



References on Opioid Receptor Research Using ALZET® Osmotic Pumps

- Q6131:** A. Kliewer, *et al.* Phosphorylation-deficient G-protein-biased mu-opioid receptors improve analgesia and diminish tolerance but worsen opioid side effects. *Nat Commun* 2019;10(1):367
ALZET Comments: Fentanyl citrate; morphine sulphate salt pentahydrate; PBS; water, sterile; SC; Mice (transgenic); 1007D; 7 days; Dose (Fentanyl (2mg/kg/day); Morphine (17 mg/kg/day)); animal info (knock-in mice with 11S/T-A mutations (Oprm1tm3.1Shlz, MGI:6117673, 11S/T-A)); behavioral testing (hot plate test; open field locomotion test); dependence; "...we used subcutaneously implanted osmotic pumps to deliver opioids at a constant rate. This approach is a powerful means of assessing both tolerance and dependence in rodents" (p.5).
- Q7171:** S. Arttamangkul, *et al.* Cellular tolerance at the micro-opioid receptor is phosphorylation dependent. *Elife* 2018;7(**ALZET Comments:** Morphine sulfate; Water; SC; Rat; 2ML1; 7 days; Dose (80mg/kg/day); animal info (5-6 Weeks); tolerance;.
- Q5922:** J. Y. Xie, *et al.* Kappa opioid receptor antagonists: A possible new class of therapeutics for migraine prevention. *Cephalalgia* 2017;37(8):780-794
ALZET Comments: Sumatriptan; Saline; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 175-200g); post op. care (gentamicin 8 mg/kg SC); behavioral testing (von Frey filaments; tail flick test); Dose (0.6 mg/kg/day);.
- Q5469:** E. Tuduri, *et al.* Acute stimulation of brain mu opioid receptors inhibits glucose-stimulated insulin secretion via sympathetic innervation. *Neuropharmacology* 2016;110(Pt A):322-32
ALZET Comments: DAMGO; Water, distilled; DMSO; saline; CSF/CNS; Mice; 5 Days; Controls received mp w/ vehicle; animal info (male, C57BL6J or alpha2A-KO, 8-10 weeks old); ALZET brain infusion kit 3 used; Dose (DAMGO 4.7 nmol/day); used 7 day pump;.
- Q4840:** Z. Jiang, *et al.* Blocking mammalian target of rapamycin alleviates bone cancer pain and morphine tolerance via u-opioid receptor. *International Journal of Cancer* 2016;138(2013-2020)
ALZET Comments: Rapamycin; CTOP; LY297002; DMSO; saline; CSF/CNS (intrathecal); Rat; 14 days; Controls received mp w/ saline; animal info (Wistar, 200-250g); 50% DMSO used; cancer (breast; bone); dose-response (pg 2015); behavioral testing (hindpaw withdrawal latency); Rapamycin is an mTOR antagonist; CTOP is an MOR antagonist; LY297002 an a PI3K inhibitor;.
- Q4836:** L. S. Hwa, *et al.* Dissociation of u-opioid receptor and CRF-R1 antagonist effects on escalated ethanol consumption and mPFC serotonin in C57BL/6J mice. *Addiction Biology* 2016;21(111-124)
ALZET Comments: CP154526; naltrexone; DMSO; CSF, artificial; CSF/CNS; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (male, C58BL/6J, 8 weeks old); functionality of mp verified by IAA drinking test or morphine-sensitive tail withdrawal; ALZET brain infusion kit 3 used; 4% DMSO used; Cannula placement verified via Nissl staining;.
- Q5226:** S. H. Lockie, *et al.* Combination cannabinoid and opioid receptor antagonists improves metabolic outcomes in obese mice. *Mol Cell Endocrinol* 2015;417(10-19)
ALZET Comments: Naloxone; Saline, normal; SC; mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info: obesity induced, C57black/6J male mice, 6 wks old; functionality of mp verified by behavioral test; dose-response (pg 13, 14); dose-response (pg 13, 14); behavioral testing (Porsolt forced swim, Elevated Plus Maze, Dowl Gnawing); delayed delivery (24 hours via a 1.5 cm vinyl catheter); Isoflurane anesthesia used; minipump combined with a dose of 1 mg/kg/day of rimonabant (rim nal) injected IP; Dose: 0.5 mg/mouse/day.
- Q5018:** K. J. Jackson, *et al.* Effects of orally-bioavailable short-acting kappa opioid receptor-selective antagonist LY2456302 on nicotine withdrawal in mice. *Neuropharmacology* 2015;97(270-4



ALZET Comments: Nicotine hydrogen tartrate salt; Saline; SC; Mice; 2002; 14 days; 28 days; Controls received mp w/ vehicle; animal info (male, ICR, 8-10 weeks old); behavioral testing (elevated plus maze; hyperalgesia); dependence; Dose (24 mg/kg/day);.

Q4319: Y. J. Bao, *et al.* Engagement of signaling pathways of protease-activated receptor 2 and μ -opioid receptor in bone cancer pain and morphine tolerance. INTERNATIONAL JOURNAL OF CANCER 2015;137(14):1475-1483

ALZET Comments: FSLRLY-NH2; Saline; CSF/CNS (intrathecal); Rat; 20 hours; Controls received mp w/ vehicle; animal info (Wistar 200-250g); cancer (bone); no stress (see pg. 1476); behavioral testing (mechanical paw withdrawal, thermal hyperalgesia); peptides;.

Q5432: D. Suarez-Boomgaard, *et al.* Dopamine D(4) receptor counteracts morphine-induced changes in micro opioid receptor signaling in the striosomes of the rat caudate putamen. Int J Mol Sci 2014;15(1):1481-98

ALZET Comments: Morphine; PD168,077; L745,870; DMSO; saline; SC; Rat; 2ML1; 6 days; Controls received mp w/ vehicle; animal info (adult male Sprague-dawley rats, 250-300g); 2% DMSO used; Combinational treatments; anesthetized with ketamine and medetomidine; PD168,077 is a dopamine D4 receptor agonist; L745,870 is a dopamine D4 receptor antagonist; Dose (morphine 20 mg/kg/day; PD168,077 1 mg/kg/day; L745,870 1 mg/kg/day);.

Q3543: A. Lantero, *et al.* TGF-beta and Opioid Receptor Signaling Crosstalk Results in Improvement of Endogenous and Exogenous Opioid Analgesia under Pathological Pain Conditions. Journal of Neuroscience 2014;34(5):5385-5395

ALZET Comments: Transforming growth factor-B1; HCl; albumin; SC; Mice (transgenic); 1002; 14 days; Controls received mp w/ vehicle; animal info (male, BAMBI-KO or WT, 14-18 weeks old); behavioral testing (von Frey monofilaments; formalin test); Transforming growth factor-B1 aka TGF-B1; sciatic nerve crush injury;.

Q3152: M. Shaqura, *et al.* Reduced Number, G Protein Coupling, and Antinociceptive Efficacy of Spinal μ -Opioid Receptors in Diabetic Rats Are Reversed by Nerve Growth Factor. JOURNAL OF PAIN 2013;14(7):720-730

ALZET Comments: Nerve growth factor; CSF, artificial; rat serum albumin; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Wistar, 225g); behavioral testing (paw pressure test); peptides; used PE-10 attached to PE-60 catheter.

Q2587: K. L. Sato, *et al.* Spinal cord stimulation reduces hypersensitivity through activation of opioid receptors in a frequency-dependent manner. EUROPEAN JOURNAL OF PAIN 2013;17(4):551-561

ALZET Comments: Naloxone; naltrindole; Saline; SC; Rat; 1007D; Control animals received mp w/ vehicle; animal info (Sprague Dawley, 250-350 g).

Q3252: T. Nakahara, *et al.* Chronic Peripheral Administration of Kappa-Opioid Receptor Antagonist Advances Puberty Onset Associated with Acceleration of Pulsatile Luteinizing Hormone Secretion in Female Rats. JOURNAL OF REPRODUCTION AND DEVELOPMENT 2013;59(5):479-484

ALZET Comments: Nor-binaltorphimine; senktide; Sodium bicarbonate; IP; Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (female, Wistar-Imamichi, 20 days old); Nor-binaltorphimine aka nor-BNI; Nor-binaltorphimine is a KOR agonist; senktide NK3R agonist;.

Q2571: S. A. Mousa, *et al.* Rab7 Silencing Prevents μ -Opioid Receptor Lysosomal Targeting and Rescues Opioid Responsiveness to Strengthen Diabetic Neuropathic Pain Therapy. Diabetes 2013;62(4):1308-1319

ALZET Comments: Nerve growth factor, beta; CSF, artificial; albumin, rat serum; CSF/CNS (intrathecal); Rat; 2001; 7 days; Control animals received mp w/ vehicle; animal info (Wistar, male, STZ induced diabetes).

Q3077: C. R. Gibbons, *et al.* Involvement of brain opioid receptors in the anti-allodynic effect of hyperbaric oxygen in rats with sciatic nerve crush-induced neuropathic pain. Brain Research 2013;1537(1):111-116

ALZET Comments: Naltrexone HCl; Saline; CSF/CNS; Rat; 1007D; 7 days; Animal info (male, Sprague Dawley, albino, 160-180g); ALZET brain infusion kit used; post op. care (ampicillin 100 mg/kg IM; meloxicam 2.0 mg/kg IM); behavioral testing (flexion reflex, flinch response, mechanical threshold pressure); Incision closed with wound clip.



Q3048: S. R. Armstrong, *et al.* The in vivo pharmacodynamics of the novel opioid receptor antagonist, TD-1211, in models of opioid-induced gastrointestinal and CNS activity. NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY 2013;386(6):471-478

ALZET Comments: Morphine; Saline; SC; Mice; 2001; 5 days; Controls received mp w/ saline; animal info (male, Swiss Webster, 20-35g); Pump not mentioned much only pg.473.

Q1813: E. M. Vadizan, *et al.* Chronic treatment with the opioid antagonist naltrexone favours the coupling of spinal cord mu-opioid receptors to G-alpha_z protein subunits. Neuropharmacology 2012;62(2):757-764

ALZET Comments: Naltrexone; SC; Rat; 2001; 7 days; Controls received mp w/ saline; animal info (Sprague Dawley, male, 250-300 g).

Q2456: H. A. Tejada, *et al.* Dysregulation of kappa-opioid receptor systems by chronic nicotine modulate the nicotine withdrawal syndrome in an age-dependent manner. Psychopharmacology 2012;224(2):289-301

ALZET Comments: Nicotine; SC; Rat; 2ML2; 14 days; Animal info (adolescent, adult, Wistar, male).

Q1879: K. Lamb, *et al.* Antinociceptive effects of herkinorin, a MOP receptor agonist derived from salvinorin A in the formalin test in rats: New concepts in mu opioid receptor pharmacology: From a symposium on new concepts in mu-opioid pharmacology. Drug and Alcohol Dependence 2012;121(3):181-188

ALZET Comments: Morphine hydrochloride; Saline; SC; Rat; 5 days; Animal info (Sprague Dawley, male, 250-275 g).

Q2420: F. Berrendero, *et al.* Influence of delta-Opioid Receptors in the Behavioral Effects of Nicotine.

Neuropsychopharmacology 2012;37(10):2332-2344

ALZET Comments: Nicotine; SC; Mice; 2001; 6 days; Animal info (C57BL/6, male, DOR KO, 8-12 wks old).

Q0846: R. S. Yamdeu, *et al.* p38 Mitogen-activated Protein Kinase Activation by Nerve Growth Factor in Primary Sensory Neurons Upregulates μ -Opioid Receptors to Enhance Opioid Responsiveness Toward Better Pain Control.

Anesthesiology 2011;114(1):150-161

ALZET Comments: Fentanyl propionanilide; buprenorphine hydrochloride; Saline, isotonic; CSF/CNS (intrathecal); Rat; 96 hours; Controls received mp w/ vehicle; animal info (male Wistar, 200-250 g); pain.

Q1406: Y. Wu, *et al.* JWA regulates chronic morphine dependence via the delta opioid receptor. Biochemical and Biophysical Research Communications 2011;409(3):520-525

ALZET Comments: Oligonucleotide, sense, JWA; oligonucleotide, antisense JWA; CSF, artificial; CSF/CNS; Rat; Animal info (adult, male, Wistar, 190 g); antisense (JWA).

Q0694: N. Quillinan, *et al.* Recovery from mu-Opioid Receptor Desensitization after Chronic Treatment with Morphine and Methadone. Journal of Neuroscience 2011;31(12):4434-4443

ALZET Comments: Morphine; methadone; Water; SC; Rat; 2ML1; 2001; 6 days; Controls received mp w/ vehicle; tolerance; animal info (adult (150-250 g, male, Sprague Dawley).

Q1441: J. N. Peart, *et al.* Sustained Ligand-Activated Preconditioning via delta-Opioid Receptors. Journal of Pharmacology and Experimental Therapeutics 2011;336(1):274-281

ALZET Comments: Naloxone; BW373U86; U50,488H; morphine-6-glucuronide; morphine-3-glucuronide; wortmannin; PKI-(14-22)-amide; SC; Mice; 1007D; 5 days; Animal info (7-12 wks old, C57/BL6, male); BW373U86 also known as (-)-4-[(R)-[2S,5R]-4-allyl-2,5-dimethyl-1-piperazinyl]-3-hydroxy-hydroxybenzyl]-N,N-diethylbenzamide is a delta opioid receptor selective agonist; U50,488H also known as *trans*-(-)-3,4-dichloro-N-methyl-N-(2-(1-pyrrolidin)cyclohexyl)-benzeneacetamide methane sulfonate hydrate is a kappa opioid selective receptor agonist.

Q0697: B. Mathew, *et al.* The Novel Role of the Mu Opioid Receptor in Lung Cancer Progression: A Laboratory Investigation. Anesthesia and Analgesia 2011;112(3):558-567



ALZET Comments: Naltrexone, methyl; SC; Mice; 1002; 12 days; Controls received mp w/ PBS; animal info (MOR KO, C57BL/6 wt); cancer (lung); Methylnaltrexone (also known as MNTX) is a mu opioid receptor inhibitor.

Q0820: H. Zheng, *et al.* μ-Opioid Receptor Agonists Differentially Regulate the Expression of miR-190 and NeuroD. MOLECULAR PHARMACOLOGY 2010;77(1):102-109

ALZET Comments: Morphine; fentanyl; Mice; 1003D; 3 days; Controls received mp w/ saline; animal info (CD1 (ICR), 6-8 wks old).

P9960: K. J. Jackson, *et al.* Effect of the selective kappa-opioid receptor antagonist JDTC on nicotine antinociception, reward, and withdrawal in the mouse. Psychopharmacology 2010;210(2):285-294

ALZET Comments: Nicotine; Mice; 1007D; 7, 14 days; Animal info (8-10 wks old, 20-25 g); 28-day pumps used; withdrawal.

Q0746: R. J. Horvath, *et al.* Inhibition of microglial P2X(4) receptors attenuates morphine tolerance, Iba1, GFAP and μ opioid receptor protein expression while enhancing perivascular microglial ED2. Pain 2010;150(3):401-413

ALZET Comments: Morphine sulfate; naloxone; SC; Rat; 2ML1; 1, 4, 7 days; Controls received mp w/ saline; animal info (male, Sprague-Dawley, 175-200 g); one pump contained morphine plus naloxone; "All morphine pumps were filled with 0.833 mg/kg/hr morphine to deliver the equivalent of twice daily 10 mg/kg injections over the course of 24 h" pg 402; tolerance.

Q0727: A. R. Waxman, *et al.* Acute and chronic fentanyl administration causes hyperalgesia independently of opioid receptor activity in mice. Neuroscience Letters 2009;462(1):68-72

ALZET Comments: Fentanyl; Saline; SC; Mice; 2001; 6 days; Controls received mp w/ vehicle; animal info (adult, male, CD-1); comparison of SC injections vs. mp; "Although acute fentanyl injection (0.25 mg/kg) caused hyperalgesia within 15 min, hyperalgesia was not similarly evident on infusion Day 1 even though pumps were filled with a fentanyl dose (10mg/kg/24 h) that dispenses ~0.42 mg/kg/h, almost double the dose given by bolus injection." pg 71.

P9868: M. S. Virk, *et al.* Buprenorphine Is a Weak Partial Agonist That Inhibits Opioid Receptor Desensitization. Journal of Neuroscience 2009;29(22):7341-7348

ALZET Comments: Buprenorphine; DMSO; water; Rat; 2ML1; Controls received mp w/ vehicle; functionality of mp verified by plasma drug levels; animal info (male, Sprague Dawley, 150-200 g.); 40% DMSO used; "the osmotic minipump delivered buprenorphine efficiently and predictably" pg. 7342.

Q0272: E. L. A. van Dorp, *et al.* Morphine-6 beta-glucuronide Rapidly increases Pain Sensitivity Independently of Opioid Receptor Activity in Mice and Humans. Anesthesiology 2009;110(6):1356-1363

ALZET Comments: Morphine-6 beta-glucuronide; MK-801; Saline; SC; Mice; 2001; Animal info (adult, male, CD-1, TrKO, B6129F1); "Osmotic pumps afford continuous opioid infusions and control for hyperalgesia associated with withdrawal in opioid-dependent subjects that potentially confounds experiments in which chronic opioid treatment is accomplished via repeated acute injections." pg 1357.

P9445: S. Sirohi, *et al.* The analgesic efficacy of fentanyl: Relationship to tolerance and mu-opioid receptor regulation. Pharmacology Biochemistry and Behavior 2008;91(1):115-120

ALZET Comments: Fentanyl hydrochloride; Saline; SC; Mice; 7 days; Controls received placebo pellets; dose-response (fig. 3); comparison of SC injections vs. mp; tolerance; animal info (male, Swiss Webster, 23-35 g.).

P9162: P. Kumar, *et al.* Hydromorphone efficacy and treatment protocol impact on tolerance and mu-opioid receptor regulation. European Journal of Pharmacology 2008;597(1-3):39-45

ALZET Comments: Hydromorphone; Saline; SC; Mice; 2001; 7 days; Controls received inert placebo pellet; tolerance; animal info (male, Swiss Webster, 22-30 g.); "There was substantially more tolerance with infusion treatment compared to injection treatment." pg. 43.

P8864: S. A. Hesketh, *et al.* Effects of chronic treatment with citalopram on cannabinoid and opioid receptor-mediated G-protein coupling in discrete rat brain regions. Psychopharmacology 2008;198(1):29-36



ALZET Comments: Citalopram; SC; Rat; 2ML2; 14 days; Comparison of IP injections vs. mp; animal info (adult, male, Sprague Dawley, 200g.); paper incorrectly states 2ML2 pump model as 2002.

P8494: D. C. Stoller, *et al.* Role of kappa and delta opioid receptors in mediating morphine-induced antinociception in morphine-tolerant infant rats. *Brain Research* 2007;1142(28-36

ALZET Comments: Morphine; SC; Rat (neonate); 1003D; 72 hours; Controls received mp w/ vehicle; tolerance; post op. care (10% povidone iodine swab); animal info (P14, 30 g); Vetbond tissue adhesive used to close incision.

P8708: S. Sirohi, *et al.* mu-opioid receptor up-regulation and functional supersensitivity are independent of antagonist efficacy. *Journal of Pharmacology and Experimental Therapeutics* 2007;323(2):701-707

ALZET Comments: Naltrexol HCl, 6B-; naloxone HCl; Saline, physiological; SC; Mice; 2001; 7 days; Controls received placebo pellets; dose-response (fig 3, 5); comparison of pellets, SC injections vs. mp; animal info (male, Swiss-Webster, 22-30g).

P7344: Q. Y. Zhang, *et al.* Continuous opioid agonist treatment dose-dependently regulates mu-opioid receptors and dynamin-2 in mouse spinal cord. *Synapse* 2005;56(3):123-128

ALZET Comments: Etorphine; Saline; SC; Mice; 2001; 7 days; Controls received placebo pellet; dose-response (p. 125, 126).

P7624: S. Tanaka, *et al.* Butorphanol dependence increases hippocampal kappa-opioid receptor gene expression. *Journal of Neuroscience Research* 2005;82(2):255-263

ALZET Comments: Butorphanol tartrate; Saline, physiological; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ vehicle; dependence; post op. care (procaine penicillin G; animal info (male, Sprague-Dawley, 250-275 g).

P6906: S. Roy, *et al.* In vivo activation of a mutant mu-opioid receptor by naltrexone produces a potent analgesic effect but no tolerance: role of mu-receptor activation and omega-receptor blockade in morphine tolerance. *Journal of Neuroscience* 2005;25(12):3229-3233

ALZET Comments: Naltrindole; SNC-80; SC; Mice; 1003D; 3 days; Controls received mp w/ vehicle.

P7012: B. C. Yoburn, *et al.* Opioid agonist and antagonist treatment differentially regulates immunoreactive mu-opioid receptors and dynamin-2 in vivo. *European Journal of Pharmacology* 2004;498(1-3):87-96

ALZET Comments: Naloxone; etorphine hcl; morphine sulfate; Saline, normal; SC; Mice; 2001; 7 days; Controls received inert, placebo pellets or saline injections; comparison of SC injections vs. pellets vs. mp; tolerance; "Intermittent naloxone and etorphine treatment did not regulate u-opioid receptor or dynamin-2, despite the fact that the total amount of drug administered was the same as continuous treatment." (pg. 94); animal info (m, 22-30 grams).

P6432: M. Hummel, *et al.* Genetic and pharmacological manipulation of mu opioid receptors in mice reveals a differential effect on behavioral sensitization to cocaine. *Neuroscience* 2004;125(1):211-220

ALZET Comments: Naltrexone; Saline; SC; Mice (knockout); 1002; 21 days; Pumps replaced at day 13; behavioral study.

P6401: A. Bailey, *et al.* Enhanced morphine withdrawal and mu-opioid receptor G-protein coupling in A2_A adenosine receptor knockout in mice. *Journal of Neurochemistry* 2004;88(4):827-834

ALZET Comments: Morphine; Saline; SC; Mice (knockout); 1007D; 7 days; Controls received mp w/ vehicle; dependence.

P6702: V. Rajashekara, *et al.* Chronic opioid antagonist treatment dose-dependently regulates mu-opioid receptors and trafficking proteins in vivo. *Pharmacology Biochemistry and Behavior* 2003;75(4):909-913

ALZET Comments: Naloxone HCL; Saline; SC; Mice; 2001; 7 days; Controls received placebo pellets; dose-response (fig.2).

P5909: A. Morinville, *et al.* Regulation of delta-opioid receptor trafficking via mu-opioid receptor stimulation: Evidence from mu-opioid receptor knock-out mice. *Journal of Neuroscience* 2003;23(12):4888-4898

ALZET Comments: Fentanyl Citrate; Saline; SC; Rat; 2001; 48 hours; Controls received mp w/ vehicle; analgesic; "because of its reported short half-life and duration of action, fentanyl citrate was also administered chronically via osmotic mini-pumps." p. 4889; multiple pumps per animal (2).



- P5962:** L. W. Fan, *et al.* Changes in the brain kappa-opioid receptor levels of rats in withdrawal from physical dependence upon butorphanol. *Neuroscience* 2003;121(4):1063-1074
ALZET Comments: Butorphanol; morphine; Saline, sterile; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; dependence; post op. care (penicillin, 0.5% sensorcaine in wound site); guide cannula with stylet was used; dental cement used to adhere cannula to skull; protective aluminum cap was placed around the cannula; tygon tubing was used; solutions were filter sterilized during filling of the pumps; brain diagram (p. 1066).
- P5226:** J. Wang, *et al.* The immunosuppressive effects of chronic morphine treatment are partially dependent on corticosterone and mediated by the mu-opioid receptor. *J Leukoc. Biol* 2002;71(5):782-790
ALZET Comments: Corticosterone; PEG 400; SC; Mice; 48 hours; Controls received mp w/ vehicle; functionality of mp verified by corticosterone plasma levels; dose-response (p. 784); immunology;.
- P5479:** S. Sinchaisuk, *et al.* Focal kappa-opioid receptor-mediated dependence and withdrawal in the nucleus paragigantocellularis. *Pharmacology Biochemistry and Behavior* 2002;74(1):241-252
ALZET Comments: Morphine sulfate; butorphanol tartrate; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ saline; dependence; minipumps were inserted 6-10 days after guide cannula implantation; stylet used.
- P5492:** B. A. Gomes, *et al.* mu-opioid receptor down-regulation and tolerance are not equally dependent upon G-protein signaling. *Pharmacology Biochemistry and Behavior* 2002;72(1-2):273-278
ALZET Comments: Etorphine HCl; morphine sulfate; Saline; SC; Mice; 3 days; Tolerance.
- P5172:** M. J. Glass, *et al.* Opioid receptor blockade in rat nucleus tractus solitarius alters amygdala dynorphin gene expression. *Am. J Physiol Regul. Integr. Comp Physiol* 2002;283(1):R161-R167
ALZET Comments: Naltrexone; CSF, artificial; CSF/CNS (nucleus of solitary tract); Rat; 1007D; 13 days; Controls received mp w/ vehicle; ALZET brain infusion kit used; 7-day recovery period; cannula placement verified by histological examination.
- P6208:** L. W. Fan, *et al.* Withdrawal from dependence upon butorphanol uniquely increases kappa1-opioid receptor binding in the rat brain. *Brain Research Bulletin* 2002;58(2):149-160
ALZET Comments: Butorphanol tartrate; morphine; Saline, sterile physiological; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; functionality of mp verified by residual drug volume; good methods (p. 150); dependence; post op. care (sensorcaine, procaine penicillin G); guide cannula & stylet used; dental cement secured cannula.
- P6207:** L. W. Fan, *et al.* Butorphanol dependence and withdrawal decrease hippocampal K-2-opioid receptor binding. *Brain Research* 2002;958(2):277-290
ALZET Comments: Butorphanol tartrate; Saline, sterile physiological; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; functionality of mp verified by residual volume; good methods (p. 279); dependence; post op. care (sensorcaine, procaine penicillin).
- P6339:** S. L. Collins, *et al.* Chronic Cocaine Increases k-Opioid Receptor Density: Lack of Effect by Selective Dopamine Uptake Inhibitors. *Synapse* 2002;45(153-158)
ALZET Comments: Cocaine; RTI-117; GBR 12909; Saline; DMSO; water, sterile; SC; Rat; 2ML1; 2ML2; 7, 14 days; Controls received mp w/ vehicle; brain tissue distribution; 50% DMSO used for GBR12909.
- P5740:** F. Berrendero, *et al.* Attenuation of nicotine-induced antinociception, rewarding effects, and dependence in mu-opioid receptor knock-out mice. *Journal of Neuroscience* 2002;22(24):10935-10940
ALZET Comments: Nicotine hydrogen tartrate; Saline; SC; Mice (knockout); 2001; 6 days; Controls received mp w/ saline; dependence.
- P4966:** K. Stafford, *et al.* Mu-opioid receptor downregulation contributes to opioid tolerance in vivo. *Pharmacology Biochemistry and Behavior* 2001;69(233-237)



ALZET Comments: Etorphine hydrochloride; Morphine sulfate; Saline; SC; mice; 2001; 7 days; controls received placebo pellet; functionality of mp verified by analgesia "tail-flick" dose-response test; comparison of morphine pellets vs. mp; tolerance; receptor downregulation; animal info (male, swiss webster, 22-40 grams).

P4912: D. M. Hutcheson, *et al.* Lack of dependence and rewarding effects of deltorphin II in mu-opioid receptor-deficient mice. *European Journal of Neuroscience* 2001;13(153-161

ALZET Comments: Deltorphin II; CSF/CNS (third ventricle); mice; 2001; 6 days; controls received mp w/ vehicle; comparison of ICV injections vs. mp; no stress (see pg. 154); good methods (mice ICV implant; p. 154); 5-day recovery period; competitive injection was by Hamilton microsyringe; histological analysis confirmed cannula placement and lack of tissue damage;.

P4674: J. Shen, *et al.* Role of cAMP-dependent protein kinase (PKA) in opioid agonist-induced m-opioid receptor downregulation and tolerance in mice. *Synapse* 2000;38(322-327

ALZET Comments: Etorphine; Morphine;; SC;; mice;; 2001;; 2, 3 days;; Controls received inert placebo pellet; opioid agonists; etorphine infused for 2 days; morphine infused for 3 days; morphine pellets also used in mp/morphine implanted mice;.

P4792: S. M. Holter, *et al.* Kappa-opioid receptors and relapse-like drinking in long-term ethanol-experienced rats. *Psychopharmacology* 2000;153(93-102

ALZET Comments: Ci-977;; Saline;; SC;; Rat;; 2 weeks;; Controls received mp w/ vehicle; tolerance; dependence; Ci-977 is a K-opioid receptor antagonist, also called enadoline; Ci-977 has a very short duration of action, therefore this drug was given chronically by osmotic mini-pumps ..." (p. 94).

P4727: A. Diaz, *et al.* Autoradiographic mapping of m-opioid receptors during opiate tolerance and supersensitivity in the rat central nervous system. *Nauyn-Schmiedeberg's Arch Pharmacol* 2000;362(101-109

ALZET Comments: Sufentanil citrate; Nimodipine;; Saline; Ethanol; Propylene glycol; Water;; SC;; Rat;; 2001;; 7 days;; Controls received mp w/ vehicle; tolerance; Group 1 received sufentanil, Group 2 received sufentanil & nimodipine, Group 3 received nimodipine, Group 4 received vehicle; Nimodipine is a Ca channel blocker; sufentanil was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water;.