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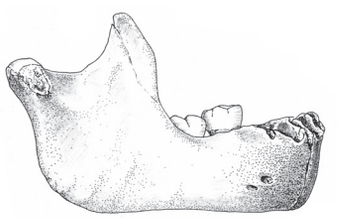

Proceedings of the European Society for the study of Human Evolution 8

Podium Presentation Session 1, Thursday 09:00

Doubling the number of high-coverage Neandertal genomes

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Over the last few years, the recovery and the analyses of genomes of ancient modern humans, Neandertals, and Denisovans have changed our understanding of the origins, the movements, and the relatedness of archaic and modern human populations. However, in many cases endogenous DNA represents such a small fraction of the DNA extracted from specimens that sequencing of the complete ancient genomes is economically infeasible. Thus, to date, only three Neandertal genomes have been sequenced to high coverage [1-3]. Even though Neandertal genome sequences of low coverage [4] can be used to reconstruct various aspects of Neandertal genetic history, many analyses, for example estimation of population size and levels of inbreeding, rely on the reliable diploid genotypes. Recent studies have shown that certain skeletal elements, such as the inner part of the petrous bone and the cementum layer in teeth [5 and references therein], may preserve DNA better over time. There is also evidence that the preservation of endogenous DNA may vary substantially even within a few millimeters distance in a single specimen [2, 4]. Due to the value and scarcity of ancient hominin remains, it is critical that the smallest possible amount of destructive sampling is involved in the recovery of genetic material. A usual sampling strategy typically involves taking around 50 mg of powder from a single location of a given bone or tooth. We investigated here whether taking multiple smaller samples in a step-wise manner of the Neandertal specimens from the Mezmaiskaya Cave in Russia and the Troisième caverne of Goyet in Belgium may improve the yield of ancient human DNA. We removed between 8.5 and 27.2 mg of bone powder from a Mezmaiskaya 1 rib fragment, between 2.5 and 35.1 mg from a Mezmaiskaya 2 skull fragment, and between 5.8 and 53.8 mg from the Goyet Q56-1 femur fragment, amounting to between 15 and 38 powder subsets per specimen and an average input of 16.6 mg of powder per extraction. Importantly, to minimize the impact of contamination, we treated each powder aliquot with 0.5% sodium hypochlorite solution prior to DNA extraction. The DNA extracts from the same specimen varied by several orders of magnitude in their proportion of endogenous DNA (between 0.07% and 54.7%), their content of nuclear genomes (between 0.01 and 78-fold coverage), as well as in the levels of present-day human contamination (0.2-50.3%). There was no significant correlation between the amount of powder used for the extraction and the overall amount of the endogenous DNA or the levels of present-day human DNA contamination. Thus, these results indicate that ancient DNA preservation varies greatly within one specimen and that the removal of multiple, small sub-samples instead of one larger sample, here coupled with a decontamination procedure, can drastically improve the likelihood of isolating large enough amounts of DNA to make whole genome sequencing feasible. This approach allowed us to identify extracts with exceptionally high endogenous DNA content and low levels of present-day human DNA contamination (<2%), enabling us to generate three additional high-coverage Neandertal genomes. The high-quality genome sequences of multiple Neandertals form a unique reference resource for the scientific community and are valuable for analyses that require reliable diploid genotypes and haplotype information. For example, these data open new opportunities to investigate Neandertal population history, to identify genetic variants that arose uniquely on the Neandertal lineage and might have changed through time, and to determine those that may underlie archaic-specific traits or adaptations.

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