



**Long Term Infusion
Using ALZET® Osmotic Pumps**

ALZET pumps range in duration from 24 hours to 6 weeks. Animals can be dosed for periods which exceed the duration of a single pump by serial reimplantation of fresh pumps. This collection of references includes only the most recent citations. However, we do have older references which include infusions of as long as 3 years and in which up to 52 serial implantations have been performed on a single animal. The following table indicates the longest published duration of administration by animal along with a reference. *(In some cases, more than one study infused for this duration.)

ANIMAL	DURATION	PUMPS REPLACED	REFERENCE
Mouse	32 weeks	Not stated	P7341 Zhou Y, Chen R, Catanzaro SE, Hu LF, Dansky HM, Catanzaro DF. Differential effects of angiotensin II on atherogenesis at the aortic sinus and descending aorta of apolipoprotein-E-deficient mice. <i>Am J Hypertens</i> 2005; 18(4):486-492
*Rabbit	36 weeks	Every 4 weeks	P8478 Ma T Modulation of allograft incorporation by growth factors over a prolonged continuous infusion of duration in vivo. <i>Bone</i> 2007; 41(3):386-392
Rat	1 year	Not stated	P0818 Murphy WM, Blatnik AF, Shelton TB, Soloway MS. Carcinogenesis in mammalian urothelium: changes induced by non-carcinogenic substances and chronic indwelling catheters. <i>J Urol</i> 1986; 135(4):840-844
Dog	18 months	Every 2-4 weeks	P0752 McRae GI, Roberts BB, Worden AC, Bajka A, Vickery BH. Long-term reversible suppression of oestrus in bitches with nafarelin acetate, a potent LHRH agonist. <i>J Reprod Fertil</i> 1985; 74(2):389-397
Cattle	8 weeks	After 28 days	P9771 Roche JR, Sheahan AJ, Chagas LM, Blache D, Berry DP, Kay JK. Long-Term Infusions of Ghrelin and Obestatin in Early Lactation Dairy Cows. <i>J Dairy Sci</i> 2008; 91(12):4728-4740
*Guinea-pig	8 weeks	Every 13 days	P4742 Tang W, Seidman MD, Henig JP, Shulman A, Stracher A. The effects of leupeptin on cochlear blood flow, auditory sensitivity, and histology. <i>International Tinnitus Journal</i> 2001; 7(1):4-12
Monkey	3 years	Every 3 weeks	P2083 Ravindranath N, Ramesh V, Krishnamurthy H, Roa AJ, Moudgal RN. Chronic suppression of testicular function by constant infusion of gonadotropin-releasing hormone agonist and testosterone supplementation in the bonnet monkey (<i>Macaca radiata</i>). <i>Fertil Steril</i> 1992; 57(3):671-676.

The short abstract following each reference in the attached list details the substance(s) infused, route of administration, animal model studied, solvent(s), model of pump, duration of infusion, and whether stress to the animal was noted.

Note: This list does not contain references in this category from before the years specified. To obtain a complete listing of earlier references, contact ALZET Technical Services at 800-692-2990 (U.S. & Canada) or by email at alzet@durect.com.



Recent References (2015-2019) on the Long Term Administration of Agents Using ALZET® Osmotic Pumps

Q6954: S. L. Payne, *et al.* Initial cell maturity changes following transplantation in a hyaluronan-based hydrogel and impacts therapeutic success in the stroke-injured rodent brain. *Biomaterials* 2019;192(309-322)

ALZET Comments: Cyclosporine A; Ethanol, Cremophor; SC; Rat; 2ML4; 56 days; Dose (15 mg/kg/day); animal info (male Sprague-Dawley rats, 350 g); post op. care (3 mg/kg- ketoprofen); behavioral testing (Montoya staircase and tapered beam test); long-term study; ischemia (stroke);.

Q7154: S. R. Subramaniam, *et al.* Chronic nicotine improves cognitive and social impairment in mice overexpressing wild type alpha-synuclein. *Neurobiol Dis* 2018;117(170-180)

ALZET Comments: Nicotine; Saline; SC; Mice; 2004; 1 or 6 months; Dose (0.4 mg/kg/h and 2.0 mg/kg/h); dose-response (); dose-response (); pumps replaced every 4 weeks; long-term study; stress/adverse reaction: Mice treated with the higher nicotine dose (2.0 mg/kg/h) lost weight after surgery and 50% died after one week. This was as a result of combined toxic effects of isoflurane and a higher dose of nicotine. Therefore, pentobarbital was used instead of isoflurane for induction of anesthesia, which reduced the mortality rate and improved weight gain in the higher dose group. (see pg. 172);.

Q7047: M. Shi, *et al.* Cisplatin nephrotoxicity as a model of chronic kidney disease. *Lab Invest* 2018;98(8):1105-1121

ALZET Comments: α Klotho protein, recomb.; Saline; SC; Mice; 1004; 20 weeks; Dose (0.3 mg/kg/month); Controls received mp w/ vehicle; pumps replaced every 4 weeks; long-term study; Therapeutic indication (Acute kidney injury);.

Q7000: U. C. Sharma, *et al.* Effects of a novel peptide Ac-SDKP in radiation-induced coronary endothelial damage and resting myocardial blood flow. *Cardio-Oncology* 2018;4(1):

ALZET Comments: Ac-SDKP; SC; Rat; 18 weeks; Dose (3.2 mg/kg/day); animal info (10–12 week old Sprague Dawley rats); long-term study; Ac-SDKP aka N-acetyl-Ser-Asp-Lys-Pro;.

Q7053: K. R. Qurania, *et al.* Systemic inhibition of Janus kinase induces browning of white adipose tissue and ameliorates obesity-related metabolic disorders. *Biochem Biophys Res Commun* 2018;502(1):123-128

ALZET Comments: Tofacitinib; Saline; SC; Mice; 10 weeks; Dose (100 μ g/day); Controls received mp w/ vehicle; animal info (C57BL6 mice); pumps replaced every 35 days; long-term study; tofacitinib is a JAK3 inhibitor; enzyme inhibitor (JAK3).

Q7010: O. S. Kornfeld, *et al.* Interaction of mitochondrial fission factor with dynamin related protein 1 governs physiological mitochondrial function in vivo. *Sci Rep* 2018;8(1):14034

ALZET Comments: P259-TAT; TAT control peptide; SC; Mice; 8 weeks; 12 weeks; Dose (3 mg/Kg/day); Controls received mp w/ vehicle; animal info (5-week old R6/2 HD and wild-type mice); pumps replaced every 4 weeks; long-term study;.

Q7189: A. U. Joshi, *et al.* Inhibition of Drp1/Fis1 interaction slows progression of amyotrophic lateral sclerosis. *EMBO Mol Med* 2018;10(3):

ALZET Comments: P110-TAT (47-57); SC; Mice; 28 day pump; 60 days; Dose (3 mg/kg/day); animal info (4–6 weeks old AdultB6SJL Tg (SOD1G93A) 1 Gur/J male mice); behavioral testing (Activity chamber); pumps replaced after 30 days; long-term study; P110 is a selective peptide inhibitor of Drp1/Fis1; neurodegenerative (amyotrophic lateral sclerosis); neurodegenerative (amyotrophic lateral sclerosis); stress/adverse reaction: (see pg. 14); .

Q7185: S. E. Iismaa, *et al.* Cardiac hypertrophy limits infarct expansion after myocardial infarction in mice. *Sci Rep* 2018;8(1):6114

ALZET Comments: Uridine, 5-bromo-2'-deoxy; DMSO, Water; SC; Mice; 2002, 2006; 9 days and 12 weeks; Dose (10 mg/kg/day); 50% DMSO/water used; animal info (16 weeks old male mice); post op. care (bupivacaine, 8 mg/kg, buprenorphine, 0.075 mg/kg); Model 2006 pumps replaced after 6 weeks; long-term study; 5-bromo-2'-deoxyuridine aka BrdU; cardiovascular; .

Q7183: P. Huehnchen, *et al.* Fingolimod therapy is not effective in a mouse model of spontaneous autoimmune peripheral polyneuropathy. *Sci Rep* 2018;8(1):5648



ALZET Comments: Fingolimod; Saline; IP; Mice; 1004; 8 weeks; Dose (1 mg/kg/day); Controls received mp w/ vehicle; animal info (CD86-/- non-obese diabetic (NOD) mice); pumps replaced every 4 weeks; long-term study; Fingolimod is a sphingosine-1-phosphate analogue; neurodegenerative (autoimmune polyneuropathy); stress/adverse reaction: (see pg. 2);.

Q7179: Y. Henning, *et al.* Retinal S-opsin dominance in Ansell's mole-rats (*Fukomys anelli*) is a consequence of naturally low serum thyroxine. *Sci Rep* 2018;8(1):4337

ALZET Comments: Thyroxine, 3,5,3'-triiodothyronine; NaOH, propylenglycol, PBS SC; Rat (mole); 2006; 12 weeks; Dose (90 ng/g of T4, 2 ng/g of T3); 15 mM NaOH, 50% propylenglycol and PBS containing 5% BSA used; Controls received mp w/ vehicle; animal info (Ansell's mole rats, mean age 2.6 ± 0.92 years); post op. care (Carprofen, 5 mg/kg for at least 3 days; animals were isolated for 24–48 h for recovery then housed as family group); pumps replaced every 6 weeks; long-term study; "Osmotic pumps deliver the test agents with a constant flow rate, thus being well-suited for long-term hormone treatments" pg. 9 ; .

Q6089: Y. Henning, *et al.* Retinal S-opsin dominance in Ansell's mole-rats (*Fukomys anelli*) is a consequence of naturally low serum thyroxine. *Sci Rep* 2018;8(1):4337

ALZET Comments: Thyroxine; Triiodothyronine, 3,5,3'-; Propylene glycol, NaOH, BSA; SC; Rat (mole); 2006; 12 weeks; Dose (T4 at 90 ng/g; T3 at 2 ng/g); Vehicle solution (15 mM NaOH, 50% propylenglycol and PBS containing 5% BSA); Controls received mp w/ vehicle; animal info (Ansell's mole-rats with mean age of 2.6 ± 0.92 years); post op. care (Carprofen, 5 mg/kg for at least 3 days; animals were isolated for 24–48 h for recovery then housed as family groups); pumps replaced every 6 weeks; long-term study (12 weeks); "Osmotic pumps deliver the test agents with a constant flow rate, thus being well-suited for long-term hormone treatments. Constant administration further overcomes the short half-life of THs in rodents" pg. 9;.

Q7139: Y. Gao, *et al.* The histone methyltransferase DOT1L inhibits osteoclastogenesis and protects against osteoporosis. *Cell Death Dis* 2018;9(2):33

ALZET Comments: EPZ5676; DMSO, Water; SC; Mouse; 2006, 2002; 8 weeks; Dose (1.6 mg/d); 50% DMSO used; Controls received mp w/ vehicle; animal info (Eight-week-old, female, FVB/N); Model 2006 pumps replaced with Model 2002 after six weeks; long-term study; EPZ5676 aka small molecule inhibitor; gene therapy;.

Q7103: A. Calevro, *et al.* Effects of chronic antipsychotic drug exposure on the expression of Translocator Protein and inflammatory markers in rat adipose tissue. *Psychoneuroendocrinology* 2018;95(28-33)

ALZET Comments: Haloperidol, olanzapine; Cyclodextrin, 2-Hydroxypropyl-B-; SC; Rat; 2ML4; 8 weeks; Dose (Haloperidol-2mg/ kg/ day, Olanzapine-10 mg/kg/ day); Controls received mp w/ vehicle; animal info (10-week old, male, Sprague-Dawley, 240–250 g); pumps replaced every 4 weeks; long-term study; dependence;.

Q5727: Y. Zhu, *et al.* Protective Effect of 17beta-Estradiol Upon Hippocampal Spine Density and Cognitive Function in an Animal Model of Vascular Dementia. *Sci Rep* 2017;7(42660)

ALZET Comments: Estradiol, 17b-; SC; Rat; 2006; Controls received mp w/ 20% cyclodextrin; animal info (male, Sprague Dawley, 250-300g, adult); functionality of mp verified by serum levels; behavioral testing (Morris water maze); replacement therapy (estradiol infusion); long-term study; cardiovascular; Dose (0.05 ug/h); "exogenous E2 replacement produced E2 levels of 25-33pg/ml" (pg 2);.

Q5933: S. Yonekubo, *et al.* Alpha1A-adrenoceptor antagonist improves underactive bladder associated with diabetic cystopathy via bladder blood flow in rats. *BMC Urol* 2017;17(1):64

ALZET Comments: Silodosin; Hartmann's solution; SC; Rat; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 6 weeks old); long-term study; diabetes; Dose (0.3 or 1 mg/kg/day);.

Q5956: J. Tam, *et al.* Peripheral cannabinoid-1 receptor blockade restores hypothalamic leptin signaling. *Mol Metab* 2017;6(10):1113-1125

ALZET Comments: Leptin; SHU-9119; PBS; SC; CSF/CNS; Mice; 2004; 12 weeks, 7 days; Controls received mp w/ vehicle; animal info (leptin-deficient ob/ob mice); long-term study; pumps replaced every 28 days; SHU-9119 is a MC4R antagonist;



Leptin dissolved in PBS and delivered SC for 12 weeks; SHU-9119 dissolved in saline and delivered ICV for 7 days; Pumps model incorrectly listed as Model 2001D. It should be Model 2004 based on description.

Q6183: M. Sudo, *et al.* Inhibition of plaque progression and promotion of plaque stability by glucagon-like peptide-1 receptor agonist: Serial in vivo findings from iMap-IVUS in Watanabe heritable hyperlipidemic rabbits. *Atherosclerosis* 2017;265(283-291

ALZET Comments: Lixisenatide; Saline; SC; Rabbits; 2ML4; 12 weeks; Dose (30 nmol/kg/day); Controls received mp w/ vehicle; animal info (Watanabe heritable hyperlipidemic); pumps replaced every 4 weeks; long-term study (12 weeks); Lixisenatide is a GLP-1 receptor agonist;

Q6180: A. Sike, *et al.* Improved method for cannula fixation for long-term intracerebral brain infusion. *J Neurosci Methods* 2017;290(145-150

ALZET Comments: Black Ink; PBS; CSF/CNS (ventricle); Mice; 2006; 50 days; Dose (PBS with 1:100 black ink); animal info (50-day old male C57BL/6J mice); functionality of mp verified by in vitro priming visualization; ALZET brain infusion kit 3 used; cyanoacrylate adhesive; no stress: The implanted pump and the cannula caused minimal discomfort to the animals and it had no effect on the moving ability (see pg.5); good methods; This report describes an improved method for better fixation of cannula during long-term brain infusion experiments using a non-toxic, soft and elastic silicone spacer.

Q5742: M. P. Serrano, *et al.* The proof-of-concept of ASS234: Peripherally administered ASS234 enters the central nervous system and reduces pathology in a male mouse model of Alzheimer disease. *J Psychiatry Neurosci* 2017;42(1):59-69

ALZET Comments: ASS234; PBS, DMSO; SC; Mice (transgenic); 2004; 4 months; Controls received mp w/ vehicle; animal info (10 weeks old, APP^{swE}/PS1^{ΔE9}); long-term study; pumps replaced every 28 days for 4 months; 3.6% DMSO ; neurodegenerative (Alzheimer's disease); behavioral testing (Object recognition task); enzyme inhibitor (AChE/MAO inhibitor); Therapeutic indication (Alzheimer's disease, AD); Dose (0.62 mg/kg/day);

Q6708: Y. J. Oh, *et al.* Role of tissue transglutaminase in age-associated ventricular stiffness. *Amino Acids* 2017;49(3):695-704

ALZET Comments: Cystamine; Saline; Mice; 2ML4; 12 weeks; Dose (60 mg/kg/day); animal info (Male Fisher 344 rats aged 6 and 18 months); pumps replaced every 4 weeks; long-term study; enzyme inhibitor (transglutaminase);

Q6195: H. Noh, *et al.* Beta 2-adrenergic receptor agonists are novel regulators of macrophage activation in diabetic renal and cardiovascular complications. *Kidney Int* 2017;92(1):101-113

ALZET Comments: Salbutamol; Rat; 12 weeks; 5 weeks; Dose (0.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Male 8-week-old ZDF rats); long-term study; Salbutamol is a beta2AR agonist; diabetes;

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;

Q6363: J. Lukas, *et al.* Glucosylsphingosine Causes Hematological and Visceral Changes in Mice-Evidence for a Pathophysiological Role in Gaucher Disease. *Int J Mol Sci* 2017;18(10):

ALZET Comments: Glucosylsphingosine; DMSO; Propylene glycol; SC; Mice; 1004; 12 weeks; Dose (10 mg/kg/day); 50% DMSO:50% propylene glycol used; Controls received mp w/ vehicle; animal info (Male C57BL/6JRj mice); functionality of mp verified by plasma levels; pumps replaced every 4 weeks; long-term study (12 weeks); Resultant plasma level (between 700 and 900 ng/mL); no stress: The pumps were well tolerated and no mortalities were observed (see pg. 11); good methods (p.10); Lyso-Gb1 levels were strongly elevated after four, eight and 12 weeks (levels ranging between 700 and 900 ng/mL). This represented a >500-fold increase compared with vehicle-treated mice.

Q6324: K. Fujiu, *et al.* A heart-brain-kidney network controls adaptation to cardiac stress through tissue macrophage activation. *Nat Med* 2017;23(5):611-622



ALZET Comments: Antibody, anti-mouse-GM-CSF, Antibody, rat isotype (IgG2a); PBS; SC; Mice; 1007D; 8 weeks; Dose (2.5 µg/d); Controls received mp w/ vehicle; pumps replaced every 4 weeks; long-term study;.

Q6222: E. C. El Hajj, *et al.* Detrimental role of lysyl oxidase in cardiac remodeling. *J Mol Cell Cardiol* 2017;109(17-26

ALZET Comments: Aminopropionitrile, beta; Saline; Rat; 12 weeks; Dose (100 mg/kg/day); Controls received mp w/ vehicle; animal info (8 week old male Sprague Dawley); post op. care (analgesia by buprenorphine HCl (1 mg/kg); long-term study; enzyme inhibitor (Lysyl oxidase);.

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 $\alpha 7nAChR$ antagonist; methyllycaconitine aka MLA; Dose (nicotine 6 mg/kg/day; MLA 3 mg/kg/day);.

Q5103: J. Yang, *et al.* Alteration of RhoA Prenylation Ameliorates Cardiac and Vascular Remodeling in Spontaneously Hypertensive Rats. *Cell Physiol Biochem* 2016;39(1):229-41

ALZET Comments: Alendronate; Saline; SC; Rat; 2004; 12 weeks; Controls received mp w/ vehicle; animal info (male, spontaneously hypertensive rat or Wistar-Kyoto, 6 weeks old); pumps replaced every 4 weeks; long-term study; cardiovascular; enzyme inhibitor (farnesyl pyrophosphate synthase); bp measured using tail cuff; Dose (100 µg/kg/day);.

Q4912: C. Yamada, *et al.* The renin-angiotensin system promotes arrhythmogenic substrates and lethal arrhythmias in mice with non-ischaemic cardiomyopathy. *Cardiovasc Res* 2016;109(1):162-73

ALZET Comments: Aliskiren; SC; Mice; 12 weeks; Controls received mp w/ vehicle; animal info (male, dnNRSF-Tg, 16 weeks old); long-term study; cardiovascular; Dose (23 mg/kg/day);.

Q5098: W. Xiaojun, *et al.* Acetylated alpha-Tubulin Regulated by N-Acetyl-Seryl-Aspartyl-Lysyl-Proline(Ac-SDKP) Exerts the Anti-fibrotic Effect in Rat Lung Fibrosis Induced by Silica. *Sci Rep* 2016;6(32257

ALZET Comments: Ac-SDKP; Saline; IP; Rat; 2ML4; 4 weeks; 8 weeks; Controls received mp w/ vehicle; animal info (male, Wistar, 3 weeks old, 180g); long-term study; peptides; Dose (800 µg/kg/day);.

Q4882: A. M. Schroeder, *et al.* Cardiac Dysfunction in the BACHD Mouse Model of Huntington's Disease. *PLoS One* 2016;11(1):1-25

ALZET Comments: Isoproterenol; Saline; SC; Mice; 2001; 3 months; Controls received mp w/ vehicle; animal info (BACHD or WT, 2-3 months old); neurodegenerative (Huntington's Disease); long-term study; cardiovascular; Dose (0.24, 0.48, 0.97 mg/day);.

Q4787: Sara K.S. Bengtsson, *et al.* Long-term continuous allopregnanolone elevation causes memory decline and hippocampus shrinkage, in female wild-type B6 mice. *Horm. Behav* 2016;78):160-167

ALZET Comments: Allopregnanolone; Captisol; SC; Mice; 1004; 20 weeks; Controls received mp w/ vehicle; animal info (C57BL6J); pumps replaced every month; 60% Captisol used; post op. care (Carprofen); behavioral testing (Morris water maze); long-term study; Industry authored (Umecrine Cognition AB);.

Q7005: L. A. Mohamed, *et al.* Role of P-glycoprotein in mediating rivastigmine effect on amyloid-beta brain load and related pathology in Alzheimer's disease mouse model. *Biochim Biophys Acta* 2016;1862(4):778-787

ALZET Comments: Rivastigmine; Water, Sterile distilled; SC; Rat; 1004; 8 weeks; Dose ((0.3 mg/kg/day); Controls received mp w/ vehicle; pumps replaced every 4 weeks; long-term study; neurodegenerative (Alzheimer's);.

Q5584: A. S. Mhashilkar, *et al.* Identification of Ecdysone Hormone Receptor Agonists as a Therapeutic Approach for Treating Filarial Infections. *PLoS Negl Trop Dis* 2016;10(6):e0004772

ALZET Comments: 20-hydroxyecdysone; Ethanol; SC; Gerbil; 2006; 150 days; pumps replaced every 42 days; long-term study; Therapeutic indication (Filarial infection); Dose (5 mg/kg/day);.



Q4859: D. Matusica, *et al.* Inhibition of motor neuron death in vitro and in vivo by a p75 neurotrophin receptor intracellular domain fragment. *Journal of Cell Science* 2016;129(517-530)

ALZET Comments: Peptide, c29; SC; Mice; 1004; Controls received mp w/ vehicle; animal info (SOD G93A, 9 weeks old); pumps replaced every month until death; neurodegenerative (amyotrophic lateral sclerosis); neurodegenerative (amyotrophic lateral sclerosis); long-term study; peptides; Dose (5 mg/kg/day);.

P0776: S. Lustigman, *et al.* Identification of Ecdysone Hormone Receptor Agonists as a Therapeutic Approach for Treating Filarial Infections. *PLOS Neglected Tropical Diseases* 2016;10(6):e0004772

ALZET Comments: Ecdysone, 20-Hydroxy-; Ethanol; SC; Gerbil; 2006; 150 days; Controls received mp w/ vehicle; animal info (male gerbil); functionality of mp verified by measurement of larvae; pumps replaced every 42 days; long-term study (150 days); "To avoid the potential for trauma induced by having to carry out multiple gavages on each animal, Alzet mini-osmotic pumps (Model number 2006) were used" pg ; Disruption of larvae development to adult stage parasites; Therapeutic indication (Filarial Infections); Dose (5 mg/kg/day);.

Q5408: S. J. Liu, *et al.* Sodium selenate retards epileptogenesis in acquired epilepsy models reversing changes in protein phosphatase 2A and hyperphosphorylated tau. *Brain* 2016;139(Pt 7):1919-38

ALZET Comments: Sodium Selenate; Sodium Chloride; SC; Rat; 2004, 2006; 4 weeks, 12 weeks; Controls received mp w/ vehicle; animal info (adult male Wistar and Long-Evans rats, 12 weeks); pumps replaced after initial 6 weeks; functionality of mp verified by residual volume; neurodegenerative (Traumatic brain injury, Alzheimer's disease); behavioral testing (neurotoxicity scale (0-4) testing); long-term study; Toxicology, sodium selenate; Epilepsy model; EEG used to monitor status epilepticus; Dose (1 mg/kg/day);.

Q5848: N. Horii, *et al.* Increased Muscular 5alpha-Dihydrotestosterone in Response to Resistance Training Relates to Skeletal Muscle Mass and Glucose Metabolism in Type 2 Diabetic Rats. *PLoS One* 2016;11(11):e0165689

ALZET Comments: Dutasteride; Sesane oil; SC; Rat; 2006; 8 weeks; Controls were sedentary or health, age-matched, non-diabetic; animal info (20 weeks old); long-term study; behavioral testing (Resistance training); diabetes; enzyme inhibitor (5α-reductase inhibitor); Therapeutic indication (Type-2 Diabetes); Dose (2 mg/kg);.

Q5858: X. Guo, *et al.* VCP recruitment to mitochondria causes mitophagy impairment and neurodegeneration in models of Huntington's disease. *Nat Commun* 2016;7(12646)

ALZET Comments: TAT peptide; HV-3 peptide; SC; Mice; 8 weeks, 9 months; Controls received mp w/ control peptide; animal info (5 weeks old, 3 months old); pumps replaced every 4 weeks in 5 week old mice, replaced every month x 9 months; long-term study; peptides; Therapeutic indication (Huntington's Disease); Dose (3 mg/kg/day);.

Q4821: Daniel G. Donner, *et al.* Trenbolone Improves Cardiometabolic Risk Factors and Myocardial Tolerance to Ischemia-Reperfusion in Male Rats With Testosterone-Deficient Metabolic Syndrome. *Endocrinology* 2016;157(1):368-381

ALZET Comments: Testosterone; trenbolone; Cyclodextrin, 2-hydroxypropyl-b-; SC; Rat; 2004; 8 weeks; Controls received mp w/ vehicle; animal info (male, Wistar, 12 weeks old, 300g); functionality of mp verified by plasma; pumps replaced every 4 weeks; 45% cyclodextrin used; ischemia (cardiac); post op. care (buprenorphine 10 ug/kg/day IM; enrofloxacin 5 mg/kg ip for 3 days); long-term study; Dose (2 mg/kg/day);.

Q5309: M. M. Clancy, *et al.* Management of Osteomyelitis Caused by Salmonella Enterica Subsp. Houtenae in a Taylor's Cantil (*Agkistrodon Bilineatus Taylori*) Using Amikacin Delivered Via Osmotic Pump. *J Zoo Wildl Med* 2016;47(2):691-4

ALZET Comments: Amikacin; SC; snake; 2002; 10 months; animal info (adult female Taylor's cantil, 6 yr old); good methods; spinal cord injury; long-term study; "This study demonstrates that the infection can be suppressed and the animal's life extended by long-term continuous infusion of amikacin and that such treatment did not result in renal compromise in this individual." pg 694; Veterinary Application; temperature adjusted pumping rate for snake; Industry authored (American Association of Zoo Veterinarians); Interesting (Veterinary use presented for treating animal with antibiotics for extended duration; minimizing need for animal handling); Dose (26ug/kg/hr);.

Q5763: K. L. Chambliss, *et al.* Nonnuclear Estrogen Receptor Activation Improves Hepatic Steatosis in Female Mice. *Endocrinology* 2016;157(10):3731-3741



ALZET Comments: Estradiol, estrogen dendrimer conjugate; IP; Mice; 2006; 12 weeks, 84 days; Controls received mp w/ vehicle; animal info (5 weeks old, ovariectomy); pumps replaced every 6 weeks; long-term study; Therapeutic indication (atherosclerosis); Dose (6 ug/day);.

Q4679: X. Zhang, *et al.* Castration of male mice prevents the progression of established angiotensin II-induced abdominal aortic aneurysms. *JOURNAL OF VASCULAR SURGERY* 2015;61(767-776

ALZET Comments: Angiotensin II; SC; Mice; 1004; 3 months; Animal info (male, ApoE -/-, 2 months old, orchietomy); pumps replaced every month; long-term study; cardiovascular; peptides;.

Q4655: J. G. Yan, *et al.* CALCITONIN PUMP IMPROVES NERVE REGENERATION AFTER TRANSECTION INJURY AND REPAIR. *MUSCLE & NERVE* 2015;51(229-234

ALZET Comments: Calcitonin; Water, distilled sterile; CSF/CNS (sciatic nerve); Rat; 2006; 12 weeks; Animal info (Sprague Dawley, 250-300g, 3 months old); half-life (p.233); long-term study; "To achieve a continuous and gradual mode of delivery, a mini-osmotic pump was implanted to deliver medication at a constant 0.15 ul/h" pg 233; "Calcitonin has short absorption and elimination half-lives of 10–15 minutes and 50–80 minutes, respectively; however, using an osmotic pump allows for gradual and prolonged release." pg233; pg230 diagram of pump implantation;.

Q4190: S. Q. Xu, *et al.* C-peptide ameliorates renal injury in type 2 diabetic rats through protein kinase A-mediated inhibition of fibronectin synthesis. *Biochemical and Biophysical Research Communications* 2015;458(674-680

ALZET Comments: C-peptide; IP; Rat; 2004; 12 weeks; Controls received mp w/ saline, isotonic; animal info (male, GK, 8 weeks old); pumps replaced every 4 weeks; long-term study; cardiovascular; peptides; diabetes;.

Q4634: M. Y. Wang, *et al.* Glucagon receptor antibody completely suppresses type 1 diabetes phenotype without insulin by disrupting a novel diabetogenic pathway. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2015;112(2503-2508

ALZET Comments: Leptin, recombinant; pramlintide acetate; liraglutide; exenatide; SC; Mice (NOD); 2001; 12 weeks; Controls received mp w/ PBS; animal info (female, NOD/ShiLtJ, 8 weeks old); pumps replaced every 7 days; long-term study; diabetes;.

Q4629: B. G. Vu, *et al.* Chronic Superantigen Exposure Induces Systemic Inflammation, Elevated Bloodstream Endotoxin, and Abnormal Glucose Tolerance in Rabbits: Possible Role in Diabetes. *MBIO* 2015;6(U999-U1008

ALZET Comments: Toxic shock syndrome toxin-1; SC; Rabbit; 2006; 6 weeks; Controls received mp w/ PBS; animal info (New Zealand White); immunology; diabetes; Toxic shock syndrome toxin-1 aka TSST-1; long-term study;.

Q5287: A. E. Vendrov, *et al.* NOX4 NADPH Oxidase-Dependent Mitochondrial Oxidative Stress in Aging-Associated Cardiovascular Disease. *Antioxid Redox Signal* 2015;23(18):1389-409

ALZET Comments: MitoTEMPO; SC; mice; 1004; 12 weeks; animal info (13mo Apoe-/- mice); functionality of mp verified by ECG; long-term study; pumps replaced every 4 weeks; cardiovascular; antihypertensive; isoflurane/O2 anesthesia; Dose (1500 ug/kg/d);.

Q5032: Uli S. Herrmann, *et al.* Structure-based drug design identifies polythiophenes as antiprion compounds. *Science Translational Medicine* 2015;7(299):1-18

ALZET Comments: LIN1001I; LIN5001; LIN5002; LIN7002; PBS; CSF/CNS; Mice; 2006; 110 days; Controls received mp w/ vehicle; animal info (WT CD1 or PrP-overexpressing mice); long-term study; pumps replaced every 42 days; post op. care (Finadyne 2.5 mg/kg BID SC; Temgesic SC injection 0.1 mg/kg; Borgal 2ml 24% in drinking water); post op. care (Finadyne 2.5 mg/kg BID SC; Temgesic SC injection 0.1 mg/kg; Borgal 2ml 24% in drinking water); long-term study; Dose (3.3 mg/kg/week); brain coordinates;.

Q5578: S. E. Thatcher, *et al.* Exogenous 17-beta estradiol administration blunts progression of established angiotensin II-induced abdominal aortic aneurysms in female ovariectomized mice. *Biol Sex Differ* 2015;6(12



ALZET Comments: Angiotensin II; Mice; 1004; 3 months; Controls received mp w/ vehicle; animal info (Female low-density lipoprotein-receptor-deficient (Ldlr^{-/-}) mice on a C57BL/6 background; 2–3 months of age); functionality of mp verified by ; long-term study; pumps replaced every 4 weeks; Dose (1000 ng/kg/min);.

Q3790: C. C. Tan, *et al.* NLRP1 inflammasome is activated in patients with medial temporal lobe epilepsy and contributes to neuronal pyroptosis in amygdala kindling-induced rat model. *Journal of Neuroinflammation* 2015;12(U1-U12)

ALZET Comments: RNA, small interfering; CSF/CNS (third ventricle); Rat; 2006; 6 weeks; Control animals received mp w/ control siRNA in aCSF; animal info (Sprague Dawley, 260-300 g); long-term study;.

Q4938: M. Sun, *et al.* Cellular repressor of E1A-stimulated genes inhibits inflammation to decrease atherosclerosis in ApoE^{-/-} mice. *J Mol Cell Cardiol* 2015;86(32-41)

ALZET Comments: CREG, recombinant human; PBS; SC; Mice; 1002; 12 weeks; Controls received mp w/ vehicle; animal info (male, ApoE^{-/-}, 10 weeks old, 20-25g); long-term study; pumps replaced every 2 weeks; cardiovascular; cardiovascular; Dose (30 ug/kg/day);.

Q4587: S. R. Shultz, *et al.* Sodium selenate reduces hyperphosphorylated tau and improves outcomes after traumatic brain injury. *BRAIN* 2015;138(1297-1313)

ALZET Comments: Sodium selenate; Saline; SC; Rat; 2006; 12 weeks; Controls received mp w/ vehicle; animal info (Long Evans hooded, 12 weeks old, 250-300g); pumps replaced every 6 weeks; long-term study; traumatic brain injury;.

Q3788: C. Sagy-Bross, *et al.* The role of cytosolic phospholipase A(2)alpha in an amyloid precursor protein induction by amyloid beta(1-42): implication for neurodegeneration. *Journal of Neurochemistry* 2015;132(559-571)

ALZET Comments: Amyloid protein, beta (1-42); Hepes; CSF/CNS; Mice; 2, 4, 8 weeks; Control animal received mp w/ vehicle; animal info (male, C57BL/6); ALZET brain infusion kit 3 used; behavioral testing (Y maze test); long-term study.

Q4285: Y. Reizel, *et al.* Gender-specific postnatal demethylation and establishment of epigenetic memory. *GENES & DEVELOPMENT* 2015;29(923-933)

ALZET Comments: Testosterone; SC; Mice; 2004; 3 months; Controls received mp w/ vehicle; animal info (C57BL6, 3 or 20 weeks old); pumps replaced every 28 days; replacement therapy (testosterone replacement); long-term study; pumps primed for 48 hours in 37C saline;.

Q4566: E. Plante, *et al.* Oxytocin Treatment Prevents the Cardiomyopathy Observed in Obese Diabetic Male db/db Mice. *ENDOCRINOLOGY* 2015;156(1416-1428)

ALZET Comments: Oxytocin; NaCl; BSA; sodium citrate; SC; Mice; 2006; 12 weeks; Controls received mp w/ vehicle; animal info (C57BL/KsJ-leptdb-leptdb); functionality of mp verified by plasma levels; pumps replaced every 6 weeks; long-term study; diabetes; "After 6 weeks, the osmotic pumps were replaced to adjust the OT concentration for body weight gain." pg 1417;.

Q4007: N. Morin, *et al.* Effect of a chronic treatment with an mGlu5 receptor antagonist on brain serotonin markers in parkinsonian monkeys. *PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY* 2015;56(27-38)

ALZET Comments: MPTP; Saline; SC; Monkey (macaque); Controls received mp w/ vehicle; animal info (female, Macaca fascicularis, ovariectomized, 4.7-7.7 years old, 2.7-4.2kg); long-term study; neurodegenerative (Parkinson's disease);.

Q4530: S. E. Mennenga, *et al.* Understanding the cognitive impact of the contraceptive estrogen Ethinyl Estradiol: Tonic and cyclic administration impairs memory, and performance correlates with basal forebrain cholinergic system integrity. *PSYCHONEUROENDOCRINOLOGY* 2015;54(1-13)

ALZET Comments: Estradiol, ethinyl; Propylene glycol; SC; Rat; 2006; 6 weeks; Controls received mp w/ vehicle; animal info (female, Fischer-344, OVX, 3 months old); functionality of mp verified by serum levels; dose-response (pg8); behavioral testing (water radial-arm maze, morris water maze, visible platform task); replacement therapy (estradiol infusion); long-term study;.



Q3984: J. O. Lo, *et al.* Vitamin C supplementation ameliorates the adverse effects of nicotine on placental hemodynamics and histology in nonhuman primates. *American Journal of Obstetrics and Gynecology* 2015;212(U271-U278)

ALZET Comments: Nicotine bitartrate; Water, bacteriostatic; SC; Monkey (macaque, pregnant); 2ML4; 134 days; Controls received mp w/ vehicle; animal info (female, Rhesus, pregnant, GD26); functionality of mp verified by blood levels; pumps replaced every 3 weeks; post op. care (cefazolin 150 mg BID); long-term study; teratology; dependence;.

Q3382: M. Llorens-Martin, *et al.* Novel connection between newborn granule neurons and the hippocampal CA2 field. *Experimental Neurology* 2015;263(285-292)

ALZET Comments: Endotoxin, LPS; PBS; SC; Mice; 1004; 8 weeks; Animal info (female, 8 wks old, C57BL/6JRcc); long-term delivery; pumps replaced after 4 weeks.

Q3981: Y. J. Liu, *et al.* Activation of AMP-activated protein kinase alpha1 mediates mislocalization of TDP-43 in amyotrophic lateral sclerosis. *Human Molecular Genetics* 2015;24(787-801)

ALZET Comments: JMF1907; Saline; SC; Mice (transgenic); 18 weeks; Controls received mp w/ vehicle; animal info (B6SJL-Tg, 6 weeks old); pumps replaced every 4 weeks; neurodegenerative (Amyotrophic lateral sclerosis); no stress (see pg. 792); behavioral testing (rotarod, forelimb grip); long-term study;.

Q4489: S. H. Lee, *et al.* Podocyte hypertrophy precedes apoptosis under experimental diabetic conditions. *APOPTOSIS* 2015;20(1056-1071)

ALZET Comments: zAsp-DCB; SC; Rat; 3 months; Animal info (male, Sprague Dawley, 250-280g, 9-10 weeks old); long-term study; diabetes; enzyme inhibitor (pan-caspase);.

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;.

Q5005: R. M. Lataro, *et al.* Acetylcholinesterase Inhibition Attenuates the Development of Hypertension and Inflammation in Spontaneously Hypertensive Rats. *Am J Hypertens* 2015;28(10):1201-8

ALZET Comments: Pyridostigmine bromide; donepezil; SC; Rat; 2004; 16 weeks; animal info (male, Wistar-Kyoto or SHR); pumps replaced every 4 weeks; long-term study; cardiovascular; bp measured using tail cuff; Dose (Pyridostigmine bromide 1.5 mg/kg/day; donepezil 1.4 mg/kg/day);.

Q4487: V. Lam, *et al.* The Vitamin D, Ionised Calcium and Parathyroid Hormone Axis of Cerebral Capillary Function: Therapeutic Considerations for Vascular-Based Neurodegenerative Disorders. *PLoS One* 2015;10(U4547-U4566)

ALZET Comments: Parathyroid hormone (1-34); Saline, isosmotic; cysteine; SC; Rat; 6 weeks; 12 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 7 weeks old); functionality of mp verified by residual volume and serum levels; 2% cysteine used; replacement therapy (parathyroid replacement); used wound clips; used 2ML size pumps; pumps primed; long-term study;.

Q5214: Y. Iwasaki, *et al.* Altered material properties are responsible for bone fragility in rats with chronic kidney injury. *Bone* 2015;81(247-54)

ALZET Comments: Parathyroid hormone, rat; SC; Rat; 2002; 16 weeks; Controls received sham operation; animal info: 12-week-old male Sprague-Dawley; functionality of mp verified by urine samples; pumps replaced every 2 weeks; pumps replaced every 2 weeks; long-term study; Dose: 0.1 µg/kg/h.

Q4461: Y. Ishikawa, *et al.* A combination of keratan sulfate digestion and rehabilitation promotes anatomical plasticity after rat spinal cord injury. *NEUROSCIENCE LETTERS* 2015;593(13-18)



ALZET Comments: Keratanase II; chondroitinase ABC; Saline; CSF/CNS (intrathecal); Rat; 2006; 6 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dalwey, 200-230g); spinal cord injury; behavioral testing (single pellet reaching task); used silicone tubing; long-term study;.

Q4442: J. C. Hardwick, *et al.* Angiotensin receptors alter myocardial infarction-induced remodeling of the guinea pig cardiac plexus. AMERICAN JOURNAL OF PHYSIOLOGY-REGULATORY INTEGRATIVE AND COMPARATIVE PHYSIOLOGY 2015;309(R179-R188)

ALZET Comments: Captopril; losartan; CGP42112A; SC; Guinea pig; 2ML4; 4 weeks; 6 weeks; Animal info (male, Hartley, 9 weeks old, 500-650g); pumps replaced every 3 weeks; cardiovascular; long-term study;.

Q4440: C. B. Hamilton, *et al.* Weight-bearing asymmetry and vertical activity differences in a rat model of post-traumatic knee osteoarthritis. OSTEOARTHRITIS AND CARTILAGE 2015;23(1178-1185)

ALZET Comments: Water, distilled; SC; Rat; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 301-325g); pumps replaced every 4 weeks; post op. care (buprenorphine 50 ug/kg SC); behavioral testing (static weight bearing, exploratory motor behavior); long-term study;.

Q3866: T. B. Dschietzig, *et al.* Relaxin-2 Does Not Ameliorate Nephropathy in an Experimental Model of Type-1 Diabetes. KIDNEY & BLOOD PRESSURE RESEARCH 2015;40(77-88)

ALZET Comments: Relaxin-2; Mice; 2006; 12 weeks; Controls received mp w/ vehicle; animal info (male, eNOS, 8 weeks old); long-term study;.

Q3738: J. G. Doria, *et al.* The mGluR5 positive allosteric modulator, CDPBB, ameliorates pathology and phenotypic signs of a mouse model of Huntington's disease. NEUROBIOLOGY OF DISEASE 2015;73(163-173)

ALZET Comments: CDPBB; DMSO; SC; Mice; 2006; 18 weeks; Control animals received mp w/ vehicle; animal info (FVB/NJ, FVB/N-Tg); long-term study; CDPBB is a mGluR5 PAM, a metabotropic glutamate receptor 5 positive allosteric modulator; neurodegenerative disease (Huntington's disease).

Q4407: D. G. Donner, *et al.* Improvements in body composition, cardiometabolic risk factors and insulin sensitivity with trenbolone in normogonadic rats. STEROIDS 2015;94(60-69)

ALZET Comments: Trenbolone; Cyclodextrin, 2-hydroxypropyl-b-; water; SC; Rat; 2004; 8 weeks; Controls received mp w/ vehicle; animal info (male, Wistar, 32 weeks old, 300g); pumps replaced every 28 days; long-term study; cardiovascular;.

Q4394: C. B. de La Serre, *et al.* Chronic exposure to Low dose bacterial lipopolysaccharide inhibits leptin signaling in vagal afferent neurons. PHYSIOLOGY & BEHAVIOR 2015;139(188-194)

ALZET Comments: Endotoxin, LPS; IP; Rat; 2004; 2006; 4 weeks; 6 weeks; Controls received mp w/ saline; animal info (male, Wistar, 237g); functionality of mp verified by circulating LPS; long-term study;.

Q3842: D. Cifuentes, *et al.* Hypertension Accelerates the Progression of Alzheimer-Like Pathology in a Mouse Model of the Disease. Hypertension 2015;65(218-+)

ALZET Comments: Angiotensin II; SC; Mice; 2006; 2.5 months; Animal info (male, APPPS1 heterozygous, 7 weeks old); pumps replaced every 6 weeks; neurodegenerative (Alzheimer's disease); behavioral testing (memory test, locomotor activity); long-term study; cardiovascular; peptides; bp measured using tail cuff;.

Q4310: M. A. Assaggaf, *et al.* Prevention of Phenytoin-Induced Gingival Overgrowth by Lovastatin in Mice. AMERICAN JOURNAL OF PATHOLOGY 2015;185(1588-1599)

ALZET Comments: Phenytoin; lovastatin; Water; propylene glycol; ethanol; SC; Mice; 2002; 12 weeks; Controls received mp w/ vehicle or saline; animal info (male, BALB/cByJ, 8 weeks old); 9% ethanol used; 41% propylene glycol used; long-term study; phenytoin and lovastatin inside one pump; used autoclips; pumps primed in 37C saline overnight;.

Q3808: T. R. Aprahamian, *et al.* The immunomodulatory parasitic worm product ES-62 reduces lupus-associated accelerated atherosclerosis in a mouse model. International Journal for Parasitology 2015;45(203-207)



ALZET Comments: ES-62; PBS; Mice; 12 weeks; Controls received mp w/ vehicle; animal info (male, Gld.apoE -/-); pumps replaced every 3 weeks; long-term study; cardiovascular; immunology; ES-62 is a phosphorylcholine-containing glycoprotein;.

Q5121: C. T. Appleton, *et al.* Reduction in disease progression by inhibition of transforming growth factor alpha-CCL2 signaling in experimental posttraumatic osteoarthritis. *Arthritis Rheumatol* 2015;67(10):2691-701

ALZET Comments: AG1478; RS504393; DMSO; water, deionized; SC; Rat; 2ML4; 10 weeks; Controls received mp w/ vehicle; functionality of mp verified by plasma levels and knee articular cartilage; pumps replaced every 4 weeks; %50 of DMSO; long-term study; enzyme inhibitor (EGFR and CCR2 inhibitors); EGFR inhibitor AG1478, CCR2 inhibitor RS504393; Dose: (AG1478) 21 nmoles/kg/hour; (RS504393) 200 nmoles/kg/hour.

Q4296: I. Aharony, *et al.* A Huntingtin-based peptide inhibitor of caspase-6 provides protection from mutant Huntingtin-induced motor and behavioral deficits. *HUMAN MOLECULAR GENETICS* 2015;24(2604-2614

ALZET Comments: ED11; Saline; water, sterile; SC; Mice; 1004; 20 weeks; Controls received mp w/ vehicle; animal info (5 weeks old); animal info (5 weeks old); neurodegenerative (Huntington's disease); behavioral testing (rotarod test, forced swim test, open field test, light dark choice test); long-term study; peptides; enzyme inhibitor (caspase-6);.