

mRNA diversity of genes by alternative splicing during neuronal differentiation of NT2 pluripotential human embryonal carcinoma cells by all-trans retinoic acid.

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ABSTRACT

To elucidate cause of disease related to neuronal differentiation, we analyzed genes and the protein-coding transcripts by alternative splicing (AS) using human NT2 teratocarcinoma cells which differentiates toward a neuron by all-trans retinoic acid (RA) induction. Gene could produce multiple protein-coding transcripts by AS. It was known that AS particularly occurs in the mammalian nervous system and plays an important role in neuronal differentiation in generating biological and functional diversity. Using DNA microarray of NT2 cells after RA induction, 358 RA-responsive genes were extracted. To understand functions of RA-responsive genes accurately, it was necessary to analyze the mRNA diversity of them. Using our FLJ Human cDNA Database, we identified 274 genes which produced multiple protein-coding transcripts by AS. Among these genes, we chose 58 genes that showed AS of alternative N-terminus, alternative C-terminus and/or alternative cassette-exon for further analysis by quantitative real-time PCR. Then we identified 42 genes which showed different RA-induced changes in the expression of their protein-coding transcripts. Furthermore, we analyzed the human mRNA diversity and consequently sequenced and identified 11,769 human full-length cDNAs whose predicted ORFs were different from other known full-length cDNAs at that point. Our analysis, which particularly focused on multiple variable first exons (FEVs) formed due to the alternative utilization of TSSs, led to the identification of 156 genes, expressed in tissue-specific manner. Among these genes, we chose 51 genes that showed AS of alternative N-terminus for further analysis by quantitative real-time PCR. Then we identified 26 genes which showed different RA-induced changes in the expression of their protein-coding transcripts. Accumulating findings such as described above on mRNA diversity of genes, we could obtain various finding on neuronal differentiation.