Abstract

Loss of hearing affects more than 10 % of the population, and one newborn in a thousand is born with defects of the inner ear. Transcriptional factors involved in the development of inner ear are important in our understanding of the causes of inner ear defects. ISLET1 is one of these factors. ISLET1 expression is detected in the sensory and neuronal cells of the inner ear. It participates in otocyst formation, and the specification and differentiation of cells of cochlea and vestibular system. The functional role of ISLET1 during inner ear development was investigated. Its role was studied by using *Pax2-Isl1* transgenic mice that overexpress *Islet1* under the control of the Pax2 promoter. Two transgenic lines were generated, *Pax2-Isl1/300* and *Pax2-Isl1/52*. Two copies of the *Pax2-Isl1* transgene were inserted to *Pax2-Isl1/300* genome and one copy was inserted to the *Pax2-Isl1/52* genome. Defects in sense of hearing were detected in both lines and circling behavior, a defect of balance, was detected in the *Pax2-Isl1/300* transgenic mice. We observed high postnatal lethality in heterozygote transgenic mice. *Pax2-Isl1/52* homozygote mutation is lethal at embryonic day 10 (E10,5). *Pax2-Isl1/300* homozygote letality couldn´t be detected because of the inability to breed heterozygote mutated mice of this line. Insertion of *Pax2-Isl1* transgene leads to increasing ISLET1 expression in the ventral part of otocyst, the part closest to the statoacoustic ganglion, and in the medial part with significant expression of PAX2. An increase of ISLET1 expression was also detected in the neuronal cells inervating the cochlear duct at embryonic day 13 (E13.5). No expression changes were found in the sensory part of forming cochlear duct or the sacculus, a vestibular organ, at embryonic day (E13.5). It was confirmed that ISLET1 is a transcription factor involved in the development of the inner ear, and that ISLET1 overexpression initiates phenotypic and functional changes of sensory organs of the developing inner ear.

Key words

Cochlear duct, Myosin VIIa, PAX2, otocyst, sacculus, transgenic model Pax2-Isl1, transcriptional factor