseresnyés
Dr.	Carl-Magnus	Svensson
Dr.	Ruman	Gerst
Dr.	Anastasia	Solomatina
Dr.	Bianca	Hoffmann
Dr.	Sandra	Timme
Dr.	Jan-Philipp	Praetorius
Dr.	Kassandra	Walluks
Dr.	Dhruv	Khatri
M.Sc.	Parastoo	Akbarimoghaddam
M.Sc.	Yann	Bachelot

M.Sc.	Arjun	Sarkar
M.Sc.	Philipp	Städter
M.Sc.	Mounir	Zerdani
M.Sc.	Simone	Piccioni
M.Sc.	Marius	Wank
M.Sc.	Karoline	Schied
M.Sc.	Jana	Wilms

Biomolecular Chemistry

Prof. Dr. Christian Hertweck

1. Research

In the year 2024, the Department of Biomolecular Chemistry (BMC) has continued achieving significant progress in the discovery and understanding of medically relevant natural products that serve as leads for therapeutics or chemical mediators of infections, delving into their biosynthesis and functions. Among the department's notable accomplishments were the discoveries of overlooked biosynthetic pathways in anaerobic bacteria and the development of tools to harness their biosynthetic potential, which led to the successful acquisition of grants, notably an ERC Advanced Grant (AnoxyGen) and the funding of the meta-CDI project in the Leibniz Collaborative Excellence Program. These projects aim at uncovering elusive virulence factors and unearthing novel antiinfectives from anaerobes.

BMC researchers advanced their ecology- and genomics-driven approach to uncovering novel bioactive compounds, leading to the identification of antiproliferative furan-substituted cyclopeptides (Angew Chem 2024), for example. The BMC's research further explored the complex symbiotic relationships between the pathogenic fungus Rhizopus microsporus and its endosymbionts (Mycetohabitans spp.), known to cause rice seedling blight and systemic infections of immunocompromised patients, BMC's investigations uncovered broader ecological functions and the molecular basis of the symbiosis (e.g. ISME J 2024, Nature 2024, with J. Vorholt, ETHZ). In addition to exploring symbiosis, the BMC has made significant advances in understanding the biosynthesis and function of virulence factors and toxins in human, animal and plant pathogens (e.g. rhizoxin, Angew Chem 2024a and 6-thioguanine, Angew Chem 2024e). Research into the infamous Burkholderia pseudomallei (BP) group—responsible for severe infections like melioidosis—has been a key area of focus. These pathogens possess a conserved gene cluster involved in the production of polyketides (malleicyprols), which are critical to their virulence. The BMC identified key enzymes for forming and incorporating the reactive cyclopropanol unit of malleicyprols, an insight that may guide the development of new antivirulence strategies against BP infections (Angew Chem 2024d). The department's advanced techniques like imaging mass spectrometry, synthetic biology, and metabolomic profiling has contributed to broader scientific inquiries in many collaborations. The support of Leibniz-HKI and FSU junior research groups and young researchers by BMC members has resulted in numerous high-impact joint publications e.g. Lackner (ISME J 2024), Beemelmanns (Angew Chem 2024c), Brunke (Nat Commun 2024), Kries (Angew Chem 2024a, 2024b), Kloss (Eur J Med Chem 2024), and Gressler (J Am Chem Soc 2024). Fruitful collaborations with MPI-CE and FSU departments (Hoffmeister, Hellmich, Mittag, Arndt, Popp) are also documented by

joint papers (e.g. Proc Natl Acad Sci USA 2024, Angew Chem 2024b, 2024f, J Am Chem Soc 2024).

2. Publications

Roman D, Meisinger P, Guillonneau R, Peng CC, Peltner LK, Jordan PM, Haensch V, Götze S, Werz O, Hertweck C, Chen Y, Beemelmanns C (2024) Structure revision of a widespread marine sulfonolipid class based on isolation and total synthesis. Angew Chem Int Ed 63(23), e202401195.

Richter I, Hasan M, Kramer JW, Wein P, Krabbe J, Woitas KP, Stinear TP, Pidot SJ, Kloss F, Hertweck C, Lackner G (2024) Deazaflavin metabolite produced by endosymbiotic bacteria controls fungal host reproduction. ISME J 18(1), wrae074.

Ishida K, Litomska A, Dunbar KL, Hertweck C (2024) An enzymatic prodrug-like route to thio and selenoamides. Angew Chem Int Ed 63(31), e202404243.

Dörner S, Trottmann F, Jordan P, Bartels B, Rogge K, Werz O, Hertweck C, Hoffmeister D (2024) The fatal mushroom neurotoxin muscarine is released from a harmless phosphorylated precursor upon cellular injury. Angew Chem Int Ed 63(52), e202417220.

Büttner H, Rassbach J, Schultz C, Popp J, Gressler M, Hertweck C (2024) Beneficial soil fungus kills predatory nematodes with dehydropeptides translocating into the animal gut. J Am Chem Soc 146(50), 34702-34710.

3. Third Party Funding

DFG: SFB ChemBioSys Teilprojekt B01, Chemische Mediatoren in komplexen Biosystemen, Sonderforschungsbereich 1127/3, B01 und Teilprojekt Z02, SFB 1127/3, Z02

DFG: Leibniz Förderpreis/ Gottfried Wilhelm Leibniz Preis 2015, HE 3469/ 7-1

Pakt Leibniz: A Molecular Targeting Approach to Combat Human Pathogenic Fungi, Projektnummer: K21712016

JSMC-TP Carl Zeiss Stiftung, Natural Products in reconstituted microbiomes

HFSP: Human Frontier Science Program: “The ecological role of bacterial specialized metabolites in bacteria-microalgae interactions”, Reference number: 885957

Freistaat Thüringen: EFRE, “Bildgebendes Massenspektrometer zur Entdeckung/ Visualisierung mikrobieller Wirkstoffe”, 2022 FGI 0010

4. Teaching

Bachelor theses

First name	Last name	Thesis title	Mentor	University	Date of submission/disputation
Dimitra	Borik	„In vivo Studien zur Inhibierung von BurG als Antivirulenz-Strategie gegen Bakterien der Burkholderia pseudomallei Gruppe“	Christian Hertweck	FSU Jena	07.11.2024

MSc/diploma theses

First name	Last name	Thesis title	Mentor	University	Date of submission/disputation
Maximilian	Meyer	“Synthesis and Functional Evaluation of Analogues of the Yellow Affinity Substance from Clostridium thermocellum“	Christian Hertweck	FSU Jena	18.06.2024

5. Young Researchers

Dissertations

First name	Last name	Thesis title	Mentor	University	Date of submission/disputation
Hannah	Büttner	„The Role of Endosymbiotic Bacteria in Micropredator Defence of Mucoromycota Fungi“	Christian Hertweck	FSU Jena	03.09.2024
Finn	Gude	“Noncanonical Polythioamide Antibiotic Biosynthesis and a Novel Self-Resistance Mechanism in Clostridia“	Christian Hertweck	FSU Jena	25.11.2024

Awards

Title	**First name**	**Last name**	**Award**	**Occasion (e.g. Conference)**	**City**	**Date**
Prof.	Christian	Hertweck	ERC Grant	ERC		07/24
Dr.	Taynara	Lopes Silva	Medac Preis	Medac GmbH	Jena	12/24
Dr.	Jana	Krabbe	Medac Preis	Medac GmbH	Jena	12/24
Dr.	Ingrid	Richter	Medac Preis	Medac GmbH	Jena	12/24
Dr.	Kirstin	Scherlach	Medac Preis	Medac GmbH	Jena	12/24
	Philipp	Wein	Medac Preis	Medac GmbH	Jena	12/24

6. International Cooperations

Title	First name	Last name	University / Institution
Prof.	Elke	Dittmann	Universität Potsdam
Prof.	Julia	Bandow	Ruhr-Universität Bochum
Prof.	Michael	Groll	TH München
Dr.	Sacha	Pidot	University of Melbourne
Prof.	Tim	Stinear	University of Melbourne
Prof.	Jesko	Koehnke	Universität Hannover
Prof.	Gabriele	Bierbaum	Universität Bonn
Prof.	Thomas	Helleday	University of Sheffield
Prof.	Markus	Künzler	ETH Zürich
Prof.	Julia	Vorholt	ETH Zürich
Prof.	Hans-Georg	Sahl	Universität Bonn
Prof.	Ute	Hellmich	FSU Jena
Prof.	Franziska	Faber	Universität Würzburg

7. Staff

Title	First name	Last name	From	To
Prof.Dr.	Christian	Hertweck		
Secretary				
	Barbara	Urbansky		
Scientists				
Dr.	Benjamin	Bartels	08/23	08/25
Dr.	Hannah	Buettner	10/17	12/24
Dr.	Katharina	Dornblut	07/24	12/24
Dr.	Jethro	Hemmann	01/24	12/24
Dr.	Keishi	Ishida		

Dr.	Mie	Ishida		06/26
Dr.	Jana	Krabbe	12/14	12/
Dr.	Taynara	Lopes Silva	04/22	06/25
Dr.	Evelyn	Molloy		12/27
Dr.	Hamideh	Rezaee	06/24	06/26
Dr.	Ingrid	Richter		06/26
Dr.	Kirstin	Scherlach		
Dr.	Guy	Schleyer	05/21	08/24
Dr.	Aiko	Teshima	06/22	01/26
Ph.D Students				
	Leo	Dumjahn	09/23	08/25
	Friedrich Johannes	Ehinger	11/21	10/25
	Romy	Feldmann	01/19	02/25
	Jonas	Fiedler	08/21	06/26
	Hale	Hamedani	06/24	06/26
	Elena	Herzog	05/21	08/25
	Philippe	Meisinger	11/22	10/25
	Mandy	Mlotek	01/22	12/25
	Philipp	Wein		
Undergratuates				
	Dimitra	Borik	03/24	09/25
	Sönke	Heeren	01/24	01/25
	Alexander	Hoff	09/24	03/25
	Hangyeol	Jung	10/23	02/25
	Maximilian	Meyer	08/23	08/24
	Pia	Müller	10/23	02/25
Technical Assistents				
	Heike	Heinecke		
	Christine	Poser		

Leibniz-Institut
für Naturstoff-Forschung
und Infektionsbiologie
Hans-Knöll-Institut

Lehrstuhl für Mikrobielle Pathogenität
Chair Microbial Pathogenicity

Prof. Dr. Bernhard Hube

1. Research

Human pathogenic fungi frequently cause infections of the skin and mucosa, however, they are also capable of causing severe, life threatening mycoses.

The research topic of the Chair Microbial Pathogenicity and the Department Microbial Pathogenicity Mechanisms (MPM) is infection biology of pathogenic fungi, one of the two main research areas of the Leibniz-HKI.

MPM explores the pathogenicity mechanisms of the most important *Candida* species (as recognized by the World Health Organization (WHO), with a focus on *C. albicans* and *C. glabrata*.

C. albicans is regarded as the most important of all medically relevant yeasts and is an extremely successful pathogen in humans. *C. glabrata* is closely related to the non-pathogenic baker's yeast *Saccharomyces cerevisiae*. However, in many cases *C. glabrata* is the second most prevalent yeast pathogen in humans after *C. albicans*.

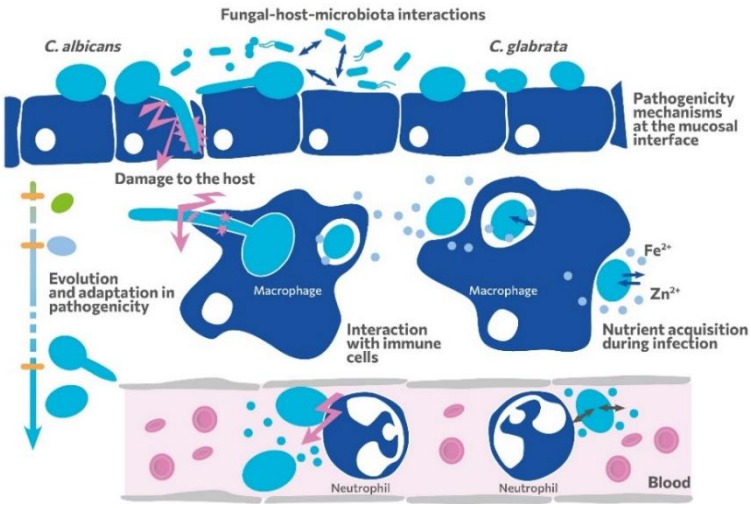
In contrast to most pathogenic fungi in humans such as *Aspergillus fumigatus*, *Cryptococcus neoformans*, or *Histoplasma capsulatum*, which are found in the environment, *C. albicans* and *C. glabrata* belong to the normal microbiota of mucosal surfaces and are regarded as harmless commensals in most circumstances. In fact, most humans are colonized with these yeasts. An intact immune system and a balanced microbial flora are normally sufficient to protect the individual from *Candida* infections. However, certain critical events such as extensive antibacterial treatment or dysfunction of the immune system may enable these fungi to overgrow the microbiota on mucosal surfaces.

MPM investigates all aspects and stages of *Candida* infections. More recently, we started to investigate the commensal life style of *C. albicans*, which is likely linked to the pathogenic potential of this fungus. We collaborate with multiple local (Leibniz-HKI, Microverse Excellence Cluster, Leibniz Campus, FSU, UKJ, Dynamic42), national (DFG priority programs, Leibniz Alliance, individual collaborations), and international partners (EU consortia, ANR/BMBF and Wellcome Trust consortia, multiple individual collaborations).

In the recent years, we continued our focus on the pathogenicity mechanisms of *Candida albicans* and *C. glabrata* (and *C. auris*) using a broad spectrum of cellular, microbial, molecular, and biochemical methods in combination with *in vitro* or *ex vivo* infection models.

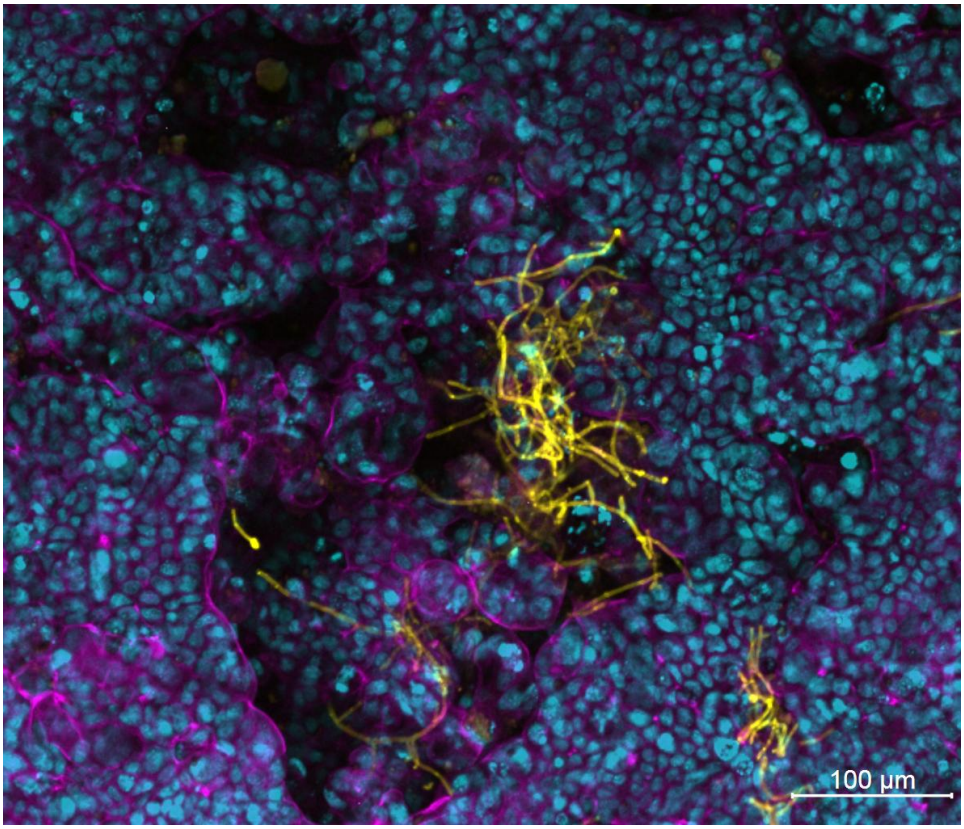
Our research topics are:

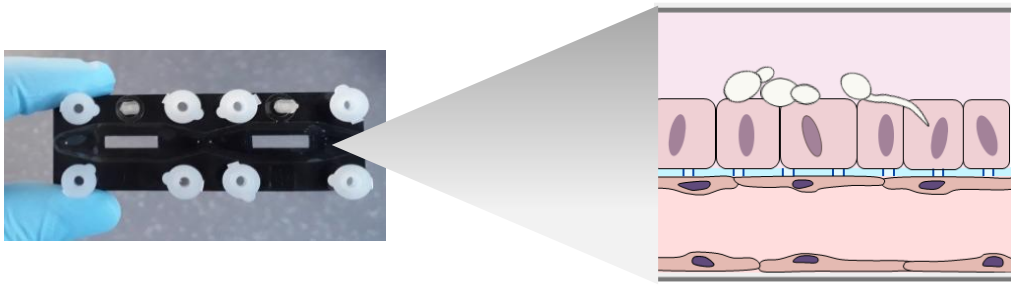
- Molecular biology of human pathogenic fungi
- Functional genomics
- Host/pathogen interactions
- Host cell reporter for stress and cell death
- Metal acquisition
- Intracellular survival and escape
- Invasion mechanisms and translocation
- Microevolution
- Morphology
- Candidalysin
- Lipases
- Interaction with bacteria and commensal growth
- Antifungal and antivirulence compound screening
- Mode of action of antifungal agents



The main topics of Department of Microbial Pathogenicity Mechanisms (MPM). For details, please visit our Leibniz-HKI homepage: https://www.leibniz-hki.de/en/microbial-pathogenicity-mechanisms.html

In 2023 - 2024, the department MPM published more than 30 original articles and reviews with contributions as first/last and/or corresponding authors or as co-authors in highly acknowledged journals, including *Biomaterials, Cell Report, EMBO Rep, J Am Chem Soc, J Biol Chem, J Clin Invest, J Exp Med, mBio* (3x), *Microbiol Mol Biol Rev, Mol Microbiol, Nature, Nat Commun* (2x), *Nat Med, Nat Microbiol* (2x), *Nucleic Acids Res,* and *PLOS Pathog*, and *Semin Immunol.*



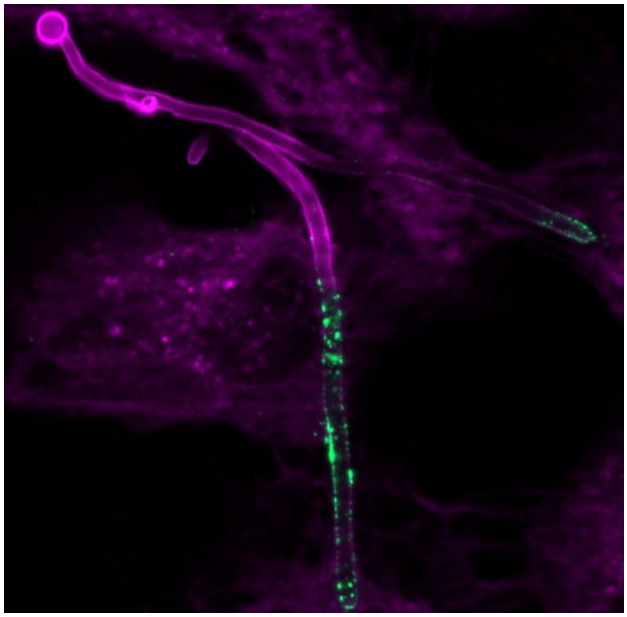


Candida albicans microcolonies in a gut-on-chip infection model (Kaden et al. 2024 Biomaterials; reviewed in Alonso-Roman et al. 2024 Nat Microbiol)

MPM publications were chosen as Paper of the Month by the Deutsche Gesellschaft für Hygiene und Mikrobiologie (DGHM), received Publication Awards of the Deutschsprachige Mykologische Gesellschaft (DMykG) and Medac Awards of the HKI and the Siegfried Czapski Publikationspreis of the Jena Alliance of Graduate Schools. MPM member received the Micoverse Early Career Scientist Award 2023 of Excellence Cluster “Balance of the Microverse” and the Roche Vortragspreis für Infektionsimmunologie and a poster award of the DMykG.

MPM Medac Award winners

As research highlights in 2023 - 2024, we made several discoveries dealing with the *C. albicans* peptide toxin candidalysin. We found that *C. albicans* translocation through the intestinal epithelial barrier is promoted by fungal zinc acquisition *via* candidalysin (*PLOS Pathogens*). Furthermore, in a translational project, we showed that candidalysin-specific nanobodies can neutralize candidalysin-mediated epithelial damage and inflammatory responses that drive vulvovaginal candidiasis pathogenesis (*mBio*). We further contributed to a study of our collaboration partner Julian Naglik (King's College London, UK), demonstrating that candidalysin amino acid sequence variations in *C. albicans* are common and identified variant toxins with differences in activity (*mBio*).



Candidalysin expression (green) during invasion of epithelial cells (Cover picture and Mogavero et al. 2021 Cell Microbiol)

We also contributed to a study of Constantin Urban (Umea University, Sweden) showing that *C. albicans* induces neutrophil extracellular traps *via* candidalysin (*EMBO Report*). We further contributed to a study of David B. Corry (Baylor College of Medicine, Houston, USA) showing that *C. albicans* is linked to chronic brain diseases such as Alzheimer's disease. This study shows that *C. albicans* enters the mouse brain from the blood and induces two neuroimmune sensing mechanisms involving secreted aspartic proteinases and candidalysin (*Cell Report*). In a further extensive study, we elucidated why candidalysin is embedded in a precursor

protein, Ece1, which consists of a signal peptide, the precursor of candidalysin, and seven non-candidalysin Ece1 peptides (NCEPs). Our data indicate that the Ece1 precursor is not required to block premature pore-forming toxicity, but rather to prevent intracellular auto-aggregation of candidalysin sequences (*Nat Microbiol*). Together with our collaboration partner Richard Bennett (Brown University, Rhode Island, USA) we made the exciting discovery that candidalysin is not only a true classical virulence factor, but also a commensal factor which promotes gut colonization (*Nature*). This publication also disproved the dogma that the hyphal morphology of *C. albicans* is detrimental for gut colonization. We also collaborated with Megan D. Lenardon (UNSW, Sydney, Australia) and dissected a synthetic peptide which kills *C. albicans* and prevents infection (*Nat Commun*). Together with Sergio Grinstein (Hospital For Sick Children) and Leah Cowen (University of Toronto) (Toronto, Canada), we identified *C. albicans* genes required for intracellular filamentation after internalization by macrophages (*mBio*). We collaborated with Steffen Jung (Weizmann Institute, Rehovot, Israel) and Petra Bacher (Christian-Albrechts University of Kiel) to identify a novel fungal species which antagonizes *C. albicans* in the gut and which can prevent *C. albicans* infections (J Ex Med).

In addition to our HKI budget, our research was funded In 2023 – 2024 by the Leibniz-Center for Photonics in Infection Biology Research (LPI), the Leibniz Campus InfectoOptics, the Leibniz Research Alliance “INFECTION”, the DFG CRC/TR 124 “FungiNet”, the DFG priority programme SPP2225 “Exit”, an individual DFG research grant “Ece1 peptides”, the Excellence Cluster “Balance of the Microverse” (Zeiss Foundation/DFG), the EU ITN FunHoMic, the EU consortium HDMFun, the ANR/BMBF project AResT, and the British Wellcome Trust.

Finally, MPM members continue to serve the scientific community and the HKI as spokesperson for the PhD students, in editorial boards of several journals (*mBio*, *Sci Rep*, *Cell Microbiol/Mol Microbiol*, *mBio*, *Curr Opin Microbiol*, and *Front Microbiol*), as chairperson of the DGHM group Eukaryotic Pathogens, as member of the program comittee of the DFG SPP 2225, and as member of the Panel/Steering Committee for Septomics and the Leibniz Research Alliance INFECTIONS.

2. Publications

Alonso-Roman R, Mosig AS, Figge MT, Papenfort K, Eggeling C, Schacher FH, Hube B[#], Gresnigt MS (2024) Organ-on-chip models for infectious disease research. *Nat Microbiol* 9(4), 891-904. (Review)

Böttcher B, Kienast SD, Leufken J, Eggers C, Sharma P, Leufken CM, Morgner B, Drexler HCA, Schulz D, Allert S, Jacobsen ID, Vylkova S, Leidel SA, Brunke S[#] (2024) A highly conserved tRNA modification contributes to *C. albicans* filamentation and virulence. *Microbiol Spectr* 12(5), e0425522.

Castaño-Cerezo S, Chamas A, Kulyk H, Treitz C, Bellvert F, Tholey A, Galéote V, Camarasa C, Heux S, Garcia-Alles LF, Millard P, Truan G (2024) Combining systems and synthetic biology for *in vivo* enzymology. *EMBO J* 43(21), 5169-5185.

Jaeger M, Dietschmann A, Austermeier S, Dinçer S, Porschitz P, Vornholz L, Maas RJA, Sprenkeler EGG, Ruland J, Wirtz S, Azam T, Joosten LAB, Hube B, Netea MG, Dinarello CA, Gresnigt MS (2024) Alpha1-antitrypsin impacts innate host-pathogen interactions with *Candida albicans* by stimulating fungal filamentation. *Virulence* 15(1), 2333367.

Kaden T, Alonso-Román R, Stallhofer J, Gresnigt MS, Hube B, Mosig AS (2024) Leveraging organ-on-chip models to investigate host-microbiota dynamics and targeted therapies for inflammatory bowel disease. *Adv Healthc Mater* , e2402756. (Review)

Kaden T[*], Alonso-Roman R[*], Akbarimoghaddam P[*], Mosig AS, Graf K, Raasch M, Hoffmann B, Figge MT[#], Hube B[#], Gresnigt MS[#] (2024) Modeling of intravenous caspofungin administration using an intestine-on-chip reveals altered *Candida albicans* microcolonies and pathogenicity. *Biomaterials* 307, 122525.

Katsipoulaki M, Stappers MHT, Malavia-Jones D, Brunke S, Hube B, Gow NAR (2024) *Candida albicans* and *Candida glabrata*: global priority pathogens. *Microbiol Mol Biol Rev* 88(2), e0002123. (Review)

King WR, Singer J, Warman M, Wilson D, Hube B, Lager I, Patton-Vogt J (2024) The glycerophosphocholine acyltransferase Gpc1 contributes to phosphatidylcholine biosynthesis, long- term viability, and embedded hyphal growth in *Candida albicans*. *J Biol Chem* 300(1), 105543.

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Liang SH, Sircaik S, Dainis J, Kakade P, Penumutchu S, McDonough LD, Chen YH, Frazer C, Schille TB, Allert S, Elshafee O, Hänel M, Mogavero S, Vaishnava S, Cadwell K, Belenky P, Perez JC, Hube B, Ene IV, Bennett RJ (2024) The hyphal-specific toxin candidalysin promotes fungal gut commensalism. *Nature* 627(8004), 620-627.

Müller R, König A, Groth S, Zarnowski R, Visser C, Handrianz T, Maufrais C, Krüger T, Himmel M, Lee S, Priest EL, Yildirim D, Richardson JP, Blango MG, Bougnoux ME, Kniemeyer O, d'Enfert C, Brakhage AA, Andes DR, Trümper V, Nehls C, Kasper L, Mogavero S, Gutsmann T, Naglik JR, Allert S, Hube B (2024) Secretion of the fungal toxin candidalysin is dependent on conserved precursor peptide sequences. *Nat Microbiol* 9(3), 669-683.

Pekmezović M, Hube B, Gresnigt MS (2024) Pathogenicity strategies of *Candida* species during interactions with epithelial cells. In: Brakhage AA, Kniemeyer O, Zipfel PF (eds.) The Mycota - Human and Animal Relationships 3. 6, pp. 35-49. Springer, Cham. ISBN: 978-3-031-64852. (Review)

Schaefer S, Corrigan N, Brunke S, Lenardon MD, Boyer C (2024) Combatting fungal infections: advances in antifungal polymeric nanomaterials. *Biomacromolecules* 25(9), 5670-5701. (Review)

Schaefer S, Vij R, Sprague JL, Austermeier S, Dinh H, Judzewitsch PR, Müller-Loennies S, Lopes Silva T, Seemann E, Qualmann B, Hertweck C, Scherlach K, Gutsmann T, Cain AK, Corrigan N, Gresnigt MS, Boyer C, Lenardon MD, Brunke S (2024) A synthetic peptide mimic kills *Candida albicans* and synergistically prevents infection. *Nat Commun* 15(1), 6818.

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Sprague JL, Schille TB, Allert S, Trümper V, Lier A, Großmann P, Priest EL, Tsavou A, Panagiotou G, Naglik JR, Wilson D, Schäuble S, Kasper L[*], Hube B[*#] (2024) *Candida albicans* translocation through the intestinal epithelial barrier is promoted by fungal zinc acquisition and limited by NFκBmediated barrier protection. *PLOS Pathog* 20(3), e1012031.

Stanca SE, Mogavero S, Fritzsche W, Krafft C, Hube B, Popp J (2024) Isotope labeled 3D-Raman confocal imaging and atomic force microscopy study on epithelial cells interacting with the fungus *Candida albicans*. *Nanomedicine* 59, 102750.

Tesfamariam M, Vij R, Trümper V, Hube B, Brunke S (2024) Shining a light on *Candida*-induced epithelial damage with a luciferase reporter. *mSphere* 9(11), e0050924.

Valentine M[*], Rudolph P[*], Dietschmann A, Tsavou A, Mogavero S, Lee S, Priest EL, Zhurgenbayeva G, Jablonowski N, Timme S, Eggeling C, Allert S, Dolk E, Naglik JR, Figge MT, Gresnigt MS[*#], Hube B[*#] (2024) Nanobody-mediated neutralization of candidalysin prevents epithelial damage and inflammatory responses that drive vulvovaginal candidiasis pathogenesis. *mBio* 15(3), e0340923.

Wickramasinghe DN, Lyon CM, Lee S, Hepworth OW, Priest EL, Maufrais C, Ryan AP, Permal E, Sullivan D, McManus BA, Hube B, Butler G, d'Enfert C, Naglik JR, Richardson JP (2024) Variations in candidalysin amino acid sequence influence toxicity and host responses. *mBio* 15(8), e0335123.

Alings F, Scharmann K, Eggers C, Böttcher B, Sokołowski M, Shvetsova E, Sharma P, Roth J, Rashiti L, Glatt S, Brunke S, Leidel SA (2023) Ncs2* mediates *in vivo* virulence of pathogenic yeast through sulphur modification of cytoplasmic transfer RNA. *Nucleic Acids Res* 51(15), 8133-8149.

Brandt P[*], Mirhakkak MH[*], Wagner L, Driesch D, Möslinger A, Fänder P, Schäuble S, Panagiotou G, Vylkova S[#] (2023) High-throughput profiling of *Candida auris* isolates reveals clade-specific metabolic differences. *Microbiol Spectr* 11(3), e0049823. (Review)

Case NT, Westman J, Hallett MT, Plumb J, Farheen A, Maxson ME, MacAlpine J, Liston SD, Hube B, Robbins N, Whitesell L, Grinstein S, Cowen LE (2023) Respiration supports intraphagosomal filamentation and escape of *Candida albicans* from macrophages. *mBio* 14(6), e0274523.

Götze S, Vij R, Burow K, Thome N, Urbat L, Schlosser N, Pflanze S, Müller R, Hänsch VG, Schlabach K, Fazlikhani L, Walther G, Dahse HM, Regestein L, Brunke S, Hube B, Hertweck C, Franken P, Stallforth P (2023) Ecological niche-inspired genome mining leads to the discovery of crop-protecting nonribosomal lipopeptides featuring a transient amino acid building block. *J Am Chem Soc* 145(4), 2342-2353.

Lange T, Kasper L, Gresnigt MS, Brunke S, Hube B (2023) "Under Pressure" - How fungi evade, exploit, and modulate cells of the innate immune system. *Semin Immunol* 66, 101738. (Review)

Martini GR, Tikhonova E, Rosati E, DeCelie MB, Sievers LK, Tran F, Lessing M, Bergfeld A, Hinz S, Nikolaus S, Kümpers J, Matysiak A, Hofmann P, Saggau C, Schneiders S, Kamps AK, Jacobs G, Lieb W, Maul J, Siegmund B, Seegers B, Hinrichsen H, Oberg HH, Wesch D, Bereswill S, Heimesaat MM, Rupp J, Kniemeyer O, Brakhage AA, Brunke S, Hube B, Aden K, Franke A, Iliev ID, Scheffold A, Schreiber S, Bacher P (2023) Selection of cross-reactive T cells by commensal and food-derived yeasts drives cytotoxic TH1 cell responses in Crohn's disease. *Nat Med* 29(10), 2602-2614.

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Himmel M, Kniemeyer O, Brakhage AA, King BL, Lupetti A, Comar M, de Seta F, Tavanti A, Blasi E, Wheeler RT, Pericolini E (2023) A new phenotype in *Candida*-epithelial cell interaction distinguishes colonization-versus culvovaginal candidiasis-associated strains. *mBio* 14(2), e0010723.

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Seelbinder B[#], Lohinai Z[*], Vazquez-Uribe R, Brunke S, Chen X, Mirhakkak M, Lopez-Escalera S, Dome B, Megyesfalvi Z, Berta J, Galffy G, Dulka E, Wellejus A, Weiss GJ, Bauer M, Hube B, Sommer MOA, Panagiotou G (2023) *Candida* expansion in the gut of lung cancer patients associates with an ecological signature that supports growth under dysbiotic conditions. *Nat Commun* 14(1), 2673.

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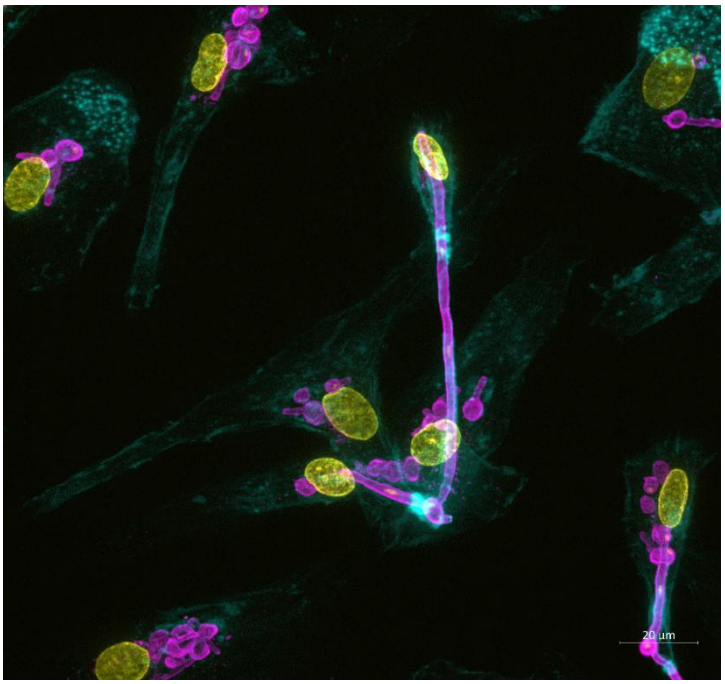
Wu Y, Du S, Bimler LH, Mauk KE, Lortal L, Kichik N, Griffiths JS, Osicka R, Song L, Polsky K, Kasper L, Sebo P, Weatherhead J, Knight JM, Kheradmand F, Zheng H, Richardson JP, Hube B, Naglik JR, Corry DB (2023) Toll-like receptor 4 and CD11b expressed on microglia coordinate eradication of *Candida albicans* cerebral mycosis. *Cell Rep* 42(10), 113240.



Candida albicans escape from macrophages – one of our two “DFG “Exit” projects (https://www.spp2225.rwth-aachen.de/cms/spp2225/Projekte/Sascha-Brunke-Bernhard-Hube/~mflff/Projekt-Strategien-des-Wirtszellaustrit/lidx/1/)

3. Third Party Funding

Funding body	Project	Period
ILRS	Steering Committee and PI	Since 2007
DFG	TR/CRC FungiNet, project C1	Since 2013
Wellcome Trust	Targeting a new kingdom: the nature and significance of Type VI secretion system-mediated anti-fungal activity	2019 - 2024
EU ITN "FunHoMic"	Deciphering the fungus-host-microbiota interplay to improve the management of fungal infections	2019 - 2022
Excellence Cluster "Balance of the Microverse" - DFG Zeiss Stiftung	Coordinator of Research Area B and projects "The interaction of Candida albicans with antagonistic bacteria in a Gut-on-Chip model" and "Evolutionary adaptations to life in the gut by Candida albicans" and "CaCom - The Candida albicans peptide toxin candidalysin as a commensal factor facilitating mucosal colonization"	Since 2019
ANR/BMBF	French-German project on antimicrobial resistance programme – "Antifungal Resistance: From Surveillance to Treatment" – AreST	Since 2020
DFG	Hu528/20-1 "Elucidating the role of Candida albicans Ece1 peptides"	Since 2020 - 2023
Leibniz Association LPI - Leibniz-Zentrum für Photonik in der Infektionsforschung, Jena	BT2 // WP8.1 „Temporally and spatially resolved host cell damage models" BT4 // WP6.1 "Temporally and spatially host cell damage reporters for use in 3D models in vitro"	Since 2020
DFG	SPP2225: EXIT Strategies of Intracellular Pathogens	Since 2021
DFG	TR/CRC FungiNet, project C2	Since 2022
Leibniz Association	Infection(21)	Since 2022

4. Teaching

Module	Lecture/course	Participants
MBC.A14 MMB011	Lecture "Moleculare und Microbial Infection Biology"	9
	Practical course "Moleculare und Microbial Infection Biology"	10
MBC.A14 MMB011	Project module	6
MBC.A14 MMB011	Specialization module	6

Bachelor theses

Johanna Wallnisch: " Die Rolle des Typ 6 Sekretionssystems von Serratia Marcescens and anderen Darm-assoziierten Bakterien bei Interaktion mit *Candida albicans"* (Sept 2023)

Lisa Denner: "The role of arginine biosynthesis for intracellular filamentation and escape of *Candida albicans* from macrophages" (Nov 2023)

Luisa Fischer: „Characterization of a *Candida glabrata* mutant lacking the protein kinase Ksp1" (Oct 2024)

Master theses

Millen Tesfamariam: "Characterizing a luciferase-based mammalian cell-line damage reporter for application in antifungal drug discovery" (April 2023)

Jonathan Ruwe: "Heterologous production and anticandidal potential of *ß*-carbolines" (Nov 2023)

Jerónimo Brom González: „Screening for fungal factors involved in *Candida glabrata* 's escape from macrophages" (March 2024)

5. Supporting Early Career Scientists

Doctoral degrees:
Jakob Sprague: “Challenging the first line of defense: *Candida albicans* interactions with epithelial barriers during infection and translocation” (Dez 2024)
Sophie Austermeier: “Adaption of *Candida albicans* to non-commensal host environments induced by circulating host proteins and immune mediators” (Dez 2024)
Rita Pforte (née Müller): “Elucidating the role of *Candida albicans* Ece1 peptides” (Dez 2024)

Jakob Sprague

Sophie Austermeier

Rita Pforte (née Müller)

6. Gender balance and family

Women	Man	Children below 12 years
17	15	10
4 PostDoc m/w		4
5 Technische Assistenten m/w		5

7. International Cooperations

Baylor College of Medicine – Houston,USA
University of Dundee – Dundee, UK
University of Toronto – Toronto,Canada
King’s College - London, UK
Raboud University Nijmegen – Nijmegen, Niederlande
University of Aberdeen – Aberdeen, UK
Umeå University – Umeå, Schweden
University of Exiter – Exeter, UK
Universität Zürich – Zürich, Schweiz
Brown University – Rhode Island, USA
Sorbonne Université – Paris, Frankreich
Trinity College Dublin – Dublin, UK
Duquesne University – Pittsburgh, USA

8. Team

Prof. Dr. Bernhard Hube

Deputy

Dr. Sascha Brunke

Technical Assistance

Himmel, Maximilian
Jablonowski, Nadja
Mantke, Julia
Wisgott, Stephanie
Schuck, Noreen

Team Assistant

Feller, Steffi

Postdoctoral Researchers

Dr. Allert, Stefanie
Dr. Trümper, Verena
Dr. Chamas, Alexandre
Dr. Sprague, Jakob

Doctoral Researchers

Alonso-Román, Raquel
Austermeier, Sophie
Elshafee, Osama
Jansen, Mathias
Katsipoulaki, Myrto
Müller, Rita
Möslinger, Anna
Lange, Teresa
Schille, Tim
Sonnberger, Johannes
Valentine, Marisa
Vij, Raghav

Students

Johanna Wallnisch
Lisa Denner
Luisa Fischer
Tesfamariam, Millen
Gonzales, Jeronimo
Ruwe, Jonathan
Schönert, Josefin
May, Hans
Böhm, Erik
Banerjee, Taniya

Mikrobielle Immunologie

Prof. Ilse Jacobsen

https://www.leibniz-hki.de/de/mikrobielle-immunologie.html

JSMC Fotowettbewerb, Sarah Vielreicher, 1. Platz: "Long-term incubation of *Serratia* and *Candida* colonies*“*

1. Research

The Research Group Microbial Immunology focuses on *C. albicans* as both a commensal and a pathogen. Both, as a commensal and pathogen, *Candida* interacts not only with the host but also with members of the bacterial microbiota. Thus, one focus of our research are interactions between *C. albicans* and bacteria, which we analyze both at the microbiome level and in the context of interactions between *C. albicans* and distinct bacterial species. Intestinal colonization with *C. albicans* furthermore serves as the main source for systemic infections. We are interested in how *C. albicans* colonization, microbiome composition, and factors such as microbiome disturbance and diet affect the host immune system and susceptibility to systemic candidiasis. Finally, we aim to address open questions regarding the pathogenesis of systemic candidiasis, especially the role of fungal factors and the interplay with the host's immune system.

Antibiotic treatment not only increases the level of *C. albicans* colonization but also colonization with facultative pathogenic bacteria in patients. We identified *Enterococcus faecalis* as synergistic interaction partner for *C. albicans*. Physical interactions, by which the fungus facilitates increased contact of bacteria to host cells, and environmental changes driven by fungal metabolism result in increased bacterial virulence and severity of fungal infections *in vivo* (Kapitan et al., bioRxiv).

Furthermore, we found that antibiotic treatment induces major changes in the immune cell composition, including the hematopoietic compartment, resulting in increased susceptibility to systemic infections due to decreased antimicrobial efficacy of myeloid cells (Merga *et al.*, in preparation). Using germ free mice, we could demonstrate that this is not due to direct effects of the antibiotics on host cells, but depends on the presence of microbiota, suggesting indirect consequences by antibiotic-induced dysbiosis. Interestingly, intestinal colonization with *C. albicans* mediates partial protection against systemic candidiasis, and reverses some of the antibiotic-induced immunmodulation. Susceptibility to systemic challenge with a homologous *C. albicans* strain is reduced by prior intestinal colonization; however, this effect coincides with increased inflammatory markers after fungal clearance (Merga *et al.*, in preparation). In addition, experimental evidence indicates that colonization-dependent protection is strain-dependent (Chakraborti *et al.*, in preparation); ongoing experiments aim to elucidate the underlying mechanisms.

Interactions between fungi and bacteria are not limited to the intestinal tract, but also occur in other body niches and the environment. *Aspergillus fumigatus* is a saprophytic fungus dwelling in soil and on decaying plant material, but also an opportunistic pathogen in immunocompromised patients. In collaboration with the department for Molecular and Applied Microbiology, and Dr. Ute Bertsche, we discovered that *A. fumigatus* secretes an endopeptidase, designated CwhA, that cleaves peptidoglycan of Gram-positive bacteria at specific residues within the peptidoglycan layer of the bacterial cell wall. This leads to bacterial lysis, and the cleavage products generated by CwhA affect the cytokine response of human immune cells. This provides an example for how fungal-bacterial interactions affect not only the microbial players, but also modulate the immune system.

2. Publications

Nikitashina L, Chen X, Radosa L, Li K, Straßburger M, Seelbinder B, Böhnke W, Vielreicher S, Nietzsche S, Heinekamp T, Jacobsen ID, Panagiotou G, Brakhage AA (2025) The murine lung microbiome is disbalanced by the human-pathogenic fungus Aspergillus fumigatus resulting in enrichment of anaerobic bacteria. Cell Rep 44(3), 115442.

Böttcher B, Kienast SD, Leufken J, Eggers C, Sharma P, Leufken CM, Morgner B, Drexler HCA, Schulz D, Allert S, Jacobsen ID, Vylkova S, Leidel SA, Brunke S# (2024) A highly conserved tRNA modification contributes to C. albicans filamentation and virulence. Microbiol Spectr 12(5), e0425522.

Jacobsen ID (2024) Infection models for human pathogenic fungi. In: Brakhage AA, Kniemeyer O, Zipfel PF (eds.) The Mycota - Human and Animal Relationships 3. 6, pp. 193-206. Springer, Cham. ISBN: 978-3-031-64853. (Review)

Jacobsen ID[#] (2023) The role of host and fungal factors in the commensal-to-pathogen transition of *Candida albicans*. *Curr Clin Micro Rpt* 10(2), 55-65. (Review)

Jacobsen ID[#] (2023) Mouse models of Mucormycosis. *Methods Mol Biol* 2667, 181-196. (Review)

Langenhorst D, Fürst AL, Alberter K, Vilhena C, Dasari P, Daud M, Heilig L, Luther CH, Dittrich M, Reiher N, Wich M, Elmowafy M, Jacobsen ID, Jungnickel B, Zipfel PF[*], Beyersdorf N[*#] (2023) Soluble enolase 1 of *Candida albicans* and *Aspergillus fumigatus* stimulates human and mouse B cells and monocytes. *J Immunol* 211(5), 804-815.

Rebai Y, Wagner L, Gnaien M, Hammer ML, Kapitan M, Niemiec MJ, Mami W, Mosbah A, Messadi E, Mardassi H, Vylkova S, Jacobsen ID, Znaidi S[#] (2023) *Escherichia coli* nissle 1917 antagonizes *Candida albicans* growth and protects intestinal cells from *C. albicans*-mediated damage. *Microorganisms* 11(8), 1929.

Refisch A[#], Sen ZD, Klassert TE, Busch A, Besteher B, Danyeli LV, Helbing D, Schulze-Späte U, Stallmach A, Bauer M, Panagiotou G, Jacobsen ID, Slevogt H, Opel N, Walter M (2023) Microbiome and immuno-metabolic dysregulation in patients with major depressive disorder with atypical clinical presentation. *Neuropharmacology* 235, 109568. (Review)

Schädel P, Czapka A, Gebert N, Jacobsen ID, Ori A[#], Werz O[#] (2023) Metabololipidomic and proteomic profiling reveals aberrant macrophage activation and interrelated immunomodulatory mediator release during aging. *Aging Cell* 22(7), e13856.

3. Teaching

WS 2023/2024 und SS 2024

Nr.	Titel	Rolle
BB032	Grundlagen der Immun- und Infektionsbiologie	beteiligt
BB3.MLS9	Molekulare Zellbiologie und Biomedizin	beteiligt
BEW016	Pathophysiologie ernährungsassoziierter Erkrankungen	beteiligt
BB011	Ringvorlesung Methoden der Mikrobiologie	beteiligt
MMB016	Translational Medical Microbiology, Vorlesung	verantwortlich
MMB016	Translational Medical Microbiology, Praktikum	verantwortlich
MMB019-7	Wildcard module: Translational Medical Microbiology Seminar	verantwortlich
MBC.A14, MMB011	Molecular and Microbial Infection Biology	beteiligt

WS 2022/2023 und SS 2023

Vertiefungs- und Projektmodule	ECTS	Anzahl Studierende
Vertiefungspraktikum Mikrobiologie BB3.MB4	10	
Vertiefungsmodul MMB 700	15	7
Projektmodul MMB 800	15	7
Biogeowissenschaftliches Projektmodul BBGW 6.3.1/2	10	2

WS 2023/2024 und SS 2024

Vertiefungs- und Projektmodule	ECTS	Anzahl Studierende
Vertiefungspraktikum Mikrobiologie BB3.MB4	10	1
Vertiefungsmodul MMB 700	15	2
Projektmodul MMB 800	15	2
Biogeowissenschaftliches Projektmodul BBGW 6.3.1/2	10	1
Projektmodul BB800	11	3

Bachelorarbeiten

Isabel Urban: Charakterisierung von Candida albicans Saccharose-Verwertungsmutanten (09/2023)

Sandra Fischer: Untersuchung der Interaktion von Candida albicans, Entercoccus faecalis und Bacteroides vulgatus (09/2023)

Anna-Chiara Nitschke: Interaktion zwischen *Candida albicans* und *Akkermansia muciniphila* (09/2024)

Masterarbeiten

Estiak Md. Khan Chowdhury: *Candida albicans* and *Enterococcus faecalis* form a complex nutritional network during in vitro coinfection altering cell damage (05/2023)

Jakia Khan: Alternative carbon sources enhance gowth and immune modulation in *Candida albicans eed1* Δ/Δ knockout mutant (07/2023)

Sarah Müller: Mycobiome analysis of wild rodents in Thuringia (11/2024)

FatemehAmir Haschchi: Characterizing the heterogeneity of the immune response to *Candida albicans* strains SC5314 and 101 in innate and adaptive immune cells (07/2024)

Staatsexamen

Jonas Baumgarten. Effects of *Phocalicola vulgatus* mpk, on epithelial cell damage caused by the human pathogen *Candida albicans* (02/2023) – Lehramt Gymnasium

Zweitbetreuung/-gutachten

2023, BSc: Jeanny Weiß
MSc: Bolaji John Samuel, Millen Tesfamariam, Teresa Zeibig
2024 MSc: Theodor Bormann, Muhammad Hamza Farooq, Sviatoslav Tsiumpala, Aftab Zafar, Karthika Muthuraj, Yuan-Chang Peng, Selina Aleta Scheu, Simranpreet Kaur

Leibniz-Institut
für Naturstoff-Forschung
und Infektionsbiologie
Hans-Knöll-Institut

Lehrstuhl für Infektionsbiologie

Sen. Prof. Dr. Peter Zipfel
2023 - 2024

1. Reserach

The complement system is a central and immediately acting component of the human immune system. We aim to understand how this defense system acts in microbial infections, how pathogenic microbes evade host complement attack, and we study the overarching role of complement in tissue homeostasis. Deregulated complement action can result in adverse reactions, tissue damage, and ultimately, disease manifestation in multiple organs. Therefore, a detailed understanding of complement action helps us to evaluate immune evasion by human pathogenic microbes and to restore protective roles in diseases such as Hemolytic Uremic Syndrome (HUS), C3 glomerulopathy, and Age-Related Macular Degeneration.

Furthermore, we design new diagnostic tools to identify the activation and intensity of the complement pathway directly in tissues for complement-mediated diseases, focusing on kidney disorders. In combination with artificial intelligence-driven analyses, this approach stratifies pathophysiological defects, allowing for personalized therapy.

Fungi and bacteria

The Department of Infection Biology evaluates how *Candida albicans* and other microbial pathogens evade host complement attack and identifies common themes in the evasion of complement by several human pathogens. Most, if not all, pathogens misguide the master regulators of complement Factor H to evade immune recognition and mimic self-surfaces.

The interplay between fungi and host complement and human immunity occurs on several levels. Therefore, fungal complement and immune evasion are studied.

Enolase 1, produced by *C. albicans* and *Aspergillus fumigatus*, is an important fungal complement and immune evasion protein. However, enolase 1 has additional roles and functions and influences the fate of immune cells. Enolase 1 derived from *C. albicans* an *A. fumigatus* binds to CD4-positive human T cells, directing the fate of these cells by inducing memory T cells. Thus, enolase 1 as a "moonlighting" protein stimulates human immune cells, such as T cells, B cells, and monocytes.

We also identified how sequence variants of the *C. albicans* Sap2 protein influence complement evasion and fungal pathogenicity in *C. albicans*, together with Dr. S. Luo's laboratory at Wuhan University in China. We identified Sap2 protein sequence variants and demonstrated that pathogenic variants more efficiently program host macrophages and induce a stronger M2-like phenotype.

Similarly, we found that PspA and PspC, two highly variable surface proteins of the human pathogen *Streptococcus pneumoniae*, interact with human endothelial cells and red blood cells. We focused on the mechanism of PspA and PspC variants expressed by *S. pneumoniae* isolated from infants with Streptococcal hemolytic uremic syndrome (Sp-HUS). Compared to other variants, the PspA and PspC variants derived from Sp-HUS-causing streptococci bound more efficiently to human endothelial cells and erythrocytes. Additionally, streptococci induce

extracellular vesicles from host cells that direct immune crosstalk and contribute to Sp-HUS pathology.

Infections, e.g., by SARS-COV-2, redirect the complement and host immune responses, influencing the pattern of morphological changes in human kidneys, as evidenced by our findings from the Pathology Laboratory at the UKE in Hamburg-Eppendorf.

Complement and Diseases

We evaluated the role of complement in several kidney disorders, including aHUS syndrome, C3 glomerulopathy, and membranous nephropathy.

As a member of an international group of experts, we established and published new guidelines for the role of complement in kidney diseases in 2024.

The role of complement was further evaluated in kidney diseases, such as membranous nephropathy. Here, a clear contribution of the classical activation pathway was demonstrated. These results impact the selection of approved complement inhibitors for treating this severe complement-mediated kidney disease.

Furthermore, new diagnostic tools were developed to identify specific complement pathway activations directly in tissues for complement-mediated diseases, focusing on kidney disorders. In combination with artificial intelligence-driven analyses, this approach stratifies pathophysiological defects, allowing for personalized therapy.

In terms of translation, we collaborated with Eleva GmbH to explore the potential of complement Factor H for treating human diseases. This cooperation included pre-clinical safety profiles initiating further clinical studies with a moss-produced variant of complement Factor H.

2. Publications

2024

Perie L, Stippa s, Saffer C, Hartmann A, Mörgelin M, Zipfel SLH, Figge MT, Wiech T, Skerka C, Zipfel PF (2024) Unique target binding by the C-terminal Region of FHR1 provides a new perception of aHUS Pathology. Front. Hematol. Sec. Immunobiology and Immunotherapy, Volume 3 - 2024 | https://doi.org/10.3389/frhem.2024.1469176

Heidenreich K, Goel D, Priyamvada PS, Kulkarni S, Chakurkar V, Khullar D, Singh R, Bale C, Zipfel PF. C3 glomerulopathy: a kidney disease mediated by alternative pathway deregulation. Front Nephrol. 2024 Oct 29;4:1460146. doi: 10.3389/fneph.2024.1460146. PMID: 39534179; PMCID: PMC11554616.

Vivarelli M, Barratt J, Beck LH, Fakhouri F, Gale DP, Goicoechea de Jorge E, Mosca M, Noris M, Pickering MC, Susztak K, Thurman JM, Cheung M, King JM, Jadoul M, Winkelmayer WC, Smith RJH; Federico Alberici F, Antonucci L, Avcin T, Bagga A, Bajema IM, Blasco M, Chauvet S, Cook HT, Cravedi P, Dragon-Durey MA, Lauren Fischer, Agnes B. Fogo, Frazer-Abe Al, Frémeaux-Bacchi V, Görlich N, Haas M, Humphreys A, Jha V, Jauhal A, Kavanagh D, Kronbichler A, Richard A. Lafayette, Lanning LD, Lemaire M, Le Quintrec M, Licht C, Liew A, McAdoo S, Nicholas R. Medjeral-Thomas NR, Meroni PL, Morelle J, Nester CM, Praga M, Ramachandran R, Reich HN, Remuzzi G, Rodríguez de Córdoba S, Robinson G, Ronco P, Rossing P, Salant DJ, Sethi A, Silkjaer M, Song WC, Spoleti F, Taylor RP, van de Kar NCAJ, van Kooten C, Woodward L, Zhang Y, Zipfel PF, Zuccato M (2024) The Role of Complement in Kidney Disease: Conclusions From a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference, Kidney Int. 2024 Sep;106(3):369-391. doi: 10.1016/j.kint.2024.05.015. Epub 2024 Jun 4.

Tschongov T, Konwar S, Busch A, Sievert C, Hartmann A, Noris M, Schaaf A, Panse J, Zipfel PF, Dabrowska-Schlepp P, Häffner K (2024) Moss-produced human complement Factor H with modified glycans has an extended half-life and improved biological activity. Frontiers Immunol 1383123. doi: 10.3389/fimmu.2024.1383123. PMID: 38799460; PMCID: PMC11117068.

Rabeeah I, Billington E, Nal-Rogier B, Sadeyen JR, Pathan A, Iqbal M, Temperton N, Zipfel PF, Skerka C, Kishore U, Shelton H (2024) Mapping the interaction sites of Influenza A viruses

and human complement Factor H. Front Immunol. 15:1352022. doi: 10.3389/fimmu.2024.1352022. PMID: 38698856; PMCID: PMC11064062.
Nguyen TH, Chen LY, Khan N, Lindenbauer A, Bui VC, Zipfel PF, Heinrich D (2024) Binding of SARS-CoV-2 Spike Protein to Platelet Factor 4: A Proposed Mechanism for the Generation of Pathogenic Antibodies 245. doi: 10.3390/biom14030245. PMID: 38540666; PMCID: PMC10967930.
Zipfel PF; Skerka C, Wiech T (2024), Komplementbasierte Glomeruläre Erkrankungen, Nephro News 004/2024, Medicom
Zipfel PF, Skerka C (2024), The host innate immune response to pathogenic Candida albicans and other fungal pathogens, Human and Animal Relationships, The Mycota, Brakhage A, Kniemeyer O Zipfel, PF. Springer Nature Berlin Heidelberg
Schmidt T, Zipfel PF, Wiech T (2024) Therapie der C3-Glomerulopathie – Immunsuppression oder Komplementinhibition? Nieren- und Hochdruckkrankheiten, Dustri Publisher,
Zipfel PF, Skerka C, Wiech T (2024). Zielstrukturen des Komplementsystem als Grundlage für Innovative Therapie. Deutsche Gesellschaft für Nephrologie.
2023
Vilhena C, Du S, Battista M, Westermann M, Kohler T, Hammerschmidt S, Zipfel PF (2023) The choline-binding proteins PspA, PspC and LytA of Streptococcus pneumoniae and their interaction with human endothelial and red blood cells. Inf Immunitiy; 91:e0015423. doi: 10.1128/iai.00154-23.
Battista M, Hoffmann B, Bachelot Y, Zimmermann L, Teuber L, Jost A, Linde S, Westermann M, Müller MM, Slevogt H, Hammerschmidt S, Figge MT, Vilhena C, Zipfel PF (2023) The role of pneumococcal extracellular vesicles on the pathophysiology of the kidney disease Hemolytic Uremic Syndrome. mSphere :e0014223. doi: 10.1128/msphere.00142-23. Epub 2023 Jun 26. PMID: 37358300; PMCID: PMC10449520.
Daud M, Dasari P, Adelfinger M, Langenhorst D, Lother J, Slavkovic-Lukic D, Berges C, Kruhm M, Galler A, Schleussner C, Luther CH, Alberter K, Althammer A, Shaikh H, Pallmann N, Bodem J, Elmowafy M, Beilhack A, Dittrich M, Topp MS, Zipfel PF, Beyersdorf N (2023) Enolase 1 of Candida albicans binds human CD4+ T cells and modulates naïve and memory responses. Eur J Immunol e2250284. doi: 10.1002/eji.202250284. Epub 2023 Aug 10. PMID: 37503840.
Langenhorst D, Fürst AL, Alberter K, Vilhena C, Dasari P, Daud P, Heilig L, Luther CH, Dittrich M, Reiher N, Wich M, Elmowafy M, Jacobsen ID, Jungnickel B, Zipfel PF*, Beyersdorf N*, (2023) Soluble Enolase 1 of Candida albicans and Aspergillus fumigatus stimulates human and mouse B cells and monocytes. J Immunol 211(5):804-815. doi: 10.4049/jimmunol.2200318. PMID: 37436030.* equal contributions as senior authors
Lin L, Wang M, Zeng J, Mao Y, Qin R, Deng J, Ouyang X, Hou X, Sun C, Wang Y, Cai Y, Li M, Tian C, Zhou X, Zhang M, Fan H, Mei H, Sarapultsev A, Wang H, Zhang G, Zipfel PF, Hu Y, Hu D, Luo S. Sequence Variation of Candida albicans Sap2 Enhances Fungal Pathogenicity via Complement Evasion and Macrophage M2-Like Phenotype Induction. Adv Sci (Weinh). 2023 Jul;10(20):e2206713. doi: 10.1002/advs.202206713. Epub 2023 May 21. PMID: 37211685; PMCID: PMC10369283.
Busch C, Rau S, Sekulic A, Perie L, Huber C, Gehrke M, Joussen AM, Zipfel PF, Wildner G, Skerka C, Strauß O (2023) Increased serum level of terminal complement complex (TCC) in AMD patients: potential functional consequences for RPE cells. Frontiers Immunol, 14, 1200725 doi: 10.3389/fimmu.2023.1200725. PMID: 37359546; PMCID: PMC10287163.
de Las Mercedes Noriega M, Husain-Syed F, Wulf S, Csala B, Krebs CF, Jabs WJ, Zipfel PF, Gröne HJ, Wiech T; CoV-Kidney Investigators. Kidney Biopsy Findings in Patients with SARS-CoV-2 Infection or After COVID-19 Vaccination. Clin J Am Soc Nephrol. 2023 May 1;18(5):613-625. doi: 10.2215/CJN.0000000000000106. Epub 2023 Feb 1. PMID: 36723286; PMCID: PMC10278827.
Seifert L, Zahner G, Meyer-Schwesinger C, Hickstein N, Dehde S, Wulf S, Köllner SMS, Lucas R, Kylies D, Froembling S, Zielinski S, Kretz O, Borodovsky A, Biniaminov S, Wang Y, Cheng H, Koch-Nolte F, Zipfel PF, Hopfer H, Puelles VG, Panzer U, Huber TB, Wiech T, Tomas NM. The classical pathway triggers pathogenic complement activation in membranous nephropathy. Nat Commun. 2023 Jan 28;14(1):473. doi: 10.1038/s41467-023-36068-0. PMID: 36709213; PMCID: PMC9884226.

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3. Third Pary Funding

Projektträger	Vorhaben	Laufzeit	Mittel in 2024
DFG	Project B6: CFHR Gene Variations Provide Insights in the Pathogenesis of the Kidney Diseases Atypical Hemolytic Uremic Syndrome and C3 Glomerulopathy.	2020 - 2024	350.000,00 €

4. Teaching

Modulnummer	Veranstaltung	ECTS	Teil-nehmer
BB032, BBC033, BEW3A25	Grundlagen der Immun- und Infektionsbiologie		30
MMB012	Spezielle Immun- und Infektionsbiologie (MBC.A13) / Immune reactions of humans to Microorganisms and Pathogens		12

Vertiefungs- und Projektmodule

Modul	ECTS	Anzahl Studierende
BB033,		23
BBC3.A4		
BEW3A26		49
MCB W 10)		15
MBC.A13		7

Abschlussarbeiten

Bachelorarbeiten

Maya	Buchholz	Die Rolle des Faktor H verwandten Proteins 1 im Komplementsystem und bei Entzündungsprozessen	Prof. Dr. Peter F. Zipfel	FSU
Elina	Fuss	Fehlregulationen des Komplementsystems bei C3 Glomerulopathie und Infektionen mit dem pathogenen Erreger Staphylococccus aureus.	Prof. Dr. Peter F. Zipfel	FSU
Laura	Teuber	Charakterisierung von wirtsunabhängigen Pneumokokken-Vesikeln	Prof. Dr. Peter F. Zipfel	FSU

Masterarbeiten

Thomas	ıebreslassie	Complement system regulation and inflammation in FHR-E deficient mice	Prof. Dr. Peter F. Zipfel	FSU

Zweitbetreuung/-Gutachten

Vandana Arakandy Acquisition of host fatty acids in *Staphylococcus aureus* infections and persistence, Medizinische Faultät der Friedrich-Schiller Universität, Jena

5. Young Reserachers

Dissertations

Svitlana	Babytch	Analysis of human extracellular vesicles induced by *Candida albicans*	Prof. Dr. Christine Skerka	FSU	1. 08. 2023
Nadine	Reiher	*Candida albicans* Tef1 bindet an Dektin-1 und Dektin-2 auf humanen Dendritischen Zellen und löst eine inflammatorische Immunantwort aus	Prof. Dr. Peter F. Zipfel	FSU	28. 11. 2023
Li-Yu	Chen	Characterization and application of new materials for better detection of platelet activating antibodies	Prof. Dr. Peter F. Zipfel	FSU	10.02.2024

6. Equal Opportunities, Diversity and Family Support

Anteil Frauen	Anteil Männer	Kindern unter 12 Jahren
15	4	0
2 PostDocs		0
5 Technische Assistentinnen		

7. International Cooperations

PD	Martin	Westermann	Centre for Electron Microscopy, Jena University Hospital, Friedrich-Schiller-University of Jena	Jena	D
Prof.	Christian	Eggeling	Friedrich-Schiller-Universität Jena	Jena	D
Prof.	Berit	Jungnickel	Friedrich-Schiller-Universität Jena	Jena	D
Prof.	Thorsten	Wiech	Universitätsklinikum Hamburg	Hamburg	D
Prof.	Rolf	Stahl	Universitätsklinikum Hamburg	Hamburg	D
PD Dr.	Eva	Decker	Albert-Ludwigs-Universität Freiburg	Freiburg	D
Prof.	Ralf	Reski	Albert-Ludwigs-Universität Freiburg	Freiburg	D
Dr.	Thi Huong	Ngyuyen	Institut für Bioprozess- und Analysenmesstechnik e.V. Heiligenstadt	Heilbad Heiligenstadt	D
Prof.	Peter	Kraiczy	Johann-Wolfgang-Goethe-Universität Frankfurt	Frankfurt	D
Prof.	Gabriele	Pradel	Rheinisch-Westfaelische Technische Hochschule Aachen	Aachen	D
Prof.	Uwe	Völker	Universität Greifswald	Greifswald	D
Prof.	Herrmann J.	Gröne	Universitätsklinikum Hamburg	Hamburg	D
Prof.	Elisabeth B.	Binder	Max Planck Institut für Psychiatrie	München	D
Dr.	Karsten	Häffner	Universitätsklinikum Freiburg	Freiburg	D
Prof.	Sven	Hammerschmidt	Ernst-Moritz-Arndt-Universität Greifswald	Greifswald	D
Prof.	Olaf	Strauß	Charité Universitätsmedizin Berlin	Berlin	D
Dr.	Niklas	Beyersdorf	Universitätsklinikum Würzburg	Würzburg	D
Prof.	Loreto	Gesualdo	Università degli Studi di Bari Aldo Moro	Bari	Italien
Dr.	Silke	Brix	Manchester University, School of Medical Sciences	Manchester	UK
Prof.	Cornelia	Speth	Medizinische Universität Inssbruck	Innsbruck	Österreich
Prof.	Christoph J.	Binder	Medical University of Vienna	Wien	Österreich
	Barbara	Bröke	Universität Greifswald	Greifswald	D

Title	First name	Last name	Company	City	Country
Prof.	Dirk	Roggenbuck	GA Generic Assays GmbH	Dahlewitz	D
PD Dr.	Andreas	Busch	eleva	Freiburg	D
Dr.	Matthias	Rohrbeck	Novartis	Nürnberg	D

8. Administration/Finances

Beschäftigungsstruktur

	Personen	Stellenanteile
Beschäftigte im Rahmen von Haushaltsmitteln		
Wissenschaftliche MitarbeiterInnen	1	100 %
Postdoc	1	100 %
Profillinie Life		
Technische Assistenz	4	100 %
Sekretariat	1	50 %

Tutorinnen		
Beschäftigte im Rahmen von Drittmitteln		
Wissenschaftliche MitarbeiterInnen	1	100 %
Wissenschaftliche Assistenten		
Studentische Assistenten		
Weiteres Personal		
Auszubildende	-	

Vertretung in Selbstverwaltungsgremien

Zipfel	Peter F.	Molecular Immunology
Zipfel	Peter F.	Frontiers in Innate Immunity
Zipfel	Peter F.	Pediatric Nephrology

9. Team

Leiter	Univ.- Prof. Dr. Peter F. Zipfel	
Technische Assistentinnen	Ina Löschmann	Andrea Hartmann
Verwaltung – Sekretärin	Ina Löschmann	
PostDocs	Dr. Hans Martin Dahse Dr. Luce Perie	Dr. Cláudia Vilhena
Promovierende	Nadine Reiher	Li Yu Chen
Studierende	Elina Fuss Tomas Ghebreselassie	

Lehrstuhl für Microbiome Sciences

Prof. Dr. Christina Warinner

https://www.mikrobiologie.uni-jena.de/institut/microbiome-sciences

1. Research

The research group Microbiome Sciences has a broad and active research program that incorporates many diverse scientific specialties, including microbial sciences, paleogenomics, paleoproteomics, metabolomics, and ethnography. Our work primarily focuses on the evolution and changing ecology of the human oral and gut microbiomes, and our research has recently expanded to also include the study of culinary microbes and their long-term role in human subsistence. We currently have active projects on three continents, and our work centers on applying both conventional and emerging scientific techniques to trace the tangled paths of people, animals, and microbes to reconstruct the Bronze Age roots of contemporary societies.

We currently have five main areas of research: (1) Evolution and Ecology of the Microbiome, (2) Origins and Diversification of Dairying, (3) Microbial Domestication and the (Pre)history of Food Fermentation, (4) Microbial Pathogen Evolution, and (5) Paleobiotechnology.

Evolution and Ecology of the Microbiome

Our research team has pioneered the evolutionary study of the microbiome with a focus on ancient dental calculus. This past year, we published the first large scale study of oral microbial diversity in ancient Oceania (Velsko et al. 2024), which included more than 100 samples from 11 Pacific Islands spanning the past 3,000 years. We also published the first microbiome study of dental plaque in hunter-gatherer populations, revealing substantially expanded oral species

diversity in non-industrialized societies (Velsko et al. 2023). We are now building on this work to create the largest oral microbiome dataset yet assembled to provide a global overview of human oral microbiome diversity over the past 100,000 years.

Origins and Diversification of Dairying

Dairy pastoralism is integral to contemporary and past lifeways on the eastern Eurasian steppe, facilitating survival in agriculturally challenging environments. To better understand the context in which dairy pastoralism first emerged, we conducted a human population genetics study of the North Caucasus region, focusing on the periods and places where mobile pastoralism first developed. We traced human genetic changes in the region and established the events that led to the continental dispersal of dairy pastoralism into Europe and Asia (Ghalichi et al. 2024). We were then invited to write a Research Briefing about this article in Nature to make the research more accessible to the broader public (Reinhold and Warinner 2024). At the other end of the temporal scale, we also examined Iron Age social changes that affected dairy pastoralism alongside the rise of the first nomadic empire, the Xiongnu Empire (Lee et al. 2023). We used ancient DNA and population genetics to reconstruct aspects of political organization and kinship along Xiongnu frontier communities, and how such political developments affected the spread of dairy technologies. Horses were key to the rise of nomadic empires – through warfare, transport, and the making of fermented mare's milk - so we also examined archaeological for changing horse technology. Through the identification of a recently discovered archaeological horse saddle, we were able to trace the history of saddle-making in Mongolia and propose a timeline for the development of equestrian technologies (Bayarsaikhan et al. 2023). Alongside this work, we also contributed to another study examining ancient equine diversity in Central Asia (Pan et al. 2024), and we are currently developing new peptide mass fingerprinting markers for equid identification in large archaeological datasets. In parallel, we have sequenced more than 1,200 ancient livestock genomes from across Central Asia that were are now analyzing to reconstruct the dispersal routes of dairy pastoralism across Asia.

Microbial Domestication and the (Pre)history of Food Fermentation

With support from the Microverse Cluster, we initiated two major new projects on microbial domestication, focusing on Roman wine and Tibetan beer. The Roman wine project focuses on metagenomic analysis of grape pomace residues recovered from wine fermentation vats at the Herodium, a palace of Herod the Great dating to ca. 20 BCE. We have reconstructed high quality microbial genomes for four species of lactic acid bacteria involved in wine fermentation and we are currently preparing a manuscript for publication. The Tibetan beer project focuses on metagenomic analysis of residues recovered from the base of a copper cauldron in a Himalayan tomb dating to ca. 400 CE. We have reconstructed a high-quality *Saccharomyces cerevisiae* genome, a medium-quality *Pichia kudriavzevii* genome, and the genomes of four lactic acid bacteria involved in fermentation, and we are currently preparing a manuscript for publication.

Microbial Pathogen Evolution

This past year we had the opportunity to investigate two disease that are poorly studied in the archaeological literature: malaria and paratyphoid fever. We contributed to a large global survey of ancient malaria and identified the world's oldest known case of Plasmodium falciparum malaria in a Nepali archaeological site we have worked at for the past 15 years. We published the study in Nature (Michel et al. 2024) and in 2023 we traveled to Nepal to return the results to local communities. We also organized two university symposia in Nepal and led scientific outreach events at three Nepali middle schools. In addition to our work in Nepal, we contributed to a major study on the immunological consequences of colonial-era paratyphoid fever epidemics in Mexico. Focusing on Chichen Itza, we conducted the largest ancient DNA study on Mexican human remains published to date, and showed large immunological shifts in Mexican populations over the past 1,000 years that could be linked to 16th century epidemic outbreaks of Salmonella enterica Paratyphi C. We published this work in Nature (Barquera et al. 2024).

Paleobiotechnology

This aspect of our work is a joint collaboration with the Leibniz Institute for Natural Product Research and Infection Biology Hans Knöll Institute in Jena (HKI) with the aim of advancing the

tools of ancient metagenomics to be able to explore the biosynethetic diversity and capabilities of ancient bacteria, and in order to communicate our vision for the future of ancient microbial research, we published an invited review in the Journal of Anthropological Research (Warinner 2022). The ultimate aim of the project is to reconstruct the genomes or gene functions of lost or extinct microorganisms, with potential applications for developing novel therapeutics, such as antibiotics. Over the past year, we have integrated our research more broadly across the field of metagenomics through initiatives like nf-core/mag, for which we have developed a pipeline specifically for ancient microbial genome *de novo* assembly (https://github.com/nf-core/mag), and nf-core/funcscan, which automates biosynthetic gene cluster discovery in MAGs (https://github.com/nf-core/funcscan). Our first major research output from this project, which has reconstructed more than 200 ancient bacterial genomes from dental calculus samples up to 100,000 years old and characterized functional biosynethic gene clusters was published in Science (Klapper et al., 2023). Building on this success, we developed a software extension to accompany the Ancient MetagenomeDir resource we created, called AMDirT, which improves ancient DNA dataset accessibility (Borry et al. 2024). We were then invited to write a Commentary in Nature about our efforts to improve ancient DNA data metadata reporting (Bergstrom et al. 2024), and we are currently building on this work in partnership with the Genomic Standards Consortium and the European Bioinformatics Institute to improve systems for ancient DNA data reporting for microbial sequences.

2. Publications

Bergstrom A, Fellows Yates J, Warinner C. (2024) Comment: Ancient DNA holds insights into past organisms and ecosystems – handle them with more care. Nature, 10 December 2024, https://www.nature.com/articles/d41586-024-03993-z

Reinhold S, Warinner C. (2024) Research Briefing: The birth of Bronze Age pastoralism where Europe meets Asia. Nature, https://www.nature.com/articles/d41586-024-03832-1

Velsko IM, Fagernäs Z, Tromp M, Bedford S, Buckley HR, Clark G, Dudgeon J, Flexner J, Leal-Tamarii A, Lewis CM, Matisoo-Smith E, Nägele K, Ozga AT, Rohrlach AB, Posth C, Shing R, Spriggs M, Willie E, Valentin Frédérique, Warinner C. (2024) Exploring the potential of dental calculus to shed light on past human migrations in Oceania. Nature Communications, https://www.nature.com/articles/s41467-024-53920-z

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Michel M, Skourtanioti E, Pierini F, Barquera R, Bianco R, Carlhoff S, Coppola Bove L, Freilich S, Giffin K, Guevara EK, Hermes T, Hiss A, Knolle F, Mötsch A, Nelson EA, Neumann G, Papac L, Penske S, Rohrlach AB, Salem N, Semerau L, Villalba-Mouco, Abadie I, Aldenderfer M, Baquedano Perez E, Brown M, Carrion Santafe EC, Chenghwa T, Conteras Martinez M, Cruz Berrocal M, Czubak JM, Damsek L, Duffett Carlson KS, Durand R, Ernée

M, Fantaneanu C, Frenzel H, García Atiénzar, Guillén S, Hsieh E, Karwowski M, Kinaston R, Küssner M, Lai L, Look C, Majander K, Mandl K, Mazzarello V, McCormick M, Murphy R, Nemeth R, Nordqvist K, Onkamo P, Olmo Enciso L, Orschiedt J, Paz de Miguel Ibáñez M, Peltola S, Romero A, Rubino S, Sajantila A, Salazar García D, Serrano E, Shaydullaev S, Slaus M, Stanco L, Swanston T, Teschler-Nicola M, Valentin F, Van der Vijver K, Varney T, Vigil-Escalera Guirado A, Waters C, Weiss-Krejci E, Winter E, Lamnidis TC, Prüfer K, Nägele K, Spyrou M, Schiffels S, Stockhammer PW, Haak W, Posth C, Warinner C, Bos K, Herbig A, Krause K. (2024) Ancient Plasmodium genomes shed light on the history of human malaria. Nature. https://www.nature.com/articles/s41586-024-07546-2

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Lee JH, Miller BK, Bayarsaikhan J, Johannesson E, Ventresca Miller A, Warinner C*, Jeong C*. (2023) Genetic population structure of the Xiongnu Empire at imperial and local scales. Science Advances 9(15):eadf3904, www.science.org/doi/10.1126/sciadv.adf3904

3. Third Party Funding

Projektträger	**Vorhaben**	**Laufzeit**	**Mittel in 2022**
WSS	Paleobiotechnology – Ancient Drugs for Modern Bugs	2020-2030	300.000,00 €
DFG	ExC Microverse: Direct investigation of microbiome evolution in paleofeces and dental calculus	2022-2024	10.000,00 € + 1 Postdoc
DFG	Ancient genome-based investigation of the dispersal and adaptive evolution of cattle across Eurasia	2024-2027	220,000 €

4. Studium und Lehre

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
		1.5	40

Offered Courses

Introduction to Ancient Metagenomics, Summer School co-sponsored by the Jena School for Microbial Communications, the Max Planck-Harvard Center for the Archaeoscience of the Ancient Mediterranean (MHAAM), the Max Planck Institute for Evolutionary Anthropology (MPI-EVA), and the Standards, Precautions, and Advances in Ancient Metagenomics community (SPAAM). (05.08.2024 – 09.08.2024), https://spaam-community.github.io/wss-summer-school/#/2024/README, 1.5 ECTS points.

ANTHRO 1270: Sick: Ten Thousand Years of Human Health and Disease, Harvard University (03.09.2024 – 20.12.2024)

5. Young Researchers

Dissertations

Maxime Borry, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "Expanding the ancient DNA bioinformatics toolbox, and its applications to archeological microbiomes". 2023

Research*Zweitbetreuung/-gutachten:*

Sandra Penske, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "Human population dynamics in southeastern and Central Europe between the 5th and 3rd millennium BCE." 2024

Howell Leung, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "The Gut Microbiome in NAFLD: Advancing Diagnosis, Understanding Pathogenesis, and Developing Novel Therapies." 2024

Bjørn Bartholdy, Faculty of Archaeology, Leiden University, PhD dissertation: "Putting Dental Calculus Under the Microscope." 2024

Vera Hopfenmüller, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "Establishing the auxin-inducible degron system for Wilms tumor protein 1 degradation in zebrafish." 2023

Domenico DiFraia, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "Integrated omics approaches to study protein complexes in neuronal differentiation and brain aging." 2023

Joscha Gretzinger, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "Paleogenomic insights into the population structure and organization of northwestern Europe during the 'long Iron Age'". 2023

Rodrigo Barquera, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "The human host-pathogen interaction in the light of ancient genomics revolution." 2023

Ron Hübler, Faculty of Biological Sciences, Friedrich Schiller University, PhD dissertation: "Method development for screening archaeological samples for ancient pathogens." 2023

Chengrui Zhang, Anthropology Department, Harvard University. PhD dissertation: „Subsistence and Ritual: Animal Economy in the Bronze Age Qaidam Basin in Northwestern China." 2024.

5. Team and Equal Opportunities

Funktion		Anteil Frauen	Anteil Männer	Mit Kindern unter 12 Jahren
Leitung	Prof. Dr. Christina Warinner	1	0	1
Wiss. Mitarbeiter	Dr. Alexander Hübner	3	7	4
	Dr. Irina Velsko			
	Dr. Matthäus Rest			
	Dr. Taylor Hermes			
	Dr. Roshan Paladugu			
	Dr. James Fellows			

	Yates			
	Dr. Maxime Borry			
	Dr. John Walden (Harvard)			
	Dr. Aja Lans (Harvard)			
	Dr. Ashley Scott (Harvard)			
Doktoranden	Maxime Borry	5	3	0
	Melina Seabrook (Harvard)			
	Megan Michel (Harvard)			
	I-Ting Huang (Harvard)			
	Keri Burge (Harvard)			
	Percy Hei Chun Ho (Harvard)			
	Jake Kalodner (Harvard)			
	Gökçe Öztürk (Harvard)			
Master Student		0	0	0
techn. Mitarbeiter	Raphaela Stahl	4	2	1
	Lena Semerau			
	Emilié Blondin (Harvard)			
	Justice Sirotek (Harvard)			
	Emily Ding (Harvard)			
	Eli Visio Johnson (Harvard)			

Lehrstuhl für Molekulare Phytopathologie

Prof. Dr. Philipp Franken

© K. Burow/ FGK

In addition to its teaching at Friedrich Schiller University Jena, the chair's primary responsibility is the scientific management of the Research Centre for Horticultural Crops (FGK). Since 2019, the FGK has been conducting four third-party funded projects based at the University of Applied Sciences Erfurt. The FGK serves as a bridge between basic research in the biosciences and answering practical questions in horticulture, focusing on "Sustainability" and "Biodiversity". Following a successful evaluation of the FGK and the allocation of new project funds valid until 31 December 2028, the four research groups were able to continue their previous work.

This report covers the activities of the research group "Plant-Microorganism Interactions in Sustainable crop production", led by the chair holder. For information about the projects of other groups at the research centre, please visit https://www.fh-erfurt.de/fgk/.

1. Research

AM responsiveness and metabolomics of Basil and Petunia

Since the working group “plant-microbe-interactions” began its work in 2019, the aim of subproject A is to identify plant genes involved in the interaction with arbuscular mycorrhizal (AM) fungi, as well as the plant's response to colonization in terms of biomass formation, habitus and phosphate uptake (AM responsiveness). For this purpose, the host plant petunia was mostly used during the first funding period.
With the start of the second funding period, a further focus was placed on herbaceous plants. Basil (*Ocimum basilicum*) was chosen as an economically important potted herbaceous plant. In an initial experiment, six different varieties were tested for their AM responsiveness. Even though hardly any significant differences in plant height or fresh and dry weight could be detected after mycorrhization, changes in plant habitus caused by colonization with AMF were evident (Fig. 1). An initial metabolome analysis was carried out at the Leibniz Institute of Plant Biochemistry (IPB) in Halle (Saale) for the ‘Netti’ variety. These preliminary results show strong differences in plant metabolites between controls and mycorrhizal plants thus giving hope for further exciting findings (Fig. 2). In parallel, research continued into the environment- and genotype-dependent AM responsiveness of petunias. For this purpose, the wild species *P. axillaris* and *P. exserta* were cultivated in a combination of different light intensities and day lengths, and root material was taken for RNA isolation. In 2025, an RNA-Seq will be performed in-house using long read sequencing with GridIon from Oxford Nanopore. This will provide insights into environmentally differentiated genes associated with AM colonization and responsiveness.

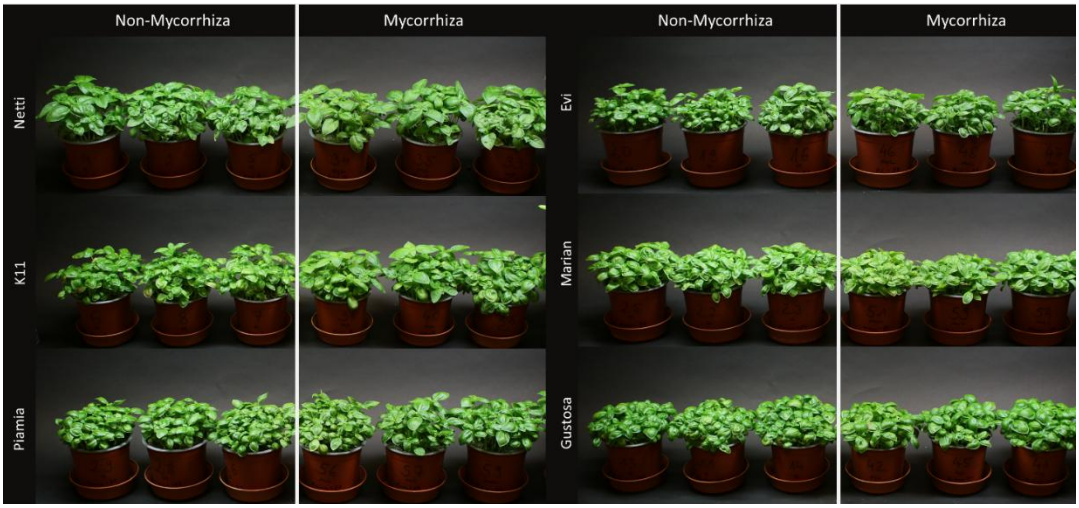

Fig. 1: Six basil varieties grown in sand/vermiculite substrate, inoculated with or without AMF. Three replicates are shown.

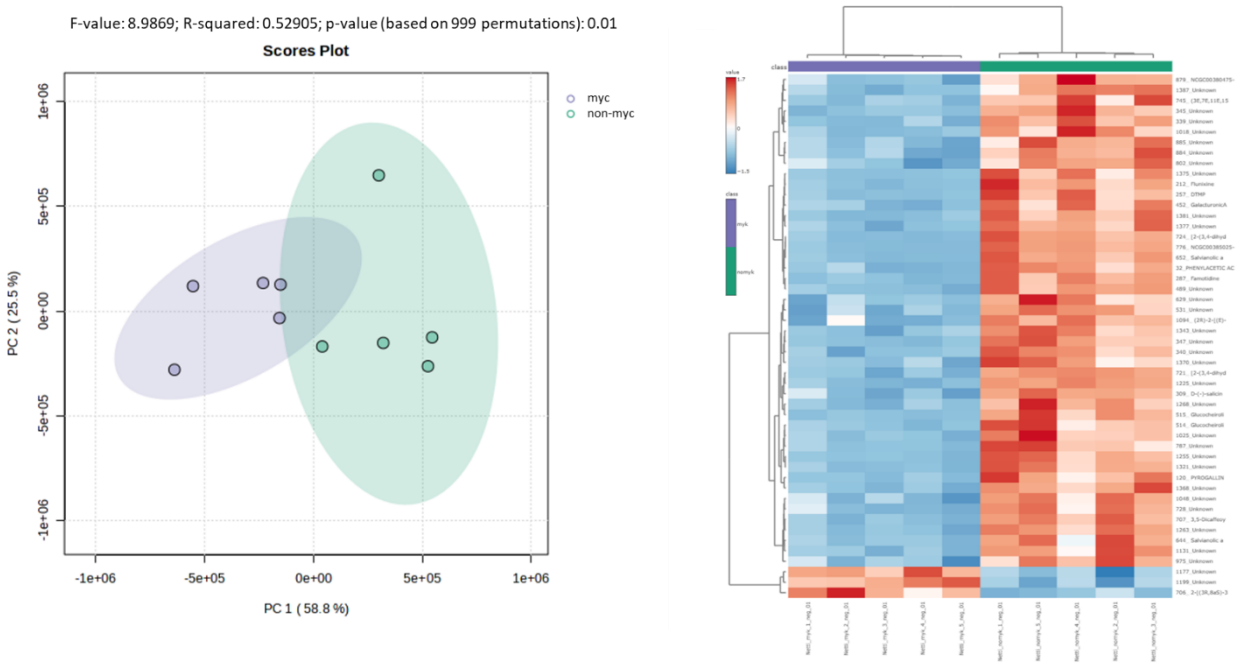

Fig. 2: Analysis of features using LC-MS negative mode (LC-MS-Neg). Left: Principal component analysis of five biological replicates of mycorrhized and non-mycorrhized basil leaves. Right: Heatmap of top 50 differentially regulated features (© J. Brandes/ FGK).

Screening of valuable plant-growth promoting (endophytic) microorganisms

In subproject B, the working group focused on investigating the interactions within microbial consortia and, in this context, on establishing a tunable *in vitro* system. Work began on isolating and characterizing representatives of additional groups of microorganisms. These include dark septate endophytes, rhizobacteria (e.g., *Paenibacillus*, *Azotobacter*, *Azospirillum*), other bacterial and fungal endophytes, as well as endophytic entomopathogenic fungi (EEMPFs). A common feature of these microorganisms is their potential application in peat-free or peat-reduced substrates. The aim of characterizing these microbial groups was to identify strains that contribute to improved nutrient availability in the substrate and thereby positively influence plant development. These microorganisms can be used to develop a microbial consortium suitable for application in peat-free or peat-reduced growing media.

Entomopathogenic fungi

In this project we are trying to isolate potential Endophytic entomopathogenic fungi (EEMPFs) against the plant pest *Bradysia difformis* (fungus gnats) (Fig. 3) which is a serious problem in pot cultures under glass and especially, highly attractive to peat free substrates. The data outcome of this study is expected to be useful for identifying entomopathogenic fungal strains as bio-control agents which also beneficially act as endophytes in Petunia and Basil plants.
Fungal strains from the German microbial collection center (DSMZ) were screened for their potential as entomopathogenic fungi against *Bradysia difformis*. The screening revealed that the strain *Metarhizium flavoviride* from DSMZ can significantly control *B. difformis* larvae, preventing their emergence into adults with a survival rate of 45.33 %. While *M. flavoviride* did not exhibit plant growth promotion through root colonization, the strain *Niesslia tinuis* showed a significant positive effect by enhancing the shoot length of *Petunia hybrida* cv. “Mitchell”. Further investigations regarding the production of cuticle-degradative enzymes, such as chitinase and protease, supported the entomopathogenic potential of *M. flavoviride* and *N. tinuis* observed in the screening.

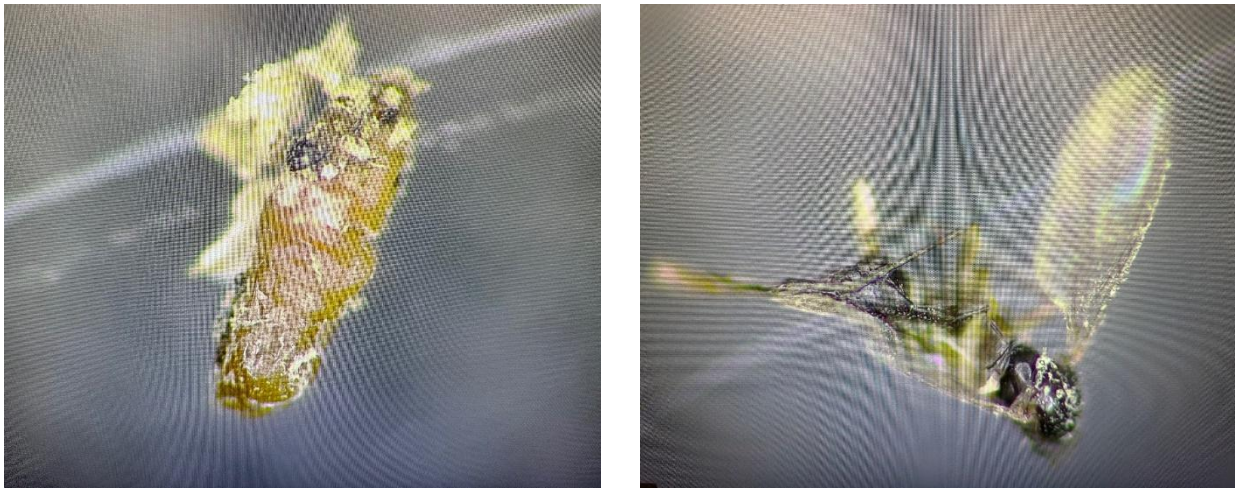

Fig. 3: Attack by an EMPF on the fungus gnat "*Bradysia difformis*" (© S. Sabu/ FGK).

Dark Septate Endophytes

Representatives of the fungal group "Dark Septate Endophytes" (DSEs) were isolated and identified from plant roots of *Ocimum basilicum*, *Hydrangea macrophylla* and various grasses, as well as from peat-free substrates. *Periconia macrospinosa* and *Sordaria* sp., which according to the literature have a positive influence on plant growth, were isolated. The growth of various DSEs on culture media with different inorganic and organic nitrogen sources was tested. In parallel, a greenhouse experiment was conducted in which the influence of two different DSEs (*Rhexocercosporidium* sp. and *Sordaria* sp.) on the development of *P. hybrida* cv. 'Mitchell' was investigated in a steamed substrate compared to an unsteamed peat-free substrate. On the one hand, it was demonstrated that the plants in a steamed substrate showed significantly better plant growth. On the other hand, there was a significant difference between the DSEs used in the steamed substrate, with the plants inoculated with *Rhexocercosporidium* sp. showing better plant development.

Application of microorganisms in peat-free or peat-reduced substrates

In frame of the projects ToPGa (Development and Evaluation of Peat-Reduced Production Systems in Horticulture) and ToSuGa (Peat reduction with safe substrates for professional horticulture), a series of experiments were conducted during the reporting years to explore sustainable alternatives to peat-based growing media and the role of beneficial microorganisms in improving plant growth and substrate quality. Special substrate compositions made from green compost and digestate were used for microbial treatments. In the experiments with *Schizophyllum commune*, this substrate supported good plant growth and also showed improved nutrient dynamics, particularly influencing nitrogen availability in both steamed and non-steamed conditions. In parallel, testing the bacterial treatment with *Priestia aryabhattai* (PGPR), significant improvements were observed in plant biomass production and nitrogen uptake.
The interaction of synthetic microbial communities with plants regarding nitrogen nutrition and overall plant health will be studied in detail using Basil and Petunia. In addition, fungal inocula will be used to enhance physical properties of the substrates, such as stability and water-holding capacity. The goal is to establish safe and functional peat-free substrates suitable for commercial horticulture.

Improvement and support of functions of root-colonizing fungi

Acclimatization of AMF and its effects on plant performance

The aim of subproject C is the acclimatization of *Rhizoglomus irregulare* (AMF) strains to high nutrient concentrations in the substrate, which can significantly increase the effectiveness of AMF strains as biostimulants in practice. After it was already shown in 2022 that an AMF strain acclimatized to high phosphate conditions achieved very good results on melon plants, these acclimatized strains were tested together with non-acclimatized strains on four different cultivars of *Hydrangea macrophylla*, two of which are tolerant and two of which are susceptible to *Botrytis cinerea*. The results showed that AMF had a significant negative impact on agronomic parameters in all four varieties.

Optimization of AMF with innovative additives and mycorrhizal helper bacteria

In this research, we explore how certain beneficial microorganisms—in particular *IAA-producing bacteria* (Fig. 4) and *arbuscular mycorrhizal fungi (AMF)*—can work together to improve plant growth and resilience, especially in Petunia cuttings. One part of the project focuses on using bacteria that naturally produce IAA, a plant hormone that encourages rooting. By comparing these bacteria to synthetic IAA treatments, the aim is to understand not just how effective the microbial version is, but also how it might offer a more sustainable and biologically compatible alternative for plant propagation. In parallel, we are working on improving how we can grow and use AMF, particularly in systems that don't rely on host plants. This includes testing whether certain bacteria can support AMF by helping the spores to germinate, extend their hyphae, or better tolerate challenging environments like high-phosphate soils.
By combining both approaches, this research is tapping into the natural strengths of microorganisms—how they interact, support each other, and benefit plants—to build a more integrated and sustainable system for plant cultivation. It's about moving beyond synthetic inputs and toward smarter, microbe-based solutions that are rooted in biology and cooperation.

Fig. 4: IAA and biofilm production of bacteria on AMF hyphae. (© N. Neetu/ FGK).

2. Publications

Peer-reviewed:

Gaber D A, Berthelot C, Blaudez D, Kovács GM and Franken P (2023) Impact of dark septate endophytes on salt stress alleviation of tomato plants. Frontiers in Microbiology 14: 1124879.

Götze S, Vij R, Burow K, Thome N, Urbat L, Schlosser N, Pflanze S, Müller R, Hänsch VG, Schlabach K, Fazlikhani L, Walther G, Dahse HM, Regestein L, Brunke S, Hube B, Hertweck C, Franken P, Stallforth P (2023) Ecological niche-inspired genome mining leads to the discovery of crop-protecting nonribosomal lipopeptides featuring a transient amino acid building block. Journal of the American Chemical Society 145(4): 2342-2353.

Azri R, Zorrig W, Debez A, Alyami N M, Burow K, Rabhi M, Fnayou B, Mliki A, Franken P, Aroca R (2024) Significance of photosystem integrity and reducing Cd accumulation in mitigating Cd stress on olive tree inoculated with bacteria consortium is variety-dependent. Plant Stress. doi.org/10.1016/j.stress.2025.100788.

Lucic-Mercy E, Mercy L, Jeschke A, Schneider C, Franken P. Short-term artificial adaptation of *Rhizoglomus irregulare* to high phosphate levels and its implications for fungal-plant interactions: phenotypic and transcriptomic insights. Front. Plant Sci. 15:1385245. doi.org/10.3389/fpls.2024.1385245.

Further publications:

Brandes J, Esposto D, Burow K, Franken P (2024) Einfluss von Lichtintensität und Tageslänge auf die Interaktion zwischen arbuskulären Mykorrhizapilzen und Petunien. Hortigate Versuchsberichte Zierpflanzenbau, online veröffentlicht am 13.11.2024.

Gaber D A, Lux J, Blaudez D, Burow K, Franken P (2024) Nutzung von Dark Septate Endophytes (DSEs) als Biostimulanzien in torffreien Substraten. Hortigate Versuchsberichte Zierpflanzenbau, online veröffentlicht am 10.12.2024.

3. Third Pary Funding

Projektträger	**Vorhaben**	**Laufzeit**	**Mittel in 2021**
TMWWDG (TMBWK)	Pflanzen-Mikroorganismen Wechselwirkungen im nachhaltigen Anbau	01.01.2024 -31.12.2028	4.000.000,00 €
DFG	Phosphatmangel bei Petunien	12 Monate	7.850,00 €
DFG	Dark & Strong “High melanisation of dark septate endophytes: an advantageous trait for plant colonisation and stress tolerance”	01.02.2024 - 31.01.2027	338.184 €
BLE	OPT4AMF	01.03.2023 – 28.02.2026	200.482,89 €
DAAD	Forschungsstipendium	2023 + 2024	2000,00 €
BMEL, FNR	Verbundvorhaben: ToSuGa	01.12.2024 – 31.01.2027	187.046,50 €

4. Studium und Lehre

Angebotene Module der Mikrobiellen Phytopathologie

Modulnummer	Veranstaltung	ECTS	Teilnehmerzahl
Sommersemester 2023			
MMB019	Endophytic fungi	5	2
Sommersemester 2024			
MMB019	Endophytic fungi	5	2

Abschlussarbeiten

Bradl M (2023) Einfluss von *Schizophyllum commune* sowie eines Bakterienkonsortiums auf die Entwicklung von *Ocimum basilicum* in torfreduziertem Substrat. Fachhochschule Erfurt, Bachelorarbeit.

Kühne, S (2023) In vitro Untersuchungen interspezifischer Wechselwirkungen eines bakteriellen Konsortiums an *Petunia hybrida* cv. ‘Mitchell‘. Fachhochschule Erfurt, Bachelorarbeit.

Möcker D (2023) Untersuchungen zur Wirkung von Mikroorganismen in torffreien Kultursubstraten. Fachhochschule Erfurt, Bachelorarbeit.

Neetu N (2023) Investigation of Beneficial Microbe-Microbe/Plant-Interaction in Sustainable Horticulture. Friedrich-Schiller-Universität Jena, Masterarbeit.

Paolucci C (2023) Effects of light regime and mycorrhization on growth on two different RILs (*P. axillaris* x *P. exserta*). University of Perugia, Italy, Bachelorarbeit.

Proma R (2023) Characterization of microbes and microbial consortia from rhizosphere and their impact on plant growth of different Petunia genotypes. Friedrich-Schiller-Universität Jena, Masterarbeit.

Lux J S (2024) Stickstoffverwertung von wurzelbesiedelnden Pilzen und deren Einfluss auf das Pflanzenwachstum. Fachhochschule Erfurt, Bachelorarbeit.

Winkler L (2024) Modifizierung eines In-vitro-Systems zur Untersuchung des Einflusses arbuskulärer Mykorrhiza-Pilze auf das Pflanzenwachstum an *Petunia axillaris* unter Verwendung verschiedener Nährmedien. Fachhochschule Erfurt, Bachelorarbeit.

5. Wissenschaftlicher Nachwuchs

Promotionsabschlüsse

Matared M (2024) Using insects as vectors for inoculation of beneficial resistance-inducing microbes in plants. Friedrich-Schiller-Universität, Dissertation.

6. Gleichstellung und Familie

Anteil Frauen	Anteil Männer	Mit Kindern unter 12 Jahren
9	1	3

7. Internationales

Kooperationen mit internationalen Universitäten

Université de Nancy **- Frankreich**

Eötvös Loránd University – **Ungarn**

University of Copenhagen – **Dänemark**

University of Amsterdam – **Niederlande**

Institute for Sustainable Plant Protection, C.N.R.– **Italien**

*Internationale Gastwissenschaftler*innen*

Dr. Mehdi Ghabooli, Malayer University, Iran, 01.07.2023 - 30.09.2023

8. Administration/Finanzen

Beschäftigungsstruktur

	Personen	Stellenanteile
Beschäftigte im Rahmen von Haushaltsmitteln		
Studentische Hilfskräfte	0	
Beschäftigte im Rahmen von Drittmitteln		
Wissenschaftliche Mitarbeiterinnen	3	2,23
Technische Assistenz	2	2,0
Studentische Hilfskräfte	4	

9. Team

Univ.-Prof. Dr. Philipp Franken

Wissenschaftlerin

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Alicia V. Alonso
Dr. Dalia Gaber

Technische Assistenz

Sabine Czekalla
Natalie Hauswald

Promovierende

Julia Brandes
Neetu Neetu
Rhedia Proma
Sneha Sabu

Studierende

Rhedia Proma (FSU Jena) (2023/2024)
Neetu Neetu (FSU Jena) (2023/2024)
Dirk Möcker (FH Erfurt) (2023/2024)
Jamie Lux (FH Erfurt) (2023/2024)
Miriam Bradl (FH Erfurt) (2023/2024)
Nathalie Wiedmann (FH Erfurt) (2023/2024)
Adriana Tinoco Gaona (FSU Jena) (2023/2024)
Benedict Werdich (FH Erfurt) (2023/2024)
Lilly Winkler (FH Erfurt) (2023/2024)

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Lilly Michalowitch (FH Erfurt)
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Eric Bierau (FH Erfurt)
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