Recent References on the Administration of Antioxidants
Using ALZET® Osmotic Pumps

AEOL10150
ALZET Comments: AEOL 10150; SC; Rat; 2002; 10 weeks; 8 days; Controls received mp w/ vehicle; functionality of mp verified by plasma AEOL 10150 concentrations; dose-response (fig. 4); long-term study; pumps replaced every 2 weeks; half-life (p. 574), short; cancer; animal info (female, Fisher-344, 150-170 grams); “Osmotic mini-pumps provided consistent and dose-dependent delivery of AEOL 10150,” "a continuous availability of antioxidant via osmotic infusion pumps throughout the study." (p. 575).

ALZET Comments: AEOL 10150; PBS; IV (jugular); Mice; 1003D; 6 hours; Controls received mp w/ vehicle;

ALZET Comments: AEOL 10150; PBS; IV (jugular); Mice; 1003D; 3 days; Controls received mp w/ vehicle; plasma levels of AEOL 10150 determined by HPLC; ischemia (cerebral); MCAO.

Ascorbic Acid
ALZET Comments: Trolox; neomycin; ascorbic acid; Perilymph, artificial; sodium bicarbonate; Ear (cochlea); Guinea pig; 2002; 26 days; Controls received mp w/ vehicle; pumps replaced after 14 days; post op. care (doxycycline); animal info (male, pigmented, 250-400g., neomycin deafening); cannula primed with 10% neomycin solution followed by a small air bubble spacer to allow neomycin infusion for first 2 days; trolox, a vitamin F analogue, and ascorbic acid delivered together in 1 mp;

ALZET Comments: Ascorbic acid; Naltrexone; Saline; SC; Rat (pregnant); Rat; 7 days; controls received mp w/ vehicle.

Catalase
Agents: Peptide, Nox2ds-tat; polyethylene glycol-conjugated catalase Vehicle: Not Stated; Route: SC; Species: Rat; mice; Pump: 2ML1; 1002; Duration: 7 days;
ALZET Comments: Controls received mp w/ scramble ds-tat or vehicle; animal info (Rat male, Wister-Kyoto, 2-3 months; mice male, C57Bl6J and p47 phox -/-, 4.5-6 months old); cardiovascular; peptides; polyethylene glycol-conjugated catalase aka PEG-CAT; arterial ligation; NOX2 is NADPH oxidase;

Agents: Catalase; Dimethyl sulfoxide; Dexamethasone; Indomethacin; Pyrilamine maleate; AA-861; Cimetidine; Phenidone Vehicle: Ethanol; Saline; Route: SC; Species: mice; Pump: 1007D; Duration: 72 hours;
ALZET Comments: all agents infused concomitantly in the same pump; preliminary study conducted to test solubility and toxicity for 5 days; enzyme inhibitors; toxicity

**Agents:** Tempol; catalase **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Gerbil; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Controls received mp with saline; agents given separately and together; ischemia (cerebral)


**Agents:** Catalase; tempol **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** monkey; **Pump:** 2ML1; **Duration:** 7 days;

**ALZET Comments:** controls received inactivated SOD and BSA; functionality of mp verified by measuring enzyme levels in CSF during infusion and testing agent released from pump in vitro for 7 days; stability verified by measuring activity of enzymes released from pumps in vitro over 7 days; daily CSF sampling performed using a subcutaneous Ommaya reservoir; authors report no cases of catheter blockage or dislodgement


**Agents:** Glutathione peroxidase; Catalase; tempol **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** no duration posted;

**ALZET Comments:** Japanese with English abstract


**Agents:** Catalase; tempol **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 10, 20 days;

**ALZET Comments:** functionality of mp verified by serum catalase; PEG-conjugated enzymes; antioxidants; stability of enzymes questioned beyond 20 days


**Agents:** Catalase, PEG **Vehicle:** Saline, balanced; **Route:** Not Stated; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;

**ALZET Comments:** controls received surgery but no mp; dose response; 3 doses of agent infused

**Dimethylthiourea**


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

**ALZET Comments:** Dose (100 mg/kg/day); animal info (Male, C57BL/6J); Blood pressure measured via Tail Cuff Method; Dimethylthiourea aka DMTU; cardiovascular;


**ALZET Comments:** Angiotensin II; Dimethylthiourea; PBS; **IP:** Rat; 2002; 7 days.; Controls received mp w/ vehicle; cardiovascular; peptides; Dimethylthiourea, also called DMTU, is an antioxidant; some animals received 2 pumps (IP): one pump for ANG II infusion and one for DMTU infusion;

**Ebselen**


**ALZET Comments:** Ebselen; DMSO; saline; SC; Rat; 2ML4; 1 week; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 200g); 80% DMSO used; cardiovascular; bp measured with radiotelemetry; Dose (10 mg/kg/day);
ALZET Comments: Ebselen; DMSO; SC; Mice; 2004; Controls received mp w/ vehicle; animal info (8 wks old, Prdx -/-, ApoE -/-);

ALZET Comments: Tempol; ebselen; DMSO; saline; SC; IV (jugular); Mice; 2ML1; 1007D; 4 days; Animal info (male, 11-13 wks old, C57BL/6, P47 phox -/-); 50% DMSO used.

ALZET Comments: Ebselen; DMSO; SC; Mice (transgenic); 14 days; Controls received mp w/ vehicle; cardiovascular; 50% DMSO; ebselen is a glutathione peroxidase-mimetic antioxidant (a.k.a Harmokisane).

EUK-189
Agents: EUK-189 Vehicle: Not Stated; Route: Not Stated; Species: Not Stated; Pump: Not Stated; Duration: Not Stated;
ALZET Comments:

Agents: EUK-189 Vehicle: Mannitol; Route: SC; Species: Mice (transgenic); Pump: 2004; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (alpha synuclein A53T Tg)

Agents: EUK-189 EUK-207 Vehicle: Mannitol; Route: SC; Species: Mice; Pump: 2004; Duration: 6 months;
ALZET Comments: Controls received mp w/ vehicle; long-term study; pumps replaced every 28 days; animal info (C57BL/6N Sim, 27-36 g, 17 months old)

Agents: EUK-189 Vehicle: Mannitol; Route: SC; Species: Mice; Pump: 2004; Duration: 28 days;
ALZET Comments: Controls received mp w/vehicle; animal info (C57BL/6, 2-12 months old); neurodegenerative

Agents: EUK-189 Vehicle: Water, distilled; Route: SC; Species: Rat; Pump: 2004; Duration: 30 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by residual volume; animal info (male, Fischer 344, 6 month old, 300-400g., 24 month old, 350-450g.)

Agents: EUK-189 Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: Not Stated; Duration: 8,10 days;
ALZET Comments: Animal info (female, 6-8 weeks old, BALB/C and C57BL/6)

Agents: EUK-189 Vehicle: Mannitol; Route: SC; Species: Mice; Pump: 2004; Duration: 28 days;
ALZET Comments: Controls received mp w/ vehicle; neurodegenerative (Parkinson’s disease)
Agents: EUK-189 Vehicle: Mannitol; Route: SC; Species: Mice; Pump: 2004; Duration: 56, 84 days;
ALZET Comments: Controls received mp w/ vehicle; long-term study; pumps replaced every 28 days; no stress (see pg.941); cancer (thymoma); EUK-189 is a synthetic catalytic antioxidant w/ both catalase & superoxide dismutase activities; neurodegenerative (ataxia telangiectasia)

Agents: EUK-189; EUK-207 Vehicle: Mannitol; water; Route: SC; Species: Mice; Pump: 2004; Duration: 3 months;
ALZET Comments: Controls received mp w/ vehicle; long-term study; pumps replaced every 28 days in same location; pumps primed for >40 hours in 5% mannitol; eukarion is a synthetic catalytic scavenger of reactive oxygen species; stress/adverse reaction: in 10% of mice, the pumps were replaced on the other side of hip area due to skin damage of original site of implantation; behavioral study

Genistein
Agents: Genistein Vehicle: DMSO; water, distilled; Route: SC; Species: Rat; Pump: 1002; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, ovariectomized); 50% DMSO used; ischemia (cerebral);

Agents: Genistein Vehicle: Cyclodextrin, hydroxypropyl beta; Route: IP; Species: Rat; Pump: 2ML1; Duration: 3 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Wistar, male, 300-350 g)

P6396: I. F. Benter, et al. Inhibition of Ras-GTPase, but not tyrosine kinases or Ca2+/calmodulin-dependent protein kinase II, improves recovery of cardiac function in the globally ischemic heart. MOLECULAR AND CELLULAR BIOCHEMISTRY 2004;259(1-2):35-42
Agents: FPT III; KN-93; Genistein Vehicle: Saline; Route: IP; Species: Rat; Pump: 2ML1; Duration: 6 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (tyrosine kinase, CaMKII); cardiovascular; ischemia

Agents: Genistein; Estradiol, 17B- Vehicle: DMSO; PEG 300; Route: SC; Species: Mice; Pump: 2002; Duration: 4 weeks;
ALZET Comments: Replacement therapy (orchiectomy); dose-response (p.336); 20% DMSO used in vehicle

Agents: Genistein Vehicle: DMSO; EtOH; water; Route: IV (superior vena cava); Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; vehicle composition: DMSO, ethanol; water (50/20/30)

Agents: Genistein; estradiol, 17B- Vehicle: DMSO; PEG 300; Route: SC; Species: Mice; Pump: 2002; Duration: Not Stated;
ALZET Comments: Controls received mp w/ vehicle

Agents: Estradiol, 17B-; Genistein Vehicle: DMSO; PEG 300; Route: SC; Species: Mice; Pump: Not Stated; Duration: 2.4 weeks;
ALZET Comments: Controls received mp w/vehicle; replacement therapy (ovariectomy);
Glutathione


**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; mouse DV: –5 mm and AP: –1.8 mm);


**Agents:** S-nitrosoglutathione **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 24 hours; 7 days;

**ALZET Comments:** Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (GRK2-C340S mice); cardiovascular


**Agents:** Ascorbate; glutathione; tocopherol, alpha- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** Not Stated;

**ALZET Comments:** Controls received mp w/saline; animal info (male, C57BL/6J, 25-30g, 10-12 weeks old); compounds were mixed and infused together as an antioxidant cocktail


**Agents:** Amyloid protein, beta (1-42), human oligomeric; lipoprotein, high density; glutathione ethyl ester **Vehicle:** HEPES; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 1004; **Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (Tg-SREBP-2, NPC1-/-, Tg-APP/PS1); neurodegenerative (Alzheimer’s Disease)


**Agents:** Glutathione **Vehicle:** Not Stated; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;

**ALZET Comments:** Controls received mp w/PBS-HEPES; animal info (obese, lean, male, Zucker, 7 wks old); cannula placement verified by angiogensin II dipsogenic effect; Plastics One cannula used; no stress (see pg 2193) "Well being of the animals (weight gain and food intake) was preserved during the infusion”; good methods


**Agents:** Glutathione, monoethyl ester; MPP+ **Vehicle:** Saline; **Route:** SC; CSF/CNS; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; dose-response (fig. 6); stability verified by incubation for 0-28 days at 37 celsius, assessed by HPLC; half-life (pg. 515) 10-14 hours in culture; brain tissue distribution; toxicology; animal info (Sprague-Dawley, 300g.); neurodegenerative (Parkinson’s disease)


**Agents:** Fibroblast growth factor-2, basic, human; Penicillamine, S-nitroso N-acetyl; glutathione, S-nitroso N-acetyl **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;

**ALZET Comments:** Peptides; animal info (male, C57BL/6, 6-8 wks old); SNAP and SNAG are nitric oxide donors
Agents: Glutathione S-transferase; glutathione S-transferase-Nogo-66 Vehicle: Not Stated; Route: CSF/CNS (sciatic nerve); Species: Rat; Pump: 2002; Duration: 14 days;
ALZET Comments: Controls received mp w/ GST or no treatment; peptides; animal info (male, Sprague Dawley, 240-260g., Sciatic nerve transection); pain; silicon tube used

Agents: Mactinin; Glutathione 5-transferase Vehicle: Saline; Route: SC; Species: Rat; Mice (transgenic); Pump: 1007D; Duration: 1, 7 days;
ALZET Comments: Controls received mp w/ vehicle, or GST; peptides; animal info (Tgu PA-/- or wt; Fisher, 150-200g); Polyvinyl alcohol sponges soaked in agent implanted SC, with mp catheter directed to center of sponge: “osmotic pumps were used to continually deliver the fragment and replenish the mactinin in the sponges” (p.125); wound healing

Agents: Glutathione monoethyl ester Vehicle: Saline; Route: CSF/CNS; Species: Rat; Pump: 2001; Duration: Not Stated;
ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit 2 used; dental cement used; post op. care (xylocaine/adrenaline injected into site of wound); neuroprotection; ischemia (cerebral); antioxidant

Agents: C3 Transferase; Glutathione S-transferase; Y-27632 Vehicle: PBS; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2002; Duration: 2-3 weeks;
ALZET Comments: Enzyme inhibitor (protein kinase); peptides; spinal cord injury; Y-27632 is a Rho-associated kinase (ROCK) inhibitor

Agents: Insulin-like growth factor binding protein-6; glutathione S-transferase Vehicle: Not Stated; Route: SC; Species: Mice (nude); Pump: 1002; Duration: 2 weeks;
ALZET Comments: Controls received mp w/ GST; dose-response (table 1); comparison of daily IP injections vs. mp; cancer (neuroblastoma); peptides; animal info (female, SP Swiss nude, 6 wk old); “The (tumor developed) delay was not evident in mice injected i.p., possibly because IGFBP-6 is rapidly degraded in the bloodstream.” (p. 2063)

Agents: Glutathione, S-(N-p-chlorophenyl-N-hydroxycarbamoyl) Vehicle: Cyclodextrin, B-; Route: IV (jugular); Species: Mice; Pump: 2002; Duration: 14 days;
ALZET Comments: Comparison of IV injections vs. mp; enzyme inhibitor; 20% hydroxypropyl-beta-cyclodextrin used; CHG (Et)2 is an enediol analog inhibitor of glycoxalase in its ester prodrug form; colon adenocarcinoma and prostate cancer

Agents: Penicillamine, S-nitroso N-acetyl-; Glutathione, S-nitroso N-acetyl; Vehicle: Cyclodextrin, B-; Route: IV (jugular); Species: Mice; Pump: 2002; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; SNAP and SNAG are nitric oxide donors; angiogenesis inhibitors.

Agents: Glutathione peroxidase; Catalase; tempol Vehicle: Not Stated; Route: Not Stated; Species: Rat; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: Japanese with English abstract
Magnolol


**ALZET Comments**: Magnolol; Alcohol; SC; Rat; 2001; 2 weeks; Dose-response (p. 129); pumps replaced every 7 days; magnolol, an active component purified from magnolia officinalis, is a commonly used Chinese medicinal herb, with reported anti-inflammatory and antioxidant effects.

Mannitol

**Q9888**: S. Yoshimoto, et al. NFAT5 promotes oral squamous cell carcinoma progression in a hyperosmotic environment. Laboratory Investigation 2021;101(1):38-50

**Agents**: Mannitol **Vehicle**: Saline; **Route**: SC; **Species**: Mice; **Pump**: 1004; **Duration**: 4 weeks;

**ALZET Comments**: Dose (289.5 ug/mouse/day); Controls received mp w/ vehicle; animal info (); cancer (Carcinoma);


**Agents**: Aminobutyric acid, Y-; mannitol **Vehicle**: Saline; **Route**: CSF/CNS (amygdala); **Species**: Rat; **Pump**: 2001; **Duration**: 7 days;

**ALZET Comments**: Controls received mp w/mannitol; functionality of mp verified by cutting open & visual inspection; dose-response (table 1); no stress (see pg. 25)


**Agents**: Mannitol; Inulin; **Vehicle**: Radio-isotopes; 3H tracer; saline; ethanol; **Route**: Ear (round window); **Species**: Guinea pig; **Pump**: 1007D; **Duration**: 7 days;

**ALZET Comments**: Tissue perfusion (round window)


**Agents**: Mannitol; Radio-isotopes **Vehicle**: Pyrrolidone, N-methyl-2-; Propylene glycol; PEG; 14C tracer; Water; Dimethylacetamide; **Route**: In vitro; **Species**: Not Stated; **Pump**: 2ML1; **Duration**: 8 days;

**ALZET Comments**: Functionality of mp verified by in vitro testing; ALZAID chemical compatibility kit used; various solvents employed to find compatibility with drug reservoir


**Agents**: Cerebrospinal fluid, artificial; Mannitol **Vehicle**: Not Stated; **Route**: CSF/CNS; **Species**: Rat; **Pump**: 2002; **Duration**: Not Stated;

**ALZET Comments**: Controls were sham operated and received mixed-concentration aCSF, received no infusions, or received aCSF w/normal physiological balance of sodium and potassium; experimental groups consisted of varying the ratio of potassium to sodium in the aCSF; mannitol added to infusate in one high-potassium group to maintain isosmolality


**Agents**: Potassium Chloride, hypertonic; Sodium chloride, hypertonic; Mannitol, hypertonic **Vehicle**: Saline, isotonic; Water; **Route**: CSF/CNS (preoptic area); **Species**: Rat; **Pump**: 2002; **Duration**: 2 weeks;

**ALZET Comments**: bilateral infusion to brain


**Agents**: Mannitol; Cerebrospinal fluid, artificial **Vehicle**: Not Stated; **Route**: CSF/CNS; **Species**: Rat; **Pump**: 2ML1; **Duration**: 4 days;

**ALZET Comments**: study of effect of agents on salt appetite; agents infused simultaneously
Melatonin (2010-Present)


**Agents:** Melatonin  
**Vehicle:** CSF, artificial;  
**Route:** CNS/CSF;  
**Species:** Rat;  
**Pump:** 1004;  
**Duration:** 1 week;

**ALZET Comments:** “Dose (0.025 ug/hr); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 220-285 g); Melatonin aka Mel; Brain coordinates (1.8 mm caudal from bregma, 0.4 mm lateral to the midline, and 7.9 mm ventral to the dorsal surface); bilateral cannula used; ischemia (Myocardial); ”


**Agents:** Melatonin  
**Vehicle:** Not Stated;  
**Route:** Not Stated;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** Not Stated;

**ALZET Comments:** animal info (Sprague-Dawley rats); comparison of infusion pump, pellets, transdermal, beads, sponge, iPRECIO vs mp; Lynch coil;


**Agents:** Melatonin  
**Vehicle:** Not Stated;  
**Route:** Not Stated;  
**Species:** Sheep (pregnant);  
**Pump:** Not Stated;  
**Duration:** Not Stated;

**ALZET Comments:**


**Agents:** Melatonin  
**Vehicle:** Saline;  
**Route:** CSF/CNS (lateral ventricle);  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 7 days;

**ALZET Comments:** Dose (1 mg•kg body wt_1•day_1); Controls received mp w/ vehicle; animal info (Male Fischer 344 rats weighing 175–200 g); Brain coordinates (_0.80 mm, ML: _1.50 mm, DV: _4.00 mm from Bregma);


**Agents:** Melatonin; luzindole  
**Vehicle:** DMSO; water;  
**Route:** Intrauterine;  
**Species:** Sheep (ewe; pregnant);  
**Pump:** 2ML4;  
**Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (female, Western white face, GD62); functionality of mp verified by serum levels; 45% DMSO used; stress/adverse reaction: (see pg.2); post op. care (For two days: flunixin meglumine 50 mg/ml IM twice a day; Penicillin G procain 300,000 u/ml once per day); tissue perfusion (uterus mesometrium); cardiovascular;


**Agents:** Melatonin; Luzindole  
**Vehicle:** DMSO; water;  
**Route:** Intrauterine (uterine horn);  
**Species:** Sheep (ewe);  
**Pump:** 2ML4;  
**Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by serum levels of melatonin taken; 45% DMSO used; stress/adverse reaction: (see pg.2); post op. care (For two days: flunixin meglumine 50 mg/ml IM twice a day; Penicillin G procain 300,000 u/ml once per day); tissue perfusion (uterus mesometrium); cardiovascular;


**Agents:** Melatonin  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Not Stated;  
**Pump:** Not Stated;  
**Duration:** 2 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; “The method of melatonin infusion via s.c. osmotic mini-pumps provided constant steady-state hormonal concentrations.” Pg. 45; Dose (10 mg/kg/day);
Agents: Gentamicin; dexamethasone; melatonin Vehicle: Not Stated; Route: Ear (round window); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (Wistar, male, 220-250 g); stability verified after 7 days (data not shown)

Agents: Melatonin; ramelteon Vehicle: Saline; ethanol; Route: SC; Species: Hamster; Pump: 2004; Duration: 8 weeks;
ALZET Comments: Controls received mp w/ vehicle; long-term study; pumps replaced after 4 weeks; animal info (Siberian, adult, male); 15% ethanol used; ramelteon is a specific MT1/MT2 agonist

Resveratrol
Agents: Resveratrol Vehicle: PEG 300; DMSO; Route: SC; Species: Rat; Pump: Not stated; Duration: 3 days;
ALZET Comments: Dose (4 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats, 400-450 g); Blood pressure measured via tail-cuff method; Resveratrol aka RSV; cardiovascular;

Agents: Resveratrol; Nicotinamide Vehicle: Cyclodextrin, 2-hydroxypropyl-b; Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 days;
ALZET Comments: Dose (resveratrol 1 mg/kg/day; nicotinamide 250 mg/kg/day); Controls received mp w/ vehicle; animal info (9-month-old YAC128 transgenic mice and age-matched WT controls); neurodegenerative (Huntington's Disease);

Agents: Resveratrol; EX-527 Vehicle: DMSO; Route: SC; Species: Mice; Pump: 1002; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (7-9 weeks; C57BL/6J); Multiple pumps per animal (2); behavioral testing (open field, elevated-plus maze, forced swim test, sucrose preference test); Plastics One guide cannula used; bilateral cannulae (one pump for each pedestal); Elective adhesives used; EX-527 is a SIRT1 antagonist; Therapeutic indication (Depression); Dose (0.1 or 0.2 ug/day, EX-527: 0.5 or 1.0 ug/day);

Agents: Resveratrol Vehicle: DMSO; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info: Male, 6-week-old C57BL/6J mice; %50 of DMSO; dose-response (pg.1257-1259); Resveratrol aka RSV; Animals fed high-fat diets concurrently; Dose: 8 mg/kg/day

Q3651: S. J. Yang, et al. Resveratrol ameliorates hepatic metaflammation and inhibits NLRP3 inflammasome activation. METABOLISM-CLINICAL AND EXPERIMENTAL 2014;63(639-701
Agents: Resveratrol Vehicle: DMSO; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6); 50% DMSO used; no stress (see pg. 697); diabetes; “Resveratrol was administered via an osmotic pump, which is a safe and standard delivery system for rodents” “no side effects were observed by monitoring weight change, behavior and inflammatory response around the implantation area.” pg 697;

**Agents:** Resveratrol  
**Vehicle:** DMSO; ethanol  
**Route:** SC  
**Species:** Mice  
**Pump:** 2002  
**Duration:** 14 days  
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (6 wks old, female, C57BL/6J); 50% DMSO used; 15% ethanol used; “Owing to the limited compatibility of the osmotic pumps with DMSO and/or ethanol, as well as the limited solubility of resveratrol in aqueous solutions, it wasn’t possible to achieve higher doses of resveratrol using osmotic pumps” pg 17585

Q3150: S. J. Sheu, et al. Resveratrol Stimulates Mitochondrial Bioenergetics to Protect Retinal Pigment Epithelial Cells From Oxidative Damage. INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 2013;54(9):6426-6438

**Agents:** Resveratrol; Coenzyme Q10  
**Vehicle:** DMSO;  
**Route:** IP  
**Species:** Rat  
**Pump:** 2004  
**Duration:** 4 weeks  
**ALZET Comments:** Controls received mp w/ vehicle or sham surgery; animal info (Female, Brown Norway, 200-265g); 0.8% DMSO used; post op. care (Procaine penicillin 1000 IU IM); Coenzyme Q10 aka ubiquinone


**Agents:** Resveratrol; chloroquine  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 14 days  
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (C57BL/6J, male, 8-10 wks old)


**Agents:** Resveratrol  
**Vehicle:** Saline, sterile  
**Route:** CSF/CNS  
**Species:** Mice  
**Pump:** 2004  
**Duration:** 5 weeks  
**ALZET Comments:** Controls received mp w/ vehicle; comparison of oral vs. SC mp; animal info (C57/BL6); 25% ethanol used


**Agents:** Resveratrol, trans  
**Vehicle:** DMSO;  
**Route:** SC  
**Species:** Mice  
**Pump:** 2004  
**Duration:** 4 weeks  
**ALZET Comments:** Controls received mp w/ vehicle; comparison of oral vs. SC mp; animal info (C57/BL6); 50% degassed DMSO


**Agents:** Resveratrol  
**Vehicle:** DMSO; PEG 300  
**Route:** SC  
**Species:** Rat  
**Pump:** 2001  
**Duration:** 7 days  
**ALZET Comments:** Controls received mp w/ vehicle; 10% DMSO used; Resveratrol is a natural phytoalexin with antioxidant properties

**Retinoic Acid**

Q8858: C. Huang, et al. Chronic retinoic acid treatment induces affective disorders by impairing the synaptic plasticity of the hippocampus. Journal of Affective Disorders 2020;274(678-689

**Agents:** Retinoic acid  
**Vehicle:** Saline; DMSO  
**Route:** CSF/CNS (lateral ventricle);  
**Species:** Rat;  
**Duration:** 21 days  
**ALZET Comments:** Dose (20 μg/day); Controls received mp w/ vehicle; animal info (Adult male Wistar rats, 220–240 g); behavioral testing (Sucrose Preference Test, Open Field Test, Elevated Plus Maze Test, Tail Suspension Test, Forced Swim Test); Retinoic acid aka RA; ALZET brain infusion kit used; Brain coordinates (AP: 0.8 mm, ML: 1.5 mm, DV: 4.0 mm); dental cement used; neurodegenerative (Depression)

**Agents:** retinoic acid  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  

**ALZET Comments:** Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 160-180g); Retinoic acid is an agonist of N-acetylglucosamine transferase V; cardiovascular;


**Agents:** Retinoic acid, 13-cis  
**Vehicle:** Ethanol;  
**Route:** SC;  
**Species:** Mice (transgenic);  
**Pump:** 1007D;  
**Duration:** 5 weeks;  

**ALZET Comments:** Controls received mp w/ vehicle; dose-response (fig. 1); no stress (see pg. 312-13); cancer (neuroblastoma)


**Agents:** Retinoic acid; Uridine, bromodeoxy  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 1, 3, 6 days;  

**ALZET Comments:** Controls received mp w/ vehicle; comparison of SC injections vs. mp; cancer (gastric); multiple pumps per animal (2)


**Agents:** Transforming growth factor; insulin-like growth factor I; retinoic acid; brain-derived neurotrophic factor;  
**Vehicle:** PBS; BSA;  
**Route:** Ear (vestibule);  
**Species:** Guinea pig;  
**Pump:** 2002;  
**Duration:** 4 weeks;  

**ALZET Comments:** Controls received mp w/ vehicle; pumps replaced after 2 weeks; peptides; IntraEAR catheter used; GFI group pumps filled with TGF, IGF and Retinoic acid; GFII group pumps filled with TGF, IGF, BDNF and retinoic acid;


**Agents:** Dipyridamole; Lazaroids; Retinoic acid  
**Vehicle:** Not Stated;  
**Route:** Not Stated;  
**Species:** Not Stated;  
**Pump:** Not Stated;  
**Duration:** Not Stated;  

**ALZET Comments:** Review of adhesion formation and prevention; mentions the use of mini-osmotic pumps to evaluate new agents to reduce experimental pelvic adhesions (p. 125).


**Agents:** Retinoic acid; Quinacrine; Dipyridamole  
**Vehicle:** PBS; Ethanol;  
**Route:** Injury site;  
**Species:** Rabbit;  
**Pump:** 2ML1;  
**Duration:** 1, 2, 3, 7 days;  

**ALZET Comments:** Controls received mp w/vehicle; tissue perfusion (surgical injury site); animals given morphine i.m. for post-operative pain; catheter stabilized in sidewall w/suture; catheter tubing was disconnected to halt flow at specific times;


**Agents:** Retinoic acid; Phorbol myristate acetate  
**Vehicle:** ETHANOL; Gibco BRL minimal essential medium; DMSO; Culture medium, serum-free;  
**Route:** CSF/CNS (cortex);  
**Species:** Rat;  
**Pump:** 2ML1;  
**Duration:** 21, 28 days;

**ALZET Comments:** controls received mp w/ vehicle; functionality of mp verified by residual volume; pumps replaced weekly

**Tempol (2011-Present)**

Q8077: T. Li, et al. Elevated Oxidative Stress and Inflammation in Hypothalamic Paraventricular Nucleus Are Associated With Sympathetic Excitation and Hypertension in Rats Exposed to Chronic Intermittent Hypoxia. Front Physiol 2018;9(840

**Agents:** Tempol  
**Vehicle:** Not stated,  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 7 days;  

**ALZET Comments:** Dose (5 ug/min); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 10 weeks old, 300-325 g); Tempol aka superoxide scavenger ; bilateral cannula used; cardiovascular;

Agents: Porphyrin-based superoxide dismutase mimetic (MnHex)
Vehicle: Not Stated
Route: SC
Species: Mice
Pump: 1004
Duration: 8 weeks
ALZET Comments: Dose (450 ug/kg/day); pumps replaced every 4 weeks; Porphyrin-based potent superoxide dismutase mimetic aka (Mn(III) meso-tetrakis-(n-hexylpyridinium-2-yl) porphyrin (MnTnHex-2-PyP5+);


Agents: mitochondrial superoxide dismutase mimetic (Hexyl)
Vehicle: Saline
Route: SC
Species: Monkey
Pump: Not Stated
Duration: 6 weeks
ALZET Comments: Dose (0.1 mg/kg/day); Controls received mp w/ vehicle; animal info (Rhesus monkeys);


Agents: Losartan; Tempol; Clonidine
Vehicle: CSF, artificial
Route: CSF/CNS (lateral ventricle)
Species: Rat
Pump: Not Stated
ALZET Comments: Dose (1 mg/kg/day losartan; 4.5 ug/kg/day tempol; 5.76 ug/kg/day clonidine); Controls received mp w/ vehicle; animal info (Five-week-old male Sprague-Dawley rats); Therapeutic indication (5/6 nephrectomy);


Agents: Tempol
Vehicle: Saline
Route: CSF/CNS (cisterna magna)
Species: Rat
Pump: 1002
Duration: 14 days
ALZET Comments: Dose (10 mM); Controls received mp w/ vehicle; animal info (Male, adult spontaneously hypertensive rats and Wistar–Kyoto rats); ALZET brain infusion kit 2 used;


Agents: FeTMPyP; Tempol
Vehicle: CSF, artificial
Route: CSF/CNS (intracisternal)
Species: Rat
Pump: 2001
Duration: 6 days
ALZET Comments: Controls received mp w/ vehicle; animal info (male adult Sprague-Dawley rats 278 +/-28 g); FeTMPyP is an active peroxynitrite decomposition catalyst; tempol is an antioxidant; Dose: FeTMPyP (100 pmol/ul/hr); tempol (4 nmol/ul/hr);

Q5692: H. Z. Toklu, et al. Intracerebroventricular tempol administration in older rats reduces oxidative stress in the hypothalamus but does not change STAT3 signalling or SIRT1/AMPK pathway. Applied Microbiology and Biotechnology 2017;42(1):59-67

Agents: Tempol
Vehicle: CSF, artificial
Route: CSF/CNS
Species: Rat
Pump: Not Stated
Duration: 3 weeks
ALZET Comments: Vehicle pumps replaced after one week; Dose (300 ug/h);


Agents: Tempol
Vehicle: Water
Route: SC
Species: Rat
Pump: Not Stated
Duration: 4 weeks
ALZET Comments: Controls received mp w/ vehicle; animal info (Diabetic rats); diabetes; Therapeutic indication (Diabetes); Dose (1.5 mM/kg/day);


Agents: Butylhydroquinone, tert-
Vehicle: Water, distilled; Ethanol
Route: CSF/CNS (right lateral ventricle)
Species: Rat
Pump: Not Stated
Duration: 6 days
ALZET Comments: Tempol 8 umol kg/day) dissolved in distilled water and delivered for 4 weeks; t-BHQ (1 mM) dissolved in 1% Ethanol in water and delivered for 6 days ICV; Controls received mp w/ vehicle; animal info (9 week old Sprague-Dawley rats weighing 290–310 g); Tempol is an antioxidant; Brain coordinates (1 mm caudal; – 1.5 mm lateral; – 3.4 mm below surface)
Agents: Butylhydroquinone, tert-; Tempol; Vehicle: CSF, artificial; DMSO; Route: CSF/CNS (hypothalamic paraventricular nucleus); Species: Rat; Pump: 1004; Duration: 2 weeks;
ALZET Comments: Dose; tBHQ (0.8 μg/day), or tempol (20 μg/h); 1% DMSO used; Controls received mp w/ vehicle; animal info (250 g–270 g spontaneously hypertensive rats and Wistar-Kyoto rats); antihypertensive; bilateral cannula used;

Q5838: H. K. Kim, et al. Tempol Ameliorates and Prevents Mechanical Hyperalgesia in a Rat Model of Chemotherapy-Induced Neuropathic Pain. Front Pharmacol 2016;7(532
Agents: Tempol Vehicle: Saline; Route: IP; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (200-350 g); cancer (Chemotherapy); behavioral testing; Therapeutic indication (Pain study, chemotherapy-induced neuropathic pain); Dose (200 mg/kg);

Q4451: Y. H. Ho, et al. Peripheral inflammation increases seizure susceptibility via the induction of neuroinflammation and oxidative stress in the hippocampus. JOURNAL OF BIOMEDICAL SCIENCE 2015;22(1619-1633
Agents: Endotoxin, LPS; NS398; tempol Vehicle: Saline; DMSO; Route: IP; CSF/CNS; Species: Rat; Pump: Not Stated; Duration: 7d
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 10 weeks old, 250-282g); ALZET brain infusion kit 2 used; 1% DMSO used; Multiple pumps per animal (2); post op. care (IM procaine penicillin 1000IU); immunology; used dental cement; NS398 is a COX-2 inhibitor and anti-inflammatory; tempol scavanges ROS;

Agents: Losartan; clonidine; tempol; hydralazine Vehicle: PBS; CSF, artificial; Route: CSF/CNS; intrastrigastric; Species: Rat; Pump: Not Stated; Duration: 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 5 weeks old, 5/6x nephrectomy); dose-response (pg 1627); cardiovascular; bp measured using catheter;

Q4181: K. L. H. Wu, et al. Role of Nitric Oxide Synthase Uncoupling at Rostral Ventrolateral Medulla in Redox-Sensitive Hypertension Associated With Metabolic Syndrome. Hypertension 2014;64(815--+
Agents: Tempol; coenzyme Q10 Vehicle: CSF, artificial; Route: CSF/CNS (cisterna magna); Species: Rat; Pump: 1007D; Duration: 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, adult, 250-275g); post op. care (1000 IU IM); tissue perfusion (cisterna magna); cardiovascular; diabetes; used PE-10 catheter;

Q3661: Q. Su, et al. Inhibition of reactive oxygen species in hypothalamic paraventricular nucleus attenuates the renin-angiotensin system and proinflammatory cytokines in hypertension. TOXICOLOGY AND APPLIED PHARMACOLOGY 2014;276(115-120
Agents: Tempol; angiotensin II Vehicle: CSF, artificial; saline, sterile; Route: CSF/CNS (paraventricular nuclei); Species: Rat; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, adult, 250-275g); functionality of mp verified by increase bp; tissue perfusion (paraventricular nucleus); immunology; "The success rate of bilateral microinjection and vein infusion is respectively 65% and 78%." pg 116; bp measured using tail-cuff;

Q4699: A. O. Awonuga, et al. THE IN-VIVO EFFECTS OF SUPEROXIDE DISMUTASE ON THE INCIDENCE AND SEVERITY OF POST-OPERATIVE ADHESION DEVELOPMENT
751. FERTILITY AND STERILITY 2014;102(E73-E73
Agents: Superoxide dismutase Vehicle: Saline; Route: IP; Species: Rat; Pump: Not Stated; Duration: 3 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Sprague Dawley);
   **Agents:** Enalapril maleate, Losartan, Tempol **Vehicle:** CSF, artificial; **Route:** CSF/CNS (ventricle); **Species:** Rat; **Pump:** 1003D; **Duration:** 14 days;
   **ALZET Comments:** Controls received mp w/ aCSF; ALZET brain infusion kit 2 used; Therapeutic indication (erectile dysfunction); Dose: Enalapril (0.5 mg/ml), losartan (2 mg/ml), tempol (50 mg/ml);

Q2125: K. Ozumi, et al. Role of Copper Transport Protein Antioxidant 1 in Angiotensin II-Induced Hypertension A Key Regulator of Extracellular Superoxide Dismutase. Hypertension 2012;60(2):476-U487
   **Agents:** Angiotensin II; Tempol **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 7 days;
   **ALZET Comments:** Controls received mp w/ vehicle; animal info (Atox1 -/-, 3 mo old); blood pressure measured via tail cuff

   **Agents:** Tempol **Vehicle:** Not Stated; **Route:** Species: Mice; **Pump:** 2002; **Duration:** Not Stated;
   **ALZET Comments:** Controls received mp w/ saline; animal info (CHOP-10 deficient, wt, 28 g, 8 wks old); ischemia

   **Agents:** Tempol **Vehicle:** DMSO; saline; **Route:** SC; IV (jugular); **Species:** Mice; **Pump:** 2ML1; 1007D; **Duration:** 4 days;
   **ALZET Comments:** Animal info (male, 11-13 wks old, C57BL/6, P47 phox -/-); 50% DMSO used

   **Agents:** Tempol **Vehicle:** CSF, artificial; **Route:** CSF/CNS; IP; **Species:** Rat; **Pump:** 2ML2; **Duration:** 8 days;
   **ALZET Comments:** Animal info (male, Wistar, Kyoto, 280-300 g)

   **Agents:** Tempol; ebselen **Vehicle:** DMSO; saline; **Route:** SC; IV (jugular); **Species:** Mice; **Pump:** 2ML1; 1007D; **Duration:** 4 days;
   **ALZET Comments:** Animal info (male, 11-13 wks old, C57BL/6, P47 phox -/-); 50% DMSO used

   **Agents:** Tempol **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 8 days;
   **ALZET Comments:** Animal info (male, Wistar, Kyoto, 280-300 g)

Thioredoxin
   **ALZET Comments:** Thioredoxin-interacting protein DNAzyme; SC; Rat; 2006; 12 weeks; Controls received mp w/ scrambled TXNIP DNAzyme; animal info (female, heterozygous (mRen-2)27, 6 weeks old); pumps replaced every 6 weeks;

   **ALZET Comments:** Thioredoxin, human recomb.; SC; Mice (nude); 2002; 2 weeks; Controls received mp w/ PBS; plasma levels taken; cancer (colon, carcinoma); peptides; animal info (female, 6 weeks old, nude); xenograft.
**ALZET® Bibliography**

**ALZET Comments:** Thioredoxin; IP; Rat; 2002; 4 weeks; controls received mp w/saline; pumps replaced after 2 weeks;

**Vitamin E**

**Q1590:** C. Y. Hsieh, *et al.* Inhibition of vascular smooth muscle cell proliferation by the vitamin E derivative pentamethyldihydroxychromane in an in vitro and in vivo study; pivotal role of hydroxyl radical-mediated PLC-gamma-1 and JAK2 phosphorylation. Free Radical Biology and Medicine 2010;49(5):881-893  
**ALZET Comments:** PMC; tocopherol, alpha; SC; Rat; 14 days; Controls received mp w/ normal saline; animal info (Wistar, male, 350-400 g); PMC, also known as (2,2,5,7,8-pentamethyl-6-hydroxychromane, is a vitamin E derivative;

**ALZET Comments:** Ascorbate; glutathione; tocopherol, alpha-; SC; Mice; 1007D; Controls received mp w/saline; animal info (male, C57BL/6J, 25-30g, 10-12 weeks old); compounds were mixed and infused together as an antioxidant cocktail.

**P3759:** T. Udaka, *et al.* The effect of combination therapy with EPC-K1 and low-dose cyclosporine to pulmonary allograft after rat lung transplantation. J. Heart Lung Transplant 1997;16(839-845  
**ALZET Comments:** Vitamin E; IP; Rat; 2001; 7 days; functionality of mp verified by measuring EPC-K1 plasma levels; immunology; EPC-K1 is a diester of a-tocopherol and ascorbic acid; agent also called D-alpha-tocopherol.

**ALZET Comments:** Phosphatidylcholine; vitamin E; Liposomes; CSF/CNS (cortex); Rat; 2001; 7 days; 2 pumps per animal,