



References on the Administration of Antioxidants Using ALZET® Osmotic Pumps

1. 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; AEOL 10150 is a catalytic antioxidant metalloporphyrin; ischemia (cerebral); MCAO.

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.

2. 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; tissue perfusion (cochlea).

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.

3. 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; Ppyrilamine maleate; AA-861; Cimetidine; Phendione
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

4. 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;.

5. 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 -/-); 80% DMSO used.



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).

6. 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 (Parkinson's disease)

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.)

7. Genistein

Q3324: R. F. Shi, *et al.* Lose dose genistein inhibits glucocorticoid receptor and ischemic brain injury in female rats. *NEUROCHEMISTRY INTERNATIONAL* 2014;65(1):14-22

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

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



ALZET Comments: Genistein; Cyclodextrin, hydroxypropyl beta; IP; Rat; 2ML1; 3 days; 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

ALZET Comments: FPT III; KN-93; Genistein; Saline; IP; Rat; 2ML1; 6 days; Controls received mp w/ vehicle; enzyme inhibitor (tyrosine kinase, CaMKII); cardiovascular; ischemia (cardiac).

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

ALZET Comments: Genistein; Estradiol, 17B-; DMSO; PEG 300; SC; Mice; 2002; 4 weeks; 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

ALZET Comments: Genistein; DMSO; ethanol; water; IV (superior vena cava); Rat; 2ML2; 14 days; Controls received mp w/ vehicle; comparison of IP injections vs IV mp; immunology; transplantation; Genistein is a soybean isoflavone; antioxidant; Vehicle composition: DMSO, ethanol; water (50/20/30).

8. 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; **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

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 angiogenesis 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

9. 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.

10. Mannitol

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

ALZET Comments: Aminobutyric acid, γ -; mannitol; Saline; CSF/CNS (amygdala); Rat; 2001; 7 days; 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 Oto-laryngologica* 2003;123(2):199-202

ALZET Comments: Mannitol; Inulin;; Radio-isotopes; 3H tracer; saline; ethanol; Ear (round window); Guinea pig; 1007D; 7 days; 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)

ALZET Comments: Mannitol; Radio-isotopes; Pyrrolidone, N-methyl-2-; Propylene glycol; PEG; 14C tracer; Water; Dimethylacetamide; in vitro; 2ML1; 8 days; 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. *Am. J. Physiol. (Heart Circ. Physiol. 37)* 1995;268(H646-H652)

ALZET Comments: Cerebrospinal fluid, artificial; Mannitol; CSF/CNS; Rat; 2002; no duration posted; 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

ALZET Comments: Potassium Chloride, hypertonic; Sodium chloride, hypertonic; Mannitol, hypertonic; Saline, isotonic; Water; CSF/CNS (preoptic area); Rat; 2002; 2 weeks; bilateral infusion to brain.

11. Melatonin

R0369: D. Ovid, *et al.* Melatonin Administration Methods for Research in Mammals and Birds. *J Biol Rhythms* 2018;33(6):567-588



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;

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); **Pump:** Not Stated; **Duration:** Not Stated;

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;

12. Resveratrol

Q8519: J. Guo, *et al.* Resveratrol Inhibits Neointimal Growth after Arterial Injury in High-Fat-Fed Rodents: The Roles of SIRT1 and AMPK. *J Vasc Res* 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; **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);

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

13. Retinoic Acid

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

ALZET Comments: Retinoic acid, 13-cis-; Ethanol; SC; Mice (transgenic); 1007D; 5 weeks; 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

ALZET Comments: Retinoic acid; uridine, bromodeoxy-; SC; Mice; 1, 3, 6 days; 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

ALZET Comments: Transforming growth factor; insulin-like growth factor I; retinoic acid; brain-derived neurotrophic factor;; PBS; BSA;; Ear (vestibule); Guinea pig; 2002; 4 weeks; 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; tissue perfusion (vestibule).

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

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



14. Tempol

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) porphyrin (MnTnHex-2-PyP5+); neurodegenerative (Ionizing radiation);

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); MnTnHex-2-PyP5+ aka hexyl; cardiovascular;

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; **Duration:** 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;

15. 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; cardiovascular; diabetes; Thioredoxin-interacting protein aka TXNIP;.

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; immunology; peptides; thioredoxin is an endogenous antioxidant protein.

16. 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; tocopherol also known as vitamin E.

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; Multiple pumps per animal (2); agent also called D-alpha-tocopherol.