



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
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); 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
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

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).

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).

6. Fasudil

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); Fasudil aka selective ROCK inhibitor; enzyme inhibitor (Rho kinase inhibitor); neurodegenerative (Traumatic Brain Injury);

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, 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)

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);



7. H89

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-SCHMIEDEBERG 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).

9. Imatinib

Q8295: 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):46

Agents: PKC inhibitor, Imatinib, or both **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days; **ALZET Comments:** Dose (PKC inhibitor- 0.5 mM, Imatinib-1 mM); Controls received mp w/ vehicle; gene therapy;

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 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

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); 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. 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); 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)

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);

10. KN92 or KN93

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); Bisindolylmaleimide aka BIM; 3-chloroacetyl-indole aka 3CAI; U0126 aka ERK1/2 inhibitor; KN-93 aka CaMKII inhibitor; PJ-34



aka PARP inhibitor VIII; SC79 aka AKT activator; ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; -3.5 mm depth); neurodegenerative (Epilepsy);

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.

11. Other

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; enzyme 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); "

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 Bisindolymaleimide 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); 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)

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; 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

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, Propionamide ditri- aka VA999272; enzyme inhibitor (PKal inhibitor); enzyme inhibitor (PKal inhibitor); Resultant plasma level (pg 2394);

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)

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:** 4 weeks;

ALZET Comments: 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

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; 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)

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;

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 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: (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

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; TAT 47-57, beta IV5-3, peptide; TAT 47-57, epsilon V1-2, peptide; TAT 47-57, carrier peptide **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 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; **Pump:** Not Stated; **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

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.