The gene flow between ancient and modern humans: how often the hybridization occurred and what are population consequences?

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One of the main factors that strongly affect the estimation of fixation rate in the mitochondrial DNA is the genetic admixing during hybridization. Paternal mtDNA in rare cases can enter the egg during fertilization and significantly alter maternal mtDNA by recombination. Such type of evolutionary events can be easily traced up to the earliest stages of human evolution, because these events are very rare, in contrast to maternal inheritance of mtDNA. In order to find the most probable ways of genetic admixing, we investigated the inheritance of human mtDNA, based on all currently available complete mitochondrial genomes. We extracted 16,810 complete mtDNA sequences of modern humans from the PhyloTree.org [1] and 5 complete mtDNAs of ancient Neanderthal and Denisova humans from GenBank. Then using IMa2 program [2] we reconstructed a picture of the most plausible migrations in ancient human populations. The analysis of migrations indicates intense hybridization (p<0.001) between the modern and ancient people, which is consistent with previously published data about nuclear genes evolution [3]. It is of interest that, the mitochondrial gene flow from ancient to modern humans occurred in three ways: from ancient humans to haplotypes L0 and L5, and to the offsprings of haplotype L2. Reverse flow of modern mtDNA gene alleles to ancient humans also detected: from the offsprings of haplotype L2 and L0. Thus, it was shown that almost all modern human mitochondrial haplotypes possesses gene alleles from ancient people. Thus, *Homo sapiens* evolution is reticulate rather than phyletic, and, therefore, we the need to change the taxonomic status of *Homo neanderthalensis* and *Homo denisova* to *Homo sapiens neanderthalensis* and *Homo sapiens denisova*.

Further, we used the obtained estimations for population genetics parameters to construct and simulate a series of computer models of modern human ancestors' evolution in

Eurasia. Several possible evolutionary scenarios were analyzed. We used the software "Diploid evolutionary constructor" to simulate populations of male-female individuals. Each individual possessed a "genome" as 360 mtDNA sequence inherited maternally. This sequence modeled a variable mtDNA region. Simulations started with two monomorphic populations (the first initiated with the sequence: Homo sapiens isolate Nairobi-020 control region, gb|AY632914.1; the second initiated with the same sequence mutated with 4 SNPs). Initial population size varied from 1000 to 10000 individuals. Population, divergence and migration processes simulated over 10000 generations (assuming 25 years per generation). Birth and death rates varied, depending on scenario in such a way that population growth changed from $1+10^{-4}$ to 1.1. Only single point mutation simulated (frequency 10^{-6} bp per generation). We considered two types of migration between populations: a) frequent migrations occurred every 100 generation for minor groups (up to 1% of a population); b) rare migrations occurred every 1000 generation for major groups (up to 20% of a population). After simulation 10000 generations we analyzed sequences of mtDNA fragments in populations. The preliminary results have shown minor influence of frequent but minor migrations on genotype variability of major populations.

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