



**Recent References (2013-Present) on the Administration of siRNA
Using ALZET® Osmotic Pumps**

Q10600: D. Mao, *et al.* Effect and Mechanism of BDNF/TrkB Signaling on Vestibular Compensation. *Bioengineered* 2021;12(2):11823-11836

Agents: Brain derived neurotrophic factor, RNA, small interfering **Vehicle:** CSF, artificial; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: animal info (Male Sprague Dawley; Weighed 200-250 g); behavioral testing (Rotarod test; Postural asymmetry; Head roll tilt; Nystagmus); tissue perfusion (Brain tissue); gene therapy;

Q8870: D. S. Lee, *et al.* PDI-Mediated Reduction of Disulfide Bond on PSD95 Increases Spontaneous Seizure Activity by Regulating NR2A-PSD95 Interaction in Epileptic Rats Independent of S-Nitrosylation. *International Journal of Molecular Sciences* 2020;21(6):

Agents: RNA, small interfering (PDI) **Vehicle:** Not Stated; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Animal info (Male Sprague Dawley rats, 7 weeks old); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth from bregma); neurodegenerative (Epilepsy);

Q8400: C. M. Campolim, *et al.* Short-term exposure to air pollution (PM2.5) induces hypothalamic inflammation, and long-term leads to leptin resistance and obesity via Tlr4/Ikbke in mice. *Scientific Reports* 2020;10(1):10160

Agents: RNA, small interfering **Vehicle:** Not stated; **Route:** CNS/CSF (lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 5 days;

ALZET Comments: small interfering RNA aka si-RNA; Brain coordinates (AP -0.5 mm; L -1.3 mm; DV -2.2 mm); Cannula placement verified via angiotensin II and measurement of water intake; toxicology;

Q8762: F. Han, *et al.* Dopamine D2 receptor modulates Wnt expression and control of cell proliferation. *Scientific Reports* 2019;9(1):16861

Agents: RNA, small interfering (Dopamine D2 Receptor) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (3 ug/day); animal info (C57BL/6, Male, 20 g, 8-10 weeks old); Dopamine D2 Receptor siRNA aka D2R Receptor ; ischemia (Renal);

R0380: A. Clavreul, *et al.* Nanocarriers and nonviral methods for delivering antiangiogenic factors for glioblastoma therapy: the story so far. *Int J Nanomedicine* 2019;14(24):2497-2513

Agents: Bevacizumab; RNA, small interfering (anti-HIF-1 α /PEG); Immunotoxin, DTAT/DSTATEGF; Endostatin; 17-ODYA; Miconazole; **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral), IV; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: enzyme inhibitor (CYP epoxygenase); cancer (glioblastoma); This review describes methods (including convection-enhanced delivery devices, implantable polymer devices, nanocarriers, and cellular vehicles) to deliver antiangiogenic factors to intracranial tumors.

Q6981: H. Chao, *et al.* Cardiolipin-dependent mitophagy guides outcome after traumatic brain injury. *J Neurosci* 2019;

Agents: RNA, small interfering (cardiolipin synthase); RNA, small interfering (Phospholipid scramblase-3) **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1003D; **Duration:** 72 hours;

ALZET Comments: Dose (30 nmol); animal info (17-day-old male Sprague-Dawley rats); Brain coordinates (-0.8 mm posterior to bregma, -1.5 mm lateral to midline, and -4.6 mm ventral to the skull surface); Traumatic brain injury;

Q7264: C. Rivat, *et al.* Inhibition of neuronal FLT3 receptor tyrosine kinase alleviates peripheral neuropathic pain in mice. *Nat Commun* 2018;9(1):1042

Agents: RNA, small interfering (Flt3, scrambled) **Vehicle:** Not Stated; **Route:** CSF/CNS(Intrathecal); **Species:** Mice; **Pump:** 1002; **Duration:** 6 days;

ALZET Comments: Dose (12.53 ng/ml); animal info (C57BL/6 naive mice, Flt3KO mice 25-30 g.); behavioral testing (reflexive tail flick); spinal cord injury; stress/adverse reaction: (see pg. 10);



Q7151: D. S. Lee, *et al.* PDI-mediated S-nitrosylation of DRP1 facilitates DRP1-S616 phosphorylation and mitochondrial fission in CA1 neurons. *Cell Death & Disease* 2018;9(9):869

Agents: RNA, small interfering (protein disulfide isomerase), L-NAME **Vehicle:** Saline; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rats; **Pump:** 1007D; **Duration:** Not Stated;

ALZET Comments: Dose (15 µg/µl L-NAME); animal info (7-week-old male Sprague-Dawley rats); Nw-nitro-L-arginine methyl ester hydrochloride aka L-name; enzyme inhibitor (protein disulfide isomerase); ALZET brain infusion kit 1 used; Brain coordinates (right lateral ventricle, 1mm posterior; 1.5 mm lateral; 3.5 mm depth from bregma);

Q7191: J. E. Kim, *et al.* P2RX7-MAPK1/2-SP1 axis inhibits MTOR independent HSPB1-mediated astroglial autophagy. *Cell Death & Disease* 2018;9(5):546

Agents: BzATP, OxATP, A740003, Compound C, 3-chloroacetyl indole, Mithramycin A, U0126, RNA, small interfering (Heat shock protein B1) **Vehicle:** Not Stated; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose: BzATP (5 mM), OxATP (5 mM) A740003 (10 µM), Comp C (100 nM), 3CAI (25 µM), MMA (25 µM), U0126 (25 µM); animal info (Male, C57BL/6J, 25-30 g, 60-90 days old); BzATP is a P2RX7 agonist, OxATP and A740003 are P2RX7 antagonists; enzyme inhibitor (mitogen-activated protein kinase 1/2); ALZET brain infusion kit 3 used; Brain coordinates (lateral cerebral ventricle 1.0mm lateral to bregma); dependence; no stress: doses were well tolerated, and no signs of neurotoxicity (hind-limb paralysis, vocalization, food intake, or neuroanatomical damage) were observed;

Q6927: A. R. Jeon, *et al.* PDI Knockdown Inhibits Seizure Activity in Acute Seizure and Chronic Epilepsy Rat Models via S-Nitrosylation-Independent Thiolation on NMDA Receptor. *Front Cell Neurosci* 2018;12(438)

Agents: RNA, small interfering; L-NAME; PACMA31 **Vehicle:** Saline; **Route:** CSF/CNS (Right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 1 week;

ALZET Comments: Controls received mp w/ vehicle; animal info (7 week old male Sprague-Dawley rats); enzyme inhibitor (PACMA31 is a selective PDI inhibitor); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth from bregma); Therapeutic indication (seizure);

Q7115: S. Y. Cheon, *et al.* Apoptosis Signal-regulating Kinase 1 Silencing on Astroglial Inflammasomes in an Experimental Model of Ischemic Stroke. *Neuroscience* 2018;390(218-230)

Agents: RNA, small interfering (ASK1) **Vehicle:** siPORTNeoFX Transfection agent; **Route:** CSF/CNS (left lateral ventricle); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Dose (1 IL/h/ day); animal info (Adult,C57BL/6, male); enzyme inhibitor (apoptosis signal-regulating kinase 1); ALZET brain infusion kit used; ALZET brain infusion kit used; ischemia (Cerebral);

Q7089: F. X. Blaudin de The, *et al.* Engrailed homeoprotein blocks degeneration in adult dopaminergic neurons through LINE-1 repression. *EMBO J* 2018;37(15):

Agents: Colominic acid, RNA, small interfering (anti-Orf2p), cell-permeable peptide Penetratin-coupled siRNA **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: 0.9% sodium chloride used; Dose (1.5 ug/ul- colomic acid, 5 uM- En 1/2); Controls received mp w/ vehicle; animal info (male, En1-het mice,); Brain coordinates (-3.8 mm dorso/ventral); neurodegenerative (dopaminergic neurons);

Q5934: D. Yu, *et al.* Multiplexed RNAi therapy against brain tumor-initiating cells via lipopolymeric nanoparticle infusion delays glioblastoma progression. *Proc Natl Acad Sci U S A* 2017;114(30):E6147-E6156

Agents: RNA, small interfering **Route:** CSF/CNS (intratumoral); **Species:** mice (nude); **Pump:** 1002, 2002; **Duration:** 14 days;

ALZET Comments: animal info (athymic nude, 6-8 weeks old); ALZET brain infusion kit 3 used; cancer (glioblastoma); "Because repeated surgery introduces stress and pain that may impact the survival of the experimental animals, we opted for the convection-enhanced delivery (CED) strategy using an Alzet osmotic pump to deliver a continuous supply of the nano RNAi combination..." pg E6151;



Q6753: P. G. Quaresma, *et al.* Cdc2-like kinase 2 in the hypothalamus is necessary to maintain energy homeostasis. *Int J Obes (Lond)* 2017;41(2):268-278

Agents: RNA, small interfering (Cdc2-like kinase 2) **Vehicle:** Saline; DMSO; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (2 µg/day); 0.3% DMSO used; Controls received mp w/ vehicle; animal info (Eight-week-old male Swiss, db/db mice (Leprdb/Leprdb) and Leprdb/+ mice); Small interference RNA aka siCLK2;

Q6597: C. Lin, *et al.* Omega-3 fatty acids regulate NLRP3 inflammasome activation and prevent behavior deficits after traumatic brain injury. *Experimental Neurology* 2017;290(115-122

Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** CSF/CNS (left lateral ventricle); **Species:** Rat; **Pump:** 1003D; **Duration:** 72 hours;

ALZET Comments: Dose (30 nmol); Controls received mp w/ vehicle; animal info (8-weeks-old male Sprague-Dawley rats); behavioral testing (Beam balance, Morris water maze)

Q6293: A. R. Ko, *et al.* TRPC6-mediated ERK1/2 phosphorylation prevents dentate granule cell degeneration via inhibiting mitochondrial elongation. *Neuropharmacology* 2017;121(120-129

Agents: RNA, small interfering; TRPC6; U0126 **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1007D;

ALZET Comments: Controls received mp w/ vehicle; animal info (7 week old male Sprague-Dawley rats); U0126 is a selective ERK1/2 inhibitor; ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; -3.5 mm depth to the bregma); Therapeutic indication (epilepsy);

Q5674: J. Y. Kim, *et al.* PDI regulates seizure activity via NMDA receptor redox in rats. *Sci Rep* 2017;7(42491

Agents: RNA, small interfering (PDI; DTNB); bacitracin; Immunoglobulin, anti-PDI; tunicamycin ; **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days, 14 days;

ALZET Comments: Controls received mp w/ vehicle or control siRNA or control IgG; animal info (male, Sprague Dawley, 7 weeks old); pumps replaced every week; ALZET brain infusion kit 1 used; behavioral testing (behavioral seizure severity);

Q5837: J. E. Kim, *et al.* Sustained HSP25 Expression Induces Clasmotodendrosis via ER Stress in the Rat Hippocampus. *Front Cell Neurosci* 2017;11(47

Agents: RNA, small interfering (HSP25) **Vehicle:** Saline; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days, 1 week;

ALZET Comments: Controls received control siRNA ; animal info (7 months old); ALZET brain infusion kit 1 used; Electrophysiology; Therapeutic indication (Heat shock proteins, ER stress);

Q5844: X. Jiang, *et al.* Gastrin stimulates renal dopamine production by increasing the renal tubular uptake of L-DOPA. *American Journal of Physiology Endocrinology and Metabolism* 2017;312(1):E1-E10

Agents: RNA, small interfering (Gastrin-specific) **Vehicle:** TransIT in vivo transfection reagent; **Route:** Kidney (subscapular space); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp with mock (nonsilencing) siRNA; ALZET polyethylene tubing used ; Therapeutic indication (Nephrology, Hypertension, L-Dopa); Dose (3 ug/day)

Q6011: S. Y. Cheon, *et al.* Regulation of Microglia and Macrophage Polarization via Apoptosis Signal-Regulating Kinase 1 Silencing after Ischemic/Hypoxic Injury. *Front Mol Neurosci* 2017;10(261

Agents: RNA, small interfering (ASK1) **Vehicle:** siPORTNeoFX Transfection agent; **Route:** CSF/CNS (Left ventricle); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: animal info (C57BL/6, 8-12 weeks) ; Therapeutic indication (Hypoxia, late inflammation, ischemic stroke);



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. *Circulation: Heart Failure* 2016;9(1-10)

Agents: AntagomiR-7b; RNA, small interfering GABBR1; angiotensin II **Vehicle:** Not Stated; **Route:** CSF/CNS (paraventricular nucleus); **Species:** Rat; **Pump:** 1004; 1002; **Duration:** 4 weeks; 2 weeks;

ALZET Comments: 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; angiotensin II 1 ng/kg/min);

Q6055: A. Minami, *et al.* Role of Sialidase in Long-Term Potentiation at Mossy Fiber-CA3 Synapses and Hippocampus-Dependent Spatial Memory. *PLoS One* 2016;11(10):e0165257

Agents: RNA, small interfering (Neu4) **Vehicle:** AteloGene transfection reagent; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (8-9 weeks); behavioral testing (Morris water maze); AteloGene = in vivo siRNA transfection reagent; coordinates (AP = -4.2 mm; ML = 0.0 mm; DV = 4.6 mm)

Q4813: Kyoung Joo Cho, *et al.* Apoptosis signal-regulating kinase 1 mediates striatal degeneration via the regulation of C1q. *Scientific Reports* 2016;6(1-11)

Agents: Nitropropionic acid, 3-; RNA, small interfering ASK1 **Vehicle:** Transfection reagent; **Route:** SC; CSF/CNS (striatum); **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6J or R6/2 HD tg, 10 weeks old); behavioral testing (rotarod apparatus);

Q5158: M. Gujrati, *et al.* Multifunctional pH-Sensitive Amino Lipids for siRNA Delivery. *Bioconjugate Chemistry* 2016;27(1):19-35

Agents: RNA, small interfering/EHCO; PEGylated EHCO **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (nude); **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Controls received treated with nonspecific PEGylated EHCO/siGFP nanoparticles (PEGGFP) and non-PEGylated EHCO/HIF-1 α ; cancer; gene therapy, RNA nanoparticle infusion; peptides; "These results indicate that PEGylation can significantly improve the stability of EHCO/siRNA nanoparticles during storage in solution, possibly by preventing the aggregation of the nanoparticles and providing better protection to the siRNA cargo from degradation" (pg 31);

Q5789: M. C. Didiot, *et al.* Exosome-mediated Delivery of Hydrophobically Modified siRNA for Huntingtin mRNA Silencing. *Mol Ther* 2016;24(10):1836-1847

Agents: Exosomes; RNA, hydrophobically-modified small interfering (anti-Huntingtin); **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; neurodegenerative (Huntingtin); "Pump implantation for the infusion of exosomes and hsiRNA-loaded exosomes have no statistically significant impact on innate immune response in vivo." Therapeutic indication(Huntingtin); Dose (p. 1884);

Q5754: R. Boukari, *et al.* Membrane progesterone receptor-beta, but not -alpha, in dorsal brain stem establishes sex-specific chemoreflex responses and reduces apnea frequency in adult mice. *J Appl Physiol* (1985) 2016;121(3):781-791

Agents: RNA, small interfering **Vehicle:** CSF, artificial; **Route:** CSF/CNS (fourth ventricle); **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks, 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (3-4 months old); antisense (siRNA against MPR-a or mPR-b); "Previous studies in adult mice showed that 2-wk infusion of nonviral siRNA in the third ventricle ensured efficient (\geq 50%) and widespread (5-6 mm around the infusion point) knockdown of target genes in the brain (48)." Pg 782; Therapeutic indication (Sex steroids, Chemoreflex);



- Q3790:** C. C. Tan, *et al.* NLRP1 inflammasome is activated in patients with medial temporal lobe epilepsy and contributes to neuronal pyroptosis in amygdala kindling-induced rat model. *Journal of Neuroinflammation* 2015;12(U1-U12)
Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Control animals received mp w/ control siRNA in aCSF; animal info (Sprague Dawley, 260-300 g); long-term study;
- Q4110:** J. Song, *et al.* The effect of ASK1 on vascular permeability and edema formation in cerebral ischemia. *Brain Research* 2015;1595(143-155)
Agents: RNA, ASK1-small interfering **Vehicle:** siPORTNeoFX; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 days;
ALZET Comments: Controls received mp w/ scrambled si-RNA; animal info (male, C57BL6, 8-12 weeks old); ischemia (transient focal cerebral);
- Q4976:** F. A. Oladosu, *et al.* Mu Opioid Splice Variant MOR-1K Contributes to the Development of Opioid-Induced Hyperalgesia. *PLoS One* 2015;10(8):e0135711
Agents: RNA, small interfering 13 antisense **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intrathecal); **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ sense siRNA; animal info (C57BL6J or CXB7/ByJ, 8-12 weeks old, 20-30g);
- Q5014:** Y. J. Kim, *et al.* The role of TRPC6 in seizure susceptibility and seizure-related neuronal damage in the rat dentate gyrus. *Neuroscience* 2015;307(215-30)
Agents: RNA, small interfering TRPC6 **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 1 week;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague Dawley, 7 weeks old); ALZET brain infusion kit 1 used; used dental cement;
- Q4386:** S. Cuevas, *et al.* Role of Nuclear Factor Erythroid 2-Related Factor 2 in the Oxidative Stress-Dependent Hypertension Associated With the Depletion of DJ-1. *HYPERTENSION* 2015;65(1251-U173)
Agents: RNA, small interfering (Drd2-); RNA, small interfering (DJ-1-) **Vehicle:** TransIT; **Route:** Kidney (subcapsular space); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ non-silencing RNA; animal info (male, C57BL6J, uninephrectomized); used PE tubing #0007701 with surgical glue; pump sutured to abdominal wall;
- Q4214:** C. J. Yu, *et al.* BACE1 RNA interference improves spatial memory and attenuates Abeta burden in a streptozotocin-induced tau hyperphosphorylated rat model. *Cell Biochemistry and Function* 2014;32(590-596)
Agents: Okadaic acid; RNA, small interfering **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 1004; **Duration:** 16 weeks;
ALZET Comments: Controls received mp w/ saline; animal info (Sprague Dawley, 11-12.5 months); pumps replaced every 4 weeks; neurodegenerative (Alzheimer's disease); behavioral testing (morris water maze); long-term study;
- Q4200:** Y. Yang, *et al.* Sestrin2 Decreases Renal Oxidative Stress, Lowers Blood Pressure, and Mediates Dopamine D(2) Receptor-Induced Inhibition of Reactive Oxygen Species Production. *Hypertension* 2014;64(825-+)
Agents: RNA, small interfering (sestrin2) **Vehicle:** Not Stated; **Route:** Kidney (renal subcapsule); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ control RNA; animal info (C57BL6J); good methods (supplement, pg 2); post op. care (buprenorphine); replacement therapy (uninephrectomy); used ALZET PE tubing; bp measured using catheter;
- Q4176:** L. Weissmann, *et al.* IKKepsilon Is Key to Induction of Insulin Resistance in the Hypothalamus, and Its Inhibition Reverses Obesity. *Diabetes* 2014;63(3334-3345)
Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ scrambled RNA; animal info (male, C57BL6J or db/db, 8 weeks old); diabetes; obesity; used Plastics One cannula;



Q3360: M. S. Tan, *et al.* IL12/23 p40 Inhibition Ameliorates Alzheimer's Disease-Associated Neuropathology and Spatial Memory in SAMP8 Mice. *Journal of Alzheimers Disease* 2014;38(3):633-646

Agents: RNA, small interfering p40 **Vehicle:** CSF, artificial; **Route:** CSF/CNS (third ventricle); **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ control siRNA, aCSF, control antibody; animal info (male, SAMP8, SAMR1, 3 month, 7 month and 11 month old); functionality of mp verified by increased expression of IL-12 and IL-23; ALZET brain infusion kit 3 used; neurodegenerative (Alzheimer); behavioral testing (Morris water maze);

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)

Agents: RNA, small interfering NLRP1; RNA, small interfering, NLRP3; RNA, small interfering caspase-1 **Vehicle:** CSF, artificial; water, RNase-free; **Route:** CSF/CNS (dorsal third ventricle); **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 8 weeks;

ALZET Comments: 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;

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

Agents: RNA, small interfering **Vehicle:** PBS; **Route:** CSF/CNS (striatum); **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: Animal info (male, Sprague Dawley); neurodegenerative (Parkinson's disease); tissue perfusion (striatum); gene therapy; used Plastics One 30g cannula; primed overnight in 37C saline;

Q3784: X. F. Meng, *et al.* Inhibition of the NLRP3 inflammasome provides neuroprotection in rats following amygdala kindling-induced status epilepticus. *Journal of Neuroinflammation* 2014;11(U1-U12)

Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;

ALZET Comments: Control animals received mp w/ aCSF; animal info (adult, male, Sprague Dawley, 260-300 g); long-term study;

Q3551: K. P. Loh, *et al.* TRPM4 inhibition promotes angiogenesis after ischemic stroke. *PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY* 2014;466(3):563-576

Agents: RNA, small interfering TRPM inhibiting **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Rat; **Pump:** Not Stated; **Duration:** 24 hours;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 300g); ischemia (cerebral); behavioral testing (rotarod apparatus); gene therapy; cardiovascular; TRPM4 aka transient receptor potential melastatin 4;

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)

Agents: RNA, small interfering TREM2 **Vehicle:** CSF, artificial; **Route:** CSF/CNS (dorsal third ventricle); **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: 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;



Q3181: T. L. Briones, *et al.* Chronic neuroinflammation and cognitive impairment following transient global cerebral ischemia: role of fractalkine/CX3CR1 signaling. *Journal of Neuroinflammation* 2014;11(:):U1-U13

Agents: RNA, small interfering CX3CR1; RNA, scrambled **Vehicle:** Transfection medium; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1002; **Duration:** 28 days;

ALZET Comments: Animal info (male, Wistar, 350-375g); ALZET brain infusion kit 2 used; ischemia (cerebral); post op. care (heating pad); behavioral testing (Morris water maze); gene therapy; immunology; Cannula stabilized using dental cement. Pumps primed in sterile saline 37C overnight.

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

Agents: GR103691; RNA, small interfering **Vehicle:** Transfection reagent (TransIT); **Route:** SC; kidney (subcapsular space); **Species:** Mice; **Pump:** 1007D; **Duration:** 4 days; 7 days;

ALZET Comments: 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;

Q4773: A. S. b. Alexander Ewe a, Sabine Barnert c, Rolf Schubert c, Achim Temmed, Udo Bakowsky e., *et al.* Storage stability of optimal liposome–polyethylenimine complexes (lipopolyplexes) for DNA or siRNA delivery. *Acta Biomaterialia* 2014;10:2663-2673

Agents: DNA, RNA, small interfering **Vehicle:** Lipopolyplexes, (PEI F25-LMW, DPPC); **Route:** SC; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** 6+ weeks;

ALZET Comments: cancer (mamma carcinoma, prostate carcinoma, colon carcinoma); PEI F25-LMW aka Polyethylenimine F-25 Low molecular weight; DPPC aka dipalmitoyl-phosphatidyl-choline

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

Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** Kidney; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: 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

Q2961: V. A. M. Villar, *et al.* Novel role of sorting nexin 5 in renal D(1) dopamine receptor trafficking and function: implications for hypertension. *FASEB Journal* 2013;27(5):1808-1819

Agents: Ringer's solution, lactated; RNA, small interfering, Snx-5, non-silencing **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5, 7 days;

ALZET Comments: Controls received mp w/vehicle or (non-silencing mock siRNA); animal info (spontaneously hypertensive rats (SHR)); antihypertensive; mp used to infuse sorting nexin 5 (SNX5). It decreases sodium excretion, and elevates systolic blood pressure. SNX5 regulated D1 receptor, which has an important therapeutic implication in the management of essential hypertension;

Q2676: F. Tao, *et al.* Role of Neuregulin-1/ErbB Signaling in Stem Cell Therapy for Spinal Cord Injury-Induced Chronic Neuropathic Pain. *Stem Cells* 2013;31(1):83-91

Agents: RNA, small interfering **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Control animals received mp w/ non target RNA; animal info (Long Evans, female, 250 g); NRG1 siRNA; spinal cord injury

Q3326: J. Song, *et al.* Apoptosis signal-regulating kinase 1 (ASK1) is linked to neural stem cell differentiation after ischemic brain injury. *Experimental & Molecular Medicine* 2013;45(:):U28-U34

Agents: RNA, Apoptosis signaling kinase 1-small interfering **Vehicle:** Transfection medium, siPORT NeoFX; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 days;

ALZET Comments: Controls received mp w/ vehicle and scrambled siRNA (negative control) or siRNA against glyceraldehyde 3-phosphate dehydrogenase (positive control); animal info (male, C57BL6, 8-12 weeks old); ischemia (transient focal cerebral); immunology;



R0314: S. Raghunathan, *et al.* Therapeutic implications of small interfering RNA in cardiovascular diseases. FUNDAMENTAL & CLINICAL PHARMACOLOGY 2013;27(1):1-20

Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** SC; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** Not Stated; **ALZET Comments:** TACE siRNA; "SHRs were infused with previously validated TACE siRNA through subcutaneously implanted ALZET osmotic minipumps in the back of the animals. This resulted in systemic knockdown of TACE expression and decreased the cross-sectional width of cardiomyocytes by 38% which successfully stopped the advance of cardiac hypertrophy evidenced by M-mode echocardiography and gross pathology studies." pg 12

Q3169: G. Pignataro, *et al.* nNOS and p-ERK involvement in the neuroprotection exerted by remote postconditioning in rats subjected to transient middle cerebral artery occlusion. NEUROBIOLOGY OF DISEASE 2013;54(1):105-114

Agents: RNA, small interfering, nNOS blocking **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 48 hours;

ALZET Comments: Controls received sham surgery, no ischemia and control siRNA (non nNOS blocking); animal info (male, Sprague Dawley, 250-300g); ischemia (cardiac; femoral artery);

Q3582: N. Niimi, *et al.* Minocycline suppresses experimental autoimmune encephalomyelitis by increasing tissue inhibitors of metalloproteinases. NEUROPATHOLOGY 2013;33(6):612-620

Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** 2002; 2004; **Duration:** 2 weeks; 4 weeks; **ALZET Comments:** Animal info (Lewis, 8-12 weeks old, experimental autoimmune encephalomyelitis); neurodegenerative (multiple sclerosis); gene therapy; immunology;

Q6737: N. Niimi, *et al.* Therapeutic gene silencing with siRNA for IL-23 but not for IL-17 suppresses the development of experimental autoimmune encephalomyelitis in rats. J Neuroimmunol 2013;254(1-2):39-45

Agents: RNA, small interfering **Vehicle:** Saline; **Route:** SC; IP; **Species:** Rat; **Pump:** 2002; 2004; **Duration:** 2 weeks; 4 weeks; **ALZET Comments:** Dose (30 µg/day); Controls received mp w/ vehicle; animal info (Lewis (LEW) rats, 8-12 weeks of age);

Q3254: O. T. W. Ng, *et al.* Small Interfering RNA Specific for N-Methyl-D-Aspartate Receptor 2B Offers Neuroprotection to Dopamine Neurons through Activation of MAP Kinase. NEURO SIGNALS 2013;21(1-2):42-54

Agents: RNA, small interfering **Vehicle:** Saline, SilentFect; **Route:** CSF/CNS (striatum); **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: Animal info (male, Sprague Dawley, 200-250g); ALZET brain infusion kit 2 used; comparison of single injection vs mp "In summary, single injection of siRNA into PD models showed no significant effect in ameliorating the motor syndrome and protection in TH-positive neurons. However, continuous infusion of NR2B-specific siRNA can effectively ameliorate the motor symptoms, attenuate the dopaminergic cell loss in the striatum and SN regions, and promote the ERK1/2 signaling pathway in parkinsonian models." pg53; neurodegenerative (Parkinson's disease); "Moreover, by using the osmotic minipump connecting with canals, this method can be easily transplanted into patients, and allow the siRNA to be infused to the target site directly at a steady and slow rate. The direct delivery has the advantages of reducing any undesired systemic side effects and lowering the dose requirement for efficacy" pg 53 ; Primed at 37C saline overnight

Q2638: D. Kesanakurti, *et al.* Role of MMP-2 in the regulation of IL-6/Stat3 survival signaling via interaction with alpha5beta1 integrin in glioma. ONCOGENE 2013;32(3):327-340

Agents: Plasmid, scrambled vector; RNA, small interfering **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (nude); **Pump:** 2004; **Duration:** Not Stated;

ALZET Comments: Animal info (nu/nu, 4-6 wks old, athymic); MMP-2 siRNA

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

Agents: RNA, small interfering, ASK1; Nitropropanoic acid, 3- **Vehicle:** Saline; **Route:** CSF/CNS (striatum); SC; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: 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