

## GENE CONVERSION AND RETROPOSITION POTENTIAL IN RECENTLY INTEGRATED ALU ELEMENTS

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Alu elements comprise greater than 10% of the human genome. We have employed computational biology to analyze the human genomic DNA sequence databases to determine the impact of gene conversion on the sequence diversity of recently integrated Alu elements, and to identify Alu elements that were potentially retroposition competent. We analyzed 269 Alu Ya5 elements and identified 23 members of new Alu subfamily termed Ya5a2 with an estimated copy number of 35 members, including the *de novo* Alu insertion in the NF1 gene. Our analysis of Alu elements containing one to four (Ya1-Ya4) of the Ya5 subfamily-specific mutations demonstrates that gene conversion contributed as much as 10-20% to the nucleotide diversity of recently integrated Alu elements. In addition, analysis of the middle A-rich region of the different Alu Ya5 members indicates a tendency toward expansion of this region and subsequent generation of simple sequence repeats. Mining the databases for putative retroposition competent elements that share 100% nucleotide identity to the previously reported *de novo* Alu insertions linked to human diseases resulted in the retrieval of 13 exact matches to the NF1 Alu repeat, three to the Alu element in BRCA2, and one to the Alu element in FGFR2 (Apert syndrome). Transient transfections of the potential source gene for the Apert's Alu with its endogenous flanking genomic sequences demonstrated the transcriptional and presumptive transpositional competency of the element.