IMAGINING THE FUTURE OF ANTHROPOGENY

Virtual Public Symposium • Saturday, November 19, 2022

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Sponsored by:
Center for Academic Research and Training in Anthropogeny (CARTA)

ABSTRACTS

Why Should We Care About Anthropogeny?

Pascal Gagneux, UC San Diego

Our species is between 300,000 and 200,000 years old. For most of this one-quarter of a million years, up until just 12,000 years ago, it appears that our ancestors lived in small populations, in small-scale societies of which we can only guess the real nature.

It is truly humbling how we remain in the dark about the age of some of the most diagnostic features of our species: our striding bipedalism, complex tool manufacture and use, fire use, language and societies defining their own identities, collaborating with and competing against neighboring societies.

New data from fossils, molecular and cellular investigations, neuroscience, and comparative psychology and behavior studies are rapidly complicating the potential scenarios leading to our species.

Data from studies of non-human animal behavior remind us of the underappreciated capacities of many other species. However, it has so far not provided evidence for any other species that shares the long list of distinctly human characteristics; chief among those, our species' capacity to not only simultaneous modify and threaten planetary ecosystems but also document and study such ecosystems across the globe.

It is realistic to expect many new and surprising contributions to anthropogeny from a number of research fields. Drill core studies provide insights into paleoclimates and paleovegetation, via markers for burnt biomass, pollen profiles, plant organic matter and stable isotopes. Much more complete and high-quality genomes now exist for humans and most great apes, and these reveal large and dynamic changes in our genomes, exciting investigations of the microbiota found in and on the bodies of humans and their close relatives also promise novel insights. Combined with new bioinformatic and machine learning tools, these help identify important non-coding parts of the genome (micro- and other non-coding RNAs) or short proteins which can then be subjected to functional studies in cells and/or model animal species including the use of induced pluripotent stem cells and derived organoids for the comparative study of organ development and function across primates. Most promising, perhaps, are the investigations of how human culture including human language, is capable of shaping human biology, by exerting 'top-down" effects on development, growth, immunity and cognition.

A better understanding of how we came to be who we are will greatly contribute to our attempts at solving important challenges facing humanity. Appreciating the evolutionary forces that shaped us into both highly pro-social and potentially compassionate primates as well as highly destructive and potentially cruel ones.

The Evolution of Linguistic Structure and the History/Future of Linguistics

Robert Kluender, UC San Diego

For the past 30 years, the frontiers of language science have been in the areas of neurolinguistics and genetics, both of which arose in conjunction with new technologies emerging in the 1990s. It is probably safe to say that these trends will continue apace as technology in these areas continues to advance, allowing for increasingly sophisticated and fine-grained analysis.

In this talk, I first look backwards in time, in a review of the provenance and history of linguistics as a field. The idea is to take stock of where we have come from in order to get a sense for where we might be headed. Much of what we do today in linguistics has its roots in what the Sanskrit grammarians did several millennia ago. However, their analysis of language was deeply rooted in the ritual culture and religious practices of the time: the primary and arguably sole aim of analyzing language was to preserve its efficacy in the performance of the ceremonial rites that it accompanied. Perhaps not coincidentally, the impetus for the study of language in the modern era again came from the "rediscovery" of Sanskrit by the European colonialists—along with its central role in Indian culture, and its unmistakable affinities with European languages.

Thus, from its inception, the study of language has been inextricably linked with cultural anthropology and the arts. It was only in the 20th century that linguistics was able to break free of its sister disciplines and establish itself as an autonomous field all its own.

After briefly reviewing this history, I suggest that at this point in its historical development, linguistics might benefit from rejoining forces with the sister disciplines it left behind, in the interest of tackling certain thorny problems in the evolution of language. The test case I cite is that of recursion, the ability to embed linguistic structures of similar types within each other. This has been touted as the sine qua non of language evolution (Hauser, Chomsky & Fitch 2002). What we propose here, following up on an old proposal by Staal (1979, 1980, 1984), and based on consistent, identifiable remnants of recursive structure in ritual practice and its accompanying arts, is that linguistic recursion could plausibly have been exapted from the elements of ritual culture from which linguistics arose in the first place.

Genome Structural Variation and the Evolution of Human-Specific Genes

Evan Eichler, University of Washington

The discovery and resolution of genetic variation is critical to understanding disease and evolution. I will present our most recent work sequencing diverse human and nonhuman primate genomes using both ultra-long and high-fidelity long-read sequencing technologies. Advances in this area have made possible the first telomere-to-telomere assemblies of the human genome and much more complete chimp, gorilla and orangutan genomes providing new biological insights into regions typically excluded from human genetic and comparative studies. We have discovered mega basepairs of duplicated sequence and/or rapidly evolving sequence present in humans that are absent from other non-human primates. These changes have predisposed our species to recurrent rearrangements associated with disease but also have led to the emergence of new genes important in the expansion of the human frontal cortex of the brain. This process of large-scale structural change continues to shape the structure of the human genome including introgressed segments from archaic species that are under selection in specific human populations. Our data suggest that large-scale genome structural variation has played and continues to play a crucial role in the evolution of the human species.

Ancient DNA and Anthropogeny

Anne Stone, Arizona State University

The first Neandertal DNA was recovered 25 years ago, and since then, ancient DNA has provided many surprising insights into human evolutionary history. Among these are the discoveries of the multiple admixture events among late Pleistocene humans and the remnants of archaic DNA in our own genomes. How does ancient DNA research contribute to the future of anthropogeny? In this talk, I will reflect on the

findings of last quarter century of ancient DNA research about archaic humans and their environment as well as examine potential questions that the next quarter century might answer.

African Genomic Analyses Shed Light on Human Evolutionary History

Sarah Tishkoff, University of Pennsylvania

Africa is thought to be the ancestral homeland of all modern human populations within the past 300,000 years. It is also a region of tremendous cultural, linguistic, climatic, and genetic diversity. Despite the important role that African populations have played in human history, they remain one of the most underrepresented groups in human genomics studies. A comprehensive knowledge of patterns of variation in African genomes is critical for a deeper understanding of human genomic diversity, the identification of functionally important genetic variation, the genetic basis of adaptation to diverse environments and diets, and the origins of modern humans. We have characterized genomic variation in thousands of ethnically and geographically diverse Africans in order to reconstruct human population history and local adaptation to variable environments and have identified candidate loci that play a role in alcohol metabolism and skin color.

An Evolutionary Perspective on Human Cognitive and Behavioral Variation

Daniel Geschwind, UCLA

Human cognition and behavior are highly heritable and so is liability to disorders that affect them. This includes neuropsychiatric disorders such as schizophrenia and autism spectrum disorder (ASD). We have been interested in understanding the genetic basis of susceptibility to ASD, as well as the more general relationship of genetic factors that influence human brain function to features of primate and human brain evolution. Since most disease associated variation impacts non-coding regions of the genome that are involved in gene regulation, we have focused heavily on understanding the regulation of gene expression and gene co-expression networks. Some of our studies suggest that derived, human-specific gene expression networks may preferentially impact human disease, especially risk for Alzheimer's disease. More recently, we have started to integrate genetic risk data with the emerging maps of gene regulation to study human specific aspects of gene expression and gene regulation. These analyses indicate that human specific aspects of gene regulation, such as genes regulated by human specific enhancers, are indeed enriched in mutations or common genetic variants that increase risk for ASD and allied neurodevelopmental disorders. This provides evidence that genetic elements underlying human brain evolution are particularly susceptible to disruption in disease. Another aspect of work in this area indicates that disease risks are related to what are considered strengths in other areas, which leads us to a view of human brain function that emphasizes individual differences.

Using Stem Cells to Study Human Origins

Carol Marchetto, UC San Diego

Since the split of *Homo sapiens* from the last common nonhuman primate (NHP) ancestor, the human brain has substantially altered its size, structure and connectivity. The human brain has a larger mass with respect to body weight, increased cortical neurons with respect to size, an expanded proliferative zone, and unique connectivity patterns.

Human-specific neurodevelopment is not only marked by physical differences, but also by temporal changes. Human neurons, during both prenatal neurodevelopment and adult neurogenesis, exhibit an exceptionally delayed time course, a characteristic termed neoteny. It is hypothesized that this longer developmental period plays a role in the aforementioned structural and connectivity differences. It has long been proposed that the phenotypic differences between closely related species may be driven, in part, by divergent transcriptional regulation rather than by novel protein-coding sequence. However, how these regulatory mechanisms play a role in the protracted maturation process in human neurons remains largely unknown.

Signatures of human-specific neoteny have been observed and reproduced across different systems including induced pluripotent stem cell (iPSC) and brain organoids models. To examine the evolutionary

constraints on the rate of neuronal maturation, we compared neurogenesis across iPSC-derived cells from five primate species - *Macaca mulatta* (rhesus), *Gorilla gorilla* (gorilla), *Pan paniscus* (bonobo), *Pan troglodytes* (chimpanzee), and *Homo sapiens* (human) - and assessed the differences in transcriptional dynamics. While the neural progenitor cells of humans, chimpanzees, and bonobos were highly similar, we found that transcriptional differences increased between all species throughout neuronal differentiation and maturation. We identified a pioneer transcription factor, *GATA3*, that exhibited elevated neuronal expression only in humans. Strikingly, down-regulation of *GATA3* increased the rate of physiological maturity in human neurons, indicating that the species-specific rate of physiological maturity is cell intrinsic and can be modulated by perturbing a single, conserved transcription factor. This finding provides evidence for the divergence of gene regulation as a contributor to human neoteny.

Computational Neuroscience and Anthropogeny

Terry Sejnowski, Salk Institute for Biological Studies

Neuroscience has made great strides in the last decade following the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative, a science and engineering grand challenge that has greatly accelerated research on large-scale recordings from neurons and reconstructions of neural circuits. Large-scale neural network models have in turn inspired major advances in artificial intelligence. These network models have been trained on large-scale data sets to recognize objects in images, caption photographs, and translate text between languages. The most recent advance has been the emergence of pre-trained foundational language models that are self-supervised and can be adapted with fine tuning to a wide range of natural language tasks, each of which previously would have required a separate network model. This is one step closer to the extraordinary versatility of human language. Language models like Generative Pre-trained Transformer 3 (GPT-3) and, more recently, Language Model for Dialogue Applications (LaMDA) can carry on dialogs with humans on many topics after minimal priming with a few examples. However, there has been a wide range of reactions and debate on whether these large language models (LLMs) understand what they are saying or exhibit signs of intelligence. I will present examples of these dialogs and let the audience decide for themselves.

Perspectives on the Future of Fossil-Based Human Origins Research

Yohannes Haile-Selassie, Institute of Human Origins, Arizona State University

Current knowledge of our deep past is primarily derived from ancient fossils of our ancestors that paleoanthropologists search for and discover in some of the most remote areas of the world. In the last two decades, significant fossil discoveries have been made and these discoveries have re-written some parts of our deep past. With these discoveries also came significant improvements in analytical methods and technological advances that helped us extract more information from the fossils we have in hand. However, the fossil record is still far from complete, primarily due to the absence of fossils from some critical geological times and the lack of robust samples for the species already identified. Unfortunately, sites that have been "worked" for decades do not seem to substantially add new information to what we already know as they do not fill in temporal gaps in the fossil record. The best way to fill these gaps and meaningfully increase the sample size is by conducting surveys and exploration to locate new areas of paleoanthropological significance. Some newer paleoanthropological sites in Africa found as a result of survey and exploration, such as Woranso-Mille, where the most convincing fossil evidence for the contemporaneous presence of more than one human ancestor species during the mid-Pliocene (3.4 million years ago) and Ledi-Geraru, where fossil evidence for the earliest occurrence of our genus at 2.8 million years ago was discovered, are good examples in this regard. Unfortunately, there seems to be reduced effort in survey and exploration to locate new paleontological sites, which when coupled with the serious decline in funding for field-based human origins research seen in the last decade, will have adverse effects on human origins research. In order to alleviate these effects, there should be a consensus among all stakeholders—federal and private funding agencies, scientists and students—that human origins research cannot happen without the fossils that come from fieldwork, Therefore, if we want to fully understand our evolutionary history, especially how we became who we are today and where we are going, continued paleoanthropological fieldwork is of paramount importance.