Recent References on the Administration of Nonsteroidal Anti-Inflammatory Drugs Using ALZET® Osmotic Pumps

Acetylsalicylic Acid

Q0421: C. Rivat, *et al.* Chronic stress induces transient spinal neuroinflammation, triggering sensory hypersensitivity and long-lasting anxiety-induced hyperalgesia. Pain 2010;150(2):358-368
Agents: CI-988; Chlordiazepoxide; Acetylsalicylic acid **Vehicle:** DMSO; Saline; **Route:** SC; CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2ML1; 2001; 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Male, Sprague-Dawley, 300-325 g, 8 wks old; ALZET intrathecal catheter used (0007740); behavioral testing (elevated plus-maze)

P8555: A. Adamek, *et al.* High dose aspirin and left ventricular remodeling after myocardial infarction. Basic Research in Cardiology 2007;102(4):334-340
Agents: Acetylsalicylic acid, lysine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ placebo; functionality of mp verified by serum salicylate concentrations; pumps replaced after 2 weeks; animal info (female, C57BL/6, 8-12 weeks old, 20-25 grams); MI induced by coronary artery ligation

P4829: M. Yuan, *et al.* Reversal of obesity- and diet-induced insulin resistance with salicylates or targeted disruption of *Ikk*b. Science 2001;293(1673-1677
Agents: Acetylsalicylic acid; Salicylate, sodium **Route:** SC; **Species:** Rat; Mice; **Pump:** 2002; 2ML2; **Duration:** 3,4 weeks;
ALZET Comments: Controls received mp w/ vehicle; 2ML2 used in rats, 2002 used in mice; acetylsalicylic acid also called aspirin: dose was 120 mg/kg/day; diabetes (type II)

P0455: T. Oshima, *et al.* Pharmacological manipulation of canine cyclooxygenase and thromboxane synthetase in vivo: differential renal and platelet recovery rates. J. Pharmacol. Exp. Ther 1984;229(2):598-602
Agents: Acetylsalicylic acid **Vehicle:** DMSO; Saline; **Route:** IV (superficial cervical vein); **Species:** Dog; **Pump:** 2ML1; **Duration:** 3 days;
ALZET Comments: Pumps primed for 4 hrs. before implant; used prefilled catheter in vein; greater solubility of ASA in DMSO allowed greater concentration in smaller total volume

Diclofenac

P5994: T. Murase, *et al.* Synergistic effects of nitric oxide and prostaglandins on renal escape from vasopressin-induced antidiuresis. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 2003;284(2):R354-R362
Agents: Vasopressin, 1-desamino-8-D arginine; L-NAME; diclofenac; ranitidine **Vehicle:** Saline; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 5 days;
ALZET Comments: Vasopressin, 1-desamino-8-D arginine was infused in the 2002 pump; L-NAME was dissolved in saline and diclofenac was dissolved in 50% DMSO; both were infused from a 2001 pump

P3383: O. Risto, *et al.* The effect of low dose diclofenac sodium administered locally on heterotopic bone formation in rats. Int. Orthopaedics (SICOT) 1995;19(392-395
Agents: Diclofenac **Vehicle:** NaCl; **Route:** Bone; **Species:** Rat; **Pump:** 2001; **Duration:** < or = 2 weeks;
ALZET Comments: Controls received mp w/saline; tissue perfusion (demineralized bone implant); functionality of mp verified by residual volume

Flurbiprofen

Q0222: C. Campanella, *et al.* Influence of prolonged exposure of a short half life non-steroidal anti-inflammatory drugs on gastrointestinal safety. Inflammopharmacology 2009;17(4):205-210
Agents: Flurbiprofen **Vehicle:** PEG 400; **Route:** IP; **Species:** Rat; **Pump:** 2002; **Duration:** 7 days;
ALZET Comments: Comparison of IP injections vs. mp; stability verified in vitro test for 14 days; animal info (male, Sprague Dawley, adult, 300-350 g.); "There was no significant difference between the two i.p. groups in the post-mortem plasma R or S-flurbiprofen concentration or in the percent of the dose excreted as glucoronidated flurbiprofen in urine on days 1 and 7"

P7625: I. Peretto, *et al.* Synthesis and biological activity of flurbiprofen analogues as selective inhibitors beta-amyloid (1-42) secretion. Journal of Medicinal Chemistry 2005;48(18):5705-5720
Agents: Flurbiprofen analogues; Flurbiprofen **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 4,7 days;
ALZET Comments: Dose-response; neurodegenerative (Alzheimer's disease); cassette dosing technology: 2-6 different analog compounds administered simultaneously to one animal

P1533: S. Offenbacher, *et al.* Changes in cyclooxygenase metabolites in experimental periodontitis in macaca mulatta. J. Periodontal Res 1989;24(63-74
Agents: Flurbiprofen **Vehicle:** Not Stated; **Route:** SC; **Species:** Monkey; **Pump:** 2ML2; 2ML4; **Duration:** 6, 12 months;
ALZET Comments: Controls received no drugs or sham pumps; multiple pumps per animal (2) (simultaneously); pumps replaced every 2 weeks or monthly; long-term study; one animal removed from study due to a 'secondary infection caused by a cage-pressure abrasion at the site of the s.c.

P1208: S. Offenbacher, *et al.* Effects of flurbiprofen on the progression of periodontitis in macaca mulatta. J. Periodontal Res 1987;22(6):473-481
Agents: Flurbiprofen **Vehicle:** Tris buffer; **Route:** SC; **Species:** Monkey; **Pump:** 2ML2; 2ML4; **Duration:** 6 months;
ALZET Comments: controls received mp w/ tris buffer; dose-response (table); 2 doses of agent infused; high dosage group received 2 pumps (2ML2); pumps replaced every 4 weeks for 2ML4, 2 weeks for 2ML2; long-term study

Ibuprofen

Q8888: L. Lucarini, *et al.* Effects of New NSAID-CAI Hybrid Compounds in Inflammation and Lung Fibrosis. Biomolecules 2020;10(9):
Agents: Bleomycin; Compound 3; Ibuprofen; Acetazolamide; **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 21 days;
ALZET Comments: Dose (1 mg/kg Compound 3; 0.5 mg/kg Ibuprofen; 0.5 mg/kg Acetazolamide); Controls received mp w/ vehicle; animal info (C57BL/6 WT mice, 2 months old, 25-30 g); Ibuprofen aka Ibu, Acetazolamide aka AAZ; cardiovascular;

Q8467: E. Fielder, *et al.* Anti-inflammatory treatment rescues memory deficits during aging in nfkb1(-/-) mice. Aging Cell 2020;19(10):e13188
Agents: Ibuprofen **Vehicle:** DMSO; PEG; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 2 months;
ALZET Comments: Dose (50 mg/kg/day); Controls received mp w/ vehicle; animal info (male C57BL/6 mice, 6 months old); pumps replaced every 28 days; dependence;

R0376: R. G. Kenny, *et al.* Toward Multi-Targeted Platinum and Ruthenium Drugs-A New Paradigm in Cancer Drug Treatment Regimens? Chemical Reviews 2019;
Agents: Chloridotetrakis (ibuprofenato)diruthenium-(II,III) **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat;
ALZET Comments: cancer (glioma);

Q7850: M. L. D. Rayner, *et al.* Developing an In Vitro Model to Screen Drugs for Nerve Regeneration. Anat Rec (Hoboken) 2018;301(10):1628-1637
Agents: ibuprofen **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 1004; **Duration:** 21 days;
ALZET Comments: Dose (7 µg/day); Controls received mp w/ vehicle; animal info (male, Wistar, 220-250g); pump was implanted locally parallel to re-connected nerve (p.1631);

Q5442: F. Streijger, *et al.* Combinatorial treatment of acute spinal cord injury with ghrelin, ibuprofen, C16, and ketogenic diet does not result in improved histologic or functional outcome. J Neurosci Res 2014;92(7):870-83
Agents: Ibuprofen **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats, 278-315 g); spinal cord injury; behavioral testing (grooming test, cylinder rearing test, Montoya staircase test, horizontal ladder test); Healing/recovery after spinal cord injury study; Dose (2.5 mL/hour);

Q3526: D. Jurk, *et al.* Chronic inflammation induces telomere dysfunction and accelerates ageing in mice. Nature Communications 2014;5(U235-U248
Agents: Ibuprofen **Vehicle:** PEG; DMSO; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 8 weeks;
ALZET Comments: Animal info (male, nfkb1 -/-, 24 weeks old); pumps replaced every 28 days; 50% DMSO used; 50% PEG used; behavioral testing (tightrope test); used 7mm wound clips;

Q4703: M. Benadiba, *et al.* Growth inhibitory effects of the Diruthenium-Ibuprofen compound, [Ru(2)Cl(Ibp)(4)], in human glioma cells in vitro and in the rat C6 orthotopic glioma in vivo
1993. JOURNAL OF BIOLOGICAL INORGANIC CHEMISTRY 2014;19(1025-1035
Agents: Diruthenium-ibuprofen **Vehicle:** Ethanol; CSF, artificial; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Animal info (female, Wistar, 250-350g); ALZET brain infusion kit used; 15% ethanol used; comparison of injection vs mp; cancer (glioma); tissue perfusion (intratumoral, glioma); "Using the orthotopic C6 model the effects of either chronic 14-day treatment by intra-peritoneal injection of chronic 14-day intra-tumour infusion by an Alzet osmotic pump attached to a brain infusion cannula were tested. Tumour growth was reduced by both routes of administration with the osmotic pump appearing to be the less harmful route in terms of haematological responses." pg 1033; Diruthenium-Ibuprofen aka RuIbp;

Q4741: K. G. Sharp, *et al.* A re-assessment of the effects of treatment with a non-steroidal anti-inflammatory (ibuprofen) on promoting axon regeneration via RhoA inhibition after spinal cord injury. Experimental Neurology 2013;248(;):321-337
Agents: Ibuprofen **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Sprague-Dawley, 9-10 weeks old); spinal cord injury; post op. care (bladders expressed BID); behavioral testing (hindlimb locomotor function; gridwalk task, footprint analysis, girdle test, plantar von frey); immunology; pumps primed primed for 16h in 37C saline;

Q1221: T. Madura, *et al.* Ibuprofen improves functional outcome after axotomy and immediate repair in the peripheral nervous system. Journal of Plastic Reconstructive and Aesthetic Surgery 2011;64(12):1641-1646
Agents: Ibuprofen **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 3 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Wistar, 200 g); stress/adverse reaction: "pressure necrosis" (see pg. 1643)

Q0207: D. Van Dam, *et al.* Ibuprofen modifies cognitive disease progression in an Alzheimer's mouse model. Journal of Psychopharmacology 2010;24(3):383-388
Agents: Ibuprofen **Vehicle:** PEG 300; Water, ultrapure; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 8 weeks;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced after 4 weeks; animal info (6 wks old, male, APP23);

P9697: X. X. Wang, *et al.* Ibuprofen Enhances Recovery from Spinal Cord Injury by Limiting Tissue Loss and Stimulating Axonal Growth. Journal of Neurotrauma 2009;26(1):81-95
Agents: Ibuprofen; naproxen **Vehicle:** PBS; **Route:** SC; **Species:** Rat; mice; **Pump:** 2004; 2ML4; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 11-12 wks old, 250-270 g., female, C57BL/6, 8-9 wks old, 20 g.); spinal cord injury; behavioral testing (BBB locomotor scale, Basso mouse scale)

P5919: C. Wagner, *et al.* Differential regulation of renin and Cox-2 expression in the renal cortex of C57Bl/6 mice. PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY 2003;447(2):214-222
Agents: Bumetanide; ibuprofen **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments:

P1145: H. Orita*, et al.* Prevention of postsurgical peritoneal adhesion formation by intraperitoneal administration of ibuprofen. Drug Development Research 1987;10(97-105
Agents: Ibuprofen **Vehicle:** PBS; Ringer's solution, lactated; **Route:** IP; **Species:** Rabbit; **Pump:** 2002; 2ML1; **Duration:** 7, 14 days;
ALZET Comments: controls rec'd mp w/ vehicle; mp connected to cath.; 2 exp.; varying doses of agent; ip + extraperitoneal pump placement; comparison of inject. vs. mp infusion; stress/adverse react. (fibrinous tissue)

Indomethacin

Q8543: Y. H. Hsieh*, et al.* Brainstem inflammation modulates the ventilatory pattern and its variability after acute lung injury in rodents. J Physiol 2020;598(13):2791-2811
Agents: Indomethacin **Vehicle:** DMSO; **Route:** CSF/CNS (intracisternal); **Species:** Rat; **Pump:** Not stated; **Duration:** 14 days;
ALZET Comments: Dose (100 ug/day); 50% DMSO used; Controls received mp w/ vehicle; animal info (adult (150–175 g) rats); Brain coordinates (0.8 mm posterior to bregma, 1.5 mm lateral to the midline and 3.5 mm ventral to the surface of the skull); dependence;

Q7826: L. Hao*, et al.* Indomethacin Enhances Brown Fat Activity. J Pharmacol Exp Ther 2018;365(3):467-475
Agents: indomethacin **Vehicle:** saline, Kolliphor HS15 buffered; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 4 weeks;
ALZET Comments: Dose (10 mg/ml at 0.15 ml/h); saline with 18.75% Kolliphor HS15 used; Controls received mp w/ vehicle; animal info (6 weeks, male, C57BL/6J); good methods ("We connected a piece of silicon tubing at the end of each pump, and sutured the tubing on the mouse back muscle to ensure that the opening of the tubing was on the iBAT of the mouse during pump implantation." p.469); controls split into three groups (saline, Kolliphor HS15, saline + Kolliphor HS15); Therapeutic indication (expression of genes involved in thermogenesis in iBAT (interscapular brown adipose tissue) and improved hyperglycemia found in DIO (diet-induced obesity) mice along with promoting mouse brown adipocyte differentiation,);

Q4542: Y. R. Na*, et al.* Consistent Inhibition of Cyclooxygenase Drives Macrophages towards the Inflammatory Phenotype. PLoS One 2015;10(U1730-U1742
Agents: NA-398; SC-560; indomethacin **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 30 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, BALB/c); immunology;

Q7687: S. D. Hursting*, et al.* Diet and cancer prevention studies in p53-deficient mice. J Nutr 2001;131(11 Suppl):3092s-4s
Agents: fenretinide; indomethacin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Duration:** 24 weeks;
ALZET Comments: animal info (6 weeks, male, p53+/-); comparison of caloric restriction vs mp; long-term study; fenretinide is a synthetic retinoid. indomethacin is a nonsteroidal anti-inflammatory drug; cancer (bladder); citation for study listed as (Hursting, S.D. and Perkins, S.N., unpublished observations, 2001);

P4819: M. C. Babin*, et al.* Systemic administration of candidate antivesicants to protect against topically applied suitor mustard in the mouse ear vesicant model (MEVM). Journal of Applied Toxicology 2000;20(S141-S144
Agents: Hydrocortisone; indomethacin; olvanil **Vehicle:** PEG 200; **Route:** SC; **Species:** Mice;**Duration:** 2 days;
ALZET Comments: Controls received mp w/ vehicle; toxicology

P4475: M. G. Zlatnik*, et al.* The effect of indomethacin and prostacyclin agonists on blood pressure in a rat model of preeclampsia. American Journal of Obstetrics & Gynecology 1999;180(5):1191-1195
Agents: Iloprost; Cicaprost; L-NAME; Indomethacin **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML2;; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/vehicle; comparison of SC injections vs. mp; cardiovascular; L-NAME is a synthase inhibitor

P3986: P. K. Henke*, et al.* Bacterial products primarily mediate fibroblast inhibition in biomaterial infection. J. Surg. Res 1998;74(17-22
Agents: Antibody, anti-interferon gamma; Antibody, indomethacin; Antibody, anti-TNFa; Antibody, interleukin 1 alpha **Vehicle:** PBS, sterile; ETHANOL; Indomethacin; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Immunology; pump implanted next to Dacron graft; peptides

P3918: P. K. Henke*, et al.* Prostaglandin E2 modulates monocyte MHC-II (Ia) suppression in biomaterial infection. J. Surg. Res 1997;69(372-378
Agents: Indomethacin; Antibody, anti-IL-1a; Antibody, anti-TNFa **Vehicle:** PBS; ETHANOL; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; immunology

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

P3614: M. Fernandez*, et al.* Acute and chronic cyclooxygenase blockade in portal-hypertensive rats: influence on nitric oxide biosynthesis. Gastroenterol 1996;110(1529-1535
Agents: Indomethacin **Vehicle:** Sodium carbonate; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 7 days;
ALZET Comments: sonication used to suspend indomethacin

P2852: T. Sakamoto*, et al.* Effect of intravitreal administration of indomethacin on experimental subretinal neovascularization in the subhuman primate. Arch Ophthalmol 1995;113(222-226
Agents: Indomethacin **Vehicle:** GBR buffer; Cyclodextrin, B-; **Route:** Eye (vitreous); **Species:** Monkey; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Control eyes received mp with vehicles; enzyme inhibitor; indomethacin is a cyclooxygenase (COX) inhibitor; empty pump implanted at time of cannula implantation to allow 1-month recovery period; beta-cyclodextrin used as a carrier molecule; some monkeys served both as control and drug treatment group (different treatment in each eye); a vitreous opacity appeared in some eyes during infusion but disappeared after the pump was disconnected

P1204: W. Schlegel*, et al.* Effect of continuous intrauterine administration of prostaglandin F2alpha and indomethacin on fertilization of rabbits. Horm. Metab. Res 1986;18(457-461
Agents: Indomethacin; Prostaglandin F2a **Vehicle:** HCl; Sodium hydroxide; Saline; **Route:** Intrauterine; **Species:** Rabbit; **Pump:** 2002; **Duration:** 11 days;
ALZET Comments: controls received mp w/ vehicle; separate and simultaneous infusion of agents; comparison of agents effects; NaOH, HCl and saline were used in combination as the vehicle for indomethacin; many different exp.; tissue perfusion

P0794: T. G. Kennedy. Intrauterine infusion of prostaglandins and decidualization in rats with uteri differentially sensitized for the decidual cell reaction. Biology of Reproduction 1986;34(2):327-335
Agents: Indomethacin; Prostaglandin E2; Prostaglandin F2a **Vehicle:** Ethanol; Gelatin; PBS; **Route:** intrauterine; **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: replacement therapy (ovariectomy); controls received mp w/ vehicle; estradiol and progesterone injected sc w/ mp PG infusion; vehicle contained indomethacin to reduce PG synthesis; tissue perfusion (uterus)

P1031: P. E. Doktorcik*, et al.* 6-Keto-prostaglandin E1 and the decidual cell reaction in rats. Prostaglandins 1986;32(5):679-689
Agents: Indomethacin; Prostaglandin E1; Prostaglandin E2 **Vehicle:** Ethanol; Gelatin; PBS; **Route:** intrauterine; **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: mp w/vehicle; dose-response; indomethacin infused with prostaglandin E1 in one group and with prostaglandin E2 in another group; tissue perfusion (uterus)

P0739: T. G. Kennedy. Evidence for the involvement of prostaglandins throughout the decidual cell reaction in the rat. Biology of Reproduction 1985;33(140-146
Agents: Indomethacin; Prostaglandin E2; Prostaglandin F2a **Vehicle:** Ethanol; PBS; **Route:** Intrauterine; **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: Replacement therapy (ovariectomy); pumps primed overnight in saline; sc adminis. of agents in comb. w/mp infusion; separate and simultaneous infusion of agents; tissue perfusion (uterus)

Ketorolac

Q10325: D. R. Seeger, *et al.* Blood-Brain Barrier Is the Major Site for a Rapid and Dramatic Prostanoid Increase upon Brain Global Ischemia. Lipids 2020;55(1):79-85
Agents: Ketorolac **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 12 hours;
ALZET Comments: Dose: (0.625 mg/kg/h); Controls received mp w/ vehicle; animal info: Mice (C57BL/6 background) at 4–6 months; Resultant plasma level (2.03 in Ketorolac concentration); ischemia (cerebral);

Q9450: D. R. Seeger, *et al.* Blood-Brain Barrier Is the Major Site for a Rapid and Dramatic Prostanoid Increase upon Brain Global Ischemia. Lipids 2020;55(1):79-85
Agents: Ketorolac **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 12 hours;
ALZET Comments: Dose (0.625 mg/kg/h); Controls received mp w/ vehicle; animal info (Mice (C57BL/6 background), 4–6 months of age); Resultant plasma level (2.03% Ketorolac concentration); ischemia (cerebral);

P8822: J. M. Scarlett, *et al.* Regulation of central melanocortin signaling by interleukin-1beta. Endocrinology 2007;148(9):4217-4225
Agents: Ketorolac **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 2 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL/6J, 4-5 wks old)

P5091: M. D. Southall, *et al.* Twenty-four hour exposure to prostaglandin downregulates prostanoid receptor binding but does not alter PGE(2)-mediated sensitization of rat sensory neurons. Pain 2002;96(285-296
Agents: Ketorolac tromethamine **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 48 hours;
ALZET Comments: controls received mp w/ vehicle; ketorolac is an NSAID sold as Toradol; cannula patency verfied by saline injection

P4204: J. V. Shufflebarger, *et al.* The effect of ketorolac on microvascular thrombosis in an experimental rabbit model. Plast. Reconstr. Surg 1996;98(140-145
Agents: Ketorolac **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Rabbit; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Controls received mp w/saline; functionality of mp verified by residual volume; comparison of i.m. injections vs. mp; ketorolac also called Toradol; NSAID

Meclofenamate

P1305: E. L. Sargent, *et al.* Intraluteal infusion of a prostaglandin synthesis inhibitor, sodium meclofenamate, causes premature luteolysis in rhesus monkeys. Endocrinology 1988;123(5):2261-2269
Agents: Meclofenamate, sodium **Vehicle:** Saline; Water; **Route:** Intraovarian (corpus luteum); IV (jugular); **Species:** Monkey; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: stress/adverse reaction (cortisol and progesterone levels); tissue perfusion

Naproxen

Q3710: A. C. Rosa, *et al.* Prevention of Bleomycin-Induced Lung Inflammation and Fibrosis in Mice by Naproxen and JNJ7777120 Treatment. Journal of Pharmacology and Experimental Therapeutics 2014;351(308-316
Agents: JNJ7777120; naproxen **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;
ALZET Comments: Control animals received mp w/ vehicle; animal info (male, C57BL/6, ~2 mo old, 25-30 g); infusion rate listed as 0.11 ul/hr; JNJ7777120 also known as (1-[(5-chloro-1H-indol-2-yl)carbonyl]-4-methylpiperazine), is a selective H4R antagonist; one group received combination of JNJ7777120 and naproxen

P8571: C. Baj-Rossi, *et al.* Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. Biosensors and Bioelectronics 2014;53(283-7
Agents: Naproxen **Vehicle:** PBS; **Route:** In vitro; **Species:** Not Stated; **Pump:** 1002; **Duration:** Not Stated;
ALZET Comments: Naproxen is anon- steroidal anti-inflammatory agent; This paper reports the characterization of an electrochemical biosensor for the continuous monitoring of Naproxen delivered by alzet pumps

Q4700: C. Baj-Rossi, *et al.* Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. BioTechniques 2014;53(;):283-287
Agents: Naproxen **Vehicle:** Methanol; **Route:** In Vitro; **Species:** Not Stated; **Pump:** 1002; **Duration:** 16 hours;
ALZET Comments: Functionality of mp verified by naproxen levels measured with sensors;

P9697: X. X. Wang, *et al.* Ibuprofen Enhances Recovery from Spinal Cord Injury by Limiting Tissue Loss and Stimulating Axonal Growth. Journal of Neurotrauma 2009;26(1):81-95
Agents: Ibuprofen; naproxen **Vehicle:** PBS; **Route:** SC; **Species:** Rat; mice; **Pump:** 2004; 2ML4; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 11-12 wks old, 250-270 g., female, C57BL/6, 8-9 wks old, 20 g.); spinal cord injury; behavioral testing (BBB locomotor scale, Basso mouse scale)

P1504: W. Y. Chan, *et al.* Effects of inhibition of prostaglandin synthesis on uterine oxytocin receptor concentration and myometrial gap junction density in parturient rats. Biology of Reproduction 1988;39(1117-1128
Agents: Naproxen, sodium **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2001; **Duration:** 3 days;
ALZET Comments: no comment posted

Superoxide Dismutase-PEG

P3263: E. H. Karran, *et al.* A simple in vivo model of collagen degradation using collagen-gelled cotton buds: the effects of collagenase inhibitors and other agents. Inflamm. Res 1995;44(36-46
Agents: Collagenase inhibitor A; Collagenase inhibitor B; Collagenase inhibitor C; tempol; Superoxide dismutase-PEG; Cytochalasin B; Pepstatin; APMSF; TLCK; SBTI; Leupeptin; E-64; Methylamine **Route:** SC; **Species:** Rat; **Pump:** 2001; 2ML1; **Duration:** 7 days;
ALZET Comments: controls received mp w/vehicle; no stress (see pg. 39); immunology; pumps connected with catheter tubing to 14C-collagen-gelled cotton buds

P3114: D. Truelove, *et al.* Neuronal protection with superoxide dismutase in repetitive forebrain ischemia in gerbils. Free Rad. Biol. Med 1994;17(5):445-450
Agents: Superoxide dismutase-PEG **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Gerbil; **Pump:** 1007D; **Duration:** 6 days;
ALZET Comments: Controls received mp with vehicle; ischemia (cerebral)

Tempol or Superoxide Dismutase (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+); 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; **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;
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); tissue perfusion (cisternae);

Q5692: H. Z. Toklu*, et al.* Intracerebroventricular tempol administration in older rats reduces oxidative stress in the hypothalamus but does not change STAT3 signalling or SIRT1/AMPK pathway. Applied Microbiology and Biotechnology 2017;42(1):59-67
Agents: Tempol **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3 weeks;
ALZET Comments: 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 the 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:** 7 days;
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; Enalapril is an ACE inhibitor; Losartan is an ANG II AT1 receptor antagonist; tempol is a SOD mimetic; 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); ischemia (renal); 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)

Tolmetin

P2007: K. E. Rodgers, *et al.* Effect of tolmetin sodium dihydrate on adhesion formation by intraperitoneal administration of antineoplastic agents. Cancer Chemotherapy and Pharmacology 1992;29(248-251
Agents: Doxorubicin HCl; Mitoxantrone; Tolmetin sodium; Bleomycin; Cisplatin; Methotrexate **Vehicle:** PBS; **Route:** IP; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Antibiotic; cancer; no stress (see p249)