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The Genetic Diversity of the Americas

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Abstract

The history of the Americas involved the encounter of millions of Native Americans, Europeans, and Africans. A variable admixture of these three continental groups has taken place throughout the continent, influenced by demography and a range of social factors. This variable admixture has had a major influence on the genetic makeup of populations across the continent. Here, we summarize the demographic history of the region, highlight some social factors that affected historical admixture, and review major patterns of ancestry across the Western Hemisphere based on genetic data.

INTRODUCTION

The United Nations includes in the Americas a total of 35 countries and 18 dependencies, currently comprising approximately 1 billion inhabitants, or approximately 14% of the world population (99). In addition to a heterogeneous native population, whose immigration from Asia starting ∼15,000 years ago spanned millennia, from the late fifteenth century, the so-called New World has received immigrants from across the planet. The genetic diversity of the present-day Americas is thus, in a sense, the genetic diversity of the world. However, four factors had a prominent impact on the current genetic makeup of the Western Hemisphere: the variable native population density at the arrival of Europeans, the extent of European immigration to specific geographic areas, the degree to which certain parts of the New World were involved in the African slave trade, and the extent to which natives, Europeans, and Africans admixed on the continent. These three populations provided the genetic ancestry components that have become predominant across the Americas, with contributions from other parts of the world generally being smaller and geographically more restricted.

Understanding the genetic diversity of the Americas has a range of evolutionary, anthropological, and biomedical implications. To provide a sharper focus, we circumscribe this review mainly to patterns of genetic diversity (particularly continental ancestry and admixture) and their historical correlates, and do not extend into the implications of these patterns for other research fields. We also largely limit ourselves to reviewing solely native, European, and African ancestry studies across the continent. In reviewing this literature it is noticeable that, other than studies of Native American populations, population genetic analyses have rarely attempted to examine genetic diversity across the whole of the Western Hemisphere. Rather, these studies have concentrated mostly on either the United States or Ibero-America (i.e., the former Spanish and Portuguese colonies) in isolation. This literature often also shows different research approaches in that population genetic studies of the United States have usually examined separately the genetic diversity of European Americans, African Americans, and Hispanics. By contrast, studies of Ibero-American countries usually examine the extent of Native American, European, and African ancestry without reference to perceived ancestry labels.

As a contribution to a rapprochement between these somewhat divergent literatures, here we review genetic ancestry studies across the Western Hemisphere in the context of a common historical narrative. The basis for this narrative is the fact that similar demographic forces have been at play across the continent, but various social factors have influenced the extent of admixture in different regions. In particular, historical analyses have suggested that Iberian America has differed from non-Iberian (particularly British) America in a range of social features that could have affected the frequency of admixture. We therefore summarize some key historical and social factors that have helped shape the genetic diversity of human populations across the Americas (particularly rates of admixture across the continent). For simplicity, in what follows we at times refer to the Americas (comprising North, Central, and South America and the Caribbean islands—i.e., the Antilles) as "America" (and "American" as an adjective referring to the continent as a whole), while throughout the text we refer to the United States of America as the United States (or the US).

THE DEMOGRAPHIC HISTORY OF AMERICA

A range of studies date the initial settlement of the American continent towards the end of the last glaciation, some 15,000 years ago, by people who migrated from northeast Asia across Beringia (the land bridge that connected Asia and North America at the time) into Alaska (28, 35, 40, 62). From the northwest tip of North America, humans dispersed southward, reaching Tierra del Fuego at

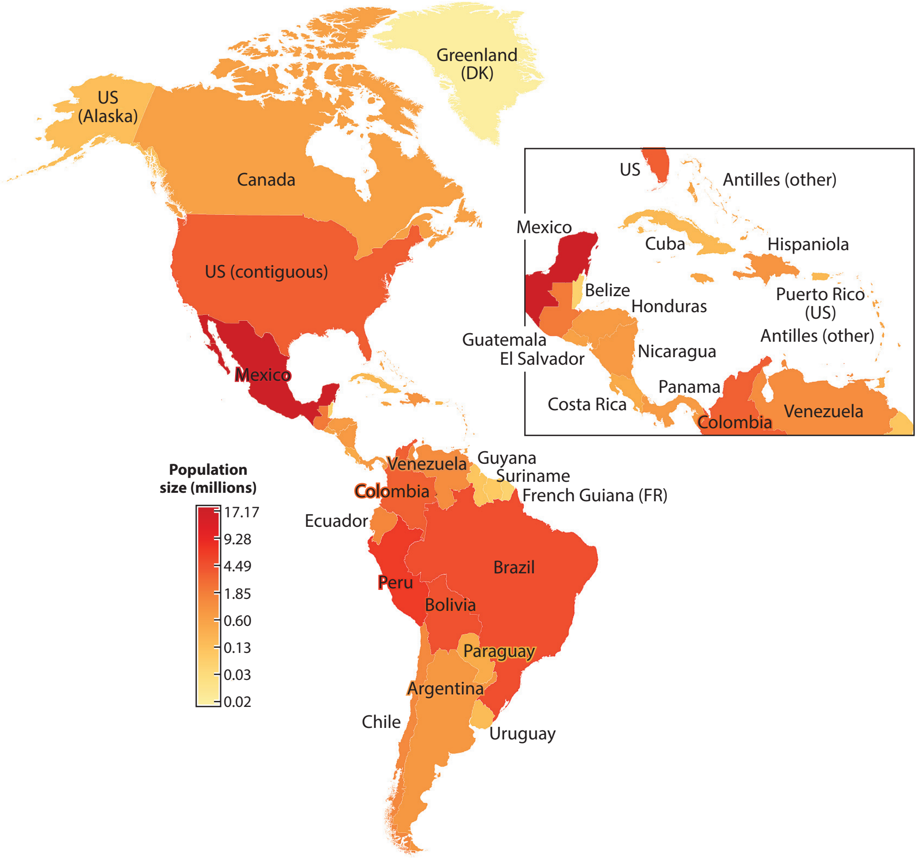

Figure 1

Estimated size of the Native American population at the time of Columbus's first landing on the continent, in 1492. To facilitate comparison with other figures in this article, population size estimates are shown by country, as defined by current borders. The actual population density varied geographically independent of these modern political borders. **Supplemental Table 1** provides exact values and sources. The population of most of the Antilles has been grouped, as has that of Haiti and the Dominican Republic, which share the island of Hispaniola. The country associated with each American dependency is indicated in parentheses (DK, Denmark; FR, France; US, United States).

Supplemental Material

the southern tip of South America in perhaps as little as 1,000 years. While expanding, these people settled a highly heterogeneous geographic environment, developing in the process a range of ways of life. The total size of the native population at the arrival of Europeans has been debated for decades; estimates differ by up to an order of magnitude (~10–100 million), with tens of millions being the most likely figure (34, 86, 96). Although definite estimates are not available, the size of the native population certainly varied greatly across the continent (**Figure 1**, **Supplemental Table 1**). This variation reflected a great diversity in means of subsistence and social organization, ranging from densely populated urban centers dependent on intensive agriculture (mainly those that developed in Mesoamerica and the Andes) to large, scarcely populated areas occupied by small hunter-gatherer communities (like parts of Patagonia and of North America) (16).

The European settlement of the American continent, set in motion by Christopher Columbus's landing in the Bahamas in 1492, was initially dominated by immigrants from Spain and Portugal (37, 47, 61). These settlers established a string of colonies in the Caribbean and on the coastal mainland (including the Pacific coast) throughout the sixteenth century. The extent of inland colonization by the Spanish and Portuguese varied widely, usually following existing Native American settlements. The Iberian expansion to America was followed by other Europeans, particularly the British and to a lesser extent the French, with others, like the Dutch, having an even smaller role. These settlements started approximately a century after the Iberians' and concentrated mainly in the Antilles and along the Atlantic seaboard, mostly of North America. Although the majority of the American territories occupied during the European colonial expansion have since become independent countries, some continue to be dependencies, particularly in the Caribbean. The current distribution of European languages across America partly reflects the colonial history of the continent (**Supplemental Figure 1**, **Supplemental Table 2**).

Supplemental Material

The introduction of African slaves to the Americas was initiated by the Spanish and the Portuguese early in the colonial period and gained strong impetus with the collapse of the native population (31, 94). It is thought that, overall, approximately 90% of the Native American population perished following the arrival of Europeans (63, 96). This population collapse was particularly drastic in areas where the pre-Columbian native population was relatively small, with European colonization essentially resulting in the annihilation of natives from those areas (e.g., in the Antilles). The non-Iberian nations further developed the African slave trade in order to exploit lands taken from the natives, particularly for the development of labor-intensive tropical plantations (initially mostly sugarcane). In many of these plantation areas, the number of Africans ultimately greatly exceeded that of Europeans, especially in the Antilles.

Although better documented than the size of the pre-Columbian native population, estimates of the number of Europeans and Africans who arrived in the New World are approximations based on records whose completeness varied by time and place. It has been estimated that during the colonial period (up to the nineteenth century), some half a million Spanish and a similar number of Portuguese migrated to the Americas, establishing settlements that include many of today's main Ibero-American cities (49, 85, 86). A prominent feature of the Iberian colonization of the Americas, particularly in its early phases, was the marked predominance of men in the immigrant population (20, 79), which in the first century of Spanish settlement represented approximately 80% of the individuals who arrived in the New World. During the colonial period, up to approximately 1 million British, French, and Dutch arrived in their American colonies (6). Although males were also predominant among these migrants, they nevertheless included a considerable number of families (10). Regarding the number of Africans introduced to America as a result of the slave trade, most calculations arrive at a figure of approximately 10 million people. Of these, it has been estimated that ∼42% were taken to Brazil, ∼25% to British colonies, ∼15% to Spanish colonies, and ∼14% to French colonies (31) (**Figure 2**, **Supplemental Table 3**).

The abolition of the slave trade in the nineteenth century interrupted this massive inflow of Africans to the New World. Nevertheless, there was a continuing strong immigration of Europeans to various parts of the continent during this period. These settled particularly in North America, with the United States being by far their primary destination; tens of millions of individuals from across Europe resettled there from the mid-nineteenth to the early twentieth century (14). After independence, several million Europeans also settled in Ibero-America (9, 49, 86) (an estimated 13 million migrated to the region between 1870 and 1930), particularly to the Southern Cone of South America (comprising Chile, Argentina, and Uruguay) and to Brazil. These originated mainly from Spain and Portugal, and in a smaller measure from Italy and Germany. In addition to Europeans, non-negligible numbers of migrants from other parts of the world moved to America

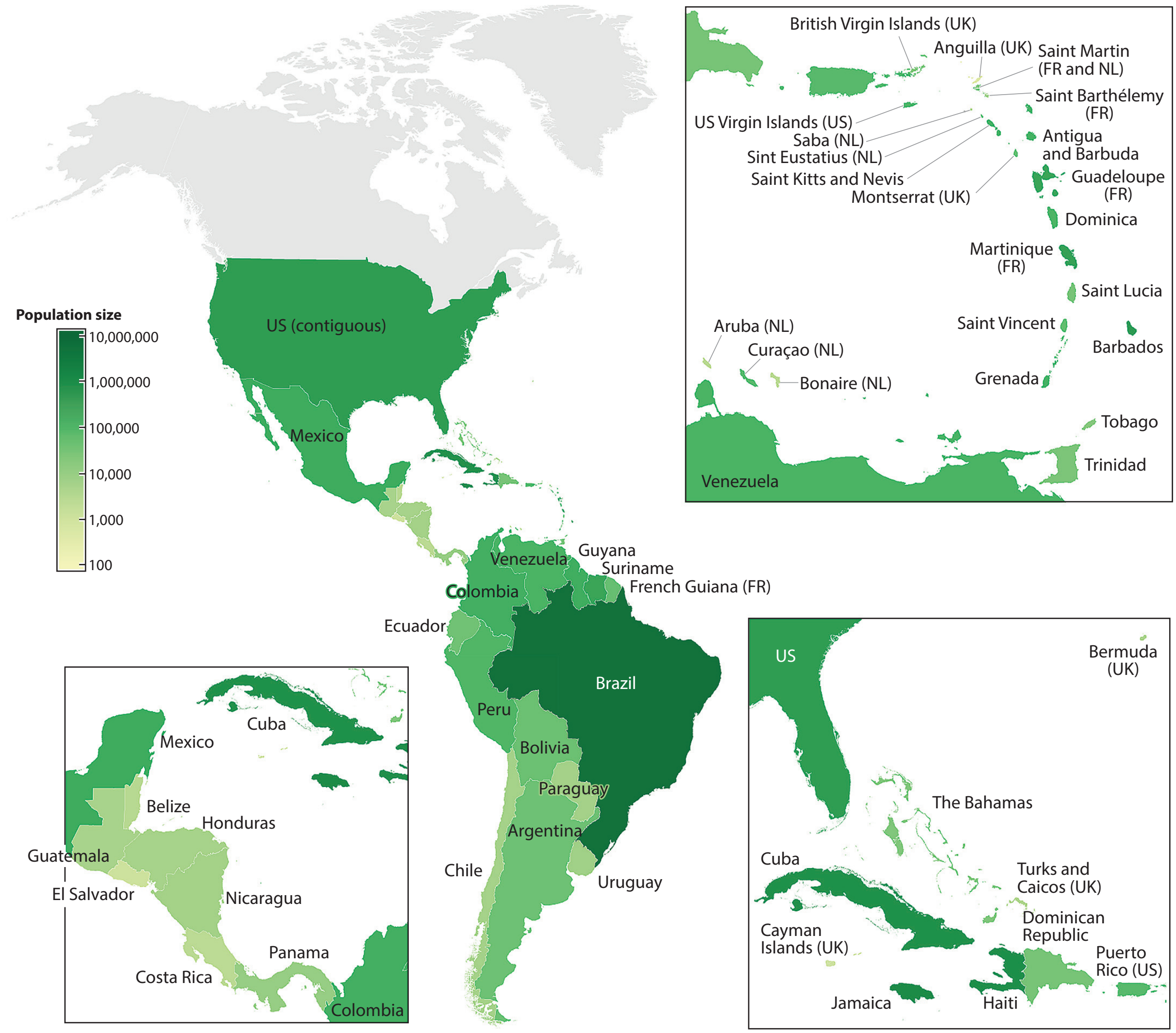

Figure 2

Estimated number of African slaves transported to the American continent. To facilitate comparison with other figures, estimates are shown by country, as defined by current borders. **Supplemental Table 3** provides exact values and sources. The country associated with each American dependency is indicated in parentheses (FR, France; NL, the Netherlands; UK, United Kingdom; US, United States).

during the nineteenth and early twentieth centuries. They also settled predominantly in the United States, but a proportion migrated to parts of Ibero-America (e.g., Chinese and Japanese to Peru and Brazil, respectively).

Supplemental Material

Today, North America remains a major recipient of migrants, whereas immigration to Ibero-America has gradually declined since the early twentieth century (49). The United States is currently the world's most popular destination for migrants. Approximately 14% of the current US population is foreign born (~46 million people); by contrast, only ~1% of the current Ibero-American population is foreign born (~8.6 million people). Ibero-America is now more a source, rather than a recipient, of migrants. In fact, in the last few decades, the main destination of migrants from Ibero-America has been the United States, where some 26 million Hispanics (~13 million of whom were born in Mexico) now live.

HISTORICAL ADMIXTURE IN THE NEW WORLD

The encounter of Native Americans with large numbers of Europeans and Africans created the opportunity for extensive admixture on the continent. However, the extent to which this admixture has taken place has been influenced by geography, the timing and magnitude of population migration, and a range of social factors, all of which have ultimately affected patterns of genetic diversity across the American continent. Importantly, historical studies indicate that there have been differences among the areas of European colonization in a range of social features that potentially affected the frequency of admixture. These differences have been particularly noticeable when comparing areas colonized by the British with those settled by the Spanish and the Portuguese (and, to some extent, the French).

The highly skewed Iberian male immigration to the Americas in the first stages of colonization occurred in the context of an extreme dominance over Native Americans (47, 67). These frontier circumstances contributed to an extensive early admixture between Iberian men and native women, a pattern abundantly documented for the most prominent Spanish conquistadors (67). Interethnic marriages were at the time officially sanctioned by the Crown (12). Later in the colonial period, admixture was facilitated by the Spanish preferentially settling in areas that were already densely populated by natives in order to exploit them as a labor force and to extract tribute (24, 37, 86). Thus, the main centers of Spanish colonial power were located in what used to be the Aztec and Inca empires, in what are now Mexico and Peru, respectively.

After the period of high admixture associated with the initial colonial expansion, several factors contributed to this being a prevalent process across Ibero-America. Although the developing colonial administration was highly hierarchical and placed Europeans at the top of society, the legal system maintained a certain flexibility with regard to interethnic relations (12, 86, 101). For instance, despite marriage between Europeans and non-Europeans being eventually forbidden, the law still allowed for a range of exceptions (e.g., the change of ethnicity affiliation through the courts). Furthermore, the strongly patriarchal nature of colonial society meant that it was of little consequence for European men to have children out of wedlock, and rates of illegitimacy (usually involving European men and native or African women) throughout this period were high (53). In relation to African admixture, although slaves (i.e., Africans, as Native Americans were not legally enslaved in Ibero-America) were at the bottom of the social hierarchy, Iberian slavery legislation (rooted in ancient Roman law) allowed for manumission under a range of circumstances, adding another element of fluidity to colonial society (44, 91, 101). As a result of the rapid increase in the admixed population (who by the eighteenth century were in many places predominant), Iberian law recognized a distinct status for individuals of mixed ancestry (separate from that of European immigrants, their descendants, natives, or slaves), even attempting to codify a wide range of mixed ancestries (denoted *castas* in the Spanish Empire).

After independence, in the nineteenth century, colonial legislation on interethnic relations and slavery were gradually abolished across Ibero-America in an effort to favor the republican ideal of the equality of citizens. Independent Ibero-American states have since embraced admixture in various ways. At times admixture has been positively valued, even actively encouraged, usually as a feature of national identity (52, 56, 57, 101). At other times, Ibero-American states have aimed at "whitening" their populations by fostering further European immigration, initiatives that (as mentioned above) were particularly successful in the Southern Cone and in Brazil (92).

In contrast to the colonization process in Ibero-America, the British settlers of the New World did not consider the native population itself to be a source of wealth. Rather, they entered into an early, sharp conflict with the natives regarding land property and use (11, 35a, 61). Continuing this policy after independence, the western expansion of the United States was often carried out at the expense of Native American populations, who were decimated or forcibly displaced so that they could be replaced with European immigrants (58, 103). British slavery legislation was stricter than the Iberian in terms of imposing segregation and restrictions on slaves (44, 91), as well as more drastic in terms of preventing marriage or sex between Europeans and non-Europeans (43, 91). Following the abolition of slavery in 1865, racial segregation legislation was reintroduced in southern US states (which had harbored most of the slave population) in the 1870s and further codified in the early twentieth century (71). This included the so-called one-drop rule, which enforced a binary view of ancestry (i.e., legally excluding the possibility of mixed ancestry). The last piece of this racial segregation legislation was abolished in the 1960s. Thus, throughout the history of the Americas, there were arguably stronger explicit social barriers to admixture between Europeans and non-Europeans in British America than in Iberian America. Beyond population segregation enforced by law, a range of other social phenomena may also have affected the rates of admixture across the Americas. Although this is a matter of debate, a substantial social sciences literature argues that racism has been different, and possibly more intense, in British America than in Iberian America (45, 59, 88, 102).

Although the admixture of natives, Europeans, and Africans has been a major historic feature shaping human diversity across America, the continent also includes a number of populations that are derived from the same three continental sources but are characterized by distinct sociocultural features. These "special" populations have been of considerable independent research interest. The most prominent examples are the many extant native populations that have maintained a relatively defined cultural identity, as manifested, for example, in the several hundred native languages currently spoken across the continent (26, 81). Other relatively isolated populations in the Western Hemisphere trace their ancestry to so-called marooned communities established by Africans fleeing slavery (e.g., the Spanish American *palenques* or the Brazilian *quilombos*) (77, 95). Finally, among the European immigrants to the New World, certain groups have maintained an identity often in relation to aspects of their specific origin in Europe, including religion. Among the largest are several German communities in South America, particularly in Chile and Brazil (49). Smaller populations include the various Anabaptist settlements across America (93).

THE GENETIC DIVERSITY OF AMERICA

Geographic Variation in Ancestry

Surveys of genetic diversity in the Americas have traditionally focused on specific populations (e.g., Native Americans). However, there has been a recent growing interest in conducting country-wide surveys of diversity. A common aim of these studies has been to relate current genetic patterns to aspects of the demographic history of the countries examined. In Brazil, for instance, the highest levels of European ancestry have been documented in the south of the country (the area of strongest European immigration during the "whitening" of Brazil), whereas the highest levels of African ancestry are in the northeast (historically the main area of African slave concentration) (75, 83). Similarly, in US African Americans, African ancestry is highest in southern states, the area historically most strongly associated with slavery (8, 22), and a south-to-north gradient of increasing European admixture has been interpreted as related to the northern migration of African Americans after the abolition of slavery (8, 22, 72, 73). In the same vein, an approach to reviewing the genetic diversity literature across the whole of the Western Hemisphere is to examine whether, globally, published studies are consistent with the demographic history of the continent.

Supplemental Material

A useful backdrop to such a review is to examine surveys on perception of ancestry across America (e.g., national censuses). These data are by definition subjective and have been collected in a heterogeneous way between countries. For instance, although at independence Ibero-American states abolished the colonial practice of recording individual ancestry, collection of this information has since been reinstated in various ways (56, 57). By contrast, the US government has systematically collected census data on ancestry decennially since 1790, although not allowing for the possibility of mixed ancestry prior to the 2000 census (a common practice across Ibero-America). Nevertheless, data on perceived ancestry provide a geographic coverage that exceeds what has been achieved by genetic studies. In **Figure 3** (see also **Supplemental Tables 4** and **5**), we summarize data on perceived continental ancestry obtained from population surveys for the 44 countries and dependencies for which information is available. We grouped the available data into five continental ancestry categories (Native American, European, African, mixed, and other). Some prominent trends are apparent. With few exceptions, the Native American, European, African, and mixed groups represent the predominant continental ancestries reported across the continent. The main exceptions where the "other" category reaches high frequency are Guyana and Suriname in South America and two of the Antilles (the Cayman Islands and Trinidad and Tobago). In these territories, a considerable fraction of the population reports South Asian ancestry (**Supplemental Table 5**). In addition, a considerable fraction of individuals in Canada (~17%) and the United States (~13%) also report other continental ancestries. Except for Greenland, where it has a reported frequency of ~88%, perceived Native American ancestry is reported by a minority of the population throughout America, although it has values above 10% in Mexico,

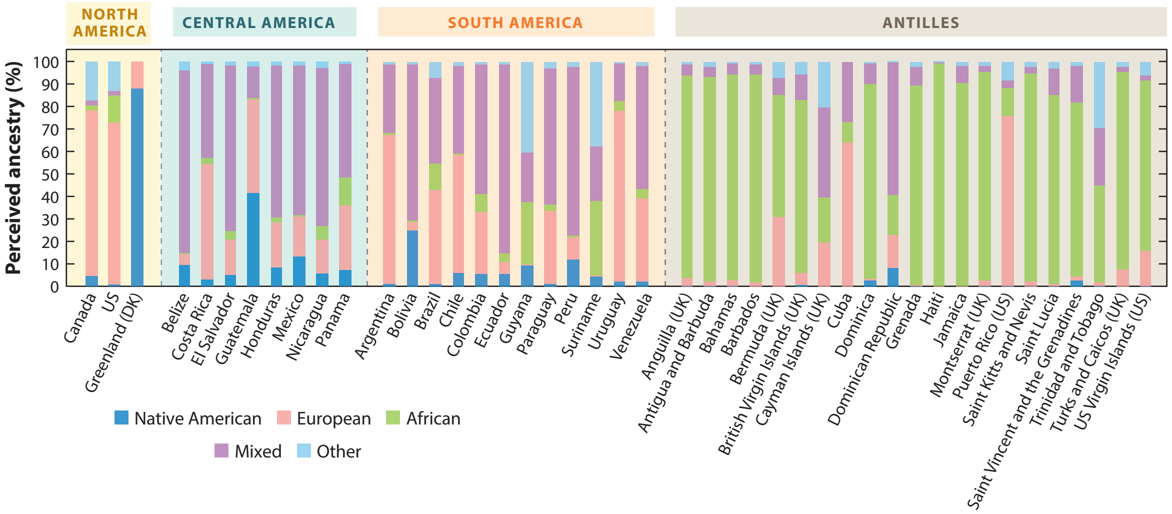

Figure 3

Perceived continental ancestry in population surveys of countries and dependencies across the American continent. **Supplemental Table 4** provides the underlying numbers. The terms used to refer to Native American, European, and African ancestry (and their mixture) vary across surveys but have been made uniform here. The "other" category refers to ancestries other than Native American, European, or African. The values shown here represent averages obtained from national censuses and samples designed to be representative of these populations (**Supplemental Table 5**). The country associated with each American dependency is indicated in parentheses (DK, Denmark; UK, United Kingdom; US, United States). Territories have been grouped into regions following the United Nations, with the exception of Bermuda, which has been included in the Antilles.

Guatemala, Peru, and Bolivia. In the Antilles, Native American ancestry is usually not reported. Perceived European ancestry is the most frequent in the United States and Canada, in four mainland Ibero-American countries, and in two of the Antilles (Cuba and Puerto Rico). The three South American countries where the European category predominates are in the Southern Cone (Chile, Argentina, and Uruguay). Uruguay has the highest frequency of perceived European ancestry in the Americas (~81%). Perceived African ancestry has a high frequency in most of the Antilles, reaching its maximum across the Americas in Haiti (~99%). The mixed-ancestry category predominates in most of continental Ibero-America, particularly in Central America and northern South America, and in one of the Antilles (the Dominican Republic). It has a low frequency in North America and in many of the Antilles.

Although heterogeneously collected and based on perceived ancestry, the data shown in **Figure 3** appear to be broadly consistent with the demographic history of the Americas, as summarized above. Natives appear to have been partly replaced by other populations in most areas (almost completely in the Antilles), although they still represent substantial proportions in the regions where the pre-Columbian population size was the largest (Mesoamerica and the Central Andes) (**Figure 1**). In most of Ibero-America, natives seem to have been replaced by a population of mixed ancestry, whereas in North America (other than Greenland) and in the non-Iberian Antilles, they appear to have been replaced mostly by Europeans and Africans, respectively.

The broad agreement of the ancestry perception data with historical records is consistent with the assumption that perceived ancestry is informative about continental genetic ancestry. To evaluate this assumption using the data in **Figure 3**, we compared perceived ancestry with published estimates of genetic ancestry obtained from study samples collected in the same territories. The genetic estimates do not suffer from the subjectivity of perceived ancestry recorded by the population surveys. However, genetic estimates have the drawback that they come from convenience samples that were not designed to be representative of the entire populations of the territories examined; they are thus likely to suffer from a range of biases, including inadequate geographic and socioeconomic sampling. There is also considerable variation in the number of published genetic ancestry estimates for different countries, the type and number of markers used, the samples used as continental reference populations, and the statistical methods employed to estimate ancestry.

In reviewing this literature, we retained only published studies that analyzed at least 30 genetic markers in samples of at least 25 individuals, so as to focus on the more reliable sample estimates (**Supplemental Tables 6** and **7**). With those restrictions, genetic ancestry estimates are available for samples from 22 American countries (or dependencies), including representatives of North, Central, and South America and the Antilles. To summarize these data, we obtained averages for each country, weighting by the size of the population being sampled (**Figure 4**, **Supplemental Table 6**). Although more scattered geographically, the variation in genetic ancestry seen across the Americas follows similar patterns as observed with the more densely distributed perceived ancestry data (**Figures 3** and **4**). There is relatively low non-European ancestry in North America (other than in Greenland), high African ancestry in the Antilles (except in Cuba and Puerto Rico), and a highly mixed ancestry across Ibero-America. Among Ibero-American countries, native ancestry is highest in Mesoamerica (Mexico and Guatemala) and in the Central Andes (Peru and Bolivia); European ancestry predominates in the Southern Cone, Brazil, Costa Rica, Cuba, and Puerto Rico; and relatively high African ancestry is seen in Brazil and Colombia. There is a strong and significant correlation between the average estimates of Native American, European, and African genetic ancestry and the frequency of the equivalent perceived ancestry categories reported in population survey data for these territories (**Figure 5**): For native ancestry, $R = 0.66$ ($p = 7 \times 10^{-4}$); for European ancestry, $R = 0.92$ ($p = 2 \times 10^{-9}$); and for African ancestry, $R = 0.96$ ($p = 4 \times 10^{-12}$). The correlation between perceived and genetically estimated ancestry is

Supplemental Material

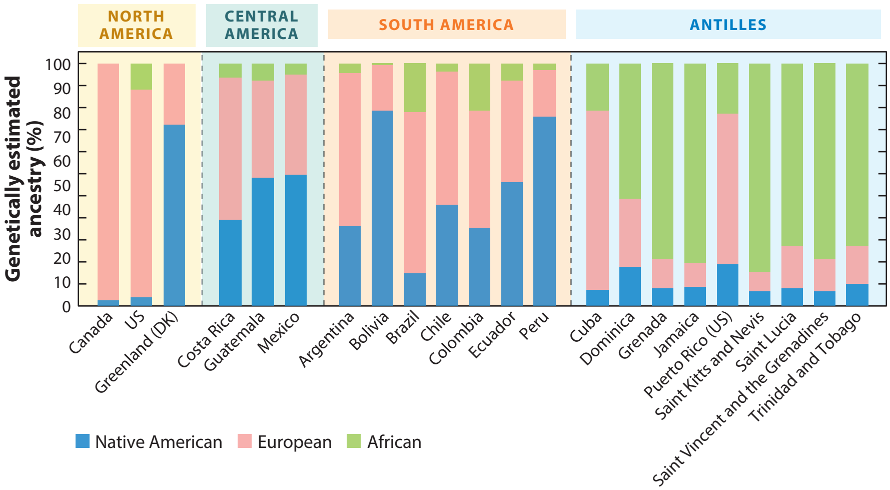

Figure 4

Average genetically estimated Native American, European, and African ancestry for samples from countries and dependencies across the American continent. When multiple studies were available for a territory, an average across studies was obtained by weighting based on the size of the population sampled. **Supplemental Tables 6** and **7** provide the underlying data and sources. The country associated with each American dependency is indicated in parentheses (DK, Denmark; US, United States).

Supplemental Material

consistent with the fact that physical appearance is partly genetic (1, 2, 4, 83) and likely an important determinant of perception of ancestry. The review of genetic data underpins the interpretation of ancestry perception data in that, globally, variation in Native American, European, and African ancestry across the Western Hemisphere bears the imprint of the region's colonial history.

Genetic Ancestry in European Americans and African Americans

Considering the correlation between perceived and genetically estimated ancestry seen in population surveys from American countries and dependencies (**Figure 5**), we reviewed studies across the continent that estimated genetic ancestry in individuals categorized previously based on perceived ancestry. By default, genetic studies of US population samples categorize individuals as European American, African American, Hispanic, or Asian. In Ibero-America, such categorization of research subjects is not standard, but studies of this type have been performed for some urban population samples (particularly in Brazil) and for certain historic isolates (e.g., African-derived Brazilian *quilombos*). Studies in Ibero-America use the terms "white" and "black" as ancestry equivalents to the European American and African American categories used in the United States; we therefore focused on a comparison of these two categories across the continent.

As above, we retained only published studies that analyzed at least 30 genetic markers in samples of at least 25 individuals. Several recent analyses of US samples have used high-density genotyping or whole-genome sequencing, but no such studies have been reported for Ibero-American samples categorized by perceived ancestry. Nevertheless, it has been shown that there is a strong correlation between genetic estimates obtained with sets of ancestry-informative markers and those obtained with high-density data in samples from Ibero-America (38, 83). A large variation has been reported in the individual estimates of ancestry within the predefined ancestry categories. Although potentially informative, it is problematic to contrast this variation across published studies because of the large differences in the number of markers examined and the sampling strategies used. We

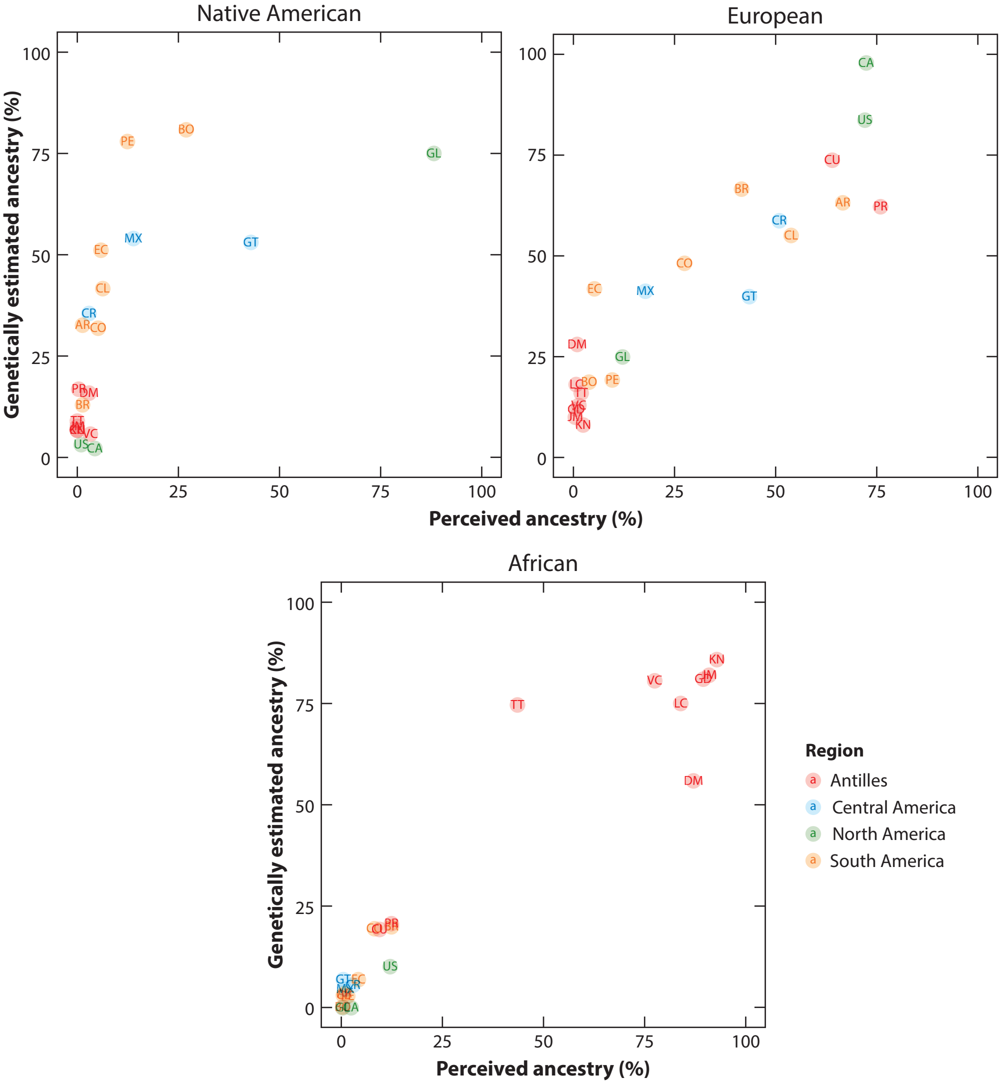

Figure 5

Contrast between perceived and genetically estimated Native American, European, and African ancestry for 20 countries and dependencies across the American continent. The values for each territory are those shown in **Figures 3** and **4**; **Supplemental Tables 4** and **6** provide the exact values. The letters are the country codes as defined by the ISO 3166-1 alpha-2 code system (**Supplemental Table 6**).

Supplemental Material

therefore focus our comparison on the average estimates of continental ancestry obtained for each sample (**Figure 6**, **Supplemental Table 8**).

Overall, there is significant differentiation in genetic ancestry between the European American/white and African American/black categories in the United States and Ibero-America (t-test p value $< 3 \times 10^{-3}$ for all ancestries, except for native ancestry in Ibero-America) (**Supplemental Table 9*a***). Notably, however, the white category sampled in the five Ibero-American countries examined shows substantial levels of non-European ancestry (ranging from 14% to 53%). By contrast, US European Americans have a very low level of mean non-European ancestry ($\leq$1%).

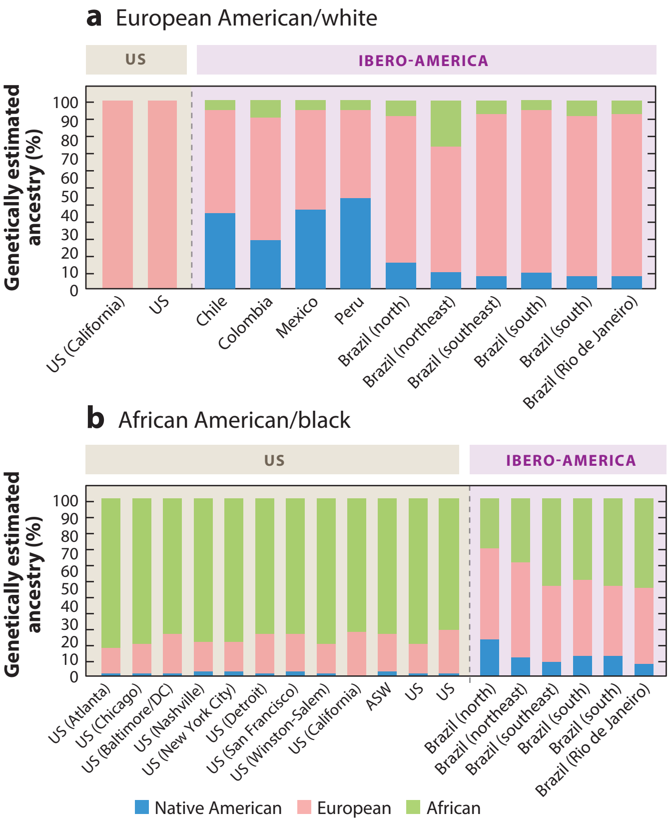

Figure 6

Genetically estimated Native American, European, and African ancestry in individuals categorized as (*a*) European American/white or (*b*) African American/black in the United States and Ibero-America. **Supplemental Table 8** provides the underlying data and sources. Abbreviation: ASW, Americans of African ancestry in the southwest United States (from the 1000 Genomes Project).

Supplemental Material

Similarly, in urban samples from Brazil, the black category shows European ancestry ranging from 39% to 54% and native ancestry ranging from 8% to 20%. By comparison, US African American samples have ≤25% European ancestry and ≤3% native ancestry. The data shown in **Figure 6** (and **Supplemental Table 8**) thus indicate that people perceived as white in Ibero-America have, on average, substantially more native and African admixture than US European Americans. Similarly, these data indicate that urban populations perceived as black in Brazil have (on average) substantially higher levels of non-African admixture than US African Americans. The differences in ancestry proportions between US European Americans/African Americans and Ibero-American whites/black are statistically significant (*t*-test *p* values $< 1 \times 10^{-2}$ for all ancestries) (**Supplemental Table 9*b***). Overall, a measure of genetic distance (F_{st}) calculated based on the admixture proportions shown in **Figure 6** (and **Supplemental Table 8**) summarizes the greater genetic differentiation between US European Americans and African Americans ($F_{st} = 0.75$) compared with the genetic differentiation of Ibero-American whites and blacks ($F_{st} = 0.18$).

It is worth noting that population surveys indicate that the black category (i.e., the one perceived as reflecting African ancestry) in Brazil represents a minority (∼12%) (**Figure 3**, **Supplemental Table 4**), whereas the mixed-ancestry category (i.e., the one perceived as

African-European admixed) represents a large proportion of the population of this country (~38%) (**Figure 3**, **Supplemental Table 4**). Consistently, Brazilians in the mixed-ancestry category have been reported to have (on average) higher non-African admixture than those in the black category (55, 75). As indicated above, no equivalent mixed-ancestry category is commonly used in population surveys or genetic studies in the United States. The ancestry estimates of **Figure 6** also highlight the comparatively scant contribution of Native Americans to admixture in the general US population. An exception is US Hispanics, whose ancestry proportions have been shown to resemble that of their country of origin in Ibero-America.

Supplemental Material

Overall, the data compared in **Figure 6** are consistent with the greater population segregation suggested by historical analyses for the United States relative to Ibero-America. Also in agreement with this, genetic studies have reported that states where native ancestry is detectable in US European Americans are mostly those that were initially colonized by the Spanish (i.e., Louisiana and the west/southwest) (22). In addition, although there is a south-to-north gradient of increasing European ancestry in US African Americans, results from Louisiana differ in that they show relatively higher levels of European and Native American ancestry (8, 22). This greater admixture in African Americans from Louisiana has been interpreted as consistent with historical studies suggesting that slaves in this state were less segregated during the period of Spanish and French rule than they were in the neighboring British colonies (91).

Subcontinental Ancestry

In addition to enabling the analysis of continental ancestry, genetic data are allowing the exploration of subcontinental ancestry in American populations, that is, to specify more narrowly the geographic location of their Native American, European, or African ancestors. An early example of such inference involving the native ancestry component of an Ibero-American population was provided by mitochondrial DNA (mtDNA) data in which haplotype frequencies were found to be most similar to existing native populations in the vicinity (27). A simple explanation for this observation was that of a genetic continuity between local pre- and post-Columbian populations (i.e., that the native population could have become amalgamated into the growing admixed population from that region). Subsequent autosomal marker surveys [including high-density single-nucleotide polymorphism (SNP) analyses] in populations from Central and South America have consistently shown that the native ancestry of these populations relates most closely to natives living in proximity (3, 64, 65, 104). These observations suggest that, despite an increased migration across Ibero-America in recent decades, this has not been extensive enough to erase the signature of pre-Columbian native population structure.

Similar studies have allowed the exploration of subcontinental European and African ancestry across the Americas. Results from early single-locus analyses have been extended more recently by high-density genome-wide data. For instance, early studies that sought to evaluate the place of origin in Africa of slaves transported to the Americas often used hemoglobin S (HbS) haplotypes, which carry the mutation that causes sickle-cell disease. In Brazil, ~61%, ~34%, and ~3% of these HbS haplotypes were found to be of the so-called CAR (Central African Republic or Bantu), Benin, and Senegal haplotypes, respectively (on the basis that these haplotypes are common in those African countries). These findings are consistent with historical information suggesting that approximately 68% and 32% of African slaves introduced to Brazil originated in west-central/southeast and west Africa, respectively (33, 85). Subsequent mtDNA and high-density genotype analyses have confirmed and extended these results, highlighting areas of non–Bantu speakers in northwest and west-central Africa as major sources for the slaves brought to the Americas, with relatively smaller contributions from other regions, such as east African

(Bantu-speaking) areas (21, 48, 60, 66, 97). Some regional variation has been reported for the relative importance of specific African source regions in the Americas; for instance, the non-Bantu component is more frequent in southern than northern Brazil, in agreement with historical information on the predominant origin of slaves introduced to different parts of this country (48).

With regard to the European ancestry of American populations, a broad genetic pattern (consistent with the colonial history of the continent) is the detection, through high-density SNP data, of relatively high levels of northern European ancestry in US European Americans and of Iberian ancestry in Spanish America and Brazil (22, 48, 64). These high-density SNP data have also revealed finer-grained geographic patterns. For instance, Scandinavian ancestry in the United States is fairly restricted to northern US states (22), and there is detectable northern European ancestry in southern Brazil (48). Given the history of Spain, an interesting question is whether there was a colonial North African and Middle Eastern genetic contribution to Ibero-America. Indeed, both Jews and Muslims represented a substantial fraction of the Spanish population in the fifteenth century and were forced by the Crown to either convert to Christianity or leave Spain in the same year as Columbus's arrival in the New World (84). Although recent converts were not legally permitted to travel to the New World, it has been argued that many in fact made the journey. Interestingly, the analysis of Y chromosome data and rare disease mutations are consistent with a genetic contribution from North Africa and the Middle East to the ancestry of Ibero-Americans (17, 27, 36, 68, 100).

Sex Bias in Admixture

As indicated above, historical studies have documented that admixture in colonial Ibero-America was strongly sex biased, reflecting the greater immigration of European men to the Americas and their dominant social role (67, 79). Genetic studies have enabled a precise assessment of the impact of this history on the genetic makeup of American populations. Initial analyses used mtDNA and Y chromosome data, which allow a direct assessment of paternal and maternal ancestry. A dramatic early example of this approach was provided by the population of Antioquia in Colombia, where ~90% of Y chromosome lineages are of European origin, whereas ~90% of mtDNA lineages are Native American, indicating that the foundation of the population from this province overwhelmingly involved European men and native women, although this is not specifically recorded in historical documents (15, 27). Similar analyses of other Ibero-American populations have often documented paternal lineages as mainly European, whereas maternal lineages are predominantly Native American or African (3). Y chromosome and mtDNA analyses have more recently been enriched by the use of X chromosome and autosomal data showing that the proportion of European ancestry estimated for the X chromosome is lower than that for the autosomes, as expected from the fact that women contribute two X chromosomes to the next generation, whereas men only contribute one (15, 106). These analyses have confirmed the widespread occurrence of a sex bias in admixture across the Americas (21–23, 30, 46, 48, 60, 66, 104). Interestingly, a similar sex bias in admixture has been documented in populations outside the American continent, indicating that the social and demographic forces at play in the Americas are not an isolated case in recent human history (41).

Special Populations

As mentioned above, certain American populations have maintained ethnographic features predating New World interactions that set them apart from predominant groups on the continent. These populations have been the focus of substantial genetics research, which has been reviewed elsewhere. We refer to these here only to highlight them as deviations from the broad patterns of diversity discussed above. The most prominent example is Native Americans, which have been the focus of genetics research for many decades. These studies have provided a range of novel insights into the evolutionary history of America, including uncovering complex and prolonged exchanges with East Asia during the pre-Columbian settlement of the continent (18, 69, 78, 82, 89, 90). These findings underline the heterogeneous Old World ancestry of Native Americans. Of the many European population isolates documented across America, some have been the subject of long-standing research mainly to identify disease genes by exploiting their relatively low genetic diversity (e.g., North American Anabaptist communities) (19, 70, 74, 93). Finally, several communities tracing their ancestry to runaway slaves have been prime objects of study in multidisciplinary analyses examining the origin in Africa of the individuals who were transported to America (77, 87). Genetic studies have shown that, although many of these populations have mainly African ancestry and show high inbreeding (7, 54), others have substantial non-African admixture, indicating that contrary to what was previously thought, maroon settlements were not always that isolated (85).

CONCLUSIONS AND PERSPECTIVES

Columbus's landing in the New World unleashed a dramatic demographic transformation of the Americas. Following his arrival, millions of Native Americans perished in arguably the most drastic human population collapse ever recorded. Through a slave trade carried out on an unprecedented scale, millions of Africans were forcibly transported to the Americas. In addition, millions of people from Europe and other continents chose to resettle to the New World, mostly in search of a better life. These events have shaped the genetic diversity of the continent. In certain regions, natives were almost entirely replaced by Europeans or Africans. In other places, the overlap of these three continental populations provided the opportunity for admixture. This admixture has been more extensive in the areas of Iberian colonization than in those settled by the British, possibly influenced by social features distinguishing these two broad areas of European colonial expansion. Despite these differences, European colonization in America was strongly patriarchal and characterized by a marked dominance of Europeans over Native Americans and Africans. The most prominent genetic signature of this history is the widespread sex bias in admixture documented by genetic studies across the continent.

The colonial history of the Americas has also had long-lasting socioeconomic effects, with important implications for public health. A prominent one has been the association of wealth with European ancestry. The wealth gap between European Americans and African Americans and Hispanics in the United States has been extensively studied (51, 98, 105). Similarly, in Ibero-America, a correlation between greater wealth and higher levels of European ancestry has been documented (83), an observation whose significance is underlined by the fact that several of these countries have some of the most unequal wealth distributions in the world (32). The difference in wealth among American populations impacts disease prevalence, as wealth correlates with a range of environmental variables influencing disease risk (5, 13, 63, 76). From a genetics perspective, environmental variables are likely to interact with disease-related genetic variants, a proportion of which are bound to be differentiated between continental populations (42, 80). Unfortunately, thus far research on genomic diversity and its role in disease susceptibility has been biased towards people of European ancestry. A broader characterization of the genetic diversity of American populations, as well as further analyses of the interaction of genetic and socioeconomic factors in disease susceptibility, is thus a priority for optimizing the future implementation in the region of health care approaches that exploit genomic information (25, 50). This need is further highlighted by projections that African Americans and Hispanics will represent approximately half of the US population by 2060 (29) and that the American continent is expected to exceed 1.2 billion inhabitants that same year, mainly through the growth of its Ibero-American population (99).

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