



**Recent References (2016-2020) on the Administration of Agents
Using Multiple ALZET® Osmotic Pumps in a Single Animal**

ALZET pumps are capable of being implanted in animals as small as mice or neonatal rats to very large animals such as cattle. Regardless of animal size, occasionally there is the need to deliver a higher concentration of compound than a single pump will allow. Implanting multiple pumps in a single animal of sufficient size is an acceptable method to achieve higher concentrations of drug delivery.

Additionally, multiple pumps may be implanted if there is a need to deliver compounds to multiple locations using two catheters. The table below contains citations, which used multiple pumps in popular animal models. To see our minimum animal size estimates for multiple pump implantations see the following webpage: http://www.alzet.com/resources/technical_tips.html#ImpMultPump

Animal	# of Pumps	Reference
Mice	3	<i>P5997</i> Kuroiwa M, et al. Continuous versus intermittent administration of human endostatin in xenografted human neuroblastoma. <i>J Pediatr Surg</i> 2003; 38(10):1499-1505. "The set of 3 osmotic pumps was retained successfully in the subcutaneous tissue of the treated and control animals throughout the experiment, no decrease in body weight was observed in either group." (p. 1501).
Rat	4	<i>P0432</i> Khan SR, et al. Experimental induction of crystalluria in rats using mini-osmotic pumps. <i>Urol Res</i> 1983; 11(5):199-205
Cat	2	<i>P7592</i> Imamura K, et al. Brain-derived neurotrophic factor enhances expression of superior cervical ganglia clone 10 in lateral geniculate nucleus and visual cortex of developing kittens. <i>Eur J Neurosci</i> 2006; 23(3):637-648
Dog	4	<i>P7118</i> Gilberto DB, et al. Use of three infusion pumps for postoperative administration of buprenorphine or morphine in dogs. <i>JAVMA</i> 2002; 220(11):1655-1660
Monkey	4	<i>P2211</i> Tarantal AF, et al. Pre and postnatal treatment of the rhesus macaque (<i>Macaca mulatta</i>) with azidothymidine: I. fetal studies. <i>Pediatr Aids HIV Infection: Fetus to Adolescent</i> 1994; 5(1):10-19
Rabbit	4	<i>P7178</i> Cellini C, et al. Effect of epidermal growth factor infusion on fetal rabbit intrauterine growth retardation and small intestinal development. <i>J Pediatr Surg</i> 2004; 39(6):891-897
Cattle	4	<i>P3546</i> Roh S-G, et al. Characteristics of growth hormone secretion responsiveness to growth hormone-releasing peptide-2 (GHRP-2 or KP102) in calves. <i>Endocrine J</i> 1996; 43(3):291-298
Pig	12	<i>P1697</i> Mukai S, et al. Changes in plasma gonadotropins, ovarian steroids and inhibin concentrations in gilts following progesterone treatment with implantable osmotic pumps. <i>Anim Reprod Sci</i> 1989; 20:287-297



Recent References (2016-2019) on the Administration of Agents Using Multiple ALZET® Osmotic Pumps in a Single Animal

Q8563: N. Kajitani, *et al.* Prefrontal cortex infusion of beta-hydroxybutyrate, an endogenous NLRP3 inflammasome inhibitor, produces antidepressant-like effects in a rodent model of depression. *Neuropsychopharmacol Rep* 2020;40(2):157-165

Agents: Beta-hydroxybutyrate **Vehicle:** PBS; **Route:** CNS/CSF (frontal cortex); **Species:** Rat; **Pump:** 2006; **Duration:** 21 days; **ALZET Comments:** Dose (80 mg/mL); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, 7-8 weeks of age); behavioral testing (forced swim test; open field test); Multiple pumps per animal (2 pumps); Beta-hydroxybutyrate aka BHB; Brain coordinates (coordinates: anteroposterior + 3.2 mm, dorsolateral \pm 0.6 mm from bregma, ventral 4.0 mm from the skull surface); bilateral cannula used; neurodegenerative (Depression);

Q8539: S. Hirakata, *et al.* Genetic Deletion of Socs3 in Smooth Muscle Cells Ameliorates Aortic Dissection in Mice. *JACC Basic Transl Sci* 2020;5(2):126-144

Agents: Aminopropionitrile, B-; Angiotensin II **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Dose (150 mg/kg/day BAPN, 1000 ng/kg/min AngII); animal info (Male mice of 11 to 14 weeks of age); Multiple pumps per animal (2 pumps); B-aminopropionitrile aka BAPN, Angiotensin II aka AngII; cardiovascular;

Q8508: G. Gomez-Correa, *et al.* Chronic Bumetanide Infusion Alters Young Neuron Morphology in the Dentate Gyrus Without Affecting Contextual Fear Memory. *Front Neurosci* 2020;14(514)

Agents: Bumetanide **Vehicle:** Propylene Glycol; **Route:** CNS/CSF (lateral ventricle); **Species:** Rat; **Pump:** 2002; **Duration:** 28 days;

ALZET Comments: Dose (0.4 mg/kg/day); Controls received mp w/ vehicle; animal info (male Wistar rats (250–350 g)); Multiple pumps per animal (2 pumps); ALZET brain infusion kit used; Brain coordinates (AP –1.4 mm; ML –2.0 mm); dependence;

Q8402: M. Carceles-Cordon, *et al.* NMDAR Antibodies Alter Dopamine Receptors and Cause Psychotic Behavior in Mice. *Ann Neurol* 2020;88(3):603-613

Agents: NMDAR-CSF **Vehicle:** CSF; **Route:** CNS/CSF (lateral ventricle); **Species:** Mice; **Pump:** Not stated; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male C57BL/6J mice, 8 to 10 weeks old (25–30g)); behavioral testing (prepulse inhibition of the acoustic startle reflex; novel object location; general locomotor activity); Multiple pumps per animal (2 pumps); NMDAR aka anti-N-methyl-D-aspartate receptor; dependence;

Q8287: Z. Min, *et al.* Asymmetrical methyltransferase PRMT3 regulates human mesenchymal stem cell osteogenesis via miR-3648. *Cell Death Dis* 2019;10(8):581

Agents: Protein arginine methyltransferase 3 inhibitor **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 2, 4, or 6 weeks;

ALZET Comments: Dose (20 mg/kg/day); animal info (8 weeks old, C57BL/6); Multiple pumps per animal (1, 2, or 3); Protein arginine methyltransferase 3 inhibitor aka SGC707; enzyme inhibitor (Protein arginine methyltransferase 3 inhibitor); gene therapy;

Q6780: Y. Izawa-Ishizawa, *et al.* Development of a novel aortic dissection mouse model and evaluation of drug efficacy using in-vivo assays and database analyses. *J Hypertens* 2019;37(1):73-83

Agents: Angiotensin II; B-aminopropionitrile **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 1 week; 6 weeks;

ALZET Comments: Dose (Angiotensin II (1000 ng/kg per day); B-aminopropionitrile (150 mg/kg/day)); Controls received mp w/ vehicle; animal info (Male C57BL/6J mice (10–12 weeks; 25–30 g)); Multiple pumps per animal (2); B-aminopropionitrile is an enzyme inhibitor (lysyl oxidase inhibitor); cardiovascular;

Q7584: J. D. Hill, *et al.* Activation of GPR55 induces neuroprotection of hippocampal neurogenesis and immune responses of neural stem cells following chronic, systemic inflammation. *Brain, Behavior, and Immunity* 2019;76(165-181)



Agents: O-1602; LPS **Vehicle:** CSF, Artificial; saline; **Route:** CSF/CNS (hippocampus); SC; **Species:** Mice; **Pump:** 1002;
Duration: 14 days;

ALZET Comments: Dose ((O-1602 4 µg/kg/day), (LPS 0.2 mg/kg/day)); O-1602 diluted in 100% EtOH before diluted in ACSF to 0.05% EtOH used; Controls received mp w/ vehicle; animal info (12-15 weeks, male and female, C57BL/6 and GPR55-/-); Multiple pumps per animal (2); O-1602 is an analog of cannabidiol and a potent GPR55 agonist. LPS (lipopolysaccharide) initiates pathological neuroinflammation; ALZET brain infusion kit 3 used; Full compound name of O-1602 is 5-Methyl-4-[(1R,6R)-3-methyl-6-(1-cyclohexen-1-yl)-1,3-benzene-diol]; Therapeutic indication (LPS-induced dysregulation of hippocampal neurogenesis);

Q8033: E. Heikkila, *et al.* The plant product quinic acid activates Ca(2+) -dependent mitochondrial function and promotes insulin secretion from pancreatic beta cells. *Br J Pharmacol* 2019;176(17):3250-3263

Agents: Quinic acid **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 12 weeks;

ALZET Comments: Dose (75 mg/kg/day); Controls received mp w/ vehicle; animal info (12 weeks old, Male, C57BL/6N); pumps replaced every ? weeks; Multiple pumps per animal (); long-term study; Quinic acid aka QA ; 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;

Q7840: M. Waldman, *et al.* PARP-1 inhibition protects the diabetic heart through activation of SIRT1-PGC-1alpha axis. *Experimental Cell Research* 2018;373(1-2):112-118

Agents: angiotensin II; INO-1001 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: "Dose ((AngII 1000 ng/kg/min), (INO-1001 5 mg/kg/day)); Controls received no pump; animal info (12-14 weeks, male, C57BLKS/J and C57BLKS/J-leprdb/leprdb); Multiple pumps per animal (2 for AT + INO group); INO-1001 is an enzyme inhibitor (PARP-1); diabetes; Therapeutic indication (PARP-1 inhibition by INO1001 promoted weight loss in the diabetic mice stressed with AT. It attenuated cardiac fibrosis and hypertension in diabetic mice and prevented oxidative stress.); "

Q7935: T. Wada, *et al.* Impact of central and peripheral estrogen treatment on anxiety and depression phenotypes in a mouse model of postmenopausal obesity. *PLoS One* 2018;13(12):e0209859

Agents: Estradiol **Vehicle:** CSF, artificial; **Route:** SC; CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1004; **Duration:** 3 weeks;

ALZET Comments: Dose ((SC 50 µg/kg/day), (ICV 1 µg/kg/day)); Controls received mp w/ vehicle; animal info (16 weeks, female, C57BL/6); behavioral testing (Open field, Light-dark box, Tail suspension, Forced swim); Multiple pumps per animal (2 for SC group); comparison of SC mp vs ICV mp; ALZET brain infusion kit 3 used; Brain coordinates (0.3 mm posterior to the bregma, 0.9 mm lateral to the central sulcus, 2.5 mm below the skull); replacement therapy (estradiol); Therapeutic indication (mouse model of postmenopausal obesity that exhibited anxiety disorder and depression phenotypes were improved by E2 replacement.);

Q7310: S. Toyama, *et al.* Protective Effect of a Mitochondria-Targeted Peptide against the Development of Chemotherapy-Induced Peripheral Neuropathy in Mice. *ACS Chemical Neuroscience* 2018;9(7):1566-1571

Agents: SS-20 **Vehicle:** Saline; **Route:** SC; **Species:** SC; **Pump:** 1004; **Duration:** 3 weeks;

ALZET Comments: Dose (5 mg/kg/day, 10 mg/kg/day); Controls received mp w/ vehicle; animal info (Male, BALB/c mice, 8 weeks old); behavioral testing (von Frey hair test, paw withdrawal); Multiple pumps per animal (2); SS-20 is a mitochondria-targeted peptide;

Q7864: J. A. Sandgren, *et al.* Arginine vasopressin infusion is sufficient to model clinical features of preeclampsia in mice. *JCI Insight* 2018;3(19):

Agents: arginine vasopressin; conivaptan; relcovaptan; tolvaptan **Vehicle:** Saline; DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1002; 1004; 1007D; **Duration:** 1, 2 weeks;



ALZET Comments: Dose ((AVP 24 ng/h), (conivaptan 22 ng/h), (relcovaptan 22 ng/h), (tolvaptan 22 ng/h)); saline or saline with 10% DMSO used; Controls received mp w/ vehicle; Multiple pumps per animal (2 if AVP plus antagonist); conivaptan is a nonselective AVPR1A and AVPR2 antagonist. relcovaptan is an AVPR1A antagonist. tolvaptan is an AVPR2 antagonist.; AVP and tolvaptan were reconstituted in saline while relcovaptan was reconstituted in saline with 10% DMSO;

Q7259: I. G. Rajapaksha, *et al.* The small molecule drug diminazene aceturate inhibits liver injury and biliary fibrosis in mice. *Sci Rep* 2018;8(1):10175

Agents: Diminazene aceturate **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Dose (10mg/kg/day); animal info (6–8 weeks old, male C57BL/6 mice); functionality of mp verified by residual volume; Multiple pumps per animal (2 pumps); Diminazene aceturate aka 4-[2-(4-carbamimidoylphenyl) iminohy-drazinyl]benzenecarboximidamide;

Q7755: R. W. Holdcraft, *et al.* A model for determining an effective in vivo dose of transplanted islets based on in vitro insulin secretion. *Xenotransplantation* 2018;25(6):e12443

Agents: Insulin, recomb. human **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3-5 days;
ALZET Comments: Dose ((female 1.5-2.0 U/day), (males 3.0-4.5 U/day)); Controls consisted of rats that did not become diabetic during the initial study period; animal info (male and female, BioBreeding diabetes-prone); Multiple pumps per animal (2 if hyperglycemic state observed. see p.4); comparison of macrobead implant vs mp; diabetes; Pilot study for CGM calibration 3-5 days followed by 1 or 3 month study using microbeads. Pump models not stated but duration length was listed at 7 or 14 days;

Q7031: M. Fregosi, *et al.* Changes of motor corticobulbar projections following different lesion types affecting the central nervous system in adult macaque monkeys. *European Journal of Neuroscience* 2018;48(4):2050-2070

Agents: Antibody, anti-Nogo-A **Vehicle:** Not Stated; **Route:** CSF/CNS (Intrathecal), SC; **Species:** Monkey (Macaca fascicularis); **Pump:** 2ML2; **Duration:** 4 weeks;
ALZET Comments: Dose (3 mg/ml); One pump administered the treatment intrathecally to the cervical spinal cord, whereas the other pump delivered the antibody close to the lesioned site in M1 below the dura; Multiple pumps per animal (2);

Q7104: E. S. Calipari, *et al.* Granulocyte-colony stimulating factor controls neural and behavioral plasticity in response to cocaine. *Nat Commun* 2018;9(1):9

Agents: Antibody, anti-GCSF neutralizing antibody, Immunoglobulin G, pre-immune **Vehicle:** Saline; **Route:** CSF/CNS (nucleus accumbens); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Dose (1 ug/day); animal info (Male, C57BL/6 J, 7 weeks old, 20–25 g); Multiple pumps per animal (2); Brain coordinates (From bregma: anteroposterior, +1.5; mediolateral, + 1.0; dorsoventral, –4.5); bilateral cannula used; The cannulae were permanently fixed to the skull with Loctite adhesive; dependence;

Q5909: L. Wang, *et al.* Sodium butyrate suppresses angiotensin II-induced hypertension by inhibition of renal (pro)renin receptor and intrarenal renin-angiotensin system. *J Hypertens* 2017;35(9):1899-1908

Agents: Angiotensin II; sodium butyrate **Vehicle:** Not Stated; **Route:** SC; Intrarenal (medulla); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-300g); Multiple pumps per animal (2); replacement therapy (uniphrectomy); tissue perfusion (renal medulla); cardiovascular; antihypertensive; peptides; Bp measured using radio telemetry (DSI); Dose (Ang II 200 ng/kg/min; NaBu 1 ug/kg/min); good bp comparison curve (pg4);

Q6701: P. Mota, *et al.* Mp17-14 Depletion of Peripheral Serotonin Synthesis Induces Benign Prostatic Growth in Mice: More Evidence for the New “Neuroendocrine Theory” in Bph Etiology. *The Journal of Urology* 2017;197(4):e216-e217

Agents: Leptin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 24 weeks;
ALZET Comments: Dose (5 mg/day; 10 mg/day); Controls received mp w/ vehicle; animal info (10-week-old male ObOb and strain-matched control mice); pumps replaced every 12 weeks; Multiple pumps per animal (2); long-term study;



Q6173: J. S. Medel-Matus, *et al.* Galanin contributes to monoaminergic dysfunction and to dependent neurobehavioral comorbidities of epilepsy. *Experimental Neurology* 2017;289(64-72

Agents: M40, M871, Galanin receptor antagonists **Vehicle:** Saline; **Route:** CSF/CNS (raphe nucleus); CSF/CNS (locus coeruleus); **Species:** Rat; **Pump:** 1007D; **Duration:** 3 days;

ALZET Comments: Dose (10 nM solution of M40, 30 nM solution of M871); Controls received mp w/ vehicle; animal info (50 day old male Wistar rats); Multiple pumps per animal (2); M40 is a Galanin receptor type 1/2 antagonist; M871 is a preferential GalR2 antagonist; PlasticsOne cannula used (28 GA; length 6.5 mm for RN, 8.0 mm for LC); bilateral cannula used for LC infusion with 2 pumps; Therapeutic indication (Epilepsy);

Q6154: Y. Li, *et al.* Brain Transforming Growth Factor-beta Resists Hypertension Via Regulating Microglial Activation. *Stroke* 2017;48(9):2557-2564

Agents: Antibody, anti-TGF β ; Angiotensin II **Vehicle:** Not Stated; **Route:** CSF/CNS (left ventricle); **Species:** Mice; **Pump:** 1002; 1004; **Duration:** 2 weeks;

ALZET Comments: Dose (TGF neutralizing antibody: 50 μ g/d; Ang II: 500 ng/kg/min); animal info (8-10 week old male adult wild-type, Tg, 34Lan, and B6.129P-Cx3cr1tm1Litt/J mice); Multiple pumps per animal (second pump with angiotensin II implanted 3 or 7 days after first pump); antihypertensive; ALZET brain infusion kit 3used; Brain coordinates (0.5 mm caudal to Bregma; 1 mm lateral to the midline; 2 mm ventral to the dura); cardiovascular;

Q6460: D. A. Howatt, *et al.* Relaxin and Matrix Metalloproteinase-9 in Angiotensin II-Induced Abdominal Aortic Aneurysms. *Circulation Journal* 2017;81(6):888-890

Agents: Angiotensin II; Relaxin **Vehicle:** Saline; Sodium acetate; **Route:** SC; **Species:** Mice (knockout); **Pump:** 2004; 1004; 2001; 1007D; **Duration:** 28 days;

ALZET Comments: Dose (Angiotensin II: 1.4 mg/kg/day; Relaxin: 0.1, 0.3, or 0.6 mg/kg/day); Controls received mp w/ vehicle; animal info (male C57BL/6 and Apoe $^{-/-}$ mice); Multiple pumps per animal (2); cardiovascular;

Q6099: C. Dai, *et al.* Age-dependent human beta cell proliferation induced by glucagon-like peptide 1 and calcineurin signaling. *J Clin Invest* 2017;127(10):3835-3844

Agents: Exendin-4; FK506 **Vehicle:** PBS; saline; **Route:** SC; **Species:** Mice (NSG), mice (NOD); **Pump:** 1004; 1002; **Duration:** 4 weeks; 2 weeks;

ALZET Comments: Dose (exendin-4: 24 nmol/kg/d; FK506: 0.25 mg/kg/d); Controls received mp w/ vehicle; animal info (NOD.Cg-Prkdcscid112rgtm1Wjl/Sz (NSG) mice); Multiple pumps per animal (2): some animals received a second pump containing FK506 after 2 weeks; diabetes;

Q4920: L. Zhao, *et al.* Prenatal nicotinic exposure upregulates pulmonary C-fiber NK1R expression to prolong pulmonary C-fiber-mediated apneic response. *Toxicol Appl Pharmacol* 2016;290(107-15

Agents: Nicotine; mecamylamine; methyllycaconitine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250-300g); pumps replaced on GD7; Multiple pumps per animal (2); no stress (see pg. 110-111); teratology; Dose (Nicotine 6 mg/kg/day; mecamylamine 0.03 mg/kg/day; methyllycaconitine 3 mg/kg/day);

Q5113: L. Zhao, *et al.* Bronchopulmonary C-fibers' IL1RI contributes to the prolonged apneic response to intra-atrial injection of capsaicin by prenatal nicotinic exposure in rat pups. *Toxicol Appl Pharmacol* 2016;303(58-64

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

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250-350g); pumps replaced every 28 days; Multiple pumps per animal (2); long-term study; teratology; MLA is an α 7nAChR antagonist; methyllycaconitine aka MLA; Dose (nicotine 6 mg/kg/day; MLA 3 mg/kg/day);

Q5713: H. Xu, *et al.* The Role of HMGB1 in Pial Arteriole Dilating Reactivity following Subarachnoid Hemorrhage in Rats. *J Vasc Res* 2016;53(5-6):349-357

Agents: HMGB1; Box A; OxPAPC **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1003D; **Duration:** 2 days;



ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-300g); Multiple pumps per animal (2); Bilateral infusion; Dose (HMGB1 120 ng/h; Box A 12-120 ng/hr; OxPAPC 20 ug/h);

Q5705: X. Wang, *et al.* Cerebral mTOR signal and pro-inflammatory cytokines in Alzheimer's disease rats. *Transl Neurosci* 2016;7(1):151-157

Agents: Rapamycin; amyloid protein, beta (1-42) **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: animal info (male, Sprague Dawley, 3-4 months old, 300-350g); Multiple pumps per animal (2); neurodegenerative (Alzheimer's); behavioral testing (Y-maze); immunology; Bilateral infusion; used jewelers' screw and dental zinc cement; Dose (10 mg/kg amyloid beta, rapamycin 500 ug/2 weeks); Brain coordinates;

Q5479: D. Wagsater, *et al.* Elevated Adiponectin Levels Suppress Perivascular and Aortic Inflammation and Prevent AngII-induced Advanced Abdominal Aortic Aneurysms. *Sci Rep* 2016;6(31414)

Agents: Angiotensin II **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 8 weeks;

ALZET Comments: Controls received mp w/ PBS; animal info (male, LDLR -/-, 8-10 weeks old); pumps replaced every 4 weeks; Multiple pumps per animal (2); post op. care (injection of bupivacaine and carprofen); cardiovascular; peptides; bp measured using tail cuff; Dose (1.5 ug/kg/min);

Q6057: J. Planaguma, *et al.* Ephrin-B2 prevents N-methyl-D-aspartate receptor antibody effects on memory and neuroplasticity. *Annals of Neurology* 2016;80(3):388-400

Agents: Ephrin-B2, **Vehicle:** CSF, patient; **Route:** CSF/CNS (ventricle); **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: animal info (8-10 weeks old, 25-30 g; C57BL/6J); behavioral testing (novel object recognition, tail suspension, forced swim test); The CSF infused was pooled from patient' samples; Multiple pumps per animal (2); Therapeutic indication (Memory, neuroplasticity);

Q6687: C. Li, *et al.* Activated Transcription Factor 3 in Association with Histone Deacetylase 6 Negatively Regulates MicroRNA 199a2 Transcription by Chromatin Remodeling and Reduces Endothelin-1 Expression. *Mol Cell Biol* 2016;36(22):2838-2854

Agents: Tubacin; Niltubacin **Vehicle:** DMSO; PBS; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 30 days;

ALZET Comments: Dose (0.0083 mg/day); 50% DMSO, 50% PBS used; animal info (4-6 month old Berkeley sickle mice); Multiple pumps per animal (2); enzyme inhibitor (HDAC6);

Q5551: E. D. Levin, *et al.* Reduction of nicotine self-administration by chronic nicotine infusion with H1 histamine blockade in female rats. *Psychopharmacology (Berl)* 2016;233(15-16):3009-15

Agents: Nicotine ditartrate, pyrilamine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2, 2ML4; **Duration:** 2 weeks,;

ALZET Comments: Controls received mp w/ vehicle; Multiple pumps per animal (2); animal info (Young adult female Sprague-Dawley rats, 8 weeks old); Nicotine dependence; Chronic nicotine infusion via sc implanted osmotic minipumps is functionally similar to the zero order kinetic of steady nicotine infusion achieved by nicotine skin patches; Therapeutic indication (Nicotine dependency); Dose (Nicotine administered for 4 weeks with 2ML4 at 2.5, 5 mg/kg/day, Pyrilamine administered for 2 weeks with 2ML2 at 25 mg/kg/day);

Q5548: K. Kohashi, *et al.* A Dipeptidyl Peptidase-4 Inhibitor but not Incretins Suppresses Abdominal Aortic Aneurysms in Angiotensin II-Infused Apolipoprotein E-Null Mice. *Journal of Atherosclerosis and Thrombosis* 2016;23(4):441-454

Agents: Angiotensin II, Glucagon-like peptide-1, Glucose-Dependent Insulinotropic Polypeptide **Vehicle:** Saline; **Route:** SC; **Species:** Mice (knockout); **Pump:** 1002; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (13 weeks old); pumps replaced every 2 weeks; Multiple pumps per animal (2); one for either Ang II, GLP-1 or GIP; enzyme inhibitor (Dipeptidyl Peptidase-4 inhibitor); Therapeutic indication (Abdominal aortic aneurysm); Dose (Angiotensin II: 2000 ng/kg/min, Angiotensin II + GIP: 25 nmol/kg/day, DPP-41: 6 mg/kg/day);

Q6049: H. D. Kim, *et al.* SIRT1 Mediates Depression-Like Behaviors in the Nucleus Accumbens. *J Neurosci* 2016;36(32):8441-52



Agents: Resveratrol; EX-527 **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (7-9 weeks; C57BL/6J); Multiple pumps per animal (2); behavioral testing (open field, elevated-plus maze, forced swim test, sucrose preference test); Plastics One guide cannula used; bilateral cannulae (one pump for each pedestal); Loctite adhesive used; EX-527 is a SIRT1 antagonist; Therapeutic indication (Depression); Dose (0.1 or 0.2 ug/day, EX-527: 0.5 or 1.0 ug/day);

Q5654: B. A. Kemp, *et al.* AT2 Receptor Activation Prevents Sodium Retention and Reduces Blood Pressure in Angiotensin II-Dependent Hypertension. *Circulation Research* 2016;119(4):532-43

Agents: Dextrose, C21, PD-123319, Angiotensin II **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 1007D, 2001; **Duration:** 1 week;

ALZET Comments: Controls received mp w/ vehicle; animal info (12 weeks); good methods (p. 546); Multiple pumps per animal (2); Multiple pumps per animal (2); Intrarenal infusion; Therapeutic indication (Hypertension); Dose (C21: 60ng/kg/min, PD-123319: 10 ng/kg/min, Dextrose/AngII: 200 ng/kg/min);

Q5576: S. T. Haller, *et al.* Rapamycin Attenuates Cardiac Fibrosis in Experimental Uremic Cardiomyopathy by Reducing Marinobufagenin Levels and Inhibiting Downstream Pro-Fibrotic Signaling. *J Am Heart Assoc* 2016;5(10):

Agents: Rapamycin, marinobufagenin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: animal info (Male Sprague-Dawley rats weighing 250–300 g); Multiple pumps per animal (2 minipumps were implanted for coadministration of rapamycin and MBG); Marinobufagenin is a cardiotonic steroid; Dose (MBG 10 ug/kg/day; rapamycin 0.2 mg/kg/d);

Q4899: y. B. S. H. H.-W. WANG, y A. CHEN, M. AHMAD,, *et al.* ROLE OF BRAIN ALDOSTERONE AND MINERALOCORTICOID RECEPTORS IN ALDOSTERONE-SALT HYPERTENSION IN RATS. *Neuroscience* 2016;314(90-105

Agents: Aldosterone; eplerenone; FAD286 **Vehicle:** CSF, artificial; acetonitrile; **Route:** SC; CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 2 weeks, 3 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 200-250g); 4% acetonitrile used; Multiple pumps per animal; cardiovascular; bp measured using radiotelemetry; bp measured using radiotelemetry; dose (1.5 and 7.5 ug/kg/hr Aldosterone, 5ug/day Eplerenone, 25 ug/day FAD286)

Q6094: L. Deng, *et al.* Prophylactic treatment with the tricyclic antidepressant desipramine prevents development of paclitaxel-induced neuropathic pain through activation of endogenous analgesic systems. *Pharmacol Res* 2016;114(75-89
Agents: Desipramine, naloxone, AM251, AM630 **Vehicle:** Water, saline, PEG 400, DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;

ALZET Comments: Dose: Desipramine (10 mg/kg/d), Naloxone (12 mg/kg/d), AM251 (3 mg/kg/d), AM630 (3 mg/kg/day); Desipramine dissolved distilled water, naloxone dissolved in saline, AM251 and AM630 dissolved in 50% PEG400 and 50% DMSO; Controls received mp w/ vehicle; animal info (Sprague-Dawley rats weighing 275–350 g); Multiple pumps per animal (2 when given the treatment of 2 different agents), Desipramine, vehicle, and all antagonists were delivered in separate osmotic pumps;

Q5750: M. L. Bertolaccini, *et al.* Complement inhibition by hydroxychloroquine prevents placental and fetal brain abnormalities in antiphospholipid syndrome. *J Autoimmun* 2016;75(30-38

Agents: Antibody, beta-2-glycoprotein, hydroxychloroquine **Vehicle:** Water, distilled; **Route:** Not Stated; **Species:** mice (pregnant); **Pump:** 1002; **Duration:** Not Stated;

ALZET Comments: animal info (Age 2-3 months old; pump inserted day 8 of pregnancy); Multiple pumps per animal (2); A group of pregnant mice received hydroxychloroquine administered by a second microosmotic pump (Alzet model 1002) on day 8 of pregnancy.; peptides; "Administration through microosmotic pumps ensures constant antibody concentrations are maintained throughout pregnancy to closely resemble the clinical condition." Pg 32 ; Therapeutic indication (Pregnancy, antiphospholipid syndrome); Dose (200 ug/mouse/day);

Q5322: M. Bazargan, *et al.* Limited fetal metabolism of rosiglitazone: Elimination via the maternal compartment in the pregnant ewe. *Reprod Toxicol* 2016;61(162-8



Agents: Rosiglitazone Maleate **Vehicle:** Water, Ethanol; **Route:** SC; **Species:** Sheep (pregnant); **Pump:** 2ML1; **Duration:** 16 days;

ALZET Comments: animal info (Singleton pregnant sheep); functionality of mp verified by plasma level, amniotic fluid samples; 15% ethanol used; Multiple pumps per animal (4); stability verified by regular plasma level measurements (reached after day 5, tested through day 16; half life of 24-48 hours in sheep); Catheters flushed with heparinized saline; Dose (2.7 mg/fetus/d);