

Global insights from microarray profiling of mammalian alternative splicing

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Recent large-scale analyses of transcript sequence and microarray data have begun to provide fundamental insights into the global properties of alternative splicing in metazoans. We have developed custom microarrays and computational tools for the global-quantitative analysis of alternative splicing patterns in mammalian cells and tissues. From profiling a diverse range of cell and tissue types, as well as cells grown under different physiological conditions, we have uncovered sets of regulated alternative exons that are concentrated in genes which operate in specific biological processes and pathways. A reoccurring observation is that primarily non-overlapping subsets of functionally-associated genes display cell/tissue-type or condition-dependent regulation at the levels of alternative splicing and transcription. The data from these studies is facilitating the identification of elements of the "code" underlying regulated alternative splicing patterns. We have also applied our quantitative profiling system to compare the alternative splicing patterns of orthologous exons in different mammalian species, including human and chimpanzee. These studies are providing among the first insights into the sets of genes which display patterns of alternative splicing that have diverged within relatively short evolutionary time intervals. Results from the above areas of investigation will be presented.