



**Recent References (2014-2019) 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

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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

ALZET Comments: Angiotensin II; B-aminopropionitrile; Saline; SC; Mice; 1002; 1 week; 6 weeks; 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;.

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

ALZET Comments: Diminazene aceturate; SC; Mice; 2 weeks; 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;.

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

ALZET Comments: Antibody, anti-Nogo-A; CSF/CNS (Intrathecal), SC; Monkey (Macaca fascicularis); 2ML2; 4 weeks; 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

ALZET Comments: Antibody, anti-GCSF neutralizing antibody, Immunoglobulin G, pre-immune; Saline; CSF/CNS (nucleus accumbens); Mice; 1007D; 7 days; 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

ALZET Comments: Angiotensin II; sodium butyrate; SC; Intrarenal (medulla); Rat; 2002; 14 days; 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

ALZET Comments: Leptin; SC; Mice; 24 weeks; 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. *Exp Neurol* 2017;289(64-72

ALZET Comments: M40, M871, Galanin receptor antagonists; Saline; CSF/CNS (raphe nucleus); CSF/CNS (locus coeruleus);; Rat; 1007D; 3 days; 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

ALZET Comments: Antibody, anti-TGF β ; Angiotensin II; CSF/CNS (left ventricle); Mice; 1002; 1004; 2 weeks; 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. *Circ J* 2017;81(6):888-890

ALZET Comments: Angiotensin II; Relaxin; Saline; Sodium acetate; SC; Mice (knockout); 2004; 1004; 2001; 1007D; 28 days; 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

ALZET Comments: Exendin-4; FK506; PBS; saline; SC; Mice (NSG), mice (NOD); 1004; 1002; 4 weeks; 2 weeks; 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)

ALZET Comments: Nicotine; mecamylamine; methyllycaconitine; SC; Rat (pregnant); 2004; 28 days; 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)

ALZET Comments: Nicotine; methyllycaconitine; Saline; SC; Rat; 2004; 28 days; 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

ALZET Comments: HMGB1; Box A; OxPAPC; CSF, artificial; CSF/CNS; Rat; 1003D; 2 days; 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 μ g/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

ALZET Comments: Rapamycin; amyloid protein, beta (1-42); CSF, artificial; CSF/CNS; Rat; 1002; 14 days; 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 μ g/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)

ALZET Comments: Angiotensin II; SC; Mice; 1004; 8 weeks; 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 μ g/kg/min);.



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

ALZET Comments: Ephrin-B2;; CSF, patient; CSF/CNS (ventricle); Mice; 1002; 14 days; 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

ALZET Comments: Tubacin; Niltubacin; DMSO; PBS; SC; Mice; 1004; 30 days; 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

ALZET Comments: Nicotine ditartrate, pyrilamine; Saline; SC; Rat; 2ML2, 2ML4; 2 weeks;; 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

ALZET Comments: Angiotensin II, Glucagon-like peptide-1, Glucose-Dependent Insulinotropic Polypeptide; Saline; SC; Mice (knockout); 1002; 4 weeks; 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

ALZET Comments: Resveratrol; EX-527; DMSO; SC; Mice; 1002; 14 days; 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. *Circ Res* 2016;119(4):532-43

ALZET Comments: Dextrose, C21, PD-123319, Angiotensin II; Water; SC; Rat; 1007D, 2001; 1 week; 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):

ALZET Comments: Rapamycin, marinobufagenin; SC; Rat; 2004; 4 weeks; 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

ALZET Comments: Aldosterone; eplerenone; FAD286; CSF, artificial; acetonitrile; SC; CSF/CNS; Rat; 2004; 2 weeks, 3 weeks; 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

ALZET Comments: Desipramine, naloxone, AM251, AM630; Water, saline, PEG400, DMSO; SC; Rat; 2ML4; 28 days; 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

ALZET Comments: Antibody, beta-2-glycoprotein, hydroxychloroquine; Water, distilled; mice (pregnant); 1002; 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

ALZET Comments: Rosiglitazone Maleate; Water, Ethanol; SC; Sheep (pregnant); 2ML1; 16 days; 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);

Q4668: Y. Yu, *et al.* Activation of Central PPAR-gamma Attenuates Angiotensin II-Induced Hypertension. *HYPERTENSION* 2015;66(403-411

ALZET Comments: Angiotensin II; pioglitazone, GW9662; DMSO; CSF, artificial; SC; CSF/CNS; Rat; 2002; 2 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-300g); functionality of mp verified by residual volume; 20% DMSO used; Multiple pumps per animal (2); cardiovascular; immunology; peptides; Cannula placement verified via histologic analysis of cannula track; bp measured using radiotelemetry (DSI);

Q4355: J. B. Wang, *et al.* Development of a rat model of D-galactosamine/lipopolysaccharide induced hepatorenal syndrome. *WORLD JOURNAL OF GASTROENTEROLOGY* 2015;21(9927-9935

ALZET Comments: Fluorescein isothiocyanate-inulin; Saline; IP; Rat; 2001; 7 days; Animal info (male, Sprague Dawley, 220 +/-20g); Multiple pumps per animal (2); used 0.22 um filter; pumps primed for 4-6 hours;

Q5577: J. Trevaskis. Synergistic metabolic benefits of an exenatide analogue and cholecystokinin in diet-induced obese and leptin-deficient rodents. *DIABETES OBESITY & METABOLISM* 2015;17(1):61-73

ALZET Comments: Amylin, Cholecystokinin-8, AC3174, , AC170236, AC170222; DMSO, water; SC; Rat; 14 or 28 days; Controls received mp w/ vehicle; animal info (Diet-induced Obese Rats); functionality of mp verified by plasma levels; Vehicle was 50% DMSO:50% water; Multiple pumps per animal (2); AC170236 is a CCK2R-selective agonist; Therapeutic indication (Obesity); Dose: amylin (50 µg/kg/day), AC3174 (10 µg/kg/day), CCK-8 (100 µg/kg/day);

Q4582: R. K. Sharma, *et al.* Role of posterior hypothalamus in hypobaric hypoxia induced pulmonary edema. *RESPIRATORY PHYSIOLOGY & NEUROBIOLOGY* 2015;205(66-76



ALZET Comments: Muscimol; SNAP; CSF, artificial; CSF/CNS (hypothalamus); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Wistar, 280g); Multiple pumps per animal (2); post op. care (Gentamycin and diclofenac 2 mg/kg for 3 days; 1ml of sterile dextrose saline given IP; daily cleaning with betadine solution and nebasulf powder until wound healed); cardiovascular; antihypertensive;.

Q4990: T. A. Paine, *et al.* Effects of chronic inhibition of GABA synthesis on attention and impulse control. *Pharmacol Biochem Behav* 2015;135(97-104

ALZET Comments: Allylglycine, L-; CSF, artificial; CSF/CNS (prefrontal cortex); Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dalwey); bilateral cannula used; Multiple pumps per animal (2); behavioral testing (standard time reaction test; locomotor activity); tissue perfusion (prefrontal cortex); enzyme inhibitor (glutamic acid decarboxylase); Dose (3.5 ug/0.5ul/h);.

Q4018: B. F. Nelson, *et al.* Protracted treatment with corticosterone reduces breeding success in a long-lived bird. *General and Comparative Endocrinology* 2015;210(38-45

ALZET Comments: Corticosterone; PEG 400; SC; Bird (kittiwake); 2002; 8 days; Controls received mp w/ vehicle; animal info (late incubation, 380g); functionality of mp verified by serum levels; Multiple pumps per animal (2);.

Q3960: J. Y. Lee, *et al.* Simultaneous Inferior Alveolar Nerve Regeneration and Osseointegration With a Nerve Growth Factor-Supplying Implant: A Preliminary Study. *Journal of Oral and Maxillofacial Surgery* 2015;73(410-423

ALZET Comments: Nerve growth factor, human B-; PBS; CSF/CNS (inferior alveolar nerve); Dog (beagle); 2ML2; 6 weeks; Controls received mp w/ vehicle; animal info (male, beagle, 18 weeks old, 10-12 kg); good methods (picture of implant pg 413); Multiple pumps per animal (2; one pump delivered NGF other delivered PBS); used rat jugular catheter, 15 cm long; pump body placed into retromandibular area; long-term study;.

Q5406: J. K. Hu, *et al.* Murine Antibody Responses to Cleaved Soluble HIV-1 Envelope Trimers Are Highly Restricted in Specificity. *J Virol* 2015;89(20):10383-98

ALZET Comments: BG505 SOSIP/664 trimer; Iscomatrix; SC; Mice; 1007D; 2001; 1002; 2002; 7 days; 14 days; animal info (129/SvJ); Multiple pumps per animal (2); stability verified by (incubation and imaging; 14 day stability. See figure 7 of supplement); immunology; Dose (various, see supplement table 6);.

Q4451: Y. H. Ho, *et al.* Peripheral inflammation increases seizure susceptibility via the induction of neuroinflammation and oxidative stress in the hippocampus. *JOURNAL OF BIOMEDICAL SCIENCE* 2015;22(U1-U14

ALZET Comments: Endotoxin, LPS; NS398; tempol; Saline; DMSO; IP; CSF/CNS; Rat; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 10 weeks old, 250-282g); ALZET brain infusion kit 2 used; 1% DMSO used; Multiple pumps per animal (2); post op. care (IM procaine penicillin 1000IU); immunology; used dental cement; NS398 is a COX-2 inhibitor and anti-inflammatory; tempol scavenges ROS;.

Q4427: K. G. F. Gerritsen, *et al.* Elevated Urinary Connective Tissue Growth Factor in Diabetic Nephropathy Is Caused by Local Production and Tubular Dysfunction. *JOURNAL OF DIABETES RESEARCH* 2015;;(U1-U11

ALZET Comments: CTGF, recombinant human; FITC-inulin; SC; Mice; 1003D; 3 days; Controls received mp w/ vehicle; animal info (male, C57BL6, 10-12 weeks old, STZ); Multiple pumps per animal (2); cardiovascular; diabetes;.

Q4962: M. T. Fuzzati-Armentero, *et al.* Dual target strategy: combining distinct non-dopaminergic treatments reduces neuronal cell loss and synergistically modulates L-DOPA-induced rotational behavior in a rodent model of Parkinson's disease. *J Neurochem* 2015;134(4):740-7

ALZET Comments: MSX-3; ANR; DMSO; PEG; SC; Rat; 2ML4; 28 days; animal info (male, Sprague Dawley, 275-300g); Multiple pumps per animal (2); stress/adverse reaction: (see pg. 742);.

Q3853: B. N. Desai, *et al.* Leptin in the hindbrain facilitates phosphorylation of STAT3 in the hypothalamus. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2015;308(E351-E361



ALZET Comments: Leptin; CSF/CNS (third ventricle; fourth ventricle); Rat; 2002; 6 days; Controls received mp w/ saline; animal info (male, Sprague Dawley, 275-300g); Multiple pumps per animal (2); tissue perfusion (third ventricle; fourth ventricle); bilateral infusion; one cannula to third ventricle second cannula to fourth ventricle; used plastics one cannula;

Q4368: W. H. Chen, *et al.* Beta-nerve growth factor promotes neurogenesis and angiogenesis during the repair of bone defects. *Neural Regeneration Research* 2015;10(1159-1165)

ALZET Comments: Nerve growth factor, b-; PBS; Evans blue dye; Bone (parietal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dalwey, 250-300g); 1% Evans blue used; good methods (picture of dual cannula implantation pg 1161); Multiple pumps per animal (2); pump with agent inserted into right pocket, pump with PBS inserted into left pocket; bilateral infusion;

Q3634: F. Zhu, *et al.* MINOCYCLINE ALLEVIATES BEHAVIORAL DEFICITS AND INHIBITS MICROGLIAL ACTIVATION INDUCED BY INTRAHIPPOCAMPAL ADMINISTRATION OF GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR IN ADULT RATS. *Neuroscience* 2014;266(275-281)

ALZET Comments: Colony stimulating factor, GM, recombinant rat; Saline; CSF/CNS (hippocampus); Rat; 1007D; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 280-320g); ALZET brain infusion kit 3 used; Multiple pumps per animal (2); behavioral testing (locomotor activity; social interaction test; PPI); used dental acrylic resin; schizophrenia;

Q3639: Z. Zhang, *et al.* Nebivolol Protects against Myocardial Infarction Injury via Stimulation of Beta 3-Adrenergic Receptors and Nitric Oxide Signaling. *PLoS One* 2014;9(U979-U988)

ALZET Comments: Nebivolol; SR59230A; Mice; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57Bl6, adult, 22-25g); Multiple pumps per animal (2); cardiovascular; BP measured using tail cuff; myocardial infarction;

Q4192: B. J. Xue, *et al.* Estrogen regulation of the brain renin-angiotensin system in protection against angiotensin II-induced sensitization of hypertension. *American Journal of Physiology-Heart and Circulatory Physiology* 2014;307(H191-H198)

ALZET Comments: Angiotensin II; estradiol, 17b-; angiotensin (1-7); A-779; Saline; DMSO; SC; CSF/CNS; Rat; 2001; 2002; 1 week; 2 weeks; Animal info (Sprague Dawley, 10-12 weeks old); ALZET brain infusion kit used; Multiple pumps per animal (2); replacement therapy (ovarectomized, estradiol infusion); cardiovascular; antihypertensive; peptides; bp measured using radiotelemetry (DSI);.

Q3696: M. Wosiski-Kuhn, *et al.* Glucocorticoid receptor activation impairs hippocampal plasticity by suppressing BDNF expression in obese mice. *Psychoneuroendocrinology* 2014;42(165-177)

ALZET Comments: Corticosterone; Cyclodextrin, 2-hydroxypropyl-b-; CSF/CNS (hippocampus); Mice; 2 weeks; Controls received mp w/ vehicle and aCSF; animal info (male, C57BL6J or db/db, 5 weeks old); functionality of mp verified by hippocampal corticosterone levels; Multiple pumps per animal (2); behavioral testing (y-maze apparatus); tissue perfusion (bilateral hippocampi); immunology; Cannula placement verified via histology; used Plastics One bilateral cannula; bilateral infusion;

Q3720: J. Wedel, *et al.* Simultaneous subcutaneous implantation of two osmotic minipumps connected to a jugular vein catheter in the rat. *Laboratory Animals* 2014;48(338-341)

ALZET Comments: Dopamine, N-octanoyl; Tween 80; saline; IV (jugular); Rat; 2ML4; 14 days; animal info (male, Brown Norway, 230-270 g, female, Wistar, 280-310 g); good methods; "Our data show that double pump implantation is a feasible alternative to changing pumps or the use of extracorporeal pump systems connected via a long wire to partly restrained animals." pg 338; N-octanoyl-dopamine also known as NOD; multiple pumps (2) used; two pumps connected to Y connector, in-house made Y-tube; "we showed that the simultaneous implantation of two slow-flow rate osmotic pumps connected to a jugular vein catheter is feasible and is not linked to additional signs of discomfort compared with single pump-implanted rats." pg 341.

Q4170: J. B. Wang, *et al.* Tumor necrosis factor-alpha-induced reduction of glomerular filtration rate in rats with fulminant hepatic failure. *LABORATORY INVESTIGATION* 2014;94(740-751)



ALZET Comments: Fluorescein isothiocyanate-inulin; Saline; IP; Rat; 7 days; Animal info (male, Sprague Dawley, 220g); functionality of mp verified by plasma fluorescent levels; Multiple pumps per animal (2); cardiovascular; bp measured using indwelling catheter;

Q5454: J. B. Wang, *et al.* Tumor necrosis factor-alpha-induced reduction of glomerular filtration rate in rats with fulminant hepatic failure. *Lab Invest* 2014;94(7):740-51

ALZET Comments: FITC-Inulin; IP; Rat; 7 days; functionality of mp verified by plasma level; 8% FITC-inulin used; dose-response, FITC-inulin clearance (pg. 746); Multiple pumps per animal (2); Severe liver injury induced by lipopolysaccharide plus D-galactosamine exposure.

Q3670: J. F. Thorson, *et al.* Pharmacologic application of native GnRH in the winter anovulatory mare, II: Accelerating the timing of pregnancy. *Theriogenology* 2014;81(4):625-631

ALZET Comments: Gonadotropin-releasing hormone; Saline; SC; Horse (mare); 2ML2; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (female, Quarter Horse grade); pumps replaced every 14 days (2ML2) or 28 days (2ML4); Multiple pumps per animal (4 2ML2 or 2 2ML4); used contralateral side for next pump implantation; pumps removed at end of study;

Q4066: L. te Riet, *et al.* Deterioration of kidney function by the (pro)renin receptor blocker handle region peptide in aliskiren-treated diabetic transgenic (mRen2)27 rats. *American Journal of Physiology-Renal Physiology* 2014;306(F1179-F1189)

ALZET Comments: Aliskiren; handle region peptide, rat; Saline; SC; Rat (transgenic); 2ML4; 3 weeks; Controls received mp w/ vehicle; animal info (Ren2 Sprague Dawley heterozygous, 400-500g); Multiple pumps per animal (2); cardiovascular; peptides; diabetes;

Q4112: V. Sriraman, *et al.* Investigation of a thiazolidinone derivative as an allosteric modulator of follicle stimulating hormone receptor: Evidence for its ability to support follicular development and ovulation. *Biochemical Pharmacology* 2014;89(266-275)

ALZET Comments: Compound 5; Solutol; SC; Rat; 1003D; 72 hours; Animal info (female, immature CD, 18-21 days old); functionality of mp verified by blood levels; Multiple pumps per animal (2); "As Compound 5 exhibited poor oral availability on the pharmacokinetic studies we chose Alzet pumps to investigate the pharmacodynamic effect. Alzet osmotic pumps ensure constant levels of compounds in the circulation by continuous delivery" pg 273;

Q4743: K. Shinohara, *et al.* Post-acquisition hippocampal NMDA receptor blockade sustains retention of spatial reference memory in Morris water maze. *BEHAVIOURAL BRAIN RESEARCH* 2014;259(1):261-267

ALZET Comments: AP5, D-; CSF, artificial; CSF/CNS (hippocampus); Rat; 1007D; 7 days; 14 days; Animal info (male, albino Wistar); pumps replaced every 7 days; Plastics One bilateral cannula used; Multiple pumps per animal (2); behavioral testing (morris water maze, probe test); tissue perfusion (hippocampus); Cannula placement verified via histological analysis; pumps primed for 24 hours in 37C saline; bilateral infusion;

Q4092: A. Secher, *et al.* The arcuate nucleus mediates GLP-1 receptor agonist liraglutide-dependent weight loss. *Journal of Clinical Investigation* 2014;124(4473-4488)

ALZET Comments: Exendin (9-39); DPBS buffer; PBS; CSF/CNS; SC; Rat; 11 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 190g); Multiple pumps per animal (2, one ICV one SC); post op. care (QD Carprofen injection); peptides; used anchoring screws; pumps primed overnight at 37C saline; obesity;

Q4085: J. M. Sasser, *et al.* Serelaxin reduces oxidative stress and asymmetric dimethylarginine in angiotensin II-induced hypertension. *American Journal of Physiology-Renal Physiology* 2014;307(F1355-F1362)

ALZET Comments: Angiotensin II; serelaxin, recombinant human; Saline; SC; Rat; 2002; 2ML2; 6 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 400-500g); pumps replaced every 2 weeks; Multiple pumps per animal (2); long-term study; cardiovascular; peptides; antihypertensive;



Q3771: T. Sakai, *et al.* Leptin restores the insulinotropic effect of exenatide in a mouse model of type 2 diabetes with increased adiposity induced by streptozotocin and high-fat diet. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2014;307(E712-E719)

ALZET Comments: Leptin, recomb.; exenatide; SC; Mice; 2002; 14 days; Control animals received mp w/ saline; animal info (STZ induced diabetes, HFD 8 wks old); multiple pumps (2) implanted.

Q3569: M. L. Rock, *et al.* The Time-to-Integrate-to-Nest Test as an Indicator of Wellbeing in Laboratory Mice. *Journal of the American Association for Laboratory Animal Science* 2014;53(1):24-28

ALZET Comments: Aldosterone; uridine, bromodeoxy-; Ethanol; saline; SC; Mice; 5 days; Controls received mp w/ vehicle; animal info (10 mouse strains; BALB/cAnNCrI, 129S2/ SvPasCrI, FVB/NCrI, C57BL/6NCrI, C3H/HeNCrI, CB17/ Icr-Prkdcscid/IcrIcoCrI, NOD.CB17-Prkdcscid/NCrCrI, CB17.Cg/ Prkdcscid Lystbg/CrI, C57BL/6NTac, and C57BL/6NJ, carotid artery injury); 11% ethanol used; Multiple pumps per animal (2); post op. care (buprenorphine 0.05 mg/kg SC); behavioral testing (nesting behavior); cardiovascular;

Q5599: M. L. Rock. The time-to-integrate-to-nest test as an indicator of wellbeing in laboratory mice. *Journal of American Association of Laboratory Animal Science* 2014;53(1):24-28

ALZET Comments: Aldosterone; bromodeoxyuridine; Ethanol; SC; Mice; 3 days; 11% ethanol used; Multiple pumps per animal (2): one for aldosterone and one for BrdU; no stress: Minipump implantation surgery did not appear to affect TINT results, yet mice were more likely to fail the TINT the morning after CAI surgery. Mice required 2 full days to return to baseline TINT levels. This lag may be due to the fact that minipump implantation surgery is adequately treated with a single dose of buprenorphine whereas CAI surgery is not (see pg. 27); post op. care: Buprenorphine (0.05 mg/kg SC); Dose: Aldosterone (6 g/kg/d;), BrdU (25 mg/kg/d);

Q3610: E. J. Rahn, *et al.* Prophylactic cannabinoid administration blocks the development of paclitaxel-induced neuropathic nociception during analgesic treatment and following cessation of drug delivery. *Molecular Pain* 2014;10(U1-U19)

ALZET Comments: AM1710; Taxol-WIN-55212-2; AM251; AM630; DMSO; PEG 400; SC; Rat; 2ML4; 28 days; Controls received mp w/ saline; animal info (male, Sprague Dawley, 300-400g); functionality of mp verified by residual volume; 50% PEG 400 used; 50% DMSO used; Multiple pumps per animal (2); stress/adverse reaction: (see pg.15); behavioral testing (mechanical threshold, cold withdrawal, locomotor activity); AM1710 is a cannabylactone CB2-selective agonist; pumps removed on day 22; WIN55,212-2 is a CB1/CB2 agonist;

Q3999: T. H. Meek, *et al.* Role of Melanocortin Signaling in Neuroendocrine and Metabolic Actions of Leptin in Male Rats With Uncontrolled Diabetes. *Endocrinology* 2014;155(4157-4167)

ALZET Comments: SHU9119; leptin; melanotan-II;; Saline; PBS; water, sterile; CSF/CNS; SC; Rat; mice; 11 days; Controls received mp w/ vehicle; animal info (rat - male, Wistar, adult; mice - STZ-DM, AgRP-deficient or WT); functionality of mp verified by decreased insulin plasma levels; Multiple pumps per animal (2); diabetes; melanotan-II aka MTII; delayed delivery - catheters filled with saline; received drug on day 5; bilateral infusion for rat;

Q3560: C. A. Martel, *et al.* Continuous low-dose infusion of tumor necrosis factor alpha in adipose tissue elevates adipose tissue interleukin 10 abundance and fails to alter metabolism in lactating dairy cows. *Journal of Dairy Science* 2014;97(4897-4906)

ALZET Comments: Tumor necrosis factor alpha; Saline; SC; Cattle (lactating); 2ML1; 7 days; Controls received mp w/ vehicle; animal info (female, Holstein, late lactation); Multiple pumps per animal (2); immunology;

Q3760: A. C. Johnson, *et al.* Magnesium Sulfate Treatment Reverses Seizure Susceptibility and Decreases Neuroinflammation in a Rat Model of Severe Preeclampsia. *PLoS One* 2014;9(U1482-U1492)

ALZET Comments: Magnesium sulfate; SC; Rat (pregnant); Animal info (Sprague Dawley, 14-16 wks old); multiple pumps (3) used; 2ML sized pumps used.

Q3859: L. L. Dugan, *et al.* Carboxyfullerene Neuroprotection Postinjury in Parkinsonian Nonhuman Primates. *Annals of Neurology* 2014;76(393-402)



ALZET Comments: C3; SC; IP; Monkey (macaque); 2ML4; 30 days; Controls received mp w/ placebo; animal info (Macaca fascicularis); Multiple pumps per animal (2); neurodegenerative (Parkinson's disease); behavioral testing (locomotor activity); stability verified by (testing at 37C, C3 is stable for >40 days); Carboxyfullerine aka C3;

Q3455: R. Dhaher, *et al.* 5-Aminovaleric acid suppresses the development of severe seizures in the methionine sulfoximine model of mesial temporal lobe epilepsy. *NEUROBIOLOGY OF DISEASE* 2014;67(18-23

ALZET Comments: Aminovaleric acid, 5-; methionine sulfoximine; PBS; SC; CSF/CNS; Rat; 2ML4; 2004; 28 days; Animal info (male, Sprague Dawley, 300-330g); Multiple pumps per animal (2); cyanoacrylate adhesive; Cannula placement verified via histological analysis; methionine sulfoximine aka MSO; 5-aminovaleric acid aka 5-AV; used Plastics One cannula; second mp implanted 5-7 days after first pump implantation; 2004 implanted CSF/CNS; 2ML4 SC; epilepsy;

Q3452: R. B. Dange, *et al.* Central blockade of TLR4 improves cardiac function and attenuates myocardial inflammation in angiotensin II-induced hypertension. *Cardiovascular Research* 2014;103(17-27

ALZET Comments: Angiotensin II; peptide, viral inhibitory; SC; CSF/CNS; Rat; 2002; 14 days; Controls received mp w/ vehicle or control peptide; animal info (male, Sprague Dawley, 10 weeks old, 250-350g); functionality of mp verified by plasma levels ELISA; Multiple pumps per animal (2); cardiovascular; peptides; viral inhibitory peptide aka VIPER; VIPER inhibits TLR4; bp measured using radiotelemetry;

Q3829: S. Cerri, *et al.* Neuroprotective Potential of Adenosine A2A and Cannabinoid CB1 Receptor Antagonists in an Animal Model of Parkinson Disease. *Journal of Neuropathology and Experimental Neurology* 2014;73(414-424

ALZET Comments: Rimobabant; MSX-3;; DMSO; PEG; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 200-225g); 50% DMSO used; 50% PEG used; Multiple pumps per animal (2); neurodegenerative (parkinson's disease);

Q3415: W. W. Batenburg, *et al.* Combined Renin Inhibition/(Pro)Renin Receptor Blockade in Diabetic Retinopathy- A Study in Transgenic (mREN2)27 Rats. *PLoS One* 2014;9(U983-U993

ALZET Comments: Aliskiren; handle region peptide; Saline; SC; Rat (transgenic); 2ML4; 3 weeks; Animal info (heterozygous Ren2 Sprague Dawley, adult, 400-500g); Multiple pumps per animal (2); cardiovascular; peptides; diabetes; handle region peptide aka HRP;

Q3220: C. Altaner, *et al.* Complete regression of glioblastoma by mesenchymal stem cells mediated prodrug gene therapy simulating clinical therapeutic scenario. *International Journal of Cancer* 2014;134(6):1458-1465

ALZET Comments: Fluorocytosine-5; stem cells, therapeutic; Saline; CSF/CNS; Rat; 2ML2; 2001D; Animal info (adult, male, CD, IGS); multiple pumps (2) used; cancer (Glioblastoma multiforme); "Continuous infusion of ThSCs by osmotic pumps allowed applying more than five times higher cell dose in comparison with the amount that is possible to deliver by stereotaxic injection."