



**Recent References (2016-2019) on Diabetes Research  
Using ALZET® Osmotic Pumps**

**Q7159:** X. J. Yu, *et al.* Chronic Intracerebroventricular Infusion of Metformin Inhibits Salt-Sensitive Hypertension via Attenuation of Oxidative Stress and Neurohormonal Excitation in Rat Paraventricular Nucleus. *Neurosci Bull* 2019;35(1):57-66

**ALZET Comments:** Metformin; CSF, artificial; CSF/CNS (lateral ventricle); Rat; 2006; Dose (25 µg/day); animal info (Eight-week-old male Dahl salt-sensitive rats); Brain coordinates (0.5 mm posterior to bregma, 1.5 mm lateral to the midline, and 2.7 mm below the skull surface); diabetes;

**Q6987:** J. Zhou, *et al.* Activation of brown adipocytes by placental growth factor. *Biochem Biophys Res Commun* 2018;504(2):470-477

**ALZET Comments:** Placenta Growth Factor; SC; Mice; 6 weeks; Controls received mp w/ vehicle; animal info (8-week old Diabetic db mice);.

**Q7041:** J. Yin, *et al.* Apelin inhibited epithelial-mesenchymal transition of podocytes in diabetic mice through downregulating immunoproteasome subunits beta5i. *Cell Death Dis* 2018;9(10):1031

**ALZET Comments:** Apelin-13, F13A; Saline; IP; Mice; 1004; 4 weeks; Dose (Apelin-13 at 30 µg/kg/d and F13A at 25 µg/kg/d); Controls received mp w/ vehicle; animal info (8-week old Male kK<sub>AY</sub> mice and control C57BL/6J mice); F13A is an Apelin-13 antagonist; diabetes;

**Q7157:** S. Tauscher, *et al.* beta Cell-specific deletion of guanylyl cyclase A, the receptor for atrial natriuretic peptide, accelerates obesity-induced glucose intolerance in mice. *Cardiovasc Diabetol* 2018;17(1):103

**ALZET Comments:** B-type natriuretic peptide; Saline; SC; Mice; 1007D; 7 days; Dose (2 ng/h/g); Controls received mp w/ vehicle; diabetes;

**Q6958:** C. L. Montgomery, *et al.* Mechanisms Underlying Early-Stage Changes in Visual Performance and Retina Function After Experimental Induction of Sustained Dyslipidemia. *Neurochem Res* 2018;43(8):1500-1510

**ALZET Comments:** Poloxamer 407; Saline; SC; IP; Mice; 2004; 1 month; Controls received mp w/ vehicle; animal info (C57BL/6Crl mice); IP delivery via a cannula connected to SC pump; functionality of mp verified by total cholesterol and true triglyceride plasma concentrations; "To more easily maintain a sustained atherogenic plasma lipid profile without the increased stress and risk of animal loss associated with repeated intraperitoneal injections, we employed implantable osmotic pumps to continuously deliver P-407 at a defined rate to mice for 1 month. " pg. 1502; Therapeutic indication (Diabetic retinopathy);.

**Q7234:** M. Mizuno, *et al.* Empagliflozin normalizes the size and number of mitochondria and prevents reduction in mitochondrial size after myocardial infarction in diabetic hearts. *Physiol Rep* 2018;6(12):e13741

**ALZET Comments:** Empagliflozin; DMSO, PEG; SC; Rat; 2 weeks; Dose (10 mg/kg per day); DMSO:PEG, 50:50 used; Controls received mp w/ vehicle; animal info (25–30 weeks); diabetes; .

**Q6960:** J. Miao, *et al.* Resistin inhibits neuronal autophagy through Toll-like receptor 4. *J Endocrinol* 2018;238(1):77-89

**ALZET Comments:** Resistin; CSF/CNS (lateral ventricle); Mice; 2002; 3 days; Dose (1.2 µg/12 µL/day); Controls received mp w/ vehicle; animal info (male C57BL6J mice (27–32 g) and TLR-4-knockout mice); Obesity and diabetes;

**Q7021:** H. Hvid, *et al.* Activation of insulin receptors and IGF-1 receptors in COLO-205 colon cancer xenografts by insulin and insulin analogue X10 does not enhance growth under normo- or hypoglycaemic conditions. *Diabetologia* 2018;61(11):2447-2457

**ALZET Comments:** Insulin, human; X10; SC; Mice (nude); Dose (insulin at 27 nmol/kg/d; X10 at 41 nmol/kg/d); Controls received mp w/ vehicle; animal info (male BALB/c nude mice); X10 is an insulin analog; cancer (colon); diabetes;

**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);.

**Q7126:** A. A. da Silva, *et al.* Control of appetite, blood glucose, and blood pressure during melanocortin-4 receptor activation in normoglycemic and diabetic NPY-deficient mice. *Am J Physiol Regul Integr Comp Physiol* 2018;314(4):R533-R539

**ALZET Comments:** Melanotan II; Saline; CSF/CNS (left lateral ventricle); Mice; 1007D; 7 days; Dose (200 ug/kg/day); Controls received mp w/ vehicle; animal info (male, 20-24 week old); antagonist aka melanocortin 3/4; diabetes;.

**Q7119:** S. Clotet-Freixas, *et al.* Sex dimorphism in ANGII-mediated crosstalk between ACE2 and ACE in diabetic nephropathy. *Lab Invest* 2018;98(9):1237-1249

**ALZET Comments:** Angiotensin II; Saline; SC; Mice; 1004; 28 days; Dose (1.44 ug/day/g); 0.9% sodium chloride used; animal info (10 week old, female and male, C57BL/6); diabetes; .

**Q7088:** N. C. Boisvert, *et al.* Hyperfiltration in ubiquitin C-terminal hydrolase L1-deleted mice. *Clin Sci (Lond)* 2018;132(13):1453-1470

**ALZET Comments:** Insulin (Humulin R); Saline; SC; Mice; 1002; 14 days; Dose (8.33 umol/ml); Controls received mp w/ vehicle; animal info (Uchl1-/-mice, 9-11-week-old, male); diabetes;.

**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);.

**Q5904:** A. Vinue, *et al.* The GLP-1 analogue lixisenatide decreases atherosclerosis in insulin-resistant mice by modulating macrophage phenotype. *Diabetologia* 2017;60(9):1801-1812

**ALZET Comments:** Lixisenatide; liraglutide; SC; Mice; 2004; 1 month; Controls received mp w/ vehicle; Controls received mp w/ vehicle; cardiovascular; immunology; peptides; diabetes; Bp measured using tail cuff; Dose (liraglutide 400 ug/kg/day; lixisenatide 10 ug/kg/day);.

**Q5997:** K. M. Thrailkill, *et al.* The impact of SGLT2 inhibitors, compared with insulin, on diabetic bone disease in a mouse model of type 1 diabetes. *Bone* 2017;94(141-151

**ALZET Comments:** Insulin (Humulin R); SC; Mice; 9 weeks; Controls were untreated diabetic mice; animal info (12 weeks); functionality of mp verified by insulin serum levels using a mouse ultrasensitive insulin ELISA; Does not indicate replacement; diabetes; 145Therapeutic indication (Diabetes); Dose (0.125 units/day);.

**Q6508:** C. Taveau, *et al.* Acute and chronic hyperglycemic effects of vasopressin in normal rats: involvement of V1A receptors. *Am J Physiol Endocrinol Metab* 2017;312(3):E127-E135

**ALZET Comments:** Vasopressin; IP; Rat; 2006; 4 weeks; Dose (500 ng/kg/day); animal info (Eight-week-old male Sprague-Dawley and lean Zucker rats); Vasopressin aka AVP; diabetes;.

**Q6184:** M. Szokol, *et al.* Long Term Osmotic Mini Pump Treatment with Alpha-MSH Improves Myocardial Function in Zucker Diabetic Fatty Rats. *Molecules* 2017;22(10):

**ALZET Comments:** Melanocyte-stimulating hormone, alpha; Saline; SC; Rat; 2006; 6 weeks; Dose (0.72 ug /h); Controls received mp w/ vehicle; animal info (Zucker Diabetic Fatty rats); diabetes;.

**Q6119:** Y. C. Shi, *et al.* Y5 receptor signalling counteracts the anorectic effects of PYY3-36 in diet-induced obese mice. *J Neuroendocrinol* 2017;29(10):



**ALZET Comments:** Peptide YY (3-36); Disodium hydrogen phosphate, NaCl, Tween 80; SC; Mice; 2004; 21 days; animal info (diet-induced obese wild-type, Y5R knockout); stability verified by (Peptide YY “was stable and functional over the period of the experiment”); Obesity and diabetes;.

**Q6762:** X. Ruiz-Herrera, *et al.* Prolactin Promotes Adipose Tissue Fitness and Insulin Sensitivity in Obese Males. *Endocrinology* 2017;158(1):56-68

**ALZET Comments:** Prolactin, ovine; SC; Rat; 28 days; Dose (0.16 mg/kg /d); Controls received mp w/ vehicle; animal info (Male Wistar rats); diabetes; “...the pumps were implanted sc in less than 2 minutes.” (P.57).

**Q6130:** Z. S. Roberts, *et al.* Chronic hindbrain administration of oxytocin is sufficient to elicit weight loss in diet-induced obese rats. *Am J Physiol Regul Integr Comp Physiol* 2017;313(4):R357-R371

**ALZET Comments:** Oxytocin; Saline; CSF/CNS (Third and fourth ventricle); Rats, Mice; 2004; 28 days; Dose (16 nmol/day); Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley (CD 1GS) rats, Long-Evans rats, C57BL/6J mice); post op. care (Mice were treated with analgesic ketoprofen and antibiotic Baytril; Rats treated with analgesic buprenorphine sustained release and the antibiotic enrofloxacin after cannulations); delayed delivery (implanted cannula and vinyl catheter were filled with sterile saline then a stainless steel 22-gauge pin plug was inserted at the end of the tubing during a 2-wk postoperative recovery period); Obesity and diabetes;.

**Q5796:** H. Qi. Glomerular Endothelial Mitochondrial Dysfunction Is Essential and Characteristic of Diabetic Kidney Disease Susceptibility. *Diabetes* 2017;66(3):763-778

**ALZET Comments:** MitoTEMPO, BQ-123; Saline; SC; Mice; 2002; MitoTEMPO, BQ-123 Controls received mp w/ vehicle; animal info (8 weeks old) diabetes; mitoTEMPO is a mitochondrial targeted potent antioxidant; BQ-123 is a peptide antagonist, which specifically inhibits the binding of Edn1 ligand to Ednra receptor; Therapeutic indication (Diabetes); Dose (1 mg/kg/day, BQ: 0.1 ng/kg/day);.

**Q6338:** D. Premilovac, *et al.* A New Method for Targeted and Sustained Induction of Type 2 Diabetes in Rodents. *Sci Rep* 2017;7(1):14158

**ALZET Comments:** Streptozotocin; Saline, citrate buffered; SC; Rat; 2ML2; 14 days; Dose (2.4–6 mg/day); Controls received mp w/ vehicle; animal info (Male Sprague Dawley rats aged 14–16 weeks); diabetes;.

**Q5820:** R. J. Perry, *et al.* Mechanism for leptin's acute insulin-independent effect to reverse diabetic ketoacidosis. *J Clin Invest* 2017;127(2):657-669

**ALZET Comments:** Leptin; Saline; SC; Mice; 1004; 2 weeks, 14 days; Controls received mp w/ vehicle; animal info (8 weeks old); diabetes; Therapeutic indication (diabetic ketoacidosis); Dose (0.624 ug/hr);.

**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;.

**Q6197:** S. Muratsubaki, *et al.* Suppressed autophagic response underlies augmentation of renal ischemia/reperfusion injury by type 2 diabetes. *Sci Rep* 2017;7(1):5311

**ALZET Comments:** Chloroquine; SC; Mice; 1 week; Dose (10 mg/kg/day); animal info (Male LETO and OLETF at ages of 25–30 weeks); diabetes; Therapeutic indication (acute kidney injury);.

**Q6199:** E. P. Mottillo, *et al.* FGF21 does not require adipocyte AMP-activated protein kinase (AMPK) or the phosphorylation of acetyl-CoA carboxylase (ACC) to mediate improvements in whole-body glucose homeostasis. *Mol Metab* 2017;6(6):471-481

**ALZET Comments:** Fibroblast growth factor-21; Saline; SC; Mice (knockout); 1002; 2 weeks; Dose (0.35 mg/kg/day); Controls received mp w/ vehicle; animal info (Mice lacking adipocyte AMPK b1b2 (ib1b2AKO); diabetes;.



**Q6350:** S. M. Morris, Jr., *et al.* Distinct roles of arginases 1 and 2 in diabetic nephropathy. *Am J Physiol Renal Physiol* 2017;313(4):F899-F905

**ALZET Comments:** Cysteine, S-(2-boronoethyl)-L-; PBS; SC; Mice (knockout); 12 weeks; Dose (2.3 mg•kg<sup>-1</sup>•day<sup>-1</sup>); Controls received mp w/ vehicle; animal info (6-wk-old male arginase-2-deficient (Arg2<sup>-/-</sup>) mice); enzyme inhibitor (arginase); Therapeutic indication (diabetes);

**Q5825:** K. P. Mori, *et al.* Increase of Total Nephron Albumin Filtration and Reabsorption in Diabetic Nephropathy. *J Am Soc Nephrol* 2017;28(1):278-289

**ALZET Comments:** Insulin; SC; Mice; 2001; 7 days; animal info (Akita, 14 weeks) ; diabetes; Therapeutic indication (Diabetes, Nephrology);

**Q6069:** E. Liepinsh, *et al.* Acute and long-term administration of palmitoylcarnitine induces muscle-specific insulin resistance in mice. *Biofactors* 2017;43(5):718-730

**ALZET Comments:** Palmitoylcarnitine hydrochloride; Saline; Saline; Mice; 2004; 28 days; Dose (50 mg/kg/day, 10 mg/kg/day); Controls received mp w/ vehicle; animal info (12 week old male CD-1 mice); diabetes;

**Q6145:** S. P. H. Lambooy, *et al.* The Novel Compound Sul-121 Preserves Endothelial Function and Inhibits Progression of Kidney Damage in Type 2 Diabetes Mellitus in Mice. *Sci Rep* 2017;7(1):11165

**ALZET Comments:** Sul-121; DMSO; SC; Mice; 2004; 8 weeks; Dose (2.2 mg/kg/day); 50% DMSO used; Controls received mp w/ vehicle; animal info (male db/db and lean controls) ; pumps replaced every 4 weeks; Resultant plasma level (p.2); diabetes;

**Q7016:** Kaczmarek P, *et al.* Chronic orexin-A (hypocretin-1) treatment of type 2 diabetic rats improves glucose control and beta-cell functions. *Journal of Physiological Pharmacology* 2017;68(5):669-681

**ALZET Comments:** Orexin-A (hypocretin-1); Saline; IP; Rat; 2ML4; 4 weeks; Dose (47 pmol/h); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (adult male Wistar rats); Orexin aka hypocretin-1; diabetes;

**Q6253:** J. Gronholm, *et al.* Metabolically inactive insulin analogue does not prevent autoimmune diabetes in NOD mice. *Diabetologia* 2017;60(8):1475-1482

**ALZET Comments:** Mimotope 3; SC; Mice; 1002; 14 days; Dose (5 µg/day); animal info (9-week-old female NOD mice); post op. care (Carprofen, 5–10 mg/kg administered s.c); mimotope 3 is a modified insulin B chain core epitope 12-23; diabetes;

**Q6386:** Dorfman MD, *et al.* Deletion of Protein Kinase C I in POMC Neurons Predisposes to Diet-Induced Obesity. *Diabetes* 2017;66(4):920-934

**ALZET Comments:** Leptin; PBS; CSF/CNS; Rat; Mice; 14 days; animal info (male Wistar rats; Eight-week-old male and female POMC-IKO and WT mice); Brain coordinates (0.8 mm posterior to bregma; 1.5 mm lateral to the sagittal suture, and 3.6 mm below the skull surface); diabetes;

**Q6024:** M. J. De Blasio, *et al.* The superoxide dismutase mimetic tempol blunts diabetes-induced upregulation of NADPH oxidase and endoplasmic reticulum stress in a rat model of diabetic nephropathy. *Eur J Pharmacol* 2017;807(12-20)

**ALZET Comments:** Tempol; Water; SC; Rat; 4 weeks; Controls received mp w/ vehicle; animal info (Diabetic rats); diabetes; Therapeutic indication (Diabetes); Dose (1.5 mM/kg/day);

**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;

**Q6021:** A. A. da Silva, *et al.* Role of autonomic nervous system in chronic CNS-mediated antidiabetic action of leptin. *Am J Physiol Endocrinol Metab* 2017;312(5):E420-E428



**ALZET Comments:** Leptin, Hexamethonium; Saline; CSF/CNS (lateral ventricle); Rat; 2002; 12 days; Controls received mp w/ vehicle; animal info (360-420g); diabetes; Therapeutic indication (Diabetes); Dose (Hexamethonium: 15 mg/kg);.

**Q6392:** A. R. Cox, *et al.* Incretin Therapies Do Not Expand beta-Cell Mass or Alter Pancreatic Histology in Young Male Mice. *Endocrinology* 2017;158(6):1701-1714

**ALZET Comments:** Exenatide; SC; Mice; 1004; 2 weeks; 18 weeks; Dose (1 nmol/kg/d); animal info (10 week old Male B6129SF1/J mice); diabetes;.

**Q6013:** C. L. Chou, *et al.* Renin inhibition improves metabolic syndrome, and reduces angiotensin II levels and oxidative stress in visceral fat tissues in fructose-fed rats. *PLoS One* 2017;12(7):e0180712

**ALZET Comments:** Aliskiren; Water, deionized; SC; Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (200-230 g.); antihypertensive; diabetes; Therapeutic indication (Oxidative stress, metabolic syndrome); Dose (100 mg/kg body weight);.

**Q6416:** V. Blasco-Baque, *et al.* Periodontitis induced by Porphyromonas gingivalis drives periodontal microbiota dysbiosis and insulin resistance via an impaired adaptive immune response. *Gut* 2017;66(5):872-885

**ALZET Comments:** Pg-lipopolysaccharides; Saline; SC; Mice; 2004; 28 days; Dose (300mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (5 week old C57Bl/6J wild-type female mice); diabetes;.

**Q5948:** M. L. Bergman, *et al.* Tolerogenic insulin peptide therapy precipitates type 1 diabetes. *J Exp Med* 2017;214(7):2153-2156

**ALZET Comments:** R22E, B9:23; SC; Mice; 1002; 14 days; animal info (4-6 weeks old) ; diabetes; Therapeutic indication (Diabetes); Dose (5 ug/day);.

**Q6417:** F. Bassil, *et al.* Insulin resistance and exendin-4 treatment for multiple system atrophy. *Brain* 2017;140(5):1420-1436

**ALZET Comments:** Exendin-4; Saline; SC; Mice; 1004; 12 weeks; Dose (3.5 pmol/kg/min or 8.75 pmol/kg/min); 0.9% Saline used; Controls received mp w/ vehicle; animal info (PLP-SYN mice); pumps replaced every 4 weeks; Resultant plasma level (2197.6 + 317.7 pg/ml for 3.5 pmol/kg/min (n = 6) and 2796.3 + 284.9 pg/ml for those receiving 8.5 pmol/kg/min); diabetes;.

**Q6428:** C. Aguayo-Mazzucato, *et al.* beta Cell Aging Markers Have Heterogeneous Distribution and Are Induced by Insulin Resistance. *Cell Metab* 2017;25(4):898-910 e5

**ALZET Comments:** S961; PBS; Saline; SC; Mice; 2001; 7 days; 0.9% saline used; animal info (C57Bl/6J mice); S961 is an insulin receptor antagonist; diabetes;.

**Q5878:** Insulin-Like Growth Factor Binding Protein 1 Could Improve Glucos Regulation and Insulin Sensitivity Through Its RGD Domain. *Diabetes* 2017;66(2):287-299

**ALZET Comments:** RGD Peptide, RAD hexapeptide; SC; Mice; 1004; 4 weeks; Controls received mp w/ RAD hexapeptide; animal info (C57BL/6, 12 weeks old); diabetes; Arg-Gly-Asp is RGD peptide sequence; Therapeutic indication (Insulin sensitivity); Dose (10 mg/ML);.

**Q5724:** X. Zhang, *et al.* Cannabinoid 2 Receptor Agonist Improves Systemic Sensitivity to Insulin in High-Fat Diet/Streptozotocin-Induced Diabetic Mice. *Cell Physiol Biochem* 2016;40(5):1175-1185

**ALZET Comments:** SEr601; SC; Mice; 2 weeks; 4 weeks; animal info (male, ICR, 4 weeks old); diabetes; Dose (20 ng/kg);.

**Q4918:** M. Zhang, *et al.* Growth factors and medium hyperglycemia induce Sox9+ ductal cell differentiation into  $\beta$  cells in mice with reversal of diabetes. *pnas* 2016;113(3):650-655

**ALZET Comments:** Gastrin; epidermal growth factor, human recombinant; Acetic acid; PBS; IP; Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, WT or Ins1 CreERT); diabetes; Dose (gastrin 3 ug/kg/hr; EGF 10 ug/kg/hr);.



**Q5108:** H. Zhang, *et al.* Intermedin/adrenomedullin 2 polypeptide promotes adipose tissue browning and reduces high-fat diet-induced obesity and insulin resistance in mice. *Int J Obes (Lond)* 2016;40(5):852-60

**ALZET Comments:** Adrenomedullin 2; Saline; SC; Mice; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 8-10 weeks old); peptides; diabetes; Dose (300 ng/kg/hr); obesity.

**Q5100:** H. Z. Xu, *et al.* 12-Lipoxygenase Inhibition on Microalbuminuria in Type-1 and Type-2 Diabetes Is Associated with Changes of Glomerular Angiotensin II Type 1 Receptor Related to Insulin Resistance. *Int J Mol Sci* 2016;17(5):

**ALZET Comments:** Hydroxyeicosatetraenoic acid, 12(S)-; Saline, normal; SC; Rat; 1002; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 180-200g); cardiovascular; diabetes; bp measured using tail cuff; Dose (1 mg/kg/day);.

**Q5706:** A. Warner, *et al.* Activation of beta3-adrenoceptors increases in vivo free fatty acid uptake and utilization in brown but not white fat depots in high-fat-fed rats. *Am J Physiol Endocrinol Metab* 2016;311(6):E901-E910

**ALZET Comments:** CL 316,243; SC; Rat; 2ML4; 3 weeks; Controls received mp w/ saline; animal info (male, Wistar); post op. care (analgesia 2 mg/kg); diabetes; "Minipump Infusion of CL has been shown to be comparable to daily CL injections" pg E902; Obesity; Therapeutic indication (obesity; diabetes); Dose (1 mg/kg/day); Industry authored (AstraZeneca);.

**Q5090:** S. Wang, *et al.* MicroRNA 152 regulates hepatic glycogenesis by targeting PTEN. *FEBS J* 2016;283(10):1935-46

**ALZET Comments:** Interleukin-6; Mice; 7 days; animal info (male, C57BL6J, 12 weeks old); diabetes;.

**Q5211:** O. O. Talton, *et al.* Maternal Hyperleptinemia Improves Offspring Insulin Sensitivity in Mice. *Endocrinology* 2016;157(7):2636-48

**ALZET Comments:** Leptin; Saline; SC; Mice (pregnant); 2004; Controls received mp w/ vehicle; animal info (female, WT); stress/adverse reaction: (see pg. 2645); teratology; diabetes; Dose (350 ng/h);.

**Q4817:** Stephanie Dal, *et al.* Oxidative stress status and liver tissue defenses in diabetic rats during intensive subcutaneous insulin therapy. *EXPERIMENTAL BIOLOGY AND MEDICINE* 2016;241(184-192

**ALZET Comments:** Insulin; SC; Rats; 2006; 1 week; 4 weeks; animal info (male, Wistar, 180-200g, STZ); immunology; diabetes; "The intensive subcutaneous insulin administration performed using a mini pump in our study led to an improvement in the metabolic control of diabetic rats, as confirmed by a decrease in fructosamine levels and an increase in body weight after four weeks of treatment. Moreover, blood insulin concentration was maintained at the same level throughout the study attesting to the efficiency of this therapy." pg 189; Dose (2 UI/200g/day);.

**Q5110:** Song-Yang Zhang, *et al.* Adrenomedullin 2 Improves Early Obesity-Induced Adipose Insulin Resistance by Inhibiting the Class II MHC in Adipocytes. *Diabetes* 2016;65(2342-2355

**ALZET Comments:** Adrenomedullin 2; Saline; SC; Mice (transgenic); 6 weeks; Controls received mp w/ vehicle; animal info (WT or aADM2-tg); peptides; diabetes; Dose (3000 ng/kg/hr); Resultant plasma level (see supplement pg 8, figure 7E);.

**Q6662:** J. Shen, *et al.* NMDA receptors participate in the progression of diabetic kidney disease by decreasing Cdc42-GTP activation in podocytes. *J Pathol* 2016;240(2):149-60

**ALZET Comments:** RNA, NR1-short hairpin; CSF/CNS (Intrathecal); Mice; Intrathecal catheter; 10.1002/path.4764; animal info (Diabetes-induced C57BL/6 J mice, 8 weeks of age); diabetes; ALZET intrathecal catheter used with another product.

**Q5196:** A. Schaschkow, *et al.* Impact of the Type of Continuous Insulin Administration on Metabolism in a Diabetic Rat Model. *J Diabetes Res* 2016;2016(8310516

**ALZET Comments:** insulin; buffer solution; SC; Rat; 28 days; animal info (male, Lewis, STZ injection); comparison of injection of insulin vs mp; post op. care (Baytril 10 mg/kg QD for 7 days); diabetes; pumps primed for 24 hours in 37C saline; "...continuous insulin delivery by pumps restored normoglycaemia, which induced the reduction of both reactive oxygen species and macrophage infiltration into the liver and omentum. Injections controlled the glucose levels for only a short period of time and therefore tissue stress and inflammation were elevated." pg 1; "pumps require no daily injection and



facilitate rat follow-up. Well-being of the animals and the homogeneity of the results permit researchers to limit the numbers of animals and experiments used to build solid and reproducible results.” pg 8; Dose (4 IU/day);.

**Q5602:** H. Sato, *et al.* Anagliptin increases insulin-induced skeletal muscle glucose uptake via an NO-dependent mechanism in mice. *Diabetologia* 2016;59(11):2426-2434

**ALZET Comments:** Exendin (9-39); Saline; SC; Mice; 1002; 8 weeks; Controls received mp w/ vehicle; animal info (8 weeks old) ; pumps replaced every 2 weeks; diabetes; Therapeutic indication (insulin resistance; diabetes);.

**Q6125:** A. Sahr, *et al.* The Angiotensin-(1-7)/Mas Axis Improves Pancreatic beta-Cell Function in Vitro and in Vivo. *Endocrinology* 2016;157(12):4677-4690

**ALZET Comments:** Angiotensin (1-7); Saline; SC; Mice; 1002; 14 days; Dose (2.47 mg/kg/day); 0.9% saline used; Controls received mp w/ vehicle; animal info (11- to 14-week-old mice deficient in the receptor Mas and wild-type); Resultant plasma level (p.4687); diabetes;.

**Q5600:** A. Rubin, *et al.* Identification of novel targets of diabetic nephropathy and PEDF peptide treatment using RNA-seq. *BMC Genomics* 2016;17(1):936

**ALZET Comments:** P78-PEDF; PBS; SC; Mice; 2006; 6 weeks; Controls received mp w/ vehicle; animal info (6 weeks, 12 weeks old); diabetes; P78-PEDF is an active 44 amino acid fragment of pigment epithelium-derived factor (PEDF); Therapeutic indication (diabetes); Dose (.3 ug/g/day);.

**Q6650:** X. M. Ren, *et al.* Atorvastatin Alleviates Experimental Diabetic Cardiomyopathy by Regulating the GSK-3beta-PP2Ac-NF-kappaB Signaling Axis. *PLoS One* 2016;11(11):e0166740

**ALZET Comments:** Atorvastatin calcium; SC; Mice; 2004; 12 weeks; Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Male C57BL/6 mice (8 wk old, 18±22 g)); cardiovascular; diabetes; Therapeutic indication (diabetic cardiomyopathy);.

**Q6647:** S. Rajan, *et al.* Chronic hyperinsulinemia reduces insulin sensitivity and metabolic functions of brown adipocyte. *J Endocrinol* 2016;230(3):275-90

**ALZET Comments:** Insulin, glargine; Saline; SC; Mice; 8 weeks; Dose (0.6 U/day); animal info (C57BL/6 mice); pumps replaced every 4 weeks; diabetes;.

**Q6075:** T. Prasad, *et al.* Beneficial Effects of Combined AT1 Receptor/Nepriylisin Inhibition (ARNI) Versus AT1 Receptor Blockade Alone in the Diabetic Eye. *Invest Ophthalmol Vis Sci* 2016;57(15):6722-6730

**ALZET Comments:** Irbesartan; Thiorphan; Saline; DMSO; Rat; 2ML4; 3 weeks; Dose (Irbesartan 15 mg/kg/day or irbesartan/thiorphan combination 0.1 mg/kg/day); 0.2% DMSO used; Controls received mp w/ vehicle; animal info (10 week old male Ren2 rats weighing 300–500g); diabetes;.

**Q5175:** Y. Pang, *et al.* Intermedin Restores Hyperhomocysteinemia-induced Macrophage Polarization and Improves Insulin Resistance in Mice. *J Biol Chem* 2016;291(23):12336-45

**ALZET Comments:** Intermedin; Saline; SC; Mice; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 6 weeks old); immunology; peptides; diabetes; Dose (318 ng/kg/h);.

**Q4868:** O. Otlivanchik, *et al.* Orexin signaling is necessary for hypoglycemia-induced prevention of conditioned place preference. *Am J Physiol Regul Integr Comp Physiol* 2016;310(R66-R73)

**ALZET Comments:** Sertraline; Ethanol; SC; Rat; 2001; 1 week; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 7-8 weeks old, 250-400g); 50% ethanol used; behavioral testing (open field); diabetes; Dose (7.5 mg/kg/day);.

**Q5171:** S. Okizaki, *et al.* Vascular Endothelial Growth Factor Receptor Type 1 Signaling Prevents Delayed Wound Healing in Diabetes by Attenuating the Production of IL-1beta by Recruited Macrophages. *Am J Pathol* 2016;186(6):1481-98

**ALZET Comments:** Placenta growth factor, recombinant human; antibody, interleukin-1B; PBS; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle or control antibody; animal info (male, C57BL6, 8 weeks old, STZ); immunology; diabetes; Dose (PIGF 10 ug/mouse; anti-IL-1B 1 ug/day);.



**Q4867:** M. K. Nøhr, *et al.* LPS-Enhanced Glucose-Stimulated Insulin Secretion Is Normalized by Resveratrol. *PLoS One* 2016;11(1):1-15

**ALZET Comments:** Endotoxin, LPS; Saline; SC; Mice; 2004; 28 days; Controls received mp w/ vehicle; animal info (male, C57BL/6N, 12 weeks old); immunology; diabetes; Dose (600 ug/kg/day);.

**Q5418:** M. Matrai, *et al.* Estrogen therapy may counterbalance eutrophic remodeling of coronary arteries and increase bradykinin relaxation in a rat model of menopausal hypertension. *Menopause* 2016;23(7):778-83

**ALZET Comments:** Angiotensin II acetate; Ringer's solution; SC; Rat; 2MI4; 4 weeks; Controls received mp w/ vehicle; animal info (Ovariectomized female Sprague Dawley rats, 210-240 g); functionality of mp verified by blood pressure; cardiovascular; diabetes; Rat model of hypertension induced by Angiotensin II; pentobarbital used for anesthesia; blood pressure measured directly by cannulation of carotid artery; Dose (100 ng/kg/min); Resultant blood pressure: 96 mmHg (control), 130 mmHg (hypertensive group).

**Q6615:** P. Martin-Mateos, *et al.* In-vivo, non-invasive detection of hyperglycemic states in animal models using mm-wave spectroscopy. *Sci Rep* 2016;6(34035)

**ALZET Comments:** Leptin; SC; Mice; 28 days; Controls received mp w/ vehicle; animal info (C57Bl6/J, albino BalbC and ob/ob mice); diabetes;.

**Q6686:** C. Lerin, *et al.* Defects in muscle branched-chain amino acid oxidation contribute to impaired lipid metabolism. *Mol Metab* 2016;5(10):926-936

**ALZET Comments:** S961; Saline; SC; Mice; 2001; Controls received mp w/ vehicle; animal info (six week old C57BL/6 male mice); enzyme inhibitor (insulin receptor antagonist); diabetes;.

**Q6653:** H. R. E. Y. Kim, *et al.* NMDA Receptors as Potential Therapeutic Targets in Diabetic

Nephropathy: Increased Renal NMDA

Receptor Subunit Expression in Akita

Mice and Reduced Nephropathy

Following Sustained Treatment With

Memantine or MK-801. *Diabetes* 2016;65(3139–3150)

**ALZET Comments:** Memantine HCl; MK-801; Saline; SC; Mice; 1004; 28 days; Dose (Memantine (2 mg/kg/day); dizocilpine (0.5 mg/kg/day)); 0.9% Saline used; Controls received mp w/ vehicle; animal info (10-week-old DBA/2J mice); Dizocilpine AKA (MK-801); diabetes.

**Q5355:** K. Karimi Galoughi, *et al.* beta3 Adrenergic Stimulation Restores Nitric Oxide/Redox Balance and Enhances Endothelial Function in Hyperglycemia. *J Am Heart Assoc* 2016;5(2):

**ALZET Comments:** S961; CL 316,243; Saline; SC; Rabbit; 2ML1; 3 days, 7 days; Controls received mp w/ vehicle; animal info (male New Zealand White rabbits, 2.2 – 2.6 kg); functionality of mp verified by plasma levels; Diabetes-induced vascular dysfunction; Hyperglycemia study; Dose (12 ug/kg/hr S961, 40 ug/kg/hr CL);.

**Q5543:** T. R. Jost, *et al.* Role of CXCR4-mediated bone marrow colonization in CNS infiltration by T cell acute lymphoblastic leukemia. *J Leukoc Biol* 2016;99(6):1077-87

**ALZET Comments:** AMD3100; PBS; IP; Mice (NSG); 1002, 1004; 14 days, 28 days; Controls received mp w/ vehicle; animal info (Immunodeficient, non-obese, diabetic);.

**Q5316:** Jeremie Boucher, *et al.* Differential Roles of Insulin and IGF-1 Receptors in Adipose Tissue Development and Function. *Diabetes* 2016;66(2201-2213)

**ALZET Comments:** Leptin; Saline; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (Fat-specific IR, IGF1R, and IR/IGF1R knockout mice; 3 month old); functionality of mp verified by blood glucose levels; dose-response (pg 2204-2206); behavioral testing (cold-resistance testing); replacement therapy (leptin); Lipoatrophic diabetes; Dose (10 ug/mouse/d);.





**Q6571:** M. A. Hye Khan, *et al.* A dual COX-2/sEH inhibitor improves the metabolic profile and reduces kidney injury in Zucker diabetic fatty rat. *Prostaglandins Other Lipid Mediat* 2016;125(40-7)

**ALZET Comments:** PTUPB; IP; Rat; 8 weeks; Dose (10 mg/kg/d); Controls received mp w/ vehicle; animal info (Male obese Zucker Diabetic Fatty and Zucker Lean rats); PTUPB aka 4-(5-phenyl-3-{3-[3-(4-trifluoromethylphenyl)-ureido]-propyl}-pyrazol-1-yl)-benzenesulfonamide; enzyme inhibitor (COX-2/sEH); Therapeutic indication (kidney injury);.

**Q6480:** C. W. Huang, *et al.* Role of n-3 Polyunsaturated Fatty Acids in Ameliorating the Obesity-Induced Metabolic Syndrome in Animal Models and Humans. *Int J Mol Sci* 2016;17(10):

**ALZET Comments:** Docosahexaenoic acid; Docosahexaenoic acid, 17R/S hydroxy; Saline; BSA; Ethanol; Mice; 15 days; Dose (Docosahexaenoic acid: 4 ug/g; 17-HDHA 50 ng/g ); animal info (Male C57BL/6J wild-type mice. Male BKS.Cg-Dock 7m+/-Leprdb/J (db/db) mice and Lean nondiabetic littermates (db/+)); comparison of injections vs mp; diabetes;.

**Q5375:** C. Huang, *et al.* Thioredoxin interacting protein (TXNIP) regulates tubular autophagy and mitophagy in diabetic nephropathy through the mTOR signaling pathway. *Sci Rep* 2016;6(29196)

**ALZET Comments:** DNazymes, Scrambled or TXNIP; Saline; SC; Rat; 2006; 12 weeks; Controls received mp w/ vehicle; animal info (6-week old, female heterozygous rats); functionality of mp verified by blood glucose levels (AMES glucometer); pumps replaced every 6 weeks; diabetes; Inhibition of TXNIP using DNA-zyme improves autophagy and mitophagy in diabetic nephropathy; Inhibition of TXNIP using DNA-zyme improves autophagy and mitophagy in diabetic nephropathy; Resultant plasma level (pg. 10);.

**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; Sesame 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 (5 $\alpha$ -reductase inhibitor); Therapeutic indication (Type-2 Diabetes); Dose (2 mg/kg);.

**Q5805:** S. Eid, *et al.* mTORC2 Signaling Regulates Nox4-Induced Podocyte Depletion in Diabetes. *Antioxid Redox Signal* 2016;25(13):703-719

**ALZET Comments:** Oligonucleotide, phosphorothioate antisense (Rictor); Oligonucleotide, phosphorothioate sense (Rictor); Saline; SC; Mice; 2006; 5 weeks; Controls received mp w/ vehicle; animal info (17 weeks old) antisense (phosphorothioated Sense and Antisense for Rictor); diabetes; Therapeutic indication (Diabetes); Dose (90 ng\* $g$  body wt<sup>-1</sup> \* day<sup>-1</sup>);.

**Q5803:** R. Dusaulcy, *et al.* Functional and Molecular Adaptations of Enteroendocrine L-Cells in Male Obese Mice Are Associated With Preservation of Pancreatic alpha-Cell Function and Prevention of Hyperglycemia. *Endocrinology* 2016;157(10):3832-3843

**ALZET Comments:** Exendin (9-39); SC; Mice; 2002; 2 weeks; animal info (10 weeks old) diabetes; Therapeutic indication (Obesity); Dose (0.5 uL/h);.

**Q5783:** H. C. Denroche, *et al.* The role of autonomic efferents and uncoupling protein 1 in the glucose-lowering effect of leptin therapy. *Mol Metab* 2016;5(8):716-24

**ALZET Comments:** Leptin, recombinant mouse; PBS; SC; Mice; 9 days; Controls received mp w/ vehicle; animal info (6 weeks old); functionality of mp verified by leptin and glucose levels: (After leptin release from the osmotic pumps had ceased (~9.2 days after pump implantation), hyperglycemia rapidly returned to pre-treatment levels in 6OHDA-leptin and sham-leptin groups, concomitant with the reduction of plasma leptin levels (Figure 3A,C)); diabetes; Temperature transponders (Implantable Programmable Temperature Transponder IPTT-300; Bio Medic Data Systems Inc, Seaford, USA) were implanted interscapularly at the same time as osmotic pumps. After leptin release from the osmotic pumps had ceased (w9.2 days after pump implantation), hyperglycemia rapidly returned to pre-treatment levels in 6OHDA-leptin and sham-leptin groups, concomitant with the reduction of plasma leptin levels (Figure 3A,C) Therapeutic indication (Diabetes Type 1, Brown adipose tissue); Dose (10, 20 ug/day);.



**Q5304:** H. C. Denroche, *et al.* Disrupted Leptin Signaling in the Lateral Hypothalamus and Ventral Premammillary Nucleus Alters Insulin and Glucagon Secretion and Protects Against Diet-Induced Obesity. *Endocrinology* 2016;157(7):2671-85

**ALZET Comments:** Leptin, recombinant mouse; SC; mice; 1007D, 1002; 15 days; Controls received mp w/ vehicle; animal info (Male Lep<sup>rflox</sup>/flox and Lep<sup>rflox</sup>/flox Syn-cre mice, 12-14 wks); functionality of mp verified by plasma levels; pumps replaced after day 10; dose-response (pg. 2679); diabetes; Dose (10 ug/d or 20 ug/d);.

**Q5640:** J. A. Davidson, *et al.* Glucagon therapeutics: Dawn of a new era for diabetes care. *Diabetes Metab Res Rev* 2016;32(7):660-665

**ALZET Comments:** Metroleptin; SC; mice; 17 days; diabetes; "While we applaud the efforts of the insulin/glucagon pump infusion studies, the delivery space cannot simulate normal physiology (Figure 1B). p.663 ; Therapeutic indication (Diabetes, Glucagon, Glucagon receptor, insulin); Dose (400 mg/day);.

**Q5791:** T. Coskun, *et al.* FGF21 Improves the Adipocyte Dysfunction Related to Seipin Deficiency. *Diabetes* 2016;65(11):3410-3417

**ALZET Comments:** LY2405319; Mice (knockout); 1004; 28 days; Controls received mp w/ vehicle; animal info (6 weeks old) ; diabetes; Therapeutic indication (Diabetes);Dose (1 mg/kg/day);.

**Q4837:** Colin M. Hyslop, *et al.* Prolactin as an Adjunct for Type 1 Diabetes Immunotherapy. *Endocrinology* 2016;157(1):150-165

**ALZET Comments:** Prolactin, recombinant mouse; Albumin, mouse; Mice (NOD); 1004; 3 weeks; Controls received mp w/ vehicle; Controls received mp w/ vehicle; diabetes; Therapeutic indication (diabetes); Dose (2.7 ug/d); resulted in serum PRL level 300-500 ng/mL;.

**Q6101:** Cochran BJ, *et al.* Impact of Perturbed Pancreatic  $\beta$ -Cell Cholesterol Homeostasis on Adipose Tissue and Skeletal Muscle Metabolism. *Diabetes*. 2016;65(12):3610-3620

**ALZET Comments:** Insulin (Humulin R); PBS; SC; Mice; 1004; 4 weeks; Dose: (Humulin R 0.1 units/day); Controls received mp w/ vehicle; animal info (16-week-old male mice); Resultant plasma level (p. 3615); diabetes;.

**Q5627:** M. P. Bhatt, *et al.* C-peptide protects against hyperglycemic memory and vascular endothelial cell apoptosis. *J Endocrinol* 2016;231(1):97-108

**ALZET Comments:** C-peptide, human; insulin, human recombinant; SC; Mice; 2004; 4 weeks; Controls underwent sham operations; animal info (6 weeks old, diabetic (non-fasting blood glucose >16mM, polyuria, and glycosuria)); diabetes; Therapeutic indication (Vasculopathy, Hyperglycemic memory); Dose (35 pmol/min/kg);.

**Q5591:** F. Ando, *et al.* Wnt5a induces renal AQP2 expression by activating calcineurin signalling pathway. *Nat Commun* 2016;7(13636)

**ALZET Comments:** Tolvaptan; DMSO; SC; Mice; 1003D; 2 days; Controls received mp w/ vehicle; animal info (8 weeks old); Therapeutic indication (nephrogenic diabetes insipidus (NDI)).

**Q5778:** Pancreatic  $\beta$ -Cells Express the Fetal Islet Hormone Gastrin in Rodent and Human Diabetes. *Diabetes* 2016;66(2):

**ALZET Comments:** S961, Insulin receptor antagonist; PBS; SC; Mice; 2001; 7 days; Controls received mp w/ vehicle; animal info (6 weeks old);diabetes; Average blood glucose level at sacrifice, 515 mg/dL Therapeutic indication (Glucose tolerance, Diabetes);Dose (12 nmol);.