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*Review*

# A history of you, me, and humanity: mitochondrial DNA in anthropological research

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**Abstract:** Within genetic anthropology, mitochondrial DNA (mtDNA) has garnered a prominent if not enduring place within the anthropological toolkit. MtDNA has provided new and innovative perspectives on the emergence and dispersal of our species, interactions with extinct human species, and illuminated relationships between human groups. In this paper, I provide a brief overview of the major findings ascertained from mtDNA about human origins, human dispersal across the globe, interactions with other hominin species, and the more recent uses of mtDNA in direct to consumer ancestry tests. Relative to nuclear DNA, mtDNA is a small section of the genome and due to its inheritance pattern provides a limited resolution of population history and an individual's genetic ancestry. Consequently, some scholars dismiss mtDNA as insignificant due to the limited inferences that may be made using the locus. Regardless, mtDNA provides some useful insights to understanding how social, cultural, and environmental factors have shaped patterns of genetic variability. Furthermore, with regard to the experiences of historically marginalized groups, in particular those of African descent throughout the Americas, mtDNA has the potential to fill gaps in knowledge that would otherwise remain unknown. Within anthropological sciences, the value of this locus for understanding human experience is maximized when contextualized with complementary lines of evidence.

**Keywords:** mitochondrial DNA (mtDNA); genetic ancestry; human origins; human evolution; migration; direct-to-consumer tests

## 1. Introduction

Situated within nucleated cells, mitochondria are organelles that are primarily responsible for energy production. Beyond their capacity to produce energy, mitochondria also have a role within apoptosis, or programmed cell death, cellular metabolism, and intracellular messaging [1]. Within human cells there are multiple copies of mitochondria and within each mitochondria, there are 2 to 10 copies of the circular 16,569 base pair genome. This extra-nuclear DNA results in hundreds to thousands of copies of the mitochondrial genome within a cell [2]. The high copy number of mitochondrial genomes within cells makes mtDNA a methodologically advantageous genetic locus to genotype. The mitochondrial genome itself contains 37 genes that code for different types of RNAs and proteins. Conventionally, only small portions of the mitochondrial genome have been utilized in genetic anthropological research. These regions are known as hypervariable region I and II (HVS I and HVS II), corresponding to nucleotide positions 16024-576 in addition to certain single nucleotide polymorphisms found throughout the coding region. Increasingly however, more recent studies utilize the whole mitochondrial genome rather than just the coding region polymorphisms and hypervariable regions. MtDNA also has a unique inheritance pattern that is unlike the inheritance of nuclear DNA. MtDNA is inherited from mother to child generally unchanged generation after generation. Only women pass their mtDNA to offspring and only female offspring pass the same mitochondrial lineage to subsequent generations. Due to this uni-parental inheritance pattern, mtDNA is particularly useful for examining questions about female migration as well as sex-biased gene flow between populations [1].

In addition to its inheritance pattern, mtDNA also has a distinct geographic distribution across global populations. Mitochondrial lineages, or haplotypes, differ in sequence from one another. The differences between the haplotypes are primarily based upon nucleotide variability in the hypervariable regions as well as polymorphisms found throughout the coding region. Phylogenetically related haplotypes can be grouped together to form haplogroups. These mitochondrial haplogroups are considered continentally specific. This means that certain haplogroups are found at high frequency among populations in one geographic region but the same haplogroup is virtually absent in other geographically distant populations. The number of mitochondrial haplogroups currently stands at 5400 [3].

MtDNA was first sequenced in 1981 [4], and the published sequence was dubbed the Cambridge Reference Sequence (CRS). However, due to errors in the original sequence, a corrected version, now referred to as the revised Cambridge Reference Sequence (rCRS), was published in 1999 [5]. The CRS/rCRS sequences have since been used as the baseline to which other sequences are compared and to which phylogenetic assessments are made to determine haplotype and haplogroup membership [6]. However, this reference sequence is not representative of the ancestral mitochondrial human sequence but instead a derived sequence belonging to haplogroup H2a2a1. The fact that the rCRS is not ancestral to known mitochondrial lineages has created complications in making assessments about the phylogenetic relationships between mitochondrial lineages. To address this issue, a new reference sequence has been published which is more representative of the root of all human mitochondrial sequences and was also constructed in relation to Neanderthal mtDNA [7]. This new reference sequence is known as the RSRS or Reconstructed Sapiens Reference Sequence. Though some researchers and direct-to-consumer (DTC) genetic testing companies have adopted the RSRS and use it adjacent to rCRS, other scientists are not as resolute in its implementation [6,8]. The primary criticism to the use of RSRS is that with the discovery of novel mitochondrial sequences the

RSRS may not actually represent the root mitochondrial lineage and consequently will need to be modified. In addition, the potential for confusion and miscommunication may increase with a transition from rCRS to the RSRS [9].

Nonetheless, as will be discussed in subsequent sections, regardless of which reference sequence is used, mtDNA has refined anthropological understandings surrounding questions of human origins, relationships with now extinct human species, and human migration. With regard to DTC genetic tests, mtDNA has proven invaluable to genetic genealogists and others interested in utilizing genetic data to learn more about familial relationships as well as long-term, or 'deep' ancestry. In addition to addressing conventional anthropological and genetic genealogic questions, mtDNA has also proven crucial in adding new perspectives to understanding how the genetics of marginalized populations have been shaped by historical processes. These insights into the 'bio-histories' of marginalized populations are best understood within the social, historical, and political contexts in which they emerged. Thus, as mtDNA and genetic data more broadly, becomes more firmly established as relevant anthropological tools, the new data may challenge old ideas about the human condition, including ideas about our origins, evolution, and human variation.

## 2. Mitochondrial studies of human origins

MtDNA was featured in the 1987 seminal paper by Rebecca Cann, Mark Stoneking, and Allan Wilson [10]. This paper became the foundation that helped to establish that the most recent common mitochondrial ancestor to all living humans lived in Africa roughly 200,000 years ago. In this study, Cann and colleagues examined mtDNA from 147 individuals sampled from five different regions of the world. They concluded that all mitochondrial lineages coalesced to one woman that lived about 200,000 years ago, most likely in Africa. The media later dubbed this common mitochondrial ancestor "Mitochondrial Eve" [11]. This study elicited criticism due to issues regarding the study design and the statistical merit of the analyses. Specifically, Cann and colleagues had sampled African Americans instead of Africans and failed to emphasize alternative but equally plausible analyses that suggested a non-African origin of our species. Four years later, a follow-up study by Vigilant et al., was published in Science [12]. This paper directly addressed some of the criticisms aimed at the Cann et al. study. Like the earlier analysis, Vigilant and colleagues also concluded that Africa was the geographic origin of *Homo sapiens*. Both the Cann et al. and Vigilant et al. papers became very influential genetics based papers to support the idea that Africa was central to the origin and evolution of our species. Within the next decade additional supporting studies that examined both mitochondrial and nuclear DNA were published [13-16]. These subsequent publications helped to solidify mtDNA as an informative marker within anthropological genetics.

Studies using mtDNA were also crucial in evaluating competing theories regarding the temporal and geographic origin of our species. The two primary human origin hypotheses, dubbed, the "Recent Out of Africa" and "Multiregionalism" theories posit different scenarios of how our species emerged. The first hypothesis, promoted by Chris Stringer and other researchers, posits that modern humans originated in Africa, migrated out into other regions of the world and completely replaced other human species with virtually no gene exchange between *Homo sapiens* and the other encountered human species [17]. The second hypothesis, advocated by Milford Wolpoff among others, also posits an African origin, but not of anatomically modern humans. According to this hypothesis, anatomically modern humans evolved from an earlier related species, *Homo erectus* that emerged from Africa and populated the world 1–2 million years ago. As a result of genetic exchange,

or gene flow, between geographical regions, anatomically modern humans emerged in several regions of the world beyond the African continent [18]. While ultimately, the details of the human origins debate remained unresolved, the work of Cann et al., Vigilant et al., and others lent support to the Recent Out of Africa hypothesis. However, additional questions about our species origins, specifically regarding the relationship between anatomically modern humans and now extinct hominins, remained unsettled [19-21].

## 3. Human migration and settlement

In addition to delineating human origins, mtDNA has also been used to trace human migration and settlement of the world. With a starting point in east Africa, humans migrated throughout the African continent as well as out into southwest Asia, Europe, Eastern Asia, and into the Americas. Mitochondrial analyses generally indicate that these dispersals began around 70,000 years ago [16,22]. The current understanding is that the initial dispersions out of Africa occurred in two routes, an earlier southern route that resulted in human presence in western and southern Asia and Australia by around 50,000 years ago [23]. The northern route was an expansion into North Africa, eastern and northern Asia and Europe. This second migration out of Africa is believed to have occurred around 40,000 years ago [24]. The final major dispersion of human groups was into the Americas and is estimated to have occurred 30,000 to 15,000 years ago [25]. In addition to movement out of Africa, mitochondrial data also support back migrations to Africa from different regions of the world [26,27].

## 4. *Homo sapiens* and other hominins

As human populations expanded beyond the African continent, they encountered other types of, now extinct, human species. According to taxonomic classifications based upon genetic data, the term hominins refers to humans and extinct human ancestors whereas the term hominids refer to human, extinct human ancestors, chimpanzees, gorillas, and orangutans [28]. Early studies analyzing mtDNA from extinct hominins, specifically Neanderthals, indicated that the variation observed among Neanderthals consistently fell outside of the variation observed for anatomically modern humans [29,30]. This suggested that, based upon mtDNA, anatomically modern humans and Neanderthals, while sharing a common ancestor that dates to 550,000 to 690,000 years ago, were not part of the same breeding population [29]. Subsequent studies analyzed mtDNA extracted from other Neanderthal specimens and also concluded that Neanderthals did not make genetic contributions to modern human populations [31,32]. However, based on studies completed within the last ten years, the finding that Neanderthals and humans did not exchange genes has been challenged with the inclusion of nuclear genomic data. The general conclusion from these studies is that for populations outside of Sub-Saharan Africa, extinct hominins including Neanderthals and Denisovans, interbred with anatomically modern humans [33-35]. In fact, low levels of genetic contributions from these species have been found in Eurasians. Around 1%–2% Neanderthal ancestry has been observed among Eurasian populations while Melanesians have 6%–8% ancestry from Denisovans [32,36-38]. Additionally, newer studies are also suggesting that genetic exchange between anatomically modern humans and now extinct hominins was not restricted to Europe and Asia, but likely occurred within African populations as well [39,40]. More data from both mitochondrial and nuclear DNA will be useful in further elucidating the nature of the relationships between our species and extinct hominins.

## 5. Direct to consumer genetic testing

Within the last twenty years, the number of companies offering mtDNA and other genetic tests to paying consumers has risen dramatically, with nearly 40 companies currently offering services [41]. These types of companies generally provide a variety of genotyping services including tests for genetic ancestry, relatedness, and disease risk [42-44]. Adding to the popularity of these services are both Internet and television advertisements in addition to media attention such as that featured in television documentaries like 'Who do you think you are?' or 'African American Lives' [45].

Beyond popular and media interest, DTC genetic tests have garnered the attention of scholars that seek to understand social impacts of these technologies. These scholars generally focus on why and how people engage with DTC technologies [46-48]. In these studies, many researchers report a variety of individual experiences, ranging from life-changing positive outcomes to confusion, anger, and regret about what genetic tests reveal [49-51]. Such studies reflect the uncertainties that surround uses of genetic tests including questions about privacy, consent, and appropriate interpretation of the results. In addition to documenting idiosyncratic experiences of DTC genetic test users, some researchers also examine the variety of ways that genetic information from DTC genetic tests impact historically marginalized communities [52-54]. For many members of historically marginalized communities, information about family and community histories are unavailable due to generations of systematic discrimination that has resulted in an obscuring of their histories. Genetic testing, consequently, potentially opens an avenue to obtaining previously unavailable information. In the case of people with African descent throughout the Americas, mitochondrial tests in addition to other ancestry informative markers illuminate the biological impacts of the Trans-Atlantic Slave trade highlighting ancestral geographic origins and evidencing admixture [55-58]. In the Spanish-speaking Caribbean islands, for example, genetic ancestry data has been referenced as support for the continued presence of indigenous Caribbean peoples. As a result, DTC ancestry tests have helped to shape the ongoing indigenous resurgence movements seen in these islands [59,60].

As part of the examination of social impacts of DTC genetic tests, researchers also have commented on the nature of the DTC testing industry. Despite the popularity of such tests, the DTC industry is unregulated and this laissez-faire approach has resulted in a wide variety of companies offering different tests that range in quality. While 'buyer-beware' is the current guiding principle to the DTC industry, increasingly, academics and federal agencies, such as the FDA, are making efforts to influence if not regulate DTC testing [41,69-71]. Accordingly, geneticists and social scientists that study the interactions between science and society are voicing concern over the lack of transparency and standardization of laboratory and statistical methods for ancestry estimations. The primary critique of DTC companies is that while genetic data, may appear precise, there are limitations to what may be inferred, in particular from genetic markers like mtDNA, and these limitations are not consistently provided to potential consumers.

## 6. The limitations of mitochondrial genetic data

Genetic anthropologists and genetic genealogists alike have lauded the advent of the Genomic age. Genetic technology has allowed for renewed investigational questions about human origins and migration, hominin species, and inter/intra regional relationships between populations. However, there are some technological and interpretive limitations of mtDNA. MtDNA does not recombine

and therefore is ideal for understanding the particular migratory histories of human groups. However, the lack of recombination also means that the scope and resolution of any interpretation based on mtDNA is comparatively limited relative to nuclear genetic markers [72]. For the purposes of genetic histories, mtDNA is essentially one genetic marker and cannot necessarily be considered as representative of the entire genome. The opposing conclusions regarding the relationship between Neanderthals and *Homo sapiens* based on mtDNA and nuclear DNA, illustrate the limitations of formulating theories about major evolutionary events using only one genetic marker. Secondly, with regard to genetic ancestry, due to the uni-parental inheritance of mtDNA, this genetic marker is only informative about the maternal lineage and not at all reflective of the entirety of an individual's genealogy. Citing a lack of substantive information content, some researchers devalue mtDNA regarding it as minimally informative [73]. However, on the scale of a population, rather than the individual, mtDNA still is quite informative about the demographic and migratory history of a population [74]. Thirdly, the assignment of genetic lineages to a specific continent is based on a frequency of how common the genetic lineage is in a particular region. In theory, this means that lineages are not stringently restricted to particular regions but instead can be found, albeit, at low frequencies, across the world. This semi-ubiquitous quality to genetic lineages can lead to an erroneous identification of an individual's geographic origin [73]. Despite these limitations, as discussed above, mtDNA have proven useful for making inferences about past evolutionary and historical processes. In addition to the general knowledge about broader questions surrounding human origins and evolution that mtDNA analyses have garnered, mtDNA data have also proven useful for addressing questions about local populations that would otherwise be left unaddressed.

## 7. MtDNA and local histories

Because of the unique maternal inheritance pattern of mtDNA, genetic genealogists, in addition to anthropologists, have found mtDNA particularly informative for tracing maternal ancestry. Considerations of mtDNA can serve as an analog to both paternally inherited Y chromosome DNA and paternally inherited surnames. Beyond tracing maternal lineages far back in time or 'deep ancestry', mtDNA can also be used to identify maternally related members of a family. Individuals that share a maternal lineage share a common ancestor, however estimating the time to that recent common ancestor is complicated due to variability of reported mutation rates for the mitochondrial genome [75,76]. Nonetheless, for the purposes of genetic genealogies, mitochondrial haplotypes that are shared between individuals generally correspond to a common mitochondrial ancestor within one to hundreds of generations ago [77,78]. MtDNA has also been marketed as a tool to help people 'discover' unknown elements of their ancestry [79]. For example, despite controversies of equating a genetic profile with any particular ethnicity, some genetic genealogy companies market the prospect of discovering Native American ancestry while other companies advertise their ability to further elucidate African ancestry [42,47]. The general theme with these uses of DTC tests is to recover knowledge that was lost as a result of colonization, enslavement, migrations, and other historical events.

Crossing disciplines, mitochondrial data have been combined with historical, ethnographic, and archaeological data to provide new insights into local histories. At times, mtDNA has been used to confirm what is generally already known. This was the case, for example, with the last royal Russian family, the Romanovs. The leading narrative was that Ural Soviets executed the entire family in 1918. However, since the bodies were deposited into unmarked graves, some historians posited that not all of the family members had died [80]. In 1991 and again in 2007, the purported remains of the family

were recovered and genetically tested. The mitochondrial and nuclear DNA tests provided confirmation that the entire family had indeed been executed in 1918 [81-83].

In other cases, mtDNA helps to radically alter primary narratives about the past. In a study led by Juan Martínez Cruzado, published in 2001, [84], the extent of indigenous Caribbean ancestry among contemporary Puerto Ricans was shown to be considerably higher than expected. General narratives of the Caribbean note that indigenous Caribbean populations were driven to extinction at the hands of European colonists soon after the turn of the 16$^{th}$ century [85]. Martínez Cruzado's work, in addition to subsequent publications from other geneticists, historians, and activists on other contemporary populations in Puerto Rico, Cuba, Dominica, St. Vincent, and Trinidad, illustrate that the extinction narrative is not correct but instead requires a more nuanced and integrative understanding of Caribbean history [86-90].

This last example from the Caribbean highlights the importance of contextualizing genetic data within larger frameworks. Using information from relevant other sources helps to interpret the genetic record. Contextualization is particularly important as cultural, social, political, economic, and biological factors affect processes that result in specific patterns of genetic variation. Relying on only genetic information while ignoring factors that shape the genetic landscape, can provide very limited, at best, or erroneous, at worse, ideas about human biological histories. While genetic data can provide novel perspectives to human experience, the experience of being human extends beyond DNA. Anthropological approaches using DNA must therefore take a holistic approach and rely upon multiple perspectives when making sense of the data.

## 8. Conclusion

Though representative of only a small percentage of the human genome, mtDNA has been quite powerful in illuminating human evolutionary history. As genotyping technology improves and comparative databases grow, mtDNA will continue to be a cornerstone in the anthropological and genetic genealogical toolkit. In particular, as the ability to recover DNA from ancient remains improves, researchers will gain better understandings of both the processes of human evolution and hominin relationships. Moreover, with an increased inclusion of people from understudied communities, researchers can work towards a refined and expanded understanding of the evolutionary processes that have shaped human histories. Finally, in light of enhanced analytical techniques and databases, genetic data are still best understood and interpreted when contextualized using additional lines of evidence. Interdisciplinary research drawing on history, archaeology, and other relevant sources will remain critical for understanding and interpreting the genetic record.

## Conflict of interest

The author declares there is no conflict of interest.

## References

1. Chinnery PF (2006) Mitochondrial DNA in *Homo sapiens*, In: *Human Mitochondrial DNA and the Evolution of Homo sapiens*: Springer, 3-15.
2. Strachan T, Read AP (2011) Human molecular genetics, 4th Eds., New York: Garland Science.
3. van Oven M, Kayser M (2009) Updated comprehensive phylogenetic tree of global human mitochondrial DNA variation. *Hum Mutat* 30: 386-394.

4. Anderson S, Bankier AT, Barrell BG, et al. (1981) Sequence and organization of the human mitochondrial genome. *Nature* 290: 457-465.
5. Andrews RM, Kubacka I, Chinnery PF, et al. (1999) Reanalysis and revision of the Cambridge reference sequence for human mitochondrial DNA. *Nat Genet* 23: 147.
6. Salas A, Coble M, Desmyter S, et al. (2012) A cautionary note on switching mitochondrial DNA reference sequences in forensic genetics. *Forensic Sci Int Genet* 6: 182-184.
7. Behar DM, van Oven M, Rosset S, et al. (2012) A "Copernican" reassessment of the human mitochondrial DNA tree from its root. *Am J Hum Genet* 90: 675-684.
8. Malyarchuk BA (2013) Improving the Reconstructed Sapiens Reference Sequence of mitochondrial DNA. *Forensic Sci Int Genet* 7: 74-75.
9. Bandelt H, Kloss-Brandstätter A, Richards MB, et al. (2014) The case for the continuing use of the revised Cambridge Reference Sequence (rCRS) and the standardization of notation in human mitochondrial DNA studies. *J Hum Genet* 59: 66-77.
10. Cann RL, Stoneking M, Wilson AC (1987) Mitochondrial DNA and human evolution. *Nature* 325: 31-36.
11. Lewin R (1987) The unmasking of mitochondrial Eve. *Science* 238: 24-26.
12. Vigilant L, Stoneking M, Harpending H, et al. (1991) African populations and the evolution of human mitochondrial DNA. *Science* 253: 1503-1507.
13. Horai S, Hayasaka K (1990) Intraspecific nucleotide sequence differences in the major noncoding region of human mitochondrial DNA. *Am J Hum Genet* 46: 828-842.
14. Kocher TD, Wilson AC (1991) Sequence evolution of mitochondrial DNA in humans and chimpanzees: control region and a protein-coding region, In: *Evolution of life*: Springer, 391-413.
15. Hasegawa M, Di Rienzo A, Kocher TD, et al. (1993) Toward a more accurate time scale for the human mitochondrial DNA tree. *J Mol Evol* 37: 347-354.
16. Ingman M, Kaessmann H, Paabo S, et al. (2000) Mitochondrial genome variation and the origin of modern humans. *Nature* 408: 708-713.
17. Stringer CB (1994) Out of Africa—a personal history, In: *Origins of anatomically modern humans*: Springer, 149-172.
18. Wolpoff M, Caspari R (1997) Race and Human Evolution, New York: Simon and Schuster.
19. Currat M, Excoffier L (2004) Modern humans did not admix with Neanderthals during their range expansion into Europe. *PLoS Biol* 2: e421.
20. Zilhão J (2006) Neandertals and moderns mixed, and it matters. *Evol Anthrop: Issue New Rev* 15: 183-195.
21. Tattersall I, Schwartz JH (1999) Hominids and hybrids: the place of Neanderthals in human evolution. *Proc Natl Acad Sci U S A* 96: 7117-7119.
22. Macaulay V, Hill C, Achilli A, et al. (2005) Single, rapid coastal settlement of Asia revealed by analysis of complete mitochondrial genomes. *Science* 308: 1034-1036.
23. Pugach I, Delfin F, Gunnarsdóttir E, et al. (2013) Genome-wide data substantiate Holocene gene flow from India to Australia. *Proc Natl Acad Sci U S A* 110: 1803-1808.
24. Maca-Meyer N, González AM, Larruga JM, et al. (2001) Major genomic mitochondrial lineages delineate early human expansions. *BMC genetics* 2: 1.
25. Kitchen A, Miyamoto MM, Mulligan CJ (2008) A three-stage colonization model for the peopling of the Americas. *PLoS One* 3: e1596.

26. Coia V, Destro-Bisol G, Verginelli F, et al. (2005) Brief communication: mtDNA variation in North Cameroon: Lack of Asian lineages and implications for back migration from Asia to sub-Saharan Africa. *Am J Phys Anthropol* 128: 678-681.
27. Gonder MK, Mortensen HM, Reed FA, et al. (2007) Whole-mtDNA genome sequence analysis of ancient African lineages. *Mol Biol Evol* 24: 757-768.
28. Wood B, Harrison T (2011) The evolutionary context of the first hominins. *Nature* 470: 347-352.
29. Krings M, Stone A, Schmitz RW, et al. (1997) Neandertal DNA sequences and the origin of modern humans. *Cell* 90: 19-30.
30. Krings M, Geisert H, Schmitz RW, et al. (1999) DNA sequence of the mitochondrial hypervariable region II from the Neanderthal type specimen. *Proc Natl Acad Sci U S A* 96: 5581-5585.
31. Ovchinnikov IV, Götherström A, Romanova GP, et al. (2000) Molecular analysis of Neanderthal DNA from the northern Caucasus. *Nature* 404: 490-493.
32. Green RE, Malaspinas A, Krause J, et al. (2008) A complete Neanderthal mitochondrial genome sequence determined by high-throughput sequencing. *Cell* 134: 416-426.
33. Noonan JP, Coop G, Kudaravalli S, et al. (2006) Sequencing and analysis of Neanderthal genomic DNA. *Science* 314: 1113-1118.
34. Green RE, Krause J, Ptak SE, et al. (2006) Analysis of one million base pairs of Neanderthal DNA. *Nature* 444: 330-336.
35. Green RE, Krause J, Briggs AW, et al. (2010) A draft sequence of the Neanderthal genome. *Science* 328: 710-722.
36. Lowery RK, Uribe G, Jimenez EB, et al. (2013) Neanderthal and Denisova genetic affinities with contemporary humans: Introgression versus common ancestral polymorphisms. *Gene* 530: 83-94.
37. Plagnol V, Wall JD (2006) Possible ancestral structure in human populations. *PLoS Genet* 2: e105.
38. Prüfer K, Racimo F, Patterson N, et al. (2014) The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature* 505: 43-49.
39. Hsieh P, Woerner AE, Wall JD, et al. (2016) Model-based analyses of whole-genome data reveal a complex evolutionary history involving archaic introgression in Central African Pygmies. *Genome Res* 26: 291-300.
40. Wall JD, Lohmueller KE, Plagnol V (2009) Detecting ancient admixture and estimating demographic parameters in multiple human populations. *Mol Biol Evol* 26: 1823-1827.
41. Royal CD, Novembre J, Fullerton SM, et al. (2010) Inferring Genetic Ancestry: Opportunities, Challenges, and Implications. *Am J Hum Genet* 86: 661.
42. Bolnick DA, Fullwiley D, Duster T, et al. (2007) Genetics. The science and business of genetic ancestry testing. *Science* 318: 399-400.
43. Tutton R (2004) "They want to know where they came from": population genetics, identity, and family genealogy. *New Genet Soc* 23: 105-120.
44. Farkas DH, Holland CA (2009) Direct-to-consumer genetic testing: two sides of the coin. *J Mol Diagn* 11: 263-265.
45. Nash C (2004) Genetic kinship. *Cult Stud* 18: 1-33.
46. Kaufman DJ, Bollinger JM, Dvoskin RL, et al. (2012) Risky business: risk perception and the use of medical services among customers of DTC personal genetic testing. *J genet counsel* 21: 413-422.

47. Nelson A (2008) Genetic Genealogy Testing and the Pursuit of African Ancestry. *Soc Stud Sci* 38: 759-760-783.
48. Wagner JK, Weiss KM (2011) Attitudes on DNA ancestry tests. *Hum Genet* 131: 41-56.
49. Belluz J (2014) Genetic testing brings families together: And sometimes tears them apart. Available from: http://www.vox.com/2014/9/9/6107039/23andme-ancestry-dna-testing.
50. Kilgannon C (2007) At a Harlem Reunion, a Rancher From Missouri Meets His 'DNA Cousins'. *The New York Times* Arts.
51. McDermott MT (2016) Meeting my DNA. *New York Times*.
52. Nelson A (2016) The Social Life of DNA: Race, Reparations, and Reconciliation After the Genome: Beacon Press.
53. Benn Torres J (2014) Prospecting the past: genetic perspectives on the extinction and survival of indigenous peoples of the Caribbean. *New Genet Soc* 33: 21-41.
54. TallBear K, Native American DNA: Tribal belonging and the false promise of genetic science. University of Minnesota Press, 2013. Available from: http://www.jstor.org/stable/10.5749/j.ctt46npt0.
55. Benn Torres J, Kittles RA, Stone AC (2007) Mitochondrial and Y chromosome diversity in the English-speaking Caribbean. *Ann Hum Genet* 71: 782-790.
56. Tishkoff SA, Reed FA, Friedlaender FR, et al. (2009) The genetic structure and history of Africans and African Americans. *Science* 324: 1035-1044.
57. Salas A, Carracedo A, Richards M, et al. (2005) Charting the Ancestry of African Americans. *Am J Hum Genet* 77: 676-680.
58. Stefflova K, Dulik MC, Barnholtz-Sloan JS, et al. (2011) Dissecting the within-Africa ancestry of populations of African descent in the Americas. *PLoS One* 6: e14495.
59. Estevez J (2008) The mtDNA debate: A diálogo on "How important is it?". *Centro J*: 218-228.
60. Haslip-Viera G (2008) Amerindian mtDNA does not matter: A reply to Jorge Estevez and the privileging of Taíno identity in the Spanish-speaking Caribbean. *Centro J* 20: 228.
61. Wilson DA, Woolsey DJ (2008) Meeting David Wilson.
62. Franklin M (1997) Power to the People: Sociopolitics and the Archaeology of Black Americans. *Hist archaeology* 31: 36-50.
63. Amsden D (2015) Building the first slavery museum in America. *N Y Times Mag*.
64. Ellis RM, Gallas KL, Perry JD (2014) Interpreting Slavery at Museums and Historic Sites. Rowman & Littlefield.
65. Mountain JL, Macpherson JM, Do CB, et al. (2011) Exceptions to the "One Drop Rule"? DNA evidence of African Ancestry in European Americans. Available from: http://blog.23andme.com/wp-content/uploads/2011/10/ASHG2011poster-Mountain-1.pdf.
66. Zimmer C (2014) White? Black? A Murky Distinction Grows Still Murkier. *New York Times*.
67. Lee SS, Mountain J, Koenig BA (2013) The Meanings of "Race" in the New Genomics: Implications for Health Disparities Research. *Yale J Health Pol Law Ethic* 1: 3.
68. Coop G, Eisen MB, Nielsen R, et al. (2014) Letters: 'A Troublesome Inheritance'. *NY Times (Print)* Sunday Book Review: BR6.
69. Annas GJ, Elias S (2014) 23andMe and the FDA. *N Engl J Med* 370: 985-988.
70. Hudson K, Javitt G, Burke W, et al. (2007) ASHG statement on direct-to-consumer genetic testing in the United States. *Am J Hum Genet* 81: 635.
71. Hauskeller C (2011) Direct to consumer genetic testing. *BMJ* 342: d2317.

72. Relethford J (2004) Reflections Of Our Past: How Human History Is Revealed In Our Genes: Westview Press.
73. Duster T (2009) Ancestry testing and DNA: uses, limits—and caveat emptor. *Gene Watch* 22: 16-17.
74. Jobling MA, Hurles M, Tyler-smith C (2004) Human evolutionary genetics: origins, peoples, and disease, Abingdon and New York: Garland Science.
75. Rieux A, Eriksson A, Li M, et al. (2014) Improved calibration of the human mitochondrial clock using ancient genomes. *Mol Biol Evol* 31: 2780-2792.
76. Henn BM, Gignoux CR, Feldman MW, et al. (2009) Characterizing the time dependency of human mitochondrial DNA mutation rate estimates. *Mol Biol Evol* 26: 217-230.
77. Walsh B (2001) Estimating the time to the MRCA for the Y chromosome or mtDNA for a pair of individuals. *Genetics* 158: 897-912.
78. Tëtushkin EY (2011) Genetic genealogy: History and methodology. *Russ J Genet* 47: 507-520.
79. Shriver MD, Kittles RA (2004) Genetic ancestry and the search for personalized genetic histories. *Nat Rev Genet* 5: 611-618.
80. Slater W (2007) The many deaths of Tsar Nicholas II: relics, remains and the Romanovs: Routledge.
81. Ivanov PL, Wadhams MJ, Roby RK, et al. (1996) Mitochondrial DNA sequence heteroplasmy in the Grand Duke of Russia Georgij Romanov establishes the authenticity of the remains of Tsar Nicholas II. *Nat Genet* 12: 417-420.
82. Gill P, Ivanov PL, Kimpton C, et al. (1994) Identification of the remains of the Romanov family by DNA analysis. *Nat Genet* 6: 130-135.
83. Coble MD, Loreille OM, Wadhams MJ, et al. (2009) Mystery solved: the identification of the two missing Romanov children using DNA analysis. *PloS one* 4: e4838.
84. Martinez-Cruzado JC (2001) Mitochondrial DNA Analysis Reveals Substantial Native American Ancestry in Puerto Rico. *Hum Biol* 73: 491-511.
85. Knight FW (1990) The Caribbean, The Genesis of a Fragmented Nationalism, New York: Oxford University Press.
86. Marcheco-Teruel B, Parra EJ, Fuentes-Smith E, et al. (2014) Cuba: exploring the history of admixture and the genetic basis of pigmentation using autosomal and uniparental markers. *PLoS genetics* 10: e1004488.
87. Mendizabal I, Sandoval K, Berniell-Lee G, et al. (2008) Genetic origin, admixture, and asymmetry in maternal and paternal human lineages in Cuba. *BMC Evolut Biol* 8: 213.
88. Vilar MG, Melendez C, Sanders AB, et al. (2014) Genetic diversity in Puerto Rico and its implications for the peopling of the Island and the West Indies. *Am J Phys Anthropol* 155: 352-386.
89. Forte MC (2002) "We are not extinct": The revival of Carib and Taino identities, the internet, and the transformation of offline indigenes into online 'N-digenes'.
90. Fraser A (2014) Revisiting the Carib Story. *Caribbean Quarterly* 60: 53.