



**Recent References (2016-Present) on the Administration of Insulin
Using ALZET® Osmotic Pumps**

- Q10944:** X. Hu, *et al.* Effects of continuous subcutaneous insulin infusion on the microstructures, mechanical properties and bone mineral compositions of lumbar spines in type 2 diabetic rats. *BMC Musculoskeletal Disorders* 2022;23(1):511
Agents: Insulin **Vehicle:** Citrate buffer; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** 2ML4; **Duration:** 4 weeks; 8 weeks;
ALZET Comments: Dose (2.5 IU/day); Controls received mp w/ vehicle; animal info (Male; 6 weeks old; 70 total; Weighed about 200 g more or less); peptides; diabetes;
- Q10738:** J. Zhan, *et al.* Positive Feedback Loop of miR-320 and CD36 Regulates the Hyperglycemic Memory-Induced Diabetic Diastolic Cardiac Dysfunction. *Molecular Therapy Nucleic Acid* 2023;31(122-138
Agents: Insulin **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;
ALZET Comments: Dose (40 mg/kg); Controls received mp w/ vehicle; animal info (C57BL/6 mice (8-week-old males); diabetes;
- Q10777:** W. Wang, *et al.* Diabetic hyperglycemia promotes primary tumor progression through glycation-induced tumor extracellular matrix stiffening. *Science Advances* 2022;
Agents: Insulin **Vehicle:** Citrate buffer; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 7 weeks;
ALZET Comments: Dose: Insulin (0.5 U of insulin per mouse per day); Controls received mp w/ vehicle; animal info: Female MMTV-PyMT mice of the FVB strain background (4 weeks of age.); diabetes;
- Q10827:** F. Li, *et al.* TEAD1 regulates Cell Proliferation Through a Pocket-Independent Transcription Repression Mechanism. *Nucleic Acids Research* 2022;50(22):12723-12738
Agents: Insulin, human **Vehicle:** Saline; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (0.2 U/day); 0.9% NaCl used; Controls received mp w/ vehicle; animal info TKO pancreatic B cell specific TEAD1 ko mice; 4-weeks old; functionality of mp verified by blood glucose levels; diabetes
- Q9968:** S. Tokumoto, *et al.* Generation and Characterization of a Novel Mouse Model That Allows Spatiotemporal Quantification of Pancreatic beta-Cell Proliferation. *Diabetes* 2020;69(11):2340-2351
Agents: Insulin Receptor Antagonist **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (8 weeks old, RIP-Cre); Insulin Receptor Antagonist aka S961; diabetes;
- Q8954:** M. M. Soundarapandian, *et al.* Activation of Protein Kinase A (PKA) signaling mitigates congenital hyperinsulinism associated hypoglycemia in the Sur1^{-/-} mouse model. *PLoS One* 2020;15(7):e0236892
Agents: Insulin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (0.2 or 0.3 U/day); Controls received mp w/ vehicle; animal info (C57BL/6J, Female, 8-10 weeks old); gene therapy;
- Q9417:** A. J. Polichnowski, *et al.* Pathophysiology of unilateral ischemia-reperfusion injury: importance of renal counterbalance and implications for the AKI-CKD transition. *American Journal of Physiology Renal Physiology* 2020;318(5):F1086-F1099
Agents: FITC-insulin **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 3 days;
ALZET Comments: Dose (40 mg/mL); animal info (6- to 8-wk-old male Sprague-Dawley rats); Blood pressure measured via radiotelemeter; ischemia (ischemia-reperfusion injury);
- Q8653:** Z. Maria, *et al.* Insulin Treatment Reduces Susceptibility to Atrial Fibrillation in Type 1 Diabetic Mice. *Frontiers in Cardiovascular Medicine* 2020;7(134
Agents: Insulin, humulin R **Vehicle:** Citrate buffer; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 7 days;
ALZET Comments: Dose (0.5 U/mouse/day); Controls received mp w/ vehicle; animal info (Male FVB/N/J mice, 8-10 weeks old); diabetes;



Q8217: T. Katahira, *et al.* Conversion of pancreatic alpha cells into insulin-producing cells modulated by beta-cell insufficiency and supplemental insulin administration. *Biochem Biophys Res Commun* 2020;521(1):178-183

Agents: Insulin **Vehicle:** Saline; **Route:** Not stated; **Species:** Mice; **Pump:** Not stated; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6J male mice, 6 or 7 weeks of age); diabetes;

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);

Q9219: G. J. Euceda, *et al.* Markers of Chronic Hyperglycemia Correlate with Attenuated Acute Lung Inflammatory Response in Murine Models of 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); dependence;

Q7653: H. Zhu, *et al.* Insulin Therapy for Gestational Diabetes Mellitus Does Not Fully Protect Offspring From Diet-Induced Metabolic Disorders. *Diabetes* 2019;68(4):696-708

Agents: Insulin, recombinant human **Vehicle:** Saline; **Route:** SC; **Species:** Mice (Pregnant); **Pump:** 1007D; **Duration:** 1 week;

ALZET Comments: Dose (0.35 IU/day); Controls received mp w/ vehicle; animal info (6-8 weeks, female, ICR, 26-28g); diabetes; Pumps were implanted on day 14.5 or 15 of pregnancy. Pups were fostered by normal females until the age of 3 weeks. "To maintain stable glycemic levels, INS dams received another injection of 0.1 units of long-acting insulin (Levemir; Novo Nordisk) ~1h before the fed state (darkness) during late gestation." p.697;

Q7634: B. P. Tooke, *et al.* Hypothalamic POMC or MC4R deficiency impairs counterregulatory responses to hypoglycemia in mice. *Mol Metab* 2019;20(194-204

Agents: Insulin; Melanotan **Vehicle:** PBS; **Route:** SC; CSF/CNS (Paraventricular Nucleus of Hypothalamus); **Species:** Mice;

Pump: 2002; 1002; **Duration:** 14 days;

ALZET Comments: Dose (10 U/kg/day); Controls received mp w/ vehicle; Brain coordinates (bregma: anteroposterior, 0.70; mediolateral, 0.22; dorsoventral, 4.80 mm); bilateral cannula used; diabetes; BIK: Plastics1, 3280PD/V/SPC;

Q9046: S. Tokumoto, *et al.* Three-dimensional analysis of β -cell proliferation by a novel mouse model. *BioRxiv* 2019;

Agents: Insulin receptor antagonist S961 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Dose (10 nmol); Controls received mp w/ vehicle; animal info (8 weeks old,); diabetes;

Q8373: S. Pushpakumar, *et al.* Hydrogen Sulfide Protects Hyperhomocysteinemia-Induced Renal Damage by Modulation of Caveolin and eNOS Interaction. *Scientific Reports* 2019;9(1):2223

Agents: Fluoresceinyl isothiocyanate-Insulin **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** 2001D; **Duration:** 1 day;

ALZET Comments: Animal info (C57BL/6J, 8-12 weeks old, 25 g); Fluoresceinyl isothiocyanate-Inulin aka FITC-Inulin; dependence;

Q7570: Z. Li, *et al.* mTOR Signaling in X/A-Like Cells Contributes to Lipid Homeostasis in Mice. *Hepatology* 2019;69(2):860-875

Agents: Grehlin, acyl-; Insulin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (11 nmol/kg/d); Controls received mp w/ vehicle; animal info (Four-week-old male mice); obesity;

Q6881: W. Deng, *et al.* Insulin ameliorates pulmonary edema through the upregulation of epithelial sodium channel via the PI3K/SGK1 pathway in mice with lipopolysaccharide-induced lung injury. *Mol Med Rep* 2019;

Agents: Insulin, human **Vehicle:** PBS; **Route:** IV (jugular); **Species:** Mice; **Pump:** Not Stated; **Duration:** 24 hours;

ALZET Comments: Dose (Human Insulin .01 U/kg/day); Controls received mp w/ vehicle; animal info (C3H/HeN mice, aged 7-9 weeks); ALZET internal jugular vein catheter used; cardiovascular;



Q7977: F. Adel, *et al.* Insulin Therapy in a Rat Model of Diabetic Cardiomyopathy Is Associated with Attenuation of the Cgmp System. *Journal of the American College of Cardiology* 2019;73(9):

Agents: insulin **Vehicle:** saline; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 1 month;

ALZET Comments: Dose (11.5 µg/kg/day); Controls received mp w/ vehicle; animal info (male, Wistar); cardiovascular; diabetes;

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;

Q8056: D. Kumar, *et al.* Chronic hyperinsulinemia promotes meta-inflammation and extracellular matrix deposition in adipose tissue: Implications of nitric oxide. *Mol Cell Endocrinol* 2018;477(15-28

Agents: Insulin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 8 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (8-10 weeks old, 20-24 g, C57BL/6J, Male); pumps replaced every 4 weeks; 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

Agents: Insulin, human; X10 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (nude); **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: 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;

Q7755: R. W. Holdcraft, *et al.* A model for determining an effective in vivo dose of transplanted islets based on in vitro insulin secretion. *Xenotransplantation* 2018;25(6):e12443

Agents: Insulin, recomb. human **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3-5 days;

ALZET Comments: Dose ((female 1.5-2.0 U/day), (males 3.0-4.5 U/day)); Controls consisted of rats that did not become diabetic during the initial study period; animal info (male and female, BioBreeding diabetes-prone); Multiple pumps per animal (2 if hyperglycemic state observed. see p.4); comparison of macrobead implant vs mp; diabetes; Pilot study for CGM calibration 3-5 days followed by 1 or 3 month study using microbeads. Pump models not stated but duration length was listed at 7 or 14 days;

Q7903: J. M. Gladding, *et al.* The Effect of Intrahippocampal Insulin Infusion on Spatial Cognitive Function and Markers of Neuroinflammation in Diet-induced Obesity. *Front Endocrinol (Lausanne)* 2018;9(752

Agents: Insulin, Humulin N **Vehicle:** Saline; **Route:** CNS/CSF (third ventricle); **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Dose (2.64 µl/day); Controls received mp w/ vehicle; animal info (Male, 8 weeks old, C57BL/6J); post op. care (Analgesia); behavioral testing (Morris Water Maze Test, Y Maze Test); ALZET brain infusion kit (not stated) used; Brain coordinates (AP-2.0mm, ML +/-1.8mm, DV-1.6mm from dura); bilateral cannula used; dependence;

Q7812: M. B. Fluit, *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;



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

Agents: Insulin (Humulin R) **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Dose (8.33 $\mu\text{mol/ml}$); Controls received mp w/ vehicle; animal info (Uchl1-/-mice, 9-11-week-old, male); diabetes;

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

Agents: Insulin (Humulin R) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 9 weeks;

ALZET Comments: 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);

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

Agents: Insulin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: animal info (Akita, 14 weeks) ; diabetes; Therapeutic indication (Diabetes, Nephrology);

Q6298: C. K. Katashima, *et al.* iNOS promotes hypothalamic insulin resistance associated with deregulation of energy balance and obesity in rodents. *Sci Rep* 2017;7(1):9265

Agents: S-nitrosoglutathione; insulin; glutathione **Vehicle:** Not Stated; **Route:** CSF/CNS (third ventricle); **Species:** Rat; mice; **Pump:** 1002; 2002; **Duration:** 1 week;

ALZET Comments: Dose (GSNO (50 μM)/insulin (0.033 UI/ μL) and GSH (50 μM)/insulin (0.033 UI/ μL)); animal info (Male 4-week-old Wistar rats, Swiss, C57BL/6 and iNOS-null (iNOS-/-) mice); S-nitrosoglutathione is an NO donor; Brain coordinates (rats DV: -8.5 mm and AP: - 0.5 mm; mice DV: -5 mm and AP: -1.8 mm);

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

Agents: Insulin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rats; **Pump:** 2006; **Duration:** 1 week; 4 weeks;

ALZET Comments: 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);

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

Agents: insulin **Vehicle:** buffer solution; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: 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);

Q5601: T. Sartorius, *et al.* Sustained Treatment with Insulin Detemir in Mice Alters Brain Activity and Locomotion. *PLoS One* 2016;11(9):e0162124

Agents: Insulin, Insulin Detemir **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 8 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (10-15 week); comparison of daily s.c. injections vs mp; behavioral testing (Locomotion); Therapeutic indication (Insulin-dependent brain activity); Dose (.6 U/d);



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

Agents: Insulin, glargine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 8 weeks;

ALZET Comments: Dose (0.6 U/day); animal info (C57BL/6 mice); pumps replaced every 4 weeks; diabetes;

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

Agents: Insulin (Humulin R) **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: 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

Agents: C-peptide, human; insulin, human recombinant **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: 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);

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

Agents: S961, Insulin receptor antagonist **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: 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);