



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

- Q5606:** W. Xie, *et al.* Resveratrol ameliorates prenatal progesterone 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);
- Q5940:** Y. Zou, *et al.* Prenatal levonorgestrel exposure induces autism-like behavior in offspring through ERbeta suppression in the amygdala. *Mol Autism* 2017;8(46)
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;
- Q6706:** Z. W. Ning, *et al.* MicroRNA-21 Mediates Angiotensin II-Induced Liver Fibrosis by Activating NLRP3 Inflammasome/IL-1beta Axis via Targeting Smad7 and Spry1. *Antioxid Redox Signal* 2017;27(1):1-20
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);
- Q5829:** N. Martinez-Sanchez, *et al.* Thyroid hormones induce browning of white fat. *J Endocrinol* 2017;232(2):351-362
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);
- Q5052:** G. Murlidharan, *et al.* CNS-restricted Transduction and CRISPR/Cas9-mediated Gene Deletion with an Engineered AAV Vector. *Mol Ther Nucleic Acids* 2016;5(7):
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;
- Q6685:** J. Y. Lee, *et al.* Jmjd3 mediates blood-spinal cord barrier disruption after spinal cord injury by regulating MMP-3 and MMP-9 expressions. *Neurobiol Dis* 2016;95(66-81)
Agents: Virus, adeno-associated shjmd3 **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;
- Q5612:** R. Rao Malla, *et al.* Knockdown of cathepsin B and uPAR inhibits CD151 and alpha3beta1 integrin-mediated cell adhesion and invasion in glioma. *Mol Carcinog* 2013;52(10):777-90
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);
- Q2986:** D. Kesanakurti, *et al.* Essential role of cooperative NF-kappaB and Stat3 recruitment to ICAM-1 intronic consensus elements in the regulation of radiation-induced invasion and migration in glioma. *ONCOGENE* 2013;32(43):5144-5155



Agents: Oligonucleotide, antisense; plasmid, scrambled vector, pSV; **PBS Vehicle: Route:** SC; **Species:** Mice (nude); **Pump:** 2004; **Duration:** **ALZET Comments:** Cancer (glioblastoma); animal info (nu/nu mice)

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: Route: Species:** Mice (nude); **Pump:** 2004; **Duration:** **ALZET Comments:** Animal info (nu/nu, 4-6 wks old, athymic); MMP-2 siRNA

Q2563: D. Kesanakurti, *et al.* Functional cooperativity by direct interaction between PAK4 and MMP-2 in the regulation of anoikis resistance, migration and invasion in glioma. *Cell Death & Disease* 2012;3(;):U78-U90

Agents: Plasmid, scrambled vector; plasmid, PAK4si **Vehicle: Route: Species:** Mice (nude); **Pump:** 2004; **Duration:** **ALZET Comments:** Animal info (female, nu/nu)

Q2565: V. R. Gogineni, *et al.* uPAR and cathepsin B shRNA impedes TGF-beta1-driven proliferation and invasion of meningioma cells in a XIAP-dependent pathway. *Cell Death & Disease* 2012;3(;):U20-U29

Agents: Plasmid, scrambled vector, pSV; plasmid, pUC **Vehicle: Route: Species:** Mice (nude); **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, puPA; plasmid, upAR; plasmid, pU2; plasmid, vector **Vehicle: PBS; Route:** CSF/CNS; **Species:** Mice (nude); **Pump: Duration:** **ALZET Comments:** Cancer (glioblastoma)

Q1640: A. K. Nalla, *et al.* Suppression of uPA and uPAR blocks radiation-induced MCP-1 mediated recruitment of endothelial cells in meningioma. *Cellular Signalling* 2011;23(8):1299-1310

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

Q1722: R. R. Malla, *et al.* Cathepsin B and uPAR knockdown inhibits tumor-induced angiogenesis by modulating VEGF expression in glioma. *Cancer Gene Therapy* 2011;18(6):419-434

Agents: Cathepsin B; vector, scrambled **Vehicle: Route: Species:** Mice (nude); **Pump:** 1002; **Duration:** **ALZET Comments:** Animal info (athymic, nu/nu, 5-7 wks old)

Q5575: P. A. Lawlor, *et al.* Aβ Infusion and Related Models of Alzheimer Dementia. 2011;48(347-370

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:);

Q2224: S. Gopinath, *et al.* Mechanism of p27 upregulation induced by downregulation of cathepsin B and uPAR in glioma. *Molecular Oncology* 2011;5(5):426-437

Agents: Plasmid, uPAR/cathepsin B; plasmid, scrambled vector **Vehicle: Route:** IP; **Species:** Mice (nude); **Pump: Duration:** 5 weeks; **ALZET Comments:** Controls received mp w/ PBS; cancer (glioma)

R0239: R. T. Richardson, *et al.* Inner ear therapy for neural preservation. *AUDIOLOGY AND NEURO-OTOLOGY* 2006;11(6):343-356

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:** 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

R0238: S. Boeckle, *et al.* Optimizing targeted gene delivery: Chemical modification of viral vectors and synthesis of artificial virus vector systems. *AAPS Journal* 2006;8(4):E731-E742

Agents: Virus, synthetic RNA **Vehicle:** **Route:** Intratumoral; **Species:** Mice (nude); **Pump:** **Duration:** **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

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:** 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-Bad¹⁴⁻³⁻³ signaling pathways*. *Journal of Biological Chemistry* 2005;280(9):8022-8030

Agents: Virus, adeno-associated; cytomegalovirus promoter **Vehicle:** **Route:** IP; **Species:** Rat; **Pump:** **Duration:** **ALZET Comments:** Cardiovascular; gene therapy; adenoviral vector harboring the human tissue kallikrein cDNA (ad. CMV-TK)

P6618: S. S. Lakka, *et al.* Inhibition of cathepsin B and MMP-9 gene expression in glioblastoma cell line via RNA interference reduces tumor cell invasion, tumor growth and angiogenesis. *ONCOGENE* 2004;23(27):4681-4689

Agents: RNA, small interfering; human cytomegalovirus promoter **Vehicle:** Empty vector; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2004; **Duration:** 5 weeks;

ALZET Comments: Cancer (glioblastoma); siRNA against mmp-9 and cathepsin; antiangiogenesis; gene therapy

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(8):8486-8496

Agents: RNA, small interfering; Virus, EV/SV vector **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** **Duration:** **ALZET Comments:** Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioma); gene therapy; antiangiogenesis; siRNA (cathepsin B); pump model not stated (0.25 ul/hr); "...local intracranial delivery of pcu using mini-osmotic pumps effectively inhibited human malignant glioma growth."

R0164: A. K. Lalwani, *et al.* Current issues in cochlear gene transfer. *Audiol. Neurootol* 2002;7(3):146-151

Agents: Gene vectors, virus **Vehicle:** **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 1007D; **Duration:** **ALZET Comments:** Gene therapy; review of various cochlear gene delivery methods; diagram of the various delivery methods (p. 147); tissue perfusion (cochlea)

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)

P4821: A. E. Luebke, *et al.* A modified adenovirus can transfect cochlear hair cells in vivo without compromising cochlear function. *Gene Therapy* 2001;8(789-794)

Agents: Adenovirus; Gene, beta-galactosidase; **Vehicle:** Perilymph, artificial;; **Route:** Ear (cochlea);; **Species:** Guinea pig;;
Pump: 2001;; **Duration:** **ALZET Comments:** Controls received mp w/ vehicle; tissue perfusion (scala tympani); functionality of mp verified by transgene expression of b-gal; gene therapy;

P7117: A. E. Luebke, *et al.* Cochlear function and transgene expression in the guinea pig cochlea, using adenovirus and adeno-associated virus-directed gene transfer. *Human Gene Therapy* 2001;12(773-781)

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)

P4781: D. T. Efron, *et al.* A novel method of studying wound healing. *Journal of Surgical Research* 2001;98(16-20)

Agents: Methylisothiourea, S-; adenovirus vector; gene, mouse iNOS cDNA sequence **Vehicle:** Saline; Dye, methylene 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);

Q3035: Interferon-alpha: an effective adjuvant for peptide-based cytotoxic T-cell vaccines. *Kurume Med J.* 2001;48(2):171-4

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 peptide 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);

P4471: J. J. Han, *et al.* Transgene expression in the guinea pig cochlea mediated by a lentivirus-derived gene transfer vector. *Human Gene Therapy* 1999;10(1867-1873)

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;

P4028: A. K. Lalwani, *et al.* Long-term in vivo cochlear transgene expression mediated by recombinant adeno-associated virus. *Gene Therapy* 1998;5(277-281)

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

P4027: A. K. Lalwani, *et al.* Expression of adeno-associated virus integrated transgene within the mammalian vestibular organs. *Am. J. Otolaryngology* 1998;19(390-395)



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

P3859: A. K. Lalwani, *et al.* Green fluorescent protein as a reporter for gene transfer studies in the cochlea. *Hear. Res* 1997;114(139-147)

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

P3860: J. Zhu, *et al.* A continuous intracerebral gene delivery system for in vivo liposome-mediated gene therapy. *Gene Therapy* 1996;3(472-476)

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)

P3410: A. K. Lalwani, *et al.* Development of in vivo gene therapy for hearing disorders: introduction of adeno-associated virus into the cochlea of the guinea pig. *Gene Therapy* 1996;3(588-592)

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