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Reply to Bianchi and Bailliet

To the Editor:

In their original study in 1994, Bianchi and Bailliet (Bailliet et al. 1994) suggested that np 16519, analyzed by *Hae*III digestion, is a phylogenetically useful site for tracing ancient migration patterns, and they used the presence/absence of this site to classify Native American mtDNA variants. In the letter above, they maintain their stance, although studies on Native Americans (Torroni et al. 1993*a,* 1993*b*), Africans (Chen et al. 1995), and Europeans (Torroni et al. 1996) have demonstrated that np 16519 is hypervariable. Bianchi and Bailliet now argue that, since all sites are subject to recurrent mutations, np 16519 is as informative as any. This argument avoids the fact that np 16519 mutates faster, on average, than other sites, such as np 16111 and 16271, which we used for phylogenetic analysis. To obtain an impression of how much faster np 16519 mutates, we counted the number of recurrent transitions of np 16519, np 16111, and np 16271 in most parsimonious trees of African mtDNA variants: the most parsimonious trees for the Chen et al. (1995) restriction-site data (140 Mandenka, Wolof, Pular, other Senegalese, Mbuti, and Biaka) require 8–10 mutations for np 16519, whereas no other site is estimated to have undergone >3 mutations. If one retained in this tree only the 99 individuals sampled from the Mandenka, Mbuti, and Biaka, then still 7 or 8 mutations at np 16519 are observed. Control-region sequences for these 99 individuals are available in the data sets of Graven et al. (1995) (Mandenka) and Vigilant (1990) (Mbuti and Biaka). Neither these 99 nor the complete set of 156 published control-region sequences from the three populations show any transitions at np 16111 or np 16271.

Bianchi and Bailliet claim that their groups A1/A2 and D1/D2 based on np 16519 are congruent with ours. This may appear to apply to published Eskimo data, which lack the *Hae*III np 16517 site (Merriwether et al. 1996) and are predominantly A2 (Forster et al. 1996); however, the *Hae*III site is also absent in the Kuna (Torroni et al. 1993*a*), who instead belong to A1 (identifiable by a 6-bp deletion at np 106; see Batista et al. 1995). Nor does group D1 (i.e., group II) in the data of Horai et al. (1993) correlate with np 16519. It thus appears that the correlation illustrated by Bianchi and Bailliet in their table 1 does not conform with previously published data sets.

Next, we would like to elaborate their narrative of group X nomenclature. Bailliet et al. (1994) were the first to notice that published sequence data indicated the presence of five founding Amerind mtDNA types, rather than four as had previously been believed (and is still occasionally reported, e.g., see Easton et al. 1996, p. 214), and the existence of this additional sequence type (which they termed "V") was confirmed by Bandelt et al. (1995), Forster et al. (1996), and Scozzari et al. (1997). Forster et al. (1996) renamed it "X," since the same mtDNA motif is found in the European group X (Torroni et al. 1996); however, Bailliet et al. (1994) also reanalyzed RFLP types, and they made the unfortunate aphylogenetic decision to group all RFLP types that lack the diagnostic A, B, C, or D RFLP sites into a new group "E." Merriwether et al. (1996) and Easton et al. (1996) followed this decision but renamed "E" as "X" and split it into further subgroups, such as "X6" and "X7"; however, one should bear in mind that a diagnostic RFLP marker can occasionally be lost because of reversion, which can often be detected by phylogenetic analysis; for example, see the discussion by Torroni and Wallace (1995) versus that by Bianchi and Rothhammer (1995). For instance, among the Yanomami there is a group D subset that is characterized by three control-region mutations, one of which is a transversion (e.g., see Yanomama 44 in the work of Torroni et al. 1993*a*). One such Yanomama (Yan 31) in the data of Easton et al. (1996) has suffered a reversion of its D-specific restriction marker, and, according to their definition, now belongs to group "X6." Therefore, it appears that groups "X6" and "X7" of Easton et al. (1996) both represent mixed bags of reverted C and D types and do not correspond to group X of Forster et al. (1996).

We also disagree that the mtDNA chronologies of human evolution need major revisions because of the 200-fold- and 9-fold-faster mutation rates proposed for coding and control regions, respectively, by Howell et al. (1996). The 200-fold-higher rate is partly due to the inclusion, among the four pedigrees used to calculate the mutation rate, of two pedigrees (QLD1 and NWC1) that were already known by 1991 (Howell et al. 1991*a,* 1991*b*) to harbor recent mtDNA mutations. The 9-fold-higher mutation rate for the control region is mainly an artifact of extrapolation of the mutation rate of the entire control region from two hypervariable nucleotide positions in the second control-region segment (Ma-

caulay et al. 1997 [in press]). A more extensive pedigree study by Bendall et al. (1996) confirms the orthodox mtDNA mutation rate.

We do agree with the comment by Bianchi and Bailliet that more research is needed in order to understand the mutational mechanisms acting on mtDNA and, specifically, on np 16519; for example, it is intriguing that np 16519 is virtually "frozen" in some haplogroups, such as group B in Amerinds and group T in Caucasoids, and in both the Caucasoid and the Amerind branches of group X.

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Paleolithic and Neolithic Lineages in the European Mitochondrial Gene Pool

To the Editor:

In a recent analysis of lineage groups derived from European and Middle Eastern samples of mtDNA D-loop sequences, Richards et al. (1996) have stated that most extant European mtDNA lineages predate the Neolithic