



References on the Administration of Antibiotics
Using ALZET® Osmotic Pumps

ActinomycinD

Q7407: J. Apulei, *et al.* Non-cell autonomous Otx2 homeoprotein regulates visual cortex plasticity through Gadd45b. Cerebral Cortex 2018;

Agents: cycloheximide; actinomycin D **Vehicle:** Saline; **Route:** CSF/CNS (visual cortex); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Dose: cycloheximide (0.1 µg/µl); actinomycin D (0.2 µg/µl); Controls received mp w/ vehicle; animal info (C57Bl/6N and Otx2+/GFP knock-in mice); Brain coordinates (lambda: x = 1.7 mm, y = 0 mm, z = 0.5 mm);

P1379: M. Kanje, *et al.* A new method for studies of the effects of locally applied drugs on peripheral nerve regeneration in vivo. Brain Research 1988;439(116-121

Agents: Actinomycin D; Cycloheximide; Mitomycin C; Vinblastine **Vehicle:** Ringer's solution; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 3, 4, 6 days;

ALZET Comments: mp connected to silicone cuff; functionality of mp verified in vivo with dye; tissue perfusion

Amikacin (2014-Present)

R0391: T. Coutant, *et al.* Advances in Therapeutics and Delayed Drug Release. Vet Clin North Am Exot Anim Pract 2019;22(3):501-520

Agents: Florfenicol voriconazole; fentanyl; amikacin **Route:** SC; in vitro; **Species:** Rat; Snake (corn, rattle); Iguana; Cat; Hamster; Gelada; Pudu; Wallaby; Monkey; Quail; Hen;

ALZET Comments: "animal info (Eastern massasauga rattlesnakes (*Sistrurus catenatus*); timber rattlesnake (*Crotalus horridus*); pudu (*Pudu puda*); wallaby (*Macropus rufogriseus*); iguanas (*Iguana iguana*); Mojave rattlesnakes (*Crotalus scutulatus*); corn snakes (*Elaphe guttata guttata*); Japanese quails (*Coturnix coturnix japonica*); hens (*Gallus domesticus*)); " Finally, the use of intracoelomic osmotic pumps was reported in iguanas (*Iguana iguana*) in a study of reproductive behavior.²⁶ No complication due to the pump placement was reported in that study." pg. 508; Advantages: Can be extracted in case of drug overdose or toxicity, Is not altered by its biological environment, Release the drug at a constant rate, Low cost, Commercially available, Release rate and operation time can be chosen; Drawbacks: Necessitate 2 light surgical procedures under anesthesia to be implanted and explanted, Can sometimes migrate in unwanted location (especially if implanted accidentally in air sacs during intracoelomic implantation) "

Q5309: M. M. Clancy, *et al.* Management of Osteomyelitis Caused by Salmonella Enterica Subsp. Houtenae in a Taylor's Cantil (*Agkistrodon Bilineatus Taylori*) Using Amikacin Delivered Via Osmotic Pump. J Zoo Wildl Med 2016;47(2):691-4

Agents: Amikacin **Vehicle:** Not Stated; **Route:** SC; **Species:** Snake; **Pump:** 2002; **Duration:** 10 months;

ALZET Comments: animal info (adult female Taylor's cantil, 6 yr old); good methods; spinal cord injury; long-term study; "This study demonstrates that the infection can be suppressed and the animal's life extended by long-term continuous infusion of amikacin and that such treatment did not result in renal compromise in this individual." pg 694; temperature adjusted pumping rate for snake; Industry authored (American Association of Zoo Veterinarians); Interesting (Veterinary use presented for treating animal w/ antibiotics for extended duration; minimizing need for animal handling); Dose (26ug/kg/hr);

R0324: P. M. Gibbons. ADVANCES IN REPTILE CLINICAL THERAPEUTICS. Journal of Exotic Pet Medicine 2014;23(1):21-38

Agents: Amikacin; Florfenicol; Gonadotropin-releasing hormone **Species:** Snake; Iguana;

ALZET Comments: Animal info (Euttata corn snake, C scutulaus Mojave rattlesnake, green iguana); stress/adverse reaction:

Bleomycin (2019-Present)

Q10060: T. Saito, *et al.* Antifibrotic therapy by sustained release of low molecular weight heparin from poly(lactic-co-glycolic acid) microparticles on bleomycin-induced pulmonary fibrosis in mice. Scientific Reports 2020;10(1):19019

Agents: Bleomycin **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2010; **Duration:** 7 days;

ALZET Comments: Dose (5 mg); animal info (Female 13-14-week-old ICR mice); Bleomycin aka BLM; dependence;



Q9811: F. Ravanetti, *et al.* Modeling pulmonary fibrosis through bleomycin delivered by osmotic minipump: a new histomorphometric method of evaluation. *American Journal of Physiology-Lung Cellular and Molecular Physiology* 2020;318(2):L376-L385

Agents: Bleomycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (0.5 ul/hr); animal info (C57BL/6, 8 weeks old, Female); cardiovascular;

Q8888: L. Lucarini, *et al.* Effects of New NSAID-CAI Hybrid Compounds in Inflammation and Lung Fibrosis. *Biomolecules* 2020;10(9):

Agents: Bleomycin; Compound 3; Ibuprofen; Acetazolamide; **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Duration:** 21 days;

ALZET Comments: Dose (1 mg/kg Compound 3; 0.5 mg/kg Ibuprofen; 0.5 mg/kg Acetazolamide); Controls received mp w/ vehicle; animal info (C57BL/6 WT mice, 2 months old, 25-30 g); Ibuprofen aka Ibu, Acetazolamide aka AAZ; cardiovascular;

Q9042: V. R. Vasquez-Garzon, *et al.* Liver damage in bleomycin-induced pulmonary fibrosis in mice. *Naunyn-Schmiedeberg's Archives of Pharmacology* 2019;392(12):1503-1513

Agents: Bleomycin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (10 U/kg); Controls received mp w/ vehicle; animal info (10 weeks old, Male, CD1); dependence;

Q7495: H. Urushiyama, *et al.* Naftopidil reduced the proliferation of lung fibroblasts and bleomycin-induced lung fibrosis in mice. *J Cell Mol Med* 2019;23(5):3563-3571

Agents: Bleomycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (50 µg/hour); animal info (Wild-type C57BL/6J mice 6 wk); Therapeutic indication (lung fibrosis);

Q8739: J. K. Park, *et al.* Bleomycin induces drug efflux in lungs: A pitfall for pharmacological studies of pulmonary fibrosis. *American Journal of Respiratory Cell and Molecular Biology* 2019;

Agents: Bleomycin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (100 U/kg); Controls received mp w/ vehicle; animal info (Male, 13 or 24 weeks old, 25-28 g);

Q8276: G. M. Marchetti, *et al.* Targeted drug delivery via caveolae-associated protein PV1 improves lung fibrosis. *Commun Biol* 2019;2(92)

Agents: Bleomycin **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 28 days;

ALZET Comments: Dose (100 mg/kg); animal info (C57BL/6); dependence;

Q7620: N. Kokuho, *et al.* Analyses of alveolar epithelial injury via lipid-related stress in mammalian target of rapamycin inhibitor-induced lung disease. *Lab Invest* 2019;99(6):853-865

Agents: Bleomycin hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 14 days;

ALZET Comments: Dose (100 mg/kg); Controls received i.p. injection w/ DMSO; animal info (7 weeks, female, C57BL/6); comparison of i.p. temsirolimus injection vs mp; BLM causes marked inflammation and epithelial injury in the lung; immunology; BLM dissolved in saline for pump (injury group) although controls used i.p. injected DMSO;

Clindamycin

Q3927: N. Ito, *et al.* Organic Cation Transporter/Solute Carrier Family 22a is Involved in Drug Transfer into Milk in Mice. *Journal of Pharmaceutical Sciences* 2014;103(3342-3348)

Agents: Acyclovir; cimetidine; clindamycin; metformin; terbutaline; verapamil; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** 72 hours;

ALZET Comments: Animal info (female, lactating, Bcrp KO or WT FVB); functionality of mp verified by plasma and milk concentrations; no stress "All mice survived the surgical procedure and appeared to be lactating normally, and all pups thrived throughout the course of the experiment." (see pg. 3343);



Q5063: N. Ito, *et al.* Contribution of protein binding, lipid partitioning, and asymmetrical transport to drug transfer into milk in mouse versus human. *Pharm Res* 2013;30(9):2410-22

Agents: acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopyramide phosphate salt, labetalol hydrochloride, nitrofurantoin +-propranolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cephapirin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, praziquantel, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide. **Vehicle:** DMSO; water; **Route:** IP; **Species:** mice; **Pump:** 1003D; **Duration:** Not Stated;

ALZET Comments: animal info: lactating mice, postnatal age of 14 days; functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer.

P1074: C. L. Astry, *et al.* Interactions of clindamycin with antibacterial defenses of the lung. *American Review of Respiratory Disease* 1987;135(10):15-1019

Agents: Clindamycin HCl; Penicillin G **Vehicle:** Sodium hydroxide; Water; **Route:** SC; **Species:** mice; **Duration:** 72 hours;

ALZET Comments: Pump model not stated; controls received mp w/water; dose-response; mp primed overnight in PSB; 2 doses of agent infused; agent infused separately; antibiotic

P0953: S. J. Hollenbach, *et al.* Early administration of methylprednisolone promotes survival in rats with intra-abdominal sepsis. *Circ. Shock* 1986;20(2):161-168

Agents: Clindamycin; Methylprednisolone; Gentamicin; Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: controls received mp w/saline; multiple pumps per animal (3); comparison of bolus injections vs. mp infusion; antibiotic

Doxycycline (2008-Present)

Q6660: J. H. Seo, *et al.* In Situ Pluripotency Factor Expression Promotes Functional Recovery From Cerebral Ischemia. *Mol Ther* 2016;24(9):1538-49

Agents: Doxycycline **Vehicle:** PBS; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose ((12 ng/day or 1,200 ng/day)); Controls received mp w/ vehicle; animal info (transgenic mice expressing Pou5f1 (Oct4), Sox2, Myc, and Klf4); Doxycycline aka DOX; ALZET brain infusion kit 3 used; Brain coordinates ((AP +0.3 mm from Bregma; ML -0.7 mm from Bregma; DV -2.0 mm from Dura); ischemia (cerebral); Therapeutic indication (Cerebral ischemia);

Q4941: P. Rai, *et al.* Renin angiotensin system modulates mTOR pathway through AT2R in HIVAN. *Experimental and Molecular Pathology* 2014;96(3):431-7

Agents: Telmisartan; PD123319; Doxycycline; aliskiren **Vehicle:** Saline; water; **Route:** SC; **Species:** mice; **Pump:** 2004; **Duration:** 2, 6 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info : Tg26 mice; FVBN mice, Tg26 mice; Vpr transgenic mice (4 week old); immunology; Dose: Telmisartan (AT1R blocker, 300 µg/day), PD123319 (AT2R blocker, 3 µg/day); Doxycycline + aliskiren (50 mg/kg)

Q1540: L. Clarke, *et al.* The Adult Mouse Dentate Gyrus Contains Populations of Committed Progenitor Cells that are Distinct from Subependymal Zone Neural Stem Cells. *Stem Cells* 2011;29(9):1448-1458

Agents: Doxycycline **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 4 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (GFP/M2, 2-3 mo old)

Q1607: A. Baysal, *et al.* Comparisons of the effects of systemic administration of L-thyroxine and doxycycline on orthodontically induced root resorption in rats. *European Journal of Orthodontics* 2010;32(5):496-504

Agents: Thyroxine, L-; doxycycline **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ physiological serum; animal info (Wistar, male, 50-60 days old, 132 g)



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

Gentamicin (2004-Present)

Q2846: A. A. Al Dayeh, *et al.* Real-time monitoring of the growth of the nasal septal cartilage and the nasofrontal suture. *American Journal of Orthodontics and Dentofacial Orthopedics* 2013;143(6):773-783

Agents: Amikacin; gentamicin **Vehicle:** Not Stated; **Route:** SC; **Species:** Pig (mini); **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Animal info (female, 3.5-4.5 mo old, 12-27 kg); 2ML sized pumps used; pump implanted in back of the neck

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

P9166: K. Guerin, *et al.* Systemic aminoglycoside treatment in rodent models of retinitis pigmentosa. *Experimental Eye Research* 2008;87(3):197-207

Agents: Gentamicin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (transgenic); **Pump:** 1007D; **Duration:** 5 days;

ALZET Comments: Animal info (S3344ter-4, heterozygous, P15)

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

Agents: Gentamicin **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)

P8198: A. I. Bakardjiev, *et al.* Listeria monocytogenes traffics from maternal organs to the placenta and back. *PLoS Pathog* 2006;2(6):e66

Agents: Gentamicin sulfate **Vehicle:** Not Stated; **Route:** SC; **Species:** Guinea pig (pregnant); **Pump:** 2ML1;

ALZET Comments: Functionality of mp verified by plasma levels taken; teratology; listeria; wound clips used

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

Agents: Gentamicin **Vehicle:** Saline; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: 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)

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

Agents: Gentamicin **Vehicle:** Hank's soln; **Route:** Ear (semicirc canals); **Species:** Chinchilla; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; Meniere's disease; microcatheter used; 27 gauge tubing used for cannulation; tissue perfusion (semicircular canals)



Metronidazole

Q5063: N. Ito, *et al.* Contribution of protein binding, lipid partitioning, and asymmetrical transport to drug transfer into milk in mouse versus human. *Pharm Res* 2013;30(9):2410-22

Agents: acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopyramide phosphate salt, labetalol hydrochloride, nitrofurantoin +-propranolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cephapirin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, praziquantel, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide. **Vehicle:** DMSO; water; **Route:** IP; **Species:** mice; **Pump:** 1003D; **Duration:** Not Stated;

ALZET Comments: animal info: lactating mice, postnatal age of 14 days; functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer

Minocycline (2018-Present)

Q8857: C. T. Huang, *et al.* Glycemic control with insulin attenuates sepsis-associated encephalopathy by inhibiting glial activation via the suppression of the nuclear factor kappa B and mitogen-activated protein kinase signaling pathways in septic rats. *Brain Research* 2020;1738(146822

Agents: Dextrose; Fluorocitrate; Minocycline; SB203580; PD98059 **Vehicle:** DMSO; **Route:** CSF/CNS (intracerebral); IV (jugular); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: 1% DMSO used; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley rats (weight, 200–250 g)); behavioral testing (Von Frey filament test, Plantar test); functionality of mp verified by residual volume; SB203580 aka p38 MAPK inhibitor, PD98059 aka extracellular signal-regulated kinase inhibitor; Brain coordinates (0.8 mm posterior and 1.3 mm lateral to the bregma, and 4.0 mm ventral to the skull surface); dependence;

Q8536: D. He, *et al.* Asthmatic Airway Vagal Hypertonia Involves Chloride Dyshomeostasis of Preganglionic Neurons in Rats. *Frontiers in Neuroscience* 2020;14(31

Agents: Minocycline **Vehicle:** CSF, Artificial; **Route:** CSF/CNS (intracerebral); IV; **Species:** Rat; **Pump:** 2002; **Duration:** 15 days;

ALZET Comments: Dose (172 ng/mL); animal info (Male Sprague-Dawley rats, seven-week-old, 170–190 g); Minocycline aka MC; ALZET brain infusion kit 2 used; Brain coordinates (0.8 mm caudal to the bregma; 1.5 mm lateral to the midline; 4 mm below the surface of the skull); dependence;

Q6949: T. Zera, *et al.* Microglia and brain angiotensin type 1 receptors are involved in desensitising baroreflex by intracerebroventricular hypertonic saline in male Sprague-Dawley rats. *Autonomic Neuroscience: Basic and Clinical* 2019;217(49-57

Agents: Minocycline, Losartan **Vehicle:** Saline, iso-osmotic, Saline, hyperosmotic; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;

ALZET Comments: Dose (Minocycline-5 µg/h; Losartan- 12.5 µg/h); 0.9% isosmotic saline with minocycline, 5% Hyperosmotic saline with Losartan used; animal info (Normotensive adult male Sprague-Dawley rats); enzyme inhibitor (microglia); ALZET brain infusion kit 2 used; Brain coordinates (1.2mm posterior to bregma, -1.8mm laterolateral from sagittal suture, diameter 0.5 mm) bilateral cannula used; cyanoacrylate adhesive; cardiovascular;

Q9272: U. Hoheisel, *et al.* Action potentials and subthreshold potentials of dorsal horn neurons in a rat model of myositis: a study employing intracellular recordings in vivo. *Journal of Neurophysiology* 2019;122(2):632-643

Agents: M=Minocycline **Vehicle:** Cerebrospinal fluid, artificial; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;

ALZET Comments: Dose (2 µg/day); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 300-470 g); bilateral cannula used; dependence;

Q7050: R. K. Sharma, *et al.* Involvement of Neuroinflammation in the Pathogenesis of Monocrotaline-Induced Pulmonary Hypertension. *Hypertension* 2018;71(6):1156-1163

Agents: Minocycline **Vehicle:** CSF, artificial; **Route:** CSF/CNS (left ventricle); **Species:** Rat; **Pump:** 2004; **Duration:** Not Stated;

ALZET Comments: Dose (5 µg/h); animal info (8 week old male Sprague-Dawley rats);



Q8109: T. Majima, *et al.* Role of microglia in the spinal cord in colon-to-bladder neural crosstalk in a rat model of colitis. *NeuroUrol Urodyn* 2018;37(4):1320-1328

Agents: Minocycline **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 7 days;
ALZET Comments: Dose (200 ug/day); animal info (24 weeks old, SD, Female); enzyme inhibitor (Microglia inhibitor);

Mitomycin (1988-Present)

P1874: X. Lu, *et al.* Inflammation near the nerve cell body enhances axonal regeneration. *J. Neurosci* 1991;11(4):972-978

Agents: Mitomycin C **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** Not Stated;
ALZET Comments: no comment posted

P1993: K. K. Fu, *et al.* Early and late effects of mitomycin C and continuous low-dose-rate irradiation on the mouse skin and soft tissues of the leg. *Int. J. Radiat. Oncol. Biol. Phys* 1991;21(1523-1528

Agents: Mitomycin C **Vehicle:** Saline; **Route:** IP; **Species:** mice; **Pump:** Not Stated; **Duration:** no duration posted;
ALZET Comments: cancer

P1302: S. Kawano, *et al.* Effect of continuous intravesical infusion of low-concentrated mitomycin-C on bladder carcinogenesis in rats treated with N-butyl-N-4-hydroxybutyl-nitrosamine. *J. Urol* 1988;139(1343-1346

Agents: Mitomycin C **Vehicle:** Not Stated; **Route:** bladder; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
ALZET Comments: mp connected to catheter; dose-response (graph, text); comparison of twice weekly injections vs. mp infusion; functionality of mp verified by urine levels; cancer/immunology; tissue perfusion

P1379: M. Kanje, *et al.* A new method for studies of the effects of locally applied drugs on peripheral nerve regeneration in vivo. *Brain Research* 1988;439(116-121

Agents: Actinomycin D; Cycloheximide; Mitomycin C; Vinblastine **Vehicle:** Ringer's solution; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 3, 4, 6 days;
ALZET Comments: mp connected to silicone cuff; functionality of mp verified in vivo with dye; tissue perfusion

Neomycin (2002-Present)

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); Ear (cochlea); Ear (scala tympani); Ear; **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; Review, see pgs. 1587 - 1589, 1591, 1593 - 1595, refs #49, 50, 60, 63, 72, 75, 102, 104, 180, 181, 194-201

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)



P5009: T. Shinohara, *et al.* Neurotrophic factor intervention restores auditory function in deafened animals. Proceedings of the National Academy of Sciences of the United States of America 2002;99(3):1657-1660

Agents: Brain-derived neurotrophic factor; Ciliary neurotrophic factor; Neomycin; **Vehicle:** Perilymph, artificial; **Route:** Ear (scala tympani); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 26 days;

ALZET Comments: controls received mp w/ vehicle; tissue perfusion (cochlea, scala tympani); pumps replaced at day 15; peptides; catheter filled with perilymph and 10% neomycin; pump filled with vehicle or neurotrophic factor solution; 48-hr infusion of neomycin to cause deafness followed by 12 or 26 day infusion of neurotrophic factor pump reservoir.

Penicillin

P6354: A. W. Harrington, *et al.* Secreted proNGF is a pathophysiological death-inducing ligand after adult CNS injury. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2004;101(16):6226-6230

Agents: Antibody, anti-nerve growth factor, neutralizing mouse; serum; immunoglobulin-G; penicillin; streptomycin **Vehicle:** PBS; **Route:** CSF/CNS (cortex); **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: Controls received mp w/ vehicle

P1263: M. Kimoto, *et al.* Recombinant murine IL-3 fails to stimulate T or B lymphopoiesis in vivo, but enhances immune responses to T cell-dependent antigens. J. Immunol 1988;140(6):1889-1894

Agents: Interleukin-3, recomb. mouse; Penicillin; Streptomycin **Vehicle:** Glycerol; PBS; **Route:** IP; SC; **Species:** Mice; **Pump:** 2001; 2002; **Duration:** 7 days, 2 weeks;

ALZET Comments: Controls received mp w/vehicle; 2002 mp infused IL-3 ip for 2 weeks, additional mps implanted sc; peptides; antibiotics; IL-3 infused simultaneously with penicillin and streptomycin

P1074: C. L. Astry, *et al.* Interactions of clindamycin with antibacterial defenses of the lung. American Review of Respiratory Disease 1987;135(1015-1019

Agents: Clindamycin HCl; Penicillin G **Vehicle:** Sodium hydroxide; Water; **Route:** SC; **Species:** Mice; **Duration:** 72 hours;

ALZET Comments: Pump model not stated; controls received mp w/water; dose-response; mp primed overnight in PSB; 2 doses of agent infused; agent infused separately; antibiotic

P0804: V. Kindler, *et al.* Stimulation of hematopoiesis in vivo by recombinant bacterial murine interleukin 3. Proc. Natl. Acad. Sci 1986;83(1001-1005

Agents: Endotoxin, E. coli; Interleukin-3, recomb. mouse; Penicillin; Streptomycin **Vehicle:** Glycerol; PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3, 7 days;

ALZET Comments: Infusion supplemented w/ip injections; interleukin activity in blood variable - aggregation in pump? (see p. 1004); mp infusion in normal and irradiated mice; half-life; peptides; antibiotic

Rapamycin (2016-Present)

Q9566: H. Xu, *et al.* Limited efficacy of rapamycin monotherapy in vascularized composite allotransplantation. Transplant Immunology 2020;61(101308

Agents: Rapamycin; Tacrolimus **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (0.5-2 mg/kg/day Rapamycin; 2 mg/kg/day Tacrolimus); animal info (Inbred male mice);

Q10146: K. W. Cheung, *et al.* Analysis of the retinal capillary plexus layers in a murine model with diabetic retinopathy: effect of intravitreal injection of human CD34(+) bone marrow stem cells. Annals of Translational Medicine 2021;9(15):1273

Agents: Rapamycin; Tacrolimus **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;

ALZET Comments: Dose: (1 µg/g/day) Rapamycin; Tacrolimus; Controls received mp w/ vehicle; animal info :Male Six-week-old C57BL/6J; Tacrolimus aka (FK506); diabetes; Diabetic retinopathy

Q9537: L. Wang, *et al.* Donor bone-marrow CXCR4+ Foxp3+ T-regulatory cells are essential for costimulation blockade-induced long-term survival of murine limb transplants. Scientific Reports 2020;10(1):9292

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose (2 mg/kg/d); animal info (WT BALB/c and WT C57BL/6 mice, 8-12 weeks old); dependence;



Q9465: M. Shi, *et al.* The tripartite interaction of phosphate, autophagy, and alphaKlotho in health maintenance. *FASEB Journal* 2020;34(2):3129-3150

Agents: α Klotho protein, recombinant; rapamycin; chloroquine **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: Dose (0.3 mg/kg body weight α Klotho protein; 28 mg/Kg rapamycin; 50 mg/Kg chloroquine); Controls received mp w/ vehicle; animal info (Wild type mice, 10-12 weeks old); dependence;

Q8533: M. Hayashi-Hori, *et al.* Therapeutic Effect of Rapamycin on Aortic Dissection in Mice. *Int J Mol Sci* 2020;21(9):

Agents: Angiotensin II; Aminopropionitrile, B-; Gefitinib; Rapamycin **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Dose (1000 ng/kg/min Angiotensin II; 150 mg/kg/day B-aminopropionitrile; 1000 mg/kg/day Gefitinib; 2 mg/kg/day Rapamycin); Controls received mp w/ vehicle; animal info (male mice aged 11–14 weeks);

Q7037: J. Zhang, *et al.* Neuroinflammation and central PI3K/Akt/mTOR signal pathway contribute to bone cancer pain. *Mol Pain* 2019;15(1744806919830240

Agents: Rapamycin, LY294002, Interleukin-1 Receptor antagonist, SC144, etanercept, **Vehicle:** CSF, artificial; **Route:** CSF/CNS (midbrain periaqueductal gray); **Species:** Rat; **Pump:** 1001D; **Duration:** Not Stated;

ALZET Comments: animal info (200–250 gr Wistar rats); ALZET brain infusion kit used; Brain coordinates (7.6 mm posterior to the bregma, 0.65mm lateral to the midline, and 4.2 mm ventral to the brain surface); Therapeutic indication (bone cancer pain);

Q8554: Z. Jiang, *et al.* Involvement of pro-inflammatory cytokines in diabetic neuropathic pain via central PI3K/Akt/mTOR signal pathway. *Archives of Physiology and Biochemistry* 2019;1-9

Agents: Rapamycin; LY294002; Interleukin-1 beta receptor antagonist; SC144; etanercept **Vehicle:** CSF, Artificial; **Route:** CSF/CNS (dorsolateral striatum); **Species:** Rat; **Pump:** 1003D; **Duration:** Not stated;

ALZET Comments: "Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats, 200-250 g); behavioral testing (Mechanical paw withdrawal threshold; Thermal Place Preference System); ALZET brain infusion kit used; Brain coordinates (7.6 mm posterior to the bregma, 0.65 mm lateral to the midline, and 4.2 mm ventral to the brain surface);"

Q8837: H. Xu, *et al.* Utility of IL-2 Complexes in Promoting the Survival of Murine Orthotopic Forelimb Vascularized Composite Allografts. *Transplantation* 2018;102(1):70-78

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (2 mg/kg/day); Controls did not receive mp; animal info (male, C57BL/6 and BALB/c); comparison of IP injection of FK506 vs mp; immunology; RPM monotherapy was about as effective as post-Tx IL-2C in prolonging survival. Co-administration of IL-2C and post-Tx RPM had additional benefits, with pre-Tx IL-2C plus RPM causing a fivefold increase in survival, and post-Tx IL-2C plus RPM causing a threefold increase in survival;

Q9887: L. Wang, *et al.* Use of TGF-beta plus Rapamycin to Induce Foxp3, promote iTreg

Development and Suppressive Function, and Induce Long-Term Allograft Survival. *Transplantation* 2018;

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (0.5 mg/kg/d); animal info (C57BL/6 with BALB/c cardiac allografts);

Q10090: I. Barone, *et al.* Fluoxetine Modulates the Activity of Hypothalamic POMC Neurons via mTOR Signaling. *Molecular Neurobiology* 2018;55(12):9267-9279

Agents: Rapamycin **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 3 weeks;

ALZET Comments: Dose (0.5 mg/kg); 20% DMSO used; Controls received mp w/ vehicle; animal info (2 month old); Rapamycin aka RAPA; enzyme inhibitor (mTOR signaling); "Our findings not only disclose novel insights into the mechanisms underlying FLX action, but could also be exploited towards an increased awareness for the use of this drug in the clinical setting, especially in the context of obesity treatment; "



Q8778: Use of TGF-beta plus Rapamycin to Induce Foxp3, promote iTreg Development and Suppressive Function, and Induce Long-Term Allograft Survival. Transplantation 2018;

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (0.5 mg/kg/d); animal info (C57BL/6); immunology; mp model not stated but listed as a 28d pump; Therapeutic indication (combined TGFb/RPM led to a doubling of Foxp3+ Tregs when assessed at day 14 post-Tx, suppressed T cell activation, and resulted in permanent cardiac allograft survival);

Streptomycin

P7559: C. C. M. Chan, *et al.* Dose-dependent beneficial and detrimental effects of ROCK inhibitor Y27632 on axonal sprouting and functional recovery after rat spinal cord injury. Experimental Neurology 2005;196(2):352-364

Agents: Y-27632; Streptomycin **Vehicle:** PBS; penicillin; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 2 wks; 2, 4 days;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by ROCK inhibitory activity in CSF; dose-response (fig. 3); stability of Y27632 verified by ROCK inhibitory activity after 13 days in mp at 37 C; enzyme inhibitor (RHO Kinase); animal info (male, Sprague-Dawley); cervical 4/5 dorsal column transection; spinal cord injury

P6354: A. W. Harrington, *et al.* Secreted proNGF is a pathophysiological death-inducing ligand after adult CNS injury.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2004;101(16):6226-6230

Agents: Antibody, anti-nerve growth factor, neutralizing mouse; serum; immunoglobulin-G; penicillin; streptomycin **Vehicle:** PBS; **Route:** CSF/CNS (cortex); **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: Controls received mp w/ vehicle

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

Agents: Streptomycin **Vehicle:** Saline; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 24 hours;

ALZET Comments: tissue perfusion (round window)

P1263: M. Kimoto, *et al.* Recombinant murine IL-3 fails to stimulate T or B lymphopoiesis in vivo, but enhances immune responses to T cell-dependent antigens. J. Immunol 1988;140(6):1889-1894

Agents: Interleukin-3, recomb. mouse; Penicillin; Streptomycin **Vehicle:** Glycerol; PBS; **Route:** IP; SC; **Species:** Mice; **Pump:** 2001; 2002; **Duration:** 7 days, 2 weeks;

ALZET Comments: Controls received mp w/vehicle; 2002 mp infused IL-3 ip for 2 weeks, additional mps implanted sc; peptides; antibiotics; IL-3 infused simultaneously with penicillin and streptomycin

P0804: V. Kindler, *et al.* Stimulation of hematopoiesis in vivo by recombinant bacterial murine interleukin 3. Proc. Natl. Acad. Sci 1986;83(1001-1005

Agents: Endotoxin, E. coli; Interleukin-3, recomb.; Penicillin; Streptomycin **Vehicle:** Glycerol; PBS; **Route:** SC; **Species:** Mice; **Duration:** 3, 7 days;

ALZET Comments: Infusion supplemented w/ip injections; interleukin activity in blood variable - aggregation in pump? (see p. 1004); mp infusion in normal and irradiated mice; half-life; peptides; antibiotic

Tetracycline

Q7265: R. K. Sharma, *et al.* Microglial Cells Impact Gut Microbiota and Gut Pathology in Angiotensin II-Induced Hypertension. Circulation Research 2019;124(5):727-736

Agents: Angiotensin II, Tetracycline-3, chemically modified **Vehicle:** Saline; CSF, artificial; **Route:** SC; CSF/CNS (left lateral ventricle); **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: Dose: Ang II (200 ng/kg/min), CMT-3 (3.5µg/h); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats (250-280g) and six-week old male SHR and their normotensive controls); Brain coordinates (1.0mm caudal to bregma, 1.8mm lateral to midline and 4.4mm ventral to the skull surface); cardiovascular;



P2384: K. Freeman, *et al.* Continuously infused calcium hydroxide: its influence on hard tissue repair. *J. Endodontics* 1994;20(6):272-275

Agents: Calcium hydroxide; Barium hydroxide; Tetracycline **Vehicle:** Glycerol; **Route:** bone (femur); **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: no stress (see pg. 274); tissue perfusion; good methods

Tobramycin

P0820: S. H. Powell, *et al.* Once-daily vs. continuous aminoglycoside dosing: efficacy and toxicity in animal and clinical studies of gentamicin, netilmicin, and tobramycin. *J. Infect. Dis* 1983;147(5):918-932

Agents: Tobramycin **Vehicle:** Not Stated; **Route:** IP; **Species:** Guinea pig; Rat; **Pump:** 2ML1; **Duration:** 7 days, 72 hours;

ALZET Comments: comparison of single injection vs. mp infusion; mps primed in saline for 4 hours; studies also used dogs and humans; one study used rabbits w/ infusaid pumps; antibiotics

Tunicamycin

Q9337: D. S. Lee, *et al.* Regional specific activations of ERK1/2 and CDK5 differently regulate astroglial responses to ER stress in the rat hippocampus following status epilepticus. *Brain Research* 2021;1753(147262)

Agents: Tunicamycin; U0126; Roscovitine **Vehicle:** Saline; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats, weight 250–280 g); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; – 3.5 mm depth; flat skull position with bregma as reference); neurodegenerative (status epilepticus);

Q5674: J. Y. Kim, *et al.* PDI regulates seizure activity via NMDA receptor redox in rats. *Sci Rep* 2017;7(42491)

Agents: RNA, small interfering (PDI; DTNB); bacitracin; Immunoglobulin, anti-PDI; tunicamycin ; **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days, 14 days;

ALZET Comments: Controls received mp w/ vehicle or control siRNA or control IgG; animal info (male, Sprague Dawley, 7 weeks old); pumps replaced every week; ALZET brain infusion kit 1 used; behavioral testing (behavioral seizure severity);

Q3396: V. Legry, *et al.* Endoplasmic reticulum stress does not contribute to steatohepatitis in obese and insulin-resistant high-fat-diet-fed foz/foz mice. *Clinical Science* 2014;127(507-518)

Agents: Tunicamycin **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: Control animals received mp w/ vehicle; animal info (HFD-fed foz/foz)

P4971: G. Orsini, *et al.* Localized infusion of tunicamycin in rat hemimandibles: Alteration of the basal lamina associated with maturation stage ameloblasts. *JOURNAL OF HISTOCHEMISTRY & CYTOCHEMISTRY* 2001;49(165-176)

Agents: Tunicamycin **Vehicle:** Saline; **Route:** bone (mandible); **Species:** Rat; **Pump:** 2001; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (bony elevation over incisor); article incorrectly states use of 2001D pump, but states 7 day delivery period and pump; Tunicamycin is an antibiotic that interferes with N-glycosylation;

P1695: H. Kubota, *et al.* Mechanisms of the B-adrenoceptor down-regulation by the treatment with antidepressants in the rat cerebral cortex: effects of continuous administration of antidepressants by an osmotic pump. *Jpn. J. Psychiatry Neurol* 1990;44(1):135-136

Agents: Tunicamycin; Cycloheximide; Desipramine; Fluoxetine; Mianserin; Trazodone **Route:** CSF/CNS; SC; **Species:** Rat; **Pump:** 2001; 2ML1; **Duration:** 4-7 days;

ALZET Comments: comparison of sc injections vs. mp; cyclo. and tunica. delivered icv for 5 days