



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

1. 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

ALZET Comments: Estrogen-dendrimer conjugate; SC; Mice; 2004; 28 days; Dose (240mg/kg/day); Controls received mp w/ vehicle; animal info (C57BL/6J mice);

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):

ALZET Comments: Estrogen-dendrimer conjugate, angiotensin II, Estetrol; DMSO; SC; Mice; 2004; 28 days; 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

ALZET Comments: Estradiol; Dendrimer; Estrogen-dendrimer conjugate; ICI182,780; SC; Mice; 2 weeks; 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); Estrogen-dendrimer conjugate aka EDC; ischemia (Cardiac);.

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

ALZET Comments: Telodendrimer nanoparticles, peptide-incorporated; CSF/CNS (Intratatumoral); Mice (nude); 7 days; Controls received mp w/ free peptide; animal info (female, athymic nude NCRU-Sp/Sp, 8 weeks old); cancer (glioblastoma U87); tissue perfusion (intratumoral); 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

ALZET Comments: Estradiol, estrogen dendrimer conjugate; IP; Mice; 2006; 12 weeks, 84 days; Controls received mp w/ vehicle; animal info (5 weeks old, ovariectomy); pumps replaced every 6 weeks; long-term study; 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

ALZET Comments: Estradiol; dendrimer, empty estradiol; IP; Mice; 2006; 6 weeks; Control animals received mp w/ vehicle; animal info (C57BL/6, female, 15 wks old); replacement therapy (ovariectomy);.

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

ALZET Comments: Estradiol; estrogen-dendrimer conjugate; DMSO; IP; Mice (SCID); 1004; 72 hours; 28 days; Controls received mp w/ empty dendrimer; cardiovascular; cancer (breast); animal info (female, ERE-Luc reporter, 10-13 weeks old; Ex3aERKO, 8-9 weeks old; C57BL/6 Apoe-/-, 6 weeks old; SCID, 8 weeks old); 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.



2. Dextran

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; neurodegenerative (Hydrocephalus);

Q5547: E. Jeffery, *et al.* The Adipose Tissue Microenvironment Regulates Depot-Specific Adipogenesis in Obesity. *Cell Metab* 2016;24(1):142-50

ALZET Comments: Estrogen, cyclodextran-coated; Water; Mouse; 1004; 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

ALZET Comments: Rhodamine-dextran; protein, Ad5-green fluorescent; Rat; 2ML1; 96 hours; 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

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

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

ALZET Comments: FITC-Dextran; Fluorescein isothiocyanate; Dextran; Saline; CSF/CNS (brain stem, pons); Rat; 2001D; 2ML1; 24 hrs; 7 days; Controls received mp w/ vehicle; good methods (p.389); cancer (glioma); brain tissue distribution; catheter from ALZET brain infusion kit 2 was used.

P4342: S. Kalyanasundaram, *et al.* A finite element model for predicting the distribution of drugs delivered intracranially to the brain. *Am. J. Physiol. (Regulatory Integrative Comp. Physiol. 42)* 1997;273(R1810-R1821)

ALZET Comments: GdDTPA; GdDTPA-dextran;; CSF/CNS; CSF/CNS (parenchyma);; rabbit;; 2002;; 8 days;; comparison of bolus injections vs. mp; brain tissue distribution of contrast agent Gd-DTPA was assessed by MRI;

3. Fullerene

Q0041: L. L. Dugan, *et al.* Carboxyfullerenes as neuroprotective agents. *Proc. Natl. Acad. Sci* 1997;94(9434-9439)

ALZET Comments: Carboxyfullerene, C3; Saline, physiological; IP; Mice (transgenic); 2004; 2 months; 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).

4. Liposome

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



ALZET Comments: Liposomes, fluorescently labeled; coatasome EL-01-C, hydrated; DMSO; water, distilled; Intrauterine; Rabbit (fetus); 2ML1; 1 week; 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; Fig 2, image of pump and catheter placement; multiple pumps used (2); teratology.

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

ALZET Comments: Fibroblast growth factor-2; syndecan-4, proteoliposome; SC; Rat; 1004; 7-16 days; 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

ALZET Comments: Cisplatin; Sodium thiosulfate; Brain-derived neurotrophic factor; Fibroblast growth factor; D-JNK1-1; BN82270; Tetrodotoxin; Perilymph, artificial; Dexamethasone; Methylprednisone; Caroverine; Methionine, D-; Thiourea; Liposome, cationic; Neomycin; SC; Ear (round window membrane); Ear (cochlea); Ear (scala tympani); Ear; Guinea pig; 3, 7, 14, 28 days; 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; Review, see pgs. 1587 - 1589, 1591, 1593 - 1595, refs #49, 50, 60, 63, 72, 75, 102, 104,180, 181, 194-201.

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

ALZET Comments: Liposomes; FITC-dextran-lysine; Saline; tris buffer; CSF/CNS (caudate putamen); CSF/CNS (intratumoral); Rat; 2001D; 24 hours; 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

ALZET Comments: Liposomes, cationic; Ear (cochlea); Guinea pig; 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

ALZET Comments: Liposomes, cationic; Gene, beta-galactosidase; Dextrose solution;; ear;; Guinea pig;; 1007D;; 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. Biochem. J 1997;326(357-360

ALZET Comments: Oestrone, oleoyl; Liposomes; IV (jugular); Rat; 2ML2; 3, 6, 10, 14 days; 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. Arch. Physiol. Biochem 1997;105(5):487-495

ALZET Comments: Estrone, oleoyl-; Liposomes; IV (jugular); Rat; 2ML2; 28 days; 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



ALZET Comments: Estrone, oleoyl-; Liposomes; IV (left jugular); Rat; 2ML2; 28 days; 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)

ALZET Comments: Liposomes; Gene, herpes simplex virus thymidine kinase; Gene, lacZ; CSF/CNS (caudate nucleus); Rat; 1003D; 3 days; 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)

ALZET Comments: Estrone, oleoyl-; Liposomes; IV (jugular); Rat; 2ML2; 14 days; 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

ALZET Comments: Interferon-gamma; S-MDP, free; S-MDP, liposome-encapsulated; SC; Rat; 7 days; 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-O-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)

ALZET Comments: Liposomes; Eye (lens); rabbit; 2ML1; no duration posted; 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)

ALZET Comments: Lovastatin; Pravastatin; Liposomes; Simvastatin; Propylene glycol; Rat; 2ML4; no duration posted; 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

ALZET Comments: Phosphatidylcholine; vitamin E; Liposomes; CSF/CNS (cortex); Rat; 2001; 7 days; 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

ALZET Comments: 8-MOP; Chromophore; Sorbinil; Liposomes; Radio-isotopes; Eye (lens); rabbit; 2ML1; 7 days; 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

ALZET Comments: Interferon-gamma; Liposomes; SC; Rat; 2001; 7 days; controls received mp w/empty liposomes; liposome encapsulated agent and free agent; comparison of iv injections vs. mp infusion; cancer/immunology; peptides.

5. PEGylated Molecules



Q6703: S. Nagata, *et al.* Anti-Inflammatory Effects of PEGylated Human Adrenomedullin in a Mouse DSS-Induced Colitis Model. *Drug Dev Res* 2017;78(3-4):129-134

ALZET Comments: Adrenomedullin, human, PEGylated; Saline; SC; Mice; 1002; 4 weeks; 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. *Bioconjug Chem* 2016;27(1):19-35

ALZET Comments: RNA, small interfering/EHCO; PEGylated EHCO; Mice (nude); 14 days; Controls received treated with nonspecific PEGylated EHCO/siGFP nanoparticles (PEGGFP) and non-PEGylated EHCO/HIF-1 α ; 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

ALZET Comments: Leptin receptor antagonist, non-pegylated; PBS; CSF/CNS; Mice; 1007D; 7 days; 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

ALZET Comments: Mouse leptin antagonist, pegylated; Water, distilled; SC; Mice; 1003D; 1007D; 3, 7 days; 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

ALZET Comments: Obestatin (1-23); obestatin (1-23), pegylated;; SC; Rat; 2002; 14 days; Controls received mp w/ saline; animal info (Sprague Dawley, male, 5 wks old); peptides.

P4291: I. Roeder, *et al.* Interactions of erythropoietin, granulocyte colony-stimulating factor, stem cell factor, and interleukin-11 on murine hematopoiesis during simultaneous administration. *Blood* 1998;91(9):3222-3229

ALZET Comments: Interleukin-11; Stem cell factor; Granulocyte-colony stimulating factor, PEGylated; Erythropoietin;; SC;; mice;; 2002; 1007D;; 7 days;; 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;