Recent References on the Administration of Protein Kinase Inhibitors Using ALZET® Osmotic Pumps

Calphostin C (2002-Present)

Q3801: P. Almela, *et al.* Crosstalk between G protein-coupled receptors (GPCRs) and tyrosine kinase receptor (TXR) in the heart after morphine withdrawal. FRONTIERS IN PHARMACOLOGY 2013;4(U1547-U1559HA-1004; calphostin c
Agents: HA-1004; calphostin c **Vehicle:** Water, sterile; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240g); 0.06% DMSO used; dependence; cardiovascular; pumps primed for 5 hours in 37C saline;

Q1721: F. Martin, *et al.* Protein kinase C phosphorylates the cAMP response element binding protein in the hypothalamic paraventricular nucleus during morphine withdrawal. British Journal of Pharmacology 2011;163(4):857-875
Agents: Calphostin C; chelerythrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Animal info (Sprague Dawley, male, 220-240 g); enzyme inhibitor (PKC, protein kinase C)

Q0669: F. Martin, *et al.* Morphine withdrawal regulates phosphorylation of cAMP response element binding protein (CREB) through PKC in the nucleus tractus solitarius-A(2) catecholaminergic neurons. Journal of Neurochemistry 2009;110(5):1422-1432
Agents: Calphostin C **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague-Dawley, 220-240 g); enzyme inhibitor (PKC, protein kinase C)

Q0460: P. Almela, *et al.* Cross-Talk between Protein Kinase A and Mitogen-Activated Protein Kinases Signalling in the Adaptive Changes Observed during Morphine Withdrawal in the Heart. Journal of Pharmacology and Experimental Therapeutics 2009;330(3):771-782
Agents: HA-1004; calphostin C **Vehicle:** Water; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Animal info (male, Sprague Dawley, 220-240 g); dependence; enzyme inhibitor (PKA, PKC);

P9085: P. Almela, *et al.* The PKs PKA and ERK 1/2 are involved in phosphorylation of TH at Serine 40 and 31 during morphine withdrawal in rat hearts. British Journal of Pharmacology 2008;155(1):73-83
Agents: HA-1004; calphostin C **Vehicle:** DMSO; water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240 g.); enzyme inhibitor (protein kinase C, protein kinase A); pumps were primed for 5 hours prior to implantation

P7899: P. Almela, *et al.* Role of PKC in regulation of Fos and TH expression after naloxone induced morphine withdrawal in the heart. NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY 2006;372(5):374-382
Agents: Calphostin C **Vehicle:** Water, Milli-Q; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; no stress (see pg. 378); enzyme inhibitor (protein kinase c); animal info (male, Sprague-Dawley, 220-240g.); mp primed 5 hours in 37 celsius saline; 0.06% DMSO; "Animals infused with calphostin c showed no untoward effects: their weights were equivalent to those of vehicle injected groups, and the rats showed no behavioural changes." (pg.378)

P7499: M. Benavides, *et al.* Role of PKC-alpha, gamma isoforms in regulation of c-Fos and TH expression after naloxone-induced morphine withdrawal in the hypothalamic PVN and medulla oblongata catecholaminergic cell groups. Journal of Neurochemistry 2005;95(5):1249-1258
Agents: Calphostin C **Vehicle:** DMSO; water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Animal info (male, Sprague-Dawley, 220-240 g); enzyme inhibitor (protein kinase C); 0.06% DMSO used

P5457: M. Cerezo, *et al.* Inhibition of protein kinase C but not protein kinase A attenuates morphine withdrawal excitation of rat hypothalamus-pituitary-adrenal axis. European Journal of Pharmacology 2002;452(1):57-66
Agents: HA-1004; calphostin C **Vehicle:** Water, sterile; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A, protein kinase C)

Cediranib

Q1928: T. L. Wang, *et al.* Brain Distribution of Cediranib Is Limited by Active Efflux at the Blood-Brain Barrier. Journal of Pharmacology and Experimental Therapeutics 2012;341(2):386-395
Agents: Cediranib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** 72 hours;
ALZET Comments: Animal info (wt, Mdr1a/b -/-, Bcrp1 -/-, and Mdr1a/b -/-, Bcrp1 -/-); cancer (glioma);

Cetuximab

Q2710: K. M. Talasila, *et al.* EGFR wild-type amplification and activation promote invasion and development of glioblastoma independent of angiogenesis. Acta Neuropathologica 2013;125(5):683-698
Agents: Cetuximab **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Rat (nude); **Pump:** 2ML4; **Duration:** 4 weeks;
ALZET Comments: Control animals received mp w/ PBS; animal info (rnu/rnu Rowett); ALZET brain infusion kit 2 used; convection enhanced delivery (CED); tissue perfusion (intratumoral)

P9680: T. Martens, *et al.* Inhibition of glioblastoma growth in a highly invasive nude mouse model can be achieved by targeting epidermal growth factor receptor but not vascular endothelial growth factor receptor-2. Clinical Cancer Research 2008;14(17):5447-5458
Agents: Cetuximab **Vehicle:** Not Stated **Route:** CSF/CNS (intratumor) **Species:** Mice (nude) **Pump:** 2004 **Duration:** Not Stated
ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit 2 used; animal info (NMRI- nu/nu, 6-8 wks old);

Chelerythrine

Q7040: S. P. Yoon, *et al.* Exogenous CGRP upregulates profibrogenic growth factors through PKC/JNK signaling pathway in kidney proximal tubular cells. Cell Biology and Toxicology 2018;34(4):251-262
Agents: Calcitonin gene-related peptide, SP600125, chelerythrine, CGRP8-37 receptor antagonist **Vehicle:** Saline; DMSO;
Route: IP, Kidney (cortical region); **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Dose (30 ng/kg/d); 10% DMSO used; Controls received mp w/ vehicle; animal info (Male C57BL/6 mice aged 8 to 10 weeks);. The catheter was anchored to the obstructed ureter, and osmotic pump placed SC; some mice were given CGRP8-37 (120 µg/kg/d), SP600125 (30 mg/kg/d), chelerythrine (5 mg/kg/d)

Q3342: K. K. Howell, *et al.* Inhibition of PKC disrupts addiction-related memory. Frontiers in Behavioral Neuroscience 2014;8(;):U1-U9
Agents: Peptide, zeta-inhibitory; chelerythrine **Vehicle:** CSF, artificial; PBS; **Route:** CSF/CNS (third ventricle); **Species:** Mice;
Pump: 1002; **Duration:** 2 days; 6 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6Jx129T2SvEms/J, adult); post op. care (buprenorphine injection); behavioral testing (locomotion, locomotor sensitization);; Lynch coil of ZIP administration for 14.5 hours;

Q1252: A. Nakajima, *et al.* PKC gamma in Vc and C1/C2 is Involved in Trigeminal Neuropathic Pain. Journal of Dental Research 2011;90(6):777-781
Agents: Chelerythrine **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (adult, male, Sprague Dawley, 200-300 g);

Q1721: F. Martin, *et al.* Protein kinase C phosphorylates the cAMP response element binding protein in the hypothalamic paraventricular nucleus during morphine withdrawal. British Journal of Pharmacology 2011;163(4):857-875
Agents: Calphostin C; chelerythrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Animal info (Sprague Dawley, male, 220-240 g); enzyme inhibitor (PKC, protein kinase C)

P9380: E. J. Cheong, *et al.* Tuning Thalamic Firing Modes via Simultaneous Modulation of T- and L-Type Ca^{2+} Channels Controls Pain Sensory Gating in the Thalamus. Journal of Neuroscience 2008;28(49):13331-13340
Agents: Phorbol 12, 13-didecanoate; chelerythrine; apamin; iberiotoxin **Route:** CSF/CNS (thalamus); **Species:** Mice;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL/6, 129S4/SvJac, wt, PLCB4 -/-); cannula position confirmed by post mortem histology; behavioral testing (visceral pain test)

P5045: H. Mollnau, *et al.* Effects of angiotensin II infusion on the expression and function of N AD(P)H oxidase and components of nitric Oxide/cGMP signaling. Circulation Research 2002;90(E58-E65
Agents: Angiotensin II; Chelerythrine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: controls received mp w/ vehicle; peptides; cardiovascular; enzyme inhibitor; some animals received ang II and the protein kinase C inhibitor chelerythrine concomitantly

R0159: N. W. Daw, *et al.* Developmental changes and ocular dominance plasticity in the visual cortex. Keio J Med 2001;50(3):192-197
Agents: Rp-8-Cl-cAMPS; Rp-8-Cl-cGMPS; Chelerythrine chloride; Peptide, inhibitory myristolated; **Species:** Cat;
ALZET Comments: Peptides; Fig. 5 mentions minipump infusion; enzyme inhibitors; protein kinase A, C, and G inhibitors

Dasatinib

Q10346: Q. Su, *et al.* Inhibition of Maternal c-Src Ameliorates the Male Offspring Hypertension by Suppressing Inflammation and Neurotransmitters in the Paraventricular Nucleus. Cardiovascular Toxicology 2021;21(10):820-834
Agents: Dasatinib **Vehicle:** Not Stated; **Route:** CSF/CNS (paraventricular nucleus); **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Dose: (0.15 µl/h,200 µl); Controls received mp w/ vehicle; animal info: Female Sprague–Dawley rats weighing 250–300 g; Blood pressure measured via:tail-cuff; Blood pressure measurement results (see pg 4); Dasatinib (DAS); cardiovascular;

Q9090: V. Tsvankin, *et al.* ABC Transporter Inhibition Plus Dexamethasone Enhances the Efficacy of Convection Enhanced Delivery in H3.3K27M Mutant Diffuse Intrinsic Pontine Glioma. Neurosurgery 2020;86(5):742-751
Agents: Dasatinib **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (2 uM); Dasatinib aka Tyrosine Kinase Inhibitor; enzyme inhibitor (Tyrosine Kinase Inhibitor);

Q7794: R. W. D'Amico, *et al.* Saracatinib and Dasatinib Fail To Prevent Heritable Pulmonary Arterial Hypertension. bioRxiv 2018;345447
Agents: Dasatinib, Saracatinib **Vehicle:** DMSO; 16-OHE; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;
ALZET Comments: Dose (1 mg/kg/day); 50% DMSO/50% 16α-hydroxyestrone (16-OHE) used; Controls received mp w/ vehicle; animal info (10-14 weeks old)cardiovascular;

Q3781: S. L. Ho, *et al.* Toxicity evaluation of prolonged convection-enhanced delivery of small-molecule kinase inhibitors in naive rat brainstem. Child's Nervous System 2015;31(221-226
Agents: Dasatinib; everolimus **Vehicle:** DMSO; ethanol anhydrous; CSF, artificial; **Route:** CSF/CNS (brain stem); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Control animals received mp w/ aCSF and coomassie blue; animal info (Sprague-Dawley, 188-250 g); convection-enhanced delivery; Plastics One cannula used; "an Elizabethan collar was placed on animals to prevent disturbance of cannula" pg 222; "brainstem targeting using pCED to infuse single and multi-drug therapy was well tolerated in these rats"

Q4317: S. Balasubramanian, *et al.* Dasatinib Attenuates Pressure Overload Induced Cardiac Fibrosis in a Murine Transverse Aortic Constriction Model. PLoS One 2015;10(U407-U425
Agents: Dasatinib **Vehicle:** DMSO; saline; **Route:** IP; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6, 3 months old); 50% DMSO used; no stress (see pg. 4); cardiovascular;

Q2412: G. Dhawan, *et al.* Amyloid-beta oligomers stimulate microglia through a tyrosine kinase dependent mechanism. NEUROBIOLOGY OF AGING 2012;33(10):2247-2261
Agents: Dasatinib; oligomer, amyloid beta (1-42) **Vehicle:** HEPES; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 14 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (C57BL/6, female, 12 mo old); ALZET brain infusion kit used; neurodegenerative (Alzheimer's disease); peptide; enzyme inhibitor (tyrosine kinase)

Q2100: G. Dhawan, *et al.* Inhibition of Src kinase activity attenuates amyloid associated microgliosis in a murine model of Alzheimer's disease. Journal of Neuroinflammation 2012;9(;):U1-U17
Agents: Dasatinib **Vehicle:** DMSO; HEPES; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, APP/PS1, 13 mo old);

Q1444: P. M. Reeves, *et al.* Variola and Monkeypox Viruses Utilize Conserved Mechanisms of Virion Motility and Release That Depend on Abl and Src Family Tyrosine Kinases. JOURNAL OF VIROLOGY 2011;85(1):21-31
Agents: Dasatinib; imatinib mesylate **Vehicle:** DMSO; water; PBS; **Route:** SC; **Species:** Mice; **Duration:** 4 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (6 wks old, female, C57/BL6); 50% DMSO used; dasatinib also known as BMS-354825; one group contained a mixture of dasatinib and imatinib mesylate in a single pump; imatinib mesylate also known as STI-571; enzyme inhibitor (tyrosine kinase, Src Abl)

Fasudil (2010-Present)

Q8367: C. S. Piao, *et al.* Depression following traumatic brain injury in mice is associated with down-regulation of hippocampal astrocyte glutamate transporters by thrombin. J Cereb Blood Flow Metab 2019;39(1):58-73
Agents: Fasudil **Vehicle:** Not stated; **Route:** CNS/CSF; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (25 gm/kg/day); Controls received mp w/ vehicle; animal info (CD1, Male, 25-30 g);

Q4825: P.-c. FU, *et al.* ROCK Inhibition with Fasudil Promotes Early Functional Recovery of Spinal Cord Injury in Rats by Enhancing Microglia Phagocytosis. J Huazhong Univ Sci Technol［Med Sci］ 2016;36(1):31-36
Agents: Fasudil **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 1007D; **Duration:** 3 days; 7 days; 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, SD, adult, 260-300g); animal info (male, SD, adult, 260-300g); behavioral testing (BBB behaviorial testing); Dose (180 ug/day);

Q4644: M. Wermke, *et al.* RNAi profiling of primary human AML cells identifies ROCK1 as a therapeutic target and nominates fasudil as an antileukemic drug. Blood 2015;125(3760-3768
Agents: Fasudil **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (NSG); **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Animal info (female, NSG, 4-6 weeks old); cancer (acute myeloid leukemia); immunology;

Q4305: A. leaume-Butaux, *et al.* Double-Edge Sword of Sustained ROCK Activation in Prion Diseases through Neuritogenesis Defects and Prion Accumulation. PLoS Pathogens 2015;11(U248-U272
Agents: Y-27632; dimethylfasudil **Vehicle:** DMSO; saline; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6J, adult); pumps replaced every 4 weeks; behavioral testing (statiic rod test); enzyme inhibitor (Rho-associated protein kinase; ROCK);

R0330: J. T. Xiao, *et al.* New Strategies in the Management of Guillain-Barr, Syndrome. Clinical Reviews in Allergy & Immunology 2014;47(274-288
Agents: Fasudil **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Animal info (EAN); neurodegenerative (Guillain-Barr syndrome);

Q2513: K. K. V. Haack, *et al.* Central Rho Kinase Inhibition Restores Baroreflex Sensitivity and Angiotensin II Type 1 Receptor Protein Imbalance in Conscious Rabbits With Chronic Heart Failure. Hypertension 2013;61(3):723-U313
Agents: Fasudil **Vehicle:** Saline, sterile; **Route:** CSF/CNS; **Species:** Rabbit; **Pump:** Not Stated; **Duration:** 4 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (New England, white, male, 3.0-4.5 kg); enzyme inhibitor (ROCK II, Rho associated protein kinase)

Q2087: L. Butruille, *et al.* Prenatal fasudil exposure alleviates fetal growth but programs hyperphagia and overweight in the adult male rat. European Journal of Pharmacology 2012;689(1-3):278-284
Agents: L-NAME; fasudil **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ normal saline; animal info (Wistar Han, 200-250 g, E14, female);

Q1757: A. A. M. Pineda, *et al.* Preventive and therapeutic effects of the selective Rho-kinase inhibitor fasudil on experimental autoimmune neuritis. Journal of the Neurological Sciences 2011;306(1-2):115-120
Agents: Fasudil **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ PBS; animal info (male, Lewis, 7-8 wks old, 250-300 g);

Q0632: M. Fujimura, *et al.* Inhibition of the Rho/ROCK pathway prevents neuronal degeneration in vitro and in vivo following methylmercury exposure. TOXICOLOGY AND APPLIED PHARMACOLOGY 2011;250(1):1-9
Agents: Fasudil **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ sterile saline; animal info (male, Wistar, 6 wks old, 260-310 g);

Q1920: S. de Frutos, *et al.* Endothelin-1 contributes to increased NFATc3 activation by chronic hypoxia in pulmonary arteries. American Journal of Physiology Cell Physiology 2011;301(2):C441-C450
Agents: HA 1152; diltiazem; fasudil **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (NFAT-luc, NFATc3-KO, wt, 20-25 g);

Q0981: J. E. Bond, *et al.* Wound Contraction Is Attenuated by Fasudil Inhibition of Rho-Associated Kinase. Plastic and Reconstructive Surgery 2011;128(5):438E-450E
Agents: Fasudil **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (8-10 wks old, Wistar Han, 200-225 g)

Q0326: S. de Frutos, *et al.* NFATc3 contributes to intermittent hypoxia-induced arterial remodeling in mice. American Journal of Physiology Heart and Circulatory Physiology 2010;299(2):U133-U140
Agents: Fasudil **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 days;
ALZET Comments: Animal info (adult, male, 9x-NFAT-luciferase reporter, NFATc3 knockout, BalB/C wild-type, 25-30 g);

Q1017: B. A. Couch, *et al.* Increased Dendrite Branching in A beta PP/PS1 Mice and Elongation of Dendrite Arbors by Fasudil Administration. JOURNAL OF ALZHEIMERS DISEASE 2010;20(4):1003-1008
Agents: Fasudil **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 24-26 days;
ALZET Comments: Animal info (naive, 3-mo old, wt, A-betaPP/PS1); ALZET brain infusion kit 3 used; artificial CSF recipe

H89

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

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);

Q4915: L. Yang, *et al.* Activation of protein kinase A in the amygdala modulates anxiety-like behaviors in social defeat exposed mice. Mol Brain 2016;9(3
Agents: 8-Br-cAMP; H-89; **Route:** CSF/CNS (basolateral amygdala); **Species:** Mice; **Pump:** 1002; **Duration:** 10 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, C57BL6J, 8 weeks old); ALZET brain infusion kit 2 used; behavioral testing (social defeat stress; social interaction; open field; elevated plus maze; rotarod test); bilateral infusion; pumps removed after 10 days; Dose (8-Br-cAMP 2 ug/day; H-89 0.3 ug/day);

Q4288: M. S. Rioult-Pedotti, *et al.* Dopamine Promotes Motor Cortex Plasticity and Motor Skill Learning via PLC Activation. PLoS One 2015;10(U529-U542
Agents: H89; U73122; U73343 **Vehicle:** Saline; DMSO; **Route:** CSF/CNS (motor cortex); **Species:** Rat; **Pump:** 1002; **Duration:** 5, 9 days
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Long-Evans 8-10 weeks old, 250-350g); post op. care (buprenorphin 0.01 mg/kg IP); behavioral testing (motor skill); Cannula placement verified via Nissl staining; "double-loaded" vehicle and agent solution for vehicle only during recovery;

Q2434: J. Menon, *et al.* A Novel Interplay between Rap1 and PKA Regulates Induction of Angiogenesis in Prostate Cancer. PLoS One 2012;7(11):U770-U779
Agents: 8CPT; H-89 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Control animals received mp w/ PBS; animal info (male, athymic, 15-20 g, 4-6 wks old);

Q0627: N. Miyamoto, *et al.* Protein kinase A-dependent suppression of reactive oxygen species in transient focal ischemia in adrenomedullin-deficient mice. Journal of Cerebral Blood Flow and Metabolism 2009;29(11):1769-1779
Agents: H89 **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1002; **Duration:** 8 days;
ALZET Comments: Controls received mp w/ saline; animal info (8 wks old, male, AM+/-, C57BL/6 Wt); enzyme inhibitor (PKA, protein kinase A); middle cerebral artery occlusion (MCAO)

P9278: R. Nasr, *et al.* Eradication of acute promyelocytic leukemia-initiating cells through PML-RARA degradation. Nature Medicine 2008;14(12):1333-1342
Agents: Bortezomib; cyclic AMP; H89 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (nude); mice (transgenic); **Pump:** Not Stated; **Duration:** 1, 3, 6, 7 days;
ALZET Comments: Controls received no treatment; animal info (nude, PLZF-RARA-RARA-PLZF; PML-RARA5873A Tg);

P5269: J. Qiu, *et al.* Spinal axon regeneration induced by elevation of cyclic AMP. Neuron 2002;34(6):895-903
Agents: H89 **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 week;
ALZET Comments: Controls received mp w/ vehicle; 1 week stability verified (results not shown); enzyme inhibitor;

HA1004

Q3801: P. Almela, *et al.* Crosstalk between G protein-coupled receptors (GPCRs) and tyrosine kinase receptor (TXR) in the heart after morphine withdrawal. FRONTIERS IN PHARMACOLOGY 2013;4(U1547-U1559HA-1004; calphostin c
Agents: HA-1004; calphostin c **Vehicle:** Water, sterile; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240g); 0.06% DMSO used; dependence; cardiovascular; pumps primed for 5 hours in 37C saline;

P9333: P. Almela, *et al.* Tyrosine hydroxylase phosphorylation after naloxone-induced morphine withdrawal in the left ventricle. Basic Research in Cardiology 2009;104(4):366-376
Agents: HA-1004 **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (protein kinase); dependence; animal info (male, SD, 220-240 g.); HA-1004 is a protein kinase selective inhibitor; pumps primed for 5 hours

Q0460: P. Almela, *et al.* Cross-Talk between Protein Kinase A and Mitogen-Activated Protein Kinases Signalling in the Adaptive Changes Observed during Morphine Withdrawal in the Heart. Journal of Pharmacology and Experimental Therapeutics 2009;330(3):771-782
Agents: HA-1004; calphostin C **Vehicle:** Water; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Animal info (male, Sprague Dawley, 220-240 g); dependence; enzyme inhibitor (PKA, PKC);

P9085: P. Almela, *et al.* The PKs PKA and ERK 1/2 are involved in phosphorylation of TH at Serine 40 and 31 during morphine withdrawal in rat hearts. British Journal of Pharmacology 2008;155(1):73-83
Agents: HA-1004; calphostin C **Vehicle:** DMSO; water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240 g.); pumps primed

P8249: P. Almela, *et al.* Differential involvement of 3', 5'-cyclic adenosine monophosphate-dependent protein kinase in regulation of Fos and tyrosine hydroxylase expression in the heart after naloxone induced morphine withdrawal. NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY 2007;374(4):293-303
Agents: HA-1004 **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A); animal info (male, SD, 220-240g)

P6875: M. Benavides, *et al.* Involvement of 3',5';-cyclic adenosine monophosphate-dependent protein kinase in regulation of Fos expression and tyrosine hydroxylase levels during morphine withdrawal in the hypothalamic paraventricular nucleus and medulla oblongata catecholaminergic cell groups. Journal of Neurochemistry 2005;92(2):246-254
Agents: HA-1004 **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; no stress (see pg. 249); (cAMP-dependent protein kinase A);

P5457: M. Cerezo, *et al.* Inhibition of protein kinase C but not protein kinase A attenuates morphine withdrawal excitation of rat hypothalamus-pituitary-adrenal axis. European Journal of Pharmacology 2002;452(1):57-66
Agents: HA-1004; calphostin C **Vehicle:** Water, sterile; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A, protein kinase C)

Imatinib (2011-Present)

Q10274: S. Hegde, *et al.* Inhibition of the RacGEF VAV3 by the small molecule IODVA1 impedes RAC signaling and overcomes resistance to tyrosine kinase inhibition in acute lymphoblastic leukemia. Leukemia 2022;36(3):637-647
Agents: IODVA1; Imatinib **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Vav3-deficient mice and Rac1Δ/Δ+Rac2-deficient mice; C57Bl/10 (females, 8–16 weeks old) and NSG (NOD/SCID/IL2RG-/- males and females, 8–14 weeks old); IODVA1 aka 2-guanidinobenzimidazole derivative with anti-tumorigenic properties; cancer (leukemia)

Q10054: L. Pandolfi, *et al.* Loading Imatinib inside targeted nanoparticles to prevent Bronchiolitis Obliterans Syndrome. Scientific Reports 2020;10(1):20726
Agents: Imatinib **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Pathogen-free, male C57BL/6 and Balb/c mice, 20-24 g); Imatinib aka GNP-HClm; toxicology;

Q6168: R. C. Nayak, *et al.* The signaling axis atypical protein kinase C lambda/iota-Satb2 mediates leukemic transformation of B-cell progenitors. Nat Commun 2019;10(1):1-16
Agents: Ro-31-8220; imatinib **Vehicle:** PBS; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (Ro-31-8220 (1 mM); imatinib (0.5 mM)); Controls received mp w/ vehicle; animal info (6-12 wk old transgenic mice);

Q10082: H. K. Ananthula, *et al.* Preclinical pharmacokinetic evaluation to facilitate repurposing of tyrosine kinase inhibitors nilotinib and imatinib as antiviral agents. BMC Pharmacology and Toxicology 2018;19(1):80
Agents: Nilotinib; Imatinib **Vehicle:** Ethanol:PEG300: Cremophor EL; Sterile water; **Route:** IV injection; Gavage; **Species:** Mice; Guinea pigs; Prairie Dogs; Cynomolgus monkeys; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Nilotinib 1.5:4.5:20 (ethanol:PEG300:Cremophor) in 3.7% dextrose solution used; animal info (Mice C57BL/6, 20g both genders; Prairie dogs wild caught male black tailed, 1-2 years; Guinea pigs male hartley 450-650g); half-life (p.1,8); Resultant plasma level (Figure 1 nilotinib, Figure 2 imatinib); enzyme inhibitor (tyrosine kinase (TKI)); good methods (elimination half-lives were quite short (1–2 h). Thus, further testing of these agents in C57BL/6 mice is feasible but may require a continuous delivery system such as an Alzet® mini pump.); didn't use Alzet pmup, but recommends using it in future studies of these agents in mice or guinea pigs;

Q6491: Tucheng Sun, *et al.* Imatinib inhibits angiotensin II-induced aortic
dissection through the c-Abl signaling pathway. International Journal for Clinical Experimental Pathology 2017;10(5):5316-5324
Agents: Angiotensin II; Imatinib mesylate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: Dose (Angiotensin II: 3 mg/kg/day; Angiotensin II + Imatinib mesylate: 60 mg/kg per day); 0.9% saline used; Controls received mp w/ vehicle; animal info (12-30 week old C57BL/6 male mice weighing 25-35g);

Q5735: R. Callahan, *et al.* Original Research: Featured Article: Imatinib mesylate (Gleevec) inhibits Notch and c-Myc signaling: Five-day treatment permanently rescues mammary development. Experimental Biology and Medicine 2017;242(1):53-67
Agents: Imatinib mesylate **Vehicle:** Saline; **Route:** SC; **Species:** Mice (pregnant); **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (10 weeks old); cancer (Breast); Therapeutic indication (Mammary gland development, Breast cancer); Dose (21 mg/mouse/week);

Q4546: R. J. Napier, *et al.* Low Doses of Imatinib Induce Myelopoiesis and Enhance Host Anti-microbial Immunity. PLoS Pathogens 2015;11(U1651-U1677
Agents: Imatinib mesylate **Vehicle:** Water; **Route:** SC; **Species:** Mice; **Pump:** 1007D; 2002; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6, 6 weeks old); functionality of mp verified by serum levels; dose-response (pg.9); immunology; enzyme inhibitor (tyrosine kinase);

Q3443: J. Chu, *et al.* Pharmacological Modulation of GSAP Reduces Amyloid-beta Levels and Tau Phosphorylation in a Mouse Model of Alzheimer's Disease with Plaques and Tangles. JOURNAL OF ALZHEIMERS DISEASE 2014;41(729-737
Agents: Imatinib **Vehicle:** CSF, artificial **Route:** CSF/CNS (intrathecal) **Species:** Mice (transgenic) **Pump:** 1007D **Duration:** 1 wk
ALZET Comments: Controls received mp w/ vehicle; animal info (triple transgenic ABBP, PS1, P301L); neurodegenerative (Alzheimer's); "Since it is known that the drug does not penetrate the blood-brain barrier efficiently, it is possible that the contradictory results reflect this property of the drug. For this reason in the current study, we delivered Imatinib by means of implanted osmotic minipumps directly in the brains of the triple transgenic mice" pg 730;

Q1933: J. M. Launay, *et al.* Serotonin 5-HT(2B) receptors are required for bone-marrow contribution to pulmonary arterial hypertension. Blood 2012;119(7):1772-1780
Agents: Imatinib mesylate **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 5 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (5HT-2b -/-, adult, 7-9 wks old); imatinib mesylate also known as Gleevec or STI-571; hypoxia; enzyme inhibitor (tyrosine kinase);

Q1444: P. M. Reeves, *et al.* Variola and Monkeypox Viruses Utilize Conserved Mechanisms of Virion Motility and Release That Depend on Abl and Src Family Tyrosine Kinases. JOURNAL OF VIROLOGY 2011;85(1):21-31
Agents: Dasatinib; imatinib mesylate **Vehicle:** DMSO; water; PBS **Route:** SC **Species:** Mice **Pump:** Not Stated **Duration:** 4 days
ALZET Comments: Controls received mp w/ vehicle; animal info (6 wks old, female, C57/BL6); 50% DMSO used; dasatinib also known as BMS-354825; one group contained a mixture of dasatinib and imatinib mesylate in a single pump; imatinib mesylate also known as STI-571; enzyme inhibitor (tyrosine kinase, Src Abl)

KN92 or KN93 (2015-Present)

Q9384: G. Nalesso, *et al.* Calcium calmodulin kinase II activity is required for cartilage homeostasis in osteoarthritis. Scientific Reports 2021;11(1):5682
Agents: KN-93 **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Dose (5 umol/kg/day); Controls received mp w/ vehicle; animal info (Ten week old, male C57BL/6 mice);

Q8571: J. E. Kim, *et al.* PKC, AKT and ERK1/2-Mediated Modulations of PARP1, NF-kappaB and PEA15 Activities Distinctly Regulate Regional Specific Astroglial Responses Following Status Epilepticus. Front Mol Neurosci 2019;12(180
Agents: Bisindolylmaleimide; 3-chloroacetyl-indole; U0126; KN-93; PJ-34; SC79 **Vehicle:** Not stated; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 1007D; **Duration:** 3 days;
ALZET Comments: Dose (25 uM Bisindolylmaleimide; 25 uM 3-chloroacetyl-indole; 25 uM U0126; 25 uM KN-93; 3 uM PJ-34; 25 uM SC79); Controls received mp w/ vehicle; animal info (adult male Sprague-Dawley rats, 250-280 g); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; -3.5 mm depth);

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);

Q9004: Z. Zhao, *et al.* Antioxidant defense and protection against cardiac arrhythmias: lessons from a mammalian hibernator (the woodchuck). FASEB Journal 2018;32(8):4229-4240
Agents: KN-92; KN-93 **Vehicle:** Not Stated; **Route:** IA (femoral); **Species:** Woodchuck; **Pump:** 2ML1; **Duration:** 24 hours;
ALZET Comments: Dose ((KN-92 125 µg/kg/h), (KN-93 125 µg/kg/h)); Controls received mp w/ KN-92; animal info (1-2 years, male and female, wild-caught, 2-3kg); cardiovascular; Therapeutic indication (inhibition of CaMKII activity by lessening its oxidized and/or phosphorylated levels may mediate its antiarrhythmic effects.);

Q4601: K. Tagawa, *et al.* Comprehensive phosphoproteome analysis unravels the core signaling network that initiates the earliest synapse pathology in preclinical Alzheimer's disease brain. HUMAN MOLECULAR GENETICS 2015;24(540-558
Agents: Go6976; MLR1023; KN-93 **Vehicle:** DMSO; PBS; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** 1003D;
ALZET Comments: Animal info (male, APP770 human double mutant); 0.1% DMSO used; neurodegenerative (Alzheimer's); behavioral testing (morris water maze, rotarod test, fear-conditioning, light-dark box, elevated plus maze);

Q4392: P. G. Daft, *et al.* The Growth and Aggressive Behavior of Human Osteosarcoma Is Regulated by a CaMKII-Controlled Autocrine VEGF Signaling Mechanism. PLoS One 2015;10(U431-U450
Agents: KN-93; CBO-P11 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Foxn1 nu, 6 weeks old); cancer (osteosarcoma);

Other (2012-Present)

Q8264: P. Liu, *et al.* Protein kinase C is involved in the neuroprotective effect of berberine against intrastriatal injection of quinolinic acid-induced biochemical alteration in mice. J Cell Mol Med 2019;23(9):6343-6354
Agents: Pan-PKC inhibitor **Vehicle:** Not stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;
ALZET Comments: "Dose (0.11 uL/hr); animal info (Male, 2 months old, 22-25 g, KM); Pan-PKC inhibitor aka Go6983; enzymWe inhibitor (PKC inhibitor); ALZET brain infusion kit 2 used; Brain coordinates (0.5 mm posterior to bregma, 3 mm below the surface of the cranium); neurodegenerative (Motor and cognitive deficit); "

Q8776: P. Wang, *et al.* Sodium butyrate triggers a functional elongation of microglial process via Akt-small RhoGTPase activation and HDACs inhibition. Neurobiology of Disease 2018;111(12-25
Agents: LY294002 **Vehicle:** CSF, Artificial, DMSO buffered; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1003D; 2002; **Duration:** 3 days;
ALZET Comments: Dose (5 µg/mL at 0.5 µL/h); 3% DMSO in aCSF used; Controls received mp w/ vehicle; animal info (8-10 weeks, male, C57BL/6J); behavioral testing (forced swimming, tail suspension, sucrose preference); SB is a sodium salt form of butyrate produced by fermentation of dietary fibers in the gut; enzyme inhibitor (protein kinase B); Brain coordinates (−0.2 mm anterior and 1.0 mm lateral relative to bregma and 2.3 mm below the surface of the skull); Cannula placement verified via stereotaxic frame; immunology; mp model 2002 was used for chronic injections and model 1003D for acute injections;

Q7815: F. Garcia-Bernal, *et al.* Protein Kinase C Inhibition Mediates Neuroblast Enrichment in Mechanical Brain Injuries. Front Cell Neurosci 2018;12(462
Agents: Bisindolymaleimide I **Vehicle:** PBS, sterile; DMSO, buffered; **Route:** CSF/CNS (cortex); **Species:** Mice; **Pump:** 1004; **Duration:** 14 days;
ALZET Comments: Dose (0.5 µM); PBS with 0.4% DMSO used; Controls received mp w/ vehicle; animal info (2 months, male, CD1); Go-6850 AKA Bisindolylmaleimide I, is a broad-spectrum PKC inhibitor,; enzyme inhibitor (protein kinase C); ALZET brain infusion kit 2 used; Therapeutic indication (facilitates the generation of neuroblasts);

Q7137: K. Fujita, *et al.* Targeting Tyro3 ameliorates a model of PGRN-mutant FTLD-TDP via tau-mediated synaptic pathology. Nat Commun 2018;9(1):433
Agents: Gö6976 **Vehicle:** PBS; **Route:** CSF/CNS (intrathecal); **Species:** Mouse; **Pump:** 2006; **Duration:** 2 weeks;
ALZET Comments: Dose (0.15 ul/h); animal info (PGRN-KI and C57BL/6J, 10-12 weeks old); behavioral testing (Morris water maze test, Fear-conditioning test, Probe test, Rotarod test, Open-field test, Light-dark box test)

Q4915: L. Yang, *et al.* Activation of protein kinase A in the amygdala modulates anxiety-like behaviors in social defeat exposed mice. Mol Brain 2016;9(3
Agents: 8-Br-cAMP; H-89 **Vehicle:** Not Stated; **Route:** CSF/CNS (basolateral amygdala); **Species:** Mice; **Pump:** 1002; **Duration:** 10 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, C57BL6J, 8 weeks old); ALZET brain infusion kit 2 used; behavioral testing (social defeat stress; social interaction; open field; elevated plus maze; rotarod test); bilateral infusion; pumps removed after 10 days; Dose (8-Br-cAMP 2 ug/day; H-89 0.3 ug/day); brain coordinates;

Q5308: A. Clermont, *et al.* Plasma Kallikrein Mediates Vascular Endothelial Growth Factor-Induced Retinal Dysfunction and Thickening. Invest Ophthalmol Vis Sci 2016;57(6):2390-9
Agents: Fluoroacetate, Propionamide ditri- **Vehicle:** PEG 400, PBS; **Route:** SC; **Species:** Rat, mice; **Pump:** 1003D, 1007D; **Duration:** 1 day, 2 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Male Sprague-Dawley (SD) rats 10 wks, plasma prekallikrein gene-deficient mice (KLKB1-/-)); functionality of mp verified by enzyme activity assays; 10% PEG 400 used; dose-response (pg 2394, 2398); stability verified by (single bolus subcutaneous injection); Fluoroacetate, Resultant plasma level (pg 2394);

Q2434: J. Menon, *et al.* A Novel Interplay between Rap1 and PKA Regulates Induction of Angiogenesis in Prostate Cancer. PLoS One 2012;7(11):U770-U779
Agents: 8CPT; H-89 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Control animals received mp w/ PBS; animal info (male, athymic, 15-20 g, 4-6 wks old); 8CPT also known as 8-pCPT-2'-O-Me-cAMP; enzyme inhibitor (PKA); cancer (prostate)

Q2500: L. C. Matavelli, *et al.* In vivo regulation of renal expression of (pro)renin receptor by a low-sodium diet. American Journal of Physiology Renal Physiology 2012;303(12):F1652-F1657
Agents: PKGi; ODQ **Vehicle:** Water, distilled, deionized; **Route:** Kidney (cortex); **Species:** Rat; **Duration:** 6 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 4 wks old); Vetbond used to glue catheter to kidney

Q2032: B. S. Huang, *et al.* Possible role of brain salt-inducible kinase 1 in responses to central sodium in Dahl rats. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 2012;303(2):R236-R245
Agents: Staurosporine **Vehicle:** CSF, artificial; ethanol; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (5-6 wks old, male, Dahl S, Wistar); guide cannula used;

PD98059 (2014-Present)

Q8857: C. T. Huang, *et al.* Glycemic control with insulin attenuates sepsis-associated encephalopathy by inhibiting glial activation via the suppression of the nuclear factor kappa B and mitogen-activated protein kinase signaling pathways in septic rats. Brain Research 2020;1738(146822
Agents: Dextrose; Fluorocitrate; Minocycline; SB203580; PD98059 **Vehicle:** DMSO; **Route:** CSF/CNS (intracerebral); IV (jugular); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: 1% DMSO used; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley rats (weight, 200–250 g)); behavioral testing (Von Frey filament test, Plantar test); functionality of mp verified by residual volume; Brain coordinates (0.8 mm posterior and 1.3 mm lateral to the bregma, and 4.0 mm ventral to the skull surface); dependence;

Q6430: S. Hitomi, *et al.* Enhancement of ERK phosphorylation and photic responses in Vc/C1 neurons of a migraine model. Neurosci Lett 2017;647(14-19
Agents: PD98059 **Vehicle:** DMSO, Saline; **Route:** Csf/cns (intracisternal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (0.1 µg/µl); 10% DMSO used;Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats); post op. care (penicillin G potassium); enzyme inhibitor (Mitogen-activated protein kinase kinase 1 inhibitor);

Q5854: H. L. Gao, *et al.* PVN Blockade of p44/42 MAPK Pathway Attenuates Salt-induced Hypertension through Modulating Neurotransmitters and Attenuating Oxidative Stress. Sci Rep 2017;7(43038
Agents: PD-98059 **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (8 weeks old) ; Controls received mp w/ vehicle; animal info (8 weeks old) ; Therapeutic indication (Oral drug delivery, Pharmacokinetics); Dose (.025 ug/hr);

Q4903: Y. Y. Shun-Guang Wei, Robert M. Weiss, Robert B. Felder. Inhibition of Brain Mitogen-Activated Protein Kinase Signaling Reduces Central Endoplasmic Reticulum Stress and Inflammation and Sympathetic Nerve Activity in Heart Failure Rats. Hypertension 2016;67(229-236
Agents: PD98059; SB203580; SP600125 **Vehicle:** CSF, artificial; DMSO; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 4wk
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, adult, 275-325g); 5% DMSO used;

Q5649: C. T. Huang, *et al.* Neurosteroid Allopregnanolone Suppresses Median Nerve Injury-induced Mechanical Hypersensitivity and Glial Extracellular Signal-regulated Kinase Activation through gamma-Aminobutyric Acid Type A Receptor Modulation in the Rat Cuneate Nucleus. Anesthesiology 2016;125(6):1202-1218
Agents: PD98059 **Vehicle:** DMSO, Ringer's solution; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls underwent median nerve CCI or sham operation; functionality of mp verified by residual volume; Dose (2, 2.5, 3.0 mM);

Q4099: K. Shimizu, *et al.* Involvement of Trigeminal Transition Zone and Laminated Subnucleus Caudalis in Masseter Muscle Hypersensitivity Associated with Tooth Inflammation. PLoS One 2014;9(U620-U630
Agents: PD98059 **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague Dawley, 250-450g); functionality of mp verified by residual volume; used PE45 tubing to catheterize IT space;

Ruxolitinib

Q10149: Z. Dai*, et al.* Selective inhibition of JAK3 signaling is sufficient to reverse alopecia areata. JCI Insight 2021;6(7):
Agents: INCB039110; CEP-33779; Fedratinib; Pacritinib; PF-06651600; Ruxolitinib; Tofacitinib **Vehicle:** DMSO; **Route:** Not Stated; **Species:** Mice; **Pump:** 1002; **Duration:** Not Stated;
ALZET Comments: Dose: INCB039110 (50 mg/kg); CEP-33779 (50 mg/kg), Fedratinib (50 mg/kg), Pacritinib (50 mg/kg), PF-06651600 (30 mg/kg), Ruxolitinib (30 mg/kg), Tofacitinib (30 mg/kg); animal info:C3H/HeJ mice with AA; Alopecia areata (AA) Autoimmune disease of the hair follicle

Q6403: J. Chen*, et al.* Cytokine receptor signaling is required for the survival of ALK- anaplastic large cell lymphoma, even in the presence of JAK1/STAT3 mutations. Proc Natl Acad Sci U S A 2017;114(15):3975-3980
Agents: Ruxolitinib **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Dose (50 mg/kg/d); cancer (lymphoma);

Q7240: W. Ju*, et al.* Augmented efficacy of brentuximab vedotin combined with ruxolitinib and/or Navitoclax in a murine model of human Hodgkin's lymphoma. Proc Natl Acad Sci U S A 2016;113(6):1624-9
Agents: Ruxolitinib **Vehicle:** PEG 300; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Dose (50 mg/kg/d); Controls received mp w/ vehicle; enzyme inhibitor (JAK1/2 inhibitor);

Q2729: K. G. Roberts*, et al.* Genetic Alterations Activating Kinase and Cytokine Receptor Signaling in High-Risk Acute Lymphoblastic Leukemia. Cancer Cell 2012;22(2):153-166
Agents: Ruxolitinib **Vehicle:** Dimethylacetamide; propylene glycol; **Route:** SC; **Species:** Mice; **Duration:** 4 weeks;
ALZET Comments: Control animals received mp w/ vehicle; animal info (BCR-JAK2); 40% DMA; 60% propylene glycol used;

Q2314: S. L. Maude*, et al.* Targeting JAK1/2 and mTOR in murine xenograft models of Ph-like acute lymphoblastic leukemia. Blood 2012;120(17):3510-3518
Agents: Ruxolitinib **Vehicle:** Dimethylacetamide; propylene glycol; **Route:** SC; **Species:** Mice (NSG); **Duration:** 3-4 weeks;
ALZET Comments: Control animals received mp w/ vehicle; animal info (NOD SCID, nonobese); ruxolitinib also known as INCB018424; stress/adverse effects "One ruxolitinib-treated mouse... experienced a wound dehiscence at the subcutaneous pump surgical site" pg 3512; cancer (leukemia); chemotherapeutic; 40% DMA used; 60% propylene glycol used;

Sorafenib

Q2916: A. Z. Dudek*, et al.* Brain Metastases from Renal Cell Carcinoma in the Era of Tyrosine Kinase Inhibitors. Clinical Genitourinary Cancer 2013;11(2):155-160
Agents: Sorafenib; sunitinib **Vehicle:** DMSO; saline; **Route:** IP; **Species:** Not Stated; **Pump:** 1003D; **Duration:** Not Stated;
ALZET Comments: Animal info (Friend virus B-type (FVB) wild type, and Abcb1a/b knockout mice); cancer (renal carcinoma and brain metastases); cancer; enzyme inhibitor (tyrosine kinase); chemotherapeutic

Q1442: S. Agarwal*, et al.* The Role of the Breast Cancer Resistance Protein (ABCG2) in the Distribution of Sorafenib to the Brain. Journal of Pharmacology and Experimental Therapeutics 2011;336(1):223-233
Agents: Sorafenib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** 48 hours;
ALZET Comments: Animal info (FVB wild-type, Mdr1a/b -/-, Bcrp1 -/-, Mdr1a/b -/-, Bcrp1 -/-); half-life pg 226 "Sorafenib half-life in plasma and brain after an intravenous dose was determined to be 1.6 and 0.9 h, respectively. Therefore an infusion lasting 48 h was considered to be sufficiently long to attain steady state in both plasma and brain.";

SU6656

Q3686: S. J. Wang*, et al.* Src Is Required for Mechanical Stretch-Induced Cardiomyocyte Hypertrophy through Angiotensin II Type 1 Receptor-Dependent beta-Arrestin2 Pathways. PLoS One 2014;9(U378-U387
Agents: SU6656 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 17 days;
ALZET Comments: Animal info (AGT KO, 8-10 weeks old); cardiovascular; SU6656 is a selective Src family kinase inhibitor;

Sunitinib

Q4264: Y. Zhu, *et al.* Hematogenous macrophage depletion reduces the fibrotic scar and increases axonal growth after spinal cord injury. NEUROBIOLOGY OF DISEASE 2015;74(114-125
Agents: Sunitinib malate **Vehicle:** DMSO; **Route:** CSF/CNS (intrathecal); **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: enzyme inhibitor (tyrosine kinase);Animal info (female, 8 weeks old); functionality of mp verified by use of evans blue dye; 2.5% DMSO used; spinal cord injury; immunology; used ALZET mouse IT catheter;

Q6739: R. K. Oberoi, *et al.* Pharmacokinetic assessment of efflux transport in sunitinib distribution to the brain. J Pharmacol Exp Ther 2013;347(3):755-64
Agents: Sunitinib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice (transgenic); mice (knockout); **Pump:** 1003D; **Duration:** 48 hours;
ALZET Comments: Dose (30 µg/h); animal info (8-10 week old wild-type and transgenic mice in which the gene for P-gp [Mdr1a/b(2/2) knockout mice], Bcrp [Bcrp1(2/2) knockout mice], and both P-gp and Bcrp [Mdr1a/b(2/2) Bcrp1(2/2) or "triple knockout" mice] was knocked out); enzyme inhibitor (tyrosine kinase);

Q2916: A. Z. Dudek, *et al.* Brain Metastases from Renal Cell Carcinoma in the Era of Tyrosine Kinase Inhibitors. Clinical Genitourinary Cancer 2013;11(2):155-160
Agents: Sorafenib; sunitinib **Vehicle:** DMSO; saline; **Route:** IP; **Species:** Not Stated; **Pump:** 1003D; **Duration:** Not Stated;
ALZET Comments: Animal info (Friend virus B-type (FVB) wild type, and Abcb1a/b knockout mice); cancer (renal carcinoma and brain metastases); cancer; enzyme inhibitor (tyrosine kinase); chemotherapeutic

TAT(47-57)

Q7189: A. U. Joshi, *et al.* Inhibition of Drp1/Fis1 interaction slows progression of amyotrophic lateral sclerosis. EMBO Molecular Medicine 2018;10(3):
Agents: P110-TAT (47-57) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 28 day pump; **Duration:** 60 days;
ALZET Comments: Dose (3 mg/kg/day); animal info (4–6 weeks old AdultB6SJL Tg (SOD1G93A) 1 Gur/J male mice); behavioral testing (Activity chamber); pumps replaced after 30 days; long-term study; P110 is a selective peptide inhibitor of Drp1/Fis1; neurodegenerative (amyotrophic lateral sclerosis); neurodegenerative (amyotrophic lateral sclerosis); stress/adverse reaction:

Q6163: M. H. Disatnik, *et al.* Potential biomarkers to follow the progression and treatment response of Huntington's disease. J Exp Med 2016;213(12):2655-2669
Agents: P110-TAT (47-57) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 1 week, 8 weeks;
ALZET Comments: Dose (3 mg/Kg/d); Controls received mp w/ vehicle; animal info (5 week old Hemizygous R6/2 HD mice); pumps replaced every 4 weeks; neurodegenerative (Huntington's);

Q2152: J. C. B. Ferreira, *et al.* Protein Quality Control Disruption by PKC beta II in Heart Failure; Rescue by the Selective PKC beta II Inhibitor, beta IIV5-3. PLoS One 2012;7(3):U373-U383
Agents: TAT 47-57, beta IIV5-3, peptide; beta IV5-3, epsilon V1-2, carrier peptide SC; **Species:** Rat; **Pump:** Not Stated;
ALZET Comments: Controls received mp w/ carrier peptide; animal info (Wistar, normotensive, 12 wks old, male, Dahl, 6 wks old); peptides; pumps replaced every 2 weeks; enzyme inhibitor (protein kinase C, PKC)

Q1288: X. Qi, *et al.* Aberrant mitochondrial fission in neurons induced by protein kinase Cdelta under oxidative stress conditions in vivo. Molecular Biology of the Cell 2011;22(2):256-265
Agents: TAT 47-57, peptide; TAT; TAT 47-57, delta conjugated, peptide **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ control peptide; animal info (DS, 11-15 wks old, male); peptides

Q0485: T. Deuse, *et al.* Sustained Inhibition of epsilon Protein Kinase C Inhibits Vascular Restenosis After Balloon Injury and Stenting. Circulation 2010;122(11):S170-S178
Agents: RACK7, psi epsilon; V1–2,10, epsilon; TAT (47-57) **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Duration:** 4, 6 weeks;
ALZET Comments: Controls received mp w/saline; animal info (male, Sprague-Dawley, 550-600 g); pumps replaced every second week; peptides; long-term study; enzyme inhibitor (epsilon PKC); epsilon V1-2 is a selective epsilon PKC inhibitor; psi epsilon RACK7 is a selective epsilon PKC activator psi epsilon receptor for activated protein kinase C

P9143: J. W. Kim, *et al.* Centrosomal PKCbetaII and pericentrin are critical for human prostate cancer growth and angiogenesis. Cancer Research 2008;68(16):6831-6839
Agents: TAT (47-57); IIV5-3, beta- **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice (nude); **Pump:** 2001; **Duration:** 5 weeks;
ALZET Comments: Controls received mp w/ vehicle or TAT (47-57); pumps replaced every 2 weeks; half-life (p. 6832) ~ 2 wks; enzyme inhibitor (PKC betaII, protein kinase C); animal info (6 wks old, male)

P8634: T. Koyanagi, *et al.* Pharmacological inhibition of epsilon PKC suppresses chronic inflammation in murine cardiac transplantation model. Journal of Molecular and Cellular Cardiology 2007;43(4):517-522
Agents: Peptide, TAT (47-57); Peptide TAT (47-57)-EV1-2 **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ TAT control peptide; pumps replaced after 14 days; no stress (see pg. 519); enzyme inhibitor (Epsilon PKC); cardiovascular; peptides; animal info (male, C57BL/6J (H-2b), 6-8 wks old);

P8460: R. Bright, *et al.* Delta PKC mediates microcerebrovascular dysfunction in acute ischemia and in chronic hypertensive stress in vivo. Brain Research 2007;1144(146-155
Agents: TAT (47-57), dv1-1-; TAT (47-57) **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 4,6 weeks; 6,7 days;
ALZET Comments: Controls received mp w/ control peptide TAT; comparison of IP injections vs. mp; pumps replaced every 2 weeks; enzyme inhibitor (Protein kinase C); cardiovascular; peptides; ischemia (cerebral); animal info (11-12 wks old, male)

Trametinib

Q8105: E. J. Macarak, *et al.* Trametinib prevents mesothelial-mesenchymal transition and ameliorates abdominal adhesion formation. J Surg Res 2018;227(198-210
Agents: Trametinib **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 8 days;
ALZET Comments: Dose (0.1, 1, or 3 mg/kg); Controls received mp w/ vehicle; animal info (C57BL/6, 18-25 g, 8-10 weeks old);

Q4893: B. W.-R. Shruthi Vaidhyanathan, Daniel J. Ma, Karen E. Parrish,, *et al.* Factors Influencing the Central Nervous System Distribution of a Novel Phosphoinositide 3-Kinase/Mammalian Target of Rapamycin Inhibitor GSK2126458: Implications for Overcoming Resistance with Combination Therapy for Melanoma Brain Metastases. The Journal of Pharmacology and Experimental Therapeutics 2016;356(251-259
Agents: GSK2126458; trametinib, dabrafenib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 48 hours;
ALZET Comments: animal info (WT, Mdr1a/b -/-, Bcrp1 -/-); functionality of mp verified by plasma concentration; pumps primed overnight in 37C saline;

Q4147: S. Vaidhyanathan, *et al.* Factors Influencing the CNS Distribution of a Novel MEK-1/2 Inhibitor: Implications for Combination Therapy for Melanoma Brain Metastases. Drug Metabolism and Disposition 2014;42(1292-1300
Agents: Trametinib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 48 hours;
ALZET Comments: Animal info (WT, Mdr1 a/b -/-, Bcrp1 -/-); functionality of mp verified by plasma levels; cancer (melanoma); post op. care (heating pad for recovery); pumps primed overnight in 37C sterile saline; enzyme inhibitior(mitogen-activated protein kinase kinase-1 (MEK)-1/2 inhibitor); good methods (p. 1294)

Vemurafenib

Q2184: R. K. Mittapalli, *et al.* Impact of P-Glycoprotein (ABCB1) and Breast Cancer Resistance Protein (ABCG2) on the Brain Distribution of a Novel BRAF Inhibitor: Vemurafenib (PLX4032). Journal of Pharmacology and Experimental Therapeutics 2012;342(1):33-40
Agents: Vemurafenib **Vehicle:** DMSO; propylene glycol; saline **Route:** IP **Species:** Mice **Pump:** Not Stated **Duration:** 48 hours
ALZET Comments: Animal info (wt, Mdr1a/b -/-, Bcrp1 -/-); infusion rate of 1 ul/hr; wound clips used; brain tissue distribution; cancer (breast); vemurafenib also known as PLX4032; 40% DMSO used; chemotherapeutic