

Supporting Text

Tajima's Nonparametric Relative Rate Tests

Lineage-specific substitutions were inferred by using parsimony. In particular, if we are testing for rate difference between two species A and B with C as the outgroup and at a particular aligned site the nucleotide from A is identical to the nucleotide from C and the nucleotide from B is different, we annotate the substitution to be B lineage specific. Because the genetic distances between the ape species analyzed are extremely small, the parsimony method is apposite. This method has been used successfully in human-chimpanzee-gorilla (1) and human-chimpanzee-baboon comparisons (2). We tested whether the number of substitutions in the human lineage (N_h in Fig. 2, Table 8) is significantly different from the number of substitutions in the chimpanzee lineage (N_c in Fig. 2, Table 8), Tajima's nonparametric relative rate test (3).

We found that humans have accumulated significantly fewer substitutions than the chimpanzee lineage since the last human-chimpanzee common ancestor, both in introns (41,070 human specific and 43,214 chimpanzee specific mutations) and intergenic regions (28742 human specific and 30,252 chimpanzee specific mutations) when considering the entire data set. In the high-quality data set 1 from chromosome 7 alone, humans have accumulated 1,132 and 1,032 fewer substitutions in introns and intergenic regions respectively. Again, the result is consistent when repetitive sequences are excluded from the alignment.

Evolution of Human Specific Life History Traits

We hypothesized that the generation time in the modern human has evolved at a certain time point since the divergence of the chimpanzee, and before that time point human and chimpanzee lineages had the same generation time. Assuming that the difference in the

neutral substitution rate per year between humans and chimpanzees is caused solely by the differences in generation time, the ratios of lineage-specific branch lengths is

$$\frac{K_{OC}}{K_{OH}} = \frac{T_1}{T_2} \left/ \left(\frac{g_1}{g_2} + \frac{T_1}{T_2} - 1 \right) \right.$$

where T_1 is time since the divergence of human and chimpanzee lineages, T_2 is time since the evolution of new generation time in human lineage, g_1 is generation time in chimpanzee lineage and in ancient humans, g_2 is generation time in modern humans, and H, C, O denotes human, chimpanzee, and the common ancestor of human and chimpanzee, respectively. If we assume the generation time for chimpanzees and ancient humans is 15 years and that of the human in the recent past is 20 years ($g_1/g_2 = 15/20 = 0.75$) and $T_1 = 7$ million years, then $T_2 \sim 10^6$ years for 3~4% slowdown in the human genome.

Correcting for Polymorphisms

The mean number of site differences between orthologous sequences from two species is equal to the mean nucleotide diversity in the ancestor population of the two species plus the amount of differentiation after separation (4). For any two species x and y whose common ancestor is a ,

$$K_{xy} = \frac{\Pi_x}{2} + P_{ax} + \Pi_a + P_{ay} + \frac{\Pi_y}{2}$$

where K_{xy} is corrected distance between orthologous sequences from x and y (in our case, the Jukes-Cantor distance), Π_a, Π_x and Π_y are the nucleotide diversities of a, x , and y respectively and P_{ax} and P_{ay} are the number of fixed substitutions between $a-x$ and $a-y$, respectively. Using the formula used in the relative rate test (5), it is easy to show that

$$K_{oc} = P_{oc} + \frac{\Pi_o}{2} + \frac{\Pi_c}{2}$$

and

$$K_{oh} = P_{oh} + \frac{\Pi_o}{2} + \frac{\Pi_h}{2}$$

for human (*h*), chimpanzee (*c*) and the common ancestor of human and chimpanzee (*o*).

The difference in fixed substitutions can be measured as the ratio P_{oc}/P_{oh} , which can be calculated from K_{oc}/K_{oh} (this requires knowledge about the levels of polymorphism in current humans and chimpanzees, as well as the polymorphism of the common ancestor of humans and chimpanzees).

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