Letter to the Editor

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The Peopling of the Americas: A Second Major Migration?

To the Editor:

Recently, Lell et al. (2002) analyzed the distribution of Y-chromosome haplogroups in a set of Siberian and Native American individuals. They inferred that there is evidence of two major migrations that originated from Siberia and peopled the Western Hemisphere. The first one coincides with our previous finding (Santos et al. 1999) and that of Karafet et al. (1999). In addition, Lell et al. (2002) suggest that a later major migration, which likely originated in eastern Siberia, would have carried the haplogroups S4Y (as previously suggested by Karafet at al. [1999]) and M45b. We argue that the claim of a second major migration is not well grounded and is altogether not necessary to explain the distribution of the haplogroups S4Y and M45b in Native American populations.

On the basis of detailed molecular information associated with the most common Native American M3 haplogroup and its immediately ancestral M45a haplogroup, Santos et al. (1999), Karafet et al. (1999), and Lell et al. (2002) have consistently identified central Siberia as the most likely region of origin of the present-day Native American Y chromosomes. We suppose that, when this "first" major migration occurred, the central Siberian population was polymorphic, like most if not all human populations. Natural populations usually contain few common alleles and several rare ones, but only a subset of the total rare alleles will be represented in a sample of, for example, 10–50 individuals (Ewens 1972; Helgason et al. 2000). When a population movement occurs, migrants reflect (more or less) the distribution of the source population. Therefore, we expect that most migrants carry common alleles but also that some of them carry rare ones. The first settlement of the Americas has been associated with a probable bottleneck event (Wallace et al. 1985; Pena et al. 1995; Bonatto and Salzano 1997*b;* Santos et al. 1999). It could have produced drastic changes in allele frequencies and reduced the number of rare alleles; however, even if this were the case, it does not mean that the genetic variability completely disappeared. The ancient haplogroup S4Y has a wide and heterogeneous distribution in eastern Asia. In central Siberia, the putative region of the "first" migration, its frequencies are 2/12 in Kets, 2/122 in Selkups (Karafet et al. 1999), 13/40 in Tuvan, 2/19 in Tofalars, and 18/31 in Yenisey Evenks (Lell et al. 2002). Among the 31 Native American populations in which the presence of the haplogroup S4Y has been tested, only four samples exhibit this allele—always at low frequencies (1%, 16%, and 7%)—and only one sample of 12 Tanana individuals from North America presents five S4Y chromosomes (95% CI 12%–62%). Therefore, it is clear that the S4Y haplogroup is a rare allele in Native American populations. Since we have no reason to believe that the individuals carrying the haplogroup S4Y were prohibited from migrating at the time of the first settlement of the continent, we do not think that it is necessary to claim an *ex novo* major migration to explain the presence of this haplogroup at low frequencies in Native American populations. Instead, the most parsimonious explanation for its presence in the American indigenous population seems to be that it entered as a rare allele during the first settlement of the continent.

Indigenous samples from Central and North America have low frequencies of the haplogroups S4Y and M45b. On the other hand, eastern Siberian samples coincidentally show the higher frequencies of the haplogroups S4Y and M45b (even if the latter is altogether a rare allele). Lell et al. (2002) present this observation as evidence that a second major migration originated in eastern Siberia. Actually, these populations exhibit frequencies of the S4Y haplogroup that are 40%–100%. Under the two-major-migrations model, the Native American population would be an admixed population with two parental ones: (1) the central Middle Siberian and (2) the Lower Amur/Okhotsk populations. We used the classical Bernstein formula (Cavalli-Sforza and Bodmer 1971) to calculate the contribution of each putative parental population to the current gene pool of Native American populations. The S4Y haplogroup could be useful for this purpose because it has the highest difference in allele frequencies among the parental population ($\delta = 0.45$) and is not affected by recent European or African migration. Using the data presented by Karafet et al. (1999) and Lell et al. (2002), we considered as parental populations the central southern Siberia region (Yenisey Ev-

enk, Tuvan, Tofalar, Buryat, Ket, and Selkup samples were clumped) and the Lower Amur/Okhotsk region (Okhotsk, Ulchi, Negidal Upp, Negidal Low, Udigey, Nivkh, Buriat, Siberian Evenk, Even, Manchurian Evenk, Oroquen, and Yakut samples were clumped). The calculated contribution of the Lower Amur/Okhotsk population to the current gene pool of the Native American population would be −26% (a negative value, because the frequency in the Native American population is lower than that in central southern Siberia). Although this is a rough measure of admixture, subject to a high stochastic variance, it illustrates that the proposal of a second major migration, even intuitively, is hardly compatible with current data. The obtained value is clearly more compatible with a null contribution of the Lower Amur/Okhotsk population. Again, we do not need to claim a second major migration to explain the variability of Native American Y chromosomes. When its wide distribution is considered, the haplogroup S4Y seems to be very ancient (Karafet et al. 1999; Underhill et al. 2000), and its presence in central southern Siberia at the time of first migration to the Americas is also compatible with current data. Furthermore, although Lell et al. (2002, p. 204) state that their data "demonstrate that the Native American RPS4Y-T haplogroup originated in the eastern Siberian populations," we were not able to find that demonstration in the article. Because the authors do not disclose to the public the complete information about the frequencies and distribution of S4Y-microsatellite haplotypes, we are not able to discuss this point. However, we anticipate that the above pending demonstration must include an adequate assessment of its statistical significance.

Lell et al. (2002) suggest that the distribution of 22 Y chromosomes belonging to the rare haplogroup M45b also supports the existence of the second major migration from eastern Siberia. According to Lell et al. (2002), the 17 M45b chromosomes observed in the Americas would have an eastern Siberian origin. We have an alternative explanation for the origin of a consistent portion of the 17 M45b chromosomes found in the Americas, which is—we think—simpler and perhaps obvious: Since the M45b haplogroup is largely the most frequent in virtually all western European populations (Semino et al. 2000), these chromosomes could have been introduced into Native American populations by Europeans during the last five centuries. In fact, evidence of European admixture in Native American populations, especially in North and Central America, is straightforward and comes from population-genetics, demographic, and historical studies (see Crawford [1998], Salzano and Callegari-Jacques [1988], and the second principal component of Amerindian genetic variability shown by Cavalli-Sforza et al. [1994]). Furthermore, several genetic studies have shown that European admixture in the Americas has been preferentially mediated by males (Merriwether et al. 1997; Carvajal-Carmona et al. 2000; Carvalho-Silva et al. 2001). Therefore, in populations in which evidence of admixture exists, like the Seminole or the Boruca (14%; Sans 2000), we should expect to find some level of European Y-chromosome contribution, as is clearly evidenced by previous studies (Pena et al. 1995; Santos et al. 1995, 1996*b;* Bianchi et al. 1997; Karafet et al. 1999; Ruiz-Linares et al. 1999). For instance, our group has previously demonstrated that the most common European Y-chromosome haplotype (defined by the alleles αh-II and DYS19-B), which we refer to as "II-B" (Santos et al. 1996*a*) and which is equivalent to M45b (data not shown), is present at higher frequencies in Native American populations such as the Muskokes of North America, who have a long documented history of contact and admixture with Europeans (Santos et al. 1996*b*). Curiously, even though Wallace's group has previously reported in the Seminole sample the presence of 11% of Y chromosomes with likely European origin (Huoponen et al. 1997), in the Lell et al. (2002) article they ignore this possibility but consider the eventuality of male African admixture, which is generally less likely than European admixture. Furthermore, in accordance with their probable recent European origin, the microsatellite haplotypes found by Lell et al. (2002) in the M45b chromosomes match very well with those present in the phylogenetically equivalent haplogroup 1 chromosomes of Basques, Catalans, Norwegians, French, and Italians (Hurles et al. 1999; Ruiz-Linares et al. 1999; Carvajal-Carmona et al. 2000; Rosser et al. 2001). Therefore, if we consider that a consistent portion of the 16 M45b chromosomes found in North and Central America very likely arrived during the last five centuries and that only 6 M45b chromosomes were found in eastern Siberia, very few chromosomes are left for making any robust inference about the genetic structure of populations or "major migrations." In any case, in Siberian populations, the association claimed by Lell et al. (2002) between central and eastern Siberia and the distribution of M45a and M45b haplogroups is far from reaching any acceptable significance level (Fisher exact test: $P = .25$), which means that any derived conclusion, such as the eastern Siberian origin of the Native American M45b chromosomes, is at least temerarious. Perhaps the only valid observation we can make is that the M45b haplogroup is a rare one either in native populations of northeastern Asia or in the Americas.

We think that Lell et al. (2002) have not provided any solid evidence about the existence of a second "major migration," and we think that the simplest way to reconcile the currently available molecular genetic data, which are mainly derived from Y chromosomes and mtDNA (Bonatto and Salzano 1997*a,* 1997*b*), is to as-

sume a single major migration from Siberia contributing to the gene pool of Native American populations.

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