



Recent References (2018-Present) on the Administration of Nicotine
Using ALZET® Osmotic Pumps

Q10070: C. Y. Tsai, *et al.* Perinatal nicotine exposure alters lung development and induces HMGB1-RAGE expression in neonatal mice. *Birth Defects Research* 2021;113(7):570-578

Agents: Nicotine **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2001; 2004; **Duration:** 7 days; 28 days;
ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (pregnant C57BL/6N mice); dependence;

Q9415: C. B. Pietrobon, *et al.* Pancreatic steatosis in adult rats induced by nicotine exposure during breastfeeding. *Endocrine* 2021;72(1):104-115

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (6 mg/kg/d); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (virgin female Wistar rats, 3 months old); Nicotine aka NIC; dependence;

Q9410: T. C. Peixoto, *et al.* Nicotine exposure during lactation causes disruption of hedonic eating behavior and alters dopaminergic system in adult female rats. *Appetite* 2021;160(105115)

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (6 mg/kg body mass); Controls received mp w/ vehicle; animal info (Wistar rats, male and female); Nicotine aka Nic; dependence;

Q9364: F. Matos-Ocasio, *et al.* Female rats display greater nicotine withdrawal-induced cellular activation of a central portion of the interpeduncular nucleus versus males: A study of Fos immunoreactivity within provisionally assigned interpeduncular subnuclei. *Drug Alcohol Depend* 2021;221(108640)

Agents: Nicotine; Mecamylamine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (3.2 mg/kg/day Nicotine; 3.0 mg/kg Mecamylamine); Controls received mp w/ vehicle; animal info (Fully outbred adult Wistar rats, 260 g females, 400 g males); dependence;

Q10004: M. A. Kwiatkowski, *et al.* Chronic nicotine, but not suramin or resveratrol, partially remediates the mania-like profile of dopamine transporter knockdown mice. *European Neuropsychopharmacology* 2021;42(75-86)

Agents: Nicotine Hydrogen Tartrate **Vehicle:** Saline, Sterile; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 26 days;
ALZET Comments: Dose (40 mg/kg/day); 0.9% Sterile Saline used; Controls received mp w/ vehicle; animal info (male wildtype C57BL/6J mice, 50 to 60 weeks old); behavioral testing (Behavioral Pattern Monitor); dependence;

Q9309: B. Kim, *et al.* Chronic nicotine impairs sparse motor learning via striatal fast-spiking parvalbumin interneurons. *Addiction Biology* 2021;26(3):e12956

Agents: Nicotine ditartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 2 weeks;
ALZET Comments: Dose (24 mg/kg/day); Controls received mp w/ vehicle; animal info (2- to 3-month-old C57BL/6J male mice); behavioral testing (Open field test; light-dark transition; rotarod test); dependence;

Q8732: L. R. Goldberg, *et al.* Paternal nicotine enhances fear memory, reduces nicotine administration, and alters hippocampal genetic and neural function in offspring. *Addiction Biology* 2021;26(1):E12859

Agents: Nicotine Hydrogen Tartrate Salt **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Dose (12.6 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male, 8 weeks old); dependence;

Q9852: P. Zhang, *et al.* Inhibition of Autophagy Signaling via 3-methyladenine Rescued Nicotine-Mediated Cardiac Pathological Effects and Heart Dysfunctions. *International Journal of Biological Sciences* 2020;16(8):1349-1362

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 30 days;
ALZET Comments: Dose (4 µg/kg/min); Controls received mp w/ vehicle; animal info (Sprague-Dawley male rats (8-months-old)); ischemia (cardiac injury);



Q10070: P. C. Tsai, *et al.* Sympathetic activation of splenic T-lymphocytes in hypertension of adult offspring programmed by maternal high fructose exposure. *Chinese Journal of Physiology* 2020;63(6):263-275

Agents: Nicotine **Vehicle:** Saline; **Route:** Abdomen; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (1 mg/kg/day); Controls received mp w/ vehicle; animal info (male and virgin female adult Sprague-Dawley rats, 12-14 weeks old); Blood pressure measured via tail-cuff method; 105 mmHg - 130 mmHg; cardiovascular;

Q8943: T. Sato, *et al.* Suppressive effect of ghrelin on nicotine-induced clock gene expression in the mouse pancreas. *Endocrine Journal* 2020;67(1):73-80

Agents: Nicotine **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (1.67 ng/0.5 uL/hr/20 g); Controls received mp w/ vehicle; animal info (Male C57BL/6J Jcl mice); Resultant plasma level (23 fmol/mL Ghrelin); dependence;

Q9431: M. A. Robble, *et al.* Differential Effects of Nicotine and Nicotine Withdrawal on Fear Conditioning in Male Rats. *International Journal of Neuropsychopharmacology* 2020;23(7):469-479

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** SMP-200; **Duration:** 21 days;

ALZET Comments: Dose (1.0 mg/d or 0.3 mg/d); Controls received mp w/ vehicle; animal info (Male Long-Evans rats, 300-350 g); dependence;

Q8847: T. C. Peixoto, *et al.* Nicotine exposure during breastfeeding reduces sympathetic activity in brown adipose tissue and increases in white adipose tissue in adult rats: Sex-related differences. *Food and Chemical Toxicology* 2020;140(11):1328

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (6 mg/kg of nicotine per day); Controls received mp w/ vehicle; animal info (Lactating Wistar rats); teratology;

Q8667: R. A. Miranda, *et al.* Thyroid redox imbalance in adult Wistar rats that were exposed to nicotine during breastfeeding. *Scientific Reports* 2020;10(1):15646

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (6 mg/kg/day); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (Pregnant female Wistar rats); Nicotine aka NIC; dependence;

Q8581: B. Kim, *et al.* Chronic nicotine impairs sparse motor learning via striatal fast-spiking parvalbumin interneurons. *Addict Biol* 2020;e12956

Agents: Nicotine ditartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 2 weeks;

ALZET Comments: Dose (24 mg/kg/day); Controls received mp w/ vehicle; animal info (2- to 3-month-old C57BL/6J male mice); behavioral testing (Open field test; light-dark transition; rotarod test); dependence;

Q9791: R. J. Keeley, *et al.* Intrinsic differences in insular circuits moderate the negative association between nicotine dependence and cingulate-striatal connectivity strength. *Neuropsychopharmacology* 2020;45(6):1042-1049

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 14 days;

ALZET Comments: Dose (1.2 or 4.8 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Sprague Dawley, 275-300 g); dependence;

Q8865: T. Kazemi, *et al.* Investigating the influence of perinatal nicotine exposure on genetic profiles of neurons in the sub-regions of the VTA. *Scientific Reports* 2020;10(1):2419

Agents: Nicotine hydrogen tartate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (Pregnant female Sprague Dawley rats); dependence;

Q8553: G. Jia, *et al.* Nicotine induces cardiac toxicity through blocking mitophagic clearance in young adult rat. *Life Sciences* 2020;257(11):8084

Agents: Nicotine **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 6 weeks;

ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats, 2-4 months old); toxicology;



- Q9250:** I. Gorna, *et al.* Electronic Cigarette Use and Metabolic Syndrome Development: A Critical Review. *Toxics* 2020;8(4):
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; Rat; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Dose (0.8 mg/kg/d; 4 mg/kg/d); Controls received mp w/ vehicle; animal info (Male C57BL/6J mice, 8 weeks old; Female and Male Sprague Dawley OFA rats); dependence;
- Q8474:** K. Fukuyama, *et al.* Upregulated Connexin 43 Induced by Loss-of-Functional S284L-Mutant alpha4 Subunit of Nicotinic ACh Receptor Contributes to Pathomechanisms of Autosomal Dominant Sleep-Related Hypermotor Epilepsy. *Pharmaceuticals (Basel)* 2020;13(4):
Agents: Zonisamide; Nicotine **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose (40 mg/kg/day Zonisamide, 10, 25 and 50 mg/kg/day Nicotine); animal info (Male S286L-TG and wild-type littermates); Zonisamide aka ZNS; neurodegenerative (Epilepsy);
- Q9225:** R. J. Flores, *et al.* Estradiol promotes and progesterone reduces anxiety-like behavior produced by nicotine withdrawal in female rats. *Psychoneuroendocrinology* 2020;119(104694)
Agents: Nicotine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (3.2 mg/kg/day); animal info (Male and female Wistar rats); behavioral testing (physical signs test, Anxiety-like behavior assessments); replacement therapy (Estradiol, progesterone);
- Q8848:** R. J. Flores, *et al.* Estradiol promotes and progesterone reduces anxiety-like behavior produced by nicotine withdrawal in female rats. *Psychoneuroendocrinology* 2020;119(104694)
Agents: Nicotine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (3.2 mg/kg/day); animal info (Male and female Wistar rats); behavioral testing (physical signs test, Anxiety-like behavior assessments); replacement therapy (Estradiol, progesterone);
- Q8379:** F. Diaz, *et al.* Simultaneous nicotine and oral contraceptive exposure alters brain energy metabolism and exacerbates ischemic stroke injury in female rats. *J Cereb Blood Flow Metab* 2020;271678X20925164
Agents: Nicotine Hydrogen Tartrate **Vehicle:** Saline; **Route:** CNS/CSF; **Species:** Rat; **Pump:** 2ML2; **Duration:** 21 days;
ALZET Comments: Dose (4.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley, 6 or 14 weeks old); ischemia (Stroke);
- Q8722:** N. d'Adesky, *et al.* Nicotine Exposure Along with Oral Contraceptive Treatment in Female Rats Exacerbates Post-cerebral Ischemic Hypoperfusion Potentially via Altered Histamine Metabolism. *Translational Stroke Research* 2020;
Agents: Nicotine Hydrogen Tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** ML2; **Duration:** 16, 21 days;
ALZET Comments: Dose (4.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Female, Sprague Dawley, 6 or 14 weeks old); ischemia (Hypoperfusion);
- Q8388:** D. Bhattacharya, *et al.* Concurrent nicotine exposure to prenatal alcohol consumption alters the hippocampal and cortical neurotoxicity. *Heliyon* 2020;6(1):e03045
Agents: Nicotine **Vehicle:** Alcohol, Saline; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** Not stated;
ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley (Time pregnant) rats); behavioral testing (Y maze); toxicology;
- Q8387:** I. M. Bertasso, *et al.* Programming of hepatic lipid metabolism in a rat model of postnatal nicotine exposure - Sex-related differences. *Environ Pollut* 2020;258(113781)
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (6 mg/kg/ day); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (pregnant lactating Wistar rat); toxicology;
- Q8340:** J. Avraam, *et al.* Perinatal Nicotine Reduces Chemosensitivity of Medullary 5-HT Neurons after Maturation in Culture. *Neuroscience* 2020;446(80-93)
Agents: Nicotine Bitartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: Dose (6 mg/kg/day or 60 mg/kg/day); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (pregnant ePET-EYFP mice); dependence;



Q8972: P. Zanos, *et al.* Chronic nicotine administration restores brain region specific upregulation of oxytocin receptor binding levels in a G72 mouse model of schizophrenia. *European Journal of Neuroscience* 2019;50(3):2255-2263

Agents: Nicotine, (-) hydrogen tartrate salt **Vehicle:** Saline, Physiological; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (24 mg/kg/day); Controls received mp w/ vehicle; animal info (10-12 weeks, female, CD-1 and G72 transgenic, 31-35g); dependence; pump model not stated;

Q7644: N. L. Yohn, *et al.* Effects of nicotine and stress exposure across generations in C57BL/6 mice. *Stress* 2019;22(1):142-150

Agents: Nicotine hydrogen tartrate, (-)- **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;

ALZET Comments: Dose (18 mg/kg/day); Controls received mp w/ vehicle; animal info (6-8 weeks, male and female, C57BL/6NTac, 20-30g); behavioral testing (stress exposure); dependence; "While the minipump does not recapitulate the pulsatile mode of NIC delivery experienced by human smokers, it does provide several experimental advantages. For example, minipumps allow for consistent administration of NIC doses across subjects, precise temporal control over the initiation and termination of NIC treatment, and their ease of use facilitated replication across cohorts." pg.143 ; pumps implanted for PND 28-56 before being removed. Stress exposure tests described in supplementary data although access to pages is limited.;

Q9112: J. Yang, *et al.* Age- and Nicotine-Associated Gene Expression Changes in the Hippocampus of APP/PS1 Mice. *Journal of Molecular Neuroscience* 2019;69(4):608-622

Agents: Nicotine Hydrogen Tartrate **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Dose (48 mg/kg/hour); Controls received mp w/ vehicle; animal info (Male, 4-6 months old); neurodegenerative (Alzheimer's Disease);

Q9019: S. Tan, *et al.* Sex differences in the reward deficit and somatic signs associated with precipitated nicotine withdrawal in rats. *Neuropharmacology* 2019;160(107756

Agents: Nicotine; Mecamylamine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (3.16 mg/kg/day nicotine; 1 mg/kg mecamylamine); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (Wistar rats, males 200-225 g, females 175-200 g); behavioral testing (Large Open Field Test; Elevated Plus Maze Test); dependence;

Q9075: T. A. Slotkin, *et al.* The Developmental Neurotoxicity of Tobacco Smoke Can Be Mimicked by a Combination of Nicotine and Benzo[a]Pyrene: Effects on Cholinergic and Serotonergic Systems. *Toxicological Sciences* 2019;167(1):293-304

Agents: Nicotine bitartrate; Benzo[a]pyrene; Both **Vehicle:** H2O; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Nicotine bitartrate or Benzo[a]pyrene or both

Q6791: R. Saravia, *et al.* Anti-inflammatory agents for smoking cessation? Focus on cognitive deficits associated with nicotine withdrawal in male mice. *Brain, Behavior, and Immunity* 2019;75(228-239

Agents: Nicotine hydrogen tartate salt **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Dose (25 mg/kg/day); animal info (8-weeks old male C57BL/6J mice (Charles River).); dependence;

Q8816: N. Raikwar, *et al.* Renal denervation and CD161a immune ablation prevent cholinergic hypertension and renal sodium retention. *American Journal of Physiology Heart and Circulatory Physiology* 2019;317(3):H517-H530

Agents: Nicotine Bitartrate Salt **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;

ALZET Comments: Dose (15 mg/kg/day); Controls received mp w/ vehicle; animal info (3-4 week old, Male); post op. care (Buprenorphine); Blood pressure measured via Tail-cuff Plethysmography;cardiovascular;

Q8791: S. J. Page, *et al.* Effects of acute and chronic nicotine on catecholamine neurons of the nucleus of the solitary tract. *American Journal of Physiology Regulatory Integrative and Comparative Physiology* 2019;316(1):R38-R49

Agents: Nicotine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 14 days;

ALZET Comments: Dose (24 mg/kg/day); animal info (8-16 weeks old, 20-30 g, C57BL/6J); dependence;



Q9359: D. Malin, *et al.* Inverse agonists of the 5-HT_{2A} receptor reduce nicotine withdrawal signs in rats. *Neuroscience Letters* 2019;713(134524)

Agents: Nicotine bitartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Dose (9 mg/kg/day); Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats, 284 to 323 g); behavioral testing (Fisher's LSD and Dunnett's tests); dependence;

Q7535: E. D. Levin, *et al.* Prolonging the Reduction of Nicotine Self-Administration in Rats by Coadministering Chronic Nicotine With Amitifadine, a Triple Monoamine Reuptake Inhibitor With CYP2B6 Inhibitory Actions. *Nicotine Tob Res* 2019;

Agents: Nicotine Ditartrate **Vehicle:** Saline; **Route:** SC, IV (jugular); **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Dose (2.5 mg/kg/day); animal info (Young adult female Sprague-Dawley rats); post op. care (ketoprofen, bupivacaine); behavioral testing (dual-lever experiment);

Q6064: R. F. Keller, *et al.* Comparison between dopaminergic and non-dopaminergic neurons in the VTA following chronic nicotine exposure during pregnancy. *Sci Rep* 2019;9(1):445

Agents: Nicotine hydrogen tartrate salt **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Duration:** 28 days;

ALZET Comments: Dose (6 mg/kg/d); Controls received mp w/ vehicle; animal info (Pregnant female Sprague-Dawley rats);

Q8219: R. J. Keeley, *et al.* Differential expression of nicotine withdrawal as a function of developmental age in the rat. *Pharmacol Biochem Behav* 2019;187(172802)

Agents: Nicotine Hydrogen Bitartrate salt **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Dose (1.2 mg/kg/d or 4.8 mg/kg/d); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, p25-p28 or p59-p62); post op. care (buprenorphine); behavioral testing (Precipitated withdrawal test); dependence;

Q7598: L. M. Hsu, *et al.* Intrinsic Insular-Frontal Networks Predict Future Nicotine Dependence Severity. *J Neurosci* 2019;39(25):5028-5037

Agents: Nicotine hydrogen tartrate salt **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 2ML4; **Duration:** 14 days;

ALZET Comments: Dose (1.2, 4.8 mg/kg/day); saline pH adjusted to 7.2+/-0.5 used; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 275-300g); behavioral testing (Precipitated withdrawal); pulsed delivery

Q7585: E. D. Holliday, *et al.* Stress and nicotine during adolescence disrupts adult hippocampal-dependent learning and alters stress reactivity. *Addiction Biology* 2019;e12769

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 12 days;

ALZET Comments: Dose (12.6 mg/kg/day); Controls received mp w/ vehicle; animal info (preadolescent (P23), adolescent (P38), or adult (P54), male, C57BL/6J); behavioral testing (fear conditioning); dependence; "While noncontingent nicotine administration does not recapitulate all aspects of human smoking, this dose and method of nicotine administration was used because it maintains blood plasma levels of nicotine similar to levels reported in smokers and it ensures that all mice receive identical doses of nicotine." pg.3; pumps were removed on day 12 of infusion;

Q7526: A. B. Hawkey, *et al.* Paternal nicotine exposure in rats produces long-lasting neurobehavioral effects in the offspring. *Neurotoxicol Teratol* 2019;74(106808)

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 56 days;

ALZET Comments: Dose (2 mg/kg/day); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 200-250 g); behavioral testing (Housing and behavioral test, Elevated plus maze test, Figure 8 apparatus test); pumps replaced every 4wks

Q8027: A. Hawkey, *et al.* Gestational exposure to nicotine and/or benzo[a]pyrene causes long-lasting neurobehavioral consequences. *Birth Defects Res* 2019;111(17):1248-1258

Agents: Nicotine or benzo [a]pyrene, or Nicotine +BaP **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Dose (Nicotine-2 mg/kg/day or BaP- 0.03 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley, Female); behavioral testing (Elevated Plus Maze Test, Radial Maze Test); neurodegenerative



Q8009: D. Gittings, *et al.* Chronic Nicotine Exposure Alters Uninjured Tendon Vascularity and Viscoelasticity. *Foot & Ankle Orthopaedics* 2019;4(2):

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 12 weeks;

ALZET Comments: Dose (36 mg/ml); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Sprague Dawley, 10-13 weeks old, 367-425 g); long-term study; dependence;

Q7998: X. Fu, *et al.* Brain Region Specific Single-Molecule Fluorescence Imaging. *Anal Chem* 2019;91(15):10125-10131

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 12 days;

ALZET Comments: Dose (0.7 mg/kg/h); Controls received mp w/ vehicle; animal info (2-5 months old, Male); dependence;

Q8193: R. J. Flores, *et al.* Estradiol promotes and progesterone reduces anxiety-like behavior produced by nicotine withdrawal in rats. *bioRxiv* 2019;

Agents: Nicotine **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (3.2 mg/kg/day); animal info (Male and female Wistar rats); behavioral testing (assessments of physical signs of withdrawal); dependence;

Q7471: K. E. Eklund, *et al.* Examination of the Gateway Hypothesis in a rat model. *Pharmacol Biochem Behav* 2019;179(89-97)

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 21 days;

ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley); post op. care (buprenorphine); dependence;

Q9764: J. B. Dwyer, *et al.* Prenatal nicotine sex-dependently alters adolescent dopamine system development. *Translational Psychiatry* 2019;9(1):304

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;

ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley); dependence;

Q7468: G. Donvito, *et al.* N-Oleoyl-glycine reduces nicotine reward and withdrawal in mice. *Neuropharmacology* 2019;148(320-331)

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Dose (24 mg/kg/day); Controls received mp w/ vehicle; animal info (6-8 weeks old, Male, 27-32 g); dependence;

Q6079: D. DiPalma, *et al.* Persistent attenuation of nicotine self-administration in rats by co-administration of chronic nicotine infusion with the dopamine D1 receptor antagonist SCH-23390 or the serotonin 5-HT_{2C} agonist lorcaserin. *Pharmacol Biochem Behav* 2019;176(16-22)

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Dose (2.5 mg/kg/day); Controls received mp w/ vehicle; animal info (young adult female Sprague-Dawley rats, aged 66–72 days with an average weight of 210 g); post op. care (ketoprofen (5 mg/kg, s.c.); topical bupivacaine); behavioral testing (lever press);

Q7279: Y. Ding, *et al.* Peroxynitrite-Mediated SIRT (Sirtuin)-1 Inactivation Contributes to Nicotine-Induced Arterial Stiffness in Mice. *Arteriosclerosis, Thrombosis, and Vascular Biology* 2019;ATVBAHA118312346

Agents: Nicotine **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** 2006; **Duration:** 4 weeks;

ALZET Comments: Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (8 weeks of age, WT and Sirt1Super mice); cardiovascular;

Q6978: R. D. Cole, *et al.* Adolescent and adult nicotine exposure differentially impacts oral nicotine and oral saccharin self-administration in mice. *Behavioural Brain Research* 2019;359(836-844)

Agents: nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;

ALZET Comments: Dose (3.0 mg/kg/d - adolescent, 6.3 mg/kg/d-adult); Controls received mp w/ vehicle; animal info (adolescent, adult); stability verified by (measuring the residual volume following surgical removal at the end of the exposure period for each time point); half-life 10 min (p.841); dependence;



Q7968: K. J. Clemens, *et al.* Pre-quit nicotine decreases nicotine self-administration and attenuates cue- and drug-induced reinstatement. *J Psychopharmacol* 2019;33(3):364-371

Agents: Nicotine, (-) hydrogen tartrate salt **Vehicle:** Saline, heparin buffered; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (2.1 mg/kg/day); saline (pH 7.4 with sodium hydroxide) with 25IU heparin used; Controls received sham surgery; animal info (male, Sprague-Dawley and Long Evans, 175–200g and 200–250g); post op. care (betadine ointment and recovery on a heating pad); behavioral testing (cue-reinstatement test); functionality of mp verified by weight after mp removal; dependence; pumps removed and reinstated on days 7 and 13. procedure listed on p.366;

Q7275: A. N. Cheema, *et al.* Nicotine impairs intra-substance tendon healing after full thickness injury in a rat model. *J Orthop Res* 2019;37(1):94-103

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 3 months;

ALZET Comments: Dose (61 mg/mL); Controls received mp w/ vehicle; animal info (adult male Sprague-Dawley rats 400-450g); pumps replaced every 4 weeks;

Q8173: L. B. Wollman, *et al.* Developmental Nicotine Exposure Alters Synaptic Input to Hypoglossal Motoneurons and Is Associated with Altered Function of Upper Airway Muscles. *eNeuro* 2019;6(6):

Agents: Nicotine Tartrate, Bi- **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 16 days;

ALZET Comments: Dose (6 mg/kg/d); Controls received mp w/ vehicle; animal info (Sprague Dawley rat pups of either sex, ranging in age from P1 through P7); dependence;

Q7398: M. Biet, *et al.* In utero exposure to nicotine abolishes the postnatal response of the cardiac sodium current to isoproterenol in newborn rabbit atrium. *Heart Rhythm* 2019;16(4):494-501

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rabbit; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (New Zealand, female); Multiple pumps per animal (2); Resultant plasma level ((100 and 150 ng/mL)); cardiovascular;

Q6986: R. B. Basse, *et al.* Combined early life stressors: Prenatal nicotine and maternal deprivation interact to influence affective and drug seeking behavioral phenotypes in rats. *Behavioural Brain Research* 2019;359(814-822

Agents: Nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2004; **Duration:** 14 days;

ALZET Comments: Dose (4 mg/kg/day); 0.9% saline used; Controls received mp w/ vehicle; animal info (Timed-pregnant Sprague-Dawley rats 250 g- 300 g); pumps implanted during gestation); behavioral testing (open field test, forced swim test); dependence;

Q7365: M. C. Arvin, *et al.* Chronic Nicotine Exposure Alters the Neurophysiology of Habenulo-Interpeduncular Circuitry. *J Neurosci* 2019;39(22):4268-4281

Agents: Nicotine hydrogen-tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Dose (12 mg/kg/d); animal info (6-24 weeks old); dependence;

Q7511: L. B. Wollman, *et al.* Developmental nicotine exposure alters glycinergic neurotransmission to hypoglossal motoneurons in neonatal rats. *J Neurophysiol* 2018;120(3):1135-1142

Agents: nicotine bitartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1004D; **Duration:** 16-21 days;

ALZET Comments: Dose (6 mg/kg/day); Controls received no mp or mp w/ vehicle; animal info (pregnant, female, Sprague-Dawley); pumps were implanted on gestational day 5 to expose pups through remaining gestation (16 days) and postnatal (0-5 days);

Q6905: L. B. Wollman, *et al.* Developmental plasticity of GABAergic neurotransmission to brainstem motoneurons. *J Physiol* 2018;596(23):5993-6008

Agents: Nicotine bitartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 1007D; **Duration:** Not Stated;

ALZET Comments: (6 mg/kg/day); Controls received mp w/ vehicle; animal info (pregnant dams on gestational day 5); post op. care (buprenorphine sc 0.5 mg/kg); dependence;



- Q7936:** M. U. Wagenhauser, *et al.* Chronic Nicotine Exposure Induces Murine Aortic Remodeling and Stiffness Segmentation-Implications for Abdominal Aortic Aneurysm Susceptibility. *Frontiers in Physiology* 2018;9(1459)
Agents: Nicotine **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 10, 40 days;
ALZET Comments: Dose (20, 25 mg/kg/day); Controls received mp w/ vehicle; animal info (10 weeks, male, C57BL/6, 24-26g); functionality of mp verified by cotinine level measurement; cardiovascular; pump model not stated. Abstract lists 20 mg/kg/day while methods states 25 mg/kg/day used.;
- Q7877:** J. M. Tumolo, *et al.* Chronic nicotine differentially alters spontaneous recovery of contextual fear in male and female mice. *Behavioural Brain Research* 2018;341(176-180)
Agents: Nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 7 days;
ALZET Comments: Dose (12.6 mg/kg/day); Controls received sham surgery; animal info (8-10 weeks, male and female, C57BL/6J); behavioral testing (contextual fear conditioning);
- Q7154:** S. R. Subramaniam, *et al.* Chronic nicotine improves cognitive and social impairment in mice overexpressing wild type alpha-synuclein. *Neurobiol Dis* 2018;117(170-180)
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 1 or 6 months;
ALZET Comments: Dose (0.4 mg/kg/h and 2.0 mg/kg/h); dose-response (); dose-response (); pumps replaced every 4 weeks; long-term study; stress/adverse reaction: Mice treated with the higher nicotine dose (2.0 mg/kg/h) lost weight after surgery and 50% died after one week. This was as a result of combined toxic effects of isoflurane and a higher dose of nicotine. Therefore, pentobarbital was used instead of isoflurane for induction of anesthesia, which reduced the mortality rate and improved weight gain in the higher dose group. (see pg. 172);
- Q7051:** S. Semenova, *et al.* Differential effects of withdrawal from intermittent and continuous nicotine exposure on reward deficit and somatic aspects of nicotine withdrawal and expression of alpha4beta2* nAChRs in Wistar male rats. *Pharmacol Biochem Behav* 2018;171(54-65)
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 20 days;
ALZET Comments: Dose (1.2, 3.16, or 6.32 mg/kg/day); animal info (male Wistar rats weighing 320-360g); dependence;
- Q8765:** G. Osterstock, *et al.* Axoglial synapses are formed onto pioneer oligodendrocyte precursor cells at the onset of spinal cord gliogenesis. *Glia* 2018;66(8):1678-1694
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Dose (10 mg/day/kg); 0.9% Saline used; Controls received mp w/ vehicle; animal info (8-12 weeks old, C57BL/6); spinal cord injury;
- Q8309:** C. F. Oliver, *et al.* Sex differences in the effects of nicotine on contextual fear extinction. *Pharmacol Biochem Behav* 2018;165(25-28)
Agents: Nicotine **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (12.6, 18, or 24 mg/kg/day); Controls received mp w/ vehicle; animal info (C57BL/6J, 8-12 weeks old); neurodegenerative (Post Traumatic Stress Disorder);
- Q6963:** D. H. Malin, *et al.* A subtype-specific neuropeptide FF receptor antagonist attenuates morphine and nicotine withdrawal syndrome in the rat. *Neurosci Lett* 2018;684(98-103)
Agents: Morphine sulfate, Nicotine bitartrate **Vehicle:** Saline, isotonic; **Route:** SC; **Species:** Rat; **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;
- Q7073:** C. Li, *et al.* Mito-Tempo prevents nicotine-induced exacerbation of ischemic brain damage. *J Appl Physiol* (1985) 2018;125(1):49-57
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Dose (2 mg/kg/day); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats);



Q6922: S. Y. Lee, *et al.* Pre- and early postnatal nicotine exposure exacerbates autoresuscitation failure in serotonin-deficient rat neonates. *J Physiol* 2018;596(23):5977-5991

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML4; **Duration:** Not Stated;
ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (female Sprague-Dawley dams);

Q7152: C. Lee, *et al.* Differential regulation of neuronal excitability by nicotine and substance P in subdivisions of the medial habenula. *Animal Cells and Systems* 2018;22(3):165-171

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 14 days;
ALZET Comments: Dose (1 mg/kg/hr); 9% NaCl used; animal info (male C57BL/6 mice, 6–8 weeks of age); dependence;

Q8064: S. L. Kyte, *et al.* Nicotine Prevents and Reverses Paclitaxel-Induced Mechanical Allodynia in a Mouse Model of CIPN. *J Pharmacol Exp Ther* 2018;364(1):110-119

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 day;
ALZET Comments: Dose (6, 12, or 24 mg/kg/day); 0.9% Saline used; animal info (Male, C57BL/6J, 8 weeks old, 20-30 g); cancer (Chemotherapy-induced peripheral neuropathy);

Q8062: M. G. Kutlu, *et al.* Nicotine exposure leads to deficits in differential cued fear conditioning in mice and humans: A potential role of the anterior cingulate cortex. *Neurosci Lett* 2018;673(142-149

Agents: Nicotine Hydrogen Tartrate Salt **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (12.6 mg/kg/d); 0.9% Saline used; animal info (Male, 8-10 weeks old, C57BL/6J); dependence;

Q7887: H. Keyworth, *et al.* Wheel running during chronic nicotine exposure is protective against mecamylamine-precipitated withdrawal and up-regulates hippocampal alpha7 nACh receptors in mice. *British Journal of Pharmacology* 2018;175(11):1928-1943

Agents: Nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (24 mg/kg/day); Controls received mp w/ vehicle; animal info (Male, C57BL/6J); dependence;

Q7013: R. F. Keller, *et al.* Investigating the genetic profile of dopaminergic neurons in the VTA in response to perinatal nicotine exposure using mRNA-miRNA analyses. *Sci Rep* 2018;8(1):13769

Agents: Nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (pregnant female Sprague-Dawley rats); minipumps released nicotine for 4 weeks from gestational day 6 to postnatal day 14;

Q7893: Y. Kamio, *et al.* Roles of Nicotine in the Development of Intracranial Aneurysm Rupture. *Stroke* 2018;49(10):2445-2452

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;
ALZET Comments: Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (9 week old, Male, C57BL/6J); cardiovascular;

Q7020: A. Jackson, *et al.* Pharmacological modulation of the alpha7 nicotinic acetylcholine receptor in a mouse model of mecamylamine-precipitated nicotine withdrawal. *Psychopharmacology (Berl)* 2018;235(7):1897-1905

Agents: Nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (24 mg/kg/day); Controls receive Jacksod mp w/ vehicle; animal info (8 week old ICR male mice);
Q7028: V. G. Garcia, *et al.* aPDT for periodontitis treatment in ovariectomized rats under systemic nicotine. *Photodiagnosis Photodyn Ther* 2018;22(70-78

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2006; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (3-month old Wistar rats);

Q7030: C. C. J. Frye, *et al.* Continuous nicotine exposure does not affect resurgence of alcohol seeking in rats. *PLoS One* 2018;13(8):e0202230

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: Dose (3 mg/kg/day); 0.9% sterile saline solution used; Controls received mp w/ vehicle; animal info (male Long Evans rats); post op. care (NSAID analgesic, an antibiotic);



Q5615: N. D. d'Adesky, *et al.* Nicotine Alters Estrogen Receptor-Beta-Regulated Inflammasome Activity and Exacerbates Ischemic Brain Damage in Female Rats. *Int J Mol Sci* 2018;19(5):

Agents: Nicotine hydrogen tartrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 16-21 days;

ALZET Comments: Dose (4.5 mg/kg/day); Controls received mp w/ vehicle; animal info (adult female Sprague-Dawley rats); ischemia (brain);

Q7111: Y. H. Chen, *et al.* Nicotine-Induced Conditional Place Preference Is Affected by Head Injury: Correlation with Dopamine Release in the Nucleus Accumbens Shell. *Int J Neuropsychopharmacol* 2018;21(10):949-961

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rats; **Pump:** 2ML1; **Duration:** 1 week;

ALZET Comments: Dose (9 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male, Sprague-Dawley, 6 weeks old, 200-250 g); behavioral testing (Open Field Test); Brain coordinates (3.8 mm posterior to bregma, 2.5 mm lateral to midline,); neurodegenerative (Concussion);

Q7106: L. M. Carcoba, *et al.* Amino acid modulation of dopamine in the nucleus accumbens mediates sex differences in nicotine withdrawal. *Addiction Biology* 2018;23(5):1046-1054

Agents: Nicotine hydrogen tartrate salt **Vehicle:** Saline; **Route:** Saline; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: 0.9% saline used; animal info (Adult male and female Wistar rats); post op. care (analgesic flunixin- 2.5 mg/kg); dependence;

Q7100: J. K. Brynildsen, *et al.* Activation of AMPK by metformin improves withdrawal signs precipitated by nicotine withdrawal. *Proc Natl Acad Sci U S A* 2018;115(16):4282-4287

Agents: Nicotine, Metformin **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;

ALZET Comments: Dose (18 mg/kg/day-nicotine, 50 ug/day-metformin); 0.85% saline used; Controls received mp w/ vehicle; behavioral testing (Marble Burying Test, Novelty-Induced Hypophagia Test); Brain coordinates (anteroposterior, -0.8 mm; mediolateral, +1.5 mm); dependence;

Q10108: D. Bhattacharya, *et al.* Assessment of the cerebellar neurotoxic effects of nicotine in prenatal alcohol exposure in rats. *Life Sciences* 2018;194(177-184)

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1004; **Duration:** Not Stated;

ALZET Comments: Dose: Nicotine (6 mg/kg/day.); 10% Alcohol; 95% Ethy alcohol used; animal info (Time pregnant Sprague Dawley); behavioral testing (Straub tail, tremor and ataxic behaviors);

Q10087: D. Bagdas, *et al.* New insights on the effects of varenicline on nicotine reward, withdrawal and hyperalgesia in mice. *Neuropharmacology* 2018;138(72-79)

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2000; **Duration:** 14 days; 28 days;

ALZET Comments: Dose (24 mg/kg/day 14 day; 36mg/kg/day 28 day); Controls received mp w/ vehicle; animal info (ICR male, 8 weeks old; genetically modified male and female for nAChRs); dependence; No stress (see pg.); Therapeutic indication (varenicline for nicotine withdrawal);