

Transcript variation: a new layer of complexity in expression analysis

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Abstract:

Alternative transcription, a catch-all phrase encompassing differential mRNA processing (splicing and polyadenylation) and alternative transcriptional start sites, is widespread among human and other complex, eukaryotic genomes. Thanks to alternative transcription, a single gene can produce multiple mRNA variants containing different regions of gene sequence. These differences between variants can have profound effects on gene function when they affect protein-coding regions or RNA sequence motifs important for message localization, transport, or stability. To study the effects of alternative transcription on protein, a data-mining method was developed that identifies genes in which the composition of conserved amino acid motifs differs between proteins encoded by the same gene. Briefly, this method uses high-quality cDNA-to-genome alignments, protein annotations, and gene classification rules to identify variants that delete or remodel conserved amino acid motifs. In one study, this method revealed that alternative transcription disrupts conserved motifs in over 30% of multi-variant human genes. Since these conserved motifs are likely to affect protein function, this result suggests that mRNA processing events that disrupt these regions are regulated by global or gene-specific mechanisms. Understanding how alternative transcription is regulated represents an important challenge facing modern-day molecular biology. New avenues for research that explore this area will be presented, including genome-based, re-analysis of micro-array data; EST data-mining; and data visualization techniques that show protein annotations in the context of genomic sequence.

Biography

Ann Loraine received her Ph.D. degree in Molecular and Cell Biology from the University of California at Berkeley, where she did research in plant biology. Intrigued by research opportunities in genomics, she did postdoctoral work in bioinformatics at the Berkeley Drosophila Genome Project. In 1999, she joined Neomorphic, a small bioinformatics company founded by colleagues from B.D.G.P. Following Neomorphic's acquisition by Affymetrix in 2000, she rejoined the new company as a Staff Bioinformatics Scientist. Together with colleagues in the Bioinformatics Dept., she published several articles on structure-based genome annotation, alternative transcription, and data visualization for genomics. Since leaving Affymetrix in July, 2003, she has been enjoying some time off and looks forward to pursuing new projects in computational biology in 2004.