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

<table>
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<tr>
<th>Reference ID</th>
<th>Authors</th>
<th>Title</th>
<th>Description</th>
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<tr>
<td>Q5606</td>
<td>W. Xie et al.</td>
<td>Resveratrol ameliorates prenatal progesterone exposure-induced autism-like behavior through ERbeta activation.</td>
<td>Mol Autism 2018;9(43&lt;br&gt;<strong>Agents</strong>: Lentivirus, ERβ knockdown&lt;br&gt;<strong>Vehicle</strong>: CSF, artificial&lt;br&gt;<strong>Route</strong>: CSF/CNS (amygdala)&lt;br&gt;<strong>Species</strong>: Rat&lt;br&gt;<strong>Pump</strong>: 2002&lt;br&gt;<strong>Duration</strong>: 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);</td>
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<td>Q5940</td>
<td>Y. Zou et al.</td>
<td>Prenatal levonorgestrel exposure induces autism-like behavior in offspring through ERbeta suppression in the amygdala.</td>
<td>Mol Autism 2017;8(46&lt;br&gt;<strong>Agents</strong>: Lentivirus, ER beta&lt;br&gt;<strong>Vehicle</strong>: CSF, artificial&lt;br&gt;<strong>Route</strong>: CSF/CNS (amygdala)&lt;br&gt;<strong>Species</strong>: Rat&lt;br&gt;<strong>Pump</strong>: 2002&lt;br&gt;<strong>Duration</strong>: 2 weeks&lt;br&gt;<strong>ALZET Comments</strong>: 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;</td>
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<td>Q6706</td>
<td>Z. W. Ning et al.</td>
<td>MicroRNA-21 Mediates Angiotensin II-Induced Liver Fibrosis by Activating NLRP3 Inflammasome/IL-1beta Axis via Targeting Smad7 and Spry1.</td>
<td>Antioxid Redox Signal 2017;27(1):1-20&lt;br&gt;<strong>Agents</strong>: Angiotensin II; Mir-21 lentivirus&lt;br&gt;<strong>Vehicle</strong>: Saline&lt;br&gt;<strong>Route</strong>: IP&lt;br&gt;<strong>Species</strong>: Rat&lt;br&gt;<strong>Pump</strong>: 2004; 2ML4&lt;br&gt;<strong>Duration</strong>: ALZET Comments: Dose (25 mg/kg/h); Controls received mp w/ vehicle; animal info (Male Wistar rats (200 –300 g); Therapeutic indication (liver fibrosis);</td>
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<td>Q5829</td>
<td>N. Martinez-Sanchez et al.</td>
<td>Thyroid hormones induce browning of white fat.</td>
<td>J Endocrinol 2017;232(2):351-362&lt;br&gt;<strong>Agents</strong>: Thyroxin, L-; Adenovirus vector; Gene, green fluorescent protein; Gene, AMP-activated protein kinase&lt;br&gt;<strong>Vehicle</strong>: CSF/CNS (hypothalamus)&lt;br&gt;<strong>Species</strong>: Rat&lt;br&gt;<strong>Pump</strong>: 2004; 2ML4&lt;br&gt;<strong>Duration</strong>: 7, 21 days&lt;br&gt;<strong>ALZET Comments</strong>: bilateral cannula used; animal info (200-250g); gene therapy; Therapeutic indication (Browning, thyroid hormones);</td>
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<td>Q5052</td>
<td>G. Murlidharan et al.</td>
<td>CNS-restricted Transduction and CRISPR/Cas9-mediated Gene Deletion with an Engineered AAV Vector.</td>
<td>Mol Ther Nucleic Acids 2016;5(7):&lt;br&gt;<strong>Agents</strong>: Viral vector, adeno-associated (AAV9, AAV2g0); Gene, CBh-ScGFP&lt;br&gt;<strong>Vehicle</strong>: Route: CSF/CNS (intrathecal)&lt;br&gt;<strong>Species</strong>: Mice&lt;br&gt;<strong>Pump</strong>: 2001D&lt;br&gt;<strong>Duration</strong>: 24 hrs&lt;br&gt;<strong>ALZET Comments</strong>: animal info (8 weeks old C57/Bi6 male mice); comparison of IT bolus injections vs mp; ALZET mouse intrathecal catheter used (lumbar cannulation); gene therapy;</td>
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<td>Q5612</td>
<td>R. Rao Malla et al.</td>
<td>Knockdown of cathepsin B and uPAR inhibits CD151 and alpha3beta1 integrin-mediated cell adhesion and invasion in glioma.</td>
<td>Mol Carcinog 2013;52(10):777-90&lt;br&gt;<strong>Agents</strong>: Cathepsin B; Scrambled vector (pSV); Plasmid&lt;br&gt;<strong>Vehicle</strong>: PBS (mock)&lt;br&gt;<strong>Route</strong>: Species: Mice (nude)&lt;br&gt;<strong>Pump</strong>: 1002&lt;br&gt;<strong>Duration</strong>: ALZET Comments: Controls received mp w/ control adeno-associated virus; animal info (adult male Sprague-Dawley rats weighing 250-270g); spinal cord injury;</td>
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| 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 (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; plasmid, PAK4si
Vehicle: Route: Species: Mice (nu/nu); Pump: 2004; Duration: ALZET
Comments: Animal info (female, nu/nu)

Agents: Plasmid, scrambled vector, pSV; plasmid, pUC
Vehicle: Route: Species: Mice (nu/nu); Pump: 2004; 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

Agents: Plasmid, puPA; plasmid, upAR; plasmid, pU2; plasmid, vector Vehicle: PBS; Route: CSF/CNS; Species: Mice (nu/nu); Pump: 2001; 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

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: IP; Species: Mice (nude); Pump: 1007D; Duration: 4,7 days; 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: Route: CSF/CNS (hippocampus); SC; Species: Mice; Pump: 2004; 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: Route: 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(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."

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)

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 (cochlea); Species: Guinea pig; Pump: 2001; Duration: Controls received mp w/ vehicle; tissue perfusion (scala tympani); 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, 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);

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);
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