

#### Recent References (2018-Present): The Rate-Controlled Modulation of Hormone Levels Using ALZET® Osmotic Pumps

This collection of references illustrates techniques by which the physiological effects of a controlled hormone infusion are determined in the absence of endogenous hormone production. In this manner, the effects that hormones have at different concentrations can be determined independent of temporal fluctuations in hormone levels. The technical notes following each reference detail the substance(s) infused, the route of administration, the animal model studied, the vehicle for infusion, the model of pump used, the duration of infusion, and notable technical achievements or results obtained.

This list does not contain references in this category from before 2016. To obtain a complete list of citations since 1975, please contact ALZET Technical Support at (800) 692-2990 or <a href="mailto:alzet@durect.com">alzet@durect.com</a>.

The inverse of this technique, or the study of the differential effects of varying regimens of pulsatile hormone administration, can be accessed through the sub-bibliography entitled "References on Pulsed Administration of Agents by ALZET Osmotic Pumps". To obtain a copy of this sub-bibliography contact ALZET Technical Support

For a more complete discussion of the capabilities of these techniques consult the following reference:

Urquhart, J., Fara, J., and Willis, K.L. (1984). Rate-controlled delivery systems in drug and hormone research. Ann. Rev. Pharmacol. Toxicol. 24, 199-236.



#### Recent References (2017-Present): The Rate-Controlled Modulation of Hormone Levels Using ALZET® Osmotic Pumps

**Q10817:** K. Kaster, et al. A Novel Assay to Assess the Effects of Estrogen on the Cardiac Calmodulin Binding Equilibrium. Life Sciences 2022;290(120247

Agents: Estradiol, 17B Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2002; Duration: 2 weeks;

**ALZET Comments:** Dose (Estradiol 30 ug/day); animal info Sprague-Dawley (9 weeks old; Female ovariectomized); replacement therapy (Estrogen);

**Q10538:** E. E. Handley, *et al.* Estrogen Enhances Dendrite Spine Function and Recovers Deficits in Neuroplasticity in the prpTDP-43(A315T) Mouse Model of Amyotrophic Lateral Sclerosis. Molecular Neurobiology 2022;59(5):2962-2976

Agents: Estradiol Vehicle: Saline; DMSO; Route: SC; Species: Mice; Pump: 2004; Duration: 60 days;

**ALZET Comments:** Dose (10 mg/ml); 50% DMSO used; Controls received mp w/ vehicle; animal info (Female; Wild-type and TDP-43; Ovariectomy); wound clips used; pumps replaced every 4 wk; replacement therapy (Estrogen); neurodegenerative (ALS)

**Q10512:** R. Das, et al. Medroxyprogesterone acetate positively modulates specific GABA(A)-receptor subtypes - affecting memory and cognition. Psychoneuroendocrinology 2022;141(105754

**Agents:** Medroxyprogesterone acetate **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 66 days; **ALZET Comments:** Dose  $(6.67 \pm 1.08 \text{ ng/ml} = 21 \text{ nM})$ ; 0.1%DMSO used; animal info (Male Sprague-Dawley rats (n = 19, weight < 130 g)Medroxyprogesterone acetate aka (MPA)replacement therapy (estradiol);

**Q10498:** M. Blanes-Garcia, et al. Using Osmotic Pumps to Induce the Production of Gametes in Male and Female European Eels. Animals (Basel) 2022;12(3):

**Agents:** Human chorionic gonadotropin, recombinant; Carp pituitary extract **Vehicle:** Saline **Route:** IP; **Species:** Eel; **Pump:** 1004; 2006; 2ML4; **Duration:** 5 weeks; 10 weeks;

**ALZET Comments:** Dose: HCG (13 IU/uL); CPE (1.05 uL); 90% saline vehicle used; animal info: European eels Male eels (mean body weight = 126.7 \_ 17.9 g), Female eels (mean body weight = 771 \_ 123.8 g)Multiple pumps per animal (3); HCG aka (Human chorionic gonadotropin); CPE aka (Carp pituitary extract); hormone replacement therapy

**Q10444:** V. N. Bailey, et al. Endocrine and ovarian responses to combined estradiol benzoate-sulpiride in seasonally anovulatory mares treated with kisspeptin. Animal Reproduction Science 2022;247(107087)

Agents: Kisspeptin-10 Vehicle: Saline; Route: SC; Species: Horse; Pump: 2ML1; Duration: 7 days;

**ALZET Comments:** Dose (50  $\mu$ g/h;); 0.9% saline used; Controls received mp w/ vehicle; animal info (18 total; Anestrous mares; Received 50 mg estradiol benzoate before pumps implanted); post op. care (Received 3 g sulpiride); peptides; replacement therapy (Estradiol infusion);

**Q10324:** Z. L. Sebo, *et al.* Testosterone metabolites differentially regulate obesogenesis and fat distribution. molecular Metabolism 2021;44(101141

**Agents:** Testosterone; Dihydrotestosterone; Estradiol; Letrozole; Bicalutamide **Vehicle:** 2-hydroxypropyl-B-cyclodextrin; PBS; DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;

**ALZET Comments:** Dose: Testosterone (2 mg/kg body weight/day); Estradiol (2 ug/kg body weight/day); Letrozole (0.4 mg/kg body weight/day); Dutasteride (0.5 mg/kg body weight/day); 10% DMSO vehicle used Controls received mp w/ vehicle; animal info: ARdY mice and mTmG mice 3 weeks of age; replacement therapy; (Testosterone)dependence;

**Q10056:** I. Peregrin-Alvarez, *et al.* Anti-Mullerian Hormone (AMH) regulates BRCA1 and BRCA2 gene expression after ovarian cortex transplantation. Gynecological Endocrinology 2021;37(4):349-352

**Agents:** Antibody, anti-Mullerian hormone **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days; **ALZET Comments:** Dose (1.23 mcg/day); Controls received mp w/ vehicle; animal info (ovariectomizeed NU/J mice or nude mice); anti-Mullerian hormone Antibody aka rAMH; replacement therapy (anti-mullerian hormone);





**Q9363:** F. Marcouiller, et al. Metabolic responses to intermittent hypoxia are regulated by sex and estradiol in mice. American Journal of Physiology Endocrinology and Metabolism 2021;320(2):E316-E325

**Agents:** 17 B-Estradiol **Vehicle:** DMSO; Propylene Glycol; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks; **ALZET Comments:** Dose (0.5 ug/day); 50% DMSO used; Controls received mp w/ vehicle; animal info (C57BL/6 mice, 2-3 months old); 17 B-Estradiol aka E2; replacement therapy (estradiol);

**Q9294:** J. O. Jansson, *et al.* A Body Weight Sensor Regulates Prepubertal Growth via the Somatotropic Axis in Male Rats. Endocrinology 2021;162(6):

Agents: Growth hormone Vehicle: Saline; Route: SC; Species: Rat; Pump: 1002; Duration: Not Stated;

**ALZET Comments:** Dose (1 ug/g); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats); Growth hormone aka GH; replacement therapy (growth hormone);

**Q9217:** D. Egli-Spichtig, *et al.* Renal Dnase1 expression is regulated by FGF23 but loss of Dnase1 does not alter renal phosphate handling. Scientific Reports 2021;11(1):6175

**Agents:** Fibroblast growth factor 23 **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 days; **ALZET Comments:** Dose (200 ng/g/day); Controls received mp w/ vehicle; animal info (9 week old Hyp mice; 6 week old Fgf23-/- mice); Fibroblast growth factor 23 aka FGF23; replacement therapy (Fibroblast growth factor);

**Q9182:** L. Chen, *et al.* Ouabain Protects Nephrogenesis in Rats Experiencing Intrauterine Growth Restriction and Partially Restores Renal Function in Adulthood. Reproductive Sciences 2021;28(1):186-196

Agents: Ouabain Vehicle: PBS, Sterile; Route: Not Stated; Species: Rat; Pump: 2004; Duration: 4 weeks;

**ALZET Comments:** Dose (10 ug/kg/day); animal info (female Sprague-Dawley rats); Blood pressure measured via tail-cuff method; replacement therapy (Ouabain);

**Q9185:** J. Chen, *et al.* Estrogen and serotonin enhance stress-induced visceral hypersensitivity in female rats by up-regulating brain-derived neurotrophic factor in spinal cord. Neurogastroenterology & Motility 2021;e14117

Agents: Alosetron Vehicle: Water; Route: Not Stated; Species: Rat; Pump: Not Stated; Duration: 14 days;

**ALZET Comments:** Animal info (Pregnant Sprague Dawley rats and female adult offspring, 5 weeks old); replacement therapy (estradiol);

**Q9879:** J. Yuan, et al. The effects of oxytocin to rectify metabolic dysfunction in obese mice are associated with increased thermogenesis. Molecular and Cellular Endocrinology 2020;514(110903

Agents: Oxytocin, synthetic Vehicle: Not stated; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;

ALZET Comments: Dose (100 nmol/d); animal info (4 week old male C57BL6/J mice); replacement therapy (oxytocin);

**Q9880:** M. Yu, et al. PTH induces bone loss via microbial-dependent expansion of intestinal TNF(+) T cells and Th17 cells. Nature Communications 2020;11(1):468

**Agents:** Human parathyroid hormone-(1-34) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks; **ALZET Comments:** Dose (80  $\mu$ g/kg/day); Controls received mp w/ vehicle; animal info (16-weeks-old female mice); Human parathyroid hormone-(1-34); aka hPTH1-34; replacement therapy (parathyroid hormone);

**Q9508:** B. Tuku, *et al.* Testosterone Protects Against Severe Influenza by Reducing the Pro-Inflammatory Cytokine Response in the Murine Lung. Frontiers in Immunology 2020;11(697

**Agents:** Testosterone **Vehicle:** "Cyclodextrin, 2-ß-Hydroxypropl-"; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 2 weeks; **ALZET Comments:** Dose (5 mg/ml); 45%% "Cyclodextrin, 2-ß-Hydroxypropl-" used; Controls received mp w/ vehicle; animal info (Six weeks old female mice); replacement therapy (testosterone);

**Q9496:** Q. Tang, et al. Sirt6 in pro-opiomelanocortin neurons controls energy metabolism by modulating leptin signaling. Molecular Metabolism 2020;37(100994

Agents: Leptin Vehicle: Saline; Route: SC; Species: Mice; Pump: 1007D; Duration: 2 days;

**ALZET Comments:** Dose (500 ng/h); Controls received mp w/ vehicle; animal info (Male mice, 6 weeks old); replacement therapy (Leptin);



**Q9492:** T. Takeda, et al. Gestational dioxin exposure suppresses prolactin-stimulated nursing in lactating dam rats to impair development of postnatal offspring. Biochemical Pharmacology 2020;178(114106

**Agents:** Prolactin **Vehicle:** Saline, sterile; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2002; **Duration:** 28 days; **ALZET Comments:** Dose (400 ng/day); Controls received mp w/ vehicle; animal info (Male (10 week-old, body weight: around 280 ~ 320 g) and female (6–7 week-old, body weight: around 160 ~ 220 g) Wistar rats); behavioral testing (Maternal Capacity Tests, Y-maze Test); ALZET brain infusion kit 2 used; Brain coordinates (antero-posterior, –1.0 mm and lateral, 1.0 mm from the bregma, and depth of 4 mm.); replacement therapy (Prolactin);

**Q9012:** J. G. Soares de Carvalho, *et al.* Administration of PGF2alpha during the periovulatory period increased fertilization rate in superovulated buffaloes. Theriogenology 2020;145(138-143

Agents: Prostaglandin F2α Vehicle: Not stated; Route: SC; Species: Buffalo; Pump: 1003D; Duration: 2 days;

**ALZET Comments:** Dose (0.833 mg/h); animal info (Crossbred Murrah x Mediterranean buffalo,  $8.5 \pm 2.2$  old); Prostaglandin F2 $\alpha$  aka PGF2 $\alpha$ ; replacement therapy (Prostaglandin F2 $\alpha$  Infusion);

**Q9443:** S. Sanchez-Bezanilla, *et al.* Growth Hormone Treatment Promotes Remote Hippocampal Plasticity after Experimental Cortical Stroke. International Journal of Molecular Sciences 2020;21(12):

**Agents:** Growth hormone, recomb. human **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days; **ALZET Comments:** Dose ((0.04 mg r-hGH per day); Controls received mp w/ vehicle; animal info (C57BL/6 mice, male, 10 weeks old); recombinant human growth hormone aka r-hGH; replacement therapy (human recombinant growth hormone);

**Q9442:** S. Sanchez-Bezanilla, *et al.* Growth Hormone Promotes Motor Function after Experimental Stroke and Enhances Recovery-Promoting Mechanisms within the Peri-Infarct Area. International Journal of Molecular Sciences 2020;21(2): **Agents:** Growth hormone, human recombinant **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days; **ALZET Comments:** Dose (0.04 mg rhGH per day); Controls received mp w/ vehicle; animal info (Male C57BL/6 mice, 10 weeks old); behavioral testing (Motor test); Recombinant human growth hormone aka rhGH; replacement therapy (growth hormone);

**Q9441:** W. Sakuma, *et al.* Antidepressant effect of BE360, a new selective estrogen receptor modulator, activated via CREB/BDNF, Bcl-2 signaling pathways in ovariectomized mice. Behavioural Brain Research 2020;393(112764 **Agents:** Estradiol, 17B-; Tamoxifen; Raloxifene; BE360 **Vehicle:** PEG 300 **Route:** SC **Species:** Mice **Pump:** 2002 **Duration:** 2 wk **ALZET Comments:** Dose (0.1 μg/day 17B-Estradiol; 1000 μg/day Tamoxifen; 1000 μg/day Raloxifene; 30 and 100 μg/day BE360); animal info (Female ddY mice (8 weeks old)); behavioral testing (Forced swimming test); 17B-Estradiol aka E2, Tamoxifen aka TAM, Raloxifene aka RAL; replacement therapy (estradiol);

**Q9414:** V. G. Piazza, et al. Exposure to growth hormone is associated with hepatic up-regulation of cPLA2alpha and COX. Molecular and Cellular Endocrinology 2020;509(110802

**Agents:** Growth hormone, porcine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 5 days; **ALZET Comments:** Dose (1 mg/kg of body weight per day); Controls received mp w/ vehicle; animal info (Adult (3–4 months old) Swiss-Webster female/male mice); Growth hormone, porcine aka GH; replacement therapy (Growth Hormone, Porcine);

**Q8646:** S. K. Mamta, et al. Controlled release of sex steroids through osmotic pump alters brain GnRH1 and catecholaminergic system dimorphically in the catfish, Clarias gariepinus. Brain Research Bulletin 2020;164(325-333

**Agents:** Estradiol, 17B-; Testosterone, 17a-methyl **Vehicle:** Ethanol; Saline; **Route:** IP; **Species:** Fish; **Pump:** 1007D; **Duration:** 21 days;

**ALZET Comments:** Dose (0.48 ug/day); Controls received mp w/ vehicle; animal info (male and female catfish); functionality of mp verified by residual volume; replacement therapy (testosterone; estradiol);

**Q8896:** K. S. Lynch, et al. Examining the disconnect between prolactin and parental care in avian brood parasites. Genes, Brain and Behaviour 2020;19(7):e12653

Agents: Prolactin ovine Vehicle: Saline; Route: SC; Species: Bird; Pump: 1007D; Duration: 7 days;

**ALZET Comments:** Dose (80 μg/day); 0.87% NaCl used; Controls received mp w/ vehicle; animal info (Female brown-headed and bronzed cowbirds); Ovine Prolactin aka Prolactin; replacement therapy (Prolactin);





**Q8591:** S. V. Koebele, et al. Characterizing the effects of tonic 17beta-estradiol administration on spatial learning and memory in the follicle-deplete middle-aged female rat. Hormones and Behavior 2020;126(104854)

Agents: Estradiol, 17-beta- Vehicle: PEG; Route: SC; Species: Rat; Pump: 2006; Duration: 6 weeks;

**ALZET Comments:** Dose (3 ug/day); Controls received mp w/ vehicle; animal info (female, virgin, Fischer-344 rats, 11 months old); 17-beta-estradiol aka E2; replacement therapy (estradiol);

**Q8584:** Z. Z. Kirshner, *et al.* Impact of estrogen receptor agonists and model of menopause on enzymes involved in brain metabolism, acetyl-CoA production and cholinergic function. Life Sciences 2020;256(117975

**Agents:** 17 B-Estradiol; 4,4',4"-(4- Propyl-[1H]-pyrazole-1,3,5-triyl) trisphenol; Diarylpropiolnitrile; G-1 **Vehicle:** DMSO; Hydroxypropyl-B-cyclodextrin; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 30 days;

**ALZET Comments:** Dose (3 ug/day 17 B-Estradiol; 5 ug/day other agonists); 10% DMSO, 20% Hydroxypropl-ß-Cyclodextrin used; Controls received mp w/ vehicle; animal info (Female Sprague–Dawley rats, 11 weeks of age); 17 B-Estradiol aka E2; 4,4',4''-(4- Propyl-[1H]-pyrazole-1,3,5-triyl) trisphenol aka PPT; Diarylpropiolnitrile aka DPN; G-1 aka GPER1 agonist; replacement therapy (estradiol);

**Q8212:** T. Iwasa, et al. The effects of chronic oxytocin administration on body weight and food intake in DHT-induced PCOS model rats. Gynecological Endocrinology 2020;36(1):55-60

Agents: Oxytocin Vehicle: Saline; Route: SC; Species: Rat; Pump: 2002; Duration: 14 days;

**ALZET Comments:** Dose (380 ug/day); Controls received mp w/ vehicle; animal info (Female Wistar rats); replacement therapy (effects of the chronic administration of oxytocin);

**Q8850:** L. Hyland, *et al.* Ghrelin infused into the dorsomedial hypothalamus of male mice increases food intake and adiposity. Physiology & Behavior 2020;220(112882

**Agents:** Ghrelin; JMV2959 **Vehicle:** Saline; **Route:** CSF/CNS (dorsomedial hypothalamus); **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (adult male C57BLJ6 mice); JMV2959 aka growth hormone secretagogue receptor antagonist; peptides; ALZET brain infusion kit used; Brain coordinates (AP 1.6 mm, ML 0.4 mm, and DV 5.25 mm); replacement therapy (Ghrelin infusion);

**Q8542:** R. Hornung, et al. Reduced activity of GAD67 expressing cells in the reticular thalamus enhance thalamic excitatory activity and varicella zoster virus associated pain. Neuroscience Letters 2020;736(135287

**Agents:** Estradiol benzoate, 17-beta- **Vehicle:** PEG; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 28 days; **ALZET Comments:** Dose (750 ng/6 ul/day); animal info (Transgenic male (300 g) and female Long Evans rats (260 g)); replacement therapy (estradiol);

**Q8208:** T. Hirayama, *et al.* Oxytocin induced labor causes region and sex-specific transient oligodendrocyte cell death in neonatal mouse brain. J Obstet Gynaecol Res 2020;46(1):66-78

Agents: Oxytocin Vehicle: Buffered Saline; Route: SC; Species: Mice; Pump: 1003D; Duration: Not stated;

**ALZET Comments:** Dose (0.6, 6, 18 or 240  $\mu$ g/day); Controls received mp w/ vehicle; animal info (Wild-type C57BL6/J mice and DBA/2 mice); replacement therapy ( associations between oxytocin induced labor and mental disorders in offspring);

**Q9245:** E. Y. Gohar, et al. Evidence for G-Protein-Coupled Estrogen Receptor as a Pronatriuretic Factor. Journal of the American Heart Association 2020;9(10):e015110

Agents: G1 Vehicle: DMSO; Route: SC; Species: Rat; Pump: 2ML4; Duration: 14 days;

**ALZET Comments:** Dose (400 ug/kg/day); 75% DMSO used; Controls received mp w/ vehicle; animal info (Male and female (16–20 weeks of age) Sprague Dawley rats); Blood pressure measured via HD- S10 transmitters;G1 aka GPER agonist; replacement therapy (estradiol);





**Q8491:** E. Y. Gohar, et al. Evidence for G-Protein-Coupled Estrogen Receptor as a Pronatriuretic Factor. J Am Heart Assoc 2020;9(10):e015110

Agents: G1 Vehicle: DMSO; Route: SC; Species: Rat; Pump: Q8491; Duration: Q8491;

**ALZET Comments:** Dose (400 ug/kg/day); 75% DMSO used; Controls received mp w/ vehicle; animal info (Male and female (16–20 weeks of age) Sprague Dawley rats); Blood pressure measured via HD- S10 transmitters;G1 aka GPER agonist; replacement therapy (estradiol);

**Q8848:** R. J. Flores, *et al.* Estradiol promotes and progesterone reduces anxiety-like behavior produced by nicotine withdrawal in female rats. Psychoneuroendocrinology 2020;119(104694

Agents: Nicotine Vehicle: Not Stated; Route: Not Stated; Species: Rat; Pump: 2ML2; Duration: 14 days;

**ALZET Comments:** Dose (3.2 mg/kg/day); animal info (Male and female Wistar rats); behavioral testing (physical signs test, Anxiety-like behavior assessments); replacement therapy (Estradiol, progesterone);

**Q9220:** G. J. Euceda, *et al.* Insulin Therapy Restores Lung Inflammatory Response to LPS-Induced Lung Injury in a Murine Model of Type 1 Diabetes. D35 Lung Injury and Repair: Cellular Mechanisms 2020;

Agents: Insulin; Humulin Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 2 weeks;

**ALZET Comments:** Dose (0.45 IU/day); Controls received mp w/ vehicle; animal info (C57BL/6CRL mice); replacement therapy (Insulin);

**Q8445:** Q. N. Dinh, et al. Aldosterone-Induced Hypertension is Sex-Dependent, Mediated by T Cells and Sensitive to GPER Activation. Cardiovascular Research 2020;

**Agents:** Aldosterone; G-1; G-15; Angiotensin II **Vehicle:** Propylene Glycol; DMSO; Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

**ALZET Comments:** Dose (0.72 mg/kg/d; 0.03 mg/kg/d; 0.3 mg/kg/d; 0.7 mg/kg/d); 87% propylene glycol used; Controls received mp w/ vehicle; animal info (C57Bl/6 (WT) mice; RAG1-deficient mice; GPER- deficient mice); Blood pressure measured via tail cuff plethysmography;G-1 aka G protein-coupled estrogen receptor 1 agonist; G-15 aka G protein-coupled estrogen receptor 1 antagonist replacement therapy (estrogen receptor);

**Q8440:** S. Dey, et al. Sex-specific brain erythropoietin regulation of mouse metabolism and hypothalamic inflammation. JCI Insight 2020;5(5):

**Agents:** Erythropoietin, recombinant human **Vehicle:** Saline; **Route:** CSF/CNS (lateral cerebral ventricle); **Species:** Mice; **Pump:** 2006; **Duration:** 14 days;

**ALZET Comments:** Dose (3000 U/kg); Controls received mp w/ vehicle; animal info (Tg21 mice); recombinant human Erythropoietin aka recombinant human EPO; ALZET brain infusion kit 3 used; Brain coordinates (midline, 1.00 mm; anteroposterior, 0.34 mm; dorsoventral, 2.30 mm); dental cement used; replacement therapy (Erythropoietin);

**Q8417:** L. Chen, et al. Ouabain Protects Nephrogenesis in Rats Experiencing Intrauterine Growth Restriction and Partially Restores Renal Function in Adulthood. Reprod Sci 2020;

Agents: Ouabain Vehicle: PBS, Sterile; Route: Not stated; Species: Rat; Pump: 2004; Duration: 4 weeks;

**ALZET Comments:** Dose (10 ug/kg/day); animal info (female Sprague-Dawley rats); Blood pressure measured via tail-cuff method; replacement therapy (Ouabain);

**Q8410:** J. R. Chen, *et al.* Nox4 Expression Is Not Required for OVX-Induced Osteoblast Senescence and Bone Loss in Mice. JBMR Plus 2020;4(8):e10376

**Agents:** Estradiol, 17B- **Vehicle:** Not stated; **Route:** Intraovarian; **Species:** Mice; **Pump:** Not stated; **Duration:** 8 weeks; **ALZET Comments:** Dose (20 ug/kg/day); animal info (Six-month-old WT C57Bl6 mice); 17B-Estradiol aka E2; replacement therapy (estradiol);



**Q7642:** W. Yan, *et al.* Treatment with a brain-selective prodrug of 17beta-estradiol improves cognitive function in Alzheimer's disease mice by regulating klf5-NF-kappaB pathway. Naunyn-Schmiedeberg's Archives of Pharmacology 2019;392(7):879-886 **Agents:** dihydroxyestra-1,4-dien-3-one,  $10\beta$ ,17 $\beta$ - **Vehicle:** propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 8 weeks;

**ALZET Comments:** Dose (2  $\mu$ g/day); Controls received sham surgery and mp w/ vehicle; animal info (6 months, female, Tg2576); behavioral testing (Morris Water Maze); pumps replaced every 4 weeks; 17beta-dihydroxyestra-1,4-diene-3-one (DHED) is a brain-selective prodrug of 17beta-estradiol; neurodegenerative (Alzheimer's); replacement therapy (estradiol); treatment groups received bilateral ovariectomies; Therapeutic indication (hinder the progression of AD and improving cognitive functions through inhibiting klf5-NF- $\kappa$ B pathway and restraining oxidative and inflammatory stress in the hippocampus);

**Q7663:** G. Shetty, *et al.* Effect of hormone modulations on donor-derived spermatogenesis or colonization after syngeneic and xenotransplantation in mice. Anesthesia & Analgesia 2019;7(2):257-265

**Agents:** Follicle stimulating hormone, recomb. human **Vehicle:** Not Stated **Route:** SC **Species:** Mice **Pump:** 2002 **Duration:** 2 weeks

**ALZET Comments:** Dose (5 IU/day); Controls received sham surgery; animal info (7-9 weeks, male, C57BL/6Law and nude); replacement therapy (FSH);

**Q7419:** T. Sato, *et al.* Disrupted tubular parathyroid hormone/parathyroid hormone receptor signaling and damaged tubular cell viability possibly trigger postsurgical kidney injury in patients with advanced hyperparathyroidism. Clinical Kidney Journal: Clinical and Translational Nephrology 2019;

Agents: Parathyroid Hormone, 1-34 Vehicle: Vehicle not stated; Route: SC; Species: Rat; Pump: 2002;

**ALZET Comments:** "Dose (0.1 mg/kg/h); animal info (13-week-old male Sprague Dawley rats weighing 350 g); replacement therapy (parathyroidectomy); "

**Q7424:** E. Noirrit, et al. Effects of conjugated estrogen and bazedoxifene on hemostasis and thrombosis in mice. Endocrine Connections 2019:

**Agents:** Estrogen, conjugated; Bazedoxifene **Vehicle:** Cyclodextrin, hydroxypropyl-beta; HEPES buffer; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 weeks;

**ALZET Comments:** Dose (BZA (10 mg/kg/day), CE (3 mg/kg/day)); animal info (Female C57BL/6J mice 4 weeks old); replacement therapy (ovariectomized);

**Q7613:** N. Nishizawa, *et al.* A new class of pentapeptide KISS1 receptor agonists with hypothalamic-pituitary-gonadal axis activation. Bioorganic & Medicinal Chemistry Letters 2019;29(4):654-658

Agents: 4-pyridyl analog Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 6 days;

**ALZET Comments:** Dose (5, 10, or 20 nmol/hr); Controls received mp w/ vehicle; animal info (9 week old, Male); replacement therapy (Testosterone);

**Q7566:** Y. Nagata, et al. Attenuated Dentin Matrix Protein 1 Enhances Fibroblast Growth Factor 23 in Calvaria in a Primary Hyperparathyroidism Model. Endocrinology 2019;160(5):1348-1358

**Agents:** Pituitary Growth Hormone 1-34, Human **Vehicle:** aminocaproic acid, 6-; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 21 days;

**ALZET Comments:** Dose (25 ug/kg/day); Controls received mp w/ vehicle; animal info (C57BL/6J, FVB/N, 75-96 weeks old); replacement therapy (parathyroidectomy); dependence;

**Q7377:** N. Morozumi, *et al.* ASB20123: A novel C-type natriuretic peptide derivative for treatment of growth failure and dwarfism. PLoS One 2019;14(2):e0212680

**Agents:** ASB20123 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 week, 12 weeks; **ALZET Comments:** Dose (0.05, 0.15 mg/kg/day); dose-response (fig 5); Controls received mp w/ vehicle; animal info (Seven-week male SD rats); comparison of injections vs mp "We also analyzed whether continuous sc infusion of ASB20123 to rats could accelerate skeletal growth, compared to the effects of multiple sc bolus injections"; long-term study; ASB20123 is a CNP/ghrelin chimeric peptide, composed of CNP(1-22) & human ghrelin (12-28, E17D); peptides; replacement therapy (dwarf)





**Q9360:** J. Mao, *et al.* Interleukin-1alpha leads to growth hormone deficiency in adamantinomatous craniopharyngioma by targeting pericytes: implication in pituitary fibrosis. Metabolism Clinical and Experimental 2019;101(153998

**Agents:** Recomb. IL-1R1a **Vehicle:** PBS; **Route:** CSF/CNS (cranium); **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days; **ALZET Comments:** Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Male Sprague–Dawley rats (weight, 135 ± 5 g)); Recombinant IL-1R1a aka rrIL-1α; Brain coordinates (4 mm posterior to the bregma and 1.4 mm lateral to the midline); dental cement used; replacement therapy (antifibrotic drugs and anti-inflammatory drugs for growth hormone function);

**Q7576:** Y. Lu, *et al.* Neuron-Derived Estrogen Regulates Synaptic Plasticity and Memory. J Neurosci 2019;39(15):2792-2809 **Agents:** Estradiol, 17 beta- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days; **ALZET Comments:** Dose (0.0167mg); Controls received mp w/ placebo; animal info (Chimera male); replacement therapy (ovariectomy);

**Q7537:** J. Y. Li, et al. IL-17 Receptor Signaling in Osteoblasts/Osteocytes Mediates PTH-Induced Bone Loss and Enhances Osteocytic RANKL Production. J Bone Miner Res 2019;34(2):349-360

**Agents:** Parathyroid Hormone 1-34, human **Vehicle:** Not Stated **Route:** Not Stated **Species:** Mice **Pump:** 1002 **Duration:** 2 wk **ALZET Comments:** Dose (80 ug/kg/day); Controls received mp w/ vehicle; animal info (16-week-old female IL-17RADOCY mice); replacement therapy (hyperparathyroidism);

**Q7976:** O. S. Dallner, et al. Dysregulation of a long noncoding RNA reduces leptin leading to a leptin-responsive form of obesity. Nat Med 2019;25(3):507-516

Agents: Leptin Vehicle: PBS; Route: SC; Species: Mice; Pump: Not stated; Duration: 14 days;

**ALZET Comments:** Dose (0.5 μg/h); Controls received mp w/ vehicle; animal info (12 weeks, female, C57BL/J6 Lep(ob))/Lep(ob)); replacement therapy (leptin);

**Q8341:** N. Aydogdu, *et al.* The Effects of Irisin on Nomega-Nitro-L-arginine Methyl Ester Hydrochloride-Induced Hypertension in Rats. Balkan Med J 2019;36(6):337-346

Agents: Irisin Vehicle: Saline; Route: IV; Species: Rat; Pump: 2ML2; Duration: 2 weeks;

**ALZET Comments:** Dose (50 nmol/day); Controls received mp w/ vehicle; animal info (adult male, 330-390 g, Sprague Dawley rats); Blood pressure measured via tail cuff method; replacement therapy (Irisin);

**Q7651:** H. Zhao, et al. Chemokine-like receptor 1 deficiency leads to lower bone mass in male mice. Cellular and Molecular Life Sciences 2018;76(2):355-367

**Agents:** dihydrotestosterone, 5alpha-; ethyltrimethylammonium iodide, 2-(alpha-naphthoyl)- **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;

**ALZET Comments:** Dose ((DHT 83.3  $\mu$ g/day), (alpha-NETA 33  $\mu$ g/day)); Controls received empty mp; animal info (8 or 10 weeks, male, C57BL/6 or CMKLR1-/-); DHT is a nonaromatizable androgen. Alpha-NETA is a small molecule reported to function as a CMKLR1 antagonist; replacement therapy (testosterone);

**Q7327:** K. Yukata, *et al.* Continuous infusion of PTH1-34 delayed fracture healing in mice. Sci Rep 2018;8(1):13175 **Agents:** Parathyroid hormone 1-34 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 2 weeks; **ALZET Comments:** Dose (40μg/kg/day); Controls received mp w/ vehicle; animal info (8 week old, male, C57BL/6J); replacement therapy (parathyroid hormone);

**Q8979:** R. Yang, *et al.* A glucose-responsive insulin therapy protects animals against hypoglycemia. JCI Insight 2018;3(1): **Agents:** Insulin, glucose-responsive; Insulin, recomb. human **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

**ALZET Comments:** Dose ((GRI1 340 nmol/kg/day), (RHI 60 nmol/kg/day)); Controls received mp w/ vehicle; animal info (male, C57BL/6); comparison of SC injection vs mp; glucose-responsive insulin aka GRI is glycosylated insulin that has been conjugated to maltose and polymerized with concanavalin A; replacement therapy (insulin); diabetes; vehicle used, but identity not stated;





**Q8977:** T. Yamauchi, *et al.* Na(+)-Cl(-) cotransporter-mediated chloride uptake contributes to hypertension and renal damage in aldosterone-infused rats. American Journal of Physiology Renal Physiology 2018;315(2):F300-F312

**Agents:** Aldosterone **Vehicle:** Water, Distilled, DMSO buffered; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 weeks; **ALZET Comments:** Dose (); Controls received sham surgery and mp w/ vehicle; animal info (8 weeks, male, Sprague-Dawley, 290-320g); replacement therapy (aldosterone); aldosterone dosage and pump model not stated in article;

**Q8975:** B. Xue, *et al.* Sex differences in maternal gestational hypertension-induced sensitization of angiotensin II hypertension in rat offspring: the protective effect of estrogen. American Journal of Physiology Regulatory Integrative and Comparative Physiology 2018;314(2):R274-R281

Agents: Angiotensin II Vehicle: Saline; Route: SC; Species: Rat; Pump: 2002; 2004; Duration: 2 weeks;

**ALZET Comments:** Dose (120, 250 ng/kg/min); Controls received mp w/ vehicle; animal info (10 weeks, male and female, Sprague-Dawley); replacement therapy (estradiol); cardiovascular; stress/adverse reaction: ("Out of a total 94 offspring studied, there were 10 animals that did not show any changes in BP after infusion of ANG II. We could not identify whether it was because the animals had no response to ANG II or whether it was due to osmotic pump failure." see pg.R275); model 2002 used to deliver 120 ng/kg/min AngII and model 2004 used to deliver 250 ng/kg/min;

**Q8828:** J. Xu, et al. Genetic identification of leptin neural circuits in energy and glucose homeostases. Nature 2018;556(7702):505-509

**Agents:** Leptin **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days; **ALZET Comments:** Dose (454 ng/μl); Controls received mp w/ vehicle; animal info (4-8 weeks, Agrp-IRES-cre and Agrp-IRES-cre::LSL-Cas9-GFP); comparison of IP injection vs mp; Brain coordinates (AP: –0.50mm, ML:±1.3mm, DV: –2.3mm); replacement therapy (leptin);

**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.);

**Q7873:** T. D. Tremaine, *et al.* Immunolocalization of angiogenic growth factors in the ovine uterus during the oestrus cycle and in response to Steroids. Reprod Domest Anim 2018;53(3):667-679

**Agents:** Buserelin acetate **Vehicle:** Saline; **Route:** SC; **Species:** Sheep; **Pump:** Not stated; **Duration:** 18 days; **ALZET Comments:** Dose (1mg/ml at 2.5 μl/hr); Controls received mp w/ agent; animal info (female, Welsh mountain); Buserelin acetate is a gonadotrophin agonist; replacement therapy (oestradiol); Buserelin used to remove the effect of endogenous gonadotrophins, luteinizing hormone and follicle stimulating hormone;

**Q7302:** R. Scott, *et al.* Oxyntomodulin analogue increases energy expenditure via the glucagon receptor. Peptides 2018;104(70-77

**Agents:** Exendin (9-39), Oxyntomodulin analogue **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days; **ALZET Comments:** Dose (100 nmol/kg/hr Ex9-39); (40 nmol/kg OX-SR); Controls received mp w/ vehicle; animal info (Male, Wistar, 222g mean); replacement therapy (Oxyntomodulin);

**Q7849:** Y. Ravussin, et al. Evidence for a Non-leptin System that Defends against Weight Gain in Overfeeding. Cell Metabolism 2018;28(2):289-299 e5

**Agents:** leptin, recomb. mouse **Vehicle:** Saline, buffered; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 33 days; **ALZET Comments:** Dose (150 ng/hr); saline (pH 8) used; Controls were WT and received mp w/ agent; animal info (4 weeks, male, C57BL/6J(Lepob/ob)); Resultant plasma level (1.8 ± 1.4 ng/mL); replacement therapy (leptin); good methods (detailed pump placement on page e3);





**R0393:** C. Physiology. Mechanisms of Sex Disparities in Cardiovascular Function and Remodeling. Compr Physiol 2018;9(1):375-411

Agents: Estradiol; Estrogen-dendrimer conjugate Vehicle: Not Stated; Route: Not Stated; Species: Not Stated; Pump: Not

Stated; Duration: 2 weeks;

ALZET Comments: ischemia (placental); replacement therapy (ovariectomy);

**Q7771:** W. H. Liao, *et al.* Aldosterone deficiency in mice burdens respiration and accentuates diet-induced hyperinsulinemia and obesity. JCI Insight 2018;3(14):

**Agents:** aldosterone **Vehicle:** CSF, artificial; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks; **ALZET Comments:** Dose (25 ng/h); Controls received mp w/ vehicle; animal info (10-12 weeks, 129SvEv or ASKO); ALZET brain infusion kit 2 used; Brain coordinates (anterior-posterior –0.220, medial-lateral +1.000, dorsal-ventral –3.000); Cannula placement verified via stereotaxic frame and at sacrifice; cyanoacrylate adhesive; replacement therapy (aldosterone); Therapeutic indication (aldosterone attenuated high fat diet-induced hyperinsulinemia through increased body energetic efficiency.);

**Q7912:** N. Hoa, et al. Estrogen receptor beta maintains expression of KLF15 to prevent cardiac myocyte hypertrophy in female rodents. Mol Cell Endocrinol 2018;470(240-250

Agents: Angiotensin II; LGND2, beta- Vehicle: Saline; Route: SC; Species: Mice (ovariectomized);

**ALZET Comments:** Dose ((AnglI 0.7 mg/kg/day), (beta-LGND2 0.5mg in 100  $\mu$ I)); Controls received mp w/ vehicle; animal info (10 weeks, female, C57/BJ6); beta-LGND2 is a highly specific ERbeta agonist,; replacement therapy (estradiol); cardiovascular; "In some mice, an E2 pellet (0.1 mg, 21-day release pellets, Innovative Research of America, Sarasota, Florida) was inserted under the skin and these mice did not receive beta-LGND2." p.241;

**Q7754:** D. Hirohama, et al. Aldosterone Is Essential for Angiotensin II-Induced Upregulation of Pendrin. J Am Soc Nephrol 2018;29(1):57-68

**Agents:** Angiotensin II; Aldosterone; Dexamethasone **Vehicle:** Not Stated **Route:** SC **Species:** Mice **Pump:** 2002 **Duration:** 7d **ALZET Comments:** Dose ((AnglI 400 μg/kg/day), (aldosterone 0.1μg/day), (dexamethasone 12 μg/kg/day)); Controls received mp w/ vehicle; animal info (8-14 weeks, male, C57BL/6J or PDS-/-); replacement therapy (aldosterone, dexamethasone; adrenalectomy); Vehicle used but identity not stated. All minipumps contained dexamethasone for glucocorticoid replacement;

**Q7819:** I. Gonzalez-Garcia, et al. Estradiol Regulates Energy Balance by Ameliorating Hypothalamic Ceramide-Induced ER Stress. Cell Reports 2018;25(2):413-423 e5

**Agents:** myriocin; tauroursodeoxycholic acid **Vehicle:** Saline; DMSO, buffered; PBS; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;

**ALZET Comments:** "Dose ((myriocin 4 μg/day), (TUDCA 10 μg/day)); saline containing 1/3 of DMSO, or PBS alone was used; Controls received sham surgery and mp w/ vehicle; animal info (female, Sprague-Dawley, 250-300g); myriocin is a serine palmitoyltransferase inhibitor. TUDCA is a chemical chaperone; Brain coordinates (1.6 mm lateral to bregma, 0.6 mm posterior, 4.5 mm deep); Cannula placement verified via stereotaxic frame; replacement therapy (estradiol); Therapeutic indication (both TUDCA and myriocin induced (in OVX rats) feeding-independent weight loss, decreased hypothalamic ER stress, a trend to increase body temperature, elevated BAT temperature and UCP1 protein levels in BAT.); "

**Q7818:** L. Gonzalez, et al. Angiotensin-(1-9) reduces cardiovascular and renal inflammation in experimental renin-independent hypertension. Biochemical Pharmacology 2018;156(357-370

**Agents:** angiotensin (1-9) **Vehicle:** Not stated; **Route:** IV (jugular); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days; **ALZET Comments:** Dose ((Ang(1-9) 600 ng/kg/min), (PD123319 28 ng/kg/min), (A779 100 ng/kg/min)); Controls received sham surgery and mp w/ vehicle; animal info (male, Sprague-Dawley, 150+/-10g); PD123319 is an AT2R blocker. A779 is a Mas receptor blocker; replacement therapy (Uninephrectomized); cardiovascular; vehicle used but identity not stated.; Therapeutic indication (Ang-(1-9) protects against hypertensive cardiovascular and kidney damage induced by volume overload by decreasing inflammation in the heart, aortic wall, and kidney; these effects are not mediated by the Mas or AT2 receptor.);









**Q7816:** X. Ge, *et al.* LEAP2 Is an Endogenous Antagonist of the Ghrelin Receptor. Cell Metabolism 2018;27(2):461-469 e6 **Agents:** Ghrelin, recombinant rat **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 17 days; **ALZET Comments:** Dose (0.5 μg/hr); Controls received standard diet and mp w/ vehicle; animal info (2-3 months, male, C57BL/6); replacement therapy (); pumps implanted 3 days prior to caloric restriction. "mice implanted with vehicle pumps failed to maintain viable glucose levels, and the entire group had to be euthanized on day 12." (p.467);

**Q7812:** M. B. Fluitt, *et al.* Chronic Insulin Infusion Down-Regulates Circulating and Urinary Nitric Oxide (NO) Levels Despite Molecular Changes in the Kidney Predicting Greater Endothelial NO Synthase Activity in Mice. Int J Mol Sci 2018;19(10): **Agents:** insulin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

**ALZET Comments:** Dose (50 U/kg/d); Controls received mp w/ vehicle; animal info (4-7 months, male, TALLYHO/Jng); replacement therapy (insulin); "Systolic BP was significantly higher in the insulin-infused mice during the early time period of infusion; however this arose primarily due to the fact that systolic BP levels tended to fall in vehicle-infused mice. We do not fully understand this response, but it may reflect recovery from the surgeries to implant the radiotelemetry transmitter and osmotic pumps." p.8;

**Q7798:** E. A. de Los Rios, *et al.* Impaired prolactin actions mediate altered offspring metabolism induced by maternal high-fat feeding during lactation. FASEB J 2018;32(6):3457-3470

**Agents:** prolactin, ovine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (lactating); **Pump:** Not Stated; **Duration:** 17 days; **ALZET Comments:** Dose (0.16 mg/kg/d); Controls received sham surgery; animal info (female, Sprague-Dawley, 300-350g); comparison of oral administration of PRL in pups vs mp; replacement therapy (prolactin); pump model not stated although listed as a 28-day rate. pumps implanted from d4 to d21 of lactation.;