SPECIAL FEATURE: PERSPECTIVE

Ancient DNA and human history

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We review studies of genomic data obtained by sequencing hominin fossils with particular emphasis on the unique information that ancient DNA (aDNA) can provide about the demographic history of humans and our closest relatives. We concentrate on nuclear genomic sequences that have been published in the past few years. In many cases, particularly in the Arctic, the Americas, and Europe, aDNA has revealed historical demographic patterns in a way that could not be resolved by analyzing present-day genomes alone. Ancient DNA from archaic hominins has revealed a rich history of admixture between early modern humans, Neanderthals, and Denisovans, and has allowed us to disentangle complex selective processes. Information from aDNA studies is nowhere near saturation, and we believe that future aDNA sequences will continue to change our understanding of hominin history.

human history | Neanderthal | Denisovan | ancient DNA | demography

The genomics revolution is well under way. At the time that the first human genomic sequences were obtained (1, 2), it was almost inconceivable that within 15 y thousands of genomes from people around the world would be sequenced, many to a high depth of coverage (3). It was probably even less conceivable that partial or complete genomic sequences would be obtained from hundreds of modern human fossils (4–6), several Neanderthal fossils (7, 8), and even fossils of a previously unknown sister group of Neanderthals, called Denisovans (9, 10) (Fig. 1). Some of these ancient genomes have been sequenced to such high depth that their error rates rival those of high-coverage sequences from present-day humans.

The wealth of present-day and ancient genomic data has greatly increased what is demanded of population geneticists. When relatively few loci could be studied using marker loci—chiefly blood groups, allozymes, and microsatellites—gross descriptive statistics, such as heterozygosity, Wright's F_{ST}, and various genetic distances were sufficient to characterize broad patterns of population differentiation. Application of these classic methods was pioneered by Luca Cavalli-Sforza and his many collaborators. As early as 1964, Cavalli-Sforza et al. (11) published a phylogenetic tree of 15 human populations based on a total of 20 alleles at 5 loci, mostly blood groups, for which adequate published data were available. The authors superimposed the tree on a world map to suggest past dispersal routes. Their map is surprisingly consistent with more recent studies based on vastly more data. Only the connection of Maori to Native Americans disagrees with currently accepted theory, that the Maori descended from Polynesians (12).

At present, not only can geneticists elucidate broad patterns of relationship among populations, but they can also provide detailed answers to historical questions of relevance to archeology and paleoanthropology. When, where, and from what source did particular human populations arise? Who admixed with whom and when did the admixture take place? Are obvious changes in the archaeological record the result of population replacement or cultural innovation? Did past cultures leave any genetic descendants? As we will discuss, analysis of ancient DNA (aDNA) has been successful in answering several of these questions, but has also raised new questions in the process. Importantly, aDNA provides a temporal dimension to genetic studies that would be inaccessible with present-day genomes alone, and only now is the full significance of aDNA being explored.

Contamination

One of the major problems that prevented the widespread sequencing of hominin aDNA for several years was contamination. Genetic material extracted and sequenced from a tissue sample of a living individual

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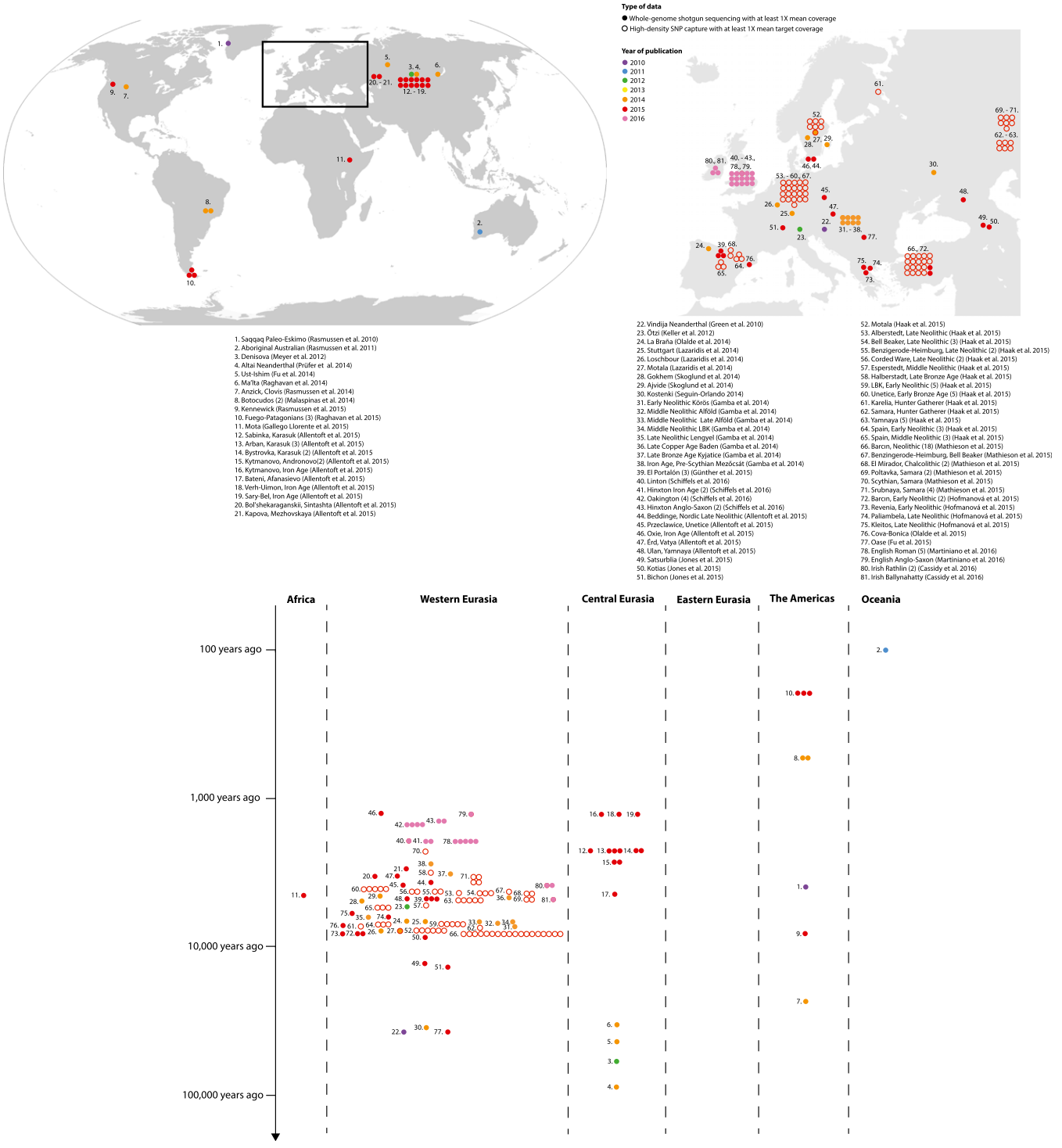

Fig. 1. A human paleogenomic revolution. The maps show the location of human remains that have yielded whole genomes (closed circles) and high-density SNP capture datasets (open circles) of medium and high average coverage (>1×) during the past 6 y. The colors denote the year of publication of each ancient DNA study. Note that some of the studies cited also include genomes and SNP capture datasets of lower coverage, which are not included in the map. The timeline displays the dating of the remains, on a logarithmic time scale. The references included in this figure but not mentioned in the main text are refs. 69–77.

will consist largely of DNA fragments from that individual (i.e., endogenous fragments) if standard laboratory practices are followed. In contrast, because aDNA is so scarce and fragmented, most of the genetic material extracted from fossils tends to be exogenous, usually either from environmental microbes or humans who handled the fossil (13). The latter type of DNA is especially troublesome, as present-day human DNA is similar in sequence to endogenous aDNA from hominin fossils, and can introduce biases in downstream analyses.

Although some of the first studies of nuclear aDNA from archaic hominins had problems with contamination (14, 15), there

have been substantial experimental and computational innovations for mitigating its effect in contemporary studies. In the past decade, researchers have developed two broad sets of approaches to correct for contamination in their aDNA samples, allowing for the study of previously unusable sequences.

First, it is now a standard practice to extract aDNA under strict clean-room conditions—including UV radiation, bleach treatment of surfaces, and filtered air systems—so as to minimize the proportion of exogenous DNA in the fossil extracts (13). Additionally, at the time of DNA library construction, scientists incorporate unique adapters to tag molecules that are present at the moment of extraction (16), to prevent additional molecules accidentally added during subsequent sequencing steps from being confused with endogenous molecules.

Second, after the DNA has been sequenced, several bioinformatic tools can be used to either remove contaminant reads or estimate the proportion of those reads present in a DNA library. A common practice is to estimate the rate of contamination using mitochondrial DNA (mtDNA), which is much more abundant than nuclear DNA and hence is sequenced to a much higher coverage than nuclear DNA. For highly divergent populations (e.g., Neanderthals), one can use diagnostic positions that distinguish the two groups and assess how many discordant reads are present at each position (17, 18). For modern human populations (e.g., ancient Europeans), one can check for reads that diverge from the consensus sequence or that do not contain molecular signatures consistent with aDNA (19, 20). There are also more sophisticated contamination rate estimation methods that use larger subsets of the data, including sex chromosomes (21, 22) and entire autosomal genomes (7, 23). Additionally, one can use patterns of cytosine deamination at the ends of fragments—a postmortem chemical damage typical of aDNA—to filter out sequenced reads that do not display this signature and are therefore not likely to be ancient (24).

Archaic Hominins

The sequencing and analysis of genomes from Neanderthals and their relatives has been nothing short of revolutionary. First, the question of interbreeding between Neanderthals and modern humans—posed by paleoanthropologists over 30 y ago—has now been convincingly answered (7, 8). Additionally, a sister group of Neanderthals, called Denisovans, was discovered and its relationship to Neanderthals and humans established (9, 10).

Neanderthals. Despite the overlapping ranges of Neanderthals and modern humans in Europe and western Asia for at least 10,000 y, there was no widely accepted archaeological evidence that Neanderthals and modern humans interacted or interbred. Krings et al. (25) found that mtDNA sequences obtained from a Neanderthal fossil lay outside the clade composed of all mtDNA sequences from modern humans. This pattern of reciprocal monyphyly has been confirmed in many later studies of Neanderthal mtDNA (17). Although the mtDNA tree was consistent with the hypothesis that there was no admixture between the two groups, it did not provide conclusive evidence against it. In fact, reciprocal monophyly would be seen with significant probability even if there had been substantial admixture (26). Before the sequencing of the first Neanderthal genome, an analysis of present-day human samples had indicated there might have been high levels of archaic ancestry in both European and West African genomes, likely stemming from a diverged hominin group (27).

Nuclear aDNA from Neanderthals resolved this problem, and its analysis showed that the actual admixture was different from what had been expected by either geneticists or paleoanthropologists. Green et al. (7) presented the first draft Neanderthal genome (~1.3× coverage) from a combined dataset of bone extracts from three individuals found in the Vindija Cave in Croatia, and convincingly showed that contamination levels were less than 1%. The genomes of individuals from three non-African populations (French, Chinese, and Papua New Guinean) were 4% more similar to the Neanderthal genome than were the genomes of individuals from two African populations (San and Yoruba). The most parsimonious explanation for this pattern was that Neanderthals and the ancestors of the present-day non-African populations had interbred in the Middle East, where their ranges were known to have overlapped. This tentative conclusion has been reinforced by numerous later studies, using both additional Neanderthal genomes and the genomes of early modern humans (8, 28, 29). All Neanderthals genomes sequenced to date show greater similarity to non-Africans than to Africans (8, 30). Additionally, identification of genomic blocks derived from Neanderthals in present-day non-African genomes confirm that admixture must have taken place (31, 32). Finally, a genome obtained from a 45,000-y-old modern human fossil from Ust'-Ishim, Siberia, contained Neanderthal tracts that were much longer than those found in present-day humans (28). This observation is consistent with admixture having taken place 7,000–13,000 before the Ust'-Ishim individual lived, as admixture tracts tend to become shorter the longer the time since the admixture event. A similar pattern was seen in the genome of Kostenki-14, a 37,000-y-old modern European (33).

Comparison of the Vindija Neanderthal genome with a larger number of present-day human genomes revealed the surprising fact that the genetic similarity of East Asians to Neanderthals is slightly but significantly greater than the similarity of Europeans to Neanderthals (10, 34). This pattern is the opposite of what was expected on purely paleoanthropological grounds, as no Neanderthal fossils have been identified in East Asia, and only a few have been found in West and Central Asia. Recently, Vernot and Akey (35) rejected the hypothesis that there was only one pulse of admixture into the common ancestors of Europeans and East Asians, suggesting either that there was additional admixture as Neanderthals expanded into the East or that the Neanderthal signal in Europeans was diluted by interbreeding with a modern human group that did not admix with Neanderthals.

Two years ago, a very high-coverage genome (52×) was obtained from a Neanderthal fossil found in the Altai Mountains in south-central Siberia and called the "Altai Neanderthal" (8). As a consequence of improvements in the ways aDNA fragments are extracted, amplified, and sequenced, sequence quality was comparable to high-quality genomes obtained from living individuals (10, 36, 37). Using the pairwise sequentially Markovian coalescent method (38), Prüfer et al. (8) found that the population ancestral to the Altai Neanderthal had a small size after it diverged from the lineage leading to modern humans. Furthermore, because there were numerous long runs of homozygosity, the individual was inferred to have an inbreeding coefficient of 1/8, meaning that her parents were either half-siblings, aunt/uncle-nephew/niece, grandparent-grandchild, or double first cousins.

More recently, the genome from a 37,000- to 42,000-y-old fossil found in Peştera cu Oase, Romania, provided dramatic confirmation that there was admixture between early modern humans and Neanderthals (29). This genome contained three

chromosomal tracts of Neanderthal ancestry longer than 50 cM, indicating that it had a Neanderthal ancestor four to six generations in the past. The total proportion of its Neanderthal ancestry (6–9%) was higher than in any present-day human genome. The Oase genome shared no more alleles with present-day Europeans than with present-day East Asians, suggesting that the population to which it belonged did not contribute substantially to present-day Europeans. Thus, although additional admixture evidently took place in Europe, the populations that admixed were replaced by modern human populations that were not involved in these later interbreeding events.

Denisovans. In 2010, researchers published a 1.9× genome from a small finger bone found in the Denisova Cave in south-central Siberia (9). The morphology of this bone was not informative enough to ascertain whether it came from a modern human, a Neanderthal, or something else. Nevertheless, its mtDNA sequence indicated that its divergence from the modern human-Neanderthal clade occurred roughly 1 million y ago (39). However, when the nuclear DNA was sequenced, it told a different story: the group represented by this bone is a sister group of Neanderthals that diverged from them after the ancestors of modern humans diverged from Neanderthals (9). That conclusion was confirmed by analysis of a high-coverage genome (30×) obtained from the same fossil (10) and the high-coverage Altai Neanderthal (8). Denisovans were the first archaic hominin group that was characterized almost completely on the basis of genomics, as the fossil remains are too scarce to provide much morphological information.

The high-coverage Denisovan genome showed a pattern of population decline similar to the Altai Neanderthal genome. However, Denisovans had a different history of admixture with modern humans. Denisovan ancestry is found in Melanesians and native Australians, and to a lesser degree in other East Asians. Although Denisovans are known only from a single cave in Siberia, the pattern of admixture suggests that they once had a broader geographic range. That conclusion is supported by the analysis of partial genomes obtained from two teeth found in the Denisova Cave (40). One of the teeth is almost 60,000 y older than the finger bone from which the first nuclear sequence was obtained, indicating that either Denisovans persisted in that region, which had a continuously harsh climate, or entered it at least twice. Furthermore, Denisovans were more genetically diverse than Neanderthals. One of the teeth sequenced has more differences from the high-coverage Denisovan genome than the differences found between Neanderthal genomes from Spain and Siberia.

Comparison of the high-coverage Denisovan and Neanderthal genomes showed that the Altai Neanderthal is slightly more similar to African genomes than is the Denisovan. That and other evidence led to the conclusion that Denisovans had received admixture from another archaic hominin group, possibly *Homo erectus*, which diverged from the common ancestor of humans, Neanderthals, and Denisovans more than 1 million y ago (8). Admixture from this group probably explains the anomalous mtDNA tree: Denisovan mtDNA likely descends from this archaic hominin group.

aDNA from Modern Humans

Arctic. The first humans started expanding into the New World Arctic 4,500 y ago. Archaeologists distinguish three major cultures in this expansion: Early Paleo-Eskimos, Late Paleo-Eskimos, and Thule. Paleo-Eskimo groups had similar technologies throughout their geographic range and persisted until roughly 1,000 y ago, when they were replaced by the Thule, who are the direct ancestors of present-day Inuit. The first ancient human genome was recovered from a Paleo-Eskimo individual (6). It provided evidence for an early Paleo-Eskimo migration from Siberia that was different from the later migrations that gave rise to present-day Native Americans.

More recently, Raghavan et al. (41) obtained 26 genomic sequences from ancient bones throughout the Arctic, and found genetic continuity in both time and space among all Paleo-Eskimos. They descended from immigrants from eastern Asia and dispersed quickly throughout the American Arctic. The later spread of technological innovations seen in the archaeological record was not accompanied by genetic changes in Paleo-Eskimos. This pattern suggests that Paleo-Eskimos were mobile and nomadic, resulting in extensive gene flow among local groups. The relative genetic continuity in time indicates a large overall effective population size resulting from high levels of gene flow.

Raghavan et al. (41) also showed that the Thule peoples descended from a separate wave of immigration from Eastern Siberia. The Thule replaced Paleo-Eskimos with no detectable interbreeding among the two groups. Park (42) argues that the lack of interbreeding calls into question claims of a 200-y period of overlap of Paleo-Eskimos and Thule. Such mobile peoples would probably have encountered one another and it seems unlikely that they would have had cultural barriers strong enough to completely prevent interbreeding.

North and South America. Native Americans in North and South America are descended from a different and earlier immigration event than the Paleo-Eskimos and the Thule (6, 41). There is widespread archeological evidence that North America was colonized by peoples associated with the Clovis technology by 13,000 y ago, and some sites in North and South America suggest earlier occupation. These observations are consistent with immigration from Eastern Siberia via Beringia, which was above sea level 22,000–17,000 y ago (41). At some early American sites, skulls were found that appear to be more similar to present-day peoples of Australia and Melanesia, raising the possibility that there was an earlier immigration of Australo-Melanesians that did not persist (41).

The sequence of a 24,000-y-old fossil from Mal'ta in south-central Siberia is important for understanding the origins of Native Americans (43). The Mal'ta genome is both basal to present-day western Eurasians and closely related to Native Americans, but it has no close affinity to present-day East Asians. Raghavan et al. (43) estimated that 14–38% of present-day Native American ancestry derives from the Mal'ta population, resulting from admixture that probably took place in Asia after the ancestors of Native Americans diverged from East Asians and before the divergence of Native American groups from one another.

The first complete genomic sequence from a Native American was presented by Rasmussen et al. (44). The individual, called Anzick-1, was associated with Clovis artifacts and is about 12,600 y old. The Anzick-1 sequence is closer to present-day Native Americans than it is to any non-American group, and hence the population to which it belongs is either directly ancestral to present-day Native American populations or very closely related to their direct ancestors. Rasmussen et al. also reported that there was a deep branch separating present-day northern Native American populations from those of southern North America and South America.

Later, Rasmussen et al. obtained a low coverage (~1×) sequence of the 8,340- to 9,200-y-old remains of an individual known as the "Kennewick Man" (45). These remains were found in the state of Washington. Its relationship to present-day Native American groups has engendered both historical and legal questions. The genomic sequence showed affinities with several present-day Native American groups living in the same geographic area, suggesting that it was a member of a population directly ancestral to those populations. Thus, although early Native Americans dispersed throughout North and South America relatively quickly, populations in the northwestern part of the United States remained in that area for several thousand years.

Two large-scale genomic studies published in the past year have helped further elucidate the history of Native Americans. Raghavan et al. (46) surveyed 31 present-day human and 23 ancient modern human genomes ranging in age from 200 to 6,000 y. They concluded that all Native Americans separated from their ancestors ~20,000 y ago, with an upper limit of 23,000 y. Within North America, Raghavan et al. (46) inferred that northern Amerindians, including Athabascans, diverged from southern North Americans and Central and South Americans ~13,000 y ago. This divergence time is close to the earliest well-established archaeological sites in the Americas, suggesting that the separation of these lineages occurred there, and not before immigration from Asia.

Raghavan et al. (46) also concluded, however, that there was not a single wave of immigration. Instead, Native Americans received significant recent gene flow from East Asians and Australo-Melanesians, possibly via the ancestors of present-day Aleutian Islanders. Raghavan et al. (46) found no evidence that any present-day Native American groups are relicts of an earlier wave of colonization. They also found no genomic evidence that fossil skulls that are morphologically similar to Australians and Melanesians were the product of an earlier wave of immigration.

Skoglund et al. (47) analyzed a large SNP dataset that included 63 individuals from 21 present-day Native American populations and reached a conclusion similar to that of Raghavan et al. (46), but one that differs somewhat. Skoglund et al. (47) found that some but not all Native American populations contained a strong signal of Australo-Melanesian ancestry, especially among certain South American populations. Furthermore, they could reject the hypothesis that Native American populations were descended from a single randomly mixing population. Instead, the authors posited that there was an intermediate population, which they called population Y, that is closely related to Australians and Melanesians and that contributed to Native American populations to varying degrees. The difference from Raghavan et al. (46) is in arguing that the admixture from population Y to the Americas occurred early in the colonization process. The problem for both the Skoglund et al. (47) and Raghavan et al. (46) scenarios is explaining why there is a stronger signal of Australo-Melanesian ancestry in native South Americans than in native North Americans.

Thus, the origin of Native Americans is still not completely clear. They do not descend from a single panmictic population that crossed Beringia, but determining where, when, and how the affinities to Australia and Melanesia arose will require the analysis of additional present-day and ancient genomes.

Western Eurasia. Populations of Western Eurasia are vastly larger than those of the Americas and their history is more complex. During the past 5 y, this region has yielded more aDNA genomes than any other in the world. The first ancient European genome sequenced came from Ötzi, a 5,300-y-old mummy found in the Tyrolean Alps. Keller et al. (48) and Sikora et al. (49) showed that, surprisingly, this individual had close genetic ties to present-day Sardinians. Furthermore, a genomic sequence from a 5,000-y-old farmer from Scandinavia was also found to have close genetic ties to Sardinians, unlike contemporaneous hunter-gatherers from the same region (50). Skoglund et al. (50) and Sikora et al. (49) posited a two-way mixture model for European origins, with the original European hunter-gatherers in the region becoming progressively more admixed with early farmers arriving from the Near East 8,000–6,000 y ago. Ötzi and the Scandinavian farmer likely belonged to this expanding population, and the uniquely high proportion of early-farmer ancestry present in the Sardinian genomes can explain their ties to these ancient genomes.

The findings from Raghavan et al. (43) discussed above suggested the existence of an ancient North Eurasian (ANE) population, with affinities to both Native Americans and Europeans. In a related study, Lazaridis et al. (51) obtained high-coverage genomes from an ancient Western European hunter-gatherer (found near Loschbour, Luxembourg) and an ancient Central European farmer (found near Stuttgart, Germany), and proposed a three-way mixture model of European origins. According to this model, the Loschbour individual belonged to the original modern human occupants of Europe, called Western hunter-gatherers (WHG). The ancestors of this population mixed with a basal Eurasian population coming from the Near East during the Neolithic to produce a population called Early European farmers (EEF), which likely brought agriculture into the region. This is the population to which the Stuttgart and Ötzi individuals belonged. Afterward, a third wave of migration from the Pontic steppe introduced the ANE ancestry component into the region.

In the past year, the number of Eurasian aDNA genomes has exploded from less than a dozen to over a hundred (4, 5, 52). Insights from whole-genome shotgun sequence data (5) as well as SNP capture data (4) have helped refine previous theories. For example, Haak et al. (4) showed that the Yamnaya—an Early Bronze Age population from the Pontic Steppe—contained ~50% ANE ancestry. Haak et al. argued that a population stemming from this source may have been the one responsible for bringing ANE ancestry into Eastern and Central Europe via a massive westward migration 4,500 y ago (the "Corded Ware" culture), and might therefore have been responsible for importing horses and Indo-European languages. Moreover, Allentoft et al. (5) found that people living in the Altai Mountains in Russia until 4,500 y ago (the Afanasievo culture) shared close genetic affinities with the Yamnaya, which could explain why Indo-European languages are also spoken in central Asia.

Haak et al. (4) also detected a resurgence of WHG ancestry immediately before the Yamnaya immigration into Europe (6,000–5,000 y ago) and placed a date on the first Near-Eastern migration of early farmers in the early Neolithic at 8,000–9,000 y ago. Additionally, Jones et al. (53) showed that the other half of the Yamnaya ancestry came from a fourth source population: the "Caucasus hunter-gatherers" (CHG), who split from the WHG ~45,000 y ago and from the EEF ~25,000 y ago. At present, it appears that western Eurasian populations are mixtures of four ancestral sources (ANE, EEF, WHG, CHG). Nevertheless, given the changes in our understanding of European history that come with each new group of fossils sequenced, it seems likely that the current models will soon be superseded.

Other Geographic Areas. Nuclear genomic sequences from fossils in other parts of the world are much less abundant. Mitochondrial and Y-chromosome sequences from human remains and genomic analysis of commensal species from Oceania have generally confirmed the Polynesian expansion model developed by archaeologists, but almost no ancient nuclear genomic data are as yet available (12). The only exception is the genome of a native Australian obtained from a 100-y-old hair sample (21). Analysis of the Australian genome supported the hypothesis that there were two waves of colonization of eastern and southeastern Asia. According to this model, the first wave may have occurred as early as 62,000–75,000 y ago.

In eastern Asia, partial nuclear sequences were obtained by Fu et al. (54) from a 40,000-y-old modern human from the Tianyuan Cave near Beijing, China. Although these sequences covered only a portion of the entire genome, they were sufficient to show that this individual belonged to a population that was ancestral to present-day East Asians and Native Americans and had already separated from the ancestors of present-day Europeans.

Ancient DNA from Africa is scarce. Studies suggest some present-day African genomes carry signatures of ancient episodes of admixture with unsampled archaic human groups (55, 56). Therefore, obtaining DNA sequence data from African fossils may help identify these groups and their evolutionary history. Sadly, environmental conditions in this part of the world make it very hard to retrieve aDNA from fossils, as biological material decays too rapidly there.

Recently, however, Gallego Llorente et al. (57) obtained the first ancient human genome from Africa. They produced a 12.5× coverage genome of a 4,500-y-old individual found in the Mota Cave in southeastern Ethiopia. The authors concluded that this individual was genetically similar to present-day inhabitants of the same region, implying genetic continuity until the present. Comparison of the Mota genome with other present-day populations indicated that the Mota population had not received admixture from European farmers, as had many present-day sub-Saharan populations (58). Instead, there was backflow into some African populations, primarily East African, from a population close to Neolithic hunter-gatherers. Although Gallego Llorente et al. (57) had originally claimed that the backflow affected all African populations, including Yoruba and Mbuti, they withdrew that claim in an online erratum (59).

Inferences About Positive Selection. The abundance of ancient DNA data has also allowed inferences about selective processes in humans. Among other things, aDNA has facilitated the search for loci that were positively selected after modern humans diverged from other archaic groups and possibly allowed modern humans to expand across the globe (7, 8, 60). Additionally, it has permitted researchers to find haplotypes introgressed from archaic groups into modern humans, and subsequently favored in modern humans by positive selection, a process known as "adaptive introgression" (31, 32, 61–65). Finally, aDNA has helped us understand recent selective events that permitted particular populations to adapt to local environments. Below, we focus on a few cases of local selection in Eurasia, where aDNA is currently most plentiful.

In one study, Allentoft et al. (5) found that the rise in frequency of the variant of the *LCT* gene—associated with lactose tolerance (rs4988235)—was likely very recent, as this variant is at low frequency in the Bronze Age, and may have possibly been introduced into Europe via the Pontic steppe migration. In another study, Mathieson et al. (52) looked for regions of the genome showing significant deviations from the EEF-ANE-WHG genome-wide mixture proportions that would be expected for each present-day population. Such anomalous patterns would occur if a region were under positive or balancing selection. The authors detected several outlier loci, including *LCT*, *SLC45A2*, *SLC24A5*, *HERC2*, and the *HLA* region. They then used the ancient genomes to study the temporal progression of these selective processes. For example, they found that a variant of *SLC24A5* contributing to light skin pigmentation rose in frequency relatively rapidly in Early Neolithic Europe, most likely because of migration. They also detected signatures of polygenic adaptation, using a method developed by Berg and Coop (66). Specifically, the authors found two independent signals of directional selection for increased and decreased height in the Iberian Neolithic and the Steppe Neolithic populations, respectively.

Discussion

The broad outlines of human history are not very different from what Cavalli-Sforza et al. (11) were able to divine based on what we now regard as paltry data. However, increasingly detailed patterns of replacement, migration, and interbreeding, which were previously invisible to researchers, are emerging in regions where abundant aDNA is available. As Pickrell and Reich (67) have emphasized, we now know that present-day populations were created by a complex history of admixture and population movement. Although local genetic continuity over long periods has been documented in a few cases, these are exceptional. The general rule is that the ancestors of present-day populations lived somewhere else.

Ancient DNA has enabled us to answer long-standing questions about the relationship between archaic and modern humans. Admixture among archaic groups and between them and modern humans seems to have occurred whenever they came into geographic proximity. In that way, they were no different from groups of modern humans. Although most present-day human ancestry can be traced to African populations that dispersed into Eurasia ∼100,000 y ago, aDNA has allowed us to also determine which parts of our genomes are from archaic hominins that occupied Eurasia before modern humans (68): all non-African genomes carry small amounts of Neanderthal ancestry, and some carry an additional component of Denisovan ancestry.

Because the paleoanthropological record of much of Asia is relatively poorly known, it is likely that more Neanderthal and Denisovan fossils will be found in this region. It is even possible that additional extinct groups of hominins will be identified using aDNA.

The more recent past has also been made clearer as a consequence of aDNA studies. Populations in both Western Eurasia and the Americas were subject to various episodes of expansion, population replacement, and admixture between divergent groups. Present-day human genomes show evidence of these events. For example, the genomes of living Europeans contain ancestry components from at least three or four ancestral populations. Other lineages were apparently genetic dead-ends—notably Paleo-Eskimos and the population to which the Oase individual belonged—and their relationship to present-day humans would have remained obscure were it not for aDNA.

The current age of genomic discovery is analogous to the age of unbridled geographic discovery by Europeans in the 16th and 17th centuries. Almost every ancient nuclear genome provides new insights into human history and opens up new horizons of

exploration and inquiry. There is no sign yet of saturation in any continental area. Temperate and Arctic regions have yielded many more aDNA sequences than tropical regions, partly because conditions are more favorable to the preservation of aDNA, and partly because they have been more intensively sampled. However, with the recent retrieval of the ancient genome from Mota Cave in Ethiopia, the outlook seems to be changing. Because of the scarcity of sequences from the tropics, each aDNA genome obtained from regions like Africa and Oceania will be precious and revealing. In the near future, more such genomes will provide new revelations about human evolution and demographic transitions.

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