



References on the Administration of Endothelins Using ALZET® Osmotic Pumps

- Q7255:** I. Prada, *et al.* Glia-to-neuron transfer of miRNAs via extracellular vesicles: a new mechanism underlying inflammation-induced synaptic alterations. *Acta Neuropathol* 2018;135(4):529-550
ALZET Comments: Endothelin A antagonist aka BQ-123 and Endothelin B antagonist aka BQ-788;; Saline; CSF/CNS (Hippocampus CA1); Mice; 1007D; 4 days; Dose (M1-EV 1.5 µg/µl, M2-EV 0.5 µl/h); Controls received mp w/ vehicle; animal info (4-month-old C57BL6 male mice); Brain coordinates (anteroposterior: 1.8 mm relative to bregma; mediolateral: +1 mm; dorsoventral: 1.5 mm relative to the dura); neurodegenerative (Multiple sclerosis);.
- Q7254:** J. Polak, *et al.* Blockade of Endothelin-1 Receptor Type B Ameliorates Glucose Intolerance and Insulin Resistance in a Mouse Model of Obstructive Sleep Apnea. *Front Endocrinol (Lausanne)* 2018;9(280)
ALZET Comments: Endothelin-1 antagonist; Saline, PEG; SC; Mice; 1002; 14 days; Dose (ETA antagonist; 200 nmol/kg/day, ETB antagonist; 200 nmol/kg/day); Controls received mp w/ vehicle; animal info (Adult male C57BL6/J mice aged 6-8 weeks); Endothelin A antagonist aka BQ-123 and Endothelin B antagonist aka BQ-788;.
- Q5489:** P. J. Wermuth, *et al.* Stimulation of Transforming Growth Factor-beta1-Induced Endothelial-To-Mesenchymal Transition and Tissue Fibrosis by Endothelin-1 (ET-1): A Novel Profibrotic Effect of ET-1. *PLoS One* 2016;11(9):e0161988
ALZET Comments: Transforming growth factor-B1; endothelin-1; Saline; Mice; 3 weeks; Controls received mp w/ vehicle; animal info (FVB/N, 4 weeks old); used 28 day model pump;.
- Q3341:** T. R. Hammond, *et al.* Astrocyte-Derived Endothelin-1 Inhibits Remyelination through Notch Activation. *Neuron* 2014;81(3):588-602
ALZET Comments: Endothelin-1; PD142,893; DAPT; Jagged1 Fc, recombinant rat; Saline; CSF/CNS; Mice; 1007D; 1002; 2 days; 7 days; 8 days; 15 days; Controls received mp w/ vehicle; animal info (TNR, C57BL6N, 8-12 weeks old); ALZET brain infusion kit 3 used; cyanoacrylate adhesive; DAPT aka N-[(3,5-Difluorophenyl)acetyl]-L-alanyl-2-phenylglycine-1,1-dimethylethyl ester; DAPT is a gamma secretase inhibitor.
- Q2397:** M. A. Saleh, *et al.* Chronic endothelin-1 infusion elevates glomerular sieving coefficient and proximal tubular albumin reuptake in the rat. *LIFE SCIENCES* 2012;91(13-14):634-637
ALZET Comments: Endothelin-1; NaCl; SC; Rat; 2 weeks; Control animals received mp w/ vehicle; animal info (Munich-Wistar, male, 200-250 g);.
- Q1784:** F. Li, *et al.* eNOS Deficiency Acts through Endothelin to Aggravate sFlt-1-Induced Pre-Eclampsia-Like Phenotype. *Journal of the American Society of Nephrology* 2012;23(4):652-660
ALZET Comments: Preproendothelin-1; SC; Mice; 1002; Controls received mp w/ saline; animal info (wt, female, nonpregnant, 3-5 mo old).
- Q2547:** J. M. Kim, *et al.* Increased expression of oxyproteins in the optic nerve head of an in vivo model of optic nerve ischemia. *BMC Ophthalmology* 2012;12(;):U1-U6
ALZET Comments: Endothelin-1; CSF/CNS (optic nerve, perineural region); Rabbit; 2, 4, 8 weeks; Animal info (New Zealand, 2.5-3.5 kg); long-term study; PE tubing used.
- Q1214:** F. Ljuca, *et al.* Contribution of Ras farnesyl transferase, MAP kinase and cytochrome P-450 metabolites to endothelin-1 induced hypertension. *Bosnian Journal of Basic Medical Sciences* 2011;11(2):84-86
ALZET Comments: Endothelin 1; FPT III; PD-98059; baicalein; ODAYA, 17-; IV (jugular); Rat; 9 days; Controls received no pump; animal info (male, Sprague Dawley); peptides; enzyme inhibitor (Ras farnesyl transferase, MAP kinase, COX); 17-ODYA is a CYP450 inhibitor; PE-60 tubing used.
- Q0303:** C. J. Wang, *et al.* (-)-Epigallocatechin Gallate Inhibits Endothelin-1-Induced C-Reactive Protein Production in Vascular Smooth Muscle Cells. *BASIC & CLINICAL PHARMACOLOGY & TOXICOLOGY* 2010;107(2):669-675



ALZET Comments: Endothelin-1; SC; Rat; 2001; 7 days; Controls received mp w/ saline; animal info (Male, Sprague-Dawley, 250 g).

Q0739: M. A. Saleh, *et al.* Endothelin-1 Increases Glomerular Permeability and Inflammation Independent of Blood Pressure in the Rat. *Hypertension* 2010;56(5):942-U427

ALZET Comments: Endothelin-1; Saline; IV (jugular); Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 225-250 g); peptides.

Q0217: V. V. Lima, *et al.* O-GlcNAcylation Contributes to Augmented Vascular Reactivity Induced by Endothelin 1. *Hypertension* 2010;55(1):180-188

ALZET Comments: Endothelin-1; Sodium chloride; IV (jugular); Rat; 14 days; Controls received mp w/ sodium chloride; animal info (male, Wistar, 8-10 wks old, 230-250 g.); 0.9% sodium chloride used.

Q1439: Y. Koyama, *et al.* Intracerebroventricular Administration of an Endothelin ET(B)-Receptor Agonist Increases Expression of Matrix Metalloproteinase-2 and -9 in Rat Brain. *JOURNAL OF PHARMACOLOGICAL SCIENCES* 2010;114(4):433-443

ALZET Comments: Endothelin-1, ala-1, 3, 11, 15-; CSF, artificial; CSF/CNS; Rat; 2002; 7 days; Controls received mp w/ vehicle; animal info (male, Wistar, 250-300 g); artificial CSF recipe listed; ALZET brain infusion kit used; ala-1, 3, 11, 15-ET-1 is an ETB-receptor agonist.

Q0138: Y. Koyama, *et al.* Decreases in rat brain aquaporin-4 expression following intracerebroventricular administration of an endothelin ET_B receptor agonist. *Neuroscience Letters* 2010;469(3):343-347

ALZET Comments: Endothelin-1, ala-1, 3, 11, 15-; CSF, artificial; CSF/CNS; Rat; 2002; 3, 7 days; Controls received mp w/ vehicle; ALZET brain infusion kit used; animal info (male, Wistar, 250-300 g.).

Q0959: Z. Aktas, *et al.* Matrix metalloproteinase-9 expression in retinal ganglion cell layer and effect of topically applied brimonidine tartrate 0.2% therapy on this expression in an endothelin-1-induced optic nerve ischemia model. *International Ophthalmology* 2010;30(3):253-259

ALZET Comments: Endothelin-1, human, porcine; Eye (optic nerve); Rabbit; 2002; 2 weeks; Animal info (New Zealand, albino); vinyl tubing used; image of pump and tubing through the upper eyelid (Fig.1, Fig 2b);

P9573: X. Wang, *et al.* Increase in endothelin B receptor expression in optic nerve astrocytes in endothelin-1 induced chronic experimental optic neuropathy. *Experimental Eye Research* 2009;88(3):378-385

ALZET Comments: Endothelin-1; CSF/CNS (optic nerve); Rat; 2004; 28 days; Post op. care (buprenorphine); animal info (adult, male, Brown Norway, 250-300g); fellow eye served as untreated control; silastic tubing used; brain tissue distribution.

Q0277: C. J. Wang, *et al.* Endothelin-1 induces the expression of C-reactive protein in rat vascular smooth muscle cells. *Biochemical and Biophysical Research Communications* 2009;389(3):537-542

ALZET Comments: Endothelin-1; Saline; SC; Rat; 2001; 7 days; Controls received mp w/ saline; animal info (male, Sprague-Dawley, 250 g).

P8717: D. E. Brooks, *et al.* Blood flow velocity response of the ophthalmic artery and anterior optic nerve head capillaries to carbogen gas in the rhesus monkey model of optic nerve head ischemia. *VETERINARY OPHTHALMOLOGY* 2007;10(;):20-27

ALZET Comments: Endothelin-1; CSF/CNS (optic nerve); Monkey (Rhesus); 2004; 8 months; Controls received mp w/ vehicle; long-term study; pumps replaced every 4 weeks; peptides; animal info (young, male, Rhesus); glaucoma.

P7183: A. Migneault, *et al.* Chronically elevated endothelin levels reduce pulmonary vascular reactivity to nitric oxide. *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE* 2005;171(5):506-513

ALZET Comments: Endothelin-1; Water; IV (jugular); Rat; 7, 20 days; Controls received sham surgery; functionality of mp verified by plasma E7-1 levels; stability verified by 7 and 28 day incubation at 37 degrees celsius and HPLC; cardiovascular; peptides.



P7257: Y. Koyama, *et al.* Endothelin increases expression of exon III-and exon IV-containing brain-derived neurotrophic factor transcripts in cultured astrocytes and rat brain. *Journal of Neuroscience Research* 2005;80(6):809-816

ALZET Comments: Endothelin-1; Ala-1, 3, 11, 15-; CSF, artificial; CSF/CNS; Rat; 2002; 7 days; Controls received mp w/ vehicle; ALZET brain infusion kit used; peptides; endothelin B receptor agonist.

P7506: Y. Koyama, *et al.* Endothelins stimulate the expression of neurotrophin-3 in rat brain and rat cultured astrocytes. *Neuroscience* 2005;136(2):425-433

ALZET Comments: Endothelin-1, Ala-1, 3, 11, 15 -; CSF, artificial; CSF/CNS; Rat; 2002; 3, 7 days; Controls received mp w/ vehicle; animal info (male, Wistar, 250-300 g).

P6957: P. Beaucage, *et al.* Position of Src tyrosine kinases in the interaction between angiotensin II and endothelin in in vivo vascular protein synthesis. *Journal of Hypertension* 2005;23(2):329-335

ALZET Comments: Angiotensin II; endothelin; SC; Rat; 1003D; 26 hours; Cardiovascular; peptides.

P7010: L. Yao, *et al.* Olmesartan improves endothelin-induced hypertension and oxidative stress in rats. *HYPERTENSION RESEARCH* 2004;27(7):493-500

ALZET Comments: Endothelin-1; Saline; IV (jugular); Rat; 2ML2; 14 days; Controls received mp w/ vehicle; cardiovascular; peptides.

P6995: Y. P. Wang, *et al.* Prevention of endothelin-1-induced increases in blood pressure: role of endogenous CGRP. *American Journal of Physiology-Heart and Circulatory Physiology* 2004;287(4):H1868-H1874

ALZET Comments: Endothelin-1; Saline, normal; IV (external jugular); Rat; 2001; 7 days; Controls received mp w/ vehicle; functionality of mp verified by confirming mp was empty and correct catheter position; cardiovascular; peptides.

P6670: B. Luo, *et al.* ET-1 and TNF-alpha in HPS: analysis in prehepatic portal hypertension and biliary and nonbiliary cirrhosis in rats. *American Journal of Physiology-Gastrointestinal and Liver Physiology* 2004;286(2):G294-G303

ALZET Comments: Endothelin-1; Saline; IV (femoral); Rat; 2002; 2 weeks; Controls received mp w/ vehicle; ET-1 plasma levels taken.

P6550: B. C. Chauhan, *et al.* Model of endothelin-1 - Induced chronic optic neuropathy in rat. *INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE* 2004;45(1):144-152

ALZET Comments: Endothelin-1; Balanced salt solution; Eye (retrobulbar optic nerve); Rat; 2004; 21,42,84 days; Controls received mp w/ vehicle and fellow eye w/ no treatment; dose-response (fig.5); long-term study; pumps replaced every 28 days; peptides; post op. care (rentamicin, buprenex).

P6541: D. E. Brooks, *et al.* Functional and structural analysis of the visual system in the rhesus monkey model of optic nerve head ischemia. *INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE* 2004;45(6):1830-1840

ALZET Comments: Endothelin; Saline; acetic acid; CSF/CNS (optic nerve); Monkey; 18 months; Controls received mp w/ vehicle; long-term study; pumps replaced every 6 weeks; no stress (see pg. 1833); peptides; "The osmotic minipumps were well tolerated by the monkeys for the length (1.5 years) of the experiment." The long exposure time was used to "mimic more closely the prolonged human glaucomatous condition." p. 1838; pump model not listed; ischemia.

P5771: L. Smith, *et al.* Endothelin-induced increases in Ca²⁺ entry mechanisms of vascular contraction are enhanced during high-salt diet. *Hypertension* 2003;41(3):787-793

ALZET Comments: Endothelin-1; IV; Rat; 5 days; Controls received mp w/ saline.

P6059: M. H. Sedeek, *et al.* Role of reactive oxygen species in endothelin-induced hypertension. *Hypertension* 2003;42(4):806-810

ALZET Comments: Endothelin-1; tempol; IV (jugular); Rat; 2002; 9 days; Peptides.



P5747: S. D. Rogers, *et al.* Endothelin B receptors are expressed by astrocytes and regulate astrocyte hypertrophy in the normal and injured CNS. *Glia* 2003;41(2):180-190

ALZET Comments: Endothelin-1; Bosentan; Dye, Evans blue; CSF, artificial; CSF/CNS (optic nerve); Rabbit; 2ML2; 14 days; Controls received mp w/ vehicle; functionality of mp verified by Evans Blue Dye; good methods p.182, 181; antihypertensive; Bosentan (commercial drug name is tracleer) is an endothelin receptor antagonist (ERA); Vialon catheter with holes used; pump/catheter schematic (p.182); pump is described as advantageous for optic nerve infusion (p.182).

P5690: B. Luo, *et al.* Increased pulmonary vascular endothelin B receptor expression and responsiveness to endothelin-1 in cirrhotic and portal hypertensive rats: a potential mechanism in experimental hepatopulmonary syndrome. *Journal of Hepatology* 2003;38(5):556-563

ALZET Comments: Endothelin-1; IV (femoral); Rat; 2002; 2 weeks; Functionality of mp verified by pump assessment; 2-week stability verified by previous studies by other groups; ET-1 plasma levels measured.

P5147: B. R. Brehm, *et al.* Modulation of the beta-adrenergic receptor system of vascular smooth muscle cells in vitro and in vivo by chronically elevated endothelin-1 levels. *Biochemical Pharmacology* 2002;63(1361-1369)

ALZET Comments: Endothelin-1; Saline; IV (superior vena cava); Rat; 2ML4; 3 weeks; controls received mp w/ vehicle; functionality of mp verified by ET-1 levels; cardiovascular; peptides.

P5051: Y. M. Ahn, *et al.* Sustained arterial narrowing after prolonged exposure to perivascular endothelin. *Neurosurgery* 2002;50(843-848)

ALZET Comments: Endothelin-1; Saline; Perivascular (femoral artery adventitia); Rat; 3 or 5 days; controls received mp w/ vehicle; tissue perfusion (adventitia); cardiovascular; peptides; ET-1 is a vasoconstrictor peptide; Arteries perfused via a custom silastic artery cuff attached to catheter tube; pump placed sc.

P4878: M. Iglarz, *et al.* Chronic blockade of endothelin receptors improves ischemia-induced angiogenesis in rat hindlimbs through activation of vascular endothelial growth factor-NO pathway. *Arterioscler Thromb Vasc Biol* 2001;21(1598-1603)

ALZET Comments: Endothelin-1; SC; IP; Rat; 2002; 3 or 28 days; ET-1 infused at a subpressor dose of 2 pmol/kg/min; ischemia (hind-limb); cardiovascular.

P4669: C. Ramirez, *et al.* Role of intrarenal endothelin 1, endothelin 3, and angiotensin II expression in chronic cyclosporin A nephrotoxicity in rats. *Experimental Nephrology* 2000;8(161-172)

ALZET Comments: Cyclosporin A; Endothelin-1; Endothelin-3;; Saline; propylene glycol; SC;; Rat;; 2ML4;; 56 days;; Controls received mp w/ vehicle; functionality of mp verified by whole blood CsA levels; long-term study, pumps replaced after 28 days; antihypertensive; cardiovascular; secretion in nephrotoxicity, relationship with Angiotensin II in renal expression propylene glycol used as vehicle for CsA.

P4492: M. Zhang, *et al.* Endothelin-1 stimulation of endothelial nitric oxide synthase in the pathogenesis of hepatopulmonary syndrome. *Am. J. Physiol. (Gastrointest. Liver Physiol. 40)* 1999;277(G944-G952)

ALZET Comments: Endothelin-1;; Saline;; IV (femoral);; Rat;; 2002;; 2 weeks;; controls received mp w/vehicle; functionality of mp verified by residual volume; stability verified by RIA after 2 weeks in vitro incubation in the pumps; peptides;.

P4526: D. Henrion, *et al.* Chronic endothelin-1 improves nitric oxide-dependent flow-induced dilation in resistance arteries from normotensive and hypertensive rats. *Arterioscler. Thromb. Vasc. Biol* 1999;19(2148-2153)

ALZET Comments: Endothelin-1;; Saline;; SC;; Rat;; 2002;; 2 weeks;; controls received mp w/vehicle; peptides;.

P4351: G. A. Cioffi, *et al.* The effect of chronic ischemia on the primate optic nerve. *European Journal of Ophthalmology* 1999;9(Supp. 1):S34-S36

ALZET Comments: Endothelin-1; CSF/CNS (optic nerve);; monkey; 2-6 months;; long-term study, pumps replaced after 4 weeks; peptides; abstract states pump implanted in rabbits also but no mention of rabbits throughout paper; ischemia.

P3977: E. Thorin, *et al.* Endothelin-1 regulates tone of isolated small arteries in the rat. *Hypertension* 1998;31(1035-1041)



ALZET Comments: Endothelin-1; Saline; IV (jugular); Rat; 2001; 7 days; functionality of mp verified by plasma levels; cardiovascular.

Q0938: M. G. Neerhof, *et al.* Endothelin 1 Induced Placental and Fetal Growth Restriction in the Rat. *The Journal of Maternal-Fetal Medicine* 1997;6(125-128)

ALZET Comments: Endothelin-1; BSA; IV (jugular); Rat; 7 days; Controls received mp w/ normal saline; animal info (female, Sprague-Dawley, 250-300 g); functionality of mp verified by residual volume.

P3475: S. Orgul, *et al.* An endothelin-1 induced model of optic nerve ischemia in the rabbit. *Invest. Ophthalmol. Vis. Sci* 1996;37(9):1860-1869

ALZET Comments: Endothelin-1; CSF/CNS (optic nerve); rabbit; 2, 8 weeks; controls received mp w/ balanced salt solution; tissue perfusion (perineural region of optic nerve); long-term study, pumps replaced every 2 weeks; peptides; pump implanted above the eye; ischemia (optic nerve).

P3477: S. Orgul, *et al.* An endothelin-1-induced model of chronic optic nerve ischemia in rhesus monkeys. *J. Glaucoma* 1996;5(135-138)

ALZET Comments: Endothelin-1; CSF/CNS (optic nerve); monkey; 2002; 7 days; controls received saline infusion; good methods; peptides; ischemia (optic nerve).

P3586: F. Martinez, *et al.* Chronic effects of endothelin-3 on blood pressure and renal haemodynamics in rats. *Nephrol. Dial. Transplant* 1996;11(270-274)

ALZET Comments: Endothelin-3; Water, distilled; IV (jugular); Rat; 3 days; controls received mp w/ vehicle; stability verified by injection of ET-3 from minipump; stable for 3 days - lost biological activity thereafter; peptides.

P3469: G. A. Cioffi, *et al.* An in vivo model of chronic optic nerve ischemia: the dose-dependent effects of endothelin-1 on the optic nerve microvasculature. *Curr. Eye Res* 1995;14(1147-1153)

ALZET Comments: Endothelin-1; Balanced salt solution; CSF/CNS (optic nerve); rabbit; 4 weeks, 3 days; controls received mp w/ vehicle; peptides; pumps implanted above the eye; ischemia (optic nerve).

P2661: G. A. Cioffi, *et al.* Microvasculature of the anterior optic nerve. *Survey of Ophthalmol* 1994;38(Suppl):S107-S117

ALZET Comments: Endothelin-1; Balanced salt solution; CSF/CNS (optic nerve); rabbit; no duration posted; controls received mp w/ vehicle; comparison of intravitreal injections vs. mp; peptides; pumps implanted above upper eyelid.

P3116: J. D. Trachtenberg, *et al.* Effect of endothelin-1 infusion on the development of intimal hyperplasia after balloon catheter injury. *J. Cardiovasc. Pharmacol* 1993;22(SUPL8):S355-S359

ALZET Comments: Endothelin-1; Albumin, bovine serum; Saline; IV (inferior vena cava); Rat; 2ML2; 2 weeks; peptides; pump implanted in groin; transmitter catheters implanted in suprarenal aorta to measure blood pressure and heart rate continuously.

P3039: M. Naruse, *et al.* Is chronic elevation of plasma endothelin levels a cause of hypertension? *Hypertension Res* 1993;16(247-251)

ALZET Comments: Endothelin-1; Saline; IV (jugular); Rat; 2ML1; 2ML4; 4 weeks; controls received mp with vehicle; functionality of mp verified by plasma levels; stability verified by examining pressor activity after 4 weeks at 37 degrees; peptides.

P2451: K. Yoshida, *et al.* Endothelin-I augments pressor response to angiotensin II infusion in rats. *Hypertension* 1992;20(3):292-297

ALZET Comments: Norepinephrine; Angiotensin II; Endothelin; Acetic acid; Saline; IP; IV (jugular); Rat; 6 days; controls received mp w/ vehicle; functionality of mp verified upon removal; peptides.

P1940: H. Kobayashi, *et al.* Cerebral vasospasm and vasoconstriction caused by endothelin. *Neurosurgery* 1991;28(5):673-679



ALZET Comments: Endothelin-1; Water; CSF/CNS (intrathecal); dog; 2001; 7 days; controls received sham op or mp w/ water; peptides.

P1803: M. Yasujima, *et al.* Chronic effects of synthetic endothelin on blood pressure and sodium excretion in rats. *Am. J. Hypertens* 1990;3(635-637)

ALZET Comments: Endothelin; Saline; IV (jugular); Rat; 6 days; stability assessed by monitoring elevated blood pressure throughout infusion period; peptides.

P1810: M. Yasujima, *et al.* Calcium channel blockers reverse the sustained elevation of blood pressure induced by chronic infusion of endothelin in conscious rats. *Tohoku J. Exp. Med* 1990;160(157-165)

ALZET Comments: Endothelin; Saline; IV (jugular); Rat; 6 days; stability assessed by comparing BP elevating activity of solution recovered from pump with fresh solution; peptides.