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Non-Invasive Blood Pressure for Mice and Rats

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Written by Joel Malkoff

BACKGROUND

Over the past 35 years, research scientists have attempted, with varying degrees of success, to measure the blood pressure in mice and rats non-invasively.

The ability to measure accurately and non-invasively the systolic and diastolic blood pressure along with the heart pulse rate and other blood flow parameters in rodents is of great clinical value to the researcher.

CONCLUSION

Non-invasive blood pressure devices that use VPR are valuable tools in research and will continue to be beneficial in many study protocols. The main advantages are that VPR devices:

- require no surgery
- are significantly less expensive than other blood pressure equipment, such as telemetry
- can screen for systolic and diastolic BP changes over time in large numbers of animals
- provide the researcher with the ability to obtain accurate and consistent blood pressure measurements over time in long-term studies

INVASIVE BLOOD PRESSURE

Direct blood pressure measurement, an invasive surgical procedure, is the gold standard for comparisons in determining the accuracy of non-invasive blood pressure technologies. Direct blood pressure should be obtained on the rodent's carotid artery when comparing to non-invasive blood pressure. “Validation in Awake Rats of a Tail Cuff Method for Measuring Systolic Pressure”, Bunag, R.D., Journal of Applied Physiology, Vol 34, Pgs 279-282, 1973.

Radiotelemetry, a highly invasive surgical procedure, is a very reliable blood pressure technology and is also used as a comparison in determining the accuracy of non-invasive blood pressure technologies. Telemetry involves implanting radio transmitters in the rodent's body. This technique is well validated and has excellent correlation with direct blood pressure.

The advantage of implantable radio telemetry is the ability to measure blood pressure continuously in free-moving laboratory animals. Its disadvantages are: (1) morbidity associated with the initial surgical implantation of the transmitter; (2) morbidity associated with surgery required to replace the short-lived battery; (3) increase in animal stress levels, especially for mice, due to the size and weight of the transmitters (2004, ATLA, 4th World Congress, Einstein, Billing, Singh and Chin); (4) abnormal behavior in animals unable to interact socially due to the one-animal-per-cage isolation required for implanted animals; (5) inability to perform high throughput screening; (6) high cost of initial equipment set-up and of transmitters that require frequent factory maintenance; (7) cost of material and human resources related to ongoing surgeries; and (8) high product and servicing costs resulting from the lack of a competitive market.

NON-INVASIVE BLOOD PRESSURE

The non-invasive blood pressure methodology consists of placing a cuff on the animal's tail to occlude the blood flow. Upon deflation, one of several types of non-invasive blood pressure sensors, placed distal to the occlusion cuff, can be used to monitor the blood pressure. There are three types of non-invasive blood pressure sensor technologies: photoplethysmography, piezoplethysmography and Volume Pressure Recording. Each method uses an occlusion tail-cuff as part of the procedure.

1. Photoplethysmography

The first and oldest method is Photoplethysmography (PPG), a light-based technology. It records the first appearance of the pulse while deflating the occlusion cuff, and the disappearance of pulses upon inflation of the occlusion cuff. PPG uses an incandescent or LED light source to record the pulse signal wave. The light source illuminates a small spot on the tail and attempts to record the pulse.

PPG is relatively inaccurate since the readings are based solely on the amplitude of a single pulse and cannot precisely measure the systolic blood pressure or the heart beat. There are many limitations to a light-based technology, such as over-saturation of the blood pressure signal by ambient light, extreme sensitivity to the rodent's movement (motion artifact) and difficulty obtaining adequate blood pressure signals in dark-skinned rodents (Pigmentation Differentiation). Light-based sensors also cause tail burns from close contact and prolonged exposure.

Diastolic blood pressure cannot be measured by PPG since the technology records only the first appearance of the pulse. If the diastolic blood pressure is displayed on the PPG instrumentation, it is an estimation only, calculated by a software algorithm, and not a true measurement.

Additional variability and inaccuracy occurs in PPG devices that rely on obtaining blood pressure readings during occlusion cuff inflation. Occlusion cuff length, another source of variability and inaccuracy, is inversely related to the accuracy of the blood pressure measurements in PPG systems. Long cuffs, predominant in PPG devices, record pressures as lower than the actual blood pressure measurements. These limitations severely compromise the consistency, dependability, and accuracy of the non-invasive blood pressure measurements obtained by devices that use light-based/LED PPG technology.

The PPG method correlates poorly with direct blood pressure measurements and is the least recommended sensor technology for non-invasive blood pressure in rodents, especially in mice.

2. Piezoplethysmography

The second non-invasive blood pressure sensor technology is piezoplethysmography. Piezoplethysmography and PPG require the same first appearance of a pulse in the tail to record the systolic blood pressure and heart rate. The two methods have similar clinical limitations.

Piezoplethysmography uses piezoelectric ceramic crystals to attempt to record a pulse signal. From a technical point of view, piezoplethysmography is far more sensitive than PPG since the signal from the sensor is the rate of change of the pulse rather than just the pulse amplitude. Therefore, even extremely small mice with high pulse rates will generate a sufficient signal to be detected with simple amplifiers.

Piezoelectric sensors are more accurate than light-based/LED sensors, but the same PPG limitations continue to produce inaccuracies in blood pressure measurements. On a positive note, the skin pigment of the rodent is not a measurement issue with piezoplethysmography as it is with PPG.

Although piezoplethysmography is better than PPG, both these non-invasive tail-cuff blood pressure technologies correlate poorly with direct blood pressure measurements.

3. Volume Pressure Recording

The third sensor technology is Volume Pressure Recording (VPR). VPR uses a specially designed differential pressure transducer to measure the blood volume in the tail non-invasively. VPR will actually measure six parameters simultaneously: systolic blood pressure, diastolic blood pressure, mean blood pressure, heart pulse rate, tail blood volume, and tail blood flow.

Since VPR uses a volumetric method to measure blood flow and blood volume in the tail, there are no measurement artifacts related to ambient light. Movement artifact is also greatly reduced. In addition, VPR is not dependent on the animal's skin pigmentation, so dark skin has no negative effect on VPR measurements. Very small 10-gram C57/BL6 black mice are easily measured with the VPR method. Special attention is afforded to the length of the occlusion cuff with VPR in order to derive the most accurate blood pressure readings.

VPR is the most reliable, consistent, and accurate method to measure the blood pressure non-invasively in rodents ranging from mice as small as 8 grams to rats over 950 grams. In a 2003 independent clinical validation study at Yale University, New Haven, Connecticut, VPR measurements correlated 99 percent with direct blood pressure: "Volume Pressure Recording is excellent. It is very accurate and dependable. We performed experiments on temperature-controlled, adult rats and the non-invasive blood pressure measurements showed almost perfect correlation with invasive blood pressure measurements. We are very pleased with the results." Numerous published research papers are listed in the Clinical Bibliography section of this Whitepaper that validate the accuracy, reliability and consistency of VPR.

RODENT HOLDERS

The ideal animal holder should comfortably restrain the animal, create a low-stress environment and allow the researcher to observe the animal's behavior constantly. A trained rat or mouse can comfortably and quietly remain in the holder for several hours.

It is very beneficial to incorporate a darkened nose cone into the rodent holder to limit the animal's view and reduce its stress level. The animal's nose should protrude through the front of the nose cone allowing for comfortable breathing. The tail of the animal should be fully extended and exit through the rear hatch opening of the holder.

The proper size animal holder is essential for proper blood pressure measurements. If the holder is too small, the limited lateral space will not allow the animal to breathe in a relaxed fashion. The animal will compensate by elongating its body, creating a breathing artifact that will cause excessive tail motion and undesirable blood pressure readings.

ANIMAL BODY TEMPERATURE

A non-invasive blood pressure system should be designed to warm the animal comfortably, reduce the animal's stress, and enhance blood flow to its tail. The rodent's core body temperature is very important for accurate and consistent blood pressure measurements. The animal must have adequate blood flow in the tail to produce a blood pressure signal. Thermo-regulation is the method by which the animal reduces its core body temperature, dissipates heat through its tail and generates tail blood flow.

Anesthetized animals may have lower body temperatures than awake animals so additional care must be taken to maintain the animal's proper core body temperature. An infrared warming blanket or a re-circulating water pump with a warm water blanket are the preferred methods for maintaining the animal's proper core body temperature. The animal should be warm and comfortable but never hot. Extreme care must be exercised never to overheat the animal. Warming devices such as hot air heating chambers, heat lamps, or heating platforms that apply direct heat to the animal's feet are not advisable for maintaining the animal's core body temperature. These heating devices will overheat the animal and increase the animal's respiratory rate and stress level. Such conditions will elicit poor thermoregulatory responses and create inconsistent and inaccurate blood pressure readings.

ENVIRONMENTAL TEMPERATURE

Room temperature at or above 26°C is essential for accurate blood pressure measurements. If the room is too cool, below 22°C for example, the animal will not thermo-regulate, tail blood flow will be reduced and it may be difficult to obtain blood pressure signals. A cold steel table or a table near an air conditioning duct are undesirable for use during animal testing.

ANIMAL PREPARATION

The animal should be in the holder at least 10 to 15 minutes before pressure measurements begin. Acclimated animals should provide faster BP measurements than non-acclimated animals. Proper animal handling is critical to consistent and accurate blood pressure measurements. A nervous, stressed animal may have diminished circulation in the tail. Most rodents will quickly adapt to new conditions and feel comfortable in small, dark, and confined spaces. Animal training is not necessary to obtain accurate blood pressure readings, however, some researchers prefer training sessions. Rodents can easily be trained in approximately three days, 15-minutes each day, before beginning your experiment.

The animal should be allowed to enter the holder freely. After the animal is in the holder, adjust the nose cone so the animal is

comfortable but not able to move excessively. The animal should never have its head bent sideways or its body compressed against the back hatch. The animal's temperature may be monitored throughout the experiment.

CONCLUSION

Tail-cuff non-invasive blood pressure measurements:

- can be accurate, consistent, and reproducible in studies of awake or anesthetized mice and rats
- make multiple animal testing very cost-effective for large scale, high throughput screening
- require that care be taken to handle the animals properly
- can benefit from training test animals and monitoring their' temperatures

The VPR method:

- provides the highest degree of correlation with telemetry and direct blood pressure
- is clearly the preferred tail-cuff sensor technology

Non-invasive blood pressure devices that use VPR are valuable tools in research and will continue to be beneficial in many study protocols. The main advantages are that VPR devices:

- require no surgery
- are significantly less expensive than other blood pressure equipment, such as telemetry
- can screen for systolic and diastolic BP changes over time in large numbers of animals
- provide the researcher with the ability to obtain accurate and consistent blood pressure measurements over time in long-term studies ●

"15" Questions to ask when choosing a tail-cuff blood pressure instrument

1. When I am submitting my experiment for peer-reviewed publications, will I be questioned and can I cite and defend my specific tail-cuff method?
2. Can I obtain reliable blood pressure measurements without increasing the animal's stress level by external heating or immobilizing the animal's tail?
3. Can I measure the blood pressure on mice as small as 8 grams?
4. Does the specific tail-cuff method have published proof that the diastolic blood pressure readings are actually measured, not an estimated calculation?
5. Can I measure awake and anesthetized mice and rats in the same non-invasive blood pressure system?
6. Can I measure the blood pressure in an MRI compatible environment?
7. Will I have difficulty measuring dark-skinned mice such as C57/BL6 mice?
8. When I begin my research study, I need to get my group "up and running" quickly. Is there a free onsite installation and clinical training?
9. Can I observe and verify that my animals are safe and stress-free throughout my experiment?
10. If I need High Throughput studies, how many animals can I measure at one time and are they simultaneous measurements? How long is each BP cycle?
11. If I have limited funds now and wish to upgrade my NIBP system at a later date, is it possible and reasonably priced?
12. If I need a small, inexpensive tail-cuff instrument for surgical blood pressure monitoring and I do not wish to use a separate computer, is it available?
13. Are there knowledgeable researchers that are familiar with the two types of tail-cuff methods that I can speak to and even visit their labs?
14. If the product has a problem, does my warranty cover 100% of all the parts and labor?
15. If I find that the product does not meet my research needs, can I have a 100% Money-Back Guarantee?

dark skinned mice

the Problem

My current NIBP instrument uses a light-based tail-cuff sensor and has trouble measuring small, 15-20 gram dark-skinned mice with diminished tail pulses.

the Study

The Chief of Vascular Surgery in a Boston university needs to measure the blood pressure in a small number of C57/BL6 mice with bilateral limb and aorta ischemia.

the Solution

The patented, Volume Pressure Recording (VPR) tail-cuff method utilizes a differential pressure transducer which measures the blood volume in the animal's tail as opposed to a light sensor which attempts to record an arterial tail pulse. VPR tail-cuff technology is non-pulse dependent and the animal's skin pigmentation is not a factor.

mri compatibility

the Problem

I need to measure the blood pressure in my anesthetized mice while in the MRI environment.

the Study

The Senior Director of the MRI Section at NIH is conducting a longitudinal mouse study determining the effects of aging on nociception.

the Solution

The patented, Volume Pressure Recording (VPR) tail-cuff sensor is 100% MRI compatible since there are no metal components. The CODA system was supplied with 15 feet of tubing to provide adequate distance between the magnet and the CODA controller.

high throughput

the Problem

My current NIBP device can only measure 4 animals at a time and I need to quickly complete a large mouse study. I only have one technician and the BP readings must be taken every morning for the next 2 months.

the Study

The Director of Cardiovascular Research in a large New Jersey pharmaceutical company has a deadline to finalize a study designed to investigate the effects of the deletion of long-form leptin receptor on the progression +/- of atherosclerosis in ApoE^{-/-}; db/db double knockout mice.

the Solution

Four (4) CODA High Throughput Systems, each capable of measuring 8 animals simultaneously, were linked together to measure 32 animals simultaneously and all the BP signals and numerical values were displayed on just one computer screen.

surgical monitoring

the Problem

I need an inexpensive method to make sure my animal is safe throughout my transplant surgery.

the Study

A researcher in the Anesthesia and Preoperative Care Department of a San Francisco university is conducting a longitudinal study on obese zucker rats to determine if ischemia pre-conditioning improves the liver transplant survival rate. There is a study requirement to monitor and quantify the animal's vital signs.

the Solution

The CODA Monitor is a self-contained, vital signs monitor (no need for a separate computer) and will intermittently measure the blood pressure during surgery.

animal stress

the Problem

We are phenotyping a very large amount of mice on a regular basis and are having difficulty obtaining reliable BP measurements. We also need a higher animal throughput to handle our increasing volume.

the Study

The Director of Drug Discovery at the leading mouse breeding institution in Maine has several 4-animal NIBP devices which use a light-based tail-cuff sensor and incorporates a magnetic plate to hold down the animals tail. The total immobilization of the animal's tail creates an adverse and stressful condition resulting in inaccurate and inconsistent BP measurements.

the Solution

The CODA High Throughput system utilizes clear, acrylic animal holders that allow the researcher to continually observe the animal. The VPR tail-cuff method allows the animal's tail to be free moving, thereby reducing animal stress. Each CODA High Throughput system measures 8 animals simultaneously. Up to 6 systems can be linked together to measure up to 48 animals automatically. This Super High Throughput Networking system displays all 48 BP measurements on one computer screen.

diastolic blood pressure

the Problem

My current NIBP instrument only calculates the diastolic blood pressure and I need an actual diastolic BP measurement for a grant submission.

the Study

The post-doctorate student in the Molecular Cardiology Department of this Washington state University is applying for a grant to conduct a longitudinal study involving spontaneously hypertensive rats. The committee requires proof that the preliminary tail-cuff measurements are clinically validated or will insist on a invasive BP technique such as telemetry or direct BP.

the Solution

The patented Volume Pressure Recording (VPR) tail-cuff method is clinically validated as published in a 2008 peer-reviewed journal. The correlation is 99% systolic blood pressure and 93% diastolic blood pressure as compared to telemetry and direct blood pressure.

Clinical Bibliographies

Publication	Article Title	Animal
2011 Heart and Circulatory Physiology	Chronic cigarette smoking causes hypertension, increased oxidative stress, impaired NO bioavailability, endothelial dysfunction, and cardiac remodeling in mice	Mouse
Neuroscience	Anti-acrolein treatment improves behavioral outcome and alleviates myelin damage in experimental autoimmune encephalomyelitis mouse	Mouse
Heart and Circulatory Physiology	Detrimental effects of thyroid hormone analog DITPA in the mouse heart: increased mortality with in vivo acute myocardial ischemia-reperfusion	Mouse
Circulation Research	Endothelial Cell-Specific Deficiency of Ang II Type 1a Receptors Attenuates Ang II-Induced Ascending Aortic Aneurysms in LDL Receptor ^{-/-} Mice	Mouse
Molecular and Cellular Biology	Mouse cardiac acyl-CoA synthetase-1 deficiency impairs fatty acid oxidation and induces cardiac hypertrophy	Mouse
Journal of Cardiovascular Pharmacology	The Effect of Selective Antihypertensive Drugs on the Vascular Remodeling-associated Hypertension: Insights from a Profilin1 Transgenic Mouse Model	Mouse
Hypertension	An Oral Formulation of Angiotensin-(1-7) Produces Cardioprotective Effects in Infarcted and Isoproterenol-Treated Rats	Rat
Kidney International	Angiotensin II induces phosphorylation of the thiazide-sensitive sodium chloride cotransporter independent of aldosterone	Rat
American Journal of Physiology (AJP)	Angiotensin-(1-7) reduces proteinuria and diminishes structural damage in renal tissue of stroke-prone spontaneously hypertensive rats	Rat
Food Chemistry	Characterization of a new antihypertensive angiotensin I-converting enzyme inhibitory peptide from <i>Pleurotus cornucopiae</i>	Rat
Hypertension	Decreased cGMP Level Contributes to Increased Contraction in Arteries From Hypertensive Rats	Rat
Journal of Renin-Angiotensin-Aldosterone System	Eplerenone suppresses aldosterone/salt-induced expression of NOX-4	Rat
Neuroscience	Gastric distention induced functional magnetic resonance signal changes in the rodent brain	Rat
International Journal of Medical Sciences	High Dose Astaxanthin Lowers Blood Pressure and Increases Insulin Sensitivity in Rats: Are These Effects Interdependent?	Rat
Neuroscience	Hypoxia-excited neurons in NTS send axonal projections to Kölliker-Fuse/parabrachial complex in dorsolateral pons	Rat
Journal of Investigative Dermatology	What Can Current Stimulation Tell Us about the Vascular Function of Endogenous Prostacyclin in Healthy Rat Skin In Vivo?	Rat
Bioorganic & Medical Chemistry Letters	Triazole incorporated pyridazinones as a new class of antihypertensive agents: Design, synthesis and in vivo screening	Rat
2010 The Journal of Biological Chemistry (JBC)	The Mitochondrial Pathway of Anesthetic Isoflurane-induced Apoptosis	Mouse
Basic Research in Cardiology	CB1 receptor inhibition leads to decreased vascular AT1 receptor expression, inhibition of oxidative stress and improved endothelial function	Mouse
The Journal of Nutrition (JN)	A High-Lipid Diet Potentiates Left Ventricular Dysfunction in Nitric Oxide Synthase 3-Deficient Mice after Chronic Pressure Overload	Mouse
PloS ONE	A New Mouse Model to Explore Therapies for Preeclampsia	Mouse
Arquivos Brasileiros de Cardiologia	Association of Physical Training with Beta-Blockers in Heart Failure in Mice	Mouse
Journal of Neuroscience Methods	Characterization of a 3-vessel occlusion model for the induction of complete global cerebral ischemia in mice	Mouse
Journal of Molecular and Cellular Cardiology	Deficiency in AMP-activated protein kinase exaggerates high fat diet-induced cardiac hypertrophy and contractile dysfunction	Mouse
Anesthesiology	Endothelial Dysfunction Enhances Vasoconstriction Due to Scavenging of Nitric Oxide by a Hemoglobin-based Oxygen Carrier	Mouse

Publication	Article Title	Animal
Arteriosclerosis, Thrombosis, and Vascular Biology	Influences of Aortic Motion and Curvature on Vessel Expansion in Murine Experimental Aneurysms	Mouse
The Journal of Neurochemistry (JNC)	Inhibition of myosin light chain kinase reduces brain edema formation after traumatic brain injury	Mouse
Journal of Biological Chemistry	Inhibitor of DNA Binding 4 (ID4) Regulation of Adipocyte Differentiation and Adipose Tissue Formation in Mice	Mouse
The Journal of Nutritional Biochemistry	Iron Overload in Hypercholesterolemic Rats affects Iron Homeostasis and Serum Lipids not Blood Pressure	Mouse
Biochimie	Isolation of an acidic phospholipase A2 from the venom of the snake <i>Bothrops asper</i> of Costa Rica: Biochemical and toxicological characterization	Mouse
BMC Research Notes	Mice lacking the C β subunit of PKA are resistant to angiotensin II-induced cardiac hypertrophy and dysfunction	Mouse
Respiratory and Critical Care Medicine	MKK3 Mediates Sepsis And Lung Injury In Mice Through IL1-2 Regulation	Mouse
Laboratory Investigation	Myocardial fibrosis in response to Angiotensin II is preceded by the recruitment of mesenchymal progenitor cells	Mouse
Arteriosclerosis, Thrombosis, and Vascular Biology	Naringenin Decreases Progression of Atherosclerosis by Improving Dyslipidemia in High-Fat-Fed Low-Density Lipoprotein Receptor-Null Mice	Mouse
Kidney International	Overexpression of VEGF-A in podocytes of adult mice causes glomerular disease	Mouse
Respiratory and Critical Care Medicine	Phosphoinositide-3 Kinase γ Activity Contributes to Sepsis and Organ Damage by Altering Neutrophil Recruitment	Mouse
American Journal of Transplantation	RGS4 Controls Renal Blood Flow and Inhibits Cyclosporine-Mediated Nephrotoxicity	Mouse
Hypertension	Targeting the Degradation of Angiotensin II With Recombinant Angiotensin-Converting Enzyme 2	Mouse
Critical Care Medicine	Toll-like receptor 2 plays a critical role in cardiac dysfunction during polymicrobial sepsis	Mouse
The Journal of Neuroscience	β -Adrenoceptor Blockers Increase Cardiac Sympathetic Innervation by Inhibiting Autoreceptor Suppression of Axon Growth	Rat
Neuroscience Letters	A putative role for hypothalamic glucocorticoid receptors in hypertension induced by prenatal undernutrition in the rat	Rat
The Journal of Immunology	Anti-Inflammatory Effects of the Activation of the Angiotensin-(1-7) Receptor, Mas, in Experimental Models of Arthritis	Rat
American Journal of Nephrology	ApoA-1 Mimetic Peptide Reverses Uremia-Induced Upregulation of Pro-Atherogenic Pathways in the Aorta	Rat
Translational Stroke Res.	Association Between Changes in Weight and Cerebral Arteries in Rats	Rat
Physiology Research	Cardiovascular Parameters in Rat Model of Chronic Renal Failure Induced by Subtotal Nephrectomy	Rat
Canadian Journal of Physiology & Pharmacology	Dual endothelin receptor antagonism prevents remodeling of resistance arteries in diabetes	Rat
Nephrology Dialysis Transplantation (NDT)	Effect of chronic kidney disease on the expression of thiamin and folic acid transporters	Rat
Frontiers in Vascular Physiology	Effect of PPAR γ inhibition during pregnancy on posterior cerebral artery function and structure	Rat
Journal of Physiology and Biochemistry	Effects of l-Canavanine and ozone on vascular reactivity in septicemic rats	Rat
Journal of Vascular Research	Effects of Pregnancy, Hypertension and Nitric Oxide Inhibition on Rat Uterine Artery Myogenic Reactivity	Rat

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Publication	Article Title	Animal
Experimental Nephrology	Epoetin Delta as an Antifibrotic Agent in the Remnant Kidney Rat: A Possible Role for Transforming Growth Factor Beta and Hepatocyte Growth Factor	Rat
Hypertension	Exercise Training and Caloric Restriction Prevent Reduction in Cardiac Ca ²⁺ -Handling Protein Profile in Obese Rats	Rat
Science Direct	Furanocoumarins-imperatorin inhibits myocardial hypertrophy both in vitro and in vivo	Rat
The Journal of Trauma Injury, Infection, & Critical Care	Hematopoietic Progenitor Cell Mobilization Is Mediated Through [beta]-2 and [beta]-3 Receptors After Injury	Rat
Acta Laboratorium Animalis Scientia Sinica	Hemodynamic Variation and Histological Alterations of the Heart in Spontaneous Hypertensive Rats at Different Weeks of Age	Rat
Psychopharmacology	Imaging brain regional and cortical laminar effects of selective D3 agonists and antagonists	Rat
Molecular Therapy	Induction of Shock After Intravenous Injection of Adenovirus Vectors: A Critical Role for Platelet-activating Factor	Rat
Human Gene Therapy	Interleukin-10 Delivery Via Mesenchymal Stem Cells: A Novel Gene Therapy Approach To Prevent Lung Ischemia-Reperfusion Injury	Rat
Hypertension	Lifetime Overproduction of Circulating Angiotensin-(1-7) Attenuates Deoxycorticosterone Acetate-Salt Hypertension-Induced Cardiac Dysfunction and Remodeling	Rat
Life Sciences	l-NAME-treatment alters ectonucleotidase activities in kidney membranes of rats	Rat
American Journal of Physiology (AJP)	Losartan increases no release in afferent arterioles during regression of l-name induced renal damage	Rat
International Journal of Medical Sciences	Maitake Mushroom Extracts Ameliorate Progressive Hypertension and Other Chronic Metabolic Perturbations in Aging Female Rats	Rat
Stress	Neurobiological constituents of active, passive, and variable coping strategies in rats: Integration of regional brain neuropeptide Y levels & cardiovascular response	Rat
Biochimie	Niacin improves renal lipid metabolism and slows progression in chronic kidney disease	Rat
American Journal of Nephrology	Novel Markers of Left Ventricular Hypertrophy in Uremia	Rat
Cardiovascular Research	Novel role of Egr-1 in nicotine-related neointimal formation	Rat
Hypertension	O-GlcNAcylation Contributes to Augmented Vascular Reactivity Induced by Endothelin 1	Rat
Medical Imaging	Optical-Flow-Based B-Mode Elastography: Application in the Hypertensive Rat Carotid	Rat
American Journal of Nephrology	Peroxisome Proliferator-Activated Receptor- γ Agonist Rosiglitazone Prevents Albuminuria but Not Glomerulosclerosis in Experimental Diabetes	Rat
Stroke	PPAR Activation Prevents Hypertensive Remodeling of Cerebral Arteries and Improves Vascular Function in Female Rats	Rat
Journal of Medicinal Food	Regulatory Function of a Malleable Protein Matrix as a Novel Fermented Whey Product on Features Defining the Metabolic Syndrome	Rat
The Journal of Nutrition (JN)	Resveratrol Arrests and Regresses the Development of Pressure Overload- but Not Volume Overload-Induced Cardiac Hypertrophy in Rats	Rat
American Journal of Hypertension (AJH)	Resveratrol Prevents the Development of Pathological Cardiac Hypertrophy and Contractile Dysfunction in the SHR Without Lowering Blood Pressure	Rat
Hypertension	Ribonucleic Acid Interference Knockdown of Interleukin 6 Attenuates Cold-Induced Hypertension	Rat
The Journal of Nutrition (JN)	Salt-Induced Cardiac Hypertrophy and Interstitial Fibrosis Are Due to a Blood Pressure-Independent Mechanism in Wistar Rats	Rat

Publication	Article Title	Animal
Investigative Ophthalmology & Visual Science (IOVS)	Systemic Propranolol Reduces b-Wave Amplitude in the ERG and Increases IGF-1 Receptor Phosphorylation in Rat Retina	Rat
Microvascular Research	Tempol, a superoxide dismutase mimetic, prevents cerebral vessel remodeling in hypertensive rats	Rat
Human & Experimental Toxicology	The effect of high fat diet-induced obesity on cardiovascular toxicity in wistar albino rats	Rat
Circulation	Vascular Endothelial Growth Factor-B Acts as a Coronary Growth Factor in Transgenic Rats Without Inducing Angiogenesis, Vascular Leak, or Inflammation	Rat
Experimental Biology and Medicine	A Profibrotic Effect of Plasminogen Activator Inhibitor Type-1 (PAI-1) in the Heart	Mouse
Circulation Research	A Role of Matrix Metalloproteinase-8 in Atherosclerosis	Mouse
American Journal of Physiology (AJP)	Abl Knockout Differentially Affects p130 Crk-associated Substrate, Vinculin, and Paxillin in Blood Vessels of Mice	Mouse
Atherosclerosis	Aldosterone blockade by Spironolactone improves the hypertensive vascular hypertrophy and remodeling in angiotensin II overproducing transgenic mice	Mouse
American Journal of Physiology (AJP)	ANG II infusion promotes abdominal aortic aneurysms independent of increased blood pressure in hypercholesterolemic mice	Mouse
Kidney International	Biomechanical strain causes maladaptive gene regulation, contributing to Alport glomerular disease	Mouse
PloS ONE	Cardiomyocyte Contractile Dysfunction in the APP ^{swe} /PS1 ^{dE9} Mouse Model of Alzheimer's Disease	Mouse
International Journal of Pharmaceutics	Complexation with β -cyclodextrin confers oral activity on the flavonoid dioclein	Mouse
European Journal of Heart Failure	Defective peroxisomal proliferators activated receptor gamma activity due to dominantnegative mutation synergizes with hypertension to accelerate cardiac fibrosis in mice	Mouse
American Journal of Physiology (AJP)	Diabetic kidney lesions of GIPR ^{dn} transgenic mice: podocyte hypertrophy and thickening of the GBM precede glomerular hypertrophy & glomerulosclerosis	Mouse
Endocrinology	Early Postnatal Nutrition Determines Somatotrophic Function in Mice	Mouse
Hypertension	Genetic Analysis of Blood Pressure in 8 Mouse Intercross Populations	Mouse
PNAS - USA	Hypertension of Kcnmb1 ^{-/-} is linked to deficient K secretion & aldosteronism	Mouse
The Journal of Allergy and Clinical Immunology	Impairing oral tolerance promotes allergy and anaphylaxis: A new murine food allergy model	Mouse
Circulation	Interferon- and the Interferon-Inducible Chemokine CXCL10 Protect Against Aneurysm Formation and Rupture	Mouse
Birth Defects Research	Intrauterine exposure to high saturated fat diet elevates risk of adult-onset chronic diseases in C57BL/6 mice	Mouse
American Journal of Physiology (AJP)	Lack of S100A1 in mice confers a gender-dependent hypertensive phenotype and increased mortality after myocardial infarction	Mouse
Journal of Visualized Experiments	Measuring blood pressure in mice using volume pressure recording, a tail-cuff method	Mouse
Atherosclerosis	Moderate kidney disease inhibits atherosclerosis regression	Mouse
American Journal of Physiology (AJP)	Myocardial lysyl oxidase regulation of cardiac remodeling in a murine model of diet-induced metabolic syndrome	Mouse
Methods in Molecular Biology	Non-invasive Blood Pressure Measurement in Mice	Mouse
Circulation	Phosphodiesterase-5 Inhibitor, Tadalafil, Protects Against Myocardial Ischemia/Reperfusion Through Protein-Kinase G-Dependent Generation of Hydrogen Sulfide	Mouse
University of California	Quantitative two-photon imaging of blood flow in cortex	Mouse

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continued

2009

Publication	Article Title	Animal
Hypertension	Regulation of Vascular Contractility and Blood Pressure by the E2F2 Transcription Factor	Mouse
American Journal of Physiology (AJP)	Temporal Analysis of Signaling Pathways Activated in a Murine Model of 2-Kidney, 1-Clip Hypertension	Mouse
PloS ONE	TGF- β Is Required for Vascular Barrier Function, Endothelial Survival and Homeostasis of the Adult Microvasculature	Mouse
Archives of Neurology	The Common Inhalational Anesthetic Sevoflurane Induces Apoptosis and Increases β -Amyloid Protein Levels	Mouse
Circulation Research	The Hedgehog Transcription Factor Gli3 Modulates Angiogenesis	Mouse
Circulation	Vascular Endothelial-Specific Dimethylarginine Dimethylaminohydrolase-1-Deficient Mice Reveal That Vascular Endothelium Plays an Important Role in Removing Asymmetric Dimethylarginine	Mouse
American Journal of Physiology (AJP)	Pulmonary Ozone Exposure Induces Vascular Dysfunction, Mitochondrial Damage, and Atherogenesis	Mouse
Wound Repair and Regeneration	[β]-1 and [β]-2, but not [α]-1 and [α]-2, adrenoceptor blockade delays rat cutaneous wound healing	Rat
Endocrinology	11 β -Hydroxysteroid Dehydrogenase Type II Inhibition Causes Cerebrovascular Remodeling and Increases Infarct Size after Cerebral Ischemia	Rat
Journal of Cerebral Blood Flow & Metabolism	Active dilation of penetrating arterioles restores red blood cell flux to penumbral neocortex after focal stroke	Rat
The Journal of Comparative Neurology	Altered balance of γ -aminobutyric acidergic and glutamatergic afferent inputs in rostral ventrolateral medulla-projecting neurons in the paraventricular nucleus of the hypothalamus of renovascular hypertensive rats	Rat
Korea Med	Altered Regulation of Renal Sodium Transporters in Salt-Sensitive Hypertensive Rats Induced by Uninephrectomy	Rat
Journal of Cardiovascular Pharmacology & Therapeutics	Anandamide Preserves Cardiac Function and Geometry in an Acute Doxorubicin Cardiotoxicity Rat Model	Rat
American Journal of Physiology (AJP)	Angiotensin II and Hypertonicity Modulate Proximal Tubular Aquaporin 1 (AQP1) Expression	Rat
Nephrology Dialysis Transplantation (NDT)	Antifibrotic effects of pioglitazone on the kidney in a rat model of type 2 diabetes mellitus	Rat
American Journal of Nephrology	Blockage of the Renin-Angiotensin System Attenuates Mortality but Not Vascular Calcification in Uremic Rats	Rat
American Journal of Physiology (AJP)	Chronic insulin treatment suppresses PTP1B function, induces increased PDGF signaling, and amplifies neointima formation in the balloon-injured rat artery	Rat
American Journal of Nephrology	Combination Therapy with Paricalcitol and Enalapril Ameliorates Cardiac Oxidative Injury in Uremic Rats	Rat
American Journal of Physiology (AJP)	Curcumin ameliorates renal failure in 5/6 nephrectomized rats: The role of inflammation	Rat
Microvascular Research	Diet-induced obesity causes cerebral vessel remodeling and increases the damage caused by ischemic stroke	Rat
Journal of Pharmacology and Experimental Therapeutics	Differential Effects of Diet-Induced Dyslipidemia and Hyperglycemia on Mesenteric Resistance Artery Structure and Function in Type 2 Diabetes	Rat
Brain Research	Early postnatal exposure to methylphenidate alters stress reactivity and increases hippocampal ectopic granule cells in adult rats	Rat
American Journal of Physiology	Effect of high-fat diet during gestation, lactation, or postweaning on physiological and behavioral indexes in borderline hypertensive rats	Rat
Clinical & Experimental Pharmacology & Physiology	Effect of Orchiectomy on Renal Function in Control and Diabetic Rats with Chronic Inhibition of Nitric Oxide	Rat

Publication	Article Title	Animal
The American Journal of the Medical Sciences	Effect of the HMG-CoA Reductase Inhibitor Rosuvastatin on Early Chronic Kidney Injury in Obese Zucker Rats Fed With an Atherogenic Diet	Rat
Hypertension	Increased Activation of Stromal Interaction Molecule-1/Orai-1 in Aorta From Hypertensive Rats	Rat
The Korean Journal of Physiology & Pharmacology	Inhibition of Arterial Myogenic Responses by a Mixed Aqueous Extract of Salvia Miltiorrhiza and Panax Notoginseng (PASEL) Showing Antihypertensive Effects	Rat
Journal of Vascular Research	Inhibition of Nitric Oxide Synthases Abrogates Pregnancy-Induced Uterine Vascular Expansive Remodeling	Rat
Molecular and Cellular Biochemistry	Long-term metabolic effects of different doses of niacin-bound chromium on Sprague-Dawley rats	Rat
Journal of Evolutionary Biochemistry and Physiology	Neonatal intermittent hypoxia and hypertension	Rat
American Journal of Physiology (AJP)	Niacin Ameliorates Oxidative Stress, Inflammation, Proteinuria, And Hypertension In Rats With Chronic Renal Failure	Rat
American Journal of Physiology (AJP)	Nitrite enhances RBC hypoxic ATP synthesis and the release of ATP into the vasculature: a new mechanism for nitrite-induced vasodilation	Rat
American Journal of Physiology (AJP)	Omega-3 Fatty Acid Supplementation Attenuates Oxidative Stress, Inflammation and Tubulo-Interstitial Fibrosis in the Remnant Kidney	Rat
Nephrology Dialysis Transplantation (NDT)	Parasympathetic regulation of heart rate in rats after 5/6 nephrectomy is impaired despite functionally intact cardiac vagal innervation	Rat
Pediatric Research	Postnatal Stress Produces Hyperglycemia in Adult Rats Exposed to Hypoxia-Ischemia	Rat
American Journal of Physiology (AJP)	PPAR- agonist rosiglitazone reverses increased cerebral venous hydraulic conductivity during hypertension	Rat
The Journal of Nutrition (JN)	Rapeseed Protein in a High-Fat Mixed Meal Alleviates Postprandial Systemic & Vascular Oxidative Stress & Prevents Vascular Endothelial Dysfunction in Healthy Rats	Rat
Journal of Neuroinflammation (JNI)	Reduction of lipoxidative load by secretory phospholipase A2 inhibition protects against neurovascular injury following experimental stroke in rat	Rat
Neuroscience Letters	Regulation of the phenylethanolamine N-methyltransferase gene in the adrenal gland of the spontaneous hypertensive rat	Rat
Hypertension	Role of Proinflammatory Cytokines and Redox Homeostasis in Exercise-Induced Delayed Progression of Hypertension in Spontaneously Hypertensive Rats	Rat
Journal of Applied Physiology	Simulated microgravity-induced aortic remodeling	Rat
American Journal of Physiology (AJP)	Spironolactone ameliorates transplant vasculopathy in renal chronic transplant dysfunction in rats	Rat
PloS ONE	Survival and Cardioprotective Benefits of Long-Term Blueberry Enriched Diet in Dilated Cardiomyopathy Following Myocardial Infarction in Rats	Rat
The Journal of Applied Biomedicine	The effect of S-nitrosocaptopril and S-nitroso-N-acetyl-D,L- penicillamine on blood glucose concentration and haemodynamic parameters	Rat
Nitric Oxide	Whole-body basal nitric oxide production is impaired in postprandial endothelial dysfunction in healthy rats	Rat
Journal of Renin-Angiotensin -Aldosterone System	Local renin-angiotensin system regulates left ventricular hypertrophy induced by swimming training independent of circulating renin: a pharmacological study	Rat
Circulation	Resveratrol Prevents the Prohypertrophic Effects of Oxidative Stress on LKB1	Rat
Nature Nanotechnology	A pilot toxicology study of single-walled carbon nanotubes in a small sample of mice	Mouse
Cardiovascular Research	A reactive oxygen species-mediated component in neurogenic vasodilatation	Mouse
American Journal of Physiology (AJP)	Angiotensin II Induced Contraction Is Attenuated By Nitric Oxide In Afferent Arterioles From The Non-Clipped Kidney In 2k1c	Mouse

Publication	Article Title	Animal
Endocrine-Related Cancer	Anti-cancer actions of a recombinant antibody (R6313/G2) against the angiotensin II AT1 receptor	Mouse
The Journal of Biological Chemistry (JBC)	Blood Pressure Is Regulated by an α 1D-Adrenergic Receptor/Dystrophin Signalingosome	Mouse
Drug Metabolism and Disposition	Deletion of the NADPH-cytochrome P450 reductase gene in cardiomyocytes does not protect mice against doxorubicin-mediated acute cardiac toxicity	Mouse
Canadian Journal of Physiology & Pharmacology	DOCA-salt treatment enhances responses to endothelin-1 in murine corpus cavernosum	Mouse
Cell	Epidermal Sensing of Oxygen Is Essential for Systemic Hypoxic Response	Mouse
Molecular & Cellular Biology	Generation and Characterization of rgs5 Mutant Mice	Mouse
PNAS - United States of America	High blood pressure arising from a defect in vascular function	Mouse
The Journal of Neuroscience	Hsp27 Protects against Ischemic Brain Injury via Attenuation of a Novel Stress-Response Cascade Upstream of Mitochondrial Cell Death Signaling	Mouse
Diabetes	Inducible Overexpression of sFlt-1 in Podocytes Ameliorates Glomerulopathy in Diabetic Mice	Mouse
Circulation	Inhaled Nitric Oxide Enables Artificial Blood Transfusion Without Hypertension	Mouse
The Journal of Neuroscience	Isoflurane-Induced Caspase-3 Activation Is Dependent on Cytosolic Calcium and Can Be Attenuated by Memantine	Mouse
American Journal of Physiology	NFATc3 is required for intermittent hypoxia-induced hypertension	Mouse
Biomedical Central (BMC) Neuroscience	Plasmalemmal Vesicle Associated Protein-1 (PV-1) is a marker of blood-brain barrier disruption in rodent models	Mouse
Journal of Cardiovascular Pharmacology	S-Nitroso-N-Acetylcysteine Prevents Myocardial Alterations in Hypercholesterolemic LDL Receptor Knockout Mice by Antiinflammatory Action	Mouse
American Journal of Hypertension (AJH)	Validation of Volume-Pressure Recording Tail-Cuff Blood Pressure Measurements	Mouse
The Journal of Experimental Medicine (JEM)	VEGF and TGF- β are required for the maintenance of the choroid plexus and ependyma	Mouse
Journal of Lipid Research (JLR)	Angiotensin II increases vascular proteoglycan content preceding and contributing to atherosclerosis development	Rat
Journal of Inorganic Biochemistry	Blood pressure lowering effects of niacin-bound chromium(III) (NBC) in sucrose-fed rats: Renin-angiotensin system	Rat
Pediatric Nephrology	Cardiac hypertrophy in neonatal nephrectomized rats: the role of the sympathetic nervous system	Rat
Nephron Physiology	Effect of Febuxostat on the Progression of Renal Disease in 5/6 Nephrectomy Rats with and without Hyperuricemia	Rat
American Journal of Physiology	Effects of acute & chronic L-arginine treatment in experimental hyperuricemia	Rat
American Journal of Physiology (AJP)	Effects of febuxostat on metabolic and renal alterations in rats with fructose-induced metabolic syndrome	Rat
Medicine & Sciences in Sports & Exercise	Exercise Preconditioning Protects against Doxorubicin-Induced Cardiac Dysfunction	Rat

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