

(ABRs) between 8–30 kHz were tested over 16 weeks. ABR thresholds, amplitudes and latencies were measured to assess for ototoxicity; cytochleograms to identify any cochlea hair cell loss and middle ear histology carried out for evidence of inflammation.

Results: At one week post insertion of antibiotic laden pellets marked ABR threshold elevation (15–40 dB) was observed ($P < 0.002$ – 0.0001) against control groups. Persistent significant elevation (25–40 dB) was apparent at 8 and 30 kHz at week 16 with some partial mid frequency recovery. No significant changes in ABR wave amplitudes and latencies were seen. Representative cytochleograms did not exhibit frank hair cell loss and middle ear histology revealed pellet remnants causing a moderate inflammatory response at 16 weeks.

Conclusions: This novel pattern of threshold elevation in the absence of frank hair cell loss has not been reported previously. The lack of significant changes in ABR latency and amplitude suggests the ototoxic effects are localised to the inner ear without accompanying neurotoxicity. Clinically, this study suggests that rifampicin and clindamycin laden pellets may not be safe to treat OME *in vivo*.

Learning Objectives: This study demonstrates that middle ear pellets laden with rifampicin and clindamycin cause an ABR threshold elevation and middle ear inflammatory response in guinea pig animal models.

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Free Papers (F812)

ID: 812.3

Wnt activation protects against neomycin-induced hair cell damage in the mouse cochlea

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Learning Objectives:

Recent studies have reported the role of Wnt/ β -catenin signaling in hair cell (HC) development, regeneration, and differentiation in the mouse cochlea; however, the role of Wnt/ β -catenin signaling in HC protection remains unknown. In this study, we took advantage of transgenic mice to specifically knock out or over-activate the canonical Wnt signaling mediator β -catenin in HCs, which allowed us to investigate the role of Wnt/ β -catenin signaling in protecting HCs against neomycin-induced damage. We first showed that loss of β -catenin in HCs made them more vulnerable to neomycin-induced injury, while constitutive activation of β -catenin in HCs reduced HC loss both *in vivo* and *in vitro*. We then showed that loss of β -catenin in HCs increased caspase-mediated apoptosis induced by

neomycin injury, while β -catenin overexpression inhibited caspase-mediated apoptosis. Finally, we demonstrated that loss of β -catenin in HCs led to increased expression of Foxo3 and Bim along with decreased expression of anti-oxidant enzymes; thus, there were increased levels of reactive oxygen species (ROS) after neomycin treatment that might be responsible for the increased aminoglycoside sensitivity of HCs. In contrast, β -catenin overexpression reduced Foxo3 and Bim expression and ROS levels, suggesting that β -catenin is protective against neomycin-induced HC loss. Our findings demonstrate that Wnt/ β -catenin signaling plays an important role in protecting HCs against neomycin-induced HC loss and thus might be a new therapeutic target for the prevention of HC death.

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Free Papers (F812)

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A comparative study evaluating the utility of EGF, FGF-2, and ofloxacin drops on eardrum regeneration

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Learning Objectives:

Objective: We compared the effects of epidermal growth factor (EGF), fibroblast growth factor-2 (FGF-2), 0.3% (w/v) ofloxacin drops, and conservative observation (only), on the healing of traumatic tympanic membrane perforations (TMPs).

Study design: A prospective, randomised, controlled clinical study.

Setting: A University-affiliated teaching hospital.

Subjects and Methods: All patients had traumatic TMPs covering >25% of the entire tympanic membrane. The closure rates, closure times, and rates of otorrhoea in patients who were treated with EGF, FGF-2, or 0.3% (w/v) ofloxacin drops, and who underwent conservative observation only, were compared.

Results: At the 6-month follow-up, the closure rates did not significantly differ among the groups ($P = 0.170$). Similarly, pairwise comparisons did not reveal any significant between-group differences ($P > 0.0083$). The mean closure time differed significantly among the four groups ($P < 0.001$); pairwise comparisons showed that the mean closure time was significantly longer in the observational group than in the test groups ($P < 0.001$). However, no significant difference in mean closure time was evident between any two experimental groups ($P > 0.0083$).

Conclusion: Topical application of EGF, FGF2, and ofloxacin drops accelerated the closure of large human traumatic TMPs. Surprisingly, neither the closure rate nor closure time differed significantly among the three test groups. This results indicate that topical application of ofloxacin drops aids in the healing of traumatic TMPs and should be considered as an alternative treatment option.