ANNUAL REVIEWS

Annual Review of Genomics and Human Genetics

Ancient Genomics of Modern Humans: The First Decade

Pontus Skoglund[1] and Iain Mathieson[2]

[1]Francis Crick Institute, London NW1 1AT, United Kingdom; email: pontus.skoglund@crick.ac.uk

[2]Department of Genetics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19103, USA; email: mathi@upenn.edu

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

Annu. Rev. Genom. Hum. Genet. 2018. 19:381–404

First published as a Review in Advance on April 25, 2018

The *Annual Review of Genomics and Human Genetics* is online at genom.annualreviews.org

https://doi.org/10.1146/annurev-genom-083117-021749

Copyright © 2018 by Annual Reviews. All rights reserved

ANNUAL REVIEWS CONNECT

www.annualreviews.org

- Download figures
- Navigate cited references
- Keyword search
- Explore related articles
- Share via email or social media

Keywords

human origins, Holocene, migration, adaptation, ancient DNA, paleogenomics

Abstract

The first decade of ancient genomics has revolutionized the study of human prehistory and evolution. We review new insights based on prehistoric modern human genomes, including greatly increased resolution of the timing and structure of the out-of-Africa expansion, the diversification of present-day non-African populations, and the earliest expansions of those populations into Eurasia and America. Prehistoric genomes now document population transformations on every inhabited continent—in particular the effect of agricultural expansions in Africa, Europe, and Oceania—and record a history of natural selection that shapes present-day phenotypic diversity. Despite these advances, much remains unknown, in particular about the genomic histories of Asia (the most populous continent) and Africa (the continent that contains the most genetic diversity). Ancient genomes from these and other regions, integrated with a growing understanding of the genomic basis of human phenotypic diversity, will be in focus during the next decade of research in the field.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

INTRODUCTION

Modern humans: humans who share a set of derived skeletal traits and genetic ancestry with living humans; they first appear in the fossil record in Africa around or before 200,000 BP

BP: years before present (where "present" is the year 1950, consistent with the radiocarbon dating convention)

The earliest ancient human genomic data were from Neanderthals—"archaic humans" that fall outside the range of present-day human phenotypic and genetic variation (34, 35, 81). Ancient DNA from prehistoric "modern humans"—those that fall within present-day genetic variation—was long thought to be almost impossible to validate using PCR-based methods, owing to the high frequency of human contamination in excavation, museum, and laboratory environments (88). PCR-based data remain difficult to authenticate, but since the mid-2000s, high-throughput sequencing has allowed sequencing of ancient DNA fragments across their entire length, allowing a twofold approach to authentication through analysis of postmortem damage and detection of secondary contaminating individuals (53). This led to the first genome-wide ancient DNA studies of modern humans, which appeared starting in 2010 (50, 106, 114, 131). These studies revealed that ancient populations often had ancestry not fully represented in present-day populations—a preview of the way in which ancient DNA would become critical for reconstructing the genetic history and evolution of modern humans. Eight years after the first sequencing of an ancient human genome, whole-genome shotgun data from hundreds of ancient modern humans are available, along with targeted capture data—analogous to data from single-nucleotide polymorphism (SNP) genotyping arrays—from more than 1,000, dating as far back as 45,000 years before present (BP). This ancient DNA revolution has allowed direct testing of hypotheses and models of human population history and evolution that were formulated in the pre-paleogenomic era based on anthropology, archaeology, and DNA from present-day people. As we will see, while some hypotheses, such as the out-of-Africa model, have been corroborated, others have been disproved. In some cases, ancient DNA has provided unforeseen insights and opened new areas of investigation. These results illustrate how ancient DNA allows us to directly study the past, rather than extrapolating information from present-day genomic variation, and could overturn many of our most closely held beliefs about human population history.

ORIGINS AND GENETIC DIVERSITY OF MODERN HUMANS

Human genetic diversity, as measured by the number of mutations observed between DNA sequences, shows a clear pattern in which Africa harbors more genetic diversity than any other part of the world (13, 98, 103). For example, the two chromosomes of a person with recent African ancestry show greater sequence divergence than any two chromosomes, ancient or modern, from any two people whose ancestry is from outside Africa (**Figure 1*a***). This can be explained by a population history where a relatively recent ancestral population carrying a subset of African diversity was the founder of the out-of-Africa expansion of modern humans (139). Another line of evidence for this model comes from the observation that all living humans today are more closely related to each other than they are to archaic humans, such as Neanderthals (34, 81) (**Figure 1*b***). While no ancient genomes from earlier than ~8,100 BP have been obtained from Africa, limiting our insight into the ancestral anatomically modern human population, more favorable preservation conditions in Eurasia have produced a wealth of direct genomic evidence. All sequenced ancient humans from outside of Africa before ~50,000 BP are archaic—in the sense that they fall outside present-day human genetic variation in the majority of the genome (34, 76, 77, 94, 96, 97, 109, 136). By contrast, all ancient genomes from modern humans outside of Africa form a clade with present-day non-Africans relative to present-day Africans (**Figure 1*b***). These observations lead us to reject models of regional continuity of archaic human populations in Eurasia in favor of models dominated by replacement (138).

However, ancient DNA has also revealed at least two independent episodes of gene flow from archaic humans into the ancestors of modern humans. Neanderthals contributed ~2% of

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

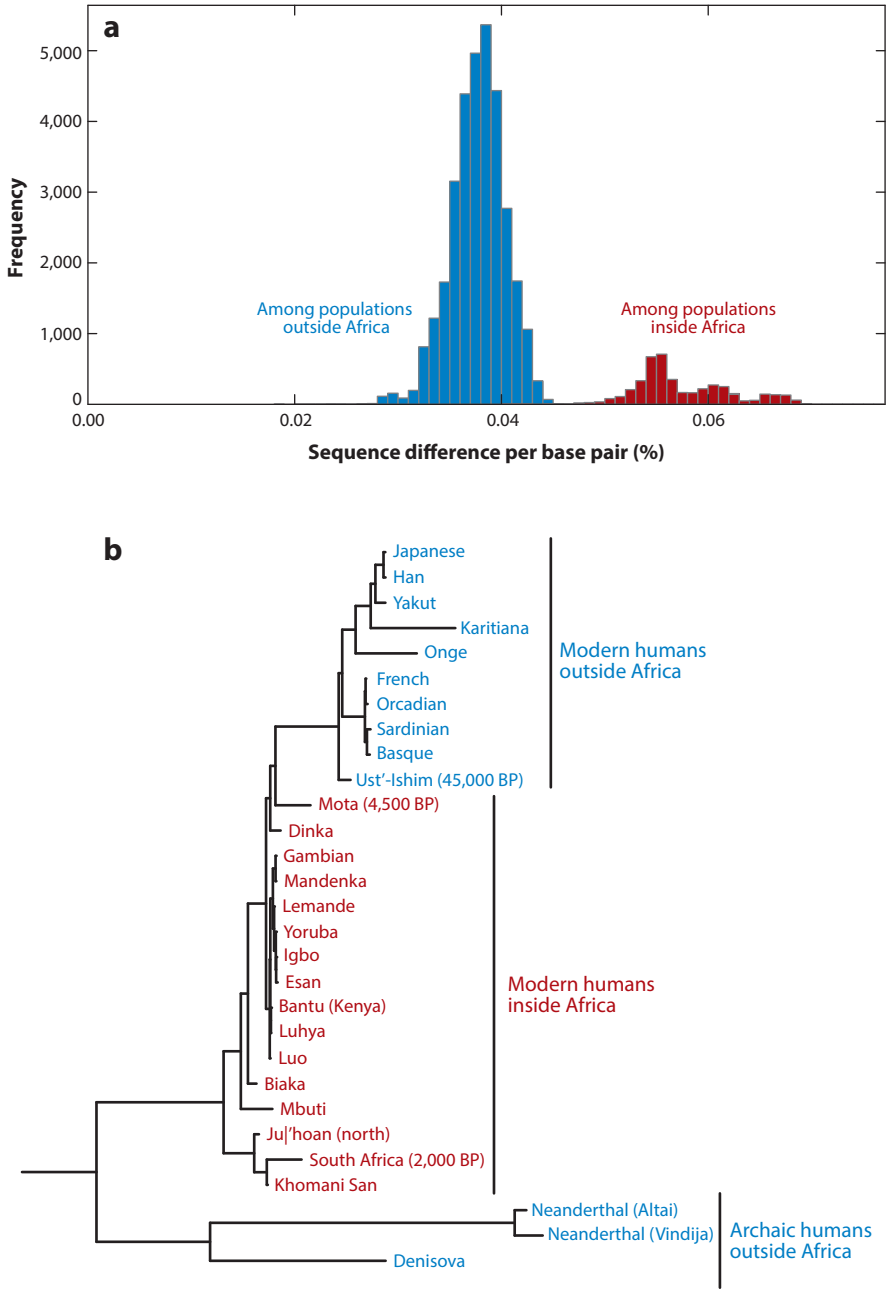

Figure 1

Patterns of modern human genomic diversity. (*a*) Sequence differences between two chromosomes from present-day modern humans inside and outside Africa (68), using positions with less than 1% missing data among all genomes in the Simons Genome Diversity Project and randomly sampling a single allele from heterozygote positions. (*b*) Maximum-likelihood tree (92) of modern and archaic humans (25, 66, 68, 135) using transversion single-nucleotide polymorphisms.

the ancestry of people of non-Africans ancestry today (34), and the still-mysterious Denisovan population contributed up to 5% of the ancestry of present-day Oceanian populations (77, 109, 133, 145) and likely also to the ancestry of East Asians (68, 116, 128). These contributions imply that not all present-day non-African ancestry is nested within African variation, referred to by Svante Pääbo as a "leaky replacement" model of Eurasian human population history (30, p. 392).

Holocene: the relatively warm and climatically stable period from around 12,000 BP to the present; it includes the growth and expansion of many human populations and all known developments of agriculture

ORIGIN AND DIVERSIFICATION OF NON-AFRICAN POPULATIONS

The ancestral out-of-Africa population was most closely related to present-day and ancient eastern African populations (141) but shows a complex pattern of affinities to African lineages (135), and there is evidence of gene flow as recently as 50,000 BP (58, 68, 118), which suggests that the ancestors of present-day non-Africans were once part of a structured, largely African, metapopulation. As modern humans expanded across the Eurasian continent, they diversified into multiple lineages. One signal of this expansion is the observation that, in present-day populations, genetic diversity successively decreases from Africa to Eurasia, from west to east across Eurasia, and then again in Oceania and America. This has been interpreted as the signature of a serial founder effect, where the expansion of modern humans was driven by the outward migration of groups with successively smaller effective population sizes owing to repeated bottlenecks (18, 63, 103). However, ancient DNA has revealed that in Europe, this pattern does not date back to the original Eurasian expansion but is a more recent phenomenon, since European populations as recently as 5,000 BP had much lower diversity than present-day populations (37, 46, 72, 84, 130) (**Figure 2*a***). Instead, the recent high diversity [and corresponding reduction in between-population differentiation (56)] in Europe is the result of Holocene migrations and admixture (**Figure 2*b***).

In Eurasia, several anatomically modern human genomes date to close to the time of the diversification of non-African lineages, which allows us to constrain the timing and structure of these events through three lines of evidence (**Figure 3**). First, directly dated ancient samples allow calibration of the human mutation rate over the relevant timescale, a parameter that can otherwise only be indirectly inferred. Analysis of the 45,000-BP Ust'-Ishim individual (25) supports an autosomal mutation rate of $\sim 0.43 \times 10^{-9}$ per base per year and a Y-chromosome mutation rate of 0.76×10^{-9} per base per year, consistent with direct measurements from pedigrees (40, 52). This autosomal mutation rate implies a split time between eastern and western Eurasians of ~47,000 BP (140), or ~50,000 BP (89) under an instant split model, or a divergence that begins around 50,000–60,000 BP under a model allowing for more gradual separation (118). Similarly, based on the ancient DNA–calibrated Y-chromosome mutation rate, the most recent common ancestor of African and non-African Y-chromosome lineages dates to ~75,000 BP, with non-African lineages diversifying around 47,000–55,000 BP (49, 95). Ancient samples also allow direct calibration of the mitochondrial mutation rate, indicating that the most recent common ancestors of African and non-African lineages date to 62,000–95,000 BP, with diversification of non-African mitochondrial clades around 45,000–55,000 BP (27, 93). This time to the most recent common ancestor of mitochondrial/Y-chromosome lineages found in different populations can be thought of as an upper bound on the time of the most recent gene flow between those populations.

Second, the rate of breakdown of Neanderthal segments of the genome since admixture, calibrated with directly dated ancient genomes, suggests that this gene flow took place around 50,000–60,000 BP (25, 79, 117, 124). Since Neanderthal ancestry is shared among all known non-African modern human genomes (24, 25, 28, 34, 68, 150), most of the ancestors of these populations must have been present at a single time and in a single region (perhaps southwestern Asia) to receive the same Neanderthal ancestry, implying that the divergence of non-African lineages cannot be older than the Neanderthal introgression. By contrast, Denisovan ancestry is restricted largely

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

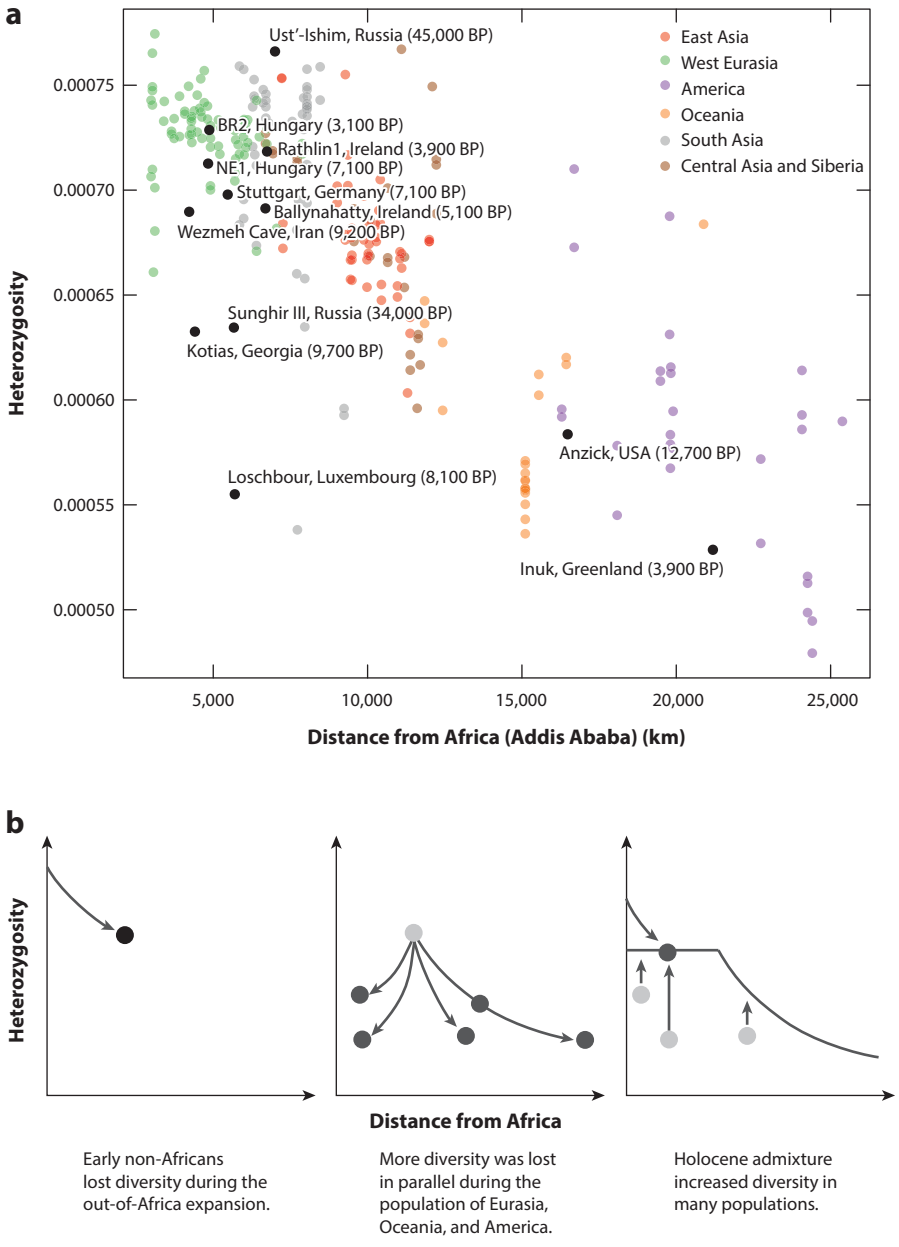

Figure 2

(*a*) Heterozygosity as a function of waypoint distance from Addis Ababa, computed for present-day non-African individuals (*colored points*) and selected ancient individuals with greater than 10× coverage (relative heterozygosity computed at transversion single-nucleotide polymorphisms ascertained in a single Khoe-San individual and rescaled) (11, 14, 25, 29, 46, 57, 104, 106). (*b*) Illustration of possible Holocene processes leading to the present-day geographic patterns of genetic diversity shown in panel *a*.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

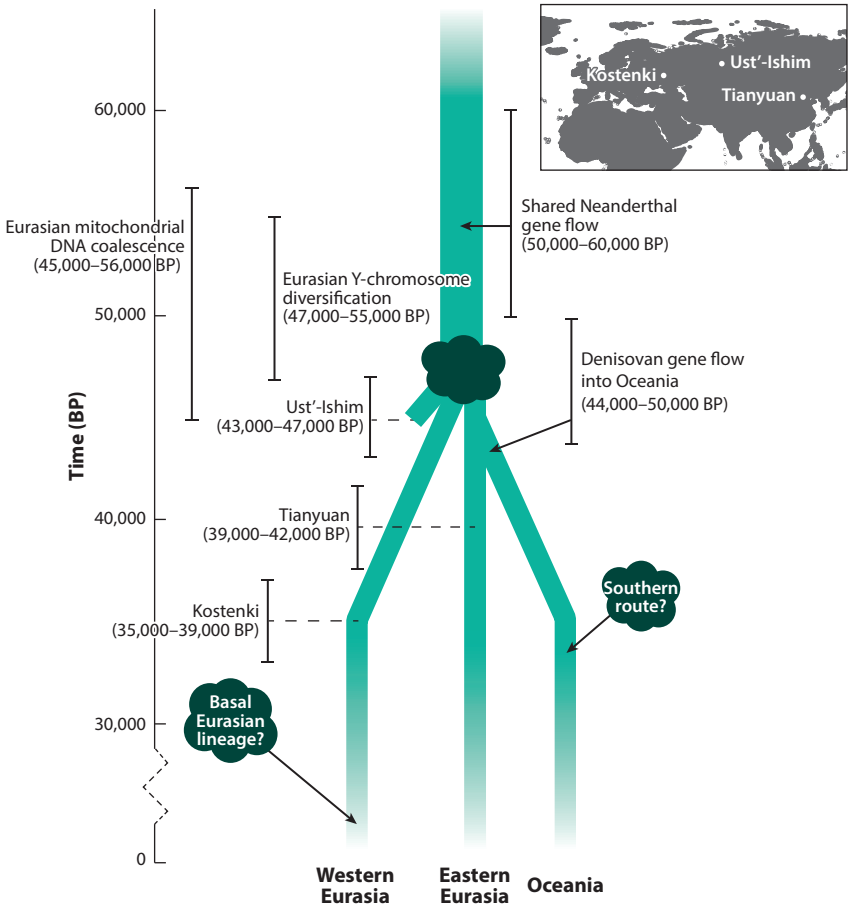

Figure 3

The origin and diversification of present-day Eurasian lineages (*green*). Dark clouds represent events with uncertain dates or structures. Black bars represent time intervals for key events or individuals. Major constraints are that western and eastern Eurasian population lineages must have diverged before the date of Tianyuan (39,000–42,000 BP) and after the date of shared Neanderthal gene flow (50,000–60,000 BP, more likely in the more recent half of this range). Furthermore, eastern Eurasian and Oceanian lineages (and therefore western and eastern Eurasian lineages) must have diverged before the date of Denisovan gene flow into the Oceanian lineage (44,000–50,000 BP). The inset at the upper right shows the locations of key ancient samples. Abbreviation: BP, years before present.

Upper Paleolithic: an archaeological term that in the context of ancient DNA studies has come to refer to technologically sophisticated hunter–gatherers during the period ~50,000–10,000 BP

to present-day Oceania and is approximately 90% as old as Neanderthal ancestry (i.e., 44,000–50,000 BP) (116). Thus, the dates of Neanderthal and Denisovan introgression must bracket the earliest divergences among non-African populations.

The third line of evidence for the time of diversification of non-African lineages comes from the 45,000-BP Ust'-Ishim individual, a modern human, who is consistent with being close to the divergence between Upper Paleolithic Europeans and the ancestors of East Asians and Aboriginal Australians (25, 61, 125). The relative lack of genetic drift separating Ust'-Ishim from these three geographically distant lineages suggests that the divergence could have happened close to 45,000 BP, when the Ust'-Ishim individual lived. Another modern human dated to ~39,000 BP from Peştera cu Oase in present-day Romania may have diverged from present-day lineages before

the Ust'-Ishim individual, although poor DNA preservation has prevented this question from being fully resolved (24, 28). A hard lower bound on ancestral Eurasian divergences comes from one individual from Kostenki, in the west of present-day Russia, dated to 36,200–38,700 BP (124) and one from Tianyuan in China dated to 39,000–42,000 BP (26, 150), which are on the western and eastern Eurasian lineages, respectively. Taken together, these lines of evidence strongly suggest that the mean divergence of the western Eurasian Upper Paleolithic lineage and the East Asian/Oceanian lineage can be fairly tightly constrained to the period 45,000–55,000 BP.

These estimates of the divergences of non-African population lineages are in tension with recent evidence of putative modern humans at very early dates, specifically remains dated to ~80,000–120,000 BP from Fuyan Cave in China (64) and ~63,000–73,000 BP from Sumatra (147), as well as artifacts from ~65,000 BP at the Madjedbebe site in Australia (15). Because these finds significantly predate the diversification of extant lineages, early populations in these regions cannot have contributed substantial ancestry to any present-day populations. Indeed, these population lineages may have gone extinct. For example, the population to which the Oase individual belonged did not contribute detectably to present-day populations (24). Could such early non-African populations have contributed any ancestry to present-day populations? Some studies have suggested a contribution to Aboriginal Australians and Papuans (89, 105), although those claims are controversial (67, 68), mainly because any such signal would be difficult to distinguish from Denisovan ancestry in Oceanian genomes. Nonetheless, current tools and data cannot exclude such an ancestral contribution on the order of a few percent.

Another key component of present-day non-African ancestry is the deeply diverging basal Eurasian lineage (57), most anciently observed around 13,000 BP in the Caucasus Mountains (46), the Levant, and northern Iran (56) and now ubiquitous in western Eurasia. This lineage is an outgroup to all other known Eurasian lineages, including the deep Ust'-Ishim (25) and Oase (24) lineages, and therefore likely diverged before 50,000 BP. In addition, this lineage carried relatively little or no Neanderthal ancestry (56), which may explain why present-day Europeans have less Neanderthal ancestry than present-day East Asians (56). The location of the hypothetical population that harbored basal Eurasian ancestry between 13,000 and 50,000 BP remains unknown but would likely be in northern Africa or southwestern Asia.

Neolithic: an archaeological term that in the context of ancient DNA studies usually refers to Stone Age groups or cultural complexes with predominantly food-producing economies

Mesolithic: an archaeological term that in the context of ancient DNA studies usually refers to human hunter–gatherer groups or cultural complexes who lived immediately prior to the Neolithic period

HOLOCENE HISTORY AND HUMAN POPULATION STRUCTURE

While the broad patterns of present-day genetic diversity outside Africa were formed by the out-of-Africa bottleneck and subsequent divergence, much of the finer-scale structure is the result of relatively recent population movements (**Figure 4**). In many cases, ancient DNA has acted as a symmetry breaker—allowing us to resolve questions about the historical processes shaping population genetic structure that could not be resolved by present-day genomes alone. In this section, we review recent results from different parts of the world and discuss what ancient DNA has taught us in general about the processes that have formed present-day genetic diversity.

Europe and Western Eurasia

Europe has provided the best example of the ability of ancient DNA to explain the genetic structure of modern humans. Empirically, genetic structure in Europe is continuous (54, 82), forming clines that were originally interpreted by Cavalli-Sforza and colleagues (75) as the signature of a Neolithic expansion of agriculturalists through a landscape of resident Mesolithic hunter–gatherer populations. However, it was later shown that exactly the same sort of patterns could arise without major expansions—as the product of an interconnected but spatially structured population evolving

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

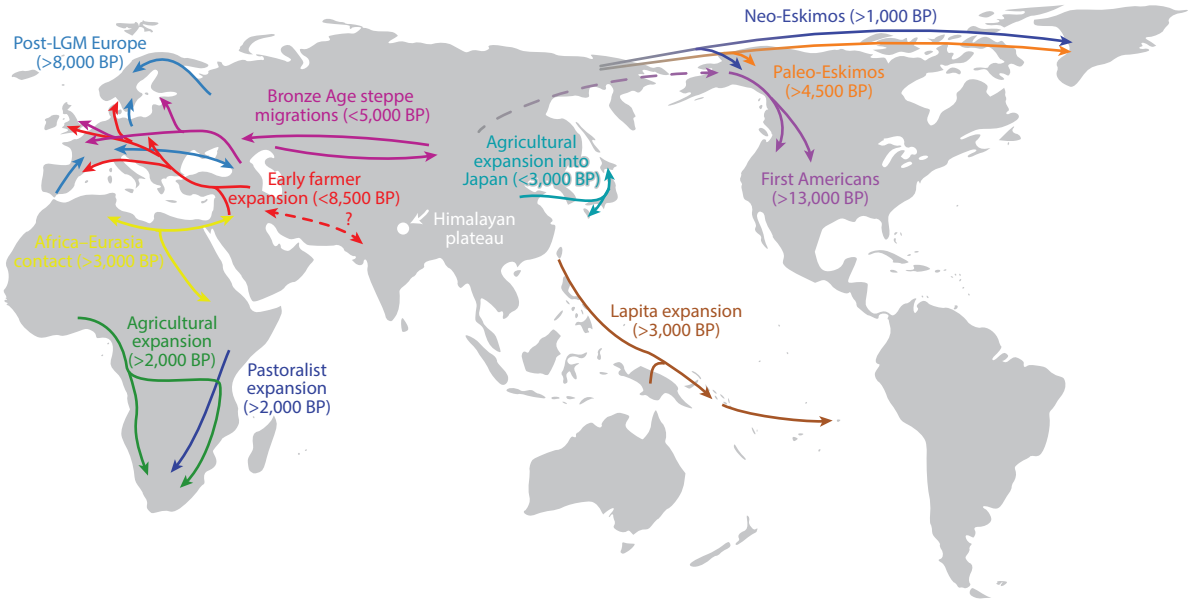

Figure 4

Major Holocene population movements and expansions that have been demonstrated using ancient DNA. Abbreviations: BP, years before present; LGM, Last Glacial Maximum.

with ongoing gene flow but without major waves or pulses of expansions and admixture (isolation by distance) (83, 137). Thus, the processes that drove the observed structure could not be resolved using present-day data alone, since both migration (see the sidebar titled Migration) and isolation by distance could, in principle, explain the data. Ancient DNA has largely resolved this question. We now know that the agricultural expansion suggested by Cavalli-Sforza and colleagues (75) indeed took place (9, 131) but did not produce the major present-day clines in Europe in the manner originally proposed. Instead, European genetic history is marked by multiple migrations (1, 10, 28, 38, 131), and patterns of genetic diversity in present-day Europe have been shaped by the admixture of at least three, not two, distinct ancestral populations (57).

Anatomically modern humans were widely distributed in Europe by at least 42,000–45,000 BP (3, 41). The oldest genomic data from a modern human in Europe are from the Oase 1 individual from present-day Romania, dated to 37,600–41,600 BP. As noted above, this individual, who had a direct Neanderthal ancestor in the past four to six generations, did not contribute detectable ancestry to later Upper Paleolithic populations (24). During the Upper Paleolithic, a major

MIGRATION

Strictly speaking, DNA can tell us only about gene flow and shared ancestry, and usually not about the movement of individuals. There is an implicit assumption that gene flow events that are dramatic, directional, and associated with cultural shifts do involve some systematic and permanent movement of people. Nonetheless, it is important to note that the migration events that are attested by ancient DNA are in many cases relatively slow, extending over hundreds or thousands of years, and do not necessarily imply the rapid movement that is often understood by the term.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

transformation occurred around 30,000–35,000 BP and was likely associated with the replacement of the Aurignacian with the Gravettian culture in western Europe (28). As the Last Glacial Maximum (LGM) came to an end and the ice sheets receded, Europe was repopulated, possibly from southern European and central Eurasian refugia (28). Another transformation may have taken place during an interstadial warm period around 14,500 BP, replacing the original recolonizers with a population that would come to form the Mesolithic populations of Europe (28, 93). These Mesolithic populations were outside the genetic diversity of present-day Europe (114, 131) and themselves display an east-to-west cline (32, 37, 38, 47, 57, 62, 72, 78, 112, 130). The origin of this cline is not clear, although it plausibly reflects two or more major sources of ancestry in the post-LGM or post-14,500-BP expansions.

Last Glacial Maximum (LGM): the peak of the last ice age, approximately 25,000–19,000 BP

Fixation index (F_{ST}): the proportion of total genetic variation that is explained by differentiation between populations

Starting from the southeast around 8,500 BP, the Mesolithic ancestry of Europe was marginalized (29, 38, 42, 130, 131) as a new type of ancestry related to that found in Neolithic northwest Anatolia (73, 87) and, ultimately, to early farming populations of the Levant and northern Iran (11, 56) expanded throughout Europe. This new ancestry rapidly reached the extreme edges of Europe, with direct evidence of its presence in Iberia at 7,300 BP (86), in Ireland at 5,100 BP (14), and in Scandinavia at 4,900 BP (131). This Anatolian Neolithic ancestry was highly differentiated from the hunter–gatherer ancestry of the populations that previously inhabited Europe [fixation index (F_{ST}) of ~0.1, similar to the divergence between present-day European and East Asian populations] (73, 132). Across Europe, its appearance was closely linked in time and space to the adoption of an agricultural lifestyle, and it is now clear that this change in lifestyle was driven, at least in part, by the migration. However, the Anatolian Neolithic migrants did not completely replace the hunter–gatherer populations. Over the next 4,000 years, the two populations merged, and by 4,500 BP, almost all European populations were admixed between these two ancestries, typically with 10–25% hunter–gatherer ancestry (29, 38, 42, 50, 62, 71, 73, 130, 131). This mixture process (10) occurred independently in different parts of Europe, likely driven by local hunter–gatherer populations who lived in close proximity to farming groups (7, 62, 72, 130).

The next substantial change is closely associated with ancestry that by around 5,000 BP extended over a region of more than 2,000 miles of the Eurasian steppe, including in individuals associated with the Yamnaya cultural complex in far eastern Europe (1, 38) and with the Afanasievo culture in the central Asian Altai mountains (1). This steppe ancestry is itself a mixture between ancestry that is related to Mesolithic hunter–gatherers of eastern Europe and ancestry that is related to both present-day populations (38) and Mesolithic hunter–gatherers (46) from the Caucasus mountains, and also to the populations of Neolithic (11) and Copper Age (56) Iran. Steppe ancestry appeared in southeastern Europe by 6,000 BP (72), northeastern Europe around 5,000 BP (47), and central Europe at the time of the Corded Ware complex around 4,600 BP (1, 38). These dates are reasonably tight constraints, because in each case there is no evidence of steppe ancestry in individuals immediately preceding these dates (47, 72). Gene flow on the steppe was extensive and bidirectional, as shown by the eastward flow of Anatolian Neolithic ancestry [reaching well into central Eurasia by the time of the Andronovo culture around 3,500 BP (1)] and the westward flow of East Asian ancestry [found in individuals associated with the Iron Age Scythian culture close to the Black Sea around 2,500 BP (143)]. Copper and Bronze Age population movements (14, 71, 78, 85, 112), as well as later movements in the Iron Age and historical period (70, 119), further distributed steppe ancestry around Europe.

Present-day western European populations can thus be modeled as mixtures of three ancestry components (Mesolithic hunter–gatherer, Anatolian Neolithic, and steppe) (38, 57). In eastern Europe, further shifts in ancestry are the result of additional or distinct gene flow from Anatolia throughout the Neolithic and Bronze Age in the Aegean (42, 51, 55, 72, 87), and gene flow from Siberian-related populations in Finland and the Baltic region (38). East-to-west gene flow also

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

brought new ancestry—related to populations from Copper Age Iran—to the Levant during the Copper and Bronze ages (39, 56).

The geographic structure of these population transformations gave rise to the population structure of present-day Europe. For example, Anatolian Neolithic ancestry is highest in southern European populations such as Sardinians and lowest in northern European populations (38). Steppe ancestry is at high frequency in north-central Europeans and at low frequency in the south. Isolation by distance may have contributed to these patterns to some extent, but the contribution must have been small. In much of Europe, extreme population discontinuity was the norm.

Siberia

The genome of a 24,000-year-old individual from the Mal'ta site close to Lake Baikal in southern Siberia showed surprisingly strong affinities to both western Eurasian and Native American populations (101), extending the known range of ancestry related to Upper Paleolithic populations of Europe. Populations related to Mal'ta contributed 10–20% of the ancestry of present-day Europeans (57) and 30–40% of the ancestry of Native Americans (101). That the Mal'ta individual falls on the western lineage of the 45,000–55,000-year-old original divergence of Eurasian populations suggests that estimates of Native American divergence from East Asians and Siberians around 20,000 BP (102, 118) may be too ancient, since they do not account for the additional deeply diverging Mal'ta-related ancestry found in Native Americans.

The Mal'ta lineage is basal to all western Eurasian Paleolithic genomes except possibly Oase (24, 28, 124, 125), including individuals dated to 34,000 BP from Sunghir, close to present-day Moscow (125). Thus, Mal'ta may be the product of a pre-34,000-BP migration through Siberia, prior to the arrival of the ancestors of the Sunghir population in the east. This migration would also likely have been after the divergence of Ust'-Ishim earlier than 45,000 BP, since the central Siberian Ust'-Ishim is basal to Mal'ta and not detectably a member of the western Eurasian Paleolithic lineage (28). The only other known representatives of the highly distinct Mal'ta lineage are two individuals dated to ∼18,000 BP from nearby Afontova-Gora (28, 101). These individuals show that the Mal'ta lineage persisted locally through the LGM. We tested (34) whether Mal'ta 1 (MA1) and Afontova-Gora 3 (AG3) are equally related to 125 present-day populations (68) and found that all Native American populations and almost no populations that are not Native American are significantly more closely related to AG3 than they are to MA1 (**Figure 5**). The observation that AG3, ∼6,000 years younger than Mal'ta, shares more genetic drift with Native Americans suggests that the major Native American population lineage may have formed after the LGM. This leaves open the possibility of a relatively late separation from Siberian ancestors and entry into Beringia.

America

Archaeological evidence supports a human presence in the Americas at least 14,500 BP (31, 74). Genetic evidence further suggests that all present-day Native Americans can trace part of their ancestry to a single population that existed at least 12,600 BP (104, 110, 134) (**Figure 5**). The most controversial hypotheses about the peopling of the Americas, including the Solutrean hypothesis of a European origin, were largely dispelled by the sequencing of a 12,600-BP individual from western Montana buried in association with Clovis stone tools (104). This individual, known as Anzick-1, falls within present-day Native American diversity and was more closely related to present-day populations from Central and South America than to geographically closer populations from North America. This >12,600-BP divergence of a northern Native American lineage has been confirmed by analyses of younger remains from North America (59, 102, 107), and the

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

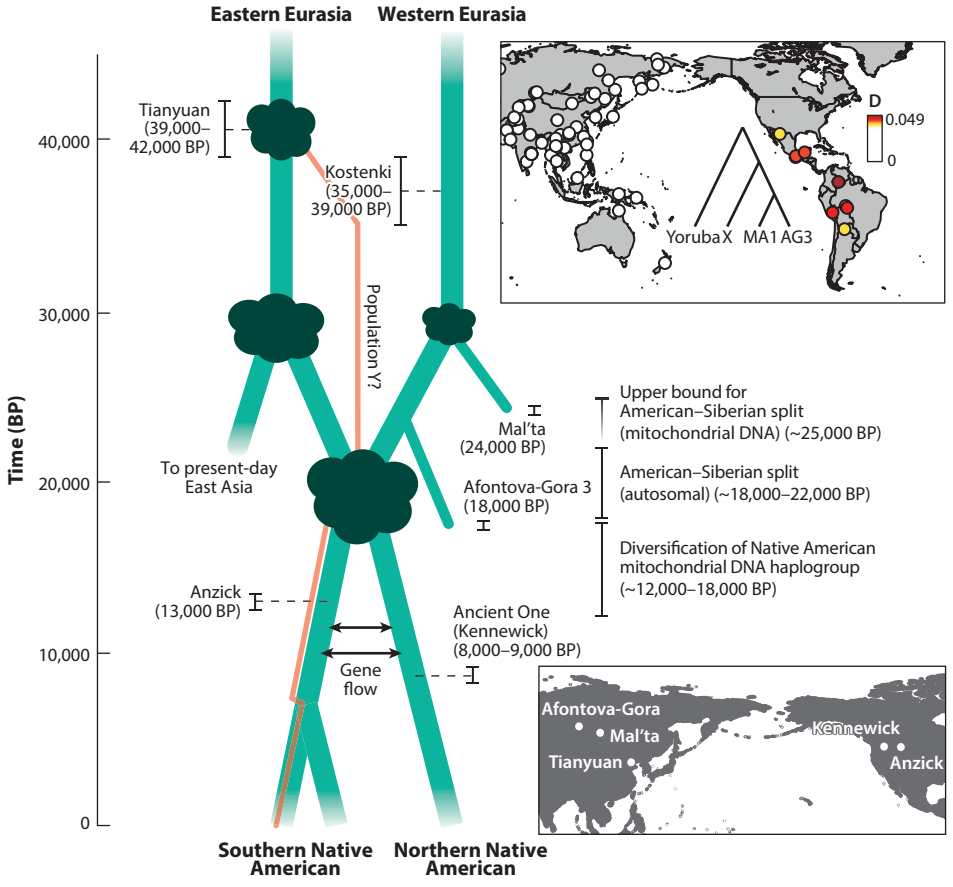

Figure 5

The origin and diversification of Native American lineages. Dark clouds represent events with uncertain dates or structures. Major constraints are that the Native American lineage must have split from Siberian ancestors around 25,000 BP at the earliest (more likely around 20,000 BP or later) and at least before the divergence of northern and southern Native American lineages (13,000–18,000 BP). The inset at the upper right is a heat map showing f_4 statistics that test the tree shown on the map—specifically, whether MA1 and AG3 are equally related to some test population (labeled X on the tree, and ranging over populations shown as circles on the map). A value close to zero, as for almost all non–Native American populations, indicates that the displayed tree is consistent with the data and thus that MA1 and AG3 are equally related to the test population, while a positive value indicates that the test population is more closely related to AG3 than to MA1. All Native American populations have values that are 3–5 standard deviations from zero, while all populations that are not Native American (except the Mansi from Siberia) have values less than 3 standard deviations from zero. The inset at the lower right shows the locations of key ancient samples. Abbreviations: AG3, Afontova-Gora 3; BP, years before present; MA1, Mal'ta 1.

diversification of Native American mitochondrial lineages around 12,000–18,000 BP (65) suggests that northern and southern lineages diverged during this time (**Figure 5**). It remains to be determined whether the population carrying the northern lineage replaced the Anzick lineage in North America from Beringia or from the south (134).

However, a genetic affinity between Amazonian and Australo-Melanesian populations suggests that we still do not have the full picture of the ancestry of the first Americans (102, 129). This

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

suggests that the expansion into the Americas was substructured, with some subpopulations retaining greater affinity to an unknown northeastern Asian population related to present-day Australo-Melanesians (129, 150). An alternative hypothesis of gene flow during the Holocene mediated by Aleutian populations (102) was rejected by direct data from prehistoric Aleuts (22). Instead, the discovery that the ~40,000-year-old Tianyuan individual from eastern China also had affinity to the Amazonian populations supports the presence of ancient substructure in Siberia contributing to the Amazonian and Australo-Melanesian connection (150).

The first ancient modern human genome sequence ever published was from an individual dated to ~4,000 BP associated with the Saqqaq culture of Greenland (106). This individual's affinity to the Koryak and Chukchi populations of northeast Siberia rather than present-day Inuit in Greenland suggested that the Saqqaq ancestors were from a separate migration to North America than those of the present-day Inuit. Since then, this model of separate Paleo- and Neo-Eskimo migrations into the Americas has been largely confirmed by direct evidence of additional Paleo-Eskimo (associated with the Middle and Late Dorset culture) and Neo-Eskimo (associated with the Thule culture) genomes (100). It is debated whether Athabascan speakers in North America have ancestry related to Paleo- or Neo-Eskimo lineages (22, 100, 102, 110). A recent study obtained support for a common northeast Siberian origin of the Paleo- and Neo-Eskimo lineages as well as the Athabascan-specific ancestry (22). These observations suggest that Paleo- and Neo-Eskimo lineages entered the Americas separately but that the distinct ancestry of Athabascan speakers involved gene flow with one or both of these lineages, rather than originating from a distinct entry into the Americas.

Africa

Poor preservation conditions make it more challenging to recover ancient DNA from Africa than from colder parts of the world. The first ancient African genome sequence was from a 4,500-BP individual from Mota Cave in highland Ethiopia (66). This and additional ancient genomes from eastern and southern Africa (135) have revealed the profound impact of an agricultural expansion associated with western African–like ancestry and Bantu languages. Archaeological evidence suggests that this expansion followed the earliest evidence of agriculture in western Mali around 4,500 BP (69) and brought farming to eastern Africa by ~2,000 BP as well as to southern Africa by ~1,500. The Bantu expansion disrupted a long-standing cline of hunter–gatherer ancestry that stretched from Ethiopia to South Africa and had existed since at least ~8,100 BP (135). In Malawi, a hunter–gatherer population that survived at least until 2,500 BP contributed almost no ancestry to present-day Bantu-speaking groups in Malawi, suggesting a complete or near-complete replacement (135). In other parts of Africa, present-day populations carry more ancestry from preagricultural populations, including the Aari in Ethiopia (66), the Hadza of Tanzania (135), and the Khoe-San of southern Africa (120, 135).

Genetic affinity between a Tanzanian individual dated to ~3,100 BP and an individual from the Western Cape of South Africa dated to ~1,200 BP (135) now confirms archaeological evidence (113) of a pastoralist expansion through eastern Africa arriving in southern Africa by ~2,000 BP. This pastoralist ancestry is also prevalent in present-day southern African Khoikhoi speakers (90, 91, 121, 135). Notably, approximately 40% of the ancestry of the ~3,100-BP Tanzanian individual was closely related to Early Neolithic individuals in the Levant (91, 135). Given that northern African Neolithic populations dated to 7,000 BP were also related to the Neolithic Levant (23), these observations demonstrate extensive Holocene gene flow between northern Africa, eastern Africa, and the Levant. Northeastern African populations also have additional ancestry related to Neolithic Levantine (56) and Iranian (135) populations, also seen in prehistoric Egypt (123). These connections emphasize the extent of Holocene interactions between Africa and Eurasia.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

Asia

Excluding the western and central Asian steppe populations discussed above, ancient DNA data from Asia are sparse. From East Asia, apart from targeted capture data from the ~40,000-BP Tianyuan individual (26, 150), autosomal genomic data are limited to eight individuals dated to 1,000–3,000 BP from Tibet (45), two individuals dated to 7,700 BP from the Devil's Gate site north of the Korean peninsula (127), and low-coverage data from two individuals associated with the Final Jomon culture of Japan, dated to around 3,000 BP (48). The Tibetan and Devil's Gate individuals appear to be relatively similar to present-day populations in their respective regions, indicating long-term population continuity that would be unusual in the context of western Eurasia (127). On the other hand, the Jomon genomes support the model that the present-day populations of Japan are admixed between the Jomon and Southeast Asian wet rice farmers associated with the Yayoi culture from 2,000–3,000 BP. Indeed, present-day variation within Japan may be driven largely by this admixture, with high levels of Jomon-related ancestry in the far northern Ainu and far southern Ryukyuan populations (48). This seems to mirror the pattern of admixture between hunter–gatherer and farming populations seen in Neolithic Europe and raises the question of whether this pattern was universal in agricultural expansions.

There are no published ancient DNA studies from South or Southeast Asia, another challenging region in terms of ancient DNA preservation. However, data from neighboring regions provide clues to the population history of this region. In particular, present-day South Asian populations share ancestry with Neolithic Iranian (11) and steppe (56) populations. This strongly suggests Neolithic or Bronze Age contact between South Asia and western/central Eurasia, although only direct ancient DNA evidence from the region will resolve the timing and structure of this contact.

Oceania

Archaeological evidence suggests that anatomically modern humans were established beyond the Wallace line in Oceania by at least 40,000–50,000 BP (8, 36). Genetic data indicate that present-day Aboriginal Australian and Papuan ancestry derives from a single founding population (67), which also contributed part of the ancestry of populations in Island Southeast Asia and the Pacific (149). However, many Pacific populations show evidence of mixture related to a later migration around 3,500 BP of mainland-East-Asian-ancestry populations associated with the Lapita culture, the spread of Austronesian languages, and food production (133, 149). Ancient DNA from ~3,000-BP remains in Vanuatu and Tonga showed that individuals associated with the Lapita culture had very little or no ancestry from Papuan or Australian populations and instead derived all of their ancestry from populations related to present-day Taiwanese populations (133). By contrast, all present-day Pacific populations surveyed have 25% or more ancestry from (primarily male) Papuan ancestors (133). The extreme eastern ends of this Austronesian expansion were the Polynesian islands of Hawaii and Rapa Nui (Easter Island)—both of which are more than 2,000 miles from the American continent. Some data, such as the presence of Native American ancestry on Rapa Nui today (80), suggest the possibility of contact between Polynesia and South America (80), although direct ancient DNA data suggest that this ancestry may postdate European contact (21).

FUNCTIONAL VARIATION AND PHENOTYPES

Because ancient DNA has transformed our ability to explain the origins of present-day patterns of genetic variation in terms of historical processes, it should also allow us to illuminate the evolutionary history of human phenotypic diversity. In particular, ancient DNA should be valuable

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

for identifying and quantifying the contribution of natural selection to phenotypic variation. Historical natural selection does leave detectable patterns in present-day genomes, but those signatures can be hard to interpret and may be mimicked by stochastic neutral processes. Ancient DNA allows us to directly detect rapid changes in allele frequencies over time—the immediate results of selection. In this section, we review areas where ancient DNA has contributed directly to our understanding of the history of phenotypic variation.

Diet and Lactase Persistence

Diet-related genes are a common target of natural selection, and analysis of ancient DNA has documented selection at several loci in Holocene Europe (73) and at taste receptor genes in the past 2,000 years in southern Africa (135). However, by far the clearest evidence of natural selection, from both ancient and modern DNA, is for lactase persistence—the ability to digest lactose and therefore milk in adulthood. In Europe, this phenotype is determined largely by a single-base mutation in the *MCM6* gene, upstream of *LCT* (rs4988235 or *−13,910*T*) (19), which shows one of the strongest signals of a hard selective sweep in the entire genome (6). This particular SNP has attracted more ancient DNA studies than any other. One potential issue with ancient DNA data for this SNP is that, because it is common in present-day populations and is a C>T mutation, contamination or deamination damage can easily lead to false inference of the derived allele. Nonetheless, ancient DNA has clearly shown that the lactase persistence allele did not become common until relatively recently. It was rare or absent in Early Neolithic farming populations (8,500–4,000 BP) (12, 73), present but rare in Europe and on the steppe around 4,500 BP (1, 73), and still rare well into the Bronze Age (up to 3,000 BP) (1, 85). The following rapid increase in the frequency of the persistence allele (to ∼70% in northern Europe today) thus came many thousands of years after evidence of dairying appears in the archaeological record (20). This delay suggests that milk consumption may have been restricted largely to children, limited to fermented products that contain less lactose, or assisted by the gut microbiome, or that any side effects might simply have been tolerated. It remains unknown why the *−13,910*T* allele was so strongly selected and why strong selection was limited to northern Europe.

Pigmentation

The evolution of light skin pigmentation is another case where ancient DNA evidence has provided new insight into the history of the trait. Depigmentation as humans moved into high-latitude environments is thought to be an adaptation to lower levels of UV radiation (44). A main conclusion from ancient DNA studies is that Upper Paleolithic Eurasians and Mesolithic western Europeans carried ancestral (i.e., relatively dark skin) alleles at the two loci that are most important for light skin pigmentation in present-day Europe, *SLC24A5* and *SLC45A2* (28, 57, 72, 73, 84, 101, 130). In the Mesolithic, both of these alleles were present in eastern Europe and Anatolia (73). The derived *SLC24A5* allele was introduced to Europe at high frequency by the Anatolian Neolithic migration, while the derived *SLC45A2* allele was introduced at lower frequency and subsequently selected. Both of these alleles are now virtually fixed in Europe. Other depigmentation alleles, including alleles at *TYR* and *GRM5*, also appear to have been selected over this period, implying a gradual depigmentation of European populations over the Holocene (1, 73, 148). It is clear that the specific combination of pigmentation alleles that is common in western Europe today is relatively recent and reached its current high frequency only within the past 5,000 years. Similarly, signals of selection in southern Africa in the past 2,000 years may also be linked to relatively recent changes in pigmentation (135).

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

Non-skin pigmentation alleles associated with eye and hair color have also been tracked using ancient DNA. In particular, the SNP rs12913832 at the *HERC2/OCA2* locus is strongly associated with light (particularly blue) eye color in Europe. The derived allele is first seen in hunter–gatherers from present-day Italy and Georgia around 13,000–14,000 BP (28, 46) and appears to have become almost fixed in parts of northern and western Europe by around 8,000 BP. This rapid increase in frequency seems likely to have been driven by selection. Direct evidence of more recent natural selection comes from time-series data in eastern and central Europe (73, 148) showing that the present-day distribution of the allele is driven by both admixture and adaptation, although the selective pressures driving this adaptation remain unknown.

The Immune System

Ancient DNA may be particularly valuable for dissecting the history of genes involved in the immune system, which exhibit complex patterns of population differentiation. In Europe, several immune-associated genes have been shown to be under selection in the past 10,000 years (73). However, in contrast to genes associated with skin pigmentation, the selected variations have been at high frequency for a relatively long time. For example, Mesolithic hunter–gatherers carried many derived variants at immune genes (84). In the Americas, ancient DNA has been used to assess evidence of positive selection before and after European contact at specific HLA alleles (60). In some cases, it is possible to recover pathogen DNA from ancient samples—demonstrating the presence of an early version of plague in Bronze Age Europe (108)—and it may be possible to use this kind of data to correlate genetic changes in humans with the presence of specific pathogens.

Height

The past decade has seen an increasing focus on polygenic adaptation as an important mode of evolution in humans. Genetic variants underlying several traits—most clearly height—have been influenced by polygenic selection acting on multiple loci that each have a small effect (4, 142). In particular, height-increasing variants have been driven by selection to higher frequency in northern European populations relative to southern European populations (5, 99, 142). Similarly, but on a larger scale, variants that increase height (in Europeans) tend to be at higher frequency in western Eurasia relative to East Asia, a pattern that is also likely driven by selection (5, 99). Analysis of ancient DNA suggests that this selection occurred in both European hunter–gatherers and the ancestors of Bronze Age steppe populations (5, 71, 73)—who may therefore have been selected for increased height at some point during or after the LGM. Variation in steppe ancestry is correlated with mean height in present-day European populations (**Figure 6**), although it remains to be determined whether this difference in height is, in fact, driven by the observed frequency differences in height-associated genetic variants. With ancient sample sizes now reaching thousands and genome-wide association study sample sizes reaching hundreds of thousands, the power of ancient DNA to explain patterns of complex trait variation in present-day populations will dramatically increase in the near future.

Functional Archaic Admixture

Admixture from archaic humans may have helped modern humans expanding outside of Africa adapt to the unfamiliar environments of Eurasia. An example is a haplotype at *EPAS1* that was shared with the Denisovan genome, is present at high frequency in present-day Tibetans, and appears to be an adaptation to life at high altitudes (43), although it is not clear what role this allele

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

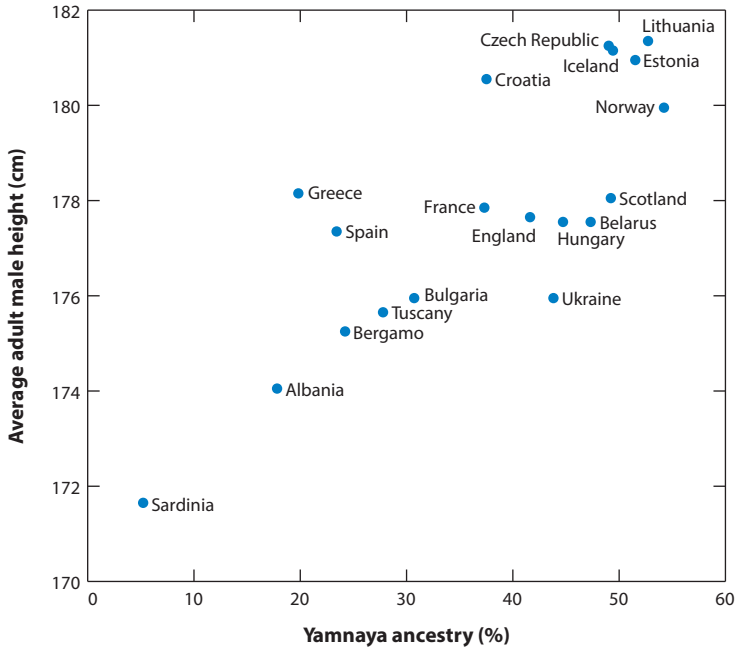

Figure 6

Average adult male height as a function of percentage of steppe ancestry. Present-day adult male height (2, 33) in Europe is predicted ($R^2 = 0.62$) by steppe ancestry (38).

played in archaic human physiology. Signs of adaptive archaic admixture have also been found in genes related to the immune system, metabolism, and skin and hair structure (16, 17, 96, 115, 116, 144, 145).

However, most archaic human ancestry is not adaptive but appears to have been selected against. There are three lines of evidence for this selection against archaic ancestry: Archaic haplotypes are depleted in more conserved parts of the genome (115, 116, 144), archaic haplotypes have decreased in frequency over time (28), and nonsynonymous archaic variants are less likely than non-archaic variants to have predicted functional consequences (16). Within European-ancestry populations, there is some evidence that archaic variants contribute significantly but with a small effect size to several phenotypes, including risk of depression, mood, skin and hair structure, and height (17, 126). Whether archaic ancestry contributes to systematic differences among present-day populations is largely unknown. Proportions of Neanderthal ancestry vary by only a small amount within Eurasia [~2.2% in Europe compared with ~2.4% in East Asia (77, 96, 97, 128, 146)], and this ancestry probably derives from the same Neanderthal population (96), but the larger differences in archaic ancestry among present-day African, Eurasian, and Oceanian populations might explain a larger proportion of phenotypic differences. We caution, however, that these differences in archaic ancestry are confounded with non-archaic genetic differentiation, so it will be difficult to design studies to resolve this question.

CONCLUDING REMARKS

Ancient DNA has greatly increased our knowledge about the expansion and diversification of the ancestors of present-day non-Africans around 50,000 BP. However, we still know relatively little

about the population from which this expansion began. Two pieces of evidence suggest that it was part of a structured population that was the source for most of the ancestry of present-day people: first, evidence of relatively recent (~50,000 BP) gene flow between the ancestors of present-day non-African and eastern, central, and western African populations, and second, the observation that some African lineages are more closely related to present-day non-African populations than others. The exact structure and location of this structured source population are unknown; it may have been geographically restricted to the African continent or may well have extended into southwestern Asia, where there is secure evidence of an anatomically modern human presence by 120,000 BP (36). The most direct way to test this speculation would be with ancient DNA from this time and region. Although conditions for ancient DNA preservation in this hot region are poor, techniques for ancient DNA extraction are continually improving, and DNA recovery is not implausible, as shown by the recent sequencing of nuclear data from an archaic human from Spain dated to 430,000 BP (76). A key challenge for ancient DNA retrieval—complicated by the fact that we have relatively little idea of where to look—would be DNA from early modern humans, on the order of 100,000–200,000 BP. These data would likely be transformative for our understanding of the origin and evolution of our species. Finally, archaic human genomes have proved extremely useful for tracking the history of modern humans, and additional archaic genomes will extend this utility. In particular, knowledge of the timing and distribution of archaic admixture allows us to build a scaffold on which specific events can be placed. For example, if we had no Denisovan genome sequence, it would be difficult to tell whether present-day Oceanians had ancestry from a separate out-of-Africa migration or an unknown archaic human population, and the timing of their ancestors' isolation from the ancestors of present-day East Asian populations would be unclear.

Discussion of Holocene ancient DNA results often focuses on what they can tell us about the spread of language—for example, the spread of Indo-European languages (1, 38). These inferences are necessarily indirect. On the other hand, for cultural features that appear in the archaeological record, ancient DNA allows us to almost directly assess links between culture and genetic history. In particular, we have direct evidence—in Africa (135), far eastern Asia (48), and Europe (9, 29, 38, 42, 130, 131)—that expansions of agriculture were associated with movements of people, as inferred from the concurrent expansion of distinctive genetic ancestries. In almost all of these cases, the agricultural population merged with the existing preagricultural population. Future research will address questions in three main directions. First, denser sampling will allow us to probe the fine-scale details of these interactions. Did agricultural populations absorb individuals from hunter–gatherer groups, or did hunter–gatherer populations transition to agriculture, with substantial genetic input from farmers? Second, data from understudied parts of the world will allow us to test whether these patterns are consistent features of the agricultural transition. In particular, were independent agricultural expansions in Central and North America, South Asia, East Asia, and Papua also associated with expansion and admixture of populations? Did they have the same fine-scale interactions? Finally, to what extent did natural selection act during and after these transitions, and how have present-day phenotypes been shaped by that adaptation?

Ancient DNA from historical times is still relatively rare, partly because it is more difficult to assess contamination from present-day individuals. However, an increasing number of studies have begun to address these periods, including studies of changes in ancestry in Britain in the Roman and Anglo-Saxon periods (70, 119), the peopling of the Canary Islands (111), the dramatic reduction of Native American population size that followed European contact (59), and the place of origin of enslaved Africans in the Caribbean (122). Analyzing these data will require geneticists to engage with historians, as they have previously engaged with anthropologists and archaeologists to interpret data from more ancient individuals. Finally, while ancient DNA analysis has historically been concentrated in European and North American laboratories, the expansion of ancient DNA

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

studies to other parts of the world—and more recent time periods—implies both an opportunity and obligation to develop analysis capacities more widely.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

ACKNOWLEDGMENTS

We thank Graham Coop, Iosif Lazaridis, Benjamin Peter, and Stephan Schiffels for constructive comments on a previous version of this article.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

LITERATURE CITED

1. Documented movements of Bronze Age steppe populations in Europe and Asia.

1. **Allentoft ME, Sikora M, Sjogren K-G, Rasmussen S, Rasmussen M, et al. 2015. Population genomics of Bronze Age Eurasia. *Nature* 522:167–72**
2. Arcaleni E. 2006. Secular trend and regional differences in the stature of Italians, 1854–1980. *Econ. Hum. Biol.* 4:24–38
3. Benazzi S, Douka K, Fornai C, Bauer CC, Kullmer O, et al. 2011. Early dispersal of modern humans in Europe and implications for Neanderthal behaviour. *Nature* 479:525–28
4. Berg JJ, Coop G. 2014. A population genetic signal of polygenic adaptation. *PLOS Genet.* 10:e1004412
5. Berg JJ, Zhang X, Coop G. 2017. Polygenic adaptation has impacted multiple anthropometric traits. bioRxiv 167551. **https://doi.org/10.1101/167551**
6. Bersaglieri T, Sabeti PC, Patterson N, Vanderploeg T, Schaffner SF, et al. 2004. Genetic signatures of strong recent positive selection at the lactase gene. *Am. J. Hum. Genet.* 74:1111–20
7. Bollongino R, Nehlich O, Richards MP, Orschiedt J, Thomas MG, et al. 2013. 2000 years of parallel societies in Stone Age central Europe. *Science* 342:479–81
8. Bowler JM, Johnston H, Olley JM, Prescott JR, Roberts RG, et al. 2003. New ages for human occupation and climatic change at Lake Mungo, Australia. *Nature* 421:837–40
9. Bramanti B, Thomas M, Haak W, Unterlaender M, Jores P, et al. 2009. Genetic discontinuity between local hunter-gatherers and central Europe's first farmers. *Science* 326:137–40
10. Brandt G, Haak W, Adler CJ, Roth C, Szecsenyi-Nagy A, et al. 2013. Ancient DNA reveals key stages in the formation of central European mitochondrial genetic diversity. *Science* 342:257–61

11. Used shotgun genome sequences from the eastern Fertile Crescent to reveal a connection to South Asia.

11. **Broushaki F, Thomas MG, Link V, López S, van Dorp L, et al. 2016. Early Neolithic genomes from the eastern Fertile Crescent. *Science* 353:499**
12. Burger J, Kirchner M, Bramanti B, Haak W, Thomas MG. 2007. Absence of the lactase-persistence-associated allele in early Neolithic Europeans. *PNAS* 104:3736–41
13. Cann RL, Stoneking M, Wilson AC. 1987. Mitochondrial DNA and human evolution. *Nature* 325:31–36
14. Cassidy LM, Martiniano R, Murphy EM, Teasdale MD, Mallory J, et al. 2016. Neolithic and Bronze Age migration to Ireland and establishment of the insular Atlantic genome. *PNAS* 113:368–73
15. Clarkson C, Jacobs Z, Marwick B, Fullagar R, Wallis L, et al. 2017. Human occupation of northern Australia by 65,000 years ago. *Nature* 547:306–10
16. Dannemann M, Andrés AM, Kelso J. 2016. Introgression of Neandertal- and Denisovan-like haplotypes contributes to adaptive variation in human Toll-like receptors. *Am. J. Hum. Genet.* 98:22–33
17. Dannemann M, Kelso J. 2017. The contribution of Neanderthals to phenotypic variation in modern humans. *Am. J. Hum. Genet.* 101:578–89
18. DeGiorgio M, Jakobsson M, Rosenberg NA. 2009. Explaining worldwide patterns of human genetic variation using a coalescent-based serial founder model of migration outward from Africa. *PNAS* 106:16057–62

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

19. Enattah NS, Sahi T, Savilahti E, Terwilliger JD, Peltonen L, Jarvela I. 2002. Identification of a variant associated with adult-type hypolactasia. *Nat. Genet.* 30:233–37
20. Evershed RP, Payne S, Sherratt AG, Copley MS, Coolidge J, et al. 2008. Earliest date for milk use in the Near East and southeastern Europe linked to cattle herding. *Nature* 455:528–31
21. Fehren-Schmitz L, Jarman CL, Harkins KM, Kayser M, Popp BN, Skoglund P. 2017. Genetic ancestry of Rapanui before and after European contact. *Curr. Biol.* 27:3209–15
22. Flegontov P, Altinisik NE, Changmai P, Rohland N, Mallick S, et al. 2017. Paleo-Eskimo genetic legacy across North America. bioRxiv 203018. **https://doi.org/10.1101/203018**
23. Fregel R, Mendez FL, Bokbot Y, Martin-Socas D, Camalich-Massieu MD, et al. 2017. Neolithization of North Africa involved the migration of people from both the Levant and Europe. bioRxiv 191569. **https://doi.org/10.1101/191569**
24. Fu Q, Hajdinjak M, Moldovan O, Constantin S, Mallick S, et al. 2015. An early modern human from Romania with a recent Neanderthal ancestor. *Nature* 524:216–19
25. Fu Q, Li H, Moorjani P, Jay F, Slepchenko SM, et al. 2014. Genome sequence of a 45,000-year-old modern human from western Siberia. *Nature* 514:445–49
26. Fu Q, Meyer M, Gao X, Stenzel U, Burbano HA, et al. 2013. DNA analysis of an early modern human from Tianyuan Cave, China. *PNAS* 110:2223–27
27. Fu Q, Mittnik A, Johnson Philip LF, Bos K, Lari M, et al. 2013. A revised timescale for human evolution based on ancient mitochondrial genomes. *Curr. Biol.* 23:553–59
28. Fu Q, Posth C, Hajdinjak M, Petr M, Mallick S, et al. 2016. The genetic history of Ice Age Europe. *Nature* 534:200–5
29. Gamba C, Jones ER, Teasdale MD, McLaughlin RL, González-Fortes G, et al. 2014. Genome flux and stasis in a five millennium transect of European prehistory. *Nat. Commun.* 5:5257
30. Gibbons A. 2011. A new view of the birth of *Homo sapiens*. *Science* 331:392–94
31. Gilbert MTP, Jenkins DL, Gotherstrom A, Naveran N, Sanchez JJ, et al. 2008. DNA from pre-Clovis human coprolites in Oregon, North America. *Science* 320:786–89
32. González-Fortes G, Jones ER, Lightfoot E, Bonsall C, Lazar C, et al. 2017. Paleogenomic evidence for multi-generational mixing between Neolithic farmers and Mesolithic hunter-gatherers in the lower Danube basin. *Curr. Biol.* 27:1801–10
33. Grasgruber P, Cacek J, Kalina T, Sebera M. 2014. The role of nutrition and genetics as key determinants of the positive height trend. *Econ. Hum. Biol.* 15:81–100
34. Green RE, Krause J, Briggs AW, Maricic T, Stenzel U, et al. 2010. A draft sequence of the Neandertal genome. *Science* 328:710–22
35. Green RE, Krause J, Ptak SE, Briggs AW, Ronan MT, et al. 2006. Analysis of one million base pairs of Neanderthal DNA. *Nature* 444:330–36
36. Groucutt HS, Petraglia MD, Bailey G, Scerri EM, Parton A, et al. 2015. Rethinking the dispersal of *Homo sapiens* out of Africa. *Evol. Anthropol.* 24:149–64
37. Günther T, Malmström H, Svensson EM, Omrak A, Sánchez-Quinto F, et al. 2018. Population genomics of Mesolithic Scandinavia: investigating early postglacial migration routes and high-latitude adaptation. *PLOS Biol.* 16:e2003703
38. Haak W, Lazaridis I, Patterson N, Rohland N, Mallick S, et al. 2015. Massive migration from the steppe is a source for Indo-European languages in Europe. *Nature* 522:207–11
39. Haber M, Doumet-Serhal C, Scheib C, Xue Y, Danecek P, et al. 2017. Continuity and admixture in the last five millennia of Levantine history from ancient Canaanite and present-day Lebanese genome sequences. *Am. J. Hum. Genet.* 101:274–82
40. Helgason A, Einarsson AW, Gumundsdottir VB, Sigursson A, Gunnarsdottir ED, et al. 2015. The Y-chromosome point mutation rate in humans. *Nat. Genet.* 47:453–57
41. Higham T, Compton T, Stringer C, Jacobi R, Shapiro B, et al. 2011. The earliest evidence for anatomically modern humans in northwestern Europe. *Nature* 479:521–24
42. Hofmanová Z, Kreutzer S, Hellenthal G, Sell C, Diekmann Y, et al. 2016. Early farmers from across Europe directly descended from Neolithic Aegeans. *PNAS* 113:6886–91
43. Huerta-Sánchez E, Jin X, Asan, Bianba Z, Peter BM, et al. 2014. Altitude adaptation in Tibetans caused by introgression of Denisovan-like DNA. *Nature* 512:194–97

28. Described a genetic record of European Upper Paleolithic populations spanning more than 30,000 years.

38. Described the contribution of Eurasian steppe populations to present-day ancestry in Europe.

44. Jablonski NG, Chaplin G. 2017. The colours of humanity: the evolution of pigmentation in the human lineage. *Philos. Trans. R. Soc. Lond. B* 372:20160349
45. Jeong C, Ozga AT, Witonsky DB, Malmström H, Edlund H, et al. 2016. Long-term genetic stability and a high-altitude East Asian origin for the peoples of the high valleys of the Himalayan arc. *PNAS* 113:7485–90
46. Jones ER, González-Fortes G, Connell S, Siska V, Eriksson A, et al. 2015. Upper Palaeolithic genomes reveal deep roots of modern Eurasians. *Nat. Commun.* 6:8912
47. Jones ER, Zarina G, Moiseyev V, Lightfoot E, Nigst PR, et al. 2017. The Neolithic transition in the Baltic was not driven by admixture with early European farmers. *Curr. Biol.* 27:576–82
48. Kanzawa-Kiriyama H, Kryukov K, Jinam TA, Hosomichi K, Saso A, et al. 2016. A partial nuclear genome of the Jomons who lived 3000 years ago in Fukushima, Japan. *J. Hum. Genet.* 62:213–21
49. Karmin M, Saag L, Vicente M, Sayres MAW, Järve M, et al. 2015. A recent bottleneck of Y chromosome diversity coincides with a global change in culture. *Genome Res.* 25:459–66
50. Keller A, Graefen A, Ball M, Matzas M, Boisguerin V, et al. 2012. New insights into the Tyrolean Iceman's origin and phenotype as inferred by whole-genome sequencing. *Nat. Commun.* 3:698
51. Kılınç Gülşah M, Omrak A, Özer F, Günther T, Büyükkarakaya Ali M, et al. 2016. The demographic development of the first farmers in Anatolia. *Curr. Biol.* 26:2659–66
52. Kong A, Frigge ML, Masson G, Besenbacher S, Sulem P, et al. 2012. Rate of de novo mutations and the importance of father's age to disease risk. *Nature* 488:471–75
53. Krause J, Briggs AW, Kircher M, Maricic T, Zwyns N, et al. 2010. A complete mtDNA genome of an early modern human from Kostenki, Russia. *Curr. Biol.* 20:231–36
54. Lao O, Lu TT, Nothnagel M, Junge O, Freitag-Wolf S, et al. 2008. Correlation between genetic and geographic structure in Europe. *Curr. Biol.* 18:1241–48
55. Lazaridis I, Mittnik A, Patterson N, Mallick S, Rohland N, et al. 2017. Genetic origins of the Minoans and Mycenaeans. *Nature* 548:214–18
56. Lazaridis I, Nadel D, Rollefson G, Merrett DC, Rohland N, et al. 2016. Genomic insights into the origin of farming in the ancient Near East. *Nature* 536:419–24
57. Lazaridis I, Patterson N, Mittnik A, Renaud G, Mallick S, et al. 2014. Ancient human genomes suggest three ancestral populations for present-day Europeans. *Nature* 513:409–13
58. Li H, Durbin R. 2011. Inference of human population history from individual whole-genome sequences. *Nature* 475:493–96
59. Lindo J, Achilli A, Perego UA, Archer D, Valdiosera C, et al. 2017. Ancient individuals from the North American Northwest Coast reveal 10,000 years of regional genetic continuity. *PNAS* 114:4093–98
60. Lindo J, Huerta-Sánchez E, Nakagome S, Rasmussen M, Petzelt B, et al. 2016. A time transect of exomes from a Native American population before and after European contact. *Nat. Commun.* 7:13175
61. Lipson M, Reich D. 2017. A working model of the deep relationships of diverse modern human genetic lineages outside of Africa. *Mol. Biol. Evol.* 34:889–902
62. Lipson M, Szécsényi-Nagy A, Mallick S, Pósa A, Stégmár B, et al. 2017. Parallel palaeogenomic transects reveal complex genetic history of early European farmers. *Nature* 551:368–72
63. Liu H, Prugnolle F, Manica A, Balloux F. 2006. A geographically explicit genetic model of worldwide human-settlement history. *Am. J. Hum. Genet.* 79:230–37
64. Liu W, Martinón-Torres M, Cai Y-J, Xing S, Tong H-W, et al. 2015. The earliest unequivocally modern humans in southern China. *Nature* 526:696–99
65. Llamas B, Fehren-Schmitz L, Valverde G, Soubrier J, Mallick S, et al. 2016. Ancient mitochondrial DNA provides high-resolution time scale of the peopling of the Americas. *Sci. Adv.* 2:e1501385
66. Llorente MG, Jones ER, Eriksson A, Siska V, Arthur KW, et al. 2015. Ancient Ethiopian genome reveals extensive Eurasian admixture throughout the African continent. *Science* 350:820–22
67. Malaspinas A-S, Westaway MC, Muller C, Sousa VC, Lao O, et al. 2016. A genomic history of Aboriginal Australia. *Nature* 538:207–14
68. Mallick S, Li H, Lipson M, Mathieson I, Gymrek M, et al. 2016. The Simons Genome Diversity Project: 300 genomes from 142 diverse populations. *Nature* 538:201–6

46. Discovered a key ancestral Eurasian population in the Caucasus mountains.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

69. Manning K, Pelling R, Higham T, Schwenniger J-L, Fuller DQ. 2011. 4500-year old domesticated pearl millet (*Pennisetum glaucum*) from the Tilemsi Valley, Mali: new insights into an alternative cereal domestication pathway. *J. Archaeol. Sci.* 38:312–22
70. Martiniano R, Caffell A, Holst M, Hunter-Mann K, Montgomery J, et al. 2016. Genomic signals of migration and continuity in Britain before the Anglo-Saxons. *Nat. Commun.* 7:10326
71. Martiniano R, Cassidy LM, O'Maolduin R, McLaughlin R, Silva NM, et al. 2017. The population genomics of archaeological transition in west Iberia: investigation of ancient substructure using imputation and haplotype-based methods. *PLOS Genet.* 13:e1006852
72. Mathieson I, Alpaslan-Roodenberg S, Posth C, Szécsényi-Nagy A, Rohland N, et al. 2018. The genomic history of southeastern Europe. *Nature* 555:197–203
73. **Mathieson I, Lazaridis I, Rohland N, Mallick S, Patterson N, et al. 2015. Genome-wide patterns of selection in 230 ancient Eurasians. *Nature* 528:499–503**
74. Meltzer DJ. 2009. *First Peoples in a New World: Colonizing Ice Age America*. Berkeley: Univ. Calif. Press
75. Menozzi P, Piazza A, Cavalli-Sforza L. 1978. Synthetic maps of human gene frequencies in Europeans. *Science* 201:786–92
76. Meyer M, Arsuaga J-L, de Filippo C, Nagel S, Aximu-Petri A, et al. 2016. Nuclear DNA sequences from the Middle Pleistocene Sima de los Huesos hominins. *Nature* 531:504–7
77. Meyer M, Kircher M, Gansauge M-T, Li H, Racimo F, et al. 2012. A high-coverage genome sequence from an archaic Denisovan individual. *Science* 338:222–26
78. Mittnik A, Wang C-C, Pfrengle S, Daubaras M, Zariņa G, et al. 2018. The genetic prehistory of the Baltic Sea region. *Nat. Commun.* 9:442
79. Moorjani P, Sankararaman S, Fu Q, Przeworski M, Patterson N, Reich D. 2016. A genetic method for dating ancient genomes provides a direct estimate of human generation interval in the last 45,000 years. *PNAS* 113:5652–57
80. Moreno-Mayar JV, Rasmussen S, Seguin-Orlando A, Rasmussen M, Liang M, et al. 2014. Genome-wide ancestry patterns in Rapanui suggest pre-European admixture with Native Americans. *Curr. Biol.* 24:2518–25
81. Noonan JP, Coop G, Kudaravalli S, Smith D, Krause J, et al. 2006. Sequencing and analysis of Neanderthal genomic DNA. *Science* 314:1113–18
82. Novembre J, Johnson T, Bryc K, Kutalik Z, Boyko AR, et al. 2008. Genes mirror geography within Europe. *Nature* 456:98–101
83. Novembre J, Stephens M. 2008. Interpreting principal component analyses of spatial population genetic variation. *Nat. Genet.* 40:646–49
84. Olalde I, Allentoft ME, Sánchez-Quinto F, Santpere G, Chiang CWK, et al. 2014. Derived immune and ancestral pigmentation alleles in a 7,000-year-old Mesolithic European. *Nature* 507:225–28
85. Olalde I, Brace S, Allentoft ME, Armit I, Kristiansen K, et al. 2018. The Beaker phenomenon and the genomic transformation of northwest Europe. *Nature* 555:190–96
86. Olalde I, Schroeder H, Sandoval-Velasco M, Vinner L, Lobón I, et al. 2015. A common genetic origin for early farmers from Mediterranean Cardial and central European LBK cultures. *Mol. Biol. Evol.* 32:3132–42
87. Omrak A, Günther T, Valdiosera C, Svensson EM, Malmström H, et al. 2015. Genomic evidence establishes Anatolia as the source of the European Neolithic gene pool. *Curr. Biol.* 26:270–75
88. Pääbo S, Poinar H, Serre D, Jaenicke-Despres V, Hebler J, et al. 2004. Genetic analyses from ancient DNA. *Annu. Rev. Genet.* 38:645–79
89. Pagani L, Lawson DJ, Jagoda E, Mörseburg A, Eriksson A, et al. 2016. Genomic analyses inform on migration events during the peopling of Eurasia. *Nature* 538:238–42
90. Pickrell JK, Patterson N, Barbieri C, Berthold F, Gerlach L, et al. 2012. The genetic prehistory of southern Africa. *Nat. Commun.* 3:1143
91. Pickrell JK, Patterson N, Loh P-R, Lipson M, Berger B, et al. 2014. Ancient west Eurasian ancestry in southern and eastern Africa. *PNAS* 111:2632–37
92. Pickrell JK, Pritchard JK. 2012. Inference of population splits and mixtures from genome-wide allele frequency data. *PLOS Genet.* 8:e1002967

73. Performed a genome-wide scan for selection over 10,000 years of European history.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

93. Posth C, Renaud G, Mittnik A, Drucker DG, Rougier H, et al. 2016. Pleistocene mitochondrial genomes suggest a single major dispersal of non-Africans and a Late Glacial population turnover in Europe. *Curr. Biol.* 26:827–33
94. Posth C, Wißing C, Kitagawa K, Pagani L, van Holstein L, et al. 2017. Deeply divergent archaic mitochondrial genome provides lower time boundary for African gene flow into Neanderthals. *Nat. Commun.* 8:16046
95. Poznik GD, Xue Y, Mendez FL, Willems TF, Massaia A, et al. 2016. Punctuated bursts in human male demography inferred from 1,244 worldwide Y-chromosome sequences. *Nat. Genet.* 48:593–99
96. Prüfer K, de Filippo C, Grote S, Mafessoni F, Korlević P, et al. 2017. A high-coverage Neandertal genome from Vindija Cave in Croatia. *Science* 358:655–58
97. Prüfer K, Racimo F, Patterson N, Jay F, Sankararaman S, et al. 2014. The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature* 505:43–49
98. Prugnolle F, Manica A, Balloux F. 2005. Geography predicts neutral genetic diversity of human populations. *Curr. Biol.* 15:R159–60
99. Racimo F, Berg JJ, Pickrell JK. 2017. Detecting polygenic adaptation in admixture graphs. bioRxiv 146043. **https://doi.org/10.1101/146043**
100. Raghavan M, DeGiorgio M, Albrechtsen A, Moltke I, Skoglund P, et al. 2014. The genetic prehistory of the New World Arctic. *Science* 345:1255832
101. Raghavan M, Skoglund P, Graf KE, Metspalu M, Albrechtsen A, et al. 2014. Upper Palaeolithic Siberian genome reveals dual ancestry of Native Americans. *Nature* 505:87–91
102. Raghavan M, Steinrücken M, Harris K, Schiffels S, Rasmussen S, et al. 2015. Genomic evidence for the Pleistocene and recent population history of Native Americans. *Science* 349:aab3884
103. Ramachandran S, Deshpande O, Roseman CC, Rosenberg NA, Feldman MW, Cavalli-Sforza LL. 2005. Support from the relationship of genetic and geographic distance in human populations for a serial founder effect originating in Africa. *PNAS* 102:15942–47
104. Rasmussen M, Anzick SL, Waters MR, Skoglund P, DeGiorgio M, et al. 2014. The genome of a Late Pleistocene human from a Clovis burial site in western Montana. *Nature* 506:225–29
105. Rasmussen M, Guo X, Wang Y, Lohmueller KE, Rasmussen S, et al. 2011. An Aboriginal Australian genome reveals separate human dispersals into Asia. *Science* 334:94–98
106. Rasmussen M, Li Y, Lindgreen S, Pedersen JS, Albrechtsen A, et al. 2010. Ancient human genome sequence of an extinct Palaeo-Eskimo. *Nature* 463:757–62
107. Rasmussen M, Sikora M, Albrechtsen A, Korneliussen TS, Moreno-Mayar JV, et al. 2015. The ancestry and affiliations of Kennewick Man. *Nature* 523:455–58
108. Rasmussen S, Allentoft ME, Nielsen K, Orlando L, Sikora M, et al. 2015. Early divergent strains of *Yersinia pestis* in Eurasia 5,000 years ago. *Cell* 163:571–82
109. Reich D, Green RE, Kircher M, Krause J, Patterson N, et al. 2010. Genetic history of an archaic hominin group from Denisova Cave in Siberia. *Nature* 468:1053–60
110. Reich D, Patterson N, Campbell D, Tandon A, Mazieres S, et al. 2012. Reconstructing Native American population history. *Nature* 488:370–74
111. Rodríguez-Varela R, Günther T, Krzewińska M, Storå J, Gillingwater TH, et al. 2017. Genomic analyses of pre-European conquest human remains from the Canary Islands reveal close affinity to modern North Africans. *Curr. Biol.* 27:3396–402
112. Saag L, Varul L, Scheib CL, Stenderup J, Allentoft ME, et al. 2017. Extensive farming in Estonia started through a sex-biased migration from the steppe. *Curr. Biol.* 27:2185–93
113. Sadr K. 2015. Livestock first reached southern Africa in two separate events. *PLOS ONE* 10:e0134215
114. Sánchez-Quinto F, Schroeder H, Ramirez O, Ávila-Arcos María C, Pybus M, et al. 2012. Genomic affinities of two 7,000-year-old Iberian hunter-gatherers. *Curr. Biol.* 22:1494–99
115. Sankararaman S, Mallick S, Dannemann M, Prufer K, Kelso J, et al. 2014. The genomic landscape of Neanderthal ancestry in present-day humans. *Nature* 507:354–57
116. Sankararaman S, Mallick S, Patterson N, Reich D. 2016. The combined landscape of Denisovan and Neanderthal ancestry in present-day humans. *Curr. Biol.* 26:1241–47
117. Sankararaman S, Patterson N, Li H, Pääbo S, Reich D. 2012. The date of interbreeding between Neandertals and modern humans. *PLOS Genet.* 8:e1002947

101. Analyzed the Mal'ta genome to reveal an ancient lineage connecting Europeans, Siberians, and Native Americans.

104. Described the first ancient American genome and showed that Native Americans descend from the first major founding population on the continent.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

118. Schiffels S, Durbin R. 2014. Inferring human population size and separation history from multiple genome sequences. *Nat. Genet.* 46:919–25
119. Schiffels S, Haak W, Paajanen P, Llamas B, Popescu E, et al. 2016. Iron Age and Anglo-Saxon genomes from East England reveal British migration history. *Nat. Commun.* 7:10408
120. Schlebusch CM, Malmström H, Günther T, Sjödin P, Coutinho A, et al. 2017. Southern African ancient genomes estimate modern human divergence to 350,000 to 260,000 years ago. *Science* 358:652–55
121. Schlebusch CM, Skoglund P, Sjödin P, Gattepaille LM, Hernandez D, et al. 2012. Genomic variation in seven Khoe-San groups reveals adaptation and complex African history. *Science* 338:374–79
122. Schroeder H, Ávila-Arcos MC, Malaspinas A-S, Poznik GD, Sandoval-Velasco M, et al. 2015. Genome-wide ancestry of 17th-century enslaved Africans from the Caribbean. *PNAS* 112:3669–73
123. Schuenemann VJ, Peltzer A, Welte B, van Pelt WP, Molak M, et al. 2017. Ancient Egyptian mummy genomes suggest an increase of sub-Saharan African ancestry in post-Roman periods. *Nat. Commun.* 8:15694
124. Seguin-Orlando A, Korneliussen TS, Sikora M, Malaspinas A-S, Manica A, et al. 2014. Genomic structure in Europeans dating back at least 36,200 years. *Science* 346:1113–18
125. Sikora M, Seguin-Orlando A, Sousa VC, Albrechtsen A, Korneliussen T, et al. 2017. Ancient genomes show social and reproductive behavior of early Upper Paleolithic foragers. *Science* 358:659–62
126. Simonti CN, Vernot B, Bastarache L, Bottinger E, Carrell DS, et al. 2016. The phenotypic legacy of admixture between modern humans and Neandertals. *Science* 351:737–41
127. Siska V, Jones ER, Jeon S, Bhak Y, Kim H-M, et al. 2017. Genome-wide data from two early Neolithic East Asian individuals dating to 7700 years ago. *Sci. Adv.* 3:e1601877
128. Skoglund P, Jakobsson M. 2011. Archaic human ancestry in East Asia. *PNAS* 108:18301–6
129. Skoglund P, Mallick S, Bortolini MC, Chennagiri N, Hünemeier T, et al. 2015. Genetic evidence for two founding populations of the Americas. *Nature* 525:104–8
130. Skoglund P, Malmström H, Omrak A, Raghavan M, Valdiosera C, et al. 2014. Genomic diversity and admixture differs for Stone-Age Scandinavian foragers and farmers. *Science* 344:747–50
131. Skoglund P, Malmström H, Raghavan M, Storå J, Hall P, et al. 2012. Origins and genetic legacy of Neolithic farmers and hunter-gatherers in Europe. *Science* 336:466–69
132. Skoglund P, Northoff BH, Shunkov MV, Derevianko AP, Pääbo S, et al. 2014. Separating endogenous ancient DNA from modern day contamination in a Siberian Neandertal. *PNAS* 111:2229–34
133. Skoglund P, Posth C, Sirak K, Spriggs M, Valentin F, et al. 2016. Genomic insights into the peopling of the Southwest Pacific. *Nature* 538:510–13
134. Skoglund P, Reich D. 2016. A genomic view of the peopling of the Americas. *Curr. Opin. Genet. Dev.* 41:27–35
135. Skoglund P, Thompson JC, Prendergast ME, Mittnik A, Sirak K, et al. 2017. Reconstructing prehistoric African population structure. *Cell* 171:59–71
136. Slon V, Viola B, Renaud G, Gansauge M-T, Benazzi S, et al. 2017. A fourth Denisovan individual. *Sci. Adv.* 3:e1700186
137. Sokal RR, Oden NL, Thomson BA. 1999. A problem with synthetic maps. *Hum. Biol.* 71:1–13
138. Stringer CB. 2014. Why we are not all multiregionalists now. *Trends Ecol. Evol.* 29:248–51
139. Stringer CB, Andrews P. 1988. Genetic and fossil evidence for the origin of modern humans. *Science* 239:1263
140. Terhorst J, Kamm JA, Song YS. 2017. Robust and scalable inference of population history from hundreds of unphased whole genomes. *Nat. Genet.* 49:303–9
141. Tishkoff SA, Reed FA, Friedlaender FR, Ehret C, Ranciaro A, et al. 2009. The genetic structure and history of Africans and African Americans. *Science* 324:1035–44
142. Turchin MC, Chiang CW, Palmer CD, Sankararaman S, Reich D, et al. 2012. Evidence of widespread selection on standing variation in Europe at height-associated SNPs. *Nat. Genet.* 44:1015–19
143. Unterländer M, Palstra F, Lazaridis I, Pilipenko A, Hofmanová Z, et al. 2017. Ancestry and demography and descendants of Iron Age nomads of the Eurasian Steppe. *Nat. Commun.* 8:14615
144. Vernot B, Akey JM. 2014. Resurrecting surviving Neandertal lineages from modern human genomes. *Science* 343:1017–21

131. Demonstrated genetic discontinuity between hunter–gatherer and agricultural populations in Europe.

135. Revealed Holocene population movements and adaptation in Africa.

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

145. Vernot B, Tucci S, Kelso J, Schraiber JG, Wolf AB, et al. 2016. Excavating Neandertal and Denisovan DNA from the genomes of Melanesian individuals. *Science* 352:235–39
146. Wall JD, Yang MA, Jay F, Kim SK, Durand EY, et al. 2013. Higher levels of Neanderthal ancestry in East Asians than in Europeans. *Genetics* 194:199–209
147. Westaway K, Louys J, Awe RD, Morwood M, Price G, et al. 2017. An early modern human presence in Sumatra 73,000–63,000 years ago. *Nature* 548:322–25
148. Wilde S, Timpson A, Kirsanow K, Kaiser E, Kayser M, et al. 2014. Direct evidence for positive selection of skin, hair, and eye pigmentation in Europeans during the last 5,000 y. *PNAS* 111:4832–37
149. Wollstein A, Lao O, Becker C, Brauer S, Trent RJ, et al. 2010. Demographic history of Oceania inferred from genome-wide data. *Curr. Biol.* 20:1983–92
150. Yang MA, Gao X, Theunert C, Tong H, Aximu-Petri A, et al. 2017. 40,000-year-old individual from Asia provides insight into early population structure in Eurasia. *Curr. Biol.* 27:3202–8

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

Annual Review of Genomics and Human Genetics

Volume 19, 2018

Contents

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.

Errata

An online log of corrections to *Annual Review of Genomics and Human Genetics* articles may be found at http://www.annualreviews.org/errata/genom

Annu. Rev. Genom. Hum. Genet. 2018.19:381-404. Downloaded from www.annualreviews.org
Access provided by North Dakota INBRE on 11/19/18. For personal use only.