Comparative deep sequencing survey of alternative splicing in human and mouse

D. Pervouchine, S. Djebali, A. Breschi, J. Lagarde, T. Gingeras, R. Guigó

We perform comparative analysis of alternative splicing by using RNA-seq data in 16 human cell lines and 30 mouse tissues. Approximately 75% of internal exons of human protein-coding genes have orthologs in mouse and vice versa. In the annotation alone there is evidence for conservation of alternative splicing: exons that are annotated alternative in one species tend to be annotated alternative in the other species. There is a negative correlation between the strengths of the consensus sequences at a splice junction and the variability of splicing ratio (percent-spliced-in,PSI) as measured by RNA-seq. This correlation is more prominent for donor sites compared to acceptor sites because the latter have more degenerate consensus sequences. Despite having biologically different samples the variability of splice junction usage is to large extent conserved between human and mouse. At the same time, splice junctions that are annotated as alternative are used more variably in the cognate species than in non-cognate species. There is evidence for conservation of association between splicing factor expression levels and splicing ratios of alternative splice junctions. At the same time, splicing regulatory networks inferred from these associations have different modular structure presumably reflecting different activated pathways in tissues and cell lines. In spite of different annotation depths, the relative contributions of major types of elementary splicing events in human and mouse are very similar. Of these, the most frequent in human are exon skipping (50%), alternative acceptor site usage (13%), alternative donor site usage (9%), multiple-exon-skipping (6%), and intron retention (5%).