



**Recent References (2016-Present) 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	4	<i>P9788</i> N. Ginovart, et al. D ₂ -Receptor Upregulation is Dependent upon Temporal Course of D ₂ -Occupancy: A Longitudinal [¹¹ C]-Raclopride PET Study in Cats. <i>Neuropsychopharmacology</i> 2009;34(3):662-671
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



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Q10218: I. Kopaliani, *et al.* Overexpression of dimethylarginine dimethylaminohydrolase 1 protects from angiotensin II-induced cardiac hypertrophy and vascular remodeling. *American Journal of Physiology and Heart Circulatory Physiology* 2021;321(5):H825-H838

Agents: Angiotensin II **Vehicle:** NaCl; **Route:** SC; **Species:** Mice; **Pump:** 1002; 1004; **Duration:** 2 weeks; 4 weeks;
ALZET Comments: Dose: (0.75 mg/kg/day); (1.5 mg/kg/day); 0.9% NaCl vehicle used; Controls received mp w/ vehicle; animal info: 12-wk-old male DDAH1 transgenic (DDAH1 TG) and wild-type male (WT) littermates (8, 20–22); All mice had C57BL/6J genetic background; Multiple pumps per animal (2 different pump model used); Blood pressure measured via: tail cuff; Angiotensin II aka (Ang II)cardiovascular;

Q9530: F. Wang, *et al.* Soluble (pro)renin receptor treats metabolic syndrome in mice with diet-induced obesity via interaction with PPARgamma. *JCI Insight* 2020;5(7):

Agents: Renin receptor, human recombinant soluble; PF429242 **Vehicle:** Not Stated; **Route:** IV (external jugular); **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: Dose (30 ug/kg/d); Controls received mp w/ vehicle; animal info (Male 36-week-old DIO C57/BL6 mice); Multiple pumps per animal (2 pumps); human recombinant soluble renin receptor aka sPRR, PF429242 aka PF; dependence;

Q10062: J. Savidan, *et al.* Cutaneous Inputs to Dorsal Column Nuclei in Adult Macaque Monkeys Subjected to Unilateral Lesion of the Primary Motor Cortex or of the Cervical Spinal Cord and Treatments Promoting Axonal Growth. *Neuroscience Insights* 2020;15(2633105520973991

Agents: Antibody, anti Nogo-A monoclonal 11C7; Brain-derived neurotrophic factor **Vehicle:** Not stated; **Route:** CSF/CNS (spinal cord); **Species:** Monkey; **Pump:** 2ML2; **Duration:** 4 weeks;
ALZET Comments: Dose (14.8 mg anti Nogo-A monoclonal antibody 11C7; 1.4 mg Brain-derived neurotrophic factor); animal info (adult monkeys, 3.0 to 5.6 kg, 4 to 6 years old); Multiple pumps per animal (2 pumps); Brain-derived neurotrophic factor aka BDNF; spinal cord injury;

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; **Pump:** 1002; 2002; **Duration:** 14 days;
ALZET Comments: Dose (2 mg/kg); Controls received mp w/ vehicle; animal info (female, Long- Evans rats, weighing 200–225 g); behavioral testing (Withdrawal testing); Multiple pumps per animal (2 or 3); dependence;

Q8910: N. Nishida, *et al.* High Salt Intake Worsens Aortic Dissection in Mice: Involvement of IL (Interleukin)-17A-Dependent ECM (Extracellular Matrix) Metabolism. *Arteriosclerosis, Thrombosis, and Vascular Biology* 2020;40(1):189-205

Agents: Aminopropionitrile, B-; Angiotensin II **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (150 mg/kg/day Aminopropionitrile, B-; 1000 ng/kg/min Angiotensin II); animal info (male mice, 11 to 14 weeks old); Multiple pumps per animal (2); B-Aminopropionitrile aka BAPN, Angiotensin II aka Ang II; cardiovascular;

Q8906: S. Nardai, *et al.* N,N-dimethyltryptamine reduces infarct size and improves functional recovery following transient focal brain ischemia in rats. *Experimental Neurology* 2020;327(113245

Agents: Tryptamine, N,N-dimethyl-; 1-(3,4-Dichlorophenethyl)-4-methyl- piperazine dihydrochloride **Vehicle:** Ethanol, Saline; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 24 hours;
ALZET Comments: Dose (2 mg/kg/hr); 70% Ethanol used; Controls received mp w/ vehicle; animal info (male Wistar rats, 280 ± 20 g body weight); behavioral testing (staircase method); Multiple pumps per animal (2 pumps); N,N-dimethyl-tryptamine aka DMT; dependence;



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. *Neuropsychopharmacology Reports* 2020;40(2):157-165
Agents: Beta-hydroxybutyrate **Vehicle:** PBS; **Route:** CSF/CNS (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);

Q8863: J. L. Jiang, *et al.* Triple reuptake inhibition of serotonin, norepinephrine, and dopamine increases the tonic activation of alpha2-adrenoceptors in the rat hippocampus and dopamine levels in the nucleus accumbens. *Progress in Neuropsychopharmacology & Biological Psychiatry* 2020;103(109987)

Agents: Nomifensine; Escitalopram **Vehicle:** 2-Hydroxypropyl-B-cyclodextrin; **Route:** SC; **Species:** Rat **Duration:** 2, 14 days;
ALZET Comments: Dose (5 mg/kg/day Nomifensine; 10 mg/kg/day Escitalopram); 20% 2-Hydroxypropyl-B-Cyclodextrin used; Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats weighing 250–350 g); Multiple pumps per animal (2 pumps); dependence;

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. *Frontiers in Neuroscience* 2020;14(514)

Agents: Bumetanide **Vehicle:** Propylene; Glycol; **Route:** CSF/CNS (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);

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, 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;

Q9767: T. W. Flanagan, *et al.* Activation of 5-HT₂ Receptors Reduces Inflammation in Vascular Tissue and Cholesterol Levels in High-Fat Diet-Fed Apolipoprotein E Knockout Mice. *Scientific Reports* 2019;9(1):13444

Agents: (R)-DOI **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 8 weeks;

ALZET Comments: "Dose (2.4 mg); Controls received mp w/ vehicle; animal info (ApoE -/-, Male, 20.6- 21.0 g); Multiple pumps per animal (2); (R)-DOI aka (R)-2,5-dimethoxy-4-iodoamphetamine aka 5-HT₂ receptor selective agonist ; cardiovascular; "

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;

Q8783: L. Wu, *et al.* C1QTNF1 attenuates angiotensin II-induced cardiac hypertrophy via activation of the AMPK α pathway. *Free Radical Biology and Medicine* 2018;121(215-230

Agents: Angiotensin II; Tumor necrosis factor related protein 1, C1q, human recombinant **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** **Duration:** 2, 4 weeks;

ALZET Comments: Dose ((AngII 1.4 mg/kg/day), (C1QTNF1 0.2 µg/g/day)); Controls received sham surgery; animal info (8-10 weeks, male, C57BL/6J and C1QTNF1 KO, 25+/-2g); Multiple pumps per animal (2); C1QTNF1 is a member of the CTRP superfamily expressed in the myocardium; cardiovascular; recombinant human globular domain of C1QTNF1 used in mp. C1QTNF1 mp implanted 2 weeks after AngII infusion;

Q7840: M. Waldman, *et al.* PARP-1 inhibition protects the diabetic heart through activation of SIRT1-PGC-1 α 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:** Mice; **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 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; **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;

Q10120: E. Brolin, *et al.* Chronic administration of morphine using mini-osmotic pumps affects spatial memory in the male rat. *Pharmacology, Biochemistry and Behavior* 2018;167(1-8)

Agents: Morphine hydrochloride **Vehicle:** DMSO; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;

ALZET Comments: Dose (17.5 mg/kg/day); 2% DMSO used; Controls received mp w/ vehicle; animal info (male Sprague Dawley); 8 wks old; behavioral testing (Tail flick, Morris water maze); Multiple pumps per animal (2); good methods (see pg 5);

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 3 used; 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-Prkdcscidll2rgtm1Wjl/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' IL1R1 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 $\alpha 7nAChR$ 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 bupivacane 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, Pylramine administered for 2 weeks with 2ML2 at 25 mg/kg/day);

Q5381: 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; **Pump:** 1002; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (ApoE -/- mice, 9 weeks old); functionality of mp verified by plasma levels, blood pressure; pumps replaced every 2 weeks; Multiple pumps per animal (2); 1 for either Ang II, GLP-1 or GIP; enzyme inhibitor (Dipeptidyl Peptidase-4 inhibitor); cardiovascular; atherosclerosis; peptides; Pathophysiology similarities btwn abdominal aortic aneurysms, atherosclerosis; Therapeutic indication (Abdominal aortic aneurysm); blood pressure measure via tail-cuff method; Dose (2000 ng/kg/min AngII, 2.16 nmol/kg/day GLP-1, 25 nmol/kg/day GIP); Resultant blood pressure (Start: 104 mmHg, End: 118 mmHg);

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);