References on the Administration of Various Nanoparticles Using ALZET® Osmotic Pumps

Dendrimer

**Agents:** Estragon-dendrimer conjugate  **Vehicle:** Not Stated;  **Route:** SC;  **Species:** Mice;  **Pump:** 2004;  **Duration:** 28 days;  
**ALZET Comments:** Dose (240mg/kg/day); Controls received mp w/ vehicle; animal info (C57BL/6J mice);


**Agents:** Estradiol; Estragon-dendrimer conjugate  **Vehicle:** Not Stated;  **Pump:** Not Stated;  **Duration:** 2 weeks;  
**ALZET Comments:** ischemia (placent); replacement therapy (ovarectomy);


**Agents:** Estragon-dendrimer conjugate, angII, Estetrol  **Vehicle:** DMSO;  **Route:** SC;  **Species:** Mice;  **Pump:** 2004;  **Duration:** 28d  
**ALZET Comments:** Dose (80 ug/kg/day-EDC, 0.5 mg/kg/day- Ang II, 6 mg/kg/day -estetrol); Controls received mp w/ vehicle; animal info (C57BL/6); cardiovascular;

Q6603: S. Menazza, et al. Non-nuclear estrogen receptor alpha activation in endothelium reduces cardiac ischemia-reperfusion injury in mice. J Mol Cell Cardiol 2017;107(41-51

**Agents:** Estradiol; Dendrimer; Estragon-dendrimer conjugate; ICI182,780  **Vehicle:** SC;  **Species:** Mice;  **Duration:** 2 weeks;  
**ALZET Comments:** Dose (Estradiol (6μg/day); (Dendrimer 6μg/day), Estrogen-dendrimer conjugate (6μg/day); ICI182,780 (2mh/kg/day0); Controls received mp w/ vehicle; animal info (11 week old C57BL/6J female mice);


**Agents:** Telodendrimer nanoparticles, peptide-incorp.  **Route:** CSF/CNS (Intratumoral);  **Species:** Mice (nude);  **Duration:** 7 days  
**ALZET Comments:** Controls received mp w/ free peptide; animal info (female, athymic nude NCRU-Sp/Sp, 8 weeks old); pumps primed overnight at 37C; Dose (0.5 ug/h); Brain coordinates (0.5 mm anterior to bregma and 2.5 mm lateral of midline);


**Agents:** Estradiol, estrogen dendrimer conjugate  **Vehicle:** DMSO;  **Route:** IP;  **Species:** Mice;  **Pump:** 2006;  **Duration:** 12 weeks, 84 days;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (5 weeks old, ovariectomy); pumps replaced 6 wk; Therapeutic indication (atherosclerosis); Dose (6 ug/day);


**Agents:** Estradiol; dendrimer, empty estradiol  **Vehicle:** Not Stated;  **Route:** IP;  **Species:** Mice;  **Pump:** 2006;  **Duration:** 6 weeks;  
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (C57BL/6, female, 15 wks old); replacement therapy


**Agents:** Estradiol; estrogen-dendrimer conjugate  **Vehicle:** DMSO;  **Route:** IP;  **Species:** Mice (SCID);  **Pump:** 1004;  **Duration:** 72 hours; 28 days;  
**ALZET Comments:** Controls received mp w/ empty dendrimer; animal info (female, ERE-Luc reporter, 10-13 wk; Ex3aERKO, 8-9 wk; C57BL/6 Apoe-/-; 6 wk; SCID, 8 wk); functionality of mp verified by serum agent levels; Estradiol Dose (6 ug/d); replacement therapy (ovaricectomy; pumps replaced after 28 days); half-life (p.2321); half life of EDC = 28 hours; stability verified by (Serum evaluation of experimental and control mice); photon recording with light emission tomography (LET) system with a CCD camera; Research Diets D10001
Dextran


**Agents:** FITC-Dextran  
**Vehicle:** Saline;  
**Route:** CSF/CNS;  
**Species:** Rat;  
**Pump:** 2001D; 2ML1;  
**Duration:** 24 hours; 5 days;  
**ALZET Comments:** Animal info (Female Sprague-Dawley rats (mean age 6 weeks, mean weight 140 g));


**Agents:** Fluorescein Isothiocyanate labeled 10 kd dextran  
**Vehicle:** Not stated;  
**Route:** CSF/CNS (Lateral Ventricle);  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 14 days;  
**ALZET Comments:** Dose (337 mOsm/L); animal info (Female, Sprague Dawley, 220-250 g); cyanoacrylate adhesive;


**Agents:** Estrogen, cyclodextran-coated  
**Vehicle:** Water;  
**Route:** Not Stated;  
**Species:** Mouse;  
**Pump:** 1004;  
**Duration:** 96 hours;  
**ALZET Comments:** animal info (8 weeks old); Cyclodextran-coated estrogen (Sigma E4389); Mice were allowed to recover for 2 weeks after pump implantation prior to experiment initiation; Therapeutic indication (obesity); Dose (2 ug/kg/day);


**Agents:** Rhodamine-dextran; protein, Ad5-green flourescent  
**Species:** Rat;  
**Pump:** 2ML1;  
**Duration:** 96 hours;  
**ALZET Comments:** Animal info (male, Harlan Sprague Dawley, adult); MRI; gene therapy;


**Agents:** Liposomes; FITC-dextran-lysine  
**Vehicle:** Saline; tris buffer;  
**Route:** CSF/CNS (caudate putamen); CSF/CNS (intratumoral);  
**Species:** Rat;  
**Pump:** 2001D;  
**Duration:** 24 hrs;  
**ALZET Comments:** Tissue perfusion (intratumoral); comparison of acute CSF/CNS injection vs. mp; half-life (p. 151) 9.9 hours; cancer (glioblastoma); ALZET brian infusion kit 2 used; brain tissue distribution; post op. care (buprenophine)


**Agents:** FITC-Dextran; Fluorescein isothiocyanate; Dextran  
**Vehicle:** Saline;  
**Route:** CSF/CNS (brain stem, pons);  
**Species:** Rat;  
**Pump:** 2001D; 2ML1;  
**Duration:** 24 hrs; 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle; good methods (p.389); cancer (glioma); brain tissue distribution;


**Agents:** GdDTPA; GdDTPA-dextran;  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (parenchyma);  
**Species:** rabbit;  
**Pump:** 2002;  
**Duration:** 8 days;  
**ALZET Comments:** comparison of bolus injections vs. mp; brain tissue distribution of contrast agent Gd-DTPA was assessed by MRI;

Fullerene


**Agents:** Carboxyfullerenes, C3  
**Vehicle:** Saline, physiological;  
**Route:** IP;  
**Species:** Mice (transgenic);  
**Pump:** 2004;  
**Duration:** 2 months;  
**ALZET Comments:** Controls received mp w/ vehicle; neurodegenerative (amyotrophic lateral sclerosis); animal info (G93A SOD1 G1, 10 weeks old); functionality of mp verified by residual volume; pumps replaced after 4 weeks; behavioral testing (motor performance)
**Liposome**


**Agents**: Liposomes, fluorescently labeled; coatasome EL-01-C, hydrated

**Vehicle**: DMSO; water, distilled

**Route**: Intrauterine

**Species**: Rabbit (fetus)

**Pump**: 2ML1; **Duration**: 1 week

**ALZET Comments**: Control animals received mp w/ liposome alone; animal info (Japanese, White, 4.2-5.4 kg, teen); tissue perfusion (fetus); “5-cm sterile PE 60 silicone catheter with silicone flange was attached to each pump” pg L209;


**Agents**: Fibroblast growth factor-2; syndecan-4, proteoliposome

**Vehicle**: Not Stated

**Route**: SC

**Species**: Rat

**Pump**: 1004; **Duration**: 7-16 days

**ALZET Comments**: Controls received mp w/ PBS; animal info (Sprague Dawley); wound clips used; ischemia


**Agents**: Cisplatin; Sodium thiosulfate; Brain-derived neurotrophic factor; Fibroblast growth factor; D-JNKI-1; BN82270; Tetrodotoxin; Perilymph, artificial; Dexamethasone; Methylprednisolone; Caroverine; Methionine, D-; Thiourea; Liposome, cationic; Neomycin

**Vehicle**: Not Stated

**Route**: SC; Ear (round window membrane); Ear (cochlea); Ear (scala tympani); Ear

**Species**: Guinea pig

**Pump**: Not Stated; **Duration**: 3, 7, 14, 28 days

**ALZET Comments**: Gene therapy; peptides; no stress; enzyme inhibitor (peroxidase); stress/adverse reaction (see pg 1593) “Ref #161 found local trauma and inflammatory responses”; tissue perfusion (scala tympani, cochlea, round window membrane); comparison of middle ear injections vs. mp;


**Agents**: Liposomes; FITC-dextran-lysinе

**Vehicle**: Saline; Tris buffer

**Route**: CSF/CNS (caudate putamen); CSF/CNS (intratumoral)

**Species**: Rat

**Pump**: 2001D; **Duration**: 24 hours

**ALZET Comments**: Tissue perfusion (intratumoral); comparison of acute CSF/CNS injection vs. mp; half-life (p. 151) 9.9 hours; cancer (glioblastoma); ALZET brian infusion kit 2 used; brain tissue distribution; post op. care (buprenophine)


**Agents**: Liposomes, cationic

**Vehicle**: Not Stated

**Route**: Ear (cochlea)

**Species**: Guinea pig

**Pump**: Not Stated

**ALZET Comments**: Gene therapy; tissue perfusion (cochlea)


**Agents**: Liposomes, cationic; Gene, beta-galactosidase

**Vehicle**: Dextrose solution

**Route**: Ear

**Species**: Guinea pig

**Pump**: 1007D; **Duration**: Not Stated

**ALZET Comments**: Tissue perfusion (cochlea); comparison of micro injections vs. mp; stress/adverse reaction: significant fibrosis and acute immune response localized at the site of cochleostomy; gene therapy; prophylactic antibiotics provided; PE50 tubing was connected to PE10;


**Agents**: Oestrone, oleoyl; Liposomes

**Vehicle**: Not Stated

**Route**: IV (jugular)

**Species**: Rat

**Pump**: 2ML2; **Duration**: 3, 6, 10, 14 days

**ALZET Comments**: controls received mp w/ liposomes; functionality of mp verified by radioimmunoanalysis of 3H-oestrone; Merlin-2 is code name for oestrone, oleoyl in liposomes

**Agents:** Estrone, oleoyl-; Liposomes

**Vehicle:** Not Stated

**Route:** IV (jugular)

**Species:** Rat

**Pump:** 2ML2

**Duration:** 28 days

**ALZET Comments:** controls received mp w/liposome suspension; pumps replaced after 14 days; oleoyl-estrone in liposomes was named Merlin-2


**Agents:** Estrone, oleoyl-; Liposomes

**Route:** IV (left jugular)

**Species:** Rat

**Pump:** 2ML2

**Duration:** 28 days

**ALZET Comments:** controls received mp w/liposomes; pumps replaced after 2 weeks; stress/adverse reaction: transient weight loss after surgical implantation of mp (pg. 790); oleoyl-estrone in liposomes referred to as “merlin-2”


**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 (37°C) for 1-3 days.” (pg.474); “continuous administration of DNA-liposome complexes did not result in significant in vivo toxicity.” (pg.474)


**Agents:** Estrone, oleoyl-; Liposomes

**Vehicle:** Not Stated

**Route:** IV (jugular)

**Species:** Rat

**Pump:** 2ML2

**Duration:** 14 days

**ALZET Comments:** no comment posted


**Agents:** Interferon-gamma; S-MDP, free; S-MDP, liposome-encapsulated

**Vehicle:** Not Stated

**Route:** SC

**Species:** Rat

**Pump:** Not Stated

**Duration:** 7 days

**ALZET Comments:** comparison of bolus tracheal injections, iv administration and mp; immunology; peptides; IFN-gamma and S-MDP were most effective when delivered either intravenously or via osmotic minipump infusion; S-MDP is lipophilic N-acetylmuramyl-6-0-stearoyl-alanyl-D-isoglutamine; recomb. mouse IFN-gamma used


**Agents:** Liposomes

**Vehicle:** Not Stated

**Route:** Eye (lens)

**Species:** Rabbit

**Pump:** 2ML1

**Duration:** Not Stated

**ALZET Comments:** Pulsed delivery described; detailed surgical methods


**Agents:** Lovastatin; Pravastatin; Simvastatin

**Vehicle:** Propylene glycol

**Route:** Not Stated

**Species:** Rat

**Pump:** 2ML4

**Duration:** Not Stated

**ALZET Comments:** comparison of injections and oral administration vs. mp; stress/adverse reaction: local cystic reaction to simvastatin and lovastatin (p. 271, 275); enzyme inhibitor (HMG-CoA reductase), sc injections of simvastatin also caused subcutaneous toxicity


**Agents:** Phosphatidylcholine; vitamin E; Liposomes

**Vehicle:** Not Stated

**Route:** CSF/CNS (cortex)

**Species:** Rat

**Pump:** 2001

**Duration:** 7 days

**ALZET Comments:** Multiple pumps per animal (2); agent also called D-alpha-tocopherol
Agents: 8-MOP; Chromophore; Sorbinil; Liposomes Vehicle: Radio-isotopes; Route: Eye (lens); Species: Rabbit; Pump: 2ML1; Duration: 7 days;
ALZET Comments: Tissue perfusion (ocular lens); liposome-encapsulated agents

Agents: Interferon-gamma; Liposomes Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: controls received mp w/empty liposomes; liposome encapsulated agent and free agent; comparison of iv injections vs. mp infusion; cancer/immunology; peptides

PEGylated Molecules
Q6703: S. Nagata, et al. Anti-Inflammatory Effects of PEGylated Human Adrenomedullin in a Mouse DSS-Induced Colitis Model. Drug Development Research 2017;78(3-4):129-134
Agents: Adrenomedullin, human, PEGylated Vehicle: Saline; Route: SC; Species: Mice; Pump: 1002; Duration: 4 weeks;
ALZET Comments: Dose (0.02, 0.1, 0.5 nmol/kg/h of 5kDa PEG-hAM; 1.0, 5.0, 25.0 nmol/kg/h of 60kDa PEG-hAM); Controls received mp w/ vehicle; animal info (Male 7-week-old C57BL/6Jcl mice); PEGylated Human Adrenomedullin aka PEG-hAM;

Agents: RNA, small interfering/EHCO; PEGylated EHCO Vehicle: Not Stated; Route: Not Stated; Species: Mice (nude); Pump: Not Stated; Duration: 14 days;
ALZET Comments: Controls received treated with nonspecific PEGylated EHCO/siGFP nanoparticles (PEGGFP) and non-PEGylated EHCO/HIF-1α; cancer; gene therapy, RNA nanoparticle infusion; peptides; "These results indicate that PEGylation can significantly improve the stability of EHCO/siRNA nanoparticles during storage in solution, possibly by preventing the aggregation of the nanoparticles and providing better protection to the siRNA cargo from degradation" (pg 31);

Agents: Leptin receptor antagonist, non-pegylated Vehicle: PBS; Route: CSF/CNS; Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6J, Mc4r -/-, Lep ob/ob); Leptin receptor antagonist, non-pegylated aka LA;

Agents: Mouse leptin antagonist, pegylated Vehicle: Water, distilled; Route: SC; Species: Mice; Pump: 1003D; 1007D; Duration: 3, 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (5 wks old, male, C57BL/6); peptides

Q1735: A. Agnew, et al. Chronic treatment with a stable obestatin analog significantly alters plasma triglyceride levels but fails to influence food intake; fluid intake; body weight; or body composition in rats. Peptides 2011;32(4):755-762
Agents: Obestatin (1-23); obestatin (1-23), pegylated Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2002; Duration: 14 days;
ALZET Comments: Controls received mp w/ saline; animal info (Sprague Dawley, male, 5 wks old); peptides

Agents: Interleukin-11; Stem cell factor; Granulocyte-colony stimulating factor, PEGylated; Erythropoietin Vehicle: Not Stated; Route: SC; Species: mice.; Pump: 2002; 1007D; Duration: 7 days;
ALZET Comments: controls received mp w/ saline; functionality of mp verified by pilot studies; no stress (see pg. 3223); peptides; recomb. human interleukin-11, EPO, & G-CSF used; recomb. rat stem cell factor used (pegylated);agents were given in every combination;