



Recent References on the Administration of Nitric Oxide Synthase Inhibitors  
Using ALZET® Osmotic Pumps

1400W

**Q10995:** S. A. Shah, *et al.* Obesity-Induced Coronary Microvascular Disease Is Prevented by iNOS Deletion and Reversed by iNOS Inhibition. *JACC Basic to Translational Science* 2023;8(5):501-514

**Agents:** 1400W **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;

**ALZET Comments:** Dose (30 mg/kg/day); animal info: mice, 8 weeks of age; Blood pressure measured via Radiotelemetry; Blood pressure measurement (see pg.9) table 2; 1400W is a highly selective iNOS inhibitor/antagonist; obesity; diabetes; cardiovascular (coronary microvascular disease, heart failure)

**Q4294:** E. I. Ager, *et al.* Blockade of MMP14 Activity in Murine Breast Carcinomas: Implications for Macrophages, Vessels, and Radiotherapy. *JOURNAL OF THE NATIONAL CANCER INSTITUTE* 2015;107(U137-U148)

**Agents:** 1400W dihydrochloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (nude); **Pump:** 1002; **Duration:** Not Stated;

**ALZET Comments:** Animal info (female, nu/nu, 6-8 weeks old); cancer (breast); enzyme inhibitor (nitric oxide synthase); immunology;

**Q3098:** F. Klug, *et al.* Low-Dose Irradiation Programs Macrophage Differentiation to an iNOS(+)/M1 Phenotype that Orchestrates Effective T Cell Immunotherapy. *Cancer Cell* 2013;24(5):589-602

**Agents:** 1400W **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (RT5); cancer (cancer immunotherapy); immunology; iNOS inhibitor

**Q1253:** M. Nishida, *et al.* Heterologous down-regulation of angiotensin type 1 receptors by purinergic P2Y(2) receptor stimulation through S-nitrosylation of NF-kappaB. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(16):6662-6667

**Agents:** 1400W; Suramin **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL/6J, 6 wks old, male); enzyme inhibitor (NO synthase, iNOS)

**P8887:** A. H. Hu, *et al.* Tonic beta-adrenergic drive provokes proinflammatory and proapoptotic changes in aging mouse heart. *Rejuvenation Research* 2008;11(1):215-226

**Agents:** 1400W **Vehicle:** Isoproterenol bitartrate; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

**ALZET Comments:** Controls received mp w/ vehicle; enzyme inhibitor (iNOS); animal info (C57BL/6, 3, 20 months old); ischemia (myocardial)

**P8870:** Y. I. Chirino, *et al.* Selective iNOS inhibition reduces renal damage induced by cisplatin. *Toxicology Letters* 2008;176(1):48-57

**Agents:** 1400W; Cisplatin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 3 days;

**ALZET Comments:** Controls received mp w/ vehicle; enzyme inhibitor (iNOS); animal info (male, Wistar, 230-275g.)

**P8466:** P. Zhang, *et al.* Inducible nitric oxide synthase deficiency protects the heart from systolic overload-induced ventricular hypertrophy and congestive heart failure. *Circulation Research* 2007;100(7):1089-1098

**Agents:** 1400W **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 2 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; cardiovascular; animal info (2-3 months old, CS7BL16)

**P7221:** F. J. Perez-Asenio, *et al.* Inhibition of iNOS activity by 1400W decreases glutamate release and ameliorates stroke outcome after experimental ischemia. *Neurobiology of Disease* 2005;18(2):375-384

**Agents:** 1400W **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2,72 hours;

**ALZET Comments:** Controls received mp w/ saline or no treatment; MCAO



**P6534:** D. E. Hu, *et al.* Tumor cell-derived nitric oxide is involved in the immune-rejection of an immunogenic murine lymphoma. *Cancer Research* 2004;64(1):152-161

**Agents:** 1400W **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;  
**ALZET Comments:** Controls received mp w/ vehicle; enzyme inhibitor (iNOS); cancer (lymphoma)

**P5175:** B. R. Sharp, *et al.* Differential response to myocardial reperfusion injury in eNOS-deficient mice. *American Journal of Physiology Heart and Circulatory Physiology* 2002;282(H2422-H2426)

**Agents:** 1400W **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice (knockout); **Pump:** Not Stated; **Duration:** Not Stated;  
**ALZET Comments:** Cardiovascular; enzyme inhibitor; 1400W is an inducible nitric oxide synthase (iNOS) inhibitor

**P5028:** A. Koarai, *et al.* Allergic airway hyperresponsiveness and eosinophil infiltration is reduced by a selective iNOS inhibitor, 1400W, in mice. *Pulmonary Pharmacology & Therapeutics* 2000;13(267-275)

**Agents:** 1400W **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1003D; **Duration:** 26 hours;  
**ALZET Comments:** Controls received mp w/ vehicle; immunology; asthma

**P4279:** M. A. Rudd, *et al.* Salt-induced hypertension in Dahl salt-resistant and salt-sensitive rats with NOS II inhibition. *American Journal of Physiology Heart and Circulatory Physiology* 1999;277(H732-H739)

**Agents:** AMT; 1400W; Ethylisourea, S- **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Duration:** 12 days;  
**ALZET Comments:** Cardiovascular; agents are NOS II inhibitors; AMT is 2-amino-5,6-dihydro-6-methyl-4H-1,3-thiazine; S-ethylisourea is also known as EIT; enzyme inhibitors; nitric oxide synthase inhibitor;

**P3742:** L. L. Thomsen, *et al.* Selective inhibition of inducible nitric oxide synthase inhibits tumor growth in vivo: studies with 1400W, a novel inhibitor. *Cancer Research* 1997;57(3300-3304)

**Agents:** 1400W **Vehicle:** Water, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 6, 12, 13 days;  
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by measurement of 1400W in plasma and tumor samples; stress/adverse reaction: unexpected symptoms in 2 mice in high dose group (12 mg/kg/h), not clear if compound toxicity or bacterial infection (see pg. 3303); cancer; 1400W is N-(3-(aminomethyl)benzyl)acetamidine, a NO synthase inhibitor

#### L-NAME (2011-Present)

**Q10451:** Y.-M. Chao, *et al.* Disparate Roles of Oxidative Stress in Rostral Ventrolateral Medulla in Age-Dependent Susceptibility to Hypertension Induced by Systemic L-NAME Treatment in Rats. *Biomedicines* 2022;10(9):

**Agents:** L-NAME **Vehicle:** Saline; **Route:** IP; CSF/CNS (cisterna magna); **Species:** Rat; **Pump:** 2002; 1007D; **Duration:** 14 days;  
**ALZET Comments:** Dose (10 mg/kg/day); 0.9% saline used; Controls received mp w/ vehicle; animal info (Male; 4 weeks old; 12 weeks old); post op. care (Procaine penicillin injection); Blood pressure measured via tail-cuff sphygmomanometer; ALZET brain infusion kit used; cardiovascular;

**Q10058:** F. Portillo, *et al.* Nitric oxide controls excitatory/inhibitory balance in the hypoglossal nucleus during early postnatal development. *Brain Structure and Function* 2020;225(9):2871-2884

**Agents:** L-NAME; D-NAME **Vehicle:** Saline, sterile; **Route:** CSF/CNS (fourth ventricle); **Species:** Rat; **Pump:** 1002; **Duration:** 2 weeks;

**ALZET Comments:** Dose (180 mg/kg/day); Controls received mp w/ vehicle; animal info (Wistar rat); post op. care (penicillin); functionality of mp verified by pump weight; ALZET brain infusion kit 3 used; dependence;

**Q10135:** D. Ceiler. Hypertension III: Flow-Induced Vascular Remodeling. *International Association for Biomedical Sciences* 2020;

**Agents:** L-NAME **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;  
**ALZET Comments:** Dose (25mg/kg/day); Controls received mp w/ vehicle; animal info: 8 week old male Wistar Kyoto; 10 week old male; post op. care:rats were kept warm with a thermostatically- controlled heating pad; Blood pressure measured via a Pressure transducer; Recorded blood pressure (148.4 vs. 119.5 mmHg) see pg 2; cardiovascular; (Hypertension)



**Q7412:** H. E. Chen, *et al.* Resveratrol prevents combined prenatal N(G)-nitro-L-arginine-methyl ester (L-NAME) treatment plus postnatal high-fat diet induced programmed hypertension in adult rat offspring: interplay between nutrient-sensing signals, oxidative stress and gut microbiota. *J Nutr Biochem* 2019;70(28-37

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 weeks;

**ALZET Comments:** Dose (60 mg/kg/day); Controls received mp w/ vehicle; animal info (12-16 weeks old, male);

**Q6918:** M. Lemery Magnin, *et al.* Assessment of Placental Perfusion in the Preeclampsia L-NAME Rat Model with High-Field Dynamic Contrast-Enhanced MRI. *Fetal Diagn Ther* 2018;44(4):277-284

**Agents:** L-NAME **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML1; **Duration:** 3 days;

**ALZET Comments:** Dose (50 mg/day); Controls received mp w/ vehicle; animal info (Pregnant female Sprague-Dawley rats on embryonic day 16);

**Q7151:** D. S. Lee, *et al.* PDI-mediated S-nitrosylation of DRP1 facilitates DRP1-S616 phosphorylation and mitochondrial fission in CA1 neurons. *Cell Death & Disease* 2018;9(9):869

**Agents:** RNA, small interfering (protein disulfide isomerase), L-NAME **Vehicle:** Saline; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rats; **Pump:** 1007D; **Duration:** Not Stated;

**ALZET Comments:** Dose (15 µg/µl L-NAME); animal info (7-week-old male Sprague-Dawley rats); Nω-nitro-L-arginine methyl ester hydrochloride aka L-name; enzyme inhibitor (protein disulfide isomerase); ALZET brain infusion kit 1 used; Brain coordinates (right lateral ventricle, 1mm posterior; 1.5 mm lateral; 3.5 mm depth from bregma);

**Q6927:** A. R. Jeon, *et al.* PDI Knockdown Inhibits Seizure Activity in Acute Seizure and Chronic Epilepsy Rat Models via S-Nitrosylation-Independent Thiolation on NMDA Receptor. *Front Cell Neurosci* 2018;12(438

**Agents:** RNA, small interfering; L-NAME; PACMA31 **Vehicle:** Saline; **Route:** CSF/CNS (Right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 1 week;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (7 week old male Sprague-Dawley rats); enzyme inhibitor (PACMA31 is a selective PDI inhibitor); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth from bregma); Therapeutic indication (seizure);

**Q6279:** L. M. Yamaleyeva, *et al.* Photoacoustic imaging for in vivo quantification of placental oxygenation in mice. *FASEB J* 2017;31(12):5520-5529

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

**ALZET Comments:** Dose (50 mg/kg/d); animal info (Female C57Bl/6 mice); L-NG-Nitroarginine methyl ester aka L-NAME;

**Q6182:** B. Sitohy, *et al.* Early Actions of Anti-Vascular Endothelial Growth Factor/Vascular Endothelial Growth Factor Receptor Drugs on Angiogenic Blood Vessels. *American Journal of Pathology* 2017;187(10):2337-2347

**Agents:** L-NAME, D-NAME **Vehicle:** PBS; **Route:** SC; **Species:** Mice (nude); **Pump:** 1003D; **Duration:** 1 day;

**ALZET Comments:** Dose: L-NAME (134 mg/kg/day); Controls received mp w/ vehicle; animal info (4 to 6-week-old female athymic nude mice, wild-type C57BL/6 and eNOS null mice); N(G)-nitro-L-arginine methyl ester aka L-NAME; N(G)-nitro-L-arginine methyl ester (inactive isomer) aka D-NAME; "Because oral administration could not be counted on to deliver a consistent amount of drug reliably over a short (1 day) period of time, L- and D-NAME were administered by way of s.c. implanted minipumps."

**Q5684:** Y. L. Tain, *et al.* Maternal melatonin or N-acetylcysteine therapy regulates hydrogen sulfide-generating pathway and renal transcriptome to prevent prenatal N(G)-Nitro-L-arginine-methyl ester (L-NAME)-induced fetal programming of hypertension in adult male offspring. *American Journal of Obstetrics & Gynecology* 2016;215(5):636 e1-636 e72

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Controls received mp w/ saline; animal info (female, Sprague Dawley); teratology; cardiovascular; Bp measured using tail cuff; Bp measured using tail cuff; Dose (60 mg/kg/day);



**Q5166:** V. A. Netti, *et al.* Effects of nitric oxide system and osmotic stress on Aquaporin-1 in the postnatal heart. *Biomedicine & Pharmacotherapy* 2016;81(225-34

**Agents:** L-NAME **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 day;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 25-50 days old); cardiovascular; L-NAME solution prepared in laminar flow cabinet and used filter; Dose (4 mg/kg/day);

**Q4123:** Y. L. Tain, *et al.* Maternal Citrulline Supplementation Prevents Prenatal N(G)-Nitro-L-Arginine-Methyl Ester (L-NAME)-Induced Programmed Hypertension in Rats. *Biology of Reproduction* 2015;92(U27-U33

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Animal info (female, Sprague Dawley, 10 weeks old); teratology; cardiovascular;

**Q4602:** Y. L. Tain, *et al.* Transcriptome Analysis in Rat Kidneys: Importance of Genes Involved in Programmed Hypertension. *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES* 2015;16(4744-4758

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Controls received mp w/ saline, iso-osmotic; animal info (female, Sprague Dawley); teratology; cardiovascular; bp measured using tail cuff;

**Q4983:** L. H. Pojoga, *et al.* Cooperative Role of Mineralocorticoid Receptor and Caveolin-1 in Regulating the Vascular Response to Low Nitric Oxide-High Angiotensin II-Induced Cardiovascular Injury. *J Pharmacol Exp Ther* 2015;355(1):32-47

**Agents:** Angiotensin II; L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** 4 days;

**ALZET Comments:** animal info (male, cav-1 KO, 12 weeks old); Dose (L-NAME 0.1 - 0.2 mg/mL; AngII 0.7-2.8 mg/kg/day);

**Q4122:** Y. L. Tain, *et al.* Long-Term Effects of Maternal Citrulline Supplementation on Renal Transcriptome Prevention of Nitric Oxide Depletion-Related Programmed Hypertension: The Impact of Gene-Nutrient Interactions. *International Journal of Molecular Sciences* 2014;15(23255-23268

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Controls received mp w/ saline; animal info (female, Sprague Dawley, 10 weeks old); teratology;

**Q3270:** E. Zana-Taieb, *et al.* Effect of Two Models of Intrauterine Growth Restriction on Alveolarization in Rat Lungs: Morphometric and Gene Expression Analysis. *PLoS One* 2013;8(11):U35-U45

**Agents:** L-NAME **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Controls received high protein diet; animal info (Female, Sprague Dawley); teratology

**Q3102:** A. Kurabayashi, *et al.* Conditional VHL Gene Deletion Causes Hypoglycemic Death Associated with Disproportionately Increased Glucose Uptake by Hepatocytes through an Upregulated IGF-I Receptor. *PLoS One* 2013;8(7):U1405-U1415

**Agents:** L-NAME; Insulin-like growth factor receptor **Vehicle:** Saline; acetic acid; **Route:** SC; **Species:** Mice; **Duration:** 14 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (VHL-KO); 25% acetic acid used; immunology

**Q2618:** L. Butruille, *et al.* Maternal hypertension induced by NO blockade does not program adult metabolic diseases in growth-restricted rat fetuses. *METABOLISM-CLINICAL AND EXPERIMENTAL* 2013;62(3):442-445

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML1; **Duration:** Not Stated;

**ALZET Comments:** Control animals received mp w/ saline; animal info (Wistar Han, female, E17)

**Q3026:** H. Abe, *et al.* Nitric Oxide Induces Vascular Endothelial Growth Factor Expression in the Rat Placenta in Vivo and in Vitro. *Bioscience, Biotechnology, and Biochemistry* 2013;77(5):971-976

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2001D; **Duration:** 24 hours;

**ALZET Comments:** Animal info (Crj Wistar); enzyme inhibitor (NOS, nitric oxide)

**Q2193:** J. Ivars, *et al.* Maternal hypertension induces tissue-specific modulations of the apelinergic system in the fetoplacental unit in rat. *Peptides* 2012;35(1):136-138

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** 5 days;

**ALZET Comments:** Animal info (Wistar, female, E17); enzyme inhibitor (nitric oxide synthase, NOS);



**Q2087:** L. Butruille, *et al.* Prenatal fasudil exposure alleviates fetal growth but programs hyperphagia and overweight in the adult male rat. *European Journal of Pharmacology* 2012;689(1-3):278-284

**Agents:** L-NAME; fasudil **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** Not Stated; **ALZET Comments:** Controls received mp w/ normal saline; animal info (Wistar Han, 200-250 g, E14, female); enzyme inhibitor (nitric oxide synthase, NOS, Rho-kinase, ROCK); one group contained mixture of fasudil and L-NAME; teratology

**Q1403:** K. Wroblewska-Seniuk, *et al.* Maternal/fetal mortality and fetal growth restriction: role of nitric oxide and virulence factors in intrauterine infection in rats. *American Journal of Obstetrics & Gynecology* 2011;205(1):U242-U248

**Agents:** L-NAME **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat (pregnant); **Pump:** 2ML1; **Duration:** Not Stated; **ALZET Comments:** Controls received mp w/ vehicle; animal info (Sprague Dawley, female, timed-pregnant);

**Q0932:** L. G. Thaete, *et al.* ENDOTHELIN AND BLOOD PRESSURE REGULATION IN THE FEMALE RAT: STUDIES IN NORMAL PREGNANCY AND WITH NITRIC OXIDE SYNTHASE INHIBITION-INDUCED HYPERTENSION. *HYPERTENSION IN PREGNANCY* 2011;19(2):233-247

**Agents:** A-127722; A-182086; A-192621; FR-139317; L-NAME **Vehicle:** EtOH; propylene glycol; NaOH; water; **Route:** SC; IV (jugular); **Species:** Rat (pregnant); **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (female, SD); multiple pumps per animal (2); wound clips used; 20% ethyl alcohol used; "It is likely that administration with the pumps resulted in more consistent drug levels..." pg 242

#### L-NMA

**P5591:** N. Presle, *et al.* Cartilage protection by nitric oxide synthase inhibitors after intraarticular injection of interleukin-1beta in rats. *Arthritis & Rheumatology* 1999;42(10):2094-2102

**Agents:** L-NMA **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 1003D; **Duration:** 72 hours;

**ALZET Comments:** Controls received mp w/ vehicle; enzyme inhibitor; nitric oxide synthase inhibitors; L-NMA also called N-monomethyl-L-arginine

**P4241:** J. Ou, *et al.* Differential effects of nonselective nitric oxide synthase (NOS) and selective inducible NOS inhibition on hepatic necrosis, apoptosis, ICAM-1 expression, and neutrophil accumulation during endotoxemia. *Nitric Oxide: Biology & Chemistry* 1997;1(5):404-416

**Agents:** Aminoguanidine; Lysine, L-N6-(1-imino-ethyl)-; V-PYRRO/NO; L-NAME; L-NMA **Vehicle:** Saline; **Route:** IV (jugular); IV (gastric); **Species:** Rat; **Pump:** 2001D; **Duration:** 16 hours;

**ALZET Comments:** controls received mp w/vehicle; good methods (p. 406); nitric oxide synthase inhibitors; PE10 catheter tubing inserted in gastric vein; some animals implanted with one pump for gastric vein and one for jugular vein; NMA is NG-monomethyl-L-arginine

#### L-NMMA

**P7793:** S. Seto, *et al.* Contribution of central nitric oxide to the regulation of blood pressure and sodium balance in DOCA-salt hypertension. *Journal of Cardiovascular Pharmacology* 2006;47(5):680-685

**Agents:** L-NMMA **Vehicle:** Not Stated; **Route:** IP; CSF/CNS; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

**ALZET Comments:** Controls received mp w/ saline; replacement therapy (nephrectomy); dose-response (fig. 1); enzyme inhibitor (no synthase); cardiovascular; animal info (male, Wistar, 7 wk. old, 240g.); cannula location confirmed by methylene blue staining

**P7271:** S. Kashiwagi, *et al.* NO mediates mural cell recruitment and vessel morphogenesis in murine melanomas and tissue-engineered blood vessels. *Journal of Clinical Investigation* 2005;115(7):1816-1827

**Agents:** L-NMMA; D-NMMA **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; Mice (SCID); **Pump:** 1002; **Duration:** 8, 21 days;

**ALZET Comments:** Controls received mp w/ D-NMMA; pumps replaced at day 14; enzyme inhibitor (NO synthase); cancer (melanoma); cardiovascular; eNOS -/- mice; iNOS -/- mice



**P6754:** Y. Momohara, *et al.* Roles of endogenous nitric oxide synthase inhibitors and endothelin-1 for regulating myometrial contractions during gestation in the rat. *Molecular Human Reproduction* 2004;10(7):505-512

**Agents:** L-NMMA **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 weeks;  
**ALZET Comments:** Controls received mp w/ saline; enzyme inhibitor (no synthase)

**P6845:** J. Hagendoorn, *et al.* Endothelial nitric oxide synthase regulates microlymphatic flow via collecting lymphatics. *Circulation Research* 2004;95(2):204-209

**Agents:** L-NMMA; D-NMMA **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 days;  
**ALZET Comments:** Controls received mp w/ D-NMMA; enzyme inhibitor (NO synthase); cardiovascular

**P4418:** M. R. Schaffer, *et al.* Inhibition of nitric oxide synthesis in wounds: pharmacology and effect on accumulation of collagen in wounds in mice. *BJS* 1999;165(262-267

**Agents:** L-NMMA; Aminoguanidine hemisulphate; MITU **Vehicle:** PBS; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 10 days;  
**ALZET Comments:** Control received mp w/vehicle; comparison of IP injections vs. mp; wound healing study; MITU is S-methyl isothiuronium, a competitive NO synthase inhibitor.

**R0140:** J. Li, *et al.* Nitric oxide IV. determination of nitric oxide protection and toxicity in liver. *American Journal of Physiology Heart and Circulatory Physiology* 1999;276(G1069-G1073

**Agents:** L-NMMA; L-NAME; Aminoguanidine **Vehicle:** Not Stated; **Route:** IV (hepatic portal); **Species:** Rat; **Pump:** Not Stated;  
**ALZET Comments:** nitric oxide synthase inhibitors;

**P4228:** Y. Wada, *et al.* Chronic inhibition of nitric oxide in central nervous system does not cause hypertension. *Hypertension Res* 1998;21(97-101

**Agents:** L-NMMA; D-NMMA **Vehicle:** Not Stated; **Route:** CSF/CNS (cisterna magna); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;  
**ALZET Comments:** controls received mp w/D-NMMA; no stress (p. 98); nitric oxide synthase inhibitor; L-NMMA is N6-monomethyl-L-arginine; silastic PE10 tubing connected to PE50 tubing; pump implanted 7 days after cannula implantation; catheter patency verified; cardiovascular

**P3522:** Y. Suzuki, *et al.* Central administration of a nitric oxide synthase inhibitor impairs spatial memory in spontaneous hypertensive rats. *Neuroscience Letters* 1996;207(105-108

**Agents:** L-NMMA **Vehicle:** Saline; Trypan blue; **Route:** CSF/CNS (dorsal third ventricle); **Species:** Rat; **Pump:** 2001;  
**ALZET Comments:** Agent is N-monomethyl-L-arginine; enzyme inhibitor: nitric oxide synthase

**P3473:** T. I. Cohen, *et al.* Intrathecal infusion of the Nitric Oxide Synthase Inhibitor N-methyl L-arginine after experimental spinal cord injury in guinea pigs. *J. Neurotrauma* 1996;13(7):361-369

**Agents:** L-NMMA; D-NMMA **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Guinea pig; **Pump:** 2001;  
**ALZET Comments:** Spinal cord injury

#### L-NNA

**P4395:** K. S. Cramer, *et al.* A role for nitric oxide in the development of the ferret retinogeniculate projection. *Journal of Neuroscience* 1996;16(24):7995-8004

**Agents:** L-NNA **Vehicle:** Saline; **Route:** CSF/CNS (lateral geniculate nucleus); **Species:** Ferret; **Pump:** 2002; **Duration:** 12 days;  
**ALZET Comments:** Controls received mp with saline; animals received antibiotics prophylactically

**P2483:** F.-Y. Lee, *et al.* N-Nitro-L-arginine administration corrects peripheral vasodilation and systemic capillary hypotension and ameliorates plasma volume expansion and sodium retention in portal hypertensive rats. *Hepatology* 1993;17(1):84-90

**Agents:** L-NNA; Heparin **Vehicle:** Saline; **Route:** IV (jugular); **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;  
**ALZET Comments:** heparin added for anticoagulation; NNA stable for at least 6 days (p. 85)



**P2574:** A. S. Kimes, *et al.* Attenuation of some signs of opioid withdrawal by inhibitors of nitric oxide synthase. *Psychopharmacology* 1993;112(521-524)

**Agents:** L-NNA **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 8 days;

**ALZET Comments:** controls received mp w/ saline; comparison of ip injections vs mp; Injected L-NNA "was more effective than continuous infusion"; L-NNA is L-N-nitroarginine and is a NOS inhibitor

### Methylisothiurea

**P9880:** K. L. H. Wu, *et al.* Nitric Oxide and Superoxide Anion Differentially Activate Poly(ADP-ribose) Polymerase-1 and Bax to Induce Nuclear Translocation of Apoptosis-Inducing Factor and Mitochondrial Release of Cytochrome c after Spinal Cord Injury. *Journal of Neurotrauma* 2009;26(7):965-977

**Agents:** Methylisothiurea, S-; PTIO, carboxy-; Coenzyme Q<sub>10</sub>; tempol; FeTMPyP; furosemide; PJ-34 **Vehicle:** CSF, artificial; sesame oil; **Route:** CSF/CNS (spinal cord); **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;

**ALZET Comments:** Controls received mp w/ vehicle; multiple pumps per animal (2); post op. care (procraine penicillin); adult, male, specific pathogen free, 200-250 g.); spinal cord injury; PE-10 catheter used;

**P4781:** D. T. Efron, *et al.* A novel method of studying wound healing. *Journal of Surgical Research* 2001;98(16-20)

**Agents:** Methylisothiurea, S-; adenovirus vector; gene, mouse iNOS cDNA sequence **Vehicle:** Saline; Dye, methylene blue; Dye, India black ink; PBS; **Route:** SC (wound healing site); **Species:** Rat; **Pump:** 2001; 2ML1; **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ saline; functionality of mp verified by dye infusion; SC-implanted pumps infused 2 hydroxyproline sponges via catheter; initial studies used 2ML1 pumps to infuse dyes in order to assess the feasibility of direct infusion with pumps; iNOS inhibitor infusion was with 2001 pumps; diagram of pump-catheter assembly and location (p. 18); "Dye infusion demonstrated both grossly and microscopically excellent delivery of the infusate to wound sponges" (p. 18);

### MITU

**P4418:** M. R. Schaffer, *et al.* Inhibition of nitric oxide synthesis in wounds: pharmacology and effect on accumulation of collagen in wounds in mice. *BJS* 1999;165(262-267)

**Agents:** L-NMMA; Aminoguanidine hemisulphate; MITU **Vehicle:** PBS; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 10 days;

**ALZET Comments:** Control received mp w/vehicle; comparison of IP injections vs. mp; wound healing study; MITU is S-methyl isothiuronium, a competitive NO synthase inhibitor.

**P3442:** M. R. Schaffer, *et al.* Nitric oxide regulates wound healing. *J. Surg. Res* 1996;63(237-240)

**Agents:** MITU **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 10 days;

**ALZET Comments:** Controls received mp w/ PBS; immunology; MITU is S-methyl isothiuronium, a competitive NO synthase inhibitor; wound healing

### MLA

**P8382:** A. Pocivavsek, *et al.* Ventral hippocampal alpha7 and alpha4beta2 nicotinic receptor blockade and clozapine effects on memory in female rats. *Psychopharmacology* 2006;188(4):597-604

**Agents:** Nicotine ditartrate; MLA; Erythroidine, dihydro-beta **Vehicle:** Saline, sterile; CSF, artificial; **Route:** SC; CSF/CNS (ventral hippocampus); **Species:** Rat; **Pump:** 2004; 2ML4; **Duration:** 4 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; multiple pumps per animal (2); animal info (female, Sprague-Dawley, 200-300g.); neurodegenerative (Alzheimer's disease); methyllycaconitine; cannula placement confirmed w/ Chicago sky-blue dye; schizophrenia

**P7098:** K. Kawakami, *et al.* Nitric oxide accelerates interleukin-13 cytotoxin-mediated regression in head and neck cancer animal model. *Clinical Cancer Research* 2004;10(15):5264-5270

**Agents:** MLA **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice (nude); **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Cancer (head, neck); MLA is NW-monomethyl-L-arginine



**P4198:** C.-Y. Yim, *et al.* Effects of nitric oxide (NO) synthesis inhibition on antitumor responses during interleukin-2 (IL-2) treatment of mice. *Korean J. Internal Med* 1996;11(2):93-100

**Agents:** MLA **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;

**ALZET Comments:** Controls received sham implantation; MLA is n-monomethyl-L-arginine, an NOS inhibitor; cancer;

**P2804:** C.-Y. Yim, *et al.* Nitric oxide synthesis contributes to IL-2-induced antitumor responses against intraperitoneal Meth A tumor. *J. Immunol* 1995;155(4):382-4390

**Agents:** MLA **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 8 days;

**ALZET Comments:** Controls received sham surgery; pumps replaced after 8 days; cancer;

**P3553:** W. E. Samlowski, *et al.* Effectiveness and toxicity of protracted nitric oxide synthesis inhibition during IL-2 treatment of mice. *J. Immunother* 1995;18(3):166-178

**Agents:** MLA **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; 1007D; **Duration:** Not Stated;

**ALZET Comments:** Controls received sham implantation or no treatments; immunology; toxicology

### Nitroindazole

**P9327:** Y. H. Tian, *et al.* 7-nitroindazole, nitric oxide synthase inhibitor, attenuates physical dependence on Butorphanol in rat. *Synapse* 2008;62(8):582-589

**Agents:** Butorphanol tartrate; Nitroindazole, 7- **Vehicle:** Saline; DMSO; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 72 hours;

**ALZET Comments:** Enzyme inhibitor (nitric oxide synthase, NOS); animal info (male, Sprague Dawley, 250-275 g.); pump connected to catheter after 1 week recovery period; 10% DMSO used; PE60 tubing used

**P8379:** T. Thippeswamy, *et al.* NO-cGMP mediated galanin expression in NGF-deprived or axotomized sensory neurons. *Journal of Neurochemistry* 2007;100(3):790-801

**Agents:** Nitroindazole, 7- **Vehicle:** DMSO; **Route:** IP; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Wistar, Albino, 250-280g.); 20% DMSO

**P7078:** E. Y. Kim, *et al.* Changes of [<sup>3</sup>H]muscimol, [<sup>3</sup>H]flunitrazepam and [<sup>3</sup>H]MK-801 binding in rat brain by prolonged ventricular infusion of 7-nitroindazole. *Neurochemical Research* 2004;29(12):2221-2229

**Agents:** Nitroindazole, 7- **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ saline; enzyme inhibitor (nitric oxide synthase); cyanoacrylate adhesive

**P3492:** T. Bazzett, *et al.* The neuronal NOS inhibitor L-MIN, but not 7-NINA, reduces neurotoxic effects of chronic intrastriatal administration of quinolinic acid. *Brain Research* 1997;775(2):229-232

**Agents:** Quinolinic acid; Nitroindazole, 7-, sodium salt; thiocitrulline dihydrochloride, methyl- **Vehicle:** PBS; **Route:** CSF/CNS (striatum); **Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;

**ALZET Comments:** Dose-response; microdialysis; quinolinic acid administered alone or w/1 other agent in same pump; enzyme inhibitor; nitric oxide synthase inhibitor;

**P3444:** M. J. O'Neill, *et al.* Neuroprotective effects of 7-nitroindazole in the gerbil model of global cerebral ischaemia. *European Journal of Pharmacology* 1996;310(1):115-122

**Agents:** Nitroindazole, 7-, sodium salt **Vehicle:** Not Stated; **Route:** IP; **Species:** Gerbil; **Pump:** 1003D; **Duration:** 72 hours;

**ALZET Comments:** Comparison of ip injections vs. mp; 2 pumps implanted in each animal; 7-nitroindazole is a neuronal nitric oxide synthase inhibitor; neuroprotection seen when 7-nitroindazole was infused via mp, but not when injected 12X after occlusion





### Thiocitrulline

**Q6948:** Y. Zhang, *et al.* Hyperbaric oxygen produces a nitric oxide synthase-regulated anti-allodynic effect in rats with paclitaxel-induced neuropathic pain. *Brain Research* 2019;

**Agents:** S-Methyl-L-thiocitrulline **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Dose ( $0.5 \pm 0.1 \mu\text{L/hr/day}$ ); 0.9% saline used; animal info (male Sprague Dawley); post op. care (Ampicillin, meloxicam); enzyme inhibitor (S-Methyl-L-thiocitrulline is a neuronal nitric oxide synthase (nNOS) inhibitor); Brain coordinates (AP-1.0 mm, ML -2.0 mm, DV -3.5mm from bregma); bilateral cannula used; dependence;

**P3492:** T. Bazzett, *et al.* The neuronal NOS inhibitor L-MIN, but not 7-NINA, reduces neurotoxic effects of chronic intrastriatal administration of quinolinic acid. *Brain Research* 1997;775(229-232)

**Agents:** Quinolinic acid; Nitroindazole, 7-, sodium salt; thiocitrulline dihydrochloride, methyl- **Vehicle:** PBS; **Route:** CSF/CNS (striatum); **Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;

**ALZET Comments:** Dose-response; microdialysis; quinolinic acid administered alone or w/1 other agent in same pump; enzyme inhibitor; nitric oxide synthase inhibitor;