

Online Repository

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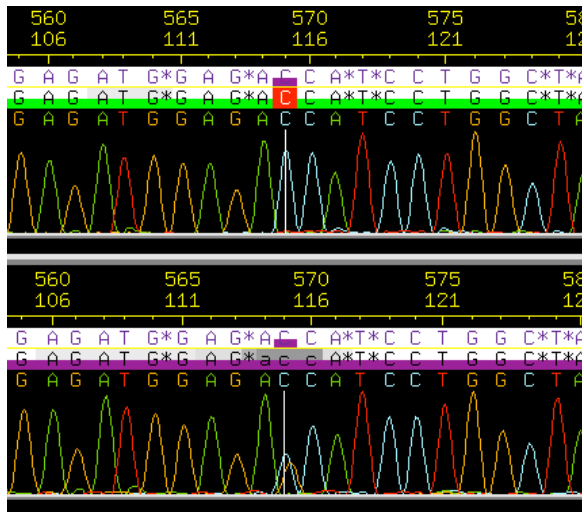
Figure E1. Chromatograms of twelve singleton variants not previously reported or verified by multiple sequence reads. Positions relative to AF395008 in Genbank are followed by rs numbers above each image. Sites are indicated by vertical white lines. Traces containing polymorphic sites appear on the bottom and traces containing the reference sequence appear on top.

Figure E2. Neighbor joining tree (constructed using Network (<http://www.fluxus-engineering.com>)<sup>1</sup> of haplotypes in Bolivians using the chimpanzee sequence as the ancestral sequence. Each circle represents a different haplotype, with the size of the circle proportional to the frequency of that haplotype in the combined sample. The proportion of each haplotype present in the case and control groups are shown as black and gray shading, respectively, in each circle. Polymorphic positions are indicated along the branches. SNPs whose frequencies differ between case and control groups at  $P < 0.05$  are shown in black boxes.

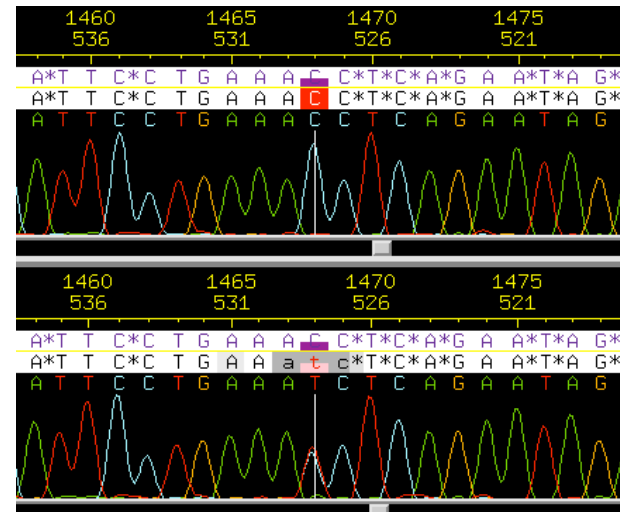
Estimates of the coalescence time for a pair of sequences (haplotypes) were calculated using  $T = D/2\mu l^2$ , where  $T$  = time to the most recent common ancestor (TMRCA) and  $D$  = number of nucleotide differences between two sequences. We used 5 and 6 million years as the divergence time between humans and chimpanzee, which was considered the ancestral sequence, resulting in a range of estimates from 38,660 to 46,392 years ago, respectively. Using the highest ( $1.3 \times 10^{-8}$ ) and lowest ( $2.5 \times 10^{-8}$ ) mutation rate estimates from Nachman and Crowell<sup>3</sup>, divergence estimates range from 25,204 to 48,469 years ago. All four combinations of estimates were used to acquire a range of plausible coalescent times, placing the split prior to the spread of modern humans into the new world<sup>4-7</sup>. It is likely, therefore, that genetic adaptations to *T. cruzi* infection and Chagas disease occurred in the Bolivian indigenous populations prior to the influx of European genes during the past approximately 500 years. Neighbor joining trees were constructed using Network, again considering the chimpanzee as the outgroup. Network is used to infer phylogenetic networks and trees and to estimate dates. This program generates a graphic display of the full information content of sequence data such that each polymorphism distinguishing two haplotypes or haplotype groups is displayed. All possible shortest, least complex (i.e. most parsimonious) trees are displayed in the output, as opposed to many tree-generating tools in which only the most likely result is displayed and all other options are ignored.

1. Bandelt HJ, Forster P, Sykes BC, Richards MB. Mitochondrial portraits of human populations using median networks. *Genetics* 1995; 141:743-53.
2. Tang H, Siegmund DO, Shen P, Oefner PJ, Feldman MW. Frequentist estimation of coalescence times from nucleotide sequence data using a tree-based partition. *Genetics* 2002; 161:447-59.
3. Nachman MW, Crowell SL. Estimate of the mutation rate per nucleotide in humans. *Genetics* 2000; 156:297-304.
4. Fagundes NJ, Kanitz R, Eckert R, Valls AC, Bogo MR, Salzano FM, et al. Mitochondrial population genomics supports a single pre-Clovis origin with a coastal route for the peopling of the Americas. *Am J Hum Genet* 2008; 82:583-92.
5. Goebel T, Waters MR, O'Rourke DH. The late Pleistocene dispersal of modern humans in the Americas. *Science* 2008; 319:1497-502.
6. Kitchen A, Miyamoto MM, Mulligan CJ. A three-stage colonization model for the peopling of the americas. *PLoS ONE* 2008; 3:e1596.
7. Tamm E, Kivisild T, Reidla M, Metspalu M, Smith DG, Mulligan CJ, et al. Beringian standstill and spread of Native American founders. *PLoS ONE* 2007; 2:e829.

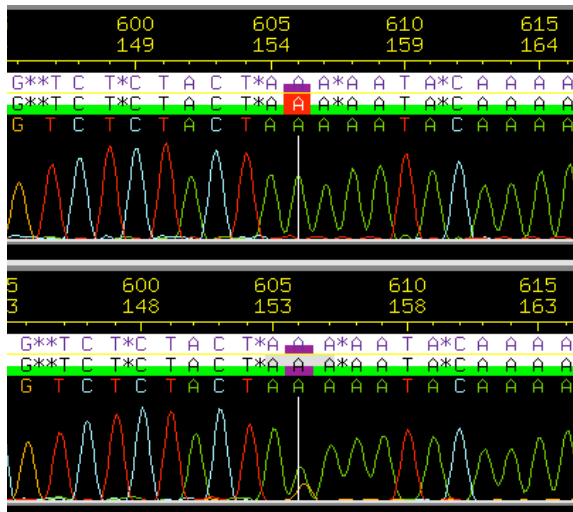
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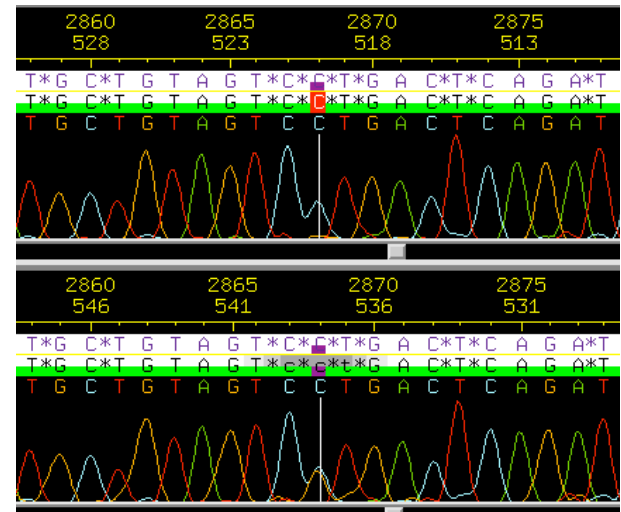
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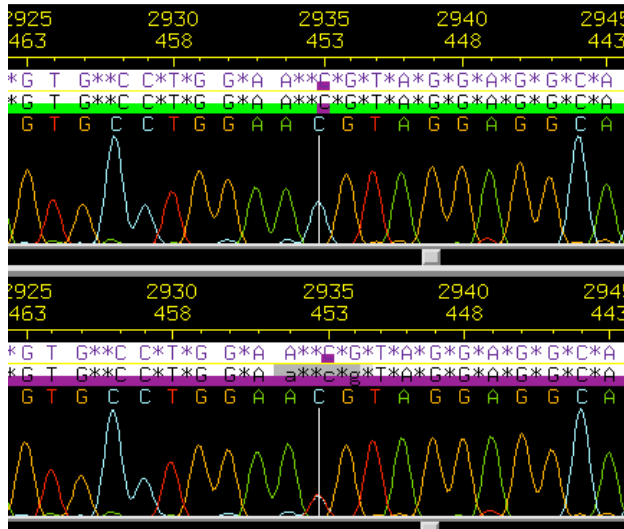
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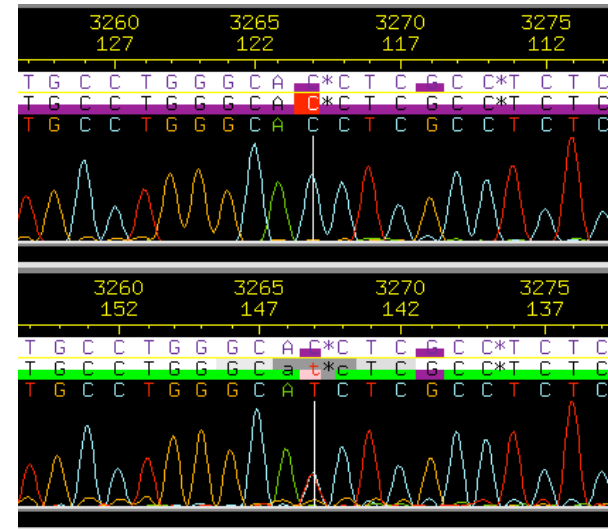
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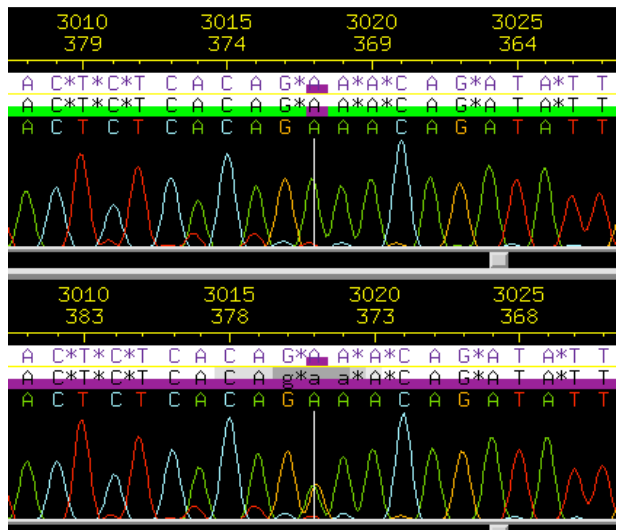
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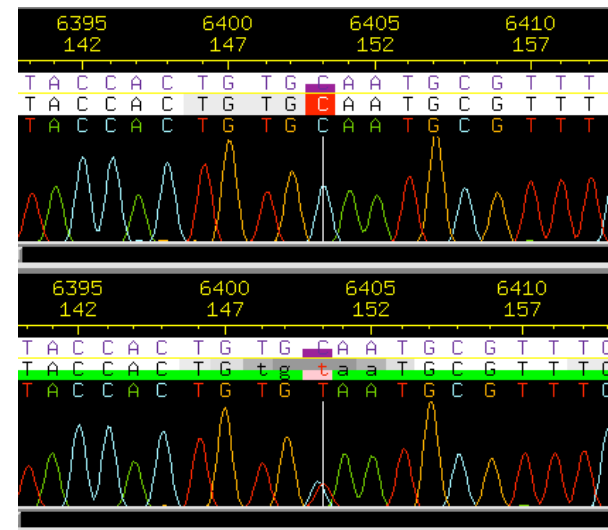
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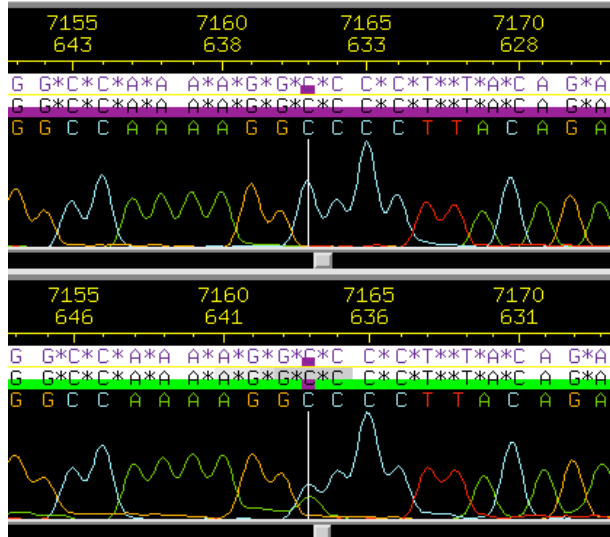
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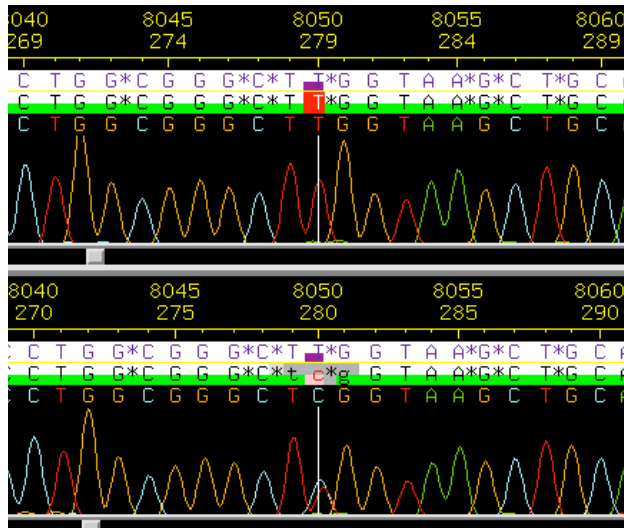
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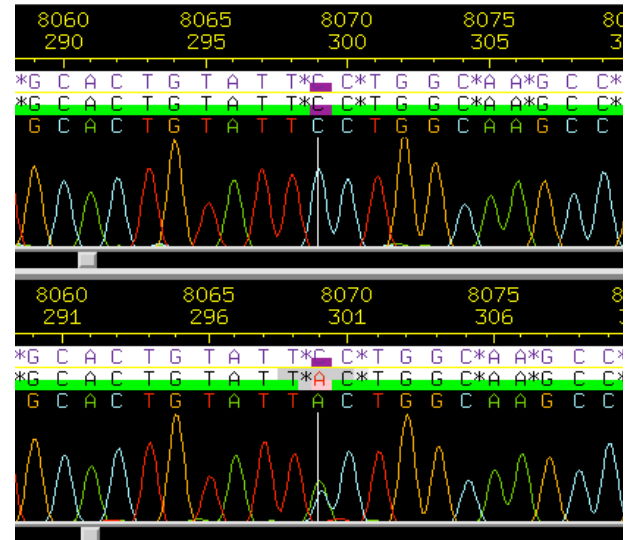
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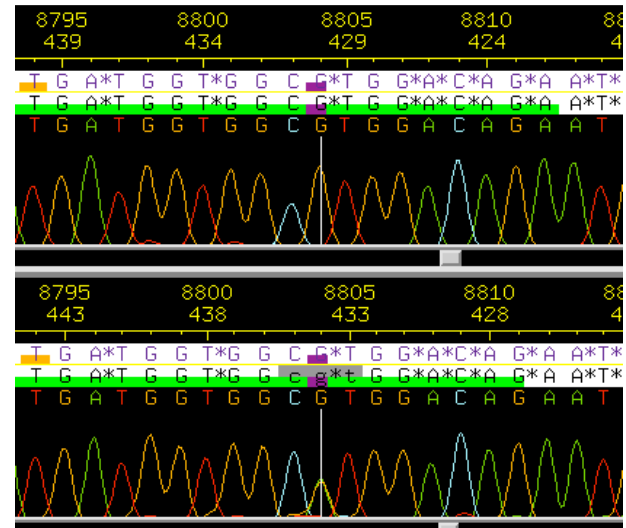
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# Ancestral

