



**Method for Use of Catheter Tubing to Delay
Drug Infusion into the CNS via ALZET® Osmotic Pumps**

Although ALZET pumps begin operating immediately upon contact with fluids, they can be adapted to allow for a period of recovery following surgery, such as following implantation of a brain cannula. In this application, the ALZET pump is filled with drug solution and attached to a length of catheter tubing, which has been loaded with a control solution (no drug). If the control solution is such that mixing could occur between it and the drug solution, then a spacer substance should be placed between the control and drug solutions. The spacer substance can be any liquid in which the drug solution is not miscible (such as oil), or it can be sterile air.

Upon implantation, the ALZET pump begins releasing the drug solution from the pump reservoir into the catheter tubing. This displaces the control solution from the catheter tubing into the animal. As the last of the control solution is being released into the animal, the drug solution reaches the end of the catheter tube and is then released into the animal at the pump's constant rate.

I. Catheter length:

For CNS infusion, the tubing length should be 25% longer than the distance between the pump (placed subcutaneously over the scapulae) and the site of cannula placement. As an example, if this distance is 8 cm, use a 10 cm length of tubing. If the 10 cm tubing is filled with control solution, the length of time for delivery of the control solution depends upon the total volume contained in the tubing and the pump model being used.

II. Catheter volume:

To determine the appropriate length of catheter tubing, use the following length-volume conversions:

Tubing Type	Size	Volume per Centimeter
Vinyl	V3/A*	3.739 µl
Polyethylene (PE)	PE-60*	4.566 µl
PE	PE-50	2.679 µl

*V3/A & PE-60 tubing are available from DURECT Corporation.
V/3A comes either separately or as part of the ALZET Brain Infusion Kits

III. Example:

A researcher desires a one-week delay following implantation of a brain cannula. Drug infusion should begin after this delay and last three weeks. The researcher is using ALZET Model 2004 with the ALZET Brain Infusion Kit, in an adult rat.

Model 2004 releases at 0.25 µl/hr** and therefore delivers 42 µl over one week. This amount of control solution, such as artificial CSF, will be loaded into the tubing.

The vinyl tubing in the brain infusion kit contains 3.739 µl per cm, so 42 µl will fill 11.2 cm. The researcher measures a distance of 8 cm between the pump and cannula implantation sites. The minimum tube length would be 25% longer than this distance or 10 cm. The 11.2 cm needed to provide the one-week delay will work well. The tubing is filled with aCSF; a small air bubble is introduced to prevent mixing with the drug solution once attached to the primed and filled pump.

Note: When using a catheter, the entire contents of the pump reservoir will not be released in the animal. (Some solution will remain in the catheter tubing at the end of the infusion period.) Despite this, the pump must be filled completely in order to operate properly.

**Nominal pumping rate for Model 2004. (Refer to the instructions inside each box for lot-specific data.)



**References on Delayed CNS Infusion
Using ALZET[®] Osmotic Pumps**

Q7803: H. M. Eggink, *et al.* Chronic infusion of tauroolithocholate into the brain increases fat oxidation in mice. *J Endocrinol* 2018;236(2):85-97

Agents: sodium tauroolithocholate; GW4064 **Vehicle:** DMSO; Saline; **Route:** CSF/CNS (lateral ventricle); IP; **Species:** Mice; **Pump:** 1004; **Duration:** 8, 23 days;

ALZET Comments: Dose ((1 μ M tLCA), (10 μ M GW4064)); 80% DMSO/saline (for GW4064) and 20% DMSO/saline (for tLCA) used; Controls received mp w/ vehicle; animal info (15 weeks, male, C57BL/6J); tLCA is a bile acid and a strong TGR5 agonist, and GW4064 is a synthetic FXR agonist; ALZET brain infusion kit 3 used; Brain coordinates (-0.45 mm anteroposterior, -1.00 mm lateral and 2.50 mm dorsoventral of bregma); cyanoacrylate adhesive (Loctite 454); delayed delivery (5 days); IP infusion of tLCA administered to control for leakage into the periphery;; Therapeutic indication (fat metabolism);

Q6945: C. Andre, *et al.* mTORC1 pathway disruption abrogates the effects of the ciliary neurotrophic factor on energy balance and hypothalamic neuroinflammation. *Brain, Behavior, and Immunity* 2018;70(325-334

Agents: Ciliary neurotrophic factor, recomb. human **Vehicle:** CSF, artificial; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1002; **Duration:** Not Stated;

ALZET Comments: Dose (63 ng/ul); Controls received mp w/ vehicle; animal info (16 week old mice); Brain coordinates (anteroposterior: -0.3mm from bregma, lateral: -1mm to bregma and dorsoventral: -2.5mm below skull); delayed delivery (2 days);

Q6509: S. Tekin, *et al.* The effects of intracerebroventricular infusion of irisin on feeding behaviour in rats. *Neurosci Lett* 2017;645(25-32

Agents: Irisin **Vehicle:** CSF, artificial; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: Dose (10 nM; 100 nM); Controls received mp w/ vehicle; animal info (male Wistar Albino rats, 240–325 g); behavioral testing (feeding behavior); ALZET brain infusion kit used; Brain coordinates (1.40 mm lateral, 0.8 mm posterior, and 4.8 mm vertical to bregma); delayed delivery (pumps were connected to cannula 7 days after surgery);

Q6130: Z. S. Roberts, *et al.* Chronic hindbrain administration of oxytocin is sufficient to elicit weight loss in diet-induced obese rats. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2017;313(4):R357-R371

Agents: Oxytocin **Vehicle:** Saline; **Route:** CSF/CNS (Third and forth ventricle); **Species:** Rats, Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Dose (16 nmol/day); Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley (CD IGS) rats, Long-Evans rats, C57BL/6J mice); post op. care (Mice were treated with analgesic ketoprofen and antibiotic Baytril; Rats treated with analgesic buprenorphine sustained release and the antibiotic enrofloxacin after cannulations); delayed delivery (implanted cannula and vinyl catheter were filled with sterile saline then A stainless steel 22-gauge pin plug was inserted at the end of the tubing during a 2-wk postoperative recovery period); Obesity and diabetes;

Q6302: M. Kapadia, *et al.* Effects of sustained i.c.v. infusion of lupus CSF and autoantibodies on behavioral phenotype and neuronal calcium signaling. *Acta Neuropathologica Communications* 2017;5(1):70

Agents: CSF, Lupus patient **Vehicle:** Not Stated; **Route:** CSF/CNS (right ventricle); **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;

ALZET Comments: animal info (6-week old CD1 male mice); Brain coordinates (-0.5 mm from Bregma, lateral 1.0 mm); delayed delivery (4 days); The vinyl tube connecting the minipump to the cannula was pre-loaded with artificial CSF to allow for 4-day postoperative recovery, and it was separated from patient CSF by a 2-mm oil "spacer".;

Q6266: R. G. Feichtinger, *et al.* Effects of alpha-melanocyte-stimulating hormone on mitochondrial energy metabolism in rats of different age-groups. *Neuropeptides* 2017;64(123-130

Agents: Melanocyte-stimulating hormone, α - **Vehicle:** Saline, pyrogen free; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: Dose (1 μ g/ μ l/h); Controls received mp w/ vehicle; animal info (Male Wistar rats aged 2, 3, 12 or 24 months); ALZET brain infusion kit used; delayed delivery (12 hours);



Q4789: Oliver J. Bosch, *et al.* Oxytocin in the nucleus accumbens shell reverses CRFR2-evoked passive stress-coping after partner loss in monogamous male prairievoles. *Psychoneuroendocrinology* 2016;64):

Agents: Astressin-2B; stresscopin; oxytocin, synthetic; receptor antagonist, oxytocin; **Vehicle:** Ringer's solution; DMSO; **Route:** CSF/CNS (nucleus accumbens); **Species:** prairie vole; **Pump:** 1007D; **Duration:** 5 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (adult, 70-100 days old); ALZET brain infusion kit 2 used; 4% DMSO used; behavioral testing (forced swim test); cyanoacrylate adhesive; delayed delivery; Astressin-2B is a CRFR2 antagonist; stresscopin is a CRFR2 agonist; bilateral infusion; Dose (Astressin-2B 1 ng/h; stresscopin 0.1 ng/h; oxytocin, synthetic 0.5 ng/hr; OT receptor antagonist 5 ng/hr); brain coordinates;

Q5419: M. Matsumoto, *et al.* Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP) Is Involved in Adult Mouse Hippocampal Neurogenesis After Stroke. *J Mol Neurosci* 2016;59(2):270-9

Agents: PACAP38 **Vehicle:** BSA, Saline; **Route:** CSF/CNS (Right lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; Brain infusion cannula used; 0.1% BSA used; ischemia (stroke); delayed delivery (1 week); Pituitary Adenylate Cyclase-Activating Polypeptide aka PACAP; Dental cement used; anesthetized with sevoflurane; PACAP involved in mouse hippocampal; Dose: 480 pmol/kg/day; Brain coordinates (0.5 mm posterior, 1.0 mm lateral, 2.2 mm ventral from bregma);

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

Agents: RG108 **Vehicle:** Cyclodextrin, hydroxypropyl- β -; **Route:** CSF/CNS (dorsal striatum); **Species:** Rat; **Pump:** 2004; **Duration:** 14 days;

ALZET Comments: 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 μ M);

Q5248: S. Parsi, *et al.* Preclinical Evaluation of miR-15/107 Family Members as Multifactorial Drug Targets for Alzheimer's Disease. *Mol Ther Nucleic Acids* 2015;4(e256

Agents: miR-16 mimic **Vehicle:** Saline; **Route:** CSF/CNS (ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Wild-type mice (C57BL/6, female, 2 months old)); ALZET brain infusion kit 2 used; dose-response (pg. 2); neurodegenerative (Alzheimer's); post op. care (Anafen); replacement therapy (miRNA replacement therapy); brain tissue distribution; delayed delivery (12 hours delivery/day); potent inhibitor of amyloid precursor protein (APP) and BACE1 expression, A β peptide production, and Tau phosphorylation in cells; Dose (4.2 μ g/ μ l); Brain coordinates; ventricle A/P = -0.22 M/L = 0.5 D/v = 3.5)

Q5026: S. Kooijman, *et al.* Central GLP-1 receptor signalling accelerates plasma clearance of triacylglycerol and glucose by activating brown adipose tissue in mice. *Diabetologia* 2015;58(11):2637-46

Agents: Exendin-4 **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 5 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6J, 20 weeks old); ALZET brain infusion kit 3 used; stress/adverse reaction: (see pg. 2638); delayed delivery for 2 days; Dose (0.75 nmol/day);

Q5154: A. Ghanbari, *et al.* Depletion of neural stem cells from the subventricular zone of adult mouse brain using cytosine b-Arabinofuranoside. *Brain and Behavior* 2015;5(11):e00404

Agents: Ara-C **Vehicle:** Saline; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week; 2 weeks;

ALZET Comments: Controls received sham operation and mp w/ vehicle; animal info: Five-week-old male C57-BL6 mice; pumps replaced once after 7 days; ALZET brain infusion kit 3 used; good methods (pg 2); post op. care (0.5 mg/kg buprenorphine every 12 h for 48 hours); cyanoacrylate adhesive (Loctite 454); delayed delivery (6-12 hours); Dose: 2% Ara-C in Saline; Brain coordinates; Paxinos mouse brain Atlas: Anterior-Posterior (AP): _0. 2, Medial-Lateral (ML): +0. 9 from the bregma point and Dorsal-Ventral: +2.7 from the top of skull



Q5152: H. O. Gautier, *et al.* Neuronal activity regulates remyelination via glutamate signalling to oligodendrocyte progenitors. *Nat Commun* 2015;6(8518)

Agents: Tetrodotoxin; Conotoxin, MVIIC w-; NBQX; Uridine, ethyldeoxy- **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1004; **Duration:** 3 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info: Female Sprague–Dawley rats aged 10–14 weeks of age (190–250 g); Plastics One brain infusion kit used; good methods; neurodegenerative (demyelination); post op. care (buprenorphine); cyanoacrylate adhesive (pg 12); delayed delivery (3 dpl and 10 dpl), using corn oil to separate drug from saline in a catheter; “The onset of drug delivery into the lesion was controlled by varying the length of the tube that connects the minipump to the cannula and by inserting a sterile corn oil drop (Sigma) to prevent diffusion of the drug solution into the initial saline solution” (pg 12); Dose: 11 mM conotoxin; 50 nM tetrodotoxin; 250 uM NBQX; 5 ug/ul EdU

Q3616: C. W. Roman, *et al.* PAC1 receptor antagonism in the bed nucleus of the stria terminalis (BNST) attenuates the endocrine and behavioral consequences of chronic stress. *Psychoneuroendocrinology* 2014;47(151-165)

Agents: Pituitary adenylate cyclase activating polypeptide **Vehicle:** Saline; BSA; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Animal info (male, adult); behavioral testing (novel object recognition, open field, elevated plus maze); stability verified by (radioimmunoassays; 4% loss per day); cardiovascular; Cannula placement verified via crestyl violet staining and visual inspection; pituitary adenylate cyclase activating polypeptide aka PACP (6-38); delayed delivery; catheters filled with vehicle; pumps primed; PACAP (6-38) is a PAC1 receptor antagonist; stress; y-connector; PACAP (6-38)75uM;

Q5066: Rakesh Kumar, *et al.* Chronic Spinal Infusion of Loperamide Alleviates Postsurgical Pain in Rats. *Indian Journal of Experimental Biology* 2014;52(317-322)

Agents: loperamide; morphine **Vehicle:** PEG, saline, ethanol; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (adult male Sprague-dawley rats, 275-350 g); dose-response (pg 319, 320); good methods (pg. 317-318); post op. care (neomycin ointment and perioperative ketoprofen [3 mg/kg, im] given); behavioral testing (stepping placing, righting reflex, and Hargreaves paw withdrawal test); delayed delivery (lynch coil filled with saline used to delay administration of drug by 3 days;); Dose: Morphine and Loperamide (0.5,1, and 2 uL/hr)

Q3596: S. Peters, *et al.* Dose-dependent effects of chronic central infusion of oxytocin on anxiety, oxytocin receptor binding and stress-related parameters in mice. *Psychoneuroendocrinology* 2014;42(225-236)

Agents: Oxytocin **Vehicle:** Ringer's solution; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 5 days; 15 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6, 19-22g, 30-35g); functionality of mp verified by serum oxytocin levels; post op. care (betaisodona; Baytril); behavioral testing (elevated plus maze; locomotor activity); Cannula placement verified via nissl-staining and histologic analysis; used dental cement and stainless steel screws; delayed delivery; catheter filled with vehicle for 1 week recovery;

Q3999: T. H. Meek, *et al.* Role of Melanocortin Signaling in Neuroendocrine and Metabolic Actions of Leptin in Male Rats With Uncontrolled Diabetes. *Endocrinology* 2014;155(4157-4167)

Agents: SHU9119; leptin; melanotan-II; **Vehicle:** Saline; PBS; water, sterile; **Route:** CSF/CNS; SC; **Species:** Rat; mice; **Pump:** Not Stated; **Duration:** 11 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (rat - male, Wistar, adult; mice - STZ-DM, AgRP-deficient or WT); functionality of mp verified by decreased insulin plasma levels; Multiple pumps per animal (2); diabetes; melanotan-II aka MTII; delayed delivery - catheters filled with saline; received drug on day 5; bilateral infusion for rat;

Q3947: S. Kooijman, *et al.* Inhibition of the central melanocortin system decreases brown adipose tissue activity. *Journal of Lipid Research* 2014;55(2022-2032)

Agents: SHU9119 **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 17 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, APOE3-Leiden.CETP); ALZET brain infusion kit 3 used; delayed delivery; catheters filled with vehicle, allowing for 4 days of recovery prior to drug delivery; obesity;



- Q3897:** R. C. Gruber, *et al.* Targeted GAS6 Delivery to the CNS Protects Axons from Damage during Experimental Autoimmune Encephalomyelitis. *Journal of Neuroscience* 2014;34(16):16320-16335
Agents: GAS6, g-carboxylated full-length human **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004;
Duration: 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6J or Gas6 -/0, 8-12 weeks old); ALZET brain infusion kit 3 used; neurodegenerative (multiple sclerosis); cyanoacrylate adhesive; Cannula placement verified via India ink dye; used dental cement; incision closed with Vetbond; pumps primed in sterile PBS at 37C; delayed delivery; catheter filled with aCSF "...mice began to receive the contents of each pump 2-3 d after attachment." pg 16321;
- Q2671:** D. Yu, *et al.* Alleviation of chronic pain following rat spinal cord compression injury with multimodal actions of huperzine A. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2013;110(8):E746-E755
Agents: Huperzine A **Vehicle:** Cyclodextrin, beta; saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** Not Stated;
Duration: 2 weeks;
ALZET Comments: Animal info (Sprague Dawley, female, adult, 200-235 g); 10% cyclodextrin used; 0.5 ul/hr rate of infusion; PE20 catheter used; wound clips used; catheter filled with 12 ul saline for delayed delivery of 24 hours; pumps replaced
- Q3359:** S. C. Robins, *et al.* Extensive regenerative plasticity among adult NG2-glia populations is exclusively based on self-renewal. *Glia* 2013;61(10):1735-1747
Agents: Uridine, bromodioxo; Ara-C **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** Not Stated;
Duration: 7 days; 12 days;
ALZET Comments: Animal info (male, NG2-CreER:tomato, 8-12 weeks old); pulsatile delivery (delayed delivery 2 days with vehicle in catheter); brain tissue distribution; cyanoacrylate adhesive used to close catheter tubing; Plastics 1 cannula and catheter
- Q5258:** S. C. Robins, *et al.* Evidence for NG2-glia derived, adult-born functional neurons in the hypothalamus. *PLoS One* 2013;8(10):e78236
Agents: Uridine, bromodeoxy; uridine, ethynyldeoxy **Vehicle:** CSF, artificial; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: animal info: NG2-CreER:tdTomato mice; functionality of mp verified post brain removal; Plastics One infusion kit used; brain tissue distribution; delayed delivery (2 days); delayed delivery (2 days); Dose: 30 ug/day (BrdU and EdU); Brain coordinates; 0.3 mm (anteroposterior), 1.0 mm (lateral), and 2.5 mm (dorsoventral, below skull)
- Q2481:** T. Noguchi, *et al.* Effects of Gold Thioglucose Treatment on Central Corticotrophin-Releasing Hormone Systems in Mice. *Journal of Neuroendocrinology* 2013;25(4):340-349
Agents: Urocortin 3 **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (C57BL/6, 22-26 g, 8 wks old); cannula placement verified post mortem by injecting methylene blue dye into the catheter; delayed delivery by filling catheter with "18 ul of saline for the first 3 days of infusion, followed by a small amount of air, and then filled with either Ucn 3" pg 341;
- Q3117:** C. B. Mantilla, *et al.* Motoneuron BDNF/TrkB signaling enhances functional recovery after cervical spinal cord injury. *Experimental Neurology* 2013;247(:):101-109
Agents: Brain-derived neurotrophic factor; **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2002;
Duration: 14 days;
ALZET Comments: 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



Q3552: I. Lundgaard, *et al.* Neuregulin and BDNF Induce a Switch to NMDA Receptor-Dependent Myelination by Oligodendrocytes. PLOS BIOLOGY 2013;11(12):U147-U164

Agents: MK-801 **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1004; **Duration:** 18 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Female, Sprague Dawley, 9-12 weeks old, 200-225g); cyanoacrylate adhesive; used anchoring screws and dental cement; used Plastics one cannula 30g; delayed delivery for 3 days; MK-801 is a NMDA receptor channel blocker;

Q1822: J. P. Shaffery, *et al.* Brain-derived neurotrophic factor (BDNF) reverses the effects of rapid eye movement sleep deprivation (REMSD) on developmentally regulated, long-term potentiation (LTP) in visual cortex slices. Neuroscience Letters 2012;513(1):84-88

Agents: Brain-derived neurotrophic factor **Vehicle:** PBS; BSA; **Route:** CSF/CNS (visual cortex); **Species:** Rat; **Pump:** 2002; 1007D; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ saline; animal info (Long-Evans Hooded, P28; immature, P22-P25); pulsatile delivery; polyethylene tubing contained saline with an air bubble separator for a 5-day drug delay and recovery period; delayed delivery;

Q2191: I. J. Clarke, *et al.* Gonadotropin-Inhibitory Hormone Is a Hypothalamic Peptide That Provides a Molecular Switch between Reproduction and Feeding. Neuroendocrinology 2012;95(4):305-316

Agents: Gonadotropin-inhibitory hormone 3 **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 5, 10 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague Dawley, male); delayed delivery by filling catheter with aCSF; ALZET brain infusion kit used; peptides

Q5370: R. P. Y. Chiang, *et al.* Melatonin reduces median nerve injury-induced mechanical hypersensitivity via inhibition of microglial p38 mitogen-activated protein kinase activation in rat cuneate nucleus. Journal of Pineal Research 2012;54(232-244)

Agents: SB203580 **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague-Dawley rats, weighing 180–250 g); dose-response (pg. 237); delayed delivery (5 days of post cannulation recovery); delayed delivery (5 days of post cannulation recovery); Brain coordinates: AP, ML, H: -6.4, 1.4, -6.4; System A; Dose (1.5, 2, 2.5 mM);

Q1970: P. Wiedmer, *et al.* Ghrelin-induced hypothermia: A physiological basis but no clinical risk. PHYSIOLOGY & BEHAVIOR 2011;105(1):43-51

Agents: Ghrelin, rat **Vehicle:** Saline, sterile; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 6 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Wistar, male, 5 wks old); delayed delivery "connecting tube was filled with saline and had a length of 21.8 cm corresponding to a pumped volume sufficient for 5 days" pg 44

Q1433: S. Soos, *et al.* Complex Catabolic Effects of Central Alpha-MSH Infusion in Rats of Altered Nutritional States: Differences from Leptin. Journal of Molecular Neuroscience 2011;43(2):209-216

Agents: MSH, alpha **Vehicle:** Saline, pyrogen free; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 2, 6 months old); vehicle inserted in to the catheter, delayed delivery for 12 hours

Q0718: E. Petervari, *et al.* Central alpha-MSH infusion in rats: Disparate anorexic vs. metabolic changes with aging. REGULATORY PEPTIDES 2011;166(1-3):105-111

Agents: Melanocyte stimulating hormone, alpha **Vehicle:** Saline, pyrogen free; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 2 mo, 3-4 mo, 12 mo, 24 mo old,); ALZET brain infusion kit used; cannula placement verified macroscopically; 12 hour delayed delivery due to "dead-space of the connecting tube"



Q1099: A. J. Grossberg, *et al.* Inflammation-Induced Lethargy Is Mediated by Suppression of Orexin Neuron Activity. *Journal of Neuroscience* 2011;31(31):11376-11386

Agents: Orexin A **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1003D; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-450 g); ALZET brain infusion kit used; "During pump assembly and priming, the catheters connecting the minipumps to the cannulae were filled with saline with a small bubble to separate the saline from the drug"; delayed delivery

Q0412: T. Yamauchi, *et al.* Olanzapine increases cell mitotic activity and oligodendrocyte-lineage cells in the hypothalamus. *Neurochemistry International* 2010;57(5):565-571

Agents: Ara-C **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1002; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/aCSF; animal info (Female C57BL/6J, 10 wks old); pumps replaced after 2 weeks; ALZET brain infusion kit 3 used; 2-day delayed infusion by filling vinyl tubing with artificial CSF; delayed delivery;

Q0471: A. N. A. Verty, *et al.* The Endogenous Actions of Hypothalamic Peptides on Brown Adipose Tissue Thermogenesis in the Rat. *Endocrinology* 2010;151(9):4236-4246

Agents: SB-334867-A; SNAP-7941; SHU9119 **Vehicle:** Cyclodextrin, 2-hydroxypropyl-b-; DMSO; water, sterile; saline, physiological; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (naïve, male, Sprague Dawley, 8 wks old, 200-300 g); 3-day delayed CNS infusion by filling tygon tubing with 40 ul of saline; cannula placement verified post mortem with cresyl violet staining; guide cannula used; obesity; endocrinology; delayed delivery;

Q0813: Y. Sugaya, *et al.* Levetiracetam suppresses development of spontaneous EEG seizures and aberrant neurogenesis following kainate-induced status epilepticus. *Brain Research* 2010;1352(:):187-199

Agents: Levetiracetam **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 8 wks old); 15 ul saline allowed for 3-day delayed delivery followed by 25-day levetiracetam delivery; "A preliminary study in which a mini-pump was filled with bromophenol blue instead of levetiracetam, confirmed that the pumped drug solution was constantly separated from the predrug saline for 3 days at 37 °C." pg 196; delayed delivery;

Q1263: E. T. Parlevliet, *et al.* GLP-1 treatment reduces endogenous insulin resistance via activation of central GLP-1 receptors in mice fed a high-fat diet. *American Journal of Physiology Endocrinology and Metabolism* 2010;299(2):E318-E324

Agents: Exendin-9; Glucagon-like phosphate-1 **Vehicle:** CSF, artificial; PBS; **Route:** CSF/CNS; SC; **Species:** Mice; **Pump:** 1004; 1002; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57Bl/6J, 12 wks old); ALZET brain infusion kit 3 used; multiple pumps per animal (2); delayed delivery for 5 days by filling catheter with aCSF; cannula placement verified by injecting 0.5% Evans blue dye through the cannula

P9952: J. W. Koo, *et al.* Nuclear factor-kappa-B is a critical mediator of stress-impaired neurogenesis and depressive behavior. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2010;107(6):2669-2674

Agents: JSH-23; SC-514 **Vehicle:** DMSO; PBS; **Route:** CSF/CNS; **Species:** Rat; mice (transgenic); **Pump:** 1004; 2004; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit 2 used; animal info (adult, male, Sprague Dawley, 230-250 g., NF-Kb/LacZ transgenic, wt, 20-30 g.); 50% DMSO used; 4-5 day delayed vehicle infusion to allow a recovery period; JSH-23 is a nuclear factor; delayed delivery;

Q0696: G. N. Neigh, *et al.* Anxiety After Cardiac Arrest/Cardiopulmonary Resuscitation Exacerbated by Stress and Prevented by Minocycline. *Stroke* 2009;40(11):3601-3607

Agents: Minocycline **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1002; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (adult, male, C57BL/6); behavioral testing (locomotor activity, rearing, central tendency); 2.5-day delayed infusion accomplished by filling catheter and cannula with vehicle; cannula placement verified with cresyl violet staining after tissue collection; delayed delivery;



P9948: O. J. Bosch, *et al.* The CRF System Mediates Increased Passive Stress-Coping Behavior Following the Loss of a Bonded Partner in a Monogamous Rodent. *Neuropsychopharmacology* 2009;34(6):1406-1415

Agents: Corticotropin-releasing factor, d-phe; CP-154526; astressin-2b **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Prairie vole; **Pump:** 1007D; **Duration:** Not Stated;

ALZET Comments: ALZET brain infusion kit 3 used; cyanoacrylate adhesive; animal info (naive, adult, male, female, 70-100 g); catheter contained ringers solution for delayed delivery of 44 hours

P9443: E. Segi-Nishida, *et al.* Electroconvulsive seizure and VEGF increase the proliferation of neural stem-like cells in rat hippocampus. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2008;105(32):11352-11357

Agents: Vascular endothelial growth factor 164, recomb. rat **Vehicle:** PBS; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days; 24 hours;

ALZET Comments: Controls received mp w/ vehicle; brain tissue distribution; peptides; animal info (male, Sprague Dawley, 175-200 g.); delayed delivery (in the 48 hour infusion, PBS infused for 24 hours to "avoid the influence of cannulation and anesthesia." (p. 11354) then VEGF infused for 24 hours)

P7353: P. Snodgrass-Belt, *et al.* Central administration of transforming growth factor-alpha and neuregulin-1 suppress active behaviors and cause weight loss in hamsters. *Brain Research* 2005;1038(2):171-182

Agents: Transforming growth factor-alpha **Vehicle:** BSA; acetic acid; CSF, artificial; **Route:** CSF/CNS (third ventricle); **Species:** Hamster; **Pump:** 2002; **Duration:** 16,20 days;

ALZET Comments: Circadian; plastics one cannula; cannula/tubing were filled with aCSF to allow for a 48 delay; behavioral study; delayed delivery;

P6887: J. P. Porter, *et al.* Effect of intracerebroventricular angiotensin II on body weight and food intake in adult rats. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2004;287(2):R422-R428

Agents: Angiotensin II **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 2,5,11 days;

ALZET Comments: Controls received mp w/ sterile saline; ALZET brain infusion kit 2 used; peptides; cyanoacrylate adhesive; ICV infusion of ANG II was delayed 2 days after surgery by prefilling the catheter between the mp and the cannula with saline instead of ANG II; delayed delivery;

P4764: P. J. Larsen, *et al.* Chronic intracerebroventricular administration of recombinant CART (42-89) peptide inhibits food intake and causes weight loss in lean and obese Zucker (*fa/fa*) rats. *Obesity Research* 2000;8(8):590-596

Agents: CART (42-89) **Vehicle:** PBS; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 7, 10 days;

ALZET Comments: Controls received mp w/ vehicle; dose-response (graph p. 592); pulsed delivery 24 hr. delay for recovery; stability verified by aspire 5 mL of pump contents, inject ICV into naive animals to verify biological activity; peptides; ALZET brain infusion kit used; recombinant CART (42-89) is a hypothalamic neuropeptide; CART (42-89) stands for cocaine-amphetamine-regulated transcript; low dose was 4.8 mg/day for 7 days, high dose was 12 mg/day for 10 days.; delayed delivery

P5244: C. Lanneau, *et al.* Involvement of the Sst1 somatostatin receptor subtype in the intrahypothalamic neuronal network regulating growth hormone secretion: an in vitro and in vivo antisense study. *Endocrinology* 2000;141(3):967-979

Agents: Oligonucleotide, antisense **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit used; antisense infusion was delayed for 4 days by vehicle infusion to allow recovery period from surgery; air bubble used as spacer to separate vehicle from antisense solution; delayed delivery;

P4659: M. J. Bradbury, *et al.* Modulation of urocortin-induced hypophagia and weight loss by corticotropin-releasing factor receptor 1 deficiency in mice. *Endocrinology* 2000;141(8):2715-2724

Agents: Urocortin **Vehicle:** CSF, artificial; **Route:** CSF/CNS (third ventricle); **Species:** Mice; **Pump:** 2001; 2002; **Duration:** 4 weeks;

ALZET Comments: Comparison of ICV injections vs mp; pumps replaced 2 times; peptides; delayed delivery; 2002 aCSF pumps were replaced with 2001 hormone pumps; then, these were replaced for 2001 aCSF pumps;



- P4478:** E. S. Redgate, *et al.* Enhanced uptake of [³H] spermidine by 9L rat brain tumors after direct intratumoral infusion of inhibitors of enzymes of the polyamine biosynthetic pathway. *Journal of Neuro-oncology* 1999;42(123-130
Agents: Spermidine; Putrescine; Ornithine, difluoromethyl- **Vehicle:** Radio-isotopes; 3H tracer; CSF; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Controls received mp w/vehicle; tissue perfusion (intratumoral); cancer; polyamines; delayed delivery for 3 days
- P3927:** B. Buwalda, *et al.* Physiological and behavioral effects of chronic intracerebroventricular infusion of corticotropin-releasing factor in the rat. *Psychoneuroendocrinology* 1997;22(5):297-309
Agents: Corticotropin-rel. factor, ovine **Vehicle:** Saline; BSA; Ascorbic acid; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002;
Duration: 10 days;
ALZET Comments: controls received mp w/ vehicle; peptides; ALZET brain infusion kit used; catheter filled w/ saline to delay agent delivery; delayed delivery;
- P4324:** E. Pellegrini, *et al.* Central administration of a growth hormone (GH) receptor mRNA antisense increases GH pulsatility and decreases hypothalamic somatostatin expression in rats. *Journal of Neuroscience* 1996;16(24):8140-8148
Agents: Oligodeoxynucleotide, antisense **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 60 hours;
ALZET Comments: Controls received anesthesia only or ICV saline; ALZET brain infusion kit used; antisense; 85 ml of saline in catheter tubing delayed antisense infusion for 7 days; delayed delivery;
- P4103:** K. Ren, *et al.* Nerve growth factor alleviates a painful peripheral neuropathy in rats. *Brain Research* 1995;699(286-292
Agents: Nerve growth factor; Antiserum, anti-nerve growth factor **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/saline; tissue perfusion (nerve cuff); perforated catheter attached to nerve cuff; delayed infusion; peptides; delayed delivery;
- P1866:** A. C. Swann. Brain Na⁺,K⁺-ATPase regulation in vivo: reduction in activity and response to sodium by intracerebroventricular tetrodotoxin. *Brain Research* 1991;543(251-255
Agents: Tetrodotoxin **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 2, 4, 7 days;
ALZET Comments: infusion delayed by loading tubing with citrate buffer; delayed delivery;
- P1731:** S. Rivest, *et al.* Effects of corticotropin-releasing factor on energy balance in rats are sex dependent. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 1989;257(R1417-R1422
Agents: Corticotropin-rel. factor, human; Corticotropin-rel. factor, rat **Vehicle:** Ascorbic acid; Albumin, bovine serum; Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: infusion delayed about 4 days by 10.6 cm saline-filled catheter; delayed delivery;
- P0607:** W. B. Jeffries, *et al.* Withdrawal syndrome follows abrupt cessation of intracerebroventricular infusion of epinephrine in spontaneously hypertensive rats. *Life Sciences* 1985;36(14):1331-1337
Agents: Epinephrine bitartrate **Vehicle:** Ascorbic acid; Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: 2 day delay of mp Epi achieved by filling connecting tubing with vehicle; some tubing externalized to allow immediate cutoff of infusion; dose-response data; delayed delivery;