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

Q5606: W. Xie, et al. Resveratrol ameliorates prenatal progestin exposure-induced autism-like behavior through ERbeta activation. Mol Autism 2018;9(43
Agents: Lentivirus, ERβ knockdown Vehicle: CSF, artificial; Route: CSF/CNS (amygdala); Species: Rat; Pump: 2002; Duration: 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: 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: 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: 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 Vehicle: Route: CSF/CNS (intrathecal); Species: Rat; Pump: 1003D; Duration: 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); Route: Species: Mice (nude); Pump: 1002; Duration: 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

Vehicle: Route: SC; Species: Mice (nu/nu); Pump: 2004; Duration: ALZET Comments: Cancer (glioblastoma); animal info (nu/nu mice)


Agents: Plasmid, scrambled vector; RNA, small interfering Vehicle: Route: Species: Mice (nu/nu); Pump: 2004; Duration: ALZET Comments: Animal info (nu/nu, 4-6 wks old, athymic); MMP-2 siRNA


Agents: Plasmid, scrambled vector, pSV; plasmid, PAK4si Vehicle: Route: Species: Mice (nu/nu); Pump: Duration: ALZET Comments: Animal info (female, nu/nu)


Agents: Plasmid, scrambled vector, pSV; plasmid, pUC Vehicle: Route: Species: Mice (nu/nu); Pump: Duration: 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

Q1958: H. Raghu, et al. Specific knockdown of uPA/uPAR attenuates invasion in glioblastoma cells and xenografts by inhibition of cleavage and trafficking of Notch -1 receptor. Molecular Cancer 2011;10(;):U1-U15

Agents: Plasmid, pT1U; plasmid, upAR; plasmid, pU2; plasmid, vector Vehicle: PBS; Route: CSF/CNS; Species: Mice (nu/nu); Pump: Duration: ALZET Comments: Cancer (glioblastoma)


Agents: Plasmid, scrambled vector; plasmid, bi-cistronic, RNA, small interfering Vehicle: Route: Species: Mice (nu/nu); Pump: 2001; Duration: ALZET Comments: Animal info (4-6 wks old)


Agents: Cathepsin B; vector, scrambled Vehicle: Route: Species: Mice (nu/nu); Pump: 1002; Duration: 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: Duration: 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 Vehicle: Route: IP; Species: Mice (nu/nu); Pump: 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:** Route: Ear (cochlea); ear (scala tympani); **Species:** Guinea pig;

**Pump:** **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

**P7904:** T. C. Harding, *et al.* AAV serotype 8-mediated gene delivery of a soluble VEGF receptor to the CNS for the treatment of glioblastoma. MOLECULAR THERAPY 2006;13(5):956-966

**Agents:** Adeno-associated virus serotype 8 vector, recomb. **Vehicle:** 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:** Route: Intratumoral; **Species:** Mice (nude); **Pump:** 1007D; **Duration:** 4,7 days;

**ALZET Comments:** Controls received mp w/ sin-EGFP

**P6905:** Y. Zhang, *et al.* Phospholipase D1-promoted release of tissue plasminogen activator facilitates neurite outgrowth. Journal of Neuroscience 2005;25(7):1797-1805

**Agents:** Virus, sinbis suspension **Vehicle:** Route: CSF/CNS (hippocampus); SC; **Species:** Mice; **Pump:** Duration: **ALZET Comments:**

**P6720:** C. S. Gondi, *et al.* RNAi-mediated inhibition of cathepsin B and uPAR leads to decreased cell invasion, angiogenesis and tumor growth in gliomas. ONCOGENE 2004;23(27):4681-4689

**Agents:** RNA, small interfering; Virus, EV/SV vector **Vehicle:** PBS; **Species:** Mice (nude); **Pump:** **Duration:** **ALZET Comments:**


**Agents:** Gene vectors, virus **Vehicle:** Route: Ear (cochlea); **Species:** Guinea pig; **Pump:** 1007D; **Duration:** **ALZET Comments:**

**P5540:** A. K. Lalwani, *et al.* In vitro and in vivo assessment of the ability of adeno-associated virus-brain-derived neurotrophic factor to enhance spiral ganglion cell survival following ototoxic insult. Laryngoscope 2002;112(8):1325-1334
Agents: Virus, adeno-associated; Gene, green fluorescent protein; Gene, brain-derived neurotrophic factor 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: Adenovirus; Gene, beta-galactosidase; Vehicle: Perilymph, artificial; Route: Ear (scala tympani); Species: Guinea pig; Pump: 2001; Duration: ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by transgene expression of b-gal; gene therapy

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: Influenza virus nucleoprotein-derived peptide; interferon, gamma Vehicle: PBS; Route: SC; Species: Mice; Pump: 1003D; Duration: 3 days;
ALZET Comments: animal info (C57BL/6 mice; 8-12 week old); comparison of SC injections vs mp; Flu pep tide administered continuously by osmotic pump with IFN injection elicited CTL response, whereas Flu peptide administered by injection with IFN did not (Figs 3 and 4); Therapeutic indication (antigen immunization);

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: Duration: no duration posted;
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: 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