TransEvo

DFG Research Training Group for
Translational Evolutionary Research

Job Advertisement

The Kiel University, the University Hospital Schleswig-Holstein (UKSH), the Max-Planck-Institute for Evolutionary Biology in Plön, and the Research Center Borstel (Leibniz Lung Center) offer

***7 PhD positions* within the Research Training Group *"Translational Evolutionary Research"* (3 year and 2.5 months fixed-term positions, 65% TV-L, TV-ÖD E13)**.

The graduate school aims at studying the relevance of evolutionary principles to applied problems. Unintended outcomes of human intervention often result from actions that influence natural selection. For example, the usage of antibiotics or anti-cancer drugs in medicine, of pesticides in agriculture, or human perturbation of the earth's ecosystems directly change natural selection and thereby affect the evolution of organisms. Surprisingly, evolutionary concepts are only rarely used to improve our understanding of these applied challenges and to develop new sustainable solutions. The RTG will train PhD students in the competences to do so.

This RTG is a joint initiative of Kiel University, the University Hospital Schleswig-Holstein (UKSH), the Max-Planck-Institute for Evolutionary Biology in Plön, the Helmholtz Center for Ocean Research Kiel (GEOMAR), the Research Center Borstel (Leibniz Lung Center), the Kiel Institute for the World Economy (IfW) and the Max-Rubner-Institute Kiel (MRI). The RTG offers an internationally competitive research environment with state-of-the-art facilities. The participating groups use a variety of different methods, including evolutionary experimental, molecular, genomic, and theoretical approaches.

The graduate program starts with a **rotation period of 2.5 months followed by a PhD project of three years** (employment by one of the involved institutions) including seminars, courses and workshops. The language of the graduate school is English. PhD projects cover the following topics:

1. *PI Remco Stam: Effects on local pathogen populations in the context of crop protec-tion.*
2. *PI Eva Stukenbrock: Recent evolutionary developments in a global wheat pathogen*
3. *PI Tal Dagan: The origins of antibiotic resistance plasmids*
4. *PI Heike Siebert: Analysis methods for phylogenetic networks*
5. *PI Stefan Niemann: Evolution-informed antibiotic therapy against Mtbc strains*
6. *PI Hinrich Schulenburg: Evolution-informed antibiotic therapy against PA strains*
7. *PI Arne Traulsen: Theoretical modeling of tumor-microbiome ecology in pancreatic cancer evolution*

To obtain further information on our PhD program, the PhD topics, and application details please visit: *https://transevo.de/*

Motivated and highly qualified candidates are welcome to apply. A Master of Science degree or a Diploma as well as a strong interest in Evolutionary Biology are prerequisites for entering the program. (You will find more information about the employment requirements with the project descriptions below). We are looking forward to your application for a PhD project in the beautiful landscape of Northern Germany.

The deadline for applications is March 27, 2025.
The selection days will be held from **June 17-18, 2025.**
The program itself starts on October 1, 2025 (a later start date is possible).

The University of Kiel sees itself as a modern and cosmopolitan employer. We welcome your application regardless of your age, gender, cultural and social origin, religion, worldview, disability or sexual identity. We support gender equality.
Women with equivalent suitability, qualifications and special abilities will be given preferential consideration in the selection process.
Kiel University is committed to the employment of people with disabilities: Applications from severely disabled persons and persons of equal status will be given preferential consideration if they are suitable.

We explicitly welcome applications from people with a migration background.

Applications should include: a letter of motivation (max. 1 page), curriculum vitae, transcripts of degree, a list of max. 3 preferred PhD topics (from among the offered projects) plus a short explanation of the preferences (max. 1 page).

We explicitly ask you to refrain from submitting photographs/application photos.

Please apply with a single PDF via the following Link by **March 27, 2025**
www.transevo.de/application

If you have any questions on the RTG program or individual projects, you may contact Dr. Sabrina Koehler (skoehler@zoologie.uni-kiel.de).

- Description of doctoral projects -

Evolution of fungal plant pathogen under anthropogenic pressure

Background - Wheat, one of the major field crops in temperate regions, is prone to several diseases that can cause significant yield losses. One of the globally most important wheat pathogens is the *ascomycete* fungus *Zymoseptoria tritici*, causing Septoria Blotch disease. It manifests as small to larger necrotic lesions and when left untreated, it can cause yield losses of up to 60% due to loss of photosynthetic potential caused by leaf necrosis. Successful infection by *Z. tritici* requires intimate interactions of specialized pathogen molecules, also called effectors, to modulate wheat defense responses and extract resources from the plant[80]. Due to the long latency (nonsymptomatic) phase of the pathogen, fungicides are applied preemptively. Over the last 25 years, several classes of fungicides with different modes of action have been used to control *Z. tritici* populations. These include Strobilurins, succinate dehydrogenase inhibitors (SDHIs) and triazoles or demethylation inhibitors (DMIs). Loss of efficacy has been observed against all abovementioned fungicide classes after several years of application[81,82]. Albeit occurring globally, *Z. tritici* shows distinct geographical and demographic patterns - yet all populations evolve fungicide resistance[83]. What remains unknown is how man-made bottlenecks like fungicide application affect the general evolutionary pattern of the pathogen and influence infection biology. In this project, we will utilize the power of two historical collections to unlock evolutionary changes of *Z. tritici* in the Anthropocene. With historical and present-day collections *of Z. tritici* we will be able to identify local adaptation across years in response to different intervention strategies.
Specifically, we will address possible unintended side-effects of crop protection strategies and possibly point to ways to prevent or overcome such effects in the future.

Overall objectives
In this project we will combine expertise in computational analyses, molecular plant pathology, and applied phytopathology in agriculture to investigate the consequences of long-term fungicide applications in populations of crop pathogens. Specifically, we will:

- Assess global and local *Z. tritici* diversity over time in two different sample collections.
- Confirm the loss of fungicide sensitivity (shifting) and the accumulation of fungicide resistance associated mutations in the populations
- Assess changes in virulence spectrum of global and local *Z. tritici* populations over time using old and modern wheat varieties.
- Perform functional analyses of candidate genes identified by genome-wide association studies (GWAS)
- Identify putative trade-offs related to fungicide resistance and virulence evolution.

Project 1: Effects on local pathogen populations in the context of crop protection (PI Remco Stam)

Possible doctoral research topics

1. Use genome sequence data to assess population structure of Schleswig-Holstein *Z. tritici* over 20 years and confirm fungicide resistance mutation accumulations
2. Analyze virulence properties of SH populations on wheat cultivars and perform GWAS
3. Validate how changes in *Z. tritici* populations affect the ability of *Z. tritici* to interact with host defense responses.

Employment requirements:

- **Master (or equivalent):** Biology or agriculture or related field.
- Background (population) genomics, hereunder proficiency in basic programming or
- Experience with experimental/molecular fungal biology or microbiology.

Employment at Kiel University

PI's Homepage*:* *https://www.phytopathology.uni-kiel.de/en/staff/remco-stam*

Project 2: Recent evolutionary developments in a global wheat pathogen (PI Eva Stukenbrock)

Possible doctoral research topics

1. Use genome sequence data to identify changes in effectors and virulence-associated genes under selection in the global *Z. tritici* collection over time
2. Phenotype virulence and fungicide tolerance based on *in planta* and *in vitro* experiments
3. Functional analyses of selected candidate genes exhibiting recent evolutionary changes

Employment requirements:

- **Master (or equivalent):** Biology or a related field.
- Background in (population) genomics, hereunder proficiency in basic programming or
- Experience with experimental/molecular fungal biology or microbiology.

Employment at Kiel University

PI's Homepage: *https://www.environmental-genomics.de/*

Evolution of plasmid-borne antibiotic resistance

Background - Plasmids play an important role in prokaryotic ecology and evolution, as they can be transferred between cells, making them potent agents of lateral gene transfer. Plasmids that encode for antibiotic resistance (AR) genes have been identified as drivers in the spread of antibiotic resistance throughout bacterial populations in diverse habitats. Antibiotics are often used in agricultural food production, where they may lead to the persistence of resistance plasmids in animal- and plant-associated bacterial communities. However, the evolutionary origins of antibiotic resistance plasmids often remains unknown. Here we aim to reconstruct the evolutionary history of resistance plasmids using a phylogenomics approach. Resistance plasmids are typically mobilizable or conjugative and are characterized by a large genome size. To reconstruct the plasmid origin, we will examine the phylogeny of plasmid-encoded genes. Similarly to bacterial chromosomes, core and accessory plasmid genes may have different evolutionary histories. Nonetheless, integrating phylogenetic information from multiple genes remains a challenge in phylogenetics. Additionally, methodology for reconstruction of ancestor-descendant relations among related plasmid variants remains unexplored. In our project we will develop methodologies for summarizing splits (i.e., tree branches) from multiple gene trees, which will enable us to reconstruct the evolution of whole plasmids. Our studies are expected to supply new information on the dissemination routes of antibiotic resistance plasmids.

Overall objectives

- Develop novel methodology for phylogenomic reconstruction of plasmid evolution.
- Reconstruct the evolution of resistance plasmids.
- Characterize the evolution of transitions in plasmid mobility and dissemination routes in the evolution of plasmids encoding antibiotic resistance genes.

Project 3: The origins of antibiotic resistance plasmids (PI Tal Dagan)

Possible doctoral research topics

1. Develop novel methodologies for the integration of plasmid (and host) gene phylogenies.
   See relevant publication: Hanke et al. (2024) *NAR* doi:10.1093/nar/gkae430
2. Reconstruct the evolution of plasmid replicons via rooted phylogenies.
   See relevant publication: Tria et al. (2017) *Nat Ecol Evol*. doi:10.1038/s41559-017-0193

Employment requirements:

- **Master (or equivalent):** Biology or Bioinformatics or related fields
- **Background** in *Molecular Evolution and/or Bioinformatics and programming.*

Employment at Kiel University

NOTE: Applicants applying to this position should include in their motivation letter a paragraph describing their motivation to engage in one (or both) of the suggested topics, a statement on the suitability of their current skills for this type of research (see the above listed publications), and which skills they expect to acquire during the PhD studies.

PI's Homepage: *http://www.mikrobio.uni-kiel.de/de/ag-dagan*

Project 4: Analysis methods for phylogenetic networks (PI Heike Siebert)

Possible doctoral research topics

1. Construction and analysis of phylogenetic networks summarizing phylogenetic trees.
2. Analysis methods for analyzing ancestor-descendant relations in phylogenetic networks.

Employment requirements:

- **Master (or equivalent):** Mathematics, physics, bioinformatics, theoretical biology or related fields.
- Background in *discrete mathematics and/or computer science/bioinformatics.*

Employment at Kiel University

PI's Homepage: *https://www.math.uni-kiel.de/de/biomathematik/heike-siebert*

Evolution-informed antibiotic therapy against human lung pathogens

Background - We are currently facing an antibiotic crisis: The intensive use of antibiotics in medical treatment and also food production has favored the spread of drug resistant pathogens that are often difficult, and in some cases impossible to treat[35,46]. The rise of antimicrobial resistance (AMR) is a major threat to human health worldwide[38,39,117]. Evolution is at the core of this threat: it is the ability of the bacteria to adapt rapidly that underlies the spread of drug resistance. Taking into account the enormous evolutionary potential of the pathogen may thus help to develop more sustainable treatment designs. This potential can be assessed by studying the history of pathogen adaptation using patient isolates, as exemplified for the recent spread of multi- and extensively drug resistant (MDR, XDR) *Mycobacterium tuberculosis* complex (Mtbc) in several parts of the world, incl. Eastern Europe, Central Asia, India, and Africa. An alternative approach to study resistance evolution is the performance of *in vitro* evolution experiments, which permit controlled tests of the efficacy of specific treatment protocols in human pathogens such as Mtbc and *Pseudomonas aeruginosa* (PA)[5,44,45,122,123]. These *in vitro* studies revealed a high efficacy of sequential treatments that include antibiotics with low rates of resistance evolution and/or drugs which express collateral sensitivity towards each other (i.e., evolution of resistance to one drug causes susceptibility towards a second drug)[9,10,44]. Most of the experimental results were obtained with laboratory strains, but only rarely clinical isolates. Importantly, these clinical isolates often show specific additional adaptations – next to full resistance – that help them to counter drug therapy, including for example (i) tolerance (i.e., reduced susceptibility to the killing effect of antibiotics), (ii) expression of persisters (i.e., dormant cells), and (iii) heteroresistance (i.e., presence of a subpopulation with high resistance). To date, the relationship between these specific, clinically relevant adaptations and evolution-informed treatment designs is unknown.

Overall objectives

- Assess the relevance of resistance rates and associated collateral effects for optimizing antibiotic therapy in clinical pathogen isolates.
- Assess the efficacy of evolution-informed treatment designs (e.g., sequential or complex combination therapy) in the presence of persisters, antibiotic tolerance, or heteroresistance
- Assess the influence of additional stressors on efficacy of evolution-informed therapy.

Project 5: Evolution-informed antibiotic therapy against Mtbc strains (PI Stefan Niemann)

Possible doctoral research topics

1. Characterize baseline resistance profiles, heteroresistance, persisters, drug tolerance for clinical Mtbc strains from defined phylogenetic lineages
2. Determine mutations rates of susceptible and resistant clinical Mtbc strains from different phylogenetic lineages with a focus on MDR/XDR TB treatment drugs

3. Assess the fitness of resistance mutations in the different phylogenetic lineages using whole genome sequencing and population genetics analysis

4. Determine the MSW for clinical Mtbc strains from different phylogenetic lineages for main drugs used in current MDR/XDR TB treatment regimens

5. Test the efficacy of sequential antibiotic therapy in consideration of resistance profiles, heteroresistance, persisters, tolerance, as well as mutation rates and MSW

Employment requirements:

- **Master (or equivalent):** Biology, bioinformatics, or related field.
- Background in *genomics and/or, medical microbiology, and/or infectious disease biology*

Employment at Research Center Borstel, (Leibniz Lung Center)

PI's Homepage: *https://fz-borstel.de/index.php/en/sitemap/priority-research-area-infections-prof-dr-ulrich-schaible/molecular-and-experimental-mycobacteriology-prof-dr-stefan-niemann/staff*

Project 6: Evolution-informed antibiotic therapy against PA strains (PI Hinrich Schulenburg)

Possible doctoral research topics

1. Characterize resistance profiles, heteroresistance, persisters, tolerance for clinical *P. aeruginosa* isolates from CF and COPD patients

2. Determine the rate of spontaneous resistance mutations towards clinically relevant antibiotics and associated collateral effects for a selection of clinical isolates

3. Assess genetics of resistance, associated collateral sensitivity, and possibly cases of phenotypic heterogeneity in different genomic backgrounds using WGS

4. Apply functional genetic manipulation in *P. aeruginosa* to characterize and confirm selected cases of the indicated genetic mechanisms

5. Use of the data on the characteristics of the clinical isolates to develop antibiotic treatment protocols, which either promote or constrain bacterial survival

Employment requirements:

- **Master (or equivalent):** Biology or related field.
- Experience in *evolutionary research, and/or bacterial genetics* Any of the following expertise is an advantage: performance of evolution experiments, statistical data analysis, and/or bacterial genome sequence analysis

Employment at Kiel University

PI's Homepage: *https://evoecogen-kiel.de/*

Project 7: Theoretical modeling of tumor-microbiome ecology in pancreatic cancer evolution (PI Arne Traulsen)

Background - Cancer ecology typically consists of characterizing tissue structure, vascularization, and spatial organization of tumors including the interaction between cancer and different non-neoplastic cell types (e.g., myofibroblasts, macrophages, T cells, endothelial cells). Besides the genetic profile of the cancer cells, the dynamic interaction between these different stromal cell populations essentially drives cancer evolution. Microbiome research has revealed a strong interdependence of hosts and bacteria that live in and on them. More recently, it has been shown that cancers are also affected by microbial communities, not only in the cancer tissue itself but also in associated tissues. Microbiome alterations have been described in pancreatic ductal adenocarcinoma (PDAC) being associated with disease progression, poor prognosis and reduced therapeutic responses. However, mechanistic and causal insights into how microbial infections of PDAC and stroma cells shape their phenotype and how these adaptive changes contribute to PDAC evolution and therapy resistance are still rare.

Overall objectives

- To understand how infection of PDAC cells and/or stroma with defined microbial species impacts cellular plasticity and functional phenotypes.
- To infer whether the presence of microbes will affect tumor or stroma cells directly or whether it changes transition rates between different plastic cell types.
- To develop a mechanistic model for the role of microbes in PDAC evolution that generates experimentally testable hypotheses.
- To model and analyze PDAC evolution in changing microenvironments in consideration of bacterial compositions, infection rates and duration of PDAC and stroma cell populations.
- To generate a novel understanding of disease progression and treatment outcome in an iterative form between an experimental and a tightly linked theoretical project.

Possible doctoral research topics

1. Generate a quantitative understanding of microbe-tumor interactions to generate new hypotheses based on a mathematical and/or computational model.
2. Develop a theoretical model that is simple enough to allow parameter inference from simulated and experimental data, adjust model/experiment if such inference turns out elusive.

Employment requirements:

- **Master (or equivalent):** Mathematics, physics, theoretical biology or related fields.
- Background in *theoretical/mathematical biology and/or physics and/or computer science, and/or evolutionary biology.*
- Strong interest and previous experience in computational models.
- Enthusiasm to work at the interface between theoretical and experimental biology.

Employment will be at Max-Planck-Institute for Evolutionary Biology, Plön

PI's Homepage: *http://web.evolbio.mpg.de/~traulsen/#home*