

Recent References (2010-Present) on Opioid Receptor Research Using ALZET[®] Osmotic Pumps

Q10665: A. Romero-Pico, *et al.* Kappa-Opioid Receptor Blockade Ameliorates Obesity Caused by Estrogen Withdrawal via Promotion of Energy Expenditure through mTOR Pathway. International Journal of Molecular Sciences 2022;23(6): **Agents:** PF-04455242 **Vehicle:** Not Stated; **Route:** CSF/CNS (intracerebroventricular); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (3.4 nmol/day); Controls received mp w/ vehicle; animal info (Female C57/BL6 WT and Oprk1-/ 8-10 weeks old); ALZET brain infusion kit 3 used; Therapeutic indication (Metabolic disorders);

Q10530: E. Gondoh, *et al.* Possible mechanism for improving the endogenous immune system through the blockade of peripheral mu-opioid receptors by treatment with naldemedine. British Journal of Cancer 2022;127(8):1565-1574 **Agents:** Methylnaltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 21 days; **ALZET Comments:** "Dose: (0.1 ml/10g)Controls received mp w/ vehicle; animal info: Male ICR mice (20–25 g)behavioral testing: Hot-plate test; methylnaltrexone is a peripheral MOR antagonist; immunology

Q8789: M. Kongstorp, *et al.* Prenatal exposure to methadone or buprenorphine alters micro-opioid receptor binding and downstream signaling in the rat brain. International Journal of Developmental Neuroscience 2020;

Agents: Methadone HCl; Buprenorphine HCl **Vehicle:** Water, Sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days; **ALZET Comments:** Dose (10 mg/kg/day Methadone HCl; 1 mg/kg/day Buprenorphine HCl); Controls received mp w/ vehicle; animal info (Female Sprague– Dawley Rat); dependence;

Q8759: T. W. Grim, *et al.* A G protein signaling-biased agonist at the mu-opioid receptor reverses morphine tolerance while preventing morphine withdrawal. Neuropsychopharmacology 2020;45(2):416-425

Agents: Morphine Vehicle: Saline; Route: SC; Species: Mice; Pump: 2001; Duration: Not Stated;

ALZET Comments: Dose (24 or 48 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL6, 10-20 weeks old); dependence;

Q8394: C. A. Browne, *et al*. Behavioral effects of the kappa opioid receptor partial agonist nalmefene in tests relevant to depression. Eur J Pharmacol 2020;872(172948

Agents: Nalmefene Vehicle: Saline; Route: SC; Species: Mice; Pump: 2004; Duration: 14 days;

ALZET Comments: Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (Male and female C57BL/6J mice, 8 weeks old); behavioral testing (forced swim test, Conditioned place aversion, Marble burying, Dark-light emergence test); Nalmefene aka NMF; neurodegenerative (Depression);

Q8391: J. M. Bossert, *et al.* In a Rat Model of Opioid Maintenance, the G Protein-Biased Mu Opioid Receptor Agonist TRV130 Decreases Relapse to Oxycodone Seeking and Taking and Prevents Oxycodone-Induced Brain Hypoxia. Biological Psychiatry 2020;88(12):935-944

Agents: Buprenophrine; TRV130 **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 14 days; **ALZET Comments:** Dose (0, 3, 6, or 9 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley rats, 250 to 350 g (males) or 175 to 225 g (females)); TRV130 aka G protein–biased mu opioid receptor agonist; dependence;

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

Agents: Fentanyl citrate; morphine sulphate salt pentahydrate **Vehicle:** PBS; water, sterile; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: 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)



Q8596: T. Kanemasa, *et al.* Pharmacologic effects of naldemedine, a peripherally acting mu-opioid receptor antagonist, in in vitro and in vivo models of opioid-induced constipation. Neurogastroenterology & Motility 2019;31(5):e13563 **Agents:** Morphine HCI **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 5 days; **ALZET Comments:** Dose (6 mg/kg); Controls received mp w/ vehicle; animal info (6-week-old Jcl Wistar male rats); dependence;

Q7450: J. Cunningham, *et al.* F160. Samidorphan, an Opioid Receptor Antagonist, Mitigates Olanzapine-Induced Metabolic Dysfunction in Female Rats. Biological Psychiatry 2019;85(10):

Agents: Olanzapine, Samidorphan Vehicle: Not stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 2 days; ALZET Comments: animal info (Female,); Olanzapine aka OLZ, Samidorphan aka SAM; dependence;

Q9050: S. Arttamangkul, *et al.* Separation of Acute Desensitization and Long-Term Tolerance of micro-Opioid Receptors Is Determined by the Degree of C-Terminal Phosphorylation. Molecular Pharmacology 2019;96(4):505-514 **Agents:** Morphine Sulfate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** Not Stated; **ALZET Comments:** animal info (5-6 weeks old, Sprague Dawley, 180-300 g); dependence;

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);

Q8073: E. S. Levitt, *et al.* Desensitization and Tolerance of Mu Opioid Receptors on Pontine Kolliker-Fuse Neurons. Mol Pharmacol 2018;93(1):8-13

Agents: Morphine Sulfate **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days; **ALZET Comments:** Dose (50 mg/kg/day); animal info (Male, Sprague Dawley, 4-7 weeks old); dependence;

Q10358: S. Arttamangkul, *et al.* Cellular tolerance at the micro-opioid receptor is phosphorylation dependent. eLife 2018;7(**Agents:** Morphine sulfate **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days; **ALZET Comments:** "Dose (80mg/kg/ml); animal info (Adult 180-300g, 5-6 week male and female Sprague-Dawley rats, MOR-knock out Sprague-Dawley rats with ZFN target site (GCTGTCTGCCACCCAgtcaaaGCCCTGGATTTC within exon 2) F3 generation); enzyme agonist (mu-opioid receptor aka MOR); dependence; The present work addresses one mechanism that underlies the development of long-term tolerance

to morphine. Elimination of phosphorylation sites on the C-terminal rendered MORs resistant to one cellular measure of long-term tolerance induced by morphine. One conclusion is that desensitization and/or internalization of MORs is necessary for the development of this form of cellular tolerance to opioids. Although there were no obvious change in cellular excitability, it could be that continued signaling through the phosphorylation deficient receptors result in downstream homeostatic mechanisms that counteract the lack of cellular tolerance and may well increase signs of withdrawal.; "

Q7171: S. Arttamangkul, *et al.* Cellular tolerance at the μ-opioid receptor is phosphorylation dependent. BioRxiv 2018; **Agents:** Morphine sulfate **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6, 7 days; **ALZET Comments:** Dose (80 mg/kg/day); Controls were untreated; animal info (5-6 weeks, male and female, Sprague-Dawley, 180-300g); dependence;

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

Agents: Sumatriptan Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;

ALZET Comments: 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

Agents: DAMGO Vehicle: Water, distilled; DMSO; saline; Route: CSF/CNS; Species: Mice; Pump: Not Stated; Duration: 5 Days; ALZET Comments: 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

Agents: Rapamycin; CTOP; LY297002 Vehicle: DMSO; saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: Not Stated; Duration: 14 days;

ALZET Comments: 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

Agents: CP154526; naltrexone Vehicle: DMSO; CSF, artificial; Route: CSF/CNS; Species: Mice; Pump: 1002; Duration: 14 days; ALZET Comments: 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

Agents: Naloxone Vehicle: Saline, normal; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;

ALZET Comments: 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, Dowel 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

Agents: Nicotine hydrogen tartrate salt **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days; 28 days; **ALZET Comments:** 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 -opioid receptor in bone cancer pain and morphine tolerance. INTERNATIONAL JOURNAL OF CANCER 2015;137(1475-1483

Agents: FSLLRY-NH2 **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** Not Stated; **Duration:** 20 hours; **ALZET Comments:** 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

Agents: Morphine; PD168,077; L745,870 Vehicle: DMSO; saline; Route: SC; Species: Rat; Pump: 2ML1; Duration: 6 days; ALZET Comments: 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(5385-5395 **Agents:** Transforming growth factor-B1 **Vehicle:** HCl; albumin; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, BAMBI-KO or WT, 14-18 weeks old); behavioral testing (von Frey monofiliments; 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 Mu-Opioid Receptors in Diabetic Rats Are Reversed by Nerve Growth Factor. JOURNAL OF PAIN 2013;14(7):720-730

Agents: Nerve growth factor **Vehicle:** CSF, artificial; rat serum albumin; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: 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

Agents: Naloxone; Naltrindole **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** Not Stated; **ALZET Comments:** 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

Agents: Nor-binaltorphimine; senktide Vehicle: Sodium bicarbonate; Route: IP; Species: Rat; Pump: 2002; Duration: 14 days; ALZET Comments: 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 mu-Opioid Receptor Lysosomal Targeting and Rescues Opioid Responsiveness to Strengthen Diabetic Neuropathic Pain Therapy. Diabetes 2013;62(4):1308-1319

Agents: Nerve growth factor, beta Vehicle: CSF, artificial; albumin, rat serum; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001; Duration: 7 days;

ALZET Comments: 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(;):111-116

Agents: Naltrexone HCl Vehicle: Saline; Route: CSF/CNS; Species: Rat; Pump: 1007D; Duration: 7 days; ALZET Comments: 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

Agents: Morphine Vehicle: Saline; Route: SC; Species: Mice; Pump: 2001; Duration: 5 days; ALZET Comments: Controls received mp w/ saline; animal info (male, Swiss Webster, 20-35g);

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 **Agents:** Naltrexone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ saline; animal info (Sprague Dawley, male, 250-300 g)



Q2456: H. A. Tejeda, *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 Agents: Nicotine Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days; ALZET Comments: 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

Agents: Morphine hydrochloride Vehicle: Saline; Route: SC; Species: Rat; Pump: Not Stated; Duration: 5 days; ALZET Comments: 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

Agents: Nicotine Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2001; Duration: 6 days; ALZET Comments: 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

Agents: Fentanyl propionanilide; buprenorphine hydrochloride **Vehicle:** Saline, isotonic; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** Not Stated; **Duration:** 96 hours;

ALZET Comments: 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

Agents: Oligonucleotide, sense, JWA; oligonucleotide, antisense JWA Vehicle: CSF, artificial; Route: CSF/CNS; Species: Rat; Pump: Not Stated; Duration: Not Stated;

ALZET Comments: 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

Agents: Morphine; methadone Vehicle: Water; Route: SC; Species: Rat; Pump: 2ML1; 2001; Duration: 6 days; ALZET Comments: 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

Agents: Naloxone; BW373U86; U50,488H; morphine-6-glucuronide; morphine-3-glucuronide; wortmannin; PKI-(14-22)-amide Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1007D; Duration: 5 days;

ALZET Comments: Animal info (7-12 wks old, C57/BL6, male);BW373U86 also known as

()-4-[(*R*)--[(2*S*,5*R*)-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 & Analgesia 2011;112(3):558-567

Agents: Naltrexone, methyl Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: 12 days; ALZET Comments: 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

Agents: Morphine; fentanyl Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: 1003D; Duration: 3 days; ALZET Comments: 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 JDTic on nicotine antinociception, reward, and withdrawal in the mouse. Psychopharmacology 2010;210(2):285-294

Agents: Nicotine Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: 1007D; Duration: 7, 14 days; ALZET Comments: 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

Agents: Morphine sulfate; naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1, 4, 7 days; **ALZET Comments:** 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