Bibliography

Recent References on the Administration of Opioids Using ALZET® Osmotic Pumps

Apomorphine (2001-Present)

Q4660: T. T. Yan, et al. Daily Injection But Not Continuous Infusion of Apomorphine Inhibits Form-Deprivation Myopia in Mice. INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 2015;56(2475-2485

Agents: Apomorphine Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57Bl6, 4 weeks old); functionality of mp verified by residual volume; pumps replaced every 2 weeks; comparison of injection vs mp;


Agents: MK-801; apomorphine HCL hemihydrate Vehicle: Saline; Ascorbic acid; Route: CSF/CNS (nucleus accumbens); Species: Rat; Pump: 2002; Duration: Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (adult, female, Sprague Dawley, 200-300 g); post op. care (dexamethasone injections to prevent brain edema); behavioral testing (mechanical allodynia, Paw withdrawal latency, cold allodynia, hotplate test, spontaneous motor activity); cannula placement verified by picomicrograph of brain section; CCI, chronic constriction injury; SNI, spared nerve injury


Agents: MPTP; L-dopa; apomorphine Vehicle: Not Stated; Route: IP; SC; Species: Mice; Pump: 2004; Duration: 1,28 days;
ALZET Comments: Controls received mp w/ saline; comparison of IP injections vs. mp; neurodegenerative (Parkinson’s disease); L-dopa and apomorphine group had SC implanted pumps; route is unclear for the MPTP group; “Continuous MPTP infusions thus recreate a disease state that mimics human PD better than acute MPTP bolus injections.” (p. 3417); MPTP group received IP pumps (2004 model), verified by e-mailing author


Agents: Apomorphine Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 days;
ALZET Comments: Controls received mp w/ vehicle; comparison of sc bolus injections vs. mp; 20-day stability verified by HPLC (p.368); neurodegenerative (Parkinson’s disease); “The neurorescue effect of continuous subcutaneous infusion of apomorphine is particularly promising from a clinical standpoint.” (p.372)


Agents: Apomorphine Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 days;
ALZET Comments: Dose (3.15 mg/kg/day); Controls received mp w/ vehicle; animal info (10 week old, C57, black);

Buprenorphine (2017-Present)


Agents: Buprenorphine Vehicle: Ethanol; DMSO; Sterile water; Route: SC; Species: Rat; Pump: 2001; 2ML1; Duration: 1 week;
ALZET Comments: Dose (0.01; 0.032 mg/kg/h); 15% ethanol, 20% DMSO, 65% sterile water used; Controls received mp w/ vehicle; animal info (Sprague-Dawley female rats, 240– 260 g, ~12 weeks old and male rats, 290– 310 g, ~11 weeks old);


Agents: Buprenorphine, nor-; Morphine Vehicle: DMSO; PEG 400; Saline, Sterile; Route: SC; Species: Rat; Pump: 2ML2; ALZET Comments: Dose (15 or 20 mg/kg/day Morphine; 0.3, 1.0, 3.0, or 10 mg/kg/day norbuprenorphine); Controls received mp w/ vehicle; animal info (timed-pregnant Long-Evans rats); norbuprenorphine aka NorBUP; dependence;
Agents: Buprenorphine Vehicle: Water; Route: SC; Species: Rat; Pump: 2ML4; Duration: 14 days;
ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (sexually mature male and female Sprague-Dawley rats, 370 g (male) and 270 g (female)); dependence;

Q8788: M. Kongstorp, et al. Prenatal exposure to methadone or buprenorphine impairs cognitive performance in young adult rats. Drug and Alcohol Dependence 2020;212(108008
Agents: Methadone HCl; Buprenorphine HCl Vehicle: Water, Sterile; Route: SC; Species: Rat; Pump: 2ML4; Duration: 5 days;
ALZET Comments: Dose (8 mg/kg/day methadone; 0.8 mg/kg/day buprenorphine); Controls received mp w/ vehicle; animal info (Female (346.9 ± 8.1 g, n = 55) and male (12 weeks, n = 28) Sprague-Dawley rats); behavioral testing (novel object recognition test, simultaneous brightness discrimination test, Morris water maze test); dependence;

Agents: Methadone; Buprenorphine Vehicle: Saline; Route: CSF/CNS; Species: Rat; Pump: 2ML4; Duration: 28 days;
ALZET Comments: Dose (Buprenorphine- 1 mg/kg/day or Methadone 10mg/kg/day); Controls received mp w/ vehicle; animal info (Female); post op. care (Metacam); dependence;

Agents: Norbuprenorphine; Morphine Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Dose (1,3 or 10 mg/kg/day); Controls received mp w/ vehicle; animal info (Long-Evans); dependence;

Agents: Morphine; buprenorphine; methadone Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 6 days;
ALZET Comments: Dose (45 mg/kg/d; 5 mg/kg/day; 60 mg/kg/day); Controls received mp w/ vehicle; animal info (Male CD-1 mice, approximately 30g); comparison of morphine alkaloid pellet vs mp;

Butorphanol (2005-Present)
Q5136: M. Meredith M. Clancy DVM, et al. Pharmacokinetics of butorphanol delivered with an osmotic pump during a seven-day period in common peafowl (Pavo cristatus). American Journal of Veterinary Research 2015;76(12):1070-1076
Agents: Butorphanol Vehicle: Not Stated; Route: SC; Species: Bird (peafowl); Pump: 2ML1; Duration: 7 days;
ALZET Comments: animal info: 14 healthy adult male common peafowl; functionality of mp verified by plasma levels; “Use of these osmotic pumps may provide options for avian analgesia.” Dose: 247 ug/kg/h); Resultant plasma level ((mean, 106.4 ug/L; range, 61.8 to 133.0 ug/L));

Agents: Butorphanol tartrate Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML1; Duration: 48 hours;
ALZET Comments: Controls received mp w/ saline; animal info (Sprague Dawley, male, 302 g); “Implantation of the pumps took less than 1 min per rat, and the length of the anesthesia was approximately 5 min per rat.” pg 576; functionality of mp verified via residual volume

Agents: Butorphanol tartrate; Nitroindazole, 7- Vehicle: Saline; DMSO; Route: CSF/CNS; Species: Rat; Pump: 2001; Duration: 72 hours;
ALZET Comments: Enzyme inhibitor (nitric oxide synthase, NOS); animal info (male, Sprague Dawley, 250-275 g.); pump connected to catheter after 1 week recovery period; 10% DMSO used; PE60 tubing used
Agents: Butorphanol tartrate Vehicle: Saline, physiological; Route: CSF/CNS; Species: Rat; Pump: 2001; Duration: 3 days;
ALZET Comments: Controls received mp w/ vehicle; dependence; post op. care (procaine penicillin G; animal info (male, Sprague-Dawley, 250-275 g)

Agents: Butorphanol tartrate Vehicle: Not Stated; Route: CSF/CNS; Species: Rat; Pump: 2001; Duration: 3 days;
ALZET Comments: Controls received mp w/ saline; dependence; animal info (male, Sprague-Dawley 230-250 g)

Dynorphin
Agents: Endorphin, B-; Enkephalin, leucine-; Enkephalin, methionine-; Dynorphin A Vehicle: Not Stated; Route: SC; CSF/CNS; Species: Rat; Pump: 2001; 2ML1; Duration: 6 days;
ALZET Comments: controls received saline infusion; peptides; ALZET brain infusion kit used

Agents: Dynorphin A (1-13); U-50,488; DuP E3800 Route: SC; Species: Cat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: Controls received mp w/ saline; no stress (see pg. 2048); ischemia (cerebral)

Agents: Dynorphin A (1-13); ICI-174,864 Vehicle: DMSO; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: controls received mp w/saline; mp connected to catheter i.t.; DMSO is vehicle for ICI-174864; functionality of mp verified; comparison of ICV vs. i.t. injections vs. mp infusion; stability

Agents: Dynorphin Vehicle: Saline; Route: Not Stated; Species: Rat; Pump: 2002; Duration: 7 days;
ALZET Comments: controls received mp w/saline; food consumption; comparison of injections vs. mp infusion; peptides

Agents: Dynorphin A Vehicle: Calcium chloride; Magnesium chloride; Potassium chloride; Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001; Duration: 1 week;
ALZET Comments: peptides

Agents: Dynorphin A(1-8); Bestatin; Captopril; Dynorphin A; Enkephalin agonist DADL; Fentanyl; Thiorphan Vehicle: Saline; Route: SC; vas deferens; Species: Mice; Pump: 2001; 2ML1; Duration: Not Stated;
ALZET Comments: Comparison of agents effects; 2ML1 pump used w/ captopril, thiorphan, and bestatin; DADL & FEN admin.

Agents: Dynorphin (1-13); Morphine sulfate Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; Duration: 2 days;
ALZET Comments: comparison of agents effects; agents given by mp alone and in combination; peptides

**Agents:** Enkephalin, Leu-; Dynorphin; Dynorphin (3-13)  
**Vehicle:** Saline; **Route:** SC; **Species:** Cat; **Pump:** 2ML1; **Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle; peptides; post op. care (penicillin E, lactated ringer’s solution); ischemia (cerebral); animal info (adult, male, MCAO)


**Agents:** Endorphin, a-neo-; DsThr; Dynorphin; Enkephalin analog DADLE; FK-33824; MR-2034; MRZ; Normorphine; Sufentanil  
**Vehicle:** Water; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 6 days;  
**ALZET Comments:** Peptides; MRZ is 5,9-dimethyl,2'S-5,9-dimethyl-2'-hydroxy-2-(2-methoxy-propyl)-6,7-benzomorphan

**Endorphin (2002-Present)**


**Agents:** B-Endorphin  
**Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 4 weeks;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male spontaneously hyperlipidemic Apoe−/− mice, 13 weeks of age); pumps replaced every 2 weeks; Blood pressure measured via tail-cuff method; 91.4 mmHg - 92.1 mmHg; Resultant plasma level (294.3 mg/dL Glucose); peptides; dependence;


**Agents:** Endorphin, beta, (1-31)  
**Vehicle:** Saline, sterile; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; 1003D; **Duration:** 3, 7 days;  
**ALZET Comments:** Animal info (Sprague Dawley, male, 200-250 g); pumps replaced


**Agents:** Endorphin, B; corticotropin releasing hormone  
**Vehicle:** CSF, artificial; **Route:** CSF/CNS (paraventricular nucleus of hypothalamus); **Species:** Rat; **Pump:** 2002; **Duration:** 16 hours;  
**ALZET Comments:** Controls received mp w/ vehicle; peptides; animal info (male, Fischer, 160-175g.)


**Agents:** Endorphin, B-  
**Route:** CSF/CNS (paraventricular nucleus); **Species:** Rat; **Pump:** 2002; **Duration:** 18 hours;  
**ALZET Comments:** Controls received mp w/ aCSF; immunology; peptides


**Agents:** Endorphin, beta  
**Vehicle:** CSF, artificial; **Route:** CSF/CNS (paraventricular nucleus); **Species:** Rat; **Pump:** 2002; **Duration:** 6 days;  
**ALZET Comments:** Plastics One bilateral guide cannula used with a Y-connector; bilateral infusion;


**Agents:** Endorphin, B-  
**Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 12 days;  
**ALZET Comments:** Cardiovascular

**Agents:** Endorphin, B-
**Vehicle:** CSF, artificial; **Route:** CSF/CNS (paraventricular nucleus of hypothalamus); **Species:** Rat; **Pump:** 2002; **Duration:** 16 hours;

**ALZET Comments:** Controls received mp w/ vehicle; peptides; mp connected w/ two infusion cannulae using a Y-connector.

Enkephalin (2000-Present)


**Agents:** [D-Ala2, N-Me-Phe4, Gly5-ol]-enkephalin
**Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; mice;

**ALZET Comments:** animal info (rat - male, adult, Sprague Dawley, 250-300g; good methods (intrathecal catheter placement pg.11704); mice - male, adult, C57BL/6, 20-25g); No pump used, catheter only for lumbar catherization


**Agents:** Morphine sulfate; Enkephalin analog DPDPE; U50,488H; Deltorphin II, D-ala2-
**Vehicle:** Saline, pyrogen free; **Route:** SC; **Species:** Mice; **Pump:** 1003D; **Duration:** 48 hours;

**ALZET Comments:** Controls received mp w/ vehicle; dose-response (fig 1); comparison of pellets vs. mp; immunology; animal info (female, 6 wk old); mp primed 4 hours in 37 C saline; “morphine pellet potently exacerbated oral salmonella infection, but morphine given by pump, at doses which were immunosuppressive had a substantially lesser effect (of infection).” (p. 251).

“Further, we and others have found that morphine pellets induce sepsis in mice.” (p. 251)


**Agents:** Enkephalin
**Vehicle:** Saline; **Route:** SC; **Species:** Mice (nude); **Pump:** 2004; **Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; OGF plasma levels taken; comparison of IP and intratumoral injections vs. SC mp; adverse reaction: (see pg. 229) “within 2 days...3 minipumps containing saline were spontaneously dislodged.” (possible pocket too small); cancer (carcinoma); peptides; enkephalin was met-5 and termed OGF or opioid growth factor


**Agents:** Morphine sulfate; Enkephalin analog DAMGO; Dermorphin-derived tetrapeptide (TAPS)
**Vehicle:** CSF, artifical; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;

**ALZET Comments:** Controls received mp w/ vehicle; pumps replaced on day 4 to achieve 6 days due to dead space in catheter; second hole with guide cannula & stylet used for bolus injections; (ALZET) cannula placement confirmed by fast green dye & the guide cannula confirmed by methylene blue; TAPS is a potent mu-opioid receptor agonist


**Agents:** Enkephalin
**Vehicle:** Saline; **Route:** SC; **Species:** Rabbit; **Pump:** 2ML1; **Duration:** 24 hours;

**ALZET Comments:** Controls received mp w/ vehicle; cardiovascular; peptides; enkephalin was met-5


**Agents:** Enkephalin analog; Naloxone
**Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 1003D; **Duration:** 1,3 days;

**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by aspirating remaining contents; peptides; Enkephalin analog ENK was (D-Met2-Pro5)enkephalinamide, inhibits epidermal growth factor
**Etorphine (2002-Present)**

**Q0665**: P. A. Madia, *et al.* Dosing protocol and analgesic efficacy determine opioid tolerance in the mouse. Psychopharmacology 2009;207(3):413-422  
*Agents*: Etorphine; Oxycodone; Hydrocodone; Methadone  
*Vehicle*: DMSO; Saline  
*Route*: SC  
*Species*: Mice  
*Pump*: 2001;  
*Duration*: 7 days;  
**ALZET Comments**: Controls received placebo pellets wrapped in nylon mesh; animal info (Male, Swiss Webster, 23-30 g); tolerance; comparison of SC injections vs mp; “Higher doses of hydrocodone, oxycodone, and methadone could not be infused due to solubility issues.” pg 415; 20% DMSO used; “infusion with hydrocodone or methadone produced greater tolerance than acute or intermittent treatment” pg 417

*Agents*: Etorphine  
*Vehicle*: Saline;  
*Route*: SC;  
*Species*: Mice;  
*Pump*: 2001;  
*Duration*: 7 days;  
**ALZET Comments**: Controls received placebo pellet; dose-response (p. 125, 126)

*Agents*: Naloxone; Etorphine hcl; Morphine sulfate  
*Vehicle*: Saline, normal;  
*Route*: SC;  
*Species*: Mice;  
*Pump*: 2001;  
*Duration*: 7 days;  
**ALZET Comments**: 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)

*Agents*: Etorphine HCl; morphine sulfate  
*Vehicle*: Saline;  
*Route*: SC;  
*Species*: Mice;  
*Pump*: Not Stated;  
*Duration*: 3 days;  
**ALZET Comments**: Tolerance

*Agents*: Etorphine hydrochloride; Morphine sulfate  
*Vehicle*: Saline;  
*Route*: SC;  
*Species*: Mice;  
*Pump*: 2001;  
*Duration*: 7 days;  
**ALZET Comments**: 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)

*Agents*: Etorphine; Morphine  
*Vehicle*: Not Stated;  
*Route*: SC;  
*Species*: Mice;  
*Pump*: 2001;  
*Duration*: 2,3 days;  
**ALZET Comments**: 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;

**Fentanyl (2011-Present)**

*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);

**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); dependency; "...we used subcutaneously implanted osmotic pumps to deliver opioids at a constant rate.

**Q7582:** B. Hunter, et al. (352) Sex Differences in Sensory Processing: The Role of Stimulus Modality ad Psychological Factors. The Journal of Pain 2019;20(4);  
**Agents:** Fentanyl  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 5 days;  
**ALZET Comments:** Dose (0.01mg/kg/hr); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley); comparison of oxycodone and morphine injection vs mp; opioids administered 1 hour, 10 days, or 28 days post-CCI (chronic constriction injury)

**Agents:** Fentanyl  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 5 days;  
**ALZET Comments:** Dose (0.01 mg/kg/hr); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 10 weeks old);

**Agents:** Florfenicol voriconazole; fentanyl; amikacin  
**Vehicle:** Not Stated;  
**Route:** SC; in vitro;  
**Species:** Rat; Snake (corn, rattle); Iguana; Cat; Hamster; Gelada; Pudu; Wallaby; Monkey; Quail; Hen;  
**Pump:** Not Stated;  
**Duration:** Not Stated;  
**ALZET Comments:** “animal info (Eastern massasauga rattlesnakes (Sistrurus catenatus); timber rattlesnake (Crotalus horridus); pudu (Pudu puda); wallaby (Macropus rufogriseus); iguanas (Iguana iguana); Mojave rattlesnakes (Crotalus scutulatus); corn snakes (Elaphe guttata guttata); Japanese quails (Coturnix coturnix japonica); hens (Gallus domesticus)); “ Finally, the use of intracoelomic osmotic pumps was reported in iguanas (Iguana iguana) in a study of reproductive behavior.26 No complication due to the pump placement was reported in that study.” pg. 508; Advantages: Can be extracted in case of drug overdose or toxicity, Is not altered by its biological environment, Release the drug at a constant rate, Low cost, Commercially available, Release rate and operation time can be chosen; Drawbacks: Necessitate 2 light surgical procedures under anesthesia to be implanted and explanted, Can sometimes migrate in unwanted location (especially if implanted accidently in air sacs during intracoelomic implantation) "

**Q7369:** J. Ball, et al. (351) The Opioids Oxycodone, Fentanyl, and Morphine Amplify Neuropathic when Given after Chronic Pain is Established. The Journal of Pain 2019;20(4);  
**Agents:** Fentanyl  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** Pump model not stated;  
**Duration:** 5 days;  
**ALZET Comments:** Dose (0.01mg/kg/hr); Controls received mp w/ vehicle; animal info (Male, Sprague-dawley); dependence;

**Q5277:** J. P. Anand, et al. The behavioral effects of a mixed efficacy antinociceptive peptide, VRP26, following chronic administration in mice. Psychopharmacology (Berl) 2016;233(13):2479-87  
**Agents:** VRP26, Fentanyl  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** mice;  
**Pump:** 1007D;  
**Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Male, female C57BL/6 wild-type, homozygous MOR knockout; 20-30 g, 8-16 wks); functionality of mp verified by in vitro testing (pg. 2481); dose-response (pg 2481); good methods (pg 2481); behavioral testing (tail suspension test, conditioned place preference and locomotor activities); behavioral testing (tail suspension test, conditioned place preference and locomotor activities); peptides; Primed for 4 hours, 37 degree Saline; antinociceptive peptide; Dose (0.3 mg/kg/day fentanyl or 10 mg/kg/day VRP26);

**Q3568:** J. D. Mitzelfelt, et al. Thermal sensitivity across ages and during chronic fentanyl administration in rats. Psychopharmacology 2014;231(1):75-84  
**Agents:** Fentanyl  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML4;  
**Duration:** 28 days;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Fischer 344 x Brown Norway, 16, 20 and 24 months old); behavioral testing (temperature preference/heat and cold sensitivity, locomotor activity); Pumps removed after 4 weeks;
**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

**Agents:** Morphine; Methadone; Fentanyl; Oxycodone **Vehicle:** Water, distilled; **Route:** SC; **Species:** Mice; **Duration:** 7 days;
**ALZET Comments:** Animal info (male, WT, barr2-KO); dependence; wound clips used

**Agents:** Fentanyl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;
**ALZET Comments:** Controls received mp w/ saline; animal info (male, Fisher 344 x Brown Norway, 12, 24, 30 mo old); behavioral testing (open field activity, grip strength, rotarod)

**Morphine (2018-Present)**

**Agents:** Naloxone; Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
**ALZET Comments:** Dose (); animal info (Male mice, 2-3 months old); behavioral testing (Morris Water Maze Test); dependence;

**Agents:** Buprenorphine, nor-; Morphine **Vehicle:** DMSO; PEG 400; Saline, Sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML2;
**ALZET Comments:** Dose (15 or 20 mg/kg/day Morphine; 0.3, 1.0, 3.0, or 10 mg/kg/day norbupernorphine); Controls received mp w/ vehicle; animal info (timed-pregnant Long-Evans rats); norbuprenorphine aka NorBUP; dependence;

Q9432: H. M. Rodgers, et al. Dopamine D1 or D3 receptor modulators prevent morphine tolerance and reduce opioid withdrawal symptoms. Pharmacology, Biochemistry and Behavior 2020;194(172935
**Agents:** Morphine hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; 2002; **Duration:** Not Stated;
**ALZET Comments:** Dose (2 mg/kg); Controls received mp w/ vehicle; animal info (female, Long- Evans rats, weighing 200–225 g); behavioral testing (Withdrawal testing); Multiple pumps per animal (2 or 3); dependence;

**Agents:** Morphone hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Duration: 7 days;
**ALZET Comments:** Dose (5 mL/kg); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL/6J); dependence;

**Agents:** Morphone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Duration: Not Stated;
**ALZET Comments:** Dose (24 or 48 mg/kg/day); Controls received mp w/ vehicle; animal info (C57BL6, 10-20 weeks old);

**Agents:** Morphone **Vehicle:** Not stated; **Route:** Not stated; **Species:** Mice; **Pump:** Not stated; **Duration:** 28 days;
**ALZET Comments:** Dose (1 mg/kg/day); dependence;

**Agents:** Morphine  
**Vehicle:** DMSO; Saline  
**Route:** CSF/CNS (intrathecal); CSF/CNS (lateral ventricle)  
**Species:** Rat  
**Pump:** Not stated  
**Duration:** 10 days  
**ALZET Comments:** 0.9% Saline used; Controls received mp w/ vehicle; animal info (adult male wistar rats, 300-350 g); behavioral testing (Nociceptive Test); dependence;


**Agents:** PD168,077; morphine  
**Vehicle:** DMSO; Saline  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML1  
**Duration:** 6 days  
**ALZET Comments:** Dose (20 mg/kg/day-75 mg/kg/day); Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats, 220–240 g)); behavioral testing (Conditioned Place Preference Test); dependence;


**Agents:** Morphine; Trimethoxy cinnamic acid, 3, 4, 5-

**Vehicle:** Saline  
**Route:** CSF/CNS (lateral ventricle)  
**Species:** Rat  
**Pump:** 2ML1  
**Duration:** 7 days  
**ALZET Comments:** Dose (26 nmol/10μ l/hr); Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats, 220–240 g)); behavioral testing (Conditioned Place Preference Test); dependence;

Q7533: C. R. Leibrand, et al. HIV-1 Tat and opioids act independently to limit antiretroviral brain concentrations and reduce blood-brain barrier integrity. J Neurovirol 2019;

**Agents:** Dolutegravir, Abacavir, Lamivudine; Morphine  
**Route:** SC  
**Species:** Mice  
**Pump:** 2001  
**Duration:** 5 days  
**ALZET Comments:** Dose (abacavir 2.5 mg/day (123.5 mg/kg/day), dolutegravir 0.2 mg/day (10.3 mg/kg/day), and lamivudine 1.2 mg/day (61.7 mg/kg/day); Morphine (2 mg/day)); Controls received mp w/ vehicle; animal info (Adult female mice, 70 days of age); post op. care (Bupivacaine);


**Agents:** DMT-DALDA; morphine sulfate  
**Vehicle:** Saline  
**Route:** CSF/CNS (intrathecal)  
**Species:** Rat  
**Pump:** 2001, 2002  
**Duration:** 7 days, 14 days  
**ALZET Comments:** Dose ((DMT-DALDA 0.3, 1, 3, or 10 pmol/μL/hour), (MS 37.5 nmol/hour)); dose-response (Figure 1a graph on page 4); Controls received mp w/ vehicle; animal info (adult, male, Sprague-Dawley, 225-300g); behavioral testing (Hargreaves-type hind paw thermal stimulator, formalin-induced flinching); DMT-DALDA (H-Dmt-D-Arg-Phe-Lys-NH2; Dmt = 2',6'-dimethyltyrosine) is a dermorphin analogue and selective mu opioid agonist; dependence; good methods (surgical techniques and pump/catheter implantation on p.2);


**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)


**Agents:** Morphine HCl  
**Vehicle:** Saline  
**Route:** SC  
**Species:** Mice  
**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);

Q8205: R. Hill, et al. Prolonged ethanol administration prevents the development of tolerance to morphine-induced respiratory depression. Drug Alcohol Depend 2019;205(107674

**Agents:** Morphine  
**Vehicle:** Saline  
**Route:** SC  
**Species:** Mice  
**Pump:** Not stated  
**Duration:** 16 days  
**ALZET Comments:** Dose (45 mg/kg/day); Controls received mp w/ vehicle; animal info (Male CD-1 mice, approximately 30 );
**Agents:** Norbuprenorphine; Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** Dose (1.3 or 10 mg/kg/day); Controls received mp w/ vehicle; animal info (Long-Evans); dependence;

**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;

**Agents:** Morphine sulfate **Vehicle:** saline; **Route:** SC; **Species:** Rat; **Pump:** pump model not stated; **Duration:** 6 days;
**ALZET Comments:** Dose (5 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (female, Sprague-Dawley, 175–200 g); behavioral testing (von Frey test, Hargreaves method); functionality of mp verified by weighing (empty, after filling, after priming, after removal); dependence;

**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);

**Agents:** Morphine sulfate, Nicotine bitartrate **Vehicle:** Sterile water; **Route:** SC; **Species:** Rats; **Pump:** 2ML1; **Duration:** 7 days;
**ALZET Comments:** Dose (morphine at 0.3 and 0.6 mg/kg/hr, nicotine at 9 mg/kg/day); Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats averaging 234 g); dependence;

**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;
**Agents:** Morphine  
**Vehicle:** Saline;  
**Route:** CSF/CNS (intrathecal);  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 7 days;  
**ALZET Comments:** Dose (15 μg/h); Controls received mp w/ vehicle; animal info (27 Male Wistar rats (350 400 g), each rat (with 12 weeks of age)); neurodegenerative ();

**Agents:** Morphine hydrochloride  
**Vehicle:** DMSO; Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML4;  
**Duration:** 28 days;  
**ALZET Comments:** Dose (17.5 mg/kg/day);  2% DMSO used; Controls received mp w/ vehicle; animal info (male Sprague Dawley); 8 wks old; behavioral testing (Tail flick, Morris water maze); Multiple pumps per animal (2); good methods (see pg 5);

Pentazocine  
**Agents:** Haloperidol; JO-1784; Pentazocine; DTG  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Rat;  
**Duration:** 2,21 days;  
**ALZET Comments:** Controls received mp w/saline; DTG is di(2-tolyl)guanidin

**Agents:** Pentazocine, d-  
**Vehicle:** Saline;  
**Species:** Rat;  
**Pump:** 2ML4;  
**Duration:** 4 weeks;  
**ALZET Comments:** no comment posted

**Agents:** Ethylketocyclazocine; Heroin; Meperidine; Oxyphophine; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; Nalbuphine; U-50,488H;  
**Vehicle:** SC;  
**Species:** Mice;  
**Duration:** 3 days;  
**ALZET Comments:** Comparison of sc morphine pellets vs. mp infusion; comparison of agents effects; controls received unspecified placebo infusion

Sufentanil (2000-Present)  
**Agents:** sufentanil; nimodipine  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** Dose ((2 μg/h sufentanil), (1 μg/h nimodipine)); Controls received mp w/ vehicle; animal info (Male, albino Wistar, 250-300g); enzyme inhibitor ((mu-opioid agonist for sufentanil), (Ca2+ channel blocker for nimodipine));

**Agents:** Sufentanil citrate; Nimodipine  
**Vehicle:** Saline; Ethanol; Propylene glycol; Water;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** 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

**Agents:** Sufentanil citrate; Nimodipine  
**Vehicle:** Saline; Ethanol; Propylene glycol; Water;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle; tolerance; Group 1 received vehicle alone, Group 2 received chronic sufentanil, Group 3 received sufentanil & nimodipine, Group 4 received nimodipine alone; Nimodipine is a CA2+ antagonist opioid; sufentanil citrate was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water