THE YEAR IN REVIEW

The Year In Genetic Anthropology: New Lands, New Technologies, New Questions

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ABSTRACT The year 2017 has been another exciting one for anthropology, revealing new and unexpected layers of human history, changing our views about how we conceptualize human variation, and leading to a deeper understanding of the biology of our species. Increases in the accessibility and resolution of genomic analysis as well as other high-throughput technologies that can now measure the functional impact of genetic variation have continued to be one of the leading drivers of innovations that can address important anthropological questions. I would like to highlight the surprising discoveries this year within the framework of three interconnected themes: (1) increased inclusion of non-European peoples into mainstream genomics studies; (2) a more comprehensive integration of new technologies beyond genomics to better contextualize human biological variation; and (3) previously underappreciated ethical discussion points emerging from these novel developments. In this review, I will attempt to briefly outline a path for genetic anthropology, primarily using examples from recent work conducted with African populations. Consequently, I will not be able to do justice to breakthrough work in primate genomics, ancient genomics studies from around the world, and other fascinating studies in biological anthropology. That said, it is an incredibly exciting time for our field. We can now ask questions that we did not know were there—and what we are finding is "stranger than we imagined." [*genomics, population genetics, human evolution, four fields*].

RESUMEN El 2017 ha sido otro año fascinante para la antropología, revelando capas nuevas e imprevistas de la historia humana, cambiando nuestros puntos de vista acerca de cómo conceptualizamos la variación humana, y conduciendo a un más profundo entendimiento de la biología de nuestras especies. Incrementos en la accesibilidad y resolución del análisis genómico, así como otras tecnologías de alto rendimiento que pueden ahora medir el impacto funcional de la variación genética han continuado siendo uno de los principales conductores de innovaciones que pueden abordar cuestiones antropológicas importantes. Quiero destacar los descubrimientos sorprendentes este año dentro del marco de tres temas interconectados: (1) mayor inclusión de pueblos no europeos en los principales estudios de genómica; (2) una integración más completa de nuevas tecnologías más allá de la genómica para contextualizar mejor la variación biológica humana, y (3) puntos de discusión ética previamente subestimados que surgen de estos desarrollos novedosos. En esta revisión, intentaré bosquejar brevemente un camino para la antropología genética, usando primariamente ejemplos de trabajo reciente conducido con poblaciones africanas. Consecuentemente, no podré hacer justicia al trabajo innovador en genómica de los primates, estudios genómicos antiguos de todo el mundo y otros estudios fascinantes en antropología biológica. Dicho esto, es un tiempo increíblemente emocionante para nuestro campo. Podemos ahora hacer preguntas que no sabíamos estaban allí —y que estamos encontrando es "más curioso de lo que habíamos imaginado." [*genética de la población, evolución humana, cuatro campos*].

AMERICAN ANTHROPOLOGIST, Vol. 120, No. 2, pp. 266–277, ISSN 0002-7294, online ISSN 1548-1433. DOI: 10.1111/aman.13032

BEYOND EUROPE: A BETTER SCIENCE OF HUMAN DIVERSITY

Beyond Europe: Thousands of Ancestors

Human genetics research has always been biased (Kevles 1985). European peoples have dominated sampling strategies in studies of human biological variation, with bias being particularly prevalent in medical genetics (Rosenberg et al. 2010). For example, the majority of genome-wide association studies exploring the relationship between genetic variation and biological traits has been conducted in European cohorts. As a result, the design of these studies is inadequate to comprehensively and accurately elucidate the human history and determine the genetic bases of variation in human traits as a whole (Lachance and Tishkoff 2013).

Insightful reviews and pointed analyses, within both anthropological (Turner 2005; Goodman, Heath, and Susan Lindee 2003) and population-genetics frameworks (Rosenberg et al. 2010; Kristiansson, Naukkarinen, and Peltonen 2008; Tishkoff 2015), have revealed the shortcomings in these human genetics studies. Anthropological genetic studies, investigating maternal and paternal genetic variation among various populations across the globe, have paved the way for a better appreciation of human diversity (Oven and Kayser 2009; Underhill et al. 2000). These earlier works have informed the design of contemporary whole-genome sequencing studies, which provide us with a platform that accurately discovers variation in a given population without any *a priori* knowledge, hence avoiding ascertainment bias. Thus, 2017 may be the year when the tides have finally turned with respect to sampling bias.

Indeed, multiple studies in 2017 have dramatically expanded our knowledge of genomic variation involving hundreds of ancient and present-day peoples from across the globe (Marciniak and Perry 2017; Nielsen et al. 2017). Maybe not surprisingly, the results of these studies have empirically confirmed that our understanding of human genetic variation was incomplete, flawed, and biased (Martin, Gignoux, et al. 2017). More relevant to this review, these studies, in addition to the massive amount of data that they produced, have also added dozens of new twists to how we perceive human variation.

Before we explore these new insights and their impacts on modern biological anthropology and anthropological genetics, we should take a step back and elaborate on the composition of the genome and how it is inherited. Each human carries two copies of each of our chromosomes, one inherited from our mother and the other from our father. Our parents' chromosomes, in turn, were inherited from their parents, and so on. In this inheritance process, the maternal and paternal chromosomes exchange genetic material through a process called recombination. The result of this inheritance pattern is that our genomes are a collection of hundreds of thousands of mosaic pieces inherited from a population of ancestors. Each piece in our genome, in theory, can be traced back to a different ancestor. A wonderful, if involved, review by Veeramah and Hammer (2014) is a great source for further information on using whole-genome data to study the history of human populations.

In contrast to whole-genome studies, those focusing on maternally inherited mitochondrial DNA or the paternally inherited non-recombining region of the Y-chromosome are limited in that they are equivalent to only a single mosaic piece, or locus, even though they can be very informative in studies investigating social organization, kinship connections, or sex-specific migration patterns (Gokcumen et al. 2011; Kennett et al. 2017; Marchi et al. 2017). Tracing back all mitochondrial DNA to a common source, for example, led to the identification of a single African mitochondrion, the now-famous Mitochondrial Eve (Cann, Stoneking, and Wilson 1987). This is a single maternal genome with which we can trace back all of the variation among present-day mitochondrial genomes. Despite the significance of this finding, it provided a fairly limited view of human history, as this single mitochondrial genome represents only one female ancestor among thousands existing at the time. Our ancestors were never a single family but instead belonged to populations. Now we have been able to sift through the genome to identify thousands of ancestors for each individual. This achievement allows us to reconstruct not only individual ancestors but also ancestral populations, as described in several breakthrough genomics studies further detailed below.

Beyond Europe: Archaic Ancestors

One of the most surprising insights from recent analyses of whole human genomes, ancient and modern alike, is the realization that unusually old lineages have remained in extant human populations (Lin et al. 2015; Plagnol and Wall 2006). Two human genomes differ from each other by only 1 in 1,000 base pairs, on average, when single nucleotide polymorphisms are considered. However, some sections show higher divergences when two human genomes are compared to each other, and these divergences cannot simply be explained by increased mutation rate. There is a small but observable portion of human genomic variation that is older than expected by our previous models.

One explanation for these unusually old variations in the genome is the effect of balancing selection: the adaptive force that favors not just one but multiple alleles in a given genomic region. Indeed, recent studies have shown that a fraction of this unusually old variation may be due to balancing selection that maintains different genetic types across millions of years (DeGiorgio, Lohmueller, and Nielsen 2014; Gokcumen, Zhu, et al. 2013; Leffler et al. 2013; Pajic et al. 2016). But these regions, as interesting as they are, represent only a handful and do not explain the majority of these unusually old variations in the genome.

Thanks to the availability of genomes from ancient hominins (Meyer et al. 2012; Prüfer et al. 2014, 2017), we now know that some of these old lineages were inherited

from Neanderthals and Denisovans (Pääbo 2015). It turns out that all Eurasians carry mosaic pieces inherited from Neanderthals, corresponding to about 2 percent of each of their genomes (Vernot et al. 2016). The current thinking posits that one major admixture event from Neanderthals to ancestors of all modern humans happened in the ancestral population to all Eurasians, possibly in Western Asia, after some human groups left sub-Saharan Africa, but before they spread into Eurasian fringes. This would explain how Neanderthal admixture seems to be confined to populations outside of sub-Saharan Africa. Other, more complex admixture events, including one affecting only East Asian populations, have also been discussed (Wall et al. 2013). In addition to the Neanderthal admixture, a more unexpected finding involves the Denisovan remains from Altai. The genomic DNA from these remains revealed a distinct hominin lineage, separate from both humans and Neanderthals. Moreover, it turned out that this lineage contributed genetic material to contemporary Southeast Asians (Reich et al. 2010). Several recent studies are now discussing how these interactions have shaped the hominin genetic variation across the globe (Gilpin, Feldman, and Aoki 2016; Rogers, Bohlender, and Huff 2017). Even though the contributions from archaic hominin populations to the present-day human gene pool is small, these findings immensely complicate our understanding of the origins and evolution of human genomic variation.

Beyond Europe: African Genetic Diversity Is Even "Deeper" Than We Have Predicted

The deepest branches of human genetic variation reside in Africa (Nielsen et al. 2017; Tishkoff et al. 2009). However, the exact origins and subsequent interactions of ancient African populations remain mostly unknown due to the lack of comprehensive sampling of contemporary societies and the paucity of ancient genome data from the continent. Here, I will highlight two papers, both published in 2017, which provide new insights into African population history and diversity by producing the first population-level ancient genome data for the continent. In the first, Skoglund et al. (2017) generated genome-wide data from fifteen sub-Saharan ancient genomes, dating from 1,200 to 8,100 years before the present. These remains were excavated in both pastoralist and hunter-gatherer archaeological contexts in present-day Kenya, Tanzania, and Malawi. In the second, Schlebusch et al. (2017) analyzed ancient genomes from seven samples from South Africa, three stone-age hunter-gatherers (about 2,000 years old) and four iron-age farmers (about 300 to 500 years old). By analyzing these ancient genomes within the context of hundreds of present-day human genomes, these studies were able to reconstruct ancestral populations of Africa at an unprecedented resolution.

In the light of these new studies, we are finding that most of the mosaic pieces in our genomes can be traced back to a single ancestral population in Africa that lived approximately 150,000 to 300,000 years ago (depending on the mutation rates and other parameters). However, there are some pieces that can be traced back to other genetic sources dating hundreds of thousands, and sometimes millions, of years before. For example, Skoglund et al. (2017) suggest that a distinct African human population diverged from extant African populations hundreds of thousands of years ago but no longer exists. Instead, small but observable genetic remains of this enigmatic population remain hidden in the genomes of present-day Western Africans. In a similar analysis, Schlebusch et al. (2017) found that relatively recent South African genomes that are only thousands of years old branch out from the present human genetic variation in Africa. This means that other isolated, distinct ancestral populations were also in Africa only two millennia ago. These populations have not survived, but their influence is visible in the genomes of ancient stone-age hunter-gatherers. These new studies confirmed the long-held suspicion that other, previously unknown human populations lived in Africa, and revealed the genetic footprint they left among extant humans.

Were the previously unknown ancestral populations described in these two studies different from each other? One potential model to explain this deeper-than-expected genetic variation in Africa is the scenario of multiple ancestral populations having lived in Africa as relatively small and mostly isolated groups. The two studies have looked at different parts of Africa and consequently found footprints of two of these previously unknown ancestral populations. Other studies investigating human remains from additional parts of Africa may reveal others. Following this model, the contemporary genetic variation, which is more homogenous, may be explained by a scenario where one of these ancestral populations expanded geographically to dominate the other groups either by subsuming them or completely replacing them. Therefore, a majority of the present genetic variation can be traced back to that single ancestral population in Africa. However, a small number of deeper lineages persist, representing the genetic legacies of the multiple ancient human populations in Africa that are long gone.

To further complicate the picture, some of these divergent mosaic pieces in African genomes are so old that, if their dating is accurate, they may indicate a species other than modern humans contributing to genetic variation in present-day African genomes (Hsieh et al. 2016; Xu et al. 2017). We now know that other hominins, including Neanderthals, have contributed genetic material to Eurasian peoples (Prüfer et al. 2017; Taskent et al. 2017). Here, the scenario is akin to earlier discussions of Neanderthals contributing to Eurasian genetic variation but involving an unknown hominin. These exciting findings are still of preliminary nature but add to the wonderful complexity that we are unearthing from ancient and modern genomes.

These genetic findings underline the importance of the concurrent expansion of the fossil record in Africa. The recently discovered 300,000-year-old modern human skull from Northern Africa (Hublin et al. 2017) and the similarly dated *Naledi* remains from South Africa (Dirks

et al. 2017), I would argue, changed the way we think about human history in Africa. Now we must envision an even more diverse picture of the Africa of the past, where multiple populations of modern humans and other hominin species roamed all corners of the continent. Recent studies in other parts of the world echo a similar complexity, albeit at a shallower timescale (Bae, Douka, and Petraglia 2017; Rogers, Bohlender, and Huff 2017). The interactions of ancient human populations with each other, and the way these interactions may have shaped the genomes of present-day humans, will remain at the very center of anthropological genetics research for the years to come.

Beyond Europe: Contemporary Human Genetic Variation across the Globe is Different Even from the Recent Past

We have known for some time that contemporary genetic variation is best explained by "geography." In other words, the closer two humans are geographically, the less their genetic variation to each other is expected to be (Novembre et al. 2008)—mostly independent of ethnicity, religion, or any other group identities. Now our field is at a stage to move beyond simple geographic distance and take the topographic features (e.g., mountains, deserts, seas, etc.) into account to visualize and understand the paths and barriers to contemporary genetic variation (Peter, Petkova, and Novembre 2017). Ancient genomics has now added a chronological twist to it. It turns out that genetic continuity in a given region across time is often an exception rather than the rule (Kılınç et al. 2016; Lazaridis et al. 2016; Skoglund et al. 2017; but see Yang et al. 2017). People move, interact with their neighbors, and create ever-changing gradients of genetic variation across time and geography.

The two studies mentioned in the previous section involving ancient African genomes provide examples as to how contemporary genetic populations in a given geographic space do not necessarily predict the genetic variation of the past. One such finding was that present-day Hadza populations, who were thought to be confined to a small region in Tanzania, may be related to genomes from Ethiopia dated to 4,500 years before the present (Skoglund et al. 2017), raising the possibility that the ancestors of forager Hadza people may have been much more widespread in Africa than they are today. The same study made another unexpected connection between an Eastern Hadza population and Southern Khoe-San populations through analyses of ancient samples. Specifically, the genetic variation of ancient samples from Tanzania, Malawi, and Kenya, as well as present-day Hadza and Khoe-San, can be explained by their relative geographical distance. However, if we do not consider the ancient samples, this geographical connection is lost. Skoglund et al. (2017) hypothesized that the ancient geographical connection between Eastern and Southern African populations was lost due to the effect of Bantu expansion. This massive population event spanned millennia starting roughly 3,000 years ago and shaped the genetic variation of modern African populations (Berniell-Lee et al. 2009).

Collectively, the genetic evidence reviewed here supports the decades-old argument by anthropologists in all four fields (and in other disciplines) that simplistic notions of discrete, isolated human populations are misleading (Goodman, Heath, and Susan Lindee 2003; Livingstone and Dobzhansky 1962; Weiss and Long 2009). This holds true even for the Khoe-San people, who are regarded as the most genetically isolated of all human populations. As it turns out, in light of ancient genomics data, the Khoe-San interacted with other African groups after they first diverged from them (Skoglund et al. 2017). Ancient genomics research advances our insights into human genetic variation, cementing our view of human variation as an ever-changing mix of complex interactions, rather than partitioned into stable, discrete population units. Instead, the new genomic data allow, for the first time, a quantification of the degrees of admixture and the nonrandom patterns with respect to geography and time.

CONTEXT MATTERS: TOWARD A BETTER UNDERSTANDING OF HUMAN BIOLOGY

Context Matters: Variation of Skin Pigmentation in Africa

One of the key contributions of genetic approaches to anthropology is the realization that most human genetic variation lies within and not between populations (Goodman, Heath, and Susan Lindee 2003). This observation naturally extends to inherited traits. Previously, skin color was thought to be one of the exceptions to this rule. Indeed, skin color and other pigmentation-related traits (e.g., eye and hair color) can be more population-specific (Jablonski 2012). Specifically, lighter pigmentation is thought to be, by those in academia as well as by the public, primarily a non-African trait. Human populations that are farther from equatorial latitudes tend to have lighter skin color (Jablonski and Chaplin 2000).

We have a reasonable evolutionary explanation for why this is the case—namely, the adaptation to low-ultraviolet-light environments within the context of metabolism of vitamin D (Jablonski and Chaplin 2000). However, this explanation has not stopped racist narratives, which view skin color as a proxy to many other biological (and cultural) traits without any scientific basis. The narrative goes that having a lighter skin color separates Europeans from Africans, which anthropologists for decades have deconstructed on multiple fronts (Jablonski 2017; Yudell et al. 2016). Two recent papers now provide a new twist to this discussion (Crawford et al. 2017; Martin, Lin, et al. 2017).

It turns out that, like other human traits, Africans harbor the majority of the genetic variation that underlies skin color in humans, as it actually was already recognized almost twenty years ago (Relethford 2000). Some genetic variants associated with lighter skin color have been previously described. However, they were thought to have evolved after humans migrated north from sub-Saharan Africa. Instead,

new studies have shown that these pigmentation-related variants have existed much longer than previously thought in Africa in low frequencies and increased in allele frequency over time, most likely under adaptive pressure from low-ultraviolet environments (Crawford et al. 2017; Martin, Lin, et al. 2017).

Another finding of these studies is that the genetic basis of pigmentation is far more complicated in African populations than in non-African populations. Specifically, researchers identified additional variants that control pigmentation in Africa that do not exist outside of Africa (Crawford et al. 2017; Martin, Lin, et al. 2017). Retrospectively, this is not surprising. Africa is a vast continent, and its inhabitants are diverse. They live in different ecological settings and inhabit a wide range of latitudes. As such, the lineages of African populations have had more time to evolve different ways to "fine tune" their skin pigmentation based on the selective pressure of ultraviolet-light incidence within Africa. Khoe-San people, for example, have lighter skin-color pigmentation than more equatorial Africans (Martin, Lin, et al. 2017).

Based on these findings, it is now clear that Eurasian adaptation to northern latitudes has happened not by evolving new variants but primarily by "hijacking" existing African variants. This is an incredibly important finding to refute racist interpretation of skin color. On the one hand, it falsifies the long-held belief that lighter pigmentation is innately a non-African trait. On the other hand, it provides further credibility to the emerging notion that "soft sweeps"—or existing variants, rather than new mutations—drive adaptation to new environments in humans (Schrider and Kern 2017). In other words, this finding implies that extant, older genetic variation—rather than newer, derived, population-specific variants—underlie the adaptive phenotypic variation in humans. This conceptual framework is about to transform the way in which we study skin color and other potentially adaptive traits.

Context Matters: Population-Specific Variations

Skin-pigmentation variation in Africa as described above is a sobering example of what was missing in past—and is still missing in many current—genomics studies. One of the most welcome additions to genetic epidemiology in the last couple of years is the general realization of the limitations of Eurocentric conceptualization of human genetic variation (Carlson 2016). For example, an extensive study involving nearly 50,000 individuals with non-European ancestry identified dozens of novel variations strongly associated with complex traits—that is, traits that are affected by a combination of multiple genetic and environmental factors (Wojcik et al. 2017). Retrospectively, this is not surprising, as anthropologists have been documenting variation in non-European populations for decades (Mielke, Konigsberg, and Relethford 2006). However, the empirical demonstration of this diversity in an indisputably large cohort is a significant milestone.

Another important finding in these studies is the realization that the effect of most genetic variants on human biology is population-specific. Two nonmutually exclusive explanations emerge from this observation. First, it is plausible that one's environment may interact with specific genetic variants to lead to the development of different biological traits. This way of thinking is especially relevant now with the rise of epigenetics studies in anthropology, allowing researchers to measure, albeit with some level of noise, the environment's impact on the regulation of gene function (reviewed in Mulligan 2016). A second way in which a particular genetic variant can have varied effects in two individuals is the difference in the rest of their genetic background. In other words, a combination of genetic variants in a given individual may have cumulative effects, where the effect of the whole is greater than its parts (reviewed in Jones, Bürger, and Arnold 2014).

Regardless of the underlying factors, this more complete understanding of the way that genetic variation affects human biology will, in my opinion, transform how we conduct anthropological genetics research. It is clear that an integrative approach involving the study of life histories, cultural practices, and environmental and genetic backgrounds has emerged as the most informative approach for thoroughly investigating variable human traits. Therefore, anthropology has never been more relevant to genetics research.

Context Matters: Microbiome, Transcriptome, and Epigenome

One of the crucial developments in anthropological genetics in 2017 is that the field continues to move to embrace other "-omics" and molecular technologies. This development has the potential to start linking previously disconnected anthropological subfields. Projects connecting genetics, transcriptomics, and microbiome data with life histories, cultural practices, and archaeological remains are not just a theoretical possibility but are viable endeavors (Han et al. 2016; Horvath et al. 2016; Manus et al. 2017; Non, Hollister, and Humphreys 2016). This year has provided some of the most amazing examples of this trend, producing results that were, indeed, stranger than we imagine.

The extent, diversity, and functional relevance of the microbiomes living in our bodies added a new layer of complexity to our understanding of the human condition. For example, studies in Indigenous populations with more traditional diets showed that their microbiome remains much more diverse than those of people consuming more uniform, modern diets (Gomez et al. 2016). A 2017 study on the microbiome of the Hadza people now adds a new layer to the story: not only is the microbiome of these hunter-gatherers much more diverse than that of people with modern diets, but it changes seasonally (Smits et al. 2017). The cyclic nature of the hunter-gatherer microbiome is likely due to the availability of different types of food and that bacterial species that adapted to such seasonal changes remain in the Hadza population. The microbiomes of industrialized societies, in

contrast, have lost these cyclic bacteria due to homogenization in their subsistence activity and diet. The consequence of this loss is unknown. The evolution and diversity of microbiomes of extant and ancient human groups, the way that diet and genetic variation shapes microbiome variation, and the biomedical outcomes of these features will undoubtedly become a new focus of anthropological genetics.

Another front that is providing fascinating insights into human biological variation is transcriptomics. One of the challenges in anthropological genetics (and human genetics in general) is linking genetic variation with phenotypes. Transcriptomics provides a high-throughput approach where variation at the genetic level can be associated with RNA-level variation. Multiple studies have already provided extensive datasets (unfortunately, mostly from cohorts with European ancestry only) of such associations between genetic and transcriptomic variation (eGTEx Project 2017). These datasets provide a robust framework in which the functional impact of anthropologically relevant genetic variation can be studied.

These studies allowed for further understanding of the reasons underlying adaptations that led to higher frequency of specific alleles in distinct populations. The most dramatic integration of such analyses in 2017 has been in measuring the impact of Neanderthal genetic variation on present-day human biological variation. Such studies have determined the genome-wide effect of Neanderthal haplotypes to expression-level change (McCoy, Wakefield, and Akey 2017) and variation in other phenotypes in human populations (Dannemann and Kelso 2017; Quach et al. 2016). Integrating these findings with ever-improving annotations of function in the human genome has even led to an estimation of the health status of the now-extinct Neanderthal population (Berens, Cooper, and Lachance 2017; Sullivan et al. 2017). These exciting inferences should be treated with a grain of salt, however. For example, it is possible that the same regulatory variants may have had different effects on expression levels and gene function due to the genomic context of Neanderthals. In other words, a single variant in a regulatory region may have different effects depending on other variations in this region. In fact, regulatory architectures (that is, the collective set of variations that determine the expression in a locus) are observably different even among human populations (Martin et al. 2014) yet alone among now-extinct hominins. Regardless, there has been an exciting flurry of discoveries with regard to ancient genomes, and now a new functional layer of transcriptomic data allows for an even deeper understanding of ancient populations and their contribution to contemporary biological diversity.

Context Matters: Emerging Studies in Mouse Models of Human Genetic Variation

Analyses of the RNA-level effect of genetic variation also provide a stepping-stone to more comprehensive studies involving mouse models—a more frequent practice among anthropologists. A study by Capellini et al. (2017) provides an excellent demonstration of this approach. The authors set out to understand why genetic variation at the Growth Differentiation Factor 5 (*GDF-5*) locus in humans shows both strong signals of selection in non-African populations and happens to be significantly associated with osteoarthritis risk. They narrowed down the variants to the regulatory enhancer region of the *GDF-5* gene and identified a single ancient African variant, similar to skin-pigmentation-associated variants, that increased in allele frequency in northern Eurasian populations under adaptive conditions. Their study took this analysis one step further by creating transgenic mouse models to demonstrate that these variants lead to decreased enhancer activity, which in turn leads to both decreased bone growth and increased susceptibility to arthritis. This study further raised the question as to why these variants were maintained in humans for millions of years and then reached major allele frequency status in many Eurasian populations, especially given the increased risk of osteoarthritis. However, what makes this study remarkable is that it poses this question by providing a concrete framework around the specific functional impact of these variants. Overall, these emerging methodologies now give anthropology a powerful means to connect genetic variation with variable human traits.

BEYOND RACE: CONSTRUCTING A HOLISTIC ETHICS OF HUMAN GENETIC DIVERSITY

Race has no biological basis, and yet the idea that it does persists. In 2017, genomics studies, including those that we mentioned in this review, have unsurprisingly shown that the genetic variation within continents, especially within Africa, is overwhelmingly higher than variation between continents. Hence, there is no basis for traditional racial categories as far as genomics is considered. On top of that, we now empirically know that even the most emblematic of traits for racial clarification, skin color, is most variable in Africa and that light skin color is not a uniquely Eurasian trait. Despite these demonstrations, the concept of race remains entrenched in public perception. As empirically scrutinized by Wagner et al. (2017), anthropology has come a long way in rejecting racial categories as biological entities while at the same time recognizing the importance of racially constructed identities for contemporary human conditions and health. As a community, we must thus remain resilient as long as these racist narratives prevail to continuously deconstruct them. It is not only an ethical responsibility; it is also a scientific one.

As our field inevitably moves into stranger and ever-more fascinating territory, the ethical concerns that follow move beyond simply the concept of race. Genomics and other "-omics" technologies are infiltrating many aspects of our lives. As a consequence, anthropological genomics is not only responsible for addressing the issue of race but also other thorny issues, such as privacy, community sensibilities, and the access to and control of anthropological datasets and narratives.

As exemplified by the studies summarized above, it is a fantastic time for anthropological genetics research. We have never known more about our biological history, and our understanding of human diversity has never been more profound. But not everyone can share in this excitement. Almost all of the cutting-edge genomics (and related) research is conducted in laboratories in North America and Europe and in a select number of East Asian countries (e.g., China, Japan, Korea). Indigenous populations and populations in many developing and underdeveloped nations are either following the anthropological genetics revolution from behind or can participate only as sample providers.

One relevant issue that genetic anthropologists increasingly face is the sheer pace at which genomic and related technologies evolve. One ethical consequence of this pace is a question of privacy (Vos et al. 2017). The types of data generated with the same samples and the resulting analyses are always changing, with implications for how we interpret the past, understand human disease, and so on. A striking example is our newly gained ability to reconstruct entire population histories from a handful of genomes. This is possible because each human genome harbors segments from a different ancestor. As a result, one can reveal immense amounts of information from individual genomes. In fact, recent high-profile studies of ancient and modern genomes rely on very detailed analyses of individual genomes to reconstruct entire population histories (Mallick et al. 2016). We can now determine the percentage of Neanderthal ancestry in a given genome (Vernot et al. 2016) and identify hundreds of new variants, estimating susceptibility to dozens of traits and diseases (Wolf, Burke, and Koenig 2015). Not even the possibility of such inferences was known a decade ago. What will have to be the ethical consideration of consent for samples collected ten years ago? Should we reconsider how we conduct informed consent and community-level permissions for future studies when undoubtedly currently unforeseen analyses will be possible? Novel analyses and interpretations of genomic data are at the core of scientific progress, although the continual reimagination of human history and variation includes very little input from the sample donors (Tindana and de Vries 2016).

In my view, the meaningful incorporation of study participants and communities in anthropological genetics is the single most pressing ethical issue facing the community, as has been argued by others more comprehensively (Malhi and Bader 2015). However, achieving this goal will not be an easy task. First, there is systemic inequality within and among nations regarding access to resources and knowledge that is far beyond genetic anthropology. Most Middle Eastern populations, who inhabit a geographic region of crucial importance to anthropologists, are living under autocratic regimes that restrict individual rights. In 2016, a comprehensive study of Middle Eastern genetic variation highlighted the extraordinary "consanguinity" in the region within a medical genetics framework but did not include necessary anthropological insights or sensibilities (Scott et al. 2016). It is evident that such genetic surveys are crucial in understanding Mendelian and high-penetrance genetic disorders that are prevalent in the region. However, from an anthropological perspective, it is not clear that such a generalistic definition of genetic variation of a diverse region of more than 200 million people is entirely benign (Taskent and Gokcumen 2017).

Anthropological insights into other types of biomedical inferences provide more insights. Excellent work by Marcia Inhorn has revealed that multiple forces, such as the now-antiquated medical practices inherited from the English colonial period (Inhorn 2003), cultural beliefs tying "manhood" to fertility (Inhorn 2004), and social stigmas regarding motherhood in the Middle East (Inhorn and Balen 2002), shape the curious spread and practices of male infertility treatments. The emerging technologies in fertility treatment are understood and practiced in a culture-specific manner. The integration of genomic technologies into diverse cultures around the world will not be much different. We have already encountered several hard ethical questions (Turner 2012): How might geography-specific cultural practices (such as patriarchal polygamy or cousin marriages), which are abhorred by Western values and by some national regimes, be handled if recorded and reported? Would self-identification as Kurdish hurt the well-being of a village community in Iran? How would individual consent in hierarchical communities be managed? Is omitting such vulnerable communities from anthropological genetics research preferable? Is such omittance itself a breach of ethics, given the increasingly central role of genetics in economics and health care?

One case is that of the Navajo Nation. Indigenous people in the Americas have a long-standing and justified suspicion of genetic research due to many past transgressions. As a result, in 2002 the Navajo Nation, the second-largest Native American territory retained in the United States, declared a moratorium on all genetic research involving their members. They are now reconsidering this ban, given the increasing importance of genetics research in the diagnosis and treatment of disease (Reardon 2017). Understandably, Navajo people want access to the best health care possible and deserve to have it on their own land. All things considered, and after decades of interacting with anthropologists, the Navajo people are now in a position of making informed decisions for themselves. Other communities may not have this luxury due to political, economic, or historical reasons. These are difficult questions with no immediately apparent answers. However, the anthropology community has been at the forefront of addressing these issues (e.g., Goodman, Heath, and Susan Lindee 2003), and undoubtedly this discussion will remain an important one in the foreseeable future.

All of these considerations highlighted above converge on one key ethical conundrum: the priorities of anthropological geneticists (e.g., understanding the history and variation of humankind) do not necessarily align with those of Indigenous populations (e.g., protecting their communities from historical and ongoing oppression and exploitation).

Nothing exemplifies this contrast more than the recent declaration of a code of ethics for researchers by the very Khoe-San people who were and still are the subject of countless genetic anthropology studies (Martin, Lin, et al. 2017; Schlebusch et al. 2017). Khoe-San peoples are, arguably, the most exciting group of individuals for anthropological geneticists to work with. Their DNA harbors the most isolated and deep genetic lineages among all human groups. They also maintain complex and unique cultural and linguistic trends that differ widely from their geographical neighbors. For example, some still practice traditional subsistence strategies that have likely persisted for thousands of years. However, the fascinating qualities of these peoples are, by definition, an outsider's view (Bankoff and Perry 2016). Their concerns about genetics research, which are very eloquently and succinctly put forward in a short document they released in 2017,[1] are not complicated (Nordling 2017). They ask to be treated respectfully, honestly, justly, and fairly. And they make a very clear case for communication to take place both ways to ensure they remain informed and also have a say in the process of genetic research. Their openness without compromising their core values gives hope and provides a potential template for future collaborations between Indigenous peoples and anthropological geneticists.

As biological technologies permeate our economy and society more and more each day, additional ethical issues are emerging. We now have a better understanding of genomic variation and its evolution. It was only a decade ago when our work identified thousands of large structural variants, suddenly increasing the known human genomic variation close to tenfold (Conrad et al. 2009; Gokcumen, Tischler, et al. 2013). We now have a more sophisticated understanding of the evolutionary forces shaping humans genomes (Antelope et al. 2017; Brinkworth 2017; Harris and DeGiorgio 2017). We now develop lists of genetic variants to predict disease outcomes more accurately (MacArthur et al. 2017). Even though it is not segregated along imagined racial boundaries, genetic variation in humans is real—and we now get closer than ever to understand its implications.

Discussion in the scientific and anthropological world has already been fierce—and this is a good thing. Would knowledge of an innate mathematical genius or an innate potential to run one hundred meters under ten seconds affect how society should treat individuals having these abilities? It likely is not a distant possibility that privacy can be breached, even in anonymous genomic datasets. Who should serve as the guardians of those datasets? Who should be authorized to convey, interpret, and use the results (Gutmann and Wagner 2013; Jarvik et al. 2014)? Experimental treatments are ongoing to repair genetic disorders, paving the road to allow for creating "designer babies" (Pei et al. 2017). Upcoming ethical conundra in our disciplines will not be in short supply.

One silver lining to all of these research issues is that, maybe as a result of past sins, anthropological genetics, in particular, and anthropology, in general, have now developed a tradition of rigorous discussion of ethics in the field, which involves not only researchers but also participants. This practice, I believe, will be the compass as we progress through exciting but uncharted territory ahead.

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NOTES

Acknowledgments. I would like to thank my students, Ozgur Taskent and Izzy Starr, as well as Dr. Marie Saito for careful reading of this manuscript. My colleagues Derek Taylor and Stefan Ruhl gave me important advice on organization and content of the manuscript. I especially want to thank the editor and reviewers, whose comments have substantially helped me to clarify and strengthen the points I am making in the manuscript. I also want to acknowledge the National Science Foundation (Grant No. 1714867) for allowing me and my students to explore new horizons in anthropology.

1. The document can be found here: http://trust-project.eu/wp-content/uploads/2017/03/San-Code-of-RESEARCH-Ethics-Booklet-final.pdf.

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