References on the Administration of Angiotensin and Phenylephrine Using ALZET® Osmotic Pumps

Q11056: D. Matsiukevich, *et al.* Characterization of a robust mouse model of heart failure with preserved ejection fraction. American Journal of Physiology Heart and Circulatory Physiology 2023;325(2):H203-H231
Agents: Angiotensin II; phenylephrine **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2004; 1002; **Duration:** 28 days; 3 days; 10 days;
ALZET Comments: Dose (1.5 µg/g/day ang II); (50 µg/g/day PE), pumps primed in 0.9% saline 24h 37degC; controls received mp w/ vehicle; animal info: 8- to 10-wk old; blood pressure measured via Noninvasive Methods; blood pressure measurement results see (p.212) Fig.3 L; behavioral testing (Treadmill exercise); cardiovascular (heart failure)

Q10526: J. F. Garbincius, *et al.* Enhanced NCLX-dependent mitochondrial Ca(2+) efflux attenuates pathological remodeling in heart failure. Journal of Molecular and Cellular Cardiology 2022;167(52-66
Agents: Angiotensin II; Phenylephrine hydrochloride **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 1004; 2004; **Duration:** 2 weeks; 4 weeks;
ALZET Comments: "Dose: Ang II (1.44 mg/kg/day) AngII/PE 10 mg/kg/day + 50 mg/kg/day); Controls received mp w/ vehicle; animal info: Adult male female TRE-NCLX x αMHC-tTA mice and age-matched αMHC-tTA between 8 and 25 weeks of age; post op. care: cefazolin at a dose of 40 mg/kg; Angiotensin II aka (Ang II)

Q10391: A. Ishikita, *et al.* GFAT2 mediates cardiac hypertrophy through HBP-O-GlcNAcylation-Akt pathway. iScience 2021;24(12):103517
Agents: Isoproterenol; 6-diazo-5-oxo-L-norleucine crystalline; Phenylephrine; Angiotensin II **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week;
ALZET Comments: Dose (ISO 15 mg/kg body weight/day; DON 0.05 ug/kg/day; AngII 1.44 mg/kg body weight/day; PE 100 mg/kg body weight/day); dose-response (see p. 18); animal info (Male; 8-10 weeks old); Blood pressure measured via tail cuff system; peptides; cardiovascular; Therapeutic indication (Cardiac hypertrophy);

Q8880: R. Liu, *et al.* Mice lacking DUSP6/8 have enhanced ERK1/2 activity and resistance to diet-induced obesity. Biochemical and Biophysical Research Communications 2020;533(1):17-22
Agents: Angiotensin II; Phenylephrine **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (1.5 mg/kg/day Angiotensin II; 50 mg/kg/day Phenylephrine); Controls received mp w/ vehicle; animal info (8-week-old mice); cardiovascular;

Q9227: J. Francisco, *et al.* Blockade of Fibroblast YAP Attenuates Cardiac Fibrosis and Dysfunction Through MRTF-A Inhibition. JACC: Basic Translational Science 2020;5(9):931-945
Agents: Angiotensin II; Phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Dose (288 ug/kg/day Angiotensin II; 100 mg/kg/day Phenylephrine); Controls received mp w/ vehicle; animal info (8 to 10 week old mice); Angiotensin II aka AngII, Phenylephrine aka PE; cardiovascular;

Q8941: R. Sabharwal, *et al.* Increased receptor activity-modifying protein 1 in the nervous system is sufficient to protect against autonomic dysregulation and hypertension. Journal of Cerebral Blood Flow & Metabolism 2019;39(4):690-703
Agents: Angiotensin II; Phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Dose (Ang II- 1000 ng/kg/min or phenylephrine- 4000 ng/kg/min); animal info (10-20 weeks old, 20-30 g); Blood pressure measured via Radiotelemetry; cardiovascular;

Q7986: L. E. Dorn, *et al.* The N(6)-Methyladenosine mRNA Methylase METTL3 Controls Cardiac Homeostasis and Hypertrophy. Circulation 2019;139(4):533-545
Agents: Angiotensin II; phenylephrine **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 4 weeks;
ALZET Comments: Dose ((Ang II 432 µg/kg/d), (phenylephrine 100 mg/kg/d)); Controls received sham surgery and mp w/ vehicle; animal info (10-32 weeks, male and female, C57BL6 and METTL3-cKO); cardiovascular; vehicle stated but identity not stated. mp model number not stated.;

Q8683: H. Aghajanian, *et al.* Targeting cardiac fibrosis with engineered T cells. Nature 2019;573(7774):430-433
Agents: Angiotensin II and Phenylephrine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Dose (Ang II- 1.5 ug/g/day, PE- 50 ug/g/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL/6); Phenylephrine aka PE ; cardiovascular;

Q6556: C. Zheng, *et al.* Gastrodin Inhibits Store-Operated Ca(2+) Entry and Alleviates Cardiac Hypertrophy. Front Pharmacol 2017;8(222
Agents: Phenylephrine; Angiotensin II **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: Dose (Phenylephrine: 70 mg/kg/day; Angiotensin II: 1.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Eight-week-old male C57 mice); cardiovascular;

Q6201: J. D. Molkentin, *et al.* Fibroblast-Specific Genetic Manipulation of p38 Mitogen-Activated Protein Kinase In Vivo Reveals Its Central Regulatory Role in Fibrosis. Circulation 2017;136(6):549-561
Agents: Angiotensin II; Phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Dose (Angiotensin II: 432 µg/kg/d; Phenylephrine: 100 mg/kg/d); animal info (LoxP-targeted Mapk14 mice); cardiovascular;

Q5401: R. Liu, *et al.* DUSP8 Regulates Cardiac Ventricular Remodeling by Altering ERK1/2 Signaling. Circulation Research 2016;119(2):249-60
Agents: Angiotensin II; Phenylephrine **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (8 – 12 weeks old); functionality of mp verified by ECG; ischemia (cardiac); cardiovascular; peptides; Transverse aortic constriction; echocardiography (ECG) used; Dose (AngII 1.5 mg/kg/day, Phenylephrine 50 mg/kg/day);

Q5546: O. Kanisicak, *et al.* Genetic lineage tracing defines myofibroblast origin and function in the injured heart. Nat Commun 2016;7(12260
Agents: Angiotensin II, Phenylephrine Hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular; Therapeutic indication (Myocardial infarction); Dose (Angiotensin II: 1.5 ug/gxd, Phenylephrine Hydrochloride: 50 ug/g/day);

Q6562: S. Ito, *et al.* Identification of the Mtus1 Splice Variant as a Novel Inhibitory Factor Against Cardiac Hypertrophy. J Am Heart Assoc 2016;5(7):
Agents: Phenylephrine; Angiotensin II **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days; 14 days; 28 days;
ALZET Comments: Dose (Phenylephrine: 75 mg/kg per day; Angiotensin II: 1000 ng/kg/minute); Controls received mp w/ vehicle; animal info (6 week old C57BL/6J male mice); cardiovascular

Q5137: R. N. Correll, *et al.* STIM1 elevation in the heart results in aberrant Ca(2)(+) handling and cardiomyopathy. J Mol Cell Cardiol 2015;87(38-47
Agents: Isoproterenol; Angiotensin II; Phenylephrine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info: STIM1 TG mice; functionality of mp verified by echocardiograph (ECG); cardiovascular; Dose: isoproterenol (60 mg/kg/d); angiotensin II (432 µg/kg/d) with phenylephrine (100 mg/kg/d),

Q4243: F. Accornero, *et al.* Genetic Analysis of Connective Tissue Growth Factor as an Effector of Transforming Growth Factor beta Signaling and Cardiac Remodeling. MOLECULAR AND CELLULAR BIOLOGY 2015;35(2154-2164
Agents: Angiotensin II; phenylephrine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (Ctgf fl/fl); cardiovascular; Dosage 100mg/kg/day phenylephrine, 432 ug/kg/day Ang II

Q2801: C. K. Tan*, et al.* SMAD3 Deficiency Promotes Inflammatory Aortic Aneurysms in Angiotensin II-Infused Mice Via Activation of iNOS. JOURNAL OF THE AMERICAN HEART ASSOCIATION 2013;2(3):U428-U455
Agents: Angiotensin II; phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** Not Stated;
ALZET Comments: Animal info (8 wks old); peptides; bp measured using tail-cuff;

Q2829: A. J. Polichnowski*, et al.* Blood pressure-renal blood flow relationships in conscious angiotensin II- and phenylephrine-infused rats. American Journal of Physiology Renal Physiology 2013;305(7):F1074-F1084
Agents: Angiotensin II; phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Animal info (Sprague Dawley, male, 250-350 g); peptides; bp measured using radiotelemetry (DSI);

Q2656: J. I. Gold*, et al.* Nuclear Translocation of Cardiac G Protein-Coupled Receptor Kinase 5 Downstream of Select Gq-Activating Hypertrophic Ligands Is a Calmodulin-Dependent Process. PLoS One 2013;8(3):U215-U229
Agents: Angiotensin II; phenylephrine; isoproterenol **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Control animals received mp w/ PBS; animal info (8 wks old, GRK5KO); peptides

Q2699: J. Mori*, et al.* Agonist-Induced Hypertrophy and Diastolic Dysfunction Are Associated With Selective Reduction in Glucose Oxidation A Metabolic Contribution to Heart Failure With Normal Ejection Fraction. Circulation: Heart Failure 2012;5(4):493-503
Agents: Angiotensin II; phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Animal info (C57BL/6, male, 9 wks old); peptides

Q2308: S. X. Jin*, et al.* Endogenous Renovascular Hypertension Combined With Low Shear Stress Induces Plaque Rupture in Apolipoprotein E-Deficient Mice. Arteriosclerosis, Thrombosis, and Vascular Biology 2012;32(10):2372-U131
Agents: Angiotensin II; phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Control animals received mp w/ normal saline; animal info (apoE -/-, 8 wks old, 20-25 g); peptides

Q0708: I. Kehat*, et al.* Extracellular Signal-Regulated Kinases 1 and 2 Regulate the Balance Between Eccentric and Concentric Cardiac Growth. Circulation Research 2011;108(2):176-U57
Agents: Angiotensin II; Phenylephrine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Animal info (Erk1-/-); peptides

Q0955: F. Accornero*, et al.* Placental Growth Factor Regulates Cardiac Adaptation and Hypertrophy Through a Paracrine Mechanism. Circulation Research 2011;109(3):272-U95
Agents: Angiotensin II; Phenylephrine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 1 week;
ALZET Comments: Animal info (wt, FVBN); Peptides

P9953: X. Wu*, et al.* TRPC channels are necessary mediators of pathologic cardiac hypertrophy. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2010;107(15):7000-7005
Agents: Angiotensin II; phenylephrine **Vehicle:** PBS; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (Nfat-luciferase, heart specific Trpc3Tg)

Q0481: J. H. van Berlo*, et al.* The Transcription Factor GATA-6 Regulates Pathological Cardiac Hypertrophy. Circulation Research 2010;107(8):1032-U178
Agents: Angiotensin II; phenylephrine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Animal info (young adult, Gata6fl/flMHC-cre Tg); peptides

Q0173: M. Maillet, *et al.* Heart-specific Deletion of CnB1 Reveals Multiple Mechanisms Whereby Calcineurin Regulates Cardiac Growth and Function. Journal of Biological Chemistry 2010;285(9):6716-6724
Agents: Angiotensin II; phenylephrine; Isoproterenol **Vehicle:** Saline, physiological; acetic acid; PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; peptides; cardiovascular; animal info (C57BL/6, wt, CnB1fl/fl-aMHC-Cre, 2 months old); behavioral response (forced swimming)

Q0001: T. Ago, *et al.* Upregulation of Nox4 by Hypertrophic Stimuli Promotes Apoptosis and Mitochondrial Dysfunction in Cardiac Myocytes. Circulation Research 2010;106(7):1253-U183
Agents: Angiotensin II; Phenylephrine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; peptides

P9623: X. Wu, *et al.* Plasma membrane Ca^{2+}-ATPase isoform 4 antagonizes cardiac hypertrophy in association with calcineurin inhibition in rodents. Journal of Clinical Investigation 2009;119(4):976-985
Agents: Phenylephrine; angiotensin II **Vehicle:** PBS; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/vehicle; animal info (Pmca4-/-); peptides; mixture of phenylephrine and angiotensin II in pump. Dose: PE (100 mg/kg/d) and Ang II (432 µg/kg/d)

Q0633: M. Maillet, *et al.* Cdc42 is an antihypertrophic molecular switch in the mouse heart. Journal of Clinical Investigation 2009;119(10):3079-3088
Agents: Angiotensin II; Phenylephrine **Vehicle:** NaCl; Acetic acid; **Route:** SC; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (Cdc MHC-cre,); peptides; Angiotensin II and phenylephrine in the same pump

P9561: S. H. H. Chan, *et al.* Oxidative Impairment of Mitochondrial Electron Transport Chain Complexes in Rostral Ventrolateral Medulla Contributes to Neurogenic Hypertension. Hypertension 2009;53(2):217-U230
Agents: Angiotensin II; phenylephrine **Vehicle:** Saline; CSF, artificial; **Route:** IP; CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/vehicle; peptides; post op. care (Penicillin); animal info (SHR, 5-6 wks old, 11-12 wks old, Wky, 5-6 wks old)

P9255: M. Maillet, *et al.* DUSP6 (MKP3) Null Mice Show Enhanced ERK1/2 Phosphorylation at Baseline and Increased Myocyte Proliferation in the Heart Affecting Disease Susceptibility. Journal of Biological Chemistry 2008;283(45):31246-31255
Agents: Angiotensin II; Phenylephrine; Isoproterenol **Vehicle:** Saline; Acetic acid; PBS; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular; peptides; animal info (C57BL/6-Sv129; Dusp6 -/-, wt, 8 wks old, transverse aortic constriction, MI, 21 g.)

P8999: Y. Sagara, *et al.* Pressor response induced by central angiotensin II is mediated by activation of Rho/Rho-kinase pathway via AT_1 receptors. Journal of Hypertension 2007;25(2):399-406
Agents: Angiotensin II; Phenylephrine; Y-27632; Valsartan **Vehicle:** CSF, artificial; **Route:** SC; CSF/CNS; **Species:** Rat; **Pump:** 1002; 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (Rho-kinase); antihypertensive; peptides; animal info (male, Wistar-Kyoto, SHR, 280-340 g.); catheter tip placement and connection confirmed

P8022: H. Nakayama, *et al.* Calcineurin-dependent cardiomyopathy is activated by TRPC in the adult mouse heart. FASEB Journal 2006;20(10):1660-1670
Agents: Phenylephrine; Isoproterenol; Angiotensin II **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular

P7438: T. Arimoto*, et al.* Cardiac-specific overexpression of diacylglycerol kinase xi prevents Gq protein-coupled receptor agonist-induced cardiac hypertrophy in transgenic mice. Circulation 2006;113(1):60-66
Agents: Angiotensin II; Phenylephrine **Vehicle:** Saline; **Route:** SC; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 3,14 days;
ALZET Comments: Controls received mp w/ vehicle; no stress (see pg. 63); cardiovascular; peptides

P8060: M. Y. Wang*, et al.* Angiotensin II activates matrix metalloproteinase type II and mimics age-associated carotid arterial remodeling in young rats. American Journal of Pathology 2005;167(5):1429-1442
Agents: Angiotensin II; Phenylephrine hydrochloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ saline; dose-response (fig 1); cardiovascular; peptides; animal info (male, Fisher 344 x Brown Norway, 8 or 30 months old)

P6154: Y. L. Liao*, et al.* Activation of adenosine A_1 receptor attenuates cardiac hypertrophy and prevents heart failure in murine left ventricular pressure-overload model. Circulation Research 2003;93(8):759-766
Agents: Adenosine receptors, CADO, 8-sulfopheyl theophylline, DPCPX, IB-MECA; phenylephrine; endotherin-1; forskolin; angiotensin II; CGS-21680; Isoproterenol; 5-ethylcarboxamidoadenosine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 4 weeks;
ALZET Comments: Pumps replaced every two weeks; cardiovascular

P5675: J. C. Braz*, et al.* Targeted inhibition of p38 MAPK promotes hypertrophic cardiomyopathy through upregulation of calcineurin-NFAT signaling. Journal of Clinical Investigation 2003;111(10):1475-1486
Agents: Isoproterenol; phenylephrine; angiotensin II **Vehicle:** PBS; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular; 3 separate pumps used (one per animal)

P7109: M. Brancaccio*, et al.* Melusin, a muscle-specific integrin $beta_1$-interacting protein, is required to prevent cardiac failure in response to chronic pressure overload. Nature Medicine 2003;9(1):68-75
Agents: Angiotensin II; Phenylephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 21 days;
ALZET Comments: Cardiovascular

P5067: C. Vecchione*, et al.* Cardiovascular influences of alpha 1b-adrenergic receptor defect in mice. Circulation 2002;105(14):1700-1707
Agents: Angiotensin II; Norepinephrine; Phenylephrine **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 18 days;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular; peptides; Ang II infused in saline, NE and PHE in 0.2% ascorbic acid