



References on Pain Research Using ALZET® Osmotic Pumps

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);

Q6999: S. J. Shiue, *et al.* Mesenchymal stem cell exosomes as a cell-free therapy for nerve injury-induced pain in rats. *Pain* 2019;160(1):210-223

Agents: Exosomes, human umbilical cord mesenchymal stem cell **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Dose (1.2 mg/mL/ hr); Controls received mp w/ vehicle; animal info (Male Sprague–Dawley rats, 200 to 250 g); Therapeutic indication (neuropathic pain);

Q7427: M. Shinoda, *et al.* Spinal glial cell line-derived neurotrophic factor infusion reverses reduction of Kv4.1-mediated A-type potassium currents of injured myelinated primary afferent neurons in a neuropathic pain model. *Mol Pain* 2019;15(1744806919841196

Agents: Glial cell line-derived neurotrophic factor, recombinant human **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Dose (0.5 mg/ml); Controls received mp w/ vehicle; animal info (adult male Sprague-Dawley rats weighing 210 to 240 g); Therapeutic indication (neuropathic pain);

Q7581: E. Nguyen, *et al.* (353) Cell-Type Specific Modulation of RBM Neurons in Nociceptive Behaviors. *The Journal of Pain* 2019;20(4):S62-S63

Agents: Fentanyl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (0.01 mg/kg/hr); animal info (Male, Sprague Dawley); neurodegenerative (Chronic pain);

Q8286: T. Miladinovic, *et al.* Spinal microglia contribute to cancer-induced pain through system xC (-)-mediated glutamate release. *Pain Rep* 2019;4(3):e738

Agents: Sulfasalazine **Vehicle:** Ammonium Hydroxide; **Route:** CNS/CSF; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Dose (6.6 mg/kg/day); Controls received mp w/ vehicle; animal info (BALB/c, 4-6 weeks old); behavioral testing (Nociception Test); Sulfasalazine aka SSZ; cancer (Cancer-induced pain);

Q7578: S. Lux, *et al.* The antinociceptive effect of resveratrol in bone cancer pain is inhibited by the Silent Information Regulator 1 inhibitor selisistat. *J Pharm Pharmacol* 2019;71(5):816-825

Agents: Selistate **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 10074D; **Duration:** 1 week;

ALZET Comments: Dose (0.5 lg/h); Controls received mp w/ vehicle; animal info (Male BALB/c mice (20–30 g)); cancer (pain); Therapeutic indication (cancer pain (nociception));

Q8248: G. W. Lee, *et al.* Central VEGF-A pathway plays a key role in the development of trigeminal neuropathic pain in rats. *Mol Pain* 2019;15(1744806919872602

Agents: VEGF-A164 antibody **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Dose (250 ng or 500 ng/day); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 200-230 g); bilateral cannula used; neurodegenerative (Neuropathic pain);



Q8189: R. de la Puerta, *et al.* BMP-7 protects male and female rodents against neuropathic pain induced by nerve injury through a mechanism mediated by endogenous opioids. *Pharmacol Res* 2019;150(104470)

Agents: recombinant BMP-7 **Vehicle:** CSF; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Dose (6µg/kg/day); Controls received mp w/ vehicle; animal info (8–10 weeks old wild type 3 (C57BL/6) and BMP-7+/- male and female mice); recombinant BMP-7 aka rBMP-7; neurodegenerative (BMP-7 and its type I receptors were detected in regions of the nervous system involved in pain transmission, processing, and modulation);

Q6900: Tramullas M, *et al.* MicroRNA-30c-5p modulates neuropathic pain in rodents. *Science Translational Medicine* 2018;10(453):

Agents: Transforming growth factor-b1 **Vehicle:** Hydrochloric acid; albumin; PBS; **Route:** Not Stated; **Species:** Mice (knockout); **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Dose (6.2 ng/hour); animal info (BAMBI-/- mice); Therapeutic indication (chronic pain);

Q7861: S. Ruoss, *et al.* Inhibition of calpain delays early muscle atrophy after rotator cuff tendon release in sheep. *Physiol Rep* 2018;6(21):e13833

Agents: calpeptin **Vehicle:** DMSO; **Route:** intramuscular (infraspinatus); **Species:** Sheep; **Pump:** 2ML4; **Duration:** 6 weeks;

ALZET Comments: Dose (0.75 mg/day); animal info (26.7+/-1.4 months, female, Swiss Alpine); pumps replaced at 2 weeks; calpeptin is a synthetic calpain inhibitor; enzyme inhibitor (calpain); tissue perfusion (m. infraspinatus); good methods (detailed pump implantation procedure on page 3.); Therapeutic indication (calpain inhibition prevented the early unloading adaptations, but not the subsequent initiation of rotator cuff disease); 75% DMSO used;

Q7732: N. Papp, *et al.* Acute and chronic escitalopram alter EEG gamma oscillations differently: relevance to therapeutic effects. *European Journal of Pharmaceutical Sciences* 2018;121(347-355)

Agents: Escitalopram-oxalate **Vehicle:** 0.3 N HCl; Distilled Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 21 days;

ALZET Comments: "Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Male Wistar Rats 250–280 g); no stress (see pg. 348 ""All

efforts were made to minimize pain, suffering and discomfort of the animals.""); Depression study; "

Q8143: K. M. Nation, *et al.* Lateralized kappa opioid receptor signaling from the amygdala central nucleus promotes stress-induced functional pain. *Pain* 2018;159(5):919-928

Agents: Morphine Sulfate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Dose (7.68 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 175-200 g); post op. care (Gentamycin); neurodegenerative (Functional Pain Syndrome);

Q7226: H. Matsuoka, *et al.* Neurotrophin((R)) Accelerates the Differentiation of Schwann Cells and Remyelination in a Rat Lysophosphatidylcholine-Induced Demyelination Model. *Int J Mol Sci* 2018;19(2):

Agents: Neurotrophin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1 Week;

ALZET Comments: Dose (24 NU/kg/day); Controls received mp w/ vehicle; animal info (male Wistar rats, 180–220 g); Neurotrophin® is a non-protein extract of inflamed rabbit skin inoculated with vaccinia virus; Therapeutic indication (neuropathic pain);

Q5934: D. Yu, *et al.* Multiplexed RNAi therapy against brain tumor-initiating cells via lipopolymeric nanoparticle infusion delays glioblastoma progression. *Proc Natl Acad Sci U S A* 2017;114(30):E6147-E6156

Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** mice (nude); **Pump:** 1002, 2002; **Duration:** 14 days;

ALZET Comments: animal info (athymic nude, 6-8 weeks old); ALZET brain infusion kit 3 used; cancer (glioblastoma);

"Because repeated surgery introduces stress and pain that may impact the survival of the experimental animals, we opted for the convection-enhanced delivery (CED) strategy using an Alzet osmotic pump to deliver a continuous supply of the nano RNAi combination..." pg E6151;



Q5695: T. L. Uhlendorf, *et al.* Efficacy of Two Delivery Routes for Transplanting Human Neural Progenitor Cells (NPCs) Into the Spastic Han-Wistar Rat, a Model of Ataxia. *Cell Transplantation* 2017;26(2):259-269

Agents: Cyclosporine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** Not Stated;

ALZET Comments: animal info (spastic Han-Wistar, 30 days); no stress (see pg. 268); behavioral testing (locomotor activity); cardiovascular; "This method of chronic delivery prevents painful daily injection and subsequent behavioral changes in treated animals. We did not detect any negative effects of cyclosporine, and no behavioral alterations were observed in treated mutants other than natural disease progression" pg 268; Dose (15 mg/kg/day);

Q5950: C. Quarta, *et al.* Molecular Integration of Incretin and Glucocorticoid Action Reverses Immunometabolic Dysfunction and Obesity. *Cell Metabolism* 2017;26(4):620-632 e6

Agents: Glucagon-like peptide-1, Dexamethasone **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; Dose (GLP-1: 0.1 mg/24h; Dexa: 0.0219mg/ml); animal info (20 week-old male C57bl6j); post op. care (meloxicam for post-surgical pain (3 mg/kg); ALZET brain infusion kit 3 used; Brain coordinates (anteroposterior: 0.5 mm from bregma, lateral: -/+1;2 mm to bregma and dorsoventral: 2.1 mm below skull); Therapeutic indication (obesity);

Q5812: M. Flinspach, *et al.* Insensitivity to pain induced by a potent selective closed-state Nav1.7 inhibitor. *Sci Rep* 2017;7(39662

Agents: JNJ63955918, Morphine **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2002, 2001; **Duration:** 14 days, 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (250-300g) behavioral testing (Hargreaves test, hotplate test, tail-flick test, formalin flinching); JNJ63955918 is a tarantula venom-derived peptide (a potent, highly selective, closed-state Nav1.7 blocking peptide); Therapeutic indication (Pain, analgesia, electrophysiology);

Q5784: K. Deseure, *et al.* Differential drug effects on spontaneous and evoked pain behavior in a model of trigeminal neuropathic pain. *J Pain Res* 2017;10(279-286

Agents: Carbamazepine, baclofen, clomipramine **Vehicle:** DMSO, PEG, Ethyl Alcohol, Acetone; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (7 weeks old); dimethyl sulfoxide, propylene glycol, ethyl alcohol, and acetone at a ratio of 42:42:15:1; post op. care (morphine 5 mg/day); behavioral testing (Facial grooming); Therapeutic indication (Trigeminal neuralgia, neuropathic pain);

Dose (30 mg/day carbamazepine (the first-line drug treatment for trigeminal neuralgia), 1.06 mg/day baclofen, 4.18 mg/day clomipramine, and 5 mg/day morphine);

Q6006: K. T. Chang, *et al.* Leptin is essential for microglial activation and neuropathic pain after preganglionic cervical root avulsion. *Life Sci* 2017;187(31-41

Agents: Leptin **Vehicle:** PBS; **Route:** CSF/CNS (Cervical); **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male and female, C57B/6 J (B6) and Ob); Therapeutic indication (Obesity, Neuropathic pain); Dose (1 ug/day);

Q6005: M. Cha, *et al.* Repetitive motor cortex stimulation reinforces the pain modulation circuits of peripheral neuropathic pain. *Sci Rep* 2017;7(1):7986

Agents: Pseudosubstrate inhibitory peptide **Vehicle:** Saline; **Route:** CSF/CNS (anterior cingulate cortex); **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (200-220g); ALZET brain infusion kit 1 used; Therapeutic indication (Neuropathic pain); Dose (10 nmol/uL);

Q6413: B. B. Braden, *et al.* A comparison of progestins within three classes: Differential effects on learning and memory in the aging surgically menopausal rat. *Behavioural Brain Research* 2017;322(Pt B):258-268

Agents: NETA, progestin **Vehicle:** Propylene glycol; **Route:** Not Stated; **Species:** Rat; **Pump:** 2006; **Duration:** Not Stated;



ALZET Comments: Dose (20µg/day); Controls received mp w/ vehicle; animal info (twelve month old Fisher-344 female rats); post op. care (Rimadyl (5 mg/mL/kg) for pain and saline (2 mL) to prevent dehydration); replacement therapy (oophorectomy);

Q5165: P. Nardelli, *et al.* Reduced motor neuron excitability is an important contributor to weakness in a rat model of sepsis. *Experimental Neurology* 2016;282(1-8)

Agents: Oxymorphone **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days;

ALZET Comments: post op. care (buprenorphine SC 0.12 mg/kg; 5 ml SC saline; Baytril SC 10 mg/kg Q12H); used 2ML size; pumps used for continuous pain relief in rat sepsis model; Dose (30 ug/kg/h);

Q6616: R. Matos, *et al.* Bladder pain induced by prolonged peripheral alpha 1A adrenoceptor stimulation involves the enhancement of transient receptor potential vanilloid 1 activity and an increase of urothelial adenosine triphosphate release. *Acta Physiologica* 2016;218(4):265-275

Agents: Phenylephrine **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 1002; **Duration:** Not Stated;

ALZET Comments: Dose (0.0498 mg/day); Controls received mp w/ vehicle; animal info (female Wistar rats); enzyme inhibitor (selective α1-adrenoceptor agonist); Therapeutic indication (chronic visceral pain);

Q5838: H. K. Kim, *et al.* Tempol Ameliorates and Prevents Mechanical Hyperalgesia in a Rat Model of Chemotherapy-Induced Neuropathic Pain. *Front Pharmacol* 2016;7(532)

Agents: Tempol **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (200-350 g); cancer (Chemotherapy); behavioral testing; Therapeutic indication (Pain study, chemotherapy-induced neuropathic pain); Dose (200 mg/kg);

Q5621: H. Kim. Pentoxifylline Ameliorates Mechanical Hyperalgesia in a Rat Model of Chemotherapy-Induced Neuropathic Pain. *Pain Physician* 2016;19(4):589-600

Agents: Pentoxifylline **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (200-350g); cancer; Chronic Pain study; Therapeutic indication (Chemotherapy); Dose (.96 mg/day);

Q5649: C. T. Huang, *et al.* Neurosteroid Allopregnanolone Suppresses Median Nerve Injury-induced Mechanical Hypersensitivity and Glial Extracellular Signal-regulated Kinase Activation through gamma-Aminobutyric Acid Type A Receptor Modulation in the Rat Cuneate Nucleus. *Anesthesiology* 2016;125(6):1202-1218

Agents: PD98059 **Vehicle:** DMSO, Ringer's solution; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls underwent median nerve CCI or sham operation; functionality of mp verified by residual volume; ALZET brain infusion kit used; <1% DMSO ; behavioral testing; Compound AKA: 2-amino-3-methoxyflavone; Therapeutic indication (Neuropathic pain); Dose (2, 2.5, 3.0 mM);

Q6048: Y. Hayano, *et al.* Dorsal horn interneuron-derived Netrin-4 contributes to spinal sensitization in chronic pain via Unc5B. *J Exp Med* 2016;213(13):2949-2966

Agents: Netrin-4 **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 1002; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (8-10 weeks old, Wistar; 200-280g); behavioral testing (von Frey filament test); Therapeutic indication (Chronic pain);

Q5815: S. Fuseya, *et al.* Systemic QX-314 Reduces Bone Cancer Pain through Selective Inhibition of Transient Receptor Potential Vanilloid Subfamily 1-expressing Primary Afferents in Mice. *Anesthesiology* 2016;125(1):204-18

Agents: QX-314 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1003D; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (20-25g); cancer; behavioral testing (pain related behavior); Therapeutic indication (Bone cancer, pain); Dose (3, 5 mg/kg);

Q5347: D. A. Figge, *et al.* Dynamic DNA Methylation Regulates Levodopa-Induced Dyskinesia. *J Neurosci* 2016;36(24):6514-24



Agents: RG108 **Vehicle:** Cyclodextrin, hydroxypropyl- β -; **Route:** CSF/CNS (dorsal striatum); **Species:** Rat; **Pump:** 2004; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male Sprague-dawley, 60 – 90 days old, 180-200 g); functionality of mp verified by behavioral testing; 5% cyclodextrin used; Plastics One unilateral guide cannula used; post op. care (7 days of care, buprenorphine and wound care for pain management); behavioral testing (forepaw adjusting steps test); tissue perfusion (brain); delayed delivery “additional polyethylene tubing was added to provide a 14 d prime of vehicle before RG-108 administration” (pg. 6515); “rats were given a unilateral dopamine lesion to the left medial forebrain bundle” (pg. 6515); Brain coordinates: anteroposterior, 0 from bregma, -3mm lateral from midline, and -3.5 mm from the dura; Dose (100 μ M);

Q5780: J. E. Dalziel, *et al.* Tracking gastrointestinal transit of solids in aged rats as pharmacological models of chronic dysmotility. *Neurogastroenterol Motil* 2016;28(8):1241-51

Agents: Loperamide, Prucalopride **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (18 months); half-life of Loperamide: 9-14hr. (p.); post op. care (Lopaine 2% was given subcutaneously around the incision site to relieve discomfort.); no stress (see pg. 1243); “Continuous dosing was necessary to administer prucalopride because it is rapidly metabolized in rats... Slow release administration also avoided the stressful twice daily restraint and subcutaneous injection otherwise required for the rats dosed with loperamide (half-life 9–14 h).” pg. 1243; Therapeutic indication (Constipation, Colon transit); Dose (1, 2, 4 mg/kg/day);

Q5315: L. Bravo, *et al.* Effect of DSP4 and desipramine in the sensorial and affective component of neuropathic pain in rats. *Prog Neuropsychopharmacol Biol Psychiatry* 2016;70(57-67

Agents: Desipramine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (Adult male Harlan Sprague-Dawley rats, 200-250 g); functionality of mp verified by pain level measurements; functionality of mp verified by pain level measurements; Noradrenaline reuptake inhibitor; Chronic Constriction Injury (CCI); Therapeutic indication (Pain); Dose (10 mg/kg/d);