

学位論文（要約）

Genetic structure of indigenous Mesoamerican populations
revealed by mitochondrial genome and
analysis of ancient genome by next-generation sequencing

（ミトコンドリアゲノムから明らかになった
メソアメリカ現生人類集団の遺伝構造ならびに
次世代シーケンサによる古人骨ゲノム分析法構築と解析）

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Abstract

Mesoamerica has played an important role in the expansion of Paleoamericans by providing a route to South America. The aims of this study were to examine the peopling of Mesoamerica, to facilitate reconstruction of the ancient dispersal of indigenous people through Mesoamerica from North to South America, and to develop a new approach essential for the explore ancient populations genetic data by next-generation sequencing (NGS).

In Chapter 1, I present the complete mitochondrial genome (mitogenome) sequences of 113 unrelated individuals from two indigenous populations of Mesoamerica, Mazahua and Zapotec. All newly sequenced mitogenomes were classified into haplogroups A2, B2, C1, and D1, but one sequence in Mazahua was classified as D4h3a, a subclade of haplogroup D4. This haplogroup has been mostly found along the Pacific coast of South America. Haplogroup X2a was not found in either of the populations. Genetic similarity determined by phylogenetic tree construction and principal component analysis showed that these two populations are distantly related to each other. Actually, the Mazahua and Zapotec shared no sequences (haplotypes) in common, while each also showed a number of unique subclades. Surprisingly, the Zapotec formed a cluster with indigenous populations living in an area from central Mesoamerica to Central America. By contrast, the Mazahua formed a cluster with indigenous populations living in external areas, including northern Mesoamerica, southwestern North America, and South America. This intriguing genetic relationship suggests the presence of two paleo-Mesoamerican groups, invoking a scenario in which one group had expanded into South America and the other resided in Mesoamerica. The availability of population-based complete mitogenome sequences from other indigenous people should greatly refine the evolutionary scenario concerning the population history of Mesoamerica hypothesized here.

Population-based ancient genome information enables us to reveal the details of the dual structure of Mesoamerican populations. Ancient mitogenomic analysis provides direct evidence of what happened in our past, such as dispersal, migration, and demography, and the relationships among populations, including admixture.

In Chapter 2, I describe a method that makes it feasible to obtain reliable high-throughput sequencing data for the target of interest from ancient material in an efficient and cost-effective manner, thus broadly relishing the benefits of NGS in the field of ancient DNA research. Because of the difficulties of deep sequencing, high-throughput sequencing of ancient DNA has been limited to exceptionally well-preserved ancient materials. The primary factor is the microbial attack often observed in buried material, which causes a marked increase in the relative ratio of microbial DNA in the extracted DNA. I present a unified strategy in which emulsion PCR is coupled with target enrichment followed by NGS. This method made it possible to efficiently obtain non-duplicated reads mapped to target sequences of interest, and this can provide deep, reliable sequencing of ancient DNA from typical materials, even if they are poorly preserved.

In Chapter 3, I describe a composite approach to the deduction of complete mitogenome sequences of ancient humans from low-depth data. I analyzed a mitochondrial genome of a sacrifice at the Moon Pyramid at Teotihuacan by applying this technique. The state of DNA preservation was extremely poor, as expected from a previous study using a conventional PCR method. I covered 89.3% of the entire mitochondrial genome by unique mapped reads; however, it was difficult to get sufficient depth by NGS. I estimated that the sacrifice belongs to haplogroup A2, one of the major haplogroups in indigenous Americans. Furthermore, I attempted a method to supplement the genome sequence by imputation based on a k-nearest neighbor (KNN) algorithm if reads were chipped off. I found that it was valid that imputation using the same haplogroup sequences because the combination of SNPs was similar in each haplogroup of mtDNA. Although this method

has the shortcoming that singletons and high-frequency polymorphic sites cannot be rescued, it can be useful in obtaining entire sequences of ancient mitogenomes for population-based analysis. I obtained a whole mitogenome sequence by rescuing 3930 bases except for one site (np 153) that was polymorphic in haplogroup A2. The availability of population-based ancient genome information enables us to reveal the details of the haplotype diversity of sacrifices. Thus, I might expect the sphere of Teotihuacan influence through the genetic origins of individuals offered as sacrifices.

In addition to modern genomic information, spatiotemporal genetic information obtained from archaeological remains makes it possible to pursue human population history chronologically. I conclude that the composite approach may be useful in obtaining entire sequences of ancient mitogenomes efficiently and reliably, even if obtaining sufficient sequence data by NGS is difficult. This approach may be useful in the analysis of population-based ancient genomes when the state of DNA preservation is extremely poor.

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