

Poster A-4

The strength of selection on ultraconserved elements



Authors:

Christina TL Chen (*Washington University at Saint Louis*)

Barak A. Cohen (*Washington University at Saint Louis*)

Short Abstract: Comparative analyses of polymorphisms and fixed differences among human, chimpanzee, and rodents indicate that ultraconserved elements are maintained by relatively weak purifying selection.

Long Abstract:

Ultraconserved elements are stretches of consecutive nucleotides that are perfectly conserved in multiple mammalian genomes. Although these sequences are identical in the reference human, mouse, and rat genomes, we identified numerous polymorphisms within these regions in the human population. To determine whether polymorphisms in ultraconserved elements may affect fitness, we genotyped more than 600 unrelated human DNA samples at loci within these sequences. For all SNPs tested in ultraconserved regions, individuals homozygous for derived alleles (alleles that differ with the mouse and rat reference genomes) were present, viable, and healthy. The distribution of allele frequencies in these human samples argues against strong, ongoing selection as the force maintaining the conservation of these sequences. We used two independent methods to determine the minimum level of selection required to generate sequences with such high conservation. Our data indicate that most ultraconserved regions are under relatively weak purifying selection. Despite the lack of fixed differences in these sequences between humans and rodents, the average level of selection on ultraconserved elements is less than that on essential genes. In addition, a small number of ultraconserved elements show more substitutions than expected, which is a hallmark of positive selection. The strength of selection that is associated with ultraconserved elements suggest that deleting these regions may have only subtle phenotypic consequences not easily detected in the laboratory.