



References on Magnetic Resonance Imaging With ALZET® Osmotic Pumps

Q9519: J. Vasquez-Vivar, *et al.* Neuronal vulnerability to fetal hypoxia-reoxygenation injury and motor deficit development relies on regional brain tetrahydrobiopterin levels. *Redox Biology* 2020;29(101407)

Agents: Sepiapterin **Vehicle:** DMSO; **Route:** Not Stated; **Species:** Rabbit; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Dose (0.6 mg/kg/day); Controls received mp w/ vehicle; animal info (pregnant New Zealand white rabbit dams at 25 days gestation); MRI;

Q7282: D. A. Duricki, *et al.* Stroke Recovery in Rats after 24-Hour-Delayed Intramuscular Neurotrophin-3 Infusion. *Annals of Oncology* 2019;85(1):32-46

Agents: Neurotrophin-3, recomb. human **Vehicle:** Saline; bovine serum, albumin; **Route:** SC; **Species:** Rat; **Pump:** 2ML2;
Duration: 4 weeks;
ALZET Comments: Dose (100 µg/ml); 0.1% bovine serum albumin used; Controls received mp w/ vehicle; animal info (Lister Hooded outbred female rats, ~4 months old, 200-300g); pumps replaced every 2 weeks; ischemia (ischemic stroke); no stress (see pg. 34); Pumps made MRI compatible

Q7982: E. Degerman, *et al.* Endolymphatic hydrops induced by different mechanisms responds differentially to spironolactone: a rationale for understanding the diversity of treatment responses in hydropic inner ear disease. *Acta Otolaryngol* 2019;139(8):685-691

Agents: vasopressin, arginine-8-; rolipram; cilostamide; spironolactone **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 4 wk
ALZET Comments: Dose (VP 0.5 mg/kg/day), (rolipram 0.4mg/kg/day), (cilostamide 0.5 mg/kg/day), (spironolactone 1.2 mg/kg/day)); Controls received mp w/ VP; animal info (8 weeks, female, CBA/J, 22-24g); enzyme inhibitor (cilostamide is a PDE3 inhibitor and rolipram is a PDE4 inhibitor); MRI; Therapeutic indication (Spironolactone prevents the development of vasopressin and rolipram-induced endolymphatic hydrops although not cilostamide-induced endolymphatic hydrops);

Q7957: Z. Chen, *et al.* USP9X deubiquitinates ALDH1A3 and maintains mesenchymal identity in glioblastoma stem cells. *J Clin Invest* 2019;129(5):2043-2055

Agents: WP1130 **Vehicle:** Not stated; **Route:** CSF/CNS (caudate nucleus); **Species:** Mice; **Pump:** Not stated; **Duration:** 7 days;
ALZET Comments: Dose (25 mg/kg at 0.5 µl/h); Controls received mp w/ vehicle; animal info (NOD/SCID); WP1130 is a USP9X inhibitor; enzyme inhibitor (USP9X); Brain coordinates (2 mm anterior, 2 mm lateral, 3 mm depth from the dura); Cannula placement verified via MRI after removal of the pump system.; cancer (glioblastoma); MRI; vehicle use stated but identity not listed in paper.; Therapeutic indication (promotes robust polyubiquitylation of ALDH1A3, which results in a marked reduction in ALDH1A3 protein levels and functional activity, leading to attenuation of the tumor-initiating ability of MES GSCs);

Q8756: A. E. Vozenilek, *et al.* Absence of Nicotinamide Nucleotide Transhydrogenase in C57BL/6J Mice Exacerbates Experimental Atherosclerosis. *Journal of Vascular Research* 2018;55(2):98-110

Agents: Manganese Chloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 15 days;
ALZET Comments: Dose (25, 50 mg/kg/day); Controls received mp w/ vehicle; animal info (10-12 weeks, male, B6129SF1/Tac); post op. care (2 mg/kg meloxicam for 3 days); behavioral testing (Morris Water Maze); comparison of IP injection vs mp; MRI; stress/adverse reaction: ("mice implanted with pumps swam more slowly on the first 2 days of training than the control animals. By day 3 this difference had normalized, and there was no effect of pumps, MnCl2 treatment, or specific treatment group on swim speed." p.417. "Some mice that received MnCl2 via osmotic pump developed skin ulceration where the solution was being released from the pump. In 4/17 cases, the ulceration was so severe that the mice had to be euthanized." p.417); "when mice are given 50 mg/kg/day MnCl2 via osmotic pump, the useable imaging window is only from day 3 to day 5. The useable imaging window for mice receiving 25 mg/kg/day is approximately 3-14 days." p.419;

Q7739: E. Shavit-Stein, *et al.* A Novel Compound Targeting Protease Receptor 1 Activators for the Treatment of Glioblastoma. *Front Neurol* 2018;9(1087)

Agents: ketone, six amino acid chloromethyl- **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 7,14 days;
ALZET Comments: Dose (0.2 ug/kg/day; 2ug/kg/day; 20 ug/kg/day); animal info (Adult Lewis rats 270-335 g); six amino acid chloromethyl-ketone aka SIXAC; enzyme inhibitor (SIXAC inhibit thrombin); ALZET brain infusion kit used; Brain coordinates (1mm lateral × 3mm posterior to the Bregma, 5.5mm deep); MRI;



Q7932: D. A. Vousden, *et al.* Continuous manganese delivery via osmotic pumps for manganese-enhanced mouse MRI does not impair spatial learning but leads to skin ulceration. *Neuroimage* 2018;173(4):11-420

Agents: manganese chloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 15 days;

ALZET Comments: Dose (25, 50 mg/kg/day); Controls received mp w/ vehicle; animal info (10-12 weeks, male, B6129SF1/Tac); post op. care (2 mg/kg meloxicam for 3 days); behavioral testing (Morris Water Maze); comparison of IP injection vs mp; MRI; stress/adverse reaction: ("mice implanted with pumps swam more slowly on the first 2 days of training than the control animals. By day 3 this difference had normalized, and there was no effect of pumps, MnCl₂ treatment, or specific treatment group on swim speed." p.417. "Some mice that received MnCl₂ via osmotic pump developed skin ulceration where the solution was being released from the pump. In 4/17 cases, the ulceration was so severe that the mice had to be euthanized." p.417); "when mice are given 50 mg/kg/day MnCl₂ via osmotic pump, the useable imaging window is only from day 3 to day 5. The useable imaging window for mice receiving 25 mg/kg/day is approximately 3-14 days." p.419;

Q7807: B. O. Erokwu, *et al.* Quantitative magnetic resonance imaging assessments of autosomal recessive polycystic kidney disease progression and response to therapy in an animal model. *Pediatr Res* 2018;83(5):1067-1074

Agents: Octreotide **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 months;

ALZET Comments: Dose (20 µg/kg/day); Controls received mp w/ vehicle; animal info (1 month, male, Sprague-Dawley and PCK); MRI; Therapeutic indication (imaging showed effect of octreotide as it slowed both kidney and liver disease progression in induced models compared to saline.);

Q6745: D. S. Poole, *et al.* Continuous infusion of manganese improves contrast and reduces side effects in manganese-enhanced magnetic resonance imaging studies. *Neuroimage* 2017;147(1-9)

Agents: Manganese Chloride **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 8 days;

ALZET Comments: Dose (30 mg/kg and 60 mg/kg); Controls received mp w/ vehicle; animal info (10 week old C57BL/6J mice); comparison of IP injections vs mp; MRI; "Our study demonstrates that the osmotic pump is able to deliver Mn to the brain (and in a suitable amount) with contrast comparable to that achieved via IP injections. Although a higher dose does appear necessary to achieve a similar contrast, this higher dose administered via osmotic pump can be used without giving side effects. Additionally, the constant delivery of manganese ensures a stable blood level and presumably a more timing-independent manganese uptake during activation. Lastly, osmotic pump delivery ensures less animal handling during the experiment, which may be a large advantage for many studies involving behavior, fear or stress, where animal handling may have a large influence on the experimental outcome." pg.8 ;

Q5049: G. Karpel-Massler, *et al.* Induction of synthetic lethality in IDH1-mutated gliomas through inhibition of Bcl-xL. *Nat Commun* 2017;8(1):1067

Agents: hydroxyglutarate, 2-R-2- **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: Dose (10mM); functionality of mp verified by adding 1% Gadolinium to the pumps and performing MRIs after removal;

Q6454: C. H. P. Jansen, *et al.* In vivo MR-angiography for the assessment of aortic aneurysms in an experimental mouse model on a clinical MRI scanner: Comparison with high-frequency ultrasound and histology. *PLoS One* 2017;12(6):e0178682

Agents: Angiotensin II **Vehicle:** Saline; **Route:** SC; **Species:** Mice (knockout); **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: Dose (1 microgram/kg/min); Controls received mp w/ vehicle; animal info (8 week old male C57BL/6J ApoE-knockout mice); cardiovascular; MRI;

Q6028: I. M. Devonshire, *et al.* Manganese-enhanced magnetic resonance imaging depicts brain activity in models of acute and chronic pain: A new window to study experimental spontaneous pain? *Neuroimage* 2017;157(5):500-510

Agents: Manganese chloride **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; behavioral testing (voluntary wheel running); MRI-compatible polyetheretherketone tubing; Therapeutic indication (osteoarthritis, fmri); Dose (80 mg/kg);



Q5781: E. Degerman, *et al.* Inhibition of phosphodiesterase 3, 4, and 5 induces endolymphatic hydrops in mouse inner ear, as evaluated with repeated 9.4T MRI. *Acta Otolaryngologica* 2017;137(1):8-15

Agents: Cilostamide, Rolipram, Sildenafil citrate **Vehicle:** DMSO, saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (22-24 g, 8 weeks old); 50% DMSO, 50% Saline MRI; Therapeutic indication (Meniere's disease); Dose (cilostamide (0.5 mg/kg/day) (Abcam, Cambridge, UK), rolipram (0.4 mg/kg/day) and sildenafil citrate (1 mg/kg/day));

Q5764: F. Charlton, *et al.* The protective effect of apolipoprotein in models of trophoblast invasion and preeclampsia. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2017;312(1):R40-R48

Agents: Tumor necrosis factor- α **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6JArc); MRI; Therapeutic indication (Hypertension, pre-eclampsia, pregnancy); Dose (500 ng/kg/day);

Q4876: R. R. Reimann, *et al.* Differential Toxicity of Antibodies to the Prion Protein. *PLoS Pathog* 2016;12(1):1-19

Agents: Antibody, 31C6; antibody, POM1 **Vehicle:** PBS; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2004; **Duration:** 21 days;

ALZET Comments: animal info (BL6.129-Prnp); post op. care (SC injections of buprenorphinum, funixin, and 5% glucose; Sulfadoxinum and sugar were added into water for 1 week post op); MRI; pumps primed in 37C PBS for 24 hours; used PEEK

Q4873: S.-L. Puhl, *et al.* Adenosine A1 receptor activation attenuates cardiac hypertrophy and fibrosis in response to α 1-adrenoceptor stimulation in vivo. *British Journal of Pharmacology* 2016;173(88-102)

Agents: Phenylephrine; Adenosine, N6-cyclopentyl **Vehicle:** NaCl; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 3 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6N, 12 weeks old, 24-25g); MRI; Dose (Phenylephrine 120 mg/kg/day; CPA 2 mg/kg/day);

Q5421: J. K. McCreary, *et al.* Altered brain morphology and functional connectivity reflect a vulnerable affective state after cumulative multigenerational stress in rats. *Neuroscience* 2016;330(79-89)

Agents: MnCl **Vehicle:** NaOH, TRIS-HCL buffer; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (120-day old MPS and non-stress control female Long-Evans rats); functionality of mp verified by plasma levels; no stress, "no toxic effects were anticipated or observed" (see pg. 81); behavioral testing (open-field exploration testing); MRI imaging every second day, total of 5 time points; Multigenerational prenatal stress model; stress response measured by plasma corticosterone levels and open-field exploration in each generation; MRI-compatible pumps used (PEEK); Dose (7.14 mg/kg);

Q5414: D. Madularu, *et al.* High estrogen and chronic haloperidol lead to greater amphetamine-induced BOLD activation in awake, amphetamine-sensitized female rats. *Horm Behav* 2016;82(56-63)

Agents: Haloperidol **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; Animal info (OVX Sprague Dawley rats, 200-250 g, 2 months old); post op. care (Anafen analgesic 0.1 mL/rat, and local antibiotic ointment); replacement therapy (estrogen replacement); MRI compatible PEEK tubing used; Dose (0.25 mg/kg/day); Therapeutic indication (Schizophrenia);

Q5342: M. Dudek, *et al.* Alcohol preference and consumption are controlled by the caudal linear nucleus in alcohol-preferring rats. *European Journal of Neuroscience* 2016;43(11):1440-8

Agents: Manganese Chloride **Vehicle:** Saline, Tris-buffered; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: animal info (male alcohol-preferring AA and male Wistar rats; 6 weeks old, 264-413 g); functionality of mp verified by MRI after pump removal; post op. care (carprofen injection); Dose (120 mg/kg/wk);

Q5770: W. J. Chung, *et al.* Apelin-13 infusion salvages the peri-infarct region to preserve cardiac function after severe myocardial injury. *Int J Cardiol* 2016;222(361-367)

Agents: Apelin-13 **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (12 weeks old, 30 g); half-life 30 minutes (p. 362); MRI; "the delivery timing and administration methods utilize continuous micro-osmotic infusion pump for 4 weeks to address the limited half-life of A13"; Therapeutic indication (Myocardial infarction, stem cell);



Q5037: D. Madularu, *et al.* Changes in brain volume in response to estradiol levels, amphetamine sensitization and haloperidol treatment in awake female rats. *Brain Research* 2015;1618(100-10)

Agents: Haloperidol **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Controls received sham surgery; animal info (female, Sprague Dawley, 200-250g 2-3 months old, OVX); post op. care (Anafen 0.1 mL/rat; antibiotic ointment); MRI; PEEK; Dose (0.25 mg/kg/day);

Q5338: T. Hoch, *et al.* Fat/carbohydrate ratio but not energy density determines snack food intake and activates brain reward areas. *Sci Rep* 2015;5(10041)

Agents: Manganese chloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: animal info (Wistar rats 571 +/-41 g); "To avoid negative side effects on basic physiology and behaviour of the animals due to the injection of the manganese chloride solution in doses sufficient for MEMRI measurement, osmotic pumps served for the gentle, but rather time-consuming continuous application of non-toxic amounts of manganese, which accumulated in the activated brain areas during the whole time course of the 7-day food test phase" (pg. 8); MRI use

Q5142: M. Dudek, *et al.* Brain activation induced by voluntary alcohol and saccharin drinking in rats assessed with manganese-enhanced magnetic resonance imaging. *Addiction Biology* 2015;20(6):1012-21

Agents: Manganese Chloride **Vehicle:** Saline, Tris-buffered; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: animal info: male alcohol-preferring AA rats, 265-335 g; post op. care (subcutaneous injection of carprofen); MRI done after infusion; brain tissue distribution; brain Mn²⁺ accumulation; Dose: 120 mg/kg/week

Q4400: B. den Hollander, *et al.* Manganese-Enhanced Magnetic Resonance Imaging Reveals Differential Long-Term Neuroadaptation After Methamphetamine and the Substituted Cathinone 4-Methylmethcathinone (Mephedrone). *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2015;18(U118-U126)

Agents: Manganese chloride **Vehicle:** Tris-buffered saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Animal info (Wistar, 6 weeks old); post op. care (SC injection carprofen 5 mg/kg); behavioral testing (locomotor activity, novel object recognition); MRI; pumps primed overnight in 37C saline;

Q5213: E. Degerman, *et al.* Vasopressin induces endolymphatic hydrops in mouse inner ear, as evaluated with repeated 9.4 T MRI. *Hear Res* 2015;330(Pt A):119-24

Agents: Vasopressin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 - 30 days;

ALZET Comments: Controls received mp w/ vehicle; animal info: Five female C57BL6 mice and 4 and 6 female CBA/J mice of body weight 22 - 24 g (8 weeks of age); functionality of mp verified by MRI; dose-response (pg 3); MRI; "EH was induced, to our knowledge for the first time, by chronic administration of vasopressin via mini-osmotic pumps in two mouse strains using 9.4 T MRI in combination with Gd contrast agent intraperitoneally as read-out" (pg 5); Dose: 50 mg/100 g/day

Q3603: D. S. Poole, *et al.* Three-dimensional inversion recovery manganese-enhanced MRI of mouse brain using super-resolution reconstruction to visualize nuclei involved in higher brain function. *NMR IN BIOMEDICINE* 2014;27(749-759)

Agents: Manganese chloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 8 days;

ALZET Comments: MRI;

Q3579: P. A. Narayana, *et al.* Chronic cocaine administration causes extensive white matter damage in brain: Diffusion tensor imaging and immunohistochemistry studies. *PSYCHIATRY RESEARCH-NEUROIMAGING* 2014;221(3):220-230

Agents: Cocaine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 280-300g); behavioral testing (fine motor movement; ambulation; rearing activities; general motor behavior); dependence; MRI; pumps primed for 24 hours in 37C saline;

Q4008: K. Moessenboeck, *et al.* Browning of White Adipose Tissue Uncouples Glucose Uptake from Insulin Signaling. *PLoS One* 2014;9(U1192-U1202)

Agents: CL 316,243 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 10 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6, 6-8 weeks old, STZ); MRI; diabetes;



Q3454: M. Desrois, *et al.* Effect of isoproterenol on myocardial perfusion, function, energy metabolism and nitric oxide pathway in the rat heart -a longitudinal MR study. NMR IN BIOMEDICINE 2014;27(529-538

Agents: Isoproterenol **Vehicle:** Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar); cardiovascular; MRI;

Q3158: B. G. Sanganahalli, *et al.* Functional MRI and neural responses in a rat model of Alzheimer's disease. NEUROIMAGE 2013;79(;):404-411

Agents: Amyloid protein, beta (1-42); ferrus sulfate heptahydrate; L-Buthionine-(S,R)-sulfoximine **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Animal info (male, FAB/Samaritan Alzheimer's, 250-350g); neurodegenerative (Alzheimer's Disease); Pumps used to induce Alzheimer's disease symptoms in FAB rat models. Pump and cannula removed prior to MRI experiments

Q4552: R. I. Menzies, *et al.* An anatomically unbiased approach for analysis of renal BOLD magnetic resonance images. American Journal of Physiology Renal Physiology 2013;305(6):F845-52

Agents: Angiotensin II **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 3 days;

ALZET Comments: MRI use; animal info: male, F344/IcoCrI, 12-16 weeks old, ; PEEK tubing; BOLD MRI; hypoxia; paper examines blood oxygen level-dependent magnetic resonance imaging (BOLD MRI) as an emerging technique to assess renal oxygen bioavailability. To cause a chronic change in R2, angiotensin II was infused; dose: 60 ng/min

Q3310: J. L. McGuire, *et al.* Traits of fear resistance and susceptibility in an advanced intercross line. European Journal of Neuroscience 2013;38(9):3314-3324

Agents: Magnesium chloride **Vehicle:** Bicine buffer; **Route:** Not Stated; **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (fear-susceptible or fear-resistant, 8-10 weeks old); behavioral testing (fear testing); MRI; manganese used to enhance MRI signal

Q5337: T. Hoch, *et al.* Manganese-enhanced magnetic resonance imaging for mapping of whole brain activity patterns associated with the intake of snack food in ad libitum fed rats. PLoS One 2013;8(2):e55354

Agents: Manganese chloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: animal info (Wistar rats, 257 +/- 21 g); good methods (pumps were incubated in isotonic saline for 12 h previous to implantation); For the use in MRI, the stainless steel flow moderator was replaced by a PEEK micro medical tubing; "Osmotic pump-assisted MEMRI proved to be a promising technique for functional mapping of whole brain activity..." (pg 1); "MnCl2 is administered by osmotic pumps, which slowly and continuously release the solution over a time period of up to seven days avoiding adverse effects on motor activity, but providing sufficient manganese accumulation for MRI analysis" (pg. 2); Dose (1 M solution);

Q4762: Hannah Botfield, *et al.* Decorin prevents the development of juvenile communicating hydrocephalus. Brain 2013;136(2842-2858

Agents: human recombinant decorin **Vehicle:** PBS; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 2002; **Duration:** 3 days, 14 days;

ALZET Comments: MRI; controls received mp w/ vehicle; 3 wk old, Sprague-Dawley rats; dose: 5 mg/ml; mp were used to infuse decorin to suppress the inflammatory response in the subarachnoid space following a hemorrhage, and to prevent ventriculomegaly.

Q4797: Hannah Botfield, *et al.* Decorin prevents the development of juvenile communicating hydrocephalus. Brain 2013;136):2842-2858

Agents: decorin, human recombinant **Vehicle:** PBS; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks; 3 days;

ALZET Comments: controls received mp w/ vehicle; 3 wk old, Sprague-Dawley rats; mp were used to infuse decorin to suppress the inflammatory response in the subarachnoid space following a hemorrhage, and to prevent ventriculomegaly; MRI; dose 5 mg/ml



Q2909: G. L. Ding, *et al.* MRI of Neuronal Recovery after Low-Dose Methamphetamine Treatment of Traumatic Brain Injury in Rats. PLoS One 2013;8(4):U175-U183

Agents: Methamphetamine **Vehicle:** Not Stated; **Route:** IV; **Species:** Rat; **Pump:** Not Stated; **Duration:** 24 hours;
ALZET Comments: Controls received mp w/ saline; animal info. (male, wistar rats, 200-300 g); functionality of mp verified by MRI measurement of fractional anisotropy

Q2115: J. Yun, *et al.* A novel adenoviral vector labeled with superparamagnetic iron oxide nanoparticles for real-time tracking of viral delivery. JOURNAL OF CLINICAL NEUROSCIENCE 2012;19(6):875-880

Agents: Rhodamine-dextran; protein, Ad5-green fluorescent **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** 2ML1; **Duration:** 96 hours;
ALZET Comments: Animal info (male, Harlan Sprague Dawley, adult); MRI; gene therapy

Q2054: A. C. Vernon, *et al.* Contrasting Effects of Haloperidol and Lithium on Rodent Brain Structure: A Magnetic Resonance Imaging Study with Postmortem Confirmation. Biological Psychiatry 2012;71(10):855-863

Agents: Haloperidol **Vehicle:** Cyclodextrin, hydroxypropyl beta; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 8 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 10 wks old); MRI; 20% cyclodextrin used; long-term study; functionality of mp verified via plasma drug levels

Q2077: M. R. Sepulveda, *et al.* Evaluation of manganese uptake and toxicity in mouse brain during continuous MnCl₂ administration using osmotic pumps. Contrast Media & Molecular Imaging 2012;7(4):426-434

Agents: Manganese chloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 12, 21 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Swiss, 2 mo old); MRI; comparison of SC injections vs SC mp; "The novel method presented in this study in mice, which is based on subcutaneously implanted mini-osmotic pumps filled with MnCl₂, appears to be a better system for delivering the agent into the interstitial tissue compared with repeated agent injections." pg 429

Q1855: S. I. Mok, *et al.* Infusion-based manganese-enhanced MRI: a new imaging technique to visualize the mouse brain. Brain Structure and Function 2012;217(1):107-114

Agents: Manganese chloride **Route:** SC; **Species:** Mice; **Pump:** 1003D; 1007D; 1002; **Duration:** 3, 7, 14 days;
ALZET Comments: Animal info (Oxtr KO, wt, 22-30 g, age-matched adult); MRI

Q1378: A. C. Vernon, *et al.* Effect of Chronic Antipsychotic Treatment on Brain Structure: A Serial Magnetic Resonance Imaging Study with Ex Vivo and Postmortem Confirmation. Biological Psychiatry 2011;69(10):936-944

Agents: Haloperidol; Olanzapine **Vehicle:** Cyclodextrin, beta-hydroxypropyl; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 8 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 240-250 g, 9 wks old); pumps replaced after 28 days; half-life 2.5 hours (p. 937); "MRI-safe" pumps; 20% cyclodextrin used; long-term study

Q1015: C. B. Colen, *et al.* Metabolic Targeting of Lactate Efflux by Malignant Glioma Inhibits Invasiveness and Induces Necrosis: An In Vivo Study. NEOPLASIA 2011;13(7):620-632

Agents: Cyano-4-hydroxycinnamate, alpha **Vehicle:** PBS; **Route:** CSF/CNS (caudate putamen); **Species:** Rat (nude); **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ saline; animal info (8-10 wks old, 250-300 g, male); cancer (glioma); tissue perfusion (intratumoral); alpha cyano-4-hydroxy also known as ACCA is a small-molecule inhibitor of lactate transport; Plastics One non-metal cannula used; MRI

Q0350: K. Schmerbach, *et al.* Effects of Aliskiren on Stroke in Rats Expressing Human Renin and Angiotensinogen Genes. PLoS One 2010;5(11):U241-U247

Agents: Aliskiren; Candesartan **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 12 days;
ALZET Comments: Controls received sham operation; animal info (dTGR, 5-6 wks old, 125-135g); MRI; ischemia (MCAO, cerebral); enzyme inhibitor (renin);



Q0113: D. Ding, *et al.* Convection-enhanced delivery of free gadolinium with the recombinant immunotoxin MR1-1. *Journal of Neuro-oncology* 2010;98(1):1-7

Agents: MR1-1; Gadolinium-DTPA **Vehicle:** Saline; Albumin, human serum; **Route:** CSF/CNS (parenchyma); **Species:** Rat; **Pump:** 2ML2; **Duration:** 5 days;

ALZET Comments: Toxicology; cancer (glioblastoma); no stress (see pg. 4); animal info (male, Fisher 344, 3 months old); dose-response (Fig.1); skin wounds closed with wound clips; behavioral testing (stepping and placing reflex and incline ramp climbing ability); CED (Convection enhanced delivery) infusion; "All rats survived the entirety of the study without clinical or histological toxicity attributable to the study drugs." (p. 1); MR1-1 is a recomb. immunotoxin of a mAb-endotoxin frag; Plastics One cannula used; MRI; brain tissue distribution

Q0994: E. Choke, *et al.* Vascular endothelial growth factor enhances angiotensin II-induced aneurysm formation in apolipoprotein E-deficient mice. *JOURNAL OF VASCULAR SURGERY* 2010;52(1):159-166

Agents: Angiotensin II **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ saline; animal info (7 mo old, ApoE -/-); peptides; MRI; adverse effects "in the placebo control group, one mouse died on day 18 after insertion of the osmotic pumps," pg 161

Q0707: Y. Tange, *et al.* Novel Antitumor Effect of Carboplatin Delivered by Intracerebral Microinfusion in a Rat Malignant Glioma Model. *NEUROLOGIA MEDICO-CHIRURGICA* 2009;49(12):572-579

Agents: Carboplatin **Vehicle:** Glucose, D-; Evans blue; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001; **Duration:** 3, 7 days;

ALZET Comments: Animal info (male, F344/N Slc, Fischer 220-260 g); brain tissue distribution; ALZET brain infusion kit used; stability verified (4 weeks) pg 573; cancer (glioma); MRI; brain tissue distribution; "... continuous intracerebral microinfusion using the osmotic mini-pump can provide broader distribution of agents than growth of the brain tumor."; "intracerebral microinfusion can attain clinically favorable drug distribution from a single infusion point." pg 576

P9286: C. Ciceroni, *et al.* Type-3 metabotropic glutamate receptors negatively modulate bone morphogenetic protein receptor signaling and support the tumourigenic potential of glioma-initiating cells. *Neuropharmacology* 2008;55(4):568-576

Agents: LY379268; LY341495 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (nude); **Pump:** Not Stated; **Duration:** 3 months;

ALZET Comments: Controls received mp w/ saline; long-term study; pumps replaced every 15-28 days; cancer (brain, glioma); MRI; animal info (male, CD-1, nude); mGlu3 receptor-agonist, antagonist

P8659: A. D. Strader, *et al.* The effects of the melanocortin agonist (MT-II) on subcutaneous and visceral adipose tissue in rodents. *Journal of Pharmacology and Experimental Therapeutics* 2007;322(3):1153-1161

Agents: Melanotan-II **Vehicle:** PBS; **Route:** SC; **Species:** Rat; Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; MRI; animal info (male, Long Evans, 225-250g; male, C57BL/6J, 5 wks old); Melanocortin receptor agonist

P8357: W. J. M. Mulder, *et al.* Early in vivo assessment of angiostatic therapy efficacy by molecular MRI. *FASEB Journal* 2007;21(2):378-383

Agents: Endostatin; Anginex **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks; 3 days;

ALZET Comments: Controls received mp w/ saline; cancer (melanoma); peptides; MRI; animal info (C57BL/6, 6 weeks old); antiangiogenesis

P9104: K. S. Monkkonen, *et al.* Intracerebroventricular antisense knockdown of G alpha_{i2} results in ciliary stasis and ventricular dilatation in the rat. *BMC Neuroscience* 2007;8(26)

Agents: Oligodeoxynucleotide, antisense; Oligodeoxynucleotide, nonsense; Oligodeoxynucleotide, mismatch **Vehicle:** Saline, sterile; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; 2002; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; no stress (see pg. 2 of 15); MRI; animal info (male, Harlan Wistar, 3-5 wks old, 50-100 g.; adult, 250 g.)



P8814: T. D. Farr, *et al.* Estrogen receptor beta agonist diarylpropionitrile (DPN) does not mediate neuroprotection in a rat model of permanent focal ischemia. *Brain Research* 2007;1185(2):275-282

Agents: Diarylpropionitrile **Vehicle:** Saline; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; replacement therapy (ovariectomy); stress/adverse reaction: (see pg. 277) infection in shoulder at mp tip (2 animals); MRI; post op. care (Baytril, Rimadyl); ischemia (cerebral); animal info (female, Lister Hooded, 180-200g, MCAO); "this strain was more susceptible to surgical wound infection than other strains" (p. 279);

P7895: K. Chen, *et al.* Induction of leptin resistance through direct interaction of C-reactive protein with leptin. *Nature Medicine* 2006;12(4):425-432

Agents: Leptin, recomb. human; C-reactive protein, human **Vehicle:** Saline; **Route:** SC; **Species:** Mice; mice (transgenic); **Pump:** Not Stated; **Duration:** 6, 7 days;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by serum concentrations; dose-response (fig.5); peptides; MRI; multiple pumps per animal (2); animal info (wt or ob/ob, 8 wk old, human CRPtg.)

P7144: M. Miyauchi, *et al.* Chronic nicotine in hearts with healed ventricular myocardial infarction promotes atrial flutter that resembles typical human atrial flutter. *American Journal of Physiology Heart and Circulatory Physiology* 2005;288(6):H2878-H2886

Agents: Nicotine **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog (mongrel); **Pump:** 2ML4; **Duration:** 28 days;

ALZET Comments: Functionality of mp verified by nicotine plasma levels; MRI; multiple pumps per animal (2)

P7388: A. Arcella, *et al.* Pharmacological blockade of group II metabotropic glutamate receptors reduces the growth of glioma cells in vivo. *Neuro-Oncology* 2005;7(3):236-245

Agents: LY341495; Ethylglutamate, alpha-25 **Vehicle:** Saline; **Route:** SC; **Species:** Mice (nude); **Pump:** 1007D; 2004; **Duration:** 7, 28 days;

ALZET Comments: Controls received mp w/ vehicle; cancer (glioma); mGlu 2/3 receptor antagonist; pumps removed prior to MRI

P6992: D. Wolfe, *et al.* Safety and biodistribution studies of an HSV multigene vector following intracranial delivery to non-human primates. *Gene Therapy* 2004;11(23):1675-1684

Agents: Ganciclovir **Vehicle:** Not Stated; **Route:** SC; **Species:** Monkey (Rhesus); **Pump:** 2ML1; 2ML2; **Duration:** 4,5,34,35 days;

ALZET Comments: Pumps replaced after 2 weeks; no stress (see pg. 1677); cancer (glioblastoma); toxicology; MRI; multiple pumps per animal (2); gene therapy

P6759: M. Shoaib, *et al.* Imaging localised dynamic changes in the nucleus accumbens following nicotine withdrawal in rats. *Neuroimage* 2004;22(2):847-854

Agents: Nicotine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ saline; dependence; MRI

P5950: N. O. Schmidt, *et al.* Antiangiogenic therapy by local intracerebral microinfusion improves treatment efficiency and survival in an orthotopic human glioblastoma model. *Clinical Cancer Research* 2004;10(4):1255-1262

Agents: Endostatin, recomb. murine **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2004; **Duration:** 21 days;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by residual volume; comparison of SC injections vs. chronic ICV mp; no stress (see pg. 1261); cancer (glioma); ALZET brain infusion kit 1 used (per Dr. Carroll); MRI; "The direct infusion of therapeutic compounds into brain tumors can overcome some of the obstacles of drug delivery." p. 1255; BIK's removed prior to MRI; "no signs of intracranial bleeding due to the presence of the pumps or antiangiogenic treatment were observed..." (p. 1261); angiogenesis inhibitor; surgical glue used to affix cannula to the skull



- P6775:** U. Gawlick, *et al.* A conjugate of a tumor-targeting ligand and a T cell costimulatory antibody to treat brain tumors. *Bioconjugate Chemistry* 2004;15(5):1137-1145
Agents: Antibody, anti-CD28 Fab/Folate; gadolinium **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by MRI w/ gadolinium infusion; comparison of IV, SC, ICV injections vs. mp; cancer (brain, choroid plexus); brain tissue distribution; MRI; cyanoacrylate adhesive; "The strongest effect on tumor growth assessed of anti-CD28 fab/Folate." (p. 1143). Plastics One cannula used
- P6869:** B. L. Falcon, *et al.* Angiotensin II type 2 receptor gene transfer elicits cardioprotective effects in an angiotensin II infusion rat model of hypertension. *Physiological Genomics* 2004;19(3):255-261
Agents: Angiotensin II **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ saline; functionality of mp verified by blood pressure measurements; cardiovascular; peptides; MRI
- P6808:** D. Engel, *et al.* Cardiac myocyte apoptosis provokes adverse cardiac remodeling in transgenic mice with targeted TNF overexpression. *American Journal of Physiology Heart and Circulatory Physiology* 2004;287(3):H1303-H1311
Agents: IDN 1965 **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1002; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced at day 14; enzyme inhibitor (caspase); cardiovascular; MRI; 50% DMSO; MRI performed at day 2 and day 28
- P7139:** Q. G. de Lussanet, *et al.* Dynamic contrast-enhanced magnetic resonance imaging at 1.5 Tesla with gadopentetate dimeglumine to assess the angiostatic effects of anginex in mice. *European Journal of Cancer* 2004;40(8):1262-1268
Agents: Anginex **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 16 days;
ALZET Comments: Controls received mp w/ vehicle; comparison of TNP-470 IP injections vs. mp; cancer (melanoma); MRI; pumps removed for MRI
- R0222:** Y. S. Ng, *et al.* Therapeutic angiogenesis for cardiovascular disease. *Current Controlled Trials in Cardiovascular Medicine* 2001;2(6):278-285
Agents: Vascular endothelial growth factor **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Pig; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Cardiovascular; peptides; MRI; ALZET pumps mentioned on pg. 279
- P5802:** W.-R. Schäbitz, *et al.* Delayed neuroprotective effect of insulin-like growth factor I after experimental transient focal cerebral ischemia monitored with MRI. *Stroke* 2000;32(5):1226-1233
Agents: Insulin-like growth factor I **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Comparison of SC injections vs. ICV mp infusion; ischemia (cerebral); MRI study (Diffusion-Weighted MRI - DWI); flow moderator not replaced
- P4643:** D. E. Cummings, *et al.* Prostate-sparing effects in primates of the potent androgen 7 α -Methyl-19-Nortestosterone: A potential alternative testosterone for androgen replacement and male contraception. *Journal of Clinical Endocrinology and Metabolism* 1998;83(12):4212-4219
Agents: Nortestosterone, 7 α -methyl-19-; Testosterone acetate **Vehicle:** Cyclodextrin, B-; **Route:** SC; **Species:** Monkey; **Pump:** Not Stated; **Duration:** 20 weeks;
ALZET Comments: Functionality of mp verified by hormone serum levels; replacement therapy (castration); dose-response (p.4213); long-term study, pumps replaced weekly during 1st treatment, bi-weekly during 2nd period, & every 4 weeks during the last 2 periods; both steroids were dissolved in 45% solution of 2-hydroxypropyl-B-cyclodextrin; MRI
- P4342:** S. Kalyanasundaram, *et al.* A finite element model for predicting the distribution of drugs delivered intracranially to the brain. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 1997;273(R1810-R1821)
Agents: GdDTPA; GdDTPA-dextran **Vehicle:** Not Stated; **Route:** CSF/CNS; CSF/CNS (parenchyma); **Species:** Rabbit; **Pump:** 2002; **Duration:** 8 days;
ALZET Comments: Comparison of bolus injections vs. mp; brain tissue distribution of contrast agent Gd-DTPA was assessed by MRI



P6871: E. Brouillet, *et al.* Systemic or local administration of azide produces striatal lesions by an energy impairment-induced excitotoxic mechanism. *Experimental Neurology* 1994;129(2):175-182

Agents: Azide, sodium **Vehicle:** Water; phosphate buffer; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 1 month;
ALZET Comments: Controls received mp w/ normal saline; dose-response; comparison of intrastriatal injections vs. mp; enzyme inhibitor (cytochrome oxidase); MRI

P6883: M. F. Beal, *et al.* Neurochemical and Histologic Characterization of Striatal Excitotoxic Lesions Produced by the Mitochondrial Toxin 3-Nitropropionic Acid. *Journal of Neuroscience* 1993;13(10):4181-4192

Agents: Nitropropionic acid, 3- **Vehicle:** Water; NaOH; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 month; 5 days;

ALZET Comments: Controls received mp w/ normal saline; comparison of intrastriatal injections vs. mp; stress/adverse reaction: (see pg. 4182), agent caused half of animals to become acutely ill, controls had no adverse reactions; toxicology; MRI

P1389: T. A. Carpenter, *et al.* Magnetic resonance imaging of the delivery of a paramagnetic contrast agent by an osmotic pump. *Drug Design and Discovery* 1988;3(263-266

Agents: GdDTPA **Vehicle:** Water; **Route:** In vitro; **Species:** Not Stated; **Pump:** 2ML1; **Duration:** 220 hours;

ALZET Comments: GdDTPA is gadolinium diethylenetriamine pentaacetic acid; MRI