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

Dendrimer

Q6903: A. Vinel, *et al.* Respective role of membrane and nuclear estrogen receptor (ER) alpha in the mandible of growing mice: Implications for ERalpha modulation. J Bone Miner Res 2018;33(8):1520-1531
Agents: Estrogen-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);

R0393: C. Physiology. Mechanisms of Sex Disparities in Cardiovascular Function and Remodeling. Compr Physiol 2018;9(1):375-411
Agents: Estradiol; Estrogen-dendrimer conjugate **Vehicle:** Not Stated; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: ischemia (placental); replacement therapy (ovarectomy);

Q7143: E. Guivarc'h, *et al.* Predominant Role of Nuclear Versus Membrane Estrogen Receptor alpha in Arterial Protection: Implications for Estrogen Receptor alpha Modulation in Cardiovascular Prevention/Safety. J Am Heart Assoc 2018;7(13):
Agents: Estrogen-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; Estrogen-dendrimer conjugate; ICI182,780 **Route:** 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);

Q5091: X. Wang, *et al.* Affinity-controlled protein encapsulation into sub-30 nm telodendrimer nanocarriers by multivalent and synergistic interactions. Biomaterials 2016;101(258-71
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);

Q5763: K. L. Chambliss, *et al.* Nonnuclear Estrogen Receptor Activation Improves Hepatic Steatosis in Female Mice. Endocrinology 2016;157(10):3731-3741
Agents: Estradiol, estrogen dendrimer conjugate; **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);

Q2622: S. M. Bartell, *et al.* Non-Nuclear-Initiated Actions of the Estrogen Receptor Protect Cortical Bone Mass. MOLECULAR ENDOCRINOLOGY 2013;27(4):649-656
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

Q0109: K. L. Chambliss, *et al.* Non-nuclear estrogen receptor-alpha signaling promotes cardiovascular protection but not uterine or breast cancer growth in mice. Journal of Clinical Investigation 2010;120(7):2319-2330
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 (ovariectomy; 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

Q9426: J. S. Rechberger, *et al.* Evaluating infusate parameters for direct drug delivery to the brainstem: a comparative study of convection-enhanced delivery versus osmotic pump delivery. Neurosurgical Focus 2020;48(1):E2
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));

Q8054: S. Krishnamurthy, *et al.* Normal macromolecular clearance out of the ventricles is delayed in hydrocephalus. Brain Res 2018;1678(337-355
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;

Q5547: E. Jeffery, *et al.* The Adipose Tissue Microenvironment Regulates Depot-Specific Adipogenesis in Obesity. Cell Metabolism 2016;24(1):142-50
Agents: Estrogen, cyclodextran-coated **Vehicle:** Water; **Route:** Not Stated; **Species:** Mouse; **Pump:** 1004;
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);

Q2115: J. Yun, *et al.* A novel adenoviral vector labeled with superparamagnetic iron oxide nanoparticles for real-time tracking of viral delivery. JOURNAL OF CLINICAL NEUROSCIENCE 2012;19(6):875-880
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

P7197: J. A. MacKay, *et al.* Distribution in brain of liposomes after convection enhanced delivery; modulation by particle charge, particle diameter, and presence of steric coating. Brain Research 2005;1035(2):139-153
Agents: Liposomes; FITC-dextran-lysine **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)

P5648: G. Occhiogrosso, *et al.* Prolonged convection-enhanced delivery into the rat brainstem. Neurosurgery 2003;52(2):388-393
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;

P4342: S. Kalyanasundaram, *et al.* A finite element model for predicting the distribution of drugs delivered intracranially to the brain. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 1997;273(R1810-R1821
Agents: GdDTPA; GdDTPA-dextran; **Vehicle:** Not Stated; **Route:** CSF/CNS; 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

Q0041: L. L. Dugan, *et al.* Carboxyfullerenes as neuroprotective agents. Proceedings of the National Academy of Sciences 1997;94(9434-9439
Agents: Carboxyfullerene, 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

Q10525: S. Fujiwara*, et al.* Age-related Changes in Trigeminal Ganglion Macrophages Enhance Orofacial Ectopic Pain After Inferior Alveolar Nerve Injury. In Vivo 2023;37(1):132-142
Agents: Liposomal clodronate; Liposome (control) **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 5 days;
ALZET Comments: Dose (0.11 µl/h,); Controls received mp w/ vehicle; animal info (23 week old male SAMP8/SAMR1 mice; Weighed 20-30 g); Brain Coordinates (2,8 mm anterior from posterior fontanelle, 1.2 mm lateral to sagitall suture); polyethylene catheter; dental cement used; aging;

Q2301: K. Nishijima*, et al.* Interactions among pulmonary surfactant, vernix caseosa, and intestinal enterocytes: intra-amniotic administration of fluorescently liposomes to pregnant rabbits. American Journal of Physiology Lung Cellular and Molecular Physiology 2012;303(3):L208-L214
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;

Q1884: E. Jang*, et al.* Syndecan-4 proteoliposomes enhance fibroblast growth factor-2 (FGF-2)-induced proliferation, migration, and neovascularization of ischemic muscle. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2012;109(5):1679-1684
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

R0266: E. E. L. Swan*, et al.* Inner ear drug delivery for auditory applications. Advanced Drug Delivery Reviews 2008;60(15):1583-1599
Agents: Cisplatin; Sodium thiosulfate; Brain-derived neurotrophic factor; Fibroblast growth factor; D-JNKI-1; BN82270; Tetrodotoxin; Perilymph, artificial; Dexamethasone; Methylprednisone; 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;

P7197: J. A. MacKay*, et al.* Distribution in brain of liposomes after convection enhanced delivery; modulation by particle charge, particle diameter, and presence of steric coating. Brain Research 2005;1035(2):139-153
Agents: Liposomes; FITC-dextran-lysine **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)

R0213: M. L. Duan*, et al.* Protection and treatment of sensorineural hearing disorders caused by exogenous factors: experimental findings and potential clinical application. Hearing Research 2002;169(169-178
Agents: Liposomes, cationic **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** Not Stated;
ALZET Comments: Gene therapy; tissue perfusion (cochlea)

P4436: M. Wareing*, et al.* Cationic liposome mediated transgene expression in the guinea cochlea. Hearing Research 1999;128(61-69
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;

P3745: D. Sanchis, *et al.* Short-term treatment with oleoyl-oestrone in liposomes (Merlin-2) strongly reduces the expression of the ob gene in young rats. Biochemical Journal 1997;326(357-360
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

P4146: F. Balada, *et al.* Effect of the slimming agent oleoyl-estrone in liposomes on the body weight of rats fed a cafeteria diet. Archives of Physiology and Biochemistry 1997;105(5):487-495
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

P3831: F. Balada, *et al.* Effect of the slimming agent oleoyl-estrone in liposomes on the body weight of zucker obese rats. Int. J. Obes 1997;21(789-795
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"

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:** 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)

P3526: D. Sanchis, *et al.* Oleoyl-estrone induces the loss of body fat in rats. Int. J. Obes 1996;20(588-594
Agents: Estrone, oleoyl-; Liposomes **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: no comment posted

P2677: D. B. Drath, *et al.* Activation of a distinct subpopulation of pulmonary macrophages following exposure to biological response modifiers. Immunol. Invest 1994;23(2):115-127
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

P1978: S. Lerman, *et al.* Miniosmotic pumps for liposomal drug delivery. Liposome Technol 1993;1(429-438
Agents: Liposomes **Vehicle:** Not Stated; **Route:** Eye (lens); **Species:** Rabbit; **Pump:** 2ML1; **Duration:** Not Stated;
ALZET Comments: Pulsed delivery described; detailed surgical methods

P2086: J. Joles, *et al.* Subcutaneous administration of HMG-CoA reductase inhibitors in hyperlipidaemic and normal rats. Lab. Anim 1992;26(269-280
Agents: Lovastatin; Pravastatin; Liposomes; 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

P2013: D. G. Stein*, et al.* Intracerebral administration of alpha-tocopherol-containing liposomes facilitates behavioral recovery in rats with bilateral lesions of the frontal cortex. J. Neurotrauma 1991;8(4):281-292
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

P1722: S. Lerman. Test models to determine potential ocular drug induced side effects. Lens Eye Toxic. Res 1989;6(1/2):1-36
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

P0957: D. B. Drath. Modulation of pulmonary macrophage superoxide release and tumoricidal activity following activation by biological response modifiers. Immunopharmacology 1986;12(2):117-126
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/6J Jcl mice); PEGylated Human Adrenomedullin aka PEG-hAM;

Q5158: M. Gujrati*, et al.* Multifunctional pH-Sensitive Amino Lipids for siRNA Delivery. Bioconjugate Chemistry 2016;27(1):19-35
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);

Q4692: N. Ottaway*, et al.* Diet-Induced Obese Mice Retain Endogenous Leptin Action. Cell Metabolism 2015;21(877-882
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;

Q1522: J. Levi*, et al.* Acute Disruption of Leptin Signaling in Vivo Leads to Increased Insulin Levels and Insulin Resistance. Endocrinology 2011;152(9):3385-3395
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