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Ancient Proteins and Middle Pleistocene Skulls Reveal the Distinctive Cranial Anatomy of Denisovans

Paleoproteomics * Human Evolution * Genomics

For more than a decade after their 2010 discovery from a juvenile finger bone in Siberia's Denisova Cave [6] , the Denisovans remained paleoanthropology's most famous "ghost lineage": an archaic human population whose complete nuclear and mitochondrial genomes were sequenced in extraordinary detail, yet whose physical face and cranial vault remained essentially unknown. Because warm, humid, or fluctuating Middle Pleistocene burial environments across East and Southeast Asia rapidly degrade ancient DNA (aDNA), dozens of enigmatic hominin skulls excavated across China over the past half-century sat in museum vaults without a molecular identity. Now, a landmark series of paleoproteomic and ancient biomolecular investigations led by Qiaomei Fu and colleagues at the Institute of Vertebrate Paleontology and Paleoanthropology (IVPP) has linked the ~138,000-to-199,000-year-old Xujiayao cranial assemblage [1] and the >146,000-year-old Harbin cranium [2, 3] directly to the Denisovan clade -- revealing a distinctive, shared craniofacial morphology across Middle Pleistocene East Asia.

Why Collagen Outlasts DNA in Middle Pleistocene Fossils

While double-stranded DNA fragments into unrecoverable short oligomers via hydrolytic depurination within 50,000 to 100,000 years outside permafrost or cold karst caves, structural bone and tooth-enamel proteins -- such as type I collagen (COL1A1 and COL1A2), amelogenin (AMELX / AMELY), and enamelin (ENAM) -- are cross-linked directly into the hydroxyapatite mineral lattice of cortical bone and dentition. Under liquid chromatography-tandem mass spectrometry (LC-MS/MS), these fossilized peptide chains preserve lineage-specific single amino acid polymorphisms (SAPs) across hundreds of thousands of years.

In their latest study published in Nature , Fu and collaborators extracted 18 endogenous ancient proteins from cranial, mandibular, and dental specimens originally excavated in the 1970s at the Xujiayao site in the Nihewan Basin of northern China, dated to between 199,000 and 138,000 years ago [1] . Mass spectrometric sequencing identified a diagnostic Denisovan-derived substitution in the alpha-2 chain of type I collagen -- specifically an arginine -to-lysine replacement at position 996 (COL1A2-R996K) -- alongside archaic hominin peptide markers shared with the high-coverage Denisova 3 genome from Siberia [1, 6] .

This molecular match builds directly on two companion breakthroughs on the nearly complete Harbin cranium from Heilongjiang Province (originally described morphologically as Homo longi or "Dragon Man"): a paleoproteomic analysis of 95 endogenous bone proteins that recovered the same Denisovan-diagnostic COL1A2 and COL1A1 variants [2] , and a targeted ancient-DNA extraction from mineralized dental calculus (calcified tooth plaque) on the Harbin molar that recovered host mitochondrial DNA nesting squarely within the early Denisovan clade [3] . Together

with proteomically confirmed Denisovan mandibles from Baishiya Karst Cave in Xiahe on the Tibetan Plateau (~160,000 years old) [5] and the Penghu Channel off Taiwan [4] , paleoproteomics has transformed an isolated Siberian genotype into a geographically widespread Asian hominin population with multiple intact skulls and jaws.

Key Molecular and Morphological Telemetry Across Confirmed Denisovan Fossils

| Specimen / Assemblage | | Geographic Region | | Estimated Age (ka) | | Primary Biomolecular Evidence | | Key Craniofacial & Dental Traits | | Reference |

| Xujiayao (20 specimens) | | Nihewan Basin, Northern China | | 199-138 ka | | 18 endogenous bone proteins; diagnostic COL1A2-R996K SAP | | Broad, low cranial vault; thick parietal bone; wide bi-parietal breadth; large megadont molars | | [1] |

| Harbin Cranium (HBSM2018) | | Heilongjiang, NE China | | >146 ka | | 95 endogenous proteins + dental calculus host mtDNA | | 1,420 cm^3 endocranial volume; massive curved supraorbital torus; flat, retracted midface; square orbits | | [2, 3] |

| Xiahe Mandible | | Baishiya Cave, Tibetan Plateau (3,280 m) | | ~160 ka | | Collagen paleoproteomics + cave sediment mtDNA | | Robust mandibular corpus; absence of chin (mental trigone); three-rooted lower second molar | | [5] |

| Penghu 1 Mandible | | Penghu Channel, Taiwan Strait | | 190-10 ka (Late Middle/Late Pleistocene) | | 51 endogenous proteins (AMELY male + Denisovan SAPs) | | Extremely thick, low mandibular body; broad anterior dental arcade; megadont molars | | [4] |

| Denisova 3 / 4 / 8 | | Denisova Cave, Altai Mountains, Siberia | | 195-50 ka | | 30x nuclear genome + mtDNA + collagen proteome | | Phalanx & isolated giant molars with flaring roots and complex occlusal crenulations | | [6] |

Anatomy of the Denisovan Face and Vault: An Evolutionary Mosaic

With both the Harbin cranium and the Xujiayao cranial fragments anchored molecularly to the Denisovan lineage, comparative morphometric analysis reveals why these fossils defied simple classification for decades: Denisovans exhibited a striking mosaic of archaic, Neanderthal-like, and derived human features [1, 2] .

* Broad, Low, and Thick-Walled Cranial Vaults: Both the Harbin and Xujiayao crania combine large endocranial capacities (~1,420 cm^3 in Harbin -- fully within the range of Homo sapiens and Neanderthals) with a low, elongated vault profile and exceptionally thick cranial walls reminiscent of earlier Asian Homo erectus [1, 2] . Unlike the globular parietal bossing of modern humans or the classic posterior "chignon" (occipital bun) of Western Eurasian Neanderthals, Denisovan vaults expand laterally across the temporal and parietal bones.

* Massive Swept Brow Ridges and Square Orbits: The upper face is dominated by a continuous, heavily buttressed supraorbital torus (brow ridge) that arches gently over wide, sub-rectangular eye sockets [2] .

* A Flat, Orthognathic Midface Under a Broad Vault: Perhaps the most unexpected feature of the Harbin cranium is its surprisingly flat, tucked-in (orthognathic)

midface with delicately contoured cheekbones that do not project forward like the midfacial prognathism of Neanderthals [2] . Previously, paleoanthropologists interpreted this flat facial profile in fossils such as Harbin, Dali, Jinniushan, and Hualongdong as evidence of early transitional Homo sapiens in East Asia. The proteomic data show instead that a retracted midface paired with a massive brow ridge and megadont dentition was a hallmark of the Denisovan lineage itself [1, 2] .

* Robust Jaws and Three-Rooted Megadont Molars: Across Xiahe, Penghu 1, Xujiayao, and Harbin, Denisovan jaws lack a projecting chin, possess thick cortical bone adapted to heavy biomechanical chewing loads, and retain huge molars -- frequently displaying an accessory third root on the lower second molar that was later inherited by some East Asian and Indigenous American modern human populations via Late Pleistocene introgression [1, 4, 5] .

Resolving the "Muddle in the Middle" Across Pleistocene Asia

For decades, hominin fossils dating between 300,000 and 100,000 years ago were grouped into an informal taxonomic bucket -- often called the "Muddle in the Middle" or split into competing regional species names such as Homo longi and Homo juluensis . By demonstrating that specimens spanning both morphotypes (including Harbin and Xujiayao) carry diagnostic Denisovan protein and mitochondrial signatures, the new molecular evidence indicates that most of these large-brained East Asian Middle Pleistocene hominins belonged to structured subpopulations of the Denisovan clade [1, 2, 3] .

Spanning subarctic Siberian steppes, the high-altitude hypoxia of the Tibetan Plateau at 3,280 meters (where Denisovans evolved the EPAS1 allele later passed to modern Tibetans), temperate northern China, and subtropical lowland shelves in Taiwan and Laos, Denisovans maintained a robust, cold- and stress-tolerant craniofacial bauplan across more than 4,000 kilometers of latitude. As high-resolution paleoproteomics is applied to additional Middle Pleistocene fossils from Jinniushan, Dali, Maba, and Narmada, researchers now have both the molecular barcode and the anatomical reference blueprint needed to map our sister lineage across Eurasia.

References & Primary Sources

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