

# Phenotypic and Expression Analysis of a Novel Spontaneous Myosin VI Null Mutant Mouse

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### Abstract :

In humans, hearing is a major factor in quality of life. Mouse models are important tools for the discovery of genes responsible for genetic hearing loss, often enabling analysis of the processes that regulate the onset of deafness in humans. Thus far, at least 400 deafness mutants have been discovered in laboratory mouse populations and used in the study of deafness. Here we report the discovery of a new spontaneous recessive Rinshoken shaker/waltzer (*rsv*) mutant derived from our in-house C57BL/6J stock, which exhibits circling and/or head-tossing behaviour and complete lack of auditory brain response to any sound pressure. The hearing and balance phenotypes are associated with structural defects, in particular, disorganisation and fusion of stereocilia in the inner ear hair cells. Two sets of intersubspecific N<sub>2</sub> mice were generated for the positional cloning of the *rsv* mutation. The mutant locus was mapped to a 4.8-Mb region of chromosome 9, which contains myosin VI (*Myo6*), a gene responsible for deafness in humans and Snell's waltzer mutation in mice. The *rsv* mutant showed reduced expressions of *Myo6* mRNA and MYO6 protein in the inner ear. Moreover, no immunoreactivity was observed in the cochlear and vestibular hair cells in the *rsv* mutant mice. We sequenced the genomic region (30,154 bp) of *Myo6*, including all coding exons, a non-coding exon, UTRs and the *Myo6* promoter; however, no mutation was discovered in these regions. We therefore speculate that loss of MYO6 expression might cause shaker/waltzer behaviour and deafness in the *rsv* mutant; also, loss of MYO6 expression might be the result of mutations in an unidentified regulatory region(s) of the gene.

### Key Word :

deafness, inner ear hair cell, mouse mutant, myosin VI, stereocilia

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