

Human-Chimp Comparative Genomics

SAKAKI Yoshiyuki

Human Genome Center, IMSUT, Genomic Sciences Center, RIKEN

Homo Sapiens is a unique organism characterized by its highly developed brain, use of complex languages, bipedal locomotion, and so on. These unique features have been acquired by a series of mutation and selection during evolution in the human lineage. It is of great interest and of great importance from biological and medical viewpoints to understand what kinds of genetic factors are involved in these complex features and how they have been established during human evolution.

Recent completion of the human genome sequence provided a solid platform for addressing these issues. However, the information obtained from the human genome alone is insufficient to discover genetic changes specific to human. The genomes of several experimental organisms such as mouse, fly and nematode have successfully characterized the human genome, but they are evolutionary too distant to zoom up human-specific changes. For these reasons, we conducted a human-chimpanzee whole chromosome comparison at the nucleotide sequence level. We chose human chromosome 21 and its genomic ortholog in chimpanzee, namely chromosome 22, as the first target, because human chromosome 21 is one of the most well-characterized human chromosomes and contains various characteristic features of the human genome such as GC-rich/gene-rich regions and AT-rich/gene-poor regions, many repeated structures, duplications, house-keeping genes and tissue-specific genes, genes with a variety of functions.

We paid special attention to obtain high-quality sequence data to precisely discover all the types of genetic changes, and sequence of 32.7Mb of the long arm of chimpanzee chromosome 22 was determined at an accuracy of more than 99.99%. The human chromosome has about 1% longer size, which can be explained by the existence of some unique DNA sequences in human, particularly, the high frequency of some subfamilies of transposable elements. Rate of overall base substitution (except centromeric and telomeric regions) is about 1.69 %, significantly higher than previously reported average substitution rate (1.23%) of the human genome. This is consistent with other study. Comparative analysis using the mouse genome as an outer group showed that among 235 genes reported, 28 have human-specific as substitution only and 23 chimp-specific only. Ka/Ks ratio suggested that most genes are well conserved but about 10% genes seemed to be positively selected during evolution. The results strongly suggest the existence of considerable number of genes free from genetic constraints over the human genome, some portion of which are rapidly evolving under some positive selections. The progress of these studies will be presented.