

Mutagenic activity of recombination hotspots

Homologous meiotic recombination is localized in small regions known as hotspots. Models about recombination hotspots are incomplete and controversial with several bizarre findings such as the hotspot paradox, rapid hotspot turnover during evolution and what appear to be heritable shifts in how hotspots are recruited for recombination. Hotspots are doomed to disappear before they can spread in the population due to the mechanism of recombination. Yet, hotspots have been around long enough to shape the association of alleles into blocks of high and low linkage disequilibrium. Several explanations regarding this “hotspot paradox” include arguments of trans-activating factors and population genetic mechanisms such as genetic drift. Interestingly, it has been argued that recombination is highly mutagenic. A high mutation activity associated with recombination could play a very important role in the evolution of hotspots, but so far there is not enough information or experimental evidence about the mutagenic activity of recombination in hominoids. In this proposal, I want to study the relationship between mutation and recombination and measure the number of new mutations introduced at recombination hotspots. Single crossovers will be collected and sequenced to identify new mutations. The mutation frequency associated with recombination, as well as the type and position of the mutations will be characterized. The estimates will be used to model the turnover and evolution of hotspots. The results of this work will provide for the first time experimental evidence that recombination hotspots are also mutation hotspots. Proof that mutation and recombination are not independent would have a profound impact in terms of our understanding in how our genomes evolve and are re-shaped by these two forces.

This project will be carried out initially with university funding. Collaborations include the University of Southern California and the University of Vienna regarding modeling and data interpretation.