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Distribution of recombination hotspots in human genome the comparison of computer simulations and real data

Analyses of meiotic recombination between homologous human chromosomes revealed the uneven distribution of recombination events along the chromosomes. This phenomenon has been observed in different genomic scales. At the megabase scale, the mean recombination rate is higher in the sub-telomeric regions than in the middle parts of chromosomes. On the other hand, at the finer scale, recombination events tend to cluster into narrow spans of a few kb in length, which are called recombination hotspots. These short regions with very high recombination frequency occur also more frequently at the ends than in the centre of chromosome. They were discovered based on high-resolution recombination maps which were inferred from high-density single-nucleotide polymorphism (SNP) data using linkage disequilibrium (LD) patterns. Recently, it has been reported a degenerate 13 bp long motif, CCNCCNTNNCCNC, which is overrepresented inside the human hotspots. Moreover, many experiments suggest that the zinc-finger protein PRDM9 binds to this motif, which can indicate the existence of a common mechanism of recombination regulation. Furthermore, hotspot locations are not shared between human and chimpanzee, which suggests their short lifespan. Understanding the function of recombination hotspots can provide insight into the linkage disequilibrium patterns and help create the accurate linkage map for disease association studies. We have found that many recombination properties, for example the uneven distribution of hotspots, can be predicted and explained by computer simulations of population evolution. Assuming spatial distribution of genes along the chromosomes and finite size of populations, simulations render a perfect picture of recombination observed in the human genome. The obtained results of simulations indicate that the distribution of crossing points are subjected to evolution. Therefore, it is expected that the distribution of the recombination motifs for the hotspot regulation should follow the uneven distribution of recombination events. In order to test our hypothesis, we check the location of the motif along the human chromosomes using both the physical and the genetic map. The analyses showed the correlation between the frequency of recombination and the location of motif. In addition, the examination of the distances between motifs confirmed their non random distribution along the human chromosomes.