



References on the Administration of Cyclosporine Using ALZET® Osmotic Pumps

Q6954: S. L. Payne, *et al.* Initial cell maturity changes following transplantation in a hyaluronan-based hydrogel and impacts therapeutic success in the stroke-injured rodent brain. *Biomaterials* 2019;192(309-322)

ALZET Comments: Cyclosporine A; Ethanol, Cremophor; SC; Rat; 2ML4; 56 days; Dose (15 mg/kg/day); animal info (male Sprague-Dawley rats, 350 g); post op. care (3 mg/kg- ketoprofen); behavioral testing (Montoya staircase and tapered beam test); long-term study; ischemia (stroke);.

R0371: M. Kockx, *et al.* Cyclosporin A-Induced Dyslipidemia and LDL Receptors. 2019;323-333

ALZET Comments: Cyclosporin A; SC; Mice; 4 weeks; Dose (20 mg/kg/day); animal info (C57Bl6 and Ildr_/_ mice);.

Q7249: L. Nusrat, *et al.* Cyclosporin A-Mediated Activation of Endogenous Neural Precursor Cells Promotes Cognitive Recovery in a Mouse Model of Stroke. *Front Aging Neurosci* 2018;10(93)

ALZET Comments: Cyclosporin A; Ethanol, Cremaphor; SC; Mice; 10.3389/fnagi.2018.00093; Dose (15 mg/kg/day); Dose (15 mg/kg/day); animal info (adult male C57BL/6 mice 6–8 weeks of age; 20–25 g); pumps replaced; ischemia (cerebral);.

Q5695: T. L. Uhlendorf, *et al.* Efficacy of Two Delivery Routes for Transplanting Human Neural Progenitor Cells (NPCs) Into the Spastic Han-Wistar Rat, a Model of Ataxia. *Cell Transplant* 2017;26(2):259-269

ALZET Comments: Cyclosporine; SC; Rat; 2004; animal info (spastic Han-Wistar, 30 days); no stress (see pg. 268); behavioral testing (locomotor activity); cardiovascular; “This method of chronic delivery prevents painful daily injection and subsequent behavioral changes in treated animals. We did not detect any negative effects of cyclosporine, and no behavioral alterations were observed in treated mutants other than natural disease progression” pg 268; Dose (15 mg/kg/day);.

Q6709: S. Oka, *et al.* PET Tracer (18)F-Fluciclovine Can Detect Histologically Proven Bone Metastatic Lesions: A Preclinical Study in Rat Osteolytic and Osteoblastic Bone Metastasis Models. *Theranostics* 2017;7(7):2048-2064

ALZET Comments: Cyclosporin A; SC; Rat; 2ML4; Dose (50 mg/mL);.

Q7248: R. L. Nuryyev, *et al.* Transplantation of Human Neural Progenitor Cells Reveals Structural and Functional Improvements in the Spastic Han-Wistar Rat Model of Ataxia. *Cell Transplant* 2017;26(11):1811-1821

ALZET Comments: Cyclosporine; SC; Rat; 2004; 28 days; Dose (15 mg/kg/day); animal info (30 days of age, male sHW mutant rats); neurodegenerative (replacement/augmentation); .

Q6203: S. J. Min, *et al.* Leptomycin B attenuates neuronal death via PKA- and PP2B-mediated ERK1/2 activation in the rat hippocampus following status epilepticus. *Brain Res* 2017;1670(14-23)

ALZET Comments: Cyclosporin A; H-89; Leptomycin B; U0126; CSF/CNS (right lateral ventricle); Rat; 1007D; 3 days; Dose [H-89 (10 uM); LMB (30 mg/ml); LMB (30 mg/ml) + H-89 (10 uM); CsA (250 uM); LMB (30 mg/ml) + CsA (250 uM); U0126 (25 uM); and LMB (30 mg/ml) + U0126 (25 uM)]; Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats weighing 320–370 g); H-89 is a PKA inhibitor; U0126 is an ERK ½ inhibitor; ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; -3.5 mm depth); Therapeutic indication (seizure);.

Q6402: K. Chen, *et al.* Sequential therapy of anti-Nogo-A antibody treatment and treadmill training leads to cumulative improvements after spinal cord injury in rats. *Exp Neurol* 2017;292(135-144)

ALZET Comments: Immunoglobulin G1, anti-Nogo-A antibody 11C7; Immunoglobulin G1, anti-cyclosporin A; CSF/CNS; Rat; 2ML2; 2 weeks; animal info (female Sprague-Dawley rats weighing 200-250 g); Therapeutic indication (spinal cord injury);.

Q6314: M. M. Adil, *et al.* Engineered hydrogels increase the post-transplantation survival of encapsulated hESC-derived midbrain dopaminergic neurons. *Biomaterials* 2017;136(1-11)

ALZET Comments: Cyclosporine; SC; Rat; Dose (10 mg/kg/day); animal info (adult female Fischer 344 rats); pumps replaced every 2 weeks;.



Q5380: M. Kockx, *et al.* Low-Density Lipoprotein Receptor-Dependent and Low-Density Lipoprotein Receptor-Independent Mechanisms of Cyclosporin A-Induced Dyslipidemia. *Arterioscler Thromb Vasc Biol* 2016;36(7):1338-49

ALZET Comments: Cyclosporine A; Ethanol; Cremophor EL; SC; Mice; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (female mice, C57Bl/6, 18-20 g); functionality of mp verified by plasma levels; 33% ethanol, 62% Cremophor EL used; toxicology; Cyclosporine A aka CsA; CsA does not induce liver or kidney toxicity; Dose (20 mg/kg/day); Resultant plasma level (1087±124 ng/mL, 711±91 ng/mL after 1 week, 4 weeks);.

Q5243: J. Oller, *et al.* C/EBPbeta and Nuclear Factor of Activated T Cells Differentially Regulate Adamts-1 Induction by Stimuli Associated with Vascular Remodeling. *Mol Cell Biol* 2015;35(19):3409-22

ALZET Comments: Vascular Endothelial Growth Factor, Angiotensin II, Losartan, Cyclosporine; Saline; SC; Mice; 21 days; Controls received mp w/ vehicle; animal info (Calcineurin (CN) B1 (Cnb1^{-/-}) conditional knockout mice, C57BL/6 mice); dose-response; vegf aka vascular endothelial growth factor; Dose (VEGF 25 ug/kg/day, AngII 1 ug/kg/min, CsA 5 mg/kg/day, Losartan 10 mg/kg/day);.

Q4344: V. Cardinale, *et al.* Profiles of Cancer Stem Cell Subpopulations in Cholangiocarcinomas. *AMERICAN JOURNAL OF PATHOLOGY* 2015;185(1724-1739

ALZET Comments: Cyclosporine; IP; Mice; 1004; 4 weeks; Animal info (male, BALB/c, 13 weeks old); cancer (cholangiocarcinoma);.

Q4077: N. Sachewsky, *et al.* Cyclosporin A enhances neural precursor cell survival in mice through a calcineurin-independent pathway. *Disease Models & Mechanisms* 2014;7(953-961

ALZET Comments: Cyclosporin; FK506; NIM811; Saline; SC; Mice; 2002; 7 days; 25 days; 32 days;; Controls received mp w/ vehicle; animal info (male, C57BL6J, 6-8 weeks old, 25-30g); pumps replaced every 2 weeks; ischemia (cerebral); post op. care (SC injection of warmed saline); behavioral testing (foot fault task);.

Q4720: H. Hamdi, *et al.* Long-Term Functional Benefits of Epicardial Patches as Cell Carriers. *CELL TRANSPLANTATION* 2014;23(1):87-96

ALZET Comments: Cyclosporine; SC; Rat; 2ML4; Animal info (female, Wistar); immunology; "Because of the planned long duration of the follow-up (6 months), concerns over daily injections of cyclosporine led us to use subcutaneously implanted microosmotic pumps preset to release the drug in a controlled fashion." pg 93;.

Q2992: E. Koellensperger, *et al.* Human Adipose Tissue Derived Stem Cells Promote Liver Regeneration in a Rat Model of Toxic Injury. *STEM CELLS INTERNATIONAL* 2013;;(;):U1-U10

ALZET Comments: Cyclosporine; IP; Rat; 2ML4; 12 weeks; Animal info (Sprague Dawley, model of toxic liver damage (two-thirds hepatectomy)); immunology; pumps replaced every 28 days; long-term study.

Q0700: N. Sachan, *et al.* Sustained Hemodynamic Stress Disrupts Normal Circadian Rhythms in Calcineurin-Dependent Signaling and Protein Phosphorylation in the Heart. *Circulation Research* 2011;108(4):437-U100

ALZET Comments: Cyclosporine; SC; Mice; Controls received mp w/ vehicle; animal info (male, C57BL/6, 6-8 wks old); wound clips used.

Q1058: V. Esteban, *et al.* Regulator of calcineurin 1 mediates pathological vascular wall remodeling. *Journal of Experimental Medicine* 2011;208(10):2125-2139

ALZET Comments: Angiotensin II; PD123319; cyclosporin A; losartan; SC; Mice; 14, 28 days; Controls received mp w/ saline; animal info (2 mo old, ApoE ^{-/-}, Rcan1 ^{-/-}); peptides.

Q1055: A. Erlandsson, *et al.* Immunosuppression promotes endogenous neural stem and progenitor cell migration and tissue regeneration after ischemic injury. *Experimental Neurology* 2011;230(1):48-57

ALZET Comments: Epidermal growth factor, recomb. human; erythropoietin; cyclosporine A; CSF/CNS; SC; Mice (NOD/SCID); 1007D; Animal info (male, C57/BL6, 8-10 wks old); pumps replaced after 7 days; ALZET brain infusion kit 3 used.



Q2198: A. Y. Chang, *et al.* Calcineurin mediates bladder wall remodeling secondary to partial outlet obstruction. *American Journal of Physiology-Renal Physiology* 2011;301(4):F813-F822

ALZET Comments: Cyclosporine A; Mice (transgenic); 2004; 2 weeks; Controls received mp w/ saline; animal info (male, pBOO tg).

Q0096: Y. Xu, *et al.* Adenovirus-Mediated Overexpression of Glutathione-S-Transferase Mitigates Transplant Arteriosclerosis in Rabbit Carotid Allografts. *Transplantation* 2010;89(4):409-416

ALZET Comments: Cyclosporin A; IP; Rabbit; Animal info (DB, NZW, 3 months old, male).

Q1648: R. Schramm, *et al.* Erythropoietin inhibits post-ischemic leukocyte adhesion but does not affect rejection in murine cardiac allografts. *Journal of Heart and Lung Transplantation* 2010;29(10):1185-1192

ALZET Comments: Cyclosporine; SC; Mice; 2004; Animal info (Balb/c, male, C57BL/6, 26-28 g).

Q0123: J. Hunt, *et al.* Cyclosporin A Has Direct Effects on Adult Neural Precursor Cells. *Journal of Neuroscience* 2010;30(8):2888-2896

ALZET Comments: Cyclosporin A; IV; SC; Mice; 2002; 14 days; Controls received mp w/ saline; animal info (male, CD1, 6-8 weeks old, 25-30 g).

Q1100: K. Groth, *et al.* Cyclosporine A exposure during pregnancy in mice: effects on reproductive performance in mothers and offspring. *Human Reproduction* 2010;25(3):697-704

ALZET Comments: Cyclosporine A; Propylene glycol; SC; Mice (pregnant); 2001; 2002; Controls received mp w/ vehicle; animal info (C57CBA-F1, female); pumps replaced after 1 weeks; 90% propylene glycol used; wound clips used.

Q0393: H. Toriumi, *et al.* Treatment of Parkinson's disease model mice with allogeneic embryonic stem cells: necessity of immunosuppressive treatment for sustained improvement. *NEUROLOGICAL RESEARCH* 2009;31(3):220-227

ALZET Comments: Cyclosporine A; Propylene glycol; SC; Mice; 2004; Animal info (C57BL/6, BALB/c, C3H/HeN PD, 129SvJ PD); pumps replaced "at 2 week intervals".

Q0590: E. A. Ingram, *et al.* Prolonged infusion of inhibitors of calcineurin or L-type calcium channels does not block mossy fiber sprouting in a model of temporal lobe epilepsy. *Epilepsia* 2009;50(1):56-64

ALZET Comments: Nicardipine; FK506; cyclosporin A; DMSO; ethanol; fluorescein; CSF/CNS (dorsal left dentate gyrus); Rat; 2004; 28 days; Controls were treated identically without status epilepticus; animal info (34-52 day old, male, Sprague-Dawley, status epilepticus); functionality of mp verified by fluorescein labeling; ALZET brain infusion kit 2 used; 50% DMSO used; 15% ethanol used.

Q0545: A. U. Hicks, *et al.* Transplantation of human embryonic stem cell-derived neural precursor cells and enriched environment after cortical stroke in rats: cell survival and functional recovery. *European Journal of Neuroscience* 2009;29(3):562-574

ALZET Comments: Cyclosporine A; PEG 400; SC; Rat; 2ML4; 2002; Controls received mp w/ vehicle; animal info (male, Wistar, 275-300 g, dMCAO); functionality of mp verified by residual volume; behavioral testing (Montoya's staircase test).

P9674: H. G. Zerwes, *et al.* The chemokine receptor Cxcr3 is not essential for acute cardiac allograft rejection in mice and rats. *AMERICAN JOURNAL OF TRANSPLANTATION* 2008;8(8):1604-1613

ALZET Comments: Cyclosporin A; NIBR2130; SC; Mice; 2002; 2ML2; 14 days; Animal info (CXCR3 deficient, C47BL/6, 8-12 wks old); NIBR2130 is a CXCR3 inhibitor; functionality of mp verified by plasma drug levels.

P9116: J. Kwun, *et al.* Unaltered graft survival and intragraft lymphocytes infiltration in the cardiac allograft of Cxcr3^{-/-} mouse recipients. *AMERICAN JOURNAL OF TRANSPLANTATION* 2008;8(8):1593-1603

ALZET Comments: Cyclosporin; SC; Mice; 1002; Animal info (male, C57BL/6, 6-8 wks old, Cxcr3^{-/-}).

P9313: C. Hippert, *et al.* Gene transfer may be preventive but not curative for a lysosomal transport disorder. *MOLECULAR THERAPY* 2008;16(8):1372-1381



ALZET Comments: Cyclosporin A; SC; Mice; 28 days; Controls received no treatment; functionality of mp verified by blood CsA levels; animal info (male, 1295v/C57BL6 Ctns -/-; 3, 5 months old); "A whole blood immunoassay demonstrated that CsA was continually administered over the 28-day period" (p.1375); metabolic disorders.

P8367: C. A. Wranning, *et al.* Rejection of the transplanted uterus is suppressed by cyclosporine A in a semi-allogeneic mouse model. *Human Reproduction* 2007;22(2):372-379

ALZET Comments: Cyclosporin A; Propylene glycol; SC; Mice; 1007D; 7-10 days; Controls received mp w/ vehicle, or no treatment; functionality of mp verified by serum CyA levels; dose-response (Table 1); immunology; post op.care (buprenorphin, carprofen, cefuroxime); animal info (female, C57BL/6, B6CBAF1, 6-8 wks old, uterine transplant).

P8541: Y. Muramatsu, *et al.* Neuroprotective efficacy of FR901459, a novel derivative of cyclosporin A, in in vitro mitochondrial damage and in vivo transient cerebral ischemia models. *Brain Research* 2007;1149(181-190

ALZET Comments: Cyclosporin A; FR901459; Cremophor EL; saline;; CSF/CNS; Rat; 1003D; 48 hours; Dose-response (fig. 7); comparison of IV bolus injections vs. mp; ischemia (cerebral); animal info (male, Wistar, 9-10 weeks old, 274-280 grams, MCAO).

P8446: J. J. A. Coenen, *et al.* Rapamycin, not cyclosporine, permits thymic generation and peripheral preservation of CD4⁺ CD25⁺ FoxP3⁺ T cells. *Bone Marrow Transplantation* 2007;39(9):537-545

ALZET Comments: Cyclosporin A; SC; Mice; 2004; 7,14,28 days; Controls received mp w/PBS; dose-response (fig. 1); cardiovascular; immunology; animal info (C3H (H-2K), BALB/C (H-2d), 8-12 wks old).

P8737: N. A. Addy, *et al.* Role of calcineurin in nicotine-mediated locomotor sensitization. *Journal of Neuroscience* 2007;27(32):8571-8580

ALZET Comments: Cyclosporin; FK506; rapamycin; PBS; Tween 20; DMSO; ethanol; cremaphor; CSF/CNS (ventral tegmental area); CSF/CNS (nucleus accumbens); Rat; 2004; 3-4 weeks; Controls received mp w/ vehicle; no stress (see pg. 8573); animal info (male, Sprague-Dawley, 200-250g); 25% DMSO.

P8173: F. Marchal, *et al.* Development of an HT29 liver metastases model in nude rats. *Oncology Reports* 2005;14(5):1203-1207

ALZET Comments: Cyclosporin A; IP; Rat (nude); 2ML4; 4 weeks; Controls received no treatment; no stress (see pg. 1204); cancer (colorectal); peptides; animal info (male, athymic Rowett nude, 300 grams).

P7104: S. B. Minami, *et al.* Calcineurin activation contributes to noise-induced hearing loss. *Journal of Neuroscience Research* 2004;78(3):383-392

ALZET Comments: FK506; cyclosporin A; Perilymph, artificial; Ear (cochlea); Guinea pig; 2002; 14 days; Controls received mp w/ vehicle, or contralateral untreated cochlea; dose-response (fig. 3); stress/adverse reaction: (see pg. 385) 4 of 43 animals developed middle ear infections; 4 of 43 animals had post surgical hearing loss; calcineurin inhibitors; "Systematic application may therefore have unwanted side effects that may be avoided by intracochlear perfusion by osmotic pump. The use of an osmotic pumps also allows relatively precise control over the timing and concentration of drugs applied to the tissues of the inner ear." (pg. 389); tissue perfusion (cochlea).

P6785: B. Luckow, *et al.* Reduced intragraft mRNA expression of matrix metalloproteinases Mmp3, Mmp12, Mmp13 and Adam8, and diminished transplant arteriosclerosis in Ccr5-deficient mice. *European Journal of Immunology* 2004;34(9):2568-2578

ALZET Comments: Cyclosporin A; SC; Mice; 2002; Heart transplant; cardiovascular.

P6525: S. Bai, *et al.* Metabolic interaction between cyclosporine and sirolimus. *Transplantation* 2004;77(10):1507-1512

ALZET Comments: Cyclosporin; sirolimus; Sandimmune IV solution; dimethylacetamide; Tween 80; PEG 400; IV (femoral); Rat; 2002; 14 days; Controls received mp w/ vehicle; multiple pumps per animal (2); CSA was purchased as sandimmune IV solution (cremophor or castor oil and 33% ethanol); sirolimus aka rapamycin; SRL was dissolved in Tween 80 (10%), PEG 400 (70%), and dimethyl acetamide, N-N- (20%); Immunology.



P5887: Y. Matsumoto, *et al.* Differential effect of cyclosporine A and SDZ RAD on neointima formation of carotid allografts in apolipoprotein E-deficient mice. *Transplantation* 2003;76(8):1166-1170

ALZET Comments: SDZ RAD; cyclosporin A; Propylene glycol; sandimmune IV solution; SC; Mice (knockout); 2002; 8 weeks; Dose-response (survival dose response) p. 1168; pumps replaced every 2 weeks; immunology; (RAD) is a novel rapamycin derivative and is an immunosuppressant, aka everolimus or certican; sandimmune IV solution used; "CSA & RAD were administered by ALZET minipumps, which we prefer because of the well-defined drug exposure." p. 1168; long-term study.

P5496: D. Haouzi, *et al.* Mitochondrial permeability transition as a novel principle of hepatorenal toxicity in vivo. *Apoptosis* 2002;7(5):395-405

ALZET Comments: Cyclosporin A; Ethanol; SC; Mice; 1003D;

P6171: Z. Nikolovski, *et al.* Efficacy of SDZ RAD compared with CsA monotherapy and combined RAD/FTY720 treatment in a murine cardiac allotransplantation model. *TRANSPLANT IMMUNOLOGY* 2001;9(43-49)

ALZET Comments: SDZ RAD; cyclosporin A; Propanediol propylene glycol, 1,2-; sandimmune IV solution; SC; Mice; 2002; 8 weeks; Controls received mp w/ vehicle; pumps replaced every two weeks; cardiovascular; SDZ RAD (everolimus or certican) is an immunosuppressant; "SDZ RAD has a shorter half-life than rapamycin; CsA was dissolved in sandimmune IV solution; long-term study.

P4669: C. Ramirez, *et al.* Role of intrarenal endothelin 1, endothelin 3, and angiotensin II expression in chronic cyclosporin A nephrotoxicity in rats. *Experimental Nephrology* 2000;8(161-172)

ALZET Comments: Cyclosporin A; Endothelin-1; Endothelin-3;; Saline; propylene glycol; SC;; Rat;; 2ML4;; 56 days;; Controls received mp w/ vehicle; functionality of mp verified by whole blood CsA levels; long-term study, pumps replaced after 28 days; antihypertensive; cardiovascular; secretion in nephrotoxicity, relationship with Angiotensin II in renal expression propylene glycol used as vehicle for CsA.

R0244: S. A. Gruber, *et al.* Local drug delivery to composite tissue allografts. *MICROSURGERY* 2000;20(8):407-411

ALZET Comments: Cyclosporin A; FK506; IA (brachial); Rabbit; 6 days; Dose-response; review, see pg. 409.

P4576: M. V. Shirbacheh, *et al.* Pharmacokinetic advantage of intra-arterial cyclosporin A delivery to vascularly isolated rabbit forelimb. I. Model development. *The Journal of Pharmacology and Experimental Therapeutics* 1999;289(3):1185-1190

ALZET Comments: Cyclosporin A; Sandimmune IV solution; IA (brachial); IV (jugular);; rabbit;; 2ML1;; 6 days; good surgical methods (p. 1186); immunology; diagram of pump/catheter system (p. 1186); PE-60 tubing was glued to PE-10 tubing; Sandimmune (CSA) solution used;

P4577: M. V. Shirbacheh, *et al.* Pharmacokinetic advantage of intra-arterial cyclosporin A delivery to vascularly isolated rabbit forelimb. II. Dose dependence. *The Journal of Pharmacology and Experimental Therapeutics* 1999;289(3):1191-1195

ALZET Comments: Cyclosporin A; Cremophor; sandimmune IV solution; IA (brachial); Rabbit; 2ML1; 6 days; Dose-response (p. 1192-1194); immunology; sandimmune (CSA) solution used; intramedic PE-60/PE-10 infusion catheter used; to achieve highest dose; two pumps were implanted and catheters were joined via a Y-connector;

P3997: D. Brandle, *et al.* Contribution of donor-specific antibodies to acute allograft rejection. *Transplantation* 1998;65(11):1489-1493

ALZET Comments: Cyclosporin A; SC; mice; no duration posted; dose-response (0, 3, 10 mg/kg/d); immunology.

P3900: S. Wehr, *et al.* Allo- and autotransplantation of carotid artery - a new model of chronic graft vessel disease. *Transplantation* 1997;64(1):20-27

ALZET Comments: Cyclosporin; SC; Rat; 2ML4; 2ML2; 8 weeks; controls received mp w/vehicle; functionality of mp verified by CsA blood levels at 1 and 8 weeks; immunology; long-term study.



P3901: S. M. Stepkowski, *et al.* Antisense ICAM-1 oligonucleotides block allograft rejection in rats. *Transplant. Proc* 1997;29(1285)

ALZET Comments: Cyclosporin; Oligodeoxynucleotide, antisense; Cremophor; IV; Rat; 7, 14 days; immunology; antisense; controls received scrambled antisense.

P3899: J.-O. Sandberg, *et al.* Xenograft rejection of porcine islet-like cell clusters in normal, interferon-gamma, and interferon-gamma receptor deficient mice. *Transplantation* 1997;63(10):1446-1452

ALZET Comments: Cyclosporin; SC; mice; 2002; 6, 12 days; controls received mp w/vehicle; functionality of mp verified by blood CsA levels and visual inspection at study end; immunology.

P3611: D. G. Tice, *et al.* Anti-VLA-4 and cyclosporine synergistically prolong rat heterotopic small bowel allografts. *Transplant. Proc* 1996;28(5):2496

ALZET Comments: Cyclosporin A; Rat; 20 days; immunology.

P3239: C. P. Larsen, *et al.* Long-term acceptance of skin and cardiac allografts after blocking CD 40 and CD 28 pathways. *Nature* 1996;381(6581):434-438

ALZET Comments: Cyclosporin A; SC; Mice; 2002; 14 days; No stress (see pg. 437); immunology; animal info (C57BL/6).

P3363: Y. Tu, *et al.* The synergistic effects of cyclosporine, sirolimus, and brequinar on heart allograft survival in mice. *Transplantation* 1995;59(2):177-183

ALZET Comments: Cyclosporin A; Rapamycin; Cremophor; Dimethylacetamide; Tween 80; PEG 400; IV (jugular); mice; 1007D; 7, 14 days; pumps replaced after 7 days; immunology; CSA and rapamycin given singly and via same pump.

P3995: S. J. Oliver, *et al.* Suppression of collagen-induced arthritis by an angiogenesis inhibitor, AGM-1470, in combination with cyclosporin: reduction of vascular endothelial growth factor (VEGF). *Cellular Immunol* 1995;166(196-206)

ALZET Comments: Cyclosporin A; PEG 300; SC; Rat; 2ML4; no duration posted; photo of rat showing implanted pump (pg. 204); no stress (see pp. 199, 204, 205); immunology; controls received sham surgeries.

P2048: S. M. Stepkowski, *et al.* Blocking of heart allograft rejection by intercellular adhesion molecule-1 antisense oligonucleotides alone or in combination with other immunosuppressive modalities. *J. Immunol* 1994;153(5336-5346)

ALZET Comments: Oligodeoxynucleotide, phosphorothioate antisense; Cyclosporin A; Rapamycin; Oligodeoxynucleotide, scrambled; Cremophor; Tween 80; Dimethylacetamide; PEG 400; IV (jugular); mice; 7,14 days; oligo of interest was IP-3082; controls received no treatment, unrelated oligo IP-1082, or scrambled oligo IP-4189; immunology; "...this study reports the first example of pharmacologic activity of an antisense PS-oligo by i.v. systemic administration in a model of a complex inflammatory process".

P2982: M. Ferrareso, *et al.* Immunosuppressive effects of defibrotide. *Transplantation* 1993;56(4):928-933

ALZET Comments: Defibrotide; Cyclosporin A; PBS; Cremophor; IA (innominate); IV (lumbar); Rat; 2002; 2ML1; no duration posted; Controls were untreated; comparison of ip injections or oral gavage vs. mp; defibrotide infused into artery of graft or recipient vein; defibrotide is an immunosuppressant w/ antithrombotic and profibrinolytic activities.

P2264: M. Ferrareso, *et al.* The mechanism of unresponsiveness to allografts induced by rapamycin and rapamycin/cyclosporine treatment in rats. *Transplantation* 1993;55(4):888-894

ALZET Comments: Cyclosporin; Rapamycin; Cremophor; Dimethylacetamide; Ethanol; PEG 400; Tween 80; IV (lumbar); Rat; 2002; 14 days; immunology.

P2246: J. F. DiJoseph, *et al.* Influence of rat strain on rapamycin's kidney effects. *Transplant. Proc* 1993;25(1):714-715

ALZET Comments: Cyclosporin A; Rapamycin; Cremophor; Dimethylacetamide; Ethanol; PEG 400; Tween; IV (jugular); Rat; 2002; 2 weeks; controls received mp w/vehicle; functionality of mp verified by HPLC analysis; immunology.

P2016: S. M. Stepkowski, *et al.* Inhibition of host-versus-graft and graft-versus-host responses after small bowel transplantation in rats by rapamycin. *Transplantation* 1992;53(2):258-264



ALZET Comments: Cyclosporin; Rapamycin; Dimethylacetamide; PEG 400; Tween; IV (lumbar); Rat; 2002; 14 days; tissue perfusion (allograft); immunology.

P1958: E. Brahn, *et al.* Suppression of collagen-induced arthritis by combination cyclosporin A and methotrexate therapy. *Arthritis Rheum* 1991;34(10):1282-1288

ALZET Comments: Cyclosporin A; PEG 300; Rat; 2ML4; 28 days; dose response (graph, p. 1284); immunology.

P1941: A. Bernareggi, *et al.* Physiologic modeling of cyclosporin kinetics in rat and man. *J. Pharmacokinet. Biopharm* 1991;19(1):21-49

ALZET Comments: Cyclosporin; Cremophor; Ethanol; SC; Rat; 6 days; blood and tissue concentrations, volume of distribution on blood and tissues.

P1729: S. C. Textor, *et al.* Altered pressor responses to NE and ANG II during cyclosporin A administration to conscious rats. *Am. J. Physiol. (Heart Circ. Physiol. 27)* 1990;258(3):H854-H860

ALZET Comments: Cyclosporin A; Olive oil; IP; Rat; 2 weeks; controls received pumps with olive oil only; two doses infused.

P1822: G. M. B. Pereira, *et al.* Mechanism of action of cyclosporine A in vivo. *J. Immunol* 1990;144(6):2109-2116

ALZET Comments: Cyclosporin A; PBS; sandimmune IV solution; mice; 2001; 7 days; functionality of mp verified by measuring CsA plasma levels (HPLC); used Sandimmune iv formulation.

P1567: S. M. Stepkowski, *et al.* Prolongation of heterotopic heart allograft survival by local delivery of continuous low-dose cyclosporine therapy. *Transplantation* 1989;47(1):17-23

ALZET Comments: Cyclosporin; Cremophor; IA (innominate); IV; Rat; 2002; 14 days; dose-response; comparison of gavage vs. mp infusion; functionality of mp verified by blood levels; tissue perfusion (heart allograft).

P1691: Y. B. Lee, *et al.* The effect of continuous injection of cyclosporine A on the cardiac allograft in the rats. *J. Catholic Med. College* 1989;42(2):459-469

ALZET Comments: Cyclosporin A; IV; Rat; 2002; 11 days; comparison of daily IV injections vs. mp; graft survival: heart transplant; Japanese with English summary, English captions on graphs and tables.

P1688: G. M. B. Pereira, *et al.* Comparative aspects of T cell activation in vivo following stimulation with anti-CD3 MAB, allogenic cells and trypanosoma cruzi. *Mem. Inst. Oswaldo Cruz* 1988;1(83):284-291

ALZET Comments: Cyclosporin A; SC; mice; 2001; no duration posted; immunology.

P0880: T. J. Ruers, *et al.* 2'Deoxycoformycin: a new immunosuppressive drug with a potency comparable to cyclosporine. *Transplant. Proc. XVII* 1985;17(1):1333-1335

ALZET Comments: Cyclosporin A; Deoxycoformycin, 2'-; Ethanol; Saline; IP; Rat; 2ML2; 12 days; controls received mp w/saline; comparison of agents effects; animals rec'd skin grafts; comparison of ip injections vs. mp infusion; immunology.