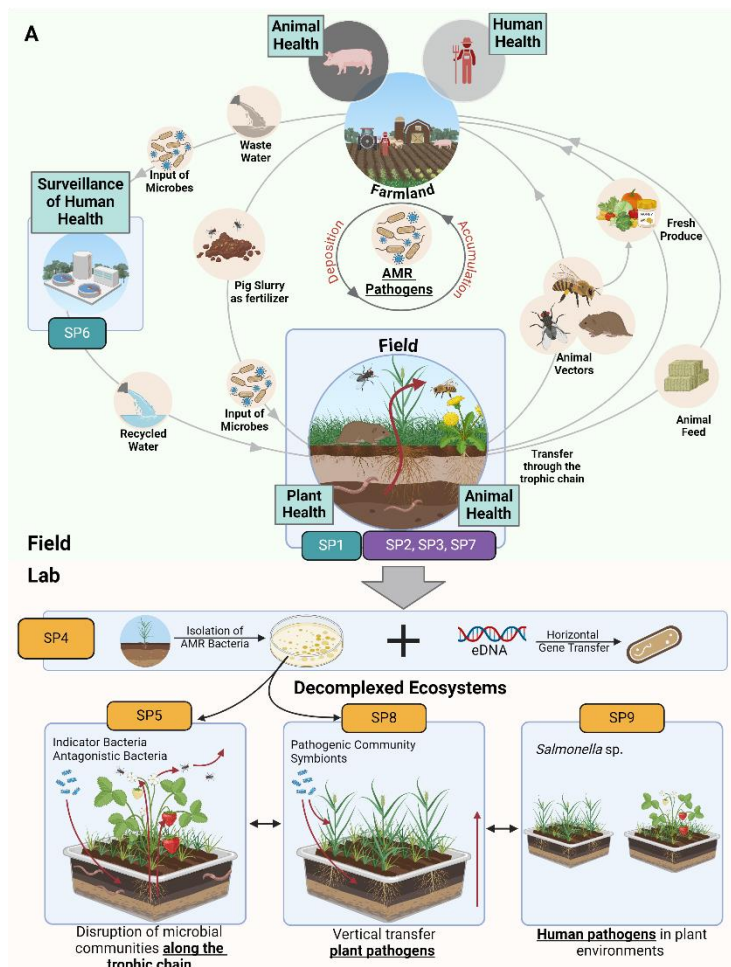# Current projects (SommerLab)

TrophicHealth: Effects of fertilization on AMR and zoonotic pathogen accumulation along the trophic chain - towards a One Health perspective in circular agriculture
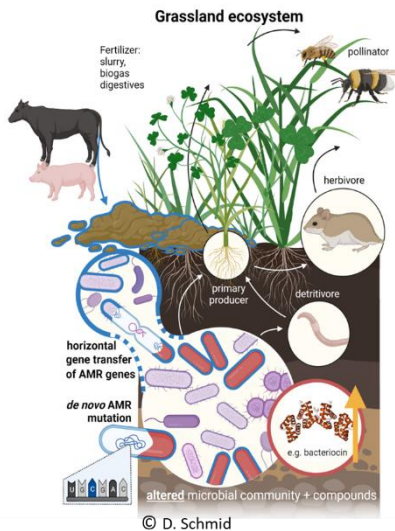

We will study how circular agriculture can spread AMR and zoonotic pathogens from livestock to the environment and back, and how ecosystem resilience may interrupt this cycle that threatens the health of humans, animals, plants, and our environment. We will combine a pan-microbiome approach with metagenomics in order to identify pathogens, AMR as well as antimicrobial peptide-producers, which may in turn stabilize microbial ecosystems preventing the spread of harmful microbes. To address this detrimental cycle inherent to circular agriculture, we will survey microbial communities from soil, wastewater, plants and potential animal vectors, and experimentally verify the potential spread and mitigation of AMR and pathogens in a series of de-complexed mesocosm experiments. TrophicHealth will refine AMR and pathogen surveillance on our doorstep and in immediate food chain, as well as identify potential mitigation strategies significantly contributing to OneHealth by blocking the cycling of harmful microbes. This work will improve surveillance by the RKI and the Umweltbundesamt, and support vets and farmers in their efforts to transition to sustainable and safe livestock farming.

Impact of agricultural land-use intensity on health functions of microbiomes along the trophic chain (IMPALA)

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Humans, animals and plants are closely related to complex microbial communities, the so-called microbiome. Its functional composition is crucial for the sensitive balance between microbiome and host. This balance is maintained by microbial diversity, genetic factors, and complex molecular-cellular interactions between host and microbiome. A disturbance of this balance (also known as dysbiosis) is often accompanied by serious illnesses. In most cases, dysbiosis is caused by changing environmental conditions and is characterized by a decrease in the diversity and abundance of important members of the microbiome and thus their functional properties. While the mutual relationships between host and microbiome in specific ecological niches have been extensively studied, little is known about the influence of environmental changes on microbiome functions in complex ecosystems. These interactions are of crucial importance for human and environmental health, as described in the OneHealth concept. Environmental factors, such as organic or inorganic fertilization, directly affect the soil microbiome by altering the nutritional and physico-chemical properties of the soil and consequently shaping the microbiome of roots, leaves and flowers. This in turn has an impact on plant fitness and the microbiome of pollinating insects and animals in the root zone, which not only absorb the respective microbiome, but also mediate its lateral transfer. Organic fertilization can also affect soil biomes and soil-living invertebrates through the entry of faecal bacteria and antibiotics contained in liquid manure or biogas fermentation residues. Last but not least, the use of antibiotics in agriculture is an important factor in the worldwide spread of antibiotic resistance and leads to an increasing number of infections in plants, livestock, wild animals and humans by antibiotic-resistant bacteria.
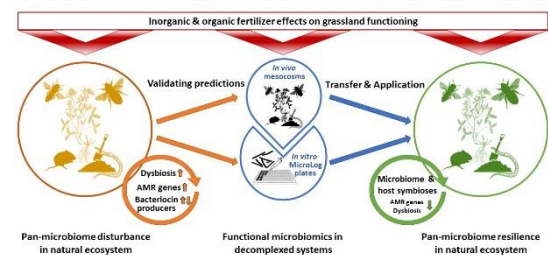

Fig. 1 Graphical abstract. The proposed project will investigate the effects of agricultural land-use intensifications on the microbiome and its functional interactions with the hosts along a trophic cascade in grassland ecosystems. Microbiome functions will be validated in model ecosystems that mimic real-world dynamics, allowing us to study and identify key determinants, such as natural bacteriocin producers. The study will contribute to the development of strategies to improve ecosystem resilience by specifically promoting beneficial microbiomes.

The IMPALA project investigate the impact of agricultural land-use intensification through the use of organic and inorganic fertilizers on the microbiome and its functional interactions with hosts along a trophic cascade in grassland ecosystems. The main goals are to determine the influence of liquid manure or biogas digestate fertilization on the function of microbiomes of soil, roots and inflorescences of plants, as well as in the gut of soil-digesting invertebrates, herbivorous mammals and pollinating insects. Genes for antibiotic resistance and production of natural antimicrobial peptides, so-called bacteriocins, are used here as parameters for the function of a microbiome.

The project thus provides important information on the effects of fertilization on the stability of an ecosystem, which are mediated through host-microbiome interactions. The generated functional data also help to evaluate different intensities of land use on the stability of a complex ecosystem. In particular, the identification of natural bacteriocin producers and their importance for the microbiome enables the development of strategies to improve the resilience of ecosystems by promoting a beneficial microbiome.

Effects of Corona and Astrovirus infections on the gut microbiomes of bats: the *Hipposideros* species complex as a model for virus-induced increase of pathogenic bacteria in highly gregarious mammals

The gut microbiome of a vertebrate has not only metabolic functions, it is also an important driver of immune defence mechanisms. To fulfil these roles, some stability and consistency within the gut microbial community is required. Enteric viruses can disturb the balance of the microbial communities, which can lead to secondary infections and to shifts towards higher number of pathogenic microbe species. If this happens in known pathogen reservoir species, a higher zoonotic risk may arise. Bats constitute the evolutionary origin and reservoirs of a high number of zoonotic pathogens. Among them are astroviruses (AstV), the worldwide leading cause of infectious diarrhoea in children, and different gastrointestinal coronavirus (CoV) species that constitute the ancestors of the viruses that recently caused highly pathogenic SARS, MERS and Covid19 epidemics / pandemics in humans. Bats are also hosts of zoonotic bacteria although these are understudied. We here employ a bat model of four ecologically similar species that – like humans – live in large groups and densities to investigate the microbiome changes induced by CoVs and AstV infections in the gut. Our aim is to identity virus-microbiome interactions and their consequences on the bacterial species community and gene function level in order to understand which pathogenetic and potentially zoonotic virus-induced population-wide microbiome changes may arise in highly gregarious mammals. More than 6500 virus-screened samples from four *Hipposideros* species from five independent locations in central Ghana are already available from the previous DFG-funded program 'German-African Cooperation Projects in Infectology'. In contrast to previous studies investigating microbiome changes in wild reservoir species, our study design provides the rare opportunity to control for phylogenetic and environmental variation which will enable us to discriminate between environmental, virus-induced and intrinsic factors driving pathogenic microbe species.

Disentangling TB epidemiology: The effects of immune gene diversity, gut microbiota and social networks on disease susceptibility in a natural meerkat model

Tuberculosis (TB) is a devastating disease that is endemic to humans and many other mammal species, including meerkats (*Suricata suricatta*). Variation in individual susceptibility and resistance to TB infection exists between individuals, and identifying the underlying causes of this variation has major implications for pathogen epidemiology and disease control. However, the biological drivers that underpin an individual's susceptibility and resistance to infectious disease (including TB) are not well understood. There is compelling evidence from laboratory studies that host genetics and gut microbes can interact to mediate host immune responses, but the extent of these interactions in natural populations and their consequences for host-pathogen dynamics are unknown. In this project, we will explore the extent to which immune genes and gut microbiota composition together shape individual TB susceptibility in a natural animal population, and integrate social network information to model key
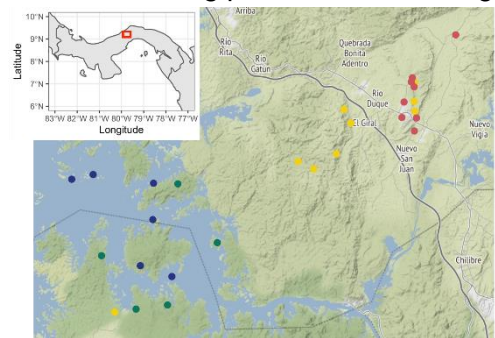
transmission routes across the study population during TB outbreaks. We will apply an exceptionally high resolution dataset on 2300 wild meerkats in the Kalahari desert, South Africa, collected over a 25 year period. This multi-layered dataset includes accurate records of behavior and movement, genetic data, and longitudinal fecal samples from virtually all individuals within the study population. Specifically, we will be able to unravel host-TB interactions, lifetime gut microbiota dynamics, the role of immune gene diversity (MHC) in life history decisions and TB resistance. We will start by examining how microbial communities prior to infection interact with host genetics to predict infection outcomes later in life. Later, we will integrate susceptibility data with social network patterns in order to build an epidemiological model aiming at identifying the main drivers of transmission. This project will not only significantly add to our understanding of the biological and social drivers of TB epidemiology, but will generate novel insights into host-microbe interactions that will provide the foundation for future research on microbial and disease ecology.

In cooperation with Prof. Dr. Marta Manser (Univ. Zürich), Prof. Dr. T. Clutton-Brock (Univ. Cambridge). Funded by DFG Sommer SO 428/15-1.

Effects of landscape-level disturbance on species diversity and abundance pattern, and associated ecological, genetic, microbial and health effects - Local diversity of host populations as determinants of reservoir-borne virus dynamics

Despite considerable research efforts during recent years, still very little is known about fundamental ecological mechanisms driving virus prevalence, evolutionary potential and emergence from wildlife reservoirs in general. Holistic approaches integrating host and viral traits are required to understand the dynamics and drivers of virus infections. This collaborative, multi-taxa project investigates the impact of anthropogenic habitat disturbance on host community composition, abundance pattern and immune genetic constitution of generalist species and relates the obtained data to local virus prevalence. Our aim is to identify ecological, behavioral and genetic constraints associated with virus evolution under the hypothesis of the dilution effect. We are focusing on three major viral vertebrate host taxa - bats, rodents and marsupials. Whereas our focus in the first funding period was on taking

baseline data and parameter correlations, we will shift in the second period to ecological validation, ecological modeling and network analyses of host-virus systems in order to investigate the development and dynamics of virus mutation hotspots in disturbed landscapes. The central task will be to understand the processes and mechanisms that determine how biodiversity loss and shifts in species abundance of resilient, less sensitive species modulate virus ecology and lead to an increased prevalence and diversification of emerging pathogens within native animal communities.

Funded by DFG Priority Program 'Ecology and species barriers in emerging viral diseases' (SPP 1596, Sommer SO 428/9-1, SO 428/9-2).

ZDF planet e: Welt der Viren (22.03.2020, 28 min)
https://www.zdf.de/dokumentation/planet-e/planet-e-welt-der-viren-100.html

Harnessing the microbiome for turtle conservation: investigating the protective effects of the eggshell microbiome against the emerging fungal disease Fusariosis using the yellow-spotted Amazon river turtle as a model system

The emergence of fungal pathogens threatening wildlife has increased exponentially, in part driven by emerging infectious diseases that are exacerbated by habitat degradation, pollution, and wildlife trade. Whilst catastrophic declines in amphibians and bats due to emerging fungal pathogens has been well documented, high mortality in sea turtles due to the emerging fungal disease *Fusariosis* has received less attention. This emerging disease is caused by the group of related pathogens in the *Fusarium solani* species complex (FSSC), involved in mass mortality of all seven sea turtle species by infecting turtle eggs during incubation and causing hatching failure. Alarmingly, this pathogen was recently detected in the Yellow-spotted Amazonian river turtle (*Podocnemis unifilis*) in the Ecuadorian Amazon, suggesting that this pathogen may also pose a threat to the 357 species of freshwater turtles and tortoises, many of which are already endangered. However, despite the imminent threat this emerging pathogen poses towards turtle biodiversity, we have very little understanding of this fungal disease, including its transmission dynamics, pathogenicity, and long-term fitness effects on turtle hosts. To address this gap, we propose to investigate *Fusarium* disease dynamics using *P. unifilis* as a model system. This species is part of a conservation program run by the Tipuni Biodiversity Station/Amazon since 2002, whereby eggs are collected at the point of laying and hatchlings are reared in captivity before being released, to avoid overharvesting of eggs for consumption and the illegal pet trade. Along this line, we will investigate the environmental and maternal sources of *Fusarium* infection at the point of laying and monitor eggs in captivity to characterise pathogenicity and infection development. Moreover, we will examine how habitat degradation due to palm oil agriculture alters *Fusarium* prevalence and pathogenicity. Lastly, we will test the role of the eggshell microbiome, which has recently been linked to *Fusarium* resistance, in mediating infection outcome and hatching success, with an aim of identifying eggshell microbes that can be harnessed for turtle conservation. Our knowledge about the development and assembly of the egg microbiome is limited to avian species and these mechanisms do not apply to turtles due to differences in parental care strategies between birds and turtles. Studies about the transmission and development of the egg bacterial and fungal microbiome in oviparous reptiles without parental care like turtles and their functional role in mediating pathogen resistance are missing. Together, these lines of research will considerably expand our understanding of *Fusarium* as an emerging infectious disease and the role of host-microbiome interactions for turtle health, thereby contributing to the development of effective turtle conservation strategies in the face of an emerging and potentially devastating threat.

In cooperation with Prof. Dr. María de Lourdes Torres, Prof. Dr. David Romo Vallejo, and Prof. Dr. Gonzalo Francisco Rivas Torres (Universidad San Francisco de Quito, Ecuador).

Pathogen resistance, adaptive genetic diversity and microbiome homeostasis and its implication for conservation

The genes of the major histocompatibility complex (MHC) and the gut microbiome play key roles in host health. We study the link between pathogen infections, MHC variation and microbiome composition in different Mammalian taxa in an ecological, evolutionary and conservation orientated context.

Small selection of finished projects (see publication list for output details)

Olfactory choice of partners – immune system, smell receptors and their adaptive importance for the level of health in mammals

Olfaction plays a central role for mate choice in mammals, but there is a lack of understanding of the underlying proximate and ultimate aspects of olfactory signal evolution. Recent studies highlighted the importance of the major histocompatibility complex (MHC) for female choice which raises the question how volatiles, olfactory receptors and the MHC co-evolved in mammalian mating systems. The project applied a broad genomic approach using 'next generation sequencing' on two species with contrasting social and mating systems, the greater sac-winged bat in Costa Rica and raccoons in Germany.

Host adaptations at the molecular and transcriptional level driven by a fast evolving pathogen, the rabbit haemorrhagic disease virus (RHDV) raging in European rabbits (*Oryctolagus cuniculus*)

Under natural conditions, pathogens are strong selective forces that drive coevolutionary processes. Studies on selective mechanisms in host species largely concentrated on analyses of major histocompatibility complex (MHC) sequence variation but did not take variance of expression in other genome-wide distributed relevant genes into account. This might be of evolutionary importance, in particular in response to fast evolving viruses. But how viruses remodel the host's gene expression patterns and the genetic constitution of host populations is still elusive. We investigate the adaptive variance on the structural and transcriptional level caused by a severe contagious viral infection, using both experimental and field approaches. Our model, the rabbit haemorrhagic disease (RHD) raging in European rabbits (*Oryctolagus cuniculus*) provides ideal preconditions for this purpose due to already available long-term field as well as genomic data. We use gene expression profiling via microarrays, qRT-PCR, MHC-genotyping and the application of GBS (Genotyping by Sequencing) to discover candidate genes and expression patterns involved in host-pathogen interactions. This changes the focus from a few to thousands of genes and multiple regulatory mechanisms. It allows us to test current selection hypotheses in more detail to improve our understanding of causes and processes of evolutionary adaptations between hosts and pathogens.

Effects of land-use changes on the bacterial load of black-backed jackals (*Canis mesomelas*) and bat-eared foxes (*Otocyon megalotis*) in Namibia – a metagenomics approach to understand the ecological and molecular attributes affecting population health in important pathogen reservoirs and vectors

Anthropogenic land-use modification is supposed to stress wildlife with negative effects on health conditions. It also facilitates the contact between wildlife and human associated livestock potentially affecting the transmission rate of pathogens which might be one reason for the increasing number of novel infectious diseases threatening our biodiversity. In the farmlands of central Namibia, we investigate how two prevalent modes of land-use (livestock versus game farming) and associated animal communities affect the health status of prominent canids and felids of southern Africa. We focus on black-backed jackals (*Canis mesomelas*), bat-eared foxes (*Otocyon megalotis*) and cheetahs (*Acinonyx jubatus*). All have been blamed as important pathogen reservoirs and vectors and occur in our study area also in modified habitats. We use a metagenomics approach applying next-generation sequencing technologies to qualify, quantify and compare the bacteria community (microbiome). Furthermore, we genotype the immune gene variability (MHC) of all species and investigate their impact on the pathogen load also using high-throughput methods and multivariate statistics. Our study will increase our understanding of the ecological and molecular attributes affecting population health of host and potential vector species as well as species barriers in viral and bacterial diseases. This will contribute to avoid eradication programs as a management tool during disease outbreaks.