14 Doctoral Positions within the Research Training Group 2501 on *Translational Evolutionary Research* (RTG TransEvo)

Evolution is the central theory of the life sciences. The core objective of the RTG TransEvo is to study and promote its key relevance 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. Therefore, the development of sustainable solutions to such emerging challenges can only be achieved by explicit consideration of the influenced evolutionary processes. Yet, to date, the translation of evolutionary concepts to applied problems is only rarely attempted. In turn, the required experimental tests in these areas have the potential to further advance evolutionary theory – to the mutual benefit of translational and basic research. Thus, the overarching aim of the RTG TransEvo is to train two main competences among doctoral candidates: On the one hand, the use of knowledge and concepts from fundamental research in evolutionary biology in order to enhance our understanding of current challenges in applied fields and, on the other hand, the use of the novel insights obtained in order to enrich our understanding of evolution. The RTG TransEvo will promote the translation of evolutionary thinking into three applied fields: (i) medicine, (ii) food production, and (iii) wildlife conservation.

The training of doctoral candidates is explicitly interdisciplinary and organized in tandem projects. Each of these consists of two sub-projects that address a related problem, yet use distinct albeit complementary research approaches, directly generating potential for synergistic interactions. The different tandem projects are interconnected at various levels, which will aid the establishment of a stimulating, interdisciplinary research network for the doctoral candidates. The doctoral research projects will be developed together with the chosen PhD students. The frameworks for research topics are given below. The RTG has a total of 14 sub-projects and thus **14 individual doctoral projects (3 year and 2.5 months fixed term positions, TV-L, TV-ÖD E13 65%)**, for which we invite applications from highly motivated and well-qualified candidates.

The deadline for applications is August 15, 2019.
The selection week will be held from October 8 - 10.
The program itself starts on December 1, 2019.

The university endeavours to increase the proportion of women in research and teaching and therefore urges appropriately qualified women to apply. Priority is given to women who have equal aptitude and professional performance.

The university is committed to the employment of severely disabled people. For this reason, severely disabled applicants will be given preferential consideration if they are suitably qualified.

We explicitly welcome applications from people with a migration background.

Applications should include: a letter of motivation (max. 1 page), curriculum vitae, a list of max. 3 preferred PhD topics (from among the offered projects) plus a short explanation of the preferences (max. 1 page), the names and addresses of 2 referees (who are familiar with the applicant's work).

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

Please send the **application as a single PDF-file** by **August 15, 2019** to:

Dr. Sabrina Koehler, Am Botanischen Garten 9, 24118 Kiel, +49 (0) 431 – 880 4148
skoehler@zoologie.uni-kiel.de

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

- Description of tandems and doctoral projects -

Tandem 1: Evolutionary management of harvested populations

Background - Almost all harvesting practises exert unwanted selection onto the target populations. One example is selection on life-history and behavioral traits in exploited fish populations. All fishing gears are selective, most often with respect to a minimal size of the fish, determined by mesh size, but also in terms of behavioral traits in case of active fishing gear (e.g. long-lining, angling). In the past decade, multiple examples of life-history changes over a few generations of heavy fishing have been documented. A dramatic outcome is that fisheries "breed" fish populations with a mean reduction in age and size at maturity, and sometimes even reduced growth rates. Such changes in vital traits may have profound cascading effects. For example, since food spectra are very much gape width driven, different sizes of fish will also eat different prey, with concomittant effects on the food-web role of a focal fish population that is now, on average, smaller. Because aquaculture cannot replace the complex environmental conditions for most wild caught fish species, harvesting of wild populations will continue. It is thus imperative to reduce, and possibly reverse, the unwanted effects of fisheries-induced selection, along with a general demographic protection of many fish stocks.

Overall objectives
- Explore how the ecological and economic processes that lead to evolutionary pressure on harvested populations can be reverted.
- Develop and model novel harvesting rules that mitigate unwanted evolutionary effects and sustain both viable levels of harvest and critical ecosystem functions.

Doctoral project 1.1: Fisheries-induced evolution (PI Thorsten Reusch)

Possible doctoral research topics
1. Perform a meta-analysis on the underlying factors that promote or restrain fishery-induced changes in fish populations (e.g., life-history characteristics, habitat and ecosystem types, fishing gear and intensity, type of management regime).
2. Assess the "selective" load that remains in the population of a fished stock and may persist over decades once the fishing pressure is alleviated, using quantitative genetic modeling.
3. Build the biological basis to reform (if required) the management regimes of exploited fish stocks in the North Atlantic area where time-series data of key traits are available.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or statistics or related fields.
- Background in evolutionary biology and/or ecology and/or fish biology
- Practical skills: Advanced statistics, computational analyses, experimental analysis of fish, genomic analysis, and/or basic molecular biology methods

PI's Homepage: *https://www.geomar.de/en/mitarbeiter/fb3/ev/treusch/*

Doctoral project 1.2: Evolutionary fishery economics and management (PI Martin Quaas)

Possible doctoral research topics
1. Understand the technical and economic factors that lead to fisheries-induced evolution
2. Investigate with a combination of ecological-evolutionary and ecological-economic models how the history of fisheries-induced evolution influences future sustainable and economically efficient fisheries management.
3. Quantify an option value of conservative fishing with adjusted selectivity patterns.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Resource Economics, Ecological Modelling, or a related field.
- Background in resource economics, ecological modeling, and/or statistics
- Practical skills: mathematical modelling, statistics, computational analyses.

PI 's Homepage: *https://www.idiv.de/groups_and_people/core_groups/biodiversity_economics.html*

Tandem 2: Evolution of sugar beet and its associated pathogens: implications for plant breeding and disease control

Background - Antagonistic interactions between plants and pathogens can result in a co-evolutionary arms race between the two partners. Plants have evolved strategies to recognize and block invading pathogens while pathogens constantly evolve to escape recognition and manipulate host defenses. The domestication of plant species has been shaped by selective breeding and strong directional selection. Such artificial selection also impacts co-evolutionary dynamics between crop plants and their pathogens. The evolution of plant pathogens is further shaped by the use of fungicides in agriculture. Their frequent application selects for resistant pathogen varieties. Sugar beet (*Beta vulgaris*) and its fungal pathogen *Cercospora beticola* provide an informative model system to study the impact of domestication, intensive crop cultivation and fungicide applications on the evolution of plant pathogens. This pathogen is increasingly important in beet production worldwide and fungicide resistance is a growing concern. *B. vulgaris* was domesticated in Germany approximately 200 years ago and is cultivated world-wide for sugar production. Leaf spot disease, as caused by *C. beticola,* is also a common pathogen of the wild progenitor of sugar beet, *B. vulgaris ssp. maritima*.

Overall objectives
- Assess the impact of selective breeding from the past 200 years on evolutionary processes by comparing genetic and functional data from cultivated and wild plant species.
- Infer patterns of evolution in pathogen populations of *C. beticola* on wild and cultivated beet species using comparative population genomics.
- Assess the ability of the fungal pathogen to adapt to fungicides and plant resistance mechanisms
- Evaluate to what extent the availability of untreated plants determines the competition between susceptible and resistant pathogen strains.

Doctoral project 2.1: Genetic analysis of leaf spot resistance (PI Christian Jung)

Possible doctoral research topics
1. Unravel the genetics of *C. beticola* resistance in beet species and investigate the genetic diversity in loci encoding resistance traits in both wild and cultivated beet species.
2. Fine-map a major QTL for *C. beticola* resistance which was identified previously.
3. Clone a quantitative trait gene from this QTL by a map-based cloning approach using a novel mapping-by-sequencing strategy.

4. Compare the diversity of resistance genes between beet and related wild species.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or agriculture or related field.
- Background in plant genomics, crop plant evolution and/or plant breeding
- Practical skills: plant genetics, genome analysis, bioinformatics, and/or plant molecular biology.

PI's Homepage: *https://www.plantbreeding.uni-kiel.de/de/Staff/prof.-dr.-christian-jung*

Doctoral project 2.2: Plant pathogen evolution on cultivated and wild plant hosts (PI Eva Stukenbrock)

Possible doctoral research topics
1. Assess the extent of host specialization and variation in virulence levels using experimental assays involving *B. vulgaris* lines from the Jung lab and *B. vulgaris ssp. maritima* as hosts.
2. Analyse the process of host specialization following host domestication by detailed analyses of genomic data and by the correlation of phenotype and genotype data.
3. Determine the potential of fungicide resistance evolution by *in vitro* fungicide assays and analyses of genome data of *C. beticola* from treated and untreated host sites.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or a related field.
- Background in fungal genomics and/or genome evolution and/or pathogen evolution
- Practical skills: Population genetics, population genomic analyses, experimental work with plant pathogens, and/or evolution experiments.

PI's Homepage: *http://web.evolbio.mpg.de/envgen/eva-h-stukenbrock.html*

Tandem 3: Evolution and spread of plasmid-borne antibiotic resistance

Background - Plasmids are genetic elements that colonize prokaryotic cells where they replicate independently of the chromosome. They are considered to be a major driving force in prokaryotic ecology and evolution as they can be transferred between cells, making them potent agents of lateral gene transfer. Many plasmids encode for antibiotic resistance genes and this enables the spread of antibiotic resistance throughout bacterial populations. This tandem explores the contribution of plasmids to the evolution of antibiotic-resistant bacteria in the context of food-related microbes. Antibiotics are used at large scale in agricultural food production, leading to the selection of resistant bacteria. Antibiotic resistant bacteria have the potential to establish within the human population, for example through direct contact with farm animals, manure used in fields, or contaminated food. Plasmids encoding for these resistance genes may be transferred to the human commensal flora, even if the food-associated bacteria are present in the human body only transiently. Surprisingly, the food dissemination route to the reservoir of resistance genes is still largely unexplored. Such information may help to understand the origin of specific resistance processes within human pathogens and possibly point to novel targets for intervention.

Overall objectives
- Characterize the evolution, spread, and persistence of resistance plasmids in the food production chain with a particular focus on bacteria from salad as a model.
- Assess how DNA acquisition during plasmid evolution contributes to the spread of antibiotic resistance genes and also the drug-resistant bacteria in food systems and beyond.

- Develop mathematical models to identify selective conditions favoring the spread of plasmid mediated resistance and to investigate how plasmids persist in bacterial populations over evolutionary time-scales.

Doctoral project 3.1: Plasmid evolution in the food industry (PI Tal Dagan)

Possible doctoral research topics
1. Characterize the persistence mechanisms of plasmids encoding antibiotic resistance genes, which were found in food bacteria.
2. Research the evolutionary trajectories of plasmid replicon types found in food bacteria.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Microbiology or molecular biology
- Background in microbiology, molecular biology.
- Practical skills: molecular microbiology techniques: DNA and RNA extraction for sequencing projects, work with environmental samples, isolation of microbial strains, plasmid engineering and generation of knockout mutant strains, evolution experiments.

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

Doctoral project 3.2: Mathematical modelling of the evolution and spread of plasmid mediated antibiotic resistance (PI Hildegard Uecker)

Possible doctoral research topics
1. Determine the probability of resistance evolution under a set of selective conditions (e.g. drug heterogeneity in time and space).
2. Explore the evolutionary dynamics for various resistance mechanisms (e.g. selfish vs cooperative resistance).
3. Study the coexistence of resistant and protected sensitive cells under cooperative resistance and the consequences for the persistence time of cooperative resistance after removal of the antibiotic.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Mathematics, physics, theoretical biology or related fields.
- Background in theoretical/mathematical biology, mathematics, physics, or computer science, and/or evolutionary biology.
- Practical skills: mathematical modelling, programming skills (e.g., C++, C, Java, Python, Matlab).

PI's Homepage: *http://web.evolbio.mpg.de/stochdyn/*

Tandem 4: The evolution of human pathogens under antibiotic therapy

Background - Pathogenic microorganisms have shaped human history through repeated epidemics and pandemics, causing enormous mortality rates. The discovery of antibiotics in the 20th century thus represented a major breakthrough, massively reducing otherwise fatal bacterial infections. Yet, the application of these drugs immediately led to the spread of antibiotic resistance. Especially the intensive use of antibiotics in humans, but also in animal husbandry and generally food production during the last decades favored multi-drug resistant pathogens that are often difficult, and in some cases impossible to treat. Evolution is at the core of the current situation. Any sustainable treatment strategy must thus take into account the enormous potential of pathogens to adapt to novel drug environments. This potential can be assessed by studying the history of pathogen adaptation using clinical pathogen isolates from patients with documented health characteristics and antibiotic treatment (e.g., phylogenomic analysis of *Mycobacterium tuberculosis* complex (Mtbc)). An alternative approach is the performance of highly controlled laboratory evolution experiments (e.g., experiments of alternative treatment protocols with the human pathogen *Pseudomonas aeruginosa*). Sequential therapy holds particular promise if two drugs that

show reciprocal collateral sensitivity are alternated. This concept implies that evolution of resistance to one drug causes susceptibility towards a second drug. Its clinical potential is as yet unclear.

Overall objectives
- Determine the efficacy of novel treatment strategies such as sequential protocols to reduce resistance evolution in clinical pathogen isolates
- Identify evolutionary trade-offs and associated molecular genetic mechanisms that influence the efficacy of antibiotic treatment protocols
- Evaluate to what extent pathogen adaptation to antibiotics under laboratory conditions reflects evolution of clinical pathogen isolates
- Assess which other factors (e.g., human immune status, strain genetic background and diversity) influence pathogen adaptation to antibiotics

Doctoral project 4.1: Adaptation of Mtbc to antibiotic treatment (PI Stefan Niemann)

Possible doctoral research topics
1. Identify potential low level resistance mutations associated with a stepwise increase in resistance against particular antibiotics and identify associated evolutionary trade-offs
2. Quantify fitness enhancing mutations that are suggested to contribute to the emergence of large multi-drug resistance Mtbc transmission networks
3. Define mutation rates in different physiological conditions (e.g. hypoxia)
4. Test alternative treatment protocols for Mtbc

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology, bioinformatics, or related field.
- Background in genomics, medical microbiology, and/or infectious disease biology
- Practical skills: genomics, phylogenetics, computational biology and/or microbiology

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*

Doctoral project 4.2: Efficacy of sequential therapy against clinical Pseudomonas (PI Hinrich Schulenburg)

Possible doctoral research topics
1. Use evolution experiments for testing the efficacy of sequential treatment protocols with *Pseudomonas aeruginosa*
2. Identify trait functions under selection during alternative antibiotic therapies using phenotypic assays and genome sequencing of experimentally evolved bacteria
3. Compare phenotypic and genomic evolutionary responses to antibiotic treatment among experimentally evolved and clinical isolates of *Pseudomonas aeruginosa*

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or related field.
- Background in evolutionary biology, and/or microbiology
- Practical skills: Evolution experiments, microbiology, genomics analysis, and/or bacterial genetics

PI's Homepage: *http://www.uni-kiel.de/zoologie/evoecogen/*

Tandem 5: Characterizing trade-offs of the human *FUT2* gene for the improvement of gut health

Background – The gene *FUT2* encodes an α1,2 fucosyltransferase responsible for the expression of ABO histo-blood group antigens on mucosal surfaces and in bodily secretions. Individuals bearing at least one functional allele are known as "secretors", whereas those homozygous for loss-of-function mutations display a "non-secretor" phenotype. The non-secretor phenotype exists in human populations and has been maintained by strong selective pressure over a period of 3 MY. This indicates the existence of strong trade-offs, whereby host-microbe interactions are a likely cause. In particular, non-secretors are resistant to infection with the Norwalk (Noro) virus, but are more susceptible to other infectious and chronic diseases involving microbes, such as inflammatory bowel disease (IBD). The *Fut2* gene is important for the assembly of the gut microbiota and its management under stress. Thus, it represents an important genetic factor to consider for the development of microbiome-related interventions, such as probiotics or fecal microbiome transplantation (FMT). Intestinal lactic acid bacteria and Bifidobacteria have been intensely investigated for their utilization as human probiotics. Probiotic microorganisms improve or restore microbial homeostasis by two scenarios: occupation of functional niches (competitive exclusion) or their antagonistic activity. It is well known that the gut microbiota interacts with human health and modulation of the microbiota by probiotics is a potential way to prevent some diseases.

Overall objectives
- Characterize the reduction of *Lactobacillus*, which is observed in both non-secreting humans and mice, at the species- and strain level.
- Evaluate whether local adaptation to *FUT2* genotype-dependent environmental differences exists among microbiomes.
- Explore whether improved understanding of functionally important microbial losses may be exploited for preventative and/or therapeutic purposes.

Doctoral project 5.1: Relationship between Lactobacillus *diversity and host FUT2 genotype (PI Charles Franz)*

Possible doctoral research topics
1. Define species-level taxonomy of *Lactobacillus* sp. that differ according to *FUT2* genotype in human fecal samples.
2. Evaluate the pan-genome of *Lactobacillus* species according to *FUT2* genotype in humans.
3. Characterize functional genomic content according to *FUT2* genotype in humans.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or related field.
- Background in microbiology, nutritional sciences and/or genomics.
- Practical skills: microbiological and molecular biology techniques, ideally anaerobic bacterial culturing, comparative genomics, metagenomics, and/or bioinformatics

PI's Homepage: *https://www.mri.bund.de/de/institute/mikrobiologie-und-biotechnologie/mitarbeiterinnenmitarbeiter/franz-charles/*

Doctoral project 5.2: Evaluating the gut microbiome for adaptation to host Fut2 genotype (PI John Baines)

Possible doctoral research topics
1. Evaluate ecological and evolutionary changes in the gut microbiome during FMT experiments with wild type and *Fut2*-deficient donor/recipient mice

2. Determine differences in inflammatory outcome of autologous vs heterologous FMT in wild type and *Fut2*-deficient mice
3. Evaluate influence of specific *Lactobacillus* strains on FMT-induced and host genotype-dependent effects on disease

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or related field
- Background in evolutionary biology, population genetics, genomics, microbiota, and/or mouse genetics.
- Practical skills: genomics, population genetic analysis, bioinformatics, ideally analysis of laboratory mouse models of disease, ideally metagenomic analysis, and/or basic molecular biology skills.

PI's Homepage: *http://web.evolbio.mpg.de/evolgenomics/*

Tandem 6: Evolution of key life history events – the sex-specific link between fertility, pregnancy and longevity

Background - Natural selection still acts on contemporary humans in developed countries despite the benefits of hygiene, modern medicine and sufficient nutrition. In particular women are under selection for later menopause and older age at last child. This increase in reproductive lifespan has been interpreted as a response to the Western standard of living. Due to low early-life mortality current selection is thought to be primarily driven by variation in fertility. In addition, there is a growing number of studies that consistently show a positive correlation between the age at last birth and healthy longevity of the mother. Brothers of women who have children late also live longer, indicating a genetic component that could mediate its effects by postponing both sexual development and ageing. The genetic link between longevity and late-life fertility is supported by the observation that variation in three longevity genes also influences age at menopause or ovary reservoir. Egg production, pregnancy, and breast-feeding are united in human maternal investment. This prevents to determine how postponed maturation and late pregnancy affect longevity. Sex-role reversal is found in syngnathid fish (pipefish, seahorses), characterized by male pregnancy. In this case, the provisioning of eggs and parental investment are decoupled: the mother provides the eggs and the father the investment during pregnancy. Syngnathids are thus ideally suited for experimental validation of the observed correlations in humans.

Overall objectives
- Investigate the correlation between late-life fertility/pregnancy and longevity in humans at the genetic and molecular level
- Experimentally validate the causal relationship between sex-specific late life fertility/ pregnancy and longevity using a sex-role reversed pipefish
- Assess genes with a function in key life history events (pregnancy, longevity) both in conventional and sex-role reversed species to assess homologous gene co-option in the convergent evolution of pregnancy in both females and males

Doctoral project 6.1: Late-life fertility and longevity in humans (PI Almut Nebel)

Possible doctoral research topics
1. Establish a list of genes and single nucleotide polymorphisms (SNPs) involved in fertility/pregnancy to be tested for an association with longevity
2. Identify novel longevity genes through a case-control association study in LLI and younger individuals by systematically analysing SNPs in the above candidate loci
3. Gain insights into mechanistic and functional processes (from genotype to phenotype) by performing *in silico* and possibly *in vitro* analyses of detected longevity-fertility genes and their associated SNPs

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or related field

- Background in genetics/genomics, human biology,, and/or aging research.
- Practical skills: Computational biology, vertebrate/human genetics; basic programming skills (ideally in R), basic molecular biology techniques

PI's Homepage: *https://www.ikmb.uni-kiel.de/people/scientists/almut-nebel*

Doctoral project 6.2: Pregnancy/late-life fertility and longevity in sex-role reversed pipefish (PI Olivia Roth)

Possible doctoral research topics
1. Experimentally analyse the late-life fertility/pregnancy and longevity trade-off in the sex-role reversed pipefish *Syngnathus typhle*
2. Experimentally evaluate sex-specific late-life fertility and longevity in the sex-role reversed pipefish *Syngnathus typhle*
3. Identify the molecular and functional basis of pregnancy, fertility and longevity in conventional and sex-role reversed lifestyle using transcriptomics and modifications of key pregnancy/fertility genes with CRISPR/cas9

Skills required and/or relevant for doctoral project
- Master (or equivalent): Biology or related field
- Background in evolutionary biology, fish biology, and/or ageing research
- Practical skills: fish experimental analysis, basic molecular biology techniques, genomics, and/or bioinformatics

PI's Homepage: *https://www.geomar.de/en/mitarbeiter/fb3/ev/oroth/*

Tandem 7: The evolution of pancreatic cancer cells under chemotherapy

Background - The evolution of drug resistance is a frequent cause for cancer treatment failure, impeding cure and prognosis of the patients. This particularly applies to pancreatic ductal adenocarcinoma (PDAC), which is mostly diagnosed at an advanced, often metastasized and hence not curable stage. Thus, even in patients undergoing successful tumor resection followed by adjuvant chemotherapy, the disease commonly progresses. However, current therapies neglect heterogeneity, evolution of tumor cell populations, and also their adaptation to chemotherapy. The concept of adaptive therapy, i.e. usage of lower dosages or intermittent phases without drugs, could be used to control tumor size, possibly improving patient health, and at the same time lowering the spread of resistance. The latter result is obtained when drug-resistant cells pay an evolutionary cost in terms of cell division rate and are then outcompeted by susceptible cells in tissues with low drug concentrations or in drug-free treatment phases. Thus, adaptive chemotherapy might help to counteract the evolution of drug resistance in PDAC cells, control tumor burden, and improve prognosis of PDAC patients. However, transferring these experimental results to patients is challenging and mathematical models can help to overcome this challenge. For example, mathematical models can yield insights into the dynamics of pre-existing and *de novo* resistance development. Mathematical modelling further allows to assess cancer evolution and therapeutic responses in an abstract, yet comprehensive form, thereby complementing experimental approaches.

Overall objectives
- Understand how the concept of adaptive therapy can be used to reduce the evolution of chemoresistance as well as inhibit tumor growth and stem cell features of PDAC cells.
- Model and analyze PDAC evolution in different changing microenvironments in consideration of: Drugs with different modes of action, drug order and concentration, recovery time between drug application, and tumor microenvironment.
- Generate predictions of treatment outcome in an iterative form between the experimental and mathematical projects.

Doctoral project 7.1: Experimental analysis of the evolution of pancreatic cancer cells under chemotherapy (PI Susanne Sebens)

Possible doctoral research topics
1. Analyze the impact of different sequential and adaptive therapy regimens on PDAC cell growth and self-renewal capacity and thereby on evolution of subclones.
2. Characterize long-term surviving PDAC cell clones after different treatment regimens. Surviving clones will be characterized at both phenotypic and genomic/transcriptomic level.
3. Analyze the impact of the tumor microenvironment on drug response of PDAC cells to different sequential and adaptive therapy regimens.
4. Validate predictions from mathematical modeling in sub-project Traulsen.

Skills required and/or relevant for doctoral project skills
- Master (or equivalent): Biochemistry, biology, medical life sciences, or related field.
- Background in oncology, molecular biology, and/or human medicine
- Practical skills: Cell culture, molecular biology and/or molecular genetics

PI's Homepage: *https://www.iet.uni-kiel.de/de/arbeitsgruppen/ag-inflammat.-karzinogenese-ss*

Doctoral project 7.2: Mathematical modelling of the evolution of pancreatic cancer cells under chemotherapy (PI Arne Traulsen)

Possible doctoral research topics
1. Develop a model to describe the dynamics of a cell population under sequentially changing selective pressures and/or adaptive therapy.
2. Model resistance evolution based on genetic mutations or phenotypic induction and assess how the arising differences of these are reflected in disease dynamics.
3. Infer the theoretically optimal sequential and/or adaptive therapy given certain dynamical assumptions and parameters.
4. Extend the model to assess the role of the tumor environment.

Skills required and/or relevant for doctoral project
- Master (or equivalent): Mathematics, physics, theoretical biology or related fields.
- Background in theoretical/mathematical biology, physics, or computer science, and/or evolutionary biology.
- Practical skills: standard methods of theoretical biology, e.g. stochastic processes or ODE based mathematical modelling, programming skills (e.g., python or a similar language).

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