References on the Administration of Naloxone and Naltrexone Using ALZET® Osmotic Pumps

1. Naloxone

Q7026: P. M. Grace*, et al.* Protraction of neuropathic pain by morphine is mediated by spinal damage associated molecular patterns (DAMPs) in male rats. Brain Behav Immun 2018;72(45-50
ALZET Comments: naloxone; A438079; YVAD-cmk, Ac-; CSF/CNS (intrathecal); Rat; 2001; Dose (naloxone: 60 ug/h; A438079: 30 ng/h; ac-YVAD-cmk: 1 ug/h); animal info (10-12 week old male Fischer 344 rats); enzyme inhibitor (caspase-1);.

Q7170: J. E. Anttila*, et al.* Post-stroke Intranasal (+)-Naloxone Delivery Reduces Microglial Activation and Improves Behavioral Recovery from Ischemic Injury. eNeuro 2018;5(2):
ALZET Comments: Naloxone; Water, ultrapure; CSF/CNS (left ventricle); Rat; 2002; 12 days; Dose (96 mg/ml, 0.5 ul/h); Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats, 200–250 g); behavioral testing (locomotor activity); half-life (1.57 +/- 0.784 h); ischemia (ischemia stroke);.

Q6219: L. V. Lima*, et al.* Short-duration physical activity prevents the development of activity-induced hyperalgesia through opioid and serotoninergic mechanisms. Pain 2017;158(9):1697-1710
ALZET Comments: Naloxone; SC; Mice; 5 days; Dose (3 mg/kg/d); Controls received mp w/ vehicle;.

Q6094: L. Deng*, et al.* Prophylactic treatment with the tricyclic antidepressant desipramine prevents development of paclitaxel-induced neuropathic pain through activation of endogenous analgesic systems. Pharmacol Res 2016;114(75-89
ALZET Comments: Desipramine, naloxone, AM251, AM630; Water, saline, PEG400, DMSO; SC; Rat; 2ML4; 28 days; Dose: Desipramine (10 mg/kg/d), Naloxone (12 mg/kg/d), AM251 (3 mg/kg/d), AM630 (3 mg/kg/day); Desipramine dissolved distilled water, naloxone dissolved in saline, AM251 and AM630 dissolved in 50% PEG400 and 50% DMSO; Controls received mp w/ vehicle; animal info (Sprague-Dawley rats weighing 275–350 g); Multiple pumps per animal (2 when given the treatment of 2 different agents), Desipramine,vehicle, and all antagonists were delivered in separate osmotic pumps;.

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, 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.

Q3949: P. R. Kramer*, et al.* Attenuation of myogenic orofacial nociception and mechanical hypersensitivity by viral mediated enkephalin overproduction in male and female rats. BMC Neurology 2015;15(U1-U12
ALZET Comments: Naloxone methiodide; naloxone; Saline; SC; Rat; 2002; 10 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, 280-300g); behavioral testing (von Frey filament);.

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).

Q3440: K. Y. Chou*, et al.* Ultra-low dose (+)-naloxone restores the thermal threshold of morphine tolerant rats. Journal of the Formosan Medical Association 2013;112(12):795-800
ALZET Comments: Morphone; naloxone; Saline; CSF/CNS (intrathecal); Rat; 5 days; Controls received mp w/ vehicle; animal info (male, Wistar, 350-400g); behavioral testing (tail-flick); dependence; IT catheter created from PE tube joined with silastic tube with epoxy resin and silicon rubber;.

Q1824: G. J. Hathway*, et al.* A critical period in the supraspinal control of pain: Opioid-dependent changes in brainstem rostroventral medulla function in preadolescence. Pain 2012;153(4):775-783
ALZET Comments: Naloxone hydrochloride; naloxone methiodide; morphine sulfate; SC; Rat; 2001; 7 days; Controls received mp w/ saline; animal info (Sprague Dawley, 200-250 g, P7, P14, P21, P28).

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*)--[(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.

Q1488: S. H. Lockie*, et al.* CNS Opioid Signaling Separates Cannabinoid Receptor 1-Mediated Effects on Body Weight and Mood-Related Behavior in Mice. Endocrinology 2011;152(10):3661-3667
ALZET Comments: Naloxone; binaltorphimine, nor; CSF/CNS; Mice; 1007D; 7 days; Animal info (129/SvEv, lacking MOR, KOR, DOR); ALZET brain infusion kit 3 used; cyanoacrylate adhesive used; post op. care (meloxiocam); cannula placement verified at end of experiment by methylene blue staining; half-life "Naloxone... has a short half-life in vivo"; "NorBNI has... an extremely long half-life" pg 3662.

P9908: S. L. Lin*, et al.* Ultra-low dose naloxone upregulates interleukin-10 expression and suppresses neuroinflammation in morphine-tolerant rat spinal cords. Behavioural Brain Research 2010;207(1):30-36
ALZET Comments: Naloxone; morphine; CSF/CNS (intrathecal); Rat; 5 days; Controls received mp w/saline; animal info (male, Wistar, 350-400 g); pumps contained morphine alone or morphine and naloxone; two intrathecal catheters implanted.

Q1210: S. L. Lin*, et al.* Co-administration of ultra-low dose naloxone attenuates morphine tolerance in rats via attenuation of NMDA receptor neurotransmission and suppression of neuroinflammation in the spinal cords. Pharmacology Biochemistry and Behavior 2010;96(2):236-245
ALZET Comments: Morphine; naloxone; CSF/CNS (intrathecal); Rat; 5 days; Controls received mp w/ saline; animal info (pathogen-free, male, Wistar, 350-400 g); infusion rate of 1 ul/hr; two catheters inserted intrathecally.

Q0909: M. R. Hutchinson*, et al.* Evidence that opioids may have toll-like receptor 4 and MD-2 effects. BRAIN BEHAVIOR AND IMMUNITY 2010;24(1):83-95
ALZET Comments: Morphine; naloxone; SC; Rat; Controls received mp w/ saline; animal info (adult, male, Sprague Dawley, 300-375 g); multiple pumps per animal (2).

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.

2. Naltrexone

Q7076: A. Levy*, et al.* Bupropion and naltrexone combination alters high fructose corn syrup self-administration and gene expression in rats. Neuropharmacology 2018;135(547-554
ALZET Comments: Bupropion hydrochloride, naltrexone hydrochloride; Saline; SC; Rat; 2ML2; 12 days; Dose (40 mg/kg/day BUP, 4 mg/kg/day NTX); Controls received sham surgery; animal info (Adult male Sprague-Dawley rats weighing 200-250 g);

behavioral testing (locomotion tests); Drugs administered together or in separate pumps; Contrave® is an adjunct pharmacotherapy for obesity that contains bupropion and naltrexone.; Therapeutic indication (Obesity);.

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;.

Q2540: F. R. Theberge*, et al.* Effect of Chronic. Delivery of the Toll-like Receptor 4 Antagonist (+)-Naltrexone on Incubation of Heroin Craving. Biological Psychiatry 2013;73(8):729-737
ALZET Comments: Naltrexone; Water, sterile; SC; Rat; 14 days; Control animals received mp w/ vehicle; 14-day pump used.

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
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.

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).

Q0724: N. J. Stagg*, et al.* Regular Exercise Reverses Sensory Hypersensitivity in a Rat Neuropathic Pain Model Role of Endogenous Opioids. Anesthesiology 2011;114(4):940-948
ALZET Comments: Naltrexone; Saline; SC; Rat; 2006; 5 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-380 g); wound clips used; neuropathic pain.

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.

Q0016: K. G. Hill*, et al.* Chronic Naltrexone Treatment and Ethanol Responsivity in Outbred Rats. ALCOHOLISM-CLINICAL AND EXPERIMENTAL RESEARCH 2010;34(2):272-279
ALZET Comments: Naltrexone HCl; Saline, physiological; SC; Rat; 2ML4; 2 weeks; Controls received mp w/vehicle; dependence; animal info (male, Long-Evans, 250 g); dose-response (fig .1).

Q1544: S. Fitting*, et al.* Interactive Comorbidity between Opioid Drug Abuse and HIV-1 Tat Chronic Exposure Augments Spine Loss and Sublethal Dendritic Pathology in Striatal Neurons. American Journal of Pathology 2010;177(3):1397-1410
ALZET Comments: Naltrexone; DMSO; saline, sterile; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (HIV-1, TAT, adult, 2-6 mo old); 50% DMSO used.

Q1577: E. Chung*, et al.* Hyperbaric Oxygen Treatment Induces a 2-Phase Antinociceptive Response of Unusually Long Duration in Mice. JOURNAL OF PAIN 2010;11(9):847-853
ALZET Comments: L-NAME; naltrexone; Saline, physiological; CSF/CNS; Mice; 2001; Controls received mp w/ vehicle; animal info (NIH, Swiss, 18-22 g); ALZET brain infusion kit used; hyperbaric oxygen.

P9480: K. F. Hauser*, et al.* HIV-1 Tat and Morphine Have Interactive Effects on Oligodendrocyte Survival and Morphology. Glia 2009;57(2):194-206

ALZET Comments: Naltrexone; DMSO; saline, sterile; SC; Mice (transgenic); 1007D; 7 days; Animal info (TAT); 50% DMSO used.

P9245: A. J. Bruce-Keller*, et al.* Morphine causes rapid increases in glial activation and neuronal injury in the striatum of inducible HIV-1 tat transgenic mice. Glia 2008;56(13):1414-1427
ALZET Comments: Naltrexone; DMSO; saline, sterile; SC; Mice (transgenic); 1007D; 2, 5-10 days; Controls received mp w/ vehicle; pumps replaced after 5 days; animal info (male, female, C3H x C57BL/6, Tat (+), Tat (-), 2-6 months old); 50% DMSO used.

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.

P5891: J. E. Jones*, et al.* Effect of naltrexone on food intake and body weight in Syrian hamsters depends on metabolic status. PHYSIOLOGY & BEHAVIOR 2003;78(1):67-72
ALZET Comments: Naltrexone; Water; sterile; SC; Hamster; 2001; 7 days; Controls received mp w/ vehicle; comparison of acute injections vs. chronic mp; naltrexone is a nonselective opiod antagonist; behavorial study.

P6029: A. Bailey*, et al.* Quantitative autoradiography of adenosine receptors in brains of chronic naltrexone-treated mice. British Journal of Pharmacology 2003;139(6):1187-1195
ALZET Comments: Naltrexone; Saline; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle.

P6162: A. S. Levine*, et al.* Naltrexone infusion inhibits the development of preference for a high- sucrose diet. American Journal of Physiology-Regulatory Integrative and Comparative Physiology 2002;283(5):R1149-R1154
ALZET Comments: Naltrexone; Saline; SC; Rat; 2001; 20 days; Pumps replaced once; post op. care (topical antibiotic).

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 verifyed by histological examination.

P5242: J. E. Jones*, et al.* Effects of naltrexone and CCK on estrous behavior and food intake in Syrian hamsters. Peptides 2001;22(4):601-606
ALZET Comments: Naltrexone; Saline; SC; Hamster; 1003D; 48 hours; Controls received mp w/ vehicle.

P4920: M. S. Cowen*, et al.* Alterations in central preproenkephalin mRNA expression after chronic free-choice ethanol consumption by fawn-hooded rats. ALCOHOLISM-CLINICAL AND EXPERIMENTAL RESEARCH 2001;25(1126-1133
ALZET Comments: Naltrexone; Saline; SC; Rat; 4 weeks; controls received mp w/ vehicle; tolerance; dependence.

Q6818: N. Boyadjieva*, et al.* Chronic Ethanol Inhibits NK Cell Cytolytic Activity: Role of Opioid Peptide -Endorphin. The Journal of Immunology 2001;167(10):5645-5652
ALZET Comments: β-endorphin; naltrexone; CSF, artificial; CSF/CNS (bilateral paraventricular nuclei); Rat; 2002; 4 hours; 16 hours; Dose (100 ng of β-EP/0.5 µl/h); Controls received mp w/ vehicle; animal info (Male Fischer-344 rats of 150–175 g body weight); naltrexone is an opiate antagonist; Brain coordinates (1.8 mm behind bregma, 1.5 mm lateral to the midline, and 7.7 mm below the skull surface); bilateral cannula used: The osmotic pump was implanted was connected with two infusion cannulae (bilateral guide cannula) using a Y-connector;.

P5752: N. Boyadjieva*, et al.* Chronic ethanol inhibits NK cell cytolytic activity: role of opioid peptide beta-endorphin. J Immunol 2001;167(10):5645-5652
ALZET Comments: Endorphin, B-; Naltrexone; CSF, artificial; CSF/CNS (paraventricular nucleus); Rat; 2002; 4,16 hours; Controls received mp w/ vehicle; naltrexone is an opiate antagonist; used a Y-connector to connect pump with a bilateral cannula; bilateral infusion;.

P4753: L. D. Middaugh*, et al.* Naltrexone effects on ethanol consumption and response to ethanol conditioned cues in C57BL/6 mice. Psychopharmacology 2000;151(321-327
ALZET Comments: Naltrexone;; Saline;; SC;; mice;; 2001;; 7 days;; Controls received mp w/ vehicle; dose-response (graph p. 324); comparison of SC injections vs. mp; good methods priming p. 322; tolerance; Naltrexone is an opioid antagonist; injected naltrexone reduced drinking behavior, infused naltrexone did not; repeated injections and infusion increased ethanol consumption; recovery period;.