Recent References on the Administration of Nucleic Acids
Using ALZET® Osmotic Pumps

DNA


Agents: vascular endothelial growth factor, DNA
Vehicle: Glucose; Route: CSF/CNS (medula); Species: Rat; Pump: 2001; Duration: 1 week;
ALZET Comments: 5% glucose used; Controls received mp w/ vehicle; animal info (Male, adult spontaneously hypertensive rats, 16 weeks old, 299 +/- 4); Blood pressure measured via telemetry transmitters; vascular endothelial growth factor aka VEGF-A; ALZET brain infusion kit 2 used; gene therapy;


Agents: Mitochondrial DNA
Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 Days;
ALZET Comments: Dose (30 ug/kg/day); animal info (Male, CD-1, 18-22 g); diabetes;


Agents: DNA aptamer (RAGE)
Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2006; Duration: 21 days;
ALZET Comments: Dose (2 x10^-4 ug/day); Controls received mp w/ vehicle; animal info (8 week old, male, C57BL/6J ); RAGE-apt is a DNA aptamer against the advanced glycation end products receptor; gene therapy;


Agents: DNAzymes, DT912
Vehicle: Saline; Route: IP; Species (nude); Pump: 1002; Duration: 14 days;
ALZET Comments: animal info (female, BLAB/c, 4-6 weeks old); cancer (Prostate PC3); “we here employed an osmotic pump as a delivery vehicle for DNAzymes via the abdominal route and demonstrated a viable means for efficient DNAzyme delivery” pg 548; Dose (12.5 mg/kg/day);

Q4843: B. Koenig, et al. Long term study of deoxyribozyme administration to XT-1 mRNA promotes corticospinal tract regeneration and improves behavioral outcome after spinal cord injury. Experimental Neurology 2016;276(51-58

Agents: DNAXT-1as
Vehicle: Not Stated; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 1007D; Duration: 2 weeks;
ALZET Comments: Controls received mp w/ control enzyme or PBS; animal info (female, Wistar, 200-250g); pumps replaced every week; spinal cord injury; post op. care (Baytril; manual bladder emptying; Rimadyl); behavioral testing (horizontal ladder task); used self-made intrathecal catheter from 32-gauge polyurethane; enzyme inhibitor (DNA enzyme of mRNA of xylosyltransferase-1);

Q5375: C. Huang, et al. Thioredoxin interacting protein (TXNIP) regulates tubular autophagy and mitophagy in diabetic nephropathy through the mTOR signaling pathway. Sci Rep 2016;6(29196

Agents: DNAzymes, Scrambled or TXNIP
Vehicle: Saline; Route: SC; Species: Rat; Pump: 2006; Duration: 12 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, heterozygous rats); functionality of mp verified by blood glucose levels (AMES glucometer); pumps replaced every 6 weeks; diabetes; Inhibition of TXNIP using DNA-zyme imporves authophagy and mitophagy in diabetic nephropathy; Resultant plasma level (pg. 10);


Agents: Thioredoxin-interacting protein DNAzyme
Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2006; Duration: 12 weeks;
ALZET Comments: Controls received mp w/ scrambled TXNIP DNAzyme; animal info (female, heterozygous (mRen-2)27, 6 weeks old); pumps replaced every 6 weeks; cardiovascular, diabetes; Thioredoxin-interacting protein aka TXNIP;
**Agents:** CpGB DNA  
**Vehicle:** Not Stated  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 7 days; 28 days  
**ALZET Comments:** Controls received mp w/ PBS; animal info (male, C57BL6 or TNFα -/- or IFNγ -/- or CXCR3 -/- or CCR5 -/- or CCL2 -/- or TLR9 -/-); functionality of mp verified by immunofluorescence at pump outlet; gene therapy; immunology; CpGB DNA is a TLR9 ligand;  

Q4752: X. H. Yu, et al. Chemosensitization of Solid Tumors by Inhibition of Bcl-xL Expression Using DNAzyme. ONCOTARGET 2014;5(9)9039-9048  
**Agents:** DNAzyme oligonucleotid  
**Vehicle:** Saline  
**Species:** Mice (nude)  
**Pump:** 1002  
**Duration:** 14 days  
**ALZET Comments:** Animal info (female, Balb/C, 4 weeks old); functionality of mp verified by plasma levels and residual volumes; cancer (prostate adenocarcinoma); "Analysis showed that the DNAzyme was stable over the treatment period and the ALZET osmotic pump provided a consistent delivery of the DNAzyme in vivo" pg 9044;  

**Agents:** Plasmid DNA-lipid complex  
**Vehicle:** Not Stated  
**Species:** Mice (SCID, CD-1)  
**Pump:** Not Stated  
**Duration:** Not Stated  
**ALZET Comments:** Therapeutic indication (Gene therapy); Brain coordinates: 3 mm lateral and 2 mm caudal to bregma;  

**Agents:** DNA, RNA, small interfering  
**Vehicle:** Lipopolyplexes, (PEI F25-LMW, DPPC)  
**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  

**Agents:** DNA, cytosine-guanine  
**Vehicle:** Not Stated  
**Route:** CSF/CNS  
**Species:** Mice  
**Pump:** 2004  
**Duration:** 4 weeks  
**ALZET Comments:** Controls received mp w/ saline; animal info (male, C57BL/6, TLR9-deficient); ALZET brain infusion kit 2 used; stress/adverse reaction: (see pg. 1117) "One C57BL/6 mouse died because of complications during the operation, and 1 TLR9-deficient mouse died for unknown reasons 2 weeks after implantation of the pump".  

**Agents:** DNAXTas  
**Vehicle:** Not Stated  
**Route:** CSF/CNS (intrathecal)  
**Species:** Rat  
**Pump:** 1007D  
**Duration:** 14 days  
**ALZET Comments:** Controls received mp w/ control deoxyribozyme or mp w/ saline; pumps replaced after 7 days; post op. care (gentamicin); animal info (female, Sprague Dawley, 200-225 g.); control also known as DNAXTmb; schematic w/ pump on fig. 1; custom cannula used  

**Agents:** DNA, plasmid  
**Vehicle:** Gene, HIV-2 gp140  
**Route:** SC  
**Species:** Mice  
**Pump:** 2004  
**Duration:** 28 days  
**ALZET Comments:** 28 day stability verified by agarose gel electrophoresis; immunology; different methods of immunization used; genetic immunization; DNA did not adhere to the osmotic minipump after 1 month since DNA concentration remained stable and intact

Agents: DNA, naked; vascular endothelial growth factor; DNA Vehicle: Water; Route: Intramuscular (left quadriceps muscle); Species: Mice; Pump: 2001; Duration: 7 days;

ALZET Comments: Controls received mp w/ saline; tissue perfusion (quadriceps muscle); gene therapy; fenestrated catheter; pump implanted IP; “we have shown that when using plasmid DNA, continuous administration is superior to multiple simultaneous IM injections.” (p. 4647)


Agents: Embryonic DNA Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001D; Duration: Not Stated;

ALZET Comments: Dose (80 ug/hr/day); animal info (Wistar, Female, Pregnant); Embryonic DNA aka BrdU; dependence;


Agents: Methylisothiourea, S-; adenovirus vector; gene, mouse iNOS cDNA sequence Vehicle: Saline; Dye, methlene blue; Dye, India black ink; PBS; Route: SC (wound healing site); Species: Rat; Pump: 2001; 2ML1; Duration: 7 days;

ALZET Comments: Controls received mp w/ saline; functionality of mp verified by dye infusion; gene therapy; enzyme inhibitor; methylisothiourea,S- is an inducible nitric oxide synthase inhibitor (iNOS inhibitor); wound healing; SC-implanted pumps infused 2 hydroxyproline sponges via catheter; initial studies used 2ML1 pumps to infuse dyes in order to assess the feasibility of direct infusion with pumps; iNOS inhibitor infusion was with 2001 pumps; pumps were designed to infuse directly into SC implanted polyvinyl sponges at the wound site; Adenovirus vector was dissolved in PBS, iNOS inhibitor was delivered in saline; diagram of pump-catheter assembly and location (p. 18); “Dye infusion demonstrated both grossly and microscopically excellent delivery of the infusate to wound sponges” (p. 18);

RNA (2007-Present)


Agents: Anti-eRNA oligos Vehicle: CSF/ artificial; Route: CNS/CSF; Species: Mice; Pump: 1003D; Duration: 3 days;

ALZET Comments: Dose: (8.3 pmole/ul); animal info (3 months old, 20-30 g, C57BL/6N); antisense (eRNA_06347: 5′-GATTTGGAATTGCTAG-3′ ; eRNA_093384: 5′-GGAAGCAGGTGAACAG-3′); ALZET brain infusion kit 3 used; ischemia (Cerebral);


Agents: siRNA Vehicle: Not Stated; Route: CSF/CNS (intratumoral); Species: Mice; Pump: 1002; Duration: 14 days;

ALZET Comments: Dose: (350 ug/kg); neurodegenerative (brain diseases); gene therapy;


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);

Q8576: J. E. Kim, et al. PLPP/CIN-mediated Mdm2 dephosphorylation increases seizure susceptibility via abrogating PSD95 ubiquitination. Exp Neurol 2020;331(113383

Agents: siRNA, Mdm2 Vehicle: Not stated; Route: CNS/CSF (lateral cerebral ventricle); Species: Mice; Pump: 1007D; Duration: 1 day;

ALZET Comments: Dose (20 μM); animal info (PLPP/CIN−/− mice); ALZET brain infusion kit 3 used; Brain coordinates (2.0 mm depth from bregma); dependence;
Agents: siRNA; TRPV1 Vehicle: CSF, artificial; Route: CSF/CNS (intrathecal); Species: Rat; Pump: Not stated; Duration: 3 days;
ALZET Comments: Dose (0.5 nmol/μL/h); Controls received mp w/ vehicle; animal info (Male Wistar rats weighing 250 to 320 g); behavioral testing (Mechanical or Thermal Stimulation); dependence;

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);

Agents: DJ-1-specific siRNA Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days;
ALZET Comments: Dose (3 ug/day); animal info (Male, C57Bl/6J, ); enzyme inhibitor (DJ-1 siRNA inhibits renal ROS production); cyanoacrylate adhesive; cardiovascular;

Agents: Bevacizumab; RNA, small interfering (anti-HIF-1α/PEG); Immunotoxin, DTAT/DTATEGF; 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.

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;

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);

Q8810: R. Prince, et al. Targeting anticoagulant protein S to improve hemostasis in hemophilia. Thrombosis and Hemostasis 2018;131(Agents: siRNA ; control siRNA Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2001; Duration: Not Stated;
ALZET Comments: Dose (1 mg/kg/day); animal info (10 weeks old, C57BL/6J); siRNA aka s72206, control siRNA aka 44S9405; cardiovascular;

**Agents:** YY1-siRNA  **Vehicle:** Not stated;  **Route:** CSF/CNS;  **Species:** Mice;  **Pump:** Not stated;  **Duration:** 4 days;  
**ALZET Comments:** animal info (Male, C57B/6, 25-35 g); Brain coordinates (mediolateral=1.0 mm, anteroposterior=0.2 mm; dorsoventral=3.1 mm); ischemia (Cerebral);


**Agents:** SNX5-specific or non silencing snRNA  **Vehicle:** Not stated;  **Route:** SC;  **Species:** Mice;  **Pump:** 1007D;  **Duration:** 7 days;  
**ALZET Comments:** Dose (3 ug/day); animal info (Male, C57BL/6J, 1 year old); SNX5-specific  aka sorting nexin 5 ; gene therapy;

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); Nω-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);


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


**Agents:** RNA, small interfering; L-NAME; PACMA31  **Vehicle:** Saline;  **Route:** CSF/CNS (left 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);


**Agents:** siHes1, scRNA NPs  **Vehicle:** Not Stated;  **Route:** CSF/CNS;  **Species:** Guinea Pig;  **Pump:** 2001;  **Duration:** 1 day;  
**ALZET Comments:** Dose (1 uL/hr); animal info (200-250 g, Female); siHes1 aka Hes1 siRNA; bilateral cannula used; cyanoacrylate adhesive; dependence;


**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);

**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);


**Agents:** RNA, micro 146a  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (corpus callosum);  
**Species:** Mice;  
**Pump:** 1007D;  
**Duration:** 7 days;  
**ALZET Comments:** animal info (8-10 week old male C57BL/6 mice); enzyme inhibitor (interleukin-1 receptor-associated kinase 1); Brain coordinates (0 mm to the bregma, 1 mm bilateral to the midline, 1.8 mm depth from the surface of the cortex);


**Agents:** RNA, small interfering  
**Vehicle:** Not Stated;  
**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;


**Agents:** shRNA, NM_133534.1; antibody, CX3CR1  
**Vehicle:** NaCl;  
**Route:** CSF/CNS;  
**Species:** Rat;  
**Pump:** 1003D;  
**Duration:** 3 days;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Sprague Dawley, P7); ALZET brain infusion kit 3 used; Brain coordinates;

Q6753: P. G. Quaresma, et al. Cdc2-like kinase 2 in the hypothalamus is necessary to maintain energy homeostasis. Int J Obes (Lond) 2017;290(115-122

**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;


**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);


**Agents:** RNA, small interfering; TRPC6; U0126  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (right lateral ventricle);  
**Species:** Rat;  
**Pump:** 1007D;  
**Duration:** Not Stated;  
**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);
Agents: RNA, small interfering (PDI; DTNB); bactracin; 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); Brain coordinates;

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);

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);

Agents: RNA, micro Vehicle: CSF, artificial; Route: CSF/CNS (right lateral ventricle); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit 2 used; behavioral testing (Rotarod); Dose (12.5 uM);