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Reply to Ho and Endicott

To the editor: Ho and Endicott (H&E) propose an alternative interpretation for our findings,¹ stating that Native American mtDNA demography is better associated to a more recent Clovis population expansion than to a pre-Clovis expansion. They base their scenario exclusively on results obtained with the use of substitution rates derived from internal calibrations for mtDNA evolution.²

We agree with H&E that improvements in mtDNA-evolutionary-rate estimation are needed to better clarify details of human prehistory, including the peopling of the New World. We also agree that perhaps a better method to achieve this could be the use of intraspecific calibration. However, there are a number of issues regarding the specific internal calibrations that they proposed for human mtDNA evolution that render their rate estimate questionable.

H&E's internal calibration is based on haplogroup diversification associated to two biogeographical events. Their oldest calibration, associated to the peopling of Sahul, uses a single haplogroup (P), even though there is at least one more haplogroup (Q) that could be associated to this event. Previously, when Haplogroup Q was used for a similar internal calibration, the mtDNA rate estimated was much slower than that of H&E, and expansion dates were closer to those of our study.³ However, H&E prefer to disregard Haplogroup Q rather than use information from both haplogroups, with the sole justification that it would result in a slower substitution rate and consequently older population expansion. Their other calibration event is also problematic. They assumed that haplogroups H1 and H3 expanded 18 thousand years (kyr) ago (95% HPD 24–11 kyr ago) in Europe around the end of the LGM (last glacial maximum). If we accept this calibration and our estimate that the Native American (NA) haplogroups expanded ~18 kyr ago, the basic diversity statistics (e.g., rho and TMRCA [time to the most recent common ancestor]) should be similar for both sets of haplogroups because such statistics are independent of any absolute rate. Moreover, if we accept the H&E estimates that the NA haplogroup expansion occurred ~12–10 kyr ago, NA hap-

logroup statistics should be ~40% lower than H1 and H3. Actually, NA haplogroup values for most of these statistics are ~70% higher than H1 and H3, thus almost three times higher than expected under H&E calibration assumptions and results. The results can be explained by accepting our estimates of ~18 kyr ago for the expansion of the NA haplogroups and ~11 kyr ago for the expansion of H1 and H3, as originally estimated⁴ with a phylogenetic mutation rate.

Another illustration of the notion that H&E's rates seem to be exaggeratedly fast can be found by the application of the substitution rate that they proposed for the noncoding region (Table 3, D-loop, in ²) to this same region of our NA mtDNA sequences (Figure 1). This results in an average coalescence time for the NA haplogroups of ~11 kyr ago and a population expansion of ~9–7 kyr ago. These dates are clearly irreconcilable with even the most radical supporters of a later entry for the peopling of the Americas (see below). Interestingly, another substitution rate based on pedigree studies⁵ indicates an expansion around 15 kyr ago, much closer to our original estimate.

The assumption that diversification of a sample (usually a single haplogroup) does not predate the biogeographical event it represents may also be an important source of error. In a previous study on mtDNA calibration,⁶ Ho et al. used the peopling of the Americas by humans as a calibration point, assuming that this event is represented by the coalescence of all sequences from all haplogroups found in a single North American tribe. This is completely mistaken, given that this coalescence can be traced back to the coalescence of macrohaplogroups M and N in Asia > 50 kyr ago.² This example illustrates very well how an uncritical use of knowledge about human evolutionary history can undermine internal calibrations.

Contrary to H&E's claims, their scenario for the peopling of the Americas is harder to reconcile with archaeological data. The coalescence of each Native American haplogroup, estimated by them as occurring ~13.9 kyr ago, must of course predate the expansion event. However, this date is too recent, given that there is now convincing evidence that humans were already in the southern tip of South America at least 14.5 kyr ago.⁷ Similarly,

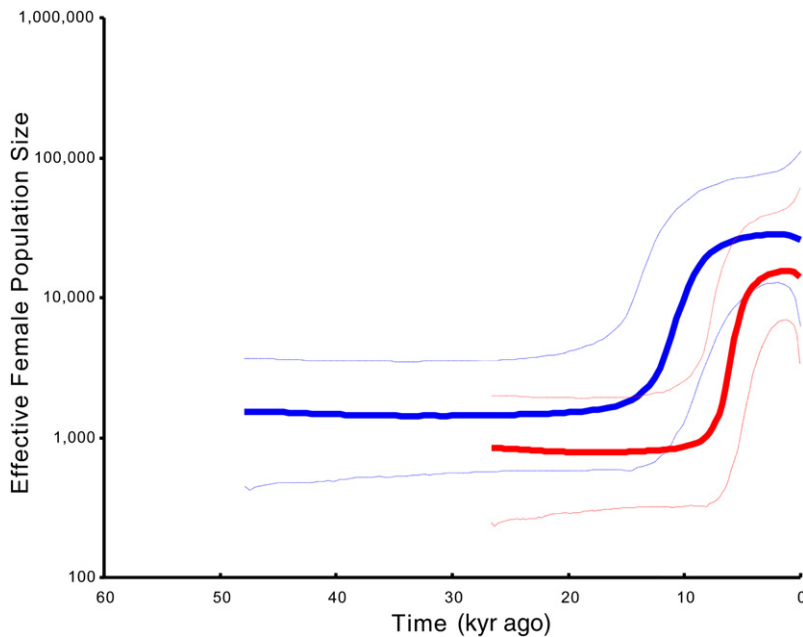


Figure 1. Bayesian Skyline Plot of Native American mtDNA

Bayesian skyline plot of noncoding (control region) mtDNA of 70 Native Americans.¹ Population sizes were estimated with the assumption of a generation time of 25 years. The time scale is given in thousand years ago (kyr ago) measurement, assuming either the evolutionary rate from Endicott and Ho² (3.02×10^{-7} subs/site/year), based on an internal calibration (in red), or that reported in Santos et al.⁵ (1.675×10^{-7}), based on a pedigree study (in blue). Thick lines represent the median estimates; thinner lines, the confidence intervals.

they suggested that the population expansion ~12–10 kyr ago that they detected might represent the expansion of the Clovis culture, purportedly representing the expansion due to the earliest colonization of the continent. Again, this is not compatible with current archeological evidence that puts human occupation of both North and South America well before the Clovis culture. Therefore, because the Clovis culture seems to represent only a later, likely localized expansion, it is, contrary to their suggestion, unlikely that it would leave any significant genetic signal across the whole continent. H&E also claim that our finding of the strong expansion occurring ~18–15 kyr ago is unlikely because it would have occurred during a period of unfavorable climate. On the contrary, the expansion occurred in the period when the climate began to ameliorate abruptly and continuously, between the ends of the LGM and the Pleistocene. Moreover, in our scenario, the population expands *out* of the colder region into the empty regions of subtropical and tropical climate of the continent south of the glaciers. Finally, several factors, which we already discussed in our original paper, could account for the lack of archaeological sites dating from ~18–15 kyr ago, such as the low population density during the initial expansion by the coastal route and the subsequent submersion of large parts of the exposed land.

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Web Resources

The URL for data presented herein are as follows:

BEAST 1.4.7, <http://beast.bio.ed.ac.uk/>

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