



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

1. Calphostin C

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
ALZET Comments: HA-1004; calphostin c; Water, sterile; DMSO; SC; Rat; 2001; 7 days; 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
ALZET Comments: Calphostin C; chelerythrine; SC; Rat; 7 days; 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
ALZET Comments: Calphostin C; SC; Rat; 2001; 7 days; 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
ALZET Comments: HA-1004; calphostin C; Water; DMSO; SC; Rat; 2001; 7 days; Animal info (male, Sprague Dawley, 220-240 g); dependence; enzyme inhibitor (PKA, PKC); 0.6% DMSO used.

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
ALZET Comments: HA-1004; calphostin C; DMSO; water; SC; Rat; 2001; 7 days; 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
ALZET Comments: Calphostin C; Water, Milli-Q; DMSO; SC; Rat; 2001; 7 days; 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
ALZET Comments: Calphostin C; DMSO; water; SC; Rat; 2001; 7 days; 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
ALZET Comments: HA-1004; calphostin C; Water, sterile; DMSO; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A, protein kinase C).



P4570: C.-L. Chen, *et al.* Quantitative high-performance liquid chromatography-based detection method for calphostin C, a naturally occurring perylenequinone with potent antileukemic activity. *Journal of Chromatography B* 1999;724(157-162)
ALZET Comments: Calphostin C;; DMSO; Tween 80; PBS;; mice;; 1007D;; 7 days;; functionality of mp verified by in vitro incubation and HPLC analysis; cancer; enzyme inhibitor (protein kinase C);.

P2315: C. Hermenegildo, *et al.* Sustained recovery of Na⁺-K⁺-ATPase activity in sciatic nerve of diabetic mice by administration of H7 or calphostin C, inhibitors of PKC. *Diabetes* 1993;42(257-262)
ALZET Comments: H7; Calphostin C; DMSO; Water; SC; mice; 3,7,10 or 14 days; controls were nondiabetic mice and untreated diabetic mice; comparison of bolus ip injections vs. mp; no stress (see pg. 259,260); enzyme inhibitor; calphostin C and H7 are PKC inhibitors; "treatment [w/ mp] did not produce any untoward effect nor affect the blood glucose levels." (pg. 260); H7 is unstable after 4 hours; Calphostin C is stable for 2 weeks.

2. 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
ALZET Comments: Cediranib; DMSO; IP; Mice; 1003D; 72 hours; Animal info (wt, Mdr1a/b -/-, Bcrp1 -/-, and Mdr1a/b -/-, Bcrp1 -/-); cancer (glioma); enzyme inhibitor (tyrosine kinase); chemotherapeutic.

3. 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
ALZET Comments: Cetuximab; CSF/CNS (intratumoral); Rat (nude); 2ML4; 4 weeks; 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
ALZET Comments: Cetuximab; CSF/CNS (intratumoral); Mice (nude); 2004; Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioblastoma); ALZET brain infusion kit 2 used; animal info (NMRI- nu/nu, 6-8 wks old); cetuximab is a monoclonal antibody against EGFR.

4. Chelerythrine

Q7040: S. P. Yoon, *et al.* Exogenous CGRP upregulates profibrogenic growth factors through PKC/JNK signaling pathway in kidney proximal tubular cells. *Cell Biol Toxicol* 2018;34(4):251-262
ALZET Comments: Calcitonin gene-related peptide, SP600125, chelerythrine, CGRP8-37 receptor antagonist; Saline; DMSO; IP, Kidney (cortical region); Mice; Dose (30 ng/kg/d); 10% DMSO used; Controls received mp w/ vehicle; animal info (Male C57BL/6 mice aged 8 to 10 weeks); CGRP is a 37-amino acid neuropeptide; enzyme inhibitor (SP600125 is a c-Jun Nterminal protein kinase (JNK), and chelerythrine is a specific protein kinase C (PKC) inhibitor); CGRP infused to the cortical region of the denervated kidney via an ALZET intrathecal catheter. 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) or vehicle (0.9% saline or 10% DMSO in 0.9% saline) via IP pump.

Q3342: K. K. Howell, *et al.* Inhibition of PKC disrupts addiction-related memory. *Frontiers in Behavioral Neuroscience* 2014;8(;):U1-U9



ALZET Comments: Peptide, zeta-inhibitory; chelerythrine; CSF, artificial; PBS; CSF/CNS (third ventricle); Mice; 1002; 2 days; 6 days; Controls received mp w/ vehicle; animal info (C57BL/6Jx129T2SvEms/J, adult); ALZET brain infusion kit 3 used; post op. care (buprenorphine injection); behavioral testing (locomotion, locomotor sensitization); pulsatile delivery; dependence; peptides; zeta-inhibitory peptide aka ZIP; Lynch coil of ZIP administration for 14.5 hours; used mineral oil; Schematic of pump implantation pg.3 Fig 1A;

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

ALZET Comments: Chelerythrine; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (adult, male, Sprague Dawley, 200-300 g); enzyme inhibitor (protein kinase C gamma).

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

ALZET Comments: Calphostin C; chelerythrine; SC; Rat; 7 days; 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 Ca²⁺ Channels Controls Pain Sensory Gating in the Thalamus. *Journal of Neuroscience* 2008;28(49):13331-13340

ALZET Comments: Phorbol 12, 13-didecanoate; chelerythrine; apamin; iberiotoxin; CSF/CNS (thalamus); Mice; 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)

ALZET Comments: Angiotensin II; Chelerythrine; Saline; SC; Rat; 7 days; 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

ALZET Comments: Rp-8-Cl-cAMPS; Rp-8-Cl-cGMPs; Chelerythrine chloride; Peptide, inhibitory myristoylated; Cat; Peptides; Fig. 5 mentions minipump infusion; enzyme inhibitors; protein kinase A, C, and G inhibitors.

5. Dasatinib

Q3781: S. L. Ho, *et al.* Toxicity evaluation of prolonged convection-enhanced delivery of small-molecule kinase inhibitors in naive rat brainstem. *Childs Nervous System* 2015;31(221-226)

ALZET Comments: Dasatinib; everolimus; DMSO; ethanol anhydrous; CSF, artificial; CSF/CNS (brain stem); Rat; 2001; 7 days; 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" pg 221; enzyme inhibitor (receptor tyrosine kinase).

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)

ALZET Comments: Dasatinib; DMSO; saline; IP; Mice; 1004; 4 weeks; 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



ALZET Comments: Dasatinib; oligomer, amyloid beta (1-42); HEPES; CSF/CNS; Mice; 1004; 14 days; 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(1):U1-U17

ALZET Comments: Dasatinib; DMSO; HEPES; SC; Mice; 1004; 28 days; Controls received mp w/ vehicle; animal info (female, APP/PS1, 13 mo old); neurodegenerative (Alzheimer's disease).

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

ALZET Comments: Dasatinib; imatinib mesylate; DMSO; water; PBS; SC; Mice; 4 days; 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).

6. Fasudil

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

ALZET Comments: Fasudil; Saline; CSF/CNS (intrathecal); Rat; 1007D; 3 days; 7 days; 14 days; Controls received mp w/ vehicle; animal info (male, Dprague Dawley, adult, 260-300g); animal info (male, Dprague Dawley, adult, 260-300g); behavioral testing (BBB behavioral 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)

ALZET Comments: Fasudil; SC; Mice (NSG); 2 weeks; 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)

ALZET Comments: Y-27632; dimethylfasudil; DMSO; saline; IP; Mice; 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)

ALZET Comments: Fasudil; Rat; 28 days; 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

ALZET Comments: Fasudil; Saline, sterile; CSF/CNS; Rabbit; 4 days; 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

ALZET Comments: L-NAME; fasudil; SC; Rat (pregnant); Controls received mp w/ normal saline; animal info (Wistar Han, 200-250 g, E14, female); enzyme inhibitor (nitric oxide synthase, NOS, Rho-kinase, ROCK); one group contained mixture of fasudil and L-NAME; teratology.



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

ALZET Comments: Fasudil; SC; Rat; Controls received mp w/ PBS; animal info (male, Lewis, 7-8 wks old, 250-300 g); enzyme inhibitor (Rho kinase).

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

ALZET Comments: Fasudil; Water, sterile; SC; Rat; 2004; 4 weeks; Controls received mp w/ sterile saline; animal info (male, Wistar, 6 wks old, 260-310 g); enzyme inhibitor (Rho kinase, ROCK).

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

ALZET Comments: HA 1152; diltiazem; fasudil; Saline; SC; Mice; 2 days; Controls received mp w/ vehicle; animal info (NFAT-luc, NFATc3-KO, wt, 20-25 g); enzyme inhibitor (RhoA/Rho kinase).

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

ALZET Comments: Fasudil; Saline; SC; Rat; 2ML4; 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

ALZET Comments: Fasudil; SC; Mice; 3 days; Animal info (adult, male, 9x-NFAT-luciferase reporter, NFATc3 knockout, BalB/C wild-type, 25-30 g); enzyme inhibitor (Rho kinase).

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

ALZET Comments: Fasudil; CSF, artificial; CSF/CNS; Mice; 1004; 24-26 days; Animal info (naive, 3-mo old, wt, A-betaPP/PS1); ALZET brain infusion kit 3 used; artificial CSF recipe.

Q0287: T. Furuya, *et al.* Treatment of rat spinal cord injury with a Rho-kinase inhibitor and bone marrow stromal cell transplantation. *Brain Research* 2009;1295(1):192-202

ALZET Comments: Fasudil; Saline; CSF/CNS (intrathecal, subarachnoid space); Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague-Dawley, 8-10 wks old, 174-236 g); post op. care (Bacitramin); spinal cord injury.

P8694: T. Ito, *et al.* Rho kinase inhibitor improves motor dysfunction and hypoalgesia in a rat model of lumbar spinal canal stenosis. *Spine* 2007;32(19):2070-2075

ALZET Comments: Fasudil hydrochloride hydrate; CSF/CNS (intrathecal); Rat; 2002; 14 days; Enzyme inhibitor (Rho-kinase); animal info (6 week, male, Sprague-Dawley, 200-250g); pain; silastic tubing used; neuroprotection.

P8286: H. Ying, *et al.* The Rho kinase inhibitor fasudil inhibits tumor progression in human and rat tumor models. *MOLECULAR CANCER THERAPEUTICS* 2006;5(9):2158-2164

ALZET Comments: Fasudil; Saline; SC; Mice (nude); 21 days; Controls received mp w/ vehicle; cancer (lung); enzyme inhibitor (rho kinase).

P6997: J. P. M. Wesselman, *et al.* Role of the RhoA/Rho kinase system in flow-related remodeling of rat mesenteric small arteries in vivo. *JOURNAL OF VASCULAR RESEARCH* 2004;41(3):277-290

ALZET Comments: Fasudil; SC; Rat; 2004; 4 weeks; Controls received mp w/ physiological saline; functionality of mp verified by fasudil and hydroxyfasudil plasma levels; enzyme inhibitor (rho kinase); cardiovascular.



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)

ALZET Comments: H89; U73122; U73343; Saline; DMSO; CSF/CNS (motor cortex); Rat; 1002; 5 days; 9 days; 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; enzyme inhibitor (protein kinase A); enzyme inhibitor (phospholipase A);.

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

ALZET Comments: H89; CSF/CNS; Mice; 1002; 8 days; 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

ALZET Comments: Bortezomib; cyclic AMP; H89; SC; Mice (nude); mice (transgenic); 1, 3, 6, 7 days; Controls received no treatment; enzyme inhibitor (PKA); cancer (acute promyelocytic leukemia); animal info (nude, PLZF-RARA-RARA-PLZF; PML-RARA5873A Tg); Bortezomib is a proteasom inhibitor; chemotherapeutic;.

P5269: J. Qiu, *et al.* Spinal axon regeneration induced by elevation of cyclic AMP. *Neuron* 2002;34(6):895-903

ALZET Comments: H89; Saline; CSF/CNS (intrathecal); Rat; 1 week; Controls received mp w/ vehicle; 1 week stability verified (results not shown); enzyme inhibitor; H89 is a protein kinase A inhibitor.

8. 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

ALZET Comments: HA-1004; calphostin c; Water, sterile; DMSO; SC; Rat; 2001; 7 days; 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

ALZET Comments: HA-1004; Water, sterile; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase); dependence; animal info (male, Sprague Dawley, 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

ALZET Comments: HA-1004; calphostin C; Water; DMSO; SC; Rat; 2001; 7 days; Animal info (male, Sprague Dawley, 220-240 g); dependence; enzyme inhibitor (PKA, PKC); 0.6% DMSO used.

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

ALZET Comments: HA-1004; calphostin C; DMSO; water; SC; Rat; 2001; 7 days; 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.



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

ALZET Comments: HA-1004; Water, sterile; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A); cardiovascular; tolerance; dependence; animal info (male, Sprague-Dawley, 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

ALZET Comments: HA-1004; Water, sterile; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; no stress (see pg. 249); enzyme inhibitor (cAMP-dependent protein kinase A); dependence.

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

ALZET Comments: HA-1004; calphostin C; Water, sterile; DMSO; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A, protein kinase C).

9. Imatinib

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

ALZET Comments: Ro-31-8220; imatinib; PBS; SC; Mice (transgenic); 2002; 14 days; Dose (Ro-31-8220 (1 mM); imatinib (0.5 mM)); Controls received mp w/ vehicle; animal info (6-12 week old transgenic mice); enzyme inhibitor (Protein Kinase C);

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

ALZET Comments: Angiotensin II; Imatinib mesylate; Saline; SC; Mice; 1002; 2 weeks; 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); enzyme inhibitor (tyrosine kinase, c-Abl); cardiovascular; Pump incorrectly noted as model #1014D.

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. Exp Biol Med (Maywood) 2017;242(1):53-67

ALZET Comments: Imatinib mesylate; Saline; SC; Mice (pregnant); 2001; 5 days; Controls received mp w/ vehicle; animal info (10 weeks old); cancer (Breast); Imatinib mesylate a.k.a Gleevec ; Therapeutic indication (Mammary gland development, Breast cancer); Dose (21 mg/mouse/week); enzyme inhibitor (tyrosine kinase);

Q4546: R. J. Napier, *et al.* Low Doses of Imatinib Induce Myelopoiesis and Enhance Host Anti-microbial Immunity. PLoS Pathogens 2015;11(U1651-U1677)

ALZET Comments: Imatinib mesylate; Water; SC; Mice; 1007D; 2002; 28 days; 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)

ALZET Comments: Imatinib; CSF, artificial; CSF/CNS (intrathecal); Mice (transgenic); 1007D; 1 week; 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; Imatinib aka STI571 aka Gleevec; used dental cement; enzyme inhibitor (tyrosine kinase);

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

ALZET Comments: Imatinib mesylate; Mice; 5 weeks; 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

ALZET Comments: Dasatinib; imatinib mesylate; DMSO; water; PBS; SC; Mice; 4 days; 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).

Q2221: R. J. Napier, *et al.* Imatinib-Sensitive Tyrosine Kinases Regulate Mycobacterial Pathogenesis and Represent Therapeutic Targets against Tuberculosis. *Cell Host & Microbe* 2011;10(5):475-485

ALZET Comments: Imatinib; Water; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, C57BL/6, 6 wks old); enzyme inhibitor (tyrosine kinase);

Q0111: M. Demestre, *et al.* Imatinib mesylate (Glivec) inhibits Schwann cell viability and reduces the size of human plexiform neurofibroma in a xenograft model. *Journal of Neuro-oncology* 2010;98(1):11-19

ALZET Comments: Imatinib mesylate; PBS; SC; Mice (nude); 2004; 28 days; Controls received mp w/ vehicle; cancer (Plexiform neurofibromas); enzyme inhibitor (receptor tyrosine kinase); stress/adverse reaction: (see pg 13) "because of inflammation at the ALZET pump site, four mice of the treatment group had to be discontinued"; animal info (female, athymic nu/nu Balb/c); agent also known as Glivec or Gleevec.

P8330: A. Raafat, *et al.* Kit and PDGFR-alpha activities are necessary for Notch4/Int3-induced tumorigenesis. *ONCOGENE* 2007;26(5):662-672

ALZET Comments: Imatinib mesylate; SC; Mice (transgenic); 2001; 1,3,4,5,7 days; Controls received mp w/ water; dose-response (fig 2); no stress (see pg. 663); cancer (mammary); animal info (female, FVB/N, 10 wks old); antiangiogenic; "Continuous release of Gleevec for a week resulted in 33% inhibition of tumor growth by day 2 and 66% by day 4." (p. 668); enzyme inhibitor (tyrosine kinase);

P8159: S. Bihorel, *et al.* Influence of hydroxyurea on imatinib mesylate (gleevec) transport at the mouse blood-brain barrier. *Drug Metabolism and Disposition* 2006;34(12):1945-1949

ALZET Comments: Imatinib mesylate; hydroxyurea; Saline; SC; Rat; 2ML2; 7, 14 days; Half-life (p. 1948) hydroxyurea <1 hour in rats; enzyme inhibitor (ribonucleotide reductase, tyrosine kinase); cancer (glioblastoma); animal info (Hanover Wistar, 270-310 grams); ATP competitive inhibitor; A.K.A, Gleevec or STI571; chemotherapeutic.

P7552: P. M. Reeves, *et al.* Disabling poxvirus pathogenesis by inhibition of Abl-family tyrosine kinases. *Nature Medicine* 2005;11(7):731-739

ALZET Comments: Imatinib mesylate; PBS; SC; Mice; 1007D; 1002; 5, 8-15 days; Controls received mp w/ vehicle; no stress (see pg. 738); enzyme inhibitor (Abl-family kinase, tyrosine kinase); animal info (female, C57/BL, 6 wk. old); agent formerly known as STI571; virology; Gleevec.

P6097: W. J. Netzer, *et al.* Gleevec inhibits beta-amyloid production but not Notch cleavage. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2003;100(21):12444-12449

ALZET Comments: Imatinib mesylate; Inhibitor 2; Saline; DMSO; CSF/CNS (Intrathecal); Guinea pig (albino); 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (abl kinase, tyrosine kinase); agent formerly known as STI571 (gleevec) is an abl kinase inhibitor (dissolved in saline); inhibitor 2 was dissolved in DMSO; "it has been shown that STI571 does not



penetrate the blood-brain barrier efficiently, we therefore delivered (p. 12447) each inhibitor intrathecally over 7 days by means of implanted osmotic minipumps."; neurodegenerative (Alzheimer's disease).

10. KN92 or KN93

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

ALZET Comments: Go6976; MLR1023; KN-93; DMSO; PBS; Mice (transgenic); 1003D; 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

ALZET Comments: KN-93; CBO-P11; Saline; SC; Mice; 1002; 2 weeks; Controls received mp w/ vehicle; animal info (male, Foxn1 nu, 6 weeks old); cancer (osteosarcoma);.

Q0651: N. Shioda, *et al.* Aberrant Calcium/Calmodulin-Dependent Protein Kinase II (CaMKII) Activity Is Associated with Abnormal Dendritic Spine Morphology in the ATRX Mutant Mouse Brain. Journal of Neuroscience 2011;31(1):346-358

ALZET Comments: KN-93; Krebs-Ringer HEPES; CSF/CNS; Mice; 1004; 2 weeks; Controls received mp w/ vehicle; animal info (ATRX-delta E2, adult, 12 wks old, male); enzyme inhibitor (Calcium/Calmodulin-Dependent Protein Kinase II, CaMKII).

P7485: S. R. Reeves, *et al.* Calcium/calmodulin-dependent kinase II mediates critical components of the hypoxic ventilatory response within the nucleus of the solitary tract in adult rats. American Journal of Physiology-Regulatory Integrative and Comparative Physiology 2005;289(3):R871-R876

ALZET Comments: KN-93; PBS; CSF/CNS (caudate nucleus solitary tract); Rat; 3 days; Controls received mp w/ vehicle; dose-response (fig. 1); brain tissue distribution; multiple pumps per animal (2); animal info (male, Sprague-Dawley, 275-300 g); CaMKII antagonist; cannula placement verified by fluorescent labeling.

P7196: A. Ogawa, *et al.* Ca²⁺/calmodulin-protein kinase II alpha in the trigeminal subnucleus caudalis contributes to neuropathic pain following inferior alveolar nerve transection. Experimental Neurology 2005;192(2):310-319

ALZET Comments: KN-93; KN-92; DMSO; CSF/CNS (medulla); Rat; 2001; 7 days; Controls received mp w/ KN-92; enzyme inhibitor (calcium-calmodulin protein kinase II); peptides; cannula placement confirmed by dissection.

P6396: I. F. Benter, *et al.* Inhibition of Ras-GTPase, but not tyrosine kinases or Ca²⁺/calmodulin-dependent protein kinase II, improves recovery of cardiac function in the globally ischemic heart. MOLECULAR AND CELLULAR BIOCHEMISTRY 2004;259(1-2):35-42

ALZET Comments: FPT III; KN-93; Genistein; Saline; IP; Rat; 2ML1; 6 days; Controls received mp w/ vehicle; enzyme inhibitor (tyrosine kinase, CaMKII); cardiovascular; ischemia (cardiac).

P5307: L. Fang, *et al.* Calcium-calmodulin-dependent protein kinase II contributes to spinal cord central sensitization. J Neurosci 2002;22(10):4196-4204

ALZET Comments: KN-92; KN-93; CSF, artificial; CSF/CNS (intrathecal); Rat; Controls received mp w/ vehicle; enzyme inhibitor; KN-93 is a calcium/calmodulin-dependent protein kinase II inhibitor; 5-day recovery period.

11. Other

Q7137: K. Fujita, *et al.* Targeting Tyro3 ameliorates a model of PGRN-mutant FTLT-TDP via tau-mediated synaptic pathology. Nat Commun 2018;9(1):433



ALZET Comments: Gö6976; PBS; CSF/CNS (intrathecal); Mouse; 2006; 2 weeks; 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); enzyme inhibitor (PKC inhibitor); gene therapy;

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)

ALZET Comments: 8-Br-cAMP; H-89; CSF/CNS (basolateral amygdala); Mice; 1002; 10 days; 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; H-89 is an enzyme inhibitor (protein kinase A); 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

ALZET Comments: Fluoroacetate, Propionamide ditri-; PEG 400, PBS; SC; Rat, mice; 1003D, 1007D; 1 day, 2 days; 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, Propionamide ditri- aka VA999272; enzyme inhibitor (PKA inhibitor); enzyme inhibitor (PKal inhibitor); 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

ALZET Comments: 8CPT; H-89; SC; Mice; 2004; 28 days; 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

ALZET Comments: PKGi; ODQ; Water, distilled, deionized; Kidney (cortex); Rat; 6 days; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 4 wks old); PKGi also known as cGMP protein kinase G inhibitor; enzyme inhibitor (protein kinase G); enzyme inhibitor (guanylyl cyclase); ODQ also known as 1H-[1, 2,4]oxadiazolo[4,3-a]quinoxalin-1-one; PE10 used; 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 Comparative Physiology* 2012;303(2):R236-R245

ALZET Comments: Staurosporine; CSF, artificial; ethanol; CSF/CNS; Rat; 2002; 2 weeks; Controls received mp w/ vehicle; animal info (5-6 wks old, male, Dahl S, Wistar); guide cannula used; 0.5% ethanol used; enzyme inhibitor (protein kinase).

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

ALZET Comments: TAT 47-57, beta IIV5-3, peptide; TAT 47-57, beta IV5-3, peptide; TAT 47-57, epsilon V1-2, peptide; TAT 47-57, carrier peptide; SC; Rat; 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).

Q1507: A. Giralt, *et al.* Increased PKA signaling disrupts recognition memory and spatial memory: role in Huntington's disease. *Human Molecular Genetics* 2011;20(21):4232-4247

ALZET Comments: cAMP, Rp-adenosine; PBS; CSF/CNS (hippocampus); Mice; 2004; Controls received mp w/ vehicle; animal info (WT, R6/2, 8 wks old); bilateral cannula used; enzyme inhibitor (protein kinase); bilateral infusion;

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

ALZET Comments: HA-1004; Water, sterile; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase); dependence; animal info (male, Sprague Dawley, 220-240 g.); HA-1004 is a protein kinase selective inhibitor; pumps primed for 5 hours.



P9217: G. B. Silva, *et al.* Angiotensin II-Dependent Hypertension Increases Na Transport-Related Oxygen Consumption by the Thick Ascending Limb. *Hypertension* 2008;52(6):1091-1098

ALZET Comments: Angiotensin II; dye, coomassie blue R250; G86976; tempol; SC; kidney (outer medulla); Rat; 1007D; 4, 7 days; Controls received mp w/ vehicle; tissue perfusion (kidney); functionality of mp verified by residual volume and dye infusion; enzyme inhibitor (PKC a/b); cardiovascular; antihypertensive; peptide; cyanoacrylate adhesive; animal info (Sprague Dawley, 7 wks old, 200-250 g.); catheter fenestrated in one side 10 mm from the tip.

P9143: J. W. Kim, *et al.* Centrosomal PKCbetall and pericentrin are critical for human prostate cancer growth and angiogenesis. *Cancer Research* 2008;68(16):6831-6839

ALZET Comments: TAT (47-57); IIV5-3, beta-; Saline; Mice (nude); 2001; 5 weeks; Controls received mp w/ vehicle or TAT (47-57); pumps replaced every 2 weeks; half-life (p. 6832) ~ 2 wks; enzyme inhibitor (PKC betall, protein kinase C); animal info (6 wks old, male).

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

ALZET Comments: TAT (47-57), dv1-1-; TAT (47-57); SC; Rat; 2ML2; 4-6 weeks; 6-7 days; 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).

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

ALZET Comments: HA-1004; Water, sterile; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A); cardiovascular; tolerance; dependence; animal info (male, Sprague-Dawley, 220-240g).

P8645: K. Adachi, *et al.* beta-Catenin signaling promotes proliferation of progenitor cells in the adult mouse subventricular zone. *Stem Cells* 2007;25(11):2827-2836

ALZET Comments: Ro3303544; Saline; CSF/CNS; Mice; 1007D; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase); animal info (adult, male, C57BL/6, 9 wks); GSK3-beta is a protein kinase.

P6503: R. Sivasankaran, *et al.* PKC mediates inhibitory effects of myelin and chondroitin sulfate proteoglycans on axonal regeneration. *Nature Neuroscience* 2004;7(3):261-268

ALZET Comments: GO-6976; Saline; CSF/CNS (intrathecal); Rat; 2002; 14 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase C).

P6428: E. Garcia-Galloway, *et al.* Glutamate excitotoxicity attenuates insulin-like growth factor-I prosurvival signaling. *MOLECULAR AND CELLULAR NEUROSCIENCE* 2003;24(4):1027-1037

ALZET Comments: Ro324032; Saline; CSF/CNS; Rat; 1007D; 7 days; Controls received mp w/ vehicle; enzyme inhibitor (PKC).

P5597: A. E. Fournier, *et al.* Rho kinase inhibition enhances axonal regeneration in the injured CNS. *Journal of Neuroscience* 2003;23(4):1416-1423

ALZET Comments: C3 Transferase; Glutathione S-transferase; Y-27632; PBS; CSF/CNS (intrathecal); Rat; 2002; 2-3 weeks; Enzyme inhibitor (protein kinase); peptides; spinal cord injury; Y-27632 is a Rho-associated kinase (ROCK) inhibitor.

P6128: L. Cancedda, *et al.* Patterned vision causes CRE-mediated gene expression in the visual cortex through PKA and ERK. *Journal of Neuroscience* 2003;23(18):7012-7020

ALZET Comments: U0126; Rp-8-cl-cAMPS; DMSO; CSF/CNS; Rat; mice (transgenic); 1007D; 7 days; Enzyme inhibitor (PKA and extracellular singal-regulated kinase); U0126 (ERK inhibitor) and Rp-8-cl-cAMPS (PKA inhibitor) were dissolved in 1% DMSO.



P5507: C. J. Beaver, *et al.* Orientation selectivity is reduced by monocular deprivation in combination with PKA inhibitors. *Journal of Neurophysiology* 2002;88(4):1933-1940

ALZET Comments: 8-chloroadenosine-3',5'-monophosphorothioate; PBS; CSF/CNS (visual cortex); Cat; 2001; 6 days; ALZET brain infusion kit used; enzyme inhibitor (protein kinase A).

P7426: C. J. Beaver, *et al.* Cyclic AMP-dependent protein kinase mediates ocular dominance shifts in cat visual cortex. *Nat. Neurosci* 2001;4(2):159-163

ALZET Comments: Rp-8-CL-cAMPS; Phosphate buffer; CSF/CNS (visual cortex); Cat (kitten); 6,14 days; Controls received mp w/ vehicle; enzyme inhibitor (protein kinase); ALZET brain infusion kit 3; post op. care (antibiotic/analgesic); animal info (25-31 days old, 15 weeks old); cannula was beveled.

12. PD98059

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)

ALZET Comments: PD98059; DMSO, Saline; Csf/cns (intracisternal); Rat; 2001; 7 days; 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)

ALZET Comments: PD-98059; CSF, artificial; CSF/CNS; Rat; 2006; 6 weeks; 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)

ALZET Comments: PD98059; SB203580; SP600125; CSF, artificial; DMSO; CSF/CNS; Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, adult, 275-325g); 5% DMSO used; cardiovascular;.

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

ALZET Comments: PD98059; DMSO, Ringer's solution; SC; Rat; 2004; 28 days; Controls underwent median nerve CCI or sham operation; functionality of mp verified by residual volume; ALZET brain infusion kit used; <1% DMSO ; behavioral testing; Compound AKA: 2-amino-3-methoxyflavone; Therapeutic indication (Neuropathic pain); 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)

ALZET Comments: PD98059; CSF/CNS (intrathecal); Rat; 2001; 7 days; 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;.

Q3151: R. Sharma, *et al.* Hyperactive Ras/MAPK signaling is critical for tibial nonunion fracture in neurofibromin-deficient mice. *Human Molecular Genetics* 2013;22(23):4818-4828

ALZET Comments: PD-98059; PBS; SC; Mice (transgenic); 1007D; 28 days; Controls received mp w/ vehicle; animal info (Col2.3Cre;Nfl flox/- and PreiCre;Nfl flox/-); PD98059 is a MEK inhibitor. Possible mistake - written that pumps released over 28 days at 0.25 ul/hr and used pump model 1007D.



Q2483: M. G. Liu, *et al.* Metabotropic glutamate receptor 5 contributes to inflammatory tongue pain via extracellular signal-regulated kinase signaling in the trigeminal spinal subnucleus caudalis and upper cervical spinal cord. *Journal of Neuroinflammation* 2012;9(;):U1-U16

ALZET Comments: PD-98059; MPEP; DMSO; saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; Animal info (Sprague Dawley, male, adult, 200-250 g); MPEP also known as 2-methyl-6-(phenylethynyl)-pyridine; PE45 tubing used; enzyme inhibitor (mitogen-activated protein kinase, MAPK); functionality of mp verified via residual drug levels.

Q1465: T. Tsujimura, *et al.* Organization of pERK-immunoreactive cells in trigeminal spinal nucleus caudalis, upper cervical cord, NTS and Pa5 following capsaicin injection into masticatory and swallowing-related muscles in rats. *Brain Research* 2011;1417(;):45-54

ALZET Comments: PD-98059; DMSO; saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (Sprague-Dawley, male, 250-350 g); enzyme inhibitor (MEK, MAPK kinase); microsilicon tubing used; 10% DMSO used.

Q1214: F. Ljuca, *et al.* Contribution of Ras farnesyl transferase, MAP kinase and cytochrome P-450 metabolites to endothelin-1 induced hypertension. *Bosnian Journal of Basic Medical Sciences* 2011;11(2):84-86

ALZET Comments: Endothelin 1; FPT III; PD-98059; baicalein; ODYA, 17-; IV (jugular); Rat; 9 days; Controls received no pump; animal info (male, Sprague Dawley); peptides; enzyme inhibitor (Ras farnesyl transferase, MAP kinase, COX); 17-ODYA is a CYP450 inhibitor; PE-60 tubing used.

Q0832: A. Kobayashi, *et al.* Mechanisms involved in extraterritorial facial pain following cervical spinal nerve injury in rats. *Molecular Pain* 2011;7(;):U1-U11

ALZET Comments: PD-98059; fluoroacetate; DMSO; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (adult, male, Sprague Dawley, 200-300 g); enzyme inhibitor (mitogen-activated protein kinase, MEK 1/2); 10% DMSO used.

Q1045: E. Dupont, *et al.* ERK Is Involved in the Reorganization of Somatosensory Cortical Maps in Adult Rats Submitted to Hindlimb Unloading. *PLoS One* 2011;6(3):U392-U400

ALZET Comments: PD-98059; CSF/CNS (cortex); Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (adult, male, Wistar, 280-320 g); enzyme inhibitor (extracellular-signal-regulated kinase 1/2, ERK 1/2); post op. care (butadiene).

Q1592: L. B. Romo, *et al.* VEGF protects spinal motor neurons against chronic excitotoxic degeneration in vivo by activation of PI3-K pathway and inhibition of p38MAPK. *Journal of Neurochemistry* 2010;115(5):1090-1101

ALZET Comments: Isoxazolepropionate, alpha amino-3-hydroxy-5-; vascular endothelial growth factor, recomb., 164; SU14980, tyrphostin; LY294002; wortmannin; PD-98059; SB203580; neurodegenerative (amyotrophic lateral sclerosis); PBS; DMSO; CSF/CNS (intrathecal, spinal cord); Rat; 2004; 2, 10, 20 days; Controls received mp w/ vehicle; animal info (Wistar, male, 270-290 g, adult); alpha amino-3-hydroxy-5-isoxazolepropionate also known as AMPA; wound clips used; post op. care, pg 1091 (penicillin); good methods, pg 1091; multiple pumps used (2); multiple intrathecal catheters used; wound clips used; 2% DMSO used; enzyme inhibitor (p38 mitogen-activated protein kinase, p38MAPK).

Q0395: K. Adachi, *et al.* Purinergic receptors are involved in tooth-pulp evoked nocifensive behavior and brainstem neuronal activity. *Molecular Pain* 2010;6(;):U1-U11

ALZET Comments: PD-98059; DMSO; CSF/CNS (intrathecal); Rat; 1 week; Animal info (male, Sprague Dawley, adult, 300-360 g); enzyme inhibitor (mitogen-activated extracellular signal-regulated kinase, MEK); 10% DMSO used.

13. Ruxolitinib

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

ALZET Comments: Ruxolitinib; Mice; 7 days; 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

ALZET Comments: Ruxolitinib; PEG 300; SC; Mice; 2 weeks; Dose (50 mg/kg/d); Controls received mp w/ vehicle; enzyme inhibitor (JAK1/2 inhibitor); cancer (Hodgkin's lymphoma);

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

ALZET Comments: Ruxolitinib; Dimethylacetamide; propylene glycol; SC; Mice; 4 weeks; Control animals received mp w/ vehicle; animal info (BCR-JAK2); enzyme inhibitor (JAK2, janus kinase 2); cancer; chemotherapeutic; 40% DMA used; 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

ALZET Comments: Ruxolitinib; Dimethylacetamide; propylene glycol; SC; Mice (NSG); 3-4 weeks; 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;

14. 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

ALZET Comments: Sorafenib; sunitinib; DMSO; saline; IP; 1003D; 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

ALZET Comments: Sorafenib; DMSO; IP; Mice; 1003D; 48 hours; 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."; good methods, pg 226 "In the intraperitoneal infusion studies, the apparent plasma clearance (CL_{app}) was calculated by using the equation, $CL_{app} = k(0)/C_{ss}$, where, $k(0)$ is the rate of infusion into the peritoneal cavity normalized to body weight (ng/h/kg), and C_{ss} is the plasma concentration at steady state (ng/ml)."; enzyme inhibitor (biaryl-urea RAF kinase, tyrosine kinase); cancer (glioma); chemotherapeutic.

15. 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)

ALZET Comments: SU6656; SC; Mice; 17 days; Animal info (AGT KO, 8-10 weeks old); cardiovascular; SU6656 is a selective Src family kinase inhibitor;

16. 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)



ALZET Comments: Sunitinib malate; DMSO; CSF/CNS (intrathecal); Mice; 1002; 2 weeks; 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

ALZET Comments: Sunitinib; DMSO; IP; Mice (transgenic); mice (knockout); 1003D; 48 hours; 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

ALZET Comments: Sorafenib; sunitinib; DMSO; saline; IP; 1003D; 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.

17. TAT(47-57)

Q7189: A. U. Joshi, *et al.* Inhibition of Drp1/Fis1 interaction slows progression of amyotrophic lateral sclerosis. *EMBO Mol Med* 2018;10(3):

ALZET Comments: P110-TAT (47-57); SC; Mice; 28 day pump; 60 days; 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: (see pg. 14); .

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

ALZET Comments: P110-TAT (47-57); SC; Mice; 1 week, 8 weeks; 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

ALZET Comments: TAT 47-57, beta IIV5-3, peptide; TAT 47-57, beta IV5-3, peptide; TAT 47-57, epsilon V1-2, peptide; TAT 47-57, carrier peptide; SC; Rat; 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

ALZET Comments: TAT 47-57, peptide; TAT; TAT 47-57, delta conjugated, peptide; SC; Rat; 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

ALZET Comments: RACK7, psi epsilon; V1–2,10, epsilon; TAT (47-57); SC; Rat; 4, 6 weeks; 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



ALZET Comments: TAT (47-57); IIV5-3, beta-; Saline; Mice (nude); 2001; 5 weeks; Controls received mp w/ vehicle or TAT (47-57); pumps replaced every 2 weeks; half-life (p. 6832) ~ 2 wks; enzyme inhibitor (PKC beta1, 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

ALZET Comments: Peptide, TAT (47-57); peptide TAT (47-57)-EV1-2; Saline, sterile; SC; Mice; 1002; 4 weeks; 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); heterotopic cardiac transplantation.

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)

ALZET Comments: TAT (47-57), dv1-1-; TAT (47-57); SC; Rat; 2ML2; 4-6 weeks; 6-7 days; 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).

18. Trametinib

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)

ALZET Comments: GSK2126458; trametinib, dabrafenib; DMSO; IP; Mice; 48 hours; 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)

ALZET Comments: Trametinib; DMSO; IP; Mice; 48 hours; 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 inhibitor(mitogen-activated protein kinase kinase-1 (MEK)-1/2 inhibitor); good methods (p. 1294).

19. 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

ALZET Comments: Vemurafenib; DMSO; propylene glycol; saline; IP; Mice; 48 hours; 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.