All Akt Isoforms (Akt1, Akt2, Akt3) Are Involved in Normal Hearing, but Only Akt2 and Akt3 Are Involved in Auditory Hair Cell Survival in the Mammalian Inner Ear

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Author(s) Brand, Y.; Levano, S.; Radojevic, V.; Naldi, A. M.; Setz, C.; Ryan, A. F.; Pak, K.; Hemmings, B. A.; Bodmer, D.
Author(s) at UniBasel Bodmer, Daniel ;
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The kinase Akt is a key downstream mediator of the phosphoinositide-3-kinase signaling pathway and participates in a variety of cellular processes. Akt comprises three isoforms each encoded by a separate gene. There is evidence to indicate that Akt is involved in the survival and protection of auditory hair cells in vitro. However, little is known about the physiological role of Akt in the inner ear-especially in the intact animal. To elucidate this issue, we first analyzed the mRNA expression of the three Akt isoforms in the inner ear of C57/BL6 mice by real-time PCR. Next, we tested the susceptibility to gentamicin-induced auditory hair cell loss in isoform-specific Akt knockout mice compared to wild-types (C57/BL6) in vitro. To analyze the effect of gene deletion in vivo, hearing and cochlear microanatomy were evaluated in Akt isoform knockout animals. In this study, we found that all three Akt isoforms are expressed in the cochlea. Our results further indicate that Akt2 and Akt3 enhance hair cell resistance to ototoxicity, while Akt1 does not. Finally, we determined that untreated Akt1 and Akt2/Akt3 double knockout mice display significant hearing loss, indicating a role for these isoforms in normal hearing. Taken together, our results indicate that each of the Akt isoforms plays a distinct role in the mammalian inner ear.

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