Abstracts of the Thirty-First Annual MidWinter Research Meeting of the

Association for Research in Otolaryngology

February 16-21, 2008

Phoenix, Arizona, USA

Peter A. Santi, PhD
Editor

Association for Research in Otolaryngology
19 Mantua Road, Mt. Royal, NJ 08061 USA

hat share some common progenitors. Sox2 is required for hair and supporting cell formation, but its role in sensory neurons, which require Neurog1 for specification, is unknown. Sox2, like Neurog1, is transiently expressed in delaminating neuroblasts. in Neurog1 null mice Sox2 is normally expressed. When Sox2 is deficient, Neurog1 is expressed and sensory neurons develop and reach with their processes areas where sensory epithelia would normally develop but soon disappear due to lack of neurotrophic support. Our data implies specification and initiation of differentiation of otic sensory neurons does not require Sox2 and is independent of development of sensory epithelia. Sox2 is however essential for maintenance of innervation and may complement but acts independently of Neurog1. Sox2 may also have a dose-dependent role in regulating the pattern of neuronal fiber outgrowth in the inner ear.

108 Sox10 is not Necessary for Auditory Neurons Survival

Ingrid Breuskin[1], Morgan Bodson[1], Nicolas Thelen[1], Marc Thiry[1], Philippe Lefebvre[1], Brigitte Malgrange[1]

[1]*CNCM - University of Liege - Belgium*

Sox10 is a HMG domain transcription factor required for proper development of neural crest cell derivatives, including melanocytes and peripheral glia. Sox10-null mutations lead to a complete absence of these derivatives, and Sox10 haploinsufficiency results in neural crest defects that causes Waardenburg-Shah syndrome in humans.

Although studies have shown the role of Sox10 in the development of the neural crest cells, its function in auditory system development is unclear. During inner ear development, Sox10 expression is first detected in the otic placode and persisted throughout its development. Sox10 is also expressed in the glial cells of the cochleo-vestibular ganglion and spiral ganglion. in Sox10-null mutant mice, spiral ganglion glial cells and melanocytes are missing. in the absence of these neural crest-derived cells, we have investigated the fate of the otocyst-derived inner ear sensory neurons. Loss of Sox10 function does not alter their morphology and does not cause reduction in their number. Our data demonstrate that as previously described in the peripheral nervous system, the neural crest-derived cells of the inner ear are missing in the Sox10-null mutant mice. But in contrast to the peripheral nervous system, our results also suggest that glial cells and Sox10 do not play a primary role in auditory neurons development and survival in the developing inner ear.

109 Functional Analysis of GATA-2 in Auditory and Neuronal System

Tomofumi Hoshino[1], Keiji Tabuchi[1], Ritsuko Shimizu[1], Masayuki Yamamoto[2], Akira Hara[1]

[1]*University of Tsukuba,* [2]*Tohoku University*

Because inner ear arises from otic vesicle under the regulation of external signal from the neural tube, both otic vesicle and neural tube are important for the inner ear development. Because transcription factor GATA-2 is expressed in both tissues, elucidation of Gata2 gene regulation is important for the understanding of inner ear development. However, roles of GATA-2 is not clarified yet, because of the embryonic lethal phenotype of Gata2 gene knockout mice. Therefore, we used the conditional knockout (CKO) system to overcome embryonic lethality.

We crossed the Gata2 flox mouse with the Nestin-Cre mouse, in which Cre recombinase is expressed specifically in neural tissues. the Gata2 CKO mice with both Gata2 flox allele and Nestin-Cre transgene were born normally and grew up to adult. We examined the ABR thresholds of 10 weeks old mice. ABR thresholds were significantly higher in Gata2 CKO mice than those of the control mice. Significant reduction of spiral ganglion cells (SGC) was observed in adult Gata2 CKO mice in the histological examination. Surprisingly SGC reduction was clearly observed in newborn pups, indicating that Gata2 CKO mice suffered from hearing impairment. On the other hand, there was no remarkable change in the organ of the Corti and the cochlear nucleus of brain stem. These results indicate that the GATA-2 is important for the inner ear development through the regulation of SGC proliferation in the embryonic period.

110 The Role of Gata3 in the Development of Auditory Neurons in Chick Inner Ear

Jennifer Jones[1], Mark Warchol[1]

[1]*Washington University*

During development of the otocyst, neuroblasts delaminate from the anteroventral region of the otic epithelium to form the auditory-vestibular ganglion (AVG) that will innervate the sensory cells of the cochlea and vestibular organs respectively. the molecular basis of cell-fate specification between auditory vs. vestibular neurons is unresolved. It has been reported that the expression of the zinc finger transcription factor Gata3 distinguishes neuroblasts destined for an auditory fate while the bHLH transcription factor, NeuroD, designates vestibular neurons (Lawoko-Kerali et al., 2004). the aim of this study was to examine the potential role of Gata3 in specifying auditory neurons. First, we examined the expression of Gata3 and NeuroD in the AVG at embryonic days E2-E7. During invagination of the otic cup (E2), Gata3 expression was restricted to the lateral wall. Following closure of the otic cup (E2.5-E3.5), Gata3 expression was detected in the lateral wall as well as the anteroventral region of the otocyst, at the site of neuroblast delamination. Notably, we observed two apparently separate populations of neuroblasts (that express either Gata3 or NeuroD) within the region of delaminating cells. As the AVG separates into the auditory ganglion and vestibular ganglion, Gata3 was restricted to auditory neurons while NeuroD was restricted to vestibular neurons. These expression data are consistent with the notion that Gata3 plays a role in specifying auditory neurons. Prior studies of Gata3 null-mutant mice suggest that GATA3 is necessary for the development of auditory neurons (Karis et al., 2001). We are currently investigating the role of Gata3 in the specification of auditory neurons by ectopically expressing Gata3 in the developing chick ear in ovo.