

Supplementary information

Sequence-based HLA genotyping identifies six candidate alleles associated with human longevity in Germans

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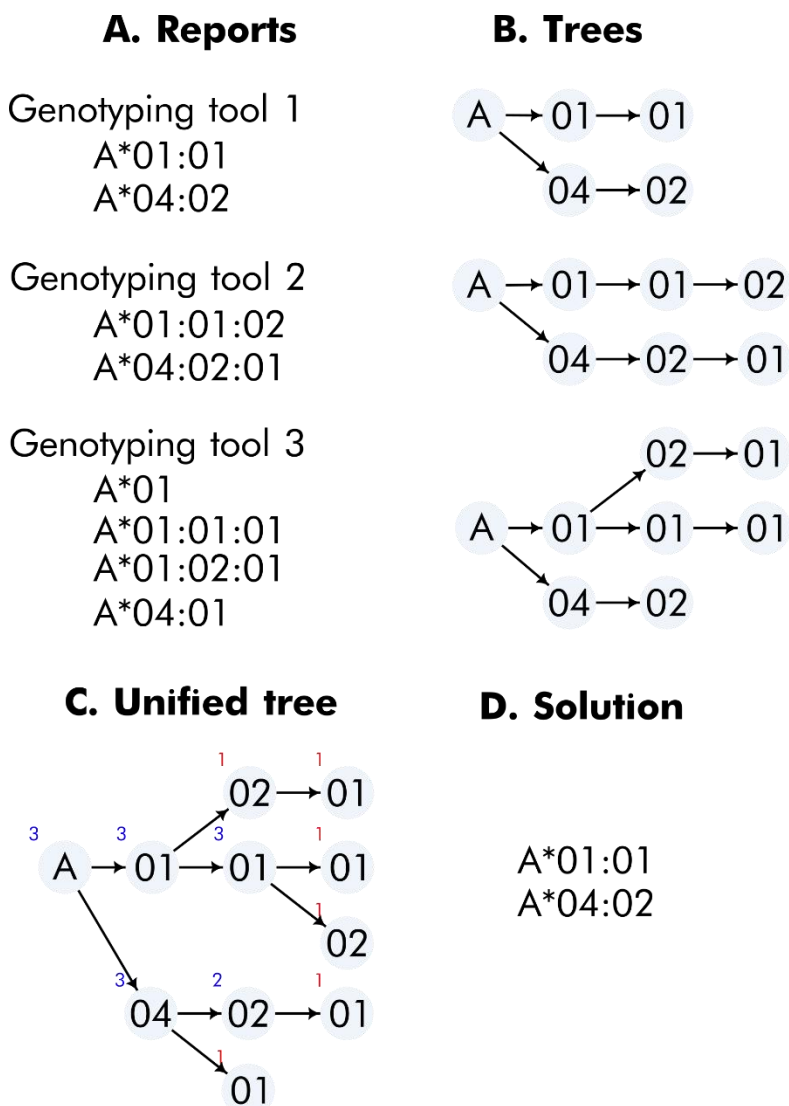


Figure S1. Workflow of the consensus genotyping algorithm.

The algorithm resolves conflicting reports from multiple HLA genotyping tools in four steps, illustrated with a simplified example using three theoretical tools. (A) Inconsistent allele calls are reported by three different tools. (B) Each report is converted into a tree structure. (C) The individual trees are merged into a single unified tree. Here, each node is annotated with a consensus score indicating the number of tools supporting that allele (Blue labels indicate a support above 60%). (D) The final diploid genotype is determined by selecting the pair of highest-resolution alleles from the unified tree that satisfy a predefined consensus threshold of 60%. This threshold is set to require agreement from the majority of the genotyping tools; in this example this means 2 agreements out of 3 possible tools.

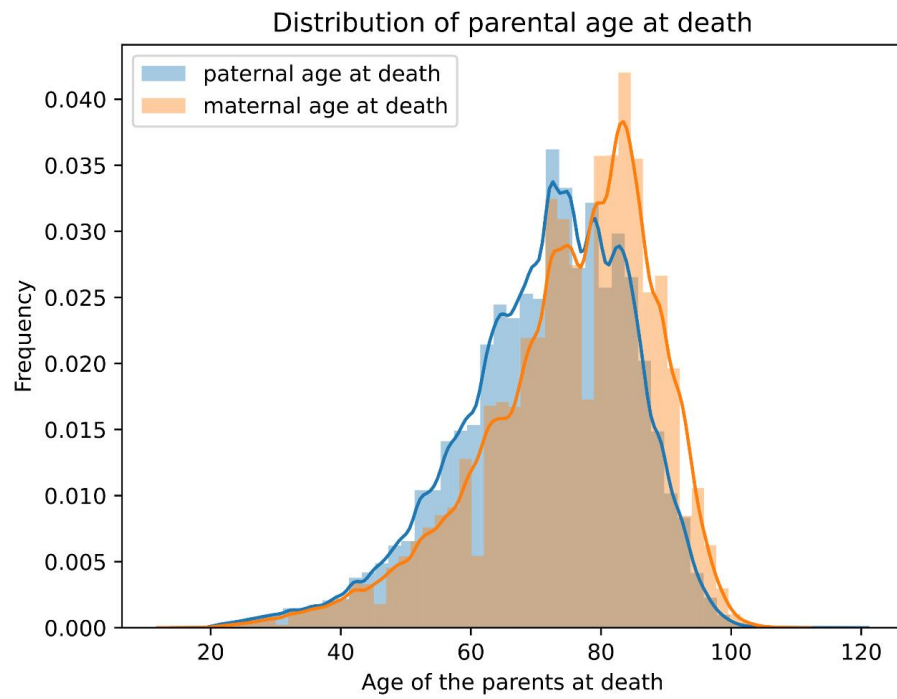


Fig. S2. Distribution of parental age at death.

The father's and mother's age-at-death distribution of samples from the UK Biobank. This distribution was used to determine the 99th percentile threshold used for the long-lived parents.

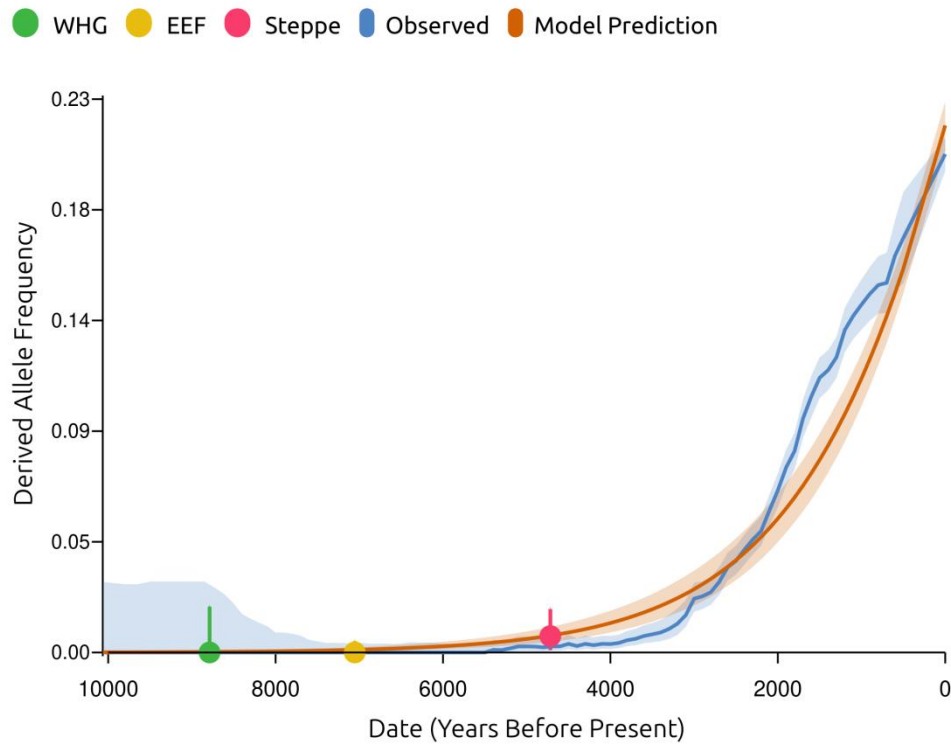


Figure S3. Predicted historical frequency change of the tag SNP of *HLA-A*01:01* (Source: <https://reich-ages.rc.hms.harvard.edu>).

Modern Europeans derive from three main ancient populations: Western Hunter-Gatherers (WHG), Early European Farmers (EEF) and Steppe Herders (Steppe). Within these populations, strong positive selection has acted on *A*01:01*, resulting in a predicted frequency increase from approximately ~0% to ~14% over the last 4,000 years. The selection coefficient was estimated to be 2.73% ($\pm 0.39\%$ SE)¹, using the SNP rs1611635(T) as a genetic proxy for this allele.

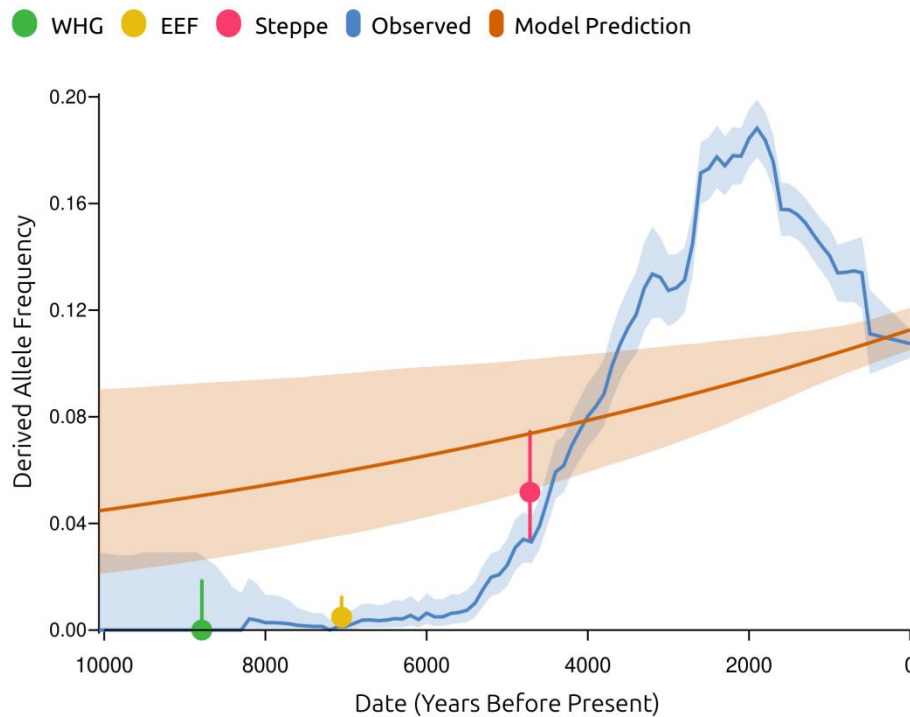


Figure S4. Predicted historical frequency change of the *HLA-DRB1*15:01* allele (Source: <https://reich-ages.rc.hms.harvard.edu>).

Modern Europeans derive from three main ancient populations: Western Hunter-Gatherers (WHG), Early European Farmers (EEF) and Steppe Herders (Steppe). In these populations, positive selection also acted on *DRB1*15:01*, resulting in a predicted frequency increase from approximately ~0% to ~18% over the last 6,000 years. The selection coefficient was estimated to be 0.57% ($\pm$ 0.22% SE)¹, using the SNP rs3135388(A) as a genetic proxy.

References:

1. Akbari A, Barton AR, Gazal S, et al. Pervasive findings of directional selection realize the promise of ancient DNA to elucidate human adaptation. bioRxiv. Preprint posted online September 15, 2024:2024.09.14.613021.

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