Selected projects

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.

In cooperation with Prof. Dr. Christian Drosten, Dr. Victor Corman (Charité, Berlin). Funded by DFG Priority Program ‘Ecology and species barriers in emerging viral diseases’ (SPP 1596, Sommer SO 428/9-1, SO 428/9-2).

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.

In cooperation with Prof. Dr. Christian Drosten, Dr. Victor Corman (Charité, Berlin). Funded by DFG Sommer SO 428/17-1.

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.

Maintenance of adaptive genetic diversity in a small populations and its implication for conservation - functional importance of MHC variation in parasite and pathogen resistance

The genes of the major histocompatibility complex (MHC) are one side of a co-evolutionary arms race between host and their parasites. They are coding for cell surface glycoproteins in vertebrates and are responsible for the recognition of foreign antigens and thereby directly linked with parasite resistance and individual fitness. We study the functional important of MHC variation and expression on parasite burden in different Mammalian radiations (e.g. in lemurs, rodents, rabbits, anteaters, cheetahs) in an ecological, evolutionary and conservation orientated context.
In cooperation with Prof. Dr. Jörg Ganzhorn (Univ. Hamburg). Funded by Deutsche Gesellschaft für Säugetierkunde, Berlin.

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 three species with

contrasting social and mating systems, the greater sac-winged bat in Costa Rica, the spotted hyena in Tanzania, 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.

Funded by DFG Priority Program 'Host-Parasite Coevolution – Rapid reciprocal adaptation and its genetic basis' (SPP 1399, DFG Sommer SO 428/7-1).

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.

Funded by DFG (Sommer SO 428/10-1).