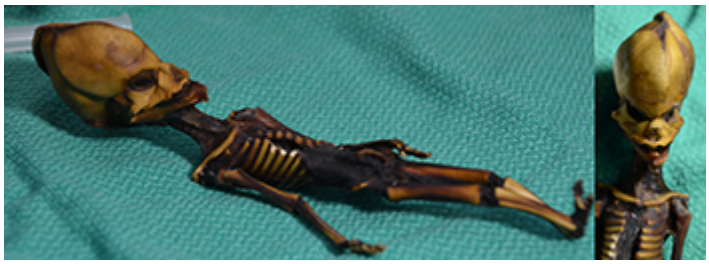
GENOME RESEARCH

6-inch tall human skeleton found to be Chilean female with multiple disease-associated mutations



Mummified specimen from Atacama region of Chile. Credit: EMERY SMITH.

March 22, 2018 – In 2003, scientists made a surprising discovery of a 6-inch mummified humanoid skeleton in the Atacama region of Chile with an estimated bone age of about 6-8 years old at the time of death. The specimen's exceptionally small stature and multiple skeletal abnormalities, including a cone-shaped skull led to widespread speculation on its origin. In a study published today in Genome Research, whole genome sequencing of the Atacama (Ata) skeleton offers insights into its ancestry and strange phenotype.

Early analyses revealed that the Ata skeleton contained high-quality DNA that was suitable for modern sequencing technology. "This was an unusual specimen with some fairly extraordinary claims put forward. … it would be an example of how to use modern science to answer the question "what is it?" says senior author Garry Nolan from Stanford University. Using DNA extracted from the bone marrow, Nolan and his colleagues conducted a whole-genome sequence analysis of Ata.

Sequencing reads were aligned to human and non-human primate reference genomes, including chimpanzee and rhesus macaque, which revealed Ata to be of human origin. Ata's Chilean ancestry was resolved by comparing single nucleotide polymorphisms (SNPs) against a database of known SNPs from diverse geographical populations. The ratio of sequence read alignment to the X and Y Chromosomes revealed that Ata was female.

The researchers next probed for genetic clues that could explain Ata's small stature, multiple bone and skull abnormalities, abnormal rib count, and premature bone age. They found multiple mutations in genes associated with diseases such as dwarfism, scoliosis, and musculoskeletal abnormalities. Surprisingly, Nolan claims Ata's "dramatic phenotype could in fact be explained with a relatively short list of mutations in genes known previously to be associated with bone development."

"This is a great example of how studying ancient samples can teach us how to analyze modern day medical samples" say co-author Atul Butte, UCSF. Future studies employing deeper sequencing and analyses of the novel sequence variations found in Ata may improve our understanding of the functional basis of genetic skeletal disorders.

Researchers from the University of California, San Francisco, Roche Sequencing Solutions, Stanford University, National Autonomous University of Mexico, Ultra Intelligence Corporation, and Stanford University School of Medicine contributed to this work. The study was supported by the Lucile Packard Foundation for Children's Health, the University of California San Francisco endowment, the Human Frontier Science Program Fellowship, and the Rachford and Carlota A. Harris Professorship.

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About the article:

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