References on the Administration of Antibiotics Using ALZET® Osmotic Pumps

1. Actinomycin D

**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


**Agents**: Florfenicol voriconazole; fentanyl; amikacin **Vehicle**: Not Stated; **Route**: SC; in vitro; **Species**: Rat; Snake (corn, rattlesnake); 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); puda (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 accidently in air sacs during intracoelomic implantation)"


**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);


**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 scutulaus Mojave rattlesnake, green iguana); stress/adverse reaction: (see pg. 23);


**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;
3. Bleomycin

Agents: Bleomycin Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 14 days;
ALZET Comments: Dose (100 μg/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;

Agents: Bleomycin hydrochloride Vehicle: Saline; 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;

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;

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

ALZET Comments: Doxycycline; PBS; CSF/CNS (right lateral ventricle); Mice (transgenic); 1007D; 7 days; Dose ((12 mg/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).
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).

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).

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

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

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)

Agents: Gentamicin Vehicle: Not Stated; Route: SC; Species: Rat (transgenic); Pump: 1007D; Duration: 5 days;
ALZET Comments: Animal info (S3344ter-4, heterozygous, P15)

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)

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;


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

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


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, Sprague Dawley, Female); enzyme inhibitor (Microglia inhibitor); dependence;


Agents: Minocycline Vehicle: Saline; Route: CSF/CNS (Lateral ventricle)  
Species: Mice  
Pump: 1007  
Duration: 7 days; 

ALZET Comments: "Dose (0.6 uL/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; "


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


ALZET Comments: Mitomycin C; CSF/CNS (intrathecal); Rat; no duration posted; no comment posted.


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

**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.


**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.


**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


**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); 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.


**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).


**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.


**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.

**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.


**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.


**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(1744806919830240

**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-a 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);


**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;
**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;

**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 midsaggital suture and to a depth of 3.5mm);

**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

**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.

**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.

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

**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.

12. Tetracycline


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;.


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

13. Tobramycin


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/ infusion aid pumps; antibiotics.

14. Tunicamycin


ALZET Comments: RNA, small interfering (PDI; DTNB); bactracin; 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;.


ALZET Comments: Tunicamycin; DMSO; SC; Mice; 1004; 4 weeks; Control animsl received mp w/ vehicle; animal info (HFD-fed foz/foz).


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;.

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.