Neuroscience Research Using ALZET® Osmotic Pumps: Drugs of Abuse

ALZET Osmotic Pumps are a valuable tool in neuroscience research, as evidenced by the thousands of publications describing their use in studies on neurodegeneration, ischemia, brain cancers, and more. Researchers have used ALZET pumps to investigate the mechanisms behind drug abuse, dependence, and withdrawal as well as potential treatments and therapies.

Highlighted below are some commonly abused drugs that have been delivered with the pumps, as well as recent research applications. The following list of references is a more extensive compilation of research within the last few years. The short abstract following each reference in the attached list details the substance(s) infused, route of administration, animal model studied, solvent(s), model of pump, duration of infusion, and relevant notes. To obtain a complete listing of earlier references or additional technical information, please contact ALZET Technical Support by email at techsupport@alzet.com.

Drugs Delivered in ALZET Pumps

- Amphetamines
- Barbiturates (pentobarbital, phenobarbital)
- Benzodiazepines (Diazepam, Midazolam)
- Cannabinoids (cannabinol)
- Fentanyl
- Heroin
- Ketamine
- MDMA
- Morphine
- Nicotine

Recent Research on Drugs of Abuse

COMPOUND	ANIMAL	DURATION	APPLICATION	REFERENCE
Nicotine	Mice	14 days	Continuous nicotine exposure to produce blood levels comparable to average human smokers and induce nicotine withdrawal	D. Kundu *et al.* Roles of metabotropic signaling of nicotine receptors in the development and maintenance of nicotine reward through regulation of dopamine D3 receptor expression. J Neurochem; 2025;169(1):e16271
Heroin	Rat	Not Stated	Chronic steady-state heroin exposure to assess efficacy of N-Oleoyl alanine in reducing somatic withdrawal responses	S.M. Ayoub *et al.* Orally Administered N-Oleoyl Alanine Blocks Acute Opioid Withdrawal Induced-Conditioned Place Preference and Attenuates Somatic Withdrawal following Chronic Opioid Exposure in Rats. Psychoactives; 2024;3(2):184-193
Morphine	Rat	7 days	Modeling morphine dependence and investigating therapeutic efficacy of mesenchymal stem cell-derived secretome	M. Quezada *et al.* Amelioration of morphine withdrawal syndrome by systemic and intranasal administration of mesenchymal stem cell-derived secretome in preclinical models of morphine dependence. CNS Neurosci Ther; 2024;30(4):e14517
Oxycodone	Mice	7 days	Developed and validated model of opioid dependence during spontaneous withdrawal in mice	K.M. Contreras *et al* Characterization and validation of a spontaneous acute and protracted oxycodone withdrawal model in male and female mice; Pharmacol Biochem Behav; 2024;242:173795
Fentanyl	Mice	7 days	Sustained fentanyl exposure to investigate comorbidity between fentanyl abuse and HIV in vivo	K.M. Rademeyer *et al.* Fentanyl dysregulates neuroinflammation and disrupts blood-brain barrier integrity in HIV-1 Tat transgenic mice. J Neurovirol; 2024 Feb;30(1):1-21

*If you are interested in a specific agent not listed, please request it at techsupport@alzet.com

Surgical Protocols:
Written protocols are available on our website. A surgical implantation video is also available, which describes proper preparation of the ALZET pump and surgical techniques for implantation in mice and rats. These can be found on https://www.alzet.com/resources/downloads/

Recent References (2018 – Present) on the Administration of Drugs of Abuse Using ALZET® Osmotic Pumps

Amphetamines

R0477: M. Ferreira, *et al.* Amphetamine and methylphenidate potential on the recovery from stroke and traumatic brain injury: a review. Reviews in the Neuroscience 2024;35(7):709-746
Agents: Amphetamine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** Not Stated **Duration:** 6d;
ALZET Comments: Dose (1 mg/kg); animal info (male 285 g); ischemia (stroke); traumatic brain injury; AMPH effects reported in pre-clinical studies;

Q9516: T. C. Uzuneser, *et al.* Presynaptic vesicular accumulation is required for antipsychotic efficacy in psychotic-like rats. Journal of Psychopharmacology 2021;35(1):65-77
Agents: Amphetamine sulfate, d- **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2001; **Duration:** 7 d
ALZET Comments: Dose (); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, 300-350 g); behavioral testing (locomotion test); d-amphetamine sulfate aka AMPH; ALZET brain infusion kit 2 used; Brain coordinates (0.8 mm posterior, 1.4 mm lateral, 4.5 mm ventral from the bregma); cyanoacrylate adhesive;

Q7057: P. Petschner, *et al.* Gene expression analysis indicates reduced memory and cognitive functions in the hippocampus and increase in synaptic reorganization in the frontal cortex 3 weeks after MDMA administration in Dark Agouti rats. BMC Medicine 2018;19(1):580
Agents: Methamphetamine, 3,4-methylenedioxy- **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (8-week old Dark Agouti rats weighing 152 +/- 3.58 g);

Q7766: A. R. Johnson, *et al.* Amphetamine maintenance differentially modulates effects of cocaine, methylenedioxypyrovalerone (MDPV), and methamphetamine on intracranial self-stimulation and nucleus accumbens dopamine in rats. Neuropsychopharmacology 2018;43(8):1753-1762
Agents: amphetamine **Vehicle:** saline, bacteriostatic; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 7, 13 days;
ALZET Comments: Dose (0.1 or 0.32 mg/kg/h), (2ML2 pump 0.5 µl/h); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 300-350g); behavioral testing (operant chambers); comparison of IP injection vs mp; dependence;

Benzodiazepines

Q10510: C. A. da Silva Junior, *et al.* Intra-uterine diazepam exposure decreases the number of catecholaminergic and serotoninergic neurons of neonate rats. Neuroscience Letters 2023;795(137014
Agents: Diazepam **Vehicle:** Propylene glycol; Benzyl alcohol; Ethyl alcohol; Sodium benzoate; Benzoic acid; Water; **Route:** SC;
Species: Rat; **Strain:** Not Stated; **Pump:** 2ML4; **Duration:** 4 hours;
ALZET Comments: 40% propylene glycol, 1.5% BnOH, 10% EtOH, 5% SB, 5% BzOH used; Controls received mp w/ vehicle; animal info (Female; Rats; Neonatal);

Q6992: R. A. Whittington, *et al.* Administration of the benzodiazepine midazolam increases tau phosphorylation in the mouse brain. Neurobiology of Aging 2019;75(11-24
Agents: Midazolam **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6; **Pump:** 2001D; **Duration:** Not Stated;
ALZET Comments: Dose (10 mg/kg or 25 mg/kg); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male, 8-10-week-old); post op. care (preemptive analgesia with carprofen 5 mg/kg s.c.); midazolam is a benzodiazepine; neurodegenerative (Alzheimers);

Cannabinoids

R0402: E. Zamberletti, *et al.* Dos(e)Age: Role of Dose and Age in the Long-Term Effect of Cannabinoids on Cognition. Molecules 2022;27(4):
Agents: Cannabinol, delta9-tetrahydro-; Cannabidiol **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Dose (3 mg/kg/day; 1 mg/kg/day each; 1:1 1 mg/kg/day THC and CBD); animal info (Male 12 and 18 months old); behavioral testing (Morris water maze; Nobel object location recognition task; Partner recognition task); toxicology;

Q11697: T. T. Wei, *et al.* Cannabinoid receptor 1 antagonist genistein attenuates marijuana-induced vascular inflammation. Cell 2022;185(10):1676-1693 e23
Agents: cannabinol, 9-tetrahydro- **Vehicle:** PMC9400797; **Route:** Saline; ethanol; cremophor; **Species:** Mice; **Strain:** Ldlr-/-; **Pump:** 2006; **Duration:** 12 weeks;
ALZET Comments: Dose: (1 mg/kg/day); 90% saline; 5% ethanol; 5% cremophor used; Controls received mp w/ vehicle; animal info: 9–12 weeks old; behavioral testing (open field activity chamber; hot plate test; bar test); Blood pressure measured via: CODA Non-Invasive Blood Pressure System; cardiovascular; atherosclerosis

Cocaine

Q9271: M. Fakhoury, *et al.* Intracranial Self-Stimulation and the Curve-Shift Paradigm: A Putative Model to Study the Brain Reward System. The Brain Reward System 2021;
Agents: Cocaine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** Not Stated;
ALZET Comments: Dose (4 mg/kg); Controls received mp w/ vehicle; dependence;

Q8149: K. Ouk, *et al.* Chronic paroxetine treatment prevents disruption of methamphetamine-sensitive circadian oscillator in a transgenic mouse model of Huntington's disease. Neuropharmacology 2018;131(337-350
Agents: Cocaine hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;
ALZET Comments: Dose (30 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (12 weeks old); neurodegenerative (Huntington's Disease);

Fentanyl

Q11888: K. M. Rademeyer, *et al.* Fentanyl dysregulates neuroinflammation and disrupts blood-brain barrier integrity in HIV-1 Tat transgenic mice. Journal of NeuroVirology 2024;30(1):1-21
Agents: Fentanyl **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** Tat transgenic; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (0.05 mg/day); controls received mp w/ vehicle; animal info (female, ~25 g; ~4 months old); dependence;

Q11863: M. M. Morgan, *et al.* Continuous fentanyl administration and spontaneous withdrawal decreases home cage wheel running in rats with and without hindpaw inflammation. Physiology & Behavior 2023;272(114376
Agents: Fentanyl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Dose: (0.32 or 1.0 mg/kg/day); controls received mp w/ vehicle; animal info (male); isoflurane anesthesia; wound clips used post op. care (CFA; 0.1 ml); half-life (p.1); behavioral testing (wheel running); dependence; "We found that fentanyl withdrawal as measured by depression of wheel running was evident with only 3 days of continuous administration." pg. 4;

Q10922: R. C. N. Marchette, *et al.* Heroin- and Fentanyl-Induced Respiratory Depression in a Rat Plethysmography Model: Potency, Tolerance, and Sex Differences. Journal of Pharmacology and Experimental Therapeutics 2023;385(2):117-134
Agents: Fentanyl citrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Long Evan; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose (0.06 mg/kg/d); 0.9% sterile saline used; animal info (Male and females; 8 weeks old); dependence

Q10949: M. R. Jain*, et al.* ZYKR1, a novel, potent, and peripherally selective kappa opioid receptor agonist reduces visceral pain and pruritus in animal models. European Journal of Pharmacology 2022;924(174961
Agents: ZYKR1; Fentanyl **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Strain:** ICR; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Dose: Fentanyl (3.2 mg/kg/day); ZYKR1 (10 mg/kg/day); Controls received mp w/ vehicle; animal info: male ICR mice; behavioral testing: the animals were observed for behavioral visceral episodes (postures) for 30 min in a transparent acrylic chamber; Resultant plasma level (at 0.25 h after IV administration of ZYKR1 (1 mg/kg) in rats, plasma level was found to be 1713.03 ±261.95 ng/ml.); pg. 7; ZYKR1 is a peripherally selective kappa opioid receptor; dependence; "The osmotic pump was used to avoid repeated intravenous administration of drug and also released the drug substance at constant rate for 7 days." p. 3

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); **Strain:** knock-in 1S/T-A mutations Oprm1tm3.1Shlz, MGI:6117673, 11S/T-A1; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Dose (Fentanyl (2mg/kg/day); Morphine (17 mg/kg/day)); animal info (mice with)); 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)

Q8735: S. M. Green-Fulgham*, et al.* Oxycodone, fentanyl, and morphine amplify established neuropathic pain in male rats. Pain 2019;160(11):2634-2640
Agents: Fentanyl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: Dose (0.01 mg/kg/hr); Controls received mp w/ vehicle; animal info (Male, 10 weeks old); dependence;

R0391: T. Coutant*, et al.* Advances in Therapeutics and Delayed Drug Release. Vet Clin North Am Exot Anim Pract 2019;22(3):501-520
Agents: Florfenicoll voriconazole; fentanyl; amikacin **Vehicle:** Not Stated; **Route:** SC; in vitro; **Species:** Rat; Snake (corn, rattle); Iguana; Cat; Hamster; Gelada; Pudu; Wallaby; Monkey; Quail; Hen; **Strain:** Sistrurus catenatus; Crotalus horridus; Pudu puda; Macropus rufogriseus; Iguana iguana; Crotalus scutulatus; Elaphe guttata guttata; Coturnix coturnix japonica; Gallus domesticus; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: animal info (Eastern massasauga rattlesnakes; timber rattlesnake; pudu; wallaby; iguanas; Mojave rattlesnakes; corn snakes; Japanese quails; hens); "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) "

Heroin

Q11814: S. M. Ayoub*, et al.* Orally Administered N-Oleoyl Alanine Blocks Acute Opioid Withdrawal Induced-Conditioned Place Preference and Attenuates Somatic Withdrawal following Chronic Opioid Exposure in Rats. Psychoactives 2024;3(2):184-193
Agents: Heroin **Vehicle:** Saline; **Route:** SC; **Species:** Rats; **Strain:** Sprague-Dawley; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Dose (7 mg/kg/day); controls received mp w/ vehicle; animal info (male; 200-225 g, isoflurane anesthesia); post op. care (carprofen); behavioral testing (somatic withdrawal observations); "For this experiment, and as previously published, heroin was selected due to solubility limits for the desired doses of morphine delivered by minipump." pg. 2;

Q10404: N. Baidoo*, et al.* Inhibition of noradrenergic and corticotrophin-releasing factor systems: Effects on enhancement of memory consolidation by unconditioned and conditioned heroin withdrawal. Neuropharmacology 2022;209(109018
Agents: Heroin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (3.5 mg/kg/day); animal info (Male; Weighed 225-250 g); behavioral testing (Conditioning chambers; Y-apparatus); dependence;

Morphine

Q11887: M. Quezada*, et al.* Amelioration of morphine withdrawal syndrome by systemic and intranasal administration of mesenchymal stem cell-derived secretome in preclinical models of morphine dependence. CNS Neuroscience & Therapeutics 2024;30(4):e14517
Agents: Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML2; **Duration:** 7 days;
ALZET Comments: Dose: (10 mg/kg/day); controls received mp w/ vehicle; animal info (eight-week-old female); dependence;

Q11878: B. J. Parks*, et al.* Limited bedding and nesting increases ethanol drinking in female rats. Pharmacology, Biochemistry and Behavior 2024;239(173756
Agents: Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Long-Evans; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (15 mg/kg/day); 0.9% saline used; controls received mp w/ vehicle; animal info (pregnant; 8-10 weeks old, isoflurane anesthesia); dependence; "Due to the relatively short half-life of morphine in rats and concerns about frequently handling and injecting pregnant rats, we induced POE using osmotic minipumps for continuous opioid delivery." pg. 10;

Q12285: Y. Kuthati*, et al.* The Melatonin Type 2 Receptor Agonist IIK7 Attenuates and Reverses Morphine Tolerance in Neuropathic Pain Rats Through the Suppression of Neuroinflammation in the Spinal Cord. Pharmaceuticals (Basel) 2024;17(12):
Agents: Morphine; IIK7 **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rats; **Strain:** Wistar; **Pump:** Not Stated;
Duration: 7 days;
ALZET Comments: Dose Morphine (15 µg/h); IIK7 (50 ng/h); controls received mp w/ vehicle; animal info (7 weeks, isoflurane anesthesia); behavioral testing (Antinociception Test; tail flick test); therapeutic indication (neuropathic pain);

Q11966: A. M. Jones*, et al.* Examining the effects of the HIV-1 protein Tat and morphine on antiretroviral accumulation and distribution within the brain. Clinical & Translational Science 2024;17(10):e70035
Agents: Abacavir; Dolutegravir; Lamivudine; Morphine **Vehicle:** Saline, normal; **Route:** SC; **Species:** Mice; **Strain:** Tat transgenic, C57 background; **Pump:** 2001; **Duration:** Not Stated;
ALZET Comments: Dose: abacavir 2.5mg/day (123.5mg/kg/day); dolutegravir 0.2mg/day (10.3mg/kg/day), lamivudine; 1.2mg/day (61.7mg/kg/day); morphine (2.5mg/day); controls received mp w/ vehicle; animal info (25 g mouse, isoflurane anesthesia); post op. care (bupivacaine);

Q11750: E. R. Jaeckel*, et al.* Chronic Morphine Induces Adaptations in Opioid Receptor Signaling in a Thalamostriatal Circuit That Are Location Dependent, Sex Specific, and Regulated by mu-Opioid Receptor Phosphorylation. Journal of Neuroscience 2024;44(3):
Agents: Morphine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** C57Bl/6J; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose: (80 mg/kg/d); controls received mp w/ saline; animal info (6-10 weeks old, isoflurane anesthesia, wound clips used)dependence; " The present study provided a direct comparison of how chronic morphine treatment differentially alters morphine signaling at presynaptic and somatic subcellular compartments within the same neuronal population in a sex-specific manner. Seven days of continuous morphine exposure facilitated morphine responses at MThal–DMS terminals in male, but not female mice, but induced tolerance at MThal cell bodies in both sexes." pg. 9;

T0017: E. R. Jaeckel. Effects of Chronic Morphine Treatment on Pre-and Postsynapti Thalamo-Cortico-Striatal Mu-Opioid Receptor Signaling. University of Michigan 2024;
Agents: Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (80 mg/kg/day); controls received mp w/ vehicle; animal info (4, 8 weeks old); dependence;

Q11714: P. M. Estave*, et al.* Co-targeting the kappa opioid receptor and dopamine transporter reduces motivation to self-administer cocaine and partially reverses dopamine system dysregulation. Scientific Reports 2024;14(1):6509
Agents: Phenmetrazine; norbinaitormorphine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2001; 2002; **Duration:** 14 days;
ALZET Comments: Dose (25 mg/kg/day); controls received mp w/ vehicle; animal info (male 325-400 g); pumps replaced every week; nBNI is a KOR antagonist; behavioral testing (food and cocaine self-administration, ANOVA; turkey's multiple comparisons, paired T-tests); dependence; " We chose to focus on phenmetrazine in this study since it is the active metabolite of phendimetrazine. Consistent with the results seen in this study, prior studies have also shown that continuous administration of phenmetrazine results in decreased cocaine breakpoints in rodents" pg. 7;

Q11344: Y. Kuthati, *et al.* Teneligliptin Co-Infusion Alleviates Morphine Tolerance by Inhibition of Spinal Microglial Cell Activation in Streptozotocin-Induced Diabetic Rats. Antioxidants (Basel) 2023;12(7):
Agents: Teneligliptin; morphine **Vehicle:** DMSO; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Strain:** Wistar; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose: mor 15 ug/h; ten 2 ug/h, or both mor + ten; 4% DMSO used; controls received mp w/ saline; animal info (Male); polyethylene catheter; behavioral testing (mechanical paw withdrawal threshold and tail-flick tests); diabetes; (neuropathic pain)

Q10953: A. Kaneguchi, *et al.* The effects of the amount of weight bearing on articular cartilage early after ACL reconstruction in rats. Connective Tissue Research 2023;64(2):186-204
Agents: Morphine hydrochloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML2; **Duration:** 14 d;
ALZET Comments: Dose (40 mg/ml); Controls received mp w/ vehicle; animal info: 8-week-old male (180–240 g); "We selected high dose of morphine hydrochloride because high doses of morphine produce prolonged antinociception and delayed tolerance" p. 4; ACL injury

Q11763: A. Kaneguchi, *et al.* The effects of weight bearing after ACL reconstruction on joint contracture in rats. Connective Tissue Research 2023;64(6):543-554
Agents: Morphine HCl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML2; **Duration:** Not Stated;
ALZET Comments: Dose (4.8 mg/day); animal info (8-week-old male); "In conclusion, continuous morphine administration after ACLR, which increases the amount of weight bearing through pain relief19, improved myogenic contractures on day 7 post-surgery. T " pg. 11;

Q11303: A. D. Dunn, *et al.* Molecular and long-term behavioral consequences of neonatal opioid exposure and withdrawal in mice. Frontiers in Behavioral Neuroscience 2023;17(1202099
Agents: Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57Bl/6NTac; **Pump:** 1004; **Duration:** 14 days;
ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Female; 8-13 weeks old); behavioral testing: pups (ultrasonic vocalizations, somatic withdrawal, and hot plate
latency), adult (elevated plus maze, tail suspension, learned helplessness, conditioned place preference, self admin; teratology;

Q11064: A. T. Amgott-Kwan, *et al.* Endomorphin analog ZH853 shows low reward, tolerance, and affective-motivational signs of withdrawal, while inhibiting opioid withdrawal and seeking. Neuropharmacology 2023;227(109439
Agents: ZH853; morphine **Vehicle:** Saline; **Route:** IV; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose: (ZH853 6 mg/day; Morphine 10 mg/day); 20% PEG in saline used; animal info: Male and female; 250-275 g and 200-225 g; dependence

Q11172: C. R. Leibrand, *et al.* Independent actions by HIV-1 Tat and morphine to increase recruitment of monocyte-derived macrophages into the brain in a region-specific manner. Neuroscience Letters 2022;788(136852
Agents: Morphine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** Tat+; Tat-; **Pump:** 2002; 2001; **Duration:** 19 days;
ALZET Comments: Dose: 0.77 mg/day; 1.5 mg/day; animal info: adult, female mice approx. 70 days of age; post op. care: bupivacaine applied to all surgical sites immediately after implantation; immunology; dependence

Q11152: K. Kawakami, *et al.* Intrathecal morphine exacerbates paresis with increasing muscle tone of hindlimbs in rats with mild thoracic spinal cord injury but without damage of lumbar alpha-motoneurons. PLoS One 2022;17(8):e0273095
Agents: Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** 1003D; **Duration:** 72 hours;
ALZET Comments: Dose: (3 ug/ul/hr); Controls received mp w/ vehicle; animal info: Adult male rats, 8–9
weeks old (weighing 240–300 g); spinal cord injury; comparison of single IT doses vs mp

Q10447: J. A. Blakeley-Ruiz, *et al.* Morphine and high-fat diet differentially alter the gut microbiota composition and metabolic function in lean versus obese mice. ISME Communications 2022;2(1):
Agents: Morphine sulfate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** Not Stated; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Control group fed standard mouse diet; 2nd group w/ diet-induced obesity by eating 60% fat diet; 3rd group fed standard diet yet obese due to spontaneous mutation of leptin receptor); immunology;

Q10661: A. Rivera, *et al.* Dopamine D(4) Receptor Is a Regulator of Morphine-Induced Plasticity in the Rat Dorsal Striatum. Cells 2021;11(1):
Agents: Morphine; PD168077 **Vehicle:** DMSO; Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** Not Stated; **Duration:** 7 days; 14 days;
ALZET Comments: Dose: (morphine 20 mg/kg/d; PD168077 1 mg/kg/d); 2% DMSO, 0.9% NaCl vehicle used; animal info (1-2 months old; Male); post op. care: animals kept warm on heating pad; dependence

Q10641: F. Pantouli, *et al.* Comparison of Morphine, Oxycodone and the Biased MOR Agonist SR-17018 For Tolerance and Efficacy in Mouse Models of Pain. Neuropharmacology 2021;185(108439
Agents: Morphine **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2001; **Duration:** 6 days;
ALZET Comments: Controls received mp w/ vehicle; animal info: 10–20 weeks of age (23–32 g)dependence; pain

Q9368: F. Meng, *et al.* Naloxone Facilitates Contextual Learning and Memory in a Receptor-Independent and Tet1-Dependent Manner. Cellular and Molecular Neurobiology 2021;41(5):1031-1038
Agents: Naloxone; Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** Not Stated; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (); animal info (Male mice, 2-3 months old); behavioral testing (Morris Water Maze Test); dependence;

Q9318: H. J. Kulbeth, *et al.* Automated quantification of opioid withdrawal in neonatal rat pups using Ethovision(R) XT software. Neurotoxicology and Teratology 2021;84(106959
Agents: Buprenorphine, nor-; Morphine **Vehicle:** DMSO; PEG 400; Saline, Sterile; **Route:** SC; **Species:** Rat; **Strain:** Long-Evans; **Pump:** 2ML2; **Duration:** Not Stated;
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 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; SCH 39166; Pramipexole **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Long- Evans; **Pump:** 1002; 2002; **Duration:** 14 days;
ALZET Comments: Dose (2 mg/kg); Controls received mp w/ vehicle; animal info (female weighing 200–225 g); behavioral testing (Withdrawal testing); Multiple pumps per animal (2 or 3); dependence;

Q9796: E. M. Lefevre, *et al.* Interruption of continuous opioid exposure exacerbates drug-evoked adaptations in the mesolimbic dopamine system. Neuropsychopharmacology 2020;45(11):1781-1792
Agents: Morphine hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (63.2mg/kg/day); 0.9% Saline used; Controls received mp w/vehicle; animal info (Oprm1 KO);

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; **Strain:** C57BL6; **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 (10-20 weeks);

Q8430: W. D. Cornwell, *et al.* Tobacco smoke and morphine alter peripheral and CNS inflammation following HIV infection in a humanized mouse model. Sci Rep 2020;10(1):13977
Agents: Morphine **Vehicle:** Not stated; **Route:** Not stated; **Species:** Mice; **Strain:** Not Stated **Pump:** Not stated **Duration:** 28d;
ALZET Comments: Dose (1 mg/kg/day); dependence;

Q8413: I. J. Chen, *et al.* The Circadian Hormone Melatonin Inhibits Morphine-Induced Tolerance and Inflammation via the Activation of Antioxidative Enzymes. Antioxidants (Basel) 2020;9(9):
Agents: Morphine **Vehicle:** DMSO; Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Strain:** Wistar; **Pump:** Not stated; **Duration:** 10 days;
ALZET Comments: 0.9% Saline used; Controls received mp w/ vehicle; animal info (adult male rats, 300-350 g); behavioral testing (Nociceptive Test); dependence;

Q7580: J. V. Negrete-Diaz, *et al.* Pharmacological activation of dopamine D4 receptor modulates morphine-induced changes in the expression of GAD65/67 and GABAB receptors in the basal ganglia. Neuropharmacology 2019;152(22-29
Agents: PD168,077; morphine **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** 2ML1; **Duration:** 6 d;
ALZET Comments: Dose (20 mg/kg/day- morphine, 1 mg/kg/day- PD168,077); 2% DMSO used; animal info (Male, 250-300g); PD168,077 aka D4R agonist; dependence.

Q8294: K. M. Nation, *et al.* Sustained exposure to acute migraine medications combined with repeated noxious stimulation dysregulates descending pain modulatory circuits: Relevance to medication overuse headache. Cephalalgia 2019;39(5):617-625
Agents: Sumatriptan succinate or Morphine Sulfate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (Sumatriptan succinate- 0.6 mg/kg/day or 3 mg/kg/day or Morphine Sulfate- 7.68 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male, 175-200g); dependence;

Q7004: S. Moon, *et al.* Morphine Dependence is Attenuated by Treatment of 3,4,5-Trimethoxy Cinnamic Acid in Mice and Rats. Neurochem Res 2019;
Agents: Morphine; Trimethoxy cinnamic acid, 3, 4, 5- **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Strain:** Sprague–Dawley; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose (26 nmol/10µ l/hr); Controls received mp w/ vehicle; animal info (male 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 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** Not Stated; **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);

Q7622: S. Kokubu, *et al.* Characterization of Analgesic Actions of the Chronic Intrathecal Infusion of H-Dmt-D-Arg-Phe-Lys-NH2 in Rat. Neuromodulation 2019;
Agents: DMT-DALDA; morphine sulfate **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Strain:** Sprague-Dawley; **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, 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);

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); **Strain:** knock-in 1S/T-A mutations Oprm1tm3.1Shlz, MGI:6117673, 11S/T-A1; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Dose (Fentanyl (2mg/kg/day); Morphine (17 mg/kg/day)); animal info (mice with)); 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 HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Jcl Wistar; **Pump:** 2ML1; **Duration:** 5 days;
ALZET Comments: Dose (6 mg/kg); Controls received mp w/ vehicle; animal info (6-week-old male rats); dependence;

Q8205: R. Hill, *et al.* Prolonged ethanol administration prevents the development of tolerance to morphine-induced respiratory depression. Drug and Alcohol Dependence 2019;205(107674
Agents: Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** CD-1; **Pump:** Not stated; **Duration:** 16 days;
ALZET Comments: Dose (45 mg/kg/day); Controls received mp w/ vehicle; animal info (Male approximately 30); dependence;

Q8013: B. A. Griffin, *et al.* In Utero Exposure to Norbuprenorphine, a Major Metabolite of Buprenorphine, Induces Fetal Opioid Dependence and Leads to Neonatal Opioid Withdrawal Syndrome. J Pharmacol Exp Ther 2019;370(1):9-17
Agents: Norbuprenorphine; Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Long-Evans; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (1,3 or 10 mg/kg/day); Controls received mp w/ vehicle; 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; **Strain:** Sprague Dawley; **Pump:** 2ML1; **Duration:** Not Stated;
ALZET Comments: Animal info (5-6 weeks old, 180-300 g); dependence;

Nicotine (2022-Present)

Q11809: S. Oh, *et al.* The Effects of Nicotine on Re-endothelialization, Inflammation, and Neoatherosclerosis After Drug-Eluting Stent Implantation in a Porcine Model. Korean Circulation Journal 2025;55(1):50-64
Agents: Nicotine **Vehicle:** Not Stated; **Route:** SC; **Species:** Pig; **Strain:** Yorkshire x Landrace; **Pump:** 2ML4; **Duration:** 8 weeks;
ALZET Comments: functionality of mp verified by blood nicotine concentration; pumps replaced after 4 weeks; dependence;

Q12092: O. Dali, *et al.* Prenatal nicotine exposure leads to epigenetic alterations in peripheral nervous system signaling genes in the testis of the rat. Epigenetics & Chromatin 2024;17(1):14
Agents: Nicotine tartrate **Vehicle:** Saline; sterile; **Route:** SC; **Species:** Rats; **Strain:** Sprague-Dawley; **Pump:** 2ML4; **Duration:** Not Stated;
ALZET Comments: Dose (6 mg/kg); controls received mp w/ vehicle; animal info (female; 9 weeks old); teratology;

Q12076: S. N. Cheeks, *et al.* Cannabidiol as a potential cessation therapeutic: Effects on intravenous nicotine self-administration and withdrawal symptoms in mice. Neuropharmacology 2024;246(109833
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (24 mg); controls received mp w/ vehicle; animal info (male and female 8+ weeks of age, isoflurane anesthesia); behavioral testing (paw, body tremors, head shakes, backing, jumps, curls, and ptosis); dependence; "The minipumps were kept at a constant flow rate to deliver 24 mg nicotine bitartrate/kg animal body weight/day for 14 days which has been show to maintain stable nicotine level and elicit nicotine withdrawal symptoms upon removal" pg. 3;

Q11905: K. Shankar, *et al.* Acute nicotine intake increases feeding behavior through decreasing glucagon signaling in dependent male and female rats. Society for Behavioral Neuroendocrinology 2024;159(105447
Agents: Nicotine **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rats; **Strain:** Wistar; **Pump:** 2ML4; **Duration:** 2 weeks;
ALZET Comments: Dose: (1 mg/kg/d); 0.9 % saline used; controls received mp w/ vehicle; animal info (adult male and female);

Q11849: W. Ma, *et al.* Application of Covalent Organic Framework-Based Solid-Phase Microextraction for Efficient and Direct Analysis of Neurotransmitters in the Striatum of Nicotine-Addicted mice. Microchemical Journal 2024;198(**Agents:** Nicotine
Vehicle: Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (6.3 mg/kg/d); controls received mp w/ vehicle; animal info (male 6-8 weeks old); dependence;

Q11807: J. V. Keady, *et al.* Sex differences in contextual fear conditioning and extinction after acute and chronic nicotine treatment. Biology of Sex Differences 2024;15(1):88
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** B6/129F1; **Pump:** 1002; **Duration:** 11; 13 days;
ALZET Comments: Dose (18 mg/kg/d); 0.9% saline used; animal info (male, female 8-13 wks); comparison of acute injection vs mp; pulsed delivery p. 4; behavioral testing (contextual fear conditioning, extinction); dependence; wound clips used;

Q11721: M. L. Fisher, *et al.* Dynamic effects of ventral hippocampal NRG3/ERBB4 signaling on nicotine withdrawal-induced responses. Neuropharmacology 2024;
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** ErbB4-floxed; B6; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (12 mg/kg/d); 0.9% saline used; controls received mp w/ vehicle; animal info (male and female; 6-8 weeks old); wound clips used; pulsed delivery; PE 60 tubing; behavioral testing (novelty-induced hypophagia test, open field exploratory); dependence; good methods (Lynch coil) p. 3; "The use of pulsatile infusions of nicotine to administer nicotine intermittently, rather than continuous delivery, allows us to accurately model the intermittent pattern of nicotine intake in cigarette smokers in a reliable manner, producing a robust WD syndrome in our model" pg. 3;

Q11665: S. N. Cheeks, *et al.* Cannabidiol as a potential cessation therapeutic: Effects on intravenous nicotine self-administration and withdrawal symptoms in mice. Neuropharmacology 2024;246(109833
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2000; **Duration:** 14 days;
ALZET Comments: Dose (24 mg/kg/d); controls received mp w/ vehicle; animal info (male and female; >8 weeks old);

Q11827: B. Buzzi, *et al.* Nelotanserin, a selective 5-HT2A receptor inverse agonist, attenuates aspects of nicotine withdrawal but not reward in mice. Behavioural Brain Research 2024;467(115019
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** ICR; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (24 mg/kg/day); controls received mp w/ vehicle; animal info (male and female; 12 weeks old; isoflurane anesthesia); behavioral testing (Maze; Conditioned place preference assessment); dependence;

Q11814: S. M. Ayoub, *et al.* Orally Administered N-Oleoyl Alanine Blocks Acute Opioid Withdrawal Induced-Conditioned Place Preference and Attenuates Somatic Withdrawal following Chronic Opioid Exposure in Rats. Psychoactives 2024;3(2):184-193
Agents: Heroin **Vehicle:** Saline; **Route:** SC; **Species:** Rats; **Strain:** Sprague-Dawley; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Dose (7 mg/kg/day); controls received mp w/ vehicle; animal info (male; 200-225 g, isoflurane anesthesia); post op. care (carprofen); behavioral testing (somatic withdrawal observations); dependence; "For this experiment, and as previously published, heroin was selected due to solubility limits for the desired doses of morphine delivered by minipump.";

Q11983: Z. Yang, *et al.* Single nucleotide polymorphisms rs148582811 regulates its host gene ARVCF expression to affect nicotine-associated hippocampus-dependent memory. iScience 2023;26(12):108335
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** WT; Arvcf KO/KO; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose: (6.3 mg/kg/day) 0.9% NaCl used; controls received mp w/ vehicle; behavioral testing (morris water maze test; novel object recognition test; fear conditioning test)dependence;

Q11014: J. Vargas-Medrano, *et al.* Sex and diet-dependent gene alterations in human and rat brains with a history of nicotine exposure. Frontiers in Psychiatry 2023;14(1104563
Agents: Nicotine **Vehicle:** Saline; **Route:** Not Stated; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (3.2 mg/kg/day); Controls received sham operation; animal info: Adult rats between 60 and 75 days of age post op. care: topical antibiotic ointment (Neosporin) on the wound, SC administration of analgesic flunixin (2.5 mg/kg;); dependence;

Q11469: G. S. Souza, *et al.* Transgenerational effects of maternal exposure to nicotine on structures of pituitary-gonadal axis of rats. Toxicology and Applied Pharmacology 2023;468(116525
Agents: Nicotine **Vehicle:** Water, bacteriostatic; **Route:** SC; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: Dose (2 mg/kg/day); controls received mp w/ vehicle; animal info (pregnant; weighed 220-260 g); pumps replaced within the first 24 h after birth; teratology; "The subcutaneous osmotic minipump is considered the best method for the chronic release of nicotine in rats, especially in pregnant animals, since it does not cause vasoconstriction in the uterus and placenta, besides avoiding other negative effects, such as stress, which would occur by daily manipulation and injection" pg. 4;

Q11000: M. L. Smith, *et al.* Identification of candidate genes for nicotine withdrawal in C57BL/6J x DBA/2J recombinant inbred mice. Genes, Brain and Behavior 2023;22(2):e12844
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; DBA/2J; BXD RI; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (24 mg/kg/day); saline used; Controls received mp w/ vehicle; animal info: 7-8 weeks; behavioral testing: plus-maze test, elevated plus maze, somatic signs; dependence

Q11892: A. Rodriguez-Vega*, et al.* Nicotine Exposure in a Phencyclidine-Induced Mice Model of Schizophrenia: Sex-Selective Medial Prefrontal Cortex Protein Markers of the Combined Insults in Adolescent Mice. International Journal of Molecular Sciences 2023;24(19):
Agents: Nicotine **Vehicle:** Water, milliQ; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6; **Pump:** 1007D; **Duration:** Not Stated;
ALZET Comments: Dose: (24 mg/kg); controls received mp w/ vehicle; post op. care (flunixin 2.5 mg/kg; enrofloxacin 2.5 mg/kg)dependence; "As for nicotine exposure, a subcutaneous osmotic minipump is an established model that has the advantage of being less stressful than other routes of administration, in addition to allowing for a constant dose and a controlled period of administration" pg. 3;

Q10960: L. D. McGill*, et al.* Prenatal nicotine exposure alters gene expression profiles of neurons in the sub-regions of the VTA during early postnatal development. Scientific Reports 2023;13(1):4911
Agents: Nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info: Pregnant, female; dependence;

Q11048: A. Kubo*, et al.* The Influence of Nicotine on Trophoblast-Derived Exosomes in a Mouse Model of Pathogenic Preeclampsia. International Journal of Molecular Sciences 2023;24(13):
Agents: Nicotine hydrogen tartrate salt **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Strain:** ICR; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Dose (3 mg/kg/day); animal info: 8–12 weeks; blood pressure measured via Tail cuff; blood pressure results see p.3 cardiovascular; therapeutic indication (Preeclampsia);

Q11044: B. A. Karamian*, et al.* Varenicline mitigates the increased risk of pseudarthrosis associated with nicotine. The Spine Journal 2023;23(8):1212-1222
Agents: Nicotine; varenicline **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley **Pump:** 2ML4 **Duration:** 8w
ALZET Comments: Dose: Nicotine 15mg/kg/day, 22.5mg/kg/day, 30mg/kg/day; Varenicline 1mg/kg/day, 2mg/kg/day; dose-response (see pg 14; graph pg 16); animal info: eight-week-old male ~300 grams; post op. care: skin closed with running sub-cuticular 4-0 Vicryl suture, incision was dressed with triple antibiotic ointment; pumps replaced every 2 weeks; functionality of mp verified by serum levels; good methods (pump replacement) p. 2-3; therapeutic indication: (Pseudarthrosis, spinal fusion)

Q10921: R. Jain. Role of Habb-e-Jawahar in Attenuating Nicotine Withdrawal in Rats. Journal of Drug and Alcohol Research 2023;12(**Agents:** Nicotine tartrate, dihydrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Wistar **Pump:** 2ML1 **Duration:** 7d
ALZET Comments: Dose (9 mg/kg/day); Controls received mp w/ vehicle; animal info (Male; Albino; Weighed 175-250 g); behavioral testing (Motor activity); dependence;

Q11105: A. Ganaway*, et al.* Investigating the Modulation of the VTA Neurons in Nicotine-Exposed Pups during Early Maturation Using Optogenetics. International Journal of Molecular Sciences 2023;24(3):
Agents: Nicotine hydrogen tartrate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley, WT; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (Female; Pregnant); dependence;

Q11707: M. Dulchavsky*, et al.* Directed evolution unlocks oxygen reactivity for a nicotine-degrading flavoenzyme. Nature Chemical Biology 2023;19(11):1406-1414
Agents: Nicotine **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML2; **Duration:** 7 days;
ALZET Comments: Dose (3.15 mg/kg/d); controls received mp w/ vehicle; animal info (adult male and female); wound clips used; dependence;

Q11253: B. Buzzi*, et al.* Differential roles of diacylglycerol lipase (DAGL) enzymes in nicotine withdrawal. Brain Research 2023;1817(148483
Agents: Nicotine bitartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** DAGL-α KO; WT (99% C57BL/6, 1% 129/ SvEv); **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Dose (24 mg/kg/day); controls received mp w/ vehicle; behavioral testing: light–dark box; somatic withdrawal signs; hot-plate test; dependence; 200 ul pump used no model specified

Q11236: J. An*, et al.* Nicotine exacerbates atherosclerosis and plaque instability via NLRP3 inflammasome activation in vascular smooth muscle cells. Theranostics 2023;13(9):2825-2842
Agents: Nicotine **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Strain:** Apoe-/-; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Dose (5 mg/kg/day); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (Male; 8 weeks old; Fed Western diet of 21% milk fat and 0.15% cholesterol); toxicology; "...nicotine infusion for 6 weeks significantly increased the plaque size and plaque area percentage of internal elastic lamina area in BA compared with that of vehicle-treated mice. These data suggest that nicotine, the core component in cigarette smoking and electronic cigarette smoking, markedly aggravates atherogenesis in Apoe-/- mice." p. 4

Q11195: Y. Alkhlaif*, et al.* L-theanine attenuates nicotine reward and withdrawal signs in mice. Neuroscience Letters 2023;807(137279
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** ICR; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (24 mg/kg); Controls received mp w/ saline; animal info (Male; 8 weeks old); dependence; behavioral testing: Light-Dark box test, hot-plate test

Q10741: J. Zubcevic*, et al.* Nicotine Exposure During Rodent Pregnancy Alters the Composition of Maternal Gut Microbiota and Abundance of Maternal and Amniotic Short Chain Fatty Acids. Metabolites 2022;12(8):
Agents: Nicotine tartrate **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** 2ML4; **Duration:** 28d
ALZET Comments: Dose (6 mg/kg); Controls received mp w/ vehicle; animal info (Female; ~9 weeks old; Virgin); teratology; toxicology

Q11593: K. Takeda*, et al.* A mouse model of weight gain after nicotine withdrawal. Biochemical Biophysical Research Communications 2022;588(140-146
Agents: Nicotine tartrate dihydrate; exendin-4 **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Dose (15 mg/kg/day nicotine base; 2.5 or 5 ug/kg/day exendin-4); Controls received mp w/ vehicle; animal info (male; 8 weeks); pumps replaced every 2 weeks; toxicology; dependence; "To mimic human subjects quitting smoking, we substituted nicotine-supplying pumps with new pumps containing either nicotine (NeN) or PBS (NeP)" pg. 3;

Q11590: H. Su*, et al.* Nicotine-mediated activation of alpha2 nAChR-expressing OLM cells in developing mouse brains disrupts OLM cell-mediated control of LTP in adolescence. Neurobiology of Learning and Memory 2022;194(107674
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** Alpha2-Cre,hM3dq; WT; **Pump:** 1002; **Duration:** Not Stated;
ALZET Comments: Dose response: (21, 2.1, 0.21 mg/kg/day); Controls received mp w/ vehicle; behavioral testing: maternal behavior (pup handling, licking, nursing, covering, contact) or non-maternal behavior (movement outside/inside nest, grooming, eating/drinking); toxicology; "We used mini pumps, because we have previously found that mouse pups exposed to nicotine via the milk of dams implanted nicotine pumps show impairments in long-term object location memory in adolescence. To investigate the underlying mechanisms, we used the same method of nicotine delivery" pg. 2;

Phencyclidine

Q9018: S. Takahashi*, et al.* ASP2905, a specific inhibitor of the potassium channel Kv12.2 encoded by the Kcnh3 gene, is psychoactive in mice. Behavioural Brain Research 2020;378(112315
Agents: Phencyclidine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (1.2 mg/day/mouse); Controls received mp w/ vehicle; animal info (male ddY mice aged 4–5 weeks); behavioral testing (Forced Swim Test; Water-Finding Task); Phencyclidine aka PCP; neurodegenerative (Schizophrenia);

Q9086: S. Thomson*, et al.* Reduced expression of synapsin II in a chronic phencyclidine preclinical rat model of schizophrenia. Synapse 2019;73(5):e22084
Agents: Phencyclidine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (5 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 250-300 g, 3 months old); Phencyclidine aka PCP; gene therapy;