



Recent References (2010-Present) on the Administration of Norepinephrine
Using ALZET® Osmotic Pumps

Q10233: C. Li, *et al.* Obesity protects against sepsis-induced and norepinephrine-induced white adipose tissue browning. *Endocrinology and Metabolism* 2021;321(3):E433-E442

Agents: Norepinephrine **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 1003D; 1007D; **Duration:** 18 hours; 72 hours;
ALZET Comments: Dose: (1.2 nmol/g/h); Controls received no mp w/ vehicle; Within this experimental group, the control mice were those that did not receive a pump nor did they get CLP (Supplemental Table S1; see <https://doi.org/10.6084/m9.figshare.14896068>). The second group consisted of mice that received the vehicle for 72; animal info: Male mice C57BL/6 mice, Six-wk-old mice; Norepinephrine aka (NE)

Q9855: B. Zhang, *et al.* The stress hormone norepinephrine promotes tumor progression through beta2-adrenoreceptors in oral cancer. *Archives of Oral Biology* 2020;113(104712)

Agents: Norepinephrine; ICI-118,551 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 3 weeks;
ALZET Comments: Dose (10 mg /kg/day); Controls received mp w/ vehicle; animal info (4-week-old female nude mice); Norepinephrine aka NE; cancer (Tumor Growth);

Q9809: F. Przygodda, *et al.* Sympathetic innervation suppresses the autophagic-lysosomal system in brown adipose tissue under basal and cold-stimulated conditions. *Journal of Applied Physiology* (1985) 2020;128(4):855-871

Agents: Norepinephrine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 1 week;
ALZET Comments: Dose (40 ug/hr); animal info (Male, Wistar, 150-170 g); dependence;

Q5605: X. P. Duan, *et al.* Norepinephrine-Induced Stimulation of Kir4.1/Kir5.1 Is Required for the Activation of NaCl Transporter in Distal Convulated Tubule. *Hypertension* 2019;73(1):112-120

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);

Q7929: S. B. Vasamsetti, *et al.* Sympathetic Neuronal Activation Triggers Myeloid Progenitor Proliferation and Differentiation. *Immunity* 2018;49(1):93-106 e7

Agents: ICI-118,551 hydrochloride; Toxin, Diphtheria; 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), (Diphtheria 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; Diphtheria 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); "

Q7917: X. Huang, *et al.* MicroRNA-21 Knockout Exacerbates Angiotensin II-Induced Thoracic Aortic Aneurysm and Dissection in Mice With Abnormal Transforming Growth Factor-beta-SMAD3 Signaling. *Arteriosclerosis, Thrombosis, and Vascular Biology* 2018;38(5):1086-1101

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;



Q5926: J. Xu, *et al.* Clinical Relevance and Role of Neuronal AT1 Receptors in ADAM17-Mediated ACE2 Shedding in Neurogenic Hypertension. *Circulation Research* 2017;121(1):43-55

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);

Q6076: M. D. Montgomery, *et al.* An Alpha-1A Adrenergic Receptor Agonist Prevents Acute Doxorubicin Cardiomyopathy in Male Mice. *PLoS One* 2017;12(1):e0168409

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-tetrahydronaphthalen-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;

Q4898: J. T. K. Kathryn R. Walsh, Joon W. Shim, and Richard D. Wainford. Norepinephrine-evoked salt-sensitive hypertension requires impaired renal sodium chloride cotransporter activity in Sprague-Dawley rats. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2016;310(R115-R124)

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);

Q4799: Kathrin Broekmans, *et al.* Angiotensin II-Induced Hypertension Is Attenuated by Reduction of Sympathetic Output in NO-Sensitive Guanylyl Cyclase 1 Knockout Mice. *The Journal of Pharmacology and Experimental Therapeutics* 2016;356):191-199

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;

Q4972: T. Nakashima, *et al.* TLR4 is a critical regulator of angiotensin II-induced vascular remodeling: the roles of extracellular SOD and NADPH oxidase. *Hypertens Res* 2015;38(10):649-55

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; Dose (Angiotensin II 1.1 mg/kg/day; norepinephrine 5.6 mg/kg/day);

Q5231: Matsuda S, *et al.* Angiotensin II Activates MCP-1 and Induces Cardiac Hypertrophy and Dysfunction via Toll-like Receptor 4. *Journal of Atherosclerosis and Thrombosis* 2015;228(8):833-844

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/kg/day);



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);

Q4491: Y. H. Lee, *et al.* Cellular origins of cold-induced brown adipocytes in adult mice. FASEB JOURNAL 2015;29(286-299

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);

Q5150: J. L. Fry, *et al.* Vascular Smooth Muscle Sirtuin-1 Protects Against Aortic Dissection During Angiotensin II-Induced Hypertension. J Am Heart Assoc 2015;4(9):e002384

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

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/ saline; animal info (male, C57BL6, 20-25g, 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; **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/ vehicle; 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:** 2004; **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;

Q3184: G. H. Deng, *et al.* Exogenous norepinephrine attenuates the efficacy of sunitinib in a mouse cancer model. *JOURNAL OF EXPERIMENTAL & CLINICAL CANCER RESEARCH* 2014;33(:):U1-U12

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.

Q3291: J. Chen, *et al.* Neuronal over-expression of ACE2 protects brain from ischemia-induced damage. *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;

Q1835: Q. Wu, *et al.* Ablation of neurons expressing agouti-related protein, but not melanin concentrating hormone, in leptin-deficient mice restores metabolic functions and fertility. *Proceedings of the National Academy of Sciences of the United States of America* 2012;109(8):3155-3160

Agents: Norepinephrine **Vehicle:** Ascorbate; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Animal info (Lep Ob+, 55 g, 14 wks old)

Q2697: T. Kurihara, *et al.* Neutrophil-Derived Matrix Metalloproteinase 9 Triggers Acute Aortic Dissection. *Circulation* 2012;126(25):3070-U532

Agents: Angiotensin II; norepinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 24 hours;
ALZET Comments: Animal info (MMP9 -/-, 7 wks old); peptides

Q1244: S. Mu, *et al.* Epigenetic modulation of the renal beta-adrenergic-WNK4 pathway in salt-sensitive hypertension. *Nature Medicine* 2011;17(5):573-U92

Agents: Norepinephrine; Isoproterenol; ICI-118,551; Metoprolol **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; Rat; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6j, male, Sprague Dawley, 250-270 g, 8 wks old, nephrectomy)

Q1137: N. Ishizaka, *et al.* Liver lipid content is reduced in rat given 7-day administration of angiotensin II. *Journal of Renin-Angiotensin-Aldosterone System* 2011;12(4):462-468

Agents: Angiotensin II, [Val 5]; Norepinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Animal info (male, Sprague Dawley, 10 wks old); peptides

Q1256: A. Penn, *et al.* Dose-Response Relationship between Norepinephrine and Erythropoiesis: Evidence for a Critical Threshold. *Journal of Surgical Research* 2010;163(2):E85-E90

Agents: Norepinephrine bitartrate; **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 1007D; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 300-350 g)



Q0026: A. P. I. Owens, *et al.* Angiotensin II Induces a Region-Specific Hyperplasia of the Ascending Aorta Through Regulation of Inhibitor of Differentiation 3. *Circulation Research* 2010;106(3):611-U108

Agents: Angiotensin II; Norepinephrine; Losartan **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks; 28 days;

ALZET Comments: Controls received mp w/vehicle; peptides; cardiovascular; animal info (male, C57BL/6, AT1aR -/-, p47phox -/-, Id3 -/-); functionality of mp verified by systolic blood pressure

Q3033: P. J. Marvar, *et al.* Central and Peripheral Mechanisms of T-Lymphocyte Activation and Vascular Inflammation Produced by Angiotensin II-Induced Hypertension. *Circulation Research* 2010;107(2):263-U186

Agents: Angiotensin II; norepinephrine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6, RAG1 -/-, OVA-specific, OT-II tg); peptides; blood pressure measured via telemetry or tail cuff

Q1545: K. Kimura, *et al.* Norepinephrine-induced nerve growth factor depletion causes cardiac sympathetic denervation in severe heart failure. *Autonomic Neuroscience: Basic and Clinical* 2010;156(1-2):27-35

Agents: Norepinephrine **Vehicle:** Saline; ascorbate; **Route:** SC; **Species:** Rat; mice; **Pump:** 2004; **Duration:** 1, 3, 7, 14, 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Wistar, male, 240-260 g, 7 wks old; 5 wks old, DBH-Cre/Floxed-EGFP); functionality of mp verified by plasma NE levels