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

AEOL10150

P8436: Z. N. Rabbani, *et al.* Long-term administration of a small molecular weight catalytic metalloporphyrin antioxidant, AEOL 10150, protects lungs from radiation-induced injury. INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS 2007;67(2):573-580
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).

P5554: R. P. Bowler, *et al.* A catalytic antioxidant (AEOL 10150) attenuates expression of inflammatory genes in stroke. Free Radical Biology and Medicine 2002;33(8):1141-1152
ALZET Comments: AEOL 10150; PBS; IV (jugular); Mice; 1003D; 6 hours; Controls received mp w/ vehicle;

P5314: H. X. Sheng, *et al.* Effects of metalloporphyrin catalytic antioxidants in experimental brain ischemia. Free Radical Biology and Medicine 2002;33(7):947-961
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

P8402: J. Maruyama, *et al.* Effects of antioxidants on auditory nerve function and survival in deafened guinea pigs. NEUROBIOLOGY OF DISEASE 2007;25(2):309-318
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;

P2797: G. I. Keshet, *et al.* Maternal naltrexone prevents morphological and behavioral alterations induced in rats by prenatal stress. Pharmacol. Biochem. Behav 1995;50(3):413-419
ALZET Comments: Ascorbic acid; Naltrexone; Saline; SC; Rat (pregnant); Rat; 7 days; controls received mp w/ vehicle.

Catalase

Q3458: M. R. DiStasi, *et al.* Nox2 and p47(phox) modulate compensatory growth of primary collateral arteries. American Journal of Physiology Heart and Circulatory Physiology 2014;306(U56-U64
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;

P4207: K. Shimoda, *et al.* Effect of antioxidants, anti-inflammatory drugs, and histamine antagonists on Sparfloxacin-induced phototoxicity in mice. Fundam. Appl. Toxicol 1996;31(133-140
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; toxicology

P3115: D. Truelove, *et al.* Superoxide dismutase, catalase, and U78517F attenuate neuronal damage in gerbils with repeated brief ischemic insults. Neurochem. Res 1994;19(6):665-671
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)

P2520: R. L. Macdonald, *et al.* Effect of intrathecal superoxide dismutase and catalase on oxyhemoglobin-induced vasospasm in monkeys. Neurosurgery 1992;30(4):529-539
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

P1931: T. Hattori, *et al.* Changes in intra-renal scavenging enzymes activities of the reactive oxygen species in experimental glomerulo-nephritis and nephrosis in rats. Nippon Jinzo Gakkai Shi 1991;33(2):191-199
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

P1741: B. T. Mossman, *et al.* Inhibition of lung injury, inflammation, and interstitial pulmonary fibrosis by polyethylene glycol-conjugated catalase in a rapid inhalation model of asbestosis. American Review of Respiratory Disease 1990;141(1266-1271
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

P1099: B. T. Mossman, *et al.* Approaches to prevention of asbestos-induced lung disease using polyethylene glycol (PEG) - congugated catalase. J. Free Radicals in Biology & Medicine 1986;2(335-338
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

Q8383: A. Kuma, *et al.* Inhibition of urea transporter ameliorates uremic cardiomyopathy in chronic kidney disease. FASEB J 2020;34(6):8296-8309
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;

P4810: G. Wolf, *et al.* Angiotensin II induces $p27^{Kip1}$ expression in renal tubules in vivo: role of reactive oxygen species. JOURNAL OF MOLECULAR MEDICINE 2001;79(382-389
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

Q4864: Esteban A.Moya, *et al.* Intermittent Hypoxia-Induced Carotid Body Chemosensory Potentiation and Hypertension Are Critically Dependent on Peroxynitrite Formation. Oxidative Medicine and Cellular Longevity 2016;2016(1-9
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);.

Q2266: J. G. Park, *et al.* Peroxiredoxin 2 Deficiency Exacerbates Atherosclerosis in Apolipoprotein E-Deficient Mice. Circulation Research 2011;109(7):739-U80
ALZET Comments: Ebselen; DMSO; SC; Mice; 2004; Controls received mp w/ vehicle; animal info (8 wks old, Prdx -/-, ApoE -/-);

Q1702: N. J. Willett, *et al.* Redox Signaling in an In Vivo Murine Model of Low Magnitude Oscillatory Wall Shear Stress. ANTIOXIDANTS & REDOX SIGNALING 2011;15(5):1369-1378
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.

P6576: J. J. Khatri, *et al.* Vascular oxidant stress enhances progression and angiogenesis of experimental atheroma. Circulation 2004;109(4):520-525
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

R0300: J. P. Williams, *et al.* Treatment for Radiation-Induced Pulmonary Late Effects: Spoiled for Choice or Looking in the Wrong Direction? Current Drug Targets 2010;11(11):1386-1394
Agents: EUK-189 **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments:

Q1593: J. Peng, *et al.* Synergistic effects of environmental risk factors and gene mutations in Parkinson's disease accelerate age-related neurodegeneration. Journal of Neurochemistry 2010;115(6):1363-1373
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)

Q0152: A. Clausen, *et al.* Prevention of cognitive deficits and brain oxidative stress with superoxide dismutase/catalase mimetics in aged mice. Neurobiology of Aging 2010;31(3):425-433
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)

P9634: J. Peng, *et al.* Iron-enhanced paraquat-mediated dopaminergic cell death due to increased oxidative stress as a consequence of microglial activation. Free Radical Biology and Medicine 2009;46(2):312-320
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

P7798: H. J. Zhang, *et al.* Chronic antioxidant enzyme mimetic treatment differentially modulates hyperthermia-induced liver HSP70 expression with aging. Journal of Applied Physiology 2006;100(4):1385-1391
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.)

P8003: G. Tocco, *et al.* Prolongation of alloskin graft survival by catalytic scavengers of reactive oxygen species. Cellular Immunology 2006;241(2):59-65
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)

P7236: J. Peng, *et al.* Superoxide dismutase/catalase mimetics are neuroprotective against selective paraquat-mediated dopaminergic neuron death in the substantial nigra - Implications for Parkinson disease. Journal of Biological Chemistry 2005;280(32):29194-29198
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)

P6477: S. E. Browne, *et al.* Treatment with a catalytic antioxidant corrects the neurobehavioral defect in ataxia-telangiectasia mice. Free Radical Biology and Medicine 2004;36(7):938-942
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)

P5936: R. L. Liu, *et al.* Reversal of age-related learning deficits and brain oxidative stress in mice with superoxide dismutase/catalase mimetics. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES O F AMERICA 2003;100(14):8526-8531
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

R0405: S. E. Yang, *et al.* Therapeutic Potential and Mechanisms of Novel Simple O-Substituted Isoflavones against Cerebral Ischemia Reperfusion. International Journal of Molecular Sciences 2022;23(18):
Agents: Genistein **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Dose (0.1 mg/kg); ischemia (Cerebral); Therapeutic indication (Cerebral Ischemia); animal info. balb/c mice

Q3324: R. F. Shi, *et al.* Lose dose genistein inhibits glucocorticoid receptor and ischemic brain injury in female rats. NEUROCHEMISTRY INTERNATIONAL 2014;65(;):14-22
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, ovarectomized); 50% DMSO used; ischemia (cerebral);

Q2856: B. Cortina, *et al.* Improvement of the circulatory function partially accounts for the neuroprotective action of the phytoestrogen genistein in experimental ischemic stroke. European Journal of Pharmacology 2013;708(1-3):88-94
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 Ca^{2+}/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

P5855: J. Wu, *et al.* Combined intervention of exercise and genistein prevented androgen deficiency-induced bone loss in mice. Journal of Applied Physiology 2003;94(1):335-342
Agents: Genistein; Estradiol, 17B- **Vehicle:** DMSO; PEG 300; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 4 weeks;
ALZET Comments: Replacement therapy (orchidectomy); dose-response (p.336); 20% DMSO used in vehicle

P5463: T. P. O'Connor, *et al.* A high isoflavone soy protein diet and intravenous genistein delay rejection of rat cardiac allografts. Journal of Nutrition 2002;132(8):2283-2287
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)

P5347: Y. Ishimi, *et al.* Genistein, a soybean isoflavone, affects bone marrow lymphopoiesis and prevents bone loss in castrated male mice. Bone 2002;31(1):180-185
Agents: Genistein; estradiol, 17B- **Vehicle:** DMSO; PEG 300; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle

P4488: Y. Ishimi, *et al.* Selective effects of genistein, a soybean isoflavone, on B-Lymphopoiesis and bone loss caused by estrogen deficiency. Endocrinology 1999;140(4):1893-1900
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

Q6298: C. K. Katashima, *et al.* iNOS promotes hypothalamic insulin resistance associated with deregulation of energy balance and obesity in rodents. Sci Rep 2017;7(1):9265
Agents: S-nitrosoglutathione; insulin; glutathione **Vehicle:** Not Stated; **Route:** CSF/CNS (third ventricle); **Species:** Rat; mice; **Pump:** 1002; 2002; **Duration:** 1 week;
ALZET Comments: Dose (GSNO (50 µM)/insulin (0.033 UI/µL) and GSH (50 µM)/insulin (0.033 UI/µL)); animal info (Male 4-week-old Wistar rats, Swiss, C57BL/6 and iNOS-null (iNOS−/−) mice); S-nitrosoglutathione is an NO donor; Brain coordinates (rats DV: −8.5 mm and AP: - 0.5 mm; mice DV: −5 mm and AP: −1.8 mm);

Q6673: Z. M. Huang, *et al.* Convergence of G Protein–Coupled Receptor and S-Nitrosylation Signaling Determines the Outcome to Cardiac Ischemic Injury. Cardiovascular Physiology 2013;6(229):ra95 (1-9)
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

P9636: D. C. Irwin, *et al.* A potential role for reactive oxygen species and the HIF-1-alpha-VEGF pathway in hypoxia-induced pulmonary vascular leak. Free Radical Biology and Medicine 2009;47(1):55-61
Agents: Ascorbate; glutathione; tocopherol, alpha- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D;
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

P9881: A. Fernandez, *et al.* Mitochondrial Cholesterol Loading Exacerbates Amyloid-beta Peptide-Induced Inflammation and Neurotoxicity. Journal of Neuroscience 2009;29(20):6394-6405
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)

Q0441: A. L. Colombani, *et al.* Enhanced Hypothalamic Glucose Sensing in Obesity: Alteration of Redox Signaling. Diabetes 2009;58(10):2189-2197
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

P8406: G. D. Zeevalk, *et al.* Characterization of intracellular elevation of glutathione (GSH) with glutathione monoethyl ester and GSH in brain and neuronal cultures: Relevance to Parkinson's disease. Experimental Neurology 2007;203(2):512-520
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)

P8631: J. J. Powell, *et al.* Neutrophil-Activating Protein-2- and Interieukin-8-Mediated Angiogenesis. Journal of Cellular Biochemistry 2007;102(2):412-420
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

P8810: L. H. Li, *et al.* Local Nogo-66 administration reduces neuropathic pain after sciatic nerve transection in rat. Neuroscience Letters 2007;424(3):145-148
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

P8211: S. D. Luikart, *et al.* Mactinin treatment promotes wound-healing-associated inflammation in urokinase knockout mice. Wound Repair and Regeneration 2006;14(2):123-128
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

P6280: M. F. Anderson, *et al.* Glutathione monoethyl ester provides neuroprotection in a rat model of stroke. Neuroscience Letters 2004;354(2):163-165
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

P5597: A. E. Fournier, *et al.* Rho kinase inhibition enhances axonal regeneration in the injured CNS. Journal of Neuroscience 2003;23(4):1416-1423
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

P7698: D. Seurin, *et al.* Insulin-like growth factor binding protein-6 inhibits neuroblastoma cell proliferation and tumour development. European Journal of Cancer 2002;38(15):2058-2065
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)

P5249: E. M. Sharkey, *et al.* Pharmacokinetics and antitumor properties in tumor-bearing mice of an enediol analogue inhibitor of glyoxalase I. Cancer Chemotherapy and Pharmacology 2000;46(2):156-166
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

P3851: J. A. Powell, *et al.* Antiangiogenesis efficacy of nitric oxide donors. Journal of Cellular Biochemistry 2000;80(104-114
Agents: Penicillamine, S-nitroso N-acetyl-; Glutathione, S-nitroso N-acetyl; **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; SNAP and SNAG are nitric oxide donors; angiogenesis inhibitors.

P1931: T. Hattori, *et al.* Changes in intra-renal scavenging enzymes activities of the reactive oxygen species in experimental glomerulo-nephritis and nephrosis in rats. Nippon Jinzo Gakkai Shi 1991;33(2):191-199
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

P6119: J. H. Chen, *et al.* Magnolol induces apoptosis in vascular smooth muscle. NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY 2003;368(2):127-133
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

Q10430: M. Crespo-Masip, *et al.* Elimination of Vitamin D Signaling Causes Increased Mortality in a Model of Overactivation of the Insulin Receptor: Role of Lipid Metabolism. Nutrients 2022;14(7):
Agents: Glucose, D-(+); Mannitol, D-; **Route:** CSF/CNS (intracerebroventricular); **Species:** Mice; **Pump:** 2006; **Duration:** 42 days;
ALZET Comments: Controls received mp w/ vehicle; animal info: Cre-negative littermates were used as controls (CNT). Twenty-one days after birth, dependence; Taken together, the results shown in the present paper point to the paramount role of an adequate (vitamin D) signaling pathway in hypoglycemia induced by overactivation of the insulin receptor. Thus, in T1 diabetic patients, especially in the lean phenotype, maintaining
correct levels of vitamin D could support proper lipid metabolism and decrease deaths induced by insulin dosing errors. (pg.13)"; diabetes

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);

P6456: J. A. Barcia, *et al.* Continuous intra-amygdalar infusion of GABA in the amygdala kindling model of epilepsy in rat. Epilepsy Research 2004;58(1):19-26
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)

P5672: L. Chelikh, *et al.* High variability of perilymphatic entry of neutral molecules through the round window. Acta Otolaryngologica 2003;123(2):199-202
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)

P4692: B. Bittner, *et al.* The impact of co-solvents and the composition of experimental formulations on the pump rate of the ALZET® osmotic pump. International Journal of Pharmaceutics 2000;205(195-198
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

P2798: S. A. Klarr, *et al.* Chronic central potassium infusion prevents deoxycorticosterone-salt hypertension in rats. American Journal of Physiology Heart and Circulatory Physiology 1995;268(H646-H652
Agents: Cerebrospinal fluid, artificial; Mannitol **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002;
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

P2170: K. M. Andrews, *et al.* Water intake during chronic preoptic infusions of osmotically active or inert solutions. Physiol. Behav 1992;52(2):241-245
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

P0854: D. A. Denton, *et al.* Species differences in the effect of decreased CSF sodium concentration on salt appetite. J. Physiol 1984;79(499-504
Agents: Mannitol; Cerebrospinal fluid, artificial **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)

Q10574: U. Kilic, *et al.* Delayed Therapeutic Administration of Melatonin Enhances Neuronal Survival Through AKT and MAPK Signaling Pathways Following Focal Brain Ischemia in Mice. Journal of Molecular Neuroscience 2022;72(5):994-1007
Agents: Melatonin **Vehicle:** Ethanol; Sodium Chloride; **Route:** IP; **Species:** Mice; **Pump:** 2004; **Duration:** 42 days;
ALZET Comments: Dose (4 mg/kg/day); 5% ethanol in 0.9% sodium chloride used; Controls received mp w/ vehicle; animal info (Male; 77 total; 8-12 weeks old; Weighed 21-26 g); behavioral testing (Grip strength test; Rotarod test); ischemia (Brain);

Q10208: U. Kilic, *et al.* Inflammatory Cytokines are in Action: Brain Plasticity and Recovery after Brain Ischemia Due to Delayed Melatonin Administration. Journal of Stroke and Cerebrovascular Diseases 2021;30(12):106105
Agents: Melatonin **Vehicle:** Ethanol; NaCl; **Route:** IP; **Species:** Mice; **Pump:** 2002; **Duration:** 55 days;
ALZET Comments: Dose: (4 mg/kg/day); 10% ethanol; 0.9% NaCl vehicle used; Controls received mp w/ vehicle; animal info: C57BL/6 mice(21-25 g, male); behavioral testing: grip strength test; Brain coordinates ((MCA) territory (2 mm posterior/6 mm lateral from bregma); Cyanoacrylate adhesive used: An intraluminal filament technique using an 8-0 nylon coated with silicon resin was applied after the ligation of the left common and external carotid arteries to obtain focal ischemia; ischemia (brain);

Q9908: J. B. Yang, *et al.* Infusion of Melatonin Into the Paraventricular Nucleus Ameliorates Myocardial Ischemia–Reperfusion Injury by Regulating Oxidative Stress and Inflammatory Cytokines. Journal of Cardiovascular Pharmacology 2019;
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); "

Q6917: K. J. McCarty, *et al.* Effect of chronic melatonin supplementation during mid to late gestation on maternal uterine artery blood flow and subsequent development of male offspring in beef cattle. J Anim Sci 2018;96(12):5100-5111
Agents: Melatonin **Vehicle:** Not Stated; **Route:** Intrauterine; **Species:** Sheep (pregnant);
ALZET Comments:

Q6359: M. McMillin, *et al.* Melatonin inhibits hypothalamic gonadotropin-releasing hormone release and reduces biliary hyperplasia and fibrosis in cholestatic rats. American Journal of Physiology Gastrointestinal and Liver Physiology 2017;313(5):G410-G418
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);

Q3870: A. W. Eifert, *et al.* Effect of melatonin or maternal nutrient restriction on vascularity and cell proliferation in the ovine placenta. Animal Science 2015;153(13-21
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; good methods (pg 15); no stress (see pg. 15); post op. care (BID IM injection flunixin meglumine; QD IP injection Penicillin G Procaine); teratology; cardiovascular; used 20 cm of PE 60 tubing; pumps primed overnight 37C saline with catheters;

Q3106: C. O. Lemley, *et al.* Uterine Infusion of Melatonin or Melatonin Receptor Antagonist Alters Ovine Feto-Placental Hemodynamics During Midgestation. Biology of Reproduction 2013;89(2):U24-U32
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;

Q5391: M. Atanasova, *et al.* Strain-dependent effects of long-term treatment with melatonin on kainic acid-induced status epilepticus, oxidative stress and the expression of heat shock proteins. Pharmacol Biochem Behav 2013;111(44-50
Agents: Melatonin **Vehicle:** Saline; DMSO; **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);

Q2064: E. Bas, *et al.* Efficacy of three drugs for protecting against gentamicin-induced hair cell and hearing losses. British Journal of Pharmacology 2012;166(6):1888-1904
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

Q0512: B. J. Prendergast. MT1 Melatonin Receptors Mediate Somatic, Behavioral, and Reproductive Neuroendocrine Responses to Photoperiod and Melatonin in Siberian Hamsters (Phodopus sungorus). Endocrinology 2010;151(2):714-721
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

Q10824: Y. Kim, *et al.* Investigation of the Feasibility of Ventricular Delivery of Resveratrol to the Microelectrode Tissue Interface. Micromachines (Basel) 2021;12(12):
Agents: Resveratrol **Vehicle:** PEG 200; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Dose (356 ug/day); animal info Sprague-Dawley (11 weeks old; About 250g); functionality of mp verified by aspirating residual volume; ALZET brain infusion kit 1 used; dental cement used; Brain coordinates: 1 mm posterior to bregma, 1.5 mm lateral to midline; good methods (pg. 8)

Q8519: J. Guo, *et al.* Resveratrol Inhibits Neointimal Growth after Arterial Injury in High-Fat-Fed Rodents: The Roles of SIRT1 and AMPK. Journal of Vascular Research 2020;57(6):325-340
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;

Q6196: L. Naia, *et al.* Comparative Mitochondrial-Based Protective Effects of Resveratrol and Nicotinamide in Huntington's Disease Models. Mol Neurobiol 2017;54(7):5385-5399
Agents: Resveratrol; Nicotinamide **Vehicle:** Cyclodextrin, 2-hydroxypropyl-b; Saline; **Route:** SC; **Species:** Mice; **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);

Q6049: H. D. Kim, *et al.* SIRT1 Mediates Depression-Like Behaviors in the Nucleus Accumbens. J Neurosci 2016;36(32):8441-52
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); Loctite adhesive 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);

Q5221: H. J. Lee, *et al.* Involvement of resveratrol in crosstalk between adipokine adiponectin and hepatokine fetuin-A in vivo and in vitro. J Nutr Biochem 2015;26(11):1254-60
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(693-701
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;

Q3733: M. R. Kanavi, *et al.* The Sustained Delivery of Resveratrol or a Defined Grape Powder Inhibits New Blood Vessel Formation in a Mouse Model of Choroidal Neovascularization. MOLECULES 2014;19(17578-17603
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;

Q2519: H. Kanamori, *et al.* Resveratrol Reverses Remodeling in Hearts with Large, Old Myocardial Infarctions through Enhanced Autophagy-Activating AMP Kinase Pathway. American Journal of Pathology 2013;182(3):701-713
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)

Q1659: A. A. Khan, *et al.* Resveratrol Regulates Pathologic Angiogenesis by a Eukaryotic Elongation Factor-2 Kinase-Regulated Pathway. American Journal of Pathology 2010;177(1):481-492
Agents: Resveratrol; Sirt1 inhibitor III; NH125 **Vehicle:** Ethanol; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6, eFK2 -/-); 25% ethanol used

P9891: G. Ramadori, *et al.* Central Administration of Resveratrol Improves Diet-Induced Diabetes. Endocrinology 2009;150(12):5326-5333
Agents: Resveratrol **Vehicle:** Saline, sterile; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 5 weeks;
ALZET Comments: Controls received mp w/vehicle; animal info (C57BL/6, male); "This daily dose of resveratrol (0.03mg/ul) is approximately 8.5 million or approximately 152 million times lower, respectively, compared with the dose orally delivered in two previous studies" pg 5327; diabetes; endocrinology

P8824: E. L. Robb, *et al.* Dietary resveratrol administration increases MnSOD expression and activity in mouse brain. Biochemical and Biophysical Research Communications 2008;372(1):254-259
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

P5513: R. Zini, *et al.* Resveratrol-induced limitation of dysfunction of mitochondria isolated from rat brain in an anoxia-reoxygenation model. LIFE SCIENCES 2002;71(26):3091-3108
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);

Q7860: N. Y. Ru, *et al.* Glycosylated CD147 reduces myocardial collagen cross-linking in cardiac hypertrophy. J Cell Biochem 2018;119(10):8022-8034
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;

P7250: T. Liu, *et al.* The retinoid anticancer signal: mechanisms of target gene regulation. British Journal of Cancer 2005;93(3):310-318
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)

P7232: S. M. Karam, *et al.* Retinoic acid stimulates the dynamics of mouse gastric epithelial progenitors. Stem Cells 2005;23(3):433-441
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)

P4739: R. D. Kopke, *et al.* Growth factor treatment enhances vestibular hair cell renewal and results in improved vestibular function. PNAS 2001;98(10):5886-5891
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;

R0148: D. Al Musawi, *et al.* Adhesion prevention: state of the art. GYNAECOLOGICAL ENDOSCOPY 2001;10(123-130
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).

P4026: K. E. Rodgers, *et al.* Reduction of adhesion formation by intraperitoneal administration of various anti-inflammatory agents. J. Invest. Surgery 1998;11(327-339
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;

P3491: M. Kaya, *et al.* Chemical induction of fenestrae in vessels of the blood-brain barrier. Experimental Neurology 1996;142(6-13
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)

Q10368: K. M. Chacko, *et al.* Tempol Alters Urinary Extracellular Vesicle Lipid Content and Release While Reducing Blood Pressure during the Development of Salt-Sensitive Hypertension. Biomolecules 2021;11(12):
Agents: Tempol **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 7 days;
ALZET Comments: Animal info (Male; Female; 13 months old); Blood pressure measured via tail cuff system; cardiovascular;

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;

Q7198: O. Le, *et al.* INK4a/ARF Expression Impairs Neurogenesis in the Brain of Irradiated Mice. Stem Cell Reports 2018;10(6):1721-1733
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) porphyrinx (MnTnHex-2-PyP5+);

Q7118: J. M. Cline, *et al.* Post-Irradiation Treatment with a Superoxide Dismutase Mimic, MnTnHex-2-PyP(5+), Mitigates Radiation Injury in the Lungs of Non-Human Primates after Whole-Thorax Exposure to Ionizing Radiation. Antioxidants (Basel) 2018;7(3):
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);

Q6941: W. Cao, *et al.* A renal-cerebral-peripheral sympathetic reflex mediates insulin resistance in chronic kidney disease. EBioMedicine 2018;37(281-293
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);

Q6541: K. L. Wu, *et al.* Effects of high fructose intake on the development of hypertension in the spontaneously hypertensive rats: the role of AT1R/gp91(PHOX) signaling in the rostral ventrolateral medulla. J Nutr Biochem 2017;41(73-83
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;

Q5333: C. Y. Tsai, *et al.* Nitrosative Stress-Induced Disruption of Baroreflex Neural Circuits in a Rat Model of Hepatic Encephalopathy: A DTI Study. Sci Rep 2017;7(40111
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 signaling 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: Controls received mp w/ vehicle; animal info (male, Fischer 344 x Brown Norway, 3 months or 23 months old); functionality of mp verified by ; Vehicle pumps replaced after one week; Dose (300 ug/h);

Q6024: M. J. De Blasio, *et al.* The superoxide dismutase mimetic tempol blunts diabetes-induced upregulation of NADPH oxidase and endoplasmic reticulum stress in a rat model of diabetic nephropathy. European Journal of Pharmacology 2017;807(12-20
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);

Q6113: E. Bouvier, *et al.* Nrf2-dependent persistent oxidative stress results in stress-induced vulnerability to depression. Mol Psychiatry 2017;22(12):1701-1713
Agents: Butylhydroquinone, tert-; Tempol **Vehicle:** Water, distilled; Ethanol; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 days, 4 weeks;
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)

Q5581: J. Bai, *et al.* Central administration of tert-butylhydroquinone attenuates hypertension via regulating Nrf2 signaling in the hypothalamic paraventricular nucleus of hypertensive rats. Toxicol Appl Pharmacol 2017;333(100-109
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(U1-U14
Agents: Endotoxin, LPS; NS398; tempol **Vehicle:** Saline; DMSO; **Route:** IP; CSF/CNS; **Species:** Rat; **Pump:** 1007D; **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;

Q4343: W. Cao, *et al.* A Salt-Induced Reno-Cerebral Reflex Activates Renin-Angiotensin Systems and Promotes CKD Progression. JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY 2015;26(1619-1633
Agents: Losartan; clonidine; tempol; hydralazine **Vehicle:** PBS; CSF, artificial; **Route:** CSF/CNS; intragastric; **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 8 weeks old, 235-296g); 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);

Q5520: H. Zheng, *et al.* Centrally mediated erectile dysfunction in rats with type 1 diabetes: role of angiotensin II and superoxide. J Sex Med 2013;10(9):2165-76
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/m), 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

Q1866: C. Loinard, *et al.* C/EBP Homologous Protein-10 (CHOP-10) Limits Postnatal Neovascularization Through Control of Endothelial Nitric Oxide Synthase Gene Expression. Circulation 2012;125(8):1014-U126
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

Q2183: S. F. Knight, *et al.* Folate Receptor-Targeted Antioxidant Therapy Ameliorates Renal Ischemia-Reperfusion Injury. Journal of the American Society of Nephrology 2012;23(5):793-800
Agents: Tempol **Vehicle:** Saline; folate; **Route:** IV (jugular); **Species:** Mice; **Pump:** Not Stated; **Duration:** 48 hours;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL/6, 11 wks old); 7-day pump used; post op. care (buprenorphine in saline)

Q1904: M. Fujita, *et al.* Sympathoexcitation by Brain Oxidative Stress Mediates Arterial Pressure Elevation in Salt-Induced Chronic Kidney Disease. Hypertension 2012;59(1):105-U259
Agents: Tempol **Vehicle:** CSF, artificial; **Route:** CSF/CNS; IP; **Species:** Rat; **Pump:** 2002; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 3 wks old); pumps replaced after 2 week; cannula placement verified by ICV injection of Evans Blue dye after euthanization

Q1702: N. J. Willett, *et al.* Redox Signaling in an In Vivo Murine Model of Low Magnitude Oscillatory Wall Shear Stress. Antioxidants & Redox Signaling 2011;15(5):1369-1378
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

Q1156: M. H. W. Kappers, *et al.* The Vascular Endothelial Growth Factor Receptor Inhibitor Sunitinib Causes a Preeclampsia-Like Syndrome With Activation of the Endothelin System. Hypertension 2011;58(2):295-U351
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

Q4605: C. Y. R. Tan, *et al.* Thioredoxin-Interacting Protein: A Potential Therapeutic Target for Treatment of Progressive Fibrosis in Diabetic Nephropathy. NEPHRON 2015;129(109-127
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;

P7999: S. Ueda, *et al.* Recombinant human thioredoxin suppresses lipopolysaccharide-induced bronchoalveolar neutrophil infiltration in rat. LIFE SCIENCES 2006;79(12):1170-1177
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.

P3398: R. L. Hawkins, *et al.* Proline, ascorbic acid, or thioredoxin affect jaundice and mortality in Long Evans Cinnamon rats. Pharmacol. Biochem. Behav 1995;52(3):509-515
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 pentamethylhydroxychromane 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;

P9636: D. C. Irwin, *et al.* A potential role for reactive oxygen species and the HIF-1-alpha-VEGF pathway in hypoxia-induced pulmonary vascular leak. Free Radical Biology and Medicine 2009;47(1):55-61
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.

P2013: D. G. Stein, *et al.* Intracerebral administration of alpha-tocopherol-containing liposomes facilitates behavioral recovery in rats with bilateral lesions of the frontal cortex. J. Neurotrauma 1991;8(4):281-292
ALZET Comments: Phosphatidylcholine; vitamin E; Liposomes; CSF/CNS (cortex); Rat; 2001; 7 days; 2 pumps per animal,