



References on the Administration of Antibiotics Using ALZET® Osmotic Pumps

1. ActinomycinD

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

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

2. Amikacin

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 **Vehicle:** Not Stated; **Route:** SC; in vitro; **Species:** Rat; Snake (corn, rattle); Iguana; Cat; Hamster; Gelada; Pudu; Wallaby; Monkey; Quail; Hen; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: "animal info (Eastern massasauga rattlesnakes (*Sistrurus catenatus*); timber rattlesnake (*Crotalus horridus*); pudu (*Pudu pudu*); 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; Veterinary

Application; temperature adjusted pumping rate for snake; Industry authored (American Association of Zoo Veterinarians); Interesting (Veterinary use presented for treating animal with 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 **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Snake; iguana; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Animal info (*E.uttata* corn snake, *C. scutulatus* Mojave rattlesnake, green iguana); stress/adverse reaction: (see pg. 23);

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 the back of the neck



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

3. Bleomycin

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 Six-week-old); Therapeutic indication (lung fibrosis);

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;

Q7769: F. Kurosaki, *et al.* AAV6-Mediated IL-10 Expression in the Lung Ameliorates Bleomycin-Induced Pulmonary Fibrosis in Mice. Hum Gene Ther 2018;29(11):1242-1251

Agents: bleomycin **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (1 µL/h of 125 mg/kg bleomycin); Controls received no vector and mp w/ vehicle; animal info (10-12 weeks, male, C57BL6/J, 25-30g); immunology;

Q8048: M. Kishi, *et al.* Blockade of platelet-derived growth factor receptor-beta, not receptor-alpha ameliorates bleomycin-induced pulmonary fibrosis in mice. PLoS One 2018;13(12):e0209786

Agents: Bleomycin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (140 mg/kg); Controls received mp w/ vehicle; animal info (5 week old, C57BL/6, female); dependence;

4. Doxycycline

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

ALZET Comments: Doxycycline; PBS; CSF/CNS (right lateral ventricle); Mice (transgenic); 1007D; 7 days; 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. Exp Mol Pathol 2014;96(3):431-7



ALZET Comments: Telmisartan; PD123319; Doxycycline; aliskiren; Saline; water; SC; mice; 2004; 2, 6 weeks; 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

ALZET Comments: Doxycycline; Saline; CSF/CNS; Mice (transgenic); 1007D; 4 days; 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

ALZET Comments: Thyroxine, L-; doxycycline; SC; Rat; 1002; 14 days; 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

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.

5. Gentamicin

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 the 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 **Vehicle:** Not Stated; **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 (data not shown)

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 **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)

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; **Duration:** Not Stated;

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

6. Minocycline

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; **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;

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 µg/day); animal info (24 weeks old, Sprague Dawley, Female); enzyme inhibitor (Microglia inhibitor); dependence;

Q8058: A. Kuroda, *et al.* Minocycline Directly Enhances the Self-Renewal of Adult Neural Precursor Cells. *Neurochem Res* 2018;43(1):219-226

Agents: Minocycline **Vehicle:** Saline; **Route:** CSF/CNS (Lateral ventricle); **Species:** Mice; **Pump:** 1007; **Duration:** 7 days; **ALZET Comments:** "Dose (0.6 µL/h); Controls received mp w/ vehicle; animal info (20-30 weeks old, Male); Brain coordinates (0.3 mm posterior to Bregma, 0.8 mm lateral, and 2.7 mm below the surface of the skull); bilateral cannula used; cyanoacrylate adhesive; gene therapy; "

Q6332: J. Zhang, *et al.* Prevention and reversal of latent sensitization of dorsal horn neurons by glial blockers in a model of low back pain in male rats. *J Neurophysiol* 2017;118(4):2059-2069

Agents: Minocycline, fluorocitrate **Vehicle:** PBS, artificial cerebrospinal fluid; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2002; **Duration:** 6 days, 3 days; **ALZET Comments:** Dose (200 µg/day); Controls received mp w/ vehicle; animal info (adult male Sprague- Dawley rats);

7. Mitomycin

P1874: X. Lu, *et al.* Inflammation near the nerve cell body enhances axonal regeneration. *J. Neurosci* 1991;11(4):972-978 **ALZET Comments:** Mitomycin C; CSF/CNS (intrathecal); Rat; no duration posted; 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

ALZET Comments: Mitomycin C; Saline; IP; mice; no duration posted; 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)

ALZET Comments: Mitomycin C; bladder; Rat; 2ML2; 2 weeks; 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)

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

P0818: W. M. Murphy, *et al.* Carcinogenesis in mammalian urothelium: changes induced by non-carcinogenic substances and chronic indwelling catheters. *J. Urol* 1986;135(4):840-844

ALZET Comments: Mitomycin; Water; bladder; Rat; 1 year and 3 weeks; pump replaced periodically; mp connected to bladder via catheter; tumors induced by infusion of water or agent; lesions reversible over time; long-term study; cancer; controls received surgery only; mps cultured upon removal; tissue perfusion.

8. Neomycin

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-JNKI-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.

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).

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

ALZET Comments: Brain-derived neurotrophic factor; Ciliary neurotrophic factor; Neomycin;; Perilymph, artificial; Ear (scala tympani); Guinea pig; 2002; 26 days; 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.

P5315: R. K. Shepherd, *et al.* A multichannel scala tympani electrode array incorporating a drug delivery system for chronic intracochlear infusion. *Hearing Research* 2002;172(1-2):92-98

ALZET Comments: Neomycin; Kanamycin; Furosenide; PBS; ear (scala tympani); Guinea pig; 2004; 28 days; Tissue perfusion (round window); functionality of mp verified by residual volume; diagram of pump and electrode assembly (p. 94); catheter patency assessed by passing fluid through the line at the end of the experiment; Neomycin infused in pilot study; Kanamycin and furosenide were co-infused in a second study.



P5489: P. Cuevas, *et al.* Inhibition of rat glioma growth by neomycin. Preliminary report. NEUROLOGICAL RESEARCH 2002;24(6):522-524

ALZET Comments: Neomycin; PBS; CSF/CNS (intratumoral); Rat; 2004; 26 days; Controls received mp w/ vehicle; tissue perfusion (tumor); cancer.

9. 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

ALZET Comments: Antibody, anti-nerve growth factor, neutralizing mouse; serum; immunoglobulin-G; penicillin; streptomycin; PBS; CSF/CNS (cortex); Rat; 2001; 1 week; 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

ALZET Comments: Interleukin-3, recomb. mouse; Penicillin; Streptomycin; Glycerol; PBS; IP; SC; mice; 2001; 2002; 7 days, 2 weeks; 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. Am. Rev. Respir. Dis 1987;135(10):15-1019

ALZET Comments: Clindamycin HCl; Penicillin G; Sodium hydroxide; Water; SC; mice; 72 hours; 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(10):1-1005

ALZET Comments: Endotoxin, E. coli; Interleukin-3, recomb. mouse; Penicillin; Streptomycin; Glycerol; PBS; SC; mice; 3 and 7 days; 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.

10. Rapamycin

Q7037: J. Zhang, *et al.* Neuroinflammation and central PI3K/Akt/mTOR signal pathway contribute to bone cancer pain. Mol Pain 2019;15(17):44806919830240

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

ALZET Comments: animal info (200-250 gr Wistar rats); rapamycin is an mTOR inhibitor; LY294002 is a PI3K inhibitor; IL-1Ra is an IL-1b receptor antagonist, SC144 is a gp130 antagonist, etanercept is a TNF- α receptor antagonist; 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);

Q5705: X. Wang, *et al.* Cerebral mTOR signal and pro-inflammatory cytokines in Alzheimer's disease rats. Transl Neurosci 2016;7(1):151-157

Agents: Rapamycin; amyloid protein, beta (1-42) **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: animal info (male, Sprague Dawley, 3-4 months old, 300-350g); Multiple pumps per animal (2); neurodegenerative (Alzheimer's); behavioral testing (Y-maze); immunology; Bilateral infusion; used jewelers' screw and dental zinc cement; Dose (10 mg/kg amyloid beta, rapamycin 500 ug/2 weeks); Brain coordinates;



Q5074: H. Z. Toklu, *et al.* Anorexic response to rapamycin does not appear to involve a central mechanism. Clinical and Experimental Pharmacology and Physiology 2016;43(9):802-7

Agents: Rapamycin **Vehicle:** DMSO; PEG 400; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, F344 Brown Norway, 23-25 months old); 10% DMSO and 90% PEG used; used PE-50 tubing; pumps initially filled with aCSF - after one week recovery, pumps replaced with rapamycin or vehicle pump; Dose (30 ug/day); Brain coordinates (1.1 mm posterior to Bregma and 1.6 mm ventral from the skull surface on the midline (medial s- sure), with the nose bar set at 4 mm below the ear bars (below zero)) pg 805;

Q5195: P. J. Scarpace, *et al.* Rapamycin Normalizes Serum Leptin by Alleviating Obesity and Reducing Leptin Synthesis in Aged Rats. J Gerontol A Biol Sci Med Sci 2016;71(7):891-9

Agents: Rapamycin **Vehicle:** DMSO; PEG 400; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, F344 x Brown Norway, 24 months old); pumps replaced after 14 days; ALZET brain infusion kit used; 10% DMSO used; 90% PEG 400 used; post op. care (rats kept warm until recovered); used aCSF filled pump for 14 days, then replaced with rapamycin or vehicle for 28 day infusion; obesity; Dose (30 ug/day); Brain coordinates (1.3 mm posterior to bregma, 1.9 mm lateral to the midsagittal suture and to a depth of 3.5mm);

Q6621: E. Moisseiev, *et al.* Intravitreal Administration of Human Bone Marrow CD34+ Stem Cells in a Murine Model of Retinal Degeneration. Invest Ophthalmol Vis Sci 2016;57(10):4125-35

Agents: FK506; Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 1 month; **ALZET Comments:** Dose (1 ug/g/day); animal info (3 week old mice); FK506 aka Tacrolimus;

11. 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

ALZET Comments: Y-27632; streptomycin; PBS, sterile; penicillin; CSF/CNS (intrathecal); Rat; 2002; 2 weeks; 2, 4 days; 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

ALZET Comments: Antibody, anti-nerve growth factor, neutralizing mouse; serum; immunoglobulin-G; penicillin; streptomycin; PBS; CSF/CNS (cortex); Rat; 2001; 1 week; 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

ALZET Comments: Streptomycin; Saline; Ear (cochlea); Guinea pig; 2002; 24 hours; 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

ALZET Comments: Interleukin-3, recomb. mouse; Penicillin; Streptomycin; Glycerol; PBS; IP; SC; mice; 2001; 2002; 7 days, 2 weeks; 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



ALZET Comments: Endotoxin, E. coli; Interleukin-3, recomb. mouse; Penicillin; Streptomycin; Glycerol; PBS; SC; mice; 3 and 7 days; 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.

12. Tetracycline

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

ALZET Comments: Angiotensin II, Tetracycline-3, chemically modified; Saline; CSF, artificial; SC; CSF/CNS (left lateral ventricle); Rat; 2004; 4 weeks; 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

ALZET Comments: Calcium hydroxide; Barium hydroxide; Tetracycline; Glycerol; bone (femur); Rat; 4 weeks; no stress (see pg. 274); tissue perfusion; good methods.

13. 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

ALZET Comments: Tobramycin; IP; Guinea pig; Rat; 2ML1; 7 days, 72 hours; 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.

14. Tunicamycin

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

ALZET Comments: RNA, small interfering (PDI; DTNB); bacitracin; Immunoglobulin, anti-PDI; tunicamycin ;; CSF/CNS; Rat; 1007D; 7 days, 14 days; 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); Brain coordinates;

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)

ALZET Comments: Tunicamycin; DMSO; SC; Mice; 1004; 4 weeks; 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)

ALZET Comments: Tunicamycin; Saline; bone (mandible); Rat; 2001; 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



ALZET Comments: Tunicamycin; Cycloheximide; Desipramine; Fluoxetine; Mianserin; Trazodone; CSF/CNS; SC; Rat; 2001; 2ML1; 4-7 days; comparison of sc injections vs. mp; cyclo. and tunica. delivered icv for 5 days.