



**Recent References (2016-Present) on the Administration of Cyclosporine
Using ALZET® Osmotic Pumps**

Q10191: J. Hu, *et al.* Angiotensin II receptor blockade alleviates calcineurin inhibitor nephrotoxicity by restoring cyclooxygenase 2 expression in kidney cortex. *Acta Physiologica* 2021;232(1):e13612

Agents: Cyclosporine A; Candesartan; Celecoxib **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 3 weeks;

ALZET Comments: Dose: Cyclosporine (25 mg/kg); Candesartan (5 mg/kg); Celecoxib ((50mg/kg) Controls received mp w/ vehicle; animal info: Adult (10 to 12 weeks) male Wistar rats; Cyclosporine A aka (CsA); Candesartan aka (RAS); Celecoxib aka (COX-2)

Q10112: M. Boehm, *et al.* Improving Right Ventricular Function by Increasing BMP Signaling with FK506. *American Journal of Respiratory Cell and Molecular Biology* 2021;

Agents: FK506; LDN-193189; Cyclosporine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Duration:** 6 weeks; 7 weeks;

ALZET Comments: Dose: FK506 low dose (0.05mg/kg/d), high dose (1mg/kg/d) LDN-193189 (2.5mg/kg/d); Cyclosporine (25mg/kg/d); Controls received mp w/ vehicle; Sham surgery; animal info: Male Bmpr2 heterozygous (Bmpr2+/-) (16), littermate controls (Bmpr2+/+) and C57Bl6/J (10-14 weeks of age); post op. care: Buprenorphine (0.05-0.1mg/mg); Tamoxifen; behavioral testing (Exercise testing); FK506 aka (Tacrolimus); LDN-193189 is a BMP2 inhibitor; cardiovascular;

Q9358: S. Maeda, *et al.* Notch signaling-modified mesenchymal stem cells improve tissue perfusion by induction of arteriogenesis in a rat hindlimb ischemia model. *Scientific Reports* 2021;11(1):2543

Agents: Cyclosporin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (10 mg/kg/day); animal info (Female Sprague-Dawley rats, 10 weeks old); pumps replaced every 2 weeks; ischemia (rat hindlimb ischemia model);

Q9500: W. M. Tierney, *et al.* Transplanted Human Neural Progenitor Cells Attenuate Motor Dysfunction and Lengthen Longevity in a Rat Model of Ataxia. *Cell Transplantation* 2020;29(963689720920275

Agents: Cyclosporine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;

ALZET Comments: Dose (15 mg/kg/d); animal info (spastic Han Wistar rat); behavioral testing (Motor Activity Testing); pumps replaced every 23 days; gene therapy;

Q8618: J. Kwun, *et al.* Cultured thymus tissue implantation promotes donor-specific tolerance to allogeneic heart transplants. *JCI Insight* 2020;5(11):

Agents: Cyclosporine A **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 months;

ALZET Comments: Dose (2.5 mg/kg/d); animal info (LW (RT-1l) and BN (RT-1n) rats); pumps replaced every month; Cyclosporine A aka CsA; immunology;

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

Agents: Cyclosporine A **Vehicle:** Ethanol, Cremophor; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 56 days;

ALZET Comments: 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);

Q7557: S. Martinez-Martinez, *et al.* Cardiomyocyte calcineurin is required for the onset and progression of cardiac hypertrophy and fibrosis in adult mice. *FEBS J* 2019;286(1):46-65

Agents: Angiotensin II, Cyclosporin A **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001, 2004; **Duration:** 21 days;

ALZET Comments: Dose (60 ug/kg/h-Ang II, 0.208 mg/kg/h- CsA); animal info (C57BL/6J, 8-12 weeks old);

R0371: M. Kockx, *et al.* Cyclosporin A-Induced Dyslipidemia and LDL Receptors. *Not Stated* 2019;323-333

Agents: Cyclosporin A **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose (20 mg/kg/day); animal info (C57Bl6 and *ldlr*_{-/-} mice);



Q8570: J. E. Kim, *et al.* Blockade of AMPA Receptor Regulates Mitochondrial Dynamics by Modulating ERK1/2 and PP1/PP2A-Mediated DRP1-S616 Phosphorylations in the Normal Rat Hippocampus. *Frontiers in Cell Neurosciences* 2019;13(179)

Agents: U0126; SP600125; Okadaic acid; Cyclosporin A **Vehicle:** Not stated; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (25 uM U0126; 10 uM SP600125; 10 uM Okadaic acid; 250 uM Cyclosporin A); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, 7 weeks old); U0126 aka ERK1/2 inhibitor, SP600125 aka JNK inhibitor, Okadaic acid aka PP1/PP2A inhibitor, Cyclosporin A aka CsA; ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; -3.5 mm depth to the bregma); dependence;

Q7349: J. E. Kim, *et al.* Perampanel Affects Up-Stream Regulatory Signaling Pathways of GluA1 Phosphorylation in Normal and Epileptic Rats. *Front Cell Neurosci* 2019;13(80)

Agents: Bisindolylmaleimide; KN-93; H-89; U0126; SP600125; okadaic acid; cyclosporin A **Vehicle:** Not Stated; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Dose (BIM 25uM, KN-93 25uM, H-89 10uM, U0126 25uM, okadaic acid 10uM, cyclosporine A 250uM); animal info (male Sprague-Dawley (SD) rats (7 weeks old)); behavioral testing (Morris Water maze test); enzyme inhibitor (BIM is a PKC inhibitor, KN-93 is a CAMKII inhibitor, H-78 is a PKA inhibitor, U0126 is an ERK 1/2 inhibitor, SPO600126 is a JNK inhibitor, cyclosporin A is a PP2B inhibitor, okadaic acid is a PP1/PP2A inhibitor); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth to the bregma); neurodegenerative (Epilepsy);

Q7938: J. E. Ahlfors, *et al.* Examining the fundamental biology of a novel population of directly reprogrammed human neural precursor cells. *Stem Cell Res Ther* 2019;10(1):166

Agents: Cyclosporin A **Vehicle:** Ethanol, Cremophor buffered; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 1, 2 weeks;

ALZET Comments: Dose (10 mg/kg/day); 65% ethanol: 35% Cremaphor used; Controls received mp w/ vehicle; animal info (8 weeks, Shi(-/-)); mp with CsA used to induce immunosuppression in Shiverer mice;

Q8157: S. L. Payne, *et al.* In Vitro Maturation of Human iPSC-Derived Neuroepithelial Cells Influences Transplant Survival in the Stroke-Injured Rat Brain. *Tissue Eng Part A* 2018;24(3-4):351-360

Agents: Cyclosporine A **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 7 days;

ALZET Comments: Dose (15 mg/kg/day); Controls received mp w/ vehicle; animal info (10 weeks old, Male, Sprague Dawley); post op. care (ketoprofen); Cyclosporine A aka CsA; neurodegenerative (Stroke);

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)

Agents: Cyclosporin A **Vehicle:** Ethanol, Cremaphor; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4-49 days;

ALZET Comments: Dose (15 mg/kg/day); ; animal info (adult male C57BL/6 mice 6-8 weeks of age; 20-25 g); pumps replaced; ischemia (cerebral); 65% ethanol and 35% cremaphor used

Q8055: J. R. Kulbe, *et al.* Continuous Infusion of Phenelzine, Cyclosporine A, or Their Combination: Evaluation of Mitochondrial Bioenergetics, Oxidative Damage, and Cytoskeletal Degradation following Severe Controlled Cortical Impact Traumatic Brain Injury in Rats. *J Neurotrauma* 2018;35(11):1280-1293

Agents: Cyclosporine A, Phenelzine **Vehicle:** Saline; Cremophor; Ethanol; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 3 days;

ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (3 months old, Sprague Dawley); neurodegenerative (Traumatic Brain Injury); 50mg/mL in saline/650 mg Cremophor/32.9% ethanol/ mL;

Q7813: T. Fuhrmann, *et al.* Combined delivery of chondroitinase ABC and human induced pluripotent stem cell-derived neuroepithelial cells promote tissue repair in an animal model of spinal cord injury. *Biomedical Research* 2018;13(2):024103

Agents: Cyclosporin A **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; 2ML4; **Duration:** 2 weeks; 8 weeks;

ALZET Comments: Dose (10 mg/kg/day); animal info (female, Sprague-Dawley, 300g); post op. care (Buprenorphine (0.05 mg/kg) every 12 h for 48 h); behavioral testing (BBB locomotor rating scale, ladder walk test); pumps replaced every 4 weeks; spinal cord injury; mp used to deliver cyclosporin A to aid transplant survival, implanted one day prior to cell transplantation;



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 Transplantation* 2017;26(2):259-269

Agents: Cyclosporine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** Not Stated;

ALZET Comments: 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

Agents: Cyclosporin A **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;

ALZET Comments: 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 Transplantation* 2017;26(11):1811-1821

Agents: Cyclosporine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: 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 Research* 2017;1670(14-23

Agents: Cyclosporin A; H-89; Leptomycin B; U0126 **Vehicle:** Not Stated; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 3 days;

ALZET Comments: 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. *Experimental Neurology* 2017;292(135-144

Agents: Immunoglobulin G1, anti-Nogo-A antibody 11C7; Immunoglobulin G1, anti-cyclosporin A **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;

ALZET Comments: 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

Agents: Cyclosporine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: 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. *Arteriosclerosis, Thrombosis, and Vascular Biology* 2016;36(7):1338-49

Agents: Cyclosporine A **Vehicle:** Ethanol; Cremophor EL; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: 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);

Q4841: A. Kawamura, *et al.* Teratocarcinomas Arising from Allogeneic Induced Pluripotent Stem Cell-Derived Cardiac Tissue Constructs Provoked Host Immune Rejection in Mice. *SCIENTIFIC REPORTS* 2016;6(1-13

Agents: Tacrolimus (cyclosporin) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 27 days;

ALZET Comments: cancer (teratocarcinoma); immunology; animal info (BALB/c); functionality of mp verified by plasma levels; pumps replaced after 14 days; BLI; Dose (1.5 mg/kg);