



Review

Damage and repair of ancient DNA

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Abstract

Under certain conditions small amounts of DNA can survive for long periods of time and can be used as polymerase chain reaction (PCR) substrates for the study of phylogenetic relationships and population genetics of extinct plants and animals, including hominids. Because of extensive DNA degradation, these studies are limited to species that lived within the past 10^4 – 10^5 years (Late Pleistocene), although DNA sequences from 10^6 years have been reported. Ancient DNA (aDNA) has been used to study phylogenetic relationships of protists, fungi, algae, plants, and higher eukaryotes such as extinct horses, cave bears, the marsupial wolf, the moa, and Neanderthal. In the past few years, this technology has been extended to the study of infectious disease in ancient Egyptian and South American mummies, the dietary habits of ancient animals, and agricultural practices and population dynamics of early native Americans. Hence, ancient DNA contains information pertinent to numerous fields of study including evolution, population genetics, ecology, climatology, medicine, archeology, and behavior. The major obstacles to the study of aDNA are its extremely low yield, contamination with modern DNA, and extensive degradation. In the course of this review, we will discuss the current aDNA literature describing the importance of aDNA studies as they relate to important biological questions and the difficulties associated with extracting useful information from highly degraded and damaged substrates derived from limited sources. In addition, we will present some of our own preliminary and published data on mechanisms of DNA degradation and some speculative thoughts on strategies for repair and restoration of aDNA.

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Keywords: Ancient DNA; DNA fragmentation; DNA repair; Interstrand cross-links; Oxidative damage

Abbreviations: aDNA, ancient DNA; ALS, alkali-labile site; AP, apurinic/aprimidinic; B.P., before present; Dsb, double-strand break; GC/MS, gas chromatography/mass spectrometry; ICL, interstrand cross-link; mtDNA, mitochondrial DNA; NAML, number average molecular length; PCR, polymerase chain reaction; PNK, polynucleotide kinase; SAP, shrimp alkaline phosphatase; Ssb, single-strand break

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Contents

1. Molecular paleobiology	266
2. The chemistry of DNA degradation	267
3. Ancient DNA damage	268
4. Studies on DNA damage in ancient permafrost	270
5. Restoration of ancient DNA	272
6. Conclusions	274
Acknowledgments	274
References	274

The past 15 years has seen a burgeoning of studies utilizing ancient DNA (aDNA) technologies to study a variety of biological problems pertinent to numerous fields of study including evolution, population genetics, ecology, climatology, medicine, molecular archeology and anthropology, cultural evolution, behavior, and exobiology to name a few [1–4]. The impact of this technology has been significant and its future holds considerable promise. This review is designed to give a brief summary, with specific examples, of aDNA insights into paleobiology and human prehistory, outline some of the problems associated with aDNA analysis with specific focus on DNA degradation and damage accumulation, and discuss the prospect of repairing aDNA and increasing the amount of sequence information available for polymerase chain reaction (PCR) analysis. Some of our recent data on aDNA damage will be summarized as well.

1. Molecular paleobiology

A major application of aDNA technology has been in the fields of evolution and population genetics. DNA extracted from a North Greenland ice core dated at 2000 and 4000 years B.P. (before the present) revealed a high diversity of fungi, plants, algae, and protists derived from the local environment as well as distant sources [5]. Similarly, aDNA extracted from five permafrost cores from Siberia, ranging from 10,000 to 400,000 years B.P., revealed a broad range of taxonomic diversity in the paleoenvironment [6]. Sequences were

identified for 19 different plant taxa as well as several mammalian species including mammoth, bison, and horse and showed significant changes in the diversity and composition of plants and animals across the late Pleistocene ice-free zone that stretched across Northeast Siberia and the Bering land bridge to Western Canada. Phylogenetic relationships have also been explored in populations of extinct horses [7], cave bears [8], ground sloths [9], the marsupial wolf [10], saber-toothed cats [11], the woolly mammoth [12], the moa [13] and most recently, Adelie penguins [14], to name a few. Recent technology has allowed DNA extraction from coprolites, fossilized fecal material, which contain sequences from both the host animal and its diet. From this material investigations on the dietary habits of ancient animals, such as the ground sloth have provided evidence for ecological and climate change in the distant past [15].

Ancient DNA analyses have also been applied to problems of human history and prehistory and promise to add invaluable and exciting insights into these fields in the near future. Hybridization of genomic DNAs isolated from modern humans with that from parietal and clavicle fossils of *Homo neanderthal* from Germany and Croatia, respectively, showed considerably more divergence than similar analyses using DNA from early *Homo sapiens* remains from Vogelherd cave in Germany. These results support the idea that Neanderthal was not in the direct lineage of modern man [16]. A similar study using mitochondria DNA from a 29,000-year-old Neanderthal specimen recovered from Mezmaiskaya Cave in the Northern

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