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

Q10254: T. Masaki, et al. GIP_HUMAN(22-51) is a new proatherogenic peptide identified by native plasma peptidomics. Scientific Reports 2021;11(1):14470

Agents: Glucose-dependent insulinotropic polypeptide; Glucose-dependent insulinotropic polypeptide neutralising antibody
Vehicle: Saline; Route: SC; Species: Mice; Pump: 1002; Duration: 4 weeks;
ALZET Comments: Dose: (0.6 nmol/kg/h) or (1.4 μg/kg/h); Controls received mp w/ vehicle; animal info: ApoE, 17 weeks of age, pumps replaced after 2 weeks; Glucose-dependent insulinotropic polypeptide aka (GIP)


Agents: Glucose-dependent insulinotropic polypeptide(3-30)-NH2; GIPR antagonist Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 days;
ALZET Comments: Dose (30 mg/mL); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL/6JRj mice, 23-week-old males); Glucose-dependent Insulinotropic Polypeptide(3-30)-NH2 aka GIP(3-30)NH2; replacement therapy (Gut Hormones);


Agents: Insulin Receptor Antagonist Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (8 weeks old, RIP-Cre); Insulin Receptor Antagonist aka S961; diabetes;


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;


Agents: FITC-insulin Vehicle: PBS; 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 FVBN/J mice, 8-10 weeks old); diabetes;


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;


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);
**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;

**Agents:** Insulin, recombinant human **Vehicle:** Saline; **Route:** SC; **Species:** Mice (Pregnant); **Pump:** 1007D; **Duration:** 1 week; 
**ALZET Comments:** Dose (0.1 units/kg/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;

**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;

**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;

**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;

**Agents:** Insulin Glargine, Pancreastatin Inhibitor **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks; 
**ALZET Comments:** Dose (1 mg/kg/day or 30 U/kg/day); Controls received mp w/ vehicle; animal info (male C57BL/6 male mice (20 ± 2 g)); Pancreastatin Inhibitor aka PSTi8; diabetes;

**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;

**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;

**Agents:** Glucose-dependent insulinotropic polypeptide  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 2 weeks;

**ALZET Comments:** 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);

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;


**Agents:** Glucose-dependent insulinotropic polypeptide  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice (knockout);  
**Pump:** 1002;  
**Duration:** Not Stated;

**ALZET Comments:** 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;


**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;


**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 ul/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;
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;

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

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);

Agents: S961 insulin receptor antagonist Vehicle: PBS; Route: SC; Species: Rat; mice;

Agents: Insulin Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2002; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6 mice, 10-wk old males); Dose (20 nmol/wk);

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);

Agents: Glucose-dependent insulintropic polypeptide Vehicle: Saline; Route: SC; Species: Rat; Pump: Not Stated; Duration: 7 days; 2 weeks;
ALZET Comments: 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);
**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);

**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);

**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);

**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;

**Agents:** Angiotensin II; Glucagon-like peptide-1; Glucose-dependent insulinotropic polypeptide **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 4 weeks;
**ALZET Comments:** 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; Multiple pumps per animal (2); 1 for either Ang II, GLP-1 or GIP; enzyme inhibitor (Dipeptidyl Peptidase-4 inhibitor); cardiovascular; atherosclerosis; peptides; Pathophysiology similarities btwn abdominal aortic aneurysms, atherosclerosis; Therapeutic indication (Abdominal aortic aneurysm); 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);

**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;

**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);