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

1. Naloxone


**Agents:** Naloxone HCl  
**Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week;

**ALZET Comments:** Dose (1 mg/100 uL); 0.9% NaCl used; animal info (four-week-old male ddY-strain mice, 24 g); behavioral testing (double activity monitoring system; Von Frey Test); spinal cord injury;

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);


**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);


**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;


**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.


**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);


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

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).

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 (−)-[R]-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.

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 (meloxicam); 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.

ALZET Comments: Naloxone; morphine; CSF/CNS (intrathecal); Rat; 5 days; Controls received mp w/saline; animal info (male, Wistar, 350-400 g); two intrathecal catheters implanted.

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 μopioid 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;


**ALZET Comments**: Naltrexone; Water, sterile; SC; Rat; 14 days; Control animals received mp w/ vehicle; 14-day pump used.


**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.


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


**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.


**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).


**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.

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

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.

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

ALZET Comments: Naltrexone; Saline; SC; Rat; 2001; 20 days; Pumps replaced once; post op. care (topical antibiotic).

**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;


**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;