



### References on the Administration to the Ear Using ALZET® Osmotic Pumps

- Q7262:** C. P. Richter, *et al.* Fluvastatin protects cochleae from damage by high-level noise. *Sci Rep* 2018;8(1):3033  
**ALZET Comments:** Fluvastatin; DMSO, Ringer's Solution; Ear (cochlea); Guinea Pig; 2004; 28 days; Dose (fluvastatin 50 µM); Dose (fluvastatin 50 µM); animal info (Outbred Hartley guinea pigs of both sexes 200–500 g); post op. care (Buprenex); Cannula used;.
- Q6165:** C. K. Kandathil, *et al.* Effects of brain-derived neurotrophic factor (BDNF) on the cochlear nucleus in cats deafened as neonates. *Hear Res* 2016;342(134-143)  
**ALZET Comments:** Brain-derived neurotrophic factor, recomb. human; Perilymph, artificial; Ear (cochlea); Cat; 1002, 2004; 10 weeks; Dose (94 mg/ml; 0.25 ml/hr); pumps replaced after 2 and 4 weeks; BDNF stability verified by neuronal cell culture survival assay (28 days);.
- Q4838:** H. JIA, *et al.* PREVENTION OF TRAUMA-INDUCED COCHLEAR FIBROSIS USING INTRACOCHLEAR APPLICATION OF ANTI-INFLAMMATORY AND ANTIPROLIFERATIVE DRUGS. *neuroscience* 2016;316(261-278)  
**ALZET Comments:** Dexamethasone; Ara-C; Perilymph, artificial; Ear (cochlea); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (Wistar, adult); animal info (Wistar, adult); stability verified by (incubation in 37C saline for 7 days see pg 268); one cochlea received vehicle only, while other received drug;.
- Q7008:** M. Y. Lee, *et al.* Continuous topical drug delivery using osmotic pump in animal cochlear implant model: Continuous steroid delivery is effective for hearing preservation. *Acta Otolaryngol* 2015;135(8):791-8  
**ALZET Comments:** Dexamethasone; Saline; Ear (cochlea); Guinea pig; 1007D; 7 days; Dose (4 mg/ml); Controls received mp w/ vehicle; animal info (female Harley Albino guinea pigs, 255–455 g, 7–9 weeks old); dependence;.
- Q4141:** Y. Tona, *et al.* Therapeutic potential of a gamma-secretase inhibitor for hearing restoration in a guinea pig model with noise-induced hearing loss. *BMC NEUROSCIENCE* 2014;15(U1-U8)  
**ALZET Comments:** MDL28170; DMSO; PBS; Ear (cochlea); Guinea pig; 1002; 14 days; Controls received mp w/ vehicle; animal info (Hartley strain, 350-400g); 0.3% DMSO used; tissue perfusion (cochlea); used Teflon tube with inner diameter of 180 µm to cannulate cochlea; MDL28170 is a gamma-secretase inhibitor;.
- Q3985:** G. Malkoc, *et al.* Histopathological and audiological effects of mechanical trauma associated with the placement of an intracochlear electrode, and the benefit of corticosteroid infusion: prospective animal study. *Journal of Laryngology and Otology* 2014;128(702-708)  
**ALZET Comments:** Dexamethasone; Saline; Ear (round window); Rat; 14 days; Controls received mp w/ vehicle; animal info (female, Albino, 250-33g, adult); used ALZET IT catheter to cannulate round window; "Dexamethasone infusion given after implantation of the intracochlear model electrode was more effective for preventing hearing loss than the administration of just one dose of dexamethasone" pg 702;.
- Q6784:** L. Waaijer, *et al.* The Peripheral Processes of Spiral Ganglion Cells After Intracochlear Application of Brain-Derived Neurotrophic Factor in Deafened Guinea Pigs. *OTOLOGY & NEUROTOLOGY* 2013;34(570-578)  
**ALZET Comments:** Brain-derived neurotrophic factor; PBS; Ear (right cochlea); Guinea pig; 2004; 4 weeks; Dose (100 µg/ml); Controls received mp w/ vehicle; animal info (10 healthy albino female guinea pigs (strain: Dunkin Hartley; weighing 250-350 g);.
- Q6721:** P. A. Leake, *et al.* Effects of brain-derived neurotrophic factor (BDNF) and electrical stimulation on survival and function of cochlear spiral ganglion neurons in deafened, developing cats. *J Assoc Res Otolaryngol* 2013;14(2):187-211  
**ALZET Comments:** Brain-derived neurotrophic factor, recomb. human; Perilymph, artificial; Ear (cochlea); Cat; 1002; 2004; 10 weeks; Dose (3.75 µg/day); animal info (deafened cats weighing 520-610g); pumps replaced every 2,4 weeks; long-term study; Because the animals were small at the time of implantation (mean body weight, 560 g; range, 520–610 g), a smaller osmotic pump (model #1002) that delivered 14 days of BDNF was implanted initially. Two weeks later, a brief surgical



procedure was performed to replace the initial pump with a larger one containing a 28-day supply of BDNF; this was replaced 1 month later with a final 28-day pump.

**Q3105:** T. G. Landry, *et al.* Chronic neurotrophin delivery promotes ectopic neurite growth from the spiral ganglion of deafened cochleae without compromising the spatial selectivity of cochlear implants. *Journal of Comparative Neurology* 2013;521(12):2818-2832

**ALZET Comments:** Neurotrophin; Brain-derived neurotrophic factor; Ear (cochlea); Guinea pig; 2004; 28 days; Controls received mp w/ artificial perilymph; animal info (young adult, 300-600g); tissue perfusion (cochlea); peptides;.

**Q2425:** H. Toyota, *et al.* A novel treatment for vestibular disorder with FGLM-NH<sub>2</sub> plus SSSR. *Neuroscience Letters* 2012;526(2):128-132

**ALZET Comments:** FGLM-NH<sub>2</sub>; SSSR; Ear (cochlea); Guinea pig; 2002; 14 days; Control animals received mp w/ artificial perilymph; animal info (male, Hartley); FGLM-NH<sub>2</sub> also known as Phenylalanine-Glycine-Leucine-Methionine-Amide; SSSR also known as Serine-Serine-Serine-Arginine; tissue perfusion.

**Q1915:** D. J. Sly, *et al.* Brain-Derived Neurotrophic Factor Modulates Auditory Function in the Hearing Cochlea.

*JARO-JOURNAL OF THE ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY* 2012;13(1):1-16

**ALZET Comments:** Brain-derived neurotrophic factor; Ear (cochlea); Guinea pig; 2004; 4 weeks; Controls received mp w/ Ringers solution; animal info (adult, male, Dunkin-Hartley pigmented, 233-815 g); post op. care (buprenorphine); "Polymers, particularly hydrogels that may be applied directly to the round window, were considered... However, most have a release profile that varies over time, so instead we chose to place a cannula attached to a mini-osmotic pump directly onto the round window." pg 2; tissue perfusion (cochlea, round window niche).

**Q2064:** E. Bas, *et al.* Efficacy of three drugs for protecting against gentamicin-induced hair cell and hearing losses. *British Journal of Pharmacology* 2012;166(6):1888-1904

**ALZET Comments:** Gentamicin; dexamethasone; melatonin; Ear (round window); Rat; 2001; 7 days; Controls received mp w/ saline; animal info (Wistar, male, 220-250 g); stability verified after 7 days (data not shown).

**Q1509:** X. Li, *et al.* Protective Role of Hydrogen Sulfide against Noise-Induced Cochlear Damage: A Chronic Intracochlear Infusion Model. *PLoS One* 2011;6(10):U487-U492

**ALZET Comments:** Sodium hydrosulfide; propargylglycine, DL-; Ear (cochlea); Rat; 2002; Controls received mp w/ artificial perilymph; animal info (Sprague Dawley, 250-350 g); tissue perfusion (cochlear); ALZET mouse jugular catheter used (#0007700); stress/adverse effects, pg e26728 "Two rats died of post-surgical infection, and one rat died of hemorrhage."

**Q1195:** P. A. Leake, *et al.* Brain-Derived Neurotrophic Factor Promotes Cochlear Spiral Ganglion Cell Survival and Function in Deafened, Developing Cats. *Journal of Comparative Neurology* 2011;519(8):1526-1545

**ALZET Comments:** Brain-derived neurotrophic factor, human; Perilymph, artificial; Ear (cochlea); Cat; 1002; 2004; 10 weeks; Controls received mp w/ vehicle; long-term study; animal info (adult, 4 wks old, deafened); functionality of mp verified via residual volume; pumps replaced after two weeks then after 28 days; tissue perfusion (cochlea); "The drug-delivery cannula within the cochlear implant... was connected to vinyl tubing..., which was connected to the regulator of the osmotic pump, which was implanted behind the right pinna."; artificial perilymph recipe.

**Q1178:** T. Kondo, *et al.* Wnt Signaling Promotes Neuronal Differentiation from Mesenchymal Stem Cells Through Activation of Tlx3. *Stem Cells* 2011;29(5):836-846

**ALZET Comments:** Wnt1; brain-derived neurotrophic factor; Ear (cochlea); Gerbil; 2004; 28 days; Controls received mp w/ saline or BDNF only; animal info (Mongolian, 4 mo old); pumps replaced after 72 hours; tissue perfusion (intracochlea).

**Q0954:** L. Abaamrane, *et al.* Intracochlear perfusion of leupeptin and z-VAD-FMK: influence of antiapoptotic agents on gunshot-induced hearing loss. *European Archives of Oto-rhino-laryngology* 2011;268(7):987-993

**ALZET Comments:** Leupeptin; z-VAD-FMK; Ear (cochlea); Guinea pig; 2001; 7 days; Controls received no treatment; animal info (albino, 400-600 g); enzyme inhibitor (caspase); artificial perilymph solution recipe; "A miniature glass pipette with a



ring of glue placed next to the tip to provide a leak-proof seal protecting the cochlea from contamination was connected to the catheter." pg 988; tissue perfusion.

**Q1665:** F. Watanabe, *et al.* Signaling through erbB receptors is a critical functional regulator in the mature cochlea.

European Journal of Neuroscience 2010;32(5):717-724

**ALZET Comments:** PD153035; 4557W; DMSO; artificial perilymph; Ear (cochlea); Guinea pig; 2002; Controls received mp w/ artificial perilymph; animal info (female, pigmented, 250-500 g); functionality of mp verified by residual volume; tissue perfusion (intracochlear); 0.1% DMSO used; enzyme inhibitor (tyrosine kinase).

**Q1391:** A. Warnecke, *et al.* Artemin improves survival of spiral ganglion neurons in vivo and in vitro. NeuroReport

2010;21(7):517-521

**ALZET Comments:** Artemin; brain-derived neurotrophic factor; Ear (scala tympani); Guinea pig; 2002; 28 days; Negative controls received mp w/ artificial perilymph; animal info (deafened, pigmented, 250-450 g); pumps replaced after 14 days; tissue perfusion (scala tympani); pump connected to silicone–polyimide tubing.

**Q1616:** H. N. Lang, *et al.* Chronic Reduction of Endocochlear Potential Reduces Auditory Nerve Activity: Further Confirmation of an Animal Model of Metabolic Presbycusis. JARO-JOURNAL OF THE ASSOCIATION FOR RESEARCH IN

OTOLARYNGOLOGY 2010;11(3):419-434

**ALZET Comments:** Furosemide; Ear (round window niche); Gerbil; 2004; 4 weeks; Controls were untreated; animal info (3-6 mo old, young adult); good methods, pg 421; tissue perfusion (round window).

**Q1685:** A. Fransson, *et al.* Post-Treatment Effects of Local GDNF Administration to the Inner Ears of Deafened Guinea Pigs.

Journal of Neurotrauma 2010;27(9):1745-1751

**ALZET Comments:** Glial-derived neurotrophic factor; Ear (cochlea); Guinea pig; 2002; 4 weeks; Controls received mp w/ artificial perilymph; animal info (deafened); silicone tube used; tissue perfusion (cochlea); pump replaced after 2 weeks; post op. care (lidocaine).

**P9515:** V. Scheper, *et al.* Effects of Delayed Treatment With Combined GDNF and Continuous Electrical Stimulation on Spiral Ganglion Cell Survival in Deafened Guinea Pigs. Journal of Neuroscience Research 2009;87(6):1389-1399

**ALZET Comments:** Glial-derived neurotrophic factor; Ear (cochlea); Guinea pig; 2002; 48 days; Controls received mp w/artificial perilymph; tissue perfusion (cochlea); long-term study; pumps replaced after 13 days; good methods (pg. 1391); animal info (male, pigmented, 250-450 g.); pumps primed; image of pump and electrode cannula device used on fig. 1.

**P9844:** H. Orita, *et al.* Unilateral intra-perilymphatic infusion of substance P enhances ipsilateral vestibulo-ocular reflex gains in the sinusoidal rotation test. Neuroscience Letters 2009;449(3):207-210

**ALZET Comments:** Substance P; neurokinin-1 receptor antagonist; Ear (round window); Guinea pig; 2002; Post op. care (piperacillin sodium); animal info (Hartley); pump was connected to a PE catheter filled with artificial perilymph for a 12-hour delayed infusion; tissue perfusion (round window).

**Q0333:** Y. Nguyen, *et al.* An animal model of cochlear implantation with an intracochlear fluid delivery system. Acta Oto-laryngologica 2009;129(11):1153-1159

**ALZET Comments:** Saline; Ear (cochlea); Guinea pig; 1007D; Controls received pump without electrode implant; animal info (albino, male, 3 to 7 months old, 290-1030 g.); good methods pg 1154; post op. care (enrofloxacin); "the pump was fixed subcutaneously between the scapulae using a vicryl 3/0 suture (Ethicon)" pg 1154; image of pump-electrode device, Fig. 1; tissue perfusion (cochlea).

**Q1126:** Z. Q. Hu, *et al.* Functional Evaluation of a Cell Replacement Therapy in the Inner Ear. OTOTOLOGY & NEUROTOLOGY 2009;30(4):551-558

**ALZET Comments:** Nerve growth factor; Hank's based salt solution; albumin, guinea pig serum; Ear (cochlea); Guinea pig; 2002; Controls received mp w/ vehicle; animal info (pigmented, adult, 270-470 g); pumps replaced after 13 days; post op. care (daily injections of cyclosporin and doxycycline); tissue perfusion.



**P9796:** A. Fransson, *et al.* In Vivo Infusion of UTP and Uridine to the Deafened Guinea Pig Inner Ear: Effects on Response Thresholds and Neural Survival. *Journal of Neuroscience Research* 2009;87(7):1712-1717

**ALZET Comments:** Uridine triphosphate; uridine; Ear (cochlea); Guinea pig; 2002; 25 days; Controls received mp w/ artificial perilymph; pumps replaced on day 13; animal info (pigmented, 280-440 g); tissue perfusion.

**Q0453:** M. J. H. Agterberg, *et al.* Enhanced Survival of Spiral Ganglion Cells After Cessation of Treatment with Brain-Derived Neurotrophic Factor in Deafened Guinea Pigs. *JARO-JOURNAL OF THE ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY* 2009;10(3):355-367

**ALZET Comments:** Brain-derived neurotrophic factor; BSA; Ear (cochlea); Guinea pig; 2004; 4 weeks; Controls were untreated; animal info (albino, female, 250-350 g); pump connected to Cochlear (R) electrode array; tissue perfusion (cochlea).

**P9856:** M. J. Adkesson, *et al.* MEDICAL AND SURGICAL MANAGEMENT OF OTITIS IN CAPTIVE BONGO (TRAGELAPHUS EURYCERUS). *JOURNAL OF ZOO AND WILDLIFE MEDICINE* 2009;40(2):332-343

**ALZET Comments:** Amikacin; Ear; Antelope (bongo); 2ML4; 24 days; Functionality of mp verified by residual volume; animal info (10 years old, male, 326 kg); "An osmotic pump was beneficial for antibiotic delivery in case 2 and may be an effective therapy for low-grade infections or for continued therapy once a severe infection is under control." pg. 340.

**P9292:** R. J. Vivero, *et al.* Dexamethasone Base Conserves Hearing from Electrode Trauma-Induced Hearing Loss. *Laryngoscope* 2008;118(11):2028-2035

**ALZET Comments:** Dexamethasone base; Perilymph, artificial; Ear (scala tympani); Guinea pig; 2001; 8 days; Controls received mp w/ vehicle; replacement therapy (cochleostomy); tissue perfusion (scala tympani); animal info (pigmented, 250-300 g.).

**R0266:** E. E. L. Swan, *et al.* Inner ear drug delivery for auditory applications. *Advanced Drug Delivery Reviews* 2008;60(15):1583-1599

**ALZET Comments:** Cisplatin; Sodium thiosulfate; Brain-derived neurotrophic factor; Fibroblast growth factor; D-JNK1-1; BN82270; Tetrodotoxin; Perilymph, artificial; Dexamethasone; Methylprednisone; Caroverine; Methionine, D-; Thiourea; Liposome, cationic; Neomycin; SC; Ear (round window membrane); Ear (cochlea); Ear (scala tympani); Ear; Guinea pig; 3, 7, 14, 28 days; Gene therapy; peptides; no stress; enzyme inhibitor (peroxidase); stress/adverse reaction (see pg 1593) "Ref #161 found local trauma and inflammatory responses"; tissue perfusion (scala tympani, cochlea, round window membrane); comparison of middle ear injections vs. mp; Review, see pgs. 1587 - 1589, 1591, 1593 - 1595, refs #49, 50, 60, 63, 72, 75, 102, 104, 180, 181, 194-201.

**P9051:** B. N. Song, *et al.* Effects of delayed brain-derived neurotrophic factor application on cochlear pathology and auditory physiology in rats. *Chinese Medical Journal* 2008;121(13):1189-1196

**ALZET Comments:** Brain-derived neurotrophic factor, recomb. human; Albumin, rat; Ringer's solution; Ear (cochlea); Rat; 2004; 28 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague Dawley, 10-12 wks old, 220-250 g.); tissue perfusion (cochlea); functionality of mp verified by residual volume; good methods pg. 1191; pumps were primed in sterile saline at 37 degree Celsius for 48 hours; 1-cm len.

**P9218:** R. K. Shepherd, *et al.* Neurotrophins and electrical stimulation for protection and repair of spiral ganglion neurons following sensorineural hearing loss. *Hearing Research* 2008;242(1-2):100-109

**ALZET Comments:** Brain-derived neurotrophic factor, recomb. human; Ringer's solution; albumin, guinea pig; Ear (scala tympani); Guinea pig; 2004; 4 weeks; Controls received no treatment to contralateral cochlea; functionality of mp verified by residual volume and intact connections; peptides; post op. care (Carprofen, Baytril); tissue perfusion (scala tympani); animal info (pigmented, 400-844 g., kanamycin/furosemide deafened).

**P9224:** J. H. Reyes, *et al.* Glutamatergic Neuronal Differentiation of Mouse Embryonic Stem Cells after Transient Expression of Neurogenin 1 and Treatment with BDNF and GDNF: In Vitro and In Vivo Studies. *Journal of Neuroscience* 2008;28(48):12622-12631



**ALZET Comments:** Doxycycline; brain-derived neurotrophic factor; glial cell line-derived neurotrophic factor; Ear (scala tympani); Guinea pig; 2002; 27 days; Controls received no treatment to contralateral ear; pumps replaced; peptides; tissue perfusion (scala tympani); animal info (NIH strain, 275-315 g., deafened); cannula and catheter contained doxycycline, mp contained BDNF/GDNF (delayed delivery) to follow, thus providing 2 days Dox, 25 days BDNF/GDNF.

**P9306:** R. Panford-Walsh, *et al.* Midazolam reverses salicylate-induced changes in brain-derived neurotrophic factor and Arg3.1 expression: Implications for tinnitus perception and auditory plasticity. *MOLECULAR PHARMACOLOGY* 2008;74(3):595-604

**ALZET Comments:** Midazolam; Ear (round window niche); Rat; 2001; 7 days; Controls received mp w/ artificial perilymph; comparison of systemic injections vs. mp; animal info (female, Wistar, 200-300 g., cochlear trauma); behavioral testing (tinnitus perception via sound/reward); tissue perfusion (round window niche).

**P9760:** E. M. Keithley, *et al.* Tumor necrosis factor alpha can induce recruitment of inflammatory cells to the cochlea. *OTOLOGY & NEUROTOLOGY* 2008;29(6):854-859

**ALZET Comments:** Tumor necrosis factor-alpha; Ear (cochlea); Guinea pig; 2001; 2-4 days; Controls received mp w/vehicle; animal info (Hartley albino); tissue perfusion.

**P9239:** J. A. Harris, *et al.* Afferent Deprivation Elicits a Transcriptional Response Associated with Neuronal Survival after a Critical Period in the Mouse Cochlear Nucleus. *Journal of Neuroscience* 2008;28(43):10990-11002

**ALZET Comments:** Tetrodotoxin; Citrate buffer; Ear (round window niche); Mice; 1003D; 24 hours; Controls received mp w/ saline or no treatment to contralateral side; tissue perfusion (round window niche); comparison of cochlear removal vs. mp; animal info (male, female, C57BL/6J, 21 days old).

**P8368:** J. Wang, *et al.* Inhibition of the c-Jun N-terminal kinase-mediated mitochondrial cell death pathway restores auditory function in sound-exposed animals. *MOLECULAR PHARMACOLOGY* 2007;71(3):654-666

**ALZET Comments:** Jun, c-, N-Terminal kinase Inhibitor-1, D-; peptide, D-TAT; Jun, c-, N-Terminal kinase Inhibitor-1-mutant; Perilymph, artificial; PBS; Ear (round window membrane); Guinea pig; 2001; 7 days; Controls received mp w/ vehicle, or inactive JNKI-1-mutant or TAT-empt peptide or contralateral untreated ear; dose-response (fig 6); comparison of acute infusion vs. hyaluronic acid gel vs.; enzyme inhibitor (c-Jun N-terminal kinase); peptides; animal info (pigmented, 250-300g.; sound trauma); D-JNKI-1 peptide contains a 10-amino acid HIV-TAT transporter sequence to facilitate its entry into cells; tissue perfusion (round window membrane).

**P8738:** P. Roehm, *et al.* Gentamicin uptake in the chinchilla inner ear. *Hearing Research* 2007;230(1-2):43-52

**ALZET Comments:** Gentamicin; Ear (round window); Chinchilla; 2002; 1, 3, 6, 14 days; 4, 8 hours; Comparison of transtympanic injections vs. mp; tissue perfusion (round window); animal info (male, female, chinchilla langier).

**P8080:** H. Nagano, *et al.* Effects of kallidinogenase on ischemic changes induced by repeated intravitreal injections of endothelin-1 in rabbit retina. *Current Eye Research* 2007;32(2):113-122

**ALZET Comments:** Kallidinogenase; Saline; IV (marginal ear vein); Rabbit; 4 weeks; Controls received mp w/ vehicle; ischemia (retinal); animal info (male, New Zealand, 2.5-3.5 kg.).

**P8661:** J. M. Miller, *et al.* Delayed neurotrophin treatment following deafness rescues spiral ganglion cells from death and promotes regrowth of auditory nerve peripheral processes: Effects of brain-derived neurotrophic factor and fibroblast growth factor. *Journal of Neuroscience Research* 2007;85(9):1959-1969

**ALZET Comments:** Brain-derived neurotrophic factor; fibroblast growth factor-1; Perilymph, artificial; albumin, guinea pig serum; Ear (scala tympani); Guinea pig; 2002; 26 days; Controls received mp w/ vehicle; pumps replaced at day 13; peptides; tissue perfusion (scala tympani); animal info (male, female, pigmented, 250-300g, deafened).

**P8402:** J. Maruyama, *et al.* Effects of antioxidants on auditory nerve function and survival in deafened guinea pigs. *NEUROBIOLOGY OF DISEASE* 2007;25(2):309-318

**ALZET Comments:** Trolox; neomycin; ascorbic acid; Perilymph, artificial; sodium bicarbonate; Ear (cochlea); Guinea pig; 2002; 26 days; Controls received mp w/ vehicle; pumps replaced after 14 days; post op. care (doxycycline); animal info



(male, pigmented, 250-400g., neomycin deafening); cannula primed with 10% neomycin solution followed by a small air bubble spacer to allow neomycin infusion for first 2 days; trolox, a vitamin F analogue, and ascorbic acid delivered together in 1 mp; tissue perfusion (cochlea).

**P8724:** R. Hori, *et al.* Pharmacological inhibition of Notch signaling in the mature guinea pig cochlea. *NeuroReport* 2007;18(18):1911-1914

**ALZET Comments:** MDL 28170; DMSO; PBS; Ear (cochlea); Guinea pig; 1002; 14 days; Tissue perfusion (cochlea); enzyme inhibitor (gamma secretase); peptides; animal info (Hartley strain, 350-400g); MDL 28170 is a gamma-secretase inhibitor; 0.3% DMSO used; "a silicon tube (180 micron OD) connected to a micro-osmotic minipump..."

**P8429:** B. L. Frederiksen, *et al.* Does erythropoietin augment noise induced hearing loss? *Hearing Research* 2007;223(1-2):129-137

**ALZET Comments:** Erythropoietin; Ear (round window); Guinea pig; 1007D; 1 week; Controls received mp w/ saline; replacement therapy (noise-induced hearing impairment); comparison of acute admin. vs. mp; peptides; animal info (male, Dunkin-Hartley); tissue perfusion (round window); mp primed 6 hours in 37 Celsius saline; correct catheter placement confirmed.

**P8068:** J. Cafaro, *et al.* Atoh1 expression defines activated progenitors and differentiating hair cells during avian hair cell regeneration. *Developmental Dynamics* 2007;236(1):156-170

**ALZET Comments:** Uridine, bromodeoxy-; PBS; Ear (perilymphatic fluid); Bird (chicken); 2002; 8 days; No stress (see p. 167); Alzet brain infusion kit used; animal info (White Legorn, 5-10 days old).

**P8388:** I. Sendowski, *et al.* Therapeutic efficacy of intra-cochlear administration of methylprednisolone after acoustic trauma caused by gunshot noise in guinea pigs. *Hearing Research* 2006;221(1-2):119-127

**ALZET Comments:** Methylprednisolone; perilymph, artificial; Perilymph, artificial; Ear (scala tympani); Guinea pig; 2001; 14 days; Controls received mp w/ vehicle, or non-implanted ear; dose-response (fig. 1); pumps replaced after 7 days of artificial perilymph; animal info (pigmented, 400-500g., acoustic trauma, gunshot); tissue perfusion (scala tympani).

**R0239:** R. T. Richardson, *et al.* Inner ear therapy for neural preservation. *AUDIOLOGY AND NEURO-OTOLOGY* 2006;11(6):343-356

**ALZET Comments:** Nerve growth factor; NT-3; adenovirus; brain-derived neurotrophic factor; perilymph, artificial; glial-derived neurotrophic factor; ciliary neurotrophic factor; fibroblast growth factor, acidic; fibroblast growth factor-1; fibroblast growth factor-2; fibroblast growth factor, basic; Ear (cochlea); ear (scala tympani); Guinea pig; 1,2,4,8 weeks; 15-60, 11-12, 26 days; Comparison of polymers, hydrogels, gene therapy, cell-based therapy, and injections vs. mp; long-term study; pumps replaced; no stress (see pg. 350); half-life (p. 344), short in blood; gene therapy; peptides; animal info (deafened); Table 2; "The mini-osmotic pump device is ideally suited to studying the effects of neurotrophic factors in the cochlea experimentally." (p. 350); tissue perfusion.

**P8176:** A. Radeloff, *et al.* Brain-derived neurotrophic factor treatment does not improve functional recovery after hair cell regeneration in the pigeon. *Acta Oto-laryngologica* 2006;126(5):452-459

**ALZET Comments:** Brain-derived neurotrophic factor, recomb. human; PBS; albumin, chicken; Hank's solution; Ear (scala tympani); Bird (pigeon); 2002; 8 weeks; Controls received mp w/ vehicle or no treatment to contralateral ear; long-term study; pumps replaced every 14 days; ALZET brain infusion kit used; peptides; animal info (Columba livia, 6 months old, 320-580 grams); deafening of both ears; tissue perfusion (scala tympani).

**P7898:** A. A. Eshraghi, *et al.* D-JNK1 treatment prevents the progression of hearing loss in a model of cochlear implantation trauma. *OTOLOGY & NEUROTOLOGY* 2006;27(4):504-511

**ALZET Comments:** Peptide, D-JNK inhibitor 1; Perilymph, artificial; Ear (cochlea); Guinea pig; 2001; 1 week; Controls received mp w/ vehicle; no stress (see pg.507); enzyme inhibitor (c-Jun N-terminal kinases); peptides; mp primed overnight in 37 celsius ringer solution; "the specificity of this molecule is high and therefore should limit the occurrence of any unwanted side effects." (pg.510); tissue perfusion.



**P7331:** A. K. Wise, *et al.* Resprouting and survival of guinea pig cochlear neurons in response to the administration of the neurotrophins brain-derived neurotrophic factor and neurotrophin-3. *Journal of Comparative Neurology* 2005;487(2):147-165

**ALZET Comments:** Brain-derived neurotrophic factor, recomb. human; NT-3; Ear (scala tympani); Guinea pig; 2004; 28 days; Controls received mp w/ Ringer's solution; cannula patency ascertained by visual inspection; tissue perfusion (scala tympani).

**P7529:** K. Tanaka, *et al.* Post-exposure administration of edaravone attenuates noise-induced hearing loss. *European Journal of Pharmacology* 2005;522(1-3):116-121

**ALZET Comments:** Edaravone; saline; Water; NaOH; Ear (cochlea); Guinea pig; 2002; 12 hours; Controls received no treatment to left ear; pumps replaced, mp w/ saline used then replaced with mp with agent; stability verified for 24 hours; post op. care (antibiotic ointment); animal info (male, Hartley, 300-450 g); tissue perfusion (cochlea).

**P7306:** R. K. Shepherd, *et al.* Chronic depolarization enhances the trophic effects of brain-derived neurotrophic factor in rescuing auditory neurons following a sensorineural hearing loss. *Journal of Comparative Neurology* 2005;486(2):145-158

**ALZET Comments:** Brain-derived neurotrophic factor, recomb. human; perilymph, artificial; Ringer's solution; albumin, recomb. guinea-pig; Ear (scala tympani); Guinea pig; 2004; 28 days; Controls received mp w/ artificial perilymph or untreated contralateral cochlea; functionality of mp verified by residual fluid, cannula connection and patency; no stress (see pg. 155); good methods; peptides; post op. care (carprofen, Baytril); mp primed 36-48 hours in 37 degrees celsius Ringer's solution; Electrode array also inserted into scala tympani; "We observed no evidence of mechanical trauma to cochlea following long-term implantation and AP or BDNF delivery." (p. 155); tissue perfusion (scala tympani).

**P7765:** R. T. Richardson, *et al.* A single dose of neurotrophin-3 to the cochlea surrounds spiral ganglion neurons and provides trophic support. *Hearing Research* 2005;204(1-2):37-47

**ALZET Comments:** NT-3, recomb. human; brain-derived neurotrophic factor; Ringer's solution; Ear (scalatympani); Guinea pig; 2004; 28 days; Comparison of bolus infusion vs. mp; peptides; animal info (adult, pigmented Dunkin-Hartley, 455g.); tissue perfusion (scala tympani).

**P8059:** H. Hara, *et al.* CGRP expression in the vestibular periphery after transient blockage of bilateral vestibular input. *ORL-JOURNAL FOR OTO-RHINO-LARYNGOLOGY AND ITS RELATED SPECIALTIES* 2005;67(5):259-265

**ALZET Comments:** Tetrodotoxin; Ear (cochlea perilymphatic space); Guinea pig; 2002; 7 days; Controls received mp w/ sterile saline; post op. care (piperacillin sodium); animal info (male, Hartley, 600g.); tissue perfusion (cochlea).

**P7209:** C. Wimmer, *et al.* Round window application of D-methionine, sodium thiosulfate, brain-derived neurotrophic factor, and fibroblast growth factor-2 in cisplatin-induced ototoxicity. *OTOLOGY & NEUROTOLOGY* 2004;25(1):33-40

**ALZET Comments:** Methionine, D-; fibroblast growth factor 2; thiosulfate, sodium tetrahydrate; brain-derived neurotrophic factor; Water; PBS; Ear (round window membrane); Guinea pig; 2001; 6 days; Controls received mp w/ saline; mp primed > 12 hours in saline; tissue perfusion (round window membrane).

**P6462:** T. Takemoto, *et al.* The clinical free radical scavenger, edaravone, protects cochlear hair cells from acoustic trauma. *European Journal of Pharmacology* 2004;487(1-3):113-116

**ALZET Comments:** Edaravone; saline; NaOH; water; HCL; Ear (cochlea); Guinea pig; 2002; 17 days; Controls received no treatment to contralateral ear; animals received mp w/saline for 3 days; then pumps replaced for mp w/edaravone; no stress (see pg. 115); post op. care (antibiotic ointment); edaravone is a free radical scavenger; tissue perfusion (cochlea).

**P6536:** K. Sugahara, *et al.* Cochlear administration of adenosine triphosphate facilitates recovery from acoustic trauma (temporary threshold shift). *ORL-JOURNAL FOR OTO-RHINO-LARYNGOLOGY AND ITS RELATED SPECIALTIES* 2004;66(2):80-84

**ALZET Comments:** Adenosine triphosphate; PPADS; Ear (cochlea); Guinea pig; 2002; Post op. care (antibiotic ointment applied); PE-10 used to target the inner ear and fixed with dental cement; for recover period, pumps and catheters were filled with saline, then pumps replaced with reagent filled pumps; infusion of agents was 12 hours post pump replacement



to allow for saline in catheter to be infused; PPADS is pyridoxal-phosphate-6-azophenyl-2',4'-disulfonic acid solution; tissue perfusion (cochlea).

**P6793:** R. M. S. Stocks, *et al.* Ototoxic protection of sodium thiosulfate: Daily vs constant infusion.

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**ALZET Comments:** Thiosulfate, sodium; Ear (middle ear space); Guinea pig; 2002; 18 days; Controls received no treatment to right ear; comparison of daily middle ear space injections vs. mp; pumps replaced after 7 days; multiple pumps per animal (2); "Continuous infusion of STS is the preferred method of administration." (p. 118) "STS continuously infused into the middle ear system provides a greater protective function than daily injection." (p. 119); tissue perfusion (middle ear space).

**P7105:** D. W. Roberson, *et al.* Direct transdifferentiation gives rise to the earliest new hair cells in regenerating avian auditory epithelium. *Journal of Neuroscience Research* 2004;78(4):461-471

**ALZET Comments:** Uridine, bromodeoxy-; Ear (cochlea); Bird (chicken); 2002; 3-11 days; Controls received untreated contralateral ear; functionality of mp verified by (epithelial immunohistochemistry); stability verified by epithelial immunohistochemistry; tissue perfusion (cochlea).

**P6458:** P. Olivius, *et al.* A model for implanting neuronal tissue into the cochlea. *BRAIN RESEARCH PROTOCOLS* 2004;12(3):152-156

**ALZET Comments:** Brain-derived neurotrophic factor; ciliary neurotrophic factor Ax1, human; Ear (scala tympani); Guinea pig; 2002; 21-22 days; Pump replaced on days 11-12; post op. care (cyclosporine, doxycycline); tissue perfusion (scala tympani).

**P6392:** T. Okuda, *et al.* Inner ear changes with intracochlear gentamicin administration in guinea pigs. *Laryngoscope* 2004;114(4):694-697

**ALZET Comments:** Gentamicin; Saline; Ear (cochlea); Guinea pig; 2002; 14 days; Controls received mp w/ vehicle; pumps replaced at day 7; pump contained saline only for the first seven days ; PE-10 used; tissue perfusion (cochlea).

**P7104:** S. B. Minami, *et al.* Calcineurin activation contributes to noise-induced hearing loss. *Journal of Neuroscience Research* 2004;78(3):383-392

**ALZET Comments:** FK506; cyclosporin A; Perilymph, artificial; Ear (cochlea); Guinea pig; 2002; 14 days; Controls received mp w/ vehicle, or contralateral untreated cochlea; dose-response (fig. 3); stress/adverse reaction: (see pg. 385) 4 of 43 animals developed middle ear infections; 4 of 43 animals had post surgical hearing loss; calcineurin inhibitors; "Systematic application may therefore have unwanted side effects that may be avoided by intracochlear perfusion by osmotic pump. The use of an osmotic pumps also allows relatively precise control over the timing and concentration of drugs applied to the tissues of the inner ear." (pg. 389); tissue perfusion (cochlea).

**Q0251:** D. M. Mills, *et al.* Metabolic Presbycusis: Differential Changes in Auditory Brainstem and Otoacoustic Emission Responses with Chronic Furosemide Application in the Gerbil. *JARO* 2004;5(1-10)

**ALZET Comments:** Furosemide; Ear (round window niche); Gerbil; 2004; 3-7 days; Controls received a bulla vent tube (no mp); no stress (see pg. 2); animal info (young adult, Mongolian, 45-65g); dose-response; tissue perfusion (round window).

**P6918:** M. Li, *et al.* Vestibular destruction by slow infusion of gentamicin into semicircular canals. *Acta Oto-laryngologica* 2004;124(35-41)

**ALZET Comments:** Gentamicin; Hank's solution; Ear (semicircular canals); Chinchilla; 1007D; 7 days; Controls received mp w/ vehicle; Meniere's disease; microcatheter used; 27 gauge tubing used for cannulation; tissue perfusion (semicircular canals).

**P7101:** C. G. Le Prell, *et al.* Chronic excitotoxicity in the guinea pig cochlea induces temporary functional deficits without disrupting otoacoustic emissions. *Journal of the Acoustical Society of America* 2004;116(2):1044-1056





**ALZET Comments:** AMPA; Perilymph, artificial; Ear (scala tympani); Guinea pig; 2002; 2004; 14-56 days; Controls received mp w/ vehicle; dose-response (fig. 2); long-term study; pumps replaced at 14 or 28 day intervals; stress/adverse reaction: (see pg. 1045) middle ear infections; tissue perfusion (scala tympani).

**P7069:** W. Jing, *et al.* Caspase inhibitors, but not c-Jun NH<sub>2</sub>-terminal kinase inhibitor treatment, prevent cisplatin-induced hearing loss. *Cancer Research* 2004;64(24):9217-9224

**ALZET Comments:** z-DEVD-fmk; z-IETD-fmk; z-LEHD-fmk; z-FA-fmk; JNKI-1, D-; Perilymph, artificial; Ear (cochlea); Guinea pig; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (caspases (-3,-8,-9), cathepsinB, JNK); peptides; tissue perfusion (cochlea).

**P6930:** L. N. Gillespie, *et al.* Delayed neurotrophin treatment supports auditory neuron survival in deaf guinea pigs. *NeuroReport* 2004;15(7):1121-1125

**ALZET Comments:** Brain-derived neurotrophic factor; nerve growth factor; NT-3; NT-4/5; Ear (scala tympani, cochlea); Guinea pig; 2004; 28 days; Tissue perfusion.

**P5983:** J. Zou, *et al.* Comparison of the protective efficacy of Neurotrophins and antioxidants for vibration-induced trauma. *ORL-JOURNAL FOR OTO-RHINO-LARYNGOLOGY AND ITS RELATED SPECIALTIES* 2003;65(3):155-161

**ALZET Comments:** Brain-derived neurotrophic factor; ciliary neurotrophic factor; Ear (scala tympani); Guinea pig; 2002; 14 days; tissue perfusion (cochlea); comparison of RWM injections vs. mp; peptides.

**P5673:** F. L. C. Wolters, *et al.* Systemic co-treatment with alpha-melanocyte stimulating hormone delays hearing loss caused by local cisplatin administration in guinea pigs. *Hearing Research* 2003;179(1-2):53-61

**ALZET Comments:** Cisplatin; Saline; Ear (cochlea); Guinea pig; 2002; 1 week; Tissue perfusion (cochlea).

**P5872:** X. B. Wang, *et al.* Blockage of immune-mediated inner ear damage by etanercept. *OTOLOGY & NEUROTOLOGY* 2003;24(1):52-57

**ALZET Comments:** Etanercept; PBS; keyhole limpet hemocyanin; Ear (scala tympani); Guinea pig; 2001; 7 days; Controls received mp w/ PBS or KLH; Etanercept is a TNF receptor; keyhole limpet hemocyanin is (KLH); tissue perfusion (scala tympani).

**P6130:** J. Wang, *et al.* A peptide inhibitor of c-Jun N-terminal kinase protects against both aminoglycoside and acoustic trauma-induced auditory hair cell death and hearing loss. *Journal of Neuroscience* 2003;23(24):8596-8607

**ALZET Comments:** D-JNKI-1; Perilymph, artificial; Ear (scala tympani); Guinea pig; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (JNK); D-JNKI-1 is a C-JUN N-terminal kinase (JNK); glass pipette was glued to PE-50 and pressed against cochlea; tissue perfusion (scala tympani).

**P6703:** J. Wang, *et al.* Local application of sodium thiosulfate prevents cisplatin-induced hearing loss in the guinea pig. *Neuropharmacology* 2003;45(3):380-393

**ALZET Comments:** Thiosulfate, sodium; Perilymph, artificial; water, sterile distilled; Ear (cochlea); Guinea pig; 2001; 7 days; Controls received mp w/ vehicle; stress/adverse reaction: (see pg.381) "Seven animals died during the course of the CDDP treatment (probably from the toxic effects of CDDP)" (p.381); cancer; "Perfusion of STS into the cochlea via an osmotic minipump completely prevented CDDP-induced hearing loss" (p.391); pump/catheter schematic (p.381); tissue perfusion (cochlea).

**P6098:** T. Takeda, *et al.* The effects of V(2) antagonist (OPC-31260) on endolymphatic hydrops. *Hearing Research* 2003;182(1-2):9-18

**ALZET Comments:** OPC-31260; Saline; Ear (cochlea); Guinea pig; 2002; Controls received mp w/ vehicle; OPC-31260 is a vasopressin type-2 antagonist; insertion site of the cannula was sealed with biobonde (biomedical adhesive); tissue perfusion (cochlea).

**P5832:** A. L. Miller, *et al.* Mechanism of electrical stimulation-induced neuroprotection: effects of verapamil on protection of primary auditory afferents. *Brain Research* 2003;966(2):218-230



**ALZET Comments:** Verapamil; Perilymph, artificial; Ear (cochlea); Guinea pig; 2002; 6 weeks; Pumps replaced every two weeks; 2 week stability verified by high pressure liquid chromatography p. 220; good methods p.220; 3 day recovery post implant; tissue perfusion (cochlea).

**P6077:** H. Lang, *et al.* Effects of chronic furosemide treatment and age on cell division in the adult gerbil inner ear. JARO-JOURNAL OF THE ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY 2003;4(2):164-175

**ALZET Comments:** Furosemide; Ear (cochlea); Gerbil; 2004; 1 week; No stress (p. 165); tissue perfusion (cochlea).

**P5659:** O. Horiike, *et al.* Protective effect of edaravone against streptomycin-induced vestibulotoxicity in the guinea pig. European Journal of Pharmacology 2003;464(1):75-78

**ALZET Comments:** Streptomycin; Saline; Ear (cochlea); Guinea pig; 2002; 24 hours; tissue perfusion (round window).

**P5669:** L. N. Gillespie, *et al.* BDNF-induced survival of auditory neurons in vivo: Cessation of treatment leads to accelerated loss of survival effects. Journal of Neuroscience Research 2003;71(6):785-790

**ALZET Comments:** Brain-derived neurotrophic factor; Ear (cochlea); Guinea pig; 2004; 4 weeks; Peptides; BDNF was recombinant human; tissue perfusion (cochlea).

**P6159:** A. Ekborn, *et al.* Intracochlear administration of thiourea protects against cisplatin-induced outer hair cell loss in the guinea pig. Hearing Research 2003;181(1-2):109-115

**ALZET Comments:** Thiourea; Perilymph, artificial; water, sterile; Ear (cochlea); Guinea pig; 2002; 14 days; good methods p. 111; microtip catheter was held in place using cyanoacrylate glue at the bulla defect, which was then sealed with dental cement; cites a detailed cannulation method; tissue perfusion (cochlea).

**P5811:** X. P. Du, *et al.* Distribution of beta-tubulin in guinea pig inner ear. ORL-JOURNAL FOR OTO-RHINO-LARYNGOLOGY AND ITS RELATED SPECIALTIES 2003;65(1):7-16

**ALZET Comments:** Tubulin, beta; PBS; Ear (scala tympani); Guinea pig; 2002; 14 days; Controls received mp w/ vehicle; tissue perfusion (cochlea); peptides.

**P5672:** L. Chelikh, *et al.* High variability of perilymphatic entry of neutral molecules through the round window. Acta Oto-laryngologica 2003;123(2):199-202

**ALZET Comments:** Mannitol; Inulin;; Radio-isotopes; 3H tracer; saline; ethanol; Ear (round window); Guinea pig; 1007D; 7 days; Tissue perfusion (round window).