



References on Gene Therapy Research Using ALZET® Osmotic Pumps

Q6966: S. Kroller-Schon, *et al.* Endothelial alpha1AMPK modulates angiotensin II-mediated vascular inflammation and dysfunction. *Basic Res Cardiol* 2019;114(2):8

ALZET Comments: Angiotensin II; Saline; SC; Mice; 1007D; 7 days; Dose (0.5 mg/kg/day); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (6 week old mice); gene therapy;

R0372: J. Hong, *et al.* Relaxin gene therapy: A promising new treatment option for various diseases with aberrant fibrosis or irregular angiogenesis. *Mol Cell Endocrinol* 2019;

ALZET Comments: Relaxin, human recomb.; SC; Rat (pregnant); Dose (2000 ng/h); Resultant plasma level (RLX level close to 0.5 ng/mL); gene therapy;

Q7242: Y. Takeda, *et al.* Epigenetic Regulation of Aldosterone Synthase Gene by Sodium and Angiotensin II. *J Am Heart Assoc* 2018;7(10):

ALZET Comments: Angiotensin II, Candesartan; PMC6015301; SC; Rat; Pump model not stated; 4 weeks; Dose (Ang II 200 ng/kg/min, Candesartan 1mg/kg/day); animal info (Male, Wistar, 6 weeks old); Candesartan aka Ang II type 1 receptor antagonist; gene therapy;

Q7266: K. Taguchi, *et al.* RAGE-aptamer attenuates deoxycorticosterone acetate/salt-induced renal injury in mice. *Sci Rep* 2018;8(1):2686

ALZET Comments: DNA aptamer (RAGE); SC; Mice; 2006; 21 days; Dose (2×10^{-4} ug/day); Controls received mp w/ vehicle; animal info (8 week old, male, C57BL/6J); RAGE-apt is a DNA aptamer against the advanced glycation end products receptor; gene therapy;

Q7223: J. Lu, *et al.* CIC-2 knockdown prevents cerebrovascular remodeling via inhibition of the Wnt/beta-catenin signaling pathway. *Cell Mol Biol Lett* 2018;23(29)

ALZET Comments: Angiotensin II; Saline; SC; Mice; 1002; 1002; Dose (1.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Male, 12 weeks old, 20-25 g, C57BL/6); gene therapy;

Q7149: K. Kamio, *et al.* Resolution of bleomycin-induced murine pulmonary fibrosis via a splenic lymphocyte subpopulation. *Respir Res* 2018;19(1):71

ALZET Comments: Bleomycin; Saline; SC; Mice; 2001; 7 days; Dose (100 mg/kg/day); Controls received mp w/ vehicle; animal info (C57BL/6); gene therapy;

Q7139: Y. Gao, *et al.* The histone methyltransferase DOT1L inhibits osteoclastogenesis and protects against osteoporosis. *Cell Death Dis* 2018;9(2):33

ALZET Comments: EPZ5676; DMSO, Water; SC; Mouse; 2006, 2002; 8 weeks; Dose (1.6 mg/d); 50% DMSO used; Controls received mp w/ vehicle; animal info (Eight-week-old, female, FVB/N); Model 2006 pumps replaced with Model 2002 after six weeks; long-term study; EPZ5676 aka small molecule inhibitor; gene therapy;

Q7138: S. Galic, *et al.* AMPK signaling to acetyl-CoA carboxylase is required for fasting- and cold-induced appetite but not thermogenesis. *Elife* 2018;7(1):1-17
ALZET Comments: Ghrelin, N-octanoylated; Ghrelin, N-octanoylated; SC; Mouse; 2002; 14 days; Dose (30 ug/day); Controls received mp w/ vehicle; animal info (Male, ACC DKI); Peptide, recombinant protein aka N-octanoylated murine ghrelin; gene therapy;

Q7137: K. Fujita, *et al.* Targeting Tyro3 ameliorates a model of PGRN-mutant FTLTDP via tau-mediated synaptic pathology. *Nat Commun* 2018;9(1):433

ALZET Comments: Gö6976; PBS; CSF/CNS (intrathecal); Mouse; 2006; 2 weeks; Dose (0.15 ul/h); animal info (PGRN-KI and C57BL/6J, 10-12 weeks old); behavioral testing (Morris water maze test, Fear-conditioning test, Probe test, Rotarod test, Open-field test, Light-dark box test); enzyme inhibitor (PKC inhibitor); gene therapy;



Q7109: S. Chakraborty, *et al.* Dexamethasone-induced Intra-Uterine Growth Restriction impacts NOSTRIN and its downstream effector genes in the rat mesometrial uterus. *Sci Rep* 2018;8(1):8342

ALZET Comments: Dexamethasone; Ethanol; SC; Rat; 2ML1; 7 days; Dose (200 ug/kg/day); 10% ethanol used; Controls received mp w/ vehicle; animal info (Sprague Dawley, 8-10 weeks old); gene therapy;

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)

ALZET Comments: Lentivirus, ER beta; CSF, artificial; CSF/CNS (amygdala); Rat; 2002; 2 weeks; 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;

Q5829: N. Martinez-Sanchez, *et al.* Thyroid hormones induce browning of white fat. *J Endocrinol* 2017;232(2):351-362

ALZET Comments: Thyroxin, L-, Adenovirus vector; Gene, green fluorescent protein; Gene, AMP-activated protein kinase; Saline; CSF/CNS (hypothalamus); Rat; 1007D; 7, 21 days; 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):

ALZET Comments: Viral vector, adeno-associated (AAV9, AAV2g0); Gene, CBh-ScGFP; CSF/CNS (intrathecal); Mice; 2001D; 24 hrs; 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;

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);

Q5312: K. Caviness, *et al.* Complex Interplay of the UL136 Isoforms Balances Cytomegalovirus Replication and Latency. *MBio* 2016;7(2):e01986

ALZET Comments: Granulocyte-colony stimulating factor; AMD3100; IP; Mice (NOD/SCID); 1007D; 1 week; animal info (NOD-scid humanized (huNSG) mice); gene therapy; immunology; Engraftment of human CD45+ cells; viral persistence; Dose (300mg/ml Colony-stim; 125 ug AMD3100);

Q5625: J. Benoit, *et al.* Epigenetic stability in the adult mouse cortex under conditions of pharmacologically induced histone acetylation. *Brain Struct Funct* 2016;221(8):3963-3978

ALZET Comments: Trichostatin A; DMSO, water; SC; Mice; 2002; 14 days, 28 days; Controls received mp w/ vehicle; animal info (6 months old); Subset of pumps replaced every 2 weeks; gene therapy;

Q5279: Y. Sztainberg, *et al.* Reversal of phenotypes in MECP2 duplication mice using genetic rescue or antisense oligonucleotides. *Nature* 2015;528(7580):123-6

ALZET Comments: Oligonucleotide, antisense MECP2; Saline; CSF/CNS; mice; 1004; 28 days; Controls received mp w/ vehicle; animal info (FVB/N pure background); functionality of mp verified by EEG; ALZET brain infusion kit 3 used; ALZET brain infusion kit 3 used; good methods (pg. 6); gene therapy; Dose (500 ug); Brain coordinates; AP = - 0.2 mm, ML = 1 mm, DV = - 3 mm.

Q4242: A. L. Mathes, *et al.* CpGB DNA activates dermal macrophages and specifically recruits inflammatory monocytes into the skin. *EXPERIMENTAL DERMATOLOGY* 2015;24(133-139)



ALZET Comments: CpGB DNA; SC; Mice; 7 days; 28 days; Controls received mp w/ PBS; animal info (male, C57BL6 or TNFa -/- or IFNg -/- or CXCR3 -/- or CCR5 -/- or CCL2 -/- or TLR9 -/-); functionality of mp verified by immunofluorescence at pump outlet; gene therapy; immunology; CpGB DNA is a TLR9 ligand;.

Q5143: A. C. Dusabineza, *et al.* Hepatic Stellate Cells Improve Engraftment of Human Primary Hepatocytes: A Preclinical Transplantation Study in an Animal Model. *Cell Transplant* 2015;24(12):2557-71

ALZET Comments: Uridine, bromodeoxy-; IP; mice; 1004; 6 hours; 4 weeks; animal info: SCID mice, females, 20–24 g; GFP+ transgenic mice, males, 35–44 g; gene therapy;.

Q3642: Q. G. Zhang, *et al.* Brain-derived estrogen exerts anti-inflammatory and neuroprotective actions in the rat hippocampus. *MOLECULAR AND CELLULAR ENDOCRINOLOGY* 2014;389(84-91

ALZET Comments: Oligodeoxynucleotide, antisense; Saline; CSF/CNS; Rat; 1007D; 7 days; Controls received mp w/ control scrambled missense oligonucleotides; animal info (female, Sprague Dawley, 3 months old, ovariectomized); ALZET brain infusion kit 2 used; antisense (oligodeoxynucleotides); ischemia (global cerebral); gene therapy; immunology;.

Q3190: C. S. Velu, *et al.* Therapeutic antagonists of microRNAs deplete leukemia-initiating cell activity. *Journal of Clinical Investigation* 2014;124(1):222-236

ALZET Comments: Antagomir, miR-21; antagomir, miR-196b; Mice; 2006; 6 weeks; Controls received mp w/control antagomirs; functionality of mp verified by analysis of peripheral white blood cells; cancer (leukemia); gene therapy; immunology; "Antagomir-treated mice did not show alteration in their normal behavior or vital organ function, as evidenced by serum chemistry panels and metabolites" pg. 226;.

Q3627: A. Sehgal, *et al.* Tissue-specific gene silencing monitored in circulating RNA. *RNA-A PUBLICATION OF THE RNA SOCIETY* 2014;20(2):143-149

ALZET Comments: RNA, small interfering; PBS; CSF/CNS (striatum); Rat; 7 days; Animal info (male, Sprague Dawley); neurodegenerative (Parkinson's disease); tissue perfusion (striatum); gene therapy; used Plastics One 30g cannula; primed overnight in 37C saline;.

Q3589: A. Ojima, *et al.* DNA aptamer raised against advanced glycation end products inhibits melanoma growth in nude mice. *LABORATORY INVESTIGATION* 2014;94(4):422-429

ALZET Comments: AGE-aptamer; IP; Mice (nude); 1004; 43 days; Controls received mp w/ control aptamer; animal info (female, nude, athymic, 6 weeks old); comparison of IP injection vs mp; cancer (G361 melanoma); gene therapy; AGE-aptamer aka advanced glycation end products;.

Q3313: J. R. Nadeau, *et al.* Induction of a reactive state in perineuronal satellite glial cells akin to that produced by nerve injury is linked to the level of p75NTR expression in adult sensory neurons. *Glia* 2014;62(5):763-777

ALZET Comments: Oligonucleotide, antisense p75; PBS; rat serum albumin; streptomycin; penicillin; CSF/CNS (intrathecal); Rat; 2001; 2 days; 3 days; 7 days; Controls received mp w/ control oligonucleotide; animal info (male, Wistar, 250-300g); functionality of mp verified by fluorescent tagged AS; antisense (oligonucleotide p75); post op. care (Temgesic SC 0.1-0.2 mg/kg); gene therapy; used silastic tubing; pumps and tubing primed overnight in PBS; 100U/ml streptomycin; 100U/ml penicillin; 1mg/ul rat serum albumin;.

Q3551: K. P. Loh, *et al.* TRPM4 inhibition promotes angiogenesis after ischemic stroke. *PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY* 2014;466(3):563-576

ALZET Comments: RNA, small interfering TRPM inhibiting; IV (jugular); Rat; 24 hours; Controls received mp w/ vehicle; animal info (male, Wistar, 300g); ischemia (cerebral); behavioral testing (rotarod apparatus); gene therapy; cardiovascular; TRPM4 aka transient receptor potential melastatin 4;.

Q3550: J. Liu, *et al.* Enhancing Virus-Specific Immunity In Vivo by Combining Therapeutic Vaccination and PD-L1 Blockade in Chronic Hepadnaviral Infection. *PLoS Pathogens* 2014;10(1):U129-U142

ALZET Comments: Entecavir; SC; Woodchuck; 12 weeks; Animal info (Marmota monax, 1 year old); pumps replaced every 4 weeks; long-term study; gene therapy; immunology; antiviral.



Q5673: R. P. Kotipatruni, *et al.* Development of plasmid-lipid complexes for direct intratumoral injection. *Methods Mol Biol* 2014;1139(467-76)

ALZET Comments: Plasmid DNA-lipid complex; Mice (SCID, CD-1); Therapeutic indication (Gene therapy); Brain coordinates: 3 mm lateral and 2 mm caudal to bregma;

Q4774: Jonathan A. Fallowfield, *et al.* Relaxin Modulates Human and Rat Hepatic Myofibroblast Function and Ameliorates Portal Hypertension InVivo. *Hepatology* 2014;59(4):1492-1504

ALZET Comments: Recombinant human H2-RLN; Sodium acetate; SC; Rat; 2ML2; 72 hrs; Controls received mp w/ vehicle; sodium acetate pH 5; minipumps were loaded with either agent or vehicle solution; animal info (Sprague-dawley, 250-300g); functionality of mp verified by plasma level in inferior vena cava or portal vein; dose-response (full dose response curve present; systemic blood levels); post op. care (warmed and received 0.9% NaCl at 10mL/kg/hr); gene therapy; RLN aka Relaxin; dose: (.5 mg/kg/day).

Q5043: J. A. Fallowfield, *et al.* Relaxin modulates human and rat hepatic myofibroblast function and ameliorates portal hypertension in vivo. *Hepatology* 2014;59(4):1492-504

ALZET Comments: H2-Relaxin, human recombinant; Sodium acetate; SC; Rat; 2ML2; 3 days; Controls received mp w/ vehicle; minipumps were loaded with either agent or vehicle solution; animal info (Sprague-dawley (250-300g)); functionality of mp verified by measuring blood levels from the inferior vena cava or portal vein ; dose-response (full dose response curve present; systemic blood levels); post op. care (warmed and received 0.9% NaCl at 10mL/kg/hr); gene therapy; RLN aka Relaxin; dose: (.5 mg/kg/day);.

Q3293: D. Crepin, *et al.* The over-expression of miR-200a in the hypothalamus of ob/ob mice is linked to leptin and insulin signaling impairment. *MOLECULAR AND CELLULAR ENDOCRINOLOGY* 2014;384(1-2):1-11

ALZET Comments: miR-200a phosphorotiate, anti-; Saline; CSF/CNS; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (male, Lep ob/ob C57BL/6, 9 weeks old)); functionality of mp verified by miRNA array; behavioral testing (food intake); gene therapy; diabetes; used dental cement and stainless steel screws;

Q3181: T. L. Briones, *et al.* Chronic neuroinflammation and cognitive impairment following transient global cerebral ischemia: role of fractalkine/CX3CR1 signaling. *Journal of Neuroinflammation* 2014;11(;) :U1-U13

ALZET Comments: RNA, small interfering CX3CR1; RNA, scrambled; Transfection medium; CSF/CNS; Rat; 1002; 28 days; Animal info (male, Wistar, 350-375g); ALZET brain infusion kit 2 used; ischemia (cerebral); post op. care (heating pad); behavioral testing (Morris water maze); gene therapy; immunology; Cannula stabilized using dental cement. Pumps primed in sterile saline 37C overnight.

Q3405: I. Armando, *et al.* Dopamine D3 receptor inhibits the ubiquitin-specific peptidase 48 to promote NHE3 degradation. *FASEB Journal* 2014;28(1422-1434)

ALZET Comments: GR103691; RNA, small interfering; Transfection reagent (TRANSIT); SC; kidney (subcapsular space); Mice; 1007D; 4 days; 7 days; Controls received mp w/ vehicle or nonsilencing "mock siRNA"; animal info (male, C57BL6J, adult); tissue perfusion (subcapsular space; kidney); gene therapy; antihypertensive; GR103691 is a D3R antagonist; used PE tubing #0007701; pump sutured to abdominal wall; surgical glue applied at puncture site to hold catheter tubing in place and to prevent leakage;

Q5521: H. M. Yun, *et al.* Acceleration of the development of Alzheimer's disease in amyloid beta-infused peroxiredoxin 6 overexpression transgenic mice. *Mol Neurobiol* 2013;48(3):941-51

ALZET Comments: Amyloid protein, beta; Saline; CSF/CNS; Mice (transgenic); 1002; 14 days; animal info (24-28 weeks); ALZET brain infusion kit 1 used; behavioral testing (Morris water maze, probe test, passive avoidance test); gene therapy (transgene); Peptides (amyloid beta); Therapeutic indication (Alzheimer's disease); Dose (300 pmol);

Q3166: J. Qiu, *et al.* Neuroprotective Effects of MicroRNA-210 on Hypoxic-Ischemic Encephalopathy. *BIOMED RESEARCH INTERNATIONAL* 2013;;(;) :U1-U5



ALZET Comments: Oligonucleotide, miR-210 mimic; inhibitor, miR-210; Saline; CSF/CNS; Rat (neonate); 1007D; 72 hours; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, P7); ischemia (hypoxic-ischemic encephalopathy); gene therapy;

Q3601: A. Pileggi, *et al.* MicroRNAs in islet immunobiology and transplantation. Immunologic Research 2013;57(1-3):185-196

ALZET Comments: Morpholinos; Kidney (renal subcapsular space); Rat; Gene therapy; diabetes; Used silicone catheter 3 french; morpholinos are DNA mimics, miRNA inhibitors.

Q3582: N. Niimi, *et al.* Minocycline suppresses experimental autoimmune encephalomyelitis by increasing tissue inhibitors of metalloproteinases. NEUROPATHOLOGY 2013;33(6):612-620

ALZET Comments: RNA, small interfering; IP; Rat; 2002; 2004; 2 weeks; 4 weeks; Animal info (Lewis, 8-12 weeks old, experimental autoimmune encephalomyelitis); neurodegenerative (multiple sclerosis); gene therapy; immunology;

Q3090: Y. Kaida, *et al.* DNA Aptamer Raised Against AGEs Blocks the Progression of Experimental Diabetic Nephropathy. Diabetes 2013;62(9):3241-3250

ALZET Comments: Advanced glycation end products aptamer; IP; Mice; 1004; 7 days; Controls received mp w/ control aptamer; animal info (male, KKay/TA or C57BL6J, 8 weeks old); functionality of mp verified by serum AGE levels; half-life 7 days (p. 3241); gene therapy; diabetes; Advanced glycation end products aptamer aka AGEs-aptamer; Pumps removed after 7 day infusion.

Q3069: S. L. DeVos, *et al.* Antisense Reduction of Tau in Adult Mice Protects against Seizures. Journal of Neuroscience 2013;33(31):12887-12897

ALZET Comments: Tau, ASO-3; Oligonucleotides, antisense scrambled; Saline; CSF/CNS; Mice; 28 days; Controls received mp w/ vehicle; animal info (C57BL6J, Tao -/-); antisense (oligonucleotides); neurodegenerative (Alzheimer's Disease); behavioral testing (elevated plus maze, Morris water maze, seizure score); gene therapy; brain tissue distribution;

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.

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

ALZET Comments: Amyloid protein, beta; virus, adeno-associated; DMSO, Hcl; CSF/CNS (ventricle); mice (transgenic); 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 μ M, DMSO:);

Q0609: Q. M. Chen, *et al.* Lipophilic siRNAs mediate efficient gene silencing in oligodendrocytes with direct CNS delivery. JOURNAL OF CONTROLLED RELEASE 2010;144(2):227-232

ALZET Comments: RNA, small interfering; cholesterol-conjugate siRNA; PBS; CSF/CNS (corpus callosum); Rat; 2ML1; 7 days; Controls received mp w/ vehicle; gene therapy; animal info (Male Sprague-Dawley); tissue perfusion (parenchyma); Agents are CNPase siRNA, Cholesterol-CNPase siRNA, Cholesterol-Luciferase siRNA.

P9511: R. Uchibori, *et al.* Retroviral vector-producing mesenchymal stem cells for targeted suicide cancer gene therapy. JOURNAL OF GENE MEDICINE 2009;11(5):373-381

ALZET Comments: Ganciclovir; IP; Mice (nude); 28 days; Controls received mp w/ PBS; animal info (6 wks old, male, Balb/c, nu/nu); gene therapy.

P8852: H. Y. Wang, *et al.* Therapeutic gene silencing delivered by a chemically modified small interfering RNA against mutant SOD1 slows amyotrophic lateral sclerosis progression. Journal of Biological Chemistry 2008;283(23):15845-15852



ALZET Comments: RNA, small interfering, modified; RNA, small interfering; PBS; CSF/CNS (intrathecal, subarachnoid space); Mice (transgenic); 1007D; 2004; 7, 28 days; 72 hours; Controls received mp w/ vehicle; functionality of mp verified by residual volume; dose-response (Fig. 3); no stress (see pg. 15846, 15849); stability verified by 28 days in vivo (see Fig. 2); half-life (p. 15846) "short"; gene therapy; brain tissue distribution; animal info (SOD1G93A Tg); neurodegenerative (ALS); mp + catheter positioning confirmed; Target (SOD1); "when infused at disease onset at the therapeutic dose for 4 weeks, this siRNA slows disease progression without detectable adverse effects." The catheter was implanted between the L5 and L6 vertebra and connected to a primed Alzet osmotic pump with the PE50 tube. The catheter was stitched to the surface muscle, and the Alzet osmotic pumps were placed under the skin on the back of the mouse.

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.

P8528: Z. C. Neal, *et al.* Flt3-L gene therapy enhances immunocytokine-mediated antitumor effects and induces long-term memory. *CANCER IMMUNOLOGY IMMUNOTHERAPY* 2007;56(11):1765-1774

ALZET Comments: Interleukin-2, recomb. human; SC; Mice; 2001; 4 days; Controls received mp w/ no treatment; cancer (neuroblastoma); peptides; animal info (female, A/J, ICR, 6-8 weeks old); gene therapy.

P8865: M. Kobayashi, *et al.* Tissue-targeted in vivo gene transfer coupled with histone deacetylase inhibitor depsipeptide (FK228) enhances adenoviral infection in rat renal cancer allograft model systems. *UROLOGY* 2007;70(6):1230-1236

ALZET Comments: Ganciclovir; IP; Rat; 7 days; Gene therapy; animal info (male, ACI, 6-8 wks old).

P8110: Y. Iwasaki, *et al.* Gene therapy of liver tumors with human liver-specific nanoparticles. *Cancer Gene Therapy* 2007;14(1):74-81

ALZET Comments: Ganciclovir; Water, sterile; SC; Rat (nude); 12 days; Controls received mp w/ agent and plasmid w/out gene therapy gene; no stress (see p.78); cancer (liver); gene therapy; animal info (male, F344/N, nu/nu, 5 wks old, 180g., NuE hepatic tumors); GCV acts as pro-drug for HSV-tk expression plasmid gene therapy.

P8510: H. R. Djalilian, *et al.* Efficacy of an osmotic pump delivered, GM-CSF-based tumor vaccine in the treatment of upper aerodigestive squamous cell carcinoma in rats. *CANCER IMMUNOLOGY IMMUNOTHERAPY* 2007;56(8):1207-1214

ALZET Comments: Colony-stimulating factor, GM, murine; interleukin-12; PBS; SC; Rat; 28 days; Controls received mp w/ vehicle; dose-response (fig 1); no stress (see pg. 1209); cancer (upper aerodigestive tract carcinoma); peptides; animal info (Fisher 344, 125-150 g); good methods; "This latter method (mp) has several advantages. First, the use of minipumps obviates the cumbersome need to transfect tumor cells and completely characterize their cytokine repertoires. Second, it allows for independent and rigorous control over the kinetics of administration of cytokine and antigen dosages. Third, it may generate less controversy than those techniques requiring "gene therapy" IRB approval." (p. 1213).

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

ALZET Comments: 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; Ear (cochlea); ear (scala tympani); Guinea pig; 1,2,4,8 weeks; 15-60, 11-12, 26 days; 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.



P7936: A. Bondanza, *et al.* Suicide gene therapy of graft-versus-host disease induced by central memory human T lymphocytes. *Blood* 2006;107(5):1828-1836

ALZET Comments: Ganciclovir; SC; Mice (NOD/SCID); 2001; 7 days; Controls received mp w/ saline; animal info (female, NOD/SCID, 6-8 weeks old, GvHD); gene therapy.

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

ALZET Comments: Virus, synthetic RNA; Intratumoral; Mice (nude); 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.

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

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

P7393: D. R. Thakker, *et al.* siRNA-mediated knockdown of the serotonin transporter in the adult mouse brain. *Molecular Psychiatry* 2005;10(8):782-789

ALZET Comments: RNA, small interfering; citalopram; RNA, mm; RNAi buffer, isotonic; CSF/CNS (dorsal third); Mice; 1002; 2 weeks; Controls received mp w/ vehicle; gene therapy; downregulation of SERT; animal info (male, BALB/C, 19-29 g); "maximally effective RNAi response requires 2 weeks of siRNA infusion." P. 783; behavioral study.

P7248: S. S. Lakka, *et al.* Specific interference of urokinase-type plasminogen activator receptor and matrix metalloproteinase-9 gene expression induced by double-stranded RNA results in decreased invasion, tumor growth, and angiogenesis in gliomas. *Journal of Biological Chemistry* 2005;280(23):21882-21892

ALZET Comments: RNA, small interfering; RNA, small interfering, uPAR; RNA, small interfering, MMP-9; CSF/CNS; Mice (nude); 1002; 2 weeks; Controls received mp w/ PBS or empty vector; cancer (glioblastoma); siRNA is within a plasmid vector (pUM vector); antiangiogenesis; gene therapy.

P7495: M. Burchardt, *et al.* Application of angiogenic factors for therapy of erectile dysfunction: protein and DNA transfer of VEGF 165 into the rat penis. *UROLOGY* 2005;66(3):665-670

ALZET Comments: Vascular endothelial growth factor, human 165; Saline, sterile; heparin; IA (renal); Rat; 2004; 28 days; Controls received mp w/ vehicle; functionality of mp verified by VEGF serum immunoassay; comparison of CDNA plasmid micro-injections vs. mp; gene therapy; peptides; animal info (male, Sprague-Dawley); urology; 2000 Units of heparin used.

P6992: D. Wolfe, *et al.* Safety and biodistribution studies of an HSV multigene vector following intracranial delivery to non-human primates. *Gene Therapy* 2004;11(23):1675-1684

ALZET Comments: Ganciclovir; SC; Monkey (Rhesus); 2ML1; 2ML2; 4,5,34,35 days; Pumps replaced after 2 weeks; no stress (see pg. 1677); cancer (glioblastoma); toxicology; MRI; multiple pumps per animal (2); gene therapy.

P6769: D. R. Thakker, *et al.* Neurochemical and behavioral consequences of widespread gene knockdown in the adult mouse brain by using nonviral RNA interference. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2004;101(49):17270-17275

ALZET Comments: RNA, small interfering; GBR 12909; RNAi buffer; CSF/CNS (dorsal third ventricle); Mice; 1007D; 1002; 1,2 weeks; Controls received mp w/ vehicle; antisense (EGFP, DAT, scrambled sequence); Plastics One cannula used; "Results highlight the temporal effects of siRNA, requiring a constant minipump-mediated infusion in the dorsal third ventricle for a stable and bilateral knockdown of gene expression in the brain." (p. 17275); gene therapy.

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

ALZET Comments: RNA, small interfering; human cytomegalovirus promoter; Empty vector; CSF/CNS; Mice; 2004; 5 weeks; 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):846-8496
ALZET Comments: RNA, small interfering; Virus, EV/SV vector; PBS; CSF/CNS (intratumoral); Mice (nude); 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."
- P5995:** G. Dorn, *et al.* siRNA relieves chronic neuropathic pain. *NUCLEIC ACIDS RESEARCH* 2004;32(5):1-6
ALZET Comments: RNA, small interfering; oligonucleotide, antisense; Saline; CSF/CNS (intrathecal); Rat; 6-7 days; Controls received mp w/ missense siRNA; no stress (see pg. 4); antisense (P2X₃); gene therapy; siRNA (P2X₃); pain research.
- Q5402:** C. D. Allen, *et al.* Germinal center dark and light zone organization is mediated by CXCR4 and CXCR5. *Nat Immunol* 2004;5(9):943-52
ALZET Comments: TE14011, 4F-benzoyl-; Saline; SC; Mice; 1007D; 7 days; Controls received mp w/saline; animal info (C57BL/6 (B6); gene therapy; immunology; Peptides (SDF-1 peptide); 4F-benzoyl-TE14011 is a CXCR4 inhibitor; Therapeutic indication (immunotherapy); Dose (40 mg/ml);
- P5966:** A. Roguin, *et al.* Restoration of blood flow by using continuous perimuscular infiltration of plasmid DNA encoding subterranean mole rat *Spalax ehrenbergi* VEGF. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2003;100(8):4644-4648
ALZET Comments: DNA, naked; vascular endothelial growth factor, DNA; Water; Intramuscular (left quadriceps muscle); Mice; 2001; 7 days; Controls received mp w/ saline; tissue perfusion (quadriceps muscle); gene therapy; fenestrated catheter; pump implanted IP; "we have shown that when using plasmid DNA, continuous administration is superior to multiple simultaneous IM injections." (p. 4647).
- P5520:** L. M. Melton, *et al.* Chronic glial activation, neurodegeneration, and APP immunoreactive deposits following acute administration of double-stranded RNA. *Glia* 2003;44(1):1-12
ALZET Comments: RNA, double stranded; statolon dsRNA; polyinosinic acid ds RNA; polycytidilic acid dsRNA; Tris/borate/EDTA buffer; CSF/CNS; Rat; 2002; 14 days; Controls received mp w/ vehicle; gene therapy; post op. care (buprenorphine); statolon is a naturally occurring dsRNA from a mycophage; neurodegenerative (Parkinson's disease, Alzheimer's); 2mM EDTA;
- P5657:** M. Herraiz, *et al.* Liver failure caused by herpes simplex virus thymidine kinase plus ganciclovir therapy is associated with mitochondrial dysfunction and mitochondrial DNA depletion. *Human Gene Therapy* 2003;14(5):463-472
ALZET Comments: Ganciclovir; Saline; IP; Rat; 2ML2; 3,7,10 days; Controls received mp w/ saline; gene therapy.
- P6138:** L. M. Smoot, *et al.* Characterization of two novel pyrogenic toxin superantigens made by an acute rheumatic fever clone of *Streptococcus pyogenes* associated with multiple disease outbreaks. *Infection and Immunity* 2002;70(12):7095-7104
ALZET Comments: rSpeL; rSpeM; rSpeC; PBS; SC; Rabbit; 15 days; rSpeL,M and C are bacteriophage genes; gene therapy; "The miniosmotic pump model of STSS was also used to assess the lethality of rSpeL and rSpeM, since these devices release a constant amount of exotoxin into subcutaneous tissue and hence resemble infection with exotoxin-producing GAS."
- P6179:** V. Mittoux, *et al.* Corticostriatopallidal Neuroprotection by Adenovirus-Mediated Ciliary Neurotrophic Factor Gene Transfer in a Rat Model of Progressive Striatal Degeneration. *Journal of Neuroscience* 2002;22(11):4478-4486
ALZET Comments: Nitropropionic acid, 3-; Water, deionized; NaOH; SC; Rat; 2ML4; 5,16 days; Controls received mp w/ nothing; gene therapy; neurodegenerative (Huntington's disease); behavioral testing; 3NP had a pH of 7.4.
- R0164:** A. K. Lalwani, *et al.* Current issues in cochlear gene transfer. *Audiol. Neurootol* 2002;7(3):146-151
ALZET Comments: Gene vectors, virus; Ear (cochlea); Guinea pig; 1007D; Gene therapy; review of various cochlear gene delivery methods; diagram of the various delivery methods (p. 147); tissue perfusion (cochlea).



R0183: A. K. Lalwani, *et al.* Developments in cochlear gene therapy. GENETIC HEARING IMPAIRMENT: ITS CLINICAL PRESENTATIONS 2002;61(1):28-33

ALZET Comments: Ear; Gene therapy; review of gene vectors and routes of delivery for cochlear gene therapy; 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

ALZET Comments: Virus, adeno-associated; Gene, green fluorescent protein; Gene, brain-derived neurotrophic factor; PBS; Ear (cochlea); Guinea pig; 1007D; 1 week; 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).

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).

P5596: F. Doetsch, *et al.* EGF converts transit-amplifying neurogenic precursors in the adult brain into multipotent stem cells. Neuron 2002;36(6):1021-1034

ALZET Comments: Epidermal growth factor; Ganciclovir; Saline; BSA; PBS; CSF/CNS; Mice; 1007D; 1002; 7 hours; 6 days; Controls received mp w/ vehicle; Gene therapy; peptides; EGF was diluted in BSA-containing saline and infused for 7 hours, or 6 days in 1007D pumps; Ganciclovir was diluted in PBS and infused for 6 days via 1002 pumps.

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

ALZET Comments: Adenovirus; Gene, beta-galactosidase;; Perilymph, artificial;; Ear (cochlea);; Guinea pig;; 2001;; 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

ALZET Comments: Adenovirus vector; virus, adeno-associated; Perilymph, artificial; Ear (scala tympani); Guinea pig; 2001; 7 days; 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).

R0184: A. Jacobs, *et al.* Positron-emission tomography of vector-mediated gene expression in gene therapy for gliomas. Lancet 2001;358(727-729

ALZET Comments: Rat; Gene therapy; brief references to minipump-infusion study (p. 728) on non-viral vector administration into rat F98 gliomas with subsequent ganciclovir treatment.

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

ALZET Comments: Methylisothiourea, S-; adenovirus vector; gene, mouse iNOS cDNA sequence; Saline; Dye, methylene blue; Dye, India black ink; PBS; SC (wound healing site);; Rat;; 2001; 2ML1;; 7 days;; 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);.

P5767: S. D. Reynolds, *et al.* Conditional clara cell ablation reveals a self-renewing progenitor function of pulmonary neuroendocrine cells. Am J Physiol Lung Cell Mol Physiol 2000;278(6):L1256-L1263



ALZET Comments: Ganciclovir; Saline; Mice (transgenic); 6,12 days; Controls received mp w/ vehicle; gene therapy.

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;.

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)

ALZET Comments: Lentivirus; gene, green fluorescent protein; Saline; PBS;; ear (cochlea);; Guinea pig;; 1007D;; 8, 3 days;; controls received mp w/vehicle; tissue perfusion (scala tympani); gene therapy;.

P4580: T. G. Bush, *et al.* Leukocyte infiltration, neuronal degeneration, and neurite outgrowth after ablation of scar-forming, reactive astrocytes in adult transgenic mice. *Neuron* 1999;23(297-308)

ALZET Comments: Ganciclovir; memantine; Saline, sterile physiological; SC; Mice (transgenic); 7, 14 days; gene therapy; ganciclovir infused for 7 days; memantin infused for 14 days.

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)

ALZET Comments: Virus, adeno-associated; Gene, lacZ; Gene, green fluorescent protein; Saline; ear (cochlea); Guinea pig; no duration posted; 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)

ALZET Comments: Virus, adeno-associated; Gene, green fluorescent protein; Gene, beta-galactosidase; PBS; ear (cochlea); Guinea pig; 1007D; 7 days; controls received mp w/vehicle, mp w/reporter gene, or no pump; tissue perfusion (scala tympani); gene therapy.

P4579: T. G. Bush, *et al.* Fulminant jejuno-ileitis following ablation of enteric glia in adult transgenic mice. *Cell* 1998;93(189-201)

ALZET Comments: Ganciclovir;; Saline, sterile physiological; SC;; mice (transgenic); 2004; 2001; 2002; 1007D; 7, 14, 28 days; controls received no treatment; 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)

ALZET Comments: Virus, adeno-associated; Gene, green fluorescent protein; PBS; ear (cochlea); Guinea pig; 1007D; 2, 7 days; controls received mp w/saline or mp w/AAV-Bgal; tissue perfusion (scala tympani); good methods (p.141); gene therapy.

P4467: J. L. Cohen, *et al.* Prevention of graft-versus-host disease in mice using a suicide gene expressed in T lymphocytes. *Blood* 1997;89(12):4636-4645

ALZET Comments: Ganciclovir;; PBS;; SC;; mice;; 2001;; 7 days;; controls received mp w/vehicle; functionality of mp verified by plasma levels; comparison of IP injections vs. mp; immunology; Gene therapy.

P3921: S. Benedetti, *et al.* Limited efficacy of the hsv-tk/gcv system for gene therapy of malignant gliomas and perspectives for the combined transduction of the interleukin-4 gene. *Human Gene Therapy* 1997;8(1345-1353)

ALZET Comments: Ganciclovir; Water; Rat; mice (nude); 2002; 2ML2; 2 weeks; comparison of IP injections vs. mp; cancer; 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)

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).

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)

ALZET Comments: Virus, adeno-associated, with bacterial gene seq; PBS; ear (cochlea); Guinea pig; 1007D; 2 weeks; controls received saline infusion; tissue perfusion (cochlea); Gene therapy.

P3574: M. Franken, *et al.* Epstein-barr virus-driven gene therapy for EBV-related lymphomas. *Nature Medicine* 1996;2(12):1379-1382

ALZET Comments: Ganciclovir; mice (SCID); 7 days; controls received p w/ saline; comparison of ip injections vs. mp; cancer; gene therapy.

P2284: P. T. Golumbek, *et al.* Herpes simplex-1 virus thymidine kinase gene is unable to completely eliminate live, nonimmunogenic tumor cell vaccines. *J. Immunother* 1992;12(224-230)

ALZET Comments: Ganciclovir; SC; mice; 2002; 2-4 weeks; controls received mp w/vehicle; pumps replaced; immunology; Gene therapy.