References on the Administration of Endothelins
Using ALZET® Osmotic Pumps

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.

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.

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).

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.

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

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

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.

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.

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.

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);

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.

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

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.

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.
**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.

**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).

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

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

**ALZET Comments:** Endothelin-1; Saline; 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.

**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.

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

**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).

**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.

**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.

**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.

**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.

**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.

**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;.

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

**ALZET Comments:** Endothelin-I; 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.

**ALZET® Bibliography**

**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.

**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).

**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; no duration posted; controls received mp w/ vehicle; peptides; pumps implanted above the eye; ischemia (optic nerve).

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

**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.

**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.

**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.

Bibliography

**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.