Recent References (2014-2019) on the Administration of Norepinephrine Using ALZET® Osmotic Pumps

**Agents:** Norepinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; Mice (knockout); **Pump:** Not Stated; **Duration:** 7 days;
**ALZET Comments:** Dose (2.5 mg/kg/d); Controls received mp w/ vehicle; animal info (C57BL/6 mice (either sex, 12 weeks old); kidney-specific conditional Kcnj10−/− or Kir4.1 knockout (Ks-Kir4.1 KO) mice);

**Agents:** ICI-118,551 hydrochloride; Toxin, Diptheria; reserpine; captopril; norepinephrine **Vehicle:** PBS; **Route:** Intrasplenic; **Species:** Mice; **Pump:** 1002; **Duration:** 1, 2, 3 weeks;
**ALZET Comments:** "Dose ((ICI-118,551 12 mg/kg/hr), (Diptheria Toxin 5 mg/kg/day), (reserpine 5mg/kg/day), (captopril 6mg/kg/day), (norepinephrine 5mg/kg/day)); Controls received mp w/ vehicle; animal info (10-12 weeks, Apoe(-/-)); comparison of intrasplenic injection vs mp; ICI-118,551 hydrochloride is a selective antagonist of the beta2 adrenergic receptor. angiotensin converting enzyme (ACE) inhibitor. Reserpine blocks the uptake of catecholamines into synaptic vesicles; Reserpine is an enzyme inhibitor (vesicular monoamine transporter 2); immunology; Diptheria toxin used to deplete TH+ leukocytes. Splenic nerves were depleted by intrasplenic DT using mp for 7 days; Therapeutic indication (ICI-118,551 reduced splenic GMP proliferation and inflammatory myeloid cell generation); "

**Agents:** angiotensin II; norepinephrine; SP600125 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;
**ALZET Comments:** Dose ((AngII 1000 ng/kg/min), (NE 5.6 mg/kg/day), (SP600125 30 mg/kg/day)); Controls received mp w/ vehicle; animal info (6-8 weeks, male, C57BL/6, miR-21(−/−), Smad3(−/−), or S3(+/−)21(−/−), 18-25g); SP600125 is an enzyme inhibitor (c-Jun N-terminal kinase); cardiovascular; "all Smad3+/−:miR-21−/− double knockout (S3+/−21−/−) mice died within 23 days of AngII infusion" p.1091;

**Agents:** Norepinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, AT1aR knockdown, 14-16 weeks old, 25-30g); cardiovascular; Dose (3.8ug/kg/min);

**Agents:** A61603; Norepinephrine **Vehicle:** Vitamin C; NaCl; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 7 days;
**ALZET Comments:** Dose (A61603 10 μg/kg/d, NE 2.5 mg/kg/d); vitamin C 100 μM in 0.9% NaCl; animal info (12 w male mice); A61603 aka N-[5-(4,5-dihydro-1H-imidazol-2-yl)-2-hydroxy-5,6,7,8-tetrahydroanaphthalen-1-yl]methanesulfonamide); cardiovascular;

Q6408: Caesar C, et al. Cyclic Strain and Hypertension Increase Osteopontin Expression in the Aorta. Cellular and Molecular Bioengineering 2017;10(2):144-152
**Agents:** Angiotensin II; Norepinephrine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (knockout); **Pump:** 2004; **Duration:** Not Stated;
**ALZET Comments:** Dose (Ang II: 0.75 mg/kg/day; Norepinephrine: 5.6 mg/kg/day); animal info (C57BL/6 (Wildtype, WT) or Osteopontin Knockout (OPN KO) mice); cardiovascular;

**Agents:** Norepinephrine; hydrochlorothiazide; losartan  
**Vehicle:** Saline; DMSO;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 14 days;  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Sprague Dalwey, 275-299g); post op. care (penicillin 0.3 ml IM 300,000 units/ml); cardiovascular; Dose (losartan 3 mg/kg/day, NE 600 ng/min; HCTZ 4 mg/kg/day);


**Agents:** Angiotensin II; norepinephrine  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1002;  
**Duration:** 2 weeks;  

**ALZET Comments:** animal info (male, NO-GC1 KO, 2-3 months old); cardiovascular; peptides; bp measured using tail cuff or radiotelemetry (DSI); Dose (Ang II 1.44 mg/kg/day; NE 2.88 mg/kg/day);good bp graph;

Q4577: B. M. Schmit, *et al.* Hypertension overrides the protective effect of female hormones on the development of aortic aneurysm secondary to Alk5 deficiency via ERK activation. American Journal of Physiology Heart and Circulatory Physiology 2015;308(H115-H125

**Agents:** Norepinephrine  
**Vehicle:** Not Stated;  
**Route:** Not Stated;  
**Species:** Mice;  
**Pump:** 2004;  
**Duration:** 28 days;  

**ALZET Comments:** Animal info (Alk5 iko or Alk5 f/f or C57BL6, 7-15 weeks old, OVX or ORX); cardiovascular; bp measured using tail cuff;  


**Agents:** Angiotensin II; norepinephrine  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1002;  
**Duration:** 2 weeks;  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, WT, 12-16 weeks old); cardiovascular; peptides; bp measured using tail cuff;  


**Agents:** Angiotensin II; norepinephrine  
**Vehicle:** Saline, physiological;  
**Route:** SC;  
**Species:** mice;  
**Pump:** 1002;  
**Duration:** 2 weeks;  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, 12-16 wks, WT Balb/c mice); functionality of mp verified by ECG; cardiovascular; peptides; peptides; Dose (Ang II – 1.1 mg/kg/day, Norepinephrine – 5.6 mg/kr/day);


**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);


**Agents:** Norepinephrine; uridine, 5-bromo-2'-deoxyuridine  
**Vehicle:** Ascorbic acid;  
**Route:** Not Stated;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 7 days;  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL6J or tdTomato);


**Agents:** Angiotensin II; Norepinephrine  
**Vehicle:** Saline; Ascorbate;  
**Route:** SC;  
**Species:** mice;  
**Pump:** 1007D; 1002;  
**Duration:** 1 week; 2 weeks;
**ALZET® Bibliography**

**ALZET Comments:** animal info: WT, SMKO, and SMTg mice aged 8 weeks (C57Bl/6J genetic background); functionality of mp verified by radiotelemetry; 1 mmol/L ascorbate; cardiovascular; antihypertensive, norepinephrine; Dose: 1 mg/kg per day of AngII; 10 mg/kg per day of norepinephrine

**Q4375:** M. J. Choi, *et al.* hTERT mediates norepinephrine-induced Slug expression and ovarian cancer aggressiveness. ONCOGENE 2015;34(3402-3412)

**Agents:** Norepinephrine  
**Vehicle:** Saline; Ascorbic acid  
**Route:** SC  
**Species:** Mice (nude)  
**Pump:** 1004  
**Duration:** 7 weeks  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (female, nude, 4 weeks old); cancer (ovarian);

**Q3828:** A. J. Case, *et al.* Redox-Regulated Suppression of Splenic T-Lymphocyte Activation in a Model of Sympathoexcitation. Hypertension 2015;65(916+  

**Agents:** Norepinephrine  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Mice  
**Pump:** 1002  
**Duration:** 14 days  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, C57BL6J, 8-12 weeks old); functionality of mp verified by plasma levels; good methods (see supplement); post op. care (incision cleaned with iodine); cardiovascular; immunology; bp measured using radiotelemetry (DSI);

**Q3654:** D. L. Xiao, *et al.* Inhibition of DNA methylation reverses norepinephrine-induced cardiac hypertrophy in rats. Cardiovascular Research 2014;101(3):373-382  

**Agents:** Norepinephrine  
**Vehicle:** Not Stated  
**Route:** Not Stated  
**Species:** Rat  
**Pump:** 2ML4  
**Duration:** 28 days  

**ALZET Comments:** Controls received mp w/ saline; animal info (male, Sprague Dawley, 6 months old); functionality of mp verified by plasma levels pg.375; dose-response (pg735, table 1); cardiovascular; arterial blood pressure measured using catheter in femoral artery;

**Q6787:** D. Xiao, *et al.* Inhibition of DNA methylation reverses norepinephrine-induced cardiac hypertrophy in rats. Cardiovascular Research 2014;101(3):373-82  

**Agents:** Norepinephrine; Cytidine, 5-aza-2'-deoxy  
**Vehicle:** Saline; Ascorbic acid  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML4  
**Duration:** 28 days  

**ALZET Comments:** Dose (norepinephrine 100 mg/kg/h; norepinephrine 200 mg/kg/h; 1 mg/kg/day 5-aza-2'-deoxycytidine); Controls received mp w/ saline; animal info (Six-month-old Sprague–Dawley male rats); cardiovascular;

**Q4059:** D. L. Rateri, *et al.* Angiotensin II Induces Region-Specific Medial Disruption during Evolution of Ascending Aortic Aneurysms. American Journal of Pathology 2014;184(2586-2595  

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

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, C57BL6J or Ldlr -/-); post op. care (topical anesthetic cream); cardiovascular; peptides; bp measured using tail cuff;

**Q3477:** Y. X. Gao, *et al.* ADAMTS-7 Expression Increases in the Early Stage of Angiotensin II-Induced Renal Injury in Elderly Mice. KIDNEY & BLOOD PRESSURE RESEARCH 2014;38(121-131  

**Agents:** Angiotensin II; norepinephrine  
**Vehicle:** Saline  
**Route:** SC  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 3 days  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, C57BL6, 36 weeks old); functionality of mp verified by increased bp; cardiovascular; immunology; peptides; bp measured using tail-cuff;


**Agents:** Norepinephrine; propranolol  
**Vehicle:** Ascorbic acid; saline  
**Route:** SC  
**Species:** Mice  
**Pump:** 1004  
**Duration:** 14 days  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (Female, C57BL6, 4-6 weeks old); cancer (melanoma; adenocarcinoma); immunology; "Seeing that microosmotic pumps (1004 type) are of the ability of pumping drugs contained incessantly for up to 4 weeks and exhibit reliable effects in mouse models, the pumps were taken into account in our research to deal with the short half life period of NE." pg 7; Primed pumps in 37C saline for 48 hours; Picture on pg 6 of pump and tumor on mouse.

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Neuropharmacology 2014;79();:550-558
Agents: Norepinephrine; A-779 Vehicle: CSF, artificial; Route: CSF/CNS; Species: Mice (transgenic); Pump: Not Stated;
Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, SARA or RA transgenic, 6-10 weeks); ALZET brain
infusion kit used; ischemia (cerebral); cardiovascular; Pumps primed overnight in 37C saline;