Recent References (2016-2020) on Cerebral Ischemia Research
Using ALZET® Osmotic Pumps

Q8343: N. Bai*, et al.* G-protein-coupled estrogen receptor activation upregulates interleukin-1 receptor antagonist in the hippocampus after global cerebral ischemia: implications for neuronal self-defense. J Neuroinflammation 2020;17(1):45
Agents: G1; G36; Oligodeoxynucleotide, IL1RA antisense; Scrambled Missense **Vehicle:** DMSO; Saline; **Route:** SC; CNS/CSF (left lateral ventricle); **Species:** Rat; **Pump:** 2004; 2002; 2001; **Duration:** 14 days;
ALZET Comments: Dose (10 ug/day; 10 nmol/day); 1% DMSO, 0.9% saline used; Controls received mp w/ vehicle; animal info (Adult female Sprague-Dawley rats); G1 aka GPER agonist; G36 aka GPER antagonist; ALZET brain infusion kit Lot no 10331-14 used; Brain coordinates (anteroposterior, 0.8 mm; lateral, 1.5 mm; depth, 3.5 mm; from bregma); ischemia (GPER neuroprotective effects);

Q7677: R. Wang*, et al.* Photobiomodulation for Global Cerebral Ischemia: Targeting Mitochondrial Dynamics and Functions. Mol Neurobiol 2019;56(3):1852-1869
Agents: Mdivi-1 **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** 1003D; **Duration:** Not Stated;
ALZET Comments: Dose (1 mg/kg/day); Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats 250–300 g); behavioral testing (Bames Maze Task, Morris Water Maze Test); enzyme inhibitor (selective inhibitor of mitochondrial fission protein Drp1);

Q4964: S. Bake*, et al.* Insulin-like Growth Factor (IGF)-1 treatment stabilizes the microvascular cytoskeleton under ischemic conditions. Experimental Neurology 2019;311(162-172
Agents: Insulin-like growth factor-I, recomb. Human; JB-1 **Vehicle:** CSF, artificial; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1003D; 1007D; **Duration:** 1 day; 5 days;
ALZET Comments: Dose (100 µg/ml rhIGF-1; 20 µg/ml JB-1); Controls received mp w/ vehicle; animal info (Female Sprague Dawley rats; 10–12 months; weight range 325–350 g); JB-1 is an IGFR inhibitor; Brain coordinates (– 1.0mm posterior to bregma,−1.4mm medial lateral, −3.5mm from dural surface); cyanoacrylate adhesive; ischemia (cerebral);

Q7313: F. Turcato*, et al.* Sequential combined Treatment of Pifithrin-alpha and Posiphen Enhances Neurogenesis and Functional Recovery After Stroke. Cell Transplantation 2018;27(4):607-621
Agents: Phenserine, (+)-; Pifithrin-a **Vehicle:** Saline, physiological; DMSO; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (25 mg/kg/day (+)-Phenserine); (2 mg/kg/day PFT-a); 10% DMSO in saline for PFT-a; Controls received mp w/ vehicle; animal info (male, 10–12-week-old, C57/BL6); behavioral testing (Accuscan activity monitor, novel object recognition); (+)-phenserine aka Posiphen; ischemia (cerebral); Therapeutic indication (stroke);

Q7876: K. Y. Tseng*, et al.* MANF Promotes Differentiation and Migration of Neural Progenitor Cells with Potential Neural Regenerative Effects in Stroke. Mol Ther 2018;26(1):238-255
Agents: neurotrophic factor, recombinant human glial cell line-derived; neurotrophic factor, mesencephalic astrocyte-derived **Vehicle:** PBS; **Route:** CSF/CNS (Lateral ventricle); **Species:** Rat; **Pump:** 2002; **Duration:** 13 days;
ALZET Comments: Dose ((GDNF 0.25 µg/µL at 12 µL/day), (MANF 0.25 µg/µL at 12 µL/day)); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 220-260g); GDNF promotes differentiation and tangential migration of cortical GABAergic neurons during brain development. MANF is a non-classical neurotrophic factor that resides in the endoplasmic reticulum; Brain coordinates (A/P 0.5; L/M +1.9; D/V 2.5); Cannula placement verified via sterotaxic frame; ischemia (Cerebral ischemia); pumps were implanted from day 3 to day 16 of experiment before being removed.; Therapeutic indication (the neuroregenerative potential of MANF via promoting neuroblast recruitment to the lesioned cortex in stroke rats);

Q7244: R. Thakkar*, et al.* 17beta-Estradiol Regulates Microglia Activation and Polarization in the Hippocampus Following Global Cerebral Ischemia. Oxid Med Cell Longev 2018;2018(4248526
Agents: Estradiol, 17b **Vehicle:** Cyclodextrin, B-; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Dose (0.0167 mg); 20% β-cyclodextrin used; animal info (3 month old, female, Sprague Dawley); ischemia (Cerebral);

Q7249: L. Nusrat*, et al.* Cyclosporin A-Mediated Activation of Endogenous Neural Precursor Cells Promotes Cognitive Recovery in a Mouse Model of Stroke. Front Aging Neurosci 2018;10(93
Agents: Cyclosporin A **Vehicle:** Ethanol, Cremaphor; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4-49 days;
ALZET Comments: Dose (15 mg/kg/day); ; animal info (adult male C57BL/6 mice 6–8 weeks of age; 20–25 g); pumps replaced; ischemia (cerebral); 65% ethanol and 35% cremaphor used

Q8096: W. Liu*, et al.* Oxidative stress-elicited YY1 potentiates antioxidative response via enhancement of NRF2-driven transcriptional activity: A potential neuronal defensive mechanism against ischemia/reperfusion cerebral injury. Biomed Pharmacother 2018;108(698-706
Agents: YY1-siRNA **Vehicle:** Not stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not stated; **Duration:** 4 days;
ALZET Comments: animal info (Male, C57B/6, 25-35 g); Brain coordinates (mediolateral=1.0 mm, anteroposterior=0.2 mm; dorsoventral=3.1 mm); ischemia (Cerebral);

Q8075: L. Li*, et al.* Combination Treatment with Methylene Blue and Hypothermia in Global Cerebral Ischemia. Mol Neurobiol 2018;55(3):2042-2055
Agents: Metheylene blue **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Dose (0.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 3 months old, 250-300 g); ischemia (Global Cerebral Ischemia);

Q7115: S. Y. Cheon*, et al.* Apoptosis Signal-regulating Kinase 1 Silencing on Astroglial Inflammasomes in an Experimental Model of Ischemic Stroke. Neuroscience 2018;390(218-230
Agents: RNA, small interfering (ASK1) **Vehicle:** siPORTNeoFX Transfection agent; **Route:** CSF/CNS (left lateral ventricle); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Dose (1 lL/h/ day); animal info (Adult,C57BL/6, male); enzyme inhibitor (apoptosis signal-regulating kinase 1); ALZET brain infusion kit used; ALZET brain infusion kit used; ischemia (Cerebral);

Q7098: M. Aleksandrowicz*, et al.* Effect of vasopressin-induced chronic hyponatremia on the regulation of the middle cerebral artery of the rat. Pflugers Arch 2018;470(7):1047-1054
Agents: Vasopressin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 3.5 days;
ALZET Comments: Dose (2.4 µg/24 h); animal info (Male Wistar rats weiging 250–300 g); ischemia (cerebral); cardiovascular; Minipumps used administer asopressin to induce prolonged hyponatremia;

Q6801: W. Xu*, et al.* Chloride Co-transporter NKCC1 Inhibitor Bumetanide Enhances Neurogenesis and Behavioral Recovery in Rats After Experimental Stroke. Mol Neurobiol 2017;54(4):2406-2414
Agents: Bumetanide **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2004; **Duration:** 21 days;
ALZET Comments: Dose (0.2 mg/kg/day); animal info (Adult male Wistar rats); enzyme inhibitor (selective Na+-K+-Cl−-co-transporter inhibitor,); ALZET brain infusion kit used; Brain coordinates (AP-0.9 mm, ML+ 1.9 mm); ischemia (cerebral);

Q6534: Y. C. Wang*, et al.* Post-acute delivery of memantine promotes post-ischemic neurological recovery, peri-infarct tissue remodeling, and contralesional brain plasticity. J Cereb Blood Flow Metab 2017;37(3):980-993
Agents: Memantine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Dose (4 or 20 mg/kg/d); animal info (8-12 week old C57BL6/j male mice weighing 23-28g); ischemia (cerebral); "…we decided to use a subcutaneous delivery strategy for memantine in this study using miniosmotic pumps, given that miniosmotic pumps allowed to achieve most stable plasma memantine levels " pg.981 ; Therapeutic indication (stroke);

Q6481: T. Shiromoto*, et al.* The Role of Endogenous Neurogenesis in Functional Recovery and Motor Map Reorganization Induced by Rehabilitative Therapy after Stroke in Rats. J Stroke Cerebrovasc Dis 2017;26(2):260-272
Agents: Cytosine-β-Darabinofuranoside **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2001;
Duration: 7 days;

ALZET Comments: 0.9% Saline used; Controls received mp w/ vehicle; Brain coordinates (1.6 mm lateral to the midline, .8 mm posterior to the bregma, and 4.0 mm deep); Therapeutic indication (cerebral ischemia);

Q6027: D. Desposito*, et al.* Neuroprotective effect of kinin B1 receptor activation in acute cerebral ischemia in diabetic mice. Sci Rep 2017;7(1):9410
Agents: Bradykinin B1 receptor agonist; Bradykinin B2 receptor agonist; **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57/BL6, 18weeks old); ischemia (cerebral); Compound AKA: SarLys[Hyp3, Igl5, DPhe8]desArg9-bradykinin and [Hyp(3),Thi(5),(N)Chg(7),Thi(8)]-bradykinin; Dose (720 nmol/kg/day and 240 nmol/Kg/day);

Q5509: N. Zhang*, et al.* MicroRNA-378 Alleviates Cerebral Ischemic Injury by Negatively Regulating Apoptosis Executioner Caspase-3. Int J Mol Sci 2016;17(9):
Agents: miR-378 **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1003D; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6J, 18-22g); ischemia (cerebral); pumps primed overnight at 37C; Brain coordinates (Bregma: - 2.2 mm, dorsoventral: 3 mm, lateral: 1 mm);

Q5508: F. Zhang*, et al.* In Vivo Targeted MR Imaging of Endogenous Neural Stem Cells in Ischemic Stroke. Molecules 2016;21(9):
Agents: Ara-C **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: animal info (C57BL6J, 8-10 weeks old, 20-25g); ischemia (cerebral);

Q5102: W. S. Xu*, et al.* Bumetanide promotes neural precursor cell regeneration and dendritic development in the hippocampal dentate gyrus in the chronic stage of cerebral ischemia. Neural Regen Res 2016;11(5):745-51
Agents: Bumetanide **Vehicle:** Water, sterile; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 21 days;
ALZET Comments: animal info (male, Wistar, 200-250g); ischemia (cerebral); behavioral testing (Morris water maze); pumps primed overnight in 37C saline; used dental cement; Dose (200 ug/kg/day); Brain coordinates (anteroposterior −0.9, mediolateral +1.5);

Q5099: J. Xing*, et al.* HIF-1alpha Activation Attenuates IL-6 and TNF-alpha Pathways in Hippocampus of Rats Following Transient Global Ischemia. Cellular Physiology and Biochemistry 2016;39(2):511-20
Agents: SC144; etanercept **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 24 hours;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 200-300g); ALZET brain infusion kit used; ischemia (cerebral); used polycarbonate tubing; SC144 is a gp130 inhibitor; Brain coordinates (3.7 mm posterior to the bregma, 4.1 mm lateral to the midline, and 3.5 mm under the dura);

Q5711: H. Xiao*, et al.* Effect of ephrin-B2 on the expressions of angiopoietin-1 and -2 after focal cerebral ischemia/reperfusion. Neural Regen Res 2016;11(11):1784-1789
Agents: Ephrin-B2-Fc, recombinant murine chimera **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: animal info (male, Sprague Dawley, 8-10 weeks old, ~280g); ischemia (cerebral); Brain coordinates;

Q5689: R. Thakkar*, et al.* NLRP3 Inflammasome Activation in the Brain after Global Cerebral Ischemia and Regulation by 17beta-Estradiol. Oxid Med Cell Longev 2016;2016(8309031
Agents: Estradiol, 17B- **Vehicle:** Cyclodextrin, B-; **Route:** SC; **Species:** Rat; Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: animal info (Rats female, Sprague Dawley, 3 months old, OVX; Mice C27BL/6 PELP1, young adult, OVX); 20% Cyclodextrin used; ischemia (cerebral); replacement therapy (estradiol infusion); immunology; Resultant plasma level (10-15 pg/mL);

Q5676: E. G. Sozmen*, et al.* Nogo receptor blockade overcomes remyelination failure after white matter stroke and stimulates functional recovery in aged mice. Proc Natl Acad Sci U S A 2016;113(52):E8453-E8462
Agents: Protein, NgR(OMNI)-Fc **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 28 days;

ALZET Comments: pumps replaced every 14 days; ischemia (cerebral); behavioral testing (pasta matrix task); Dose (0.77 mg/28 days);

Q6660: J. H. Seo*, et al.* In Situ Pluripotency Factor Expression Promotes Functional Recovery From Cerebral Ischemia. Mol Ther 2016;24(9):1538-49
Agents: Doxycycline **Vehicle:** PBS; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Dose ((12 ng/day or 1,200 ng/day); Controls received mp w/ vehicle; animal info (transgenic mice expressing Pou5f1 (Oct4), Sox2, Myc, and Klf4); Doxycycline aka DOX; ALZET brain infusion kit 3 used; Brain coordinates ((AP +0.3 mm from Bregma; ML −0.7 mm from Bregma; DV −2.0 mm from Dura); ischemia (cerebral); Therapeutic indication (Cerebral ischemia);

Q4880: E. H. Sanchez-Mendoza*, et al.* Implantation of Miniosmotic Pumps and Delivery of Tract Tracers to Study Brain Reorganization in Pathophysiological Conditions. Journal of Visualized Experiments 2016;107(1-9
Agents: Erythropoietin, recombinant human **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 30 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6); good methods (Jove Video; picture of pump and implantation pg. 4); ischemia (cerebral); post op. care (Carprofen 4 mg/kg); behavioral testing (rotarod test; hand grip strength); cyanoacrylate adhesive; “In this work we have shown the method of implantation of minipumps with a cannula connected to the skull in order to deliver the plasticity promoting protein rhEpo directly into the ventricle, thus circumventing the BBB.” pg 8; Cannula placement verified via histologic analysis "The are no evident severe tissue alterations based on Nissl staining as compared to the corresponding contralateral area";

Q6631: J. D. Nicholson*, et al.* SUR1-Associated Mechanisms Are Not Involved in Ischemic Optic Neuropathy 1 Day Post-Injury. PLoS One 2016;11(8):e0148855
Agents: Glibenclamide **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 day;
ALZET Comments: Dose (10 µg/kg); Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats); ischemia (cerebral);

Q5411: X. Liu*, et al.* Interleukin-4 Is Essential for Microglia/Macrophage M2 Polarization and Long-Term Recovery After Cerebral Ischemia. Stroke 2016;47(2):498-504
Agents: Interleukin-4 **Vehicle:** Saline; **Route:** CSF/CNS (ventricle); **Species:** Mice (knockout); **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57/BL6 mice; 8-10 weeks, 25-30 g); ischemia (cerebral; stroke model); behavioral testing (Rotarod, corner, foot fault, and Morris water maze tests); healing, recovery; learning, memory; Therapeutic indication (Cerebral ischemia); Dose (60 ng/day); Brain coordinates: −0.20 mm anterior and 1.00 mm lateral to bregma;

Q4852: C. Li*, et al.* Chronic nicotine exposure exacerbates transient focal cerebral ischemiainduced brain injury. J Appl. Physiol 2016;120(328-333
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague Dawley, 250-300g); ischemia (cerebral); “The subcutaneous osmotic minipump releases nicotine at a constant rate, which resulted in stable plasma nicotine and cotinine levels that match the chronic smokers. The doses of nicotine used in the present study have been reported to result in stable plasma nicotine levels corresponding reasonably well with plasma levels in habitual light (0.5–1 pack/day) and moderate (2 packs/day) smokers” pg 331; traumatic brain injury; Dose (2 or 4 mg/kg/day);