Analysis of abnormalities in gene expression and splicing patterns of spinocerebellar ataxia type 6 knockin mice using RNA-seq

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Keywords: RNA-seq, spinocerebellar ataxia type 6, alternative splicing

Spinocerebellar ataxia (SCA) is a neurodegenerative disease characterized by a loss of motor coordination and balance capability. SCA is one of the polyglutamine (poly-Q) diseases including subtypes of SCAs and Huntington disease. Among them, SCA6 is late-onset autosomal dominant neurodegenerative disease caused by a poly-Q expansion in CACNA1A gene that encodes Cav2.1 voltage-gated calcium channel subunit. [1] Since there is no treatment for this congenital disease, the development of novel therapies is strongly needed. It has been reported that the poly-Q expansion causes Purkinje cell degeneration, but the detailed pathogenesis pathway is still unclear. Therefore, we developed a knockin mouse model that had a 118 CAG repeat tract (118Q) in CACNA1A and investigated abnormalities in gene expression and splicing patterns in this model mice. [2]

In this research, we aimed to analyze genes differentially expressed and spliced between cerebellar tissues of a wild-type mouse and an SCA6 model mouse. We obtein 1.6 hundred million reads (16 billion bases) from the wild-type and 1.5 hundred million reads(15.3 billion bases) from the SCA6 model mouse using HiSeq 2000 (Illumina).The TopHat package[3] was used for the alignment of the short reads to the mm10 reference genome, followed by Cufflinks[4] for transcript assembly RNA expression and alternative splicing analysis.We investigated several genes and pathways that might be associated with pathogenesis of SCA6 such as degeneration of Purkinje cells.

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