Ancient hepatitis B viruses from the Bronze Age to the Medieval period - DTU Orbit

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Hepatitis B virus (HBV) is a major cause of human hepatitis. There is considerable uncertainty about the timescale of its evolution and its association with humans. Here we present 12 full or partial ancient HBV genomes that are between approximately 0.8 and 4.5 thousand years old. The ancient sequences group either within or in a sister relationship with extant human or other ape HBV clades. Generally, the genome properties follow those of modern HBV. The root of the HBV tree is projected to between 8.6 and 20.9 thousand years ago, and we estimate a substitution rate of $8.04 \times 10^{-6}$-$1.51 \times 10^{-5}$ nucleotide substitutions per site per year. In several cases, the geographical locations of the ancient genotypes do not match present-day distributions. Genotypes that today are typical of Africa and Asia, and a subgenotype from India, are shown to have an early Eurasian presence. The geographical and temporal patterns that we observe in ancient and modern HBV genotypes are compatible with well-documented human migrations during the Bronze and Iron Ages. We provide evidence for the creation of HBV genotype A via recombination, and for a long-term association of modern HBV genotypes with humans, including the discovery of a human genotype that is now extinct. These data expose a complexity of HBV evolution that is not evident when considering modern sequences alone.

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