Factors Impacting Mutation Rates in Mitochondrial DNA with Relevance to Neanderthals, Denisovans, and Modern Human Common Ancestry

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ABSTRACT

The marked genetic divergence observed between archaic and modern humans is a challenge to explain within the timeframe of the Biblical genealogies. However, emerging evidence suggests that environmental pollutants and intrinsic physiological susceptibilities may have elevated mitochondrial DNA (mtDNA) mutation rates in *Homo neanderthalensis* and Denisovans. Discoveries regarding aryl hydrocarbon receptor (AHR) sensitivity, polycyclic aromatic hydrocarbon (PAH) exposure from controlled fire, environmental lead bioaccumulation, and the functional disruption of DNA polymerase gamma (Pol *γ)* are useful for understanding mechanisms causing accelerated mtDNA divergence. These factors provide a plausible explanation for mtDNA divergence between modern and archaic humans within a timeframe that fits the Biblical genealogies.

Keywords: *Neanderthal, Denisovan, archaic hominins, mutation rates, harmful mutations, lead exposure, hypermutation, de novo mutation, biblical timeline*

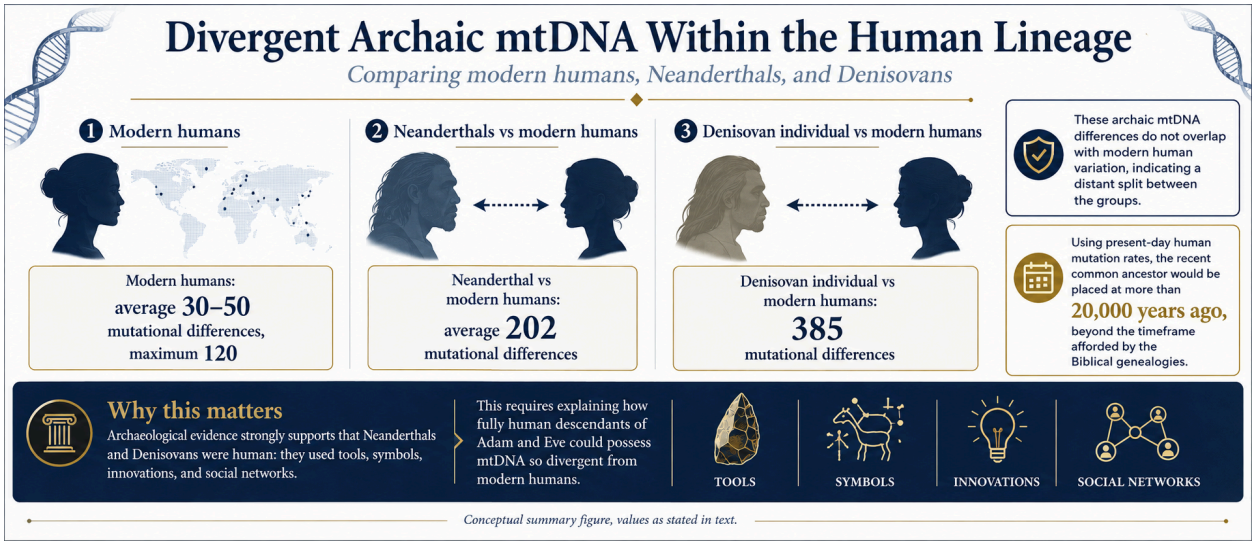
Introduction

The low diversity of human mitochondrial DNA is strong evidence of a recent common female ancestor. Ironically, in secular literature she is referred to as “Mitochondrial Eve,” and secular scientists recognize that all humans descended from this one maternal lineage. The observed mutation rates in mtDNA place Mitochondrial Eve within the timeframe of the Biblical genealogies, at less than 10,000 years.[1] However, when we consider the diversity of Neanderthal mtDNA, and trace that back to a common ancestor, it does not fit within the Biblical timeline.

While there is an average of 30-50 mutations between humans (and a maximum of 120 mutational differences), between Neanderthal and humans the average number of mutational differences is 202[2], and a related Denisova individual has 385 mutational differences[3]. Additionally, these mutations do not overlap with modern humans, which indicates a distant split between these groups. If we use present day mutation rates in humans, it will put our recent common ancestor at more than 20,000 years ago, which is clearly outside the period afforded by the Biblical genealogies.

[1] Parsons TJ, Muniec DS, Sullivan K, Woodyatt N, Alliston-Greiner R, Wilson MR, Berry DL, Holland KA, Weedn VW, Gill P, Holland MM. A high observed substitution rate in the human mitochondrial DNA control region. Nat Genet. 1997 Apr;15(4):363-8. doi: 10.1038/ng0497-363. PMID: 9090380.
[2] Krause, J., Fu, Q., Good, J. et al. The complete mitochondrial DNA genome of an unknown hominin from southern Siberia. Nature 464, 894–897 (2010). https://doi.org/10.1038/nature08976
[3] Krause, J., Fu, Q., Good, J. et al. The complete mitochondrial DNA genome of an unknown hominin from southern Siberia. Nature 464, 894–897 (2010). https://doi.org/10.1038/nature08976

There is compelling evidence that Neanderthals and Denisovans were human, based on their practices of using tools, symbols, innovations, and social networks.[4] Therefore, we must consider their placement as descendants of Adam and Eve, and how they may have ended up with mtDNA that is so divergent from modern humans.



Environmental pollutants are known to affect mutation rates in mitochondrial DNA in various ways, and this may provide the key to understanding how Neanderthal and Denisovan mtDNA mutated rapidly.

Fire Use, AHR Receptor Sensitivity, and PAH Mutagenesis

Paleoanthropological evidence demonstrates extensive fire use among Neanderthals.[5] A study examining the DNA of Neanderthals and Denisovans found that they possessed a variant at codon 381 (A381) that modern humans do not have. That variant in modern humans is in the aryl hydrocarbon receptor (AHR), which allows humans to respond quickly to environmental toxins such as polycyclic aromatic hydrocarbons (PAHs). A study in 2016 found, "Increased PAH [polycyclic aromatic hydrocarbon] binding and DNA binding, in conjunction with enhanced *Cyp1a1/1b1* expression, provides evidence that Neanderthals, expressing the A381 AHR [aryl hydrocarbon receptor] variant, may have been more susceptible than modern humans to exogenous AHR ligand mediated toxicities."[6] High levels of exposure to PAHs increases production of reactive oxygen species (ROS), and the oxidative stress is known to cause damage to the mitochondrial genome.[7]

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[4] Villa P, Roebroeks W. Neandertal demise: an archaeological analysis of the modern human superiority complex. PLoS One. 2014 Apr 30;9(4):e96424. doi: 10.1371/journal.pone.0096424. PMID: 24789039; PMCID: PMC4005592.

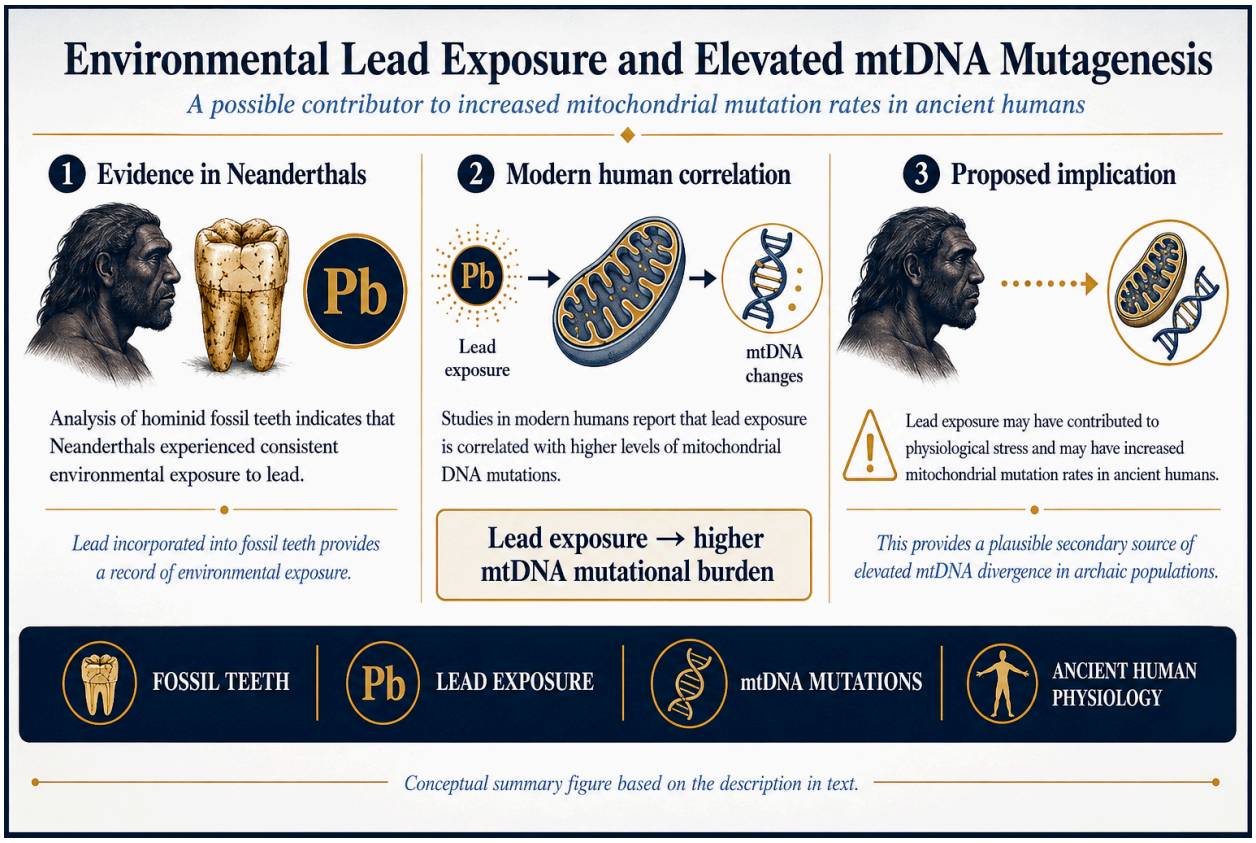
[5] Hubbard, T. D., Murray, I. A., Bisson, W. H., Sullivan, A. P., Sebastian, A., Perry, G. H., Jablonski, N. G., & Perdew, G. H. (2016). Divergent Ah Receptor Ligand Selectivity during Hominin Evolution. Molecular biology and evolution, 33(10), 2648–2658. https://doi.org/10.1093/molbev/msw143

[6] Hubbard, T. D., Murray, I. A., Bisson, W. H., Sullivan, A. P., Sebastian, A., Perry, G. H., Jablonski, N. G., & Perdew, G. H. (2016). Divergent Ah Receptor Ligand Selectivity during Hominin Evolution. Molecular biology and evolution, 33(10), 2648–2658. https://doi.org/10.1093/molbev/msw143

[7] F. Yakes, & B. Van Houten, Mitochondrial DNA damage is more extensive and persists longer than nuclear DNA damage in human cells following oxidative stress, Proc. Natl. Acad. Sci. U.S.A. 94 (2) 514-519, https://doi.org/10.1073/pnas.94.2.514 (1997).

Environmental Lead Exposure

Environmental lead exposure is another source of elevated mtDNA mutagenesis. Analysis of hominid fossil teeth demonstrates that Neanderthals had consistent environmental exposure to lead which may have contributed to physiological challenges.[8] A study of modern humans showed that lead exposure is correlated with higher levels of mtDNA mutations[9], so this may be another source of increased mutation rates in ancient humans.



Polymerase Gamma Disruption

The main enzyme responsible for replicating and proofreading the mitochondrial genome is DNA polymerase gamma (Pol *γ,* encoded by POLG). Any disruption to the POLG gene or the DNA polymerase gamma causes rapid acceleration in mtDNA mutation rates. A study of mice demonstrated that a mutation in POLG caused mutant mice to accumulate mtDNA mutations at 3 to 8 times the rate of non-mutant mice.[10] While we do not have evidence of DNA mutations in ancient human POLG genes, environmental toxins are known to cause disruption to Pol *γ* functions.[11]

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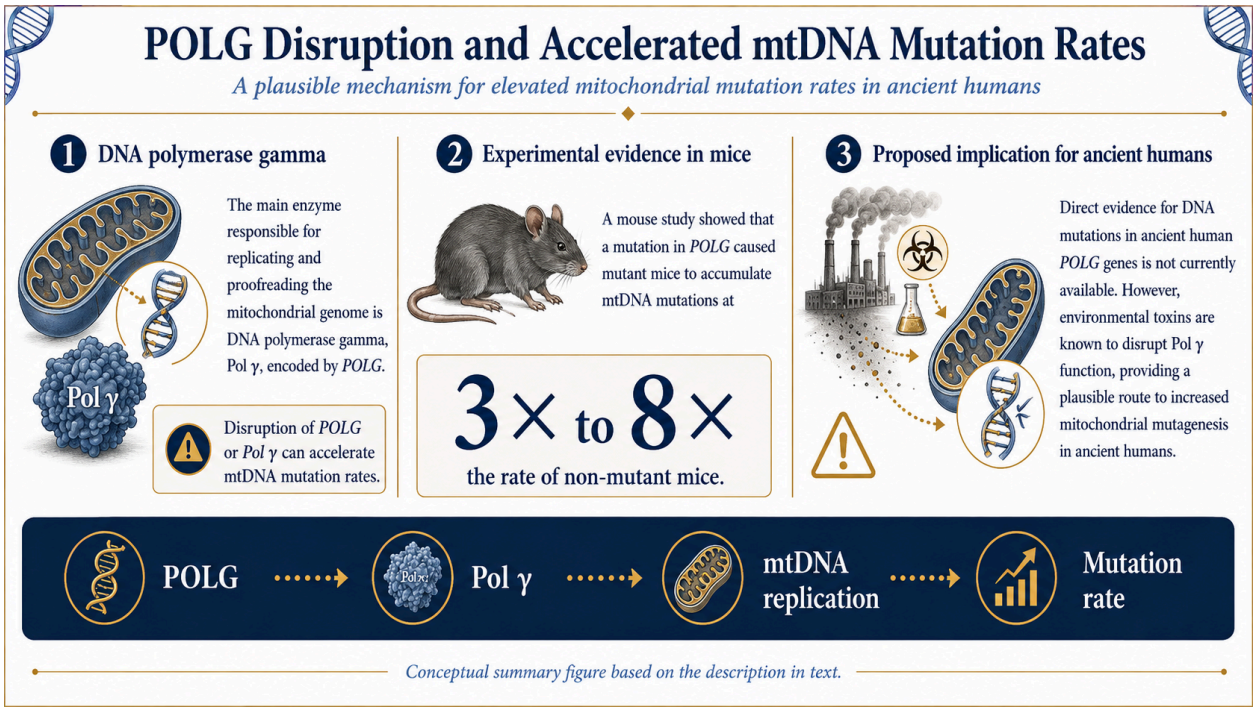
[8] Renaud Joannes-Boyau et al. ,Impact of intermittent lead exposure on hominid brain evolution.Sci. Adv.11,eadr1524(2025).DOI:10.1126/sciadv.adr1524

[9] Leuthner, Tess & Meyer, Joel. (2021). Mitochondrial DNA Mutagenesis: Feature of and Biomarker for Environmental Exposures and Aging. Current Environmental Health Reports. 8. 10.1007/s40572-021-00329-1

[10] G. C. Kujoth et al. ,Mitochondrial DNA Mutations, Oxidative Stress, and Apoptosis in Mammalian Aging.Science309,481-484(2005).DOI:10.1126/science.1112125

[11] Leuthner, Tess & Meyer, Joel. (2021). Mitochondrial DNA Mutagenesis: Feature of and Biomarker for Environmental Exposures and Aging. Current Environmental Health Reports. 8. 10.1007/s40572-021-00329-1.



Conclusion

Increased AHR receptor sensitivity to indoor smoke, chronic exposure to environmental lead, and chemical disruption of Pol *γ* replication provide possible explanations for the high mtDNA mutation rate among Neanderthals and Denisovans when compared with modern humans. While we do not have certainty about the reasons for the high mutational divergence, the studies cited in this article provide evidence that ancient humans were exposed to the environmental stressors that are known to cause high rates of mutation in mitochondrial DNA. With this evidence in mind, ancient human mtDNA divergence does not provide strong evidence against the Biblical timeframe for Adam and Eve, and mtDNA continues to provide good evidence of a recent common female ancestor for all humans.