WORDS BONES GENES TOOLS

Tracking Linguistic, Cultural, and Biological Trajectories of the Human Past

8TH ANNUAL SYMPOSIUM

PHENOTYPE-GENOTYPE INTERACTIONS

DFG CENTER FOR ADVANCED STUDIES

DECEMBER 14TH—15TH

ALTE AULA

UNIVERSITY OF TÜBINGEN

EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN

DFG

The DFG Center for Advanced Studies

Inaugurated in 2015, the DFG Center for Advanced Studies "Words, Bones, Genes, Tools: Tracking Linguistic, Cultural, and Biological Trajectories of the Human Past" aims to help establish the theoretical foundations for a new cross-disciplinary field of bio-cultural coevolution by pushing the limits of cooperation between traditional disciplines. The center is therefore a forum for interdisciplinary discussion, bringing together scholars from the relevant fields to exchange ideas and develop common research questions and methodological approaches. The University of Tübingen is particularly well positioned to host such a center, with a tradition of excellence in prehistorical and linguistic research. The center is funded by the German Research Foundation (DFG), which currently sponsors 21 Centers of Advanced Studies across Germany.

The University of Tübingen

The University of Tübingen, founded in 1477, looks back on rich academic traditions, yet is home to world-class institutions conducting state-of-the-art research in the Life Sciences, Humanities and Social Sciences. As one of the German government's designated Universities of Excellence, with significant extra funding from the state and federal governments and a rising amount of third-party sponsorship, it has been able to boost top-level research and attract outstanding international researchers. The university comprises some 28.400 students, 551 professors, and more than 5.500 academic staff.

The German Research Foundation

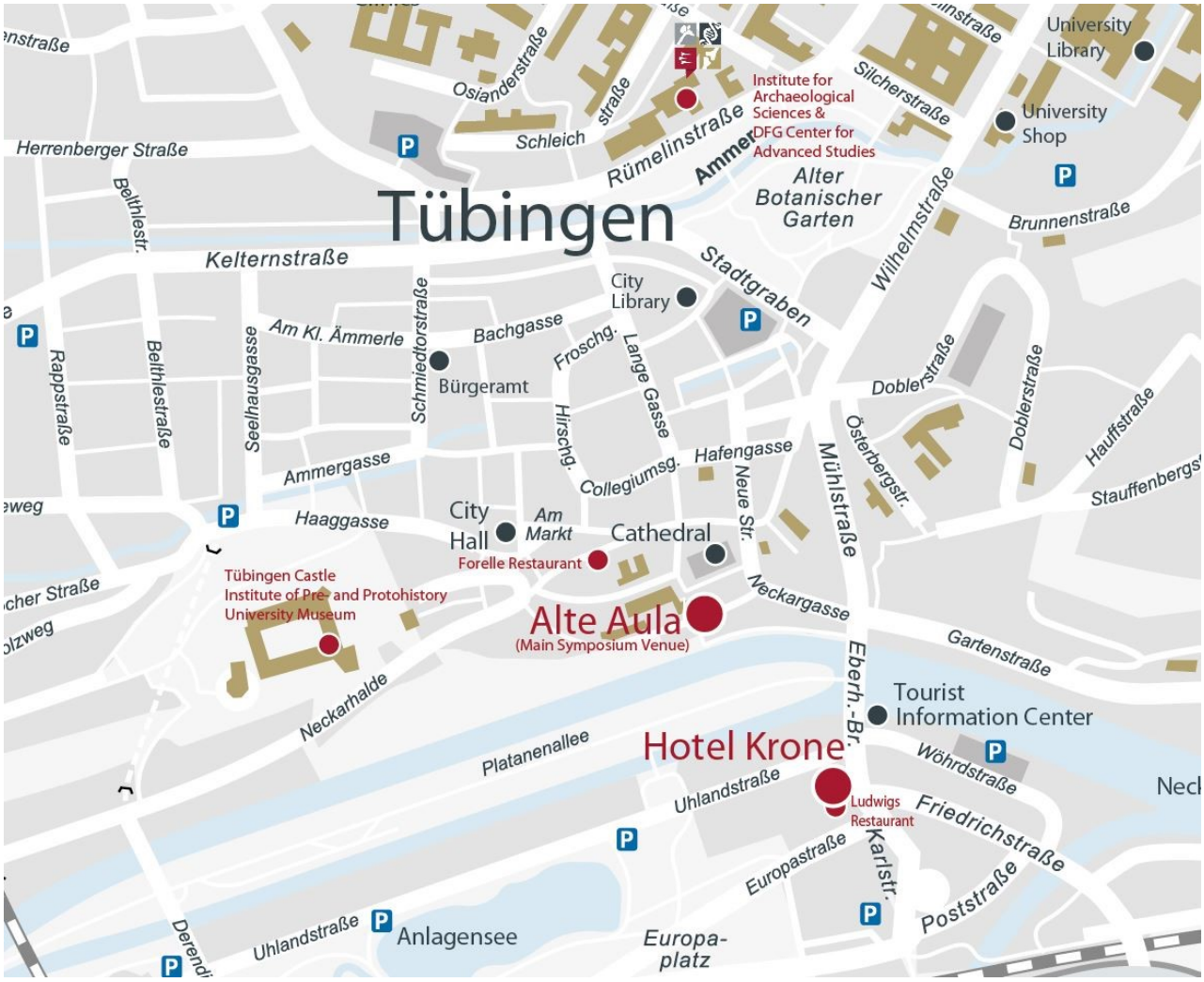
DFG Deutsche Forschungsgemeinschaft

The German Research Foundation (Deutsche Forschungsgemeinschaft or DFG) is the central self-governing research funding organization in Germany. It serves all branches of science and the humanities by funding research projects at universities and other research institutions. The DFG promotes excellence and quality by selecting the best research projects on a competitive basis and actively encourages international research cooperation. It is particularly dedicated to the promotion of young researchers and to gender equality in science and academia. It also advises legislatures and government agencies on scientific matters. The DFG's annual budget of about 2.5 billion euros is underwritten by Germany's federal (67.1%) and state governments (32.7%), as well as the European Union and private donors.

Locations

Alte Aula, Münzgasse 30
Main symposium venue

Hotel Krone, Uhlandstrasse 1
Accommodations



Institute of Archaeological Sciences – Rümelinstrasse 23

Institute of Linguistics – Wilhelmstrasse 19

Paleontology Museum – Sigwartstrasse 10
Recommended (self-guided), Monday-Friday 9-17:00

Schedule

THURSDAY, 14 DECEMBER

09:00 Welcome & Introduction to DFG Center, **Katerina Harvati, Gerhard Jäger and Cosimo Posth**

Biological adaptation in humans
Session chaired by Cosimo Posth

09:30 **Iain Mathieson,** University of Pennsylvania (in person)
Genetics, environment, culture and the evolution of human stature

10:00 **Anna di Rienzo,** University of Chicago (in person)
The history of human functional evolution: adaptation to high altitude

10:30 **Coffee Break**

11:00 **Aida Andrés,** University College London (via zoom)
Human local genetic adaptation to life in cold habitats

11:30 **Lara R. Arauna,** University of Tübingen (in person)
Biological adaptive history of Oceanians

12:00 **Guy Sella,** Columbia University (in person)
Simple scaling laws control the genetic architectures of human complex traits

12:30 **Discussion**

13:00 **Lunch Break**

Genetics of human phenotype variation
Session chaired by Katerina Harvati

14:30 **Ruth Ley**, Max Planck Institute for Biology, Tübingen (in person)
Integrating host-microbiota interactions into human evolution

15:00 **Tesla Monson,** Western Washington University (in person)
Investigating the evolution of phenotype:genotype patterning requires spanning scales from molecular to geological

15:30 **George Perry,** Pennsylvania State University (via zoom)
An integrative skeletal and paleo genomic analysis of stature variation suggests relatively reduced health for early European farmers

16:00 **Coffee Break**

Schedule

16:30 **Brenna Henn,** UC Davis (in person)
Global population genomics for genetic architecture

17:00 **Mashaal Sohail,** National Autonomous University of Mexico (in person)
Mexican Biobank advances population and medical genomics of diverse ancestries

17:30 **Alicia Martin,** Massachusetts General Hospital (via zoom)
Genomics for the world: a comprehensive framework for genetic studies in diverse modern humans

18:00 **Discussion**

Friday, 15 December

Archaic Hominins: Genetics and Morphology
Session chaired by Katerina Harvati

09:00 **David Gokhman,** Weizmann Institute of Science (via zoom)
Identifying Denisovan specimens using DNA mythylation maps

09:30 **Philipp Gunz,** Max Planck Institute for Evolutionary Anthropology (in person)
Decoding the evolution of human cranial shape

10:00 **Katerina Harvati,** University of Tübingen (in person)
Exploring the relationship between skeletal phenotype and neutral genetic variation

10:30 **Coffee Break**

11:00 **Tony Capra,** University of California (in person)
Resurrecting Ancient Molecular Phenotypes using Machine Learning

11:30 **Janet Kelso,** Max Planck Institute for Evolutionary Anthropology (in person)
Hominin gene flow in the Pleistocene

12:00 **Fernando Racimo,** University of Copenhagen (via zoom)
Adaptation in human societies: from Holocene to the Capitalocene

12:30 **Discussion**

13:00 **Lunch Break and Group Photo**

Schedule

Cognitive evolution and language

Session chaired by Gerhard Jäger

14:30 **Dan Dediu,** ICREA/University of Barcelona (in person)
Genes and cultural evolution influence language at multiple levels: focusing on the vocal tract and speech

15:00 **Wolfgang Enard,** LMU Munich (in person)
A molecular perspective on speech and language evolution

15:30 Coffee Break

16:00 **Cedric Boeckx,** ICREA/University of Barcelona (in person)
How did we become hunter-gatherers of words:
Seeking to link genotype and phenotype

16:30 **Brian Hare,** Duke University (via zoom)
Dogs and humans evolved cooperative-communication through self-domestication

17:00 **Discussion & Closing**

Abstracts

Human local genetic adaptation to life in cold habitats

Aida M. Andrés

UCL Genetics Institute
University College London, London, UK

Jasmin S. Rees, Sergio Latorre, Dean Cornish, Harrison J . Ostridge and Aida M. Andrés

The colonization of new habitats by modern humans after the out-of-Africa migration was marked by pressures to adapt to novel environments. Cold ambient temperature was likely among such strong pressures. Temperature perception was likely critical, as it is necessary for thermoregulation and thus survival. We identified signatures of local genetic adaptation in *TRPM8*, the gene that encodes the TRP cation channel that mediates perception of cold —a protein that has mediated adaptation to cold environments across mammals. The derived allele of *TRPM8* SNP rs10166942 is among the most strongly differentiated genetic variants among populations in the human genome (with 5% frequency in Nigeria and 88% in Finland), and its allele frequencies correlate with latitude and temperature beyond what can be explained by population history. The gene's patterns of linked variation show signatures of positive selection on standing variation, with the strength of selection also correlating with latitude and temperature. Using novel methods and genomes, including the growing number of available aDNA genomes, we decipher the evolution of the gene in Europe in further detail. We infer that rs10166942's was subject to strong positive selection shortly after the out-of-Africa migration, and as a consequence had very high frequency in many early European groups. Nevertheless, not all early European populations had identical frequencies of the allele, suggesting a possible series of selective events recently in Europe. This is interesting because the rs10166942 derived allele has been associated with increased expression of *TRPM8*, increased sensitivity to cold and higher risk of migraine. It is thus possible that local adaptation has shaped both temperature perception and the risk of migraine in certain human populations.

Resurrecting ancient molecular phenotypes using machine learning

Tony Capra

Bakar Computational Health Sciences Institute
University of California, San Francisco, USA

The sequencing of genomes from archaic hominins and modern humans has transformed our understanding of recent human history. However, due to the difficulty of inferring phenotypes from genotypes, ancient DNA has yet to yield major new insights into the traits of ancient individuals.

In this talk, I will describe how my group is using powerful machine learning methods to infer molecular phenotypes from ancient genetic sequences. I will illustrate how leveraging sequence-based deep neural networks can quantify protein structures, gene expression, splicing, and genome three-dimensional (3D) structure in archaic individuals. These analyses have revealed substantial similarities and differences between modern and ancient individuals that highlight molecular divergence in systems relevant to known phenotypic differences in the immune, metabolic, and skeletal systems. For example, the 3D folding of the genome is critical for regulating gene expression; however, its role in recent human evolution has not been explored because the degradation of ancient samples does not permit experimental determination of 3D genome organization. To fill this gap, we applied deep learning methods for inferring 3D genome organization from DNA sequence to Neanderthal, Denisovan, and diverse modern human genomes. Using the resulting genome-wide 3D contact maps, we identified 167 distinct regions with diverged 3D genome organization between humans and archaic hominins. We showed that these 3D-diverged loci are enriched for genes related to the function and morphology of the eye, supra-orbital ridges, hair, lungs, immune response, and cognition. Despite these specific diverged loci, the 3D genome is overall more similar than expected based on sequence divergence, suggesting that the pressure to maintain 3D genome organization constrained hominin sequence evolution. We also find that 3D genome organization constrained the landscape of Neanderthal ancestry in modern humans: regions more tolerant of 3D variation are enriched for introgression in modern Eurasians. Finally, we identify loci where modern Eurasians have inherited novel 3D genome folding from Neanderthal ancestors and show that these provide a putative molecular mechanism for phenotypes associated with the introgressed haplotypes.

In summary, deep learning applied to ancient DNA sequences has great potential to reveal previously unobservable molecular differences between humans and our closest relatives.

Genes and cultural evolution influence language at multiple levels: focusing on the vocal tract and speech

Dan Dediu

Department of Catalan Philology and General Linguistics
University of Barcelona, Barcelona, Spain

If something became clear during the last decades is that genes do not have any strong, direct, and "transparent" effect on language and speech, but instead their effects are subtle and involve complex interactions with the environment and, importantly, with the cultural evolutionary processes. Here I will argue that the cultural evolution of language is sometimes influenced by ((very) weak) biases that show inter-individual and (sometimes) inter-group variation, biases that are, in the right circumstances, amplified by the repeated use and transmission of language in complex networks of heterogeneous agents. Such biases have a complex architecture, sometimes emerging from the wider environment and other cultural practices (e.g., diet), but I will focus here on biases that, arguably, have some genetic component. I will start by reviewing recent advances concerning the 2007 proposal that the distribution of tone languages is influenced by the geographic distribution of two variants of ASPM and MCHP1, continuing with a 2022 study involving MRIs of 600 twins investigating the heritability of various structures of the human vocal tract, and the 2023 discovery, in more than 12,000 Icelanders, that voice pitch is heritable and is influenced by ABCC9. Then I will change gears and become more speculative, and I will argue that there may be genetic and evolutionary factors behind the world-wide distribution of abnormal color deficiency and the presence of a dedicated word for 'blue'. Finally, I will present recent computational and experimental work concerning the amplification of such (very weak) biases from the level of individual idiosyncrasies to that of linguistic diversity. Overall, the message I will try to convey is that, on the one hand, genes influence language and speech through a complex causal network involving other genes, the environment and culture, and, on the other, that we shouldn't look only at "universals" and "species-specific" characteristics, but also at inter-individual and between-group variation and the related processes of biased cultural amplification in heterogeneous groups.

Biological adaptive history of Oceanians

Lara R. Arauna

Institute for Archeological Sciences
University of Tübingen, Tübingen, Germany

During the settlement of Oceania populations had to adapt to island environments, including new diets, and new pathogens. Biological adaptations interacted with the demographic processes of the region that impacted the genetic diversity. Oceania was first settled by modern humans carrying Papuan-related ancestry, around 50,000 years ago. The settlement led to a strong early bottleneck in the populations and a rapid divergence between the populations of New Guinea, the Bismarck Archipelago, and the Solomon Islands. A second large expansion, only around 5,000 years ago, brought East Asian-related ancestry into the unsettled territories of Micronesia, Santa Cruz, Vanuatu, New Caledonia, Fiji and Polynesia. The subsequent demographic events within Oceania resulted in the admixture between the Papuan-related and the East Asian-related ancestries in different proportions across the different islands. Furthermore, Oceanians also acquired new variation from gene-flow from Neanderthals and Denisovans.

Our previous results on contemporary Oceanians highlighted the importance of metabolic and immunological adaptations. These processes occurred through positive selection, including a strong classic sweep in Papuan-related populations around gene RANBP-17, associated to lipid metabolism. But it also occurred in a polygenic manner, since we detected polygenic adaptation also among Papuan-related populations for lower levels of HDL cholesterol. Moreover, introgressed genetic variants from archaic hominins played an important role in the adaptation to the new environments. Here, we study the genetic variants identified in contemporary populations to understand biological adaptation and its phenotypic consequences through time.

How did we become hunter-gatherers of words: Seeking to link genotype and phenotype

Cedric Boeckx

Department of Catalan Philology and General Linguistics
University of Barcelona, Barcelona, Spain

In line with the overall theme of the meeting, “Genotype-Phenotype interactions’, I’ll be revisiting the difficult problem of the evolution of the human capacity for language. I’ll be articulating the talk around specific claims, such as (i) the evolution of human language is as complex and mosaic-like as the evolution of the sapiens lineage; (ii) fields adjacent to linguistics now offer a wealth of data that enable us to strengthen evolutionary narratives with numbers; (iii) although discussion of the human language capacity still tends to focus on the “biological endowment” that made it possible, taking into account the ecology of language use is just as important; (iv) I will summarize what we have learned from various experimental approaches concerning early brain development and how this information could be combined with findings from neurodevelopmental disorders to constrain the narratives put forward in the context of language evolution, and specifically concerning what made our brain “language-ready”.

The history of human functional evolution: adaptations to high altitude

Anna Di Rienzo

Human Genetics
University of Chicago, Chicago, USA

Throughout their history, humans encountered and adapted to a diversity of environments. Elucidating the genetic bases and the molecular mechanisms underlying beneficial traits and the history of how they evolved is central to our understanding of human evolution. Within this broad framework, indigenous high altitude populations have emerged as an ideal system to study the genetic architecture of adaptive traits and provide a rare opportunity to observe human evolution in action. These populations have phenotypes distinct from those of lowlanders at high altitude and from each other, such as the unelevated hemoglobin concentration in Tibetans. Strong selective sweep signals have previously been detected in Tibetans at the EGLN1 and EPAS1 loci, with alleles that are common in Tibetans but rare elsewhere being associated with lower Hb. The mechanisms resulting in the selective advantage conferred by these alleles remain poorly understood at a molecular, cellular and organismal levels. We have developed cell culture and animal models that attempt to address these complex questions with regard to high altitude hypoxia, but they may have broader applicability for the study of human adaptations to a variety of environmental stressors.

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A molecular perspective on speech and language evolution

Wolfgang Enard

Faculty of Biology
Ludwig Maximilian University Munich, Munich, Germany

Humans are a remarkable species, especially because of the remarkable properties of their brain. Since the split from the chimpanzee lineage, the human brain has evolved the capacities for vocal learning and language usage. Understanding the molecular basis of these changes is interesting from an evolutionary, biomedical and cultural perspective. However, obtaining direct evidence for linking particular genetic and molecular changes to human brain evolution is not possible as humans and chimpanzees cannot be crossed or genetically manipulated. I will sketch approaches for obtaining indirect evidence and discuss findings related to the speech-associated gene FOXP2.

Searching for Denisovan fossils using genetic phenotyping

David Gokhman

Department of Molecular Genetics
Weizmann Institute of Science, Rehovot, Israel

Denisovans are an extinct group of humans whose morphology remains little understood. The paucity of verified Denisovan fossils makes it challenging to study how they differed in their anatomy, and how well they were adapted to their environment. To gain insight into their evolutionary history, we developed a method to reconstruct a key regulatory mark of the genome – DNA methylation. The Denisovan methylation maps allowed us to identify genes that were differentially regulated in these humans. We then used these maps to identify gene regulatory changes that likely altered Denisovan skeletal morphology. Using these data, we reconstructed a morphological profile of the Denisovan. We suggest that Denisovans likely shared with Neanderthals traits such as an elongated face and a wide pelvis. We also identified Denisovan-derived changes, such as an increased dental arch and lateral cranial expansion. We then scanned East Asian skulls to identify unclassified specimens that match our Denisovan profile and thus might have belonged to Denisovans. We found that the Xiahe, Harbin and Dali specimens almost perfectly match our predicted Denisovan profile. We conclude that DNA methylation can be used to reconstruct anatomical features, including some that do not survive in the fossil record, and that it could then be used to classify unidentified specimens.

Decoding the evolution of human cranial shape

Philip Gunz

Department of Human Origins
Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

I will present ongoing collaborative efforts to decode the biological underpinnings of human cranial shape. Compared with our fossil ancestors and Neanderthal kin, modern humans have evolved a distinctive skull shape, with a rounder braincase and a more delicate face. Competing explanations for this rounder skull have either linked it to evolutionary changes in brain organisation, or seen it as a by-product of gracilization. Using geometric morphometrics we analysed endocranial globularity from MRI brain scans and genetic data from several thousand adults. The genetic loci significantly associated with globularity show genetic overlap with the brain's ventricular system, white matter microstructure, and sulcal morphology. The associated genes exhibit enriched expression during prenatal and early childhood development in the brain. Intriguingly, we find these genes also exhibit pronounced activity in systems beyond the brain, specifically in the cardiovascular and female reproductive systems. Based on this cross-system activity we propose a co-evolutionary model whereby evolutionary changes impacting factors such as energy needs, pregnancy, or fertility concurrently shape the brain and its structure. Taken together our findings suggest proximate developmental and ultimate evolutionary factors shaping a uniquely modern phenotype.

Dogs and humans evolved cooperative-communication through self-domestication

Brian Hare

Department of Evolutionary Anthropology
Duke University, Durham, USA

Humans evolved cultural cognition that allows for the fastest and highest fidelity social learning in the animal world. Our derived cultural cognition enhances cooperative-communication, develops early in infancy and is not shared with other great ape species. I will present evidence that domestic dogs (*Canis familiaris*) possess cognition that allows for similar forms of cooperative-communication as seen in human infants. I will make the case (relying on comparisons between dogs, wolves and foxes) that these human-like abilities evolved in dogs convergently as a result of self-domestication. The unusual skills dogs demonstrate for working and communicating with humans are by-products of selection for friendliness toward humans that altered their cognitive development. I will conclude by suggesting that dogs provide a powerful model for how human cultural cognition evolved through a similar process of self-domestication.

Exploring the relationship between skeletal phenotype and neutral genetic variation

Katerina Harvati

Institute for Archeological Sciences
University of Tübingen, Tübingen, Germany

Skeletal morphology has long been used to infer evolutionary relationships and to make decisions on taxonomy. However, it has been equally long recognized that not all aspects of the skeleton are equal in their preservation of a phylogenetic signal. Some skeletal elements, for example, are considered to change rapidly in response to outside factors, such as environment or activity patterns, during life or during ontogeny; while others, especially those that form early in development, are considered more useful in inferring population history and evolutionary relationships. With the advent of large datasets of genetic information, it has become possible to investigate the relationship of skeletal morphology and its different components with neutral genetic markers to clarify the potential of morphology in general, and of specific regions in particular, in inferring population history and phylogeny. Here I will review the work that I and colleagues have conducted in recent years to evaluate the relationship between the skeletal phenotype and neutral genetic variation among recent human populations.

Global Population Genomics for Genetic Architecture

Brenna Henn

Department of Anthropology
University of California, Davis, USA

There is a pressing need for population genomic research in diverse cohorts - allowing geneticists to characterize the genetic determinants of disease and phenotype for any human community. Based on the last decade of genetic research, it is clear that predicting phenotypic traits and disease in diverse populations performs poorly when training on European-descent cohorts. This could be because a phenotype is influenced by alleles that are population-specific, there is heterogeneity in effect size, or gene x environment strongly impacts prediction. A primary objective of my lab is to extend trait mapping and evolutionary genetic techniques to identify genetic loci associated with biomedical traits in African-descent populations where collection of large cohort sizes remains challenging. I will discuss improvements in genetic architecture inference when considering imputation, ascertainment-bias, and admixture. For example, we demonstrate improved statistical power when mapping traits with admixed populations, but also describe complications which occur when causal alleles differ in frequency between the parental source ancestries. Finally, I will describe how the aggregation of recessive alleles affects completed fertility (i.e. number of offspring) and how small cohorts can contribute to a greater understanding of the genetic architecture of traits.

Hominin gene flow in the Pleistocene

Janet Kelso

Department of Evolutionary Genetics
Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

The recovery of genome sequences from the skeletal remains of Neandertals, Denisovans and modern humans has provided a number of important insights into the history and interactions of these groups. Strikingly, we have found that although the ancestors of modern humans and Neandertals/Denisovans separated 630-520ka, and the ancestors of Neandertals and Denisovans subsequently split 440-390ka, there was recurrent gene flow between all these groups after they separated. Understanding the genetic and phenotypic diversity of Pleistocene hominins over their geographic and temporal ranges, and determining the extent to which gene flow has contributed to this diversity, is of major interest. However, identifying introgressed and lineage-specific genetic variation that could be informative about the phenotypes and adaptations of Neandertals, Denisovans and modern humans is complicated by the limited number of archaic individuals for whom we have genomic data. In particular, there is only a single Denisovan genome available for comparison. We have recently reconstructed a new high-quality genome from a Denisovan individual estimated to have lived approximately 200kya. This has provided us with new insights into Denisovan population history, and their relationships with Neandertals and modern humans. Furthermore, the availability of a second high-coverage Denisovan genome also allows us to refine the list of genetic changes that have arisen specifically on the Denisovan lineage, and that may distinguish Denisovans from other hominins.

Integrating host-microbiota interactions into human evolution

Ruth E. Ley

Department of Microbiome Science
Max Planck Institute for Biology Tübingen, Tübingen, Germany

As human populations spread across the world, they adapted genetically to local conditions. So too did the resident microorganism communities that everyone carries with them. However, the collective influence of the diverse and dynamic community of resident microbes on host evolution is poorly understood. The taxonomic composition of the microbiota varies among individuals and displays a range of functions that modify the physicochemical environment of the host and may alter selection pressures. I will present our recent work that shows how humans and certain oral and gut microbes share an evolutionary history. I will also present our unpublished work on microbially-acquired lactose tolerance, which is an example of how gut microbes can compensate for human genotype, thereby potentially allowing time for cultural and genetic adaptation.

Genomics for the world:

A comprehensive framework for genetic studies in diverse modern humans

Alicia Martin

Massachusetts General Hospital, Boston, USA

Genomic studies have matured over the last decade and are poised to improve biomedical outcomes via precision medicine. The primary ethical and scientific obstacle preventing their imminent and routine translation, however, is that they are vastly Eurocentric—current studies would provide systematically greater benefits to European descent populations than to those already most underserved. Moreover, multi-ethnic studies create major scientific opportunities missed by Eurocentric studies. They uniquely inform the extent to which heritable and environmental factors are shared or population specific. To realize equitable benefits of genetics in precision medicine, we are developing analytical methods, tools, community resources, and massive data analyses to facilitate genetic studies across diverse ancestries. In this talk, I will focus on work advancing gene-discovery efforts in globally diverse populations using large-scale meta-analysis across global biobanks. Additionally, I will describe work underway setting up the largest genetic studies of psychiatric phenotypes in underrepresented populations, including over 120,000 participants spanning Latin America and Africa. Lastly, I will describe work evaluating how genetic and exposure risks together predict disease outcomes in diverse populations.

Genetics, environment, culture and the evolution of human stature

Iain Mathieson

Department of Genetics, Perelman School of Medicine
University of Pennsylvania, Pennsylvania, USA

Despite intensive study, we still do not fully understand the genetic and environmental determinants of human height. Here, we combine genetic, anthropological and archaeological data to perform integrated analysis of human stature from thousands of ancient Europeans. We first show that polygenic scores for height derived from present-day genome-wide association studies can be used to robustly predict stature from genetic data in ancient Europeans. Further we show that we can measure the effects of individual variants, for example we show that the variant associated with adult lactase persistence has a 0.5 standard deviation effect on height in Bronze Age Europe.

We also show that long-term changes in genetically predicted height correlate with population-level changes in phenotypic height, including relatively tall stature in the Upper Paleolithic and Bronze Age, and relatively short stature in the Mesolithic and Neolithic. We also replicate previous results that Neolithic farmers are phenotypically shorter than expected based on genetics, likely due to the environmental stress of agricultural life. Finally, we investigate fine-scale dynamics of stature in Early Neolithic Europe. We show that very high sexual dimorphism in Central Europe is explained by neither genetics nor environment and likely reflect cultural differences in male preference in resource allocation. This analysis indicates that biological effects of sex-specific inequities can be linked to cultural influences at least as early as 7000 years before present.

Investigating the evolution of phenotype: genotype patterning requires spanning scales from molecular to geological

Tesla Monson

Department of Anthropology
Western Washington University, Bellingham, USA

Tesla A. Monson, Andrew P. Weitz, Marianne F. Brasil

Understanding how the forces of evolution interact with one another to produce phenotypic variation remains a complex endeavor that requires spanning scales from molecular to geological. Phenotype:genotype mapping is one approach to this problem, with phenotypic covariation providing insight into underlying genetic and developmental systems. Pleiotropy, where a gene has multiple effects, has the potential to generate phenotypic correlations across the skeletal system. Variation in some traits can thus reflect selection on linked phenotypes. The dentition is a particularly good system for investigating covariation and pleiotropy since the teeth develop early and are highly heritable.

In this talk, I will summarize nearly a decade of our work investigating covariation across craniodental tissues, focusing on how extant variation can illuminate past evolutionary processes. I will also present new and ongoing research expanding these covariation studies to other parts of the skeleton. We have recently turned our attention to the evolution of human encephalization. Body mass and endocranial volume covary through geologic time, with distinct patterns of allometry characterizing different lineages. In contrast to currently held views that encephalization has increased throughout human evolution, our results demonstrate that derived allometric scaling of brain:body size evolved in hominids around 3 Ma, in the Late Pliocene. Human-like encephalization is thus shared among all Pleistocene fossil hominids, including humans, and evolved much earlier than currently presumed. The significant change of allometric trajectory seen in the Late Pliocene suggests that some genetic or developmental factor may act on either brain or body size at least semi-independently. Based on patterns of phenotypic covariation, we can generate novel hypotheses about candidate gene pathways implicated in the evolution of the human brain.

This project was supported by funding from the National Science Foundation (NSF 2235771 to T.A.M. and M.F.B.) and the European Research Council (ERC-2021-ADG Project 101054659-Tied2Teeth to L. Hlusko). A.P.W. was supported by the Washington Research Foundation, and M.F.B. was partially supported by the John Templeton Foundation and the Human Evolution Research Center at UC Berkeley for the duration of this research.

An integrative skeletal and paleogenomic analysis of stature variation suggests relatively reduced health for early European farmers

George Perry

Department of Anthropology
Pennsylvania State University, Pennsylvania, USA

Human culture, biology, and health were shaped dramatically by the onset of agriculture 12,000 y B.P. This shift is hypothesized to have resulted in increased individual fitness and population growth as evidenced by archaeological and population genomic data alongside a decline in physiological health as inferred from skeletal remains. Here, we consider osteological and ancient DNA data from the same prehistoric individuals to study human stature variation as a proxy for health across a transition to agriculture. Specifically, we compared “predicted” genetic contributions to height from paleogenomic data and “achieved” adult osteological height estimated from long bone measurements for 167 individuals across Europe spanning the Upper Paleolithic to Iron Age (□38,000 to 2,400 B.P.). We found that individuals from the Neolithic were shorter than expected (given their individual polygenic height scores) by an average of 23.82 cm relative to individuals from the Upper Paleolithic and Mesolithic (P = 0.040) and 22.21 cm shorter relative to post-Neolithic individuals (P = 0.068), with osteological vs. expected stature steadily increasing across the Copper (+1.95 cm relative to the Neolithic), Bronze (+2.70 cm), and Iron (+3.27 cm) Ages. We also incorporated observations of paleopathological indicators of nonspecific stress that can persist from childhood to adulthood in skeletal remains into our model. Overall, our work highlights the potential of integrating disparate datasets to explore proxies of health in prehistory.

Adaptation in human societies: from the Holocene to the Capitalocene

Fernando Racimo

Globe Institute
University of Copenhagen, Copenhagen, Denmark

The fate of human societies is intimately tied to the environment in which they live, and how they adapt to its changes. Humans modify the biomes they occupy, while at the same time, biotic and climatic processes determine how humans organise their livelihoods. Thus, a complete view of human history can only be obtained by unifying data across disparate fields, including archeology, genetics, ecology and the social sciences. In this talk, I will talk about ongoing efforts in our group to understand adaptation in the past and the present. I will explain how we are integrating genomic, paleoclimatic, archaeobotanical and archaeozoological records to disentangle how humans modified the landscape in the Neolithic and Bronze Age, even as they were evolving themselves, to adapt to new conditions. I will also talk about how Holocene environmental changes are dwarfed by environmental changes the Earth is experiencing today. Thanks to ongoing governmental support for fossil fuels, and an economic system that prioritizes profit over well-being, we are now rapidly exiting the climate safe zone of the past 10,000 years, in which most of our civilization has developed for centuries. According to the last IPCC report, we are entering a rapidly warming world, characterized by a magnified frequency of natural catastrophes, droughts, crop collapses and social unrest. In the last part of my talk, I will talk about how academia has failed to properly engage with the public about this crisis, and how it can adapt to effectively connect with society moving forwards. By embracing advocacy and activism - which were once prevalent in academia - scientists today can help avert the worst consequences of climate and ecological breakdown.

Simple scaling laws control the genetic architectures of human complex traits

Guy Sella

Department of Biological Sciences
Columbia University, New York, USA

Yuval B. Simons, Hakhamanesh Mostafavi, Courtney J. Smith, Jonathan K. Pritchard, and **Guy Sella**

Genome-wide association studies have revealed that the genetic architectures of complex traits vary widely, including in terms of the numbers, effect sizes, and allele frequencies of significant hits. However, at present we lack a principled way of understanding the similarities and differences among traits. Here, we describe a probabilistic model that combines mutation, drift, and stabilizing selection at individual sites with a genome-scale model of phenotypic variation. In this model, the architecture of a trait arises from the distribution of selection coefficients of mutations and from two scaling parameters. We fit this model for 95 highly polygenic quantitative traits of different kinds from the UK Biobank. Notably, we infer similar distributions of selection coefficients across all these traits. This shared distribution implies that differences in architectures of highly polygenic traits arise mainly from the two scaling parameters: the mutational target size and heritability per site, which vary by orders of magnitude among traits.

Mexican Biobank advances population and medical genomics of diverse ancestries

Mashaal Sohail

Center for Genomic Sciences
National Autonomous University of Mexico, Mexico City, Mexico

Latin America continues to be severely underrepresented in genomics research, and fine-scale genetic histories and complex trait architectures remain hidden due to a lack of sufficient data. To fill this gap, the Mexican Biobank project genotyped 6,057 individuals from 898 rural and urban localities across all 32 states in Mexico at 1.8 million genome-wide markers with linked complex trait and disease information creating a valuable nationwide genotype-phenotype database. Using ancestry deconvolution and inference of identity-by-descent (IBD) segments, we inferred ancestral population sizes across Mesoamerican regions over time, unraveling indigenous, colonial, and post-colonial demographic dynamics. We observed variation in runs of homozygosity (ROH) among genomic regions with different ancestries reflecting distinct demographic histories and in turn, different distributions of rare deleterious variants. We conducted genome-wide association studies (GWAS) for 22 complex traits and found that several traits are better predicted using the MXB GWAS compared to the UK Biobank GWAS. We identified genetic and environmental factors associating with trait variation, such as the length of the genome in ROH as a predictor for body mass index, triglycerides, glucose, and height. This study provides new insights into the genetic histories of individuals in Mexico and dissects their complex trait architectures, both crucial for making precision and preventive medicine initiatives accessible worldwide.