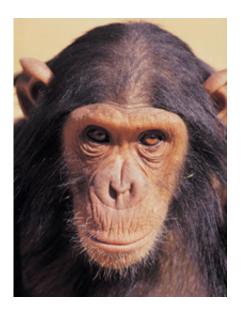


## Scientists map hotspots for genetic exchange in chimpanzees

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Georgia Tech scientists found that the rate of molecular evolution of chimpanzees is closer to that of humans than it is to other apes.

Scientists at the University of Oxford and the University of Chicago have constructed the world's first genetic map in chimpanzees of recombination – the exchange of genetic material within a chromosome that makes us all unique. The study, published today in *Science Express*, shows surprising differences compared to how the process occurs in the human genome.

Recombination is a biological process that shuffles parental DNA during



the production of sperm and eggs. This fundamental process is shared by almost every form of life – without shuffling, we would all be genetically identical. Natural selection operates on this diversity to drive the 'survival of the fittest', selecting advantageous genetic profiles.

The project to investigate how recombination has evolved in recent human and primate history was led by Professors Gil McVean, and Peter Donnelly from the Wellcome Trust Centre for Human Genetics at the University of Oxford, and Dr Molly Przeworski from the Howard Hughes Medical Institute. To study this evolution, they sequenced the entire genomes of ten western chimpanzees and identified differences between their DNA sequences.

The researchers observed that in the chimpanzee genome, for every one thousand bases – the molecules identified by the letters A, C, G and T in DNA – around one base was different. By analysing these DNA differences, they were able to map where recombination events had shuffled genetic material in the chimpanzees' ancestors and to compare this map to patterns of recombination in humans from other studies.

In a previous study, the researchers, together with Dr Simon Myers from the University of Oxford, had shown that in both chimpanzees and humans, recombination only occurs at specific locations of the genome, known as 'recombination hotspots'. Around 40% of these hotspots occur where a particular thirteen letter sequence of DNA is present.

In this new study, funded by the Wellcome Trust and the National Institutes of Health, the researchers found that there was no overlap in the location of recombination hotspots between humans and chimpanzees. This was an extraordinarily unexpected finding given the 98.5 per cent similarity between the human and chimpanzee genomes and extensive similarities at the cellular and organism level.



Professor McVean explains: "Genetic recombination has been likened to shuffling a deck of cards, which ensures that children are given a different genetic 'hand' than their parents. We know that in many cases recombination occurs where a particular thirteen letter sequence is present – this is like a run of hearts from ace to king determining where we cut the deck of cards. Because humans and chimpanzees are genetically very similar, we might explain that you can only 'cut the cards' at the same point – in fact, we find that this is not true."

Recent research found that a protein called PRDM9 binds to the 13 letter DNA motif; this protein is thought to play a central role in identifying where recombination events can occur in humans and other species. However, the gene that produces this protein differs significantly between humans and chimpanzees, and even within chimpanzees. The researchers believe this may explain the lack of overlap – the difference in the PRDM9 gene is likely to lead to the proteins targeting different locations for recombination within the chimpanzee and human genomes.

Professor Donnelly says: "This is an exciting difference between humans and chimpanzees. PRDM9 is potentially one of the fastest evolving genes since humans split from chimpanzees 6.5 million years ago. It supports studies which suggest that the gene somehow determines where recombination occurs."

PRDM9 has been linked previously to speciation in mice – two similar animals are defined as separate species if they are unable to mate together to produce viable offspring. When the gene was switched off in mice, they were rendered infertile.

Even though the recombination hotspots differ in location between humans and chimpanzees, the rate of recombination events is similar in humans and <u>chimpanzees</u>. However, the process has been disrupted



where chromosomes have undergone major rearrangements in evolution – for example, the human chromosome 2 is a fusion of two separate chimpanzee chromosomes, and this affects the rate of recombination events at this part of the genome.

Oliver Venn, a Wellcome Trust DPhil student at the University of Oxford, adds: "This is the first genome-wide study of genetic variation in our closest living relatives. Whilst, the aim of the research is to improve our understanding of recombination and how it has evolved, it may well tell us something about how and why new species arise."

**More information:** Auton, A et al. A fine-scale chimpanzee genetic map from population sequencing. *Science Express*; e-pub 15 March 2012

Provided by Wellcome Trust

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