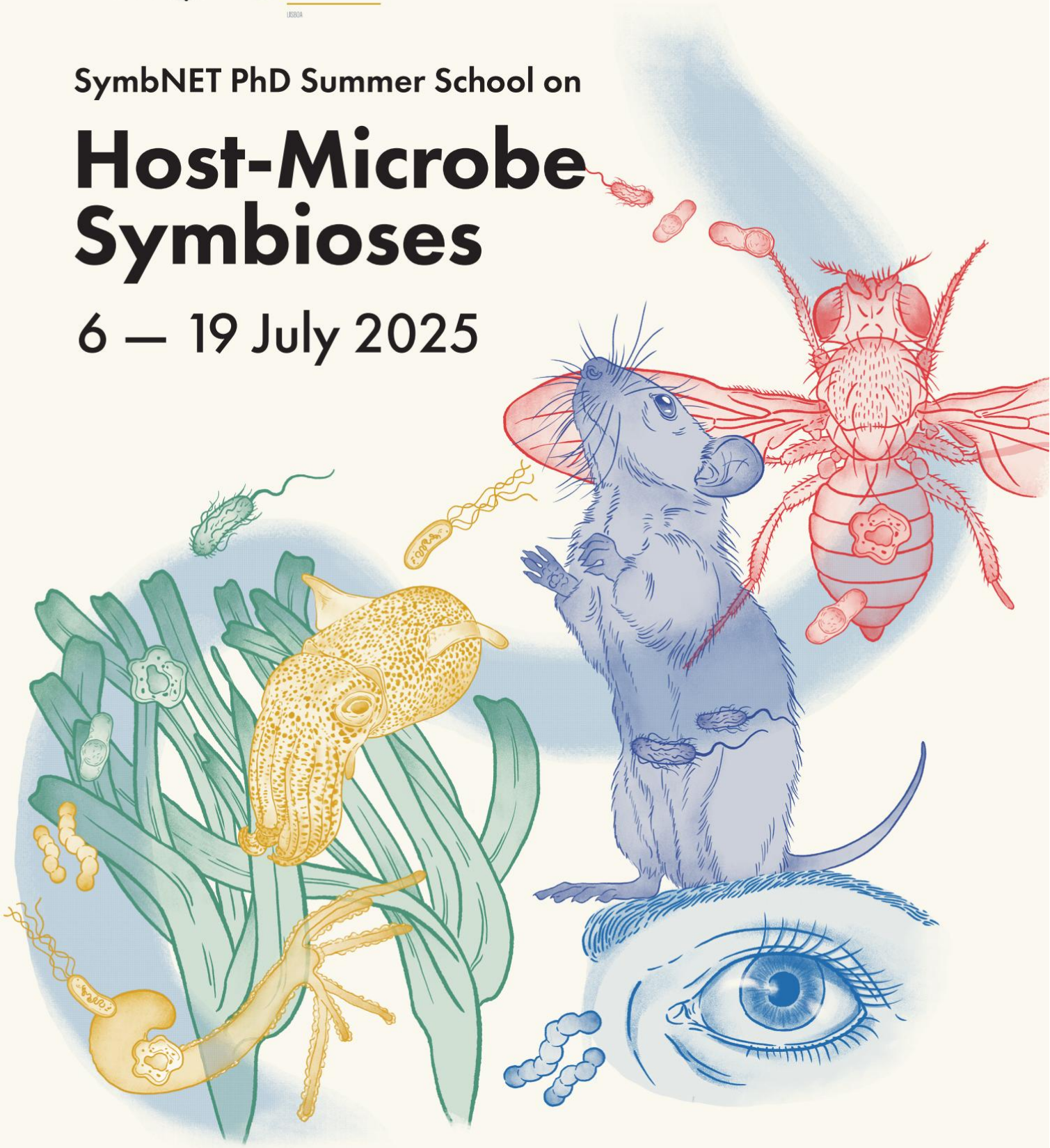
GIMM

CATÓLICA BIOMEDICAL RESEARCH CENTRE
LISBOA

SymbNET PhD Summer School on

Host-Microbe Symbioses

6 — 19 July 2025



GORDON AND BETTY MOORE FOUNDATION

META ORGANISMS
COLLABORATIVE RESEARCH CENTRE 1182

CIFAR

Hour	Sunday 06 Jul	Monday 07 Jul	Tuesday 08 Jul	Wednesday 09 Jul	Thuesday 10 Jul	Friday 11 Jul	Saturday 12 Jul
09.00 am		Welcome	Nicole Dubilier	Takema Fukatsu	Howard Ochman	Nancy Moran	
09.30		Margaret McFAll-Ngai					
10.00			Giulia Ghedini	Karina Xavier	Jewelna Akorli	Ned Ruby	
10.30		Nancy Moran	Poster session 1 with lunch	Coffee Break	Coffee Break	Coffee Break	
11.00		Coffee Break		Karen Guillemin	Martin Blaser	Luis Teixeira	
11.30		Ilana Gabanyi				Break	Bus at 11:40 from Hotel Riviera to the Dock, Alcântara
12.00				Thomas Bosch	Laila Partida Martinez	Takema Fukatsu GIMM Seminar	
12.30		Lunch		Lunch	Lunch		Boat trip with Lunch
1.00pm						Lunch	
1.30		Poster Flash Talks by the students	Break				
2.00			Laila Partida Martinez	Ilana Gabanyi	Project Presentations		
2.30				Cristina Ferreira GIMM Seminar		Maria Gloria Dominguez-Bello	
3.00		Introduction to project	Project	Project			
3.30		Coffee Break			Coffee Break	Project	
4.00		Project			Project Presentations		
4.30							
5.00					Project		
5.30							
6.00	Welcome reception					Nicole Dubilier	
6.30		Karen Guillemin	Howard Ochman	Spencer Nyholm		BBQ and Party	
7.00							
7.30	Welcome Dinner	Dinner	Dinner	Dinner	Dinner		

Hour	Sunday 13 Jul	Monday 14 Jul	Tuesday 15 Jul	Wednesday 16 Jul	Thuesday 17 Jul	Friday 18 Jul
09.00 am		Rob Knight	Waldan Kwong	Luis Teixeira	Spencer Nyholm	Thomas Bosch
09.30						
10.00		M G Dominguez-Bello	José Lourenço	Aileen Berasategui	Waldan Kwong	Coffee Break
10.30		Coffee Break	Poster session 2 with lunch	Coffee Break	Coffee Break	Project Presentations 1
11.00		Aileen Berasategui Lopez		Ned Ruby	Jewelna Akorli	
11.30						Break
12.00		Tina Keller-Costa		Pedro Leão	Naama Geva-Zatorsky	Martin Blaser GIMM Seminar
12.30		Lunch		Lunch	Lunch	
1.00pm						Lunch
1.30			Break			
2.00		Sean Meaden	Karina Xavier	Project	Project	
2.30						Project Presentations 2
3.00						
3.30		Project	Project			
4.00						
4.30						Coffee Break
5.00						Project Presentations 3
5.30						
6.00						
6.30		Margaret McFall Ngai	Sean Meaden	Rob Knight		
7.00						
7.30		Dinner	Dinner	Dinner	Dinner	Closing Dinner

ABOUT

Host-microbe interactions shape each other's physiology, ecology, and evolution. Human health, for instance, can be strongly influenced by the symbiotic microbial community. The impact of these interactions extends to the ecology of terrestrial and aquatic ecosystems. This is an expanding field of research in biology and there is a current need to summarize and integrate the knowledge that is being generated, and to extrapolate general principles to be incorporated in future innovative research projects. This Summer School aims at training the next generations of researchers in host-microbe symbioses.

The SymbNET PhD Summer School on Host-microbe Symbioses 2025 is for PhD students from diverse geographies and academic backgrounds, interested in acquiring in depth understanding of the field of Host-Microbe Symbioses from different perspectives. The Summer School is designed to teach concepts, identify new research questions, and present state of the art approaches in host-microbe symbiosis. It will consist of lectures from experts in the field, incorporating a variety of research models and topics. It will also involve the conceptual development of new research projects, by the students. The project exercise aims to promote thinking deeply about questions, future directions, and creative research approaches.

The Summer School will be two weeks long, with 25 lecturers and 35 international PhD students, fostering a continuous and strong interaction between faculty and students. The students will acquire critical knowledge for their future choice of research direction.

ORGANISING INSTITUITIONS

Gulbenkian Institute for Molecular Medicine

Católica Biomedical Research Centre, Portugal

Moore Foundation, USA

"This course is funded by the Gordon and Betty Moore Foundation through Grant GBMF11550.01 to GIMM"

Origin and Function of Metaorganisms Collaborative Research Centre 1182 (CRC1182), Germany

Canadian Institute or Advanced Research, Canada

ORGANISERS

Scientific organising committee

Martin Blaser | Rutgers University, New Brunswick, USA

Thomas Bosch | Kiel University (CAU), Kiel, Germany

Margaret McFall-Ngai | California Institute of Technology, Pasadena, USA

Luís Teixeira | Católica Biomedical Research Centre (CBR), Lisbon, Portugal

Karina Xavier | Gulbenkian Institute for Molecular Medicine (GIMM), Oeiras, Portugal

Course managemet

Ana Teles | Gulbenkian Institute for Molecular Medicine (GIMM), Oeiras, Portugal

Instituitional affairs

Regina Fernandes | Gulbenkian Institute for Molecular Medicine (GIMM), Oeiras, Portugal

Graphical Design

Lúcia Antunes | Católica Biomedical Research Centre (CBR), Lisbon, Portugal

VENUE

Please note that GIMM Institute has two sites, one in Lisbon and one in Oeiras. The venue for our event is at **Gulbenkian Institute for Molecular Medicine (GIMM) – Oeiras Site:**
Rua da Quinta Grande nº 6, 2780-156, Oeiras, Portugal

Welcome reception and Dinner - Patio
Lectures and most seminars – Ionians Auditorium
Late afternoon seminars – Patio
Coffee Breaks – Jardim das Rosas; Patio
Poster sessions – Leucippus Room
Lunch and dinner - Canteen

PROGRAMME

Sunday, 6th July 2025	
17:30 – 19:00	Welcome reception
19:00 – 21:00	Dinner

Monday, 7th July 2025	
09:00 – 09:15	Welcome address
09:15 – 10:15	Lecture: Margaret McFall-Ngai “Introduction - Two billion years of eukaryotic symbioses: major transition and cellular innovations”
10:15 – 10:45	Research Seminar: Nancy Moran “Warfare in the bee gut”
10:45 – 11:15	Coffee break
11:15 – 12:15	Lecture: Ilana Gabanyi “Understanding the interactions between gut microbiota and the central nervous system”
12:15 – 13:30	Lunch
13:30 – 15:00	Poster Flash Talks
15:00 – 15:30	Introduction to Project
15:30 – 16:00	Coffee break
16:00 – 18:30	Project
18:30 – 19:00	Research Seminar: Karen Guillemin “Stimulating interactions between microbes and their hosts: lessons from gnotobiotic zebrafish”
19:00	Dinner

Tuesday, 8th July 2025	
09:00 – 10:00	Lecture: Nicole Dubilier “Chemosynthetic Symbioses in Marine Environments”
10:00 – 10:30	Research Seminar: Giulia Ghedini “How phytoplankton species interactions affect community biomass and metabolism”
10:30 – 13:30	Poster Session 1 - With Lunch
13:30 – 14:00	Break
14:00 – 15:00	Lecture: Laila Partida Martinez “Ecology of fungal holobionts”
15:00 – 18:30	Project
18:30 – 19:00	Research Seminar: Howard Ochman “The Emergence of Genes in Bacterial Genomes”
19:00	Dinner

Wednesday, 9th July 2025	
09:00 – 10:00	Lecture: Takema Fukatsu “Symbiosis, Evolution, and Biodiversity”
10:00 – 10:30	Research Seminar: Karina Xavier “Gut protective Keystone species promotes microbiota recovery, pathobiont clearance and prevents inflammation”
10:30 – 11:00	Coffee Break
11:00 – 12:00	Lecture: Karen Guillemin “Microbiota and Host Development”
12:00 – 12:30	Research Seminar: Thomas Bosch “Microbes as architects of animal design”

12:30 – 14:00	Lunch
14:00 – 14:30	Research Seminar: Ilana Gabanyi "Bacterial derived muropeptides: How do they reach and impact brain neurons ?"
14:30 – 15:00	GIMM Seminar (via Zoom): Cristina Ferreira
15:00 – 18:30	Project
18:30 – 19:00	Research Seminar: Spencer Nyholm "The Hawaiian bobtail squid as a model host for studying defensive symbioses"
19:00	Dinner

Thursday, 10th July 2025	
09:00 – 10:00	Lecture: Howard Ochman "The First Epoch of Bacterial Genomics"
10:00 – 10:30	Research Seminar: Jewelna Akorli "Microbial dynamics: Key to unlocking symbiont-mediated mosquito control strategies"
10:30 – 11:00	Coffee Break
11:00 – 12:00	Lecture: Martin Blaser "Human Microbiota in Health and Disease"
12:00 – 12:30	Research Seminar: Laila Partida Martinez "Microbiome-derived tools from the desert for a planet under global warming"
12:30 – 14:00	Lunch
14:00 – 15:30	Project Presentations
15:30 – 16:00	Coffee Break
16:00 – 17:00	Project Presentations
17:00 – 19:00	Project
19:00	Dinner

Friday, 11th July 2025	
09:00 – 10:00	Lecture: Nancy Moran "Symbiosis and Genome Evolution"
10:00 – 10:30	Research Seminar: Ned Ruby "Diverse and specific targeting of host-cell compartments by a bacterial symbiont's small RNAs"
10:30 – 11:00	Coffee Break
11:00 – 11:30	Research Seminar: Luis Teixeira "Functional genomics in Wolbachia"
11:30 – 12:00	Break
12:00 – 13:00	GIMM Seminar: Takema Fukatsu "Experimental evolutionary approaches to insect-microbe symbiosis"
13:00 – 14:30	Lunch
14:30 – 15:30	Lecture: Maria Gloria Dominguez-Bello "Microbial Anthropology"
15:30 – 18:00	Project
18:00 – 18:30	Research Seminar: Nicole Dubilier "Strain diversity matters in chemosynthetic symbioses"
18:30	BBQ and Party

Saturday, 12th July 2025	
11:40	Bus from Riviera Hotel to the Dock "*Gare Marítima da Rocha Conde de Óbidos"* in Alcântara
12:30 – 15:30	Boat trip (Boat "Principe do Tejo") in the Tagus River – With Buffet Lunch

Monday, 14th July 2025	
09:00 – 10:00	Lecture: Rob Knight “Advances and Challenges in Microbiome Research”
10:00 – 10:30	Research Seminar: Maria Gloria Dominguez-Bello “From Soil to Skin: Microbial Transitions in the Built World”
10:30 – 11:00	Coffee Break
11:00 – 12:00	Lecture: Aileen Berasategui Lopez “The chemical ecology of insect-microbe symbioses”
12:00 – 12:30	Research Seminar: Tina Keller-Costa “From marine symbiosis to enzymes: Discovering functional chitinases in the octocoral microbiome”
12:30 – 14:00	Lunch
14:00 – 15:00	Lecture: Sean Meaden “Bacteria-Phage Interactions”
15:00 – 18:30	Project
18:30 – 19:00	Research Seminar: Margaret McFall Ngai “Host-symbiont cross-talk is more extensive than we imagined: The partner 'conversation' during initiation and early development of the squid-vibrio association”
19:00	Dinner

Tuesday, 15th July 2025	
09:00 – 10:00	Lecture: Waldan Kwong “Inter-microbe interactions in symbiosis”
10:00 – 10:30	Research Seminar: José Lourenço “Modelling the ecology and epidemiology of mosquito-borne viruses”
10:30 – 13:30	Poster Session 1 - With Lunch
13:30 – 14:00	Break
14:00 – 15:00	Lecture: Karina Xavier “Bacterial Chemical Communication in Microbiota Communities”
15:00 – 18:30	Project
18:30 – 19:00	Research Seminar: Sean Meaden “The Ecology of Defence: Insights into Phage Resistance Using Metagenomics and Experimental Evolution”
19:00	Dinner

Wednesday, 16th July 2025	
09:00 – 10:00	Lecture: Luis Teixeira “Defensive Symbiosis”
10:00 – 10:30	Research Seminar: Aileen Berasategui Lopez “Origin and evolution of a defensive symbioses in tortoise beetles”
10:30 – 11:00	Coffee Break
11:00 – 12:00	Lecture: Ned Ruby “Signaling Modes in Symbioses”
12:00 – 12:30	Research Seminar: Pedro Leão “Unique Natural Products and Enzymes from Cyanobacteria”
12:30 – 14:00	Lunch
14:00 – 18:30	Project
18:30 – 19:00	Research Seminar: Rob Knight “Towards microbiome digital twins for precision medicine””
19:00	Dinner

Thursday, 17th July 2025	
09:00 – 10:00	Lecture: Spencer Nyholm “Bacterial Symbionts Shaping Development of Host Immune Responses”
10:00 – 10:30	Research Seminar: Waldan Kwong “Symbioses in the honey bee gut”
10:30 – 11:00	Coffee Break
11:00 – 12:00	Lecture: Jewelna Akorli “Insect symbionts and vector competence”
12:00 – 12:30	Research Seminar: Naama Geva-Zatorsky
12:30 – 14:00	Lunch
14:00 – 18:30	Project
19:00	Dinner

Friday, 18th July 2025	
09:00 – 10:00	Lecture: Thomas Bosch “Innate Immunity and Specificity in Symbiosis”
10:00– 10:30	Coffee Break
10:30 – 11:45	Project Presentations 1
11:45 – 12:00	Break
12:00 – 13:00	GIMM Seminar: Martin Blaser “A model of juvenile diabetes leads to microbiome mining for new bioactive compounds”
13:00 – 14:30	Lunch
14:30 – 16:30	Project Presentations 2
16:30 – 17:00	Coffee Break
17:00 – 18:15	Project Presentations 3
18:30	Closing Dinner at Restaurant TorreMar – Praia da Torre

PROJECT TOPICS

1) Specificity of interactions.

How much of the microbiota is host specific? How is this specificity achieved? How does the host and symbiont recognise one another?

2) Symbiosis and Development.

How do nested ecosystems develop (succession, habitat change, historicity)? How do symbionts and hosts influence each other development? How are symbiont niches established?

3) Maintenance of symbiosis.

How is symbiosis and its diversity maintained over the life of an individual (Control of symbiont number)? Resilience to perturbation (e.g. circadian rhythms, infection with pathogens). How is symbiosis maintained between generations (horizontal and vertically-transmitted symbionts)?

4) Duality and transition between pathogenesis and mutualism.

Are the molecular interactions of the host with pathogens and mutualists the same or different? Which environmental or intrinsic changes lead to transitions along the spectrum of mutualism to pathogenesis?

5) Symbiosis, speciation and evolution.

To what extent is there co-evolution with the specific host and their bacteria? Does the microbiome reflect an ancestral footprint of evolution? Does natural selection operate at the level of the holobiont? How does sexual and asexual reproduction affect symbiosis?

6) Symbiosis, physiology, and behavior.

How does symbiosis influence physiology of the partners? How is this controlled (immune system, metabolome)? How does host and symbiont physiology affect behavior?

7) Symbiont – Symbiont interactions within host.

How do symbionts affect colonisation and the interaction of other symbionts with host (e.g. competitive exclusion, defensive mutualism, syntrophy, auto-induction)? How are consortiums defined? How to modulate communities of symbionts?

LECTURERS

Jewelna Akorli | Mosquito-microbiota interactions

University of Ghana, Accra, Ghana

https://noguchi.ug.edu.gh/fellows/dr-jewelna-efua-birago-akorli/

Jewelna Akorli is a Principal Investigator and Wellcome Trust Intermediate Fellow at the University of Ghana. Her work centers on mosquito-associated endosymbionts and variations in vector competence in natural mosquito populations.

Aileen Berasategui | Molecular and chemical ecology of symbiotic interactions

Vrije University Amsterdam, Netherlands

https://www.berasateguilab.com/people

Aileen Berasategui is an assistant Professor at the Vrije University Amsterdam. Her research focuses on the chemical ecology and evolution of insect-microbe symbioses, currently focusing on the interaction between fungi, insects and their host plant.

Martin Blaser | Resident microbes and the ecology of human diseases

Rutgers University, New Brunswick, NJ, USA

https://cabm.rutgers.edu/person/martin-j-blaser

Martin Blaser serves as the Henry Rutgers Chair of the Human Microbiome and as Director of the Center for Advanced Biotechnology and Medicine at Rutgers University. His current research interest focuses on the role of the human microbiome in early life development and the mechanisms of diseases.

Thomas Bosch | Evolution and the ecology of development

Kiel University-CAU / Metaorganisms CRC1182, Kiel, Germany

https://www.bosch-lab.de/

Thomas Bosch is Senior Professor of Zoology at the University of Kiel. He is an evolutionary developmental biologist, working for many years on the evolution of the immune system, in particular the role of microorganisms in the evolution and development of animals and humans. In 2016 he founded the Collaborative Research Center 1182 “Origin and Function of Metaorganisms” at Kiel University. He uses Hydra as a model system to understand the evolution of host-microbe interactions.

Maria Gloria Dominguez-Bello | Microbiota in early life and microbial anthropology

Rutgers University, New Brunswick, NJ, USA

https://sites.rutgers.edu/mgdblab/

Maria Gloria Dominguez-Bello is a Professor of Microbiome and Health at Rutgers University. She studies the development of gut microbiota in the early life of mammalian hosts, including humans, and is also interested in how human populations' lifestyle and diet shape their microbiota.

Nicole Dubilier | Marine Symbioses

Max Planck Institute (MPI) for Marine Microbiology, Bremen, Germany

https://www.mpi-bremen.de/en/Nicole-Dubilier.html

Nicole Dubilier heads the Symbiosis Department, as a Director at the MPI for Marine Microbiology, and is a professor at the University of Bremen. Her research has provided a critical contribution to marine microbiology and ecology by showing how wide-spread symbioses between marine invertebrates and bacteria are.

Takema Fukatsu | Evolution and Microbial symbioses in Insects

AIST, Tsukuba, Japan

https://bpri.aist.go.jp/en/staff/fukatsu-takema

Takema Fukatsu is a Prime Senior Researcher at the Bioproduction Research Institute, AIST. He uses experimental evolutionary approaches to study associated mechanisms and functions of microbial symbioses in insects.

Ilana Gabanyi | Neuronal responses to bacterial signals

Gulbenkian Institute for Molecular Medicine (GIMM), Oeiras, Portugal

https://gimm.pt/lab/ilana-gabanyi-lab/

Ilana Gabanyi is a principal investigator at GIMM. Her studies focus on the microbiota-gut-brain axis and the direct interactions between gut-bacterial signals and brain neurons.

Naama Geva-Zatorsky | The importance of the microbiome's functions in different environments

Rappaport Faculty of Medicine, Technion – Israel Institute of Technology

https://geva-zatorsky.net.technion.ac.il/

Naama Geva-Zatorsky is an Associate Professor and Head of department at the Rappaport Faculty of Medicine, Technion, RTICC. In her lab, she is applying computational and experimental approaches to study mechanisms of microbiota-host interactions, with a focus on bacterial functional plasticity and bacteriophage interactions, both during health and disease.

Giulia Ghedini | Community Ecology and Evolution

https://www.giuliaghedini.com/

Gulbenkian Institute for Molecular Medicine (GIMM), Oeiras, Portugal

Giulia Ghedini is a Principal Investigator at GIMM where she combines ecology, physiology, and experimental evolution approaches. Her lab uses marine phytoplankton as a model system to identify the mechanisms that regulate organismal metabolism and to understand how changes in energy use, at the individual-level, affect community properties.

Karen Guillemin | Host-microbe interactions in development and disease

University of Oregon, Eugene, USA

http://molbio.uoregon.edu/guillemin/

Karen Guillemin is a Professor at the University of Oregon. Her working interests are host-microbe systems in development and disease. Karen pioneered the use of zebrafish to study host-microbe interactions, including the influence of the gut microbiome on development, metabolism, and immunity.

Tina Keller-Costa | Marine Microbiomes

IBB - Instituto Superior Técnico, Lisbon, Portugal

https://ibb.tecnico.ulisboa.pt/people/members/Tina-Keller-Costa/

Tina Keller-Costa is a Research Scientist and Invited Assistant Professor at Instituto Superior Técnico. Her research focuses on the molecular mechanisms of marine host-microbial interactions; the response of the octocoral holobiont to climate change; and the sustainable use of marine resources, particularly chitinases.

Rob Knight | High-throughput sequencing to study microbial diversity

University of California San Diego, CA, USA

https://knightlab.ucsd.edu

Rob Knight is a Professor at UCSD. Rob studies evolution of the composition of metabolites, genomes, and communities in different ecosystems, including the complex microbial ecosystems of the human body. He has developed main computational and experimental techniques used worldwide to study these processes.

Waldan Kwong | Microbial Genomics and Symbiosis

Gulbenkian Institute for Molecular Medicine (GIMM), Oeiras, Portugal

https://www.kwonglab.com/people

Waldan Kwong is a Principal Investigator at GIMM. His research focuses on ecology, evolution, and function of microorganisms. To understand the diverse ways microorganisms have evolved to interact and thrive in their environments, he uses a multitude of approaches, from classical microbiology to high-throughput genomics and animal models, such as social bees and corals.

Pedro Leão | Cyanobacterial Natural Products

CIIMAR, Porto, Portugal

https://www.ciimar.up.pt/teams/cyanobacterial-natural-products/

Pedro Leão is Principal Investigator and ERA Chair Holder in Blue Biotechnology and Bioengineering at CIIMAR, where he leads the Research Line in Marine Biotechnology and is the head of the Research Group “Cyanobacterial Natural Products”. His research focuses on the chemistry, biosynthesis and chemical ecology of cyanobacterial natural products.

José Lourenço | Evolution, Ecology & Epidemiology of pathogens

Católica Biomedical Research Centre (CBR), Oeiras, Portugal

https://cbr.fm.ucp.pt/people/jose-lourenco

José Lourenço is Assistant Professor and Group Leader at CBR. His lab uses computational approaches to biological data related to pathogens, associated diseases, hosts and environments. Their main interests remain focused on antigenically variable viral and bacterial pathogens, and those that are mosquito-borne.

Margaret McFall-Ngai | Invertebrate-microbe symbiotic interactions

California Institute of Technology, Pasadena, CA, USA

https://www.glowingsquid.org/people_mm.php

Margaret McFall-Ngai is a faculty associate at California Institute of Technology in Pasadena and a staff scientist at the Carnegie Institution for Science. Her research focuses on understanding host responses to interactions with beneficial microbes. Using the squid-vibrio model, she explores this question at spatial, molecular and mechanistic levels.

Sean Meaden | Bacteria-viruses Interactions

University of York, UK

https://www.york.ac.uk/biology/people/sean-meaden/

Sean Meaden is a BBSRC Discovery Fellow. His work is focused on the interactions between bacteria and their viruses, and the ecological and evolutionary processes that shape such interactions.

Nancy Moran | Evolution of biological complexity

University of Texas at Austin, TX, USA

http://web.biosci.utexas.edu/moran/nancymoran.html

Nancy Moran is a Professor at the University of Texas at Austin. Her research focuses on the evolution of symbiosis between multicellular hosts and microbes. Her work has a strong emphasis on genome evolution of bacterial symbionts of insects.

Spencer Nyholm | Symbiosis and comparative immunology

University of Connecticut, USA

https://mcb.uconn.edu/person/spencer-nyholm

Spencer Nyholm is a Professor at UCONN. His lab works on the mechanisms by which animal hosts and microbial symbionts communicate with an emphasis on how components of the innate immune system may influence these interactions.

Howard Ochman | Microbial Evolution

University of Texas at Austin, TX, USA

web.biosci.utexas.edu/ochman

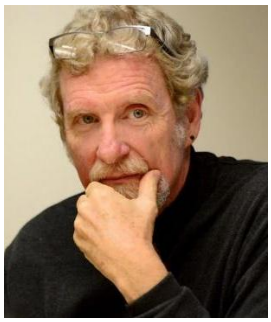
Howard Ochman is interested in the evolution and adaptation of microbial genomes and how genome structure affects bacterial lifestyle. He is also interested in co-evolution of microbiota bacteria with primate hosts, including humans.

Laila Partida-Martinez | Microbial Interactions and Ecology

CINVESTAV, Irapuato, Mexico

https://orcid.org/0000-0001-8037-2856

Laila Partida-Martinez is the director and principal investigator at Cinvestav-Irapuato. She is interested in fungal-bacterial interactions, plant-microbe interactions, microbial ecology and natural products produced by microorganisms.

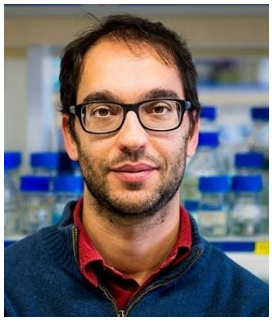


Edward (Ned) Ruby | Biology of the squid symbiont *Vibrio fischeri*

California Institute of Technology, Pasadena, CA, USA

https://www.glowingsquid.org/people_profile_nr.php?id=68

Ned Ruby is a Faculty Associate at the California Institute for Technology. He studies the role of bacterial behavior and physiology in the beneficial colonization of host tissues. He uses the natural squid-vibrio model of symbiosis to address how the partners communicate with each other at the molecular level.



Luis Teixeira | Host-microorganism interactions

Católica Biomedical Research Centre (CBR), Oeiras, Portugal

https://fm.ucp.pt/pt-pt/pessoa/luis-teixeira

Luis Teixeira is a Principal Investigator at CBR. His lab studies host-microbe symbioses using Drosophila as a model system. He is interested not only in how viruses, Wolbachia and gut microbiota interact with flies but also how these microbes influence each other.

Karina Xavier | Bacterial signalling

Gulbenkian Institute for Molecular Medicine (GIMM), Oeiras, Portugal

https://karinaxavierlab.weebly.com/people-and-projects.html

Karina Xavier is a Principal Investigator at GIMM. She studies interspecies cell-to-cell communication in bacteria and its role in beneficial and hostile interactions in multispecies bacterial communities. Her work includes elucidation of the molecular mechanisms involved in bacterial quorum sensing and their role in shaping gut microbiota composition.

STUDENTS


Anthony_Allan Cardoso


Julien Amoros


Veronika Andriienko


Lachlan Bartrop


Meghan Blaszynski


Sara Brites de Oliveira


André Cairrão


Isabella Changsut


Giulia Ghisleni


Bonface Gichuki


Arno Hagenbeek


Rowan Hart


Pi Johansen


Fabiyi Kafayath


Slipa Kanungo


Mary Lally


Yehonatan Levin


Teresa Maia


Marcos Martins


Inmaculada Mena Guzman


Jesus U. Mendez Leyva


Katharina Müller


Kateryna Pantiukh


Christos Paschalidis


Camilo Perez Salazar


Ehsan Sakib


Marcella Santiago


Mei Shimizu


Isa Silva


Pratyaksh Singh


Alexej Sinner


Natalia Sommario

Natchapon Srinak

Daisuke_Yamagishi

Xiaotong Zhang

1. Understanding the characteristics and host impacts of freshwater gregarines

Anthony Allan-Cardoso[1,2], Sonja Rückert[1,2, 3]

1 - Department of Eukaryotic Microbiology, Universität Duisbrg-Essen, Universitätsstrasse 2, 45141 Essen, Germany
2 - Zentrum für Wasser- und Umweltforschung (ZWU), Universität Duisbrg-Essen, Universitätsstrasse 2, 45141 Essen, Germany
3 - Centre for Conservation and Restoration Science, Edinburgh Napier University, Sighthill Court, Edinburgh, EH11 4BN, United Kingdom

As an ancestral group of symbionts infecting invertebrates, gregarines are supposed to have an important position for understanding the evolutionary development of parasitism in the phylum Apicomplexa. However, due to their lack of direct clinical significance to humans, gregarines have been largely overlooked in research.
Most known species have barely been examined since their initial descriptions, which often predate the advent of modern sequencing and electron microscopy techniques. As a result, only a fraction of gregarine species has been documented with ultrastructural or molecular data, with this gap being particularly pronounced among those infecting freshwater hosts.
Furthermore, for most gregarine species, it is unknown how they affect their hosts and how these effects might alter under different environmental conditions, though various studies have displayed that described effects span the whole spectrum of symbiosis.
To address these knowledge gaps, the present project has screened through over 60 common freshwater invertebrate species in stream systems in North Rhine-Westphalia and identified over a dozen gregarine species. Comprehensive characterisation of this small collection of freshwater gregarine species has been achieved through obtaining SSU DNA sequences and SEM micrographs.
Additionally, this project is currently utilising a novel aquatic host-gregarine model system to generate infected and uninfected host populations. These populations will be deployed in experiments measuring various metrics of host fitness (e.g., fecundity, mortality, food consumption, etc.) whilst being exposed to modulated environmental conditions (e.g., water temperature, water pH, pollutant levels, food type, food availability, etc.). Ultimately a generalised linear regression model will be applied to examine the relationship between infection status, environmental condition and fitness metrics.

2. Diversity and spread of cytoplasmic incompatibility genes among maternally inherited symbionts: *Wolbachia* do not walk alone

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Cytoplasmic Incompatibility (CI) causes embryonic lethality in arthropods, resulting in a significant reduction in reproductive success. In most cases, this reproductive failure is driven by *Wolbachia* endosymbionts through their *cifA/cifB* gene operon, whose products disrupts arthropod DNA replication during reproduction. While *cif* operon has been considered a hallmark of *Wolbachia*, its presence and functional significance in other bacterial lineages remains poorly investigated. Here, we conducted a comprehensive survey of 762 genomes spanning non-*Wolbachia* endosymbionts and their close relatives, revealing that *cif* operon is far more widespread than previously recognized. We identified *cif* loci in 8.4% of the surveyed genomes, with a striking incidence of 17.4% in facultative symbionts. Beyond *Wolbachia*, *cif* operon occurs across eight bacterial genera spanning α-Proteobacteria, γ-Proteobacteria, Mollicutes, and Bacteroidota. Notably, *cif* operon has been identified in several intracellular pathogens of mammals showing high rate of transovarial transmission in their arthropod hosts, suggesting a potential role of *cif* operon and CI in vector-borne disease dynamics. Structural analyses further reveal that PD(D/E)-XK nucleases and AAA-ATPase-like motifs are consistently conserved across *cif* operons in all bacterial taxa. Moreover, *cif* operons are frequently integrated within diverse mobile genetic elements, from transposons to large intact WO prophages in *Wolbachia* and RAGEs in Rickettsiaceae. Phylogenetic analyses reveal recent and potentially ongoing horizontal transfers of *cif* operon between distantly related bacterial lineages, a process potentially facilitated by mobile genetic elements. Indeed, the PDDEXK2 transposase exhibits a phylogenetic pattern consistent with the co-transmission of *cif* genes, suggesting that it may facilitate horizontal transfers of *cif* across bacterial lineages. Furthermore, the detection of endosymbionts harboring *cif* operon in arthropod groups where *Wolbachia* is scarce, such as ticks, suggests that CI may be more widespread than previously known, with significant implications for arthropod symbiosis, reproductive manipulation, and future biocontrol strategies.

3. Exploring nested symbiosis and microbial dynamics in *Aphrodes* leafhoppers

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Bacterial symbioses play a central role in the biology and evolution of Hemiptera, enabling these insects to exploit nutritionally unbalanced diets and adapt to diverse ecological niches. In Auchenorrhyncha – a group that includes leafhoppers, planthoppers, spittlebugs, and cicadas – such relationships originated approximately 300 million years ago with the acquisition of two obligate symbionts: *Sulcia* (phylum Bacteroidetes) and a representative of Betaproteobacteria. Descendants of these ancestral symbionts persist in many modern lineages, although in some clades they have been replaced or supplemented by additional partners, leading to remarkable diversity in symbiotic systems.

Leafhoppers of the genus *Aphrodes* exhibit an unusual arrangement: in addition to *Sulcia* and *Nasuia*, they harbour the bacterium *Sodalis*, which resides within the cytoplasm of *Sulcia* – a rare case of nested symbiosis. Using light and electron microscopy, we confirmed the presence of *Sodalis* within *Sulcia* cells in bacteriomes, during migration through the follicular epithelium, and in mature oocytes, suggesting transovarial transmission and stable integration of this symbiont with the host.

To explore the diversity of *Sodalis*, we analysed 16S rRNA gene amplicons from 112 individuals representing three species of *Aphrodes* in 16 geographically separated European populations. The presence of *Sodalis* varied among populations, and multiple strains frequently co-occurred within individual hosts. Metagenomic sequencing of a subset of 30 selected samples confirmed the presence of genetically distinct *Sodalis* strains and enabled assessment of their metabolic potential. In contrast to the highly reduced genomes of *Sulcia* and *Nasuia*, *Sodalis* retains a broader gene repertoire, consistent with more recent integration.

The *Aphrodes* symbiotic system thus combines the stability of ancestral symbionts with the dynamic variability of additional partners. Our study reveals a complex, evolving symbiosis and positions *Aphrodes* leafhoppers as a valuable model for investigating nested symbioses, strain-level symbiont variation, and the evolutionary dynamics of insect–microbe associations.

4. Re-structuring the search for antibiotic resistance genes from human microbiomes

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The enthusiasm after the discovery of antibiotics was rapidly overshadowed by the rise of bacteria exhibiting antimicrobial resistance (AMR), a problem that has grown to become one of the most pressing global public health challenges of our time. Antibiotic resistance genes (ARGs) – key drivers of AMR – mostly emerge from environmental microbiomes. Elevated antibiotic levels create selection pressures for the emergence of novel ARGs and their horizontal transfer to the human microbiome via mobile genetic elements (MGEs). Identifying previously uncharacterized proteins from the human microbiome which confer resistance to clinical antibiotics is a crucial component of AMR within its One-Health context, for accurate surveillance, diagnostics, and antibiotic stewardship. Current attempts to identify novel ARGs mainly rely on the similarity of their amino acid sequences to known ARGs. However, often these sequences differ considerably from known ARGs, revealing an important limitation. Protein structures are generally more conserved than sequences, so we sought to leverage the increased accuracy of computational predictions simulating protein structure by training a one-class support vector machine (SVM) on the pairwise primary protein structure (seqID) and tertiary protein structure (TM-scores) of highly conserved structural regions of an ARG class. We applied the SVM to five human microbiome project (HMP) strains and functionally confirmed four novel dfrs, two novel beta-lactamases, and a novel pencillin binding protein (PBP). One novel dfr was identified in *Pseudomonas aeruginosa* and the remaining novel dfr and the class C beta-lactamase co-localize with signature sequences of MGEs, increasing their risk of transfer to human pathogens. This represents a precise and computationally efficient method of identifying previously uncharacterized ARGs from DNA databases.

5. Shifts in *Sinorhizobium* Fitness Across Non-Leguminous Plant Hosts

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Facultative mutualisms are widespread across many ecosystem types and provide important ecosystem services. However, it remains unclear how these mutualisms are maintained over time, as the free-living and partner-associated states often impose distinct, and at times, conflicting selective pressures. It is thus critical to understand how fitness trade-offs between host-associated and free-living periods drive the evolution of symbionts. Using the *Medicago-Sinorhizobium* model system and multiple sympatric non-legume hosts that *Sinorhizobium* is likely to encounter in the environment, I will address if the fitness of *Sinorhizobium* strains change between nodulating and non-nodulating hosts. My previous work has shown that *Avena barbata*, a co-occurring non-legume, selects for a different *Sinorhizobium* strain than *Medicago truncatula*. If interactions in non-legume rhizospheres influence the relative fitness of *Sinorhizobium* strains, this could have significant implications for the *Medicago-Sinorhizobium* facultative mutualism, especially if low partner quality strains gain a selective advantage in the non-legume rhizosphere. To test if plant-mediated selection varies between legume and non-legume hosts, both *M. truncatula* and six non-leguminous hosts will be inoculated with equal starting concentrations of the twenty-seven characterized *Sinorhizobium* strains. After six weeks, I will extract DNA from the roots of all hosts and the nodules of *M. truncatula* and assess each strain's relative abundance. If strain fitness does change across plant hosts, this could explain how rhizobial variation is maintained in nature, despite variable partner quality in *M. truncatula*. This would be pivotal for the understanding how alternative selective pressures shape the evolution of the legume-rhizobia interaction and broaden our view of the partnership.

6. Integrin-mediated symbiont uptake in Cnidarians

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Corals and most sea anemones share a symbiotic relationship with a dinoflagellate alga, *Symbiodiniaceae*. They are born without symbionts, meaning that they inherently possess mechanisms to determine appropriate partners. Although poorly understood, symbiont recognition and uptake are the first steps to a successful symbiosis.
Using the sea anemone *Exaiptasia diaphana* (Aiptasia), as a model organism, is much more convenient than corals: they are much easier to grow and maintain, reliably and consistently produce offspring. Preliminary results of the Guse lab suggest that the presence of symbionts within host cells alter the expression of multiple host integrins. Integrins are heterodimeric cell-surface receptors, known for their function of binding cells to the extracellular matrix, as well as binding to foreign particles and facilitating phagocytosis in vertebrate immune cells. When human cells overexpress integrins, symbiont uptake is increased and if integrin binding sites are blocked in Aiptasia larvae, uptake if inhibited. Suggesting that integrins bind specifically to symbionts to enhance phagocytosis.
To uncover the molecular mechanisms behind these first insights, the next steps would shed light onto the contribution of the integrin signaling pathway and a potential post-phagocytic retention. Additionally, identifying the ligand(s) of this interaction and the extent of their specificity would be a breakthrough in unraveling the actors of this interaction.
Insights into integrin ligand interactions between the host and symbiont has the potential to guide coral reef restoration efforts, and more generally add valuable information of how symbiotic relationships are formed.

7. Volatile Profiles and Antimicrobial Activity of *Asparagopsis armata* Extracts: Insights for Biotechnological Applications

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The invasive alga *Asparagopsis armata* is a threat to Portugal's marine ecosystems; its abundant biomass and unique chemical properties, however, presents opportunities for various biotechnological applications. This work focuses on the production of extracts from *A. armata* through green methods, the characterization of their volatile organic compounds (VOCs) content, and the assessment of their antimicrobial potential against a broad range of microorganisms, including gram-positive and gram-negative bacteria, filamentous fungi and yeasts. Seasonal variations in the VOCs composition were found, with peaks of bioactivity identified in specific harvesting months. GC-MS chemical profiling revealed that the main VOCs present were halomethanes, among which bromoform was a major one, particularly in bioactive samples. This compound, however, at the concentrations observed in the extracts did not exhibit significant antimicrobial activity, suggesting the presence of possible synergistic interactions within the extracts. NMR analysis provided additional chemical fingerprint data of the samples, giving an overview of their composition and highlighting the presence of fatty acids. Our findings emphasize the potential of *A. armata* as a source of new bioactive compounds against human pathogens, while providing technical guidelines for the quick analysis and identification of bioactive water-based *A. armata* extracts. We strive to achieve and encourage sustainable harvesting and extraction strategies to mitigate the ecological impact of *A. armata*, transforming its invasiveness into a resource while promoting market value through bioprospecting and blue bioeconomy approaches.

8. Establishing *Astrangia poculata* as a model for investigating symbiosis-immune interplay

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Coral communities worldwide are in decline in part, due to disease. Yet, the intricacies of the relationship between the coral holobiont (coral host, algae, and microbes) and coral immune system remain relatively unexplored. *Astrangia poculata* is a temperate, facultatively symbiotic coral which is able to be readily collected and maintained in the lab with ease. While it is not subject to the same biotic factors as its tropical, reef-building counterparts, these traits enable us to use *A. poculata* as a model for understanding holobiont-immune interplay. This dissertation aims to establish *A. poculata* as such. In particular, the first chapter aims to describe immune system ontogeny across larval development. To investigate immune system ontology, I collected samples across larval stages and evaluated development using gene expression data. In addition to describing the development of the immune system, I will evaluate the relationship between holobiont members (coral host, algal symbiont, and microbiome) and host immunity across the geographic range. I will describe all aspects of the holobiont including microbiome, algal symbionts, and the coral host transcriptomics and immunity using a variety of molecular and biochemical methods. Finally, I will evaluate the interplay between these elements of the holobiont and host immunity to elucidate larger correlations between microbiome diversity and abundance and host immunity within and across populations. Overall, this work will aid in the establishment of *A. poculata* as a model for symbiosis-immune interplay and provide the molecular resources to support future research.

9. Reuniting Science and Society: A Participatory and Evolutionary Approach to Urban Microbiome Research

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Urbanization has drastically altered human-microbial interactions, contributing to a decline in environmental and human microbiota diversity with critical implications for public health. As evolutionary mismatches between our immune systems and modern lifestyles give rise to "diseases of civilization," preserving microbial biodiversity has become urgent. Yet, scientific research alone cannot address this challenge: public engagement and participatory approaches are essential.
We present two synergistic initiatives - Bicocca Sampling Days (BSDs) and UniBiome - that merge scientific inquiry with citizen participation to investigate the urban microbiome and its relationship to human health. BSDs is a reproducible, scalable model for participatory environmental microbiome sampling, tested through year-long campaigns involving 76 undergraduate volunteers who collected over 2,400 samples across urban sites in Milan. Through hands-on activities and pre/post assessments, participants significantly improved their knowledge, self-efficacy, and perceived skills in microbiome sampling.
Complementing this, the UniBiome project, part of the EU-funded MUSA initiative, involved over 160 students across two Italian universities. The project mapped microbial communities in both human (skin and gut) and environmental samples in two seasons, generating a rich dataset that highlights the interconnectedness of urban and human microbiomes. Data shows that factors such as the level of urbanization of the residence town, lifestyle, and time spent in highly urbanized environments significantly shape students' microbiome.
Together, these projects demonstrate how integrating participatory methods with cutting-edge microbiome research can generate high-quality data while fostering public awareness and microbiology literacy. By engaging students and citizens directly in sample collection and analysis, both initiatives build trust, empower communities, and offer a scalable framework for microbiome monitoring and intervention. These efforts affirm that science with society is not only possible but essential to addressing complex, cross-disciplinary challenges at the intersection of urban ecology and human health.

10. A genomic catalogue of cultivated gut bacteria from children in non-industrialised populations

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Gut bacterial culture collections from humans allow for precision medicine from the microbiome by enabling high-resolution metagenomic profiling and phenotypic strain characterisation for the targeted population. However, most gut bacteria from children in non-industrialised countries remain uncultured hence their functions are yet to be characterised. Here, I present the Childhood Acute Illness and Nutrition Network (CHAIN) Bacterial Collection (CBC), a comprehensive catalogue of 1,396 whole-genome sequenced gut bacterial isolates representing 304 unique species (70 novel species) from children under two years across six countries in Africa and South Asia. The CBC more than doubles the existing cultivated species from children and significantly improves read mapping of non-industrialised early-life gut metagenomes beyond the strain-level resolution compared to a public genome database. Further genomic analysis revealed enrichment of metabolic functions associated with human breastmilk- and plant-derived polysaccharides utilisation among key bacteria such as *Bifidobacterium* and *Prevotella*. This valuable resource enables preservation of infant microbiota diversity amid global lifestyle transition and rational design of next-generation probiotics to promote healthy childhood growth and development.

11. Investigating microbe function as the main driver of microbiome composition across animal phyla

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It is now well-established that animal microbiomes significantly affect their host's biology. However, the mechanisms that shape the structure and evolution of animal microbiomes remain poorly understood. Arguably the most prominent theory for microbiome evolution and formation is holobiont theory, which posits that host and microbiome form a single cooperative unit, subject to selection and evolution collectively.
Holobiont theory is an attractive theory, due to the many examples of host-microbiome coevolution. However, the notion that whole microbiomes coevolve with their hosts contradicts observations that microbiomes are typically not heritable and tend to differ significantly even within the same host species.
The "It's the song, not the singer" (ITSNTS) hypothesis (Doolittle & Booth. 2017) accounts for these contradictions by positing that microbiomes are shaped based on microbe function, not taxonomy. This suggests a situation where microbiomes are not formed by the host selectively recruiting coevolved partners, but instead by the reconstruction of a desired metabolic landscape using suitable microbes available in the environment.
This study aims to assess the accuracy of ITSNTS across the animal kingdom. By acquiring and analyzing shotgun metagenomes from 25 phyla (80% of animal phyla), both the metabolic and taxonomic composition of microbiomes can be assessed across the majority of the animal kingdom. If metabolic functions are more conserved than taxonomic composition this would strongly support the ITSNTS hypothesis.

12. Host-symbiont cophylogeny within a population

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Cophylogeny, the study of phylogenetic similarity between interacting organisms, provides insights into the strength and shared evolutionary history of symbiotic interactions. While cophylogenetic analyses have traditionally focused on macroevolutionary relationships between species, increasing availability of paired host and symbiont population genomic data opens up opportunities to explore cophylogeny within populations. However, the causes and manifestations of cophylogeny at the macroevolutionary scale are likely to differ from those at the population level, which remain largely unexplored. In particular, host phylogenies within a population are not congruent across the genome and change dramatically across genomic regions due to meiotic recombination. Here, we leverage recent methodological advancements to infer ancestral recombination graphs in the host and offer an approach to measure cophylogeny within a population across the host genome. This allows us to disentangle genome-wide non-genetic signals, such as shared population structure and transmission mode, from locus-specific host-symbiont genetic interactions. We use single-locus simulations to validate our approach and investigate how processes such as symbiont transmission, population structure, and allele matching can impact cophylogeny within a host population. We then apply this framework to two datasets: (1) the Human Microbiome Project to identify human genetic loci interacting with genetic variation in bacterial symbionts, and (2) mitonuclear interactions in the 1000 Genomes Project to examine cophylogeny in a structured population with known demographic history and transmission dynamics.

13. A global atlas of dietary fiber utilization and production of health-beneficial short-chain fatty acids by the human gut microbiota

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The human gut microbiota has an important task in breaking down dietary fibers, which humans cannot digest due to the limited range of carbohydrate-active enzymes (CAZymes) encoded in the human genome. Saccharides of different structures are selectively degraded by specific intestinal bacteria, ultimately leading to the production of a broad range of metabolites, including short-chain fatty acids (SCFAs), which promotes intestinal barrier function and have been linked to overall human health and protection against inflammatory and metabolic diseases. Intervention studies with dietary fibers often show distinct groups of responders and non-responders, likely due to differences in gut microbiota composition and CAZyme repertoire. This study explores the ability of the human gut microbiota to convert dietary fibers into health-beneficial SCFAs and investigates interindividual variability to move towards personalized approaches to dietary interventions for disease prevention.
We analyzed 9,633 microbial species from the human gut microbiota, identifying more than 600,000 CAZymes, including more than 100,000 that utilize dietary fibers. Through this, we discovered vast differences between bacterial phyla in CAZyme richness, diversity and fiber targets. We linked the fiber-degrading potential of bacterial genomes to the presence of metabolic pathways that produce the SCFAs acetate, propionate and butyrate. We investigated the abundance of dietary fiber-degrading CAZymes and bacteria in 760 individuals including 305 from non-westernized populations, which revealed substantial inter-individual variability, emphasizing that abundant SCFA producers can be targeted by different dietary fibers depending on the individual.
This comprehensive atlas of dietary fiber utilization and SCFA-production by human gut bacteria enhances our understanding of the metabolic potential of the human gut microbiota and facilitates the development of personalized nutraceuticals through targeted promotion of SCFA-producing bacteria by supplementation of selective dietary fiber components, ultimately contributing to improved metabolic outcomes and disease prevention.

14. Combating bacterial resistance to antibiotics in Benin: characterization of phages and perception of their use in human and animal health

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Antibiotic resistance (AMR) is a major public health concern. The discovery of new antimicrobials is strongly encouraged as an alternative solution to antibiotic use. The aim of this study is to assess the potential of Benin phages against multi-resistant pathogenic bacteria (MRB). To this end, the first phase of work focused on the identification by MALDI-TOF and determination of resistance profiles of bacteria from environmental samples (wastewater, sediment and faeces) taken from Lake Nokoué. The second phase was carried out on the same environmental samples to isolate, classify and assess the lytic activity of phages.
The results showed that of the 34 samples analyzed, *Escherichia coli* (32.85%), followed by *Klebsiella pneumoniae* (30.71%), *Acinetobacter baumannii* (15.71%) were the most isolated bacterial species. *K. pneumoniae strains* (97.67%) showed resistance to ampicillin, and all *Pseudomonas spp* strains (100%) showed resistance to aztreonam, imipenem, ceftadizime, cefipime and ciprofloxacin. The blaSHV, blaTEM and blaOXA genes were the most characterized. Forty-two phages were isolated, mainly against *K.pneumoniae*, *P. aeruginosa*, *A.baumanni* and *E. coli*, with an overall success rate of 35%. All phages formed clear lysis plaques with high titers of up to 10^{10} PFU/mL Although some phages showed a narrow host range, others were able to infect several multidrug-resistant clinical strains, including those of *A. baumannii* and *P. aeruginosa*. They showed good stability between pH 3 and 9, as well as at temperatures ranging from 4°C to 50°C, but high sensitivity to extremes of acidity and heat.
This study demonstrates that locally isolated phages have favorable characteristics for therapeutic use against multidrug-resistant bacteria. It highlights that the effective adoption of phage therapy in Benin requires a comprehensive understanding of bacterium-phage-host interactions within natural ecosystems and underscores the role of environmental viromes in addressing antimicrobial resistance (AMR).

15. 'Decoding' Quorum sensing (QS) homologues in the key members of the gut microbiota: A dual *In silico* and *In vitro* approach

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The gut microbiota is crucial for host health. Microbiota populations are dynamic, and their relative densities are monitored via intercellular communication systems, of which quorum sensing is the best studied. By quorum sensing, bacteria coordinate behaviour in response to changes in population density by releasing chemical signals called autoinducers (AIs). While quorum sensing is well-studied in pathogens, its role in gut symbionts remains poorly understood. Our lab's prior research showed that, during antibiotic treatment, manipulating the quorum sensing signal mediating interspecies signaling, AI-2, altered gut microbiota composition of the major phyla, favoring Bacillota over Bacteroidota. In Bacillota, production of the interspecies signal AI-2, via the synthase LuxS is prevalent, and autoinducer peptide signals are also common as species-specific quorum sensing signals. However, in Bacteroidota signalling mechanisms are less known. Recently, our group showed that *Bacteroides* produce pyrazinone signals as a novel quorum sensing signal, produced by theronine dehydrogenase, encoded by the *tdh* gene.
Here, we have used a bioinformatics approach to search for quorum sensing signal synthase homologues involved in production of AI-2 and pyrazinone in gut microbiota members belonging to the Bacillota and Bacteroidota. Our analysis shows that *luxS* is prevalent in Bacillota, while the *tdh* and the associated threonine degradation pathway gene *kbl* are prevalent in the Bacteroidota. Preliminary results reveal that roughly 62% accounts for *tdh-kbl* homologues tends to co-occur in Bacteroidota, compared to only 12% in Bacillota. Moreover, the co-occurrence of *tdh-kbl* suggests a potential co-regulation of the expression of these two genes and we plan to study their regulation under different environmental conditions to understand the mechanism involved in regulating pyrazinone biosynthesis in Bacteroidota.
Additionally, to validate the bioinformatics data, we have implemented assays using reporter strains to detect the activity of AI-2 and pyrazinones quorum sensing signals. Overall, this study will help to provide insights into bacterial communication mechanisms involved in gut microbial communities.

16. Acute Physiological Responses to Treatment with a Non-Absorbable Antibiotic

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For human and veterinary applications, non-absorbable drugs are often considered safe due to their limited systemic absorption. However, we hypothesize that their impact on the gut microbiome leads to systemic changes. To investigate the potential systemic effects of non-absorbable agents, we focused on vancomycin, a non-absorbable glycopeptide antibiotic. We gavaged 8-9-week-old specific pathogen free (SPF, n=65) or germ-free (GF, n=10) mice with 1 or 3 doses of vancomycin, or with PBS/saline (negative control). Using 16S rRNA sequencing, we confirmed that the antibiotic significantly altered the α- and β-diversity of the SPF mouse microbiota. Hybrid LC-MS metabolomics revealed a dozen metabolites, mostly amino acids, in both the portal and systemic circulation that were altered in vancomycin-treated conventional mice. Comparison of the GF and SPF metabolomes also indicated that microbial production of phenol was significantly decreased in GF mice and following vancomycin treatment. Hepatic transcriptomics identified >50 differentially expressed genes, and KEGG pathway enrichment analysis revealed upregulation of the steroid biosynthetic pathway in the 3-dose vancomycin-treated mice versus PBS-controls. Using flow cytometry to assess effects of dysbiosis on the innate and adaptive immune response, we found an upward trend in splenic monocytes ($CD19^{-}CD3^{-}CD11b^{+}Ly6C^{+}$) in 3-dose vancomycin-treated mice at Day 4; consistent with the elevation observed 12, 24 and 48 hours after a single dose. Ten days after vancomycin treatment began, there were significant decreases in the frequencies of splenic B cells (CD19+) and cytotoxic T cells ($CD45^{+}CD19^{-}TCRb^{+}CD8A$) together with robust responses in the colon, mesenteric lymph nodes, and Peyer's patches. These findings show that vancomycin-induced microbiome disruption elicits acute systemic effects, including metabolic, transcriptional, and innate and adaptive immune changes, and underscores the need to consider the systemic implications of microbiome-alteration from luminally active agents.

17. Antibiotics damage the colonic mucus barrier in a microbiota-independent manner

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Antibiotic use is a risk factor for the development of inflammatory bowel diseases (IBDs). IBDs are characterized by a damaged mucus layer, which does not separate the intestinal epithelium from the microbiota. Here, we hypothesized that antibiotics affect the integrity of the mucus barrier, which allows bacterial penetrance and predisposes to intestinal inflammation. We found that antibiotic treatment led to breakdown of the colonic mucus barrier and penetration of bacteria into the mucus layer. Using fecal microbiota transplant, RNA sequencing followed by machine learning, ex vivo mucus secretion measurements, and antibiotic treatment of germ-free mice, we determined that antibiotics induce endoplasmic reticulum stress in the colon that inhibits colonic mucus secretion in a microbiota-independent manner. This antibiotic-induced mucus secretion flaw led to penetration of bacteria into the colonic mucus layer, translocation of microbial antigens into circulation, and exacerbation of ulcerations in a mouse model of IBD. Thus, antibiotic use might predispose to intestinal inflammation by impeding mucus production.

18. Natural variation of *Wolbachia* antiviral protection strength in *Drosophila melanogaster*

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Wolbachia are maternally transmitted intracellular bacteria, widely prevalent in insects, known to confer antiviral protection to their hosts, such as *Drosophila melanogaster* and mosquitoes. Currently, deployment of *Wolbachia*-carrying mosquitoes in the wild is a successful strategy to block the transmission of arboviruses in endemic areas, reducing dengue cases by 77%. However, the mechanisms underlying *Wolbachia*-mediated antiviral protection remain unclear. Higher proliferation of *Wolbachia* positively correlates with the strength of antiviral protection, and other induced phenotypes, but also has a cost for the host. We introduced 174 *Wolbachia* variants into the same *D. melanogaster* isogenic background and tested their growth inside the host and antiviral strength upon Drosophila C virus infection. We performed a Genome Wide Association Study (GWAS) to identify polymorphisms associated with these phenotypes. While the GWAS identified polymorphisms associated with growth, the strength of protection was not associated with specific polymorphisms independently of *Wolbachia* titres. There is a general correlation between the antiviral protection strength and the levels of *Wolbachia* inside the host. Understanding how *Wolbachia* titers are regulated is, therefore, important to understand its biology and modulation of antiviral activity.

19. Persistence of an influential passenger: the endosymbiotic association of *Wolbachia* with the neotropical fly *Drosophila willistoni*

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The endosymbiotic bacterium *Wolbachia* is widespread in arthropods, largely due to its remarkable capacity to manipulate host reproduction and confer fitness-related traits. These traits—such as antiviral protection, altered host behavior, and increased fecundity—are often modulated by environmental factors, especially temperature. Temperature also affects *Wolbachia* bacterial densities (titer) and maternal transmission efficiency. While high *Wolbachia* titers are often necessary for beneficial traits like pathogen protection, they may also impose costs to the host. Despite extensive research in model organisms, little is known about how these dynamics play out in non-model Neotropical species, where *Wolbachia* presence and diversity remains underexplored.

In *Drosophila willistoni*, *Wolbachia* exhibits variable prevalence, with two infection types reported: systemic (present in all tissues) and restricted (limited to neural and germline cells). Unlike other hosts, *Wolbachia* in *D. willistoni* does not appear to manipulate reproduction, raising questions about its persistence. Here, we investigated (1) *Wolbachia* titer stability across temperatures, (2) associations between titer and strain variation, and (3) links between titer, host fitness, and antiviral protection.

We analyzed *D. willistoni* isolines from the Atlantic rainforest, identifying high-titer (HT) and low-titer (LT) infections. HT strains showed systemic distribution and stable titers across temperatures and host ages, while LT strains were unstable and lost over generations. Genomic analysis revealed HT strains were closely related to *w*Wil and *w*Au, whereas LT strains resembled *w*Mel and carried cytoplasmic incompatibility (CI) genes. Despite high titers and systemic infection, HT-infected flies exhibited no antiviral protection against Drosophila C virus (DCV).

Our findings demonstrate the coexistence of two divergent *Wolbachia* strains in *D. willistoni*, with distinct persistence strategies. The absence of CI or antiviral protection in HT strains suggests alternative mechanisms maintain this infection. This study highlights the diversity of *Wolbachia*-host interactions and the need to explore symbiont persistence in ecological contexts.

20. Coevolution of the bacterium Bacteroides thetaiotaomicron and the host mucosal immunity mediated by Polysaccharide Utilization Loci

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The mammalian intestine is inhabited by a complex microbial community, i.e., gut microbiota. The gut microbiota plays a crucial role in establishing a symbiotic relationship with the host by fermenting undigestible nutrients, producing essential nutrients, fostering immune development and tissue growth, and providing pathogen defense. Microbial diversity and stability of gut microbiota are essential, but factors like diet, infections, and medications commonly cause imbalances, which are associated with increased gut disorders such as inflammatory bowel disease, metabolic syndrome, and even with susceptibility to opportunistic infections. Bacterium Bacteroides thetaiotaomicron is a predominant gut microbiota member, specialized in the consumption of fibers and plant polysaccharides, as well as the host glycans. We previously showed that the genes responsible for the degradation of polysaccharides, i.e., Polysaccharide Utilization Loci (PULs), were highly targeted during the evolutionary adaptation to the mouse gut, and this was diet independent. One of the ways in which B. thetaiotaomicron interacts with the mammalian host is through the immunoglobulin A (IgA). IgA has two roles: it helps colonization of commensal bacteria and eliminates pathogenic microorganisms. Our main hypothesis is that the PULs synergistically co-evolved with IgA. By employing techniques such as experimental evolution in laboratory conditions and in mice lacking partial or complete adaptive immune system (IgA-/- and Rag1-/- knockouts, respectively), whole-genome sequences, IgA-SEQ of gut bacteria coated with IgA, and Immune Repertoire Sequencing, we aim to identify key mutations that modulate B.theta-IgA interaction. Characterizing mutations that enhance interaction with IgA and increase its diversity will provide insights into the role of IgA in the mechanisms underlying genetic and functional composition of the gut microbiota, as well as allow us to propose novel strategies to avoid diversity loss and promote its recovery. Our results will provide a unique perspective on the symbiotic relationships essential for human physiology and bacterial evolution.

21. Genomic analysis unravels distinct co-evolution patterns of *Sitophilus spp.* with their endosymbiotic bacteria

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Most insects thriving on unbalanced diets have evolved obligate associations with intracellular symbionts (endosymbionts) that complement their diet with nutrients lacking in their habitat. Endosymbiosis is a fundamental driver of evolutionary success, enabling hosts to adapt to diverse environments while facilitating niche expansion and phenotypic diversification. However, these obligate associations are not permanent and endosymbionts have been lost or replaced during insects' evolutionary history. Phylogenetic studies on weevils from the *Sitophilus* genus showed a recent endosymbiont replacement (≈30 KYA) by a Gram-negative bacterium of the *Sodalis-allied* clade, constituting an ideal model to study the evolutionary processes of endosymbiogenesis. The *Sitophilus* genus consists of 14 described species and shows a variety of host-bacteria interactions and ecological niches. *S. oryzae* and *S. zeamais* infest both cereal fields and cereal-containing silos. However, *S. granarius* is restricted to silos, while other species dwell in trees, such as *S. rugicollis* that infects the seeds of the *Myrtaceae* family. This study investigates the host and endosymbiont genetic hallmarks underlying the contrasted phenotypic diversification observed. We revealed differences in endosymbiont genome size and content, showing distinct levels of genome degradation. Following a metagenomic assembly approach, we discovered the co-occurrence of multiple symbionts in *Sitophilus* weevils. Focusing on the five *Sodalis* endosymbionts detected, we reconstructed a pangenome showing a core genome composed of around 400 genes and accessory genes ranging from 4 to 352 depending on the *Sodalis* studied. These findings provide insights into the molecular bases of endosymbiogenesis and the varied trajectories of host-symbiont co-evolutionary routes.

22. Unraveling the impact of protein synthesis inhibitors on *Bacteroides uniformis*

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Protein synthesis inhibitors (PSIs), such as macrolides like erythromycin, are textbook bacteriostatic antibiotics. They have been associated with strong dysbiosis within the human gut microbiome and have also been shown to induce lysis in certain gut bacterial species. In this study, we aim to clarify the molecular mechanisms by which macrolides impact *Bacteroides uniformis* and broaden our understanding to encompass other strains and additional PSIs. Our findings indicate that various PSIs can induce lysis in *B. uniformis* and survival assays revealed that clindamycin and erythromycin exert the strongest effects. We used a transposon library of *B. uniformis* to enrich for mutants surviving erythromycin treatment and conducted follow-up experiments to measure their survival and minimum inhibitory concentrations (MIC). In a next step, this selection of mutants will be expanded, and the disrupted genes responsible for the loss of susceptibility will be identified. These genes will serve as a foundation for further experiments aimed at unraveling the molecular mechanisms underlying lysis. Finally, we will utilize a panel of 48 different *B. uniformis* strains to assess survival for each strain. By integrating the obtained results, we want to determine whether the genes identified from the transposon library mutants can be used to predict the effects of PSIs. Altogether, our results will shed light on the actual mode of action of PSIs in gut microbes, which might advance our understanding of why these antibiotics induce long-term dysbiosis in the gut microbiota of patients.

23. Metagenome-assembled genomes of Estonian Microbiome cohort reveal novel species and their links with prevalent diseases

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Recently established large biobanks have enabled the systematic study of the relationship between the microbiome and human health on a large scale. New approaches, such as *de novo* metagenome assembly, make it possible to include many previously unknown bacterial species in these studies and to move beyond simple association studies toward genome-resolved analyses. However, despite being essential, these advanced approaches remain challenging to implement, especially at a large scale.
Here we introduce a strategy for population-based early disease detection. At first step, we first expand the human gut bacterial reference database by incorporating population-specific bacteria identified through metagenome-assembled genomes. From 1,878 samples with deep sequencing, we reconstructed 84,762 MAGs representing 2,257 species, 15.6% of which were novel. Using this expanded database, we profiled the microbiome of all 2,509 Estonian cohort samples and conducted species-level association studies across all common diseases. We identified significant associations with 15 of the 33 diseases analyzed, including novel species associations in 7 diseases.
To assess within-species genetic diversity, we introduced the Strain Richness Index (SRI), a simple metric reflecting strain-level variation based on metagenome-assembled genome (MAG) data. Using SRI, we selected *Odoribacter splanchnicus* for further analysis and identified a specific strain (N1) significantly associated with gastritis and duodenitis, a signal not detected at the species level.
This scalable strategy provides both a methodological framework for future microbiome research and a valuable resource, such as SRI metrics for key gut species, to guide downstream strain-level analyses.

24. A story of a frog, a fungus and some bacteria: Microbiome mediated colonisation resistance via siderophore production

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Batrachochytrium dendrobatidis (Bd) is a fungal pathogen responsible for chytridiomycosis, a disease that has caused catastrophic declines in amphibian populations worldwide by infecting amphibians' skin. This infection disrupts skin permeability and electrolyte balance, leading to cardiac arrest and death. One of the host's primary defence strategies is nutritional immunity—limiting access to essential metals like iron, zinc, and manganese—to inhibit pathogen growth and virulence.
In parallel, the amphibian skin microbiome plays a crucial role in chytridiomycosis resistance by producing antifungal metabolites. However, the impact of host-driven metal restriction on these microbial communities remains largely unexplored. Our preliminary data suggest that iron limitation triggers skin bacteria to produce siderophores, specialized iron-chelating molecules with strong antifungal properties. This points to a potentially important synergy whereby host nutritional immunity and skin commensals' siderophore production act together to reduce iron bioavailability, critically limiting *Bd*'s access to this essential micronutrient.
To investigate this interaction, we isolated bacterial strains from the skin of *Alytes obstetricans* and assembled a minimal bacterial community representing the most abundant bacterial phylogroups. Using a high-throughput screening method, we found that most isolates, tested so far, produce siderophores under iron limitation, and that environmental factors such as pH and carbon source significantly influence siderophore production.
Importantly, our functional assays revealed that Bd: 1) cannot exploit any of the tested siderophores, 2) lacks competitive iron acquisition systems, and 3) cannot degrade siderophores. This suggests that microbial siderophores effectively reinforce host-imposed iron limitation, creating an environment hostile to Bd.
Together, these findings reveal a novel mechanism by which the amphibian skin microbiome complements nutritional immunity, enhancing protection against Bd. Understanding this interplay could pave the way for microbiome-based strategies to mitigate chytridiomycosis and aid amphibian conservation.

25. Role of phosphite in gene regulation of *T. atroviride* and interaction with other organisms

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As the global population continues to grow, the demand and consumption of food has increased, leading to the search for alternative strategies to meet this demand. Among these strategies, the use of plant growth-promoting microorganisms (PGPMs) that are environmentally friendly, as well as other beneficial molecules, has gained attention. Phosphites are molecules considered to promote plant growth and act as inhibitors of various phytopathogenic bacteria and fungi. However, little is known about the effects that phosphites may have on beneficial microorganisms involved in plant growth promotion. In this study, we performed a transcriptomic RNA-Seq analysis of the fungus *Trichoderma atroviride*, a well-known growth-promoting fungus and biocontrol agent against various phytopathogenic fungi, widely used in agriculture worldwide.
We evaluated the effect of potassium phosphite (Phi) on gene expression in *T. atroviride* using RNA-Seq, and we also assessed the influence of Phi on *T. atroviride* during its interactions with plants and phytopathogenic fungi. The results showed that low concentrations of Phi promote the growth of *T. atroviride* by activating genes related to the cell cycle and growth. Moreover, direct confrontation assays between *T. atroviride* and *Rhizoctonia solani* revealed that the presence of Phi in the medium enhanced the inhibition of the phytopathogen's growth at a faster rate. This work represents the first report on the effect of Phi at the gene expression level in a beneficial fungus widely used in agriculture.

26. Decoding Neuronal Aging in *Hydra*: A Non-Senescent System Shaped by Microbiota

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Life history processes such as aging result from a complex interplay between genetic endowment and environmental exposures during a lifetime. For instance, the molecular and cellular hallmarks of aging include changes in the microbiome. As aging research advances, so does the need for experimental animal models that allow a functional understanding of the genetic and environmental factors involved. In the freshwater polyp *Hydra*, a non-aging invertebrate with an ancient phylogenetic history, biological immortality is largely driven by continuously self-renewing stem cells, regulated by Wnt and FoxO signaling. Both these pathways are influenced by microbial cues. FoxO deficiency disrupts stem cell maintenance, immune balance, and AMP expression, impairing microbiota selection (Boehm, 2012; Mortzfeld, 2018). Recently, we have shown that microbial signals affect neural circuit formation (Noack, 2025) and behavior (Giez, 2023). Here, we use FoxO KD mutants, which exhibit an aging phenotype, including a changed microbiome, to address at a mechanistic level how microbial signals may influence the aging process through the three-way interaction of genes, neural circuits, and behavior. We found that knocking down TF FoxO severely impacts feeding behavior by impairing mouth opening. Current efforts are focused on developing new transgenics with neuronal subpopulation-specific markers to gain a deeper understanding of the microbiome's influence on an aging nervous system.

27. Microbiome Disruption by Environmental Plasticizers: A Multi-Model Approach

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Plasticizers are widespread environmental contaminants with known endocrine-disrupting effects, but their impact on the gut microbiome (GM) remains largely underexplored. We assessed the effects of plasticizers on GM composition using *in vitro* and *in vivo* models. To this aim, we exposed human fecal material and a synthetic bacterial community (Comm20) to ten plasticizers (0–1024µM) for 24 hours. We found a dose-dependent impact on community growth, particularly for the plasticizers DEHP, DEHT, and DINCH. Based on this, we selected five plasticizers (DEHP, DEHT, BBP, ATBC, and DOA/DEHA) extended exposure of 3x24 hours followed by 16S rRNA sequencing. This assay revealed induced marked alterations in bacterial composition by DEHP, which is why we further investigated its impact on the gut microbiome *in vivo*.

We colonized germ-free B6NTac mice with Comm20 and administered DEHP (500 mg/kg/day) for five days. Although alpha and beta diversity remained unchanged, DEHP changed the abundance of specific taxa: *Bacteroides fragilis* and *Eggerthella lenta* decreased, while *Bacteroides thetaiotaomicron* and *Clostridium perfringens* increased. To evaluate the effects of a longer and environmentally relevant exposure, we exposed male Wistar rats to DEHP (48 mg/kg/day) from postnatal day (PND) 25 to 90. Fecal samples from PND25, 53, and 90 underwent 16S rRNA sequencing. Alpha diversity was unaffected, but beta diversity was significantly altered at PND53. Members from the Muribaculaceae family had its abundance decreased at PND53 and 90, while *Paramuribaculum* increased only at PND90.

Notably, even short-term exposure in a simplified community altered specific bacterial abundances without changing the overall microbiome diversity. Conversely, long-term exposure in a complex microbiota resulted in broader community shifts, including beta diversity alterations and changes in key genera. Together, the results demonstrate that DEHP exposure leads to microbiome alterations specific to both the host model and exposure regimen, reinforcing the relevance of integrating microbiome endpoints into toxicological studies of environmental pollutants.

28. Exploring the molecular basis of “optimal pairing” on Cnidarian-Dinoflagellate symbiosis

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Endosymbiosis has driven major evolutionary innovations. In marine ecosystems, it underlies the essential relationship between cnidarians and dinoflagellates, a partnership that sustains coral reefs. Yet, the molecular cues that govern symbiotic specificity remain poorly understood, especially in early life stages of the host.
Here, we investigated symbiont compatibility in the sea anemone model organism *Exaiptasia diaphana* (Aiptasia) by exposing larvae and polyps to two symbiotic dinoflagellates: the native *Breviolum minutum* (SSB01) and the thermotolerant *Durusdinium trenchii* (Clade D). We assessed infection rates, colonization dynamics, and photosynthetic efficiency.
Aiptasia displayed stronger compatibility with SSB01 in all metrics tested, while Clade D exhibited reduced infection success and slower colonization. At the cellular level, immunohistochemistry revealed distinct molecular environments within the symbiosomes, with SSB01 symbionts being significantly more enriched in proteins linked to cellular signaling and nutrient transport. Transcriptomic analysis further supported this, revealing increased expression of nutrient transport genes in SSB01 hosting larvae.
While previous research primarily contrasted symbiotic and non-symbiotic interactions in the larval state, our study further investigated the compatibility within symbiotic dinoflagellate pairing, allowing us to pinpoint the molecular basis for the “optimal” pairing. This work advances our understanding of symbiotic specificity and may inform coral conservation strategies under climate change.

29. Interplay of Bioactive Peptides and the Gut-Skin Axis: A Novel Perspective on Psoriasis Therapy

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Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by keratinocyte hyperproliferation and immune dysregulation, involving the activation of Th1/Th17 cells and elevated levels of cytokines such as TNF-α, IL17, and IL-23. Although current treatments range from topical corticosteroids to systemic biologics, recent studies highlight the importance of the gut–skin axis in psoriasis pathogenesis, where gut dysbiosis and increased intestinal permeability contribute to systemic inflammation. This emerging link underscores the need for therapeutic strategies that address both gut and skin homeostasis. We developed a PhD project hypothesizing that bioactive peptides (BPeps) derived from natural dietary sources can modulate inflammation and epithelial barrier integrity in both the gut and skin, offering a novel therapeutic avenue for psoriasis based on host–microbe interactions and personalised nutraceuticals. Selected using bioinformatics and machine learning tools, 4 BPeps were synthesized and will be screened in intestinal cell models to evaluate their immunomodulatory effects in gut dysbiosis and psoriasis. This includes profiling cytokine expression and analyzing NF-κB and JAK-STAT signaling pathways. Promising peptides will undergo simulated gastrointestinal digestion, and their colonic fractions will be tested in gut fermentation models to assess effects on microbiota composition, short-chain fatty acid production, and barrier function. Absorbed peptide fractions and microbiota-derived metabolites will then be applied to in vitro and ex vivo 3D psoriatic skin models to assess their influence on inflammation, tissue regeneration, and skin barrier restoration. In parallel, intact BPeps will be directly tested on psoriatic skin to evaluate local activity. This approach enables a comparative evaluation of peptide effects in both gut and skin systems and the gut-skin axis. By bridging immunonutrition, microbiome science, and dermatology, this research advances novel peptide-based therapies and deepens our understanding of host–microbe symbioses in chronic inflammatory diseases

30. Rapid wire: The fast pace of endosymbiont evolution in novel hosts

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Endosymbiotic bacteria of the genus *Spiroplasma*, a member of the mycoplasmas, are known to infect a wide range of arthropods. The occurrence rate of *Spiroplasma* in arthropods is estimated to be between 5% and 10% and are involved in array of symbiotic relationships – from commensalism to pathogenicity. These symbiotic relationships are short-lived on an evolutionary time scale, with endosymbionts often jumping to different host species - a phenomenon known as host shifting. To better understand how host-shifting occurs, we performed experimental evolution using the *Drosophila-Spiroplasma* system. We transfected different *Spiroplasma* strains into two novel Drosophila host and allowed them to evolve for 21 host generations. The aim was to investigate whether and how *Spiroplasma* can evolve in a different host species and to identify what genetic factors are responsible for such adaptations. To end this, we initially performed fitness assay at the start and at the end of experiment. To corroborate the phenotypic data, we performed re-sequencing at both start and the end of experiment, and measured endosymbiont titre across generations. We found that different *Spiroplasma* strains can adapt differently in different hosts. The fecundity of the new host across all the experimental replicates differs from that of the native hosts, indicating phenotypic changes over time. Moreover, we observed changes in host longevity across different experimental lines, supporting the idea of host/line-specific evolutionary trajectories. the genomic analysis of the adapted symbionts will provide insights into the genetic changes potentially associated with the observed phenotypic differences. This study highlights the evolutionary plasticity of endosymbionts like *Spiroplasma* and provides experimental evidence that they can rapidly adapt to new host environments. Our findings underscore the importance of both phenotypic plasticity and genetic change in facilitating host shifts.

31. Association between MHC genetic variability and T cell receptor repertoire richness in humans

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Recognition of pathogens by the adaptive immune system requires self/non-self-discrimination, mediated by major histocompatibility complex (MHC) molecules that present peptides on cell surfaces. T cells, through their T cell receptors (TCRs), survey these MHC:peptide complexes to recognize pathogen-derived peptides and initiate immune responses. MHC molecules are genetically encoded by the highly polymorphic MHC locus, which harbors thousands of alleles in humans. In contrast to these diverse but genetically hard-wired MHC proteins, TCRs are generated through somatic V(D)J recombination, a process that splices together variable gene segments to produce hypervariable receptors. However, variability is restricted during T cell development in the thymus: while T cells are positively selected for recognizing MHC:peptide complexes, negative selection eliminates overly self-reactive T cells to reduce the risk of autoreactivity.
The immense variability of TCRs together with the restriction during thymic development has made understanding TCR repertoire dynamics challenging. Sequencing results suggest that the TCR repertoire is influenced by factors such as age, disease history, the microbiome, and the MHC genotype. Here, we analyze TCR repertoire data from public human datasets to investigate differences in repertoire diversity, richness, and structural composition. Various estimators were evaluated to quantify functional diversity from both the antigen recognition (TCR) and antigen presentation (MHC) side. Preliminary findings indicate that, after adjusting for the effect of age and infection status, TCR repertoire richness is non-linearly associated with the MHC variability, indicating a TCR repertoire maximum at a medium-to-high number of unique MHC alleles within an individual. In future work, we aim to use experimentally generated TCR repertoires from sticklebacks, a fish model used to study natural genetic variation and evolution, to investigate how the microbiome affects repertoire characteristics.

32. Mycobacteriophages remain infective after internalization into pulmonary epithelial cells

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Bacteriophages are classically known for their role as bacterial predators; however, they are now increasingly recognized as active players in eukaryotic biology. While it has been well established that phages can cross the cellular membrane, the extent of their interactions with eukaryotic cells remains largely unclear. For our research, we use a genetically modified TM4 bacteriophage that naturally infects mycobacteria, including the pathogen *Mycobacterium tuberculosis*. Our phage injects the $mCherry_{bomb}$ gene into its host and, following expression, the fluorescent reporter accumulates in the bacteria. Our first experiments involved staining the phage DNA with SYTOX Green, allowing us to corroborate that they indeed could be internalized into A549 human pulmonary epithelial cells. Next, we added LysoTracker to phage-treated cells, a dye that stains acidic compartments including lysosomes. We found that the signal intensity of LysoTracker increases after phage treatment, reaching its peak after two hours of phage incubation rather than overnight. Finally, to reveal phage infectivity after internalization, we incubated phages with cells previously infected with *M. tuberculosis*. As evidenced by the expression of mCherry in bacteria, we showed that, at the times used in this experiment, phages are capable of reaching and infecting intracellular bacteria. Overall, we show that TM4 can be internalized into A549 cells and remain infective afterwards. Now we are focusing on establishing the bacteriophage's mechanisms of entry and intracellular trafficking, and how the eukaryotic cell responds to this event.

33. Influence of host-microbe-environment interactions to structure of microbial community in Hydra-microbiome context

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Microorganisms play essential roles in all eukaryotic hosts, from nutrient acquisition to protection against pathogens. A key factor influencing microbial function is community composition, which can be shaped by external environments, microbe-microbe interactions, and host-microbe dynamics. In this study, we investigate how microbial composition and function respond to external metabolite perturbations using the freshwater cnidarian *Hydra* as a model organism.
We analyzed 16S rRNA and metagenomic data from *Hydra*-associated microbiomes exposed to a range of metabolite supplements to identify associations changes in microbial diversity and functional potential. Our results show that some metabolite categories, particularly amino acids, peptides and analogues; as well as carbohydrates and carbohydrates conjugates, tend to alter microbial alpha and beta diversity. The direction and extent of these changes were metabolite-specific. For example, L-methionine increased alpha diversity, while L-arginine reduced it. Thereby we observed two dominant microbiome community states – one dominated by the native main colonizer *Curvibacter*, associated with high alpha diversity and one dominated by *Pseudomonas*, which exhibited lower alpha diversity. By integrating 16S rRNA data with metagenomic derived microbial genomes, we explored functional shifts in the microbiome. We found that metabolically related compounds, such as L-arginine, L-ornithine, and putrescine, led to similar functional profiles. This result indicates common microbial community shifts dominated by metabolic functionality.
In the next step, we will incorporate microbe-microbe and host-microbe interactions using genome-scale metabolic modelling approach. We aims to reveal the mechanistic basis of how and to what extend metabolic host-microbe-environment interactions influence microbial community structure and function.

34. Flexible Amoebozoan photosymbioses: Fitness and plasticity in amoeba-algal endosymbiotic interactions

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Photosymbiosis is a form of symbiosis between non-photosynthetic eukaryotes and microalgae. Although photosymbioses have been reported across a wide range of taxa, research has mainly focused on only a few models, e.g. cnidarians and ciliates, largely because of the challenges in culturing and experimental methods in other lineages, particularly in amoebozoan. Despite more than 100 years of research, only a few amoeba-algal symbioses were described, and the mechanisms by which photosymbiosis is established and their evolutionary significance remain unclear.
To understand from a broader perspective how photosymbiosis affects host fitness and how flexible it is, we aimed to evaluate the plasticity of photosymbiotic relationships in a photosymbiotic amoebozoan, *Mayorella viridis*, that hosts green algal symbionts *Chlorella* spp. inside their cells.
Through various chemical treatments, we found that a herbicide, 2-amino-3chloro-1,4-naphthoquinone (ACN), could induce the removal of algal symbionts from the amoebae host cells. In contrast, photosynthesis inhibitor 3-(3,4-chlorophenyl)-1,1-dimethylurea (DCMU) could not induce an apo-symbiotic (“bleached”) state, suggesting that photosynthesis activities may not be related to establishing this amoeba-algal symbiosis.
While apo-symbiotic amoebae could grow to the same extent as symbiotic ones with enough food supply, their survival rate under starvation conditions was lower than symbiotic ones. Furthermore, by feeding two *Chlorella* strains to apo-symbiotic *M. viridis* cells and evaluating their symbiotic abilities, we found the differential ingestion efficiency and retention rates of algal cells depending on algal strains. In addition, cytological and gene expression analyses have allowed more detailed characterizations of this amoeba-algal symbiosis.
Our study suggests that the symbiotic abilities of algae and the fitness of host amoebae vary depending on phylogenetic relationships and environmental conditions, which provides a flexible basis for this photosymbiosis. Moreover, we will report a photosymbiotic amoebozoan newly isolated from a freshwater environment as a novel model organism.

35. How does IgA shape the gut microbiome dynamics

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The gastrointestinal tract is home to a complex community of commensal bacteria – known as the microbiota - which provide beneficial functions for human health. However, the forces that shape the predictable dynamics of the gut microbiome assembly remain largely unknown. A major mechanism through which the host can shape the microbiota is via the intestinal immune system, and Immunoglobulin A (IgA) is the most common antibody in the gut. In my PhD project, I'll address these questions: how do host IgA and maternal IgA shape initial microbiome assembly? How does IgA influence microbiome stability? How does IgA affect individual microbe-microbe interactions?
By sampling immune-deficient and immune-competent mice from 2 weeks old to 2 months old frequently and challenging the gut microbiome with a medium dose of antibiotics, I have built a rich longitudinal dataset to address these questions. So far, through IgA ELISA and flow cytometry, I have found that the week before and after weaning is a crucial period. Mice obtain IgA from their mother prior to weaning, and immune-competent mice gradually generate their own IgA postweaning. Moreover, antibiotic perturbations appear to cause an increase in IgA coating percentage in the gut microbiota. Now, I am integrating this immune data with absolute metagenomics data (sequencing currently underway) to understand how these immune changes influence microbiome dynamics.

Map of GIMM – Oeiras Site

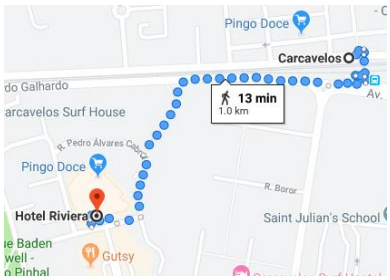
Internet access (Wi-Fi at the GIMM)

Login: IGC | Password: chemokine

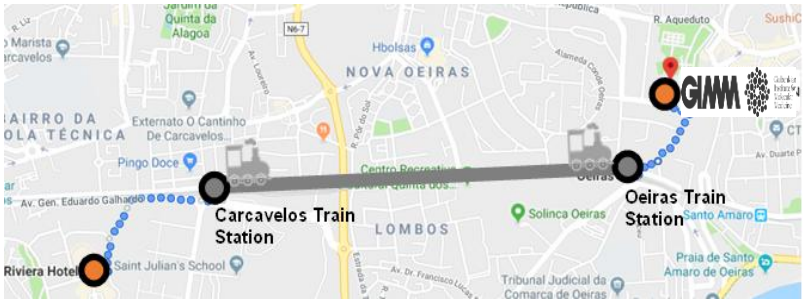
How to get to the GIMM – Oeiras Site

GIMM – Oeiras
Rua da Quinta Grande, nº6. 2780-156 Oeiras
https://maps.app.goo.gl/oZBTeLQriLVKT2xU8

1) From Riviera Hotel, walk to Carcavelos train station.



2) Get the train (direction Cascais > Lisbon Cais do Sodré), exit in Oeiras (just one stop after Carcavelos) and walk for about 7 minutes to the Institute:



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