



Recent References on the Administration of Immunosuppressants
Using ALZET® Osmotic Pumps

Cyclosporin (2014-Present)

Q10492: P. K. Aujla, *et al.* Loss of ADAM15 Exacerbates Transition to Decompensated Myocardial Hypertrophy and Dilation Through Activation of the Calcineurin Pathway. *Hypertension* 2023;80(1):97-110

Agents: Cyclosporin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; 1004; **Duration:** 6 weeks;
ALZET Comments: Dose (25 mg/kg/day); animal info (Male; Wildtype and ADAM15-deficient; C57BL/6J background; 8-10 weeks old); cardiovascular;

Q10948: H. Ishigooka, *et al.* Novel Complement C5 Small-interfering RNA Lipid Nanoparticle Prolongs Graft Survival in a Hypersensitized Rat Kidney Transplant Model. *Transplantation* 2022;106(12):2338-2347

Agents: Cyclosporin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Strain:** Lewis; **Pump:** 2ML4; **Duration:** 7 days;
ALZET Comments: Dose (CsA 0.3 mg/body/day); animal info (Male); immunology (CsA is an immunosuppressant); nephrology

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);

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 **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

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 BMPR2 inhibitor; cardiovascular;

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); CsA aka Cn inhibitor cyclosporin A; enzyme inhibitor (Cn inhibitor); cardiovascular;

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 Ildr_/_ mice);

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;

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 **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 SD rats, 7 wks); Brain coordinates (1 mm posterior; 1.5 mm lateral; -3.5 mm depth to the bregma);

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); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth to the bregma); neurodegenerative (Epilepsy);

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 Phenezine, 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, Phenezine **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):024-103

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 1/2 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);

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

Agents: Vascular Endothelial Growth Factor, Angiotensin II, Losartan, Cyclosporine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 21 days;

ALZET Comments: 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)

Agents: Cyclosporine **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: 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)

Agents: Cyclosporin; FK506; NIM811 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 7 days; 25 days; 32 days;

ALZET Comments: 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);

Deoxyspergualin

R0346: F. Thomas, *et al.* 15-Deoxyspergualin: a novel immunosuppressive drug with clinical potential. Annals of the New York Academy of Sciences 1993;685(175-92)

Agents: Deoxyspergualin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle (saline); stability verified by (in-vitro cultures, stable for up to 14 days at pH 3 to 4); Immunology (Immunosuppressant); "These authors noted the superiority of a continuous infusion of DSG delivered by a mini-osmolar pump in graft prolongation when compared to intramuscular injection." Pg.177; Dose (2.5 mg/kg/day);

P2065: K. Nishikawa, *et al.* Treatment schedule dependency of antitumor effect of deoxyspergualin. Jpn. J. Antibiot 1991;44(9):917-925

Agents: Deoxyspergualin **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 2001; **Duration:** 1,2,4, or 8 days;

ALZET Comments: Comparison of injections vs. mp; cancer; detailed formulation information; time-dependent systemic toxicity characterized; 'continuous infusion produced higher efficacy' over injections

P0971: J. Plowman, *et al.* Preclinical antitumor activity and pharmacological properties of deoxyspergualin. Cancer Research 1987;47(685-689)

Agents: Deoxyspergualin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 24, 48, 72, 96 hours;

ALZET Comments: Dose-response; mps primed in saline at 37C prior to implant; mice w/sc L1210 leukemia cells; comparison of bolus injections vs. mp infusion; functionality of mp verified by plasma conc.; cancer



FK506 (2014-Present)

Q10726: H. V. Willingenburg, *et al.* Validation of a Dried Blood Spot Method to Measure Tacrolimus Concentrations in Small Volumes of Mouse Blood. *Bioanalysis* 2022;

Agents: Tacrolimus **Vehicle:** DMSO; EtOH; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Dose (1 or 3 mg/kg/day); 50% DMSO and EtOH used; animal info (Female; Male; 12-20 months old); immunology;

Q10602: O. Mashinchian, *et al.* An Engineered Multicellular Stem Cell Niche For The 3D Derivation of Human Myogenic Progenitors From iPSCs. *Embo Journal* 2022;41(14):e110655

Agents: Tacrolimus **Vehicle:** EtOH; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** Not Stated;

ALZET Comments: Dose: (2.5 mg/kg/day) 70% EtOH; 0.9% NaCl vehicle used Controls received mp w/ vehicle; animal info: Male C57BL/10ScSn-Dmdmdx/J (Mdx mice) 4 and 8 weeks, tacrolimus aka FK-506

Q9354: T. Y. Liu, *et al.* Healing of Sub-Critical Femoral Osteotomies in Mice is Unaffected By Tacrolimus and Deletion of Recombination Activating Gene 1. *European Cells and Materials* 2021;

Agents: Tacrolimus **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1003D; 1007D; **Duration:** 3, 7 days;

ALZET Comments: Dose (1 or 10 mg/kg/day); Controls received mp w/ vehicle; animal info (male C57BL/6 mice, 11 weeks old); dependence;

Q10236: Y. Li, *et al.* Tacrolimus inhibits oral carcinogenesis through cell cycle control. *Biomedicine & Pharmacotherapy* 2021;139(111545)

Agents: Tacrolimus **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose: (5 mg/kg/d); Controls received mp w/ vehicle; animal info: Male Sprague-Dawley (SD) rats (6–8 weeks old); Tacrolimus aka (TAC, FK506) is a major calcineurin inhibitor; cancer ();

Q9203: H. B. Dai, *et al.* Adrenomedullin Attenuates Inflammation in White Adipose Tissue of Obese Rats Through Receptor-Mediated PKA Pathway. *Obesity (Silver Spring)* 2021;29(1):86-97

Agents: Tacrolimus **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: Dose (0.25 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley obese); Tacrolimus aka TAC; dependence;

Q10146: K. W. Cheung, *et al.* Analysis of the retinal capillary plexus layers in a murine model with diabetic retinopathy: effect of intravitreal injection of human CD34(+) bone marrow stem cells. *Annals of Translational Medicine* 2021;9(15):1273

Agents: Rapamycin; Tacrolimus **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;

ALZET Comments: Dose: (1 µg/g/day) Rapamycin; Tacrolimus; Controls received mp w/ vehicle; animal info :Male Six-week-old C57BL/6J; Tacrolimus aka (FK506); diabetes; Diabetic retinopathy

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; **Pump:** Not Stated; **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 Bmpr2 inhibitor; cardiovascular;

Q9889: S. Yoshida, *et al.* Syngeneic Mesenchymal Stem Cells Reduce Immune Rejection After Induced Pluripotent Stem Cell-Derived Allogeneic Cardiomyocyte Transplantation. *Scientific Reports* 2020;10(1):4593

Agents: Tacrolimus **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 15 days;

ALZET Comments: Dose (1.5 mg/kg body weight); animal info (Adult male BALB/c mice (6–7 weeks old, 17–22 g)); pumps replaced every 13 days; immunology;



Q9114: A. Yazdanyar, *et al.* Effects of intravitreal injection of human CD34(+) bone marrow stem cells in a murine model of diabetic retinopathy. *Experimental Eye Research* 2020;190(107865)

Agents: Tacrolimus; Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 5 weeks;

ALZET Comments: Dose (1 ug/g/day); animal info (6-week-old male C57BL/6J mice); Tacrolimus aka FK506; dependence;

Q9566: H. Xu, *et al.* Limited efficacy of rapamycin monotherapy in vascularized composite allotransplantation. *Transplant Immunology* 2020;61(101308)

Agents: Rapamycin; Tacrolimus **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (0.5-2 mg/kg/day Rapamycin; 2 mg/kg/day Tacrolimus); animal info (Inbred male mice); Rapamycin aka RPM, Tacrolimus aka FK506; cardiovascular;

Q9206: R. E. De la Vega, *et al.* Effects of FK506 on the healing of diaphyseal, critical size defects in the rat femur. *European Cells & Materials* 2020;40(160-171)

Agents: FK-506 **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Dose (1 mg/kg/day); animal info (male Fischer F344 rats, 16 weeks old); post op. care (buprenorphine); FK506 aka Tacrolimus; immunology;

Q8432: C. Dai, *et al.* Tacrolimus- and sirolimus-induced human beta cell dysfunction is reversible and preventable. *JCI Insight* 2020;5(1):

Agents: Tacrolimus **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: Dose (0.25 mg/kg/day); Controls received mp w/ vehicle; animal info (Male NSG mice, age 12–18 weeks); Tacrolimus aka TAC; dependence;

Q8598: N. Kashiyama, *et al.* Vasculogenically conditioned peripheral blood mononuclear cells inhibit mouse immune response to induced pluripotent stem cell-derived allogeneic cardiac grafts. *PLoS One* 2019;14(5):e0217076

Agents: Tacrolimus **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 7 days;

ALZET Comments: Dose (0.5 mg/kg/day); animal info (C57BL/6 male mice, 10 weeks old, 20-25 g); cardiovascular;

Q8737: V. Hartwig, *et al.* Human skin-derived ABCB5(+) stem cell injection improves liver disease parameters in Mdr2KO mice. *Archives of Toxicology* 2019;93(9):2645-2660

Agents: Tacrolimus **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002, 2004; **Duration:** 2, 4 weeks;

ALZET Comments: Dose (1 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Balb/c, 16 weeks old); dependence;

Q7455: R. E. De la Vega, *et al.* Specific, Sensitive, and Stable Reporting of Human Mesenchymal Stromal Cell Chondrogenesis. *Tissue Engineering Part C Methods* 2019;25(3):176-190

Agents: FK-506, SEW2871 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Dose (0.15 mg/kg/day- FK-506, 0.075 mg/kg/day- SEW2871); Controls received mp w/ vehicle; animal info (Male, 14 weeks old, Fischer-344); gene therapy;

Q7885: C. Vandenbussche, *et al.* Tacrolimus-induced nephrotoxicity in mice is associated with microRNA deregulation. *Archivos de Zootecnia* 2018;92(4):1539-1550

Agents: Tacrolimus **Vehicle:** Serum, physiological; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Dose (1 mg/kg/d); Controls received mp w/ vehicle; animal info (4 weeks, male, CD-1, 30-40g); enzyme inhibitor (Calcineurin); toxicology; Tacrolimus actively participates to chronic allograft dysfunction through miR-21-5p modulation.;

Q8307: G. Oldani, *et al.* Chimeric liver transplantation reveals interspecific graft remodeling. *J Hepatol* 2018;69(5):1025-1036

Agents: Tacrolimus **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; Rat; **Pump:** 1002 or 2002; **Duration:** 14 days or 28 days;

ALZET Comments: Dose (0.3, 0.6, or 1.2 mg/kg); animal info (C57BL/6J, 23-31 g, Male; Lewis. Male, 47-60 g); pumps replaced every 2 weeks; dependence;



Q6099: C. Dai, *et al.* Age-dependent human beta cell proliferation induced by glucagon-like peptide 1 and calcineurin signaling. *J Clin Invest* 2017;127(10):3835-3844

Agents: Exendin-4; FK506 **Vehicle:** PBS; saline; **Route:** SC; **Species:** Mice (NSG), mice (NOD); **Pump:** 1004; 1002; **Duration:** 4 weeks; 2 weeks;

ALZET Comments: Dose (exendin-4: 24 nmol/kg/d; FK506: 0.25 mg/kg/d); Controls received mp w/ vehicle; animal info (NOD.Cg-Prkdcscidll2rgtm1Wjl/Sz (NSG) mice); Multiple pumps per animal (2): some animals received a second pump containing FK506 after 2 weeks; diabetes;

Q6178: S. Schworer, *et al.* Epigenetic stress responses induce muscle stem-cell ageing by Hoxa9 developmental signals. *Nature* 2016;540(7633):428-432

Agents: FK-506 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** Not Stated;

ALZET Comments: Dose (5 mg/kg); animal info (young adult (3–4 months) and aged (22–28 months) C57/BL6J mice); immunology;

Q6621: E. Moisseiev, *et al.* Intravitreal Administration of Human Bone Marrow CD34+ Stem Cells in a Murine Model of Retinal Degeneration. *Invest Ophthalmol Vis Sci* 2016;57(10):4125-35

Agents: FK506; Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 1 month;

ALZET Comments: Dose (1 ug/g/day); animal info (3 week old mice); FK506 aka Tacrolimus;

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);

Q4071: L. Rojanathammanee, *et al.* Attenuation of microglial activation in a mouse model of Alzheimer's disease via NFAT inhibition. *Journal of Neuroinflammation* 2015;12(U14-U26)

Agents: FK506; tat-VIVIT; tat-VEET **Vehicle:** DMSO; HEPES; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, APP/PS1, 12 months old); neurodegenerative (Alzheimer's); behavioral testing (t maze); peptides; FK506, tat-VIVIT are NFAT inhibitors; VEET is a negative control scrambled peptide;

Q4100: K. Shin, *et al.* Hedgehog Signaling Restrains Bladder Cancer Progression by Eliciting Stromal Production of Urothelial Differentiation Factors. *Cancer Cell* 2014;26(521-533)

Agents: FK506 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 1 month;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, GilCreER/WT; SMPflox/flox, 8-10 weeks old); cancer (bladder); used wound clips;

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)

Agents: Cyclosporin; FK506; NIM811 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 7 days; 25 days; 32 days;

ALZET Comments: 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);

Q3418: C. F. Bentzinger, *et al.* Wnt7a stimulates myogenic stem cell motility and engraftment resulting in improved muscle strength. *Journal of Cell Biology* 2014;205(97-111)

Agents: FK506 **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 3 days;

ALZET Comments: Animal info (C57BL6); FK-506 aka tacrolimus; FK506 is an immunosuppressant



Methyldeoxyspergual

P3365: S. Suzuki, *et al.* Continuous administration of methyldeoxyspergualin prolongs xenograft survival in hamster-to-rat cardiac transplantation. *Transplant. Proc* 1993;25(1):430-431

Agents: Methyldeoxyspergualin **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** 2001; 2ML2; **Duration:** 8, 14 days;

ALZET Comments: immunology

Rapamycin (2009-Present)

Q10895: J. Zheng, *et al.* cPKCgamma Deficiency Exacerbates Autophagy Impairment and Hyperphosphorylated Tau Buildup through the AMPK/mTOR Pathway in Mice with Type 1 Diabetes Mellitus. *Neuroscience Bulletin* 2022;38(10):1153-1169

Agents: Rapamycin **Vehicle:** DMSO; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose: (0.2 mg/kg); Controls received mp w/ vehicle; animal info: Adult male wild-type (cPKCγ^{-/-}) and cPKCγ knockout (cPKCγ^{-/-}) C57BL/6 mice (18 g–22 g, 6–8 weeks) diabetes mellitus; behavioral testing: Morris Water Maze (MWM) Test; Brain coordinates (AP - 0.5 mm, ML + 1.0 mm, and DV - 2.8 mm relative to bregma); diabetes;

Q10855: S. Yuan, *et al.* Ras Drives Malignancy Through Stem Cell Crosstalk With the Microenvironment. *Nature* 2022;612(7940):555-563

Agents: Leptin; VEGFA; Rapamycin **Vehicle:** PBS; DMSO; **Route:** SC; **Species:** Mice (nude); **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose: Leptin (2 mg/ml; 0.5 mg/ml); 0.5 mg/ml SMLA; VEGFA 50ug/ml; 10 mM rapamycin; 10% DMSO used; Controls received mp w/ vehicle; animal info (Nude mice); cancer (Squamous cell carcinomas);

Q10682: P. J. Siska, *et al.* Kynurenine Induces T Cell Fat Catabolism and Has Limited Suppressive Effects in Vivo. *EBioMedicine* 2021;74(103734)

Agents: Rapamycin **Vehicle:** DMSO; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days; 10 days;

ALZET Comments: Dose (0.5 mg/kg/d); Controls received mp w/ vehicle; animal info (C57BL6; Female; 8-12 weeks of age; D-kynurenine diet or control chow); cancer (head and neck);

Q10018: Z. Jiang, *et al.* RETRACTED ARTICLE: Involvement of pro-inflammatory cytokines in diabetic neuropathic pain via central PI3K/Akt/mTOR signal pathway. *Archives of Physiology and Biochemistry* 2021;127(6):I-IX

Agents: Rapamycin; LY294002; Interleukin-1 beta receptor antagonist; SC144; etanercept **Vehicle:** CSF, Artificial; **Route:** CSF/CNS (dorsolateral striatum); **Species:** Rat; **Pump:** 1003D; **Duration:** Not Stated;

ALZET Comments: "Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats, 200-250 g); behavioral testing (Mechanical paw withdrawal threshold; Thermal Place Preference System); Interleukin-1 beta receptor antagonist aka IL-1b receptor antagonist; ALZET brain infusion kit used; Brain coordinates (7.6 mm posterior to the bregma, 0.65 mm lateral to the midline, and 4.2 mm ventral to the brain surface); diabetes; "

Q10146: K. W. Cheung, *et al.* Analysis of the retinal capillary plexus layers in a murine model with diabetic retinopathy: effect of intravitreal injection of human CD34(+) bone marrow stem cells. *Annals of Translational Medicine* 2021;9(15):1273

Agents: Rapamycin; Tacrolimus **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;

ALZET Comments: Dose: (1 µg/g/day) Rapamycin; Tacrolimus; Controls received mp w/ vehicle; animal info :Male Six-week-old C57BL/6J; Tacrolimus aka (FK506); diabetes; Diabetic retinopathy

Q9148: J. Y. Cao, *et al.* Autophagosome protects proximal tubular cells from aldosterone-induced senescence through improving oxidative stress. *Renal Failure* 2021;43(1):556-565

Agents: Aldosterone; Rapamycin; Choroquine **Vehicle:** DMSO; PBS; **Route:** IP; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: Dose (1 mg/kg/day Rapamycin; 60 mg/kg/day Aldosterone); 0.5% DMSO, 99.5% PBS used; Controls received mp w/ vehicle; animal info (healthy male Sprague-Dawley rats, 180-200 g); Aldosterone aka Aldo, Rapamycin aka Rap, Choroquine aka CQ; dependence;



Q9114: A. Yazdanyar, *et al.* Effects of intravitreal injection of human CD34(+) bone marrow stem cells in a murine model of diabetic retinopathy. *Experimental Eye Research* 2020;190(107865)

Agents: Tacrolimus; Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 5 weeks;

ALZET Comments: Dose (1 ug/g/day); animal info (6-week-old male C57BL/6J mice); Tacrolimus aka FK506; dependence;

Q9566: H. Xu, *et al.* Limited efficacy of rapamycin monotherapy in vascularized composite allotransplantation. *Transplant Immunology* 2020;61(101308)

Agents: Rapamycin; Tacrolimus **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (0.5-2 mg/kg/day Rapamycin; 2 mg/kg/day Tacrolimus); animal info (Inbred male mice); Rapamycin aka RPM, Tacrolimus aka FK506; cardiovascular;

Q9537: L. Wang, *et al.* Donor bone-marrow CXCR4+ Foxp3+ T-regulatory cells are essential for costimulation blockade-induced long-term survival of murine limb transplants. *Scientific Reports* 2020;10(1):9292

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose (2 mg/kg/d); animal info (WT BALB/c and WT C57BL/6 mice, 8-12 weeks old); dependence;

Q9465: M. Shi, *et al.* The tripartite interaction of phosphate, autophagy, and alphaKlotho in health maintenance. *FASEB Journal* 2020;34(2):3129-3150

Agents: αKlotho protein, recombinant; rapamycin; chloroquine **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: Dose (0.3 mg/kg body weight αKlotho protein; 28 mg/Kg rapamycin; 50 mg/Kg chloroquine); Controls received mp w/ vehicle; animal info (Wild type mice, 10-12 weeks old); dependence;

Q8533: M. Hayashi-Hori, *et al.* Therapeutic Effect of Rapamycin on Aortic Dissection in Mice. *Int J Mol Sci* 2020;21(9):

Agents: Angiotensin II; Aminopropionitrile, B-; Gefitinib; Rapamycin **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Dose (1000 ng/kg/min Angiotensin II; 150 mg/kg/day B-aminopropionitrile; 1000 mg/kg/day Gefitinib; 2 mg/kg/day Rapamycin); Controls received mp w/ vehicle; animal info (male mice aged 11–14 weeks); B-aminopropionitrile aka BAPN, Angiotensin II aka AngII; dependence;

Q7037: J. Zhang, *et al.* Neuroinflammation and central PI3K/Akt/mTOR signal pathway contribute to bone cancer pain. *Mol Pain* 2019;15(1744806919830240)

Agents: Rapamycin, LY294002, Interleukin-1Receptor antagonist, SC144, etanercept, **Vehicle:** CSF, artificial; **Route:** CSF/CNS (midbrain periaqueductal gray); **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: animal info (200–250 gr Wistar rats); ALZET brain infusion kit used; Brain coordinates (7.6 mm posterior to the bregma, 0.65mm lateral to the midline, and 4.2 mm ventral to the brain surface); Therapeutic indication (bone cancer pain);

Q8554: Z. Jiang, *et al.* RETRACTED ARTICLE: Involvement of pro-inflammatory cytokines in diabetic neuropathic pain via central PI3K/Akt/mTOR signal pathway. *Arch Physiol Biochem* 2019;1-9

Agents: Rapamycin; LY294002; Interleukin-1 beta receptor antagonist; SC144; etanercept **Vehicle:** CSF, Artificial; **Route:** CSF/CNS (dorsolateral striatum); **Species:** Rat; **Pump:** 1003D; **Duration:** Not stated;

ALZET Comments: "Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats, 200-250 g); behavioral testing (Mechanical paw withdrawal threshold; Thermal Place Preference System; Brain coordinates (7.6 mm posterior to the bregma, 0.65 mm lateral to the midline, and 4.2 mm ventral to the brain surface); diabetes; "

Q8837: H. Xu, *et al.* Utility of IL-2 Complexes in Promoting the Survival of Murine Orthotopic Forelimb Vascularized Composite Allografts. *Transplantation* 2018;102(1):70-78

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (2 mg/kg/day); Controls did not receive mp; animal info (male, C57BL/6 and BALB/c); comparison of IP injection of FK506 vs mp; immunology; RPM monotherapy was about as effective as post-Tx IL-2C in prolonging survival. Co-administration of IL-2C and post-Tx RPM had additional benefits, with pre-Tx IL-2C plus RPM causing a fivefold increase in survival, and post-Tx IL-2C plus RPM causing a threefold increase in survival;



Q9887: L. Wang, *et al.* Use of TGF-beta plus Rapamycin to Induce Foxp3, promote iTreg Development and Suppressive Function, and Induce Long-Term Allograft Survival. *Transplantation* 2018;

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Dose (0.5 mg/kg/d); animal info (C57BL/6 with BALB/c cardiac allografts);

Q5705: X. Wang, *et al.* Cerebral mTOR signal and pro-inflammatory cytokines in Alzheimer's disease rats. *Transl Neurosci* 2016;7(1):151-157

Agents: Rapamycin; amyloid protein, beta (1-42) **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: animal info (male, Sprague Dawley, 3-4 months old, 300-350g); Multiple pumps per animal (2); neurodegenerative (Alzheimer's); behavioral testing (Y-maze); immunology; Bilateral infusion; used jewelers' screw and dental zinc cement; Dose (10 mg/kg amyloid beta, rapamycin 500 ug/2 weeks); Brain coordinates

Q5074: H. Z. Toklu, *et al.* Anorexic response to rapamycin does not appear to involve a central mechanism. *Clinical and Experimental Pharmacology and Physiology* 2016;43(9):802-7

Agents: Rapamycin **Vehicle:** DMSO; PEG 400; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, F344 Brown Norway, 23-25 months old); 10% DMSO and 90% PEG used; used PE-50 tubing; pumps initially filled with aCSF - after one week recovery, pumps replaced with rapamycin or vehicle pump; Dose (30 ug/day); Brain coordinates (1.1 mm posterior to Bregma and 1.6 mm ventral from the skull surface on the midline (medial s- sure), with the nose bar set at 4 mm below the ear bars (below zero)) pg 805;

Q5195: P. J. Scarpace, *et al.* Rapamycin Normalizes Serum Leptin by Alleviating Obesity and Reducing Leptin Synthesis in Aged Rats. *J Gerontol A Biol Sci Med Sci* 2016;71(7):891-9

Agents: Rapamycin **Vehicle:** DMSO; PEG 400; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, F344 x Brown Norway, 24 months old); pumps replaced after 14 days; ALZET brain infusion kit used; 10% DMSO used; 90% PEG 400 used; post op. care (rats kept warm until recovered); used aCSF filled pump for 14 days, then replaced with rapamycin or vehicle for 28 day infusion; obesity; Dose (30 ug/day); Brain coordinates (1.3 mm posterior to bregma, 1.9 mm lateral to the midsagittal suture and to a depth of 3.5mm);

Q6621: E. Moisseiev, *et al.* Intravitreal Administration of Human Bone Marrow CD34+ Stem Cells in a Murine Model of Retinal Degeneration. *Invest Ophthalmol Vis Sci* 2016;57(10):4125-35

Agents: FK506; Rapamycin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 1 month;

ALZET Comments: Dose (1 ug/g/day); animal info (3 week old mice); FK506 aka Tacrolimus;

Q4840: Z. Jiang, *et al.* Blocking mammalian target of rapamycin alleviates bone cancer pain and morphine tolerance via u-opioid receptor. *International Journal of Cancer* 2016;138(2013-2020)

Agents: Rapamycin; CTOP; LY297002 **Vehicle:** DMSO; saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ saline; animal info (Wistar, 200-250g); 50% DMSO used; cancer (breast; bone); dose-response (pg 2015); behavioral testing (hindpaw withdrawal latency);

Q5576: S. T. Haller, *et al.* Rapamycin Attenuates Cardiac Fibrosis in Experimental Uremic Cardiomyopathy by Reducing Marinobufagenin Levels and Inhibiting Downstream Pro-Fibrotic Signaling. *J Am Heart Assoc* 2016;5(10):

Agents: Rapamycin, marinobufagenin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: animal info (Male Sprague-Dawley rats weighing 250-300 g); Multiple pumps per animal (2 minipumps were implanted for coadministration of rapamycin and MBG); Dose (MBG 10 ug/kg/day; rapamycin 0.2 mg/kg/d);

Q4415: J. Fields, *et al.* HIV-1 Tat Alters Neuronal Autophagy by Modulating Autophagosome Fusion to the Lysosome: Implications for HIV-Associated Neurocognitive Disorders. *JOURNAL OF NEUROSCIENCE* 2015;35(1921-1938)

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 2 weeks;

ALZET Comments: Animal info (GFAP-Tat tg, 7-8 months old); "Because Rapam poorly crosses into the CNS, it was infused intracerebrally into the lateral ventricle of 9-month-old mice at a concentration of 20 mg/kg." pg 1923;



Q3222: H. L. Li, *et al.* Suppression of the mTORC1/STAT3/Notch1 pathway by activated AMPK prevents hepatic insulin resistance induced by excess amino acids. *American Journal of Physiology Endocrinology and Metabolism* 2014;306(2):E197-E209

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 months;

ALZET Comments: Control animals received mp w/ vehicle; animal info (C57BL/6, 12 wks old, male)

Q1974: S. B. Yang, *et al.* Rapamycin Ameliorates Age-Dependent Obesity Associated with Increased mTOR Signaling in Hypothalamic POMC Neurons. *Neuron* 2012;75(3):425-436

Agents: Rapamycin **Vehicle:** PEG 400; DMSO; cremophor; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1004;

ALZET Comments: Animal info (C57BL/6, 2, 12 mo); ALZET brain infusion kit used; 10% DMSO, 60% PEG 400; 30% cremophor

Q2380: G. N. Paliouras, *et al.* Mammalian Target of Rapamycin Signaling Is a Key Regulator of the Transit-Amplifying Progenitor Pool in the Adult and Aging Forebrain. *Journal of Neuroscience* 2012;32(43):15012-15026

Agents: Rapamycin; epidermal growth factor **Vehicle:** DMSO; **Route:** CSF/CNS; **Species:** Mice (pregnant); **Pump:** 1007D;

Duration: 7 days;

ALZET Comments: Control animals received mp w/ vehicle; animal info (C57BL/6, female, 2, 10, 18 mo old); ALZET BIK used

Q2046: J. Klucken, *et al.* Alpha-synuclein aggregation involves a bafilomycin A1-sensitive autophagy pathway. *Autophagy* 2012;8(5):754-766

Agents: Bafilomycin, A1; rapamycin **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 2 weeks;

ALZET Comments: Animal info (wt, alpha synuclein, 9 mo old); neurodegenerative (Parkinson's disease)

Q5955: S. Haller. Marinobufagenin induced uremic cardiomyopathy : the role of passive immunization, rapamycin, and CD40 signaling in the generation of renal fibrosis. *Theses and Dissertations* 2012;331(**Agents:** Rapamycin; Marinobufagenin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: animal info (Male Sprague Dawley rats weighing between 250-300 gms); marinobufagenin is a cardiotonic steroid; Agents administered alone or in combination; Dose (rapamycin administered 0.2mg/kg/day and MBG at 10µg/kg/day);

Q0422: S. H. Qi, *et al.* Activation of mammalian target of rapamycin signaling in spatial learning. *Neuroscience Research* 2010;68(2):88-93

Agents: Rapamycin **Vehicle:** DMSO; Saline; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Pump:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 2-3 months old); 0.5 ul/hr pump used; behavioral testing (Radial-arm maze task)

Q0084: L. Crews, *et al.* Selective Molecular Alterations in the Autophagy Pathway in Patients with Lewy Body Disease and in Models of alpha-Synucleinopathy. *PLoS One* 2010;5(2):U163-U178

Agents: Rapamycin **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; cyanoacrylate adhesive; animal info (alpha-syn, Tg); neurodegenerative (dementia with Lewy bodies, Parkinson's Disease)

Q0508: C. Y. Wang, *et al.* Obesity Increases Vascular Senescence and Susceptibility to Ischemic Injury Through Chronic Activation of Akt and mTOR. *Science Signaling* 2009;2(62):U8-U18

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

ALZET Comments: Controls received mp w/ vehicle; animal info (Akt1 null)

Q0824: C. Phornphutkul, *et al.* The Effect of Rapamycin on Bone Growth in Rabbits. *Journal of Orthopaedic Research* 2009;27(9):1157-1161

Agents: Rapamycin **Vehicle:** DMSO; **Route:** Bone (proximal tibial growth plates); **Species:** Rabbit; **Pump:** 2004; **Duration:** 8 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (5 wks old, New Zealand White); long-term study; pumps replaced after 4 weeks; 5% DMSO used; good methods pg 1158



P9753: P. S. Buckmaster, *et al.* Inhibition of the Mammalian Target of Rapamycin Signaling Pathway Suppresses Dentate Granule Cell Axon Sprouting in a Rodent Model of Temporal Lobe Epilepsy. *Journal of Neuroscience* 2009;29(25):8259-8269

Agents: Rapamycin **Vehicle:** DMSO; ethanol; fluorescein; **Route:** CSF/CNS (dentate gyrus); **Species:** Rat; **Pump:** 2004;

Duration: 1-2 months;

ALZET Comments: Controls received mp w/vehicle; functionality of mp verified by fluorescein labeling; long-term study; pumps replaced after 1 month; ALZET brain infusion kit 2 used; animal info (male, Sprague Dawley, 34 days old); 50% DMSO used; 15% ethanol used

Q0461: K. R. Bridle, *et al.* Rapamycin Inhibits Hepatic Fibrosis in Rats by Attenuating Multiple Profibrogenic Pathways. *LIVER TRANSPLANTATION* 2009;15(10):1315-1324

Agents: Rapamycin **Vehicle:** DMSO; PEG 400; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 21 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (normal, male, Wistar, 450-550 g, 214-320 g)