

Navigation

- ▶ Latest Releases
- ▶ Release Archives
- ▶ About i-newsWire
- ▶ I-NewsWire Updates
- ▶ i-newsWire Reach
- ▶ Submit Release
- ▶ Premium Partner
- ▶ Request Syndication
- ▶ Press Release Help
- ▶ Partner PR Firms
- ▶ Terms of Service
- ▶ Contact Our Team
- ▶ Free XML Feeds

Also visit:



Home > 'Punctuated' evolution in the human genome

Researchers report today that regions of the human genome have been hotspots for acquiring duplicated DNA sequences - but only at specific time-points during evolution. It appears that long periods of genomic stasis, at least with regard to the accretion of duplicated DNA fragments, are "punctuated" by relatively brief episodes of duplicative activity. This is the first time that such temporal bias has been documented for DNA duplications, and it challenges the evolutionary paradigm that continuous alterations occur during the course of genome evolution.

i-NewsWire, - The scientists, who are affiliated with the University of Washington (Seattle, WA), Case Western Reserve University (Cleveland, OH), the University of Bari (Bari, Italy), Washington University (St. Louis, MO), Washington State University (Pullman, WA), and Duke University (Durham, NC), report their findings online today in the journal *Genome Research*.

Dr. Evan E. Eichler, Associate Professor of Genome Sciences at the University of Washington, heads the team. "Primate genomic sequence comparisons are becoming useful for elucidating the evolutionary history and organization of our own genome," he explains. "Such studies are particularly informative within human pericentromeric regions - areas of rapid change in genomic structure."

Pericentromeric regions are sequences of DNA that lie in close proximity to the centromere, which plays a critical role in chromosomal separation during cell division. Pericentromeric regions contain an abundance of segmental duplications, which are large DNA sequences that exhibit strong similarity to the euchromatic ancestral loci from which they were copied. According to Eichler, the limited number of comparisons of pericentromeric regions among closely related primates suggests extraordinary dynamism, where duplication, deletion, and rearrangement of large segments of DNA occur at an unprecedented scale.

Eichler's group performed a comprehensive structural and evolutionary analysis of a 700-kilobase (Kb) pericentromeric region on the short arm of human chromosome 2. This chromosome has intrigued evolutionary and primate biologists for years because it appears to have formed from the fusion of two mid-sized ape chromosomes, and it is the primary cytogenetic distinction separating humans and their evolutionary progenitors.

Within this 700 Kb region of human chromosome 2, the researchers identified segments of DNA that originated from 14 ancestral loci. These DNA segments, or "duplicons," ranged from 4-77 Kb in length and exhibited 94-99% sequence identity to their euchromatic predecessors.

The scientists then performed a comparative analysis of these duplicons in other primate species, including chimpanzee, gorilla, orangutan, baboon, and macaque. This analysis revealed that the duplicative transposition events leading to the establishment of these duplicons within the pericentromeric region occurred during a relatively narrow window of evolutionary time between 10-20 million years ago. This corresponds to the time period following the divergence of humans and Old World monkeys, but before the divergence of humans and great apes. For the past 10 million years, however, no such "duplicative seeding" events appear to have occurred in this region of the genome.

"It is unclear why pericentromeric seeding events have occurred so frequently during this period of human/great-ape evolutionary history," says Eichler. "It is also unclear as to why they suddenly cease, at least in the case of this pericentromeric region of chromosome 2."

Clearly, factors other than DNA sequence are necessary for such "punctuated" duplicative transposition events to occur during genome evolution. During the divergence of the human/great-ape lineage from the Old World monkey lineage, the genome may have been particularly permissive to segmental duplication events. The scientists speculate that the molecular driving forces behind this "punctuated" duplicative activity may have been changes in transcriptional status or chromatin conformation.

"Other regions may show different temporal biases," explains Eichler. "The important implication

here is that episodic bursts of activity challenge the concept of gradual clock-like changes during the course of genome evolution. Since duplications are important in the birth of new genes and large-scale chromosomal rearrangements, it may follow that these processes may have gone through similar episodes of activity followed by quiescence."

Contact: Maria A. Smit
smit@cshl.edu
516-422-4013
Cold Spring Harbor Laboratory
<http://www.cshl.org>

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Published on:

2005-06-20

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