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PASIREOTIDE, A SOMATOSTATIN ANALOGUE AS NOVEL TREATMENT FOR HEARING LOSS

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Sensory hair cells in the inner ear are the primary receptors of auditory signals and hair cells degeneration is the primary event in most cases of hearing loss. Gentamicin is a widely used antibiotic for the treatment of gram-negative bacterial infections; although, its use often results in significant and permanent hearing loss. Strategies to overcome the apparently irreversible loss of hair cells in mammals are crucial for hearing protection. Here author report that the somatostatin analogue pasireotide protects mouse cochlear hair cells from gentamicin damage using a well-established *in vitro* gentamicin-induced hair cell loss model, and that the otoprotective effects of pasireotide are due to Akt up-regulation via PI3K-Akt signal pathway activation. They demonstrate active caspase signal in Organ of Corti explants exposed to gentamicin and show that pasireotide treatment activates survival genes, reduces caspase signal and increases hair cell survival. The neuropeptide somatostatin and its selective analogues have provided neuroprotection by activating five somatostatin receptor (SSTR1-SSTR5) subtypes. Pasireotide has high affinity for SSTR2 and SSTR5 and addition of SSTR2- and SSTR5-specific antagonists lead to a loss of protection. The otoprotective effects of pasireotide were also observed in a gentamicin-injured animal model. *In vivo* studies showed that 13 days of subcutaneous pasireotide application prevents gentamicin-induced hair cell death and permanent hearing loss in mice. Auditory brainstem response analysis confirmed the protective effect of pasireotide, and they found a significant threshold shift at all measured frequencies (4, 8, 16, 24 and 32 kHz). Together, these findings indicate that pasireotide is a novel otoprotective peptide acting via the PI3K-Akt pathway and may be of therapeutic value for hair cell protection from ototoxic insults.

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