

Recent References (2015-Present) on Angiogenesis Research Using ALZET[®] Osmotic Pumps

Q10803: P. Xiao, *et al.* RTN4/Nogo-A-S1PR2 Negatively Regulates Angiogenesis and Secondary Neural Repair Through Enhancing Vascular Autophagy in the Thalamus After Cerebral Cortical Infarction. Autophagy 2022;18(11):2711-2730 **Agents:** RTN4-d20-Fc; Immunoglobulin G, recombinant **Vehicle:** PBS; PEG 300; **Route:** CSF/CNS (right lateral ventricle); **Species:** Rat; **Pump:** 1003D; **Duration:** 24 hours;

ALZET Comments: Dose: (40 µg/kg); 2% DMSO; 40% PEG300 vehicle used Controls received mp w/ vehicle; animal info: Sprague-Dawley (SD) rats weighting 90–110 g; Recombinant human IgG Fc aka (IgG Fc); Brain coordinates (into the right lateral ventricle under a stereotaxic apparatus (–1.0 mm anteroposterior, 1.4 mm mediolateral, –4.0 mm dorsoventral relative to the bregma); neurodegenerative (cerebral cortical infarction);

Q10876: C. Zhang, *et al.* Sirtuin 3 Deficiency Aggravates Angiotensin II-Induced Hypertensive Cardiac Injury by the Impairment of Lymphangiogenesis. Journal of cellular and Molecular Medicine 2021;25(16):7760-7771

Agents: Angiotensin II Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 days;

ALZET Comments: Dose: (1000 ng/kg per minute); Controls received mp w/ vehicle; animal info: Eight-week-old male mice; Blood pressure measured via: non-invasive tail-cuff; Angiotensin II aka (Ang II)cardiovascular;

Q10330: M. Sharma, *et al.* Decreased Cyclic Guanosine Monophosphate-Protein Kinase G Signaling Impairs Angiogenesis in a Lamb Model of Persistent Pulmonary Hypertension of the Newborn. American Journal of Respiratory Cell and Molecular Biology 2021;65(5):555-567

Agents: Sildenafil Vehicle: Saline; Route: SC; Species: Lamb; Pump: Not Stated; Duration: 6 days; ALZET Comments: Dose: (6 mg/day); Controls received mp w/ vehicle; animal info: Fetal lamb model of PPHN; Cardiovascular

Q9452: D. R. Seeger, *et al.* Cyclooxygenase inhibition attenuates brain angiogenesis and independently decreases mouse survival under hypoxia. Journal of Neurochemistry 2021;158(2):246-261

Agents: Ketoralac Vehicle: Saline; Route: SC; Species: Mice; Pump: 2002; Duration: 10 days;

ALZET Comments: Dose (0.64, 1.28, 6.4 mg/kg/hr); dose-response (); Controls received mp w/ vehicle; functionality of mp verified by ketorolac and prostaglandin levels in plasma and brain; hypoxia and normoxia

Q8506: B. Gomes de Almeida Schirmer, *et al.* The NO-donor MPC-1011 stimulates angiogenesis and arteriogenesis and improves hindlimb ischemia via a cGMP-dependent pathway involving VEGF and SDF-1alpha. Atherosclerosis 2020;304(30-38 **Agents:** MPC-1011; Cilostazol **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** Not stated; **ALZET Comments:** Dose (3.6 mg/day MPC-1011; 100 mg/kg/bi-daily Cilostazol); animal info (Four-week-old male Sprague-Dawley rats); MPC-1011 aka novel NO-donor; cardiovascular;

Q8469: A. Frisch, *et al.* Apelin Controls Angiogenesis-Dependent Glioblastoma Growth. International Journal of Molecular Sciences 2020;21(11):

Agents: Apelin-13 **Vehicle:** CSF, Artificial; **Route:** CSF/CSN; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days; **ALZET Comments:** Dose (30 μg); Controls received mp w/ vehicle; animal info (APLNKO mice); Apelin-13 aka APLN; ALZET brain infusion kit 3 used; Brain coordinates (1 mm anterior and 1.5 mm right to the bregma); cancer (Glioblastoma);

Q8459: S. Esteban, *et al.* Endothelial MT1-MMP targeting limits intussusceptive angiogenesis and colitis via TSP1/nitric oxide axis. EMBO Molecular Medicine 2020;12(2):e10862

Agents: GDGRGDACK Vehicle: Dextran, sulfate; Route: SC; Species: Mice; Pump: 1003D; Duration: 3 days; ALZET Comments: Dose (2.4 mg/mouse/day); 1% Dextran Sulfate used; animal info (C57BL/6 wild-type mice, 8-20 weeks old); peptides; gene therapy;



Q9124: Z. Y. Zhai, *et al.* Constraint-induced movement therapy enhances angiogenesis and neurogenesis after cerebral ischemia/reperfusion. Neural Regeneration Research 2019;14(10):1743-1754

Agents: NEP1-40 Vehicle: DMSO/Saline; Route: CSF/CNS; Species: Rat; Pump: 2ML4; Duration: 1, 3 weeks;

ALZET Comments: Dose (1 mg); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 8-10 weeks old, 280-320 g); behavioral testing (Beam Walking Test, Morris Water Maze Test); NEP1-40 aka Specific antagonist of the Nogo-66 receptor; ALZET brain infusion kit 2 used; Brain coordinates (anteroposterior -0.9 mm and mediolateral +2.0 mm); ischemia (Cerebral)

Q8836: S. Xing, *et al.* EphrinB2 activation enhances angiogenesis, reduces amyloid-b deposits and secondary damage in thalamus at the early stage after cortical infarction in hypertensive rats. Journal of Cerebral Blood Flow & Metabolism 2019;39(1776–1789

Agents: Ephrin B2-Fc, human recombinant; Fc-IgG, human recombinant Vehicle: PBS, Human Serum Albumin buffered; Route: CSF/CNS (lateral ventricle); Species: Rat; Pump: Not Stated; Duration: 3 days;

ALZET Comments: Dose ((EphB2-Fc 100 μl), (IgG-Fc 100 μl)); 0.01M phosphate-buffered saline (pH7.4) containing 0.1% human serum albumin used; Controls received sham surgery; animal info (male, Sprague-Dawley, 80-100g); post op. care (Body temperature of animals kept at 37+/-0.5C with a heating pad during recovery); behavioral testing (Adhesive removal test); Brain coordinates (1.0 mm anteroposterior, 1.4 mm lateral, 4.0 mm dorsoventral relative to bregma); Cannula placement verified via stereotaxic frame; ischemia (cerebral infarction); pump model not stated although flow rate listed as 100ul; Therapeutic indication (EphB2-Fc treatment significantly accelerated the sensory recovery compared with those in the IgG-Fc group. Activation of ephrinB2 can promote angiogenesis, decrease Abeta deposits and rescue the secondary neurodegeneration of thalamus after cerebral infarction.);

Q7604: S. Perveen, *et al.* MIF inhibition enhances pulmonary angiogenesis and lung development in congenital diaphragmatic hernia. Pediatr Res 2019;85(5):711-718

Agents: MIF inhibitor, Nitrofen Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 21 days; ALZET Comments: Dose (200 mg- Nitrofen, 1.8 mg/kg/day- MIF inhibitor); animal info (Adult,);

Q8258: Y. T. Lin, *et al.* Cordycepin Suppresses Endothelial Cell Proliferation, Migration, Angiogenesis, and Tumor Growth by Regulating Focal Adhesion Kinase and p53. Cancers (Basel) 2019;11(2):

Agents: Cordycepin **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 7 days; **ALZET Comments:** Dose (2.4 mg/kg/day); Controls received mp w/ vehicle; animal info (BALB/c,); dependence;

Q7343: X. Huang, *et al.* Resveratrol Promotes Diabetic Wound Healing via SIRT1-FOXO1-c-Myc Signaling Pathway-Mediated Angiogenesis. Front Pharmacol 2019;10(421

Agents: EX-527; 10068-F4 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: 4 weeks; ALZET Comments: Dose (EX-527 5 mg/kg/day, 10068-F4 30mg/kg/day); Controls received mp w/ vehicle; animal info (BKS.Cg-Dock7mC=CLeprdb=J mice, 8 weeks old); diabetes;

R0372: J. Hong, *et al.* Relaxin gene therapy: A promising new treatment option for various diseases with aberrant fibrosis or irregular angiogenesis. Mol Cell Endocrinol 2019;

Agents: Relaxin, human recomb. Vehicle: Not Stated; Route: SC; Species: Rat (pregnant); Pump: Not Stated; ALZET Comments: Dose (2000 ng/h); Resultant plasma level (RLX level close to 0.5 ng/mL); gene therapy;

Q7543: J. Zhou, *et al.* Lactate potentiates angiogenesis and neurogenesis in experimental intracerebral hemorrhage. Experimental & Molecular Medicine 2018;50(7):78

Agents: oxamate; L-lactate, Sodium Vehicle: CSF, Artifical; Saline, Sterile; Route: CSF/CNS (lateral ventricle); CSF/CNS (globus pallidus); Species: Rat; Pump: Not Stated; Duration: 2, 7, 14 days;

ALZET Comments: oxamate 7 or 14 days; L-lactate 2 or 7 days; Dose ((OXA 10, 25, 50 mM), (L-lactate 5, 10, 25 mM)); Controls received sham surgery and mp w/ vehicle; animal info (male, Sprague-Dawley, 220-250g); behavioral testing (modified neurological severity score); oxamate aka OXA is an LDH inhibitor; enzyme inhibitor (lactate dehydrogenase); ischemia (intracerebral hemorrhage); pump model not stated but flow rate was listed at 0.5 µL/h; Therapeutic indication (lactate may assist to facilitate angiogenesis and neurogenesis following ICH);



Q8989: L. Zhai, *et al.* Endogenous calcitonin gene-related peptide suppresses ischemic brain injuries and progression of cognitive decline. Journal of Hypertension 2018;36(4):876-891

Agents: Peptide, human alpha calcitonin gene-related Vehicle: Saline, Sterile Physiological; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 days;

ALZET Comments: Dose (1 µmol/l at 0.5µl/h); Controls received mp w/ vehicle; animal info (8 weeks, male, C57BL/6); CGRP is a 37-amino acid peptide produced as a consequence of alternative RNA processing of the calcitonin gene; ischemia (cerebral ischemia); only WT mice were used for mp experiments; Therapeutic indication (Calcitonin gene-related peptide administration promotes cerebral blood flow recovery, suppresses astrocyte activation and increases angiogenesis after cerebral ischemia);

Q7165: Yanru Zhao1, Mengwen Yan1,2,*, Chen Chen1,*, Wei Gong1,3, Zhongwei Yin1, Huaping, *et al.* MiR-124 aggravates failing hearts by suppressing CD151-facilitated angiogenesis in heart. Oncotarget 2018;9(18):14382-14396 **Agents:** Angiotensin II **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days; **ALZET Comments:** Dose (1.5 mg/kg/day); animal info (Male C57BL/6 mice (22–25 g));

Q8087: H. Lin, *et al.* Extracellular Lactate Dehydrogenase A Release From Damaged Neurons Drives Central Nervous System Angiogenesis. EBioMedicine 2018;27(71-85

Agents: CD31 antibody, LHDA **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week; **ALZET Comments:** Dose (0, 10, 100 ug/kg/day-LHDA,); Controls received mp w/ vehicle; animal info (C57BL/6J); Brain coordinates (0.2 mm posterior, 2.5 mm left, and 3 mm depth from the skull surface); bilateral cannula used;

Q7908: Z. C. Hesp, *et al.* Proliferating NG2-Cell-Dependent Angiogenesis and Scar Formation Alter Axon Growth and Functional Recovery After Spinal Cord Injury in Mice. J Neurosci 2018;38(6):1366-1382 **Agents:** Ganciclovir **Vehicle:** Saline, physiological; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1002; 1007D; **Duration:** 7, 11, 14 days; **ALZET Comments:**

Q6336: M. L. Zhu, *et al.* Berberine promotes ischemia-induced angiogenesis in mice heart via upregulation of microRNA-29b. Clinical and Experimental Hypertension 2017;39(7):672-679

Agents: miR-29b antagomir **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (8–12 week-old male C57BL6 mice); cardiovascular;

Q5725: S. Zhao, *et al.* Tetramethylpyrazine attenuates carbon tetrachloride-caused liver injury and fibrogenesis and reduces hepatic angiogenesis in rats. Biomedicine & Pharmacotherapy 2017;86(521-530

Agents: Angiotensin II Vehicle: Not Stated; Route: Not Stated; Species: Rat; Pump: 2004; 2ML4; Duration: 5 weeks; ALZET Comments: Controls received mp w/ saline; animal info (male, SD, 180-220g); cardiovascular; Dose (25 ug/kg/hr);

Q6470: A. L. Guan, *et al.* Role of Jagged1-Hey1 Signal in Angiotensin II-induced Impairment of Myocardial Angiogenesis. Chin Med J (Engl) 2017;130(3):328-333

Agents: Angiotensin II **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks; **ALZET Comments:** Dose (200 ng/kg/min); animal info (8-week-old male C57BL/6 mice); cardiovascular;

Q5811: L. Feng, *et al.* EphA4 may contribute to microvessel remodeling in the hippocampal CA1 and CA3 areas in a mouse model of temporal lobe epilepsy. Mol Med Rep 2017;15(1):37-46

Agents: unclustered ephrin A5 Fc, clustered (C) ephrin A5 Fc, antibody, IgG Vehicle: CSF, artificial; Route: CSF/CNS; Species: Mice; Pump: 1007D; Duration: Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6, 5-6 weeks old) ALZET brain infusion kit 3 used; no stress "All mice survived, and no apparent behavioral discomfort was observed. " (see pg. 41); Therapeutic indication (angiogenesis, Temporal lobe epilepsy); Dose (50 ug/mL);



Q6017: N. Clere, *et al.* Pro-Angiogenic Effects of Low Dose Ethoxidine in a Murine Model of Ischemic Hindlimb: Correlation between Ethoxidine Levels and Increased Activation of the Nitric Oxide Pathway. Molecules 2017;22(4):

Agents: Ethoxide, glucose Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: 2004; Duration: 21 days; ALZET Comments: animal info (8 weeks); 5% glucose; average plasma concentration between 18.34 and 46.97 nM ethoxidine; Therapeutic indication (ischemia; angiogenesis; neovascularization); Dose (0.14 ng/kg)

Q6321: S. C. Chen, *et al.* Administration of sonic hedgehog protein induces angiogenesis and has therapeutic effects after stroke in rats. Neuroscience 2017;352(285-295

Agents: Sonic hedgehog protein, Cyclopamine, antibody, anti-VEGF **Vehicle:** PBS; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (1 mg/mL Shh, 20 μM Shh plus Cyc, 25 μg/ml Shh plus VEGF antibody); animal info (Male Sprague–Dawley rats); Cyclopamine is a sonic hedgehog protein inhibitor; Brain coordinates (bregma -0.8 mm anteroposterior, ±1.5 mm mediolateral, and -4.5 mm dorsoventral);

Q5856: M. Goda, *et al.* Nerve growth factor facilitates perivascular innervation in neovasculatures of mice. J Pharmacol Sci 2016;131(4):251-8

Agents: Nerve Growth Factor Vehicle: Saline; Route: SC; IP; Species: Mice; Pump: 1003D, 1007D, 1002; Duration: 3 days, 7 days, 10 days, 14 days;

ALZET Comments: Controls received mp w/ vehicle; Therapeutic indication (Angiogenesis);

Q6037: Q. Duan. Deregulation of XBP1 expression contributes to myocardial vascular endothelial growth factor-A expression and angiogenesis during cardiac hypertrophy in vivo. Aging Cell 2016;

Agents: Isoproterenol hydrochloride Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: 1007D, 1002; Duration: 2 weeks;

ALZET Comments: Controls received sham surgery; animal info (C57BL/6, 8 weeks old); Therapeutic indication (ER stress, Heart failure); Dose (15 mg/kg/day);

Q5311: L. Chen, *et al.* 20-HETE contributes to ischemia-induced angiogenesis. Vascular Pharmacology 2016;83(57-65 **Agents:** DDMS; 6,15-20-HEDGE **Vehicle:** Not Stated; **Route:** Intramuscular (hindlimb gracilis); **Species:** Mice; **Pump:** 2002, 2004; **Duration:** 32 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Balb/c mice, 12 wk old); functionality of mp verified by blood pressure and blood perfusion scans; dose-response (pg. 61); good methods (pg. 58); ischemia (peripheral); tissue perfusion (intramuscular); Polyethylene catheter tubing used (inner ID 0.8 mm); Dose (5 mg/kg/day);

Q4886: Y. S. B. X. Q. W. T. L. Y. D. &, *et al.* The Ephrin-A5/EphA4 Interaction Modulates Neurogenesis and Angiogenesis by the p-Akt and p-ERK Pathways in a Mouse Model of TLE. MOLECULAR NEUROBIOLOGY 2016;53(561-576 **Agents:** Ephrin-A5-Fc; immunoglobulin G2A **Vehicle:** CSF, artificial; **Route:** CSF/CNS (hippocampus); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6, 18-21g, 5-6 weeks old); ALZET brain infusion kit used; no stress (see pg. 563) All mice survived the operation, remained active, ate well, and appeared to be well groomed."; behavioral testing (seizure frequency); Cannula placement verified via histological analysis; pumps primed in 37C PBS overnight; used dental acrylic;

Q4538: S. Morita, *et al.* Vascular endothelial growth factor-dependent angiogenesis and dynamic vascular plasticity in the sensory circumventricular organs of adult mouse brain. Cell and Tissue Research 2015;359(865-884 **Agents:** Ara-C **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2002; **Duration:** 10 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6J, adult, P70-P84); comparison of IP injection vs mp; cardiovascular; "This infusion method is effective for suppressing cell proliferation in the subventricular zone and minimizes surgery damage to brain tissues" pg 867;



Q4241: Y. Minami, *et al.* Prostaglandin 12 analog suppresses lung metastasis by recruiting pericytes in tumor angiogenesis. INTERNATIONAL JOURNAL OF ONCOLOGY 2015;46(548-554

Agents: Betaprost sodium **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 weeks; **ALZET Comments:** Controls received mp w/ water, distilled; animal info (female, C57BL6, 8-10 weeks old, 20-25g); cancer

Q5225: Y. Liu, *et al.* Angiotensin-(1-7) Suppresses Hepatocellular Carcinoma Growth and Angiogenesis via Complex Interactions of Angiotensin II Type 1 Receptor, Angiotensin II Type 2 Receptor and Mas Receptor. Mol Med 2015;21(626-36 **Agents:** Angiotensin (1-7), A-779, PD123319 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 21 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info: Male BALB/c mice (6–8 wks old); functionality of mp verified by measurement of tumor volumes; cancer (Hepatocellular Carcinoma); peptides; Dose: (200 ng/kg/min) Ang-(1–7), (800 ng/kg/min) Ang-(1–7), (800 ng/kg/min) A779, (10 mg/kg/day) PD123319

Q4501: J. Liu, *et al.* The effect of chronic stress on anti-angiogenesis of sunitinib in colorectal cancer models. PSYCHONEUROENDOCRINOLOGY 2015;52(130-142

Agents: Norepinephrine bitartrate hydrate; propranolol Vehicle: Ascorbic acid; PBS; Route: SC; Species: Mice; Pump: 1004; Duration: 20 days;

ALZET Comments: Animal info (female, BALB/c, 5-7 weeks old); cancer (colorectal carcinoma, human);

Q3977: Y. C. Lim, *et al.* Proinsulin C-Peptide Prevents Impaired Wound Healing by Activating Angiogenesis in Diabetes. Journal of Investigative Dermatology 2015;135(269-278

Agents: C-peptide Vehicle: PBS; Route: SC; Species: Mice; Pump: 2004; Duration: 2 weeks;

ALZET Comments: Controls received sham surgery; animal info (male, C57BL6J, 6 weeks old, streptozotocin induced diabetes); cardiovascular; peptides; diabetes;

Q4457: J. Z. Hu, *et al.* miR-126 promotes angiogenesis and attenuates inflammation after contusion spinal cord injury in rats. Brain Research 2015;1608(191-202

Agents: miR-126 Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 1003D; Duration: Not Stated; ALZET Comments: Controls received mp w/ control agomir; animal info (male, Sprague Dawley, 180-220g); spinal cord injury; post op. care (Ringer's solution administered IP 5 ml, penicillin G 40000 U IM QD for 3 days, bladders manually expressed BID); behavioral testing (locomotor testing, open field); immunology; pumps primed overnight at 37C

Q5034: T. Hongu, *et al.* Arf6 regulates tumour angiogenesis and growth through HGF-induced endothelial beta1 integrin recycling. Nat Commun 2015;6(7925

Agents: SecinH3 Vehicle: DMSO; glycerol; Route: SC; Species: Mice; Pump: 2001; Duration: 16 days; ALZET Comments: Controls received mp w/ vehicle; animal info (male, Arf6 flox/flox, 8 weeks old); pumps replaced every 4 days; 50% DMSO used; 50% glycerol; cancer (B16 melanoma or LLC); xenograft model;

Q4436: L. S. Gutierrez, et al. Thrombospondin peptide ABT-898 inhibits inflammation and angiogenesis in a colitis model. WORLD JOURNAL OF GASTROENTEROLOGY 2015;21(6157-6166

Agents: ABG-898 Vehicle: Glucose, sterile; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days; ALZET Comments: Controls received mp w/ vehicle; animal info (WT or TSP-1 -/-); 5% glucose used; cardiovascular; immunology; peptides;

Q4414: P. Escudero, *et al.* Combined treatment with bexarotene and rosuvastatin reduces angiotensin-II-induced abdominal aortic aneurysm in apoE(-/-) mice and angiogenesis. British Journal of Pharmacology 2015;172(2946-2960

Agents: Rosuvastatin, Angiotensin II **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 5 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (apoE -/-, 8 weeks old); cardiovascular; peptides; "Because the s.c. administration of the statin using an osmotic minipump allows 100% drug bioavailability and its p.o. administration results in 34.5% bioavailability in mice (Peng et al., 2009), we chose the former route to ensure a full dosage effect." pg 2948; comparison of mp vs. oral gavage