



References on the Administration of Antihypertensive Agents Using ALZET® Osmotic Pumps

1. Atenolol

Q7652: W. B. Zhao, *et al.* Stimulation of beta-adrenoceptors up-regulates cardiac expression of galectin-3 and BIM through the Hippo signalling pathway. *British Journal of Pharmacology* 2019;176(14):2465-2481

Agents: Isoproterenol; propranolol; carvedilol; atenolol; ICI-118551 **Vehicle:** saline; ascorbic acid, buffered; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 1 day; 2 days; 7 days;

ALZET Comments: Dose ((ISO 0.6, 6, 20 mg/kg/d), (Prop 2 mg/kg/d), (Carv 2 mg/kg/d), (AT 2 mg/kg/d), (ICI 1 mg/kg/d)); saline with 0.4 mM ascorbic acid used; Controls were non-transgenic and received mp w/ vehicle; animal info (12-16 weeks, Male, (C57BL/6J, beta2-TG, Mst1-TG, or dnMst1-TG)); ICI-118551 is a beta2-antagonist with the structure (2R,3S)-1-[[7-methyl-2,3-dihydro-1H-inden-4-yl]oxy]-3-(propan-2-ylamino)butan-2-ol; cardiovascular; Minipumps were removed to allow for washout of ISO overnight prior to imaging;

Q7241: M. N. Nguyen, *et al.* Mechanisms responsible for increased circulating levels of galectin-3 in cardiomyopathy and heart failure. *Sci Rep* 2018;8(1):8213

Agents: Isoproterenol, Atenolol, ICI-118551 **Vehicle:** Saline, ascorbic acid; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 48 Hours;

ALZET Comments: Dose: ISO (2, 6 or 30 mg/kg/day; atenolol (2 mg/kg/day), ICI-118551 (1 mg/kg/day)); 0.4 mM ascorbic acid used; animal info (12~14 week-old C57Bl/6 mice); cardiovascular;

Q6161: C. Disdier, *et al.* Brain Inflammation, Blood Brain Barrier dysfunction and Neuronal Synaptophysin Decrease after Inhalation Exposure to Titanium Dioxide Nano-aerosol in Aging Rats. *Sci Rep* 2017;7(1):12196

Agents: Atenolol **Vehicle:** PEG 200; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001D; **Duration:** 4 hours;

ALZET Comments: Dose (0.25 mg/kg/h); 50% PEG 200 used, 50% DMSO used; animal info (19 month old Fischer rats); Resultant plasma level (p.10);

Q6167: W. L. Lin, *et al.* Sleep-related changes in cardiovascular autonomic regulation in left coronary artery ligation rats: Neural mechanism facilitating arrhythmia after myocardial infarction. *Int J Cardiol* 2016;225(65-72

Agents: Atenolol **Vehicle:** DMSO, PEG 300; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;

ALZET Comments: Dose (10 mg/kg/d); 50% PEG 300/50% DMSO used; animal info (8 to 10-week-old male Wistar-Kyoto rats); Atenolol is a selective beta1-blocker;

Q4508: C. Disdier, *et al.* Tissue biodistribution of intravenously administrated titanium dioxide nanoparticles revealed blood-brain barrier clearance and brain inflammation in rat. *Particle and Fibre Toxicology* 2015;12(U1-U20

Agents: Atenolol; digoxin; prazosin **Vehicle:** PEG 200; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001D; **Duration:** Not Stated;

ALZET Comments: Animal info (male, Fisher F344, 8 weeks old, 180-250g); 50% PEG 200 used; 50% DMSO used;

2. Benazepril

P9490: M. Abu-Taha, *et al.* Menopause and Ovariectomy Cause a Low Grade of Systemic Inflammation that May Be Prevented by Chronic Treatment with Low Doses of Estrogen or Losartan. *Journal of Immunology* 2009;183(2):1393-1402

ALZET Comments: Estradiol, 17b-; benazepril; DMSO; SC; Rat; 2004; Controls received mp w/ vehicle or sham operation; animal info (male, female, Sprague Dawley, OVX); 50% DMSO used; dose (5 ug/kg/d).

P6345: S. Yagi, *et al.* Combined treatment with an AT₁ receptor blocker and angiotensin converting enzyme inhibitor has an additive effect on inhibiting neointima formation via improvement of nitric oxide production and suppression of oxidative stress. *HYPERTENSION RESEARCH* 2004;27(2):129-135

ALZET Comments: Valsartan; benazepril; Potassium hydroxide; HCL; SC; Rat; Controls received mp w/ vehicle; dose-response (p131); pump model not stated.



P6612: M. Mizukami, *et al.* Gene expression profile revealed different effects of angiotensin II receptor blockade and angiotensin-converting enzyme inhibitor on heart failure. *Journal of Cardiovascular Pharmacology* 2003;42(S1-S6)
ALZET Comments: Benazepril; candesartan; SC; Rat; 2ML4; Blood pressure taken.

P3188: L. Chow, *et al.* Improved glucose metabolism following blockade of angiotensin converting enzyme but not angiotensin AT receptors. *Eur. J. Pharmacol* 1995;282(77-86)
ALZET Comments: Benazepril; Valsartan; Water, distilled; NaOH; HCl; IP; Rat; 2ML4; 12 weeks; controls received mp with saline; long-term study, pumps replaced every 28 days; valsartan is an angiotensin AT1 receptor antagonist; antihypertensive.

3. Benazeprilat

Q2883: Q. C. Yong, *et al.* Angiotensin type 1a receptor-deficient mice develop diabetes-induced cardiac dysfunction, which is prevented by renin-angiotensin system inhibitors. *Cardiovascular Diabetology* 2013;12(1):U1-U13
ALZET Comments: Aliskiren; benazeprilat; valsartan; PD123319; Saline; SC; Mice; 1004; 10 weeks; Cardiovascular; peptides; animal info (12 wks old, male, AT-KO); functionality of mp verified by echocardiography; pumps replaced every 4 weeks; enzyme inhibitor (renin);

Q2934: C. M. Thomas, *et al.* Direct renin inhibition prevents cardiac dysfunction in a diabetic mouse model: comparison with an angiotensin receptor antagonist and angiotensin-converting enzyme inhibitor. *Clinical Science* 2013;124(7-8):529-541
ALZET Comments: Insulin (Humulin N); aliskiren (renin inhibitor); benazeprilat (ACEi); valsartan (ARB); streptozotocin; Saline; SC; Mice; 1004; 10 weeks; Controls received mp w/vehicle, or (0.1M sodium citrate buffer (pH 4.5)); cardiovascular; animal info (male, C57b16/J, 12 weeks, blood glucose > 250 mg/dl); pumps replaced every 4 weeks; enzyme inhibitor (renin); diabetes;

P3939: R. L. Webb, *et al.* Effects of valsartan and hydrochlorothiazide alone and in combination on blood pressure and heart rate in conscious-telemetered spontaneously hypertensive rats (SHR). *Am. J. Hypertens* 1998;11(59-65)
ALZET Comments: Valsartan; Hydrochlorothiazide; Benazeprilat; NaOH; SC; Rat; 2ML2; 2 weeks; controls received mp w/vehicle; functionality of mp verified by residual volume and plasma assays; dose-response; stability verified by pilot expt; antihypertensive; cardiovascular; agents administered alone and in combination.

P4059: R. L. Webb, *et al.* Protective effects of valsartan and benazeprilat in salt-loaded stroke-prone spontaneously hypertensive rats. *Clin. Exp. Hypertens* 1998;20(7):775-793
ALZET Comments: Valsartan; Benazeprilat; NaOH; SC; Rat; 2ML2; 9.5 weeks; controls received mp w/vehicle; long-term study, pumps replaced every 2 weeks; radiotelemetric devices implanted concomitantly for blood pressure and heart rate measurement; antihypertensive; cardiovascular; ischemia (cerebral); long-term study.

P2830: R. L. Webb, *et al.* Development of tolerance to the antihypertensive effects of highly selective adenosine A2a agonists upon chronic administration. *J. Pharmacol. Exp. Ther* 1993;267(1):287-295
ALZET Comments: CGS-21680C; CGS-22989; CGS-22492; Benazeprilat; DMSO; Sodium bicarbonate; IV (jugular); Rat; 2ML2; 2 weeks; controls received mp w/ vehicle; tolerance.

4. Bendroflumethiazide

P2385: H. E. Lunau, *et al.* Renal adaptations to continuous administration of furosemide and bendroflumethiazide in rats. *Pharmacol. Toxicol* 1994;74(216-222)
ALZET Comments: Bendroflumethiazide; Furosemide; Lithium citrate; Ethanolamine; IP; Rat; 2ML1; 7 days; antihypertensive.



5. Bisoprolol

Q3145: C. C. Sucharov, *et al.* beta-Adrenergic receptor antagonism in mice: a model for pediatric heart disease. *Journal of Applied Physiology* 2013;115(7):979-987

ALZET Comments: Isoproterenol HCl; Bisoprolol; Nebivolol; Metoprolol, CGP2712A; Saline; DMSO; Ascorbic acid; SC; Mice; 1007D; 2001; 7 days; Controls received mp w/ vehicle; animal info (FVB); 40% DMSO used for CGP20712A & nebivolol vehicle; post op. care (Carpofen 5 mg/kg); cardiovascular; antihypertensive;.

P3796: H. Hamada, *et al.* Age-related effects of norepinephrine on rat ventricular hypertrophy. *Jpn. Heart J* 1997;38(3):433-443

ALZET Comments: Norepinephrine HCl; Norepinephrine bitartrate; Bunazosin; Bisoprolol; SC; Rat; 2002; 7, 14 days; controls received mp w/saline or norepinephrine; dose-response; antihypertensive; cardiovascular; 2 pumps implanted in each animal.

6. Bunazosin

P3796: H. Hamada, *et al.* Age-related effects of norepinephrine on rat ventricular hypertrophy. *Jpn. Heart J* 1997;38(3):433-443

ALZET Comments: Norepinephrine HCl; Norepinephrine bitartrate; Bunazosin; Bisoprolol; SC; Rat; 2002; 7, 14 days; controls received mp w/saline or norepinephrine; dose-response; antihypertensive; cardiovascular; 2 pumps implanted in each animal.

7. Candesartan

Q8609: L. M. H. Krause, *et al.* Renal functional effects of the highly selective AT2R agonist, beta-Pro7 Ang III, in normotensive rats. *Clin Sci (Lond)* 2020;134(7):871-884

Agents: Candesartan **Vehicle:** Dextrose; **Route:** SC; **Species:** Rat; **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: Dose (0.01 mg/kg/min); 5% dextrose used; animal info (12-week-old female Sprague-Dawley rats); Candesartan aka CAND; dependence;

Q7624: B. A. Kemp, *et al.* Defective Renal Angiotensin III and AT2 Receptor Signaling in Prehypertensive Spontaneously Hypertensive Rats. *J Am Heart Assoc* 2019;8(9):e012016

Agents: candesartan **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: Dose (0.01 mg/kg/min); Controls received mp w/ agent; animal info (4 weeks, male and female, Wistar-Kyoto (WKY) and spontaneously hypertensive (SHR)); enzyme inhibitor (Ang type-1 receptor); all animals received pump with candesartan 24h prior to experiments to block systemic AT1Rs.;

Q7311: L. J. Trigiani, *et al.* Pleiotropic Benefits of the Angiotensin Receptor Blocker Candesartan in a Mouse Model of Alzheimer Disease. *Hypertension* 2018;72(5):1217-1226

Agents: Candesartan **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 2 months;

ALZET Comments: Dose (1 mg/kg per day,); 25% DMSO used; 25% DMSO used; animal info (male and female, C57BL6 mice with APP mutations, 3–4 months old); behavioral testing (Morris water maze); pumps replaced at 34 days; comparison of oral delivery via drinking water vs mp; neurodegenerative (Alzheimer disease); “It is thus possible that delivery of candesartan through osmotic minipumps (cohort 1) compared with drinking water (cohort 2) allowed for better control of drug concentration and steady-state levels that conferred a better drug efficacy despite a shorter treatment, ” pg. 1224;



Q7242: Y. Takeda, *et al.* Epigenetic Regulation of Aldosterone Synthase Gene by Sodium and Angiotensin II. *J Am Heart Assoc* 2018;7(10):

Agents: Angiotensin II, Candesartan **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks; **ALZET Comments:** Dose (Ang II 200 ng/kg/min, Candesartan 1mg/kg/day); animal info (Male, Wistar, 6 weeks old); Candesartan aka Ang II type 1 receptor antagonist; gene therapy;

Q8306: Y. Okuyama, *et al.* The effects of anti-hypertensive drugs and the mechanism of hypertension in vascular smooth muscle cell-specific ATP2B1 knockout mice. *Hypertens Res* 2018;41(2):80-87

Agents: Amlodipine or Candesartan **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 2 weeks; **ALZET Comments:** Dose (Amlodipine- 5 mg/kg/day, Candesartan-0.5 mg/kg/day); animal info (ATP2B1 loxP/loxP); cardiovascular;

8. Captopril

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); "

Q7067: W. L. Lin, *et al.* Neural mechanism of angiotensin-converting enzyme inhibitors in improving heart rate variability and sleep disturbance after myocardial infarction. *Sleep Med* 2018;48(61-69

Agents: Captopril **Vehicle:** PEG 300; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks; **ALZET Comments:** Dose (30 mg/kg/d); Controls received mp w/ vehicle; enzyme inhibitor (ACE);

Q4497: W. C. Li, *et al.* Angiotensin II regulates brain (pro)renin receptor expression through activation of cAMP response element-binding protein. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2015;309(R138-R147

Agents: Losartan; captopril; CAS92-78-4 **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 3 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6J); cardiovascular; CAS92-78-4 is a CREB-CBP interaction inhibitor;

Q4442: J. C. Hardwick, *et al.* Angiotensin receptors alter myocardial infarction-induced remodeling of the guinea pig cardiac plexus. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2015;309(R179-R188

Agents: Captopril; losartan; CGP42112A **Vehicle:** Not Stated; **Route:** SC; **Species:** Guinea pig; **Pump:** 2ML4; **Duration:** 4 weeks; 6 weeks;

ALZET Comments: Animal info (male, Hartley, 9 weeks old, 500-650g); pumps replaced every 3 weeks; cardiovascular; long-term study;

Q3953: S. Lankhorst, *et al.* Treatment of Hypertension and Renal Injury Induced by the Angiogenesis Inhibitor Sunitinib Preclinical Study. *Hypertension* 2014;64(1282-U260

Agents: Captopril **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 8 days;



ALZET Comments: Animal info (male, Wistar Kyoto, 280-300g); cardiovascular; antihypertensive; bp measured using radiotelemetry (DSI);

9. Clonidine

Q6941: W. Cao, *et al.* A renal-cerebral-peripheral sympathetic reflex mediates insulin resistance in chronic kidney disease. *EBioMedicine* 2018;37(281-293

Agents: Losartan; Tempol; Clonidine **Vehicle:** CSF, artificial; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Dose (1 mg/kg/day losartan; 4.5 ug/kg/day tempol; 5.76 ug/kg/day clonidine); Controls received mp w/ vehicle; animal info (Five-week-old male Sprague-Dawley rats); Therapeutic indication (5/6 nephrectomy);

Q6376: G. D. Fink, *et al.* Can we predict the blood pressure response to renal denervation? *Autonomic Neuroscience: Basic and Clinical* 2017;204(112-118

Agents: Clonidine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** 2006; **Duration:** Not Stated;

ALZET Comments: Dose (125 µg/kg/day); animal info (Male SHR); antihypertensive;

Q4646: B. A. Williams, *et al.* Multimodal Perineural Analgesia with Combined Bupivacaine-Clonidine-Buprenorphine-Dexamethasone: Safe In Vivo and Chemically Compatible in Solution. *PAIN MEDICINE* 2015;16(186-198

Agents: Bupivacaine; clonidine; dexamethasone **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, albino, CD[SD]); no stress (see pg. 192); post op. care (IM butorphanol tartrate 0.05 mg/kg, ceftiofur sodium 5 mg/kg); stability verified by (pg. 195); used polyurethane catheter 0.5mm ID 0.9 mmOD; pumps removed after 1 week; dose (66.6 ug/mL)

Q4343: W. Cao, *et al.* A Salt-Induced Reno-Cerebral Reflex Activates Renin-Angiotensin Systems and Promotes CKD Progression. *JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY* 2015;26(1619-1633

Agents: Losartan; clonidine; tempol; hydralazine **Vehicle:** PBS; CSF, artificial; **Route:** CSF/CNS; intragastric; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 5 weeks old, 5/6x nephrectomy); dose-response (pg 1627); cardiovascular; bp measured using catheter;

P6722: A. Quartilho, *et al.* Production of paradoxical sensory hypersensitivity by alpha₂-adrenoreceptor agonists. *Anesthesiology* 2004;100(6):1538-1544

Agents: Clonidine; MK-801; dexmedetomidine; idazoxan **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal, lumbar); SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;

ALZET Comments: Comparison of IT injections vs. IT and SC mp; idazoxan and MK-801 infused intrathecally in a separate infusion

10. Digoxin and digoxin

Q5206: B. Sjogren, *et al.* Digoxin-Mediated Upregulation of RGS2 Protein Protects against Cardiac Injury. *J Pharmacol Exp Ther* 2016;357(2):311-9

ALZET Comments: Digoxin; DMSO; saline; SC; Mice; 2002; 3 days; 7 days; 10 days; Controls received mp w/ vehicle; animal info (male, C57BL6J or RGS2 -/-, 8-18 weeks old); 0.04% DMSO used; dependence; pumps primed overnight in 37C saline; Dose (2 ug/kg/day);.

Q5344: U. Eskiocak, *et al.* Synergistic effects of ion transporter and MAP kinase pathway inhibitors in melanoma. *Nat Commun* 2016;7(12336



ALZET Comments: Digoxin; Promethylcellulose, Tween80, DMSO; SC; mice; Controls received mp w/ vehicle; animal info (NSG mice); 0.5% used Promethylcellulose, 0.2% Tween80 used, 5% DMSO; cancer (xenograft models); dose-response (pg. 14); Dose (10 mg/kg/day);.

Q4508: C. Disdier, *et al.* Tissue biodistribution of intravenously administrated titanium dioxide nanoparticles revealed blood-brain barrier clearance and brain inflammation in rat. *Particle and Fibre Toxicology* 2015;12(U1-U20)

ALZET Comments: Atenolol; digoxin; prazosin; PEG 200; DMSO; SC; Rat; 2001D; Animal info (male, Fisher F344, 8 weeks old, 180-250g); 50% PEG 200 used; 50% DMSO used;.

Q2688: B. Sjoegren, *et al.* Cardiotonic Steroids Stabilize Regulator of G Protein Signaling 2 Protein Levels. *MOLECULAR PHARMACOLOGY* 2012;82(3):500-509

ALZET Comments: Digoxin; DMSO; saline; SC; Mice; 2002; 7 days; Control animals received mp w/ vehicle; animal info (C57BL/6, male, 8-13 wks old); 0.4% DMSO used.

R0295: M. P. Blaustein, *et al.* How NaCl raises blood pressure: a new paradigm for the pathogenesis of salt-dependent hypertension. *American Journal of Physiology-Heart and Circulatory Physiology* 2012;302(5):H1031-H1049

ALZET Comments: Digoxin; ouabain; Saline; SC; Rat; 42 days; Controls received mp w/ vehicle; animal info (normal); blood pressure measured via tail cuff.]

11. Doxazosin

Q6678: J. Kim, *et al.* Renal nerves drive interstitial fibrogenesis in obstructive nephropathy. *J Am Soc Nephrol* 2013;24(2):229-42

ALZET Comments: Doxazosin; Atipamezole; Metoprolol; ICI118551; L748337; BRL44408; Imiloxan; Spiroxatine; PBS; DMSO; IP; Mice; 10 days; Dose (doxazosin (α 1-AR antagonist, 12 mg/kg/d), atipamezole (α 2-AR antagonist, 2.4mg/kg/d), metoprolol (β 1-AR antagonist, 12 mg/kg/d), ICI118551 (β 2-AR antagonist, 2.4 mg/kg/d), L748337 (β 3-AR antagonist, 2.4 mg/kg/d), BRL44408 (α 2A-AR antagonist, 12 mg/kg/d), imiloxan (α 2B-AR antagonist, 12 mg/kg/d), spiroxatine (α 2C-AR antagonist, 12mg/kg/d)); 10% DMSO used; animal info (8-10 week old male 129S1/SvlmJ mice);.

P6787: M. Yono, *et al.* Doxazosin treatment causes differential alterations of α 1-adrenoceptor subtypes in the rat kidney, heart and aorta. *LIFE SCIENCES* 2004;75(21):2605-2614

ALZET Comments: Doxazosin; DMSO; SC; Rat; 12 weeks; Controls received mp w/ vehicle; functionality of mp verified by plasma doxazosin levels; long-term study; antihypertensive; 50% DMSO; doxazosin supplemented orally in drinking water.

P7070: H. J. Foster, *et al.* Effects of chronic administration of doxazosin on α 1-adrenoceptors in the rat prostate. *Journal of Urology* 2004;172(6):2465-2470

ALZET Comments: Doxazosin; DMSO; SC; Rat; 8,12 weeks; Controls received mp w/ vehicle; dose-response (table 2); long-term study; cancer (prostatic hyperplasia); 50% DMSO; due to limitations in solubility mp was combined with oral dosing to deliver higher doses.

P3785: E. M. van Kleef, *et al.* Doxazosin blocks the angiotensin II-induced smooth muscle cell DNA synthesis in the media, but not in the neointima of the rat carotid artery after balloon injury. *Cardiovasc. Res* 1996;31(324-330)

ALZET Comments: Angiotensin II, [val 5]; Doxazosin; Uridine, bromodeoxy-; Saline; DMSO;; SC;; Rat;; 2002; 2ML1;; 2 weeks;; controls received mp w/vehicle; 2ML1 pumps replaced after 1 week; antihypertensive; cardiovascular; multiple pumps per animal (2) - 1 w/drug, 1 w/BrdU.



12. Enalapril

Q5520: H. Zheng, *et al.* Centrally mediated erectile dysfunction in rats with type 1 diabetes: role of angiotensin II and superoxide. *J Sex Med* 2013;10(9):2165-76

ALZET Comments: Enalapril maleate, Losartan, Tempol; CSF, artificial; CSF/CNS (ventricle); Rat; 1003D; 14 days; Controls received mp w/ aCSF; ALZET brain infusion kit 2 used; Enalapril is an ACE inhibitor; Losartan is an ANG II AT1 receptor antagonist; tempol is a SOD mimetic; Therapeutic indication (erectile dysfunction); Dose: Enalapril (0.5 mg/m), losartan (2 mg/mL), tempol (50 mg/mL);.

Q2220: S. Bae, *et al.* Preventing progression of cardiac hypertrophy and development of heart failure by paricalcitol therapy in rats. *Cardiovascular Research* 2011;91(4):632-639

ALZET Comments: Enalapril; SC; Rat; 4 weeks; Controls received vehicle injections; animal info (HSS, Harlan Sprague Dawley); post op. care (meloxicam); low-dose enalapril at 90 mg/day;.

P8202: M. Hamai, *et al.* Comparison of inhibitory action of candesartan and enalapril on brain ischemia through inhibition of oxidative stress. *Neuropharmacology* 2006;51(4):822-828

ALZET Comments: Candesartan; enalapril; IP; Mice; 1002; 10 days; Dose-response (fig.1); cardiovascular; ischemia (cerebral, induced by MCAO); animal info (male, C57BL/6J, 10 wks old); neurology.

P4840: C. J. Blais, *et al.* Effects of the vasopeptidase inhibitor omapatrilat on cardiac endogenous kinins in rats with acute myocardial infarction. *Peptides* 2001;22(953-962

ALZET Comments: Enalapril; Omapatrilat;; Saline;; SC;; Rat;; 1007D;; 5 days;; Controls received mp w/ vehicle; functionality of mp verified by serum ACE inhibition; cardiovascular; antihypertensive; omapatrilat is a vasopeptidase inhibitor; Enalapril is an Angiotensin Converting Enzyme (ACE) inhibitor;.

P2744: V. J. D. da Silva, *et al.* Chronic converting enzyme inhibition facilitates baroreceptor resetting to hypertensive levels. *Hypertension* 1994;23(1 Supp):168-172

ALZET Comments: Enalapril; Hoe 140; SC; Rat; 2001; 7 days; comparison of oral dosing vs. mp; enzyme inhibitor; enalapril is an antihypertensive.

13. Enalaprilat

Q3528: Y. M. Kang, *et al.* Chronic infusion of enalaprilat into hypothalamic paraventricular nucleus attenuates angiotensin II-induced hypertension and cardiac hypertrophy by restoring neurotransmitters and cytokines. *TOXICOLOGY AND APPLIED PHARMACOLOGY* 2014;274(3):436-444

ALZET Comments: Angiotensin II; enalaprilat; Saline; CSF, artificial; SC; CSF/CNS (paraventricular nucleus); Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, adult, 275-300g); functionality of mp verified by increased bp; post op. care (buprenorphine); tissue perfusion (bilateral paraventricular nucleus); cardiovascular; peptides; antihypertensive; bp measured using tail-cuff; pumps primed in 37C saline; used wound clips; enalaprilat is an ACE inhibitor; Plastics One bilateral PVN cannulae; bilateral infusion.

R0364: R. Gatti, *et al.* Enhanced Cough, Animal Models. *Methods in Pharmacology and Toxicology* 2012;1(17):343-360

ALZET Comments: Enalaprilat; Lisinopril; Imidapril; Saline; IP; Guinea pig; 2ML1; Dose (enalaprilat (0.1, 0.5, 1, 5, 10, 20 mg/ml), lisinopril (0.1, 0.5, 1, 5, 10, 20 mg/ml), imidapril (1, 5, 10, 20, 30 mg/ml)); Controls received mp w/ vehicle; enzyme inhibitor (angiotensin-converting-enzyme); cardiovascular;.

P5889: D. Lamireau, *et al.* Altered vascular function in fetal programming of hypertension. *Stroke* 2002;33(12):2992-2998

ALZET Comments: Enalaprilat; Saline; Rat (pregnant); 1 week; Controls received mp w/ vehicle; enzyme inhibitor (ACE).



P4975: Y. Sawada, *et al.* Comparative study of effects of angiotensin II receptor antagonist, KD 3-671, and angiotensin converting enzyme inhibitor, enalaprilat, on cough reflex in guinea pig. *European Journal of Drug Metabolism and Pharmacokinetics* 2001;26(1/2):47-52

ALZET Comments: KD3-671; enalaprilat; Sodium phosphate; Sodium carbonate; IP; Guinea pig; 2ML1; functionality of mp verified by plasma drug levels; antihypertensive dose-response (fig 2. p. 50); KD3-671 is an angiotensin II antagonist which causes persistent hypotension; enalaprilat is an angiotensin converting enzyme inhibitor, prevents inactivation of bradykinin.

P4922: K. M. Denton, *et al.* Chronic angiotensin converting enzyme inhibition enhances renal vascular responsiveness to acetylcholine in anaesthetized rabbits. *Journal of Hypertension* 2001;19(1497-1503)

ALZET Comments: Enalaprilat; PBS; SC; rabbit; 2ML4; 6 weeks; controls received "dummy pump"; pumps replaced after 4 weeks; cardiovascular; antihypertensive; dummy pump implanted in controls was PVC plastic balloon of the same size and shape as pump. Enalaprilat is an Angiotensin Converting Enzyme (ACE) inhibitor.

P3773: A. K.-. Laflamme, *et al.* Effects of renin-angiotensin blockade on sympathetic reactivity and B-adrenergic pathway in

14. Eprosartan

Q0529: S. Mukaddam-Daher, *et al.* Hemodynamic and Cardiac Effects of Chronic Eprosartan and Moxonidine Therapy in Stroke-Prone Spontaneously Hypertensive Rats. *Hypertension* 2009;53(5):775-U58

ALZET Comments: Moxonidine; eprosartan; Saline; NaOH; HCl; SC; Rat; 2004; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (SP-SHR, 14 wks old, 250-275 g); antihypertensive; pumps replaced after 4 weeks; long-term study; multiple pumps per animal (2); moxonidine or eprosartan were infused separately or in combination.

P7557: T. Karram, *et al.* Effects of spironolactone and eprosartan on cardiac remodeling and angiotensin-converting enzyme isoforms in rats with experimental heart failure. *American Journal of Physiology-Heart and Circulatory Physiology* 2005;289(4):H1351-H1358

ALZET Comments: Spironolactone; eprosartan; PEG 400; sodium bicarbonate; IP; Rat; 2ML2; 2ML4; 14, 28 days; Controls received mp w/ vehicle; functionality of mp verified by plasma levels (H1353); cardiovascular; animal info (male, Wistar 300 g); aldosterone antagonist; ANG II receptor antagonist.

P7356: A. Dendorfer, *et al.* Peripheral sympatholytic actions of four AT₁ antagonists: are they relevant for long-term antihypertensive efficacy? *Journal of Hypertension* 2005;23(10):1861-1867

ALZET Comments: Candesartan; losartan; eprosartan; irbesartan; NaOH; IP; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; functionality of mp verified by blood pressure taken; dose-response (fig. 1); cardiovascular; antihypertensive; animal info (male, SHR, 10 wk old, 250-280 g).

P7583: Y. Chen, *et al.* Heat shock treatment suppresses angiotensin II-induced SP-1 and AP-1 and stimulates Oct-1 DNA-binding activity in heart. *INFLAMMATION RESEARCH* 2005;54(8):338-343

ALZET Comments: Angiotensin II; eprosartan; norepinephrine; Saline; SC; IP; IV (jugular); Rat; 2001; 2ML2; 3, 7 days; Controls received mp w/ vehicle or sham HS surgery; cardiovascular; peptides; animal info (male, Sprague-Dawley 280-310 g).

P6492: Y. Chen, *et al.* Heat shock treatment protects against angiotensin II-induced hypertension and inflammation in aorta. *CELL STRESS & CHAPERONES* 2004;9(1):99-107

ALZET Comments: Angiotensin II; eprosartan; norepinephrine; Saline; SC; IP; IV (vena cava); Rat; 2001; 2002; 2ML2; 1,3,5,7,11,14 days; Controls received empty mp for 7 days; functionality of mp verified by SBP; cardiovascular; peptides.



15. Felodipin

P5185: X. J. Zhou, *et al.* Defective calcium signalling in uraemic platelets and its amelioration with long-term erythropoietin therapy. *NEPHROLOGY DIALYSIS TRANSPLANTATION* 2002;17(992-997)

ALZET Comments: Felodipine; Rat; 6 weeks; Cardiovascular; antihypertensive; calcium channel blocker.

P3960: E. M. A. Mervaala, *et al.* Influence of dietary salts on the cardiovascular effects of low-dose combination of ramipril and felodipine in spontaneously hypertensive rats. *British J. Pharmacol* 1998;123(195-204)

ALZET Comments: Felodipine; Water, distilled; SC; Rat; 2ML4; 4 weeks; controls received mp w/ NaCl; antihypertensive; cardiovascular.

P3540: E. M. A. Mervaala, *et al.* Cardiovascular effects of a low-dose combination of ramipril and felodipine in spontaneously hypertensive rats. *Br. J. Pharmacol* 1997;121(503-510)

ALZET Comments: Felodipine; SC; Rat; 2ML4; 4 weeks; controls received mp w/ saline; antihypertensive; cardiovascular.

16. Furosemide

Q6899: N. Tokonami, *et al.* Uromodulin is expressed in the distal convoluted tubule, where it is critical for regulation of the sodium chloride cotransporter NCC. *Kidney Int* 2018;94(4):701-715

ALZET Comments: Furosemide; DMSO; Saline; SC; Mice; 2001; 50% DMSO used; animal info (8–12-week-old C57BL6J male mice);.

Q4455: R. W. Hunter, *et al.* Hypertrophy in the Distal Convoluted Tubule of an 11-Hydroxysteroid Dehydrogenase Type 2 Knockout Model. *JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY* 2015;26(1537-1548)

ALZET Comments: Uridine, bromodeoxy-; furosemide; DMSO; SC; Mice; 1007D; 2001; 7 days; Animal info (WT or Hsd1 1b2 -/-); 50% DMSO used; pumps primed overnight in 37C saline;.

Q3156: I. M. Schiessl, *et al.* Dietary salt intake modulates differential splicing of the Na-K-2Cl cotransporter NKCC2. *American Journal of Physiology-Renal Physiology* 2013;305(8):F1139-F1148

ALZET Comments: Furosemide; Angiotensin II; NaCl; Acetic Acid; SC; Mice; 1002; 7 days; Controls received mp w/ vehicle; animal info (male, C57BL6, 8-10 weeks); functionality of mp verified by increased arterial BP; cardiovascular; bp measured using tail-cuff;.

Q2841: S. Seidel, *et al.* Annexin A1 modulates macula densa function by inhibiting cyclooxygenase 2. *American Journal of Physiology-Renal Physiology* 2012;303(6):F845-F854

ALZET Comments: Furosemide; Rat; 2ML1; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male).

Q1616: H. N. Lang, *et al.* Chronic Reduction of Endocochlear Potential Reduces Auditory Nerve Activity: Further Confirmation of an Animal Model of Metabolic Presbycusis. *JARO-JOURNAL OF THE ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY* 2010;11(3):419-434

ALZET Comments: Furosemide; Ear (round window niche); Gerbil; 2004; 4 weeks; Controls were untreated; animal info (3-6 mo old, young adult); good methods, pg 421; tissue perfusion (round window).

17. Guanabenz

Q4951: F. G. Vieira, *et al.* Guanabenz Treatment Accelerates Disease in a Mutant SOD1 Mouse Model of ALS. *PLoS One* 2015;10(8):e0135570

ALZET Comments: Guanabenz acetate; Ethanol; water; propylene glycol; SC; Mice; 2004; Controls received mp w/ vehicle; animal info (SOD1-G93A); pumps replaced every 28 days; dose-response (pg 4); neurodegenerative (amyotrophic lateral



sclerosis); post op. care (antibiotic ointment; buprenorphine 0.1 mg/kg); used lot#10284-12; Dose (0.45, 1.5, or 4.5 mg/kg/day);.

P2311: C. A. Hamilton, *et al.* Do centrally-acting antihypertensive drugs act at non-adrenergic as well as alpha-2 adrenoceptor sites? Clin. and Exper. Hyper. -Theory and Practice 1992;A14(5):815-835

ALZET Comments: Guanabenz; Clonidine; Rilmenidine; Water, sterile; Ethanol; IV (femoral); rabbit; 6 days; controls received mp w/ vehicles; agents are antihypertensives; mp and catheter embedded in thigh muscle; antihypertensive.

18. Hydralazine

Q6070: P. Lemkens, *et al.* Dual NEP/ECE inhibition improves endothelial function in mesenteric resistance arteries of 32-week-old SHR. Hypertens Res 2017;40(8):738-745

ALZET Comments: SOL1, Losartan, Hydralazine; Saline; SC; Rat; 2ML4; 4 weeks; Dose: SOL1 (50 mg/kg/d), Losartan (20 mg/kg/d), hydralazine (9 mg/kg/d); Controls received a dummy device (polyethylene tube of the same size as the 2ML4 pumps); animal info (28 week old SHR); enzyme inhibitor (endothelin-converting enzyme; neutral endopeptidase); cardiovascular;.

Q4476: H. Kawahata, *et al.* Continuous infusion of angiotensin II modulates hypertrophic differentiation and apoptosis of chondrocytes in cartilage formation in a fracture model mouse. HYPERTENSION RESEARCH 2015;38(382-393

ALZET Comments: Angiotensin II; olmesartan; hydralazine; Saline; sodium bicarbonate; SC; Mice; 2004; 2 weeks; 4 weeks; Controls received mp w/ vehicle; animal info (female, C57BL/6NJ, 20-22g); dose-response (p. 385); cardiovascular; antihypertensive; peptides; bp measured using tail cuff;.

Q4343: W. Cao, *et al.* A Salt-Induced Reno-Cerebral Reflex Activates Renin-Angiotensin Systems and Promotes CKD Progression. JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY 2015;26(1619-1633

ALZET Comments: Losartan; clonidine; tempol; hydralazine; PBS; CSF, artificial; CSF/CNS; intragastric; Rat; 2 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 5 weeks old, 5/6x nephrectomy); dose-response (pg 1627); cardiovascular; bp measured using catheter;.

Q1307: Y. Sakurai-Yamashita, *et al.* Lercanidipine Rescues Hippocampus Pyramidal Neurons from Mild Ischemia-Induced Delayed Neuronal Death in SHRSP. Cellular and Molecular Neurobiology 2011;31(4):561-567

ALZET Comments: Hydralazine; lisinopril; valsartan; SC; Rat; 1 week; 14 days; Controls received mp w/ vehicle; animal info (SHRHP, 16 wks old).

Q1140: M. Iwamoto, *et al.* Connective tissue growth factor induction in a pressure-overloaded heart ameliorated by the angiotensin II type 1 receptor blocker olmesartan. HYPERTENSION RESEARCH 2010;33(12):1305-1311

ALZET Comments: Olmesartan; hydralazine; SC; Rat; 2ML2; 14 days; Controls received mp w/ saline; animal info (male, Sprague-Dawley, 250-300 g); antihypertensive.

19. Hydrochlorothiazide

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. Am J Physiol Regul Integr Comp Physiol 2016;310(R115-R124

ALZET Comments: Norepinephrine; hydrochlorothiazide; losartan; Saline; DMSO; SC; Rat; 2ML2; 14 days; 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);.

Q2139: A. Ashek, *et al.* Activation of Thiazide-Sensitive Co-Transport by Angiotensin II in the cyp1a1-Ren2 Hypertensive Rat. PLoS One 2012;7(4):U1890-U1899



ALZET Comments: Hydrochlorothiazide; spironolactone; losartan; Saline; DMSO; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; animal info (male, cyp1a1-Ren2 TGR, Fischer 344, 12-14 wks old); 50% DMSO used.

P9509: H. R. Jang, *et al.* Effects of Thiazide on the Expression of TRPV5, Calbindin-D_{28K}, and Sodium Transporters in Hypercalciuric Rats. *Journal of Korean Medical Science* 2009;24(1):S161-S169

ALZET Comments: Hydrochlorothiazide; Ethanolamine; SC; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 6 wks old, 160-180 g.).

P8602: K. Y. Na, *et al.* Chronic furosemide or hydrochlorothiazide administration increases H⁺-ATPase B1 subunit abundance in rat kidney. *American Journal of Physiology- Renal Physiology* 2007;292(6):F1701-F1709

ALZET Comments: Furosemide; hydrochlorothiazide; Ethanolamine; SC; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; no stress (see pg. F1703-4); animal info (male, Sprague-Dawley, pathogen-free, 170-230 grams).

20. Imidapril

Q1882: R. Ishibashi, *et al.* Imidapril Inhibits Cerebral Aneurysm Formation in an Angiotensin-Converting Enzyme-Independent and Matrix Metalloproteinase-9-Dependent Manner. *Neurosurgery* 2012;70(3):722-730

ALZET Comments: Imidapril hydrochloride; DMSO; IP; Rat; 2ML4; 1 month; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 7 wks old); enzyme inhibitor (ACE, angiotensin converting enzyme).

R0364: R. Gatti, *et al.* Enhanced Cough, Animal Models. *Methods in Pharmacology and Toxicology* 2012;1(17):343-360

ALZET Comments: Enalaprilat; Lisinopril; Imidapril; Saline; IP; Guinea pig; 2ML1; Dose (enalaprilat (0.1, 0.5, 1, 5, 10, 20 mg/ml), lisinopril (0.1, 0.5, 1, 5, 10, 20 mg/ml), imidapril (1, 5, 10, 20, 30 mg/ml)); Controls received mp w/ vehicle; enzyme inhibitor (angiotensin-converting-enzyme); cardiovascular;

P5298: Y. Kurosawa, *et al.* Tissue Angiotensin-converting enzyme activity plays an important role in pressure overload-induced cardiac fibrosis in rats. *J Cardiovasc. Pharmacol* 2002;39(4):600-609

ALZET Comments: Imidapril; Saline; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; cardiovascular; enzyme inhibitor; imidapril is an angiotensin-converting enzyme inhibitor.

P5293: M. Kakoki, *et al.* Effects of hypertension, diabetes mellitus, and hypercholesterolemia on endothelin type B receptor-mediated nitric oxide release from rat kidney. *Circulation* 1999;99(9):1242-1248

ALZET Comments: Imidapril; SC; Rat; 2ML4; 4 weeks; Cardiovascular; enzyme inhibitor (ACE inhibitor).

P4062: Y. Hirata, *et al.* Nitric oxide release from kidneys of hypertensive rats treated with imidapril. *Hypertension* 1996;27(pt 2):672-678

ALZET Comments: Imidapril; Saline, sterile; SC; Rat; 2ML4; 4 weeks; controls received mp w/vehicle; dose-response (1 or 10 mg/kg); antihypertensive; cardiovascular.

21. Isoproterenol

Q8614: S. Kumari, *et al.* Musa balbisiana Fruit Rich in Polyphenols Attenuates Isoproterenol-Induced Cardiac Hypertrophy in Rats via Inhibition of Inflammation and Oxidative Stress. *Oxid Med Cell Longev* 2020;2020(7147498)

Agents: Isoproterenol **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 14 days;

ALZET Comments: Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (Male Sprague- Dawley rats (250 g)); cardiovascular;

Q8520: N. Gupta, *et al.* Targeted Inhibition of Gut Microbial Trimethylamine N-Oxide Production Reduces Renal Tubulointerstitial Fibrosis and Functional Impairment in a Murine Model of Chronic Kidney Disease. *Arterioscler Thromb Vasc Biol* 2020;40(5):1239-1255



Agents: Isoproterenol **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Dose (30 mg/kg per day); animal info (male C57BL/6J mice); cardiovascular;

Q8481: W. Gao, *et al.* HTR2A promotes the development of cardiac hypertrophy by activating PI3K-PDK1-AKT-mTOR signaling. *Cell Stress Chaperones* 2020;25(6):899-908

Agents: Isoproterenol **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Dose (50 mg/kg/day); Controls received mp w/ vehicle; animal info (8–12-week-old male C57BL/6 mice); Isoproterenol aka ISO; cardiovascular;

Q8480: W. Gao, *et al.* Carboxypeptidase A4 promotes cardiomyocyte hypertrophy through activating PI3K-AKT-mTOR signaling. *Biosci Rep* 2020;40(5):

Agents: Isoproterenol **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Dose (50 mg/kg/day); Controls received mp w/ vehicle; animal info (8–12 weeks old male C57BL/6 mice); Isoproterenol aka ISO; cardiovascular;

Q8455: T. R. Eijgenraam, *et al.* The phospholamban p.(Arg14del) pathogenic variant leads to cardiomyopathy with heart failure and is unresponsive to standard heart failure therapy. *Sci Rep* 2020;10(1):9819

Agents: Isoproterenol **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;
ALZET Comments: Dose (30 mg/kg/day); animal info (adult (10-week-old) PLN-R14Δ/+ mice); cardiovascular;

22. Ketanserin

P9838: O. Lairez, *et al.* Genetic deletion of MAO-A promotes serotonin-dependent ventricular hypertrophy by pressure overload. *Journal of Molecular and Cellular Cardiology* 2009;46(4):587-595

ALZET Comments: Ketanserin; M100907; DMSO; saline; hydrochloric acid; IP; Mice (transgenic); 4 weeks; Controls received mp w/ vehicle; animal info (male, Tg8 MAO-A KO, wt, 10 wks old); 10% DMSO used; 5-HT_{2A} receptor antagonists.

P5895: H. Jorgensen, *et al.* Serotonergic involvement in stress-induced vasopressin and oxytocin secretion. *European Journal of Endocrinology* 2002;147(6):815-824

ALZET Comments: Ketanserin; Ly-53857; ICS-205930; Saline; CSF/CNS; Rat; 2ML4; 24 hours; Stylet used; pump implanted IP; drugs were 5-ht antagonists.

P4222: Q. Gu, *et al.* Involvement of serotonin in developmental plasticity of kitten visual cortex. *Eur. J. Neurosci* 1995;7(11):1146-1153

ALZET Comments: Dihydroxytryptamine, 5,7-; Methysergide; Ketanserin; Saline; Ascorbic acid; CSF/CNS (visual cortex); cat (kitten); 2001; 3,7 days; controls received mp w/saline; 5,7-dihydroxytryptamine is a neurotoxin; serotonin receptor blockers; antihypertensive.

P2499: G. Balasubramaniam, *et al.* Differences in the chronic hypotensive mechanism of action of ketanserin in spontaneously hypertensive and wistar-kyoto rats. *J. Hypertens* 1994;12(7-14)

ALZET Comments: Ketanserin; Dextrose; IV (femoral); Rat; 2ML1; 7 days; controls received mp w/ vehicle; antihypertensive.

P2173: G. Balasubramaniam, *et al.* Differences in the acute and chronic antihypertensive mechanism of action of ketanserin in spontaneously hypertensive rats. *J. Pharmacol. Exp. Ther* 1993;264(1):129-134

ALZET Comments: Ketanserin; Dextrose, isotonic; IV (femoral); Rat; 2ML1; 7 days; antihypertensive.



23. Losartan

Q8409: Y. M. Chao, *et al.* Anomalous AMPK-regulated angiotensin AT1R expression and SIRT1-mediated mitochondrial biogenesis at RVLM in hypertension programming of offspring to maternal high fructose exposure. *J Biomed Sci* 2020;27(1):68

ALZET Comments: Losartan **Vehicle:** CSF, Artificial; **Route:** CSF/CNS (cistern magna); **Species:** Rat; **Pump:** 1007D; **Duration:** 4 weeks; **ALZET Comments:** Dose (3 µg·µL⁻¹·h⁻¹); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats at age of 10 weeks); functionality of mp verified by drainage of cerebrospinal fluid; Blood pressure measured via tail-cuff method; 130 mmHg - 160 mmHg; cardiovascular;

Q7063: T. Nozaki, *et al.* The angiotensin II type I receptor antagonist losartan retards amygdala kindling-induced epileptogenesis. *Brain Res* 2018;1694(121-128)

ALZET Comments: Losartan; Saline; CSF/CNS (lateral ventricle); Rat; 2004; 3 weeks; Dose (0.5 mg/kg/day; 1.0 mg/kg/day; 3.0 mg/kg/day); Controls received mp w/ vehicle;

Q7194: T. Kishi. Disruption of Central Antioxidant Property of Nuclear Factor Erythroid 2-Related Factor 2 Worsens Circulatory Homeostasis with Baroreflex Dysfunction in Heart Failure. *Int J Mol Sci* 2018;19(3):

ALZET Comments: Losartan, Butylhydroquinone, tert; CSF, artificial; CSF/CNS (lateral ventricle); Rat; 2002; 14 days; Dose (1 mg/kg/day-Losartan, 1mM -t-BHQ); Controls received mp w/ vehicle; animal info (Sprague-Dawley, 14-16 week old, 450-650 g, Male); Losartan is an AT1R blocker, tBHQ is a Nrf2 activator; cardiovascular;

Q7186: K. L. Jackson, *et al.* Circadian Differences in the Contribution of the Brain Renin-Angiotensin System in Genetically Hypertensive Mice. *Front Physiol* 2018;9(231)

ALZET Comments: Losartan; Ringer's solution; CSF/CNS (lateral ventricle), SC; CSF/CNS (lateral ventricle), SC; 1002; 7 days; Dose (22 nmol/h); animal info (BPH/2J mice); behavioral testing (MAP responses, dirty cage-switch stress); Brain coordinates (0.5mm posterior from bregma, 1.2mm lateral from the midline, and 2.2mm ventral to the skull surface); Right angle cannula (30G) used; 1.0 cheese-head screws and dental cement used ;

Q6941: W. Cao, *et al.* A renal-cerebral-peripheral sympathetic reflex mediates insulin resistance in chronic kidney disease. *EBioMedicine* 2018;37(281-293)

ALZET Comments: Losartan; Tempol; Clonidine; CSF, artificial; CSF/CNS (lateral ventricle); Rat; Dose (1 mg/kg/day losartan; 4.5 µg/kg/day tempol; 5.76 µg/kg/day clonidine); Controls received mp w/ vehicle; animal info (Five-week-old male Sprague-Dawley rats); Therapeutic indication (5/6 nephrectomy);

24. Metoprolol

Q6485: J. Skrzypecki, *et al.* Renal denervation decreases blood pressure and renal tyrosine hydroxylase but does not augment the effect of hypotensive drugs. *Clin Exp Hypertens* 2017;39(3):290-294

ALZET Comments: Losartan; Metoprolol; Indapamide; Saline; SC; Rat; 2ML2; 2ML4; 14 days; 28 days; Dose (Losartan: 10 mg/kg/day; Metoprolol: 10 mg/kg/day; Indapamide: 1 mg/kg/day); Controls received mp w/ vehicle;

Q6264: T. Feridooni, *et al.* Effects of beta-adrenergic receptor drugs on embryonic ventricular cell proliferation and differentiation and their impact on donor cell transplantation. *Am J Physiol Heart Circ Physiol* 2017;312(5):H919-H931

ALZET Comments: Isoproterenol; Metoprolol; SC; Mice; 2001; 3 days; Dose (Isoproterenol: 0.025 g/ml; Metoprolol: 0.0684 g/ml); animal info (CD1 and C57BL/6 (BL6) mice);

Q5500: L. Yang, *et al.* Loss of beta-adrenergic-stimulated phosphorylation of CaV1.2 channels on Ser1700 leads to heart failure. *Proc Natl Acad Sci U S A* 2016;113(49):E7976-E7985

ALZET Comments: Metoprolol; SC; Mice; 4 weeks; Controls received mp w/ vehicle; animal info (SA or WT, 3 months old); cardiovascular; Dose (2.5 mg/kg/hr);



Q4145: M. A. Ulleryd, *et al.* Metoprolol Reduces Proinflammatory Cytokines and Atherosclerosis in ApoE(-/-) Mice. BIOMED RESEARCH INTERNATIONAL 2014;;(U1-U7

ALZET Comments: Metoprolol; Saline; SC; Mice; 1002; 2006; 11 weeks; Animal info (male, C57BL6J or ApoE -/-, 12 weeks old); functionality of mp verified by plasma levels with mass spectrometry; pumps replaced every 6 weeks; cardiovascular; immunology; antihypertensive;.

Q3379: V. Saran, *et al.* Combined metoprolol and ascorbic acid treatment prevents intrinsic damage to the heart during diabetic cardiomyopathy. Canadian Journal of Physiology and Pharmacology 2014;92(827-837

ALZET Comments: Metoprolol; SC; Rat; 2ML4; 2006; Animal info (male, Wistar, 200-220 g).

25. Minoxidil

P1899: Y.-J. Kuo, *et al.* Captopril increases norepinephrine spillover rate in conscious spontaneously hypertensive rats. J. Pharmacol. Exp. Ther 1991;258(1):223-231

ALZET Comments: Minoxidil HCl; Captopril; Enalaprilat; Acetic acid; Ethanol; Propylene glycol; Saline; Water; SC; Rat; 5 days; no comment posted; antihypertensive.

26. Moxonidine

Q5529: N. Honda, *et al.* Moxonidine-induced central sympathoinhibition improves prognosis in rats with hypertensive heart failure. J Hypertens 2013;31(11):2300-8; discussion 2308

ALZET Comments: Moxonidine; CSF, artificial; CSF/CNS (lateral ventricle); Rat; 2006; 42 days; Controls received mp w/ vehicle; ALZET brain infusion kit 2 used; Therapeutic indication (Heart failure); Dose (4 mmol/L);.

Q0906: A. M. Stabile, *et al.* Functional and molecular effects of imidazoline receptor activation in heart failure. LIFE SCIENCES 2011;88(11-12):493-503

ALZET Comments: Moxonidine; Saline, normal; SC; Hamster; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (BIO 14.6, male, 6, 10 m old).

Q0529: S. Mukaddam-Daher, *et al.* Hemodynamic and Cardiac Effects of Chronic Eprosartan and Moxonidine Therapy in Stroke-Prone Spontaneously Hypertensive Rats. Hypertension 2009;53(5):775-U58

ALZET Comments: Moxonidine; eprosartan; Saline; NaOH; HCl; SC; Rat; 2004; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (SP-SHR, 14 wks old, 250-275 g); antihypertensive; pumps replaced after 4 weeks; long-term study; multiple pumps per animal (2); moxonidine or eprosartan were infused separately or in combination.

P6728: R. Van Kerckhoven, *et al.* Pharmacological therapy can increase capillary density in post-infarction remodeled rat hearts. Cardiovascular Research 2004;61(3):620-629

ALZET Comments: Moxonidine; Saline, acidified; SC; Rat; 2001; 21 days; Pumps replaced every 7 days; cardiovascular.

R0228: S. Mukaddam-Daher, *et al.* Imidazoline receptors in the heart: a novel target and a novel mechanism of action that involves atrial natriuretic peptides. Brazilian Journal of Medical and Biological Research 2004;37(8):1239-1245

ALZET Comments: Moxonidine; Saline; SC; 2ML2; 2ML4; 1,4 days; Controls received mp w/ vehicle; dose-response (Fig.2); cardiovascular; antihypertensive; review.

27. Nifedipine

Q0062: P. Fossat, *et al.* Knockdown of L Calcium Channel Subtypes: Differential Effects in Neuropathic Pain. Journal of Neuroscience 2010;30(3):1073-1085



ALZET Comments: Nicardipine; CSF/CNS (intrathecal); Rat; 1007D; 5 days; Animal info (adult, Wistar, 250-300 g.); PE-10 catheter used.

Q0590: E. A. Ingram, *et al.* Prolonged infusion of inhibitors of calcineurin or L-type calcium channels does not block mossy fiber sprouting in a model of temporal lobe epilepsy. *Epilepsia* 2009;50(1):56-64

ALZET Comments: Nicardipine; FK506; cyclosporin A; DMSO; ethanol; fluorescein; CSF/CNS (dorsal left dentate gyrus); Rat; 2004; 28 days; Controls were treated identically without status epilepticus; animal info (34-52 day old, male, Sprague-Dawley, status epilepticus); functionality of mp verified by fluorescein labeling; ALZET brain infusion kit 2 used; 50% DMSO used; 15% ethanol used.

P9054: Q. Hao, *et al.* Increased tissue perfusion promotes capillary dysplasia in the ALK1-deficient mouse brain following VEGF stimulation. *American Journal of Physiology-Heart and Circulatory Physiology* 2008;295(6):H2250-H2256

ALZET Comments: Hydralazine; nicardipine; CSF/CNS; Mice; 1002; 14 days; Controls received mp w/ saline; animal info (adult, male, ALK1 +/-); fig. 1 illustrates cannula placement; cannula placement verified by CBF measurements.

P4055: M. Kurooka, *et al.* High incidence of esophageal cancer in esophageal achalasia by the oral administration of N-amyl-N-methylnitrosamine and its prevention by nicardipine hydrochloride in mice. *Cancer Letters* 1998;127(55-61)

ALZET Comments: Nicardipine HCl; SC; mice; 2002; no duration posted; calcium-channel blocker; cancer; antihypertensive.

P1991: K. Hewitt, *et al.* Combined treatment with MK-801 and nicardipine reduces global ischemic damage in the gerbil. *Stroke* 1992;23(1):82-86

ALZET Comments: Nicardipine; SC; gerbil; 1003D; 3 days; no comment posted; antihypertensive; ischemia (cerebral).

28. Nifedipine

Q8043: S. Ikeda, *et al.* Blockade of L-type Ca(2+) channel attenuates doxorubicin-induced cardiomyopathy via suppression of CaMKII-NF-kappaB pathway. *Sci Rep* 2019;9(1):9850

Agents: Nifedipine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (9-10 weeks, C57BL/6J); Nifedipine aka L-type Ca2+ blocker ; gene therapy;

Q7519: Z. Gao, *et al.* Effects of Dissolution Medium pH and Simulated Gastrointestinal Contraction on Drug Release From Nifedipine Extended-Release Tablets. *J Pharm Sci* 2019;108(3):1189-1194

Agents: Nifedipine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Dose (30 mg, 60 mg); dependence;

Q3125: J. G. Yan, *et al.* The effect of calcium modulating agents on peripheral nerve recovery after crush. *Journal of Neuroscience Methods* 2013;217(1-2):54-62

Agents: Nifedipine; calcitonin **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2006; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ saline or sham only; animal info (3 month old, male, Sprague-Dawley 250-300g); functionality of mp verified by decrease in calcium levels; peptides; Picture of MP p56, Fig1A. MP Pump setup p56, Fig1B;

Q2251: Z. Tian, *et al.* Nifedipine increases energy expenditure by increasing PGC-1alpha expression in skeletal muscle. *HYPERTENSION RESEARCH* 2011;34(11):1221-1227

Agents: Nifedipine **Vehicle:** PEG 400; ethanol; water; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 4 months;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, eNOS KO); 15% PEG 400 used; 15% ethanol used; long-term study



Q0127: T. Kaimoto, *et al.* Nifedipine Inhibits Vascular Smooth Muscle Cell Dedifferentiation via Downregulation of Akt Signaling. *Hypertension* 2010;56(2):247-U133

Agents: Nifedipine **Vehicle:** Ethanol; **Route:** IV (jugular); **Species:** Rat; **Pump:** 2ML4; **Duration:** 3 weeks;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular; animal info (male, Sprague-Dawley, 12 weeks old, balloon injury model)

29. Nilvadipine

P3418: S. Kawamura, *et al.* Protective effect of nilvadipine on focal cerebral ischemia in spontaneously hypertensive rats. *Neurol. Med. Chir* 1996;36(151-155)

ALZET Comments: Nilvadipine; PEG; SC; Rat; 2ML1; 7 days; controls received vehicle infusion; antihypertensive; ischemia (cerebral).

30. pd123319

R0374: C. Shimbori, *et al.* The Role of Mast Cells in the Pathophysiology of Pulmonary Fibrosis. *Not Stated* 2019;135-173
Agents: TY-51469, H4R antagonist, MK-571, PD123319 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Dose: TY-51469 (0.1 or 1.0 mg/kg/day), H4R antagonist (40 mg/kg); PD123319 (0.5 or 5 mg/kg/d); animal info (ICR, C57BL/6 mice); TY-51469 is a Chymase inhibitor; enzyme inhibitor (Chymase); cardiovascular;

Q7364: M. E. Arce, *et al.* Age-Related Changes in Ang II Receptor Localization and Expression in the Developing Auditory Pathway. *Neurochem Res* 2019;44(2):412-420

Agents: Angiotensin II, AT2 antagonist PD123319 **Vehicle:** Saline; **Route:** Saline; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: Dose (1.0 mg/kg/day); Controls received mp w/ vehicle; animal info (Pregnant Wistar, 230-250 g); PD123319 aka AT2 antagonist; enzyme inhibitor (PD123319); neurodegenerative (Brain development);

Q7782: A. Chakrabarty, *et al.* Inflammatory Renin-Angiotensin System Disruption Attenuates Sensory Hyperinnervation and Mechanical Hypersensitivity in a Rat Model of Provoked Vestibulodynia. *J Pain* 2018;19(3):264-277

Agents: PD123319 difluoroacetate **Vehicle:** Water, distilled; **Route:** IP; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley rats, ~60 days, 190-200 g); behavioral testing (perivaginal mechanical sensitivity via Semmes-Weinstein monofilaments); PD123319 difluoroacetate aka PD; enzyme inhibitor (PD is an angiotensin II antagonist);

Q5654: B. A. Kemp, *et al.* AT2 Receptor Activation Prevents Sodium Retention and Reduces Blood Pressure in Angiotensin II-Dependent Hypertension. *Circulation Research* 2016;119(4):532-43

Agents: Dextrose, C21, PD-123319, Angiotensin II **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 1007D, 2001; **Duration:** 1 week;

ALZET Comments: Controls received mp w/ vehicle; animal info (12 weeks); good methods (p. 546); Multiple pumps per animal (2); Multiple pumps per animal (2); Intrarenal infusion; Therapeutic indication (Hypertension); Dose (C21: 60ng/kg/min, PD-123319: 10 ng/kg/min, Dextrose/AngII: 200 ng/kg/min);

Q6605: Angiotensin type II receptor protects cardiovascular functions at the onset of atherosclerosis in young apolipoprotein E-deficient mouse. *Journal of the American College of Cardiology* 2016;68(16):C175

Agents: Angiotensin II, PD123319 **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** 2002; **Duration:** 7 days;
ALZET Comments: Dose (12 µg/kg/hr Ang II, 10mg/kg/day PD123319); Controls received mp w/ vehicle; animal info (9-week-old male C57BL/6 and apoE(-/-)); PD123319 is a AT2R antagonist; cardiovascular;



31. Perindopril

Q4275: Z. Qu, *et al.* Effects of angiotensin-converting enzyme inhibition and bradykinin peptides in rats with myocardial infarction. *INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL PATHOLOGY* 2015;8(3410-3417

ALZET Comments: Perindopril; bradykinin; Saline; SC; Rat; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, Wister, 8-12 weeks old, 200-250 g); cardiovascular; peptides;.

P4534: J. Higaki, *et al.* In vivo evidence of the importance of cardiac angiotensin-converting enzyme in the pathogenesis of cardiac hypertrophy. *Arterioscler. Thromb. Vasc. Biol* 2000;20(428-434

ALZET Comments: Perindopril;; Saline; PEG 400;; IP;; Rat;; 3 days;; controls received mp w/vehicle; cardiovascular;.

P3146: Y. Tokita, *et al.* Role of the tissue renin-angiotensin system in the action of angiotensin-converting enzyme inhibitors. *P. S. E. B. M* 1995;208(391-396

ALZET Comments: Captopril; Perindopril; Saline; IP; Rat; 6 days; controls received mp with saline; antihypertensive.

P2387: J. M. Mathews, *et al.* B-adrenoceptor subtypes in the atrioventricular conducting system and myocardium of spontaneously hypersensitive rats: effects of angiotensin-converting enzyme inhibition by perindopril. *J. Cardiovasc. Pharmacol* 1994;23(691-697

ALZET Comments: Perindopril; Water; SC; Rat; 2002; 14 days; antihypertensive.

32. Pindolol

P4963: N. Haddjeri, *et al.* Effects of sustained (+/-)pindolol administration on serotonin neurotransmission in rats. *JOURNAL OF PSYCHIATRY & NEUROSCIENCE* 2000;25(378-388

ALZET Comments: Pindolol; Saline; SC; Rat; 2 weeks; controls received mp w/ vehicle; comparison of ip injections vs. mp;.

P4052: N. Haddjeri, *et al.* Effect of the reversible monoamine oxidase-A inhibitor befloxatone on the rat 5-hydroxytryptamine neurotransmission. *Eur. J. Pharmacol* 1998;343(179-192

ALZET Comments: Befloxatone; Pindolol; Water; Ethanol; SC; Rat; 2, 21 days; controls received mp w/vehicle; befloxatone is an antidepressant; agents infused separately or concomitantly; antihypertensive.

P4647: N. Haddjeri, *et al.* Acute and long-term actions of the antidepressant drug mirtazapine on central 5-HT neurotransmission. *Journal of Affective Disorders* 1998;51(255-266

ALZET Comments: Mirtazapine; Pindolol;; NaCl; Ascorbic acid;; SC;; Rat;; 2, 21 days;; controls received mp w/ vehicle; comparison of IV injections vs mp; antidepressant; pindolol infused for 2 days; mirtazapine administered for 21 days.

P1826: C. Nanoff, *et al.* Desensitization pattern of cardiac B-adrenoceptor subtypes by prolonged in vivo infusion of pindolol and celiprolol in rats. *Basic Res. Cardiol* 1990;85(88-95

ALZET Comments: Celiprolol; Pindolol; Isoprenaline; Propranolol; HCl; Saline; SC; Rat; 2001; 7 days; antihypertensive.

33. Prazosin

Q4508: C. Disdier, *et al.* Tissue biodistribution of intravenously administrated titanium dioxide nanoparticles revealed blood-brain barrier clearance and brain inflammation in rat. *Particle and Fibre Toxicology* 2015;12(U1-U20

Agents: Atenolol; digoxin; prazosin **Vehicle:** PEG 200; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001D; **Duration:** Not Stated; **ALZET Comments:** Animal info (male, Fisher F344, 8 weeks old, 180-250g); 50% PEG 200 used; 50% DMSO used;

Q4103: M. J. Skelly, *et al.* Chronic treatment with prazosin or duloxetine lessens concurrent anxiety-like behavior and alcohol intake: evidence of disrupted noradrenergic signaling in anxiety-related alcohol use. *Brain and Behavior* 2014;4(468-483



Agents: Prazosin; propranolol; duloxetine **Vehicle:** DMSO; saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Long Evans, adult, 300g); functionality of mp verified by residual volume; 10% DMSO used; stress/adverse reaction: (see pg. 472); post op. care (ketoprofen 3 mg/kg SC); behavioral testing (ethanol intake, open field test, locomotor activity, elevated plus maze); dependence; "Drug doses were calculated based on the estimated mean weight of animals in each group halfway through the drug delivery period (taking the mean weight at baseline and adding projected weight gain across 2 weeks)" pg 470; pumps removed after 4 weeks;

Q0916: J. Yazaki, *et al.* Alpha1-Adrenoceptor Antagonists Improve Bladder Storage Function Through Reduction of Afferent Activity in Rats With Bladder Outlet Obstruction. *NEUROUROLOGY AND URODYNAMICS* 2011;30(3):461-467

Agents: Silodosin; prazosin **Vehicle:** Hartmann's solution; saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (12 wks old, male, Sprague--Dawley)

Q2249: B. M. Shao, *et al.* Prolonged Hepatomegaly in Mice That Cannot Inactivate Bacterial Endotoxin. *Hepatology* 2011;54(3):1051-1062

Agents: Prazosin **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated; **ALZET Comments:** Animal info (male, C57BL/6 Aoah -/-, uMT Aoah -/-); 100 ul sized pump used

Q2278: N. Haga, *et al.* Effect of Long-Term Prazosin and Yohimbine Administration on c-Fos Expression in Spinal Neurons: Inhibitory Effect of Alpha-1 and Alpha-2 Adrenoceptors on Afferents from the Lower Urinary Tract. *UROLOGIA INTERNATIONALIS* 2011;87(2):230-237

Agents: Prazosin; yohimbine **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (Sprague Dawley, female, 12 wks old)

34. Propranolol

Q7425: X. Zhi, *et al.* Adrenergic modulation of AMPKdependent autophagy by chronic stress enhances cell proliferation and survival in gastric cancer. *Int J Oncol* 2019;54(5):1625-1638

Agents: Propranolol Hydrochloride **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** Not stated; **ALZET Comments:** Dose (2 mg/kg/day); Controls received mp w/ vehicle; animal info (Male BALB/c nude mice (5weeks old, weighing ~20 g)); cancer (gastric cancer);

Q7652: W. B. Zhao, *et al.* Stimulation of beta-adrenoceptors up-regulates cardiac expression of galectin-3 and BIM through the Hippo signalling pathway. *British Journal of Pharmacology* 2019;176(14):2465-2481

Agents: Isoproterenol; propranolol; carvedilol; atenolol; ICI-118551 **Vehicle:** saline; ascorbic acid, buffered; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 1 day; 2 days; 7 days; **ALZET Comments:** Dose ((ISO 0.6, 6, 20 mg/kg/d), (Prop 2 mg/kg/d), (Carv 2 mg/kg/d), (AT 2 mg/kg/d), (ICI 1 mg/kg/d)); saline with 0.4 mM ascorbic acid used; Controls were non-transgenic and received mp w/ vehicle; animal info (12-16 weeks, Male, (C57BL/6J, beta2-TG, Mst1-TG, or dnMst1-TG)); ICI-118551 is a beta2-antagonist with the structure (2R,3S)-1-[(7-methyl-2,3-dihydro-1H-inden-4-yl)oxy]-3-(propan-2-ylamino)butan-2-ol; cardiovascular; Minipumps were removed to allow for washout of ISO overnight prior to imaging;

Q6697: Q. Long, *et al.* Chronic stress accelerates the development of endometriosis in mouse through adrenergic receptor beta2. *Hum Reprod* 2016;31(11):2506-2519

Agents: Propranolol hydrochloride **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days; **ALZET Comments:** Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (female Balb/C mice); enzyme inhibitor (ADRB antagonist); Therapeutic indication (endometriosis);

Q4687: L. Zhao, *et al.* Effect of Chronic Psychological Stress on Liver Metastasis of Colon Cancer in Mice. *PLoS One* 2015;10(U1894-U1908)



Agents: Propranolol hydrochloride; ICI-118,551 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (nude); **Pump:** 1004;
Duration: 35 days;

ALZET Comments: Animal info (male, BALB/C nu/nu, 4 weeks old); cancer (colon, HT-29);

Q5463: A. Perino, *et al.* Combined inhibition of PI3K β and PI3K γ reduces fat mass by enhancing α -MSH-dependent sympathetic drive. *Science* 2015;7(352):1-13

Agents: TGX-221; AS605240; Propranolol; SR59230A **Vehicle:** PBS; Tween 20; **Route:** SC; CSF/CNS (right cerebral ventricle); **Species:** Mice; **Pump:** Not Stated; **Duration:** 10 days; 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Knock-in mice with catalytically inactive p110 γ (encoded by KR γ) or p110 β (encoded by KR β)); ALZET brain infusion kit 2 used; 0.1% Tween 20 used; Dental cement used; Obesity; Propranolol and SR59230A are Beta blockers; Therapeutic indication (obesity); Dose (700 nM TGX-221, 500 nM AS605240, 2 mg/kg/day Propranolol, 1 mg/kg/day SR59230A); Brain coordinates (anteriorposterior, +0; medial-lateral, +1; dorsal-ventral, -2),

35. Ramiprilat

P3734: M. S. Fernandez-Alfonso, *et al.* Early induction of angiotensin I-converting enzyme in rat carotid artery after balloon injury. *Hypertension* 1997;30(pt 1):272-277

ALZET Comments: Ramiprilat; HR 720; DMSO; Water; SC; Rat; 2ML2; 2ML4; 21 days; 2ML2 pumps replaced after 14 days; antihypertensive; cardiovascular; some animals received multiple pumps per animal (2); ramiprilat is the active metabolite of ramipril; HR 720 is an angiotensin II receptor antagonist.

36. Reserpine

Q0550: J. E. Ghia, *et al.* Reactivation of Inflammatory Bowel Disease in a Mouse Model of Depression. *Gastroenterology* 2009;136(7):2280-2288

ALZET Comments: Reserpine; choline chloride; methyllycaconitine; Water; acetic acid; CSF/CNS; IP; Mice; 5, 10, 14 days; Controls received mp w/ vehicle; animal info (male, C57BL/6, 7-9 wks old, alpha 7nAChR -/-); post op. care (buprenorphine); Plastics One cannula used with PE60 tubing.

P8751: J. E. Ghia, *et al.* Impaired parasympathetic function increases susceptibility to inflammatory bowel disease in a mouse model of depression. *Journal of Clinical Investigation* 2008;118(6):2209-2218

ALZET Comments: Reserpine; Acetic acid; CSF/CNS; Mice; 14 days; Controls received mp w/ vehicle; dose-response (Fig. 1); comparison of IP injection vs. mp; no stress (see pg. 2210); antihypertensive; cyanoacrylate adhesive; animal info (male, female, C57BL/6, op/op, wt, 7-9 wks old, colitis, vagotomy); animal model of depression; plastics one cannula used; PE-60 used.

P5124: S. Shafi, *et al.* Long-term low-dose treatment with reserpine of cholesterol-fed rabbits reduces cholesterol in plasma, non-high density lipoproteins and arterial walls. *Journal of Cardiovascular Pharmacology* 2002;40(67-79)

ALZET Comments: Reserpine; Citric acid; SC; Rabbit; 2ML4; 6 weeks; controls received mp w/ vehicle; pumps replaced after 3 wks; cardiovascular; antihypertensive; vehicle included 4% citric acid.

P0429: M. Girgis. A combined histochemical-neurophysiological technique for investigating the extent of diffusion of intracerebrally injected drugs. *Acta Anat* 1983;117(248-256)

ALZET Comments: Physostigmine; Reserpine; CSF/CNS (limbic system); cat; Guinea pig; monkey; rabbit; 3, 5, and 7 days; comparison of injec by microsyringe vs. mp infusion, infused hippocampus, septum, hypothalamus, caudate-putamen; chemitrode, mp advant. for icv admin; antihypertensive.

37. Rilmenidine



Q5047: K. L. Jackson, *et al.* Actions of rilmenidine on neurogenic hypertension in BPH/2J genetically hypertensive mice. *J Hypertens* 2014;32(3):575-86

ALZET Comments: rilmenidine; Ringer's solution; CSF/CNS (ventricles); mice; 1002; 1 week; Controls received mp w/ ringer's solution vehicle; animal info (BPH/2J and BPN/3J mice); functionality of mp verified by behavioral tests; dose-response (pg 577-582, description and graphical representation); behavioral testing (pg 577; mice were exposed to aversive behavioral stimuli; restraint stress and dirty cage-switch tests conducted); tissue perfusion (brain tissue); antihypertensive; antihypertensive; Dose: 15ug/hr of rilmenidine.

P9686: S. L. Burke, *et al.* Cardiac and renal baroreflex control during stress in conscious renovascular hypertensive rabbits: effect of rilmenidine. *Journal of Hypertension* 2009;27(1):132-141

ALZET Comments: Rilmenidine; Saline; SC; Rabbit; 2ML4; 3 weeks; Controls received mp w/ vehicle; comparison of IV injections vs. SC mp; antihypertensive; animal info (mixed breed, male, female, 2.4-3.2 kg.).

P9041: I. L. Signolet, *et al.* Improvement of cardiac Diastolic function by long-term centrally mediated sympathetic inhibition in one-kidney, one-clip hypertensive rabbits. *American Journal of Hypertension* 2008;21(1):54-60

ALZET Comments: Rilmenidine; metoprolol; SC; Rabbit; 2ML2; 6 weeks; Controls received mp w/ vehicle; animal info (New Zealand, White, 4-6 wks old, male, 0.7-0.9 kg., nephrectomized); long-term study.

P6378: L. Monassier, *et al.* Chronic treatment with rilmenidine in spontaneously hypertensive rats: Differences between two schedules of administration. *Journal of Cardiovascular Pharmacology* 2004;43(3):394-401

ALZET Comments: Rilmenidine; Saline; IP; Rat; 2002; 1 month; Comparison of IP injections vs. IP mp; pumps replaced at 15 days; stability verified (30 days at 37 degrees Celsius); cardiovascular; antihypertensive.

P5646: M. L. Parkin, *et al.* Importance of imidazoline-preferring receptors in the cardiovascular actions of chronically administered moxonidine, rilmenidine and clonidine in conscious rabbits. *Journal of Hypertension* 2003;21(1):167-178

ALZET Comments: Moxonidine; clonidine; rilmenidine; Saline; HCl; Sodium hydroxide; SC; Rabbit; 2ML2; 4 weeks; Controls received mp w/ vehicle; functionality of mp verified by residual volume; pumps replaced after 2 weeks; antihypertensive; moxonidine dissolved in saline/HCl/NaOH; other agents dissolved in saline; moxonidine & rilmenidine are imidazoline receptor agonists.

38. Tertaolol

P3658: Y. Y. Tan, *et al.* B-adrenoceptor regulation in rat heart, lung and skin after chronic treatment with (-)-tertatolol or (-)-propranolol. *J. Auton. Pharmac* 1995;15(4):421-436

ALZET Comments: Tertatolol; Propranolol; HCl; SC; Rat; 2002; 14 days; controls received mp w/ vehicle; antihypertensive; cardiovascular; beta-adrenoceptor antagonists; examined heart rate and systolic blood pressure.

39. Valsartan

Q3611: T. A. Ramirez, *et al.* Aliskiren and valsartan mediate left ventricular remodeling post-myocardial infarction in mice through MMP-9 effects. *Journal of Molecular and Cellular Cardiology* 2014;72(3):326-335

Agents: Aliskiren; valsartan **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (MMP-9 null or WT); cardiovascular; bp measured using MC4000 bp analysis system;

Q3218: M. Zeniya, *et al.* Dietary Salt Intake Regulates WNK3-SPAK-NKCC1 Phosphorylation Cascade in Mouse Aorta Through Angiotensin II. *Hypertension* 2013;62(5):872-878

Agents: Valsartan; angiotensin II; aldosterone **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;



ALZET Comments: Animal info (C57BL/6J. male); peptides

Q2883: Q. C. Yong, *et al.* Angiotensin type 1a receptor-deficient mice develop diabetes-induced cardiac dysfunction, which is prevented by renin-angiotensin system inhibitors. *Cardiovascular Diabetology* 2013;12(:):U1-U13

Agents: Aliskiren; benazeprilat; valsartan; PD123319 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 10 weeks;

ALZET Comments: Cardiovascular; peptides; animal info (12 wks old, male, AT-KO); functionality of mp verified by echocardiography; pumps replaced every 4 weeks; enzyme inhibitor (renin);

Q2934: C. M. Thomas, *et al.* Direct renin inhibition prevents cardiac dysfunction in a diabetic mouse model: comparison with an angiotensin receptor antagonist and angiotensin-converting enzyme inhibitor. *Clinical Science* 2013;124(7-8):529-541

Agents: Insulin (Humulin N); aliskiren (renin inhibitor); benazeprilat (ACEi); valsartan (ARB); streptozotocin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 10 weeks;

ALZET Comments: Controls received mp w/vehicle, or (0.1M sodium citrate buffer (pH 4.5)); cardiovascular; animal info (male, C57b16/J, 12 weeks, blood glucose > 250 mg/dl); pumps replaced every 4 weeks; enzyme inhibitor (renin); diabetes;

Q6760: K. P. Roos, *et al.* Adenylyl cyclase VI mediates vasopressin-stimulated ENaC activity. *J Am Soc Nephrol* 2013;24(2):218-27

Agents: Valsartan **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (knockout); **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (5 mg/kg per day); animal info (CDAC6 KOmice);