



References (2005-Present) on the Administration to the Ear
Using ALZET® Osmotic Pumps

Q11269: F. Depreux, *et al.* Statins protect mice from high-decibel noise-induced hearing loss. *Biomedicine & Pharmacotherapy* 2023;163(114674)

Agents: Fluvastatin **Vehicle:** DMSO; **Route:** Ear (cochlea); **Species:** Mice; **Strain:** CBA/CaJ; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Dose (50 µM); 0.5% DMSO used; Controls received mp w/ vehicle; animal info (Male; 10 weeks old); comparison of mp vs oral delivery; good methods (cochleostomy) p. 3

Q10598: K. Malfeld, *et al.* Prevention of Noise-Induced Hearing Loss In Vivo: Continuous Application of Insulin-like Growth Factor 1 and Its Effect on Inner Ear Synapses, Auditory Function and Perilymph Proteins. *International Journal of Molecular Sciences* 2022;24(1):

Agents: IGF-1, Recombinant human **Vehicle:** Perilymph. artificial; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2006;
Duration: 7 days;
ALZET Comments: Dose (2 µg/mL) Controls received mp w/ vehicle; animal info (male Dunkin Hartley guinea pigs); weighting between 350 g and 426 g; post op. care (0.2 mg/kg meloxicam and 10 mg/kg enrofloxacin.) to reduce pain & prevent infection; catheter; dental cement used; (UV cement)

R0444: M. Magdy, *et al.* Localized drug delivery to the middle ear: Recent advances and perspectives for the treatment of middle and inner ear diseases. *Journal of Drug Delivery Science and Technology* 2022;69(**Agents:** Liposome; Gd-DOTA **Vehicle:** Not Stated; **Route:** Ear (intratympanic); **Species:** Rat; **Strain:** Not Stated; **Pump:** Not Stated; **Duration:** 17 days;
ALZET Comments: toxicology; Therapeutic indication (Middle and inner ear diseases);

Q9343: S. Li, *et al.* FGF22 promotes generation of ribbon synapses through downregulating MEF2D. *Aging* 2020;
Agents: Adeno-associated virus **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Mice; **Pump:** 1004; **Duration:** 4 days;
ALZET Comments: Animal info (male CBA/J mice, aged 6 weeks, weight around 18g); toxicology;

Q7262: C. P. Richter, *et al.* Fluvastatin protects cochleae from damage by high-level noise. *Sci Rep* 2018;8(1):3033
Agents: Fluvastatin **Vehicle:** DMSO, Ringer's Solution; **Route:** Ear (cochlea); **Species:** Guinea Pig; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Dose (fluvastatin 50 µM); animal info (Outbred Hartley guinea pigs 200–500 g); post op. care (Buprenex);

Q5813: A. Fransson, *et al.* Structural changes in the inner ear over time studied in the experimentally deafened guinea pig. *J Neurosci Res* 2017;95(3):869-875
Agents: Glial cell-line derived neurotrophic factor **Vehicle:** artificial perilymph; **Route:** Ear, Cochlea; **Species:** Guinea Pig;
Pump: 2002; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (200-320g); Artificial perilymph : ringer-acetate; Therapeutic indication (Delayed treatment, degeneration, cochlear implant, hearing);

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)
Agents: Brain-derived neurotrophic factor, recomb. human **Vehicle:** Perilymph, artificial; **Route:** Ear (cochlea); **Species:** Cat;
Pump: 1002, 2004; **Duration:** 10 weeks;
ALZET Comments: 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 INTRACOCHELEAR APPLICATION OF ANTI-INFLAMMATORY AND ANTIPROLIFERATIVE DRUGS. *neuroscience* 2016;316(261-278)
Agents: Dexamethasone; Ara-C **Vehicle:** Perilymph, artificial; **Route:** Ear (cochlea); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: 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 Otolaryngologica* 2015;135(8):791-8

Agents: Dexamethasone **Vehicle:** Saline; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: 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)

Agents: MDL28170 **Vehicle:** DMSO; PBS; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: 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 um 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)

Agents: Dexamethasone **Vehicle:** Saline; **Route:** Ear (round window); **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: 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)

Agents: Brain-derived neurotrophic factor **Vehicle:** PBS; **Route:** Ear (right cochlea); **Species:** Guinea pig; **Pump:** 2004;
Duration: 4 weeks;

ALZET Comments: 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

Agents: Brain-derived neurotrophic factor, recomb. human **Vehicle:** Perilymph, artificial; **Route:** Ear (cochlea); **Species:** Cat;
Pump: 1002; 2004; **Duration:** 10 weeks;

ALZET Comments: 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

Agents: Neurotrophin; Brain-derived neurotrophic factor **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ artificial perilymph; animal info (young adult, 300-600g); tissue perfusion

Q2425: H. Toyota, *et al.* A novel treatment for vestibular disorder with FGLM-NH₂ plus SSSR. *Neuroscience Letters* 2012;526(2):128-132

Agents: FGLM-NH₂; SSSR **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Control animals received mp w/ artificial perilymph; animal info (male, Hartley); FGLM-NH₂ 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

Agents: Brain-derived neurotrophic factor **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2004; **Duration:** 4 weeks; **ALZET Comments:** 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

Agents: Gentamicin; dexamethasone; melatonin **Route:** Ear (round window); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ saline; animal info (Wistar, male, 220-250 g); stability verified after 7 days

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

Agents: Sodium hydrosulfide; propargylglycine, DL- **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Rat; **Pump:** 2002; **ALZET Comments:** 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

Agents: Brain-derived neurotrophic factor, human **Vehicle:** Perilymph, artificial; **Route:** Ear (cochlea); **Species:** Cat; **Pump:** 1002; 2004; **Duration:** 10 weeks; **ALZET Comments:** 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

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

Q0954: L. Abamrane, *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

Agents: Leupeptin; z-VAD-FMK **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2001; **Duration:** 7 days; **ALZET Comments:** 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

Agents: PD153035; 4557W **Vehicle:** DMSO; artificial perilymph; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002 **ALZET Comments:** 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

Agents: Artemin; brain-derived neurotrophic factor **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 28 days;

ALZET Comments: 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

Agents: Furosemide **Vehicle:** Not Stated; **Route:** Ear (round window niche); **Species:** Gerbil; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: 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

Agents: Glial-derived neurotrophic factor **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 4 weeks;

ALZET Comments: 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

Agents: Glial-derived neurotrophic factor **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 48 days;

ALZET Comments: 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

Agents: Substance P; neurokinin-1 receptor antagonist **Vehicle:** Not Stated; **Route:** Ear (round window); **Species:** Guinea pig; **Pump:** 2002; **Duration:** Not Stated;

ALZET Comments: 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 Otolaryngologica* 2009;129(11):1153-1159

Agents: Saline **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 1007D; **Duration:** Not Stated;

ALZET Comments: 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. *Otology & Neurotology* 2009;30(4):551-558

Agents: Nerve growth factor **Vehicle:** Hank's based salt solution; albumin, guinea pig serum; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** Not Stated;

ALZET Comments: 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

Agents: Uridine triphosphate; uridine **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 25 days;

ALZET Comments: 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

Agents: Brain-derived neurotrophic factor **Vehicle:** BSA; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: 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

Agents: Amikacin **Vehicle:** Not Stated; **Route:** Ear; **Species:** Antelope (bongo); **Pump:** 2ML4; **Duration:** 24 days;

ALZET Comments: 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

Agents: Dexamethasone base **Vehicle:** Perilymph, artificial; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2001; **Duration:** 8 days;

ALZET Comments: 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

Agents: Cisplatin; Sodium thiosulfate; Brain-derived neurotrophic factor; Fibroblast growth factor; D-JNKI-1; BN82270; Tetrodotoxin; Perilymph, artificial; Dexamethasone; Methylprednisone; Caroverine; Methionine, D-; Thiourea; Liposome, cationic; Neomycin **Route:** SC; Ear (round window membrane, cochlea, scala tympani); **Species:** Guinea pig; **Duration:** 3, 7, 14, 28 days;

ALZET Comments: 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;

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

Agents: Brain-derived neurotrophic factor, recomb. human **Vehicle:** Albumin, rat; Ringer's solution; **Route:** Ear (cochlea); **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: 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

Agents: Brain-derived neurotrophic factor, recomb. human **Vehicle:** Ringer's solution; Albumin, guinea pig; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: 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

Agents: Doxycycline; Brain-derived neurotrophic factor; Glial cell line-derived neurotrophic factor **Vehicle:** Not Stated; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 27 days;

ALZET Comments: 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

Agents: Midazolam **Vehicle:** Not Stated; **Route:** Ear (round window niche); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: 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

Agents: Tumor necrosis factor-alpha **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2001; **Duration:** 2-4 days;

ALZET Comments: 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

Agents: Tetrodotoxin **Vehicle:** Citrate buffer; **Route:** Ear (round window niche); **Species:** Mice; **Pump:** 1003D; **Duration:** 24 hours;

ALZET Comments: 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

Agents: Jun, c-, N-Terminal kinase Inhibitor-1, D-; peptide, D-TAT; Jun, c-, N-Terminal kinase Inhibitor-1-mutant **Vehicle:** Perilymph, artificial; PBS; **Route:** Ear (round window membrane); **Species:** Guinea pig; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: 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 sequece 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

Agents: Gentamicin **Vehicle:** Not Stated; **Route:** Ear (round window); **Species:** Chinchilla; **Pump:** 2002; **Duration:** 1, 3, 6, 14 days; 4, 8 hours;

ALZET Comments: 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

Agents: Kallidinogenase **Vehicle:** Saline; **Route:** IV (marginal ear vein); **Species:** Rabbit; **Pump:** Not Stated; **Duration:** 4 weeks; **ALZET Comments:** 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

Agents: Brain-derived neurotrophic factor; fibroblast growth factor-1 **Vehicle:** Perilymph, artificial; lbumin, guinea pig serum; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 26 days;

ALZET Comments: 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

Agents: Trolox; Neomycin; Ascorbic acid **Vehicle:** Perilymph, artificial; Sodium bicarbonate; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 26 days;

ALZET Comments: 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

Agents: MDL 28170 **Vehicle:** DMSO; PBS; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: 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

Agents: Erythropoietin **Vehicle:** Not Stated; **Route:** Ear (round window); **Species:** Guinea pig; **Pump:** 1007D; **Duration:** 1 week;

ALZET Comments: 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

Agents: Uridine, bromodeoxy- **Vehicle:** PBS; **Route:** Ear (perilymphatic fluid); **Species:** Bird (chicken); **Pump:** 2002; **Duration:** 8 days;

ALZET Comments: 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

Agents: Methylprednisolone; Perilymph, artificial **Vehicle:** Perilymph, artificial; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2001; **Duration:** 14 days;

ALZET Comments: 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. *Auditory Neuroscience* 2006;11(6):343-356
Agents: 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 **Vehicle:** Not Stated; **Route:** Ear (cochlea); ear (scala tympani); **Species:** Guinea pig; **Pump:** Not Stated; **Duration:** 1,2,4,8 weeks; 15-60, 11-12, 26 days;
ALZET Comments: 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 Otolaryngologica* 2006;126(5):452-459
Agents: Brain-derived neurotrophic factor, recomb. human **Vehicle:** PBS; Albumin, chicken; Hank's solution; **Route:** Ear (scala tympani); **Species:** Bird (pigeon); **Pump:** 2002; **Duration:** 8 weeks;
ALZET Comments: 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-JNK1-1 treatment prevents the progression of hearing loss in a model of cochlear implantation trauma. *OTOLOGY & NEUROTOLOGY* 2006;27(4):504-511
Agents: Peptide, D-JNK inhibitor 1 **Vehicle:** Perilymph, artificial; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2001; **Duration:** 1 week;
ALZET Comments: 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
Agents: Brain-derived neurotrophic factor, recomb. human; NT-3 **Vehicle:** Not Stated; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: 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
Agents: Edaravone; saline **Vehicle:** Water; NaOH; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 12 hours;
ALZET Comments: 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
Agents: Brain-derived neurotrophic factor, recomb. human; perilymph, artificial **Vehicle:** Ringer's solution; Albumin, recomb. guinea-pig; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: 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)