## Recent References (2009-Present) on the Administration of Agents to Nerves Using ALZET® Osmotic Pumps

**Q9130:** W. Zhong, *et al.* Blockade of peripheral nociceptive signal input relieves the formation of spinal central sensitization and retains morphine efficacy in a neuropathic pain rat model. Neuroscience Letters 2020;716(134643
**Agents:** Ropivacaine **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
**ALZET Comments:** Dose (10 µl/hour); 0.9% NaCl used; animal info (male Sprague-Dawley rats, 200–250 g, aged 6–8 weeks); spinal cord injury;

**Q9475:** H. Y. Shin, *et al.* Alteration in global DNA methylation status following preconditioning injury influences axon growth competence of the sensory neurons. Experimental Neurology 2020;326(113177
**Agents:** Cytidine, 5-aza-2'-deoxy-; Methionine, S-adeno-syl- **Vehicle:** DMSO; PBS; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
**ALZET Comments:** Dose (1 mM 5-aza-2'-deoxycytidine; 1mM S-adeno-sylmethionine); Controls received mp w/ vehicle; animal info (Adult female Sprague Dawley rats, 250–300 g); 5-aza-2'-deoxycytidine aka 5-aza; S-adeno-sylmethionine aka SAM;

**Q7850:** M. L. D. Rayner, *et al.* Developing an In Vitro Model to Screen Drugs for Nerve Regeneration. Anat Rec (Hoboken) 2018;301(10):1628-1637
**Agents:** ibuprofen **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 1004; **Duration:** 21 days;
**ALZET Comments:** Dose (7 µg/day); Controls received mp w/ vehicle; animal info (male, Wistar, 220-250g); pump was implanted locally parallel to re-connected nerve (p.1631);

**Q7084:** M. Caillaud, *et al.* Local low dose curcumin treatment improves functional recovery and remyelination in a rat model of sciatic nerve crush through inhibition of oxidative stress. Neuropharmacology 2018;139(98-116
**Agents:** Curcumin **Vehicle:** Saline; **Route:** CSF/CNS (Sciatic nerve); **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;
**ALZET Comments:** Dose (0.2mg/day); 0.9% saline used; post op. care (buprenorphine 0.05 mg/kg); behavioral testing (Von Frey's filament test, SSI test, beam walking test); neurodegenerative (nerve regeneration);

**Q7085:** M. Buffelli, *et al.* Activity-dependent vs. neurotrophic modulation of acetylcholine receptor expression: Evidence from rat soleus and extensor digitorum longus muscles confirms the exclusive role of activity. European Journal of Neuroscience 2018;47(12):1474-1481
**Agents:** Tetrodotoxin **Vehicle:** Saline; **Route:** CSF/CNS (left sciatic nerve); **Species:** Rat; **Pump:** 2ML4; 2ML2; **Duration:** 20 days;
**ALZET Comments:** Dose (10.2 ug/day); animal info (Adult male Wistar, 400–600 g); neurodegenerative (Skeletal muscles); Pump connected with a silicone tubing to a custom-made silicone cuff (9 mm length, 1.4/5.0 mm ID/OD) placed around the nerve;

**Q5901:** N. H. Tu, *et al.* Na(+) /K(+) -ATPase coupled to endothelin receptor type B stimulates peripheral nerve regeneration via lactate signalling. European Journal of Neuroscience 2017;46(5):2096-2107
**Agents:** Ouabain **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** mice; **Pump:** 1004; **Duration:** 4 weeks;
**ALZET Comments:** animal info (male, Thy1-YFP tg, 8-10 weeks old); post op. care (heater until mice could move freely); behavioral testing (hind paw withdrawal); Used ALZET catheter to infuse to sciatic stump; see diagram (pg 2098);

**Q6158:** A. G. Fisher, *et al.* Transcriptomic and epigenetic regulation of disuse atrophy and the return to activity in skeletal muscle. FASEB J 2017;31(12):5268-5282
**Agents:** Tetrodotoxin **Vehicle:** Saline; **Route:** CSF/CNS (peroneal nerve); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
**ALZET Comments:** Dose (350mg/ml); 0.9% saline used; Controls received mp w/ vehicle; animal info (Male Wistar rats weighing between 350–450 g); delivery tubes were channeled to a silicone rubber cuff that was carefully placed around the common peroneal nerve of the left hind limb (Fig.1);

**Q4655:** J. G. Yan*, et al.* CALCITONIN PUMP IMPROVES NERVE REGENERATION AFTER TRANSECTION INJURY AND REPAIR. MUSCLE & NERVE 2015;51(229-234
**Agents:** Calcitonin **Vehicle:** Water, distilled sterile; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2006; **Duration:** 12 weeks;
**ALZET Comments:** Animal info (Sprague Dawley, 250-300g, 3 months old); half-life (p.233); long-term study; "To achieve a continuous and gradual mode of delivery, a mini-osmotic pump was implanted to deliver medication at a constant 0.15 ul/h" pg 233; "Calcitonin has short absorption and elimination half-lives of 10–15 minutes and 50–80 minutes, respectively; however, using an osmotic pump allows for gradual and prolonged release." pg233; pg230 diagram of pump implantation;

**Q4646:** B. A. Williams*, et al.* Multimodal Perineural Analgesia with Combined Bupivacaine-Clonidine-Buprenorphine-Dexamethasone: Safe In Vivo and Chemically Compatible in Solution. PAIN MEDICINE 2015;16(186-198
**Agents:** Bupivacaine; clonidine; dexamethasone **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, albino, CD[SD]); no stress (see pg. 192); post op. care (IM butorphanol tartrate 0.05 mg/kg, ceftiofur sodium 5 mg/kg); stability verified by (pg. 195); used polyurethane catheter 0.5mm ID 0.9 mmOD; pumps removed after 1 week; dose (66.6 ug/mL)

**Q3960:** J. Y. Lee*, et al.* Simultaneous Inferior Alveolar Nerve Regeneration and Osseointegration With a Nerve Growth Factor-Supplying Implant: A Preliminary Study. Journal of Oral and Maxillofacial Surgery 2015;73(410-423
**Agents:** Nerve growth factor, human B- **Vehicle:** PBS; **Route:** CSF/CNS (inferior alveolar nerve); **Species:** Dog (beagle); **Pump:** 2ML2; **Duration:** 6 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, beagle, 18 weeks old, 10-12 kg); good methods (picture of implant pg 413); Multiple pumps per animal (2; one pump delivered NGF other delivered PBS); used rat jugular catheter, 15 cm long; pump body placed into retromandibular area; long-term study;

**Q3330:** S. Unezaki*, et al.* Involvement of Na(x) sodium channel in peripheral nerve regeneration via lactate signaling. European Journal of Neuroscience 2014;39(5):720-729
**Agents:** Lactate; hydroxycinnamic acid, alpha-cyano-4; **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Mice (transgenic); **Pump:** 1004; **Duration:** 4 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; animal info ([B6.Cg-Tg (thy1-YFP)16Jrs/J, Nax -/-, 8-15 weeks old); behavioral testing (von frey filaments, neurometer analysis); alpha-cyano-4 hydroxycinnamic acid aka CIN; used catheter tubing #7701 to attach pump to silicone tubing sutured to nerve stump; schematic of surgery on pg.725, figure 3A;

**Q3625:** C. D. Schuh*, et al.* Prostacyclin mediates neuropathic pain through interleukin 1beta-expressing resident macrophages. Pain 2014;155(3):545-555
**Agents:** CAY10441 **Vehicle:** PBS; DMSO; **Route:** CSF/CNS (sciatic nerve); **Species:** Mice; **Pump:** 1007D; **Duration:** 4 days; 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL6N or IP receptor KO mice); 1% DMSO used; behavioral testing (paw withdrawal latency); immunology; sciatic nerve injury; used RenaSil tube attached to PE-60, and fixed by Stabiloblast 2-component glue; pumps primed in 37C saline; pumps implanted subcutaneously and fixed with 6-0 Prolene suture to muscle; CAY10441 is an IP receptor antagonist;

**R0327:** M. Favero*, et al.* The Timing of Activity Is a Regulatory Signal During Development of Neural Connections. Journal of Molecular Neuroscience 2014;53(324-329
**Agents:** Tetrodotoxin **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** Not Stated; **Duration:** 7,10 days;
**ALZET Comments:** Animal info (AO Rat); nerve injury; functionality of mp verified by establishment of a chronic conduction block; tissue perfusion (sciatic nerve);

**Q4705:** M. J. Buys, *et al.* Novel Use of Perineural Pregabalin Infusion for Analgesia in a Rat Neuropathic Pain Model 1809. Anesthesia & Analgesia 2014;119(481-488
**Agents:** Pregabalin **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 8-9 weeks old); behavioral testing (Hargreaves' radient heat testing, guarding behavior, incapacitance testing); pump and catheter secured using 4-0 silk suture; sciatic nerve injury;

**Q3125:** J. G. Yan, *et al.* The effect of calcium modulating agents on peripheral nerve recovery after crush. Journal of Neuroscience Methods 2013;217(1-2):54-62
**Agents:** Nifedipine; calcitonin **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2006; **Duration:** 4 weeks;
**ALZET Comments:** Controls received mp w/ saline or sham only; animal info (3 month old, male, Sprague-Dawley 250-300g); functionality of mp verified by decrease in calcium levels; peptides; Picture of MP p56, Fig1A. MP Pump setup p56, Fig1B;

**Q2637:** B. C. Gill, *et al.* Neurotrophin therapy improves recovery of the neuromuscular continence mechanism following simulated birth injury in rats. NEUROUROLOGY AND URODYNAMICS 2013;32(1):82-87
**Agents:** Albumin **Vehicle:** Saline, sterile; **Route:** CSF/CNS (pudendal nerve); **Species:** Rat; **Pump:** 1007D; 2002; **Duration:** 1, 2 weeks;
**ALZET Comments:** Animal info (Sprague Dawley, female, virgin, 200-225 g); bilateral cannula used; "localized continuous neurotrophin supplementation has been most effective at promoting nerve regeneration and provided the rationale behind utilizing miniature osmotic pumps in this study." pg 86; bilateral infusion;

**Q2687:** V. T. Ribeiro-Resende, *et al.* Bone marrow-derived fibroblast growth factor-2 induces glial cell proliferation in the regenerating peripheral nervous system. Molecular Neurodegeneration 2012;7(;):U1-U17
**Agents:** Antibody, Fibroblast growth factor-2, mouse, monoclonal **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve);
**Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;
**ALZET Comments:** Animal info (male, Lister Hooded, 3 mo old)

**Q1798:** J. A. Martinez, *et al.* Comparison of central versus peripheral delivery of pregabalin in neuropathic pain states. Molecular Pain 2012;8(;):U7-U26
**Agents:** Pregabalin, $I^{125}$; pregabalin, unlabeled **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); CSF/CNS (sciatic nerve);
**Species:** Rat; **Pump:** 2002; **Duration:** 72 hours;
**ALZET Comments:** Controls received mp w/ saline; animal info (Sprague Dawley, male, 200-225 g); catheter patency and functionality of mp verified via pump infusion of india ink; neuropathic pain

**Q2547:** J. M. Kim, *et al.* Increased expression of oxyproteins in the optic nerve head of an in vivo model of optic nerve ischemia. BMC Pharmacology 2012;12(;):U1-U6
**Agents:** Endothelin-1 **Vehicle:** Not Stated; **Route:** CSF/CNS (optic nerve, perineural region); **Species:** Rabbit; **Pump:** Not Stated; **Duration:** 2, 4, 8 weeks;
**ALZET Comments:** Animal info (New Zealand, 2.5-3.5 kg); long-term study; PE tubing used

**Q2157:** M. Favero, *et al.* Spike timing plays a key role in synapse elimination at the neuromuscular junction. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2012;109(25):E1667-E1675
**Agents:** Tetrodotoxin **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;
**ALZET Comments:** Animal info (AO strain, 200-400 g, Harlan); fig 1, schematic of pump and placement of conduction block

**Q2413:** D. I. Carrasco, *et al.* Motor terminal degeneration unaffected by activity changes in SOD1(G93A) mice; a possible role for glycolysis. NEUROBIOLOGY OF DISEASE 2012;48(1):132-140
**Agents:** Tetrodotoxin; dexamethasone **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Mice; **Pump:** 2002;
**Duration:** Not Stated;
**ALZET Comments:** Animal info (SOD1 G93A); good methods, pg 133

**Q1387:** X. Y. Wang, *et al.* Impaired Activity-Dependent Plasticity of Quantal Amplitude at the Neuromuscular Junction of Rab3A Deletion and Rab3A Earlybird Mutant Mice. Journal of Neuroscience 2011;31(10):3580-3588
**Agents:** Tetrodotoxin **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Mice; **Duration:** 7-8 days;
**ALZET Comments:** Animal info (Rab3a +/-, male, female, 2.5-3.5 mo old, C57BL/6J); silastic cuff used

**Q1435:** X. Y. Wang, *et al.* Activity-Dependent Regulation of the Binomial Parameters p and n at the Mouse Neuromuscular Junction In Vivo. Journal of Neurophysiology 2010;104(5):2352-2358
**Agents:** Tetrodotoxin **Vehicle:** NaCl; **Route:** CSF/CNS (sciatic nerve); **Species:** Mice; **Pump:** 1002; **Duration:** Not Stated;
**ALZET Comments:** Animal info (unaffected litter mates of ClCn1adr-mto2J, 2-4 mo old); catheter tubing was filled with saline so that "after surgery the foot muscles were not paralyzed" pg 2353

**Q1362:** R. N. Toledo, *et al.* The Action of Topical Basic Fibroblast Growth Factor in Facial Nerve Regeneration. OTOLOGY & NEUROTOLOGY 2010;31(3):498-505
**Agents:** Fibroblast growth factor, basic; albumin, human **Vehicle:** Ringer lactate solution; **Route:** CSF/CNS (facial nerve anastomosis); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ sodium heparin, human albumin in Ringer lactate solution; animal info (male, Wistar, adult); functionality of mp verified by residual volume; good methods, pg 499; stress/adverse reaction: (see pg. 501) "neuroma at the anastomosis", "hemoatoma at the surgical incision"; tissue perfusion (epineural anastomosis); vinyl catheter used; "We chose to use minipumps because this method allows better control of the quantity of bFGF delivered at the target site and is compatible with standard facial nerve surgical techniques. Furthermore, the isolate reservoir of the minipumps prevents the contact of the study drug with substances that could inactivate it" pg 502

**Q0898:** L. J. Kasselman, *et al.* Application of Angiotensin II to Healthy Rat Sciatic Nerve Can Produce Neuropathy Without Associated Vasculopathy. Muscle & Nerve 2010;42(6):959-965
**Agents:** Angiotensin II **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2004; **Duration:** 12 weeks;
**ALZET Comments:** Controls received mp w/ PBS; animal info (male, Wistar, 250-300 g); peptides; long-term study; good methods, pg 960; no stress (see pg. 961) "All animals from both groups survived the surgery without complications"; pump connected to silicone tube that was connected to a piece of Gelfoam; Fig. 1, schematic of pump, tube, and gelfoam. pg 960

**Q0133:** M. Favero, *et al.* The Timing of Impulse Activity Shapes the Process of Synaptic Competition at the Neuromuscular Junction. Neuroscience 2010;167(2):343-353
**Agents:** Tetrodotoxin **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2002; 2ML4; **Duration:** Not Stated;
**ALZET Comments:** Animal info (adult, male, Wistar, 180-350 g)

**Q0154:** P. J. Apel, *et al.* Effect of Locally Delivered IGF-1 on Nerve Regeneration During Aging: An Experimental Study in Rats. Muscle & Nerve 2010;41(3):335-341
**Agents:** Insulin-like growth factor-I, recomb. human **Vehicle:** Not Stated; **Route:** CSF/CNS (tibial nerve); **Species:** Rat; **Pump:** 2004; **Duration:** 12 weeks;
**ALZET Comments:** Controls received mp w/ saline; long-term study; pumps replaced after 6 weeks; animal info (Fischer 344 x Brown Norway, Sprague Dawley; 8 months old, 24 months old); diagram of pump with custom-made T-tube

**P9573:** X. Wang, *et al.* Increase in endothelin B receptor expression in optic nerve astrocytes in endothelin-1 induced chronic experimental optic neuropathy. Experimental Eye Research 2009;88(3):378-385
**Agents:** Endothelin-1 **Vehicle:** Not Stated; **Route:** CSF/CNS (optic nerve); **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;
**ALZET Comments:** Post op. care (buprenorphine); animal info (adult, male, Brown Norway, 250-300g); fellow eye served as untreated control; silastic tubing used; brain tissue distribution

**Q0436:** G. Vrbova, *et al.* Chemical communication between regenerating motor axons and Schwann cells in the growth pathway. European Journal of Neuroscience 2009;30(3):366-375
**Agents:** Gallamine triethiodide; tubocurarine; atropine; suramin **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2ML4; **Duration:** 2-4 weeks;
**ALZET Comments:** Controls received mp w/saline; animal info (female, adult, Sprague Dawley, 200-220 g); schematic illustration of pump with silastic catheter, Fig 1b

**P9872:** S. Unezaki, *et al.* Effects of neurotrophic factors on nerve regeneration monitored by in vivo imaging in thy1-YFP transgenic mice. Journal of Neuroscience Methods 2009;178(2):308-315
**Agents:** Nerve growth factor; glial-derived neurotrophic factor **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Mice (transgenic); **Pump:** 1004; **Duration:** 4 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; half-life (p. 308) "short"; animal info (10 wks old, 20 g., Thy1-YEP); image of pump pg. 309; schematic of drug delivery system with pump+silicone, fig. 1); "Because of the short biological half-life of neurotrophic factors, a delivery system that protects the protein and slowly releases it locally over a prolonged period of time is required." pg. 308; tissue perfusion (sciatic nerve)

**Q0519:** C. C. Toth, *et al.* Locally Synthesized Calcitonin Gene-Related Peptide Has a Critical Role in Peripheral Nerve Regeneration. Journal of Neuropathology and Experimental Neurology 2009;68(3):326-337
**Agents:** Cycloheximide; puromycin **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
**ALZET Comments:** Animal info (adult, male, Sprague-Dawley, 250-300 g)

**Q0748:** H. K. Lee, *et al.* Nidogen Plays a Role in the Regenerative Axon Growth of Adult Sensory Neurons Through Schwann Cells. Journal of Korean Medical Science 2009;24(4):654-659
**Agents:** Alkaline phosphatase tag; eTEM-AP, recomb. **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 1002; **Duration:** 2 weeks;
**ALZET Comments:** Controls received mp w/ alkaline phosphatase tag; animal info (adult, male, Sprague-Dawley, 150-300 g); peptides