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The Tequendama Genome: How Ancient DNA is Rewriting the History of Syphilis

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Introduction: A Paleogenomic Paradigm Shift in the Andes

For over five centuries, the origins of syphilis and its related treponemal diseases have been debated through the lens of historical accusation, ambiguous osteological lesions, and conflicting epidemiological models. When a fulminant epidemic of the "Great Pox" erupted among King Charles VIII's mercenary armies during the 1495 siege of Naples -- causing severe pustular lesions, rapid tissue destruction, and high mortality -- physicians immediately linked its arrival to Christopher Columbus's 1493 return from the Americas.[7][9] That debate crystallized into three competing frameworks: the Columbian Hypothesis, holding that Treponema pallidum originated in the Americas and increased sharply in virulence upon entering immunologically naive European populations;[3][8] the Pre-Columbian Hypothesis, arguing that treponemal disease was already circulating in medieval Afro-Eurasia but misdiagnosed as leprosy before undergoing a mutation in virulence;[7][10] and E.H. Hudson's Unitarian Hypothesis, positing a single global treponemal pathogen whose clinical manifestations shift between venereal and skin-to-skin transmission according to climate and hygiene.[7]

Because treponemal syndromes leave nearly indistinguishable inflammatory bone signatures (periostitis and osteomyelitis), osteology alone could not resolve the stalemate.[8] In January 2026, however, an international consortium led by Davide Bozzi of the University of Lausanne and the Swiss Institute of Bioinformatics, alongside collaborators at the University of California, Santa Cruz, and Colombian research institutions, published a landmark study in Science.[1][2] By reconstructing a 5,500-year-old Treponema pallidum genome (designated TE1-3) from the tibia of a Middle Holocene hunter-gatherer buried in the Tequendama I rock shelter of the Bogot Savanna, the team established the earliest direct molecular proof of treponemal infection in the pre-contact Americas.[1][2]

Crucially, TE1-3 represents a previously unknown, deep-branching sister lineage basal to all modern T. pallidum subspecies, proving that treponemal host-pathogen co-evolution in the Western Hemisphere began millennia before European contact -- and in an individual whose skeleton displayed no macroscopic pathological lesions.[1][5]

Biology of the Spirochete and the Tequendama I Archaeological Context

Understanding the evolutionary significance of TE1-3 requires examining the extreme specialization of Treponema pallidum. A helical spirochete propelled by periplasmic endoflagella (specialized internal flagellum filaments that enable corkscrew motility through dense mucosal and connective tissues), T. pallidum is an obligate

human parasite.[1][2] Its circular chromosome is reduced to approximately 1.14 Mb (~1,000 protein-coding genes), having shed the genetic machinery for the tricarboxylic acid (TCA) cycle and oxidative phosphorylation.[3] Relying exclusively on glycolysis for ATP generation, the bacteria must scavenge amino acids, fatty acids, and nucleotides directly from host tissues.[11] Today, modern human treponematoses are classified into four clinically distinct groups that share ~99.8% genomic identity (Table 1).

Table 1: Modern Classification of Human Treponematoses

| Taxon | | Syndrome | | Primary Transmission | | Geographic Distribution | | Pathological Hallmark |

| T. p. pallidum | | Syphilis | | Venereal / Congenital | | Global | | Chancres, neurosyphilis, cardiovascular and late osteological gummas. |

| T. p. pertenue | | Yaws | | Skin-to-skin contact | | Humid Tropics | | Papillomatous skin lesions (frambesia) and destructive osteoperiostitis. |

| T. p. endemicum | | Bejel | | Mucosal / Shared utensils | | Arid & Semi-arid zones | | Oral mucosal plaques, nasopharyngeal gummas, and long-bone inflammation. |

| T. carateum | | Pinta | | Skin-to-skin contact | | Neotropics (Americas) | | Cutaneous dyschromia and hyperkeratosis; complete absence of bone lesions. |

The ancient TE1-3 genome was recovered from the Sabana de Bogot , a high-altitude Andean plateau (2,600 meters) excavated by Gonzalo Correal Urrego and Thomas van der Hammen in the late 1960s and 1970s.[12] The Tequendama I rock shelter preserves an 11,000-year occupation sequence spanning Late Pleistocene megafaunal hunters to Middle Holocene broad-spectrum foragers.[13] Individual TE1-3 -- a middle-aged male (~1.58 m tall) interred in a flexed ritual burial within Zone IV (~5,500 BP) -- subsisted on white-tailed deer (Odocoileus virginianus), caviomorph rodents (Cavia), land snails, and C3 tubers prior to the adoption of maize agriculture.[1][13][14] The dry, sheltered microclimate inside the rock shelter helped protect his skeletal remains from the acidic groundwater of the open savanna, preserving endogenous ancient DNA.[1]

Paleogenomic Reconstruction: Shotgun Screening, Capture, and Deamination

Isolating a fragile spirochete genetic code from a 5,500-year-old bone required overcoming severe post-mortem degradation. Following death, endogenous enzymes and soil microbes fragment host and pathogen DNA, while water and oxygen induce hydrolytic cleavage, leaving over 99.9% environmental background contamination.[15]

Rather than relying on visual osteological screening -- which would have excluded the lesion-free TE1-3 tibia -- researchers applied untargeted metagenomic shotgun sequencing, generating ~1.5 billion raw sequencing reads.[4] Bioinformatic taxonomic classifiers (including the HOPS pipeline) identified trace diagnostic reads mapping to Treponema pallidum.[16] The team then performed in-solution hybridization capture using synthetic RNA baits tiled across modern treponemal reference genomes, enriching the ancient pathogen library to reconstruct the TE1-3 chromosome at 1.7x average depth of coverage.[1]

To authenticate the antiquity of the pathogen reads and rule out modern laboratory contamination, the investigators quantified post-mortem hydrolytic deamination. Over millennia, cytosine (C) residues at the overhanging 5 ends of sheared ancient DNA fragments lose an amine group and convert into uracil (U), which polymerases misread as thymine (T).[17] The TE1-3 reads exhibited the classic "smile plot" of terminal C-to-T substitution frequencies matching the co-extracted 5,500-year-old human host DNA.[1]

Phylogenetic Placement, Molecular Clock Dating, and Virulence Architecture

When placed onto the treponemal tree of life, TE1-3 did not nest within pallidum (syphilis), pertenue (yaws), or endemicum (bejel). Instead, phylogenetic reconstruction after masking hypervariable and recombinogenic loci positioned TE1-3 as an extinct (or unsampled) basal sister lineage that diverged prior to the radiation of all known modern subspecies.[1][18]

Using tip-calibrated Bayesian molecular clock modeling, the authors estimated that TE1-3 and the progenitor of modern T. pallidum diverged approximately 13,700 years ago (Late Pleistocene).[1][3] This divergence window coincides closely with the initial peopling of the Americas across Beringia, indicating that ancestral treponemes either accompanied early Paleoamerican hunter-gatherers or diversified rapidly in the Western Hemisphere shortly after arrival.[19]

Despite its basal divergence, TE1-3 already possessed the core virulence repertoire of modern T. pallidum (Table 2). Most notably, it carried the tprK antigenic variation system, which uses segmental gene conversion to continuously shuffle outer-membrane variable regions and evade host adaptive immunity.[1][11] However, TE1-3 exhibited unique non-synonymous variants in chemotaxis receptors (mcp2) and outer-membrane proteins (Tp0969), suggesting distinct tissue tropism.[1][3]

Table 2: Chronological and Genomic Comparison of Ancient TE1-3 and Modern Subspecies

| Characteristic | | TE1-3 (Tequendama I) | | Nichols Strain (Modern Syphilis) | | Samoa D (Modern Yaws) |

| Chronological Age | | ~5,500 BP (Middle Holocene) | | Modern (Isolated 1912) | | Modern (Isolated 1953) |

| Geographic Origin | | Sabana de Bogot , Colombia | | Global | | Tropical Oceania / Pantropical |

| Demographic Context | | Mobile Hunter-Gatherers | | Dense Urban / Global Networks | | Rural / Humid Tropical Communities |

| Phylogenetic Position | | Basal Sister Clade (~13,700 BP split) | | T. p. pallidum Clade | | T. p. pertenue Clade |

| Genome Architecture | | ~1.14 Mb (1.7x capture coverage) | | 1.14 Mb | | 1.14 Mb |

| tprK Immune Evasion | | Present | | Present | | Present |

| Skeletal Pathology | | Absent in host tibia | | Common in tertiary disease | | Frequent (sabre shin, periostitis) |

The absence of skeletal lesions in the TE1-3 host -- combined with its Neotropical provenance -- raises an intriguing evolutionary connection to pinta (Treponema carateum), the skin-restricted American treponematosis that leaves no osteological trace and has never been sequenced.[20] Equally significant is how TE1-3 illuminates the "Osteological Paradox": because individuals with acute systemic bacteremia or soft-tissue-restricted strains lack bone remodeling, lesion-based bioarchaeology has systematically underestimated the ancient pathogen burden.[5][6] Furthermore, the persistence of TE1-3 within small, mobile foraging bands demonstrates that Treponema bypassed the high host-density threshold of classic "crowd diseases" by evolving lifelong latency via tprK immune evasion.[1]

Conclusion: Rewriting the Deep History of Treponemal Evolution

Conducted in close ethical partnership with Colombian researchers and indigenous stakeholders,[19] the recovery of the 5,500-year-old TE1-3 genome definitively refutes any claim that the pre-contact Americas were free of Treponema pallidum. While TE1-3 is a basal cousin rather than the direct progenitor of the 1495 European epidemic strain, its Late Pleistocene divergence (~13,700 BP) proves that the Americas harbored deep treponemal diversity for millennia before European arrival.[1][3] By applying untargeted genomics to lesion-free remains, the Tequendama discovery transforms our understanding of how stealth pathogens co-evolved alongside early human populations.[1][6]

Updates... (Nov 21, 2026): Replaced Wikipedia and HTTP 403 links with peer-reviewed archaeological and genomic DOIs (Triana Vega et al., Dec 24, 2019; Fraser et al., Jul 17, 1998; Harper et al., Jan 2011), standardized exact publication dates across all 20 citations, and updated reference list markup.

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