References on the Administration of Immunosuppressants Using ALZET® Osmotic Pumps

1. Cyclosporin

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 ldlr_/_ 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; 4-49 days; 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.

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_/fl) 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.

2. Deoxyspergualin

R0346: F. Thomas*, et al.* 15-Deoxyspergualin: a novel immunosuppressive drug with clinical potential. ANNALS NEW YORK ACADEMY OF SCIENCES 1993;685(175-92
ALZET Comments: Deoxyspergualin; Saline; SC; Rat; 14 days; 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
ALZET Comments: Deoxyspergualin; Saline; IP; mice; 2001; 1,2,4, or 8 days; 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 Res 1987;47(685-689
ALZET Comments: Deoxyspergualin; Saline; SC; mice; 2001; 24, 48, 72, and 96 hours; 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.

3. FK506

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
ALZET Comments: Exendin-4; FK506; PBS; saline; SC; Mice (NSG), mice (NOD); 1004; 1002; 4 weeks; 2 weeks; 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
ALZET Comments: FK-506; SC; Mice; 2004; 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
ALZET Comments: FK506; Rapamycin; SC; Mice; 1004; 1 month; Dose (1 ug/g/day); animal info (3 week old mice); FK506 aka Tacrolimus;.

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
ALZET Comments: FK506; tat-VIVIT; tat-VEET; DMSO; HEPES; SC; Mice (transgenic); 1004; 28 days; 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
ALZET Comments: FK506; SC; Mice; 2004; 1 month; 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
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);.

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
ALZET Comments: FK506; Mice (transgenic); 3 days; Animal info (C57BL6); FK-506 aka tacrolimus; FK506 is an immunosuppressant.

P9923: N. Zhou*, et al.* Mechanical stress-evoked but angiotensin II-independent activation of angiotensin II type 1 receptor induces cardiac hypertrophy through calcineurin pathway. Biochemical and Biophysical Research Communications 2010;397(2):263-269
ALZET Comments: FK506; losartan; PBS; SC; Mice; 2002; Controls received mp w/vehicle; animal info (atg -/-, 8-10 wks old).

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.

Q0556: J. F. Chabas*, et al.* FK506 Induces Changes in Muscle Properties and Promotes Metabosensitive Nerve Fiber Regeneration. Journal of Neurotrauma 2009;26(1):97-108
ALZET Comments: FK506; IP; Rat; 2ML4; 12 weeks; Controls were unoperated; animal info (8 wks old male, Sprague-Dawley, 250-300 g); long-term study; stress/adverse reaction: (see pg. 98) "untreatable infection".

P9280: T. Mitamura*, et al.* Effect of pharmacokinetic profile on the pancreatic toxicity and efficacy of tacrolimus in rats. JOURNAL OF TOXICOLOGICAL SCIENCES 2008;33(5):575-584
ALZET Comments: FK506; Propylene glycol; ethanol; castor oil, hydrogenated; IV (femoral); Rat; 2002; 9, 14 days; Controls received mp w/ vehicle; functionality of mp verified by blood drug concentration; dose-response (fig. 4); comparison of bolus IV injections vs. mp; immunology; toxicology; animal info (male, Jcl:SD, 9 wks old: Fischer, WKAtt, 8 wks old; skin allograft); 15% EtOH used; "The sustained blood concentration of tacrolimus (via ALZET) with an AUC similar to that of bolus administration was better tolerated and had the same efficacy...These results indicate that the sustained-release formulation of tacrolimus has the potential to improve the safety of tacrolimus." (p. 583); also known as FK-506.

P9419: M. E. Katz*, et al.* Immunosuppressant calcineurin inhibitors phase shift circadian rhythms and inhibit circadian responses to light. Pharmacology Biochemistry and Behavior 2008;90(4):763-768
ALZET Comments: FK506; CSF/CNS (third ventricle); Hamster; 2002; 2 weeks; Controls received mp w/ saline; no stress (see pg. 766); enzyme inhibitor (calcineurin); animal info (Syrian, male, 4-6 months old); behavioral testing (locomotor activity); cannula placement verified post mortem; "The continuous administration of a drug directly to the SCN via an osmotic pump in vivo has been shown to be very useful to assess reversible effects of different compounds" (p. 767).

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.

P8021: K. Zen*, et al.* Myocardium-targeted delivery of endothelial progenitor cells by ultrasound-mediated microbubble destruction improves cardiac function via an angiogenic response. Journal of Molecular and Cellular Cardiology 2006;40(6):799-809
ALZET Comments: FK506; SC; Hamster; 2004; Cardiovascular; animal info (8 weeks old).

4. 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
ALZET Comments: Methyldeoxyspergualin; IP; Rat; 2001; 2ML2; 8, 14 days; immunology.

5. Rapamycin

Q7037: J. Zhang*, et al.* Neuroinflammation and central PI3K/Akt/mTOR signal pathway contribute to bone cancer pain. Mol Pain 2019;15(1744806919830240
ALZET Comments: Rapamycin, LY294002, Interleukin-1Receptor antagonist, SC144, etanercept,; CSF, artificial; CSF/CNS (midbrain periaqueductal gray); Rat; animal info (200-250 gr Wistar rats); rapamycin is an mTOR inhibitor; LY294002 is a PI3K inhibitor; IL-1Ra is an IL-1b receptor antagonist, SC144 is a gp130 antagonist, etanercept is a TNF-a receptor antagonist; 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);.

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

ALZET Comments: Rapamycin; amyloid protein, beta (1-42); CSF, artificial; CSF/CNS; Rat; 1002; 14 days; 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. Clin Exp Pharmacol Physiol 2016;43(9):802-7
ALZET Comments: Rapamycin; DMSO; PEG 400; CSF/CNS (third ventricle); Rat; 4 weeks; 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
ALZET Comments: Rapamycin; DMSO; PEG 400; CSF/CNS; Rat; 28 days; 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 midsaggital 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
ALZET Comments: FK506; Rapamycin; SC; Mice; 1004; 1 month; 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
ALZET Comments: Rapamycin; CTOP; LY297002; DMSO; saline; CSF/CNS (intrathecal); Rat; 14 days; 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); Rapamycin is an mTOR antagonist; CTOP is an MOR antagonist; LY297002 an a PI3K inhibitor;.

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):
ALZET Comments: Rapamycin, marinobufagenin; SC; Rat; 2004; 4 weeks; animal info (Male Sprague-Dawley rats weighing 250–300 g); Multiple pumps per animal (2 minipumps were implanted for coadministration of rapamycin and MBG); Marinobufagenin is a cardiotonic steroid; 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
ALZET Comments: Rapamycin; CSF/CNS; Mice; 1007D; 2 weeks; Animal info (GFAP-Tat tg, 7-8 months old); neurodegenerative (HIV-associated neurocognitive disorder); "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; Rapamycin is an autophagy activator;.

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
ALZET Comments: Rapamycin; Mice; 2 months; 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
ALZET Comments: Rapamycin; PEG 400; DMSO; cremophor; CSF/CNS; Mice; 1004; Animal info (C57BL/6, 2, 12 mo old); ALZET brain infusion kit used; 10% DMSO used; 60% PEG 400 used; 30% cremophor used.

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
ALZET Comments: Rapamycin; epidermal growth factor; DMSO; CSF/CNS; Mice (pregnant); 1007D; 7 days; Control animals received mp w/ vehicle; animal info (C57BL/6, female, 2, 10, 18 mo old); ALZET brain infusion kit 3 used.

Q2046: J. Klucken*, et al.* Alpha-synuclein aggregation involves a bafilomycin A1-sensitive autophagy pathway. Autophagy 2012;8(5):754-766
ALZET Comments: Bafilomycin, A1; rapamycin; CSF/CNS; Mice; 1007D; 2 weeks; 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(**ALZET Comments:** Rapamycin; Marinobufagenin; SC; Rat; 2004; 4 weeks; animal info (Male Sprague Dawley rats weighing between 250-300 gms); marinobufagenin is a cardiotonic steroid; Agents administered alone or in combination; Dose (rapamycin was administered at 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
ALZET Comments: Rapamycin; DMSO; saline; CSF/CNS (third ventricle); Rat; 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
ALZET Comments: Rapamycin; CSF/CNS; Mice (transgenic); 1007D; 2 weeks; 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
ALZET Comments: Rapamycin; SC; Mice; 4 weeks; 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
ALZET Comments: Rapamycin; DMSO; Bone (proximal tibial growth plates); Rabbit; 2004; 8 weeks; 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
ALZET Comments: Rapamycin; DMSO; ethanol; fluorescein; CSF/CNS (dentate gyrus); Rat; 2004; 1-2 months; 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
ALZET Comments: Rapamycin; DMSO; PEG 400; SC; Rat; 21 days; Controls received mp w/ vehicle; animal info (normal, male, Wistar, 450-550 g, 214-320 g).

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.

P7922: C. Segrelles*, et al.* Molecular determinants of Akt-induced keratinocyte transformation. ONCOGENE 2006;25(8):1174-1185
ALZET Comments: Rapamycin; PBS; BSA; SC; Mice (nude); 2002; 2 weeks; Cancer; animal info (nude, 5-6 weeks old, female).

P7354: T. E. Krahe*, et al.* Protein synthesis-independent plasticity mediates rapid and precise recovery of deprived eye responses. Neuron 2005;48(2):329-343
ALZET Comments: Cycloheximide; rapamycin; tetrodotoxin; PBS; Ferret; 4 days; Controls received mp w/ vehicle; 0.25 ul model pump used.

P7287: M. Guba*, et al.* Dosing of rapamycin is critical to achieve an optimal antiangiogenic effect against cancer. TRANSPLANT INTERNATIONAL 2005;18(1):89-94
ALZET Comments: Rapamycin; DMSO; IP; Mice; 2002; 7-35 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; cancer (colon adenocarcinoma); "The most effective inhibition of tumor growth occurred in rapamycin-treated mice on the continuous pumping system.;" "Survival data also show the most positive effect with continuous drug delivery." P. 91.