The demographic and adaptive history of central African hunter-gatherers and farmers

Etienne Patin, Lluis Quintana-Murci

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Etienne Patin[1,2,3] and Lluis Quintana-Murci[1,2,3]

[1]Unit of Human Evolutionary Genetics, Department of Genomes and Genetics, Institut Pasteur, 75015 Paris, France

[2]Centre National de la Recherche Scientifique (CNRS) UMR2000, 75015 Paris, France

[3]Center of Bioinformatics, Biostatistics and Integrative Biology, Institut Pasteur, 75015 Paris, France

Correspondence to: epatin@pasteur.fr or quintana@pasteur.fr

Abstract

Central Africa, a forested region that supports an exceptionally high biodiversity, hosts the world's largest group of hunter-gatherers, who live in close proximity with groups that have adopted agriculture over the past 5,000 years. Our understanding of the prehistory of these populations has been dramatically hampered by the almost total absence of fossil remains in this region, a limitation that has recently been circumvented by population genomics approaches. Different studies have estimated that ancestors of rainforest hunter-gatherers and Bantu-speaking farmers separated more than 60,000 years ago, supporting the occurrence of ancient population structure in Africa since the Late Pleistocene. Conversely, the Holocene in central Africa was characterized by large-scale population migrations associated with the emergence of agriculture, and increased genetic interactions between autochthonous rainforest hunter-gatherers and expanding Bantu-speaking farmers. Genomic scans have detected numerous candidate loci for positive selection in these populations, including convergent adaptation for short stature in groups of rainforest hunter-gatherers and local adaptation to endemic malaria in western and central Africans. Furthermore, there is recent increasing evidence that adaptive variation has been acquired by various African populations through admixture, suggesting a previously unappreciated role of intraspecies gene flow in local adaptation. Ancient and modern DNA studies will greatly broaden, and probably challenge, our view on the past history of central Africa, where introgression from yet uncharacterized archaic hominins and long-term adaptation to distinct ecological niches are suspected.

Introduction

The central African belt — a vast territory that extends from the Congo Basin in its western part to Lake Victoria in its easternmost part — is mostly covered by dense rainforests and supports one of the highest levels of biodiversity worldwide. This region is key to understand African prehistory, population structure and dynamics as it harbours both the largest living group of active hunter-gatherers, the rainforest hunter-gatherers, as well as Bantu-speaking, agriculturalist communities [1-3]. These two groups differ not only in their subsistence patterns (i.e., broadly, although not exclusively, hunting and gathering *versus* farming) but also in their lifestyle, ecologies and exposure to environmental pressures [4] and diseases [5]. While most farming communities are sedentary and live in rural or urban areas, rainforest hunter-gatherers traditionally live in huts in the rainforest, moving regularly from one camp to another.

African rainforest hunter-gatherers (RHG) — collectively known by the historical and derogatory term "Pygmies" — are broadly subdivided into two groups that reflect their geographic location [6]. Western RHG inhabit the Congo Basin and include multiple populations such as the Baka, Aka, Koya or Bongo, whereas Eastern RHG live close to the Ituri rainforest and Lake Victoria and comprise groups such as the Asua, Sua, Efe or BaTwa. In addition to a forest-dwelling mode of subsistence, Western and Eastern RHG share distinctive cultural and phenotypic traits, such as specific hunting and honey-gathering techniques and a trait known as the "pygmy phenotype", i.e., small adult body size distinctive of certain African, Southeast Asian and South American populations [7]. African RHG, particularly those of the Ituri rainforest, show the lowest average adult stature worldwide, of < 155 cm [8].

Bantu-speaking, agriculturalist populations of central Africa are thought to descend from early farming communities that recently expanded across sub-Saharan Africa [9]. The central African belt is also key in this respect, as it is adjacent to the postulated homeland of Bantu languages, where agriculture possibly emerged 3-5 Ky ago, in the area that corresponds today to Southeast Nigeria and Western Cameroon [3]. The appearance of pottery and polished stone tools within this time frame, together with the shared languages and oral traditions of farmers and hunter-gatherers, indicates an early and extensive history of economic and technological exchanges between the ancestors of these two communities [1-3,8,10]. These contacts have been maintained until today; for example, some groups of rainforest hunter-gatherers remain sedentary for some time due to strong socioeconomic dependence on neighbouring farmers.

The lacks of archaeological data for central Africa, in particular for the Congo Basin owing to the rapid disintegration of fossil remains in the rainforest's acidic soils, have hampered the understanding of demography and adaptation of populations inhabiting this region. How the increasing availability of genomic data from populations of the region has counteracted this limitation is the goal of this review. We focus on how genomic studies of rainforest hunter-gatherers and farmers have been of paramount importance to infer their past demography — population splits, sizes changes and gene flow — as well as their history of biological adaptation, highlighting the importance of admixture as a possible source of new adaptive variation.

Deep divergence of central African populations in the Late Pleistocene

While the late Pleistocene is thought to have witnessed modern human diversification within Africa [11], the human fossil record of central Africa is exceptionally sparse for this period [12].

The oldest samples studied have been dated at 20-25 Ky, and suggest that the biological and cultural diversity of central Africa during this period was considerable [13]. However, it is currently unknown if such diversity was a local exception, or a general rule in the diverse ecological regions composing central Africa.

The study of the genetic diversity of present-day populations represents an alternative, powerful approach to infer past population histories and ecologies. Population genetic studies have shown that present-day RHG and farming populations are characterized by one of the deepest splits in human evolution [14,15]. The combined modelling of 16 high-coverage whole genomes supports a separation of the ancestors of RHG and the west African Yoruba 90 Ky (85–92) or 155 Ky (139–164) ago, assuming either instantaneous or continuous asymmetric gene flow between the two groups [14]. A similar approach recently applied on 300 exomes of RHG and Bantu-speaking farmers has estimated that their ancestors diverged 135 Ky (57–259) ago [15] (**Figure 1**), assuming the most recent estimations of mutation rate [16] and generation time [17]. Under the same assumptions, the former study supports a population split as old as 300 Ky ago, while previous studies based on independent autosomal regions support a separation ~110 Ky ago [18,19]. Despite discrepancies between estimates, which may be due to imperfections in the models, low sample sizes, or the effects of background selection, they all support ancient structure among the ancestors of rainforest hunter-gatherer and farmer populations, in agreement with the proposed human diversification within Africa during the Late Pleistocene [11].

Seminal ancient genomic studies have revealed that Neanderthals contributed ~2% of the genetic variation of present-day non-Africans [20-22], while Denisovans contributed ~5% of genetic variation to modern Melanesians [23-25]. Despite the coexistence throughout Africa of diverse forms of *Homo* with both archaic and modern traits during the Pleistocene [26], few studies have yet provided robust evidence of archaic introgression in Africa. Reference-free methods have nonetheless identified in RHG genomes hundreds of candidate introgressive loci, which are strongly depleted in genic regions [27-29]. Whether these observations reflect archaic admixture or ancestral structure [30] remains to be determined.

Demographic transitions and admixture during the Holocene

The Holocene in central Africa was characterized by a global warming after the Last Glacial Maximum, and the increase of forested areas followed by short episodes of forest contraction from 4 Ky onward [31,32]. These deforestation events were concomitant with the well-documented expansion of Bantu languages from the modern-day Nigeria-Cameroon border [3,33,34]. The Bantu expansion is thought as one of the most influential cultural events of African prehistory, as it spread a new, more sedentary lifestyle that ultimately led to the diffusion of agriculture and iron-smelting technology across sub-Saharan Africa. Population genetic studies have revealed that present-day Bantu-speaking populations (BSP) of central, eastern and southern Africa present little differentiation [35-37], supporting their recent separation during the Bantu expansion. Haplotype-based approaches, together with linguistics [34] and archaeoclimate data [9], all support a model in which early BSP first moved southward through the rainforest, before migrating toward eastern and southern Africa [37-39]. Interestingly, the signal of population growth observed in BSP genomes cannot be solely explain by an expansion occurring 3-5 Ky ago, suggesting that their ancestors were already a demographically successful group prior to agriculture emergence [40,41].

As they dispersed throughout central Africa, BSP encountered local RHG populations. Several studies indicate that admixture occurred between the ancestors of these two groups [18,35-37,41-45]. Model-based methods have estimated that gene flow from BSP to RHG was greater than the opposite [14,15] (**Figure 1**), resulting in high BSP ancestry among some RHG groups [18,41,43-45]. Furthermore, uniparentally-inherited and X-linked markers have revealed that gene flow from BSP to RHG was male-biased [41,44,46]. However, asymmetrical male-biased gene flow is not systematically observed across western RHG groups [41,44], suggesting variable intermarriage customs. While modelling approaches based on the site frequency spectrum have estimated a time of admixture as old as ~7 Ky [14,15] (**Figure 1**), decay of admixture linkage disequilibrium is compatible with admixture occurring mostly during the last millennium [37,41]. We anticipate that methodological improvements allowing parameter estimation under both instantaneous and continuous admixture models [47] will help resolving these apparent discrepancies.

Population size changes and the burden of deleterious mutations

Understanding how demographic events such as explosive growth or bottlenecks have affected the ability of populations to purge deleterious variants is crucial for the dissection of the genetic architecture of diseases [48-50]. Fuelled by the availability of population sequencing data, there has been increased interest on whether human populations carry differential burdens of deleterious alleles (i.e. mutational load). Despite some initial controversy, the consensus today is that the demographic events experienced by the majority of human populations have not been long or severe enough to impact, at least to a detectable extent, mutational load under an additive model of dominance, whereas they may impact load under a recessive model [51-53].

The question of how population size changes affect mutational load is especially relevant in hunter-gatherer history, as their subsistence patterns are expected to be associated with a unique demography [15,18,19,41]. Based on exome sequencing data from RHG and BSP from western and eastern central Africa, a recent study has explored, using simulations, the trajectories of mutational load across populations, and examined the model of dominance that is most compatible with the patterns of deleterious variation [15]. Despite the marked population collapses and expansions experienced by RHG and BSP, respectively (**Figure 1**), both groups exhibit similar load under an additive model. Furthermore, the historically large effective population size of RHG, together with the gene flow received from neighbouring farmers, have counteracted the predicted effect of the recent and strong population decline of RHG on their recessive load.

In the absence of knowledge of the average distribution of dominance coefficients across the genome and full consideration of rare variants located in both coding and non-coding regions, the question of the extent of mutational load differences between hunter-gatherers and farmers, and more generally among human populations, remains open.

Signatures of local adaptation in rainforest hunter-gatherers and farmers

Despite rainforest hunter-gatherers and farmers cohabit along the central African belt, their history of population divergence dates back to > 60 Ky ago [14,15,18,43]. Their differences in effective population sizes appear to result from demographic events that predate the first farmers' expansions 3-5 Ky ago [41], suggesting a long — and probably different — history of biological adaptation.

The “pygmy phenotype” [7] appears to have a genetic basis, at least in Africa [45,54,55], and its adaptive nature — proposed to be associated with higher fitness in rainforest environments through thermoregulation, food limitation, improved mobility or earlier reproduction [7,8,56,57] — is increasingly supported [58]. Population genetic studies have detected signatures of positive selection targeting a largely non-overlapping set of genes in various RHG groups [14,29,45,55,59-62], possibly reflecting false positives. The relevance of some candidate loci is nonetheless supported by functional and epidemiological studies; for example, *FLNB* and *EPHB1* present not only robust signatures of positive selection but also variation that affect body size in model organisms or is associated with human height [14,29,45] (**Figure 2**). That studies of different RHG groups detect different candidate genes for the pygmy phenotype may also reflect convergent adaptation within Africa, as supported by population genetics data [55] and analysis of longitudinal growth rates in western and eastern RHG groups [63].

Functional categories of candidate genes evolving adaptively among RHG also involve reproduction, cell signalling, neural development and immune functions [14,29]. Beside all these cases of candidate selective sweeps, signals of polygenic adaptation [64] have been also detected among RHG, related to the pygmy phenotype [55] and immunity-related processes (i.e. antigen binding and pattern recognition receptor activity) [14].

Genetic adaptation related to host defence against pathogens has been pervasive among African populations [65,66]. The pressure imposed by *Plasmodium* — the causative agent of malaria —

largely characterises the history of positive selection of sub-Saharan Africans [67], particularly that of western and central African farming communities [36,37]. Highly supported cases of genes that have evolved adaptively in response to malaria include *HBB*, *DARC* (*ACKR1*), *G6PD*, *CR1* and *CD36* [36,68-74] (**Figure 2**), variation in which confers protection against *falciparum* or *vivax* malaria [67]. Other cases of genetic adaptation include *APOL1*, conferring resistance to *Trypanosoma brucei* [75], *LARGE*, implicated in Lassa virus infectivity and immunity [76], *TLR5*, associated with decreased NF-κB activity [77], as well as several loci putatively involved in adaptation to temperature and osmoregulation [36]. All these studies have collectively broadened our understanding of the ecological pasts of populations of central Africa that differ in their carrying capacities and modes of subsistence.

Admixture as a vehicle of genetic adaptation

Recent studies have highlighted a previously unappreciated role of admixture and gene flow as an important source of adaptive genetic variation, from ancient hominins such as Neanderthals or Denisovans [30,78,79], or between modern human populations [37,80,81].

Within Africa, BSP rapidly dispersed in less than 3 Ky, and had to adapt to new ecosystems. Recent data has shown that during their dispersals, BSP acquired advantageous genetic variation via admixture with the local populations they encountered [37]. For example, BSP from western central Africa acquired adaptive variants at the *HLA-D* gene locus through admixture with RHG, and BSP from eastern Africa acquired the lactase persistence trait through gene flow from east African pastoralists [37] (**Figure 2**). Another study has reported strong changes in local ancestry in the genome of the Fula population from west Africa; the region overlapping the lactase persistence trait (*LCT/MCM6*) exhibits the highest proportion of Eurasian ancestry, while *DARC*, where the Duffy null allele confers almost complete resistance to *vivax* malaria, exhibits the highest proportion of African ancestry [81]. That adaptation can be accelerated by gene flow is also supported by studies of African-descent, admixed populations of Madagascar and Pakistan, where the Duffy null allele is, again, observed at higher frequencies than expected [82-84].

Conclusions and perspectives

Human evolutionary genomics in central Africa has contributed new knowledge of the history and evolution of human groups inhabiting this ecologically unique region. Deep population divergence between populations with historically distinct subsistence strategies, as well as compelling signatures of local adaptation, suggest an early prehistory of central Africa characterized by isolation between populations relying on different ecosystems. Conversely, the Holocene witnessed the geographical expansion of demographically-successful, sedentary Bantu-speaking peoples, resulting ultimately in asymmetric and male-biased admixture with several groups of rainforest hunter-gatherers.

Despite these new insights, important aspects of the evolutionary past of central Africans remain unclear, because of inherent limitations of modern population genomics and the scarcity of high-quality genomic data for both modern and ancient human DNA. Uncertainties in the geographic distribution of ancestors of present-day populations and in mutation rates impede the interpretation of the demographic models fitted on the available genetic data [85]. The overall genetic diversity of central Africans remains to be fully characterized, as the geographic distribution of sampled populations is still fragmented, particularly in the Demographic Republic of Congo where several hunter-gatherer groups live, such as the Twa and the Cwa [1] (**Figure 2**). The extreme scarcity of human fossils and the low preservation of ancient DNA in these regions also hamper ancient genomics, yet this field is essential to confirm that archaic admixture with ancient hominins did occur in Africa, and if so, to determine which modern populations were mostly introgressed.

Finally, the contrasted demographic histories and ecologies of central African populations are expected to impact their present-day phenotypic diversity, both benign and disease-related. While compelling evidence support that a number of distinctive traits of rainforest hunter-gatherers and farmers are adaptive, the genetic architecture of such traits, as well as that of diseases endemic of this region, is yet to be determined. Future studies combining rich phenotype data with innovative methodological tools to detect the footprints of polygenic selection and adaptive introgression will provide invaluable insights into the determinants of human biological diversity.

BOX 1 - The genetic legacy of the Transatlantic Slave Trade

Millions of individuals from western and central Africa were forcibly brought to the Americas by slave traders from the 16th to the 19th centuries. Subsequent admixture between the descendants of slaves and European- or Native-American-descent Americans impacted greatly the genetic landscape of the New World. Contemporary American populations of African descent show considerable variation in African ancestry proportions, ranging from <5% in Puerto Ricans to more than 95% in the Noir Marron from north-eastern South America [86-91]. Within North America, innovative approaches modelling ancestry and recent relatedness estimated that admixture occurred in the first half of the 19th century mainly in the South, followed by ancestry-biased migration towards the North [90].

Although rich historical records documented slave embarkations from different coastal regions of western and central Africa [92], they could not inform the precise geographical origins of African-descent Americans. These origins were recently revealed by genetic surveys that estimated the relative genetic contribution of western and central African populations to African-Americans [37,91], highlighting Angola as an important source of slaves in both South and North America [93].

Leveraging the rich genealogical and genetic records of Iceland, a seminal study reconstructed the African genome of Hans Jonatan, an Icelandic immigrant born in the Caribbean in 1784 to an enslaved African mother and European father, from the genomes of 182 of his descendants in Iceland, and inferred his mother originated from western central Africa [94].

Conflict of interest statement

Nothing declared.

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Integrates simulations with empirical data to assess the temporal trajectories of mutational load in central African hunter-gatherers and farmers. Despite their contrasting demographic pasts, both groups present today similar loads under additive and recessive models of dominance, owing to various demographic events that have hampered hunter-gatherers to accumulate recessive load.

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Figures

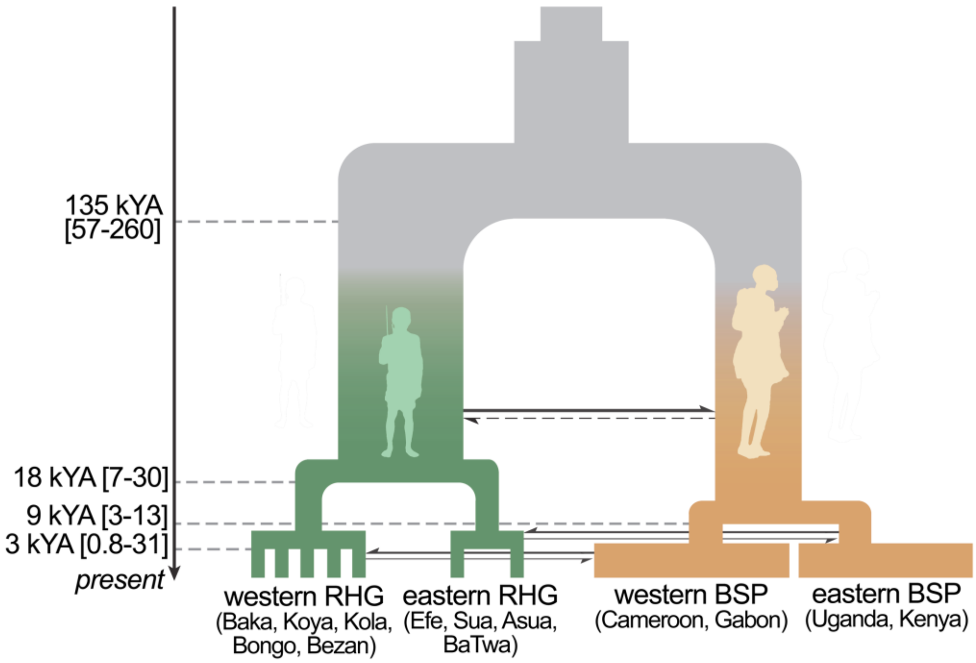

Figure 1. A general demographic model of rainforest hunter-gatherer and farmer populations. This model recapitulates estimations of the demographic history of rainforest hunter-gatherers (RHG) and neighbouring Bantu-speaking farmer populations (BSP) of central Africa [15,41,43]. Times are given in thousands of years from present (kYA). Inferred changes in effective population size are shown by changes in branch width, and gene flow by arrows.

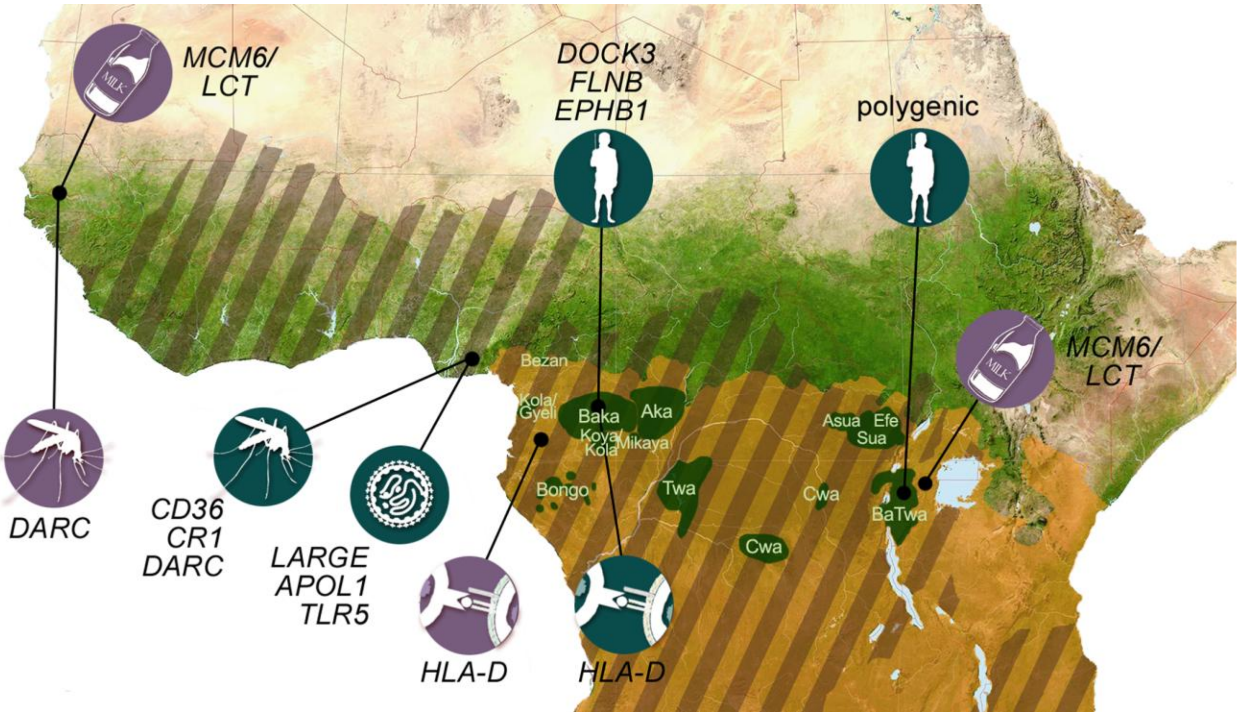

Figure 2. A map of human local adaptations in central Africa. Blue circles indicate case examples of candidate local adaptations and corresponding positively-selected genes in western/central Africa. Violet circles indicate candidate cases of adaptive admixture, when adaptive variation was acquired through admixture or gene flow. The orange area shows where Bantu languages are spoken today (adapted from [3]). Dark green areas indicate the geographic areas that the different RHG groups occupy (adapted from [1]). The maroon hatched areas indicate predicted areas of high *Plasmodium falciparum* malaria endemicity [95].