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Mitochondrial DNA and Y Chromosome Diversity and the Peopling of the Americas: Evolutionary and Demographic Evidence

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ABSTRACT A number of important insights into the peopling of the New World have been gained through molecular genetic studies of Siberian and Native American populations. While there is no complete agreement on the interpretation of the mitochondrial DNA (mtDNA) and Y chromosome (NRY) data from these groups, several generalizations can be made. To begin with, the primary migration of ancestral Asians expanded from south-central Siberia into the New World and gave rise to ancestral Amerindians. The initial migration seems to have occurred between 20,000–15,000 calendar years before present (cal BP), i.e., before the emergence of Clovis lithic sites (13,350–12,895 cal BP) in North America. Because an interior route through northern North America was unavailable for human passage until 12,550 cal BP, after the last glacial maximum (LGM), these ancestral groups must have used a coastal route to reach South America by 14,675 cal BP, the date of the Monte Verde site in southern Chile. The initial migration appears to have brought mtDNA haplogroups A-D and NRY haplogroups P-M45a and Q-242/Q-M3 to the New World, with these genetic lineages becoming widespread in the Americas. A second expansion that perhaps coincided with the opening of the ice-free corridor probably brought mtDNA haplogroup X and NRY haplogroups P-M45b, C-M130, and R1a1-M17 to North and Central America. Finally, populations that formerly inhabited Beringia expanded into northern North America after the LGM, and gave rise to Eskimo-Aleuts and Na-Dené Indians. Am. J. Hum. Biol. 16:420–439, 2004.

Over the past 7 years there has been a great proliferation of molecular anthropological studies of different human populations across the world. These studies have clarified various aspects of migrations into the major continental regions of the world, shed light on the emergence of linguistic and archeological traditions, and provided insights into differential male and female gene flow within local populations. Not surprisingly, many new data have also been obtained from Native American and Siberian populations. Such data have been used to address several major questions about the peopling of the New World, namely, when ancestral Native Americans first arrived in the Americas, how many population expansions or migrations were involved in this colonization process, and where in Asia/Eurasia that these ancestral groups came from. This genetic evidence has yielded new insights into the origins of Native Americans, while also raising a number of additional and intriguing questions about their prehistory.

The two genetic systems most commonly used in studies of Native American and Siberian population variation have been the mitochondrial DNA (mtDNA) and the nonrecombining portion of the Y chromosome (NRY). Each of them possesses a series of different markers that help to define or identify specific genetic lineages (maternal and paternal, respectively) present in human groups. By analyzing the sequence variation in these two genomes, one can identify the genetic lineages that are present within populations and ascertain the manner in which they have been spread across geographic areas. Moreover, by measuring the sequence variation that has accumulated within them,

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one can estimate their approximate ages in a particular part of the world, assuming certain assumptions about the initial population size, etc.

In this article, we explore the prehistory of the Americas from three different perspectives. The first examines the antiquity of genetic lineages in Native American groups and how it relates to the timing of the initial human entry in the New World. The second focuses on the demographic aspects of population expansions into the Americas—in particular, the way in which such expansions leave signatures in the genetic diversity of extant populations. The third considers the genetic evidence for the occurrence of multiple migrations into the New World. In the final section, we synthesize the molecular data in the context of other anthropological evidence to generate a current view of the peopling of the Americas.

GENETIC DIVERSITY OF NATIVE AMERICAN POPULATIONS

mtDNA haplogroups in the Americas

The vast majority of mtDNAs from modern Native American populations belong to primarily five different haplogroups, which have been designated A–D and X (Schurr et al., 1990; Torroni et al., 1992, 1993a, 1994a,b; Forster et al., 1996; Brown et al., 1998). Each of these is distinguished by a unique combination of coding region RFLPs and HVR-I sequence polymorphisms. Together, they comprise 95–100% of all mtDNAs in indigenous populations of the New World (Schurr, 2001, 2002, and references therein). The same pattern of variation is also observed in ancient Amerindian samples (Merriwether et al., 1994; Fox, 1996; Monsalve et al., 1996; Parr et al., 1996; Ribeiro-Dos-Santos et al., 1996; Lalueza et al., 1997; Stone and Stoneking, 1998; Carlyle et al., 2000; O'Rourke et al., 2000; Kaestle and Smith, 2001). Therefore, these five haplogroups are clearly the main founding mtDNA lineages in Native American populations.

However, a certain number of haplotypes not belonging to these five maternal lineages have been detected in different Native American groups (Bailliet et al., 1994; Easton et al., 1996; Merriwether et al., 1994, 1995; Lorenz and Smith, 1996, 1997; Ribeiro-Dos-Santos et al., 1996; Rickards et al., 1999; Santos et al., 1996; Torroni et al., 1993a; Ward et al., 1991). Most of these have been shown to belong to haplogroup X, derive from haplogroups A–D mtDNAs, or result from non-native admixture (Schurr and Wallace, 1999; Smith et al., 1999; Schurr, 2002, 2004a). The remaining haplotypes were not sufficiently analyzed to determine their haplogroup status (e.g., Bailliet et al., 1994; Ribiero-dos-Santos et al., 1996).

Haplogroup A–D mtDNAs are observed in indigenous populations from North, Central, and South America (summarized in Schurr, 2001, 2002, and references therein). Among Amerindians, haplogroup A generally occurs at higher frequencies in North America relative to other regions, whereas haplogroups C and D generally occur at higher frequencies in South America. There does not appear to be a distinct clinal distribution for haplogroup B, but it is virtually absent from northern North America (Schurr et al., 1990; Torroni et al., 1992, 1993a, 1994a,b; Fox, 1996; Lorenz and Smith, 1996, 1997; Malhi et al., 2001, 2002). In contrast, haplogroup X is found nearly exclusively in North America (Torroni et al., 1992, 1993a; Scozzari et al., 1997; Brown et al., 1998; Smith et al., 1999; Malhi et al., 2001, 2002; Bolnick et al., 2003). These distributions likely reflect both the original pattern of settlement of the Americas and the subsequent genetic differentiation of Native American populations within these continental areas.

Haplogroup A–D mtDNAs have also been detected in populations representing the three Native American linguistic groups (Amerind, Na-Dené, Eskimo-Aleut) proposed by Greenberg (1987). Although haplogroups A–D usually appear together in Amerindian populations, many tribes lack haplotypes from at least one of these haplogroups (Torroni et al., 1992, 1993a, 1994a,b; Batista et al., 1995; Kolman et al., 1995; Easton et al., 1996; Lorenz and Smith, 1996, 1997; Kolman and Bermingham, 1997; Scozzari et al., 1997; Rickards et al., 1999; Moraga et al., 2000; Bert et al., 2001). This pattern likely reflects the extent to which genetic drift and founder events have influenced the distribution of mtDNA haplotypes in New World populations.

However, ancestral populations for the Na-Dené Indians and Eskimo-Aleuts may not have possessed all four of these haplogroups. These populations show different haplogroup profiles than Amerindians, which consist largely of haplogroup A and D mtDNAs. In

addition, they essentially lack haplogroup B and have very low frequencies of haplogroup C. Moreover, none of them have haplogroup X mtDNAs (Torroni et al., 1992, 1993a; Shields et al., 1993; Ward et al., 1993; Starikovskaya et al., 1998; Saillard et al., 2000; Rubicz et al., 2003). Thus, circumarctic groups appear to have experienced different population histories than Amerindians.

NRY haplogroups in the Americas

In characterizing NRY variation in Native Americans, researchers have employed a number of different single nucleotide (SNP) and short tandem repeat (STR) loci to define the paternal lineages present within them (Pena et al., 1995; Underhill et al., 1996, 1999, 2000; Bianchi et al., 1997, 1998; Hammer et al., 1997; Karafet et al., 1997, 1999; Lell et al., 1997, 2002). However, these research groups have not used the same combination of genetic markers in their studies, leading to alternative and sometimes confusing nomenclatures for NRY haplotypes and haplogroups. A recent synthesis of these data has resulted in a consensus nomenclature based on known single nucleotide polymorphisms (SNPs) (Y Chromosome Consortium 2002), and it will be used in this article. This system identifies a NRY haplogroup by a letter and the SNP that defines it (e.g., G-M201).

Native American NRY haplotypes derive from subsamples of the haplogroups present in Siberia. These include haplogroups Q-M3, R1a1-M17, P-M45, F-M89, and C-M130. Two of them, Q-M3 and P-M45, represent the majority of Native American Y-chromosomes. Q-M3 haplotypes appear at significant frequencies in most Native American populations and are distributed in an increasing north-to-south cline within the New World (Bianchi et al., 1996, 1998; Underhill et al., 1996; Karafet et al., 1997, 1999; Lell et al., 1997, 2002; Santos et al., 1999). The STR data from Q-M3 haplotypes also reveal significant differences in haplotype distributions between North/Central and South American populations, suggesting different population histories in the two major continental regions (Bianchi et al., 1997, 1998; Karafet et al., 1997, 1999; Lell et al., 1997, 2002; Ruiz-Linares et al., 1999; Santos et al., 1999).

Haplogroup P-M45 is also widely distributed among Native American populations and represents ~30% of their NRY haplotypes (Ruiz Linares et al., 1999; Santos et al., 1999; Lell et al., 2002; Bortolini et al., 2003). In addition, phylogenetic analysis has revealed two distinct sets of P-M45 haplotypes in Native American populations. The first of these (M45a) is more broadly distributed in populations from North, Central, and South America, whereas the second (M45b) appears in only North and Central American groups (Lell et al., 2002).

Most of the remaining NRY haplotypes belong to one of several different haplogroups, and comprise only 5% of Native American Y chromosomes. In general, these haplotypes have limited distributions in the New World. For example, C-M130 haplotypes have only been detected in the Na-Dené-speaking Tanana, Navajo and Chipewayan, and the Amerindian Cheyenne (Bergen et al., 1999; Karafet et al., 1999; Lell et al., 2002; Bortolini et al., 2003). In addition, R1a1-M17 haplotypes have only been observed in the Guaymi (Ngöbe), a Chibchan-speaking tribe from Costa Rica (Lell et al., 2002). Neither of these haplogroups has been detected in South American Indian populations.

TIMING OF THE INITIAL COLONIZATION OF THE AMERICAS

Having defined the genetic lineages present in Native American populations, we can now turn to the question of when ancestral populations first entered the New World. Considerable attention has been paid to this question for several reasons. First, the Americas were the last continental regions to be settled by modern humans, who entered areas previously uninhabited by people. For this reason, genetic studies of Native American groups will illuminate the process and rate of human migration and adaptation to new environments. Second, there is great interest in knowing how much time was required to generate the biocultural diversity observed in contemporary Native American populations. Assigning a temporal starting point for the accumulation of this diversity will provide a calibration point for estimating into how fast languages and cultures can change, particularly if a single primary migration gave rise to all Amerindian populations. Third, estimates for the timing of the initial migration to the New World based on genetic studies have ranged from 30,000–14,000 calendar years before present (cal BP). However, this range encompasses the Last Glacial Maximum (LGM) (~24,000–13,050 cal BP),

a period of time when human movement into the New World through an interior route was not possible because of glacial barriers. Therefore, reconciling the genetic data with archeological and geological evidence will be crucial for determining whether the First Americans arrived before or after the LGM, and whether they followed an interior or coastal route into the New World during this time period.

Antiquity of mtDNA haplogroups in Siberia and the Americas

While there is little controversy about the number and type of founding haplogroups in the New World, the ages of these maternal lineages continues to be contested. Early studies of RFLP variation in Native American populations produced time depths for haplogroups A, C, D, and X of between 35,000–20,000 cal BP (Torroni et al., 1992, 1993a, 1994a). These estimates were viewed as reflecting the genetic diversity that had accumulated in the American branches of these mtDNA lineages, hence, the time at which modern humans first entered the Americas. Additional support for these findings came from the fact that Native American and Siberian populations did not share any specific haplotypes (Torroni et al., 1993b; Starikovskaya et al., 1998; Schurr et al., 1999). By contrast, the age for haplogroup B in the New World was estimated at 17,000–13,000 cal BP, suggesting that it was brought to the Americas in a later and separate migration from the earlier one that brought the other four lineages. The age of haplogroup X based on RFLP haplotype data was identical to that of haplogroup B, although it increased in age when estimated from HVS-I sequence data (Brown et al., 1998).

Subsequent analyses of HVS-I sequence variation in Native Americans provided somewhat different perspectives on the antiquity of these haplogroups. Several of them showed that haplogroups A, B, and C had roughly the same extent of genetic diversification in North America, and that haplogroup B could possibly have been present in the New World by 30,000–20,000 cal BP (Lorenz and Smith, 1997; Bonatto and Salzano, 1997; Stone and Stoneking, 1998). The older date also implied that haplogroup B arrived in the Americas around the same time that haplogroups A, C, D, and X did. In fact, most HVS-I studies have provided ages for the four major founding haplogroups that range between 35,000–15,000 cal BP, with the earliest dates being 14,000–12,000 cal BP (Shields et al., 1993). A recent analysis of coding region sequence variation in Native American populations has also generated average dates for haplogroups A–D of between 20,000–15,000 cal BP (Silva et al., 2002a). Thus, most molecular studies favor an entry time for these mtDNA lineages that is somewhat earlier than the dates associated with the Clovis lithic culture in North America.

Two other important issues about haplogroup ages have arisen in this debate. The first centers on the question whether the older haplogroup age estimates actually reveal the timing of human expansion(s) into the New World. Because the genetic divergence or coalescence times of genetic lineages do not necessarily correspond to the timing of population splits, it has been suggested that the older dates may reflect the emergence of these mtDNA lineages in Asia rather than their entry into the Americas (e.g., Shields et al., 1993). On the other hand, only the founding RFLP haplotypes for haplogroup A–D have been shown to be present in both Siberia and the Americas (Torroni et al., 1992, 1993a; Schurr et al., 1999). These data suggested that the temporal split between the ancestral Amerindian population and its Asian precursor mirrored the split in the branches of each respective haplogroup. This issue will be reexamined below when considering demographic aspects of New World colonization.

The second issue is the number of founding haplotypes that were brought with each founding haplogroup. The number of founders present in a genetic lineage will affect estimates of its age because a certain amount of the diversity present in that lineage will have accumulated from each founding type. If more than one founding haplotype was present within a haplogroup, then the age of this mtDNA lineage would be inflated due to the fact that the diversity of haplotypes that accumulated from each founding haplotype was not taken into account in the coalescence estimates. For Native Americans, the presence of multiple founding haplotypes would imply that the ages of haplogroups A–D would be less than 30,000–20,000 cal BP; hence, the colonization date of the Americas would be more consistent with a late entry (Clovis-first) migration model.

As noted above, there appears to be only one founding RFLP haplotype each for

haplogroups A–D and X (Torroni et al., 1992, 1993a, 1994a,b; Brown et al., 1998; Schurr et al., 1999). These founder haplotypes are the most widely distributed mtDNAs in the Americas, and central to the diversification of their respective haplogroups. However, other investigators have suggested that more than one founding haplotypes from haplogroups A–D were among the original set of founding Native American mtDNAs (Bailliet et al., 1994; Merriwether et al., 1994, 1995; Easton et al., 1996; Santos et al., 1996; Rickards et al., 1999). Unfortunately, none of these studies have provided additional RFLP or HVR-I sequence data to demonstrate that these are actually the same founding haplotypes defined in other studies (Schurr and Wallace, 1999; Schurr, 2004b).

At the same time, Malhi et al. (2002) argue that there could possibly be more than one founder HVS-I sequence for at least some of these haplogroups, due to these sequences being identical to ones present in Asian and Siberian populations. However, they also recognize the difficulty in delineating ancestral sequences from derivative forms that have lost or gained key polymorphisms that distinguish American from Asian sequence motifs, due to the recurrent mutations that typically occur in the mtDNA control region (Gurven, 2000; Stoneking, 2000). Thus, additional coding region data must be obtained from these mtDNAs to confirm their status as founder haplotypes.

Antiquity of NRY haplogroups in Siberia and the Americas

The methods for dating NRY haplogroups have employed both the SNPs that define them and the STR loci that occur on each Y chromosome. Because SNPs are rare, if not unique, evolutionary events, it is difficult to estimate when they evolved in a particular paternal lineage using only this kind of data. To get around this problem, Underhill et al. (2001) used an average mutation rate estimated from SNP variation in three NRY genes (Thomson et al., 2000) to date the various branches (haplogroups) of their phylogeny. This estimate of 1.24×10^{-9} produced an age for the major expansion of modern humans out of Africa of ~59,000 cal BP. Using this date for the Most Recent Common Ancestor (MRCA) of their SNP phylogeny, Underhill et al. (2000) estimated an average SNP evolution rate of one per every 6,900 years. With this rate, it is possible to tentatively date the origins of the major branches of the phylogeny, as well as other points of SNP haplotype diversification.

An alternative strategy for dating the ages of NRY haplogroups is to analyze variation in the faster evolving STR loci that co-occur on each SNP haplotype. In this case, the extent of allelic diversity of a set of STR loci are measured and averaged over all loci, with the average then being multiplied by an STR mutation rate to determine the actual age of the NRY lineage. Recent mutation rates have been estimated across multiple generations of males (meiotic transmissions) in human families. Although these rates vary somewhat depending on the type of STR used for the estimates (di-, tri-, tetra-), most studies have found that the average mutation rate of NRY STRs is around 2.80×10^{-3} per generation (Heyer et al., 1997; Kayser et al., 1997, 2000; Bianchi et al., 1998; Thomson et al., 2000).

Considerable effort has been made to estimate the age of Q-M3 haplotypes, given that they appear to signal the initial entry of ancestral populations into the New World. Using the SNP mutation rate of Underhill et al. (2000), one obtains an age for haplogroup Q-M3 of ~13,800 cal BP (Schurr, 2004a). The estimates made with STR mutation rates have ranged from 30,000–7,600 cal BP (Underhill et al., 1996; Bianchi et al., 1998; Hammer et al., 1998; Karafet et al., 1999; Forster et al., 2000). Together, these analyses of NRY variation in Native American populations do not clearly point to an early or late entry of the Q-M3 lineage into the New World, but tend to favor the latter.

The P-M45 lineage is considerably older than the Q-M3 lineage, which derives from it. Using the SNP mutation rate of Underhill et al. (2000), P-M45 haplotypes are estimated to be at least 30,000 years old. This degree of antiquity is also reflected by their widespread distribution in Siberia and Eurasia (Underhill et al., 2000; Lell et al., 2002). In addition, the P-M45 lineage has been present in Siberia long enough to diversify into different subhaplogroups. This is shown by the presence of two different types of NRY haplotypes in Native Americans, a central Siberian set (P-M45a) that is shared with all Native American populations, and an eastern Siberian set (P-M45b) that appears only in Native Americans from North and Central America (Lell et al., 2002).

The ages of several other NRY lineages present in Siberia and the Americas have also been estimated. One of the older lineages in Siberia, K-M9, has been dated at >50,000 cal BP (Karafet et al., 1999; Underhill et al., 2000). The antiquity of the K-M9 lineage is consistent with the presence of this SNP in a sizeable majority of Siberian Y chromosomes (Karafet et al., 1999; Santos et al., 1999; Underhill et al., 2000; Lell et al., 2002). The oldest SNP in the Eurasian branch of the NRY phylogeny, F-89, dates to ~62,000 cal BP (Schurr, 2004a), and predates the occurrence of the K-M9 lineage, since it appears in all haplotypes bearing the latter mutation. F-89 is an important SNP because it marks the initial diversification and spread of non-African NRY lineages into the rest of the world.

By contrast, the C-M130 lineage is somewhat younger than the F-M89 or K-M9 lineages, having been dated at ~30,000–25,000 cal BP (Karafet et al., 1999; Underhill et al., 2000). Its age is generally consistent with its broad distribution in East and Southeast Asia, in which it appears to have originated, and its haplotypic diversity in eastern Siberian and Asian populations (Su et al., 1999; Lell et al., 2002).

The estimated age of haplogroup R1a1-M17 is rather intriguing. Using the SNP evolution rate of Underhill et al. (2000), an age of 13,800 cal BP was obtained for this lineage, one that falls into the very end of the LGM (Schurr, 2004a). These haplotypes constitute a distinct branch within R1a, and are not especially common in Siberian populations, although occurring across a broad geographic area (Lell et al., 2002). The data suggest that R1a1-M17 haplotypes did not emerge in Siberia until after the Americas had already been colonized and were brought to the New World through a secondary expansion of ancient Asian populations, along with C-M130 and P-M45b haplotypes (Lell et al., 2002).

The most recent efforts to date the NRY haplotypes present in Native American populations have utilized a newly identified SNP, Q-M242, to make this estimate (Bortolini et al., 2003; Seielstad et al., 2003). The Q-M242 marker occurred within haplogroup P-M45 in Central Asia prior to the emergence of the Q-M3 SNP and the expansion of its haplotypes in the Americas. As such, the M242 marker may better define the initial entry into the Americas than M3. Using STR mutation rates, researchers have dated the age of M242 haplotypes in the New World at ~18,000–15,000 cal BP (Bortolini et al., 2003; Seielstad et al., 2003).

DEMOGRAPHY OF NATIVE AMERICAN POPULATIONS

The manner in which a population enters and establishes itself in a geographic area should be reflected in the pattern of variation in its genes. A sudden population expansion shows certain demographic features that distinguish it from a more uniform pattern of growth and dispersal. In the former case, a founding population rapidly grows from small numbers until reaching some plateau. Concomitantly, the extent of genetic diversity also increases substantially because of this rapid spread of human groups and their genetic divergence from each other because of being geographically isolated from one another. Such diversification appears as a multiplication of the branches and subbranches in a gene genealogy, with the major bifurcation points or nodes corresponding to the initial phase of expansion.

If the resulting haplotypes are compared for pairwise mutational differences, one can generate a frequency plot of these differences and determine the parameters of this expansion (Rogers and Harpending, 1992). The resulting curve should show the speed and nature of the expansion, based on the initial slope and shape of the curve, respectively. A steep upward trajectory of the curve suggests the rapid expansion of the population, whereas a more modest slope indicates a somewhat slower growth process. If the curve is unimodal and smooth, then the growth or expansion probably occurred as a single event. However, if it is bimodal or ragged (multiple peaks), then two or more expansions may have contributed to the genetic make-up of that population. Alternatively, the population may have undergone fluctuations in size because of various stochastic processes, such as population bottlenecks. Thus, we can distinguish several basic parameters of populations having undergone different demographic processes through this kind of sequence analysis.

Such signatures of population expansion have been examined through the analysis of mismatch and crossmatch distributions in mtDNA sequence data (Harpending and Rogers, 1992; Harpending et al., 1993, 1998; Sherry et al., 1994). Mismatch distributions

refer to pairwise comparisons between all members in a single population (or haplogroup), while crossmatch distributions refer to all pairwise comparisons between members of two separate populations (or haplogroups). Given these empirical distributions and the locus-specific generational mutation rate, μ, it is possible to estimate when an episode of population expansion began or when two populations diverged, both events being measured in units of mutational time.

In mtDNA studies, mismatch distributions can be estimated from either HR-RFLP haplotype or HVR-I sequence data, or even whole genome sequences. Ordinarily, when considering DNA sequence data, mismatch and crossmatch distributions are simply tabulations of the number of mutational differences between all pairs of individuals in a sample, and the estimation of the per-site mutation rate, μ, is simply the product of μ and the number of nucleotides sequenced. However, when HR-RFLP data are being analyzed, a unit conversion has to be performed because haplotype scores (0 and 1 for the absence or presence of a RFLP, respectively) are not equivalent to single nucleotide substitutions, due to the fact that each restriction enzyme surveys variation across 4–6 nucleotides within each recognition site (Table 1). However, once converted into sequence format, the haplotype data can be analyzed with the mismatch and crossmatch techniques as though they were HVS-I sequences.

Using this analytical approach, we investigated whether all of the founding haplogroups in Native Americans showed the same pattern of haplotypic diversity. If these mtDNA lineages were brought to the Americas at the same time through a single expansion event, then the mismatch and crossmatch distributions should look essentially identical, i.e., the same shape of the curve, and the same average number of mutation differences between haplotypes or HVS-I sequences. By contrast, if one or more of them arrived at different times through independent expansions, then the distributions should vary between the mtDNA lineages. Furthermore, if any of the haplogroups were brought to the Americas more than once, then the mismatch distributions for those haplogroups could be bimodal or ragged, depending on how much time passed between the expansions. Thus, we are able to make some predictions as to what the mismatch profile of these mtDNA lineages might look like under different demographic or migration scenarios.

Two different kinds of mismatch analyses were performed with the HR-RFLP haplotype data from haplogroups A–D and X (Torroni et al., 1992, 1993a, 1994a,b). In the first analysis (Analysis I), the entire HR-RFLP dataset was analyzed, with expansion times for the haplogroups and divergence times between the haplogroups being computed. In the second (Analysis II), the dataset was analyzed after removing the RFLPs that define each haplogroup, as these sites are known to predate the entry of ancestral Native American populations into the New World. Comparison of the results of these two analyses would, therefore, provide approximate dates for the expansion of these mtDNA lineages in Asia/Siberia (Analysis I) and their expansions in the New World (Analysis II).

The results of Analysis I showed that haplogroups C and D were the first haplogroups

TABLE 1. Unit conversion of RFLP haplotype data into sequence data

RFLP study	Haplotype estimate	2μ estimate for DNA sequence data*		
		2%	3%	4%
Cann et al. 1987	μ	0.126	0.189	0.252
V = 236, r = 4, T = 370	2μ	0.252	0.378	0.503
Torroni et al. 1993a, 1994a,b	μ	0.247	0.370	0.494
V = 149, r = 4, T = 459	2μ	0.494	0.740	0.988

T = total number of restriction sites inspected, V = the number of reported variable sites, and r = average recognition sequence length. The conversion of μ to an RFLP-equivalent μ was defined as $\mu = 2\mu/[V/rT]$. This formula is also written $\hat{u} = 2\mu k$, with k being equal in expectation to the average number of nucleotide sites per haplotype that are covered by restriction sites in the data (Harpending and Rogers, 1992).

*The 2μ value represents the nucleotide divergence rate. The data for each population consisted of haplotype frequencies and designations (AM01-AM96) for 149 polymorphic sites (Torroni et al. 1993a, 1994a,b). All of the polymorphisms included in these analyses were presumed to be the product of simple point mutations. As a result, the Region V 9-bp deletion, which is frequently used as a marker of Asian ancestry and almost completely defines haplogroup B, was excluded from analysis. This exclusion is justified by the fact that Region V deletions arise by a different mutational process than that generating RFLPs, one that has not been incorporated into the analytical theory underlying this method.

TABLE 2. Parameter estimates for Amerindian mtDNA haplogroups

		Analysis I (full data set)			Analysis II (haplogroup-defining sites removed)		
Haplogroup	N	$\tau \pm$ SE (τ)	θ	Time	$\tau \pm$ SE (τ)	θ	Time
Mismatch analysis (population expansion)							
A	156	1.94 ± 0.65	0.74	17,600	1.58 ± 0.63	0.75	14,900
B	93	0.33 ± 0.40	0.82	3,000	0.33 ± 0.66	0.82	3,100
C	61	3.58 ± 0.60	0.00	32,400	3.06 ± 0.21	0.00	28,900
D	59	2.13 ± 0.48	0.00	19,300	1.68 ± 0.26	0.00	15,800
X	8	2.11 ± 0.45	0.00	19,100	2.11 ± 0.68	0.00	20,000
TOTAL	377	3.47 ± 0.80	1.14	31,400	1.72 ± 0.45	0.50	16,270
Crossmatch analysis (population divergence)							
A × B	249	3.72 ± 2.00	0.00	33,600	1.04 ± 0.79	0.85	9,800
A × C	217	7.24 ± 3.10	0.00	65,600	2.89 ± 0.69	0.00	27,200
A × D	215	6.53 ± 3.42	0.00	59,000	2.18 ± 0.66	0.00	20,600
A × X	164	5.00 ± 2.93	0.00	45,400	2.18 ± 0.66	0.00	30,000
B × C	154	6.03 ± 2.61	0.00	54,800	2.18 ± 0.66	0.00	21,800
B × D	152	5.45 ± 3.16	0.00	49,400	2.18 ± 0.66	0.00	16,400
B × X	101	2.78 ± 1.24	0.00	25,200	2.18 ± 0.66	0.00	26,200
C × D	120	5.04 ± 2.19	0.00	45,600	2.18 ± 0.66	0.00	24,200
C × X	69	7.28 ± 3.38	0.00	65,800	2.18 ± 0.66	0.00	33,600
D × X	67	6.40 ± 3.31	0.00	58,000	2.18 ± 0.66	0.00	25,400

All mismatch distributions were constructed by comparing each haplotype against every other one, for a total of n (n−1)/2 comparisons, and tallying the number of differences in a vector indexed by i number of differences, where the index value i = 0, 1, 2, ... Crossmatch distributions, which define the distribution and relative divergence of a pair of samples, were constructed by comparing each haplotype in one sample against every other haplotype, for a total of nm comparisons, in the same manner as mismatch distributions. The two-parameter method of moments developed by Rogers (1994) was used to estimate the time of population growth, τ (tau), and the pre-expansion parameter θ (theta), which is defined as $\theta = 2N\mu$ for mtDNA. The standard errors reported for estimates of θ and τ were computed from simulation trials after Harpending et al. (1993). The distribution raggedness r, a measure of growth magnitude, was computed after Harpending (1994) and Sherry et al. (1994).

to expand in Siberia and the New World, beginning around 35,000–25,000 cal BP (Table 2; Fig. 1). This result is consistent with their widespread distribution throughout North and East Asia, and with other estimates of their ages in these regions (Torroni et al., 1993b; Sukernik et al., 1996; Starikovskaya et al., 1998; Derenko et al., 1998; Schurr et al., 1999; Schurr and Wallace, 2003). Haplogroups A and X expanded somewhat later, around 20,000–18,000 cal BP, while haplogroup was the last mtDNA lineage to expand within the Americas, beginning around 15,000–12,000 cal BP. These estimates are generally concordant with the divergence values previously estimated from the same haplotype dataset.

In contrast, the results of Analysis II were inconsistent with a great antiquity for haplogroups A–D and X in the New World. When the haplogroup-defining sites were removed, the haplogroups appeared to have expanded on average about 18,000 cal BP (Fig 1). This date was compatible with a scenario of population growth and fission upon entry into the New World. Interestingly, the Analysis II estimates gave recent (~15,000–12,000 cal BP) expansion times for haplogroups A and B in the Americas, and earlier expansion times for haplogroups C and D (~25,000 cal BP), with haplogroup X falling in between them (~20,000 cal BP). The Analysis I expansion times were proportionately similar, indicating that the inclusion of haplogroup-defining sites did not greatly bias the mismatch calculations towards older expansion times. It should also be pointed out that the haplogroup A expansion time estimate in this analysis was based solely on Native American HR-RFLP haplotypes, not those from the Chukchi and Siberian Eskimos, as was the case for a more recent divergence time estimate for this mtDNA lineage (Starikovskaya et al., 1998; Schurr et al., 1999).

To determine the consistency of the patterns obtained for these mtDNA lineages, an additional set of mismatch and crossmatch analyses were carried out with the HR-RFLP haplotype data. In this case, the HR-RFLP haplotypes were partitioned into the 24 Native American populations in which they were first characterized before being analyzed. In general, the mismatch distributions for these groups were quite variable (Tables 3 and 4, Fig. 2). Some populations appeared to

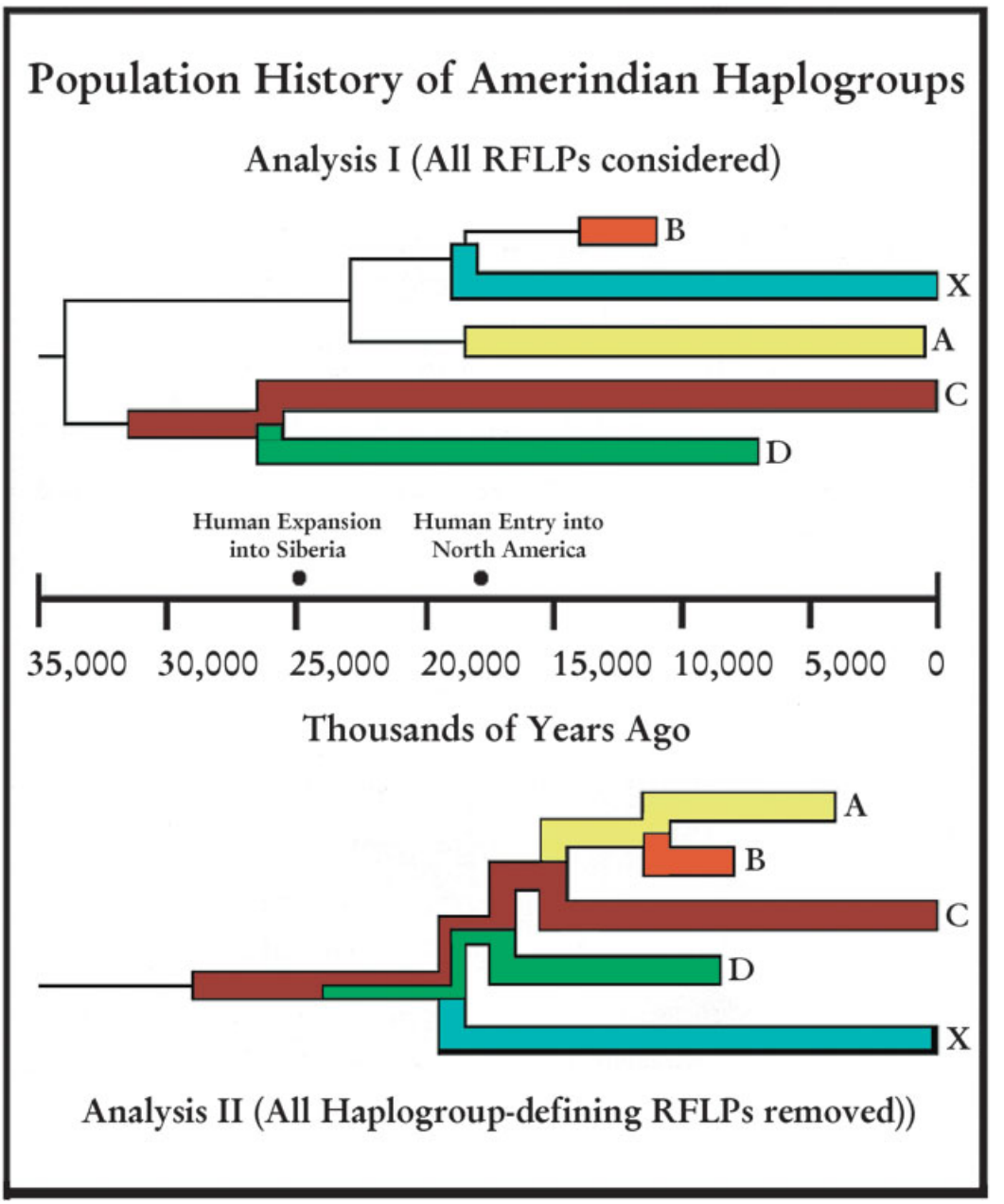

Fig. 1. Pairwise mismatch analysis of Native American haplogroups. Each figure portrays a possible population history of Amerindian haplogroups. The overall structure provides haplogroup fissioning times (crossmatch data), while the shaded overlays indicate periods of population expansion [estimated from $\tau \pm SE$ (τ) values (Table 2). For Analysis II, the RFLPs defining each haplogroup were removed from the haplotypes being analyzed, since they were common to both Asian and Native American mtDNAs belonging to these lineages. This step allowed an estimate of the times at which new haplotypes within each haplogroup began to accumulate diversity or expand in the New World. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

TABLE 3. Mismatch distributions for 20 Native American populations analyzed by RFLP haplotype analysis

Population	F_0	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}
Dogrib	.448	.460	.092	0	0	0	0	0	0	0	0	0
Ojibwa	.161	.023	.013	.018	.008	.098	.230	.230	.071	.077	0	0
Navajo	.175	.244	.173	.198	.086	.042	.056	.026	0	0	0	0
Pima	.064	.110	.117	.126	.067	.113	.205	.166	.032	0	0	0
Maya	.063	.122	.140	.143	.111	.222	.103	.032	.048	.008	.008	0
Teribe/Naso	.663	0	0	0	0	.337	0	0	0	0	0	0
Guatuso	.637	0	0	.011	.263	.089	0	0	0	0	0	0
Boruca	.505	0	.022	.110	.220	0	.110	.022	0	.011	0	0
Bribri/Cabecar	.229	0	.254	0	.518	0	0	0	0	0	0	0
Guaymi/Ngobe	.183	.267	.109	.192	.208	.042	0	0	0	0	0	0
Kuna (San Blas)	.875	0	0	.125	0	0	0	0	0	0	0	0
Yanomama	.156	.022	.043	.029	.355	.181	.087	.112	.014	0	0	0
Makiritare	.222	0	.022	.111	.111	.133	.245	.089	.022	.045	0	0
Wapishana	.364	0	0	.106	.152	.060	.318	0	0	0	0	0
Makushi	.022	0	.067	.067	.067	.177	.244	.222	.067	.067	0	0
Piaroa	.267	0	.400	0	.200	0	.133	0	0	0	0	0
Ticuna	.066	.048	.063	.188	.098	.119	.225	.153	.040	0	0	0
Kraho	.132	0	.077	.176	.220	.186	.132	.077	0	0	0	0
Marubo	.200	0	0	.155	.044	.156	.267	.156	.022	0	0	0
Mataco/Wichi	.404	0	.080	0	0	.516	0	0	0	0	0	0

Note: Histogram values were normalized to unit area to permit comparisons between distributions drawn from unequal sample sizes.

TABLE 4. Amerindian population expansion times estimated from RFLP haplotype data

Population	N	Mean	Variance	τ	θ	"Expansion Time"
Dogrib	30	0.62	0.41	0.62	0.00	5,643
Ojibwa	28	5.17	8.49	3.35	1.82	30,365
Navajo	48	2.21	3.39	1.13	1.08	10,223
Pima	30	4.06	5.90	2.70	1.36	24,496
Mixe	16	4.20	5.68	2.99	1.21	27,108
Mixtec-Alta	15	3.64	7.62	1.65	2.00	14,959
Mixtec-Baja	14	2.39	1.60	2.39	0.00	21,656
Zapotec	16	4.50	5.94	3.30	1.20	29,905
Maya	27	3.62	5.23	2.36	1.27	21,371
Teribe	20	1.60	5.44	−0.36	1.96	−3,261
Guatuso	20	1.46	4.10	−0.17	1.63	−1,548
Boruca	14	2.01	5.72	0.08	1.93	753
Bribri/Cabecar	24	2.47	2.80	1.90	0.58	17,192
Guaymi	16	1.97	2.50	1.24	0.73	11,251
Kuna	16	0.35	0.93	−0.41	0.76	−3,716
Yanomami	24	3.78	5.09	2.64	1.14	23,298
Makiritare	10	3.74	7.95	1.69	2.05	15,306
Wapishana	12	2.88	6.72	0.91	1.96	8,290
Macushi	10	5.08	6.35	3.95	1.13	35,838
Piaroa	10	2.00	4.00	0.59	1.41	5,313
Ticuna	28	4.31	5.26	3.33	0.98	30,180
Kraho	14	3.55	4.66	2.50	1.05	22,674
Marubo	10	3.86	7.28	2.01	1.85	18,235
Mataco	28	2.64	5.77	0.87	1.77	7,899
All-Amerindians*	377	4.61	5.92	3.47	1.14	31,454
All-Amerindians**	377	2.22	2.47	1.72	0.50	16,274

*All RFLPs were used for these estimates.
**Haplogroup-defining RFLPs (HaeIII 663, HincII 13259, AluI 13262, AluI 5176, DdeI 10394, and AluI 10397) were excluded for these estimates.

have very recently expanded in the New World, such as some Chibchan-speaking groups of Central America and the Canadian Dogrib, while others seemed to have done so very early, such as the Ticuna and Yanomami of South America. A number of the populations also showed a bimodal distribution of pairwise sequences, suggesting they could have experienced a population bottleneck or reduction after the Americas had been colonized, or perhaps as a consequence of contact with Europeans, beginning in the 16th century.

The overall expansion time for this set of populations using an Analysis I approach was 31,454 cal BP, a date consistent with early divergence times for the mtDNA haplogroups in the Americas. However, when haplogroup-specific RFLPs were excluded from the mismatch estimates (Analysis II), the expansion time dropped by half, to 16,275 cal BP (Fig. 3). This date is concordant with similar estimates for the five haplogroups when the same RFLP sites were excluded. These results point to expansion times for Native American populations that are somewhat more recent than those inferred from previous estimates for haplogroup divergence based on the same data sets (e.g., Torroni et al., 1993a, 1994b).

While these results are intriguing, one must also consider the effects of sampling on these mismatch expansion estimates. For these analyses, relatively small sample sizes from each Native American population (10–24 individuals) were analyzed. These numbers are clearly not representative of the overall sizes of the populations being analyzed, nor are these estimates fully reflective of the genetic diversity present within these groups. In addition, the vast majority of Native American mtDNAs examined for variation has not been analyzed by the HR-RFLP method and, hence, is not available for comparable mismatch analyses. These facts, along with the apparent sensitivity of the mismatch method to demographic effects occurring in human populations (Marjoram and Donnelly, 1994), suggests that the shallowness of the expansion times for both haplogroups and populations could possibly underestimate their actual expansions times.

Similar mismatch studies have been carried out with HVS-I sequence data from Native Americans. In their analysis of ancient and modern Native American samples, Stone

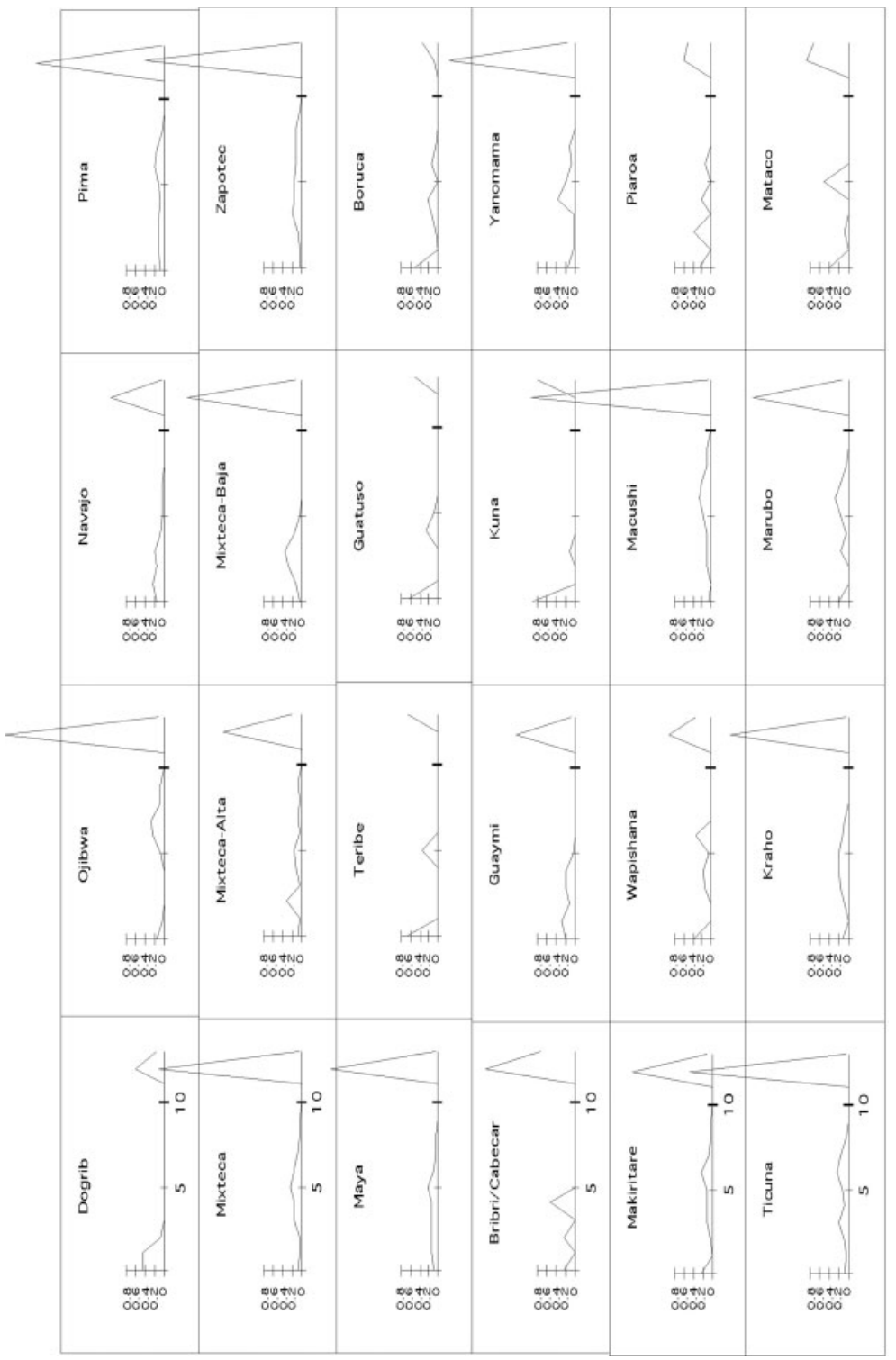

Fig. 2. Mismatch distributions for individual Native American populations using RFLP haplotypes. The distributions are presented as normalized values to permit comparisons between populations of unequal sample sizes. These values are indicated along the *y*-axis, while the number of site differences between haplotypes is shown along the x-axis, with the scale indicated in units of five.

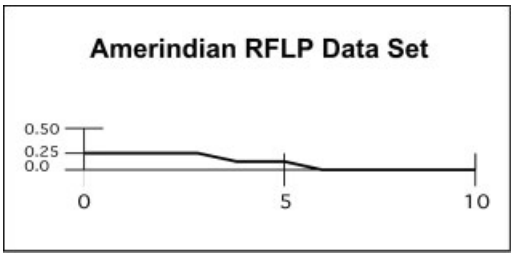

Fig. 3. Mismatch distribution for all Native American RFLP haplotypes. The frequency distribution of mismatches is indicated along the y-axis, while the number of site differences between haplotypes is shown along the x-axis, with the scale indicated in units of five.

and Stoneking (1998) estimated that haplogroups A–D and X began expanding, on average, between 37,000–22,000 cal BP, with haplogroups A and D being the oldest and haplogroups B and C being slightly younger. These estimates fall within analogous coalescence dates estimated from equivalent HVR-I sequence data by Bonatto and Salzano (1997). In contrast to the RFLP mismatch results, however, neither of these studies generated later expansion dates for haplogroups A and B. Instead, the HVS-I sequences gave relatively smooth unimodal distributions that revealed similar dates of expansion of haplogroups A–D in the Americas. Furthermore, neither study excluded the HVS-I sequence polymorphisms that define the sequence motif of each haplogroup when making their coalescence estimates.

MIGRATIONS TO THE NEW WORLD

There has been considerable discussion about the number of migrations that reached the New World and gave rise to ancestral Native Americans. Based on nonmolecular data, this number has ranged from one to eight or more, depending on the dataset being used (craniometric, dental, classical blood group markers, GM allotypes, HLA haplotypes). There is general agreement that the Eskimo-Aleuts and Na-Dené Indians represent the last significant population expansion into the New World (Shields et al., 1993; Starikovskaya et al., 1998; Schurr et al., 1999; Saillard et al., 2000; Rubicz et al., 2003), and, for this reason, the emergence of circumarctic groups will not be addressed here.

The primary question is the number of migrations responsible for the genetic diversity of Amerindian groups. The alternative migration scenarios can be evaluated by scrutinizing the evidence for multiple entries of genetic lineages into the New World. By identifying the number of founding lineages and haplotypes present in Siberia and the Americas, one can determine whether or not multiple founder types were brought to the New World at different times. In addition, by examining the patterns of mutations present in these haplotypes, it may be possible to find specific mutations that demarcate the movement of certain of these haplotypes or genetic lineages, hence, human groups, into the New World.

Number of migrations based on mtDNA haplogroup data

Several different models for the peopling of the New World have been proposed based on mtDNA data. Most of them have suggested a region extending from the Altai Mountains to South-Central Siberia and northern China as the potential source area(s) for ancestral Native American populations (Kolman et al., 1996; Merriwether et al., 1996; Sukernik et al., 1996; Santos et al., 1999). However, there is no complete agreement on the numbers of migrations that left this region and entered the New World.

Many researchers have asserted that haplogroups A–D were brought to the New World in a single migratory event. This view is based on the fact that all four founding haplogroups are present throughout the Americas (Merriwether et al., 1995, 1996; Forster et al., 1996; Kolman et al., 1996), and that statistical and pairwise mismatch analyses of their HVR-I sequences indicate similar levels of diversity in each mtDNA lineage (Bonatto and Salzano, 1997; Stone and Stoneking, 1998; Silva et al., 2002). According to this view, the pattern of genetic variation seen in modern Native American groups is largely attributed to in situ differentiation and population movements occurring after the initial colonization of the New World, rather than a consequence of sequential expansions.

Other investigators have argued for the occurrence of two or more migrations to the Americas. It has been proposed that ancestral Amerindian populations brought haplogroup A, C, and D mtDNAs from Siberia during the initial colonization(s) of the New World, with haplogroup B possibly representing a second independent migration. This view was based on the fact that haplogroup B appeared to be

younger than the other founding lineages, was absent from most of northern Asia from East Asia to the Americas, and was widely distribution in East and Southeast Asia (Torroni et al., 1993a,b; Starikovskaya et al., 1998). Others have asserted that each haplogroup represents a separate migratory wave to the New World (Horai et al., 1993). However, evidence indicating similar levels of diversity in haplogroups A–D in the Americas complicates these interpretations.

On the other hand, haplogroup X may still represent a separate migration from somewhere in Eurasia. It is absent in nearly all indigenous Siberian populations (Torroni et al., 199b; Starikovskaya et al., 1998; Schurr et al., 1998, 2000; Derenko et al., 1998, 2001; Schurr and Wallace, 2003), and appears only in North American Amerindian populations (Torroni et al., 1992, 1993a; Scozzari et al., 1997; Huoponen et al., 1997; Brown et al., 1998; Smith et al., 1999; Malhi et al., 2001, 2003; Bolnick et al., 2003). Its estimated age in Eurasia ranges from 35,000–20,000 cal BP (Torroni et al., 1998; Richards et al., 1998, 2000; Simoni et al., 2001; Reidla et al., 2003), and is somewhat younger in the Americas (17,000–13,000 cal BP based on RFLP data; Brown et al., 1998), suggesting that it could have been brought to the New World within a relatively broad time range.

It also remains possible that mtDNAs from haplogroups A–D were introduced into the Americas in separate expansion events. This scenario receives tentative support from the fact that, in addition to the consensus founder haplotypes for these haplogroups, there are other HVS-I sequences shared between Asian/Siberian and Native American populations that could potentially be additional founder haplotypes (see above). These putative founder haplotypes are not widespread in Asia and the Americas, but appear in populations living in the vicinity of the hypothesized source area for ancestral Native Americans (Schurr and Wallace, 1999; Malhi et al., 2002; Schurr, 2002). However, further investigation of HVR-I sequence and coding region variation in both Siberian and Native American populations will be necessary to resolve this issue.

Number of migrations based on NRY haplogroup data

At least six different paternal haplotypes have been identified in Siberia and the Americas using SNP markers (DE-M1, Q-M3, R1a1-M17, P-M45, N3-M46, and C-M130). Only two of these, P-M45 and Q-M3, fundamentally contributed to the initial peopling of the New World, either through single (Underhill et al., 1996; Bianchi et al., 1998; Santos et al., 1999) or multiple (Karafet et al., 1999; Lell et al., 2002, Bortolini et al., 2003) migration events. The founding Q-M3 haplotype is the most frequent haplotype in Native American populations, and is widely distributed throughout the New World (Bianchi et al., 1998; Karafet et al., 1999; Lell et al., 2002; Bortolini et al., 2003). In addition, the ancestral P-M45a haplotype, the direct ancestor to the Q-M3 founder haplotype, has the widest geographic distribution of all of those present in the Americas, occurring in populations from central Siberia to South America (Lell et al., 2002; Bortolini et al., 2003).

A second and later expansion(s) of human groups from Beringia into the Americas brought with it a different set of P-M45 haplotypes. These P-M45b haplotypes show a different array of STR alleles than the Q-M3/P-M45a haplotypes that came with the initial expansion into the New World, as well as the M173 SNP. This second set of P-M45b haplotypes is also shared between eastern Siberian and North and Central American groups, but are absent in those from central Siberia and South America (Lell et al., 2002). The secondary expansion may also have contributed the R1a1-M17 and C-M130 haplotypes to Amerindian populations. Based on their distribution in Siberia, P-M45b and C-M130 haplotypes were proposed to have come from the Amur River region (Karafet et al., 1999; Lell et al., 2002).

Bortolini et al. (2003) supports the proposal that there were two major expansions of NRY haplogroups into the New World. However, they argue that both NRY migrations came from southern/central Siberia to the Americas. In their view, this interpretation is more consistent with the generally high frequency of haplogroup K-M9 in eastern Siberia and its absence in the Americas.

DISCUSSION

As attested by the new molecular data, the diversity of mtDNA and NRY haplogroups in Siberia and the Americas points to the dynamic quality of human movements in

these regions over the course of the last 30,000 years. However, there continues to be discussion about the incongruity between the late (14,675–13,050 cal BP) archeological visibility of the early colonizers of the Americas and the greater antiquity (35,000–15,000 cal BP) of the genetic lineages brought to these regions by the founding populations of Native Americans. The initial problem with the older age estimates for mtDNA and NRY haplogroups was that some were equal to the oldest known human occupation sites in southeastern Siberia (40,000–30,000 cal BP), and much older than the archeological sites in northeastern Siberia (Goebel, 1999; Goebel et al., 2001). However, the expanded datasets from Siberian and Native American populations, and the refinement of methods used to estimate mutation rates, effective population sizes, and genetic diversity now give ages for these genetic lineages that are more consistent with archeological data from these regions. Furthermore, with the recent discoveries of pre-Clovis cultures in the Americas, the dates for the earliest archeological sites in the Americas and the expansion times for these genetic lineages are slowly drawing closer together.

Both mtDNA and NRY data generally provide an initial entry time of ancestral Native Americans of between 20,000–15,000 cal BP. While this expansion time would seem to favor a late entry of ancestral Native Americans and is more consistent with archeological data from the New World, it presents other interesting problems. For one thing, these dates fall in the middle of the LGM, before the earliest time at which an ice-free corridor was available for passage by modern human population (~13,050–12,550 cal BP). In addition, the ages of the earliest archeological sites in the New World are somewhat older than the time at which the ice-free corridor became available for human movement. The Clovis sites long held as the benchmark of human colonization span a range of 13,350–12,895 cal BP (Haynes, 1992, 1993; Boldurian and Cotter, 1999; Fiedel, 1999), the pre-Clovis Monte Verde site has been dated at ~14,675 cal BP (Dillehay, 1997), and other pre-Clovis sites in South America are only slightly younger than Monte Verde (Dillehay, 1999; Dixon, 2001, 2002). Thus, one could conclude that ancestral Native American populations were already present in the New World before the LGM.

If glacial coalescence prevented access to North America via an interior route until ~12,550 cal BP, and if sites in South America were occupied by 14,675 cal BP, then how did human populations arrive in the New World prior to, or during, the LGM? Despite no clear evidence for human occupation of northeastern Siberia before 22,000–20,000 cal BP (Goebel, 1999; Goebel et al., 2001), it is possible that ancestral Amerindians moved from Beringia into North America before the beginning of the LGM around 24,000 cal BP. In this case, the expansion across Beringia and down into northern North America would likely to have been relatively quick, given the periglacial conditions in this ice-free corridor.

An alternative explanation for these data is that ancestral Amerindians followed a coastal route into the New World. This idea was put forward a number of years ago based on both geological and linguistic evidence (Fladmark, 1979, 1983; Gruhn, 1987, 1992a,b). However, only recently has geological evidence of deglaciation of the Northwest Coast of North America by between 16,800–14,850 cal BP clearly indicated that human occupation of this area during the LGM was possible (Blaise et al., 1990; Bobrowsky et al., 1990; Mann and Hamilton, 1995; Jackson and Duk-Rodkin, 1996; Josenhans et al., 1997; Mandryk et al., 2000; Fedje and Christiansen, 1999; Fedje et al., 2001; Fedje, 2002). In addition, computer simulations of a colonization process by interior and coastal routes using demographic data from hunter-gatherer groups has suggested that the patterns of genetic diversity in Amerindian populations are more consistent with a coastal model that allowed an earlier and rapid expansion into the Southern hemisphere (Fix, 2002).

Therefore, based on the existing anthropological data, one can generate the following picture of the peopling of the New World. There was a pre-Clovis entry of ancestral Asian groups into the Americas during the LGM. These immigrants used a coastal route to reach the areas below the glaciated areas of northern North America somewhere between 18,000–15,000 cal BP. They apparently brought mtDNA haplogroups A–D and NRY haplogroups P-M45a and Q-242/Q-M3 haplotypes with them to the Americas, with these being dispersed throughout all continental areas of the New World. A subsequent expansion probably brought mtDNA haplogroup X

and NRY haplogroups P-M45b, C-M130, and R1a1-M17, with these being disseminated in only North and Central America. This expansion may have coincided with the opening of the ice-free corridor around 12,550 cal BP. A somewhat later expansion likely involved the emergence of circumarctic populations, such as Eskimos, Aleuts, and Na-Dené Indians (Shields et al., 1993; Starikovskaya et al., 1998; Schurr et al., 1999; Saillard et al., 2000; Rubicz et al., 2003).

Of course, this model, like others before it, will continue to evolve as more archeological, genetic, and geological data are gathered from Siberia and the Americas. However, the increasing congruence between these different lines of anthropological evidence would seem to indicate that we are gaining a much better understanding of the processes that gave rise to the diversity of Native American peoples and cultures.

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LITERATURE CITED

Bailliet G, Rothhammer F, Carnese FR, Bravi CM, Bianchi NO. 1994. Founder mitochondrial haplotypes in Amerindian populations. Am J Hum Genet 54:27–33.

Batista O, Kolman CJ, Bermingham E. 1995. Mitochondrial DNA diversity in the Kuna Amerinds of Panama. Hum Mol Genet 4:921–929.

Bergen AW, Wang C-Y, Tsai J, Jefferson K, Dey C, Smith KD, Park SC, Tsai SJ, Goldman D. 1999. An Asian-Native American paternal lineage identified by RPS4Y resequencing and microsatellite haplotyping. Ann Hum Genet 63:63–80.

Bert F, Corella A, Gené M, Pérez-Pérez A, Turbón D. 2001. Major mitochondrial DNA haplotype heterogeneity in highland and lowland Amerindian populations from Bolivia. Hum Biol 73:1–16.

Bianchi NO, Bailliet G, Bravi CM, Carnese RF, Rothhammer R, Martinez-Marignac VL, and Pena SD. 1997. Origin of Amerindian Y chromosomes as inferred by the analysis of six polymorphic markers. Am J Phys Anthropol 102:79–89.

Bianchi NO, Catanesi CI, Bailliet G, Martinez-Marignac VL, Bravi M, Videl-Rioja LB, Herrera RJ, Lopez-Camelo JS. 1998. Characterization of ancestral and derived Y-chromosome haplotypes of New World native populations. Am J Hum Genet 63:1862–1871.

Blaise B, Clague JJ, Matthewes RW. 1990. Time of maximum Late Wisconsin glaciation, west coast of Canada. Quaternary Res 34:282–295.

Bobrowsky PT, Catto NR, Brink JW, Spurling NE, Gibson TH, Rutter NW. 1990. Archeological geology of sites of western and northwestern Canada. Centennial special, vol. 4. Boulder, CO: Geological Society of America. p 87–122.

Boldurian AT, Cotter JL. 1999. Clovis revisited. Philadelphia: University of Pennsylvania Museum Press.

Bolnick DA, Smith DG. 2003. Unexpected patterns of mitochondrial DNA variation among Native Americans from the southeastern United States. Am J Phys Anthropol 122:336–354.

Bonatto SL, Salzano FM. 1997. Diversity and age of the four major mtDNA haplogroups, and their implications for the peopling of the New World. Am J Hum Genet 61:1413–1423.

Bortolini M-C, Salzano FM, Thomas MG, Stuart S, Nasanen SPK, Bau CHD, Hutz MH, Layrisse Z, Petzl-Erler ML, Tsuneto LT, Hill K, Hurtado AM, Castro-de-Guerra D, Torres MM, Groot H, Michalski R, Nymadawa P, Bedoya G, Bradman N, Labuda D, Ruiz-Linares A. 2003. Y-Chromosome evidence for differing ancient demographic histories in the Americas. Am J Hum Genet 73:524–539.

Brace CL, Nelson AR, Seguchi N, Oe H, Sering L, Qifeng P, Yongyii L, Tumen D. 2001. Old World sources of the first New World human inhabitants: a comparative craniofacial view. Proc Natl Acad Sci USA 98: 10017–10022.

Brown MD, Hosseini SH, Torroni A, Bandelt H-J, Allen J-C, Schurr TG, Scozzari R, Cruciani F, Wallace DC. 1998. Haplogroup X: an ancient link between Europe/Western Asia and North America? Am J Hum Genet 63:1852–1861.

Carlyle SW, Parr RL, Hayes MG, O'Rourke DH. 2000. Context of maternal lineages in the Greater Southwest. Am J Phys Anthropol 113:85–101.

Derenko MV, Malyarchuk BA, Dambueva IK, Shaikhaev GO, Dorzhu CM, Nimaev DD, Zakharov IA. 2000. Mitochondrial DNA variation in two south Siberian aboriginal populations: implications for the genetic history of North Asia. Hum Biol 72:945–973.

Derenko MV, Grzybowski T, Malyarchuk BA, Czarny J, Miscicka-Sliwka D, Zakharov IA. 2001. The presence of mitochondrial haplogroup X in Altaians from South Siberia. Am J Hum Genet 69:237–241.

Dillehay TD. 1997. Monte Verde: a Late Pleistocene settlement in Chile, vol. 2. Washington, DC: Archeological Context, Smithsonian Institution Press.

Dillehay TD. 1999. The late Pleistocene cultures of South America. Evol Anthropol 7:206–216.

Dixon EJ. 2001. Human colonization of the Americas: timing, technology and process. Q Sci Rev 20: 277–299.

Dixon EJ. 2002. How and when did people come to North America? Athena Rev 3:23–27.

Easton RD, Merriwether DA, Crews DE, et al. 1996. mtDNA variation in the Yanomami: evidence for additional New World founding lineages. Am J Hum Genet 59:213–225.

Fedje D. 2002. The early post-glacial history of the northern Northwest Coast: a view from Haida Gwaii and Hecate Strait. Athena Rev 3:28–30.

Fedje DW, Christensen T. 1999. Modeling paleoshorelines and locating early Holocene coastal sites in Haida Gwai. Am Antiq 64:635–652.

Fedje DW, Wigen RJ, Mackie Q, Lake CR, Sumpter ID. 2001. Preliminary results from investigations at Kilgii Gwaay: an early Holocene archaeological site on Ellen Island, Haida Gwaii, British Columbia. Can J Archeol 25:98–120.

Fiedel SJ. 1999. Older than we thought: implications of corrected dates for Paleoindians. Am Antiq 64: 95–115.

Fix AG. 2002. Colonization models and initial genetic diversity in the Americas. Hum Biol 74:1–10.

Fladmark KR. 1979. Routes: alternative migration corridors for early man in North America. Am Antiq 44: 55–69.

Fladmark KR. 1983. Times and places: environmental correlates of Mid-to-Late Wisconsin human population expansion in North America. In: Shutler R, editor. Early Man in the New World. Beverly Hills, CA: Sage Publications. p 13–42.

Forster P, Harding R, Torroni A, Bandelt H-J. 1996. Origin and evolution of Native American mtDNA variation: a reappraisal. Am J Hum Genet 59:935–945.

Forster P, Röhl A, Lünnermann P, Brinkmann C, Zerjal T, Tyler-Smith C, Brinkmann B. 2000. A short tandem repeat-based phylogeny for the human Y chromosome. Am J Hum Genet 67:182–196.

Fox CL. 1996. Mitochondrial DNA haplogroups in four tribes from Tierra del Fuego-Patagonia: inferences about the peopling of the Americas. Hum Biol 68: 855–871.

Goebel T. 1999. Pleistocene human colonization of Siberia and peopling of the Americas: an ecological approach. Evol Anthropol 8:208–227.

Goebel T, Waters MR, Meshcherin MN. 2001. Masterov Kliuch and the early Upper Palaeolithic of the Transbaikal, Siberia. Asian Perspect 39:47–70.

Greenberg JH. 1987. Language in the Americas. Stanford, CA: Stanford University Press.

Gruhn R. 1987. On the settlement of the Americas: South American evidence for an expanded time frame. Curr Anthropol 28:363–364.

Gruhn R. 1992a. Linguistic evidence in support to the coastal route of the earliest entry into the New World. Man 23:77–100.

Gruhn R. 1992b. The Pacific coast route: an alternative model of the initial peopling of the Americas. In: Taylor AR, editor. Proceedings of the Conference on Language and Prehistory, Boulder, CO, March 1990. Stanford, CA: Stanford University Press.

Gurven M. 2000. How can we distinguish between mutational "hot spots" and "old sites" in human mtDNA samples? Hum Biol 72:455–471.

Hammer MF, Spurdle AB, Karafet T, Bonner WR, Wood ET, Novelletto A, Malaspina A, Mitchell RJ, Horai S, Jenkins T, Zegura ST. 1997. The geographic distribution of human Y chromosome variation. Genetics 145:787–805.

Hammer MF, Karafet T, Rasanayagam A, Wood ET, Altheide TK, Jenkins T, Griffiths RC, Templeton AR, Zegura SL. 1998. Out of Africa and back again: nested cladistic analysis of human Y chromosome variation. Mol Biol Evol 15:427–441.

Harpending HC. 1994. Signature of ancient population growth in a low-resolution mitochondrial DNA mismatch distribution. Hum Biol 66:591–600.

Harpending HC, Sherry ST, Rogers AR, Stoneking M. 1993. The genetic structure of human populations. Curr Anthropol 34:483–496.

Harpending HC, Batzer MA, Gurven MA, Jorde LB, Rogers AR, Sherry ST. 1998. Genetic traces of ancient demography. Proc Natl Acad Sci USA 95: 1961–1967.

Haynes CV Jr. 1992. Contributions of radiocarbon dating to the geochronology of the peopling of the New World. In: Taylor, Long, Kra, editors. Radiocarbon after four decades. New York: Springer. p 355–374.

Haynes CV Jr. 1993. Clovis-Folsom geochronology and climatic change. In: Soffer O, Praslov ND, editors. From Kosteniki to Clovis. New York: Plenum Press. p 219–326.

Heyer E, Puymirat J, Dieltjes P, Bakker E, de Knijff P. 1997. Estimating Y chromosome specific mutation frequencies using deep rooted pedigrees. Hum Mol Genet 6:799–803.

Horai S, Kondo R, Nakasawa-Hattori Y, Hayashi S, Sonoda S, Tajima K. 1993. Peopling of the Americas, founded by four major lineages of mitochondrial DNA. Mol Biol Evol 10:23–47.

Huoponen K, Torroni A, Wickman PR, Sellitto D, Gurley DS, Scozzari R, Wallace DC. 1997. Mitochondrial and Y chromosome-specific polymorphisms in the Seminole tribe of Florida. Eur J Hum Genet 5:25–34.

Jackson LE Jr, Duk-Rodkin A. 1996. Quaternary geology of the ice-free corridor: glacial controls on the peopling of the New World. In: Akazawa T, Szathmary EJE, editors. Prehistoric Mongoloid dispersals. Oxford: Oxford University Press.

Jantz RL, Owsley DW. 2001. Variation among early North American crania. Am J Phys Anthropol 114:146–155.

Josenhans HW, Fedje DW, Barrie JV, Mathewes RW, Pietnitz R. 1997. Early humans and rapidly changing Holocene sea levels in the Queen Charlotte Islands-Hecate Strait, British Columbia, Canada. Science 277:71–74.

Kaestle FA, Smith DG. 2001. Ancient mitochondrial DNA evidence for prehistoric population movement: the Numic expansion. Am J Phys Anthropol 115:1–12.

Karafet TM, Zegura SL, Vuturo-Brady J, Posukh O, Osipova L, Wiebe V, Romero F, Long JC, Harihara S, Jin F, Dashnyam B, Gerelsaikhan T, Omoto K, Hammer MF. 1997. Y-Chromosome markers and trans-Bering Strait dispersals. Am J Phys Anthropol 102:301–314.

Karafet TM, Zegura SL, Posukh O, Osipova L, Bergen A, Long J, Goldman D, Klitz W, Harihara S, de Knijff P, Wiebe V, Griffiths RC, Templeton AR, Hammer MF. 1999. Ancestral Asian source(s) of New World Y-chromosome founder haplotypes. Am J Hum Genet 64:817–831.

Kayser M, Caglià C, Corach D, Fretwell N, Gehrig C, Graziosi G, Heidorn F, Herrmann S, Herzog B, Hidding M, Honda K, Jobling M, Krawczak M, Leim K, Meuser S, Meyer E, Oesterreich W, Pandya A, Parson W, Penacino G, Pérez-Lezaun A, Piccinini A, Prinz M, Schmitt C, Schneider PM, Szibor R, Teifel-Greding J, Weichhold G, de Knijff P, Roewer L. 1997. Evaluation of Y-chromosomal STRs: a multicenter study. Int J Leg Med 110:125–133.

Kolman CJ, Bermingham E. 1997. Mitochondrial and nuclear DNA diversity in the Choco and Chibcha Amerinds of Panama. Genetics 147:1289–1302.

Kolman CJ, Bermingham E, Cooke R, Ward RH, Arias TD, Guionneau-Sinclair F. 1995. Reduced mtDNA diversity of the Ngöbé Amerinds of Panamá. Genetics 140:275–283.

Kolman CJ, Sambuughin N, Bermingham E. 1996. Mitochondrial DNA analysis of Mongolian populations and implications for the origin of New World founders. Genetics 142:1321–1334.

Lalueza C, Pérez-Pérez A, Prats E, Cornudella L, Turbón D. 1997. Lack of founding Amerindian mitochondrial DNA lineages in extinct aborigines from Tierra del Fuego-Patagonia. Hum Mol Genet 6:41–46.

Lell JT, Brown MD, Schurr TG, Sukernik RI, Starikovskaya YB, Torroni A, Moore LG, Troup GM, Wallace DC. 1997. Y chromosome polymorphisms in Native American and Siberian populations: identification of founding Native American Y chromosome haplotypes. Hum Genet 100:536–543.

Lell JT, Sukernik RI, Starikovskaya YB, Jin L, Su B, Schurr TG, Underhill P, Wallace DC. 2002. The dual origins and Siberian affinities of Native American Y chromosomes. Am J Hum Genet 70:192–206.

Lorenz JG, Smith DG. 1996. Distribution of four founding mtDNA haplogroups among native North Americans. Am J Phys Anthropol 101:307–323.

Lorenz JG, Smith DG. 1997. Distribution of sequence variations in the mtDNA control region of native North Americans. Hum Biol 69:749–776.

Malhi RS, Schultz BA, Smith DG. 2001. Distribution of mitochondrial lineages among Native American tribes of northeastern North America. Hum Biol 73:17–55.

Malhi RS, Eshleman JA, Greenberg JA, Weiss DA, Shook BAS, Kaestle FA, Lorenz JG, Kemp BM, Johnson JR, Smith DG. 2002. The structure of diversity within New World mitochondrial DNA haplogroups: implications for the prehistory of North America. Am J Hum Genet 70:905–919.

Malhi RS, Mortensen HM, Eshleman JA, Mesa N, Munera JG, Bedoya G, Velez ID, Garcia LF, Pérez-Lezaun A, Bertranpetit J, Feldman MW, Goldstein DB. 2003. Native American mtDNA prehistory in the American Southwest. Am J Phys Anthropol 120: 108–124.

Mandryk CA, Josenhans H, Fedje DJ, et al. 2001. Late Quaternary paleoenvironments of northwestern North America: implications for inland versus coastal migration routes. Quaternary Sci Rev 20:301–314.

Mann DH, Hamilton TD. 1995. Late Pleistocene and Holocene paleoenvironments of the North Pacific coast. Quaternary Sci Rev 14:449–471.

Marjoram P, Donnelly P. 1994. Pairwise comparisons of mitochondrial DNA sequences in subdivided populations and implications for early human evolution. Genetics 136:673–683.

Merriwether DA, Rothhammer F, Ferrell RE. 1994. Genetic variation in the New World: ancient teeth, bone, and tissue as sources of DNA. Experientia 50:592–601.

Merriwether DA, Rothhammer F, Ferrell RE. 1995. Distribution of the four-founding lineage haplotypes in Native Americans suggests a single wave of migration for the New World. Am J Phys Anthropol 98:411–430.

Merriwether DA, Hall WW, Vahlne A, Ferrell RE. 1996. mtDNA variation indicates Mongolia may have been the source for the founding population for the New World. Am J Hum Genet 59:204–212.

Merriwether DA, Huston S, Iyengar S, Hamman R, Norris JN, Shetterly SM, Kamboh MI, Ferrell RE. 1997. Mitochondrial versus nuclear admixture estimates demonstrate a past history of directional mating. Am J Phys Anthropol 102:153–159.

Monsalve MV, Cardenas F, Guhl F, Delaney AD, Devine DV. 1996. Phylogenetic analysis of mtDNA lineages in South American mummies. Ann Hum Genet 60: 293–303.

Moraga ML, Rocco P, Miquel JF, Nervi F, Llop E, Chakraborty R, Rothhammer F, Carvallo P. 2000. Mitochondrial DNA polymorphisms in Chilean aboriginal populations: implications for the peopling of the Southern Cone of the continent. Am J Phys Anthropol 113:19–29.

O'Rourke DH, Hayes MG, Carlyle SW. 2000. Spatial and temporal stability of mtDNA haplogroup frequencies in native North America. Hum Biol 72:15–34.

Parr RL, Carlyle SW, O'Rourke DH. 1996. Ancient DNA analysis of Fremont Amerindians of the Great Salt Lake wetlands. Am J Phys Anthropol 99: 507–518.

Pena SDJ, Santos FR, Bianchi NO, Bravi CM, Carnese FR, Rothhammer F, Gerelsaikhan T, Munkhtuja B, Oyunsuren T. 1995. A major founder Y-chromosome haplotype in Amerindians. Nat Genet 11:15–16.

Reidla M, Kivisild T, Metspalu E, Kaldma K, Tambets K, Tolk H-V, Parik J, Loogvali E-L, Derenko M, Malyarchuk B, Bermisheva M, Zhadanov S, Pennarun E, Gubina M, Golubenko M, Damba L, Fedorova S, Gusar V, Grechanina E, Mikerezi I, Moisan J-P, Chaventre A, Khusnutdinova E, Osipova L, Stepanov V, Voevoda M, Achilli A, Rengo C, Rickards O, De Stefano GF, Papiha S, Beckman L, Janicijevic B, Rudan P, Anagnou N, Michalodimitrakis E, Koziel S, Usanga E, Geberhiwot T, Herrnstadt C, Howell N, Torroni A, Villems R. 2003. Origin and diffusion of mtDNA haplogroup X. Am J Hum Genet 73:1178–1190.

Ribeiro-Dos-Santos AKC, Santos SEB, Machado AL, Guapindaia V, Zago MA. 1996. Heterogeneity of mitochondrial DNA haplotypes in Pre-Columbian natives of the Amazon region. Am J Phys Anthropol 101: 29–37.

Richards M, Macaulay VA, Bandelt H-J, Sykes BC. 1998. Phylogeography of mitochondrial DNA in western Europe. Ann Hum Genet 62:241–260.

Richards M, Macaulay V, Hickey E, Vega E, Sykes B, Guida V, Rengo C, Sellitto D, Cruciani F, Kivisild T, Villems R, Thomas M, Rychkov S, Rychkov O, Rychkov Y, Golge M, Dimitrov D, Hill E, Bradley D, Romano V, Cali F, Vona G, Demaine A, Papiha S, Triantaphyllidis C, Stefanescu G, Hatina J, Belledi M, Di Rienzo A, Novelletto A, Oppenheim A, Norby S, Al-Zaheri N, Santachiara-Benerecetti S, Scozzari R, Torroni A, Bandelt HJ. 2000. Tracing European founder lineages in the Near Eastern mtDNA pool. Am J Hum Genet 67:1251–1276.

Rickards O, Martiñez-Labarga C, Lum JK, De Stefano GCF, Cann RL. 1999. mtDNA history of the Cayapa Amerinds of Ecuador: detection of additional founding lineages for the Native American populations. Am J Hum Genet 65:519–530.

Rogers AR, Harpending H. 1992. Population growth makes waves in the distribution of pairwise genetic differences. Mol Biol Evol 9:552–569.

Ross AH, Ubelaker DH, Falsetti AB. 2002. Craniometric variation in the Americas. Hum Biol 74:807–818.

Rubicz R, Schurr TG, Babb P, Crawford MH. 2003. Mitochondrial DNA diversity in modern Aleuts, and their genetic relationship with other circumarctic populations. Hum Biol 75:809–835.

Ruiz-Linares A, Ortiz-Barrientos D, Figueroa M, et al. 1999. Microsatellites provide evidence for Y chromosome diversity among the founders of the New World. Proc Natl Acad Sci USA 96:6312–6317.

Saillard J, Forster P, Lynnerup N, Bandelt H-J, Nørby S. 2000. mtDNA variation among Greenland Eskimos: the edge of the Beringian expansion. Am J Hum Genet 67:718–726.

Santos FR, Rodriguez-Delfin L, Pena SD, Moore J, Weiss KM. 1996a. North and South Amerindians may have the same major founder Y chromosome haplotype. Am J Hum Genet 58:1369–1370.

Santos SEB, Ribeiro-Dos-Santos AKC, Meyer D, Meyer D, Zago MA. 1996b. Multiple founder haplotypes of mitochondrial DNA in Amerindians revealed by RFLP and sequencing. Ann Hum Genet 60:305–319.

Santos FR, Pandya A, Tyler-Smith C, Pena SDJ, Schanfield M, Leonard WR, Osipova L, Crawford MH, Mitchell RJ. 1999. The central Siberian origin for Native American Y-chromosomes. Am J Hum Genet 64:619–628.

Schultz BA, Malhi RS, Smith DG. 2001. Examining the proto-Algonquian migration: analysis of mtDNA. In: Nichols JD, Ogg A, editors. Proceedings of the 32d Algonquian Conference. Ottawa: Carleton University Press. p 470–492.

Schurr TG. 2000. Mitochondrial DNA variation in Native Americans and Siberians and its implications for the peopling of the New World. Am Sci 88: 246–253.
Schurr TG. 2002. A molecular anthropological view of the peopling of the Americas. Athena Rev 3:59–77.
Schurr TG. 2004a. Genetic diversity in Siberians and Native Americans suggests an early migration to the New World. In: Madsen DB, editor. Entering America: northeast Asia and Beringia before the last glacial maximum. Salt Lake City: University of Utah Press.
Schurr TG. 2004b. An anthropological genetic view of the peopling of the Americas. In: Clark GA, Barton CM, Yesner D, Pearson G, editors. The settlement of the American continents: a multidisciplinary approach to human biogeography. Tucson: Arizona State University Press.
Schurr TG, Wallace DC. 1999. MtDNA variation in Native Americans and Siberians and its implications for the peopling of the New World. In: Bonnichsen R, editor. Who were the first Americans. Proceedings of the 58th Annual Biology Colloquium, Oregon State University. Corvallis: Center for the Study of the First Americans. p 41–77.
Schurr TG, Wallace DC. 2003. Genetic prehistory of Paleoasiatic-speaking peoples of northeastern Siberia and their links to Native American populations. In: Kendall L, Krupnik I, editors. Constructing cultures then and now: celebrating Franz Boas and the Jesup North Pacific Expedition. Baltimore: Smithsonian Institution Press. p 239–258.
Schurr TG, Ballinger SW, Gan Y-Y, Hodge JA, D. Merriwether DA, Lawrence DN, Knowler WC, Weiss KM, Wallace DC. 1990. Amerindian mitochondrial DNAs have rare Asian variants at high frequencies, suggesting they derived from four primary maternal lineages. Am J Hum Genet 46:613–623.
Schurr TG, Sukernik RI, Starikovskaya EB, Wallace DC. 1999. Mitochondrial DNA diversity in Koryaks and Itel'men: ancient and recent population expansions and dispersals in Okhotsk-Bering Sea region. Am J Phys Anthropol 108:1–40.
Scozzari R, Cruciani F, Santolamazza P, Sellitto D, Cole DEC, Rubin LA, Labuda D, Marini E, Succa V, Vona G, Torroni A. 1997. mtDNA and Y-chromosome-specific polymorphisms in modern Ojibwa: implications about the origin of their gene pool. Am J Hum Genet 60:241–244.
Seielstad M, Yuldasheva N, Singh N, Underhill P, Oefner P, Shen P, Wells RS. 2003. A novel Y-chromosome variant puts an upper limit on the timing of the first entry into the Americas. Am J Hum Genet 73:700–705.
Sherry ST, Rogers AR, Harpending H, Soodyall H, Jenkins T, Stoneking M. 1994. Mismatch distributions of mtDNA reveal recent human population expansions. Hum Biol 66:761–775.
Shields GF, Schmiechen AM, Frazier BL, Redd A, Voevoda MI, Reed JK, Ward RH. 1993. mtDNA sequences suggest a recent evolutionary divergence for Beringian and northern North American populations. Am J Hum Genet 53:549–562.
Silva WA, Bonatto SL, Holanda AJ, et al. 2002. Mitochondrial genome diversity of native Americans supports a single early entry of founder populations into America. Am J Hum Genet 71:187–192.
Simoni L, Calafell F, Pettener D, et al. 2000. Geographic patterns of mtDNA diversity in Europe. Am J Hum Genet 66:262–278.
Smith DG, Malhi RS, Eshleman J, Kaestle FA, Lorenz JG. 1999. Distribution of haplogroup X among native North Americans. Am J Phys Anthropol 110:271–284.
Smith DG, Lorenz J, Rolfs BK, et al. 2000. Implications of the distribution of Albumin Naskapi and Albumin Mexico for New World prehistory. Am J Phys Anthropol 111:557–572.
Starikovskaya YB, Sukernik RI, Schurr TG, Wallace DC. 1998. Mitochondrial DNA diversity in Chukchi and Siberian Eskimos: implications for the genetic prehistory of ancient Beringia. Am J Hum Genet 63: 1473–1491.
Stoneking M. 2000. Hypervariable sites in the mtDNA control region are mutational hotspots. Am J Hum Genet 67:1029–1032.
Stone AC, Stoneking M. 1998. mtDNA analysis of a prehistoric Oneota population: implications for the peopling of the New World. Am J Hum Genet 62:1153–1170.
Su B, Xiao J, Underhill P, Deka R, Zhang W, Akey J, Huang W, Shen D, Lu D, Luo J, Chu J, Tan J, Shen P, Davis R, Cavalli-Sforza LL, Chakraborty R, Xiong M, Du R, Oefner P, Chen Z, Jin L. 1999. Y-Chromosome evidence for a northward migration of modern humans into eastern Asia during the last Ice Age. Am J Hum Genet 65:1718–1724.
Sukernik RI, Schurr TG, Starikovskaya YB, Wallace DC. 1996. Mitochondrial DNA variation in Native Siberians, with special reference to the evolutionary history of American Indians: studies on restriction endonuclease polymorphism. Genetika 32:432–439.
Thomson R, Pritchard JK, Shen P, Oefner PJ, Feldman MW. 2000. Recent common ancestry of human Y chromosomes: evidence from DNA sequence data. Proc Natl Acad Sci USA 97:7360–7365.
Torroni A, Schurr TG, Yang C-C, Szathmary EJE, Williams RC, Schanfield MS, Troup GA, Knowler WC, Lawrence DN, Weiss KM, Wallace DC. 1992. Native American mitochondrial DNA analysis indicates that the Amerind and the Na-Dené populations were founded by two independent migrations. Genetics 130:153–162.
Torroni A, Schurr TG, Cabell MF, Brown MD, Neel JV, Larsen M, Smith DG, Vullo CM, Wallace DC. 1993a. Asian affinities and the continental radiation of the four founding Native American mtDNAs. Am J Hum Genet 53:563–590.
Torroni A, Sukernik RI, Schurr TG, Starikovskaya YB, Cabell MF, Crawford MH, Comuzzie AG, Wallace DC. 1993b. mtDNA variation of aboriginal Siberians reveals distinct genetic affinities with Native Americans. Am J Hum Genet 53:591–608.
Torroni A, Neel JV, Barrantes R, Schurr TG, Wallace DC. 1994a. A mitochondrial DNA "clock" for the Amerinds and its implications for timing their entry into North America. Proc Natl Acad Sci USA 91: 1158–1162.
Torroni A, Chen Y-S, Semino O, Santachiara-Beneceretti AS, Scott CR, Lott MT, Winter M, Wallace DC. 1994b. MtDNA and Y-chromosome polymorphisms in four native American populations from southern Mexico. Am J Hum Genet 54:303–318.
Torroni A, Lott MT, Cabell MF, Zamudio S, Zhuang J, Droma T, Wallace DC. 1994c. mtDNA and the origin of Caucasians: identification of ancient Caucasian-specific haplogroups, one of which is prone to a recurrent somatic duplication in the D-loop region. Am J Hum Genet 55:760–776.
Torroni A, Huoponen K, Francalacci P, Petrozzi M, Morelli L, Scozzari R, Obinu D, Savontaus M-L, Wallace DC. 1996. Classification of European mtDNAs from an analysis of three European populations. Genetics 144: 1835–1850.
Underhill PA, Jin L, Zemans R, Oefner PJ, Cavalli-Sforza L-L. 1996. A pre-Columbian Y chromosome-

specific transition and its implications for human evolutionary history. Proc Natl Acad Sci USA 93: 196–200.

Underhill PA, Jin L, Lin AA, Jenkins T, Vollrath D, Davis RW, Cavalli-Sforza L-L, Oefner PJ. 1997. Detection of numerous Y chromosome biallelic polymorphisms by denaturing high performance liquid chromatography. Genome Res 7:996–1005.

Underhill PA, Shen P, Lin AA, Jin L, Passarino G, Yang WH, Kauffman E, Bonné-Tamir B, Bertranpetit J, Francalacci P, Ibrahim M, Jenkins T, Kidd JR, Mehdi SQ, Seielstad MT, Wells RS, Piazza A, Davis RW, Feldman MW, Cavalli-Sforza L-L, Oefner P. 2000. Y chromosome sequence variation and the history of human populations. Nat Genet 26: 358–361.

Ward RH, Redd A, Valencia D, Frazier B, Pääbo S. 1993. Genetic and linguistic differentiation in the Americas. Proc Natl Acad Sci USA 90:10063–10067.

Y Chromosome Consortium. 2002. A nomenclature system for the tree of human Y-chromosomal binary haplogroups. Genome Res 12:339–348.