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A 40 Kb Genomic Deletion Including *tmie* (Transmembrane Inner Ear Protein) Gene Causes Deafness, Circling and Head Tossing in Circling Mice

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Abstract

Circling (*cir*) mouse is a spontaneous mutant in the inner ear that was first reported in Korea. The mutation is transmitted by an autosomal recessive gene with 100 %- penetrance.. Homozygous mice are characterized by head-tossing, bi-directional circling behavior and deafness. Histologicalexamination of the inner ear reveals abnormalities of the region around the organ of Corti, spiral ganglion neurons, and outer hair cells. In the previous study, the *cir* gene was mapped to a region between *D9Mit116/D9Mit15* and *D9Mit38* on the mouse chromosome 9 at a site indistinguishable from that of the spinner (*sr*) mouse. Since the *sr* gene of the spinner mouse is closely linked to the *cir* gene, we performed mating experiments to investigate the relationship between the *sr* and *cir* genes using allelism test. We also compared the phenotypes of compound heterozygous (*sr/cir*) to those of circling and spinner homozygous. The results of allelism tests between circling and spinner indicated that *cir* is allelic with *sr*. Originally the *sr* allele consists of 40 kb genomic deletion including *tmie* (transmembrane inner ear protein). In our study of *tmie* expression analysis demonstrated that *cir* allele also have 40 kb defective genomic sequence including *tmie* gene. Further characterization of the impact of *tmie* mutations in the inner ears of circling mice will provide insight into pathways that are critical for normal maturation of sensory cell function. Since the cir locus is homologous to DFNB6, human deafness locus, analysis of circling and spinner will also help to define the molecular mechanism of hearing loss in humans with defects at the DFNB6 locus, and will provide a system in which to investigate potential therapies that rescue sensory cells and preserve auditory function.

Key words: ***Circling mice, Deafness, Spinner mouse***