References on the Administration of Viral Vectors
Using ALZET® Osmotic Pumps

Agents: Estrogen receptor beta; Oxytocin; Lentivirus Vehicle: CSF, artificial; Route: CSF/CNS; Species: Mice; Pump: 2002; Duration: 2 weeks;
ALZET Comments: Animal info (Male mice, 6 weeks old); behavioral testing (Animal Behavior Test); Brain coordinates (anteroposterior (AP) = -1.4, mediolateral (ML) = ±3.5, dorsoventral (DV) = -5.1); neurodegenerative (Autism spectrum disorders);

Agents: Lentivirus Vehicle: CSF, artificial; Route: CSF/CNS (amygdala); Species: Rat; Pump: 2002; Duration: 1 week;
ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague–Dawley 2-month female rats); dependence;

Q9343: S. Li, et al. FGF22 promotes generation of ribbon synapses through downregulating MEF2D. Aging 2020;
Agents: Adeno-associated virus Vehicle: Not Stated; Route: Ear (cochlea); Species: Mice; Pump: 1004; Duration: 4 days;
ALZET Comments: Animal info (male CBA/J mice, aged 6 weeks, weight around 18g);

Q8160: K. Arnaud, et al. Non-cell autonomous choroid plexus-derived sAPPα regulates adult hippocampus proliferation and plasticity. Hyper Articles en Ligne 2020;
Agents: Cre recombinase protein, Vectored Vehicle: Saline, DMSO; Route: CSF/CNS (right lateral ventrile); Species: Mice;
Pump: Not stated; Duration: 15 days;
ALZET Comments: Dose (3.5 μg); 1.8% NaCl, 15% DMSO used; Controls received mp w/ vehicle; animal info (Janvier Mice); behavioral testing (water maze); Vectored Cre recombinase protein aka Cre-Tat; Brain coordinates (x, -0.58 mm; y, +1.28 mm; z, -2 mm); neurodegenerative (Alzheimer disease);

Agents: Adeno-associated viral vector serotype 9 Route: SC; Species: Mice; Pump: 2001D; Duration: 1 day;
ALZET Comments: Dose (2 ul/min/day); animal info (12-20 weeks old, Male, C57BL/6); neurodegenerative (Adrenoleukodystrophy);

Q5606: W. Xie, et al. Resveratrol ameliorates prenatal progestin exposure-induced autism-like behavior through ERβ activation. Mol Autism 2018;9(43
Agents: Lentivirus, ERβ knockdown Vehicle: CSF, artificial; Route: CSF/CNS (amygdala); Species: Rat; Pump: 2002;
ALZET Comments: animal info (8 week old Sprague Dawley rat); behavioral testing (marble burying test and social interaction test); 26 Gauge Plastics One cannula used; Brain coordinates (~ 2.0 mm posterior to the bregma, ± 4.2 mm from the midline, and ~ 7.2 mm from the skull surface);

Agents: Virus, recombinant adeno-associated Vehicle: Saline; Route: CSF/CNS (subarachnoid space); CSF/CNS (lateral ventricle); Species: Mice; Pump: 2001D; Duration: 40, 42 hours;
ALZET Comments: Dose (1·10^{11}, 2·10^{12} GC in 200 μL); Controls received mp w/ vehicle; animal info (6 weeks, male and female, C57BL/6J, 20g); post op. care (200 μL of 0.9% saline by i.p. injection); comparison of IT injection vs mp; recombinant adeno-associated viruses (rAAVs) packaged in several serotypes such as AAV9 and AAV.rh10 can cross the BBB and transduce neurons and glia in rodents and nonhuman primates; Brain coordinates ((-0.9,-0.2) for the left ventricle, or (+0.9, -0.2) for the right ventricle); Cannula placement verified via stereotaxic frame; cyanoacrylate adhesive for icv delivery (Loctite); gene therapy; good methods (detailed pump installation instructions for IT and ICV delivery of agent on p.77-83); “IT pump infusion resulted in more widespread and higher transduction of the spinal cord than a bolus IT injection” pg.83; recombinant adeno-associated virus serotype 9 (rAAV9) used for examples;

**Agents:** Lentivirus, ER beta  
**Vehicle:** CSF, artificial  
**Route:** CSF/CNS (amygdala)  
**Species:** Rat  
**Pump:** 2002  
**Duration:** 2 weeks  

**ALZET Comments:** Controls received mp w/ empty lentivirus; animal info (male, Sprague Dawley, 8 weeks old); functionality of mp verified by India ink injection; behavioral testing (marbles burying test, social interaction, elevated plus maze, open-field test); gene therapy; Used Plastics One cannula;


**Agents:** Angiotensin II; Mir-21 lentivirus  
**Vehicle:** Saline  
**Route:** IP  
**Species:** Rat  
**Pump:** 2004; 2ML4  
**Duration:** Not Stated  

**ALZET Comments:** Dose (25 mg/kg/h); Controls received mp w/ vehicle; animal info (Male Wistar rats (200–300 g); Therapeutic indication (liver fibrosis);


**Agents:** Thyroxin, L-; Adenovirus vector; Gene, green fluorescent protein; Gene, AMP-activated protein kinase  
**Vehicle:** Saline  
**Route:** CSF/CNS (hypothalamus)  
**Species:** Rat  
**Pump:** 1007D  
**Duration:** 7, 21 days  

**ALZET Comments:** bilateral cannula used; animal info (200-250g); gene therapy; Therapeutic indication (Browning, thyroid hormones);


**Agents:** Viral vector, adeno-associated (AAV9, AAV2g0); Gene, CBh-ScGFP  
**Vehicle:** Not Stated  
**Route:** CSF/CNS (intrathecal)  
**Species:** Mice  
**Pump:** 2001D  
**Duration:** 24 hrs  

**ALZET Comments:** animal info (8 weeks old C57/Bl6 male mice); comparison of IT bolus injections vs mp; ALZET mouse intrathecal catheter used (lumbar cannulation); gene therapy;


**Agents:** Virus, adeno-associated shjmjd3  
**Route:** CSF/CNS (intrathecal)  
**Species:** Rat  
**Pump:** 1003D  

**ALZET Comments:** Controls received mp w/ control adeno-associated virus; animal info (adult male Sprague-Dawley rats weighing 250-270g); spinal cord injury;


**Agents:** Cathepsin B; Scrambled vector (pSV); Plasmid  
**Vehicle:** PBS (mock)  
**Species:** Mice (nude)  
**Pump:** 1002  

**ALZET Comments:** Controls received mp w/ vehicle; cancer (Glioma); Therapeutic indication (Cancer, Glioma); Dose (1.5 mg/mL);


**Agents:** Oligonucleotide, antisense; plasmid, scrambled vector, pSV; PBS  
**Route:** SC  
**Species:** Mice (nude)  
**Pump:** 2004  

**ALZET Comments:** Cancer (glioblastoma); animal info (nu/nu mice)


**Agents:** Plasmid, scrambled vector; RNA, small interfering  
**Species:** Mice (nude)  
**Pump:** 2004  

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


**Agents:** Plasmid, scrambled vector; plasmid, PAK4si  
**Species:** Mice (nude)  
**Pump:** 2004  

**ALZET Comments:** Animal info (female, nu/nu)

Agents: Plasmid, scrambled vector, pSV; plasmid, pUC; Species: Mice (nu/nu, athymic); pUC is a bicistronic shRNA constructs targeting uPAR and cathepsin B

ALZET Comments: Control animals received mp w/ scrambled vector; animal info (nu/nu, athymic); pUC is a bicistronic shRNA constructs targeting uPAR and cathepsin B


Agents: Plasmid, puPA; plasmid, upAR; plasmid, pU2; plasmid, vector Vehicle: PBS; Route: CSF/CNS; Species: Mice (nude); Cancer (glioblastoma)

ALZET Comments: Cancer (glioblastoma)


Agents: Plasmid, scrambled vector; plasmid, bi-cistronic, RNA, small interfering Vehicle: Not Stated; Route: Not Stated; Species: Mice (nude); Pump: 2001; Duration: Not Stated;

ALZET Comments: Animal info (4-6 wks old)


Agents: Cathepsin B; vector, scrambled Vehicle: Not Stated; Route: Not Stated; Species: Mice (nude); Pump: 1002; Duration: Not Stated;

ALZET Comments: Animal info (athymic, nu/nu, 5-7 wks old)


Agents: Amyloid protein, beta; virus, adeno-associated Vehicle: DMSO, Hcl; Route: CSF/CNS (ventricle); Species: mice (transgenic); Pump: Not Stated; Duration: Not Stated;

ALZET Comments: ALZET brain infusion kit used; behavioral testing (Morris water maze, passive avoidance, novel object recognition); gene therapy (viral vector); “Use of an osmotic mini-pump to deliver Ab has the advantage of providing the continuous release and presence of Ab in the brain throughout the experiment.” Pg. 353; Therapeutic indication (Alzheimer’s disease); Dose (Amyloid beta: 100 μM, DMSO:);


Agents: Plasmid, uPAR/cathepsin B; plasmid, scrambled vector Route: IP; Species: Mice (nude); Duration: 5 weeks;

ALZET Comments: Controls received mp w/ PBS; cancer (glioma)


Agents: Nerve growth factor; NT-3; adenovirus; brain-derived neurotrophic factor; perilymph, artificial; glial-derived neurotrophic factor; ciliary neurotrophic factor; fibroblast growth factor, acidic; fibroblast growth factor-1; fibroblast growth factor-2; fibroblast growth factor, basic Vehicle: Not Stated; Route: Ear (cochlea); ear (scala tympani); Species: Guinea pig; Pump: Not Stated; Duration: 1,2,4,8 weeks; 15-60, 11-12, 26 days;

ALZET Comments: Comparison of polymers, hydrogels, gene therapy, cell-based therapy, and injections vs. mp; long-term study; pumps replaced; no stress (see pg. 350); half-life (p. 344), short in blood; gene therapy; peptides; animal info (deafened); Table 2; “The mini-osmotic pump device is ideally suited to studying the effects of neurotrophic factors in the cochlea experimentally.” (p. 350); tissue perfusion


Agents: Adeno-associated virus serotype 8 vector, recomb. Vehicle: Not Stated; Route: CSF/CNS (intratumoral); Species: Rat; Pump: 2001D; Duration: 24 hours;

ALZET Comments: Controls received mp w/ AAV control; cancer (glioblastoma multiforme, u-251 MG); gene therapy; animal info (male, athymic, 6 wk. old); rAAV contains soluble VEGF inhibitor, sVEGFR1/R2; “Implantation of the mini pump allows the slow infusion of a rAAV vector...to transduce more effectively the intracranial tumor mass.” (pg. 962); antiangiogenesis

**Agents:** Virus, synthetic RNA  
**Vehicle:** Not Stated;  
**Route:** Intratumoral;  
**Species:** Mice (nude);  
**ALZET Comments:** Cancer (glioblastoma); “Control animals within 30 days after tumor implantation, all treated animals survived for >1 year and were completely cured.” (p. E738); gene therapy


**Agents:** Virus, sinbis suspension  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (hippocampus); SC;  
**Species:** Mice;  
**Pump:** 1007D;  
**Duration:** 4,7 days;  
**ALZET Comments:** Controls received mp w/ sin-EGFP

P7335: H. Yin, et al. Kallikrein/kinin protects against myocardial apoptosis after ischemia/reperfusion via Akt-glycogen synthase kinase-3 and Akt-Bad-14-3-3 signaling pathways*. Journal of Biological Chemistry 2005;280(9):4681-4689

**Agents:** RNA, small interfering; human cytomegalovirus promoter  
**Vehicle:** Empty vector;  
**Route:** CSF/CNS;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 5 weeks;  
**ALZET Comments:** Cancer (glioblastoma); siRNA against mmp-9 and cathepsin; antiangiogenesis; gene therapy


**Agents:** RNA, small interfering; virus, EV/SV vector  
**Vehicle:** PBS;  
**Route:** Ear (cochlea);  
**Species:** Guinea pig;  
**Pump:** 1007D;  
**Duration:** 1 week;  
**ALZET Comments:** Gene therapy; cochlea cannulated with PE10 attached to PE50; virus contained gene for brain-derived neurotrophic factor and/or green fluorescent protein; tissue perfusion (cochlea)


**Agents:** Virus, adeno-associated; Gene, green fluorescent protein; Gene, brain-derived neurotrophic factor  
**Vehicle:** PBS;  
**Route:** Ear (cochlea);  
**Species:** Guinea pig;  
**Pump:** 1007D;  
**Duration:** Not Stated;  
**ALZET Comments:** Gene therapy; cochlea cannulated with PE10 attached to PE50; virus contained gene for brain-derived neurotrophic factor and/or green fluorescent protein; tissue perfusion (cochlea)


**Agents:** Adenovirus; Gene, beta-galactosidase;  
**Vehicle:** Perilymph, artificial;  
**Route:** Ear (cochlea);  
**Species:** Guinea pig;  
**Pump:** 2001;  
**Duration:** Not Stated;  
**ALZET Comments:** Controls received mp w/ vehicle; tissue perfusion (scala tympani); functionality of mp verified by transgene expression of b-gal; gene therapy
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Bibliography


Agents: Adenovirus vector; Virus, adeno-associated Vehicle: Perilymph, artificial; Route: Ear (scala tympani); Species: Guinea pig; Pump: 2001; Duration: 7 days;

ALZET Comments: Controls received mp w/ vehicle, and no treatment to contralateral ear; no stress (see pg. 778); good methods; gene therapy; cyanoacrylate adhesive; tissue perfusion (scala tympani)


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);


Agents: Lentivirus; gene, green fluorescent protein Vehicle: Saline; PBS; Route: Ear (cochlea); Species: Guinea pig; Pump: 1007D; Duration: 8, 3 days;

ALZET Comments: Controls received mp w/vehicle; tissue perfusion (scala tympani); gene therapy


Agents: Virus, adeno-associated; Gene, lacZ; Gene, green fluorescent protein Vehicle: Saline; Route: Ear (cochlea); Species: Guinea pig; Pump: Not Stated; Duration: Not Stated;

ALZET Comments: Controls received mp w/vehicle; tissue perfusion (cochlea); functionality of mp verified by gene expression; gene therapy


Agents: Virus, adeno-associated; Gene, green fluorescent protein; Gene, beta-galactosidase Vehicle: PBS; Route: Ear (cochlea); Species: Guinea pig; Pump: 1007D; Duration: 7 days;

ALZET Comments: Controls received mp w/vehicle, mp w/reporter gene, or no pump; tissue perfusion (scala tympani); gene therapy


Agents: Virus, adeno-associated; Gene, green fluorescent protein Vehicle: PBS, Route: Ear (cochlea); Species: Guinea pig; Pump: 1007D; Duration: 2, 7 days;

ALZET Comments: Controls received mp w/saline or mp w/AAV-Bgal; tissue perfusion (scala tympani); good methods (p.141); gene therapy

**Agents:** Liposomes; Gene, herpes simplex virus thymidine kinase; Gene, lacZ **Vehicle:** Not Stated; **Route:** CSF/CNS (caudate nucleus); **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;

**ALZET Comments:** controls received mp w/LacZ gene; tissue perfusion (tumor); functionality of mp verified by gene expression; comparison of intracerebral injections vs. mp; no stress (see pg.473); stability verified by gene expression; ALZET brain infusion kit used; cancer; gene therapy; “DNA-liposome complexes were stable within minipumps at body temperature (37C) for 1-3 days.” (pg.474); “Continuous administration of DNA-liposome complexes did not result in significant in vivo toxicity.” (pg.474)


**Agents:** Virus, adeno-associated, with bacterial gene seq **Vehicle:** PBS; **Route:** ear (cochlea); **Species:** Guinea pig; **Pump:** 1007D; **Duration:** 2 weeks;

**ALZET Comments:** controls received saline infusion; tissue perfusion (cochlea); Gene therapy