Recent References (2018-2020) on Diabetes Research Using ALZET® Osmotic Pumps

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, 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;

Agents: Fibroblast growth factor-21, recomb. human Vehicle: Not Stated; Route: IP; Species: Mice; Pump: Not Stated; Duration: 10 days;
ALZET Comments: "Dose (3 mg/kg/day); Controls were db/+ and received mp w/ vehicle; animal info (16 weeks, male, db/db); FGF21 is a robust regulator of metabolism through interactions with FGF receptor 1c and co-factor beta-Klotho.; diabetes; Therapeutic indication (obesity-induced reducing cognitive dysfunction and anxiety-like behavior through reducing glucose tolerance, insulin resistance, and hyperlipidemia); "

Agents: Metformin Vehicle: CSF, artificial; Route: CSF/CNS (lateral ventricle); Species: Rat; Pump: 2006; Duration: Not Stated;
ALZET Comments: Dose (25 ug/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;

Agents: Peptide-1, recombinant human glucagon-like Vehicle: Saline; Route: IV; Species: Rat; Pump: 2004; Duration: 12 weeks;
ALZET Comments: "Dose (1.5 pmol/kg/min);Controls received mp w/ vehicle; animal info (Eight-week-old male/female Wistar rats weighing 300 – 10 g); diabetes; "

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: angiotensin II Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;
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Bibliography

ALZET Comments: Dose (1,000 ng/kg/min); Controls contained functional AT1aR (pancreatic angiotensin type 1 receptor) gene; animal info (8-10 weeks, male, AT1aR(fl/fl) or AT1aR(pdx) transgenic); diabetes; All transgenic mice were of C57BL/6 origin. Mice were fed HF diet throughout this portion of the study;

Agents: CL-316,243 Vehicle: PBS; Route: Not Stated; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Dose (1 mg/kg/day); Controls received mp w/ vehicle; animal info (Six -week-old C57Bl6J and db/db mice); diabetes;

Agents: Dexmedetomide Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML4, 2002; Duration: 28 days;
ALZET Comments: Dose (1 ug/kg/hr); animal info (Sprague Dawley, 8-10 weeks old); Dexmedetomide aka DEX; diabetes;

Agents: Angiotensin II Vehicle: Not stated; Route: SC; Species: Mice; Pump: 2004; Duration: 28 days;
ALZET Comments: Dose (1000 ng/kg/min); animal info (ApoE -/-, C57BL/6, Male, 8-10 weeks old, 20-30g); diabetes;

Agents: Canagliflozin Vehicle: DMSO, PEG; Route: SC; Species: SC; Pump: Not Stated; Duration: 2 weeks;
ALZET Comments: Dose (1 mg/kg/day); 1:1 DMSO:PEG used; animal info (Male LETO and OLETF age 25–30 weeks); functionalty of mp verified by blood pressure and pulse rate via tail-cuff method; cardiovascular; diabetes; Therapeutic indication (type 2 diabetes mellitus);

Agents: Angiotensin II, Nitroglycerin Vehicle: NaCl, Citrate Buffer; Route: Not stated; Species: Rat; Pump: Not Stated; Duration: 7 days, 4 days;
ALZET Comments: Dose (1.0 mg/kg/d or 6.6 ug/kg/min); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (male Wistar Rats, 6 weeks, 300 g); Angiotensin II aka AT-II, Nitroglycerin aka GTN; diabetes;

Agents: Incretin Mimetic Exenatide Vehicle: Not stated; Route: Not stated; Species: Mice; Pump: 1004; Duration: Not stated;
ALZET Comments: Dose (10 ug/kg/day); animal info (Seven week-old C57Bl/6J female mice); diabetes;

Agents: EX-527; 10068-F4 Vehicle: Saline; Route: SC; Species: Mice; Pump: 2004; Duration: 4 weeks;
ALZET Comments: Dose ( EX-527 5 mg/kg/day, 10068-F4 30mg/kg/day ); Controls received mp w/ vehicle; animal info (BKS.Cg-Dock7mC=CLeprdb=J mice, 8 weeks old); enzyme inhibitor (EX-527 is an SIRT1 inhibitor, 10058-F$ is a c-Myc inhibitor); diabetes;

Agents: Insulin Glargine, Pancreastatin InhibitorVehicle: 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:** Aldosterone, d-
  **Vehicle:** Ethanol; Propylene Glycol; Distilled Water; **Route:** Not Stated; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;
  **ALZET Comments:** Dose (2.9 mg/mL); 9% ethanol, 87% propylene glycol, 4% dH2O; Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats); diabetes;

  **Agents:** Anti-GCGR monoclonal antibody
  **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 2 weeks;
  **ALZET Comments:** Dose (3 mg/ml); Controls received mp w/ vehicle; animal info (2-4 months old); diabetes;

  **Agents:** Prolactin
  **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
  **ALZET Comments:** Dose (18 ug/day); Controls received mp w/ vehicle; animal info (5 months old, ob/ob, 56 g); Prolactin aka Prl; diabetes;

  **Agents:** Angiotensin II
  **Vehicle:** saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;
  **ALZET Comments:** Dose (700 ng/min/kg); Controls received agent; animal info (129S6 Akita); diabetes; mp used to accelerate kidney damage;

  **Agents:** Mitochondrial DNA
  **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 Days;
  **ALZET Comments:** Dose (30 ug/kg/day); animal info (Male, CD-1, 18-22 g); diabetes;

  **Agents:** Exendin-4
  **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 2 weeks;
  **ALZET Comments:** Dose (24 nmol/kg/day); Controls received sham surgery; animal info (10 weeks, male, C57BL/6J and db/db); ischemia (coronary artery occlusion); cardiovascular; diabetes; "As there has been no published protocol for long-term EX administration in mice, we followed the initial EX injection with prolonged Exendin-4 administration via osmotic pump for 2 weeks" p.35-36;

  **Agents:** insulin
  **Vehicle:** saline; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 1 month;
  **ALZET Comments:** Dose (11.5 μg/kg/day); Controls received vehicle; animal info (male, Wistar); cardiovascular; diabetes;

  **Agents:** Placenta Growth Factor
  **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (8-week old Diabetic db mice);


Agents: Apelin-13, F13A Vehicle: Saline; Route: IP; Species: Mice; Pump: 1004; Duration: 4 weeks;

ALZET Comments: 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 kkAy mice and control C57BL/6J mice); F13A is an Apelin-13 antagonist; diabetes;


Agents: Angiotensin II Vehicle: Saline; Route: SC; Species: Rat; Pump: Pump model not stated; Duration: Not Stated;

ALZET Comments: Dose (200 ng/kg/min); Controls received mp w/ vehicle; animal info (Male, Wistar, 6-8 weeks old, 180-220 g); diabetes;

Q7319: Q. Wang, et al. Danhong Injection Alleviates Mechanical Allodynia via Inhibiting ERK1/2 Activation and Elevates BDNF Level in Sciatic Nerve in Diabetic Rat. Evidence-Based Complementary and Alternative Medicine 2018;2018(5798453

Agents: U0126 Vehicle: DMSO; CSF, artificial; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 1007D; Duration: 1 week;

ALZET Comments: Dose (0.5 ug/ul/hr); 10% DMSO used; Controls received mp w/ vehicle; animal info (Male, Sprague-Dawley, 180-200 g); behavioral testing (Stimulus test); U0216 is a Mitogen-activated protein kinase (MAPK) kinase 1/2 inhibitor; enzyme inhibitor (Mitogen-activated protein kinase); Intrathecal catheters were inserted into subarachnoid spaces through atlantooccipital membrane; diabetes;


Agents: angiotensin II; INO-1001 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 4 weeks;

ALZET Comments: "Dose ((AngII 1000 ng/kg/min), (INO-1001 5 mg/kg/day)); Controls received no pump; animal info (12-14 weeks, male, C57BLKS/J and C57BLKS/J-leprdb/leprdb); Multiple pumps per animal (2 for AT + INO group); INO-1001 is an enzyme inhibitor (PARP-1); diabetes; Therapeutic indication (PARP-1 inhibition by INO1001 promoted weight loss in the diabetic mice stressed with AT. It attenuated cardiac fibrosis and hypertension in diabetic mice and prevented oxidative stress.);"

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. Cardiovascular Diabetology 2018;17(1):103

Agents: B-type natriuretic peptide Vehicle: Saline; Route: SC; Species: Mice; Pump: Not stated; Duration: 7 days;

ALZET Comments: Dose (2 ng/h/g); Controls received mp w/ vehicle; diabetes;


Agents: Tumor necrosis factor, alpha Vehicle: Saline, BSA Buffered; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days;

ALZET Comments: Dose (6.44 μg/ml at 1 μl/h); Controls received mp w/ vehicle; animal info (9 weeks, male, Gulo(-/-)); diabetes;


Agents: Amyloid-B(25-35) Vehicle: Saline; Route: SC; Species: Rat; Pump: Not stated; Duration: 14 days;

ALZET Comments: Dose (3.6 nmol/day); animal info (Sprague Dawley, 202 g, ); diabetes;

Q8144: G. Navarro, et al. Androgen excess in pancreatic beta cells and neurons predisposes female mice to type 2 diabetes. JCI Insight 2018;3(12):
Agents: Dihydrotestosterone  
**Vehicle:** Not stated;  
**Route:** CSF/CNS (lateral ventricle);  
**Species:** Mice;  
**Pump:** Not stated;  
**Duration:** 4 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (8 weeks old, Female, C57BL/6J); Dihydrotestosterone aka DHT, nonaromatizable AR agonist ; Brain coordinates (L +1 mm, AP –0.2 mm, DV –2 mm); bilateral cannula used; diabetes;

Q7730: G. Navarro, et al. Androgen excess in pancreatic beta cells and neurons predisposes female mice to type 2 diabetes. JCI Insight 2018;3(12):

**Agents:** Dihydrotestosterone  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (lateral ventricle);  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** Not Stated;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (littermate mice aged 10 –16 weeks.); dihydrotestosterone aka DHT; Brain coordinates ((coordinates compared with the bregma L +1 mm, AP – 0.2 mm, DV –2 mm)); diabetes;


**Agents:** Poloxamer 407  
**Vehicle:** Saline;  
**Route:** SC; IP;  
**Species:** Mice;  
**Pump:** 2004;  
**Duration:** 1 month;

**ALZET Comments:** 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

**Agents:** Empagliflozin  
**Vehicle:** DMSO, PEG;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 2 weeks;

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


**Agents:** Resistin  
**Vehicle:** Not stated;  
**Route:** CSF/CNS (lateral ventricle);  
**Species:** Mice;  
**Pump:** 2002;  
**Duration:** 3 days;

**ALZET Comments:** 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;


**Agents:** Angiotensin II  
**Vehicle:** Not stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1004;  
**Duration:** 4 weeks;

**ALZET Comments:** Dose (1 ug/min/kg); animal info (8-10 weeks old, 20-24 g, C57BL/6J, Male); pumps replaced every 4 weeks; diabetes;


**Agents:** S961  
**Vehicle:** PBS;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1007d;  
**Duration:** 1 week;

**ALZET Comments:** dose-response (5 nmol/week or 10 nmol/week); Controls received mp w/ vehicle; animal info (Male, C57BL/6J); diabetes;


**Agents:** Clozapine-N-Oxide  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 4 weeks;
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Bibliography

Agents: phlorizin Vehicle: propylene glycol; Route: SC; Species: Mice; Pump: 2004; Duration: 11 weeks;
ALZET Comments: Dose (120 mg/kg/day); 40% w/v of agent in propylene glycol used; Controls received mp w/ agent; animal info (4 weeks, female, C57BL/6 or Akita); pumps replaced every 4 weeks; phlorizin is an inhibitor of sodium-glucose linked transporter types 1 and 2 that prevents glucose reabsorption in the kidney; enzyme inhibitor (sodium-glucose linked transporter types 1 and 2 (SGLT1 and SGLT2)); diabetes; Therapeutic indication (normalized serum glucose in diabetic-prone mice while increasing the urine output and reducing inflammation in the bladder);

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: Fingolimod Vehicle: Saline; Route: IP; Species: Mice; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: 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);

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;

Agents: S961 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 6 days;
ALZET Comments: Dose (1.2 nmol/day); Controls received mp w/ vehicle; animal info (10-12 weeks, male, beta-CB1R+/+, beta-CB1R−/− or MIPCre/ERT); S961 is an insulin receptor antagonist; diabetes; Vehicle used but identity not stated.;

Q7814: M. Gao, et al. Redox signal-mediated TRPM2 promotes Ang II-induced adipocyte insulin resistance via Ca(2+)-dependent CaMKII/JNK cascade. Metabolism 2018;85(313-324
Agents: angiotensin II; anthranilic acid, N-(p-amylcinnamoyl)− Vehicle: PBS; Route: SC; Species: Mice; Pump: Not Stated; Duration: 4 weeks;
ALZET Comments: Dose ((AngII 1.5 mg/kg/d), (ACA 25 mg/kg/d)); Controls received mp w/ vehicle; animal info (8 weeks, male, C57BL/6J); ACA aka N-(p-amylcinnamoyl)anthranilic acid; diabetes; Therapeutic indication (insulin sensitivity increased in ACA-treated hypertensive mice);

Agents: Melanotan II Vehicle: Saline; Route: CSF/CNS (left lateral ventricle); Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: 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
Agents: Angiotensin II Vehicle: Saline; Route: SC; Species: Mice; Pump: 1004; Duration: 28 days;
ALZET Comments: Dose (1.44 ug/day/g); 0.9% sodium chloride used; animal info (10 week old, female and male, C57BL/6); diabetes;

Agents: Reparixin Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days;
ALZET Comments: Dose (5.4 mg/h/kg); animal info (Male, C57BL/6, Balb/c, 8-9 weeks old, 24-6 g ); Reparixin aka CXCR1/2 inhibitor; enzyme inhibitor (CXCR1/2 inhibitor); diabetes;

Agents: S961 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: Dose (40 nmol/week); S961 is a insulin receptor antagonist; diabetes;

Agents: Trimethylamine; PF06650833 Vehicle: Saline; Route: SC; Species: Mice; Pump: 2006; Duration: 6 weeks;
ALZET Comments: Dose (TMA 0.1 mM in circulation or PF06650833 50 nM in circulation); Controls received mp w/ vehicle; animal info (Five-week-old C57BL/6J mice); diabetes;

Agents: Angiotensin II Vehicle: Not stated; Route: SC; Species: Mice; Pump: 2004; Duration: 4 weeks;
ALZET Comments: Dose (Ang II 1000 ng/kg per minute); animal info (E1841K mutation); diabetes;

Agents: Exendin-4 Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML4; Duration: 28 days;
ALZET Comments: Dose (5 ug/kg/day); Controls received mp w/ vehicle; animal info (6 male Wistar and 12 GK rats (8 months old)); Ex-4 aka Exendin-4; diabetes; Therapeutic indication (Alzheimer’s disease);

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); diabetes;