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

Acetylsalicylic Acid


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)


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 IkB. 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)


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


 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


 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
ALZET®

Bibliography

Flurbiprofen


**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 glucuronidated flurbiprofen in urine on days 1 and 7”


**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


**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.


**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 nfkbeta1(-/-) 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;


**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);
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<thead>
<tr>
<th>ID</th>
<th>Authors</th>
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<th>Agents</th>
<th>Vehicle</th>
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<th>Species</th>
<th>Pump</th>
<th>Duration</th>
<th>ALZET Comments</th>
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<tbody>
<tr>
<td>Q5442</td>
<td>F. Streijger et al.</td>
<td>Combinatorial treatment of acute spinal cord injury with ghrelin, ibuprofen, C16, and ketogenic diet does not result in improved histologic or functional outcome.</td>
<td>J Neurosci Res 2014;92(7):870-83</td>
<td></td>
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<td>Ibuprofen</td>
<td>PBS; Route: SC; Species: Rat; Pump: Not Stated; Duration: Not Stated;</td>
<td>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);</td>
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<tr>
<td>Q3526</td>
<td>D. Jurk et al.</td>
<td>Chronic inflammation induces telomere dysfunction and accelerates ageing in mice.</td>
<td>Nature Communications 2014;5(U235-U248</td>
<td></td>
<td></td>
<td></td>
<td>Ibuprofen</td>
<td>Vehicle: PEG; DMSO; Route: SC; Species: Mice; Pump: 2004; Duration: 8 weeks;</td>
<td>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;</td>
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<td>Q4703</td>
<td>M. Benadiba et al.</td>
<td>Growth inhibitory effects of the Diruthenium-Ibuprofen compound, [Ru(2)Cl(Ibp)(4)], in human glial cells in vitro and in the rat C6 orthotopic glioma in vivo</td>
<td>JOURNAL OF BIOLOGICAL INORGANIC CHEMISTRY 2014;19(1025-1035</td>
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<td>Diruthenium-Ibuprofen</td>
<td>Vehicle: Ethanol; CSF, artificial; Route: CSF/CNS (intratumoral); Species: Rat; Pump: 2002; Duration: 14 days;</td>
<td>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 Rublp;</td>
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<td>Q4741</td>
<td>K. G. Sharp et al.</td>
<td>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.</td>
<td>Experimental Neurology 2013;248(:);321-337</td>
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<td>Ibuprofen</td>
<td>Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML4; Duration: 4 weeks;</td>
<td>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;</td>
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<td>Q1221</td>
<td>T. Madura et al.</td>
<td>Ibuprofen improves functional outcome after axotomy and immediate repair in the peripheral nervous system.</td>
<td>Journal of Plastic Reconstructive and Aesthetic Surgery 2011;64(12):1641-1646</td>
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<td></td>
<td>Ibuprofen</td>
<td>Vehicle: PBS; Route: SC; Species: Rat; Pump: 2ML4; Duration: 3 weeks;</td>
<td>Controls received mp w/ vehicle; animal info (female, Wistar, 200 g); stress/adverse reaction: “pressure necrosis” (see pg. 1643)</td>
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<td>Q0207</td>
<td>D. Van Dam et al.</td>
<td>Ibuprofen modifies cognitive disease progression in an Alzheimer's mouse model.</td>
<td>Journal of Psychopharmacology 2010;24(3):383-388</td>
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<td></td>
<td>Ibuprofen</td>
<td>Vehicle: PEG 300; Water, ultrapure; Route: SC; Species: Mice; Pump: 2004; Duration: 8 weeks;</td>
<td>Controls received mp w/ vehicle; pumps replaced after 4 weeks; animal info (6 wks old, male, APP23);</td>
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<td>P9697</td>
<td>X. X. Wang et al.</td>
<td>Ibuprofen Enhances Recovery from Spinal Cord Injury by Limiting Tissue Loss and Stimulating Axonal Growth.</td>
<td>Journal of Neurotrauma 2009;26(1):81-95</td>
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<td>Ibuprofen; naproxen</td>
<td>Vehicle: PBS; Route: SC; Species: Rat; mice; Pump: 2004; 2ML4; Duration: 4 weeks;</td>
<td>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);</td>
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<td>P5919</td>
<td>C. Wagner et al.</td>
<td>Differential regulation of renin and Cox-2 expression in the renal cortex of C57Bl/6 mice.</td>
<td>PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY 2003;447(2):214-222</td>
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<td>Bumetanide; ibuprofen</td>
<td>Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;</td>
<td>ALZET Comments:</td>
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</table>
**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**

**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;

**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,);

**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;

**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; toxicity

**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

**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
Agents: Indomethacin; Antibody, anti-IL-1α; Antibody, anti-TNFα Vehicle: PBS; Ethanol; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; immunology

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

Agents: Indomethacin Vehicle: Sodium carbonate; Route: SC; Species: Rat; Pump: 2ML2; Duration: 7 days;
ALZET Comments: sonication used to suspend indomethacin

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

Agents: Indomethacin; Prostaglandin F2α Vehicle: HCl; Sodium hydroxide; Saline; Route: Intrauterine; Species: Rabbit; Pump: 2002; Duration: 11 days;
ALZET Comments: controls received mp w/ vehicle; dose-response; indomethacin infused with prostaglandin E1 in one group and with prostaglandin E2 in another group; tissue perfusion (uterus)

Agents: Indomethacin; Prostaglandin E2; Prostaglandin F2α 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)

Agents: Indomethacin; Prostaglandin E1; Prostaglandin F2α 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)

Agents: Indomethacin; Prostaglandin E2; Prostaglandin F2α 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


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);


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(283-296

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


Agents: Ketorolac Vehicle: Not Stated; Route: IV (jugular); Species: Rabbit; Pump: 2ML1; Duration: 7 days;

ALZET Comments: Controls received mp w/ vehicle; ketorolac also called Toradol; NSAID

Meclofenamate


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


Agents: JNJ7777120; naproxen Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1004; Duration: Not Stated;

ALZET Comments: Control animals received mp w/ vehicle; one group received combination of JNJ7777120 and naproxen


Agents: Naproxen Vehicle: PBS; Route: In vitro; Species: Not Stated; Pump: 1002; Duration: Not Stated;

ALZET Comments: Naproxen is an an- steroidal anti-inflammatory agent; This paper reports the characterization of an electrochemical biosensor for the continuous monitoring of Naproxen delivered by alzet pumps


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;
**ALZET® Bibliography**

**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)

**Agents:** Naproxen, sodium  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat (pregnant);  
**Pump:** 2001;  
**Duration:** 3 days;  
**ALZET Comments:** no comment posted

**Superoxide Dismutase-PEG**

**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

**Agents:** Superoxide dismutase-PEG  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Gerbil;  
**Pump:** 1007D;  
**Duration:** 6 days;  
**ALZET Comments:** Controls received mp w/vehicle; ischemia (cerebral)

**Tempol or Superoxide Dismutase (2011-Present)**

**Q8077:** T. Li, *et al.* Elevated Oxidative Stress and Inflammation in Hypothalamic Paraventricular Nucleus Are Associated With Sympathetic Excitation and Hypertension in Rats Exposed to Chronic Intermittent Hypoxia. Front Physiol 2018;9(840)  
**Agents:** Tempol  
**Vehicle:** Not stated;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 7 days;  
**ALZET Comments:** Dose (5 ug/min); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 10 weeks old, 300-325 g); Tempol aka superoxide scavenger; bilateral cannula used; cardiovascular;

**Q7198:** O. Le, *et al.* INK4a/ARF Expression Impairs Neurogenesis in the Brain of Irradiated Mice. Stem Cell Reports 2018;10(6):1721-1733  
**Agents:** Porphyrin-based superoxide dismutase mimetic (MnHex)  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1004;  
**Duration:** 8 weeks;  
**ALZET Comments:** Dose (450 ug/kg/day); pumps replaced every 4 weeks; Porphyrin-based potent superoxide dismutase mimetic aka (Mn(III) meso-tetrakis-(n-hexylpyridinium-2-yl) porphyrin (MnTnHex-2-PyP5+ ); neurodegenerative (Ionizing radiation);

**Q7118:** J. M. Cline, *et al.* Post-Irradiation Treatment with a Superoxide Dismutase Mimic, MnTnHex-2-PyP(5+), Mitigates Radiation Injury in the Lungs of Non-Human Primates after Whole-Thorax Exposure to Ionizing Radiation. Antioxidants (Basel) 2018;7(3)  
**Agents:** mitochondrial superoxide dismutase mimetic (Hexyl)  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Monkey;  
**Duration:** 6 weeks;  
**ALZET Comments:** Dose (0.1 mg/kg/day); Controls received mp w/ vehicle; animal info (Rhesus monkeys);

**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);

**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;


**Agents:** FeTMPyP;  
**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);


**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);


**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);


**Agents:** Butylhydroquinone, tert-;  
**Tempol** Vehicle:** Water, distilled; Ethanol;  
**Route:** CSF/CNS (right lateral ventricle);  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 2 weeks;  
**ALZET Comments:** 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;

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;

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);

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);

Q1215: 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;

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
**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)

**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

**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

**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**

**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)