



References on Pain Research Using ALZET® Osmotic Pumps

R0377: X. S. Zeng, *et al.* Neurotoxin-Induced Animal Models of Parkinson Disease: Pathogenic Mechanism and Assessment. *ASN Neuro* 2018;10(1759091418777438

ALZET Comments: Rotenone, MPTP; IV, IP; Rat; 14 days, 33 days; Dose (Rotenone (3 mg/kg/day); MPTP (46 mg/kg/day)); neurodegenerative (Parkinson's);.

Q7084: M. Caillaud, *et al.* Local low dose curcumin treatment improves functional recovery and remyelination in a rat model of sciatic nerve crush through inhibition of oxidative stress. *Neuropharmacology* 2018;139(98-116

ALZET Comments: Curcumin; Saline; CSF/CNS (Sciatic nerve); Rat; 2004; 4 weeks; Dose (0.2mg/day); 0.9% saline used; post op. care (buprenorphine 0.05 mg/kg); behavioral testing (Von Frey's filament test, SSI test, beam walking test); neurodegenerative (nerve regeneration);.

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

ALZET Comments: Resveratrol; Nicotinamide; Cyclodextrin, 2-hydroxypropyl-b; Saline; SC; Mice; 28 days; 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);.

Q5737: M. Ishido, *et al.* Neonatal rotenone lesions cause onset of hyperactivity during juvenile and adulthood in the rat. *Toxicol Lett* 2017;266(42-48

ALZET Comments: Rotenone; SMSO, PEG 300; SC; Rat (neonate); Controls received mp w/ vehicle; animal info (5-14 days); 50% DMSO: 50% PEG 300 used; Therapeutic indication (Hyperactivity disorder); Dose (3.0 mg/kg/day);.

Q6371: Gao Q, *et al.* Azilsartan ameliorates apoptosis of dopaminergic neurons and rescues characteristic parkinsonian behaviors in a rat model of Parkinson's disease. *ONCOTARGET* 2017;8(15):24099-24109

ALZET Comments: Rotenone; CSF/CNS (right supranigral); Rat; 2ML4; 4 weeks; Dose (2.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Male Lewis rats weighing 280-300 g); Brain coordinates (anteroposterior: 5.5 mm; mediolateral: 2.5 mm; dorsoventral: 7.0 mm, from bregma as a reference); neurodegenerative (Parkinson's disease);.

Q5502: T. Yayeh, *et al.* Morphine dependence is attenuated by red ginseng extract and ginsenosides Rh2, Rg3, and compound K. *J Ginseng Res* 2016;40(4):445-452

ALZET Comments: Ginsenoside, Rg3; ginsenoside, Rh; compound K; morphine; Saline; CSF/CNS; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240g); behavioral testing (conditioned place preference; escaping behavior); dependence; cyanoacrylate wound closure; Dose (morphine 26nmol/10ul/hr, ginsenoside 10 ug/ul/h); Brain coordinates (L: 1.3 mm; AeP: e0.5 mm; and DeV: e4.3 mm);.

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

ALZET Comments: Resveratrol; EX-527; DMSO; SC; Mice; 1002; 14 days; 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);.

Q5596: M. F. Almeida, *et al.* Aged Lewis rats exposed to low and moderate doses of rotenone are a good model for studying the process of protein aggregation and its effects upon central nervous system cell physiology. *Arq Neuropsiquiatr* 2016;74(9):737-744

ALZET Comments: Rotenone; DMSO, PEG; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (aged at 10 months old) ; 50:50 DMSO: PEG used; neurodegenerative (protein aggregation); Therapeutic indication (Neurodegeneration); Dose (1 mg/kg/day, 2 mg/kg/day);.



Q4971: S. Murakami, *et al.* Long-Term Systemic Exposure to Rotenone Induces Central and Peripheral Pathology of Parkinson's Disease in Mice. *Neurochem Res* 2015;40(6):1165-78

ALZET Comments: Rotenone; DMSO; PEG; SC; Mice; 2004; 1 week; 3 week; 6 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 20-25g, 9 weeks old); pumps replaced every 3 weeks; 50% DMSO used; 50% PEG used; neurodegenerative (Parkinson's disease); behavioral testing (locomotor activity); Dose (50 mg/kg/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

ALZET Comments: Resveratrol; DMSO; SC; mice; 1004; 4 weeks; 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.

Q4356: C. Z. Chang, *et al.* Curcumin, encapsulated in nano-sized PLGA, down-regulates nuclear factor kappaB (p65) and subarachnoid hemorrhage induced early brain injury in a rat model. *BRAIN RESEARCH* 2015;1608(215-224

ALZET Comments: Nanocurcumin; Rat; 5 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 18 weeks old, 300-400g); dose-response (pg 218-219); Curcumin aka diferuloylmethane;.

Q3651: S. J. Yang, *et al.* Resveratrol ameliorates hepatic metaflammation and inhibits NLRP3 inflammasome activation. *METABOLISM-CLINICAL AND EXPERIMENTAL* 2014;63(693-701

ALZET Comments: Resveratrol; DMSO; SC; Mice; 1004; 4 weeks; 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;.

Q4749: E. S. Yamada, *et al.* Annonacin, a natural lipophilic mitochondrial complex I inhibitor, increases phosphorylation of tau in the brain of EDP-17 transgenic mice. *EXPERIMENTAL NEUROLOGY* 2014;253(;):113-125

ALZET Comments: Annonacin; DMSO; PEG 400; SC; Mice (transgenic); 1003D; 3 days; Controls received mp w/ vehicle; animal info (male, R406W -/- or +/-, 16-18 weeks old, 30-40g); 50% DMSO used; 50% PEG 400 used; dose-response (pg 116); stress/adverse reaction: (death noted at 12 mg/kg/day annonacin see pg. 114); pumps primed in 37C saline for 4 hours; annonacin is a plant-derived mitochondrial inhibitor;.

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

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;.

Q3747: S. Murakami, *et al.* Neuroprotective Effects of Metallothionein Against Rotenone-Induced Myenteric Neurodegeneration in Parkinsonian Mice. *NEUROTOXICITY RESEARCH* 2014;26(285-298

ALZET Comments: Rotenone; DMSO; PEG; SC; Mice; 2004; 4, 6 weeks; Control animals received mp w/ vehicle; animal info (normal, C57BL/6, MT-1, MT-2 KO, 9 wks old); 50% DMSO used; 50% PEG used;.

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

ALZET Comments: Resveratrol; DMSO; ethanol; SC; Mice; 2002; 14 days; 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.

Q3127: L. Wu, *et al.* Inhibition of endoplasmic reticulum stress is involved in the neuroprotective effects of candesartan cilexetil in the rotenone rat model of Parkinson's disease. *Neuroscience Letters* 2013;548(;):50-55



ALZET Comments: Rotenone; DMSO; PEG 300; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (male, Lewis, 10 weeks, 300-350g); 50% DMSO used; neurodegenerative (Parkinson's disease); behavioral testing (grid test, bar test); Primed overnight at 37C. Pumps delivered pesticide to model Parkinson's symptoms.

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

ALZET Comments: Resveratrol; Coenzyme Q10; DMSO; IP; Rat; 2004; 4 weeks; 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;

Q3019: P. Mulcahy, *et al.* The behavioural and neuropathological impact of intranigral AAV-alpha-synuclein is exacerbated by systemic infusion of the Parkinson's disease-associated pesticide, rotenone, in rats. *Behavioural Brain Research* 2013;243(:):6-15

ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; 4 weeks; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 279 +/- 10 g); 50% DMSO used; 50% PEG used; neurodegenerative (Parkinson's disease).

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

ALZET Comments: Resveratrol; chloroquine; SC; Mice; 14 days; Control animals received mp w/ vehicle; animal info (C57BL/6J, male, 8-10 wks old).

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).

Q3195: R. S. Chaves, *et al.* Dynein c1h1, dynactin and syntaphilin expression in brain areas related to neurodegenerative diseases following exposure to rotenone. *Acta Neurobiologiae Experimentalis* 2013;73(4):541-556

ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; 4 weeks; Control animals received mp w/ vehicle; animal info (male, Lewis, 12 mo old); 50% DMSO used; 50% polyethylene glycol used.

R0315: N. Xiong, *et al.* Mitochondrial complex I inhibitor rotenone-induced toxicity and its potential mechanisms in Parkinson's disease models. *Critical Reviews In Toxicology* 2012;42(7):613-632

ALZET Comments: Rotenone; DMSO; polyethylenimine; PEG; IV (jugular); SC; Rat; Animal info (Sprague Dawley, Lewis); 50% DMSO used; summarized results from various studies that used ALZET pumps for rotenone infusion.

Q2943: L. T. Tien, *et al.* Neonatal exposure to lipopolysaccharide enhances dopamine transporter protein expression and accumulation of alpha-synuclein aggregation in the substantia nigra in responses to rotenone challenge in later life. *SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER* 2012;42(:):U213-U214

ALZET Comments: Rotenone; DMSO; PEG-300; SC; 2ML4; 14 days; Controls received mp w/ DMSO/PEG-300; toxicology; animal info (male Sprague-Dawley rats, pregnant); neurodegenerative (Parkinson's); minipumps used to infuse rotenone to investigate whether neonatal LPS exposure causes long lasting changes in a-synuclein aggregation and DAT expression;

Q2362: T. K. Lin, *et al.* Mitochondrial Dysfunction and Oxidative Stress Promote Apoptotic Cell Death in the Striatum via Cytochrome c/Caspase-3 Signaling Cascade Following Chronic Rotenone Intoxication in Rats. *International Journal of Molecular Sciences* 2012;13(7):8722-8739

ALZET Comments: Rotenone; DMSO; polyethylene glycol; SC; Rat; 2ML4; 28 days; Control animals received mp w/ vehicle; animal info (adult, male, Lewis, 300-350 g); post op. care (penicillin).

Q1395: Y. Wen, *et al.* Alternative Mitochondrial Electron Transfer as a Novel Strategy for Neuroprotection. *Journal of Biological Chemistry* 2011;286(18):U932-U943



ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 230-250 g, 10 wks old); 50% DMSO used; 50% PEG used.

Q1120: A. Hineno, *et al.* Ceruloplasmin Protects Against Rotenone-Induced Oxidative Stress and Neurotoxicity. *Neurochemical Research* 2011;36(11):2127-2135

ALZET Comments: Rotenone; SC; Mice; 28 days; Controls received mp w/ vehicle; animal info (CP +/+, CP -/-, 13 wks old).

Q1060: L. W. Fan, *et al.* Neonatal exposure to lipopolysaccharide enhances vulnerability of nigrostriatal dopaminergic neurons to rotenone neurotoxicity in later life. *NEUROBIOLOGY OF DISEASE* 2011;44(3):304-316

ALZET Comments: Rotenone; DMSO; PEG 300; SC; Rat (pregnant); 2ML4; 14 days; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, pregnant); neurodegenerative (Parkinson's disease); 50% DMSO used; 50% PEG 300 used.

Q1241: B. Monti, *et al.* Valproic Acid is Neuroprotective in the Rotenone Rat Model of Parkinson's Disease: Involvement of alpha-Synuclein. *NEUROTOXICITY RESEARCH* 2010;17(2):130-141

ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; animal info (adult, male, Wistar, 280-300 g, 330-250 g; neurodegenerative (Parkinson's disease); 50% DMSO used; 50% PEG.

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

ALZET Comments: Resveratrol; Sirt1 inhibitor III; NH125; Ethanol; SC; Mice; 14 days; Controls received mp w/ vehicle; animal info (C57BL/6, eFK2 -/-); 25% ethanol used.

Q0231: H. Chai, *et al.* In Vivo Assessment of the Effects of Ginsenoside Rb1 on Intimal Hyperplasia in ApoE Knockout Mice. *Journal of Surgical Research* 2010;162(1):26-32

ALZET Comments: Ginsenoside Rb1; homocysteine; Saline, normal; IP; Mice; 2004; 28 days; Animal info (12 wks old, ApoE -/-); one group contained Hcy and Rb1 in the same pump.

Q0953: Y. Sai, *et al.* Phosphorylated-ERK 1/2 and neuronal degeneration induced by rotenone in the hippocampus neurons. *ENVIRONMENTAL TOXICOLOGY AND PHARMACOLOGY* 2009;27(3):366-372

ALZET Comments: Rotenone; DMSO; PEG 300; SC; Rat; 4 weeks; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 280-320 g).

P9621: F. Richter, *et al.* Neurons Express Hemoglobin alpha-and beta-Chains in Rat and Human Brains. *Journal of Comparative Neurology* 2009;515(5):538-547

ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; 1 week; Controls received mp w/vehicle; animal info (adult, male, Lewis).

P9891: G. Ramadori, *et al.* Central Administration of Resveratrol Improves Diet-Induced Diabetes. *Endocrinology* 2009;150(12):5326-5333

ALZET Comments: Resveratrol; Saline, sterile; CSF/CNS; Mice; 1004; 5 weeks; 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.

P9745: B. H. Meurers, *et al.* Low dose rotenone treatment causes selective transcriptional activation of cell death related pathways in dopaminergic neurons in vivo. *NEUROBIOLOGY OF DISEASE* 2009;33(2):182-192

ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; 1 week; Controls received mp w/vehicle; no stress (see pg. 186); stress/adverse reaction: (see page. 186); "Except for the animal that died on day four of the treatment period, there were no signs of general distress, such as irritability or reduced responsiveness..." pg 186; animal info (adult, male, Lewis); neurodegenerative (Parkinson's disease); 50% DMSO used; 50% PEG used.

R0252: A. Jacob, *et al.* Mechanism of the Anti-inflammatory Effect of Curcumin: PPAR-gamma Activation. *PPAR Research* 2009;2007(89369):



ALZET Comments: Curcumin; IV; Rat; 2ML1; 3 days; Immunology; phytochemical component in turmeric; antioxidant properties; anti-inflammatory.

Q0232: H. Chai, *et al.* Ginsenoside Rb1 Attenuates Homocysteine-Augmented Guidewire Injury-Induced Intinnal Hyperplasia in Mice. *Journal of Surgical Research* 2009;157(2):193-198

ALZET Comments: Ginsenoside Rb1; homocysteine; Saline; IP; Mice; 2004; 28 days; Controls received mp w/ vehicle; animal info (C57BL/6, 12 wks old); one group contained Hcy and Rb1 in the same pump.

P9608: H. Bayir, *et al.* Peroxidase Mechanism of Lipid-dependent Cross-linking of Synuclein with Cytochrome c PROTECTION AGAINST APOPTOSIS VERSUS DELAYED OXIDATIVE STRESS IN PARKINSON DISEASE. *Journal of Biological Chemistry* 2009;284(23):15951-15969

ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; 4 weeks; Controls received mp w/vehicle; animal info (male, Lewis, 300-350g); 50% DMSO used; 50% PEG used.

P9720: J. G. Yu, *et al.* Arterial baroreflex dysfunction fails to mimic Parkinson's disease in rats. *JOURNAL OF PHARMACOLOGICAL SCIENCES* 2008;108(1):56-62

ALZET Comments: Rotenone; DMSO; PEG; SC; Rat; 2ML4; 4 weeks; Animal info (male, Sprague Dawley, 270-300 g); neurodegenerative (Parkinson's disease).

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

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

R0255: A. Lannuzel, *et al.* Atypical Parkinsonism in the Caribbean Island of Guadeloupe: Etiological Role of the Mitochondrial Complex I Inhibitor Annonacin. *Movement Disorders* 2008;23(15):2122-2128

ALZET Comments: Annonacin; Rat; 28 days; No stress (see pg. 2126); neurodegenerative (Parkinson's disease); Review see ref #26, p. 2126.

P9337: K. Kaneko, *et al.* Increased vulnerability to rotenone-induced neurotoxicity in ceruloplasmin-deficient mice. *Neuroscience Letters* 2008;446(1):56-58

ALZET Comments: Rotenone; DMSO; oil, peanut; SC; Mice; 4 weeks; Controls received mp w/ vehicle; animal info (13 wks old, Cp -/-).