Max Planck Institute for Evolutionary Biology

ROBERT KOCH INSTITUT

One Past Health

Workshop on zoonotic diseases and ancient DNA

February 15 - 17, 2017

Venue:

Max Planck Institute for
Evolutionary Biology
August-Thienemann-Str. 2
24306 Plön, Germany

Cover photo credit: Fabian Leendertz, Ben Krause-Kyora

Program overview

Wednesday, 15th		Thursday, 16th		Friday, 17th	
09:00		09:00	**Plenary: Simone Sommer**	09:00	**Plenary: Frank Kirchhoff**
10:00		10:00	**Plenary: Christian Drosten**	10:00	Jatin Arora
					Alex Greenwood
			Coffee		Coffee
11:00		11:00	Florian Binder	11:00	Jamie Winternitz
			Hamzah Hasyim		Sébastien Calvignac-Spencer
			Federica Pierini		Scientific discussion
12:00		12:00	Máté Manczinger	12:00	
			Lunch (at restaurant)		Lunch (at institute)
13:00		13:00		13:00	
			Tour of the institute		Conclusion and farewell
14:00	Check in & Registration	14:00	**Plenary: Philippe Lemey**	14:00	
15:00	Welcome address	15:00	Simon Frost	15:00	
	Plenary: Johannes Krause		Coffee		
16:00		16:00	**Plenary: Charles Nunn**	16:00	
	Coffee				
	Alexander Herbig		Anne Stone		
17:00	Aida Andrades Valtueña	17:00	Scientific discussion	17:00	
	Verena Schuenemann				
	Kirsten Bos				
18:00	Felix Key	18:00	Walk to restaurant	18:00	
	Dinner (at institute)		Dinner (at restaurant)		
19:00		19:00		19:00	
	Scientific discussion + Mixer (at institute)		Scientific discussion cont. (at restaurant)		

Workshop program

Wednesday, February 15

14:00 - 15:00	Check in & Registration
15:00 - 15:30	Welcome address
15:30 - 16:20	**Plenary: Johannes Krause**
16:20 - 16:40	Coffee
16:40 - 17:00	**Alexander Herbig**
17:00 - 17:20	**Aida Andrades Valtueña**
17:20 - 17:40	**Verena Schuenemann**
17:40 - 18:00	**Kirsten Bos**
18:00 - 18:20	**Felix Key**
18:20 - 19:20	Dinner (at institute)
19:20 -	Scientific discussion + Mixer (at institute)

Thursday, February 16

09:00 - 09:50	**Plenary: Simone Sommer**
09:50 - 10:40	**Plenary: Christian Drosten**
10:40 - 11:00	Coffee
11:00 - 11:20	**Florian Binder**
11:20 - 11:40	**Hamzah Hasyim**
11:40 - 12:00	**Federica Pierini**
12:00 - 12:20	**Máté Manczinger**
12:20 - 13:40	Lunch (at restaurant)
13:40 - 14:20	Tour of the institute
14:20 - 15:10	**Plenary: Philippe Lemey**
15:10 - 15:30	**Simon Frost**
15:30 - 15:50	Coffee
15:50 - 16:40	**Plenary: Charles Nunn**
16:40 - 17:00	**Anne Stone**
17:00 - 18:00	**Scientific discussion**
18:00 - 18:30	Walk to restaurant
18:30 - 19:20	Dinner (at restaurant)
19:20 -	Scientific discussion cont. (at restaurant)

Friday, February 17

09:00 - 09:50	**Plenary: Frank Kirchhoff**
09:50 - 10:10	**Jatin Arora**
10:10 - 10:30	**Alex Greenwood**
10:30 - 10:50	Coffee
10:50 - 11:10	**Jamie Winternitz**
11:10 - 11:30	**Sébastien Calvignac-Spencer**
11:30 - 12:30	**Scientific discussion**
12:30 - 13:30	Lunch (at institute)
13:30 - 14:00	Conclusion and farewell

Wednesday, 15:30

Ancient Pathogen Genomics: What we learn about Zoonosis from the past

Johannes Krause

Presenting author:
Johannes Krause
Max Planck Institute for the Science of Human History, Archeogenetics, Jena, Germany

High throughput sequencing has revolutionized the field of archaeogenetics in the last decade, providing a better understanding of human history, past population dynamics and host pathogen interactions through time. Targeted DNA capture approaches have allowed reconstructing complete ancient bacterial genomes providing direct insights into the evolution and origin of some of the most infamous pathogens known to humans such as Yersinia pestis, Mycobacterium tuberculosis or Mycobacterium leprae. Here the potential of ancient pathogen genomics is discussed in the light of zoonosis research. Phylogenetic comparisons of modern and ancient bacterial genomes are presented that have provided direct evidence for zoonotic transmissions between humans and animals in the past that might have been responsible for the dissemination of M.tuberculosis in the Americas before European contact. Furthermore genome wide studies of Y.pestis over 5000 years of human history are discussed that provide evidence that major virulence factors essential for the transmission of bacteria by fleas have evolved rather late in human history. Temporal studies of pathogens might thus throw new light on the zoonotic origin of human diseases and potentially allow predicting and preventing further zoonotic transmissions in the future.

Thursday, 09:00

Ecological and genomic drivers of wildlife infections

Simone Sommer

Presenting author:
Simone Sommer
University of Ulm, Evolutionary Ecology and Conservation Genomics, Ulm, Germany

Anthropogenic environmental change and loss of biodiversity has been shown to increase the infection prevalence in wildlife reservoirs and drive zoonotic diseases. However, despite recent advances in theoretical concepts and mathematical models, empirical data concerning the ecological and genomic drivers of infections in wild animal populations, especially from the tropics, remain scarce. I will first summarize current concepts on the ecological and genomic drivers of wildlife infections and then use one of our projects to illustrate the complex interaction between various drivers. We have studied small mammal and bat populations in three tropical landscapes in central Panama differing in their degree of human disturbance to test whether changes in species richness affect host population density and virus prevalence. Our results indicate that the transformation of continuous habitat into partly connected or discrete habitat patches is indeed associated with changes in these community traits. We have detected an increasing prevalence of directly transmitted Hepacivirus, driven by increasing host density and sex-specific constraints. We furthermore investigated the effects of host adaptive (TLR, MHC) diversity on infection and resistance pattern to infer the impact of genomic constraints and reduced genetic diversity. Our study has revealed ecological and genomic mechanisms by which human-induced landscape change can have significant effects on zoonotic diseases.

Thursday, 09:50

Virus ecology: studying animal reservoirs to understand viral emergence

Christian Drosten

Presenting author:
Christian Drosten
University of Bonn, Institute of Virology & Charité, Bonn, Germany

Fifteen years after the SARS epidemic, zoonotic and emerging viruses have become a growing field of research. Some remarkable novel virus descriptions in animals have demonstrated how ignorant we are of the diversity of viruses around us. In our efforts to delineate viral origins we may have to re-asess our concept of reservoir. In many instances, we are mixing up ecological and epidemiological implications of viral evolution. Among the biggest challenges in this field is the integration of the concepts of virus-host codivergence, and viral host switching. In addition, assessments of viral reservoirs with the intention to predict future pandemic threats would have to take into account important host and virus traits which cannot be predicted merely from virus genes. For example, we need to know whether there are hosts which have a higher propensity to carry broader spectra or higher concentrations of viruses, potentially without being affected. Among the viruses borne in such reservoirs, there may be some that are more promiscuous in their choice of hosts than others, potentially due to the conservedness of their receptor structures or the way they interfere with conserved- or not-so-conserved immune properties. A synopsis of available approaches demonstrates how much work needs to be done before we will be able to assess functional, rather than genetic diversity of reservoir-borne viruses.

Thursday, 14:20

Data integration in Bayesian phylogenetic reconstruction to elucidate pathogen phylodynamics

Philippe Lemey

Presenting author:
Philippe Lemey
KU Leuven, Clinical and Epidemiological Virology, Leuven, Belgium

The field of phylodynamics has witnessed a rich development of statistical inference tools, with increasing levels of sophistication, that assist in uncovering pathogen evolutionary and epidemiological processes. A Bayesian phylogenetic framework that focuses on time-measured trees has proven fertile ground for integrating such approaches. Here, I will discuss emerging concepts of data integration that are stimulating new advances in Bayesian evolutionary inference methodology. Specifically, I will highlight how simple generalised linear modelling can be implemented in sequence evolutionary models, discrete trait diffusion models and coalescent models in order to test and quantify the contribution of covariates to these processes. Applications involve divergence dating for HIV-1, host jumping in a multi-host bat rabies virus system and testing predictors of spatial spread of Ebola virus during the 2013-2016 West African epidemic.

Thursday, 15:50

Understanding Zoonoses Using Comparative Data: The Global Mammal Parasite Database

Charles L. Nunn

Presenting author:
Charles Nunn
Duke University, Evolutionary Anthropology & Duke Global Health Institute, Durham, USA

Significant effort has aimed to understand zoonoses using genetic data from infectious agents circulating today, or by using ancient DNA. In this talk, I consider another source of information on the history of zoonoses: large-scale comparative analyses of the parasites and pathogens of primates. I focus on analyses of primate parasites from the Global Mammal Parasite Database. First, I review research on the sharing of parasites among primates. These analyses reveal that multiple factors predict sharing of parasites among primates, including phylogenetic closeness, a larger geographic range, higher population density, and phenotypic similarity of species. Next, I consider whether humans are more heavily parasitized than other primates, perhaps due to our close contact with domesticated animals and more sedentary lifestyles. Using new phylogenetic methods to predict human phenotypes based on other primates - and controlling for vast differences in sampling effort and geographic distributions of humans compared to other primates - we find that humans are not particularly exceptional in their parasite richness. Nonetheless, other findings suggest that the composition of human parasites has shifted, consistent with the role of zoonotic events in shaping the parasite communities of humans.

Friday, 09:00

Origin of HIV and adaptation to the human host

Frank Kirchhoff

Presenting author:
Frank Kirchhoff
Ulm University Medical Center, Institute of Molecular Virology, Ulm, Germany

Simian immunodeficiency viruses (SIVs) are found in about 40 different monkey and ape species in Sub-Saharan Africa and three of them (Sooty mangabeys, gorillas and chimpanzees) have transmitted their virus to humans. Only one of at least thirteen independent zoonotic transmissions, however, is responsible for the AIDS pandemic. Here, I will describe the origin and evolution of the different groups of HIV-1 and discuss their respective human-specific adaptations and reasons for their differential spread in the human population. First, it will be shown that only group M HIV-1 strains are “perfectly” adapted to human and are fully capable of evading or counteracting all of our defence mechanisms. Next, evidence will be presented that adaptation of rare group N and epidemic group O HIV-1 strains is currently ongoing. Finally, I will discuss that HIV-1 not only counteracts restriction factors directly but also suppresses their induction and expression by modulating NF-kB activity and DNA damage repair pathways. In summary, the presentation will show that the striking adaptability of primate lentiviruses was a prerequisite for one of the deadliest pandemics in modern times.

Wednesday, 16:40

MALT: Fast alignment and analysis of metagenomic DNA sequence data applied to the Tyrolean Iceman

Alexander Herbig, Frank Maixner, Kirsten I. Bos, Albert Zink, Johannes Krause & Daniel H. Huson

Presenting author:
Alexander Herbig
Max Planck Institute for the Science of Human History, Department of Archaeogenetics, Jena, Germany

By the utilization of modern sequencing technologies huge amounts of DNA sequence data can be produced in large-scale metagenomic experiments, which allows for studying the complexity of microbial communities in unprecedented detail. For these analyses high-throughput computational methods are required that can process sequencing data in a time efficient manner while retaining a high level of sensitivity and precision. Here we present MALT (Megan ALignment Tool), a program for the fast alignment of DNA sequencing reads to large reference databases. With MALT hundreds of millions of reads can be processed within only a few hours. In addition to the alignment step MALT implements a taxonomic binning algorithm that assigns reads to specific species. MALT output can be directly loaded by the interactive metagenomic analysis software MEGAN, which allows for further analysis and visualization of the results. These analyses can be performed in a comparative manner for studying the dynamics of microbial communities over time, or from different habitats or hosts. In this context human or animal related microbiomes are of major interest. They are comprised of a large number of commensals, but potentially also pathogens that have evolved with their host. To gain insights into these evolutionary relationships, the field of paleogenetics aims to study ancient metagenomes based on DNA extracted from archaeological remains. We demonstrate MALT by applying it to the analysis of two ancient microbiomes based on oral cavity and lung samples from the 5,300-year-old Tyrolean Iceman. Despite a strong environmental background, MALT is able to detect the weak signal of the endogenous microbiomes and identifies multiple species that are typical representatives of the respective host environment.

Wednesday, 17:00

The Stone Age Plague: 1000 years of Persistence in Eurasia

Aida Andrades Valtueña, Alissa Mittnik, Ken Massy, Raili Allmäe, Mantas Daubaras, Rimantas Jankauskas, Mari Tõrv, Saskia Pfrengle, Maria A. Spyrou, Michal Feldman, Wolfgang Haak, Kirsten I. Bos, Philipp W. Stockhammer, Alexander Herbig & Johannes Krause

Presenting author:
Aida Andrades Valtueña
Max Planck Institute for the Science of Human History, Archaeogenetics, Jena, Germany

Yersinia pestis is the aetiological agent of plague. Plague is a zoonotic disease associated with rodents and their fleas that has affected human populations in three historic pandemics during the past: the Plague of Justinian in the 6th century AD; the second pandemic, which started with the infamous Black Death in the middle of the 14th century; and the most recent third pandemic, which started in the 19th century when Y. pestis spread world-wide and has become endemic in many regions all over the world. The discovery of molecular signatures of Yersinia pestis in Late Neolithic and Early Bronze Age (LNBA) Eurasian individuals suggests the presence of a form of plague long before the first historically documented pandemic. Here, we present the first four European Y. pestis genomes from this time period. Through comparative phylogenetic analysis with 14 ancient and 160 modern Y. pestis strains we show that all currently reconstructed LNBA strains from Eurasia form a distinct clade that seems to be nowadays extinct. In the context of recent findings from human ancient DNA research and the age of the Y. pestis genomes, we propose that Y. pestis entered Europe from Central Eurasia during an expansion of Eurasian steppe pastoralists, persisted in Europe and travelled back to Central Eurasia with subsequent human movements. We further explore the mode of transmission of Y. pestis during this time based on the genomic data. The LNBA strains may have been transmitted by fleas but in a less efficient manner than the their modern counterparts. The potential hosts of Y. pestis during the LNBA remain unknown. The most parsimonious scenario suggests that Y. pestis was transmitted to human populations by fleas with a rodent population as a reservoir, as known from modern zoonotic events. However, whether other animals, such as livestock or birds, or other vectors, such as lice, could have played a role in the spread of Y. pestis still needs to be explored.

Wednesday, 17:20

Ancient leprosy genomics: Retracing the evolutionary history of Mycobacterium leprae using ancient DNA

Verena J. Schuenemann, Charlotte Avanzi, Alexander Seitz, Ben Krause-Kyora, Alexander Herbig, Andrej Benjak, Sarah Inskip, Ella Reiter, Christian Urban, Jesper L. Boldsen, G. Michael Taylor, Pushpendra Singh, Graham T. Stewart, Petr Velemínský & Jakub Liko

Presenting author:
Verena Schuenemann
University of Tübingen, AG Paleogenetics, Institute for Archaeological Sciences, Tübingen, Germany

Ancient DNA studies can provide new perspectives for evolutionary history of pathogens. This includes Mycobacterium leprae, the causative agent of leprosy, one of the oldest recorded and most feared diseases in human history, which was prevalent in Europe until the 16th century and is still endemic in many countries with over 200,000 new cases reported annually. Previously, an exceptional DNA preservation of M. leprae in medieval skeletons enabled us to successfully reconstruct a late medieval leprosy genome by de novo assembly, thus offering the opportunity to retrace M. leprae's pre-historic origin. Furthermore, the analysis of medieval M. leprae genomes indicates a pre-medieval origin of most contemporary human and armadillo M. leprae lineages and suggested a presence of two distinct lineages in medieval northwestern Europe. Our new data provide new insights into the evolutionary history of leprosy in Europe from genome wide data of different time points and geographic origin including a 1500-year-old M. leprae genome from one of the earliest known cases of leprosy in the UK, a skeleton from the Great Chesterford cemetery with a calibrated date of 415–545 AD. A phylogenetic analysis including these novel medieval genomes points to a more complex picture of the geographic lineages distributed in medieval Europe than previously assumed: we found up to four distinct lineages suggesting a high diversity of M. leprae strains in medieval Europe. With the Great Chesterford M. leprae genome, the so far oldest M. leprae genome, we were able to trace one of the lineages, lineage 3, back to the 6th century. These results develop and refine previous models for the geographic distribution of M. leprae lineages in the past indicating a higher complexity and point out the necessity of studying ancient M. leprae strains to understand the history of leprosy worldwide.

Wednesday, 17:40

Zoonotic infections of Mycobacterium tuberculosis in the precontact New World

Kirsten I Bos, Åshild Vågene, Tanivi Honap, Alexander Herbig, Jane Buikstra, Anne Stone & Johannes Krause

Presenting author:
Kirsten Bos
Max Planck Institute for the Science of Human History, Archeogenetics, Jena, Germany

Pre-contact Peruvian cultures are among the first New World populations to show skeletal indications of tuberculosis, and recent molecular analyses have revealed that three individuals were afflicted with a rare zoonotic form of the disease acquired from marine mammals. This form is no longer circulating in the human population, and it appears to have been replaced by the European variant after contact. While the ancient disease was presumably acquired through either the consumption or manipulation of tissues from affected seals or sea lions, little is known about its range in the human population and whether or not it subsequently became human-adapted. This talk will explore our recent work on the molecular evaluation of additional skeletal material from the Americas that show physical evidence of tuberculosis infections. Our analyses are conducted with the aim of exploring the different forms of tuberculosis that were circulating in the New World before contact, their relationship to the Peruvian form, and the potential evidence for human adaptation.

Wednesday, 18:00

High-throughput pathogen detection in ancient metagenomic data

Felix M Key, Ron Hübler, Wolfgang Haak, Johannes Krause & Alexander Herbig

Presenting author:
Felix M Key
Max Planck Institute for the Science of Human History, Department of Archaeogenetics, Jena, Germany

Analysis of pathogens associated with ancient humans has long been limited to characteristic skeletal lesions. The rising availability of metagenomic DNA obtained from ancient human remains offers a new possibility for detection of pathogen presence, thereby granting us direct evidence of pathogens and the human disease burden even if phenotypic lesions are absent. Further, the genomic information retrieved from pathogens helps to elucidate the evolution of the pathogen and thus its adaptation to the human host. Manual approaches for pathogen detection in ancient metagenomic data are laborious and error prone. Aiming at the development of an in-silico pipeline to automate the detection of bacterial pathogens in ancient metagenomic data we employ a set of summary statistics indicative for the presence of true ancient pathogens. We demonstrate our approach by applying it to a massive, and diverse ancient metagenomic dataset to infer the presence of pathogens for over 10.000 years of human evolution.

Thursday, 11:00

Host-Associated Absence of Human Puumala Virus Infections in Northern and Eastern Germany

Stephan Drewes, Hanan Sheikh Ali, Moritz Saxenhofer, Ulrike M. Rosenfeld, Florian Binder, Fabian Cuypers, Mathias Schlegel, Susanne Röhrs, Gerald Heckel & Rainer G. Ulrich

Presenting author:
Florian Binder
Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany

Puumala virus (PUUV) is a hantavirus causing a mild to moderate form of hemorrhagic fever with renal syndrome in humans. Its reservoir host, the bank vole (Myodes glareolus), is widely distributed in Europe. PUUV outbreaks mainly affect western and southern Germany. In contrast, very low numbers of human cases have been recorded in Northeastern Germany. The objective of our study is to find out potential reasons for the inhomogeneous distribution of PUUV infections in Central Europe. Our hypothesis is that the presence of different evolutionary lineages of the rodent host represents a major reason. For this purpose, bank voles from relevant regions of Germany were tested for PUUV infection. Serological and molecular analyses demonstrated a usually medium to high PUUV prevalence in endemic areas. In contrast, bank voles from various sites in the northeastern part of Germany were seronegative. Initial cytochrome b analyses of bank voles suggested the presence of the Eastern and Carpathian evolutionary lineages in the Northeast of Germany, but the Western evolutionary lineage in the endemic regions. Future investigations will have to prove if the different genetic lineages of the bank vole differ in susceptibility to PUUV and might be a cause of the inhomogeneous distribution of this hantavirus in Central Europe.

Thursday, 11:20

Does livestock protect from malaria or serve as a source of malaria? A cross-sectional study in endemic rural areas of Indonesia

Hamzah Hasyim, Meghnath Dhimal, Doreen Montag, David A. Groneberg, Ulrich Kuch & Ruth Müller

Presenting author:
Hamzah Hasyim
Goethe University, Department of Tropical Medicine and Public Health, Frankfurt am Main, Germany

Since malaria was first acknowledged as being transmitted by zoophilic vectors, zooprophylaxis has been used to prevent malaria. While the existence of livestock as a variable of importance for malaria risk has already been assessed, the outcomes of such studies are still highly debated. In the present study, the association amongst the presence of livestock raised in households and the prevalence of malaria was assessed from a large-scale survey from Indonesian basic health research. Here, the subset included 259,885 participants who reside at 176 regencies of 15 provinces in the rural area. In this study, we could demonstrate that residents who raised goats, sheep and pigs had 1.6 times greater risk of getting malaria compared to participants who did not keep livestock, when adjustments were made for other covariates in the areas under investigation. Adjusted odds ratio (AOR) 1.64, 95% CI 1.44-1.86, $P < 0.001$. In summary, our results imply that livestock has to be considered as a source of malaria rather than as a prophylactic tool. We firmly recommend the implementation of an overall \One Health\ strategy as part of a programme to eliminate malaria, with the aim of a malaria-free Indonesia by 2030.

Thursday, 11:40

Ancient HLA immune gene polymorphism in pre-European contact Native American populations

Federica Pierini, Austin W. Reynolds, Jaime Mata-Míguez, Marcel Nutsua, Lisa Böhme, Almut Nebel, Ben Krause-Kyora, Deborah A. Bolnick & Tobias L. Lenz

Presenting author:
Federica Pierini
Max Planck Institute for Evolutionary Biology, Evolutionary Ecology, Plön, Germany

It has been proposed that selection for resistance to infection drives the evolution of genetic variability at the major histocompatibility complex (MHC). In humans, a number of studies suggest that specific alleles of the human leukocyte antigen (HLA) are associated with susceptibility or resistance to a number of infectious diseases (i.e. HIV, malaria, tuberculosis, hepatitis) but, unlike for several other species, convincing evidence for pathogen-driven selection is still awaited. In this light, the recent development of genomic tools for analysis of ancient DNA (aDNA) provide a unique opportunity to unravel selection processes throughout human history. Archeological, historical and genetic studies indicate that Native Americans experienced a strong population bottleneck following European contact. It has been proposed that Native Americans' HLA genes may have lacked both genetic polymorphism generally and specific resistance alleles to a variety of new pathogens introduced by European colonizers, resulting in an increased susceptibility to new diseases (i.e. smallpox, measles, diphtheria, rubella, and mumps). Here we use in-solution targeted capture on aDNA samples to analyze HLA polymorphism in an ancient Native American population. We will use this technology to investigate potential HLA allele frequency shifts from pre- to post-European contact. This work is expected to highlight possible signatures of emerging selection in response to specific new pathogens, so-called virgin-soil epidemics, introduced by European colonizers.

Thursday, 12:00

Parasite load drives rapid evolution of promiscuous peptide binding in human MHC-II alleles

Máté Manczinger, Gábor Boross, Benjamin Papp, Balázs Papp, Csaba Pál & Lajos Kemény

Presenting author:
Máté Manczinger
University of Szeged, Department of Dermatology and Allergology, Szeged, Hungary

The adaptive immune system must detect a wide variety of parasites and distinguish them from the organism's own healthy tissue. By recognizing peptide segments (epitopes), the major histocompatibility complex (MHC) molecules shape the clonal immune response against parasites and tolerance to self-peptides. How do these molecules evolve in human populations facing different sets of parasites? We demonstrate that in geographical regions of low parasite diversity, human MHC-II molecules specifically recognize epitopes derived from endemic extracellular parasites. By contrast, when parasite diversity is high, evolution of MHC-II alleles takes a different route. In such regions, individual MHC-II alleles have exceptionally high epitope binding repertoire, indicating that they can promote immune response against a greater breadth of parasites. These promiscuous MHC-II alleles are not confined to a single geographic area or a human race, cover different segments of the epitope genotype space, and have multiple independent evolutionary origins. The switch towards increased epitope-binding repertoire of MHC-II molecules has been very rapid during the course of human evolution, driven by positively selected mutations. In sum, our work indicates that MHC class II epitope binding repertoire shows large variation worldwide and evolves rapidly with implications on genetic susceptibility to extracellular parasites.

Thursday, 15:10

Modeling the phylodynamics of zoonoses

Simon D.W. Frost, Bethany L. Dearlove & Erik M. Volz

Presenting author:
Simon Frost
University of Cambridge, Veterinary Medicine, Cambridge, United Kingdom

While some zoonotic infections in humans arise from a single host jump, others, such as MERS-Coronavirus and Lassa Fever, are characterized by ongoing spillover from the reservoir population. Pathogen sequence data can provide information on the number and timing of host jumps, based on the phylogenetic pattern of samples from the reservoir and from humans. However, sampling is often highly biased, particularly in an emerging epidemic, with relatively small numbers of samples, particularly from the reservoir population. We present a phylodynamic framework for comparing the number of host jumps in a population with those inferred from a sample of sequences, using parsimony and likelihood-based models. We demonstrate, both in theory and in practice, how biased sampling can lead to the inferred direction of host jumps being reversed (i.e. from humans to the reservoir). Even when host jumps are constrained in one direction, parsimony underestimates the number of jumps, particularly those in the recent past. We show how external knowledge on directionality and the sample fraction can be integrated with a likelihood-based model in order to generate accurate inferences of host jumps.

Thursday, 16:40

Non-human primate Mycobacterium leprae strains and their relationship to human leprosy strains

Tanvi P. Honap, Luz-Andrea Pfister & Anne C. Stone

Presenting author:
Anne Stone
Arizona State Unversity, School of Human Evolution and Social Change, Tempe, Arizona, United States

Leprosy is one of the most ancient documented human diseases, but when and where it first afflicted humans and its zoonotic origin remains unclear. Mycobacterium leprae and the recently identified M. lepromatosis are the causative agents of leprosy in humans. Both pathogens have been found in red squirrels in the United Kingdom and Ireland, and M. leprae infects nine-banded armadillos, which serve as a reservoir for this pathogen in the Americas. Occasionally, natural leprosy has also been observed in nonhuman primates. It is not known whether leprosy in nonhuman primates occurs due to incidental infections from humans or if nonhuman primates carry these pathogens and can also transmit them to other species. Here we report the results of sequencing strains from three naturally infected nonhuman primates (a chimpanzee from Sierra Leone, a sooty mangabey from Nigeria, and a cynomolgus macaque from the Philippines). All animals were born in the wild and developed signs of leprosy during captivity despite never having any contact with a known source. We sequenced the genomes of these strains using in-solution whole-genome capture and next-generation sequencing technology, and conducted phylogenetic analyses to determine their relationship to modern and ancient human M. leprae and M. lepromatosis strains. The cynomolgus macaque has an M. leprae strain belonging to a human M. leprae lineage found in Asia. The chimpanzee and sooty mangabey strains are closely related to each other and belong to a human M. leprae lineage found in West Africa. The close relationship of the two African nonhuman primate M. leprae strains suggests that different nonhuman primate species may transmit M. leprae among themselves.

Friday, 09:50

HIV epitope prediction provides functional link between HLA genotype and viral load

Jatin Arora, Paul J. McLaren, István Bartha, Nimisha Chaturvedi, Jacques Fellay & Tobias L. Lenz

Presenting author:
Jatin Arora
Max Planck Institute for Evolutionary Biology, Evolutionary Ecology, Plön, Germany

Genetic variation in the peptide-binding groove of HLA molecules has repeatedly been associated with HIV infection and progression to AIDS, suggesting a key role for HLA-presentation of HIV-1 epitopes in disease control. However, the responsible repertoire of specific HLA-bound HIV-1 epitopes remains largely elusive. Using data from 6,311 HIV-1 patients, we computationally screen the entire HIV-1 proteome for disease-associated epitopes. We characterize a core set of HLA-presented HIV-1 epitopes that together account for the same amount of variation in set point viral load as all previously associated independent genetic variants in the HLA. Our findings thus provide a novel functional explanation for the association between HLA and HIV-1 control, and prioritize specifically Env-derived but also other strongly disease-associated epitopes as potential new therapeutic targets.

Friday, 10:10

Directly observing retroviral evolution using DNA from museum samples

Alex D. Greenwood

Presenting author:
Alex Greenwood
Leibniz Institute for Zoo and Wildlife Research, Wildlife Diseases, Berlin, Germany

Here I present a summary of the use of historical and ancient DNA to examine wildlife retroviral evolution directly using museum samples. Retroviruses are unique among viruses in that during replication they must insert a DNA copy of their genome, into the host cell genome where it becomes permanently integrated. If this occurs in the genome of a germ cell, the retrovirus becomes a permanent part of the host genome and will be transmitted vertically as a Mendelian trait. Such proviral integrations are termed endogenous retroviruses (ERVs). While many of the general evolutionary features of ERV evolution post genome invasion can be studied using modern DNA, the evolutionary trajectory during the invasion process become obscured over time. Unfortunately, most ERVs integrated and became fixed in their host genome millions of years ago largely obscuring the adaptations that resulted in their endogenization. The koala retrovirus, KoRV, is one of the few retroviruses that is known to be currently invading the genome of its host the koala (Phascolarctos cinereus). Using museum skins from the 19th and early 20th centuries, we have been able to show the rate of evolution and identify some of the mechanisms underlying KoRV endogenization in the koala genome which may generally explain aspects of the establishment of ERVs. Switching timescales, I will summarize the results of examining ERV evolution from extant sloths and elephants and their extinct Pleistocene giant ground sloth and woolly mammoth relatives. The results highlight the dependency of viral lineages on the fates of their host species over both medium and short term evolutionary timescales.

Friday, 10:50

Host–pathogen evolutionary signatures reveal dynamics and future invasions of vampire bat rabies

Daniel G. Streicker, Jamie C. Winternitz, Dara A. Satterfield, Rene Edgar Condori-Condori, Alice Broos, Carlos Tello, Sergio Recuenco, Andrés Velasco-Villa, Sonia Altizer & William Valderrama

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Anticipating how epidemics will spread across landscapes requires understanding host dispersal events that are notoriously difficult to measure. Here, we contrast host and virus genetic signatures to resolve the spatiotemporal dynamics underlying geographic expansions of vampire bat rabies virus (VBRV) in Peru. Phylogenetic analysis revealed recent viral spread between populations that, according to extreme geographic structure in maternally inherited host mitochondrial DNA, appeared completely isolated. In contrast, greater population connectivity in biparentally inherited nuclear microsatellites explained the historical limits of invasions, suggesting that dispersing male bats spread VBRV between genetically isolated female populations. Host nuclear DNA further indicated unanticipated gene flow through the Andes mountains connecting the VBRV-free Pacific coast to the VBRV-endemic Amazon rainforest. By combining Bayesian phylogeography with landscape resistance models, we projected invasion routes through northern Peru that were validated by real-time livestock rabies mortality data. The first outbreaks of VBRV on the Pacific coast of South America could occur by June 2020,which would have serious implications for agriculture, wildlife conservation, and human health. Our results show that combining host and pathogen genetic data can identify sex biases in pathogen spatial spread, which may be a widespread but underappreciated phenomenon, and demonstrate that genetic forecasting can aid preparedness for impending viral invasions.

Friday, 11:10

The evolution of dsDNA viruses in hominines

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Humans are infected with many double-stranded DNA (dsDNA) viruses, including a number of herpesviruses, papillomaviruses and polyomaviruses. Most of these viruses are suspected to have co-evolved with their vertebrate hosts over extended timescales. Therefore, it is often assumed that human-infecting dsDNA viruses are heirloom parasites, i.e. parasites which infected the human lineage long before the first epidemiological transition. Investigating the diversity of dsDNA viruses in African great apes and modeling their evolution provide opportunities to formally test this hypothesis. Here, we will discuss recent findings that documented long-term codivergence of dsDNA viruses with members of the hominine lineage and leveraged this knowledge to pinpoint the (sometimes zoonotic) origins of human dsDNA viruses. We will highlight how this evolutionary framework may generate new hypotheses that could be tested using aDNA approaches and how it may also provide a sensible roadmap for the discovery of new dsDNA viruses in humans.

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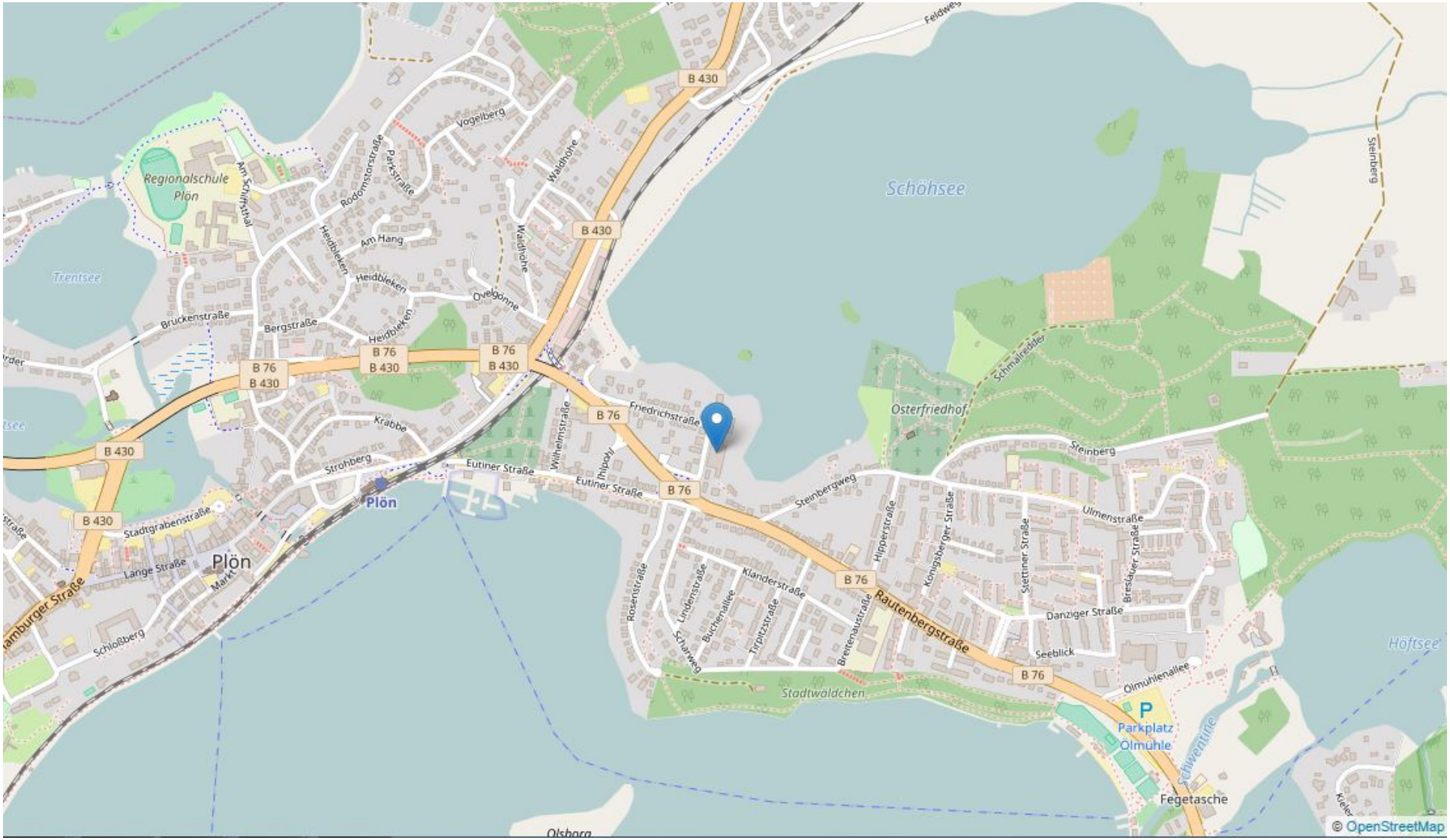
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