



References on the Administration of Insulin Using ALZET® Osmotic Pumps

- 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;
ALZET Comments: Insulin, human; PBS; IV (jugular); Mice; 24 hours; 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;.
- Q7160:** Y. W. Yu, *et al.* Glucose-Dependent Insulinotropic Polypeptide Mitigates 6-OHDA-Induced Behavioral Impairments in Parkinsonian Rats. *Int J Mol Sci* 2018;19(4):
ALZET Comments: Glucose-dependent insulinotropic polypeptide; Saline; SC; Rat; 2002; 2 weeks; Dose (7.8 or 15 nmol/kg/day); Controls received mp w/ vehicle; behavioral testing (Open field test); functionality of mp verified by plasma levels; Resultant plasma level (GIP administration at 15 nmol/kg/day resulted in total GIP plasma levels of 203.9 pmol/L); neurodegenerative (Parkinson's);.
- Q6914:** Y. Mori, *et al.* Glucose-Dependent Insulinotropic Polypeptide Suppresses Peripheral Arterial Remodeling in Male Mice. *Endocrinology* 2018;159(7):2717-2732
ALZET Comments: Glucose-dependent insulinotropic polypeptide; SC; Mice (knockout); 1002; Dose (GIP(1-42) and GIP(3-42) were 50 nmol/kg/d, except for experiment 2, where GIP(1-42) at 25 nmol/kg/d was also administered); animal info (Seven-week-old male C57BL/6 (wild-type) and db/db mice); peptides; cardiovascular;.
- 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;.
- 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;.
- 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);.
- Q5962:** H. Okamoto, *et al.* Glucagon receptor inhibition normalizes blood glucose in severe insulin-resistant mice. *Proc Natl Acad Sci U S A* 2017;114(10):2753-2758
ALZET Comments: S961 insulin receptor antagonist; PBS; SC; Mice; 2002; 14 days; Controls received mp w/ vehicle; animal info (C57BL/6 mice, 10-wk old males); Dose (20 nmol/wk);.
- 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);.
- 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
ALZET Comments: S-nitrosoglutathione; insulin; glutathione; CSF/CNS (third ventricle); Rat; mice; 1002; 2002; 1 week; 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);

Q5505: Y. W. Yu, *et al.* Glucose-Dependent Insulinotropic Polypeptide Ameliorates Mild Traumatic Brain Injury-Induced Cognitive and Sensorimotor Deficits and Neuroinflammation in Rats. *J Neurotrauma* 2016;33(22):2044-2054

ALZET Comments: Glucose-dependent insulinotropic polypeptide; Saline; SC; Rat; 7 days; 2 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-300g, adult); functionality of mp verified by plasma levels (pg 2049); behavioral testing (Morris water maze; recognition memory test; beam walking test; novel object recognition); peptides; traumatic brain injury; Dose (21.58 or 38.85 ug/kg/day); Resultant plasma level (58.6 +/- 11.8 pmol/L);

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);

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);

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

ALZET Comments: Insulin, Insulin Detemir; Saline; SC; Mice; 8 days; 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

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;

Q5381: K. Kohashi, *et al.* A Dipeptidyl Peptidase-4 Inhibitor but not Incretins Suppresses Abdominal Aortic Aneurysms in Angiotensin II-Infused Apolipoprotein E-Null mice. *Journal of Atherosclerosis and Thrombosis* 2016;23(4):441-454

ALZET Comments: Angiotensin II; Glucagon-like peptide-1; Glucose-dependent insulinotropic polypeptide; Saline; SC; Mice; 1002; 4 weeks; Controls received mp w/ vehicle; animal info (ApoE^{-/-} mice, 9 weeks old); functionality of mp verified by plasma levels, blood pressure; pumps replaced every 2 weeks; cardiovascular; atherosclerosis; peptides; Pathophysiology similarities btwn abdominal aortic aneurysms, atherosclerosis; blood pressure measure via tail-cuff method; Dose (2000 ng/kg/min AngII, 2.16 nmol/kg/day GLP-1, 25 nmol/kg/day GIP); Resultant blood pressure (Start: 104 mmHg, End: 118 mmHg);

Q5548: K. Kohashi, *et al.* A Dipeptidyl Peptidase-4 Inhibitor but not Incretins Suppresses Abdominal Aortic Aneurysms in Angiotensin II-Infused Apolipoprotein E-Null Mice. *Journal of Atherosclerosis and Thrombosis* 2016;23(4):441-454

ALZET Comments: Angiotensin II, Glucagon-like peptide-1, Glucose-Dependent Insulinotropic Polypeptide; Saline; SC; Mice (knockout); 1002; 4 weeks; Controls received mp w/ vehicle; animal info (13 weeks old); pumps replaced every 2 weeks;



Multiple pumps per animal (2); one for either Ang II, GLP-1 or GIP; enzyme inhibitor (Dipeptidyl Peptidase-4 inhibitor); Therapeutic indication (Abdominal aortic aneurysm); Dose (Angiotensin II: 2000 ng/kg/min, Angiotensin II + GIP: 25 nmol/kg/day, DPP-4i: 6 mg/kg/day);.

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

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);.

Q5778: Pancreatic β -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);.

Q4939: N. M. Templeman, *et al.* Suppression of hyperinsulinaemia in growing female mice provides long-term protection against obesity. *Diabetologia* 2015;58(10):2392-402

ALZET Comments: Insulin2, murine peptide; SC; Mice; 2004; 28 days; Controls received mp w/ vehicle; animal info (Ins1 -/-; 25 weeks old); functionality of mp verified by plasma insulin; peptides; diabetes; Dose (0.1 U/day);.

Q4039: G. Pandey, *et al.* Insulin Regulates Nitric Oxide Production in the Kidney Collecting Duct Cells. *Journal of Biological Chemistry* 2015;590(5582-5591

ALZET Comments: Insulin (Humulin R); SC; Mice; 1007D; 14 days; 28 days; Animal info (male, C57BL6J, 5 months old); cardiovascular;.

Q5241: Keunhee Oh, *et al.* In Vivo Differentiation of Therapeutic Insulin-Producing Cells from Bone Marrow Cells via Extracellular Vesicle-Mimetic Nanovesicles. *ACS Nano* 2015;9(12):11718-11727

ALZET Comments: Insulin; SC; Mice (NOD); 14 days; animal info (BALB/c, NOD male mice, aged 7-10 wks); functionality of mp verified by blood glucose levels; diabetes; Dose (0.14 units/day);.

Q3779: G. T. Dodd, *et al.* Leptin and Insulin Act on POMC Neurons to Promote the Browning of White Fat. *Cell* 2015;160(88-104

ALZET Comments: Leptin; insulin, human; CSF/CNS; CSF/CNS (intra-arcuate nucleus of the hypothalamus); Mice; 1002; 6 days; Control animals received mp w/ vehicle; animal info (8 wks old, C57BL/6); ALZET brain infusion kit (3) used; Plastics One bilateral cannula used with PEG tubing and a Y connector.

R0323: W. R. Crowley, *et al.* Neuroendocrine Regulation of Lactation and Milk Production. *COMPREHENSIVE PHYSIOLOGY* 2015;5(255-291

ALZET Comments: Leptin; insulin; SC; Rat; Animal info (female);.

Q3794: L. Adzovic, *et al.* Insulin improves memory and reduces chronic neuroinflammation in the hippocampus of young but not aged brains. *Journal of Neuroinflammation* 2015;12(U1-U10

ALZET Comments: Insulin, recombinant cat; endotoxin, LPS; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, F-344, 3 months old, 21 months old); bilateral cannula used; behavioral testing (morris water maze); tissue perfusion (fourth ventricle); bilateral infusion; used tygon tubing to attach cannula to pump;.



Q4000: P. Mehrotra, *et al.* Pathogenicity of Mycobacterium tuberculosis Is Expressed by Regulating Metabolic Thresholds of the Host Macrophage. PLoS Pathogens 2014;10(U589-U608)

ALZET Comments: Insulin, bovine; UK5099; SC; Mice; Controls received mp w/ vehicle; animal info (female, BALB/C, 4-6 weeks old); immunology; diabetes;.

R0325: V. F. H. Jensen, *et al.* Effect of Insulin-Induced Hypoglycaemia on the Peripheral Nervous System: Focus on Adaptive Mechanisms, Pathogenesis and Histopathological Changes. Journal of Neuroendocrinology 2014;26(482-496)

ALZET Comments: Insulin (Humulin R); SC; Mice; rats; 9-14 days; Animal info (mice; female, B6C3F1, 9-10 or 95weeks old, 20-26g rats; female, 9-10 weeks old, 216-228g); pumps replaced every 5-10 days; diabetes;.

Q3329: K. Tsuchiya, *et al.* Liver Sinusoidal Endothelial Cells Link Hyperinsulinemia to Hepatic Insulin Resistance. Diabetes 2013;62(5):1478-1489

ALZET Comments: Insulin; PBS; Mice; 1003D; 72 hours; Controls received mp w/ vehicle; animal info (male, VECKO); functionality of mp verified by plasma insulin; no stress (see pg.1480); peptides; diabetes;.

Q2934: C. M. Thomas, *et al.* Direct renin inhibition prevents cardiac dysfunction in a diabetic mouse model: comparison with an angiotensin receptor antagonist and angiotensin-converting enzyme inhibitor. Clinical Science 2013;124(7-8):529-541

ALZET Comments: Insulin (Humulin N); aliskiren (renin inhibitor); benazeprilat (ACEi); valsartan (ARB); streptozotocin; Saline; SC; Mice; 1004; 10 weeks; Controls received mp w/vehicle, or (0.1M sodium citrate buffer (pH 4.5)); cardiovascular; animal info (male, C57b16/J, 12 weeks, blood glucose > 250 mg/dl); pumps replaced every 4 weeks; enzyme inhibitor (renin); diabetes;.

Q3175: A. C. Palei, *et al.* Euglycemic Hyperinsulinemia Increases Blood Pressure in Pregnant Rats Independent of Placental Antiangiogenic and Inflammatory Factors. American Journal of Hypertension 2013;26(11):1445-1451

ALZET Comments: Insulin; SC; Rat (pregnant); 1007D; 7 days; Animal info (female, Sprague Dawley); functionality of mp verified by serum insulin levels; cardiovascular; peptides; diabetes;.

Q2893: L. Novikova, *et al.* Variations in Rodent Models of Type 1 Diabetes: Islet Morphology. JOURNAL OF DIABETES RESEARCH 2013;;(;):U1-U13

ALZET Comments: Insulin; SC; Rat; 4 weeks; Peptides; animal info (BBDR, rat, 23-25 days); functionality of mp verified by measuring blood glucose levels; diabetes;.

Q2520: L. J. Li, *et al.* Reduced ENaC activity and blood pressure in mice with genetic knockout of the insulin receptor in the renal collecting duct. American Journal of Physiology-Renal Physiology 2013;304(3):F279-F288

ALZET Comments: Insulin (Humulin R); SC; Mice; 1007D; 7 days; Animal info (AQP2-Cre, wt).

Q2956: S. N. Hokke, *et al.* Altered Ureteric Branching Morphogenesis and Nephron Endowment in Offspring of Diabetic and Insulin-Treated Pregnancy. PLoS One 2013;8(3):U453-U461

ALZET Comments: Insulin; Saline; Mice; 1007D; Controls received mp w/ saline; Peptides; animal info (8-12wk, C57BL/6J, mice (pregnant)); mp used to infuse insulin to study the effect of hyperglycemia and glycemic control on ureteric branching during pregnancy; diabetes;.

Q2960: H. Frikke-Schmidt, *et al.* Adipose Weight Gain during Chronic Insulin Treatment of Mice Results from Changes in Lipid Storage without Affecting De Novo Synthesis of Palmitate. PLoS One 2013;8(9):U1010-U1016

ALZET Comments: Insulin, human; SC; Mice; 1002; Controls received mp w/ phosphate buffer; animal info (15 weeks old, female, C57BL6/J).

Q4780: Christian W. Grant, *et al.* Testing Agents for Prevention or Reversal of Type 1 Diabetes in Rodents. PLoS One 2013;8(8):1-14



ALZET Comments: ISO-092, Insulin (Humulin R); SC; Rat; not specified; 21 days; 22 days; animal info: LEW.1WR1, male and female, 21-25 days old; functionality of mp verified by glycosuria, blood glucose levels >250 mg/dl; dose response: Fig. 6; insulin (0.25 U/day); ISO-092 is a small molecule MIF inhibitor.

Q2010: Y. Nogi, *et al.* Glucose-Dependent Insulinotropic Polypeptide Prevents the Progression of Macrophage-Driven Atherosclerosis in Diabetic Apolipoprotein E-Null Mice. *PLoS One* 2012;7(4):U967-U974

ALZET Comments: Glucose-dependent insulinotropic polypeptide; Saline; SC; Mice; 1007D; 4 weeks; Controls received mp w/ vehicle; animal info (8 wks old, ApoE -/-); functionality of mp verified via plasma drug levels.

Q2734: C. W. Grant, *et al.* Development of Standardized Insulin Treatment Protocols for Spontaneous Rodent Models of Type 1 Diabetes. *COMPARATIVE MEDICINE* 2012;62(5):381-390

ALZET Comments: Insulin (Humulin R); SC; Mice (NOD); 1002; 14 days; Animal info (diabetic, NOD); Humulin R used; wound clips used; diabetes; dose response (Table 1); "Compared with injected insulin, osmotic insulin pumps provided superior glycemic control, although diabetic NOD mice did experience events of hypoglycemia. diabetes;".

Q2730: S. Fredersdorf, *et al.* Increased myocardial SERCA expression in early type 2 diabetes mellitus is insulin dependent: In vivo and in vitro data. *Cardiovascular Diabetology* 2012;11(;):U1-U11

ALZET Comments: Insulin; SC; Rat; 2ML2; 2ML4; 6 weeks; animal info (male, Zucker, 118 g, 13 wks old); pumps replaced after 2 weeks; diabetes; "Pumps were changed after 2 weeks and the insulin dose was adapted to normalize blood glucose levels" pg 3; long-term study;.

Q2180: Q. Ding, *et al.* Caloric restriction increases adiponectin expression by adipose tissue and prevents the inhibitory effect of insulin on circulating adiponectin in rats. *JOURNAL OF NUTRITIONAL BIOCHEMISTRY* 2012;23(8):867-874

ALZET Comments: Insulin; Saline, isotonic; plasma, rat, stripped; SC; Rat; 2002; 1 week; Controls received mp w/ vehicle; animal info (male, brown, Norway, 4 mo old).

Q1309: S. J. Salpeter, *et al.* Glucose Regulates Cyclin D2 Expression in Quiescent and Replicating Pancreatic beta-Cells Through Glycolysis and Calcium Channels. *Endocrinology* 2011;152(7):2589-2598

ALZET Comments: Insulin; Mice; 2001; 5 days; Animal info (1 mo old, ICR, D2 +/-).

Q1284: S. Polakof, *et al.* Glucose homeostasis in rainbow trout fed a high-carbohydrate diet: metformin and insulin interact in a tissue-dependent manner. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 2011;300(1):R166-R174

ALZET Comments: Insulin, bovine; metformin; IP; Fish (rainbow trout); 1003D; 11 days; Controls received mp w/ saline; animal info (200 g); multiple pumps per animal (2); no stress (see pg. R167); post op. care (antibiotic gel); "No symptoms of stress, including alterations in feeding behavior, were observed as a consequence of pump implantation."

Q0655: S. Polakof, *et al.* Insulin Stimulates Lipogenesis and Attenuates Beta-Oxidation in White Adipose Tissue of Fed Rainbow Trout. *Lipids* 2011;46(2):189-199

ALZET Comments: Insulin, bovine; IP; Fish (Rainbow trout); 5, 11 days; Controls received mp w/ saline; animal info (rainbow trout, 200 g); post op. care (antibiotic gel).

Q1271: M. Oelze, *et al.* Vascular Dysfunction in Streptozotocin-Induced Experimental Diabetes Strictly Depends on Insulin Deficiency. *JOURNAL OF VASCULAR RESEARCH* 2011;48(4):275-284

ALZET Comments: Insulin; SC; Rat; 2, 8 weeks; Animal info (male, Wistar, 6 wks old, 250 g, STZ induced); diabetes; long-term study.

Q1519: M. Nagashima, *et al.* Native incretins prevent the development of atherosclerotic lesions in apolipoprotein E knockout mice. *Diabetologia* 2011;54(10):2649-2659

ALZET Comments: Glucagon-like peptide-1 (7-36) amide; glucagon-like peptide-1 (9-36) amide; exendin (9-39) amide; glucose-dependent insulinotropic polypeptide (1-42); glucose-dependent insulinotropic polypeptide (3-42);



glucose-dependent insulinotropic polypeptide, pro 3; Saline; Mice; 1007D; 4 weeks; Controls received mp w/ vehicle; animal info (apoE -/-, 17 wks old); peptides.

Q1344: A. Shimotoyodome, *et al.* RS4-type resistant starch prevents high-fat diet-induced obesity via increased hepatic fatty acid oxidation and decreased postprandial GIP in C57BL/6J mice. AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM 2010;298(3):E652-E662

ALZET Comments: Insulin; SC; Mice; 1002; Controls received mp w/ saline; animal info (male, C57BL/6J, 8 wks old).

Q0030: Y. M. Searls, *et al.* Intracellular Ca²⁺ regulating proteins in vascular smooth muscle cells are altered with type 1 diabetes due to the direct effects of hyperglycemia. Cardiovascular Diabetology 2010;9(1):U1-U17

ALZET Comments: Insulin (Humulin R); SC; Rat; 2004; 28 days; Controls received mp w/saline; peptides; animal info (male, DR-BB Wistar, 21-26 days old); comparison of SC injections vs. mp; replacement therapy (anti-RT6 mAB-induced diabetes); endocrinology; Humulin R, Humulin U and Humulin N used;

Q0182: S. Polakof, *et al.* Insulin-induced hypoglycaemia is co-ordinately regulated by liver and muscle during acute and chronic insulin stimulation in rainbow trout (*Oncorhynchus mykiss*). Journal of Experimental Biology 2010;213(9):1443-1452

ALZET Comments: Insulin, bovine; Saline; IP; Fish (trout); 1003D; 4 days; Controls received mp w/ vehicle; peptides; animal info (rainbow trout, 170 g); post op. care (antibiotic ointment); comparison of IP injections vs. mp; 17 degrees C; endocrinology.

Q1649: S. Polakof, *et al.* Effects of insulin infusion on glucose homeostasis and glucose metabolism in rainbow trout fed a high-carbohydrate diet. Journal of Experimental Biology 2010;213(24):4151-4157

ALZET Comments: Insulin, bovine; IP; Fish (rainbow trout); 1003D; 5 days; Controls received mp w/ saline; animal info (immature); post op. care (antibiotic gel).

P9976: L. Nordquist, *et al.* Proinsulin C-peptide prevents type-1 diabetes-induced decrease of renal Na⁺-K⁺-ATPase alpha-1-subunit in rats. DIABETES-METABOLISM RESEARCH AND REVIEWS 2010;26(3):193-199

ALZET Comments: C-peptide, human; insulin, recomb. human; SC; Rat; 2ML2; 1 weeks; Controls received mp w/ saline; animal info (male, Sprague Dawley, 15 wks old, 350-450 g.); replacement therapy (STZ-induced Diabetes); peptides.

Q0322: F. Annaba, *et al.* Ileal apical Na(+)-dependent bile acid transporter ASBT is upregulated in rats with diabetes mellitus induced by low doses of streptozotocin. American Journal of Physiology-Gastrointestinal and Liver Physiology 2010;299(4):G898-G906

ALZET Comments: Insulin, human; SC; Rat; 2ML1; 3 days; Animal info (Sprague-Dawley, males, 7-8 wks old, 200-250 g); diabetes; "Upon insulin treatment from subcutaneous osmotic pumps, glucose levels were restored to normal" pg G904; streptozotocin-induced diabetes.

Q0506: A. Adam, *et al.* Altered cardiac bradykinin metabolism in experimental diabetes caused by the variations of angiotensin-converting enzyme and other peptidases. Neuropeptides 2010;44(2):69-75

ALZET Comments: Insulin (Humulin R); IP; Rat; 2ML2; 7 days; Controls received no treatment; animal info (diabetic, Sprague Dawley, 125-150 g.); diabetes.

Q0568: J. Xu, *et al.* Regulation of Food Intake and Gonadotropin-Releasing Hormone/Luteinizing Hormone during Lactation: Role of Insulin and Leptin. Endocrinology 2009;150(9):4231-4240

ALZET Comments: Insulin, human; leptin, rat; Saline; SC; Rat; 1003D; 48 hours; Controls received mp w/ vehicle; animal info (d 8-9 post partum, 6 d post ovariectomy); multiple pumps per animal (2); replacement therapy (ovariectomized).

P9941: S. Polakof, *et al.* Glucose homeostasis is impaired by a paradoxical interaction between metformin and insulin in carnivorous rainbow trout. American Journal of Physiology-Regulatory Integrative and Comparative Physiology 2009;297(6):R1769-R1776

ALZET Comments: Metformin; insulin, bovine; SC; Fish; 1007D; Controls received mp w/ saline; post op.care (antibiotic gel); animal info (rainbow trout); one group contained metformin and insulin.



Q0939: S. Park, *et al.* Long-Term Intracerebroventricular Infusion of Insulin, but Not Glucose, Modulates Body Weight and Hepatic Insulin Sensitivity by Modifying the Hypothalamic Insulin Signaling Pathway in Type 2 Diabetic Rats. *Neuroendocrinology* 2009;89(4):387-399

ALZET Comments: Insulin (Humulin); glucose; CSF/CNS; Rat; 4 weeks; Controls received mp w/ artificial CSF; animal info (Sprague-Dawley, male, 215 g); one group contained insulin + glucose; pump connected to catheter after 1 week recovery period.

P8758: J. P. Warne, *et al.* The gastroduodenal branch of the common hepatic vagus regulates voluntary lard intake, fat deposition, and plasma metabolites in streptozotocin-diabetic rats. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2008;294(1):E190-E200

ALZET Comments: Insulin (Humulin R); IV (superior mesenteric); Rat; 2002; 10 days; Controls received mp w/ saline; replacement therapy (STZ-induced Diabetes, gastroduodenal branch vagotomy); Humulin R U500 used.

P9611: C. Takimoto, *et al.* Candesartan and Insulin Reduce Renal Sympathetic Nerve Activity in Hypertensive Type 1 Diabetic Rats. *HYPERTENSION RESEARCH* 2008;31(10):1941-1951

ALZET Comments: Insulin; SC; Rat; 2 weeks; Controls received mp w/ vehicle; animal info (male, 13 wks old, SHR); replacement therapy (STZ-induced Diabetes).

P9376: W. E. Rodriguez, *et al.* PPAR gamma agonist normalizes glomerular filtration rate, tissue levels of homocysteine, and attenuates endothelial-myocyte uncoupling in alloxan induced diabetic mice. *International Journal of Biological Sciences* 2008;4(4):236-244

ALZET Comments: FITC-Insulin; IP; Mice; 2001D; 24 hours; Replacement therapy (Alloxan-induced diabetes); cardiovascular; animal info (male, C57BL/6J); endocrinology.

P8753: L. Koch, *et al.* Central insulin action regulates peripheral glucose and fat metabolism in mice. *Journal of Clinical Investigation* 2008;118(6):2132-2147

ALZET Comments: Leptin; insulin; SC; CSF/CNS; Mice; 1002; 2001; 7 days; Controls received mp w/ vehicle; functionality of mp verified by serum leptin levels; ALZET brain infusion kit 3 used; peptides; cyanoacrylate adhesive; animal info (C57BL/6, wt, IR-d-wb, 10-14 wks old); cannula position confirmed post mortem with methylene blue.

P8767: M. E. Johansson, *et al.* Hyperinsulinemic rats are normotensive but sensitized to angiotensin II. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 2008;294(4):R1240-R1247

ALZET Comments: Insulin; losartan; SC; Rat; 6 weeks; Controls received mp w/ no treatment; cardiovascular; peptides; animal info (female, Sprague Dawley, 180g.); endocrinology.

P8701: J. P. Warne, *et al.* Mapping brain c-fos immunoreactivity after insulin-induced voluntary lard intake: Insulin- and lard-associated patterns. *Journal of Neuroendocrinology* 2007;19(10):794-808

ALZET Comments: Insulin (Humulin R); Saline; IV (jugular); Rat; 2002; 10 days; Controls received mp w/ vehicle; replacement therapy (STZ-induced diabetes); no stress (see pg. 797); peptides; post op. care (Ketoprofen); animal info (male, Sprague-Dawley, 300g); "The presence of an osmotic mini-pump at either site did not cause any obvious signs of pains or discomfort in the rats." (p. 797); Humulin R U500 used.

P8620: J. P. Warne, *et al.* Afferent signalling through the common hepatic branch of the vagus inhibits voluntary lard intake and modifies plasma metabolite levels in rats. *JOURNAL OF PHYSIOLOGY-LONDON* 2007;583(2):455-467

ALZET Comments: Insulin (Humulin R); IV (superior mesenteric); Rat; 2002; 10 days; Controls received mp w/ saline; replacement therapy (STZ-induced diabetes); peptides; animal info (male, Sprague-Dawley, 300 g); catheter position verified; Humulin R U500 used.

P8957: S. Tiwari, *et al.* Reduced expression of insulin receptors in the kidneys of insulin-resistant rats. *Journal of the American Society of Nephrology* 2007;18(10):2661-2671



ALZET Comments: Insulin (Humulin R); SC; Rat; 2002; 28 days; Controls received sham operation; pumps replaced; peptides; animal info (Sprague Dawley, 250-280 g.); nephrology; Research Diets.

P8310: A. K. Singh, *et al.* Transplanting fragments of diabetic pancreas into activated omentum gives rise to new insulin producing cells. *Biochemical and Biophysical Research Communications* 2007;355(1):258-262

ALZET Comments: Insulin; SC; Rat; 28 days; Replacement therapy (STZ-induced diabetes, pancreatectomy and autotransplanted into omentum; immunology; animal info (male, Sprague-Dawley, 150-200g.); nephrology.

P8972: S. Prabhakar, *et al.* Diabetic nephropathy is associated with oxidative stress and decreased renal nitric oxide production. *Journal of the American Society of Nephrology* 2007;18(11):2945-2952

ALZET Comments: Insulin, porcine; Glycerine; ethanol; SC; Rat; 2004; 12 weeks; Controls received no treatment; long-term study; pumps replaced every 4 wks; multiple pumps per animal (2); animal info (ZSF1, 8 wks old, 200-250 g.); 50% ethanol used.

P8149: P. Kovacs, *et al.* The effect of diabetes and centrally administered insulin on anterior hypothalamic estrogen receptor alpha immunoreactivity. *ACTA DIABETOLOGICA* 2007;44(1):38-44

ALZET Comments: Insulin (Humulin); Saline; CSF/CNS (third ventricle); Rat; 2002; 14 days; Controls received mp w/ vehicle; replacement therapy (STZ-induced Diabetes, ovariectomy); peptides; animal info (female, Sprague-Dawley, 175-200g.); tissue perfusion (ventricle).

P8734: S. J. Kim, *et al.* Resistin is a key mediator of glucose-dependent insulinotropic polypeptide (GIP) stimulation of lipoprotein lipase (LPL) activity in adipocytes. *Journal of Biological Chemistry* 2007;282(47):34139-34147

ALZET Comments: Glucose-dependent insulinotropic polypeptide; PBS; IP; Rat; 2 weeks; Controls received mp w/ vehicle; peptide; animals info (VDF Zucker, Fa/Fa or lean; 8 weeks old).

P8073: C. C. Hoppe, *et al.* Combined prenatal and postnatal protein restriction influences adult kidney structure, function, and arterial pressure. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 2007;292(1):R462-R469

ALZET Comments: Insulin; aminohippuric acid, p-; Radio-isotopes; 3H tracer; SC; Rat; 2ML1; 3 days; Cardiovascular; animal info (Sprague-Dawley, male, 132 days old, 340-425g.); nephrology.

P8516: L. Z. Hong, *et al.* Hyperinsulinemia Instead of Insulin Resistance Induces Baroreflex Dysfunction in Chronic Insulin-Infused Rats. *American Journal of Hypertension* 2007;20(4):451-458

ALZET Comments: Insulin, porcine; Glycerin; ethanol; SC; Rat; 2002; 8 weeks; Controls received mp w/ vehicle; long-term study; pumps replaced every 14 days; post op. care (penicillin); animal info (male, Sprague-Dawley, 200-250 grams); 50% ETOH used [manufacturer suggests 15% or less ETOH; for pump compatibility purposes].

P8683: M. Garcia-San Frutos, *et al.* Impaired central insulin response in aged Wistar rats: Role of adiposity. *Endocrinology* 2007;148(11):5238-5247

ALZET Comments: Insulin, human; PBS; CSF/CNS; Rat; 2001; 7 days; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose-response (fig. 1, p. 5241); peptides; animal info (Wistar, 3, 8, 24 month, male); endocrinology.

P8167: A. K. Bidani, *et al.* Spontaneously reduced blood pressure load in the rat streptozotocin-induced diabetes model: potential pathogenetic relevance. *American Journal of Physiology-Renal Physiology* 2007;292(2):F647-F654

ALZET Comments: Insulin; SC; Rat; 16-20, 36-40 weeks; Replacement therapy (STZ-induced Diabetes); long-term study; pumps replaced every 4 weeks; peptides; animal info (male, Sprague-Dawley, 8 weeks old, 250 grams).

P7985: J. P. Warne, *et al.* Comparison of superior mesenteric versus jugular venous infusions of insulin in streptozotocin-diabetic rats on the choice of caloric intake, body weight, and fat stores. *Endocrinology* 2006;147(11):5443-5451



ALZET Comments: Insulin (Humulin R), methylene blue; Saline; IV (jugular); Rat; 2002; Functionality of mp verified by dye infusion; replacement therapy (diabetic); no stress (see pg. 5444); good methods; peptides; animal info (male, Sprague-Dawley, 275 grams); diabetes; PE-60 fused to PE-5.

P7928: C. Toth, *et al.* Rescue and regeneration of injured peripheral nerve axons by intrathecal insulin. *Neuroscience* 2006;139(2):429-449

ALZET Comments: Insulin; Saline; CSF/CNS (intrathecal, lumbar, peroneal nerve); Rat; 2002; 2 weeks; Controls received mp w/ vehicle; peptides; animal info (adult male, Sprague-Dawley, 250-300 grams); silicone catheters (0.012" x 0.025") used between L6-S1 vertebrae; nerve perfusion chamber used for nerve infusion; nerve injury; India Ink in pumps to verify delivery; behavioral testing.

P8004: H. Toba, *et al.* Hyperinsulinaemia increases the gene expression of endothelial nitric oxide synthase and the phosphatidylinositol 3-kinase/Akt pathway in rat aorta. *Clinical and Experimental Pharmacology and Physiology* 2006;33(5-6):440-447

ALZET Comments: Insulin (Humulin); Saline; SC; Rat; 2 weeks; Controls received mp w/ vehicle; insulin plasma levels taken; cardiovascular; peptides; animal info (male, Wistar, 280-300 grams).

P7758: J. Song, *et al.* Regulation of blood pressure, the epithelial sodium channel (ENaC), and other key renal sodium transporters by chronic insulin infusion in rats. *American Journal of Physiology-Renal Physiology* 2006;290(5):F1055-F1064

ALZET Comments: Insulin (Humulin R); Water; SC; Rat; 2002; 28 days; Controls received sham surgery; pumps replaced at 2 weeks; no stress (see pg. F1056); animal info (male, Sprague-Dawley, 250-280g.); Humulin-R; continuous radiotelemetry to record blood pressure; ; Humulin R U500 used.

P7451: C. Fekete, *et al.* Differential effects of central leptin, insulin, or glucose administration during fasting on the hypothalamic-pituitary-thyroid axis and feeding-related neurons in the arcuate nucleus. *Endocrinology* 2006;147(1):520-529

ALZET Comments: Leptin, recomb. mouse; insulin; glucose; CSF, artificial; CSF/CNS; Rat; 1003D; 3 days; Controls received mp w/ vehicle; functionality of mp verified by agent levels in CSF+ serum; peptides; post op. care (bacitracin ointment); animal info (male Sprague-Dawley, 200-250 g); cannula placement confirmed by light microscope.

P8304: S. Chakrabarty, *et al.* Ovarian dysfunction in peripubertal hyperinsulinemia. *JOURNAL OF THE SOCIETY FOR GYNECOLOGIC INVESTIGATION* 2006;13(2):122-129

ALZET Comments: Insulin; SC; Rat; 2004; 4 weeks; Controls received mp w/ physiological saline; no stress (see pg. 126); peptides; animal info (female, Sprague-Dawley, 28 days old); "This method of drug delivery eliminates the stress and trauma of daily injections." (p. 126).

P8217: J. M. Castellano, *et al.* Expression of hypothalamic KiSS-1 system and rescue of defective gonadotropic responses by kisspeptin in streptozotocin-induced diabetic male rats. *Diabetes* 2006;55(9):2602-2610

ALZET Comments: Insulin; leptin; Saline; HCl; CSF/CNS; Rat; 2001; 6 days; Controls received mp w/ vehicle, or nondiabetic; replacement therapy (STZ-induced Diabetes); peptides; animal info (male, Wistar, adult).

P6903: J. Nyberg, *et al.* Glucose-dependent insulinotropic polypeptide is expressed in adult hippocampus and induces progenitor cell proliferation. *Journal of Neuroscience* 2005;25(7):1816-1825

ALZET Comments: Glucose-dependent insulinotropic polypeptide; PBS; CSF/CNS (third ventricle); Rat; 2001; 5 days; Controls received mp w/ vehicle; ALZET brain infusion kit 2; peptides; GIP.

P7329: S. J. Kim, *et al.* Glucose-dependent insulinotropic polypeptide (GIP) stimulation of pancreatic beta-cell survival is dependent upon phosphatidylinositol 3-kinase (PI3K)/protein kinase B (PKB) signaling, inactivation of the forkhead transcription factor Foxo1, and down-regulation of bax expression. *Journal of Biological Chemistry* 2005;280(23):22297-22307

ALZET Comments: Glucose-dependent insulinotropic polypeptide (1-42), synthetic porcine; IP; Rat; 2 weeks; Replacement therapy (diabetic); immunology; peptides.



P6949: M. Fowler, *et al.* Assessment of pancreatic islet mass after islet transplantation using in vivo bioluminescence imaging. *Transplantation* 2005;79(7):768-776

ALZET Comments: Insulin, human; SC; Mice (SCID); 1002; 7,10 days; Diabetes; bioluminescence imaging (BLI); IVIS 200 system used after pumps were removed.

P7358: A. El Midaoui, *et al.* Increases of spinal kinin receptor binding sites in two rat models of insulin resistance. *Peptides* 2005;26(8):1323-1330

ALZET Comments: Insulin; SC; Rat; 2002; 2 weeks; Peptides; diabetes.

P6956: A. El Midaoui, *et al.* Effects of glucose and insulin on the development of oxidative stress and hypertension in animal models of type 1 and type 2 diabetes. *Journal of Hypertension* 2005;23(3):581-588

ALZET Comments: Insulin; Saline; glutamic acid; Rat; 2002; 2 weeks; Controls received mp w/ vehicle; insulin plasma levels taken; cardiovascular; peptides; diabetes; 0.7% glutamic acid added to prevent insulin aggregation; replacement therapy (STZ-induced Diabetes).

P7673: C. Dragonas, *et al.* Role of insulin in the progression of ovarian sex cord stromal tumors in rats. *Journal of Cancer Research and Clinical Oncology* 2005;131(11):751-757

ALZET Comments: Insulin; SC; Rat; 28, 56, 84 days; Controls received mp w/ saline; replacement therapy (ovariectomy, STZ-induced diabetes); long-term study; pumps replaced every 28 days; no stress (see pg.753); cancer (sex cord stromal); animal info (female, Lewis, 60 days old, 150-210 g).