Chapter 18
How did Evolutionary Processes Influence the Genetic Structure of Humans in the Neotropics?

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Contents

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Abstract The Neotropics, encompassing Central and South America, stand out for their extraordinary biodiversity and cultural richness. Indigenous Americans exhibit remarkable cultural and linguistic diversity, but their genetic diversity is among the lowest among human populations. Environmental factors, including altitude, temperature, and biodiversity, have influenced the genetic makeup of Indigenous Americans since the earliest peopling of the America. Additionally, human impact, such as hunting, harvesting, and wildlife management, has significantly affected neotropical biodiversity. Niche construction, driven by plant and animal domestication and landscape modification, has played a crucial role in agriculture and has heavily influenced the genetic diversity of the region. The interplay between humans and their environment has shaped human genetic adaptations concerning diet and susceptibility to infectious diseases, affecting contemporary indigenous and admixed populations. Furthermore, migrations have played a significant role in shaping the genetic structure of neotropical human populations. Over time, multiple migration waves have contributed to the genetic diversity observed in present-day populations. The peopling of the America involved successive migrations dating back at least 15,000 years, followed by later post-contact migrations from various world regions. The study of genetic variation in neotropical populations has provided insights into their evolutionary history, demographic changes, and the impact of historical events like colonization and the transatlantic slave trade. Understanding the complex interplay of genetic, environmental, and historical factors is vital for conserving the biodiversity of humans and ecosystems. This chapter discusses the importance of migrations, demographic changes and natural selection in shaping the genetic diversity of neotropical human populations.

Keywords Genetic diversity · Indigenous Americans · Migration · Demographic Changes · Natural Selection

Learning Objectives

1. Understand the origins of Indigenous populations from America and how the peopling of the American continent have shaped the genetic diversity of ancient and present-day human populations.
2. Examine the genetic evidence, in the light of the archaeological and linguistic data regarding human occupation, population movements and demographic dynamics in this region, as well as their lasting effects on genetic diversity.
3. Explore the unique genetic profiles of Neotropical human populations, examining adaptations to diverse environments, diets, and pathogens.
4. Analyze the practical significance of studying human genetic diversity, considering its impact on human health.

18.1 Introduction

The Neotropical region is characterized by its rich and varied geography, including dense rainforests, expansive savannas, mountain ranges, and extensive river systems in the tropical areas of the American continent, spanning from Mexico to Argentina (Palma-Silva et al. 2022). This region comprised an astonishing array of plant and animal species, accounting for almost one third of global biodiversity (Rull 2008, 2011; Palma-Silva et al. 2022). Also, the Neotropics area includes the Amazon Rainforest, the biggest tropical rainforest in the world, and home to an enormous variety of plants, insects, mammals, and birds (Hoorn et al. 2010; Antonelli et al. 2018).

Regarding human history, Neotropics have a rich cultural scenario, with ancient civilizations that flourished in these regions during at least 15,000 years before European contact. Pre-contact civilizations diversified over this time, giving rise to various peoples, such as the great Mesoamerican and Andean empires (e.g., the Maya and Inca), as well as numerous different cultures of the lowlands of Central and South America (e.g., Tupi and Taino). These Indigenous peoples left behind a legacy of advanced agricultural practices, monumental architecture, intricate material culture, landscape modifications, and a vast number of domesticated, and semi-domesticated, species of plants, along with a few animals (Larson et al. 2014; Clement et al. 2015; Neves and Heckenberger 2019; Iriarte et al. 2020). These societies also held considerable knowledge about diverse topics including astronomy, engineering, medicine, writing, mathematics, among others (Graeber and Wengrow 2021).

Humans have been modifying and shaping the Neotropics region since their first arrival. One striking example suggests the human influence on the Late Pleistocene extinctions, especially of megafaunal species, not only in America, but also globally (Bergman et al. 2023). The extent to which this process was influenced by various other factors, including climate change and the repercussions of the end of the last glacial period, remains a subject of ongoing debate. During the Holocene humans also started to perform different types of niche construction, generating considerable environmental changes, such as the construction of domesticated landscapes, as represented by the Amazonian dark earths mostly concentrated along riverside areas, and also earthworks (particularly geoglyphs) which are currently estimated to number in the thousands in the Amazonian area (Iriarte et al. 2020; Peripato et al. 2023). Notably, this also includes the domestication of at least 83 plant species within the Amazon, making it one of the world's major crop domestication centers (Clement et al. 2015).

From a scientific perspective, the Neotropics provide a valuable setting for research in various disciplines, including ecology, biology, anthropology and genetics. Thus, regarding the study of human population genetics, first and foremost, the Neotropical region is characterized by unique and diverse ecosystems, leading to distinct genetic profiles among its human populations (Rull 2008, 2011; Adhikari et al. 2017; Castro E Silva et al. 2022; Palma-Silva et al. 2022). Understanding this genetic diversity offers insights into the historical processes of human migration, adaptation, health and the complex interactions between populations and their environments over time.

In this perspective, the purpose of this chapter is to provide an overview of some of the key questions surrounding the genetic diversity, history and evolution of humans in the Neotropics. In the first section we start by looking at how humans first came to be in this region and then explore some of the complex processes that have shaped the genetic makeup of people throughout the Neotropics over time. We also examine how human genetic diversity is distributed across the Neotropics, analyzing the connections between various populations and evaluating evidence of long-standing patterns of genetic continuity. Furthermore, we explore the genetic adaptations caused by natural selection in Neotropical environments in greater detail in the second section. We also highlight a few instances where native populations have adapted to the Neotropical environments, pathogens and food resources. In its third section, the chapter also considers the consequences arising from the genetic diversity of present-day Neotropical peoples, exploring the implications on both native and non-native populations. This chapter concludes with a consideration of the wider ramifications and importance of the knowledge that has been generated about the genetic diversity of humans in the Neotropics.

18.2 Neotropical Human Genetic Diversity

18.2.1 Peopling of the America

The peopling of the American continent trace back its origins to human migrations from East and Northeast Asia. Human history in Northeast Asia predates the Last Glacial Maximum (LGM; 26.5 to 19 thousand years ago) (Lambeck et al. 2014), by the presence of the Ancient North Siberians (Sikora et al. 2019) as evidenced by archaeological findings at sites like Yana River (31,600 years ago) and Mal'ta (24,000 years ago) (Raghavan et al. 2014; Graf and Buvit 2017). Although the Ancient North Siberians did not persist, their genetic legacy endured through admixture with East Asians around 20–18,000 years ago, likely giving rise to the ancestors of the Indigenous Americans peoples, or Native Americans (Figs. 18.1 and 18.2).

According to the Beringian standstill hypothesis, the ancestors of Native Americans experienced a period of isolation, either preceding or during their initial migration to America (Bonatto and Salzano 1997; Tamm et al. 2007; Hoffecker et al. 2023). This isolation is estimated to have endured for a minimum of 4600 years (Pinotti et al. 2019), though likely lasted more than 10,000 years (Tamm et al. 2007; Hoffecker et al. 2023). The precise reasons for this isolation, whether ecological barriers or Beringia acting as a bioclimatic refugium during the Last Glacial Maximum, are still not understood (Figs. 18.1 and 18.2) (Bonatto and Salzano

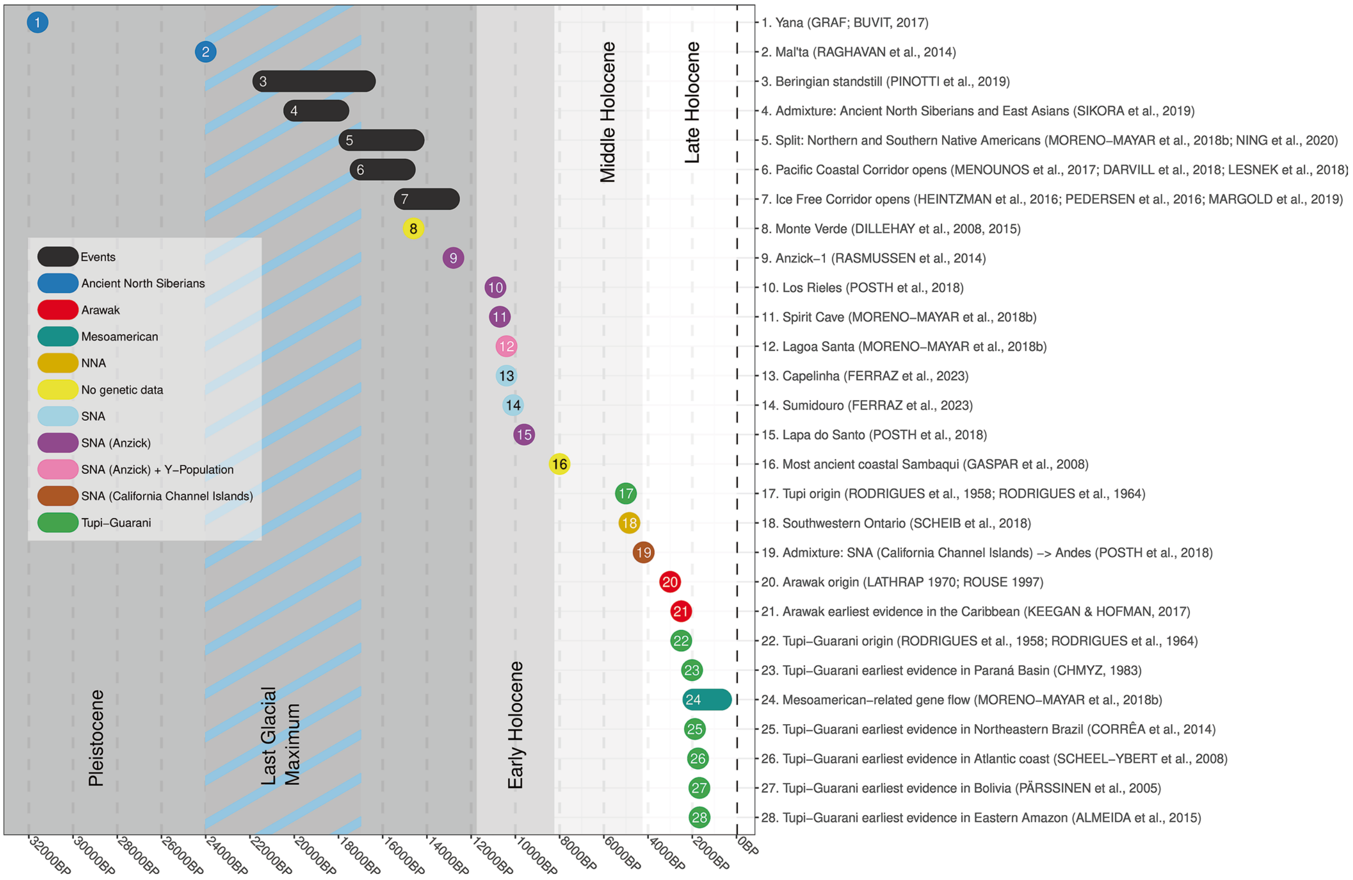

Fig. 18.1 Temporal overview of key events shaping neotropical human diversity. The timeline depicts major milestones in the history of Neotropical indigenous populations, as discussed in the text. These events are organized chronologically according to start date (confidence intervals are not shown), assigned numerical identifiers, and accompanied by concise descriptions and references. The back panel of the plot incorporates shades of gray to denote geological periods, with bright blue stripes representing the Last Glacial Maximum. Specific genetic or ethnolinguistic affiliations are color-coded, as indicated in the legend on the right of the plot. The events and their numerical identifiers presented in this figure are further detailed and geographically contextualized in Figs. 18.2 to 18.4

Fig. 18.2 Initial peopling of the America. This schematic representation illustrates the key milestones in the origin of Indigenous American peoples. The timeline encompasses the formation of Indigenous American ancestors in Northeast Asia through the admixture of Ancient North Siberians (ANS) and East Asians (EAS). It further highlights the Beringian standstill, which prompted the development of distinctive genetic diversity, followed by the fast post-Last Glacial Maximum dispersion into the American continent. The figure finishes with the major population split that gives rise to Northern and Southern Native American lineages (NNA and SNA, respectively). The ice sheet distribution during the Last Glacial Maximum is indicated in white. The map was plotted using the ‘sf’ and ‘ggplot2’ R packages, using the Orthographic projection centering on the North Pole (Latitude = 90; Longitude = 0). Points represent the approximate location of important archeological sites and events cited in the text, while the arrows simply indicate the direction of hypothetical dispersal routes. The numerical sequence of points has been arranged chronologically, referencing the primary timeline depicted in Fig. 18.1

1997; Tamm et al. 2007; Sikora et al. 2019). Subsequently, around 17.5 to 14.6 thousand years ago, the ancestors of Native Americans underwent genetic differentiation, leading to the divergence into northern and southern Native American branches (Figs. 18.1 and 18.2) (Moreno-Mayar et al. 2018b). This period of genetic divergence marks a crucial moment in the early history of Native American populations, shaping the foundational genetic structure of northern and southern branches that persisted through subsequent millennia.

Throughout the Last Glacial Maximum, extensive continental glaciers obstructed an inland route to the American continent from Beringia (Meltzer 2010). However, following the Last Glacial Maximum, an ice-free corridor opened along the Rocky Mountains, offering a feasible passage for human migration approximately 15–13 thousand years ago (Figs. 18.1, 18.2, and 18.3) (Perego et al. 2009; Potter et al. 2018). An alternative migratory route is the Pacific coastal corridor, supported by evidence of human arrival dating back to 17–15 thousand years ago (Figs. 18.1, 18.2, and 18.3). The latter pathway is currently considered the most plausible based on a convergence of multiple lines of evidence, spanning archaeological findings to genetic analyses (Perego et al. 2009; Lesnek et al. 2018). Although, both routes might have been used at different times, as the glaciers in Northern North America began to melt, creating pathways for our species to enter the new continent (Figs. 18.1, 18.2, and 18.3) (Lambeck et al. 2014; Potter et al. 2018). Then, likely around 16,000 years ago, humans started to migrate from Beringia into the American continent, marking the first time any hominin set foot on this continent (Skoglund and Reich 2016; Willerslev and Meltzer 2021; Silva et al. 2022).

Indigenous Americans, as revealed by extensive studies, predominantly trace their ancestry to either the Northern Native American (NNA) or Southern Native American (SNA) branches, with limited exceptions (Posth et al. 2018; Moreno-Mayar et al. 2018b). Notably, South American populations exhibit exclusive SNA ancestry, indicating that their initial dispersion occurred subsequent to the divergence of the SNA and NNA branches. While some populations in Central and South America display contributions from both lineages, it is inferred that these admixture events took place after the initial settlement (Scheib et al. 2018). However, distinctive cases are observed among speakers of Na-Dené and Eskimo-Aleut languages in northern North America, requiring additional gene flow from East Asian groups to explain their genetic diversity (Rasmussen et al. 2010; Reich et al. 2012; Moreno-Mayar et al. 2018a; Flegontov et al. 2019).

Other exceptions are several contemporary Indigenous groups in the Amazon (Karitiana and Suruí), as well as the Xavante from the Brazilian central plateau, along with an ancient individual from the Lagoa Santa site in Minas Gerais dating back to 10,000 years ago, which display an increased genetic affinity with Australasian populations (Figs. 18.1 and 18.3) (Raghavan et al. 2015; Skoglund et al. 2015; Moreno-Mayar et al. 2018b; Campelo dos Santos et al. 2022). Recent findings have expanded this connection to include two additional modern-day groups from the Central-West Brazilian region (Guaraní Kaiowá) and the northern Peruvian Pacific coast (Chotuna), indicating a wider distribution of this ancestry contribution (e Silva et al. 2021). This apparent excess affinity with Australasians in certain South American populations has been attributed to the contribution of an unsampled population, known as "*Ypikuéra*" (meaning "ancestral" in Tupi language) or "Y." This discovery implies a more intricate population history, involving either an additional influx from Beringia or a significant genetic structure in the ancestors of Native Americans. However, the percentage of this additional ancestry in the identified groups remains relatively low, ranging from 1% to 3% of the total genetic makeup (Skoglund et al. 2015; e Silva et al. 2021).

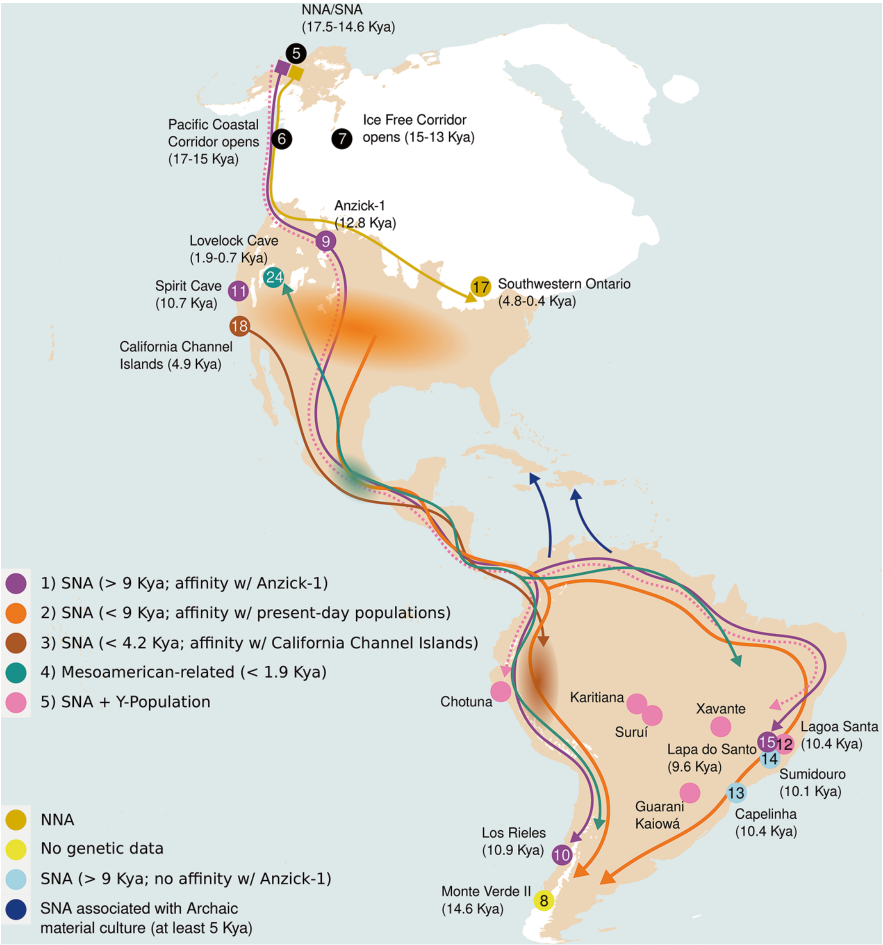

Fig. 18.3 Origins of Caribbean, Central, and South American natives. This figure shows the four main ancestry components that formed South American Indigenous populations. After splitting from the Northern Native American (NNA; green) lineage, the initial wave of settlers in the region corresponds to a Southern Native American (SNA) group genetically linked to Anzick-1 (purple). Subsequently, a second SNA influx (orange), distinct in its lack of this genetic affinity to Anzick-1 and higher affinity to present-day Indigenous populations, at least partially replaced the first group starting approximately 9000 years ago, however some exceptions contradict this model (red). Beyond these two primary dispersals, a distinctive genetic contribution emerged after 4.2 thousand years ago and geographically confined to Central Andes. This component is genetically linked to SNA ancient individuals from the California Channel Islands (brown). A fourth ancestry is detected as an excess affinity between some contemporary and ancient individuals and Australasian populations (pink), modeled as the contribution of an unsampled group called Y-population. At least 5 thousand years ago an SNA group associated with so-called Archaic material culture started to appear in Caribbean Islands (dark green). The map was plotted using the ‘sf’ and ‘ggplot2’ R packages, using the Orthographic projection centering on the Caribbean (Latitude = 20; Longitude = −80). The ice sheet distribution during the Last Glacial Maximum is indicated in white. The numerical sequence of points has been arranged chronologically, referencing the primary timeline depicted in Fig. 18.1

An intriguing hypothesis posits that the genetic connection observed between certain Indigenous American and Australasian populations may stem from shared archaic introgression, potentially involving Denisovans, Neanderthals, or another unidentified archaic hominin. The widespread signal of low Denisovan ancestry across Eastern Eurasian and Native American populations raises questions (Qin and Stoneking 2015; Peyrégne et al. 2023). Notably, Oceania displays a heightened Denisovan ancestry compared to Eastern Eurasians and Indigenous Americans. In Oceania, this ancestry correlates with a New Guinean ancestry rather than an Australian ancestry, suggesting recent gene flow from New Guinea as a contributing factor. Conversely, Denisovan ancestry in Eastern Eurasians and Indigenous American populations correlates equally with both New Guinea and Australian ancestry, pointing toward a common source for Denisovan ancestry in these groups (Qin and Stoneking 2015). If this shared Denisovan ancestry plays a role in the observed genetic affinity between certain Indigenous Americans and Australasian populations is still an open question. To date, there is no supporting evidence indicating a correlation between Denisovan ancestry in Asians or Native Americans and Australasian ancestry (Peyrégne et al. 2023).

In conclusion, in South America, existing data strongly suggest the occurrence of three distinct dispersals of SNA populations into the continent (Posth et al. 2018). The initial group, closely related to Anzick-1, gave way around 9000 years ago to a second SNA influx lacking this genetic affinity but demonstrating increased affinity with contemporary Indigenous populations, hinting at a scenario of at least partial demographic replacement (Figs. 18.1 and 18.3). Furthermore, a third population influx, with genetic ties to individuals from the California Channel Islands, contributed to populations in the central Andes before 4200 years ago, potentially associated with the diffusion of agriculture from Mesoamerica (Figs. 18.1 and 18.3) (Sutter 2021). Notably, another study (Moreno-Mayar et al. 2018b (https://www.science.org/doi/10.1126/science.aav2621)) identified a significant and recent influx of Mesoamerican-related ancestry into Indigenous populations spanning both North and South America (Figs. 18.1 and 18.3). While this genetic signal underscores a shared demographic history across geographically distant regions, including the Lovelock Cave site in North America and contemporary South American Indigenous populations, its potential relationship to the aforementioned evidence of North American gene flow into Andean populations remains unclear. This admixture likely reflects the movement of relatively small groups that, while contributing genetically to local populations, did not lead to their complete demographic or cultural replacement. The predominant genetic and archaeological evidence supports a settlement of the continent after the Last Glacial Maximum. However, a handful of potential archaeological sites dating back to the Last Glacial Maximum era, or even earlier, introduces the possibility of a more prolonged human presence on the continent, albeit the evidence supporting this possibility remains very limited (Silva et al. 2022).

18.3 Holocene Population Dynamics in the Neotropics

18.3.1 Amazonia and Andes

South America experienced a rapid human dispersal with the arrival of initial populations approximately 15–16 thousand years ago (Prates et al. 2020). Early populations from this region likely separated into two groups, independently migrating along the west and east coasts (Bodner et al. 2012; Goldberg et al. 2016; Brandini et al. 2018; Gómez-Carballa et al. 2018; Prates et al. 2020). An alternative hypothesis proposes that the Andes, Amazon, and coastal areas in South America were colonized by three distinct lineages that diverged before entering the continent (Rothhammer and Dillehay 2009), with the possibility that the Andean region was settled through a later split from the Pacific coastal branch (Skoglund and Reich 2016). Population history models for indigenous Peruvians support the latter idea, with an inferred split date of around 12,000 years ago, aligning with the trifurcation hypothesis (Harris et al. 2018). These findings indicate that significant lineage splits occurred early in the settlement of South America, and their dispersion was rapid. This is supported by the earliest evidence of human presence in the Southern Cone, which comes from Monte Verde II archeological site, dated to 14.6 thousand years ago (Figs. 18.1 and 18.3) (Dillehay 2009; Dillehay et al. 2015) and the discovery of ancient human remains dating back more than 9000 years ago on both sides of the continent. Noteworthy locations include Cuncaicha in Peru and Los Rieles in Chile on the Pacific side, as well as Lapa do Santo and Lagoa Santa in Brazil on the Atlantic side (Figs. 18.1 and 18.3) (Posth et al. 2018; Moreno-Mayar et al. 2018b). Notably, there is evidence of long-term genetic continuity within significant continental areas. For instance, permanent settlements in the Andes began around 9000 years ago, while genetic analyses suggest enduring continuity in the Lake Titicaca region, possibly dating back to 3.8 or even 7 thousand years ago, persisting in present-day Aymara and Quechua-speaking peoples (Lindo et al. 2018).

Eastern South America boasts some of the earliest human remains in America, found at sites in the Lagoa Santa region in southeastern Brazil, dating back to 10.4–9.6 thousand years ago (Box 18.1). Individuals from these sites are inferred to be descendants of the first southern Native American population influx (Posth et al. 2018; Moreno-Mayar et al. 2018b). As discussed before, around 9000 years ago, a new southern Native American group began to arrive, partially displacing the early migrants, as evidenced by their reduced affinity with Anzick1 and increased affinity with modern South American indigenous peoples (Posth et al. 2018; Moreno-Mayar et al. 2018b). However, a recent study (Ferraz et al. 2023) analyzing 34 ancient individuals from coastal and riverine Sambaqui sites (Box 18.1) has revealed individuals older than 9000 years ago lacking substantial affinity to Anzick-1 (Capelinha and Sumidouro; Figs. 18.1 and 18.3), contradicting the narrative of two sequential waves of migration into South America, one with Anzick-1-related ancestry and another without (Ferraz et al. 2023).

Box 18.1: Lagoa Santa peoples and Sambaqui mound builders

Lagoa Santa sites are famous for their well-preserved early Holocene human skeletons. The sites comprise caves with a sheltered area and have a rich history of human occupation spanning three distinct phases: early, middle, and late Holocene (Strauss et al. 2020). Excavations since 2001 have uncovered 39 human burials, predominantly from the late phase of the early Holocene (Posth et al. 2018; Moreno-Mayar et al. 2018b), placing Lagoa Santa as one of the most densely populated sites in this period. Ritualistic treatment of the dead, including mutilation and defleshing was practiced around 9600–9400 calBP, depicting the ancient case of ritualistic funeral in the neotropics (Strauss et al. 2015). Sediments indicate repeated combustion activities, suggesting an early Archaic economy focused on staple carbohydrates and hunting. The lithic assemblage consists mainly of small flakes and cores, with a shift towards locally available crystal quartz as the dominant raw material around 9900 calBP. Also, low mobility is supported by isotopic and anthropological studies (Strauss et al. 2020). The individuals excavated from the archaeological sites of Lagoa Santa exhibit Paleoamerican craniofacial morphology (Neves and Hubbe 2005), meaning they are morphologically different from present-day Native Americans. However, genomic studies have shown that the skeletons recovered from this region, although morphologically distinct, originate from the early Beringian populations that populated South America, genetically closely related to present-day Indigenous peoples (Posth et al. 2018; Moreno-Mayar et al. 2018b). In this sense, both the emblematic Luzia and her contemporaries from Lagoa Santa are believed to originate from a dispersal through Beringia, as all the earliest inhabitants of the American continent. The morphological differences between Paleoamericans and other ancient and modern individuals from America may be explained by microevolutionary factors following the arrival of the first Americans on the continent (González-José et al. 2008).

The Sambaqui, a term used by Tupi speakers, are shell mounds produced by diverse fisher-gatherer communities, along the Atlantic coast, as well as riverside, and lake areas, starting at least 8000 years ago (Gaspar et al. 2008). These groups likely occupied the Brazilian coast until the arrival of Tupi-Guarani and Macro-Jê speakers, suggested by the presence of ceramics from Tupiguarani and Taquara/Itararé traditions in the uppermost layers of some Sambaqui (Gaspar et al. 2008). Due to the limited number of individuals studied, the relationship between the builders of Sambaqui mounds and contemporary indigenous populations remains largely unexplored. Nevertheless, recent data suggests a stronger affinity between the Sambaqui builders and present-day Jê speakers when compared to other indigenous groups in eastern South America. It is crucial to interpret this finding cautiously, given that the analyzed Jê-speaking communities exhibit a high degree of endogamy (Castro E Silva et al. 2020, 2022; Ferraz et al. 2023). The observed high level of endogamy can result in an accelerated genetic drift effect, potentially introducing biases in inferences related to genetic similarity (Moorjani and Hellenthal 2023).

After the initial population dispersals, South America's diverse climates and environments led to a demographic and evolutionary history characterized by significant variation across time and space. In this sense, a comprehensive analysis incorporating calibrated radiocarbon datings from 13 to 2 thousand years ago and spanning 5464 datings from 1147 archaeological sites, reveals two main phases in this demographic history (Goldberg et al. 2016). The first phase, from 13 to 5.5 thousand years ago, witnessed rapid geographic expansion followed by density-dependent population growth. Population sizes increased swiftly until reaching carrying capacity, after which they would have remained relatively constant between 9 and 5.5 thousand years ago. Additionally, a recent analysis of high-quality curated radiocarbon dates supports that demographic stability was achieved by 11 thousand years ago (Prates et al. 2020). Around 5.5 thousand years ago, the adoption of a sedentary lifestyle and intensified food production marked the onset of a new phase characterized by exponential population growth, particularly in cultural centers, notably those situated in the central and northern Andes. According to this model, more than half of the population growth occurred during this second stage (Goldberg et al. 2016). However, studies indicate that population growth rates varied significantly between regions and over time. In the Andes, expansion began around 9000 years ago, earlier than in other eastern regions such as Patagonia, where a more gradual and late expansion initiated between 7.5 and 5 thousand years ago (Perez et al. 2016, 2017; Prates et al. 2020).

The shift in human population growth rates aligns with a Middle Holocene climatic change, transitioning from previously dry and variable precipitation to consistently increased precipitation in the Southern Hemisphere's tropical forests (Iriarte et al. 2017). In this sense, an increase in precipitation expanded tropical rainforests between 5 and 1 thousand years ago, fostering human population growth and movement, especially in the southern Amazon forest (Iriarte et al. 2017). This shift to wetter climates also led to increased sedentism and the prominence of agriculture, evidenced by an elevated rate of landscape modifications during the Late Holocene (Iriarte et al. 2020). Plant domestication in South America broadly coincided with the extinction of the last megafauna species around 9–8 thousand years ago, with some plant species fully domesticated by 6 thousand years ago. However, the initial use of various plants dates back to the Late Pleistocene or Early Holocene (Iriarte et al. 2020). Although the boost in food production did not directly translate into an increased population growth rate, it mainly occurred in specific cultural centers, especially in the Andes, where intensive agricultural systems took precedence as the primary subsistence strategy (Goldberg et al. 2016; Perez et al. 2017).

Some studies propose that this second phase of exponential growth continued until the arrival of Europeans, especially in Amazonia (Arroyo-Kalin 2017). In contrast, other research suggests a slowdown or even a decline in population size in certain areas, potentially due to reaching carrying capacity, autochthonous diseases, or environmental and social changes (Arroyo-Kalin and Riris 2021; Bush et al. 2021). Nevertheless, as expected the majority of genetic and archaeological evidence indicates the most significant population decrease rate occurred after the arrival of Europeans in America (Browning et al. 2018; Castro E Silva et al. 2022).

The Andes-Amazon divide model, historically utilized to understand various archaeological, ethnolinguistic, genetic, and demographic patterns in South America, more recently has been criticized for limiting and biasing the study of indigenous peoples, particularly regarding genetic diversity (Pearce et al. 2020). This model prompts an evolutionary framework where opposing dynamics have historically shaped the Andes and Amazonia (Tarazona-Santos et al. 2001). The Andes, characterized by long-standing large populations and intensive food production, led to highly hierarchical and interconnected societies with preserved genetic diversity within populations and reduced genetic differentiation across populations. In contrast, Amazonia, inhabited by small and isolated hunter-gatherer groups in diverse environments, exhibited low within-population genetic diversity and high among-population genetic differentiation due to limited gene flow.

The reassessment of cultural and demographic complexity in the Andes and Amazonia is ongoing as evidence of denser occupation and complex cultures in the Amazon grows (Heckenberger et al. 2003; Heckenberger and Neves 2009; Roosevelt 2013; Piperno et al. 2015; Clement et al. 2015; Pearce et al. 2020). Recent findings reveal highly populated permanent settlements along major rivers, establishing Amazonia as a major center for crop domestication with at least 83 domesticated species, thousands of geoglyphs and even cities within the Amazon (Iriarte et al. 2020; Peripato et al. 2023; Rostain et al. 2024). These developments involved extensive environmental modifications, including the creation of Amazonian dark earths (ADEs), crucial for plant domestication and food production, contributing to increased population growth rates (Clement et al. 2015; Neves and Heckenberger 2019; Iriarte et al. 2020).

18.3.2 Central America and the Caribbean

Certain regions, shaped by unique geographical factors, exhibit distinctive genetic variation patterns, such as Central America, the Caribbean, and the Southern Cone. Central America, was the exclusive entry point for the dispersal of humans into South America and the crucial link between distinct genetic lineages from North and South America, witnessing through time extensive population movements and the exchange of resources, ideas, and populations (Capodiferro et al. 2021). The archaeological and paleoecological records strongly suggest a continuous human occupation of the Isthmo-Colombian region dating back 16 thousand years (Ranere and Cooke 2021). Whereas, patterns of regional genetic continuity in some indigenous communities in continental Central America have been inferred through the analysis of mitochondrial DNA data and nuclear genomes (Reich et al. 2012). While the examination of ancient individuals predating the arrival of Europeans (around 1.4–0.6 thousand years ago) reveals a remarkable genetic continuity spanning nearly a thousand years, with these ancient lineages persisting in the Indigenous

American component present in contemporary admixed populations from the region (Capodiferro et al. 2021).

The analysis of ancient individuals from the Isthmo-Colombian region also unveiled the presence of a unique ancestry component distinct from other areas of the continent. This distinctive ancestry component can be modeled as the result of an admixture event between two distinct SNA lineages originating in North America. Notably, one of these lineages involves an additional contribution from another unsampled population, referred to as unsampled population I (Capodiferro et al. 2021). In turn, the oldest archaeological sites discovered in the Caribbean Islands date back approximately 8 thousand years before the present and are located on the island of Trinidad near the northern coast of South America (Napolitano et al. 2019). Dating between 5.8 and 2.5 thousand years ago, archaeological sites showcasing stone tool technologies from the Lithic and Archaic eras are dispersed across Barbados, Cuba, Hispaniola, Puerto Rico, St. Martin, and Tobago (Napolitano et al. 2019). Comparatively, the oldest archaeological sites identified in Jamaica, San Salvador, and St. Lucia date back to at most 1800 years ago.

The genetic composition of Caribbean human populations is thought to have been shaped by at least two major dispersal events occurring at different times. The first, dating back at least 6 thousand years ago, brought individuals with so-called Archaic stone tool technologies (Fig. 18.3) (Napolitano et al. 2019), although earlier studies proposed two separate population dispersals from South America during this period (Schroeder et al. 2018; Nägele et al. 2020). Analyses suggest that individuals associated with the Archaic period in Cuba derive from a single source (Fernandes et al. 2021), contradicting previous evidence of additional migration with an affinity to North American individuals (Nägele et al. 2020). Approximately 2500 years ago, a new wave of people from the Ceramic Age, originating from Arawak-speaking populations in northern South America, is believed to have arrived (Figs. 18.1 and 18.4). The dispersal of the Ceramic Age ancestry component into the Caribbeans will be further explored in the following section.

18.3.3 Southern Cone

Whereas, in the Southern Cone, the Monte Verde II site in Patagonia stands as the earliest indisputable evidence of human activity, dating back to 14.6 thousand years ago (Figs. 18.1 and 18.3) (Dillehay 2009). Additionally, the region has yielded the most ancient DNA ever genotyped in the continent (Los Rieles site in Chile), dating back 12 thousand years (Posth et al. 2018). These findings highlight an exceptionally rapid colonization of the Southern Cone following the initial arrival on the continent around 16–15 thousand years ago (Prates et al. 2020). Even Tierra del Fuego, the continent's southernmost point, was inhabited before 8000 years ago, a time when it remained connected to South America due to substantially lower sea levels (Morello et al. 2012).

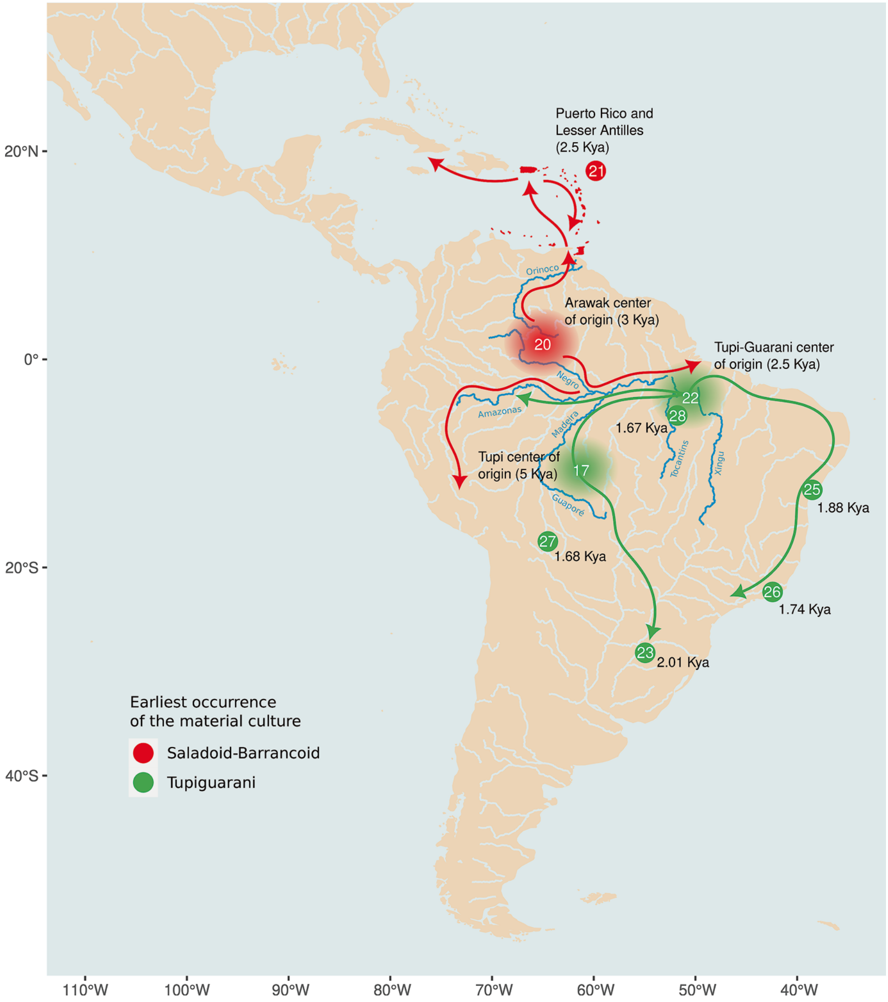

Fig. 18.4 Late Holocene population expansions. This figure summarizes the hypothesis for the Arawak and Tupi-Guarani demic diffusion based on linguistic, archaeological and genetic data, as discussed in the text. Green points on the map pinpoint the approximate location of the earliest Tupiguarani material culture occurrences in the limits of their geographic expansion. While the Caribbean Islands, highlighted in red, indicate where the most ancient evidence of Saladoid-Barrancoid culture was found. Meanwhile, arrows are used to illustrate the hypothetical dispersal routes. Shaded areas represent the center of origin of the Arawak, Tupi and Tupi-Guarani linguistic groups. Important rivers mentioned in the text are labeled and highlighted in a darker tone of blue. The map was generated using the ‘sf’ and ‘ggplot2’ R packages, employing the Robinson projection. The numerical sequence of points has been arranged chronologically, referencing the primary timeline depicted in Fig. 18.1

During the Middle Holocene, the ancestors of Southern Cone populations underwent divergence into three primary lineages, as evidenced by ancient individuals from the Argentinean Pampas, Patagonia, and the Center-Southern region of Chile. The lineage originating from the Center-Southern region of Chile represents a group of ancestors to contemporaneous Mapuche population, while the Patagonian lineage corresponds to ancestors of present-day peoples in the Patagonia region (Nakatsuka et al. 2020). Notably, present-day populations from the Southern Cone exhibit elevated genetic affinities among themselves and with contemporary indigenous communities in Central-Southern Chile (Raghavan et al. 2015; la Fuente et al. 2018).

18.4 Population Expansions of the Late Holocene

A transformational time marked by unprecedented population growth along with major worldwide population movements arose during the Late Holocene (Loog et al. 2017; Stoneking et al. 2023). Evidence indicates this demographic growth was sustained by the intensification of food production, impulsed by long processes of landscape modification, the transition to sedentary lifestyles, advancements in technology, but most importantly by plant and animal domestication. The confluence of these factors played a pivotal role in creating demographic expansions and large-scale migratory patterns that have left enduring imprints on the patterns of genetic and cultural diversity distribution across the world (Sokal et al. 1991; Cordaux et al. 2004; Wen et al. 2004; de Filippo et al. 2012; Ammerman and Cavalli-sforza 2014).

These processes also significantly increased the impact of infectious diseases, due to the close proximity between humans and their domesticated animals. Also, the concentration of human populations in densely inhabited areas enhanced pathogen transmission between populations due to migrations (Stoneking et al. 2023). Many infectious diseases, including tuberculosis, plague, herpes, and chickenpox, have their origins in this period (Sikora et al. 2023). The increased selective pressure originated by this wide range of diseases has been recently implicated in the evolution of immune genes, likely contributing to an increased genetic risk of autoimmune diseases such as multiple sclerosis (Barrie et al. 2024).

Furthermore, according to the agricultural expansion hypothesis, between approximately 10,500 and 4500 years ago, the development of food production, centered on the domestication of a limited number of wild plant and animal species, occurred independently in at least nine agriculture and herding homelands, distributed across the world, leading to the transition from hunter-gatherer to farming (and/or herding) subsistence strategy in these places (Diamond and Bellwood 2003).

In line with this hypothesis, the agricultural expansions can be attributed to three key advantages acquired by farmers over hunter-gatherers. Firstly, farmers achieved higher food yields per unit of productive land. Secondly, while usually hunter-gatherer societies are mobile, food-producing societies adopted a sedentary lifestyle, allowing them to accumulate stored food surpluses. Lastly, epidemic infectious diseases that originated from domestic animals provided an additional advantage when facing hunter-gatherer groups. These combined advantages facilitated the displacement, replacement or assimilation of hunter-gatherers in the areas of expansion of these early farmers/herders (Diamond and Bellwood 2003). Numerous examples of this phenomenon have been documented across the world, including the expansion of the Bantu in Africa, the Austronesian in South Asia, Oceania, Polynesia, and Madagascar, and most famously the Indo-European in Eurasia (Stoneking et al. 2023).

By the Late Holocene populations in Central and South America are believed to have broadly settled into more or less cohesive regions, showing prolonged continuity for several thousand years prior to the European arrival (Willerslev and Meltzer 2021). Despite the emergence of Andean civilizations (e.g. Norte Chico, Nazca, Wari, Tiwanaku, and Inca) the population movements during this time are supposed to have been relatively smaller in scale compared to earlier periods of the continent. In this sense, the territorial expansion of these populations over large areas may not have entailed extensive, widespread movements of people.

In spite of that, South America's linguistic landscape reveals compelling correlations with its material culture traditions, particularly the material culture traditions of the Late Holocene. Major language families from South American lowlands, namely Arawak, Karib, Jê (a linguistic family of the Macro-Jê stock), and Tupi-Guarani (a linguistic family of the Tupi stock), are posited to have origins and dispersal centers in the Amazonian region (Dixon and Aikhenvald 2006; Neves 2011). While lacking complete correspondence, existing evidence supports the hypothesis that the geographic distribution of these language families aligns at least partially with some Late Holocene material culture traditions (Noelli 2008; Castro E Silva et al. 2020; Gregorio de Souza et al. 2020; Nägele et al. 2020). Demic diffusion is proposed as the mechanism through which these languages and material culture were propagated together (Box 18.2) (Gregorio de Souza et al. 2020).

Box 18.2: Demic or cultural diffusion?

What are the mechanisms governing the diffusion of farming practices and languages? Did these phenomena occur through migrations of farming communities, thereby introducing their lifestyle and languages (referred to as demic diffusion), or did local hunter-gatherer groups adopt farming and language from nearby farmers (characterized as cultural diffusion)? Moreover, in the context of demic diffusion, the fate of local hunter-gatherer groups becomes crucial: were they entirely displaced/replaced, or did they undergo partial assimilation into the expanding farmer communities?

Although archaeology, biological anthropology, and linguistics were the only sources of evidence in the past, currently the ultimate resolution usually lies within the realm of genetics. Assuming the identification of the homeland of the original farming group and recognizing genetic distinctions between these individuals and the groups into whose territories they expanded, genetic investigations can elucidate the degree to which contemporary populations possess ancestry derived from farmers versus indigenous hunter-gatherer populations (Stoneking et al. 2023).

Specifically, evidence suggests that the Arawak, Karib, Jê, and Tupi-Guarani linguistic families respectively overlap to the Saladoid-Barrancoid, Incised-Punctate, Una, and Tupiguarani material culture traditions (Noelli 2008; Corrêa 2015). Notably, only the Saladoid-Barrancoid and Tupiguarani cultural complexes exhibit a broader geographical presence outside de boundaries of the Amazonian basin. The Saladoid-Barrancoid culture extended its influence to the Caribbean islands of Puerto Rico and Hispaniola, while the Tupiguarani complex spanned over 5000 kilometers across eastern South America, encompassing diverse ecosystems such as the Brazilian highlands, Caatinga, Atlantic forests, and the Argentine pampas (Keegan 1995; Noelli 1998, 2008). Subsequently, we undertake a more intricate exploration of the Tupi Expansion, which is the most well-known from a genetic standpoint. Additionally, we provide a brief discussion of the Late Holocene dispersals into the Caribbean islands, representing the only portion of the Arawak expansion studied using genetic data. The aim is to present a comprehensive illustration of how genetics is being used to infer population dynamics in the Neotropics throughout the Late Holocene.

18.4.1 Tupi Expansion

Tupi speakers represent a group of Amazonian peoples which originated and adapted specifically to the challenges of forest life, particularly thriving in riverine forest environments. The widespread geographical distribution of the Tupi people has been a subject of considerable interest for archaeologists and linguists for a long time. Over the years, there has been a prevailing hypothesis suggesting that the Tupi people originated and expanded from a unique common origin in the Amazon (Noelli 1998, 2008; Castro E Silva and Hünemeier 2023). Several lines of evidence converge to support that the Tupi's center of origin lies in the region between the Madeira and Guaporé rivers in Southwestern Amazonia (Figs. 18.1 and 18.4). One compelling line of evidence is the higher linguistic diversity among Tupi speakers in this area, notably characterized by the presence of the most deeply diverged languages within the Tupi language family (Campbell and Grondona 2012; Walker et al. 2012). Additionally, genetic diversity in populations from this region exceeds that found in populations from other areas (Ramallo et al. 2013; Santos et al. 2015). Particularly in the case of the Tupi-Guarani, the most widespread of the 10 Tupi linguistic families, evidences suggest a center of dispersal in a region of eastern Amazonia between the Xingu and Tocantins rivers (Figs. 18.1 and 18.4) (Almeida and Neves 2015; Souza Mello and Kneip 2017; O'Hagan et al. 2019).

Aligned with the agricultural expansion hypothesis, the Tupi people developed an agricultural food production system, however diverging significantly from the prevalent strategies adopted by agriculturalists worldwide. In contrast to the common practice of monocultures involving one or more cereal species in highly anthropized environments, the Tupi developed a system known as polyculture agroforestry (Neves 2013; Iriarte et al. 2020). This distinctive approach seamlessly integrated the cultivation of domesticated plants with the management of semi and non-domesticated plants within forest environments. The Tupi's agricultural practices showcase their cultural adaptation to the intricate ecosystems of the Amazon rainforest, reflecting a profound understanding of sustainable and resilient food production systems tailored to their unique environmental context.

The available evidence, including genetic analyses, support a demic diffusion model aligning with a longstanding hypothesis positing that the dispersal of the Tupi-Guarani population from Amazonia was propelled by continuous demographic expansion sustained by the development of their agriculturalist food production systems (Brochado 1984; Corrêa 2015; Castro E Silva et al. 2020). Moreover, insights from paleoecological and paleoclimatic investigations suggest that a more humid climate during the Late Holocene led to forest expansions in the southern Hemisphere around 3 to 2 thousand years ago, coinciding with the onset of the Tupi Expansion (Iriarte et al. 2017). The expansion of riverine forests, in particular, would have presented an ecological opportunity for the Tupi-Guarani population to expand, as it provided the essential environmental conditions conducive to their adapted polyculture agroforestry practices for food production. This highlights how the confluence of ongoing cultural evolution of Indigenous communities in the region, encompassing aspects such as plant domestication, landscape modification, and the development of food production systems with opportune environmental changes, resulted in heightened rates of population growth and, subsequently, territorial expansion in some instances.

The Tupiguarani material culture tradition can be internally classified into three primary sub traditions: Guaraní, Amazon Tupinambá, and Atlantic Forest Tupinambá. These subtraditions are primarily distributed in the Paraná Basin, southeastern Amazonia, and the Atlantic coast, respectively (Almeida and Neves 2015). Current archeological evidence indicates the initial appearance of Tupiguarani ceramics in these regions occurred approximately between 1600 and 2010 years ago (Figs. 18.1 and 18.4) (Chmyz 1983; Pärssinen et al. 2005; Scheel-Ybert et al. 2008; Corrêa 2015; Almeida and Neves 2015). The model that emerges for the expansion of the Tupi-Guarani, with support from the current genetic evidence, is that a branch of the Tupi-Guarani migrated southward, settling in the Paraná basin and eventually giving rise to the Guarani (Fig. 18.4). Simultaneously, another branch radiated towards the mouth of the Amazon river, subsequently dispersing along the Atlantic coast, extending down to present-day Southeastern Brazil, forming the Tupi coastal populations, collective denoted as Tupinambá (Fig. 18.4) (Brochado 1984; Corrêa 2015; Castro E Silva et al. 2020).

18.4.2 Arawak Expansion into the Caribbean Islands

In turn, a connection between the Saladoid-Barrancoid ceramics and Arawakan languages was first proposed by American archeologist Donald Lathrap (Lathrap 1970). According to existing evidence, it is posited that the Arawak population originated from a dispersion center located in the northwestern Amazonian region, spanning from the Upper Amazon river in Brazil to the Middle Orinoco river in Venezuela (Figs. 18.1 and 18.4) (Lathrap 1970; Rouse 1997). Linguistic analysis suggests that approximately 3000 years ago, Arawak-speaking communities experienced a rapid dispersion across the Negro and Orinoco floodplains. This dispersion extended through the Amazon, reaching as far as the Caribbean and Guyana coasts, and finally the Antilles (Figs. 18.1 and 18.4) (Hill and Santos-Granero 2002; Heckenberger 2013).

In recent years, genetic studies have played a pivotal role in shedding light on the intricate details of human settlement in the Caribbean islands by Arawak speaking populations. These investigations have provided a more nuanced understanding of the population dynamics and migratory patterns that shaped the genetic landscape of the region. By delving into the genomic data of present-day populations and analyzing ancient DNA from archaeological sites, researchers have been able to trace the footsteps of these ancestral communities.

The image that emerges from this research is that, circa 2500 years ago, Saladoid material culture started to appear in Puerto Rico and the northern Lesser Antilles marking the start of the Ceramic Age in the Caribbean (Figs. 18.1 and 18.4) (Keegan and Hofman 2017). The Ceramic Age newcomers would have encountered Archaic Age peoples and interacted, yet little to no evidence of admixture has been identified (Napolitano et al. 2019; Nägele et al. 2020). In the majority of the Greater Antilles, the Archaic Age ancestry component underwent a substantial replacement (>98%) by Ceramic Age ancestry. Contrarily, in Cuba, the Archaic Age ancestry persisted with minimal admixture for over 2500 years (Fernandes et al. 2021). Most Ceramic Age individuals are inferred to be largely genetically homogenous and linked to a northwestern South America origin (Fernandes et al. 2021), the hypothesized Arawak homeland (Lathrap 1970; Rouse 1997). Finally, present-day individuals from Puerto Rico and Cuba exhibit approximately 14% of their ancestry attributed to the Ceramic Age ancestors.

18.5 Human Genetic Adaptations to the Neotropical Environments

Neotropical America, with its vast expanses of tropical rainforests, high mountains, savannas, and deserts, is home to a rich diversity of ethnic groups and cultures. Over millennia, evolutionary processes, especially natural selection, have played a crucial role in shaping the genetic diversity and differentiation of these populations. This selective force has led to genetic (Fig. 18.5), physiological and cultural adaptations in response to the region's diverse environmental, climatic and pathogenic conditions. In this diverse landscape, human evolution unfolded, with local conditions and resources playing a fundamental role in driving natural selection.

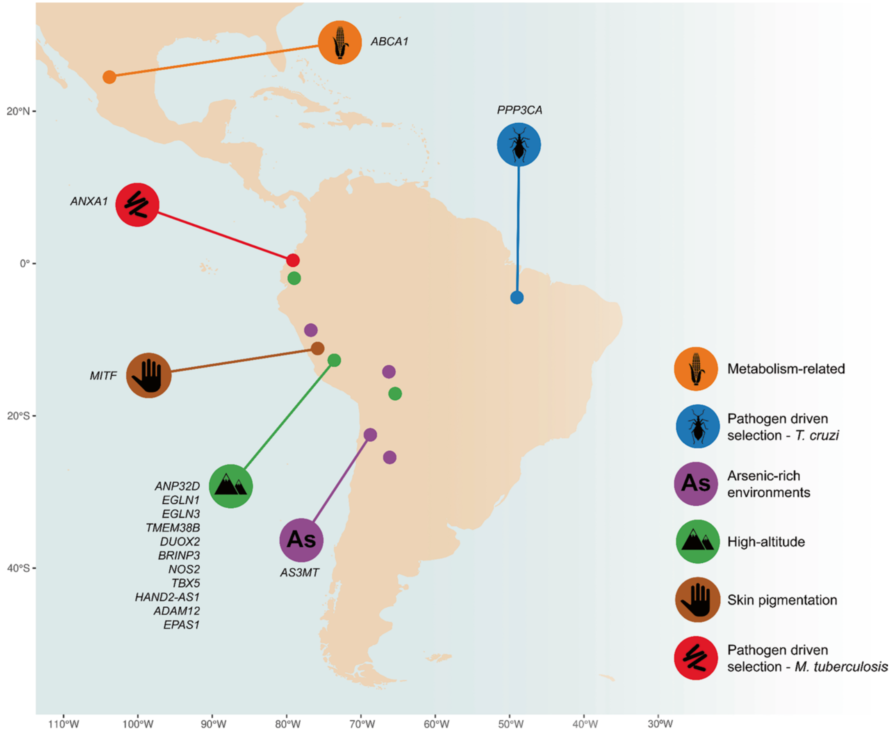

Fig. 18.5 Genetic Adaptations to the Neotropical Environments. This figure highlights some genetic signatures of natural selection found in the Neotropical environment. The dots in orange represent signs of selection in genes related to metabolism, in blue, selection directed by the pathogen *T. cruzi*, in red by *M. tuberculosis*, in purple the arsenic-rich environment, and in brown and green in response to high altitudes. (Modified from Hünemeier (2024))

18.5.1 Adaptations to the Andean highlands

Continuously inhabited for at least 12,000 years by modern humans (Rademaker et al. 2014), the Andes highlands stand as one of the most extreme environments in the Neotropical region, imposing a myriad of challenges on organisms that necessitate physiological and ecological adaptations for survival (Espinoza-Navarro et al. 2011). With average altitudes reaching 4000 meters, the Andes present low oxygen concentrations, extreme temperatures, harsh weather conditions, and harmful doses of ultraviolet radiation, all compounded by limited resources. These local characteristics have spurred numerous studies to understand how organisms respond to this seemingly inhospitable environment.

Undoubtedly, the primary challenge posed by the Andean highlands is the reduction in atmospheric pressure, leading to a diminished availability of oxygen. This condition, referred to as hypoxia, significantly impacts the health and well-being of individuals residing at high altitudes. To cope with hypoxia, physiological adaptations come into play, involving adjustments in respiratory and circulatory functions. Andean populations frequently exhibit an augmented respiratory response characterized by increased breathing frequency and depth, facilitating more effective oxygen uptake. Additionally, circulatory adaptations, including alterations in heart rate and cardiac output, work to optimize the transport of oxygen to the body's tissues. A notable response to hypoxia is the heightened production of red blood cells, known as polycythemia. This adaptive mechanism enhances the oxygen transport capacity, thereby improving the efficiency of the cardiovascular system in high-altitude environments (Moore 2001; Beall 2007).

From a genetic standpoint, studies reveal that numerous genes exhibit signs of positive selection in the Andes. Specifically, candidate genes associated with the *Hypoxia Inducible Factor* (HIF) have been identified, including *EGLN1* (Bigham et al. 2009, 2010), *EGLN3* (Caro-Consuegra et al. 2022; Joseph et al. 2023), *PRKAA1* (Bigham et al. 2009; Eichstaedt et al. 2014), *ANP32D* (Zhou et al. 2013; Eichstaedt et al. 2014) and *EPAS1* (Lawrence et al. 2024). The HIF pathway holds significance in regulating oxygen homeostasis, encompassing physiological adaptations in skeletal and heart muscles during situations of oxygen reduction, such as those induced by muscular effort and ischemic cardiomyopathy, respectively.

Other genes, such as *BRINP3* (Crawford et al. 2017; Caro-Consuegra et al. 2022; Joseph et al. 2023), *NOS2* (Bigham et al. 2009; Crawford et al. 2017), and *TBX5* (Crawford et al. 2017; Caro-Consuegra et al. 2022), are involved in the Nitric Oxide pathway (NOS), which at high altitudes acts as a vasodilator, relaxing blood vessels to enhance oxygen transport to tissues. The NOS pathway plays a pivotal role in regulating blood flow, immune responses, and cardiovascular health. Positive selection signals have been also identified in the *DUOX2* gene (Jacovas et al. 2018; Borda et al. 2020; Caro-Consuegra et al. 2022), associated with the generation of Reactive Oxygen Species (ROS). Exposure to reduced atmospheric pressure and oxygen levels at high altitudes induces oxidative stress, surpassing the body's detoxification capacity and leading to an increased production of ROS. Organisms acclimated to high altitudes exhibit adaptive responses, enhancing antioxidant defense mechanisms to counteract excessive ROS and mitigate oxidative stress. While excessive ROS levels can be detrimental, moderate levels play a pivotal role in cellular signaling pathways associated with adaptive responses, including angiogenesis (Schieber and Chandel 2014).

Additionally, numerous candidate genes exhibit a TP53 pathway selection signal, centered around the p53 protein, which safeguards genomic stability at high altitudes by orchestrating DNA repair mechanisms in response to elevated ultraviolet radiation, oxidative stress, and reduced oxygen levels (Eichstaedt et al. 2014; Jacovas et al. 2015, 2018). The TP53 pathway is also involved in regulating apoptosis versus cell survival, influencing tissue homeostasis in the face of stressors like hypoxia. The pathway's involvement in mitigating oxidative stress and collaborating with other signaling pathways highlights its central role in cellular adaptation to the unique challenges of high-altitude environments.

Beyond hypoxia, other signs of selection have been identified. In Andean Peruvians, a notable signal was found in *MITF*, a gene involved in the development of melanocytes, which is associated with both pigmentation and the vitamin D receptor (Caro-Consuegra et al. 2022). Additionally, a recent study uncovered selective signals in genes associated with the immune response. Specifically, the study identified signs of positive selection in genomic regions linked to the immune response against tuberculosis (*Mycobacterium tuberculosis*) (Joseph et al. 2023). The candidate genes *ANXA1*, *CD44*, and *ADGRE*1 were highlighted for their roles in the direct recognition of bacterial antigens by innate immune macrophages, while the genes *KCNA3* and *FCRL4* were implicated in the pro-inflammatory adaptive immune response. This suggests that, alongside adaptations to hypoxia, there are evolutionary changes in genes related to immune responses in high-altitude environments, particularly in the context of combating infectious diseases.

The dynamic interactions between indigenous people and their environment in the Andes offer a wealth of opportunities to investigate not only physiological adaptations, but also the underlying genetic, molecular, and ecological processes that contribute to their resilience. Although there are other regions of the world where people live at high altitudes, such as Tibet and Ethiopia, most of the selective signals observed in the Andean highlands are unique. This uniqueness underscores the importance of studying Andean populations as a distinct and valuable resource for understanding human adaptation to extreme environments.

18.5.2 Adaptations to the Andean Arsenic-rich Environments

One of the most intriguing examples of natural selection is observed in arsenic-rich Andean environments. Arsenic contamination of groundwater is a prevalent issue in many parts of the Andean region, often stemming from natural sources of arsenic in geological formations or mining activities (Cooke and Abbott 2008). This contamination can result in elevated levels of arsenic in rivers and drinking water, posing a significant threat to the health of local populations (Smith et al. 2006; Van Den Bergh et al. 2010). Prolonged exposure to high levels of arsenic through drinking water is associated with various health problems, including skin lesions and cancer (Martinez et al. 2011; Sage et al. 2017). Over thousands of years, human communities in the Andean highlands have coped with drinking water tainted by arsenic, prompting the question of whether these populations have developed adaptations over time to thrive in their potentially toxic environment.

Initial insights emerged from studies conducted on indigenous women in the northern Argentine Andes who regularly consumed drinking water with elevated arsenic concentrations. These women displayed genetic variations in the *AS3MT* gene, a pivotal player in arsenic metabolism. Individuals carrying the arsenic tolerance haplotype can metabolize arsenic more rapidly. Consequently, by minimizing exposure to toxic metabolites, they may have gained a selective advantage in environments with high arsenic content (Schlebusch et al. 2015).

Since the initial report of arsenic adaptation in humans, signatures of natural selection in *AS3MT* gene have been identified in studies involving indigenous populations from various regions of the Andes, including Argentina, Chile, Peru, and Bolivia (Eichstaedt et al. 2015; Apata et al. 2017; Jacovas et al. 2018; De Loma et al. 2022). These findings strongly support the hypothesis that arsenic exposure has been a driving force for human adaptation, leading to enhanced tolerance through more efficient arsenic detoxification in diverse Andean populations.

In the realm of environmental adaptations, numerous organisms have demonstrated the ability to tolerate toxic chemicals in their surroundings. Surprisingly, our understanding of human adaptations to such toxic chemicals remains limited. The discoveries regarding protective variants of the *AS3MT* gene open a new avenue for exploring how human populations might develop genetic resilience to environmental toxins, shedding light on the intricate mechanisms of adaptation within the human genome not only in the Neotropics but in other environments around the world.

18.5.3 Adaptations to the Amazon Rainforest

The Amazon rainforest is frequently acknowledged as one of the most biodiverse areas on the planet, given its extensive variety of plant, animal, and microbial species. The wealth of biodiversity in the Amazon rainforest is contrasted by the formidable challenges it presents, rendering it a harsh environment for long-term human habitation. Despite its nutrient-rich characteristics, the Amazon introduces distinctive obstacles to sustained human survival, characterized by the unpredictable availability of food resources (Bailey et al. 1989; Headland and Bailey 1991), restricted light penetration resulting from the dense canopy (Ratnam et al. 2011), and a diverse array of pathogens (Guernier et al. 2004). Notably, tropical forests, including the Amazon, are estimated to harbor approximately 70% more pathogens compared to temperate forests (Guernier et al. 2004). This elevated pathogenic diversity makes pathogens and tropical diseases potential contributors to local selective pressures.

Regardless of the unique characteristics of the Amazon environment, there remains a scarcity of studies that have assessed natural selection within this region. In 2015, Amorim et al. conducted a study evaluating convergent evolution between populations in the Amazonian and African rainforest. Identifying shared selective signals, the study primarily pinpointed genes associated with the immune system (*CCL28, CWH43, SCP2*), lipid metabolism (*CWH43, SCP2*), and thermoregulation (*HSF2*), among others (Amorim et al. 2015). This research provides insights into the genetic adaptations of populations in rainforests, shedding light on specific pathways influenced by natural selection in response to the challenges posed by these diverse and intricate environments.

Another study, focused on indigenous populations from the Peruvian Amazon and the Amazon lowlands, revealed indications of selection in the *PTPRC* gene. This gene plays a crucial role in the production of the CD45 protein, which is involved in the recognition of pathogens, particularly viral ones (Borda et al. 2020). Furthermore, in another investigation, indications of selection were noted in the *CBLB* and *CARD8* genes among indigenous individuals from the Peruvian Amazon. The *CBLB* gene encodes a negative regulator of adaptive immune responses, while *CARD8* mediates inflammasome activation in response to pathogens and other signals (Caro-Consuegra et al. 2022).

Finally, in a recent genomic and functional exploration within indigenous populations of the Brazilian Amazon, a prominent signal of natural selection was identified in a cluster of genes associated with the immune response to *Trypanosoma cruzi* infection (*PPP3CA* and *DYNC1I1*) and to the mosquito bite reaction (*NOS1AP*). *T. cruzi* is the parasite responsible for Chagas disease, endemic to America. The study uncovered that a variant of the *PPP3CA* gene provided a protective effect against Chagas disease infection. Through comprehensive functional studies, it was demonstrated that this gene plays a role in reducing the infection rate among carriers, unveiling a potential mechanism contributing to resistance against Chagas disease in Amazonian populations (Couto-Silva et al. 2023). This study underscores the potential significant role of Chagas disease in driving natural selection within native Amazonian populations. The findings highlight the imperative for more comprehensive exploration of human adaptations within the intricate environmental dynamics of the Amazon rainforest.

18.6 Adaptations Gene-culture Coevolution

Human evolution is not solely driven by the natural environment, climate, and pathogens; rather, it is profoundly shaped by cultural practices, knowledge, and innovations that influence how societies adapt to their surroundings. One of the most compelling examples of natural selection involving cultural factors in human populations is linked to the emergence of agriculture. The development of agriculture was a pivotal milestone in human history, often signifying a transition from nomadic, foraging societies to settled communities engaged in farming and animal husbandry.

Genetic adaptations might have occurred in response to the new dietary and environmental challenges introduced by agriculture (Balaresque et al. 2007; O'Brien and Laland 2012). For example, the increased reliance on cereal grains and domesticated animals could have led to genetic changes related to the metabolism of new food sources (Perry et al. 2007), lactose tolerance (Bersaglieri et al. 2004; Voight et al. 2006; Tishkoff et al. 2007), and resistance to certain diseases associated with agricultural settlements (Balaresque et al. 2007; O'Brien and Laland 2012).

In the Neotropical region, the most striking example of selection driven by agricultural practices comes from the indigenous populations of Mexico. Agricultural practices originated in Mexico between 10,000 and 7000 yBP, and the region is considered, along with the Andes, one of the primary centers for plant domestication and the development of agricultural practices in America (Pope et al. 2001; Zizumbo-Villarreal and Colunga-GarcíaMarín 2010). The cultivation of crops such as beans, squash, and especially maize formed the foundational basis for early agricultural societies in Mesoamerica (Zizumbo-Villarreal and Colunga-GarcíaMarín 2010).

A previous study revealed that Native American populations exhibit a natural selective signature on an autochthonous allele of the *ABCA1* gene (rs9282541) from America. These days, this allele is associated with low HDL cholesterol levels and obesity-related comorbidities. However, in the past, this variant may have favored intracellular cholesterol retention and energy storage (Acuña-Alonzo et al. 2010).

Upon further study of this variant, Hünemeier et al. discovered a significant correlation between the frequency of the *ABCA1*230Cys*-derived allele and the distribution of *Zea* pollen relics in Mesoamerican populations (Hünemeier et al. 2012). Using a Bayesian approach, the authors estimated the age of the derived allele at 7500 yBP, aligning with the age of domestication of maize in southwestern Mexico, approximately 10,000–6200 yBP. These discoveries reveal how a constructed agricultural niche and an autochthonous Native American allele became the focal points of an ongoing directional selective sweep as a consequence of the origin and spread of maize culture in ancient Mesoamerica.

This is an example of niche construction, showcasing how human beings, rather than remaining passive to their environment, actively engage in shaping it. Niche construction underscores the active role organisms play in molding their ecological and cultural surroundings. The subsequent modifications to this environment can, in turn, influence natural selection and evolutionary processes by favoring traits that prove advantageous within the altered niche. However, according to the thrifty genotype hypothesis, some authors argue that evolutionary history did not end there. Some of these genetic variants, which played a crucial role during the agricultural food transition process, are now associated with the development of a range of metabolic diseases in our contemporary society, characterized by an abundance of food resources and ultra-processed foods (see Box 18.3) (Neel 1962; Acuña-Alonzo et al. 2010; Yang and Ye 2021; Johnson et al. 2022).

Box 18.3: Thrifty Genotype Hypothesis and Domestication of Maize in Mesoamerica

The thrifty genotype hypothesis, proposed by geneticist James V. Neel in 1962, suggests that genetic variants advantageous in times of food scarcity have undergone positive selection throughout human evolutionary history. These variants promoted efficient energy utilization in ancient times, aiding adaptation to fluctuating food availability. However, in modern societies with abundant food resources, these same variants may lead to metabolic disorders.

The introduction of maize cultivation in Mesoamerica brought significant shifts in settlement patterns, with communities heavily reliant on maize as a primary food source. Despite expectations, agricultural and sedentary lifestyles did not guarantee food stability, as evidenced by periodic crop failures (Wells and Stock 2020). In this context, carriers of the ABCA1 variant (rs9282541) may have experienced selective advantages. This variant, associated with reduced cholesterol efflux, likely facilitated intracellular cholesterol and energy storage, benefiting adipose tissue in various functions such as energy regulation, reproduction, and immune support. In current Neotropical native populations, this variant is observed with an average frequency of 12% (ranging from 0% to 31%) (Acuña-Alonzo et al. 2010). However, in contemporary societies, these variants may contribute to metabolic diseases like low HDL levels, obesity (Villarreal-Molina et al. 2007; Acuña-Alonzo et al. 2010), cardiovascular disease and type 2 diabetes (Ochoa-Guzmán et al.

2020; Peña-Espinoza et al. 2024). This juxtaposition highlights the dual nature of the thrifty genes, wherein beneficial adaptations in ancestral environments can predispose individuals to health risks in modern contexts of excess resources (Fig. 18.6).

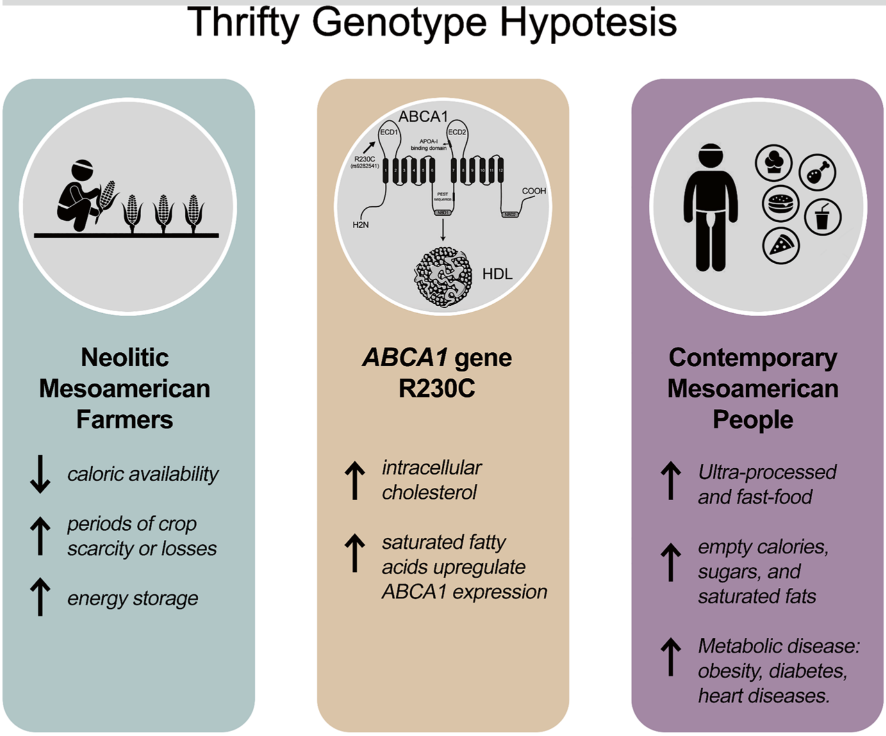

Fig. 18.6 Thrifty Genotype Hypothesis applied to autochthonous *ABCA1 R230C* variant (rs92822541) in Neotropical Mesoamerica. *ABCA1* is a protein playing a fundamental role in cholesterol homeostasis, mediating the formation of high-density lipoproteins and facilitating cholesterol efflux. Functional studies indicate that the *R230C* variant (rs9282541) demonstrates reduced cholesterol efflux. The presence of this variant favors the accumulation of 30% more intracellular cholesterol and may impact energy storage. This energy reserve could have conferred an adaptive advantage to Neolithic Mesoamerican populations during the transition from hunter-gatherer to maize farming lifestyles, particularly due to low caloric availability following the advent of agriculture and periods of crop scarcity or losses. Conversely, numerous studies conducted in the current Mesoamerican population have linked this variant to metabolic diseases such as obesity, cardiovascular disease, and diabetes. It's recognized that recent decades have witnessed a significant dietary transition marked by the prevalence of industrialized and ultra-processed foods, which are rich in empty calories, sugars, and saturated fats. Recent research indicates that diets high in saturated fatty acids upregulate *ABCA1* expression. Furthermore, the R230C variant interacts with dietary macronutrients, impacting plasma lipid levels, BMI, HDL-C, and serum adiponectin levels, which are often associated with metabolic diseases. Thus, this example may support the hypothesis of thrifty genotypes in Neotropical Mesoamerica.

(*continued*)

Box 18.3: (Continued)

The cultivation of maize in Mesoamerica not only shaped genetic adaptations but also influenced patterns of human disease. The transition from traditional maize-based diets to modern diets rich in processed foods may have increased metabolic disorders among indigenous populations in the region (Mendoza-Caamal et al. 2020). Understanding the relationship between maize cultivation, genetic adaptations, and human disease offers insights into the evolutionary origins of metabolic disorders. Furthermore, integrating genetics, anthropology, and public health can inform strategies to address health challenges posed by the mismatch between ancestral biology and modern lifestyles.

18.7 Natural Selection Post-contact

Natural selection is an ongoing evolutionary process that remains active even in recent times. As further detailed in the next section, during the last five centuries, the American continent experienced an influx of transatlantic migrants from regions including Europe, Africa, and more recently, the Middle East and East Asia. These foreign genomes, shaped by millennia of evolution in diverse environments, were now admixing and encountering novel challenges in the Neotropical environment. Now, scientists are striving to comprehend how genetic variants with diverse ancestral origins respond to the selective pressures of this new ecosystem.

In the past decade, a recurring observation in studies of natural selection in admixed Latino populations has been the presence of selective signatures in the Major Histocompatibility Complex (MHC) region, typically characterized by an increased frequency of variants of African origin (Meyer et al. 2018). This region stands out as one of the most gene-dense areas in the human genome, with a majority of its genes closely associated with the immune response. Within this complex, the HLA gene family holds particular prominence, playing a critical role in the immune system. These genes encode proteins that are integral to recognizing foreign substances (antigens), including pathogens and toxins, showcasing the vital role of the HLA in shaping immune responses and reflecting its significance in the genetic landscape of admixed Latino populations.

Two additional studies, focusing on identifying signs of selection across the genomes of admixed Latino populations, observed signals in genes related to the immune system, metabolism, and diseases. In one study encompassing populations from Colombia, Mexico, Peru, and Puerto Rico, genes associated with the immune system, particularly in pathways related to cytokine receptor interaction, T cell receptor signaling, and antigen presentation, were identified. The analysis also highlighted genes related to metabolism, including drug and xenobiotic metabolism, and steroid hormone biosynthesis. Furthermore, the study discovered genes associated with specific diseases such as type I diabetes, Alzheimer's disease, and

Leishmaniasis (Norris et al. 2018). The other study, involving populations from Brazil, Chile, Colombia, Mexico, and Peru, identified 15 genes associated with the development or regulation of the immune system and 9 genes related to dietary practices through their association with metabolism-related phenotypes or anthropometric measurements (Mendoza-Revilla et al. 2022).

In the exploration of post-contact natural selection within Latin populations, researchers have unearthed genetic variants stemming from different ancestral origins, encompassing African, European, and Native American roots. This discovery underscores the intriguing possibility that alleles originating from various genetic backgrounds may confer adaptive advantages in the context of Neotropical America. It is noteworthy that the observed selection signals may exhibit commonality across multiple populations, indicating shared adaptive responses. However, the specificity of these signals to particular populations adds an additional layer of complexity, highlighting the intricate interplay of genetic diversity and adaptation within the diverse mosaic of Latin American populations.

18.8 Genetic Distinctiveness of Contemporary Neotropical Populations

The last five centuries, the American continent has witnessed unprecedented population dynamics, movements, and demographic shifts, beginning with the European contact in 1492. The colonization process initiated a profound demographic transformation, leading to the extermination of over 90% of the indigenous populations, numbering in the millions at the time (Adhikari et al. 2017). Various factors contributed significantly to this decimation process, encompassing epidemics, enslavement, extermination through wars of conquest, manipulation of conflicts between rival indigenous groups, forced displacement from ancestral territories, habitat destruction, disruption of traditional subsistence strategies, and the erosion of indigenous knowledge, among other impactful elements (Thornton 1987; Stannard 1992). Some evidence suggests that the depopulation was more intense later during the colonization period in more isolated areas (Jones et al. 2021).

The colonization era also witnessed extensive admixture among Indigenous populations, European colonizers, and enslaved Africans forcibly brought to the continent, shaping the genetic landscape in unprecedented ways. The unique combination of these factors highlights the distinctiveness of the Western Hemisphere, particularly in terms of human genetic history of Latin America. This region experienced a much more widespread admixture process compared to North America, where the segregation between Indigenous Americans, European, and African populations was more pronounced (Adhikari et al. 2017). Hence, the genetic study of these populations presents a valuable opportunity to explore the effects of large-scale admixture and population reduction events on human genetic diversity patterns and evolution.

In this sense, the historical trajectory of America has resulted in the contemporary genetic diversity of the region encompassing a substantial portion of the world's human genetic variability, as previously highlighted by others (Adhikari et al. 2017). Although the predominant ancestry of present-day populations in America can be traced to the three primary continental ancestral populations (Native Americans, Europeans, and Africans) and the contribution from ancestors originating in Asia, Oceania, and other global regions has been minimal and largely confined to specific geographic areas. Furthermore, the genetic makeup of contemporary American populations is a consequence of the varying contributions from these three major continental ancestry components. These components were intermixed in diverse proportions and timelines, influenced by various socioeconomic and demographic factors.

Another phenomenon contributing to the distinctive contemporary human genetic diversity in America and the Neotropical region is the pronounced non-random mating dynamics in the admixture processes that shaped these populations, including more evidently the sex-biased admixture, most prevalent during the initial period of the colonization (Adhikari et al. 2017). This non-random mating primarily occurred between European men and Indigenous American and African women (Pena 2002; Kehdy et al. 2015). Several factors led to this pattern, including the predominance of European male settlers, their dominant socioeconomic roles, the elevated mortality rate among Indigenous and African men, who were also prevented from leaving descendants, along with the sexual violence against women from these latter groups.

Analyses of mitochondrial DNA and Y chromosome have unequivocally demonstrated that the majority of paternal genetic lineages trace back to European ancestors, while the predominant maternal lineages can be linked to Indigenous American or African origins (Carvajal-Carmona et al. 2000; Bedoya et al. 2006; Adhikari et al. 2016). The investigation of the X chromosome, as well as autosomal genetic variation, has consistently corroborated these findings (Adhikari et al. 2016; Webster and Wilson Sayres 2016). An additional important factor influencing the patterns of genetic diversity of American populations is the ancestry-assortative mating, which happens when individuals select mates with comparable amounts of ancestry (Kehdy et al. 2015). Socioeconomic factors are likely important underlying causes of this phenomenon, given that they are often linked with ancestry proportions, influencing mating probabilities and genetic diversity patterns (Mas-Sandoval et al. 2023).

In general, recognizing the genetic diversity of present-day Neotropical populations necessitates an understanding that it is shaped by a complex interplay of past demographic events and the proportional contributions from continental ancestral populations. This insight is paramount for the formulation of effective public health policies and the development of tailored health treatments that account for the specific genetic risks inherent in these diverse populations. By unraveling this intricate genetic history, geneticists pave the way for targeted interventions that address the unique health challenges faced by Neotropical communities, ultimately fostering more equitable and effective healthcare strategies.

18.9 Final Remarks

The intricate history of the peopling of America, shaped by human migrations originating from Asia, reveals a multifaceted evolutionary and demographic history. This process encompasses the enduring genetic legacy arising from the contact and intermixing dynamics of Northeast and East Asian ancestral populations, the emergence of a distinctive genetic diversity within the Beringian ancestors, the rapid dispersal of the ancestors of Native Americans following the Last Glacial Maximum, and the subsequent successive population turnovers. This extensive history unfolds against the backdrop of an intricate process of biological and cultural adaptation, prompted by the immensely diverse environments encountered across the continent.

This process of adaptation has produced in the Neotropics not only incredibly rich cultural diversity, including multiple strategies of food production integrated to their ecosystems, but also the evolution of genetic adaptations to the local environmental challenges, encompassing adaptations to consumption of the food resources and to respond to pathogens. The study of this complex history provides profound insights into how human demographic dynamics and evolution has shaped their genetic diversity and impact the health of present-day populations.

The study of human occupation in the Neotropical region also provides a compelling illustration of the profound influence of past climate changes on human demography. This encompasses critical aspects such as the distribution, growth rates, and movement patterns of populations. These past climatic shifts altered the selective pressures within environments, sometimes even creating ecological opportunities that facilitated the thriving and expansion of certain groups. These findings underscore how historical climatic shifts have shaped human history, offering valuable insights into the complex interplay between environmental factors and human demographic patterns.

The long-term consequences of this genetic history can be found in both modern native and non-native populations throughout the region, where they had a considerable influence on phenotypic diversity and, more importantly, health outcomes. This impact includes genetic risks and adaptations linked with traditional and modern industrialized diets, susceptibility to infectious and auto-immune diseases, the genetic burden of deleterious mutations introduced by diverse global populations and propelled to higher frequencies by genetic drift, among other health-related aspects. The complex relationship between historical genetic legacies and present-day health underscores the significant impact of the human recent and distant past on the well-being of populations in the region.

Key Points

- Indigenous American populations trace their ancestry back to ancestors who lived in Northeast and East Asia during the Late Pleistocene.
- Distinct ancestry components were formed within the American continent and several population turnovers and demographic shifts shaped and reshaped the genetic makeup of the continent.
- Serial population bottlenecks and founder events led to an increased effect of genetic drift, both reducing the genetic diversity and increasing the proportion of deleterious variants in present-day indigenous and admixed American populations.
- The European colonization of America dramatically changed the genetic diversity patterns of human populations, causing intense population reductions and widespread admixture of at least three continental ancestry components (African, European and Indigenous American).
- Human populations, both in the past and present, adapted to Neotropical environments, diets and pathogens. Several examples have been documented, including resistance to Chagas disease, adaptations to high-altitude and arsenic-rich environments, among others.

Questions

1. How do Indigenous American populations relate to other human populations, and what distinguishes the genetic diversity of Indigenous Americans from that of other groups?
2. Analyze the profound demographic transformation initiated by European contact in 1492, including the population bottlenecks and admixture events. How have these factors influenced the genetic diversity of human populations in the American continent?
3. What significance does the study of human genetic diversity hold in enhancing our understanding of human diseases? Furthermore, why is it particularly important to focus on the study of underrepresented populations?
4. In what ways have evolutionary processes, particularly natural selection, influenced the genetic diversity of populations in the Neotropical America? Can you provide examples of human genetic adaptations evolved in response to Neotropical environments?

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