



Recent References (2016-2018) on the Administration of siRNA Using ALZET® Osmotic Pumps

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:** 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 Dis* 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:** **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 Dis* 2018;9(5):546

Agents: BzATP, OxATP, A740003, Compound C, 3-chloroacetyl indole, Mithramycin A, U0126, RNA, small interfering (Heat shock protein B1) **Vehicle:** 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 **Vehicle:** 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. *Exp Neurol* 2017;290(115-122

Agents: RNA, small interfering **Vehicle:** 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 **Vehicle:** Route: CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** **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:** 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); Brain coordinates;

Q5837: J. E. Kim, *et al.* Sustained HSP25 Expression Induces Clasmatodendrosis 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. *Am J Physiol Endocrinol Metab* 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 µg/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. *Circ Heart Fail.* 2016;9(1-10)
Agents: AntagomiR-7b; RNA, small interfering GABBR1; angiotensin II **Vehicle:** **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; antiotensin 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:** **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (8-9 weeks); behavioral testing (Morris water mazex); 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. *Bioconjug Chem* 2016;27(1):19-35
Agents: RNA, small interfering/EHCO; PEGylated EHCO **Vehicle:** **Route:** **Species:** Mice (nude); **Pump:** **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 (~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);