

A Molecular Anthropological Perspective on the Peopling of the Americas

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The past decade has been an enormously productive period for research into questions concerning the peopling of the Americas. During this time, investigators from all subfields of anthropology and from many different laboratories across the world have focused their attention on determining who the First Americans were. Like their intellectual predecessors, these investigators have attempted to elucidate when ancestral Native Americans first arrived in the New World, how many population expansions or migrations were involved in this colonization process, and where in Asia/Eurasia that these ancestral groups came from. Their efforts have yielded new insights into the origins of Native Americans, while also raising a number of additional and intriguing questions about Native American prehistory.

Until recently, the dominant explanation for the colonization of the Americas was the Clovis-first model, hypothesizing that modern humans first entered the Americas between 13,500-12,000 cal BP (calendar years before present) and then rapidly expanded into the uninhabited areas of these continental regions (see also Collins, p.31). Because no older Paleoindian sites had been discovered or confirmed, and because all other lithic traditions in the Americas seemed to derive from the Clovis culture, many archaeologists believed that the Clovis points demarcated the earliest occupancy of the Americas by modern human groups.

However, recent archaeological data have brought the Clovis-first model into question. Meadowcroft (PA), Cactus Hill (VA), the Topper Site (SC), and especially Monte Verde in southern Chile, have all been dated to between 16,000-14,500 cal BP, dates that are older than those associated with Clovis lithic sites in North America. In addition, these sites have yielded lithic tools and other cultural materials that indicate that they were not created by Clovis peoples. These important novel findings suggested that ancestral Native Americans settled the New World earlier than 13,500 cal BP, predating the Clovis lithic tradi-

tion. Furthermore, because glacial ice sheets blocked the movement of human groups from Beringia through the interior of North America until after 14,000 cal BP, these early immigrants may have followed a coastal route into the American continents, a path that was also suggested by recent linguistic studies of Native American languages (see Gruhn p.109).

Moreover, recent studies of craniometric variation in the New World have revealed significant biological differences between the earliest settlers of the Americas, the Paleoindians, and populations dating from the Archaic period (7,000 cal BP) forward, including modern Native American populations (e.g. Brace, pp.53-61). These data suggested that Paleoindians and later Amerindian populations derived from two

and Y-chromosome. These genomes possess a series of different markers that define or identify specific genetic lineages present in human populations. Thus, by analyzing the sequence variation in these two genomes, one can identify the genetic lineages that are present within populations, characterize the extent of diversity within them, and ascertain the manner in which they have been spread into neighboring groups. Due to the insights into the genetic prehistory of Native American populations that they provide, these two molecular data sets will be explored in some detail.

Mitochondrial DNA Variation in Siberia and the Americas:

Genetic Properties of the Mitochondrial DNA: The human mtDNA has a number of distinct properties that make it a valuable tool for molecular anthropological studies. These properties have been discussed in detail elsewhere, ^{50a,147} but include its maternal inheritance, rapid evolutionary rate, and lack of recombination, all of which allow mutations to accumulate in a more or less "linear" or chronological fashion within extended maternal lineages. In addition, many mtDNA mutations correlate with the geographic region in which they first occurred. ^{2,18,19,132,133,137} This property allows researchers to reconstruct ancient migration patterns based on the distribution of these mutations in different populations. Moreover, because of their sensitivity to stochastic processes such as genetic drift and founder effects that result from geographic isolation, migration, or population splits, ^{88a} mtDNA sequences often contain genetic signals of these past events.

The human mtDNA consists of two basic regions that have been analyzed in genetic studies of human populations (fig.1). The first encompasses all of the coding regions of the mtDNA genome, including genes that control for ribosomal RNAs (rRNAs), transfer RNAs (tRNAs), and proteins involved in oxidative phosphorylation (OXPHOS), the major biochemical process that takes place within the mitochondrion. ¹⁴⁷ These coding regions represent roughly 94% of the total mtDNA sequence. The remainder of the mtDNA genome is comprised of the non-coding Displacement Loop (D-loop), or control region (CR), in which mtDNA replication is initiated and regulated.

RFLP Analysis: Two different molecular methods have been typically used to analyze these regions of the mtDNA genome. The first

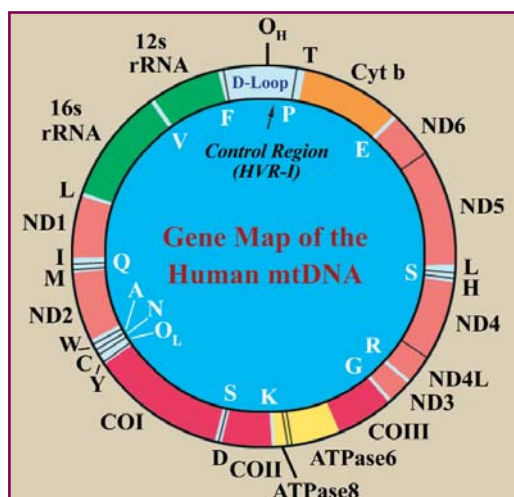


Fig.1: Schematic diagram of the mitochondrial genome (after the Mitochondrial DNA Morbid Map, <http://www.gen.enory.edu/MITOMAP/mitomapgenome.pdf>).

temporally distinct migrations that originated in different parts of Asia. On top of this, the putative Eurasian/East Asian appearance of the Paleoindian crania, and the lack of an obvious Siberian precursor to the Clovis lithic culture, has led some researchers to propose that ancient Eurasian/European peoples were among the first to enter the New World. Whether or not this turns out to be the case, the new anthropological data imply that the colonization of the New World was a more complex process than previously thought, one in which multiple expansions of ancient peoples contributed to the genetic diversity observed in Native American populations.

The same issues concerning the origins and affinities of Native Americans have also been approached through molecular genetic studies, in particular, those involving analysis of two uniparentally inherited, non-recombining genomes, the mitochondrial DNA (mtDNA)

method is called restriction fragment length polymorphism (RFLP) analysis. RFLP analysis surveys individual mtDNAs for sequence variation using a series of restriction enzymes that cleave the mtDNA molecule at different recognition sites (i.e. locations in the sequence that contain specific combinations of nucleotide bases, such as GCGC) within it. Point mutations, the source of most sequence variation in DNAs, either eliminate recognition sites in mtDNAs by altering their nucleotide base composition (from GCGC to GCAC) or create new recognition sites from semi-sites that are one nucleotide away from being real recognition sites (e.g. GCAC to GCGC). As a result, RFLP analysis catalogues the sequence changes that have occurred within the recognition sites of these mtDNAs.

The combination of all of the RFLPs present in a mtDNA define its “haplotype.” Those haplotypes sharing a specific set of RFLPs are said to belong to a “haplogroup,” or “lineage,” because of their genetic relatedness. Since the majority of the polymorphisms detected by this method occur in the coding sequences of the mitochondrial genome, they generally reflect the pattern of variation in, and the relative evolutionary rate of, mtDNA sequences that are under functional constraints. By measuring the extent of RFLP variation within and among mtDNA haplogroups, one can estimate their relative time depths in a particular geographic region.

Due to the cost of screening the whole mtDNA genome for RFLP variation, many researchers have elected to use an alternative method that takes advantage of the ability of RFLP analysis to detect specific maternal lineages in human populations. While numerous RFLPs have been detected in various world

populations, only a small percentage of them actually define these maternal lineages, which represent smaller branches in the larger modern human mtDNA phylogeny. As noted above, a number of these maternal lineages have been shown to have specific geographic origins (e.g. haplogroup L in the African continent^{18,19}). Consequently, it is possible to screen mtDNAs from a particular population for the RFLPs defining these maternal lineages, and then determine the number of haplotypes that originated in different geographic regions within that population. However, since this screening process examines a limited subset of the total number of RFLPs present within mtDNAs, the amount of sequence information obtained through this method is more limited than that acquired through whole genome RFLP analysis.

HVR-I Sequencing: A second important method involves the direct sequencing of the first hypervariable segment (HVR-I) of the mtDNA control region (CR; fig.1). In contrast to RFLP analysis, HVR-I sequencing provides a nucleotide-by-nucleotide reading of this segment of the mtDNA genome, rather than a general scan of the genome for small regions of sequence changes, as provided by RFLP analysis. The HVR-I also mutates more rapidly than the coding sequences in the rest of the mtDNA genome.^{46, 47,145,149} Because of this feature, one can obtain a very detailed assessment of mutational changes that have occurred within the HVR-I through direct sequencing. In addition, like RFLPs, certain combinations of mutations in the HVR-I (sequence motifs) help to delineate specific mtDNA haplogroups in human populations, whereas the remaining polymorphisms generally reveal the extent of genetic differentiation of these

mtDNAs in different geographic areas. By statistically assessing the level of HVR-I sequence variation within haplogroups, one can estimate their relative time depths in a particular geographic region.

For various reasons, researchers analyzing mtDNA diversity through HVR-I sequencing developed a separate nomenclature to describe mtDNA variants detected by this

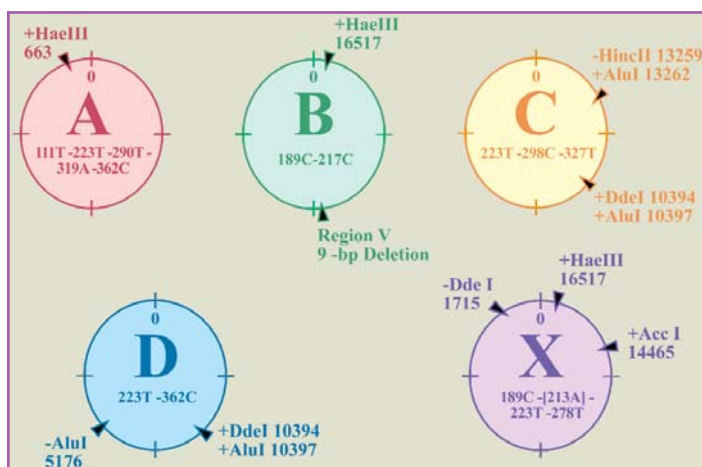


Fig.2: Five founding Native American mtDNA haplogroups. RFLPs that define each haplogroup are shown outside of circular mtDNA molecules representing the 5 maternal lineages; HVR-I polymorphisms forming sequence motifs of each group shown inside each circle.

Glossary of terms used in evolutionary biology

allele: for genes, it is a variant of a single gene, inherited at a particular genetic locus, consisting of a particular sequence of nucleotides, and coding for messenger RNA (mRNA); for other genetic markers, it represents alternative forms of those markers (e.g. deleted/nondeleted, A or G, presence/absence).

Alu insertion element: one of a family of repeated sequences about 300 base pairs in length that derive from the 7SL RNA gene. They have the ability to duplicate and insert themselves into different chromosomal locations. Over the course of hominid evolution, Alu sequences have inserted themselves into these chromosomes over a million times, and now constitute 10% of all human DNA.

amino acid: the molecular building block of proteins; they are specified by groups of three nucleotide bases in the DNA sequence called codons. A protein is a chain of amino acids in a certain sequence; its properties are determined by this sequence of amino acids.

autochthonous: indigenous, native; forming or originating in the place where it is found.

biallelic: a polymorphism (trait) that is either present or absent in an allele.

chromosome: one of the linear DNA-containing structures found in the cell nucleus that contains all or most of the genes of an individual.

control region (CR): (also known as the D-loop) region that initiates and regulates the replication of the mtDNA genome; it is non-coding (i.e. does not contain genes that encode specific traits).

craniometric: standardized measurements of different skull dimensions (e.g. facial breadth).

D-loop: displacement loop, see control region.

DNA: deoxyribonucleic acid; the molecule that contains the genetic code spelled out in nucleotide bases; it exists as a double helix, and the nucleotide base pairs form the rungs of the helix, or ladder. DNA is the main component of chromosomes.

enzyme: a special protein that triggers and oversees chemical reactions in the body.

exon: the nucleotide sequences of most genes consist of parts that code for amino acids (proteins) and others that do not code for amino acids interspersed among them. The coding parts, which are translated into proteins in the ribosome, are called exons; the interspersed non-coding parts are called introns.

fixation: an allele or gene has achieved fixation when it reaches a frequency of 100% in a population.

founder effect: the loss of genetic variation when a new population is formed by a very small number of individuals from a larger population.

gene: units of inheritance; a sequence of DNA base pairs that codes for a specific function or trait.

method. In these studies, the term “lineage” was used to describe each unique HVR-I sequence in a given population. Every set of related lineages was then called a “cluster,” with the nodal or root types of these clusters being considered their “founding” lineages. This parallel terminology has resulted in confusion over the relative comparability of mtDNA haplotypes defined by RFLP analysis and HVR-I sequencing, hence, the number of founding haplotypes and lineages (haplogroups) that have been brought to the New World. To avoid similar problems here, I will use the term “haplotype” to refer to a mtDNA genotype defined by either RFLP analysis or HVR-I sequencing, and “lineage” to refer to the haplogroup to which the haplotypes belong.

It should also be pointed out here that the mutations detected by both RFLP analysis and HVR-I sequencing are associated on a single mtDNA molecule. Consequently, they create complex haplotypes that remain recognizable even when reversion and/or parallel mutations occur and potentially obscure the phylogenetic affiliation of the mtDNA in which they are present.¹⁴⁰ This association highlights the importance of using both RFLP haplotyping and HVR-I sequencing to characterize human mtDNAs. Without this dual approach, it may be difficult to judge how genetically similar that the Native American haplotypes defined by HVR-I sequencing actually are to those defined by RFLP analysis.

Founding mtDNA Lineages in the Americas (Haplogroups): Studies of mtDNA variation in modern Native American populations have shown that their haplotypes belong to primarily four different haplogroups, or lineages, which have been designated A-D.^{111,139,140} Collectively, these four haplogroups comprise 95%-100% of all mtDNAs in modern indigenous populations of the New World.^{1,3,6,25,30,31,50,61,62,71,72,76,79,80,86,99,107,108,135,141,148-150} They also encompass the vast majority of mtDNAs in ancient populations of the Americas.^{6,29,42,53-55,79,85,91,97,125} Thus, they can unequivocally be considered founding lineages in Native American populations.

Recent work has also shown that the majority of mtDNAs not falling into haplogroups A-D belong to haplogroup X,^{14,28,114,122} a mtDNA lineage that is also observed in European and West Asian populations.^{20,74,132,133} Amerindian haplogroup X mtDNAs share a set of RFLP and HVR-I sequence mutations with those from Eurasian haplogroup X, which reveals their

deeper genetic links, but have otherwise diverged from their Eurasian counterparts by at least several different mutations.^{14,122} In addition, haplogroup X has been detected in a pre-Columbian North American population,¹²⁵ and may possibly be present in a few ancient Floridian⁴¹ and Brazilian samples.⁹⁷ Together, these data indicate that haplogroup X was present in the New World prior to historical European contact, and that it is a fifth founding mtDNA lineage in Native Americans.

These five haplogroups possess a unique set of mutations, or genetic markers, that distinguish them from each other (fig.2). These markers include both coding region RFLPs^{111,139,140} and HVR-I sequence polymorphisms.^{30,49,140,149} Occasionally, haplotypes that appear to have diagnostic RFLP markers from two different haplogroups have been detected.^{1,108,140} However, after careful comparison of the RFLP and HVR-I sequence data from them, it becomes apparent that these so-called “compound” or “unusual” haplotypes are haplogroup A or D mtDNAs that have accumulated RFLPs which also appear in other haplogroups (e.g. Region V 9-bp deletion, -HincII 13259) or have lost diagnostic RFLPs for a particular haplogroup (e.g. +HaeIII 663).^{109,122,140}

In addition to the five founding haplogroups, some studies have detected the presence of “Other” (non-haplogroup A-D and X) haplotypes in different Native American groups.^{1,71,79,80,122,140,149} The presence of “Other” haplotypes in Native Americans is important because they could potentially represent previously unidentified founding mtDNA lineages that were brought to the New World during its initial phase of colonization. On the other hand, these haplotypes could have been



Fig.3: Eskimo women from Wales Bay, Alaska showing distinct craniometry in terms of facial breadth (Hrdlicka 1930, *BAE* vol.46).

acquired through non-native admixture in a post-Columbian context. Thus, a fuller definition of these haplotypes is critical for resolving the number of founding lineages brought to the Americas. This is especially true because most of the “Other” haplotypes were detected in studies in which the mtDNAs were only screened for the RFLP markers of haplogroups A-D.

One possible additional founding mtDNA lineage has been observed among South American Indians.^{25,79,80} These so-called X6/X7 haplotypes have the +DdeI 10394 and +AluI 10397 sites (+DdeI/+AluI sites) that occur in haplogroup M, a macrocluster that encompasses 55%-70% of all Asian mtDNAs, including haplogroups C and D,^{2,60,92,93,113,140,141} but otherwise lack the diagnostic RFLPs of haplogroups C and D. For this reason, X6/X7 haplotypes are not related to those from haplogroup X. [The similarity of the names of these two putative mtDNA lineages (X6/X7 versus X) arose because they were described in two separate papers published in the same year by different researchers using different nomenclatures.] Because putatively similar mtDNAs had been identified in other Native American populations,^{79,80,140} X6/X7 haplotypes were proposed to represent an additional founding lineage of Asian origin.^{25,79,80,82} However, when the HVR-I sequences from X6/X7 mtDNAs were phylogenetically analyzed with those from other Native American populations, they clustered within haplogroups C and D.^{109,110,125} These results indicated that X6/X7 mtDNAs were probably autochthonous haplotypes deriving from haplogroup C and D mtDNAs after the peopling of the Americas, rather than ones belonging to a new founding lineage from haplogroup M.

The majority of the remaining “Other” mtDNAs are likely to have been acquired through historical non-native gene flow. Several studies have revealed slight but non-negligible European admixture in North American Indian groups by the presence of West Eurasian haplogroups H, J and K.^{114,122,138} This finding is not surprising given that previous nuclear genetic studies had indicated the occurrence of European admixture among these indigenous groups. With further RFLP analysis, additional North American Indian populations with “Other” mtDNAs may exhibit the same kinds of haplotypes. However, due to the predominately male-mediated gene flow into native populations during the last several centuries, it is also likely that European mtDNAs will com-

prise a small minority of the “Other” haplotypes present in Native American groups.

By contrast, there is increasing evidence of historical African gene flow into a number of different Amerindian populations. Various studies have revealed the presence of African haplogroup L mtDNAs in native populations from both North and Central America.^{50,122,141} Similar haplotypes have also been found in admixed populations of North, Central and South America, such as Black Caribs,⁸⁴ Cubans,¹³⁶ Puerto Ricans,⁷⁷ Mexican-Americans,⁸¹ and Afro-Brazilian and Afro-Uruguayan populations.^{12,13} As more “Other” haplotypes are screened for the +HpaI 3592 site that defines African haplogroup L,^{18,19} the number of Native American populations shown to have African mtDNAs may increase. Furthermore, because many of these admixed or multiethnic populations represent indigenous groups that no longer exist as distinct tribal entities,⁷⁷ their mtDNAs may provide clues to the settlement of the regions of the Americas in which they reside.

Despite evidence to the contrary, it remains possible that additional haplogroups are present in Native American populations. Because relatively few ancient Native American samples have been molecularly characterized, and most of these have come from samples dated to 6,000 cal BP and later, an expanded analysis of pre-Columbian remains from various parts of the Americas could reveal the presence of heretofore unidentified ancient haplogroups. However, based on existing mtDNA data sets, most of these haplogroups would appear to have been lost from Amerindian populations in the relatively distant past, while some could possibly have been lost during the major demographic crash initiated by European colonization of the Americas. Even if detected, however, mtDNAs not belonging to haplogroups A-D and X will comprise a tiny minority of all of the haplotypes that were once present in ancient and modern Native American populations.

Distribution of Founding mtDNA Lineages in the Americas: An examination of the cumulative data from these studies reveals several broad patterns of haplogroup distribution across the Americas that may reflect its settlement history. To begin with, the four major founding haplogroups (A-D) are observed in Amerindian populations from North, Central and South America (fig.5). These four haplogroups have also been detected in Na-Denè Indian and

Eskimo-Aleut populations (fig.3),^{79,100,102,113,117,124,140} but it is not clear that all of them were originally present in these Native American groups (see below). Among Amerindians, there is a decreasing north-to-south frequency cline for haplogroup A, and an increasing north-to-south frequency cline for haplogroups C and D. In addition, South American haplogroup A, C and D mtDNAs are generally distinctive from those seen in North and Central America,^{50,136,139-141} as also seen with GM and HLA allotype data for Amerindian groups.^{24a,116a} Thus, based on these data, mtDNA diversity in the Americas shows some amount of geographic structuring.

In contrast, there is no particular clinal distribution for haplogroup B, aside from its being virtually absent in northern North America^{71,72,76,79,80,111,135,139-141} (fig.5). Haplogroup B occurs

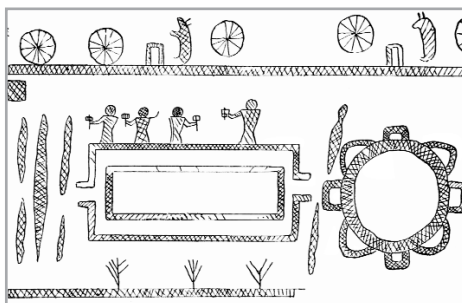


Fig.4: Detail from a birch-bark drawing of the Ojibwa creation myth from Red Lake, Minnesota. The circle at right is the world; at center is a ceremonial lodge, where four shamans hold healing rattles, warding off vertical serpent spirits at left (*Hoffman 1891, BAE vol.7, pl.IIIa*).

at its highest frequency among Amerindian populations of the US Southwest,^{140,71} but also appears at relatively high frequencies along the Andean coast of South America,^{79,80} probably due to recent population expansions there.¹⁴⁰ Other researchers have also suggested that Polynesian populations bearing haplogroup B may have genetically contributed to ancestral South American Indian groups.^{15,73} However, these putative contacts have not been supported by other genetic data.¹⁰

Unlike haplogroups A-D, haplogroup X is found nearly exclusively in North American populations (fig.5). It occurs at its highest frequencies among Algonkian-speaking groups such as the Ojibwa, and has been detected in various other Native American populations.^{14,76,114,122,140} While this haplogroup seems to be associated with the expansion of Algonkian speakers, it also appears in the Na-Denè-speaking Navajo. Its presence in the Navajo could reflect the occurrence of admixture between ancestral Na-Denè and Amerindian populations as the

former expanded southward from Canada around 1,000 years ago.^{139,140} Alternatively, it is possible that haplogroup X was brought to the Americas with ancestral Athapaskans and subsequently disseminated into Amerindian populations through contact between these groups, as implied by the distribution of the albumin Naskapi variant in North American native populations.¹²⁰ In either case, a more extensive mtDNA analysis of Canadian Athapaskan groups will be needed to test these hypotheses.

Although mtDNAs from haplogroups A-D and X often occur together in Amerindian populations, many tribes lack haplotypes from at least one of these haplogroups.^{111,135,138-141} This pattern probably reflects the extent to which genetic drift and founder events have influenced the stochastic extinction and fixation of mtDNA haplotypes. In other words, once a small group moves away from its founding population and becomes isolated, its gene pool may not have the full range of polymorphisms (or traits, variants, etc.) that the larger, original group had. This event shapes the genetic makeup of the population's future generations (founder effect). Furthermore, the frequencies of various polymorphisms can be significantly different in the smaller group from the founding group, while genetic mutations in a smaller group can have a larger effect on the population as a whole (genetic drift).

This interpretation is also supported by the high frequency of “private haplotypes” (i.e. unique genetic variants that are exclusive to a small isolated group or set of related groups and have a limited distribution) in different Amerindian tribes.¹⁴⁰ These are analogous to the “private polymorphisms” detected in nuclear genes for many of these same populations.⁸⁷ The general congruence of nuclear and mitochondrial genetic data supports the idea that early tribal isolation and founder effects led to the divergence of tribal gene pools.^{88,140} In fact, there is some evidence that this process has occurred at a regional level, as in the sharing of unique haplotypes among spatially adjacent and/or linguistically related populations, such as Chibchan groups of Costa Rica.^{3,61,62,135,140,141}

However, the genetic composition of ancient populations may or may not be the same as extant groups occupying the same geographic region because of these population genetic processes. For example, based on its haplogroup frequencies, the ancient Stillwater Marsh population does not appear to be ances-

Glossary of terms used in evolutionary biology

gene flow: the movement of genes into or through a population by interbreeding, or migration and interbreeding, with another population.

genetic drift: random changes in gene frequency in a population; may be caused by a reduction in population size (bottleneck), a small group moving away from its parent population (founder effect), or other stochastic processes.

genome: the complete genetic material of an individual or species; it is sometimes used to refer to the genetic map of the mtDNA (which has its own genome, like its precursors, bacteria).

haplotype: combination of genetic markers or polymorphisms present in a gene or genome, such as the mtDNA, and are inherited together as a unit.

haplogroup/haplolineage: group of haplotypes that share a specific set of polymorphisms (genetic markers), reflecting their genetic relatedness. Five mtDNA (A, B, C, D, and X), and six Y-chromosome haplogroups (M1, M3, M17, M45, M89, and M130), found in varying frequencies in Native American populations, provide keys to past genetic input to the different populations.

HVR-I: the first hypervariable region of the mtDNA control region. This region mutates more rapidly than the coding sequences in the rest of the mtDNA genome, and, thus, on average, exhibits a larger number of mutations than coding sequences. Its hypermutability reveals a detailed report of genetic changes in human mtDNAs.

hypermutable: susceptible to rapid mutations.

lineage: although there are several technical definitions, this article refers to it as the haplogroup to which specific haplotypes belong.

locus: the location in the DNA occupied by a particular gene or genetic marker.

microsatellite: short tandem repeat polymorphism (see STR).

mitochondria: (*sing.* mitochondrion) organelles (mini, self-contained units) in cell cytoplasm (outside the nucleus) that produce energy for cell functions and have DNA distinct from the nuclear DNA.

mtDNA: DNA of mitochondria. Because mitochondria occur outside of the cell nucleus, mtDNA is typically only passed on through the female, and hence reveals matrilineal relationships.

mRNA: messenger RNA; a type of single-stranded RNA molecule that copies portions of the DNA (segments known as exons) and brings the codes to the ribosome (structures in the cytoplasm of cells) for protein synthesis.

mutation: a change in the structure of DNA, either in the nucleotide bases, or in the number and/or form of chromosomes.

non-recombining: (recombination defined on next page) Those portions of the human genome that do not recombine include the mtDNA and the majority of the Y-chromosome (NRY). Because they are non-recombining, the mutations that occur in these segments of DNA are not reshuffled/mixed into new combinations, and hence, accumulate in a linear or chronological fashion.

tral to the modern Amerindian populations living in the Great Basin region of Nevada (see also *AR* 3,1 pp.94-98).⁵³⁻⁵⁵ Conversely, ancient and modern Eskimo and Aleut samples have nearly the same haplogroup frequencies as their modern antecedents.^{71,80,90,42,43,100,102,117,124} The same thing is true for the ancient Anasazi and Fremont cultures with modern Puebloan Indian groups,^{16,91} ancient Oneota with modern Algonkian groups,^{76,125} and ancient and modern Patagonians and Fuegians.^{29,65a,86} Ongoing work with ancient Californian,²⁶ Southeast US,¹⁵² and Ohio Valley⁸³ populations will reveal whether this trend holds true for those regions, as well. Overall, these data suggest that, once becoming genetically distinct from surrounding groups, many regional Amerindian populations maintained their genetic integrity over a considerable length of time.

In light of these observations, it is intriguing that none of the oldest (Holocene) skeletal samples analyzed for mtDNA variation (10,000-8,000 cal BP) have yet been shown to possess haplogroup A mtDNA.¹²¹ This finding would seem to suggest that this haplogroup was brought to the Americas later than the other four. However, the number of very ancient samples that have been successfully analyzed for mtDNA variation are rather small (15-20), and are drawn from only North American locations. Therefore, while suggestive, this trend in haplogroup distribution among Paleoamerican samples requires further confirmation through the analysis of additional skeletal remains.

Eskimo-Aleut populations differ from Amerindian ones in having predominantly haplogroup A and D mtDNAs^{80,100,102,113,117,124,140} (fig.5). Siberian and Alaskan Eskimos (Yupik and Inupik) have higher frequencies of haplogroup A, while the Aleuts differ from Eskimo populations in having mostly haplogroup D mtDNAs.^{80,89,90,100,102,113,117,124,140} Both groups also exhibit very low frequencies of haplogroup C mtDNAs, and essentially lack haplogroup B.^{79,117,118,124,139,140} These findings suggest that haplogroup C could represent a founding mtDNA lineage in Eskimo-Aleut populations.^{113,124} At the same time, European gene flow into the Alaskan Eskimos and Aleuts and Chukchi gene flow into the St. Lawrence Eskimos,^{20a,26a} as well as tribal interactions between Alaskan Eskimo and Northwest Coast Amerindian groups,^{130a} may be the sources of the very low frequencies of haplogroup B and “Other” mtDNAs that appear in Alaskan Eskimos and Aleuts.⁷⁹

Na-Denè Indians also exhibit somewhat different haplogroup profiles than either Amerindian or Eskimo-Aleut populations. Virtually all of the northern Na-Denè mtDNAs belong to haplogroup A, and show genetic affinities with those of other circumarctic populations. However, while having clear biological links to northern Na-Denè groups, the Southern Na-Denè Indians (Navajo and Apache) also have mtDNAs belonging to haplogroups B-D and X (fig.6).^{14,71,79,122,139,140} These observations are consistent with data indicating that the Southern Na-Denè populations have become admixed with neighboring Amerindian populations since their arrival in the American Southwest some 1,000-500 years ago.

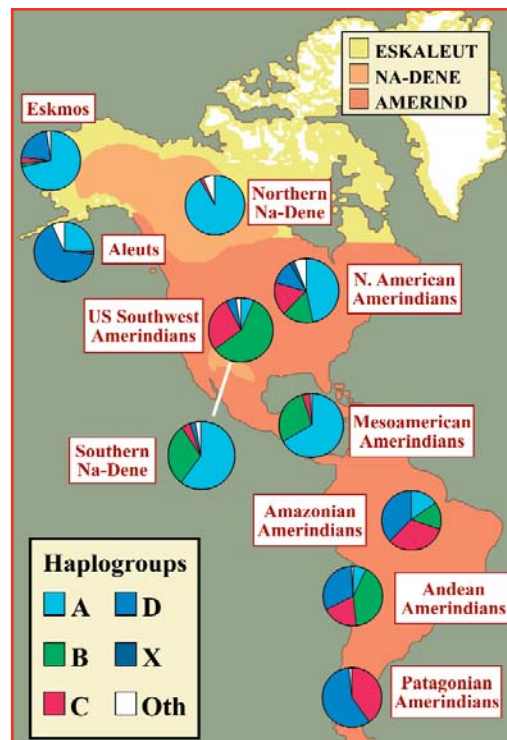


Fig.5: mtDNA haplogroup frequencies in Native American populations. Charts located in different geographic regions summarize the overall haplogroup frequencies for a number of populations inhabiting those areas. “Other” category represents mtDNAs that have not yet been shown to belong to haplogroups A-D and X. Haplogroup X occurs in Southern Na-Denè at a 2.7% frequency and in North American Amerindians at 2.8%.

Origins of mtDNA Haplogroups in Asia and Siberia: It has been suggested that the region between Mongolia and the Lake Baikal area represents the source area for ancestral Native Americans because populations from these regions have polymorphic frequencies of haplogroups A-D.^{63,82} However, it is now known that haplogroup A-D mtDNAs are found together in populations originating as far west as the Altai Mountain region to Japan and Korea in the east, with Mongolia and the Lake Baikal region falling in the middle of the two locations.^{2,22,22a, 24,48,63,82,112,130,134} Thus, if the presence of these founding haplogroups in an Asian population is the sole criterion for identifying the potential source area of ancestral Native Americans, then the range of possibilities is now expanded well beyond Mongolia *per se*.

Haplogroups A-D actually represent a minority of mtDNA lineages in many Siberian and East Asian populations (fig.10). In fact, most Siberian populations have only haplogroups A, C and D.^{113,112,124,130,138} Haplogroup A is absent or at low frequencies in most Siberian populations, but rises in frequency in Tuvans, Buryats, and Mongolians, while appearing at its highest frequency in northeastern Siberian populations.^{24,113,124,130,138} In contrast, haplogroup C and D mtDNAs are found at significant frequencies in every eastern Siberian population, from the Yenisey River in the west to the Bering Sea in the east,^{112,113,124,130,138} and appear in many East Asian populations as well.^{2,48} Thus, these two mtDNA lineages either represent some of the first haplogroups to have expanded into this region of the world and/or have been spread throughout northern regions through later population expansions.

Interestingly, nearly all Siberian groups lack haplogroup B mtDNAs. Those that do possess these haplotypes live along the southern margin of Siberia adjacent to Mongolia and northern China.^{22,63,95,113,117,118,124} (fig.10). The frequency of this mtDNA lineage is relatively low in these Siberian/Asian populations, and increases as one moves into East and Southeast Asia.^{3,39,45,48,78,96} The most significant increase of this lineage in Asia occurs in Melanesia and Oceania as a result of the expansion of Austronesian speaking groups.^{73,78,82a,96,98} This distribution suggests that haplogroup B arose somewhere in East Asia rather than in southeastern Siberia, where haplogroups A, C and D probably evolved, or else has been lost through genetic drift in most northern Asian populations.

Siberian and East Asian populations also appear to lack haplogroup X mtDNAs^{48,113, 124,130,138} (fig.10). These haplotypes appear at low frequencies in a number of European and West Asian populations,^{19a,20,32,74,114,133,98} and do not appear in groups east of Kazakhstan. The only exceptions are Altayan populations, who very recently were found to possess low frequencies of haplogroup X mtDNAs.^{22a} This discovery suggests that at least some ancestral Amerindians may have arisen in south-central Siberia rather than somewhere closer in East Asia.

Various other Eurasian and Asian haplogroups comprise the rest of the Siberian mitochondrial gene pool (indicated as "Other" haplogroups in fig.10). This distribution probably reflects population dynamics in Siberia before and after the colonization of the New World, such as the expansion of

Paleoasiatic speakers in northeast Asia,^{113,124} the spread of Tungusic speaking populations throughout east and central Siberia,^{22,110,113,140} the spread of Uralic speakers in northern Asia,⁶⁴ and the northward expansion of Turkic speakers into Siberia (Yakuts¹³³). At this time, none of these Eurasian or Asian haplogroups have been seen in Native American populations.

Glossary of terms used in evolutionary biology

nucleotide base: basic unit of a DNA sequence, made of a sugar, a phosphate group, and one of four nitrogenous bases (adenine, guanine, thymine, and cytosine; commonly referred to as A, G, T and C). These nucleotides bond with one another in fixed ways (always A with T and G with C) to form base pairs, the "rungs" of the "ladder" of the DNA double helix.

3' oligo tails: all Alu elements have additional stretches of A's (adenine nucleotides) at the 3'-end of their sequences ("oligo" means multiple occurrences of the same nucleotide). The Asian form of the M1 Alu insertion found on the Y-chromosome has a longer series of A's at its end compared to the African form. This difference allows the distinction between the two types genetically, and the inference of the ancestral-descendant form of this Alu element evolutionarily.

oxidative phosphorylation (OXPHOS): a process occurring in mitochondria that provides energy to the cell.

phylogeny: a tree or network showing the branching relationships among a species or gene; a genetic genealogy. Through a phylogeny, one can determine the most recent common ancestor of a species or gene.

point mutation: a change in a single nucleotide base in a DNA sequence. These can either be transitions (A to G, C to T) or transversions (C to G, A to T).

polymorphism: the condition in which a population possesses more than one allele at a locus; sometimes defined as the condition of having more than one allele with a frequency of 5% in the population. The term is more generically used to refer to any kind of mutation occurring in a particular gene or at a locus.

population: a group of organisms (of the same species) sharing one gene pool.

recombination: an event, occurring by the crossing over of chromosomes during meiosis (gamete formation), in which DNA is exchanged between a pair of chromosomes. This process reshuffles the locations of genes or alleles on chromosomes, and produces greater genetic variability by creating novel combinations of genes.

restriction enzyme: an enzyme that recognizes a specific combination of nucleotides (e.g. GTAC) in a DNA sequence, and cuts the DNA only at those locations.

RFLP: a restriction fragment length polymorphism (RFLP) is a series of DNA fragments of varying size that results from the use of a restriction enzyme to cut up a DNA molecule.

RFLP analysis: a method that utilizes the ability of restriction enzymes to cut DNA at specific locations to detect variation in DNA sequences, as point mutations will either eliminate or create new sites. The presence of new mutations is determined by comparing the sample RFLPs with that of a standard reference DNA.

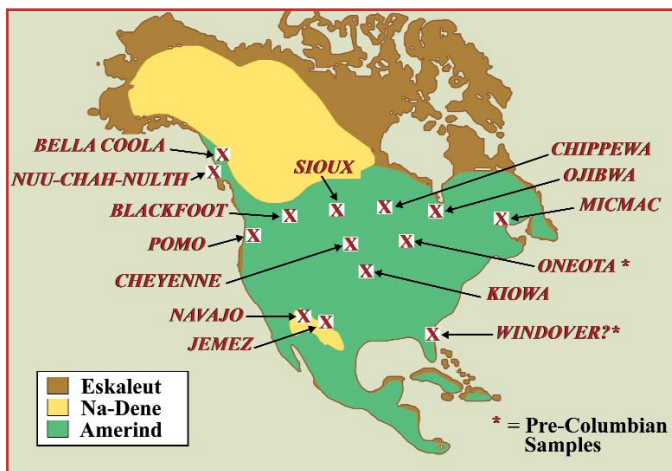


Fig.6: Native North American populations having haplogroup X mtDNAs (populations/samples that are pre-Columbian in origin marked with *); does not show all of the populations known to possess these haplotypes, but includes most of them.

Antiquity of mtDNA Haplogroups in Siberia and the Americas: One of the most hotly debated questions concerning the origins of Native Americans is the antiquity of the ancestral populations who entered the New World. This question has been approached by examining the antiquity and pattern of diversity of the five founding haplogroups in Native American populations. Researchers analyzing RFLP haplotype data have estimated ages for haplogroups A, C, and D in the Americas of between 35,000-20,000 cal BP.^{113,139-141} Comparably ancient dates have also been obtained for these three mtDNA lineages in Asia and Siberia.^{113,124,138} Additional support for these findings comes from the fact that Native American and Siberian populations seem to lack any mtDNAs in common, even those which appear to be identical on the basis of their RFLP haplotypes, due to their having different HVR-I sequences.^{113,124,140} These findings imply that estimates of haplogroup divergence may well reflect the genetic diversity that has accumulated in the American branches of these mtDNA lineages, hence, the time at which modern humans first entered the Americas. By contrast, the age estimate for haplogroups B and X were smaller than that of haplogroups A, C, and D.^{14,113,124,138} These estimates suggested that haplogroups B and X could have been brought to the Americas in later separate migrations from the earlier one(s) that brought haplogroups A, C, and D here.

However, recent estimates of HVR-I sequence diversity in Native American groups indicate considerable antiquity for all five founding haplogroups. These studies have provided ages for haplogroups A, C, and D of 35,000-20,000 cal BP,^{11,27,125} with a comparable age being estimated for haplogroup X in the Americas and Europe.^{14,98,119,132,133} In addition, studies using HVR-I sequence data have suggested that haplogroup B was present in the New World by 30,000-25,000 cal BP,^{11,125} a date consistent with those estimated for this mtDNA lineage in Asia using both RFLP and HVR-I sequence data (32,000-24,000 cal BP).^{2,73,96} As such, these estimates imply that haplogroups B and X could have been brought to the Americas at about the same time as haplogroups A, C, and D. Therefore, most molecular studies point to an early, rather than a later, entry time of these mtDNA lineages in the Americas.

Still other researchers have argued that the ~25,000 cal BP ages for the mtDNA haplogroups in the Americas overestimate the time

at which the initial colonization process took place. They instead suggest that these estimates represent the times at which the haplogroups diverged or originated in Asia, hence, the emergence of the common ancestral population for Native Americans.^{117,149} Based on their analysis of HVR-I sequence data, Shields et al. (1993) proposed a “late” entry time (14,000-12,000 cal BP) of ancestral Amerindians to the New World. However, these data were taken from mostly Northwest Coast Amerindian and circumarctic populations who are known to share a number of HVR-I sequences from haplogroups A, C and D.^{72,113,117,124,148} As a consequence, this date may underestimate the antiquity of these groups in the New World. On the other hand, Shields et al. (1993) proposed late entry for circumarctic populations (7,000-5,000 cal BP) is generally consistent with other mtDNA diversity estimates in these groups.^{102,113,124}

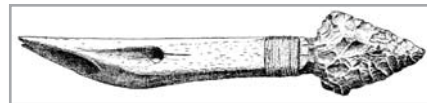
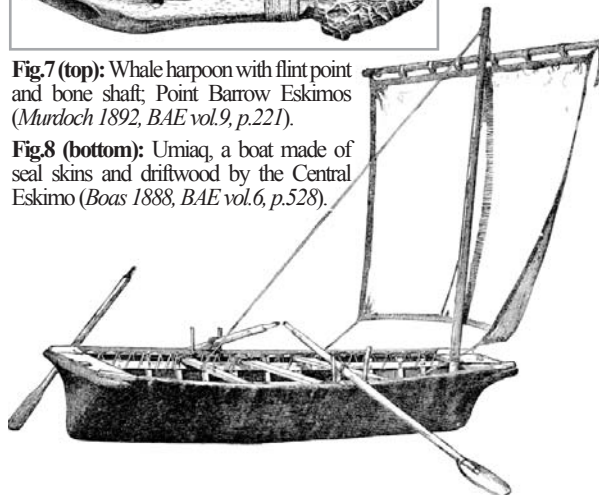


Fig.7 (top): Whale harpoon with flint point and bone shaft; Point Barrow Eskimos (Murdoch 1892, *BAE* vol.9, p.221).

Fig.8 (bottom): Umiak, a boat made of seal skins and driftwood by the Central Eskimo (Boas 1888, *BAE* vol.6, p.528).



It has further been suggested that the ancient haplogroup divergence dates are overestimates because they did not consider that multiple haplotypes from haplogroups A-D were brought to the Americas by ancestral Amerindian populations.^{1,25,79,80} In this view, haplogroup sequence divergences are inflated because the diversity of haplotypes accumulating from each founding haplotype (two per haplogroup) was combined, not analyzed separately. If divergence values were estimated for the subbranches of haplogroups A-D that are defined by these two founding haplotypes, then the overall divergence time for each mtDNA lineage would, therefore, be less than 30,000-20,000 cal BP, and the colonization date of the Americas would be consistent with a “late” entry, or Clovis-first migration model.

The problem with this view is that the proposed founding haplotypes for each haplogroup (e.g. A1, A2, B1, B2, etc.) are delineated by the hypermutable +HaeIII 16517 site.^{1,25,79,80} Its hypermutability causes the +HaeIII 16517 site to appear in a number of distinct mtDNA haplogroups, and between otherwise identical haplotypes, as a result of independent mutational events. For Native American populations, these mtDNAs include not only the putative founding haplotypes for haplogroups A-D but also numerous pairs of tribal-specific haplotypes for both Native American and Siberian populations.^{110,124,135,138-140} As a consequence, it is difficult to determine which of the mtDNAs from each haplogroup are actually “founding” haplotypes and which are “derived” haplotypes by screening them for only the haplogroup-defining RFLPs and the +HaeIII 16517 site. Thus, the +HaeIII 16517 site provides little information that would allow one to estimate the age of a haplogroup based on RFLP data.

A comparison of the HVR-I sequence data from Asia and the Americas allows further inferences about the number of founding mtDNAs brought to the New World. Not surprisingly, those HVR-I sequences indicated as being founder mtDNAs in the Americas are the most common sequences for each haplogroup among Native American populations, and are also the stem types from which most other HVR-I sequences have evolved.^{3,25,30,49,62,63,72,86,99,107,108,140,148-150} HVR-I

sequences identical to the ancestral Asian sequences have also been detected in some Amerindian populations. But without further RFLP and HVR-I sequence analysis, it is impossible to determine whether or not these are really ancestral sequences or instead derivatives that have lost the key polymorphisms that delineate American from Asian mtDNAs through secondary mutations.

Judging from the HVR-I data, there are potentially two founding HVR-I sequences for haplogroups A, C, D, and X, and only one for haplogroup B. If confirmed, then the previous estimates of mtDNA lineal diversity will have to be revisited. However, all other mutations in the HVR-I sequences appear to have arisen in either Asian/Siberian or Native American populations after their shared ancestral popula-

tion(s) separated. There are some instances of recurrent mutations appearing in both sets of mtDNAs, with these appearing as parallel mutations in different haplogroups.^{138,140} This finding is not unexpected given that many nucleotide sites are known to undergo mutation more often than others in the HVR-I.^{33,40,50a,126,146}

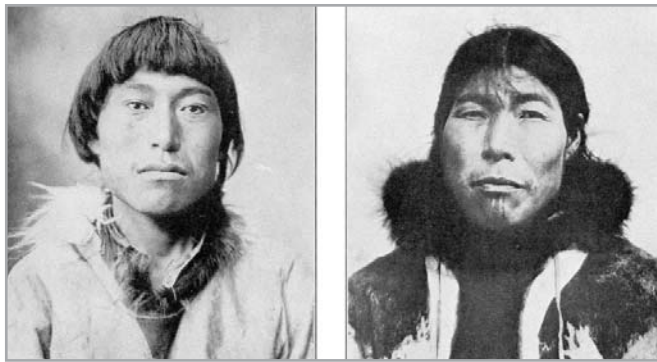


Fig.9: Eskimo men from the North Bering Sea region (photo: Lomen Bros.; Hrdlicka 1930, BAE vol.46).

Nevertheless, there may still be only 5-8 definitive founding *RFLP haplotypes*, and at the same time twice as many associated founding *HVR-I sequences*, among New World populations, in part because of the different evolutionary rates of the coding (slower) and non-coding (faster) portions of the mtDNA genome. Yet, the fact that both *RFLP haplotype* and *HVR-I* sequence data have revealed the presence of a small number of founding mtDNAs in Native American populations that inhabit a broad geographic expanse continues to indicate that either some degree of reduction in genetic diversity occurred during the colonization of the New World, or a geographically-specific subset of Asian mtDNAs were brought to the Americas by ancient Asian populations.

Number of mtDNA Migrations to the New World: Based on these Siberian and Asian mtDNA data, several different models for the peopling of the New World have been proposed (fig.11). Most of them have suggested a region extending from the Altai Mountains to southeastern Siberia and northern China as the potential source area(s) for ancestral Native American populations. However, there is not complete agreement on the numbers of migrations that left this region and entered the New World. Some researchers have suggested that ancestral Amerindian populations brought at least 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 from East Asia to the Americas.^{124,138,140} In addition, it was suggested that haplogroup X might also represent a separate migration from somewhere in Eurasia, given its absence in Siberia and much of the Americas.¹⁴ Some have even argued that each haplogroup represents a separate migratory wave to the New World.⁴⁹

However, many researchers assert that haplogroups A-D were brought to the New World in *Athena Review* Vol.3, No.2

a single migratory event.^{27,63,72,79-81} This view is based in part on the fact that haplogroups A-D are present in all Amerindian populations, and in part on the fact that the HVR-I sequences from these haplogroups have approximately the same levels of diversity, implying that they arrived as part of a single migration to the New World.^{11,72,125} From this perspective, the pattern of HVR-I variation in modern Native American groups largely resulted from *in situ* differentiation of ancestral Native American groups, as well as population expansions and movements occurring after the initial colonization of the New World.

Recent work provides yet another view on this question, that populations originating in both south-central and far eastern Siberia could have brought ancestral haplotypes to the New World. This suggestion is based on the possibility that two different founding haplotypes from haplogroups C and D were brought to the Americas with ancestral populations. More specifically, haplotypes with the most common HVR-I sequence motifs for haplogroups C (16223T-16298C-16325C-16327T) and D (16223T-16325C-16362C) in Native American groups are rarely encountered in Asian and Siberian populations, but have been seen in Amur River and East Asian groups.^{47,112} In contrast, haplotypes with the most common HVR-I sequence motif for haplogroups C (16223T-16298C-16327T) and D (16223T-16362C) in Asian/Siberian populations are not very frequent, if present at all, in most Native American groups.^{3,6,25,30,49,61,62,72,76,86,99,107,108,140,148-150} If substantiated, then the overall ages of haplogroups C and D would be somewhat less than 35,000-20,000 cal BP, because the diversity in these mtDNA lineages would have derived from two rather than one founding haplotypes. This would mean that the Americas could have been settled later than indicated by the older haplogroup age estimates, but would also imply that

multiple population expansions from different parts of northern Asia contributed to the genetic make-up of Amerindian populations.

There is also the issue of where haplogroup X came from. Because haplogroup X is present in a number of modern European populations,^{20,74,98,119,132,133,137} the Amerindian haplogroup X data have been used to argue for a prehistoric movement of ancient European (Solutrean) peoples across the Atlantic Ocean during the last glacial maximum.^{17a,123a} In this view, the distribution of haplogroup X in North America reflects the expansion of ancient peoples from Western Europe some 18,000-16,000 cal BP, the descendants of whom eventually developed the Clovis lithic technology that spread across North America between 13,500-12,100 cal BP.

Aside from the issue of whether or not the Clovis and Solutrean lithic traditions are actually related, this model is consistent with the proposed age of haplogroup X in Europe and Eurasia (30,000-20,000 cal BP).^{74,98,119,132} However, most ancient and modern European populations also exhibit an array of mtDNA haplogroups (H-K, T-X)^{20,74,98,103,119,132,133,137} that are not commonly seen in northern (or any) Native American populations. Furthermore, it is unclear as to why this hypothesized trans-Atlantic migration would primarily involve a haplogroup that typically comprises no more than 2% of the mtDNAs in modern Eurasian populations as opposed to another one such as haplogroup H that represents ~40% of mtDNAs in all of these groups. Thus, presently, there is very little support from the mtDNA data for an ancient trans-Atlantic migration.

Y-Chromosome Variation in Siberia and the Americas:

Genetic Properties of the Y-Chromosome: Many new and exciting insights into the peopling of Siberia and the New World have been recently obtained through studies of Y-chromosome variation in populations from these two areas. The Y-chromosome exhibits strict paternal transmission, and encompasses large regions of non-recombining sequence.^{37,51} As a consequence, mutations accumulate in a more or less linear, or chronological, fashion within extended paternal lineages, and patterns of accumulated sequence changes in Y-chromosomes along branching male lineages can be reconstructed with relatively minimal ambiguity.

Although the sequence evolution rate of the Y-chromosome is slower than that of the

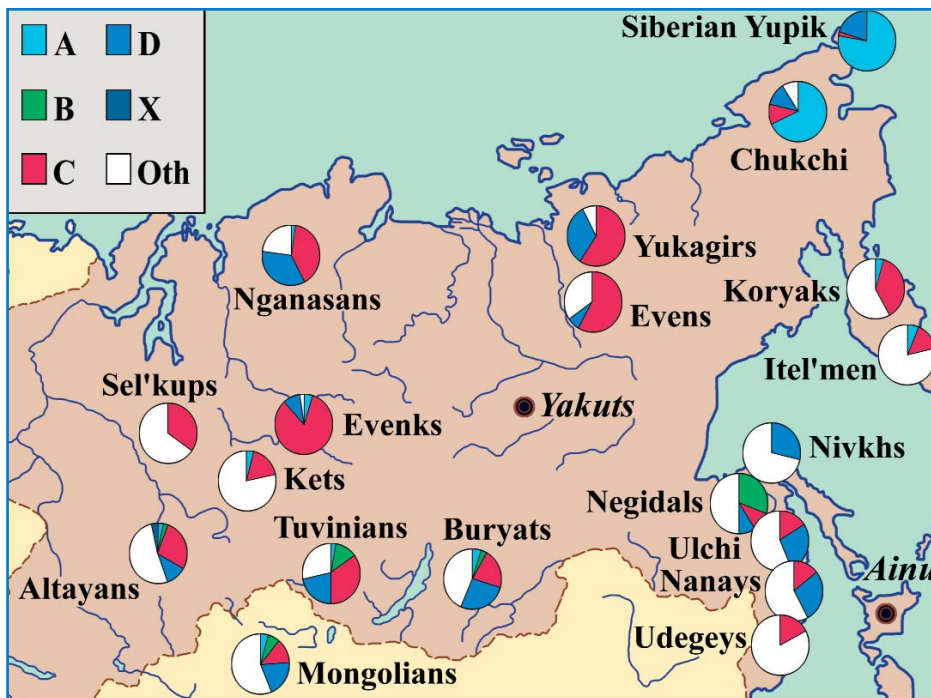


Fig.10: mtDNA haplogroup frequencies in native Siberian populations. The pie charts located in the different geographic regions indicate haplogroup frequencies for each population. The “Other” category represents mtDNAs that do not belong to haplogroups A-D and X (i.e. belong to other Asian or Eurasian haplogroups).

mtDNA,^{37,51} it contains several different types of polymorphic genetic systems that have different mutational mechanisms and rates. These include single nucleotide polymorphisms (SNPs), which consist of point mutations and small insertions or deletions, short tandem repeat (STR) polymorphisms, also known as microsatellites, and Alu insertion elements^{21,35,37,51,52,58} (fig.12). STRs are comprised of multiple copies of short nucleotide sequences, such as GCG or GATA, with each “allele” representing a certain number of sequence repeats (e.g. 9, 10, 11, etc.) for a particular STR marker, or locus, i.e. the number of repeats present at a particular locus determines its “allele size.” Over time, STR markers usually increase or decrease in allele size in a stepwise fashion (6 to 7, to 8, etc.), and, typically mutate much more rapidly than the other genetic systems (SNPs and Alus), thereby providing a finer resolution of sequence change in the Y-chromosome.

All of these genetic markers can collectively be used to construct Y haplotypes that are informative for tracing male migration and ascertaining phylogenetic relationships amongst various populations. To classify these Y-chromosome haplotypes, researchers use a genealogical approach based on a hierarchical ranking of different marker systems.^{21,36,38,51,67-70,105} In this approach, sets of Y-chromosomes are divided into distinct lineage clusters, or hap-

logroups, defined by one to several infrequently occurring biallelic polymorphisms (SNPs), which largely represent unique evolutionary events. Haplotypes belonging to these haplogroups are further assayed for diversity using more variable loci such as STRs, in which multiple alleles of different sizes are present within a population. The resulting “compound” haplotypes comprised of biallelic and multiallelic markers are then compared with those occurring in various world populations to reconstruct the genetic prehistory of these groups.

It should be pointed out here that multiallelic STR markers typically subdivide biallelic Y-chromosome haplotypes, but not in exactly the same way that HVR-I sequences subdivide RFLP haplotypes in the mtDNA. Unlike HVR-I mutations, STR loci do not provide additional markers that confirm the identity of a particular paternal lineage. Instead, the overall pattern of allelic variation at multiple STR loci gives information about the evolutionary trajectory of a paternal lineage. To elaborate, the same biallelic haplotype may have several different alleles for a particular STR locus because the higher mutation rate of the STR produces a large number of alleles that distinguish otherwise identical SNP haplotypes from each other. In addition, the same STR allele from a particular locus may be observed in different Y haplotypes, either because of the recent expansion or contraction

Glossary of terms used in evolutionary biology

RNA: ribonucleic acid; similar to DNA in nucleotide base composition except that it uses Uracil (U) rather than thymine (T) in its sequence, and is single stranded. When DNA is transcribed (read), messenger RNA containing the DNA sequence is produced and then translated into amino acids (proteins) by ribosomes.

ribosomal RNA: the RNA that, along with small proteins, constitutes ribosomes, and provides a site for translation of mRNA into protein.

sequence: the specific order of nucleotide base pairs in a DNA molecule or gene.

sequencing: method of determining the specific order of nucleotide base pairs in a given stretch of DNA or gene.

SNP: single nucleotide polymorphism; a genetic marker consisting of either point mutations or small insertion/deletions. The term is generally used to describe the occurrence of these mutations anywhere in a DNA sequence, but, in this report, refers to those occurring on the Y-chromosome.

STR: short tandem repeat, a.k.a. microsatellite. A genetic marker composed of multiple copies of a short nucleotide sequence (e.g. GATA) at a single locus. Allele size differences for STRs are based on the number of repeats present at that locus (e.g. 6,7,8, etc.). STR markers typically mutate more rapidly than the other genetic systems (SNPs and Alus), providing a finer resolution of change in the Y-chromosome.

tRNA: transfer RNA; binds to specific amino acids and transports them to the ribosome (structures in the cell cytoplasm) for protein synthesis.

Y-chromosome: a chromosome unique to males, on which sex-determination genes are located; consists largely of non-recombining sequence (NRY). Genetic variation on the Y-chromosome can show the inheritance of specific genes or mutations through the paternal line, and also track male migrations through time and space.

of allele sizes at this STR locus, or the convergence of STR allele sizes in the two SNP haplotypes. For these reasons, several to many different STR loci are usually analyzed for every Y-chromosome, as this combination of loci reveals the directionality of allele size changes that occurred within them, hence, how they evolved within these paternal lineages.

Over the course of the last five years, researchers have employed a variety of different SNPs to define Y-chromosome haplotypes. These include DYS287 [M1],³⁵ the α alphoid system, SRY1532 and 92R7;^{9,108} DYS199 [M3];¹⁴³ DYS7C;⁵² PN1, PN2, PN3 [M29], DYS257, SRY4064 [M40], SRY9138, and SRY10831;^{36,38} M9 and M17;⁴² Tat [M46];¹⁵³

RPS4Y [M130];^{4,5} and M45, M89, M119, and M122,¹²⁷ with the M numbers referring to the SNP nomenclature of Underhill et al. (1997, 2000). A comparable battery of STRs has been used for world populations.^{21,58} However, most researchers have employed at least some part of an informative set of STRs when analyzing Asia/Siberian and Native American populations, which includes the DYS19, DYS388, DYS389a, b, DYS390, DYS391, DYS392, and DYS393 loci.^{8,9,66-70,105}

This profusion of markers has led to the generation of a number of different nomenclatural systems for defining Y haplotypes, which, unfortunately, do not overlap to any great extent. Most studies have used a naming system in which unique Y-chromosomes defined by SNPs are called “haplotypes.” In this paper, I will use a system modeled after that employed with the mtDNA. Each unique Y-chromosome lineage defined by SNP markers will be referred to as a Y-chromosome “haplogroup” or “lineage,” with the SNP names deriving from the M nomenclature of Underhill et al. (1997, 2000). As shorthand for discussion, each haplotype will be assigned to a particular haplogroup based on the most recently occurring SNP marker that it has acquired. For example, the haplogroup defined by the presence of the M89, M9, M45 and M3 markers (oldest to youngest) will be referred to as haplogroup M3 (fig.13). Although this system contrasts with that pro-

posed by Underhill et al. (2000), who observed ten major haplogroups in world populations (I-X), it is possible to generally relate the two nomenclatures. More specifically, M1 is present in haplogroups III and IV; M89 is present in haplogroups VI-X; M9 is in haplogroups VII-X; M45 is present in haplogroups IX and X; M3 is present in haplogroup X; M17 is present in haplogroup IX; M46 occurs in haplogroup VIII; and M130 occurs in haplogroup V in Underhill et al. (2000).

Distribution of Y-Chromosome Lineages in Asia and Siberia: All studies to date have indicated that a variety of Y-chromosome haplogroups are present among Asian and Siberian populations at various frequencies. These include the M1, M3, M9, M17, M45, M46, M89, and M130 lineages (figs.13,14). Not all of these Y lineages were disseminated into the Americas in its initial colonization, and those that were may not have been brought there through a single population expansion. To draw out these distinctions more clearly, each lineage and its distribution will first be described in Asia and Siberia, and then in the Americas.

The M9 lineage, which is defined by a C to G transversion at the M9 locus, defines a major Eurasian branch of Y chromosome haplotypes.^{36,142,144} Based on existing data sets, most East Asian and Siberian groups exhibit M9-G haplotypes hence, represent Y-chromosomes that evolved from the ancestral M9-C African haplotypes, as do those in Native American populations.^{36,57,67-70,142,144} In the case of Asian, Siberian and Native American Y haplotypes, the M9 polymorphism is associated with the M3, M17, M45, and M46 lineages, but not the M130 lineage (fig.13). Overall, the M9 SNP encompasses a large number of the Y haplotypes seen in Siberians.^{36, 57,67-70,142,144}

Defined by a G to A transition, haplogroup M45 is observed in populations throughout Siberia, including those inhabiting Chukotka, Kamchatka, the Amur/Okhotsk region, and central Siberia (fig.14). However, this haplogroup is almost completely absent in East Asian populations,¹²⁷ suggesting that it arose in northern Asia and has not been widely disseminated in regions farther

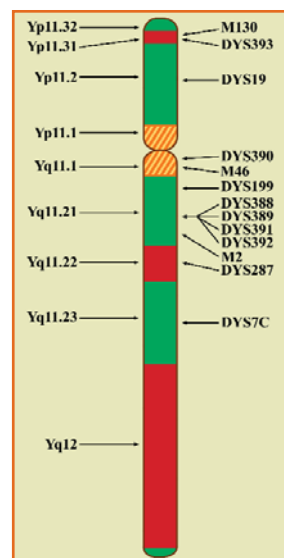


Fig.12: Schematic diagram of the Y-chromosome. SNP and STR markers commonly used for studies of Y-chromosome variation in indigenous Siberians and Native Americans are indicated along the right side of the chromosome. The markers along the left side represent different “geographic” positions along the chromosome.

south. M45 haplotypes also include the most recent ancestors of the M3 lineage that, on the basis of other SNP and STR marker data, are found in the central Siberian Kets, Sel’kups and Altayans.^{67,68,104} Defined by a C to T transition at the M3 locus, this lineage is the major paternal one seen in Native American populations, but in Siberia, is detected only in Chukchi and Siberian Eskimos.^{8,9,56,57,66-70,104,143}

The M1 lineage is defined by an Alu element insertion at Yq11, which has also been called the Y Alu Polymorphic element (YAP).³⁵ It defines a major branch of the human Y-chromosome phylogeny that originated in Africa. The M1 lineage appears at intermediate to high frequencies (46%-78%) in African populations and at low frequencies (0-11%) in European populations.^{35,123,65,144} Interestingly, it has also been detected at low to moderate frequencies in Central and East Asian populations, such as the Japanese,³⁴ Koreans,⁵⁹ Tibetans, Mongolians, Yakuts, Altayans and Tuvans,^{36,56,57,66-70} and represents a distinct haplogroup (IV) within them.¹⁴⁴ However, the Asian M1 haplotypes differ from those in African populations by having longer 3' oligo (dA) tails on the Alu element, and lacking the DYS271 (M2) SNP, which has been found only on African M1 chromosomes.^{115,116}

The M46 lineage is defined by a T to C transition at the RBF5, or Tat, locus.¹⁵³ Many of the haplotypes from this lineage also possess a 50-bp deletion at the DYS7C locus.^{52,57,69,70} Recent studies suggest that the M46 lineage arose in southeastern Siberia, as this is where its ancestral haplotypes appear at the highest frequencies.^{52, 69,70,153} Ancestral populations bearing these haplotypes then influenced the Kets, Altayans and Buryats, as well as Mongolians, Yakuts and

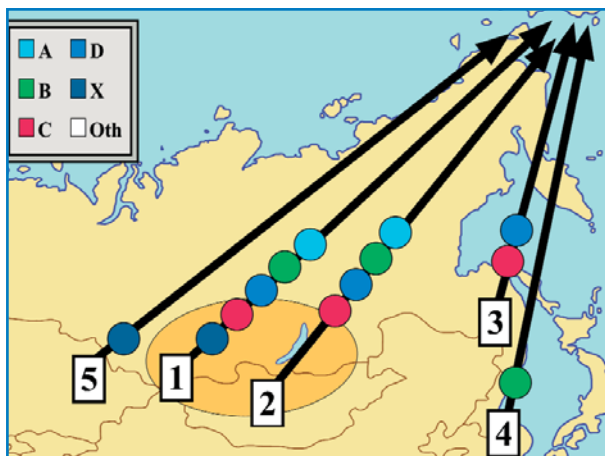


Fig.11: Possible New World migrations involving mtDNA haplogroups: *Scenario I:* all haplogroups were brought in from south-central Siberia at the same time (arrow 1); *II:* haplogroups A-D were brought together from south-central Siberia (arrow 2) and X came from Eurasia independently (arrow 5); *III:* haplogroups A, C and D came from south-central Siberia (arrow 2), with B brought in as part of a separate migration from East Asia (arrow 4), and haplogroup X brought in from Eurasia independently (arrow 5); *IV:* at least some haplogroup C and D mtDNAs were brought from the Amur River region (arrow 3), regardless of where the other haplogroup A-D and X originated. *V:* Less likely, and not shown here is that all 5 haplogroups represent separate migrations to the Americas.

Chinese Han populations.^{52,69,70,104,153} Furthermore, the M46 lineage appears at polymorphic frequencies in northern European populations such as the Finns and Saami, as well as Uralic-speakers of western Siberia.^{52,65,69,70,104,144,153} Its widespread distribution implies that this haplogroup was disseminated across Eurasia through a major population expansion, perhaps that associated with the spread of reindeer herding technology in the Neolithic.

Interestingly, M46 haplotypes are common in northeastern Siberian groups, including the Chukchi (fig.14) and Siberian Eskimos, but occur far less frequently in Amur River groups.^{57,67-70} Among Okhotsk/Amur populations, the M46 lineage appears only in those groups who have had recent contact, or shared origins, with central Siberians, such as the Okhotsk Evenks, Ulchi, Nanays and downriver Negidals. In contrast, it was absent in those groups that have maintained greater geographic and/or linguistic isolation, namely, the Udegeys, Nivkhs and upriver Negidals.^{67,68,70} These data suggest that the M46 haplogroup was recently introduced into the Okhotsk/Amur region, probably from south-central Siberia.

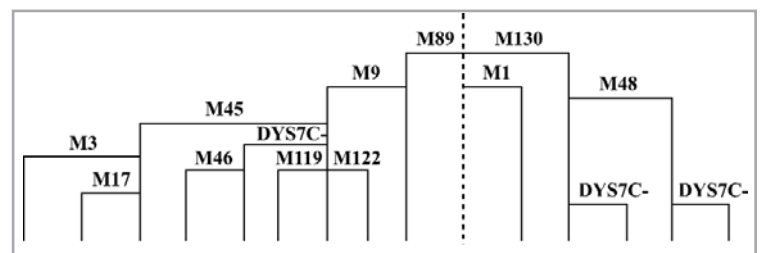
The M119 lineage is defined by an A to C transversion at this locus. Only a few Siberian populations exhibit the M119 lineage, with the Buryats having the highest frequency of this haplogroup (fig.14). However, this lineage occurs at significant frequencies in various ethnic Chinese populations. Its presence in Siberian populations is consistent with the northward migration of this haplogroup from East Asia.^{127,128} Conversely, Siberian populations lacked the M122 lineage,⁶⁸ a haplogroup that represents a large proportion of northern Chinese and East Asian Y-chromosomes.^{127,128} Thus, this haplogroup does not appear to have been brought to Siberia through northern expansions of ethnic Chinese groups.

The M130 lineage is defined by a C to T transition occurring at np 711 within the 7th exon of the RPS4Y (ribosomal protein S4 gene on the Y-chromosome) locus.^{4,5} Unlike most of the other Y haplogroups, the M130 lineage appears to be quite ancient and widespread in East and Southeast Asia, appearing in populations as far apart as Australia and Chukotka^{4,5, 57,67-70} (fig.14). Based on the STR patterns for its Y haplotypes in Siberian populations, the M130 lineage may have arisen in East Asian populations rather than the Altai-Sayan/Lake Baikal region, where nearly all other Y lineages are thought to have evolved.^{5,57,67-70,104} This inter-

pretation is supported by the high frequencies and diversity of M130 haplotypes in the Amur River region and northeastern Siberia, where both Kamchatkan and Amur River populations exhibit distinct sets of M130 haplotypes.⁶⁷⁻⁷⁰ This lineage later spread west from East Asia into the Baikal region, where it now appears at significant frequencies in Central Asian and central Siberian populations.^{5,57,69,70}

The remainder of Siberian Y-chromosomes belonged to less frequently occurring haplogroups. The first of these, the M89 lineage, is defined by a C to T transition at this locus. It is one of the most ancient SNPs in human Y-chromosomes, and distinguishes most Eurasian

Fig.13: Y-chromosome SNP phylogeny showing the general relationships of the SNP markers used to define Y-chromosome haplotypes in Native American and Siberian populations [after Underhill et al. (2000)].



from African Y haplotypes (haplogroups VI-X¹⁴⁴). Among Siberian populations, Y haplotypes with this SNP marker only appear in the Buryats (fig.14). By contrast, the M17 lineage, which is defined by a 1-bp deletion at that locus, seems to be one of the more recent lineages in Siberia. It is present at low frequencies in a small, but not insignificant, number of Siberian populations, and occurs at the highest frequency among the Itel'men, whereas it is absent from the neighboring Koryaks.⁶⁷⁻⁷⁰

Founding Y-Chromosome Lineages in Native Americans: Two paternal lineages encompass most Native American Y-chromosomes, haplogroups M3 and M45 (fig.15). The M3 lineage appears at significant frequencies in most Native American populations, and is distributed in an increasing north-to-south cline within the New World.^{7,8,56,57,66-70,104,143} However, it has yet to be found in any African or European populations.^{57,104,142-144} The STR data from M3 Y-chromosomes also reveal significant differences in haplotype distributions between North/Central and South American Indian populations, suggesting different population histories in the two major continental regions.^{8,57,67-70,101,104}

Other studies of Y-chromosome variation in Siberian and Native American populations have shown similar patterns of haplotypic variation. Several researchers have defined Y hap-

lotypes by analyzing variation in the aliphoid heteroduplex (α) type II gene along with additional SNP and STR markers.^{7,8,94,104,105} These studies revealed the presence of a major founding Y haplotype, A0, in Native American populations defined by the combination of the α II/DYS19/M3 markers. The A0 haplotype is almost certainly synonymous with the M3 lineage, and appears to have originated somewhere in central-east Siberia. Like the M3 lineage, this A0 haplotype occurs at its highest frequencies in South American populations, and at its lowest in North American ones.

In contrast, the M3 lineage is essentially absent from any Siberian and Asian populations

except the Siberian Eskimos and the Chukchi,^{66,69,70,56,57,143} along with a single Even individual.^{56,57} The absence of the M3 lineage in nearly every Siberian and central Asian population, and its presence in all major linguistic subdivisions of Native Americans, implies that it evolved in the ancestral Native American population(s), either in Beringia or in the Americas, after leaving this part of northern Asia. The M3 lineage also appears to have been maintained in the ancestral Beringian population(s) that was ancestral to modern day Eskimo-Aleuts and Chukchi, who show genetic affinities with other circumpolar populations.^{27,113,117,124,138} However, it is possible that the Chukchi acquired this lineage through back-migration and gene flow from Alaskan Eskimos across the Bering Strait.^{56,57}

The second most frequent Y-chromosome lineage observed in the Americas is haplogroup M45 (fig.15). Haplogroup M45 is widely distributed among Native American populations, with about 29% of their Y-chromosomes belonging to this paternal lineage. Other researchers using different sets of SNPs and STRs to characterize their Y-chromosomes have also noted the presence of a second major paternal lineage in the Americas, which, in all likelihood, is synonymous with the M45 lineage.^{101,104}

Phylogenetic analysis of the M45 lineage further revealed two distinct sets of haplotypes in Native American populations. The first of these

is broadly distributed in indigenous populations from North, Central, and South America, and appears to have arisen in south-central Siberia. Based on the associated STR alleles, this sublineage of M45 (M45a) is most closely related to the M3 lineage. By contrast, the second set of M45 haplotypes exhibit an additional SNP called M173, and emerged in East Asia/Siberia (Amur River region). Interestingly, this sublineage (M45b) is observed only in North and Central American populations, and, thus, appears to have been brought to the Americas in a secondary expansion of ancestral populations.^{67,68,70}

The remaining 5% of Y-chromosome haplotypes in Native Americans belong to one of several different haplogroups seen in Asian/Siberian populations. M46 haplotypes are completely absent in Native American populations,^{57,69,70,104,153} whereas the M130 lineage has only been seen in the Na-Dené speaking Tanana and Navajo and the Amerindian Cheyenne^{4,5,57,67-70} (fig. 15). In addition, the M17 lineage is completely absent from Native American populations, with the exception of the Guaymi, a Chibcha-speaking tribe from Costa Rica.⁶⁷⁻⁷⁰ Because the STR patterns for these Native American Y haplotypes are consistent with those present in eastern Siberian groups, they appear to have been brought to the Americas through a secondary expansion of ancient Asian peoples, rather than with the initial immigrants to the New World (i.e. these haplotypes had less time to diversify indicating that the geographic separation was relatively more recent).⁶⁷⁻⁷⁰

In the New World, the M1 lineage has been observed in several Native American populations. These include the Mixe from southern Mexico,^{57,66} the Seminoles of Florida,⁵⁰ and several Central and South American populations⁵⁷ (fig. 15). However, the two Mixe with the M1 haplotypes also exhibited DYS1 alleles previously observed in other non-Native American populations,⁶⁶ and the Central and South American Indian groups exhibited additional SNPs that typically occur in African M1 haplotypes.^{67,69,70} Therefore, these Native American populations probably acquired their M1 haplotypes through intermarriage with persons having African ancestry.

A few Y haplotypes found in Native American populations do not belong to any of these paternal lineages, and hence, were placed into the “null haplotype” category.^{67,68} These are likely to have been acquired through non-native admixture because of the higher frequencies of

null haplotypes in African populations^{36, 38,142} However, additional screenings for newly discovered SNPs¹⁴⁴ will further define their origins and affinities, hence, the region or source of these haplotypes.

Age of Y-Chromosome Haplogroups in Siberia and the Americas: The method of dating the ages of Y-chromosome haplogroups relies on the diversity of STR loci that occur on each SNP haplotype. This has to be the case because SNPs are rare occurring events. For this reason, it is difficult to estimate when SNPs evolved in a particular paternal lineage using only this data set. On the other hand, the faster evolving STR loci that co-occur on each SNP haplotype can be used for this purpose. In this case, the extent of allelic diversity of a set of STR loci is measured and then averaged over all loci, with this average then being multiplied by a known STR mutation rate to determine the actual age of the SNP haplogroup.

Y-chromosome STR mutation rates have been estimated in various ways. Recent studies have made estimates across multiple generations of males (meiotic transmissions) in human families to obtain mutation rates per generation. Although these rates vary somewhat depending on the type of STR used for the estimate (di-, tri-, tetranucleotide repeats),^{21,58} most of these studies have found that the average mutation rate of Y STRs is around 2.80×10^{-3} .^{8,44,58,58a,131} However, some researchers caution that the mutation rate of a given STR can vary considerably depending on the size (number of repeats of the variable block) of the founder allele at each STR locus.¹⁷

By contrast, Underhill et al. (2000) used an average mutation rate estimated from SNP variation in three Y genes,¹³¹ rather than from STR loci, to date the various branches, or haplogroups, of this phylogeny. Their estimate of 1.24×10^{-9} produced an average SNP evolution rate of one per every 6,900 years. Using this rate, it is possible to date the origins of the major branches of their phylogeny, which is based on 167 different SNPs, as well as other points of SNP diversification, since SNPs represent unique mutational events that have occurred once over evolutionary time.

All studies in which Y SNP variation has been characterized in Native Americans have attempted to date the age of the M3 lineage, since it appears to signal the entry of ancestral populations into the New World. The first of these studies estimated the age of M3 haplotypes at 30,000 cal BP, based on the linkage of the M3 SNP and

DYS19 alleles, and an autosomal STR mutation rate of 1.5×10^{-4} .¹⁴³ However, an alternative faster mutation rate of 2.1×10^{-3} for the DYS19 locus gave an age for the M3 lineage of 2,147 cal BP. Although the latter age was clearly an underestimate of initial New World colonization, it raised the possibility that the M3 marker arose in a Beringian or American population after, rather than before, the initial entry of human populations into the New World.

Using different methods, Hammer et al. (1998) and Karafet et al. (1999) also estimated a shallow time depth for the M3 lineage, between 10,000-7,600 cal BP. By contrast, Forster et al. (2000) estimated a 20,000 cal BP age for the M3 mutation based on a mutation rate of 2.6×10^{-4} mutations/20 years for slowly evolving Y STRs, and Bianchi et al. (1998) estimated the age of the ancestral Native American α II/DYS19/M3 lineage of 22,270 cal BP. On the other hand, using the SNP evolution rate of Underhill et al. (2000) (hereafter called the “SNP mutation rate”), one obtains an age for M3 haplotypes of ~13,800 cal BP. Thus, while most analyses of Y-chromosome variation in Native American populations suggest an “early” rather than a “late” entry of ancestral populations into the New World, the data are not unequivocal on this issue.

The M45 lineage is considerably older than the M3 lineage, which derives from it. Using the SNP mutation rate, M45 haplotypes appear to be at least 30,000 years old. This degree of antiquity is also reflected by their widespread distribution in Siberia and Eurasia.^{67-70,144} In addition, the M45 lineage has been around Siberia long enough to become diversified within this region. This degree of differentiation is evident by the presence of two different sets of M45 haplotypes in Native Americans, the first being a central Siberian set shared with all Native American populations, and the second an eastern Siberian set shared only with Native Americans from North and Central America.^{67,68} The older central Siberian M45 haplotypes showed a greater diversity of STR alleles than the younger eastern Siberian haplotypes, which is a pattern not observed in the M3 haplotypes from either North/Central or South America.^{67,68} Based on these data, the ~30,000 cal BP age of the M45 lineage may overestimate the antiquity of these haplotypes in the New World, since two branches of the same lineage were brought to this region at different times. For this reason, it will be necessary to estimate the ages of the M45a and M45b sublineages to more accurately date

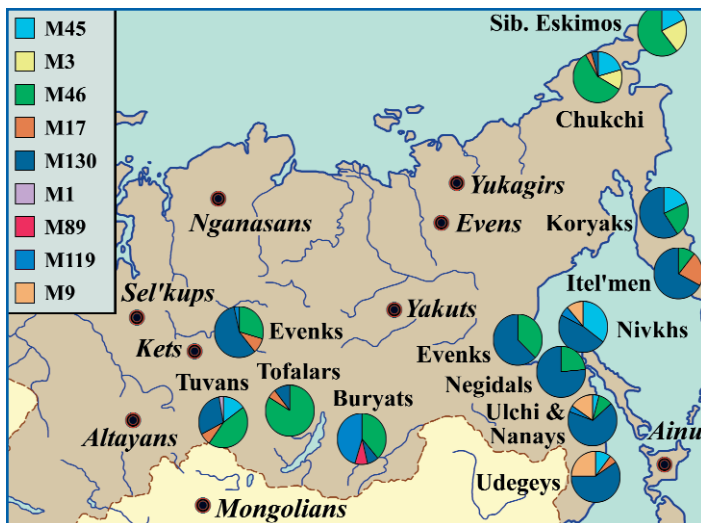


Fig.14: Y-chromosome haplogroup frequencies in indigenous Siberian populations.

the presence of these haplotypes in the Americas.

Many of the other Y lineages present in Siberia and the Americas have also been dated. Two of the older lineages in Siberia, M1 and M9, have been dated at >50,000 cal BP.^{57,144} The M1 lineage is clearly ancient because of its frequency and diversity in African populations,³⁶ but probably reached Central Asia somewhat later, given its more limited distribution and diversity of its haplotypes in Central and East Asia.^{34,38,66,69,70} On the other hand, the antiquity of the M9 lineage is consistent with the presence of its mutation in a sizeable majority of Siberian Y-chromosomes.^{57,67,68,70,104,144} The oldest SNP in the Y phylogeny, M89, has been dated to ~62,000 cal BP,¹⁴⁴ and, therefore, predates the occurrence of the M9 lineage, since it appears in all haplotypes bearing the M9 mutation (fig. 13).

The M130 lineage appears to be somewhat younger than the M89 or M9 lineages, having been dated at ~30,000-25,000 cal BP.^{57,144} This date is generally consistent with its broad distribution in East Asia, in which it appears to have originated, and its haplotypic diversity in eastern Siberian and Asian populations.^{67,68,70,127,128} However, its age may increase once more STR data from Asian M130 haplotypes are analyzed.

On the other hand, the widely distributed M46 lineage is much younger than the other Y haplogroups. It appears to have expanded in Siberia between 4,000-2,400 cal BP¹⁵³ and 8,400-7,000 cal BP.⁵⁷ Using the SNP mutation rate, the age of M46 haplotypes (6,900 cal BP) falls into the middle of this range. This shallow time depth is consistent with the limited diversity of M46 haplotypes in Siberian populations.⁶⁷⁻⁷⁰ It also suggests that the M46 lineage arose in

Siberia after the initial settlement of the New World, perhaps with the expansion of reindeer herding culture in northern Asia and Eurasia.¹⁵³

The estimated age of the M17 lineage is rather intriguing. Using the SNP mutation rate, one obtains a 13,800 cal BP age for this lineage, a date that falls towards the end of the LGM (last glacial maximum). These haplotypes constitute a distinct

branch with the human Y phylogeny, and are not especially common in Siberian populations, although occurring across a broad geographic area. Such data suggest that M17 haplotypes did not emerge in Siberia until after the Americas had been settled, and probably entered the New World through a secondary expansion of ancient Asian populations.

It is also interesting that one of the major lineages present in northern Chinese and East Asian populations, M122, has been dated at ~60,000 cal BP.^{127,128} As noted above, haplotypes bearing this marker have not yet been seen in Siberian populations. Thus, despite its antiquity in East Asia, this haplogroup does not appear to have been brought to Siberia, even in recent times. At the same time, while not yet clearly dated, the M119 lineage must be old enough to have been disseminated into some Siberian populations through the northward migration of this haplogroup from East Asia.

Number of Migrations Based on Y-Chromosome Variation: From a Y-chromosome perspective, there are clear linkages between Siberia and the Americas, as well as population dynamics within Siberia itself that have led to the distribution of various paternal lineages within it. These linkages can be summarized as follows. First, among the variety of SNP lineages that have been identified in Siberia and the Americas, only two of these (M3 and M45) fundamentally contributed to the initial peopling of the New World, either through single^{8,104,143} or multiple^{57, 67-70} migration events (fig.16). Three of the other major Y lineages present in Siberia either arose after the colonization of the New World, since they are distributed almost exclusively in Siberia (M17, M46), or else originated outside of the geo-

graphic region from which ancestral Native American populations bearing the M3 and M45 lineages evolved (M130).

A later, secondary expansion(s) of human groups from Beringia into the Americas brought with it a different set of M45 haplotypes as well as the M17 and M130 lineages, with these possibly being contributed from populations originating in the Amur River region. While the additional M45b haplotypes could have been introduced into Native American populations through post-Columbian gene flow with non-native populations, the STR data suggest otherwise. On the other hand, the high frequency, specific distribution, and relative homogeneity of these M45b haplotypes makes it probable that

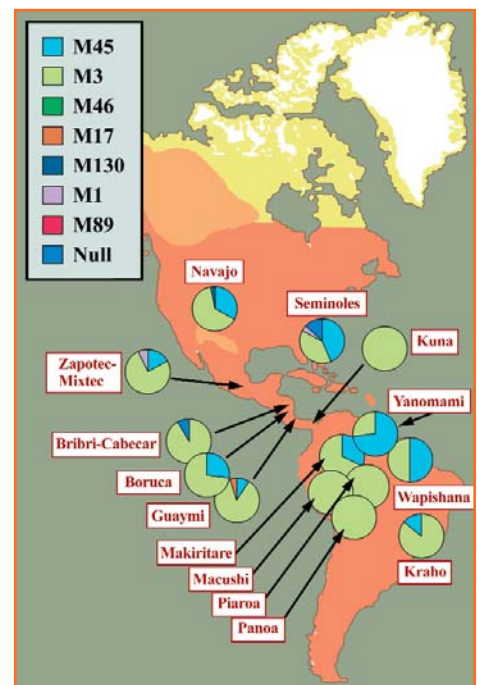


Fig.15: Y-chromosome haplogroup frequencies in Native American populations.

they had a Siberian origin that was temporally and geographically distinct from the migration bringing the more diverse M45a haplotypes that are shared between all Native American and central Siberian populations. Therefore, these M45b haplotypes appear to represent a second migration into the Americas that occurred after the M3/M45a migration.

This secondary expansion probably also contributed the M17 and M130 lineages to Amerindian populations, with both the lineages probably being contributed from the Amur River region.^{57,67,68,70,128} By contrast, M46 haplotypes appear to not have been introduced into the New World at all. Instead, they were widely dispersed throughout Siberia and Eurasia during Neolithic

times. Finally, the M1 haplotypes present in Native American populations were acquired through non-native admixture, rather than being contributed by founding Asian populations.

Summary of Molecular Genetic Data:

Given all of these molecular genetic data, what general patterns of biological affinities and origins for Native Americans can be ascertained? To begin with, all of these studies support a primary Asian origin of Native American populations. Most of them have indicated the potential source area(s) for ancestral Native American populations as lying in a region extending from central Siberia to the Altai Mountains in the west to southeastern Siberia and northern China in the east. However, the mtDNA data also suggests a possible Eurasian genetic influence with presence of haplogroup X in North America, and Y-chromosome data suggest both south-central and eastern Siberia as source areas for the paternal lineages brought to the New World.

While there is a growing consensus about the general source area for ancestral Amerindian populations, there is less agreement among these studies about the number of migratory events bringing these populations to the New World. The number of migrations proposed to have given rise to Amerindians ranges from one^{8,63,79,80,82,125} to two or more.^{14,49,57,67-70,104,140} Regardless of the number of migrations that reached the New World, the molecular data are consistent in showing the distinctiveness and greater haplotypic diversity of Amerindians relative to Eskimo-Aleut and Na-Denè Indian groups, hence, the earlier immigration of ancestral Amerindians to the New World. The Na-Denè Indians and Eskimo-Aleuts represent two later

population expansions into North America that possibly arose from the remnants of ancestral Beringian population(s) that were ancestral to Amerindians.

Perhaps the most controversial aspect of recent molecular studies is the early colonization dates for the Americas that they have suggested. Although no one argues that the colonization of the New World represents the terminal Pleistocene expansion of modern humans, there has been considerable debate about when this expansion occurred. What has concerned researchers, particularly archaeologists, is the apparent incongruity between the late (15,000-12,000 cal BP) archaeological visibility of the early colonizers of the Americas and the greater antiquity (35,000-20,000 cal BP) of the genetic lineages brought to the Americas by these founding populations. This is an important concern because geological and climatological data indicate that glacial barriers prevented human movements into the Americas between 20,000-14,000 cal BP (see Dixon, Fedje pp.23-30). On the other hand, the dates for the earliest archaeological sites in the Americas (e.g. Monte Verde, Meadowcroft, Cactus Hill, etc.) and the range of expansion times for these genetic lineages are slowly drawing closer together. Ongoing analyses of the mutation rates of mtDNA and Y-chromosome loci may ultimately narrow this time range for these genetic lineages, or perhaps push the initial entry time closer to the earliest archaeological dates in the Americas. Irrespective of the initial entry time for ancestral Amerindians, the molecular data sets are consistent in dating the emergence of the Eskimo-Aleuts and Na-Denè Indians at between 8,000-5,000 cal BP, well after ancestral Paleoindians arrived in the New World.

Moreover, the mtDNA and Y-chromosome data have shown that settlement of the Americas after their initial colonization was not a static process. Although most studies show genetic differences between North/Central and South America, there is also evidence for both population contact and gene flow between these regions. Underlying these broader patterns is considerable evidence for regional and tribal differentiation of populations in the major continental regions of the New World, particularly South America, with these patterns

being shaped by geographic isolation, linguistic differentiation, and genetic drift.

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Author's biographical note:

Theodore Schurr has spent the last twelve years investigating the genetic prehistory of Asia and the Americas through laboratory studies of mtDNA and Y-chromosome variation in Asian, Siberian and Native American populations. As part of these research efforts, he has also conducted joint field projects with Russian anthropologists among indigenous peoples of north-eastern Siberia.

Among his current projects are studies of genetic diversity in modern Aleuts, indigenous peoples of south-central Siberia and the Russian Far East, and archaeological populations from the Lake Baikal region. Aside from these projects, Schurr serves as an Associate Editor for *Current Research in the Pleistocene*, a Scientific Consultant for the "Kennewick Man" case, Bonnicksen et al. v. USA and the Department of the Army, and a Scientific Consultant for Family Tree DNA. As a Post-Doctoral Scientist at the Southwest Foundation for Biomedical Research, he was involved in the mapping and identification of genes that contribute to cardiovascular disease risk in Native American groups. Dr. Schurr is currently an Assistant Professor in the Department of Anthropology, and a Consulting Curator in the Physical Anthropology Section of the Museum of Anthropology and Archeology, at the University of Pennsylvania.

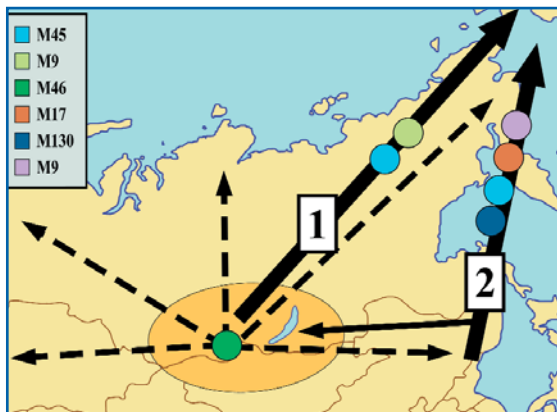


Fig.16: A map of possible New World migrations involving Y-chromosome haplogroups. The initial migration (1) appears to have involved primarily haplogroups M3 and M45, whereas the second and later migration (2) may have involved haplogroups M17, M89, and M130, as well as an additional set of M45 haplotypes.

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Suggested Readings:

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