



Targeted Delivery of Agents Using ALZET® Osmotic Pumps

ALZET pumps allow researchers to understand and optimize the key determinants of drug action. These determinants are the level of drug exposure and its duration, and the spatial distribution of drug relative to the target tissue. By manipulating these variables, drug effects can be optimized early in preclinical development, allowing clinical studies to be conducted at lower cost and with better results. Accumulated literature offers numerous examples of targeted delivery in which ALZET pumps expose a specific, limited region to a compound. Through a catheter introduced into the arterial blood supply of an organ, or affixed within or adjacent to the target tissue, the pump provides continuous and controlled input of a compound. A variety of organs and tissues have become target sites for drug delivery using this method.

Targeted infusion offers significant advantages over systemic administration. Daemen *et al.* (*Trends Pharmacol Sci* 1988;9:138) assert that "for the clinician, drug delivery should ideally be direct to its target tissue. Its distribution should be confined to the target site (thus avoiding any systemic drug effects), where it should reach high concentration." This ideal has two key facets:

- achieving sufficiently high concentrations at the target site
- minimizing systemic concentrations

To demonstrate a drug's efficacy, it must reach the target tissue at a concentration sufficient to elicit a therapeutic effect. There are many obstacles that can make it difficult to achieve sufficient concentration at the target site, such as drug metabolism, drug excretion, and permeability barriers. Infusing drug to the target tissue can circumvent these barriers, and can improve the drug's efficacy as compared with systemic administration.

Even if the concentration at the target site is sufficient, the desired effect may or may not be recognized. If the drug is administered such that significant systemic concentrations are also produced, simultaneous or cascading drug effects in multiple tissues may result. These systemic effects may alter the effect from the target tissue by diminishing, antagonizing, or simply obscuring it. Additionally, unwanted systemic effects may be toxic to the target tissue or even lethal, thus preventing the desired effect from ever developing.

References in which the following organs or tissues were infused via ALZET pumps are included in this list, with the exception of brain infusion. (References on brain infusion can be obtained at www.alzet.com or by contacting ALZET Technical Support at 1-800-692-2990 or by email at alzet@direct.com.)



**Targeted Delivery of Agents
Using ALZET® Osmotic Pumps**

Arterial Wall
Articular Cavity
Bladder
Bone
Brain (Solid Tissue)
Brain (Ventricles)
Ear
Esophagus
Eye
Gallbladder
Intestine
Kidney+
Liver+
Lymph Node
Mammary Gland
Muscle
Myocardial
Nerve
Ovary
Pericardial Space
Prostate
Skin
Spleen
Stomach
Testis+
Trachea
Tumor
Uterus

+ Perfused directly and via arterial supply.

The technical notes following each reference detail the substance(s) infused, route of administration, animal model studied, infusion vehicle, model of pump used, duration of infusion, and notable technical achievements or results obtained. For a more complete discussion of the capabilities of solid tissue microperfusion, consult the following reference:

R0051 Urquhart, J., Fara, J., and Willis, K.L. Rate-controlled delivery systems in drug and hormone research. *Ann. Rev. Pharmacol. Toxicol.* 24, 199-236, 1984.

Note: This listing does not contain abstracts in this category, nor references from before the years indicated. To obtain abstracts or additional references, contact ALZET Technical Services at (800) 692-2990 or by email at alzet@direct.com.



**Recent References (2013-2018) on the Targeted Delivery of Agents
Using ALZET® Osmotic Pumps**

Q7861: S. Ruoss, *et al.* Inhibition of calpain delays early muscle atrophy after rotator cuff tendon release in sheep. *Physiol Rep* 2018;6(21):e13833

Agents: calpeptin **Vehicle:** DMSO; **Route:** intramuscular (infraspinatus); **Species:** Sheep; **Pump:** 2ML4; **Duration:** 6 weeks; **ALZET Comments:** Dose (0.75 mg/day); animal info (26.7+/-1.4 months, female, Swiss Alpine); pumps replaced at 2 weeks; calpeptin is a synthetic calpain inhibitor; enzyme inhibitor (calpain); tissue perfusion (m. infraspinatus); good methods (detailed pump implantation procedure on page 3.); Therapeutic indication (calpain inhibition prevented the early unloading adaptations, but not the subsequent initiation of rotator cuff disease); 75% DMSO used;

Q5909: L. Wang, *et al.* Sodium butyrate suppresses angiotensin II-induced hypertension by inhibition of renal (pro)renin receptor and intrarenal renin-angiotensin system. *J Hypertens* 2017;35(9):1899-1908

ALZET Comments: Angiotensin II; sodium butyrate; SC; Intrarenal (medulla); Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-300g); Multiple pumps per animal (2); replacement therapy (uniphrectomy); tissue perfusion (renal medulla); cardiovascular; antihypertensive; peptides; Bp measured using radio telemetry (DSI); Dose (Ang II 200 ng/kg/min; NaBu 1 ug/kg/min); good bp comparison curve (pg4);

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)

ALZET Comments: FeTMPyP; Tempol; CSF, artificial; CSF/CNS (intracisternal); Rat; 2001; 6 days; 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);

Q5894: S. Thammacharoen, *et al.* Effects of Hindbrain Infusion of an Estrogen Receptor Antagonist on Estrogenic Modulation of Eating Behavior. *Neurophysiology* 2017;49(1):72-77

ALZET Comments: ICI 182,780; DMSO; Saline; CSF/CNS (fourth ventricle); Rat; 1002; animal info (female, Wistar, 250-300g, OVX); 1% DMSO used; post op. care (enrofloxacin IV 2.5-5 mg/kg, ibuprofen PO 15 mg/kg); replacement therapy (estradiol infusion); tissue perfusion (fourth ventricle); Cannula placement verified via injection of Evans Blue dye; Used PlasticsOne cannula;

Q5104: Q. Y. Yi, *et al.* Paraventricular Nucleus Infusion of Epigallocatechin-3-O-Gallate Improves Renovascular Hypertension. *Cardiovasc Toxicol* 2016;16(3):276-85

ALZET Comments: gallate, Epigallocatechin-3-O; CSF, artificial; CSF/CNS (paraventricular nucleus); Rat; 1004; 4 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-275g); bilateral cannula used; post op. care (buprenorphine 0.01 mg/kg SC 12 hours post); tissue perfusion (paraventricular nucleus); tissue perfusion (paraventricular nucleus); tissue perfusion (paraventricular nucleus); Dose (20 ug/h); Brain coordinates "1.8 mm posterior, 0.4 mm lateral to the bregma and 7.9 mm ventral to the zero level" pg 277;

Q5097: K. L. Wu, *et al.* Impaired Nrf2 regulation of mitochondrial biogenesis in rostral ventrolateral medulla on hypertension induced by systemic inflammation. *Free Radic Biol Med* 2016;97(58-74)

ALZET Comments: Endotoxin, LPS; coenzyme Q10; tempole; Interleukin-1 receptor antagonist; butylhydroquinone, tert-; Saline; CSF, artificial; IP; ;CSF/CNS (cisterna magna); Rat; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 8 weeks old, 250-280g); ALZET brain infusion kit 2 used; post op. care (IM procaine Penicillin 1000 IU); tissue perfusion (cisterna magna); cardiovascular; bp measured using tail cuff; Dose (LPS 1.2 mg/kg/day; coenzyme Q10 3.25 ug/ul/hr; tempol 5 ug/ul/hr; IL-1Ra 0.5 ug/ul/h);

Q5091: X. Wang, *et al.* Affinity-controlled protein encapsulation into sub-30 nm telodendrimer nanocarriers by multivalent and synergistic interactions. *Biomaterials* 2016;101(258-71)

ALZET Comments: Telodendrimer nanoparticles, peptide-incorporated; CSF/CNS (Intratatumoral); Mice (nude); 7 days; Controls received mp w/ free peptide; animal info (female, athymic nude NCRU-Sp/Sp, 8 weeks old); cancer (glioblastoma



U87); tissue perfusion (intratumoral); pumps primed overnight at 37C; Dose (0.5 ug/h); Brain coordinates (0.5 mm anterior to bregma and 2.5 mm lateral of midline);.

Q5080: J. Urra, *et al.* In vivo blockade of acetylcholinesterase increases intraovarian acetylcholine and enhances follicular development and fertility in the rat. *Sci Rep* 2016;6(30129)

ALZET Comments: Huperzine A; Intraovarian (ovarian bursa); Rat; 2004; 4 weeks; Controls received mp w/ saline; animal info (female, Sprague Dawley, 250-300g, hemi-OVX); tissue perfusion (ovarian bursa); enzyme inhibitor (acetylcholine esterase);.

Q5212: T. Tamagawa, *et al.* Involvement of Microglial P2Y12 Signaling in Tongue Cancer Pain. *J Dent Res* 2016;95(10):1176-82

ALZET Comments: MRS2395; DMSO; PBS; CSF/CNS (cisterna magna); Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (male, Fischer, 100-200g); 25% DMSO used; cancer (tongue squamous cell carcinoma SCC-158, JCRB0231; JCRB); behavioral testing (head-withdrawal); tissue perfusion (cisterna magna); used PE tubing 0.8mm diameter; MRS2395 is an P2Y12R antagonist;.

Q4895: Y. A. Syed, *et al.* Antibody-mediated neutralization of myelin-associated EphrinB3 accelerates CNS remyelination. *Acta Neuropathol. (Berl)* 2016;131(281-298)

ALZET Comments: Fc-IgG; ephrineB3, pre-clustered; PBS; CSF/CNS (caudal cerebellar peduncle); Rats; mice; 11 days; 18 days; Controls received mp w/ Fc-IgG only; animal info (Rats - female, Sprague Dawley; mice - EphrinB3 KO); neurodegenerative (multiple sclerosis); tissue perfusion (caudal cerebellar peduncle); Cannula placement verified via infusion of Evan's Blue;.

Q4900: P. Q. H. Renjun Wang, MD; Rui Zhou, BSc; Zengxiang Dong, PhD, *et al.* Sympathoexcitation in Rats With Chronic Heart Failure

Depends on Homeobox D10 and MicroRNA-7b Inhibiting GABBR1 Translation in Paraventricular Nucleus. *Circ Heart Fail.* 2016;9(1-10)

ALZET Comments: AntagomiR-7b; RNA, small interfering GABBR1; angiotensin II; CSF/CNS (paraventricular nucleus); Rat; 1004; 1002; 4 weeks; 2 weeks; animal info (male, Wistar, 180-200g); pumps replaced after 4 weeks; bilateral cannula used; tissue perfusion (paraventricular nucleus); cardiovascular; peptides; bilateral infusion; Dose (AntagomiR-7b or Ad-siGABBR1 40 ng/h; antiotensin II 1 ng/kg/min);.

Q4862: Matthew McMillin, *et al.* Bile Acid Signaling Is Involved in the Neurological Decline in a Murine Model of Acute Liver Failure. *American Journal of Pathology* 2016;186(2):

ALZET Comments: Vivo-morpholino; CSF/CNS (frontal cortex); Mice; 3 days; Controls received mp w/ mismatched control morpholino; animal info (male, C57BL6, 25-30g); tissue perfusion (frontal cortex); tissue perfusion (frontal cortex);.

Q5395: T. H. Lin, *et al.* NF-kappaB decoy oligodeoxynucleotide mitigates wear particle-associated bone loss in the murine continuous infusion model. *Acta Biomater* 2016;41(273-81)

ALZET Comments: Ultra-high molecular weight polyethylene particles; oligodeoxynucleotide, decoy; oligodeoxynucleotide, scrambled; Endotoxin, LPS; Brain-derived neurotropic factor;; Saline; In Vitro (cell culture); Bone (Femur); Mice (nude); 2006; 4 weeks; Controls received mp w/ vehicle; animal info (Male athymic nude mice, 10-15 weeks old); stability verified by (in vitro experiment); dose-response (pg. 277); good methods (pg. 276); tissue perfusion (bone); Dose (15 mg/ml UHMWPE, 50uM decoy, 1 ug/ml LPS); Therapeutic indication (Bone loss, chronic inflammation);.

Q5390: H. B. Li, *et al.* TLR4/MyD88/NF-kappaB signaling and PPAR-gamma within the paraventricular nucleus are involved in the effects of telmisartan in hypertension. *Toxicol Appl Pharmacol* 2016;305(93-102)

ALZET Comments: Telmisartan; Losartan; GW9662; CSF, artificial; CSF/CNS (Hypothalamic paraventricular nucleus); Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (12-week-old male normotensive Wistar-Kyoto); functionality of mp verified by blood pressure; bilateral cannula used; dose-response (pg. 94); post op. care (buprenorphine 0.04 mg/kg, sc); tissue perfusion (hypothalamic paraventricular nucleus); cardiovascular; antihypertensive; Dose (10 ug/hr TEL, 20 ug/hr LOS, 100 ug/hr GW); Brain coordinates (1.8mm posterior to bregma, 0.4mm from midline, and 7.9mm ventral to dura);.



Q5382: D. B. Kurland, *et al.* The Sur1-Trpm4 channel regulates NOS2 transcription in TLR4-activated microglia. *J Neuroinflammation* 2016;13(1):130

ALZET Comments: Endotoxin, LPS; Saline, normal; CSF/CNS (striatum); Rat; 1007D; 7 days; Controls received mp w/ vehicle; animal info (Male Wistar rats aged 8-12 weeks); ALZET brain infusion kit 2 used; good methods (pg. 3); tissue perfusion (striatum); model to study TLR4 activation in vivo; nitrosative/oxidative stress and neuroinflammation; Brain coordinates; 1-mm burr hole was made over the right striatum [AP, +0.75 mm; ML, +1.7 mm relative to bregma]; Dose (5 ug/day);.

Q5367: F. Higuchi, *et al.* Hippocampal MicroRNA-124 Enhances Chronic Stress Resilience in Mice. *J Neurosci* 2016;36(27):7253-67

ALZET Comments: LMK-135, LY2090314; Water; CSF/CNS (hippocampus); Mice; 1002, 1004; 2 weeks, 4 weeks; animal info (BALB mice); behavioral testing (social interaction test, forced swim test, novelty-suppressed feeding test); tissue perfusion (hippocampus); brain tissue distribution; Bilateral infusion; Dose (LMK-235 (100 nM or 1 uM), LY2090314 (10 or 100 nM));.

Q6041: L. German-Castelan, *et al.* Intracellular Progesterone Receptor Mediates the Increase in Glioblastoma Growth Induced by Progesterone in the Rat Brain. *Arch Med Res* 2016;47(6):419-426

ALZET Comments: Oligodeoxynucleotide, antisense; Propylene glycol; CSF/CNS; Rat; 15 days; animal info (250-300g) ; tissue perfusion (brain tissue); Guide cannula used; Therapeutic indication (Astrocytomas, CNS tumor); Dose (0.5 ug/day);.

Q5347: D. A. Figge, *et al.* Dynamic DNA Methylation Regulates Levodopa-Induced Dyskinesia. *J Neurosci* 2016;36(24):6514-24

ALZET Comments: RG108; Cyclodextrin, hydroxypropyl-β-; CSF/CNS (dorsal striatum); Rat; 2004; 14 days; Controls received mp w/ vehicle; animal info (male Sprague-dawley, 60 – 90 days old, 180-200 g); functionality of mp verified by behavioral testing; 5% cyclodextrin used; Plastics One unilateral guide cannula used; post op. care (7 days of care, buprenorphine and wound care for pain management); behavioral testing (forepaw adjusting steps test); tissue perfusion (brain); delayed delivery “additional polyethylene tubing was added to provide a 14 d prime of vehicle before RG-108 administration” (pg. 6515); “rats were given a unilateral dopamine lesion to the left medial forebrain bundle” (pg. 6515); Brain coordinates: anteroposterior, 0 from bregma, -3mm lateral from midline, and -3.5 mm from the dura; Dose (100 uM);.

Q5311: L. Chen, *et al.* 20-HETE contributes to ischemia-induced angiogenesis. *Vascul Pharmacol* 2016;83(57-65

ALZET Comments: DDMS; 6,15-20-HEDGE; Intramuscular (hindlimb gracilis); Mice; 2002, 2004; 32 days; Controls received mp w/ vehicle; animal info (Balb/c mice, 12 wk old); functionality of mp verified by blood pressure and blood perfusion scans; dose-response (pg. 61); good methods (pg. 58); ischemia (peripheral); tissue perfusion (intramuscular); Polyethylene catheter tubing used (inner ID 0.8 mm); Dose (5 mg/kg/day);.

Q4673: M. Zamykal, *et al.* Inhibition of intracerebral glioblastoma growth by targeting the insulin-like growth factor 1 receptor involves different context-dependent mechanisms. *NEURO-ONCOLOGY* 2015;17(1076-1085

ALZET Comments: IMC-A12; Saline; CSF/CNS (intratumoral); Mice; 2004; 3 weeks; 4 weeks; Controls received mp w/ vehicle; animal info (Foxn1nu, 6-8 weeks old); cancer (glioblastoma); tissue perfusion (glioblastoma); IMC-A12 aka cixutumumab;.

Q4217: K. Yuyama, *et al.* A potential function for neuronal exosomes: Sequestering intracerebral amyloid-beta peptide. *FEBS Letters* 2015;589(84-88

ALZET Comments: Exosome; PBS; CSF/CNS (hippocampus); Mice; 14 days; Animal info (APP or C57BL6J, 13 months old); ALZET brain infusion kit used; neurodegenerative (Alzheimer's disease); tissue perfusion (hippocampus);.

Q4656: H. J. Yang, *et al.* Red peppers with moderate and severe pungency prevent the memory deficit and hepatic insulin resistance in diabetic rats with Alzheimer's disease. *Nutrition & Metabolism* 2015;12(U15-U26

ALZET Comments: Amyloid protein, beta (25-35); CSF/CNS (hippocampus); Rat; 14 days; Controls received mp w/ scrambled amyloid protein; animal info (male, Sprague Dawley, 192 +/-30g,); neurodegenerative (Alzheimer's disease); behavioral testing (locomotive activity, passive avoidance, Morris water maze); tissue perfusion (CA1 subregion of hippocampus); diabetes;.



Q5008: Yael Kusne, *et al.* Targeting aPKC disables oncogenic signaling by both the EGFR and the proinflammatory cytokine TNF α in glioblastoma. *Science Signaling* 2015;7(338):1-15

ALZET Comments: PZ09; CSF/CNS (lateral ventricle); mice; 7, 14 days; animal info (Six- to 8-week-old female NOD-SCID, TNF α -/-, and control mice); dose-response (pg. 2-5); tissue perfusion (brain; glioblastomas); PZ09 aka small-molecule, benzimidazole

adenosine triphosphate-competitive aPKC inhibitor; xenografts; Dose: 10 μ M PZ09.

Q4593: R. Stark, *et al.* Acyl Ghrelin Acts in the Brain to Control Liver Function and Peripheral Glucose Homeostasis in Male Mice. *ENDOCRINOLOGY* 2015;156(858-868)

ALZET Comments: Ghrelin, acyl; CSF, artificial; CSF/CNS (third ventricle); Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, C57BL6); ALZET brain infusion kit 3 used; tissue perfusion (third ventricle);.

Q4990: T. A. Paine, *et al.* Effects of chronic inhibition of GABA synthesis on attention and impulse control. *Pharmacol Biochem Behav* 2015;135(97-104)

ALZET Comments: Allylglycine, L-; CSF, artificial; CSF/CNS (prefrontal cortex); Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dalwey); bilateral cannula used; Multiple pumps per animal (2); behavioral testing (standard time reaction test; locomotor activity); tissue perfusion (prefrontal cortex); enzyme inhibitor (glutamic acid decarboxylase); Dose (3.5 μ g/0.5 μ l/h);.

Q5000: H. Liu, *et al.* The distinct role of NR2B subunit in the enhancement of visual plasticity in adulthood. *Mol Brain* 2015;8(49)

ALZET Comments: PPPA; TCN 201; Ro 25-6981; PBS; CSF/CNS (visual cortex); Mice; 1007D; 1002; 5 days; 2 weeks; Controls received mp w/ vehicle; animal info (C57BL6); tissue perfusion (visual cortex); cyanoacrylate adhesive; brain coordinates;.

Q4995: H. B. Li, *et al.* Central blockade of salusin beta attenuates hypertension and hypothalamic inflammation in spontaneously hypertensive rats. *Sci Rep* 2015;5(11162)

ALZET Comments: Immunoglobulin G, antisalusin b; CSF/CNS (paraventricular nucleus); Rat; 1004; 2 weeks; Controls received mp w/ vehicle and control antibody; animal info (male, Wistar Kyoto, SHR, 10 weeks old); bilateral cannula used; post op. care (buprenorphine SC); tissue perfusion (paraventricular nucleus); cardiovascular; Cannula placement verified via histological analysis; bilateral infusion; bp measured using tail cuff; Dose (50, 100, 150 ng/kg/day);.

Q4970: D. H. Kim, *et al.* Peptide fragment of thymosin beta4 increases hippocampal neurogenesis and facilitates spatial memory. *Neuroscience* 2015;310(51-62)

ALZET Comments: Ac-SDKP; PBS; CSF/CNS (third ventricle); Mice; 1007D; 7 days; animal info (male, C57BL6J), 25-28g, 8 weeks old); behavioral testing (Morris water maze); tissue perfusion (third ventricle); peptides; Cannula placement verified via histologic analysis; used Plastics one cannula; brain coordinates;.

Q3920: S. C. Hopp, *et al.* Differential Neuroprotective and Anti-Inflammatory Effects of L-Type Voltage Dependent Calcium Channel and Ryanodine Receptor Antagonists in the Substantia Nigra and Locus Coeruleus. *Journal of Neuroimmune Pharmacology* 2015;10(35-44)

ALZET Comments: Endotoxin, LPS; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 2004; 28 days; Animal info (male, F-344, 3 months old); behavioral testing (rotarod; open field test; forced swim test); tissue perfusion (fourth ventricle); immunology;.

Q3780: R. Hiramatsu, *et al.* Tetrakis(p-Carboranylthio-Tetrafluorophenyl)Chlorin (TPFC): Application for Photodynamic Therapy and Boron Neutron Capture Therapy. *Journal of Pharmaceutical Sciences* 2015;104(962-970)

ALZET Comments: Tetrakis(pcarboranylthiotetrafluorophenyl) Chlorin; CSF/CNS (intratumoral); Rat; 2001D; Animal info (male, 200-250 g, F344 Fischer); ALZET brain infusion kit 2 used; TPFC, also known as Tetrakis(p-Carboranylthio-Tetrafluorophenyl)Chlorin, is a carboranyl-containing chlorin of high boron content; cancer (glioma); tissue perfusion; convection-enhanced delivery.



Q4425: S. Garofalo, *et al.* Enriched environment reduces glioma growth through immune and non-immune mechanisms in mice. *Nature Communications* 2015;6(U26-U38)

ALZET Comments: Interleukin-15; brain-derived neurotrophic factor; PBS; CSF/CNS (striatum); Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, C57BL6, 3 weeks or 2 months old); ALZET brain infusion kit 3 used; cancer (glioma, U87MG human); tissue perfusion (right striatum); immunology; pumps primed in 37C saline overnight;

Q4405: J. M. do Carmo, *et al.* Role of hindbrain melanocortin-4 receptor activity in controlling cardiovascular and metabolic functions in spontaneously hypertensive rats. *JOURNAL OF HYPERTENSION* 2015;33(1201-1206)

ALZET Comments: SHU-9119; CSF/CNS (fourth ventricle); Rat; 2002; 10 days; Animal info (male, Spontaneously hypertensive or Wistar-Kyoto, 275-325g, 15-17 weeks old); behavioral testing (food intake); tissue perfusion (fourth ventricle); cardiovascular; Cannula placement verified via Evan's Blue dye; bp measured using radiotelemetry (DSI);

Q3853: B. N. Desai, *et al.* Leptin in the hindbrain facilitates phosphorylation of STAT3 in the hypothalamus. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2015;308(E351-E361)

ALZET Comments: Leptin; CSF/CNS (third ventricle; fourth ventricle); Rat; 2002; 6 days; Controls received mp w/ saline; animal info (male, Sprague Dawley, 275-300g); Multiple pumps per animal (2); tissue perfusion (third ventricle; fourth ventricle); bilateral infusion; one cannula to third ventricle second cannula to fourth ventricle; used plastics one cannula;

Q5135: P. Cheng, *et al.* Protein phosphatase 2A (PP2A) activation promotes axonal growth and recovery in the CNS. *J Neurol Sci* 2015;359(1-2):48-56

ALZET Comments: Sphingosine, D-erythro; saline; SC; Rat; 2002; 2 weeks; Controls received mp w/ vehicle; sham operation; animal info: adult Sprague–Dawley (SD) male rats, 240 - 260 g; spinal cord injury; tissue perfusion (spinal cord); D-erythro-sphingosine aka DES; Dose: DES (200 µl 1 µg/ml solution).

Q4347: N. Carrier, *et al.* The Anxiolytic and Antidepressant-like Effects of Testosterone and Estrogen in Gonadectomized Male Rats. *BIOLOGICAL PSYCHIATRY* 2015;78(259-269)

ALZET Comments: Fadrozole; Saline, sterile; CSF/CNS (dentate gyrus); Rat; 2004; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-270g, adult, orchidectomized); bilateral cannula used; behavioral testing (sucrose preference test, open field test); tissue perfusion (dentate gyrus); Cannula placement verified via a posteriori by sectioning on cryostat; bilateral infusion; coordinates; pumps primed for 48 hours in 37C sterile saline; used Plastics One cannula;

Q5123: R. F. Barth, *et al.* Evaluation of TK1 targeting carboranyl thymidine analogs as potential delivery agents for neutron capture therapy of brain tumors. *Appl Radiat Isot* 2015;106(251-5)

ALZET Comments: N5-2OH; DMSO; CSF/CNS (intracerebral); IV; Rat; 2001D; 24 hr; Controls received mp w/ vehicle, untreated controls; 35% of DMSO; cancer (brain tumor; F98 glioma model); tissue perfusion (brain tissue); brain tissue distribution; Animals were irradiated for 5 min at the MITR-II reactor; "intracerebral. administration of BPA did not increase the tumor boron uptake compared to that obtained following i.v. administration" (pg. 252); Dose: 500 ug.

Q4320: E. Barbier, *et al.* DNA Methylation in the Medial Prefrontal Cortex Regulates Alcohol-Induced Behavior and Plasticity. *JOURNAL OF NEUROSCIENCE* 2015;35(6153-6164)

ALZET Comments: RG108; Cyclodextrin, 2-hydroxypropyl-b-; CSF/CNS; CSF/CNS (medial prefrontal cortex); Rat; 2002; 2004; 1 week; Controls received mp w/ vehicle; animal info (male, Wistar, 200-225g); 5% cyclodextrin used; behavioral testing (two bottle free choice; alcohol self-administration); tissue perfusion (medial prefrontal cortex); dependence;

Q3794: L. Adzovic, *et al.* Insulin improves memory and reduces chronic neuroinflammation in the hippocampus of young but not aged brains. *Journal of Neuroinflammation* 2015;12(U1-U10)

ALZET Comments: Insulin, recombinant cat; endotoxin, LPS; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, F-344, 3 months old, 21 months old); bilateral cannula used; behavioral testing (morris water maze); tissue perfusion (fourth ventricle); bilateral infusion; used tygon tubing to attach cannula to pump;



Q4233: Y. B. Zhou, *et al.* Intermedin in Paraventricular Nucleus Attenuates Sympathetic Activity and Blood Pressure via Nitric Oxide in Hypertensive Rats. *Hypertension* 2014;63(330-+)

ALZET Comments: Intermedin; AM22-52; CSF, artificial; CSF/CNS (paraventricular nucleus); Rat; 1004; 15 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 160-180g); ALZET brain infusion kit used; tissue perfusion (paraventricular nucleus); antihypertensive; cardiovascular; Cannula placement verified via 2% Evans Blue dye injection; Intermedin aka IMD; AM22-52 is an adrenomedullin receptor antagonist; bp measured using tail cuff;.

Q4225: F. Zhang, *et al.* Apelin-13 and APJ in paraventricular nucleus contribute to hypertension via sympathetic activation and vasopressin release in spontaneously hypertensive rats. *ACTA PHYSIOLOGICA* 2014;212(17-27)

ALZET Comments: Apelin-13; CSF/CNS (paraventricular nucleus); Rat; 1002; 15 days; Controls received mp w/ saline; animal info (male, Wistar Kyoto, 13 weeks old); tissue perfusion (paraventricular nucleus); cardiovascular; "Osmotic minipumps were used for continuously delivering chemicals at controlled rate for several weeks without the need for external connections, frequent handling or repeated dosing" pg 19; bp measured using tail cuff; hypertension;.

Q4216: K. Yuyama, *et al.* Decreased Amyloid-beta Pathologies by Intracerebral Loading of Glycosphingolipid-enriched Exosomes in Alzheimer Model Mice. *Journal of Biological Chemistry* 2014;289(24488-24498)

ALZET Comments: Exosome solution, glycosphingolipid-enriched; PBS; CSF/CNS (hippocampus); Mice (transgenic); 1002; 14 days; Controls received mp w/ vehicle; animal info (APP, 4 months old); ALZET brain infusion kit 3 used; neurodegenerative (Alzheimers); tissue perfusion (hippocampus);.

Q4184: Y. W. Wu, *et al.* Central adiponectin administration reveals new regulatory mechanisms of bone metabolism in mice. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2014;306(E1418-E1430)

ALZET Comments: Adiponectin, globular; adiponectin, full-length; CSF, artificial; CSF/CNS (third ventricle); Mice; 28 days; Controls received mp w/ vehicle; animal info (male, APN-KO or WT, 20-25g, 4-6 weeks old); ALZET brain infusion kit 2 used; tissue perfusion (third ventricle); cyanoacrylate adhesive; Cannula placement verified via micrograph imaging; used tygon tubing to attach BIK cannula to pump;.

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-+)

ALZET Comments: Tempol; coenzyme Q10; CSF, artificial; CSF/CNS (cisterna magna); Rat; 1007D; 2 weeks; 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;.

Q3696: M. Wosiski-Kuhn, *et al.* Glucocorticoid receptor activation impairs hippocampal plasticity by suppressing BDNF expression in obese mice. *Psychoneuroendocrinology* 2014;42(165-177)

ALZET Comments: Corticosterone; Cyclodextrin, 2-hydroxypropyl-b-; CSF/CNS (hippocampus); Mice; 2 weeks; Controls received mp w/ vehicle and aCSF; animal info (male, C57BL6J or db/db, 5 weeks old); functionality of mp verified by hippocampal corticosterone levels; Multiple pumps per animal (2); behavioral testing (y-maze apparatus); tissue perfusion (bilateral hippocampi); immunology; Cannula placement verified via histology; used Plastics One bilateral cannula; bilateral infusion;.

Q4173: Y. K. Wang, *et al.* Overexpression of angiotensin-converting enzyme 2 attenuates tonically active glutamatergic input to the rostral ventrolateral medulla in hypertensive rats. *American Journal of Physiology-Heart and Circulatory Physiology* 2014;307(H182-H190)

ALZET Comments: A779; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 1007D; 1 week; Controls received mp w/ vehicle; animal info (male, SHR and WKY); tissue perfusion (fourth ventricle);.

Q4141: Y. Tona, *et al.* Therapeutic potential of a gamma-secretase inhibitor for hearing restoration in a guinea pig model with noise-induced hearing loss. *BMC NEUROSCIENCE* 2014;15(U1-U8)

ALZET Comments: MDL28170; DMSO; PBS; Ear (cochlea); Guinea pig; 1002; 14 days; Controls received mp w/ vehicle; animal info (Hartley strain, 350-400g); 0.3% DMSO used; tissue perfusion (cochlea); used Teflon tube with inner diameter of 180 um to cannulate cochlea; MDL28170 is a gamma-secretase inhibitor;.



Q4135: E. Tavares, *et al.* Immunoneutralization of Endogenous Aminoprocaltinin Attenuates Sepsis-Induced Acute Lung Injury and Mortality in Rats. *American Journal of Pathology* 2014;184(3069-3083

ALZET Comments: Antibody, anti-aminoprocaltinin; Saline; IP; Rat; 2001D; 18 hours; Controls received mp w/ control antibody; animal info (male, Wistar, 280-300g); tissue perfusion (peritoneum); immunology; peptides; Catheter used to cannulate peritoneum;

Q4128: M. S. Tan, *et al.* Amyloid-beta induces NLRP1-dependent neuronal pyroptosis in models of Alzheimer's disease. *Cell Death & Disease* 2014;5(U228-U239

ALZET Comments: RNA, small interfering NLRP1; RNA, small interfering, NLRP3; RNA, small interfering caspase-1; CSF, artificial; water, RNase-free; CSF/CNS (dorsal third ventricle); Mice (transgenic); 8 weeks; Controls received mp w/ vehicle or control RNA; animal info (male, APP/PS1); functionality of mp verified by knockdown of targeted gene; ALZET brain infusion kit 3 used; neurodegenerative (Alzheimer's disease); no stress "This dose of NLRP1 siRNA, caspase-1 siRNA or NLRP3 siRNA infusion was well tolerated, and no signs of neurotoxicity including hind-limb paralysis, vocalization, food intake, or neuroanatomical damage were observed in preliminary study." (see pg. 10); behavioral testing (morris water maze); tissue perfusion (dorsal third ventricle); "Our study using this approach of pump-mediated siRNA infusion is efficient in downregulation of NLRP1 mRNA (by about 60%) and protein (by about 50%) levels in APP/PS1 brain. And the treatment with control siRNA did not alter cerebral NLRP1 mRNA and protein levels compared with No siRNA-treated APP/PS1 mice, excluding an effect of pump-mediated infusion on NLRP1 expression levels." pg 8;

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

ALZET Comments: Tempol; angiotensin II; CSF, artificial; saline, sterile; CSF/CNS (paraventricular nuclei); Rat; 1004; 4 weeks; 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;

Q4743: K. Shinohara, *et al.* Post-acquisition hippocampal NMDA receptor blockade sustains retention of spatial reference memory in Morris water maze. *BEHAVIOURAL BRAIN RESEARCH* 2014;259(:):261-267

ALZET Comments: AP5, D-; CSF, artificial; CSF/CNS (hippocampus); Rat; 1007D; 7 days; 14 days; Animal info (male, albino Wistar); pumps replaced every 7 days; Plastics One bilateral cannula used; Multiple pumps per animal (2); behavioral testing (morris water maze, probe test); tissue perfusion (hippocampus); Cannula placement verified via histological analysis; pumps primed for 24 hours in 37C saline; bilateral infusion;

Q3627: A. Sehgal, *et al.* Tissue-specific gene silencing monitored in circulating RNA. *RNA-A PUBLICATION OF THE RNA SOCIETY* 2014;20(2):143-149

ALZET Comments: RNA, small interfering; PBS; CSF/CNS (striatum); Rat; 7 days; Animal info (male, Sprague Dawley); neurodegenerative (Parkinson's disease); tissue perfusion (striatum); gene therapy; used Plastics One 30g cannula; primed overnight in 37C saline;

Q3351: M. G. Mohammad, *et al.* Immune cell trafficking from the brain maintains CNS immune tolerance. *Journal of Clinical Investigation* 2014;124(3):1228-1241

ALZET Comments: Fingolimod; DMSO; CSF/CNS (forebrain; hippocampus); SC (cervical lymph nodes); Mice (transgenic); 8 days; 4 weeks; Controls received mp w/ vehicle; animal info (female, C57BL6, 6-12 weeks old; 2D2 transgenic); ALZET brain infusion kit 3 used; 50% DMSO used; neurodegenerative (multiple sclerosis); tissue perfusion (forebrain, hippocampus, cervical lymph nodes); immunology; Cannula placement verified via Nissl staining;

Q3986: J. Malmevik, *et al.* Selective transfection of microglia in the brain using an antibody-based non-viral vector. *Brain Research* 2014;1586(12-22



ALZET Comments: Scavenger receptor class B, type I; CSF/CNS (hippocampus); Rat; 1004; 14 days; Animal info (male, Sprague Dawley, 250-350g); tissue perfusion (CA3 area of hippocampus); immunology; brain tissue distribution; Scavenger receptor class B, type I akd SR-BI;

Q3556: J. H. Ma, *et al.* Chronic brain inflammation causes a reduction in GluN2A and GluN2B subunits of NMDA receptors and an increase in the phosphorylation of mitogen-activated protein kinases in the hippocampus. *MOLECULAR BRAIN* 2014;7(U1-U10)

ALZET Comments: Endotoxin, LPS; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 2004; 28 days; Controls received mp w/ vehicle; animal info (male, Fischer-344); behavioral testing (morris water maze); tissue perfusion (fourth ventricle); immunology; LPS from E.coli, serotype 055:B5;

Q3963: J. Lee, *et al.* Intrauterine Coadministration of ERK1/2 Inhibitor U0126 Inhibits Interferon TAU Action in the Endometrium and Restores Luteolytic PGF(2alpha) Pulses in Sheep. *Biology of Reproduction* 2014;91(U177-U185)

ALZET Comments: U0126; serum protein, ovine; interferon tau, recombinant ovine; DMSO; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 6 days; Controls received mp w/ vehicle; animal info (female, Suffolk Ovis aries); 3% DMSO used; tissue perfusion (uterine horn); cyanoacrylate adhesive; used cyanoacrylate glue to anchor pump; interferon tau aka IFNT;

Q3956: T. A. Larson, *et al.* Reactive Neurogenesis in Response to Naturally Occurring Apoptosis in an Adult Brain. *Journal of Neuroscience* 2014;34(13066-13076)

ALZET Comments: Z-VAD-FMK; Z-DEVD-FMK; Z-LEHD-FMK; DMSO; CSF/CNS (HVC); Bird (sparrow); 1007D; 5 days; Controls received mp w/ vehicle; animal info (male, Gambel's white-crowned sparrows, adult); 1% DMSO used; behavioral testing (song behavior); tissue perfusion (control nucleus HVC); Cannula placement verified via histologic analysis; "We placed osmotic pumps into sealed microcentrifuge tubes filled with saline and mounted the tubes into custom-made "backpacks" that allowed the birds to fly freely." pg 13067; enzyme inhibitor (caspase-3, caspase-9, pan-caspase); bilateral infusion; used dental cement;

Q5009: M. D. Kritzer, *et al.* The scaffold protein muscle A-kinase anchoring protein beta orchestrates cardiac myocyte hypertrophic signaling required for the development of heart failure. *Circ Heart Fail* 2014;7(4):663-72

ALZET Comments: Isoproterenol; mice; 2 weeks; animal info (C57BL/76 mice; 8-week-old mAKAPfl/fl); ischemia (cardiac); behavioral testing (physiological hypertrophy induced with 5-wk swimming regimen, Hargreaves test); tissue perfusion (heart); cardiovascular; Iso aka Isoproterenol; Dose: 60 mg/kg/day.

Q4727: B. Koneru, *et al.* Mineralocorticoid receptor in the NTS stimulates saline intake during fourth ventricular infusions of aldosterone. *AMERICAN JOURNAL OF PHYSIOLOGY-REGULATORY INTEGRATIVE AND COMPARATIVE PHYSIOLOGY* 2014;306(1):R61-R66

ALZET Comments: Aldosterone; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 2004; 28 days; Animal info (Wistar-Kyoto, 275g); tissue perfusion (fourth ventricle); cardiovascular;

Q3528: Y. M. Kang, *et al.* Chronic infusion of enalaprilat into hypothalamic paraventricular nucleus attenuates angiotensin II-induced hypertension and cardiac hypertrophy by restoring neurotransmitters and cytokines. *TOXICOLOGY AND APPLIED PHARMACOLOGY* 2014;274(3):436-444

ALZET Comments: Angiotensin II; enalaprilat; Saline; CSF, artificial; SC; CSF/CNS (paraventricular nucleus); Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, adult, 275-300g); functionality of mp verified by increased bp; post op. care (buprenorphine); tissue perfusion (bilateral paraventricular nucleus); cardiovascular; peptides; antihypertensive; bp measured using tail-cuff; pumps primed in 37C saline; used wound clips; enalaprilat is an ACE inhibitor; Plastics One bilateral PVN cannulae; bilateral infusion.

Q3521: T. Jiang, *et al.* Triggering receptor expressed on myeloid cells 2 knockdown exacerbates aging-related neuroinflammation and cognitive deficiency in senescence-accelerated mouse prone 8 mice. *NEUROBIOLOGY OF AGING* 2014;35(1243-1251)

ALZET Comments: RNA, small interfering TREM2; CSF, artificial; CSF/CNS (dorsal third ventricle); Mice; 1004; 4 weeks; Controls received mp w/ vehicle or control siRNA; animal info (SAMP8, 6 months old); functionality of mp verified by



decrease TREM2 protein levels pg. 1246; ALZET brain infusion kit used; neurodegenerative (Alzheimers); no stress (see pg. 1244); behavioral testing (Morris water maze); tissue perfusion (third ventricle); immunology;

Q5047: K. L. Jackson, *et al.* Actions of rilmenidine on neurogenic hypertension in BPH/2J genetically hypertensive mice. *J Hypertens* 2014;32(3):575-86

ALZET Comments: rilmenidine; Ringer's solution; CSF/CNS (ventricles); mice; 1002; 1 week; Controls received mp w/ ringer's solution vehicle; animal info (BPH/2J and BPN/3J mice); functionality of mp verified by behavioral tests; dose-response (pg 577-582, description and graphical representation); behavioral testing (pg 577; mice were exposed to aversive behavioral stimuli; restraint stress and dirty cage-switch tests conducted); tissue perfusion (brain tissue); antihypertensive; antihypertensive; Dose: 15ug/hr of rilmenidine.

Q3510: M. Iijima, *et al.* Antidepressant and anxiolytic profiles of newly synthesized arginine vasopressin V(1B) receptor antagonists: TASP0233278 and TASP0390325. *British Journal of Pharmacology* 2014;171(3511-3525

ALZET Comments: Allylglycine, 1-; CSF/CNS (hypothalamus); Rat; Animal info (male, Sprague Dawley, 211-246g); behavioral testing (forced swimming test, elevated plus maze, locomotor activity); tissue perfusion (dorsomedial hypothalamus); I-AG is a GAD inhibitor;

Q3338: W. H. Gmeiner, *et al.* Selective anti-tumor activity of the novel fluoropyrimidine polymer F10 towards G48a orthotopic GBM tumors. *Journal of Neuro-oncology* 2014;116(3):447-454

ALZET Comments: F10; PBS; CSF/CNS (thalamus); Mice (nude); 1007D; 7 days; Controls received mp w/ vehicle; animal info (nu/nu, 7 weeks old); ALZET brain infusion kit 3 used; cancer (human glioblastoma G48a); dose-response (pg.451-452, fig.3b and fig.4); no stress (see pg. 451); tissue perfusion (posterior thalamus); immunology; "F10 does not penetrate the BBB in healthy mice (data not shown), thus intra-cranial (i.c.) administration of F10 results in high local concentrations that may be therapeutically beneficial. Dose-finding studies in nude mice demonstrate that F10 administered i.c. using an Alzet osmotic mini-pump at doses up to 200 mg/kg administered over 7 days are well-tolerated and do not cause damage to normal brain (Fig. 2b)." pg 451; Pumps primed in 37C saline overnight; F10 is a novel antitumor agent;

R0327: M. Favero, *et al.* The Timing of Activity Is a Regulatory Signal During Development of Neural Connections. *Journal of Molecular Neuroscience* 2014;53(324-329

ALZET Comments: Tetrodotoxin; CSF/CNS (sciatic nerve); Rat; 7-10 days; Animal info (AO Rat); nerve injury; functionality of mp verified by establishment of a chronic conduction block; tissue perfusion (sciatic nerve);

Q3337: J. R. Erion, *et al.* Obesity Elicits Interleukin 1-Mediated Deficits in Hippocampal Synaptic Plasticity. *Journal of Neuroscience* 2014;34(7):2618-2631

ALZET Comments: IL-1 receptor antagonist; CSF, artificial; CSF/CNS (hippocampus); Mice; 2 weeks; Animal info (male, db/db C57BL6J); functionality of mp verified by ELISA of hippocampal IL1ra; behavioral testing (spatial recognition memory testing, novel-object preference, treadmill running); tissue perfusion (hippocampus); immunology; diabetes; Cannula placement verified via histology; Used Plastics One cannula.

Q3212: S. Eberstaal, *et al.* Intratumoral COX-2 inhibition enhances GM-CSF immunotherapy against established mouse GL261 brain tumors. *International Journal of Cancer* 2014;134(11):2748-2753

ALZET Comments: Parecoxib; valdecoxib; IP; CSF/CNS (intratumoral); Mice; 1004; 7 days; 34 days; Animal info (C57BL/6, female, 8-10 wks old); cancer; tissue perfusion (intratumoral).

Q3185: J. J. Donegan, *et al.* A Novel Role for Brain Interleukin-6: Facilitation of Cognitive Flexibility in Rat Orbitofrontal Cortex. *Journal of Neuroscience* 2014;34(3):953-962

ALZET Comments: Antibody, anti-IL-6; Saline; CSF/CNS (orbitofrontal cortex); Rat; 1004; Controls received mp w/ goat IgG; animal info (male, Sprague Dawley, adult, 220-240g); behavioral testing (learning); tissue perfusion (orbitofrontal cortex); immunology; Cannula placement verified via histology; Used dual-injection, osmotic pump compatible cannulae from Plastics One.



Q3336: J. W. Cordeira, *et al.* Hypothalamic Dysfunction of the Thrombospondin Receptor alpha2beta-1 Underlies the Overeating and Obesity Triggered by Brain-Derived Neurotrophic Factor Deficiency. *Journal of Neuroscience* 2014;34(2):554-565

ALZET Comments: Gabapentin; Saline; CSF/CNS (ventromedial hypothalamus); Mice; 1004; 10 days; Controls received mp w/ vehicle; animal info (male, BDNF 2L/2Lck-Cre, 8-10 weeks old); behavioral testing (feeding, locomotor activity); tissue perfusion (ventromedial hypothalamus); Cannula placement verified via post hoc histological analysis ;.

Q3815: D. N. Bochner, *et al.* Blocking PirB up-regulates spines and functional synapses to unlock visual cortical plasticity and facilitate recovery from amblyopia. *Science Translational Medicine* 2014;6(U13-U22)

ALZET Comments: Paired immunoglobulin-like receptor B, soluble; BSA; PBS; CSF/CNS (primary visual cortex); Mice; 1002; 11 days; Controls received mp w/ vehicle; animal info (PirB -/-, P21); functionality of mp verified by staining for sPirB; tissue perfusion (primary visual cortex);.

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)

ALZET Comments: Diruthenium-ibuprofen; Ethanol; CSF, artificial; CSF/CNS (intratumoral); Rat; 2002; 14 days; 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 Rulbp;.

Q3414: I. Bardou, *et al.* Age and duration of inflammatory environment differentially affect the neuroimmune response and catecholaminergic neurons in the midbrain and brainstem. *NEUROBIOLOGY OF AGING* 2014;35(5):1065-1073

ALZET Comments: Endotoxin, LPS; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 2006; 21 days; 56 days; Controls received mp w/ vehicle; animal info (male, F-344 rats, 3 months or 9 months or 23 months old); post op. care (lidocaine 1% on wound; 2ML isotonic saline SC injection; 2% tylenol in drinking water 3 days after surgery); tissue perfusion (fourth ventricle); long-term study; immunology; LPS aka lipopolysaccharide;.

Q3410: E. Avolio, *et al.* ANTIHYPERTENSIVE AND NEUROPROTECTIVE EFFECTS OF CATESTATIN IN SPONTANEOUSLY HYPERTENSIVE RATS: INTERACTION WITH GABAERGIC TRANSMISSION IN AMYGDALA AND BRAINSTEM. *Neuroscience* 2014;270(48-57)

ALZET Comments: Catestatin; muscimol; Saline; PBS; CSF/CNS (amygdala, central nucleus); Rat; 2004; 15 days; Controls received mp w/ vehicle; animal info (male, Spontaneously Hypertensive Rat, 3, 6, or 9 months old); ALZET brain infusion kit 2 used; tissue perfusion (central nucleus of amygdala); cardiovascular; antihypertensive; peptides; Cannula placement verified via histological analysis and methylene blue injection; Catestatin aka CST; muscimol aka MUS; used acrylic dental cement; bp measured using radiotelemetry; CST is a catecholamine release inhibitor; muscimol is a GABAa receptor agonist;.

Q3180: N. Asavapanumas, *et al.* Experimental mouse model of optic neuritis with inflammatory demyelination produced by passive transfer of neuromyelitis optica-immunoglobulin G. *Journal of Neuroinflammation* 2014;11(1):U1-U11

ALZET Comments: Antibody, rAb-53; complement, human; CSF/CNS (optic chiasm); Mice; 1003D; 3 days; Controls received mp w/ non-NMO control IgG and complement; animal info (AQP4+/+ and AQP4-/-, 8-10 weeks old); tissue perfusion (optic chiasm); immunology; Cannula placement verified via Evan's blue dye; rAb-53 aka NMO-IgG;.

Q3405: I. Armando, *et al.* Dopamine D3 receptor inhibits the ubiquitin-specific peptidase 48 to promote NHE3 degradation. *FASEB Journal* 2014;28(1422-1434)

ALZET Comments: GR103691; RNA, small interfering; Transfection reagent (TransIT); SC; kidney (subcapsular space); Mice; 1007D; 4 days; 7 days; Controls received mp w/ vehicle or nonsilencing "mock siRNA"; animal info (male, C57BL6J, adult); tissue perfusion (subcapsular space; kidney); gene therapy; antihypertensive; GR103691 is a D3R antagonist; used PE tubing



#0007701; pump sutured to abdominal wall; surgical glue applied at puncture site to hold catheter tubing in place and to prevent leakage;.

Q3795: Y. Aghazadeh, *et al.* Induction of Androgen Formation in the Male by a TAT-VDAC1 Fusion Peptide Blocking 14-3-3epsilon Protein Adaptor and Mitochondrial VDAC1 Interactions. *MOLECULAR THERAPY* 2014;22(1779-1791
ALZET Comments: TVG167; TVS167; Water; IP; intratesticular; Rat; 24 hours; Controls received mp w/ vehicle; animal info (male, Sprague Dawley); tissue perfusion (testis); peptide; TVS167 and TVG167; pump infused at 1.0 ul/hr;.

Q3369: Q. Wu, *et al.* NR2B subunit of the NMDA glutamate receptor regulates appetite in the parabrachial nucleus. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2013;110(36):14765-14770
ALZET Comments: Lithium chloride; RO25-6981; bretazenil; Saline; CSF/CNS (fourth ventricle; parabrachial nucleus); Mice; 1002; 14 days; Controls received mp w/ vehicle or sham surgery; animal info (male, Agrp DTR/+ or WT); bilateral cannula used; dose-response (pg.14766, fig.3; pg.14769, fig.6); behavioral testing (food intake); tissue perfusion (fourth ventricle; parabrachial nucleus); Cannula placement verified; RO25-6981 is a NR2B antagonist; bilateral infusion;.

Q2471: V. M. Villar, *et al.* Sorting Nexin 1 Loss Results in D(5) Dopamine Receptor Dysfunction in Human Renal Proximal Tubule Cells and Hypertension in Mice. *Journal of Biological Chemistry* 2013;288(1):152-163
ALZET Comments: RNA, small interfering; Kidney; Mice; 7 days; Control animals received mp w/ vehicle or non-silencing mock siRNA; animal info (C57BL/6, BALB/c, nephrectomized, adult, male); Snx-1 specific siRNA; infusion rate of 0.5 ul/hr; tissue perfusion (kidney); PE catheter used.

Q2710: K. M. Talasila, *et al.* EGFR wild-type amplification and activation promote invasion and development of glioblastoma independent of angiogenesis. *Acta Neuropathologica* 2013;125(5):683-698
ALZET Comments: Cetuximab; CSF/CNS (intratumoral); Rat (nude); 2ML4; 4 weeks; Control animals received mp w/ PBS; animal info (rnu/rnu Rowett); ALZET brain infusion kit 2 used; convection enhanced delivery (CED); tissue perfusion (intratumoral).

Q3353: K. Ohira, *et al.* Fluoxetine-Induced Cortical Adult Neurogenesis. *Neuropsychopharmacology* 2013;38(6):909-920
ALZET Comments: Ara-C; PBS; CSF/CNS (frontal lobe); Mice; 1004; 4 weeks; Controls received mp w/ vehicle; animal info (male, 3 months old, C57BL/6J); ALZET brain infusion kit 3 used; ischemia (cerebral); Multiple pumps per animal (two 1004 pumps, two Brain infusion kits); tissue perfusion (frontal lobe); brain tissue distribution;.

Q3248: Y. Morishima, *et al.* Critical Period of Experience-Driven Axon Retraction in the Pharmacologically Inhibited Visual Cortex. *Cerebral Cortex* 2013;23(10):2423-2428
ALZET Comments: Muscimol; Ringer's solution; CSF/CNS (primary visual cortex); Cat (kitten); 2001; 2002; 7 days; 8 days; Animal info (3 age groups: early phase P22-26, late phase P40-60, and adults >P500); post op. care (xylocane pump spray; entofloxacin 5 mg/kg); tissue perfusion (primary visual cortex);.

Q3245: F. Montarolo, *et al.* Early Enriched Environment Exposure Protects Spatial Memory and Accelerates Amyloid Plaque Formation in APP(Swe)/PS1(L166P) Mice. *PLoS One* 2013;8(7):U653-U666
ALZET Comments: Tetrodotoxin; Saline; CSF/CNS (dorsal hippocampus); Mice (transgenic); 1004; 4 weeks; Controls received mp w/ vehicle; animal info (APP swe/PSI L166P, 2 months old); neurodegenerative (Alzheimer's); behavioral testing (Morris water maze, eight radial arm maze, escape latency); tissue perfusion (hippocampus); used dental cement to attach cannula; polyvinyl tubing.

Q3243: T. Miki, *et al.* Activity-Dependent Neurotrophin Signaling Underlies Developmental Switch of Ca(2+) Channel Subtypes Mediating Neurotransmitter Release. *Journal of Neuroscience* 2013;33(48):18755-18763
ALZET Comments: Tetrodotoxin; K252a; Saline; CSF/CNS (cerebellum); Rat (neonate); 1007D; 7 days; Controls received mp w/ vehicle; animal info (Wistar/ST, Postnatal day 6); ALZET brain infusion kit 1 used; tissue perfusion (cerebellum); teratology; good methods(pg. 18757); Pump implantation shown figure 6A pg.P18761. K252a is a CaM kinase and phosphorylase inhibitor;.



Q3117: C. B. Mantilla, *et al.* Motoneuron BDNF/TrkB signaling enhances functional recovery after cervical spinal cord injury. *Experimental Neurology* 2013;247(1):101-109

ALZET Comments: Brain-derived neurotrophic factor;; CSF/CNS (intrathecal); Rat; 2002; 14 days; Animal info (male, Sprague Dawley, adult); spinal cord injury; post op. care (Acetaminophen orally and buprenorphine IM for 3 days); pulsed delivery (delayed delivery for 3 days - aCSF only in catheter); tissue perfusion (C4 segment of spine); peptides; "Mini-osmotic pumps were successfully implanted for intrathecal delivery at the C4 level and functioned properly throughout the 14 day duration of the experiment." pg 103 "Differences in survival rates across groups were likely unrelated to the possible additional morbidity associated with intrathecal catheter and miniosmotic pump implantation, as the survival rate was 70% (28 out of 40) compared to 84% (26 out of 31) in rats not implanted with an intrathecal pump (p = 0.17)." pg 103; PE-10 intrathecal cannula, 10 cm.

Q3106: C. O. Lemley, *et al.* Uterine Infusion of Melatonin or Melatonin Receptor Antagonist Alters Ovine Feto-Placental Hemodynamics During Midgestation. *Biology of Reproduction* 2013;89(2):U24-U32

ALZET Comments: Melatonin; Luzindole; DMSO; water; Intrauterine (uterine horn); Sheep (ewe); 2ML4; 28 days; Controls received mp w/ vehicle; functionality of mp verified by serum levels of melatonin taken; 45% DMSO used; stress/adverse reaction: (see pg.2); post op. care (For two days: flunixin meglumine 50 mg/ml IM twice a day; Penicillin G procain 300,000 u/ml once per day); tissue perfusion (uterus mesometrium); cardiovascular;

Q3105: T. G. Landry, *et al.* Chronic neurotrophin delivery promotes ectopic neurite growth from the spiral ganglion of deafened cochleae without compromising the spatial selectivity of cochlear implants. *Journal of Comparative Neurology* 2013;521(12):2818-2832

ALZET Comments: Neurotrophin; Brain-derived neurotrophic factor; Ear (cochlea); Guinea pig; 2004; 28 days; Controls received mp w/ artificial perilymph; animal info (young adult, 300-600g); tissue perfusion (cochlea); peptides;

Q3103: S. Kurata, *et al.* Nerve Growth Factor Involves Mutual Interaction between Neurons and Satellite Glial Cells in the Rat Trigeminal Ganglion. *ACTA HISTOCHEMICA ET CYTOCHEMICA* 2013;46(2):65-73

ALZET Comments: Carbenoxolone; Saline; CSF/CNS (trigeminal ganglion); Rat; 2001; 3 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 200-250g); tissue perfusion (Trigeminal ganglion, left maxillary division); Carbenoxolone aka carbenoxolone, CBX;

Q3093: B. A. Kermath, *et al.* Effects of Chronic NMDA-NR2b Inhibition in the Median Eminence of the Reproductive Senescent Female Rat. *Journal of Neuroendocrinology* 2013;25(10):887-897

ALZET Comments: Ifenprodil; Tartaric acid; CSF/CNS (median eminence); Rat; 1004; 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 9-11 months, persistent oestrus); stress/adverse reaction: (see pg. 888. One female died after surgery); post op. care (Carprofen SC injection 5 mg/kg; Pramoxine HCl on incision); tissue perfusion (Median eminence); used ALZET PE-60 catheter.

Q2864: S. Fritzell, *et al.* Intratumoral temozolomide synergizes with immunotherapy in a T cell-dependent fashion. *CANCER IMMUNOLOGY IMMUNOTHERAPY* 2013;62(9):1463-1474

ALZET Comments: Temozolomide; CSF/CNS (intratumoral); Mice; 1003D; 3 days; Animal info (C57BL/6, female, syngenic, 8-10 wks old); ALZET brain infusion kit 3 used; cyanoacrylate; tissue perfusion (intratumoral); temozolomide (TMZ) is an alkylating agent.

Q3335: K. J. Cho, *et al.* Apoptosis signal-regulating kinase-1 aggravates ROS-mediated striatal degeneration in 3-nitropropionic acid-infused mice. *Biochemical and Biophysical Research Communications* 2013;441(2):280-285

ALZET Comments: RNA, small interfering, ASK1; Nitropropanoic acid, 3-; Saline; CSF/CNS (striatum); SC; Mice (transgenic); 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, SOD1-tg); functionality of mp verified by Western blotting; Multiple pumps per animal (2); neurodegenerative (apoptotic striatal degeneration); behavioral testing (rotarod test); tissue perfusion (striatum); 3-NP delivered SC, ASK1-siRNA delivered CSF/CNS.

Q2463: V. Chandramohan, *et al.* Recombinant anti-podoplanin (NZ-1) immunotoxin for the treatment of malignant brain tumors. *International Journal of Cancer* 2013;132(10):2339-2348



ALZET Comments: Immunotoxin, NZ-1; immunotoxin, P588; PBS-HSA; CSF/CNS (intratumoral); Mice; 1003D; 3 days; Control animals received mp w/ vehicle; tissue perfusion (intratumoral); cancer (brain).

Q3075: D. Cantinieaux, *et al.* Conditioned Medium from Bone Marrow-Derived Mesenchymal Stem Cells Improves Recovery after Spinal Cord Injury in Rats: An Original Strategy to Avoid Cell Transplantation. *PLoS One* 2013;8(8):U18-U32

ALZET Comments: Conditioned medium, bone marrow-derived mesenchymal stem cells; CSF/CNS (intrathecal); Rat; 1007D; 7 days; Controls received mp w/ control medium; animal info (female, Wistar, adult, 200g); spinal cord injury; post op. care (manually emptied bladder until rats regained control); behavioral testing (BBB open-field test, grid navigation test); tissue perfusion (spinal cord injury site); cardiovascular; immunology; Bone marrow-derived mesenchymal stem cells conditioned medium aka BMSC-CM; Pumps removed after 7 days.

Q3056: T. J. Brozoski, *et al.* Local NMDA Receptor Blockade Attenuates Chronic Tinnitus and Associated Brain Activity in an Animal Model. *PLoS One* 2013;8(10):U388-U398

ALZET Comments: AP5, D-; Saline; CSF/CNS (paraflocculus); Rat; 2002; 2 weeks; Controls received mp w/ methylene dye; animal info (male, Long-Evans, 60 days old); functionality of mp verified by residual volume; tissue perfusion (paraflocculus); brain tissue distribution; Used PE-50 tubing. D-AP5 is an NMDA antagonist. Pumps anchored to muscle/connective tissue via nylon suture.

Q3423: H. M. Brothers, *et al.* Riluzole Partially Rescues Age-Associated, but not LPS-Induced, Loss of Glutamate Transporters and Spatial Memory. *Journal of Neuroimmune Pharmacology* 2013;8(5):1098-1105

ALZET Comments: Endotoxin, LPS; CSF, artificial; CSF/CNS (fourth ventricle); Rat; 2004; 3 weeks; Controls received mp w/ vehicle; animal info (Fisher F-344, 3 months old); behavioral testing (Morris water maze); tissue perfusion (fourth ventricle); immunology;.

Q3055: N. Brazda, *et al.* A mechanical microconnector system for restoration of tissue continuity and long-term drug application into the injured spinal cord. *Biomaterials* 2013;34(38):10056-10064

ALZET Comments: Antibody, human IgG; Saline; CSF/CNS (intrathecal); Rat; 2001; 3 days; 7 days; Controls received mp w/ vehicle; animal info (Female, Wistar, 200-230g); spinal cord injury; post op. care (Baytril for one week, manual bladder emptying twice per day); behavioral testing (locomotor behavior); tissue perfusion (spinal cord); pump attached to mechanical microconnector system (mMS).

Q3328: L. Biddlestone-Thorpe, *et al.* ATM Kinase Inhibition Preferentially Sensitizes p53-Mutant Glioma to Ionizing Radiation. *Clinical Cancer Research* 2013;19(12):3189-3200

ALZET Comments: KU-60019; PBS; CSF/CNS (intratumoral); Mice (nude); 1007D; 1002; 2002; 7 days; 19 days; Controls received mp w/ vehicle; animal info (female, nude, athymic, 15-20g, 5-6 weeks old); ALZET brain infusion kit 3 used; cancer (glioma); tissue perfusion (glioma); "To reach meaningful drug concentrations of KU-60019 within the tumor, the BBB/BTB need to be bypassed or drugs administered locally. Both osmotic pumps, as well as clinically used CED, partially bypass the BBB/BTB and deliver drugs directly to the tumor to improve efficacy and reduce potential systemic toxicity" pg3194; KU-60019 is a kinase inhibitor.

Q3684: J. V. Berg, *et al.* Intratumoral IL-12 combined with CTLA-4 blockade elicits T cell-mediated glioma rejection. *Journal of Experimental Medicine* 2013;210(13):2803-2811

ALZET Comments: Interleukin-12, murine; PBS; CSF/CNS (intratumoral); Mice; 1004; 2004; 28 days; Controls received mp w/ vehicle; animal info (C57BL6); cancer (glioma); tissue perfusion (tumor; glioma); immunology; pumps primed at 37C; pumps explanted after 28 days;.