Abstract

Identification of transcription factors involved in a complex network regulating the development of neurosensory cells in the inner ear is a key point for understanding the pathophysiology of hearing loss, development of new therapeutic tools, and for hearing loss prevention. The aim of this thesis was to elucidate the function of the transcription factor NEUROD1 in the development of the inner ear and sensory neurons. Using the Cre-loxP recombination system, a unique mouse model was created with tissue-specific deletion of *Neurod1* in NEUROD1-Cre positive cells (*Neurod1ST*). In the inner ear, *Neurod1* was deleted only in neurons permitting to identify the secondary effects of *Neurod1* elimination in neurons on sensory cell development. We showed that neither the early development of the inner ear nor the formation of the statoacoustic ganglia was significantly affected by *Neurod1* deletion. The primary consequence of the deletion was manifested by increased neuronal death due to apoptosis, which resulted in a reduced number of differentiated neurons in the inner ear. Spiral and vestibular ganglia were smaller in the mutants, and there was a number of neurons misplaced, indicating impaired migration. The cochlear sensory epithelium was shortened probably due to the reduced number of neurons within the spiral ganglion. Correspondingly, the size of all vestibular organs was smaller in the inner ear of *Neurod1* mutant. Furthermore, decreased expression of selected genes encoding transcription factors, signaling molecules, and receptors that play an important role during the development of the inner ear and inner ear neurons have been identified. These results confirm an important role of the transcription factor NEUROD1 in the formation of spiral ganglion, migration and survival of neurons, as well as the formation of cochlear innervation.

Key words: neurons, inner ear, bHLH transcription factor NEUROD1, Cre-loxP system, mouse model