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Worldwide genetic and cultural change in human evolution

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Both genetic variation and certain culturally transmitted phenotypes show geographic signatures of human demographic history. As a result of the human cultural predisposition to migrate to new areas, humans have adapted to a large number of different environments. Migration to new environments alters genetic selection pressures, and comparative genetic studies have pinpointed numerous likely targets of this selection. However, humans also exhibit many cultural adaptations to new environments, such as practices related to clothing, shelter, and food. Human culture interacts with genes and the environment in complex ways, and studying genes and culture together can deepen our understanding of human evolution.

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Introduction

The study of worldwide genetic variation has made great strides in the 25 years since researchers first convened to plan the Human Genome Diversity Panel (HGDP) [1]. The initial analyses of HGDP data showed that the vast majority of genetic variation occurs within human populations; however, the small fraction of between-population genetic variation could be used to characterize clusters of individuals, which generally correspond to geographic regions and can often be further segmented into population-level groups [2]. The data produced as a result of this initiative, combined with the HapMap and 1000 Genomes initiatives and additional samples from modern and ancient populations, continues to shed light on important aspects of human evolution, including demographic history, migration patterns, admixture between groups, selection pressures, and mutation rates [3••,4•,5–10].

Meanwhile, it has become increasingly clear that human culture interacts with genetic variation in complex ways. Culture can evolve through similar processes to genetic evolution: cultural variants can have differential survival and reproduction, but there are notable differences between cultural transmission, mutation, and inheritance and their genetic analogues [11–13]. Cultural transmission does not obey the precise rules that Mendelian inheritance imposes on single genes, and it may occur between unrelated individuals. Culturally transmitted traits, such as norms and preferences, can change within the course of a human generation, and cultural inheritance may occur over many generations, between groups rather than individuals, and depend on the environmental or social context in which an individual lives. Further, genes and culture often interact: several researchers have suggested that genetic changes, for example those that affect brain architecture, can promote large-scale changes in human culture [14,15], but cultural changes can also alter the selective advantage of genetic mutations, fostering their spread [16–18]. In one classic example, the spread of dairy farming and animal domestication in multiple geographic regions led to a corresponding regional increase in the frequency of genetic variants associated with lactase persistence, allowing more individuals to benefit from drinking milk into adulthood [19,20]. This interaction between genetic and cultural evolution has been studied under several research umbrellas, including gene–culture coevolution, dual inheritance theory, and cultural niche construction [19,21,22]. Here, we review the literature on human genetic and cultural variations, the interactions between them, and the importance of considering both genes and culture in studies of human evolutionary history.

Patterns of worldwide genetic variability and the influence of cultural practices

Geographic patterns of human demographic history have left detectable signatures on the human genome. For example, the human migration out of Africa likely occurred by repeated founder events, in which a small group of people broke away from a larger population to establish a new settlement [23]. Since each subsequent founder event constitutes a sample of the genotypes of the larger group, the serial founder effect model predicts a decrease in genetic diversity with geographic distance from the putative human origin in Africa [24]. Patterns of human

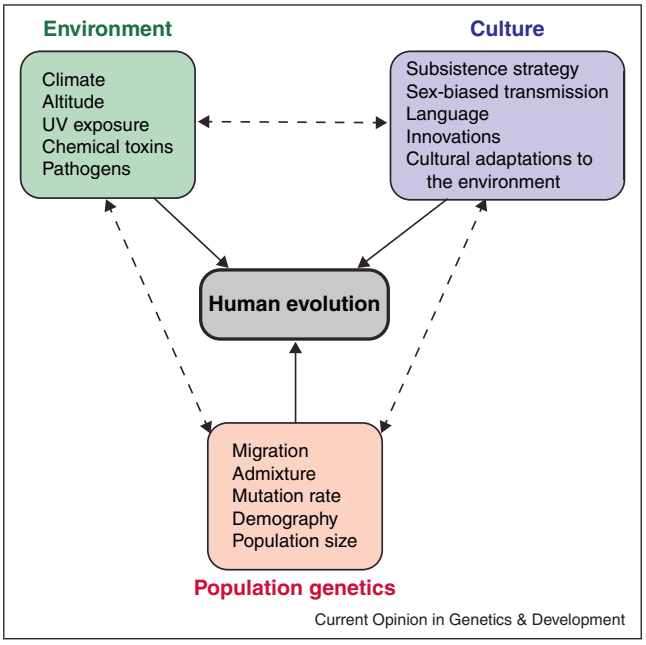
genetic variation have also shed light on the extent of admixture between different populations [25]. This admixture can be a result of relatively recent events in human history, such as colonialism or the advent of technology that facilitates long-distance transportation [4•,8,25,26]. However, recent studies have illustrated that ancient admixture events, such as between modern humans and Neanderthals or Denisovans, are also detectable in the modern human genome [27••,28••].

As researchers accumulate genetic data from more human populations and develop more sophisticated computational techniques, the effects of various forces in population genetics — for example, recent population growth [29], population separation [30•], range expansion [31], neutral genetic variation [32,33], and mutational load [34•] — can be understood in much greater detail. However, signals of population genetic and demographic processes in the human genome are complicated by cultural factors. For example, runs of homozygosity (ROH) are stretches of the genome where heterozygous nucleotides are absent or extremely rare, indicating that an individual's two chromosomes share a recent ancestor, with the length of each run dependent on the number of generations since the common ancestor [35]. ROH can provide evidence for population bottlenecks and ancestral relationships between populations, but it is important to note that the length of these runs can be dramatically influenced by cultural practices, particularly those surrounding marriages between relatives [35–37]. Indeed, homozygosity-based measurements can be used to estimate inbreeding more accurately than can be achieved with family pedigrees [38], particularly in cases where parental relatedness is elevated for many generations [39]. This inbreeding can, in turn, be negatively associated with phenotypes that are relevant to fitness and health, such as height, educational attainment [40], and hypertension [41].

Consanguinity and the cultural practices surrounding it provide one example of a culturally transmitted behavior that leaves an identifiable signature on the human genome. Other aspects of human culture, such as religion [42,43] and sex-specific demographic features [44] including sex-biased migration and sex-specific definition of cultural belonging, can also shape a population's trajectory of genetic evolution. By separately tracing the evolution of maternally transmitted mitochondrial sequences and paternally transmitted Y chromosomes, researchers can test the genetic effects of cultural practices such as matrilineality and patrilineality [45], as well as other sex-biased patterns of human demography that are culturally determined (Figure 1).

For example, the deep phylogenetic history of mitochondrial DNA sequences suggests that human populations were matrilineally structured before the out-of-Africa expansion [46]. A further study of Eurasian and African populations found a discrepancy between the Y chromosome and mitochondrial DNA in the signal of expansion events, implying that male gene flow might have been restricted in some ancestral lineages [47]. Marital practices in which a man relocates to his wife's village upon marriage have left a genetic signature of reduced effective population size and genetic diversity for females in Timor [48]. In contrast, patrilineal societies exhibit male-biased transmission of reproductive success, likely culturally transmitted, which leads to reduced genetic diversity [49]. The sex-specific cultural practices surrounding age of reproduction can also leave a mark on genetic variation, with faster matrilineal genetic evolution in Iceland attributed to a shorter generation interval in women [50]. In the specific example of the Hindu caste system, the cultural tradition of hypergamy, in which women are permitted to marry into a higher social caste in some circumstances but men are not socially mobile, has led to female-specific gene flow and, in some cases, genetic stratification of the populations [51]. Thus, societal systems and cultural norms can have an affect on genetic evolution; however specific cultural events can also leave a mark on the genome. For example, known migration events or significant cultural innovations in human history may correspond to dramatic expansions of the male human lineage, detectable on the Y chromosome [52••]. Although some of the effects of culture on

Figure 1



Genetic, environmental, and cultural factors are capable of influencing one another (dashed arrows), and all three have an impact on human evolution (solid arrows).

patterns of genetic diversity are due to the ways in which culturally transmitted practices alter effective population size, others may be due to the spread of the attitudes, preferences, or norms that have no direct demographic impact.

Genetic and non-genetic adaptations to the environment

Underlying these patterns of worldwide genetic variation is a human tendency to explore previously uninhabited geographic regions. As a result of this cultural propensity to migrate to new areas, humans have adapted to differences in climate, altitude, and resource availability. Some of these adaptations to new environments are themselves cultural practices: for example, clothing and foot coverings that are suited to the climate, as well as novel tools and techniques for food acquisition and cultivation. Migration to new environments also alters the selection pressures on the human genome, and comparative genetic studies have pinpointed certain loci that were likely targets of this selection [53,54]. For example, highly pigmented skin protects against skin cancer but reduces the synthesis of vitamin D3 by the skin, so differences in the amount of ultraviolet radiation in the environment place different selection pressures on pigmentation genes [55]. Polymorphic loci in several genes contribute to variation in pigmentation, including *MC1R* and *SLC45A2* in skin [56–59] and *SLC24A4* in the hair and eyes [59], whose effects on health can be modified by clothing and shelter practices.

Migration to high altitude also alters selection pressures, and the mechanism of genetic adaptation to altitude appears to differ among Andean, Tibetan, and Ethiopian highland populations [60]. On the Tibetan Plateau, residents have a decreased hemoglobin phenotype that appears to accommodate the reduced oxygen levels at high altitude; this phenotype is associated with polymorphisms in genes such as *EPAS1* and *EGLN1* [61,62]. Humans have also adapted to local chemical environments; for example, high environmental arsenic levels in the Argentinean Andes have been linked to changes in a putative gene for arsenic metabolism, *AS3MT* [63•]. Evolutionary pressures may change when humans migrate to new climates, but a changing climate also appears to have an impact on human migration: historical fluctuations in climate occurred concurrently with the timing of migration events predicted by analysis of ancient DNA from South America [64].

Whereas older statistical methods were used to evaluate signals of environmental adaptation in single nucleotide polymorphisms and candidate genes, newer Bayesian algorithms have enabled genome-wide scans for adaptation to the local environment [54], with the caveat that results of this type of analysis are more stable when averaged over multiple runs [65]. Across the genome, climate differences are correlated with polymorphisms in genes related to UV radiation and metabolism of starch and sugar, among others, and cultural practices related to both subsistence strategy and food sources appear to have had measurable genetic effects [66,67]. Diet provides another pathway by which culture can interact with the environment, shaping selection pressures on the human genome [66].

In addition to associations between environmental variables and single gene polymorphisms, recently developed techniques can reveal signatures of local adaptation in phenotypes controlled by more than one gene, for example, a polygenic association between latitude and skin pigmentation [68•]. Another technique, which detects signals of polygenic selection within one population, has shown that genes related to lactose digestion, immune function (HLA), and hair and eye pigmentation have been under selection in the United Kingdom [69]. However, one researcher estimated that 'local adaptations are over 10-fold more likely to affect gene expression than amino acid sequence' and found polygenic associations between the local environment and gene expression levels in several pathways, including those involved in response to UV radiation, diabetes, and the immune system [70].

Local adaptation involves responding to selection pressures, not only related to the climate, altitude, and resource availability, but also to the pathogens in the local environment. In fact, the pathogenic environment may play a more important role than climate in driving local adaptation [71]. Further, past adaptive responses to environmental pathogens might have implications for present-day human health: genes found to be linked to pathogen-driven selection were associated with susceptibility to celiac disease, type 1 diabetes, and other autoimmune diseases [71]. Other chromic diseases also show signatures of environmental adaptation, since risk alleles for numerous diseases are significantly associated with environmental variables [72]. For example, risk alleles for asthma were found to be strongly correlated with summer humidity levels, and risk alleles for several autoimmune diseases, such as Crohn's disease, ulcerative colitis, and systemic lupus erythematosus, appear to be associated with various features of the local climate [72]. In contrast, risk alleles for type 2 diabetes seem to follow the predictions of the serial founder effect model of migration out of Africa, with the frequency of risk alleles decreasing with distance from Africa [72–74].

Patterns of worldwide cultural variation

Human genetic and cultural transmission differ in that culture can be inherited not only from parents but also from teachers and peers, and thus patterns of cultural evolution may often diverge from population genetic histories [11,19]. Even so, some widespread culturally

transmitted phenotypes appear to show geographic signatures of human demographic history [75,76•,77]. Cultural traits can also respond to selection pressures, as genes do; for example, in a study of Polynesian canoes, functional elements evolved more slowly than symbolic elements, suggesting purifying selection on the properties of canoes most relevant to the survival of the human passengers [78]. Since they are transmitted differently but closely linked, cultural and genetic traits can be studied using a coevolutionary framework developed for co-speciating hosts and parasites, as opposed to framing such traits as two sources of data from the same organism [79].

Languages, genes, and geography

Language is a culturally transmitted human characteristic that has been studied for centuries and has recently been considered in the context of genetic variation. In a recent global comparison of genetic variation with inventories of phonemes, the smallest units of sound capable of distinguishing meaning between words, both genetic distance and phonemic distance between populations were significantly correlated with geographic distance [76•]. The pattern of worldwide phonemic variation contains signals of both historical migrations and recent population contact [76•]. However, most studies of regional language and genetic variation highlight local features that are more complex than this global pattern (although some regions, such as Daghestan [80] and New Britain [81], show a relatively straightforward correlation between genetic and linguistic diversity). For example, in Northern island Melanesia [81], North America [82], and northeastern Thailand [83], language boundaries do not appear to act as a barrier to gene flow, so genetic distance does not show a strong association with linguistic distance. In contrast, in Europe [84], the Caucasus [85], the Niger-Congo populations of sub-Saharan Africa [86], and the Kra-Dai linguistic family in Thailand [87], language seems to be a better predictor of genetic differences than geography, so genetic distance shows a stronger association with linguistic than geographic distance.

Language and sex-biased gene flow

Comparisons of linguistic, genetic, and geographic distances can also provide evidence for sex-biased demography. For example, Y-chromosome genetic distance among African populations was reported to be more closely correlated with linguistic distance than with geographic distance [86,88], whereas mtDNA genetic distance was associated with both linguistic and geographic distance [88], suggesting that culturally determined sex-biased demographic patterns, such as patrilocality and male-biased language transmission, could have played a role in the evolution of these populations. In contrast, among a set of Austronesian populations, language was more closely associated with genetic differences in mtDNA than Y-chromosome DNA [89], implying a pattern of sex-biased transmission, such as matrilineality and female-biased language transmission, that differs from the pattern of male-biased transmission suggested by the study of African populations. We can speculate that variation in the extent to which language differences form a barrier to gene flow might be related to child-rearing practices, in particular the transmission of parental attitudes that result in children's lifelong preferences.

Cultural homophily

Human culture can also bias genetic evolution through culturally mediated mating preferences. Through assortative mating or homophily, humans often choose mates who are similar to themselves in certain ways. People assort on numerous phenotypes, from polygenic traits such as eye color [90], height, and IQ [91–93] to behavioral traits such as generosity [94], risk attitude [95], smoking [96], and education level [97•]. This assortment may affect fitness; more similar mates tend to have higher fertility [98]. Further, assortative mating on religion and educational attainment corresponds to differences in the length of runs of homozygosity in homophilic groups [99,100], which could be interpreted as evidence for inbreeding if assortative mating is not taken into account. The tendency for assortative mating can itself be culturally transmitted or may be partially genetic [92], and evolutionary simulations indicate that increased assortative mating can have a strong effect on evolution by facilitating the spread of rare cultural and genetic traits [101,102]. The tendency for culturally similar individuals to come into contact more frequently than by chance was called 'assortative meeting' by Eshel and Cavalli-Sforza; their theoretical analysis showed that such homophily can have a positive effect on the spread of cooperative behavior and that the tendencies to homophily and altruistic behavior may coevolve [103]. Thus, assortative mating represents an important mechanism of interaction between genes and culture that is not often accounted for in genetic studies.

Conclusions

In sum, researchers can better understand evolutionary patterns and human demographic history when both genes and culture are considered. In the 25 years since the Human Genome Diversity Panel was first proposed, our understanding of human population structure, local adaptation, admixture, and gene-culture coevolution has dramatically improved. That said, the juxtaposed study of genes and culture has potential pitfalls when poorly deployed, particularly when researchers fall victim to the use of incomplete data, faulty statistics, or logical fallacies. Recent examples include (1) the assertion by Ashraf and Galor that the high genetic diversity in Africa and low genetic diversity in the Americas are both detrimental to economic development whereas the 'intermediate level' of genetic diversity in Europe is conducive to such economic development [104], and (2) the proposition

by Wade that differences between 'races' in wealth, IQ, and societal institutions have a genetic basis [105]; the methods and conclusions of both works have been strongly criticized on biological and anthropological grounds [106–108]. Extreme care is needed here to guard against the erroneous conclusion that the genetic diversity of a population in any sense determines whether members of that population are subject to a lack of wealth or intelligence; such claims run the risk of providing pseudo-scientific support for those seeking to justify economic or social policies such as ethnic cleansing, systematically mistreating immigrants, or halting humanitarian aid. With these caveats in mind, and in light of increased genetic sampling and improved analysis techniques, the next 25 years hold great promise for the study of human evolution by considering both its genetic and cultural components.

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