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;


ALZET Comments: Calphostin C; chelerythrine; SC; Rat; 7 days; Animal info (Sprague Dawley, male, 220 -240 g); enzyme inhibitor (PKC, protein kinase C).


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).


ALZET Comments: HA-1004; calphostin C; Water; DMSO; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 220-240 g); enzyme inhibitor (PKA, PKC); 0.6% DMSO used.


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


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).


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.


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).
2. Cediranib


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


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).


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


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.


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).


ALZET Comments: Calphostin C; chelerythrine; SC; Rat; 7 days; Animal info (Sprague Dawley, male, 220-240 g); enzyme inhibitor (PKC, protein kinase C).


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).


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.


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

5. Dasatinib


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).


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 (CS7BL/6, female, 12 mo old); ALZET brain infusion kit used; neurodegenerative (Alzheimer's disease); peptide; enzyme inhibitor (tyrosine kinase).


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).


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


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


ALZET Comments: Y-27632; dimethylfasudil; DMSO; saline; IP; Mice; Controls received mp w/ vehicle; animal info (CS7BL6J, adult); pumps replaced every 4 weeks; behavioral testing (static rod test); enzyme inhibitor (Rho-associated protein kinase; ROCK).


ALZET Comments: Fasudil; Rat; 28 days; Animal info (EAN); neurodegenerative (Guillain-Barr syndrome).


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).


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.
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).

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).

ALZET Comments: Fasudil; Saline; SC; Rat; 2ML4; Controls received mp w/ vehicle; animal info (8-10 wks old, Wistar Han, 200-225 g).

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).

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.

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.

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.

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

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.

**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).


**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).


**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;


**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.


**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.

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).


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.


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


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).


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.


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).


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).


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);

ALZET Comments: Imatinib mesylate; Mice; 5 weeks; Controls received mp w/ vehicle; animal info (SHT-2b -/-, adult, 7-9 wks old); imatinib mesylate also known as Gleevec or STI-571; hypoxia; enzyme inhibitor (tyrosine kinase).

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-71; enzyme inhibitor (tyrosine kinase, Src Abl).

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).

ALZET Comments: Imatinib mesylate; PBS; SC; Mice (nude); 2001; 1,3,4,5,7 days; Controls received mp w/ vehicle; dose-response (fig 2); no stress (see pg. 663); 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.

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).

ALZET Comments: Imatinib mesylate; hydroxyurea; Saline; DMSO; CSF/CNS (Intrathecal); Guinea pig (albino); 2001; 7 days; Controls received mp w/ vehicle; 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.

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.

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).


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).


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).


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.


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 Ca^{2+}/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).


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

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.


ALZET Comments: 8-Br-cAMP; H-89; CSF/CNS (basolateral amygdala); Mice; 2002; 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.


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).


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).


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.


ALZET Comments: Stauorosporine; 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).
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.

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 betaII, protein kinase C); animal info (6 wks old, male).

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).

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).

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.

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.

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.

**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).


**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


**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).


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


**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).


**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.


**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 an MEK inhibitor. Possible mistake - written that pumps released over 28 days at 0.25 ul/hr and used pump model 1007D.

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.


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.


ALZET Comments: Endothelin 1; FPT III; PD-98059; baicalein; ODYA; 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.


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.


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).


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).


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


ALZET Comments: Ruxolitinib; Mice; 7 days; Dose (50 mg/kg/d); cancer (lymphoma).
**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).

**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;

**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

**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.

**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 (Clapp) was calculated by using the equation, Clapp = k0/Css, where, k0 is the rate of infusion into the peritoneal cavity normalized to body weight (ng/h/kg), and Css 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

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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;


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);


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)


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);


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);


ALZET Comments: TAT 47-57, beta IV5-3, peptide; TAT 47-57, delta conjugated, peptide; SC; Rat; Controls received mp w/ control peptide; animal info (DS, 11-15 wks old, male); peptides.

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 47-57, delta conjugated, peptide; SC; Rat; Controls received mp w/ control peptide; animal info (DS, 11-15 wks old, male); peptides.


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.

**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 betaII, protein kinase C); animal info (6 wks old, male).


**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**


**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, Mdr1a/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**


**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.