BIOGRAPHICAL SKETCH
Senior Trainer

NAME: **Sathish Kumar**

eRA COMMONS USER NAME: kusathis

POSITION TITLE: Associate Professor (tenured)

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Tamil Nadu Veterinary & Animal Sciences University (TANUVAS), India	DVM	1996	Veterinary Medicine
TANUVAS	MVSc	1999	Pharmacology & Toxicology
Indian Veterinary Research Institute, India	PhD	2003	Veterinary Pharmacology
Southern University and A&M College (SUBR), Baton Rouge, Louisiana	Fellowship	2007	Cardiovascular Toxicology
University of Texas Medical Branch (UTMB), Galveston, Texas	Fellowship	2009	Cardiovascular Physiology

A. PERSONAL STATEMENT

I have a broad background and training in reproductive biology, cardiovascular physiology, and regulation of fetal growth. I have expertise in key research areas for this application, such as using fine vessel wire myography for vascular reactivity studies, blood pressure monitoring using invasive and noninvasive methods, and histopathology and molecular studies including real-time PCR and Western blotting. I characterized the nitric oxide- and α_2 adrenoceptor-mediated vascular signaling mechanisms in pulmonary arteries. We showed that inhibition of CGRP peptides during pregnancy causes fetal growth retardation and hypertension and sex steroid hormones modulate many of the vascular effects. I established my independent research group in the department of Ob/Gyn at UTMB – Galveston in 2010 and then expanded my vascular studies to include maternal vascular adaptation and fetal programming of adult cardiovascular diseases. As a PI on multiple NIH funded grants, I laid the ground work to develop a pregnant rat model of androgen exposure and provide strong evidence that elevated testosterone levels during pregnancy affects maternal cardiovascular adaptation and increases the risk of hypertension in adult offspring. I had successfully administered the projects (eg, staffing, research, and budget), collaborated with other researchers, and produced many peer-reviewed publications from each project. I moved to University of Wisconsin last year and got affiliated with Cellular and Molecular Pathology (CMP) graduate program.

Our laboratory is interested in understanding the physiological and pathophysiological mechanisms underlying blood pressure control during pregnancy and the fetal origins of adult metabolic disorders. We use an integrated approach that combines basic science, molecular laboratory techniques, and state-of-the-art cardiovascular tools to study: a) The mechanisms that contribute to normal cardiovascular adaptations during pregnancy, focusing on steroid hormones and the renin-angiotensin system, b) Why these cardiovascular changes are perturbed in certain pregnant women and whether an unhealthy lifestyle and disease during pregnancy have a role (i.e. stress, smoking, hypoxia etc.), c) How disorders in the mother induce organizational and structural changes in the heart and vasculature of the fetus, with emphasis on the level of adrenal and gonadal hormones, genes and inflammatory factors, and d) How the mechanisms of hypertension and diabetes are different between males and females, with focus on the endothelium and vascular smooth muscle signaling. An understanding of these pregnancy and fetal mechanisms will help to prevent abnormal maternal vascular function and the consequent development of adult-life diseases — this provides a novel approach of bringing preventive medicine back into the womb. Understanding the sex effects in hypertension and diabetes will provide knowledge for the development of sex-specific treatments for these disorders. I have mentored 5 postdoctoral fellows, 2 graduate students and 3 undergraduate student in my lab. Excellence in mentoring is demonstrated through the awards garnered by my students and fellows: Presidents Pfizer Award, Lalor Foundation Award and Excellence in Basic Science Research Award. Many trainees have taken a faculty position and industrial job.

Kumar's name in publications prior to 2017 appear as Sathishkumar K

1. Mishra JS, Gopalakrishnan K, **Kumar S**. Pregnancy upregulates angiotensin type 2 receptor expression and increases blood flow in uterine arteries of rats. Biol Reprod. 2018 Jun 1. PubMed PMID: 29860295.

2. Chinnathambi V, Blesson CS, Vincent KL, Saade GR, Hankins GD, Yallampalli C, **Sathishkumar K**. Elevated testosterone levels during rat pregnancy cause hypersensitivity to angiotensin II and attenuation of endothelium-dependent vasodilation in uterine arteries. Hypertension. 2014 Aug; 64(2):405-14. PubMed PMID: 24842922; PubMed Central PMCID: PMC4096063.

3. Yallampalli C, Chauhan M, **Sathishkumar K**. Calcitonin gene-related family peptides in vascular adaptations, uteroplacental circulation, and fetal growth. Curr Vasc Pharmacol. 2013 Sep; 11(5):641-54. Review. PMID:24063381;

4. Chinnathambi V, Balakrishnan M, Ramadoss J, Yallampalli C, **Sathishkumar K**. Testosterone alters maternal vascular adaptations: role of the endothelial NO system. Hypertension. 2013 Mar; 61(3):647-54. PubMed PMID: 23339170; PubMed Central PMCID: PMC3596870.

B. POSITIONS AND HONORS

Positions and Employment

1998 - 2000	Deputy Manager, Alved Pharma and Foods Pvt. Ltd., Chennai
2003 - 2004	Research Scientist, Ranbaxy Research Laboratories, Gurgaon
2004 - 2007	Cardiovascular Toxicology Fellowship, Southern University and A&M College, Baton Rouge, LA
2007 - 2009	Postdoctoral Fellow, Department of Obstetrics & Gynecology, UTMB, Galveston, TX
2009 - 2010	Instructor, Department of Obstetrics & Gynecology, UTMB, Galveston, TX
2010 - 2016	Assistant Professor (tenure-track), Department of Obstetrics & Gynecology, UTMB, Galveston
2014 – 2016	Assistant Professor, Biochemistry and Molecular Biology Graduate Program, UTMB, Galveston
2014 –2016	Assistant Professor, NIEHS Center for Environmental Toxicology, UTMB, Galveston, TX
2016– 2017	Associate Professor (Tenured), Department of Obstetrics & Gynecology, UTMB, Galveston, TX.
2017–	Associate Professor (Tenured), Department of Comparative Biosciences, University of Wisconsin, Madison, WI
2017–	Associate Professor (Adjunct), Department of Obstetrics & Gynecology, University of Wisconsin, Madison, WI

Other Experience and Professional Memberships

2005 - 2009	Member, North American Vascular Biology Organization
2008 -	Member, Society for Study of Reproduction
2011 -	Member, Developmental Origins of Health and Disease
2011 -	Member, American Heart Association
2013 -	Member, Perinatal Research Society
2014 -	Member, Society for Reproduction Investigation
2014 -	Editorial Board Member, Austin Journal of Obstetrics and Gynecology
2014 -	Editorial Board Member, Biology of Reproduction
2016	ad-hoc member, NIH grant review study sections (PN)
2016 -	Standing member, NIH grant Review, Obstetrics and Maternal-Fetal Biology subcommittee (CHHD B)
2018	ad-hoc member, NIH grant review, Vascular and Hematology (ZRG1 VH-N (80) A)

Honors

1999	Best Postgraduate Student, Madras Veterinary College, Chennai
1999	Gold medal for being topper in master's degree program and excellence in Pharmacology, Madras Veterinary College, Chennai
1999	Best Student in the Subject of Pharmacology, Madras Veterinary College, Chennai
2002	Senior Research Fellowship, Indian Council of Agricultural Research, New Delhi, Indian Council of Agricultural Research, New Delhi
2008	Excellence in Basic Science Research, 6th annual meeting of Center for Interdisciplinary Research in Women's Health (CIRWH), UTMB, Galveston, TX
2009	Travel award, 42nd Annual Meeting of the Society for Study of Reproduction, Pittsburgh, PA
2010	Young Investigator Award, Perinatal Research Society, Avon, CO
2011	Presidents Pfizer Award for meritorious research presentation, Society for Gynecological Investigation, San Diego, CA

2014	Researcher of the Month April/May, UTMB Research Services
2014	Lalor Foundation Award for Outstanding Research, Society for Study of Reproduction, Grand Rapids, MI
2015	Presidents Pfizer Award for meritorious research, Society for Reproductive Investigation, San Francisco, CA
2017	Presidents Pfizer Award for meritorious research, Society for Reproductive Investigation, Orlando, FL

C. CONTRIBUTION TO SCIENCE

Dr. Sathish Kumar's early publications directly addressed the molecular mechanisms by which ozone inflicts damage to the heart and brain. Ozone does not penetrate far beyond the air-tissue boundary (≤2 µm) in the lung to cause damage to distant organs like heart and brain. Dr. Sathish Kumar demonstrated that secosterols, the reaction product formed in the lung due to ozone's interaction with cholesterol, are a mediator of cytotoxic effect of environmental ozone in heart cells and neuronal cells. Dr. Sathish Kumar also established that secosterols promote aggregation of β-amyloid proteins, the pathognomonic feature in Alzheimer's disease. These observations were consistent with the identification of cholesterol secoaldehyde in brain samples of Alzheimer's patients. Using genomic approaches including microarray and real-time PCR technologies, Dr. Sathish Kumar demonstrated activation of the plasma membrane-bound NADPH oxidase system in neuronal cells exposed to secosterols, and that antioxidants efficiently reverses these ill-effects. Following these findings, Dr. Sathish Kumar was invited to contribute 2 book chapters to Free Radicals and Antioxidant Protocols for the Methods in Molecular Biology series (Humana Press, Totowa, NJ). The U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, cited Dr. Sathish Kumar findings in their review of the "national ambient air quality standards for ozone." His finding is also cited in a well known resource book "Research Progress in Alzheimer's disease and Dementia" that is frequently referenced by medical students and clinical practitioners.

a. **Sathishkumar K**, Haque M, Perumal TE, Francis J, Uppu RM. A major ozonation product of cholesterol, 3beta-hydroxy-5-oxo-5,6-secocholestan-6-al, induces apoptosis in H9c2 cardiomyoblasts. FEBS Lett. 2005 Nov 21;579(28):6444-50. PubMed PMID: 16288747.
b. **Sathishkumar K**, Murthy SN, Uppu RM. Cytotoxic effects of oxysterols produced during ozonolysis of cholesterol in murine GT1-7 hypothalamic neurons. Free Radic Res. 2007 Jan;41(1):82-8. PubMed PMID: 17164181.
c. **Sathishkumar K**, Xi X, Martin R, Uppu RM. Cholesterol secoaldehyde, an ozonation product of cholesterol, induces amyloid aggregation and apoptosis in murine GT1-7 hypothalamic neurons. J Alzheimers Dis. 2007 Jun;11(3):261-74. PubMed PMID: 17851176.
d. **Sathishkumar K**, Gao X, Raghavamenon AC, Parinandi N, Pryor WA, Uppu RM. Cholesterol secoaldehyde induces apoptosis in H9c2 cardiomyoblasts through reactive oxygen species involving mitochondrial and death receptor pathways. Free Radic Biol Med. 2009 Sep 1;47(5):548-58. PubMed PMID: 19477266.

Dr. Sathish Kumar began working on the mechanisms that impair cardiovascular adaptations to pregnancy in 2007. Dr. Sathish Kumar initially received support for this work with an NIH R03 developmental grant. In contrast to most studies that examined the beneficial effects of estradiol and progesterone, Dr. Sathish Kumar discovered that androgens adversely affect maternal vascular and placental function. Dr. Sathish Kumar developed a unique rat model that mimics human testosterone levels and pattern as observed in preeclamptic pregnancies and showed that elevated testosterone levels during pregnancy incudes key features seen in women with preeclampsia, such as hypertension, proteinuria, endothelial dysfunction, exaggerated vascular contractile response to angiotensin II, placental insufficiency with decreased nutrient transport capacity, and fetal growth restriction. This study was published in Hypertension in 2013. Later, a commentary appeared in Hypertension stating that this this study used a well-controlled experimental model, is novel and provides critical mechanistic insight and potential therapeutic targets for gestational hypertension, and emphasized the need for clinical translation of this important work. Dr. Sathish Kumar was invited to present this finding in the "Late Breaking Science" session of the 18th World Congress of International Society for Study of Hypertension in Pregnancy in Geneva, Switzerland. Further work stemming from these findings led us to examine the placentas of preeclamptic women to find that the placenta contributes to increased androgen production and expresses higher androgen receptor levels. The implication is that understanding testosterone's influences on the maternal

cardiovascular system could lead to new therapeutic approaches to ameliorate hypertensive effects during pregnancy.

a. **Sathishkumar K**, Balakrishnan M, Chinnathambi V, Chauhan M, Hankins GD, Yallampalli C. Fetal sex-related dysregulation in testosterone production and their receptor expression in the human placenta with preeclampsia. J Perinatol. 2012 May;32(5):328-35. PubMed PMID: 21904298; PubMed Central PMCID: PMC3712643.
b. Chinnathambi V, Balakrishnan M, Ramadoss J, Yallampalli C, **Sathishkumar K**. Response to Testosterone and Sympathetic Nerve Activity during Pregnancy. Hypertension. 2013; 61:e45.
c. Chinnathambi V, Balakrishnan M, Ramadoss J, Yallampalli C, **Sathishkumar K**. Testosterone alters maternal vascular adaptations: role of the endothelial NO system. Hypertension. 2013 Mar;61(3):647-54. PubMed PMID: 23339170; PubMed Central PMCID: PMC3596870.
d. Chinnathambi V, Blesson CS, Vincent KL, Saade GR, Hankins GD, Yallampalli C, **Sathishkumar K**. Elevated testosterone levels during rat pregnancy cause hypersensitivity to angiotensin II and attenuation of endothelium-dependent vasodilation in uterine arteries. Hypertension. 2014 Aug;64(2):405-14. PubMed PMID: 24842922; PubMed Central PMCID: PMC4096063.

In his early work, Dr. Sathish Kumar discovered that prenatal insults, such as protein restriction and elevated testosterone levels, lead to adult life hyperandrogenism and hypertension that is more pronounced in males than females. This sex-related difference in cardiovascular risk has been attributed to the protective effects of estrogens. Dr. Sathish Kumar's studies provide a different approach, addressing the effects of postnatal androgens. His work led to the important observation that elevated testosterone levels during adult life dynamically regulate blood pressure and that this effect is mediated via heightened angiotensin II type 1 receptor (AGTR1)- and protein kinase C (PKC)-mediated signaling. Dr. Sathish Kumar identified a novel androgen-mediated mechanism that controls the expression of PKCδ in mesenteric artery smooth muscle cells through positive regulation of PKCδ transcript and protein levels. He identified the functional androgen response and enhancer element that binds androgen receptor in response to androgen stimulation in the PKCδ gene promoter and intron 1, respectively. These studies provide a paradigm shift in exploring the role of androgens in hypertension, not only in males, but also in females. Dr. Sathish Kumar served as the primary investigator or co-investigator in all of these studies.

a. Chinnathambi V, Balakrishnan M, Yallampalli C, **Sathishkumar K**. Prenatal testosterone exposure leads to hypertension that is gonadal hormone-dependent in adult rat male and female offspring. Biol Reprod. 2012 May;86(5):137, 1-7. PubMed PMID: 22302690; PubMed Central PMCID: PMC3364920.
b. **Sathishkumar K**, Balakrishnan M, Chinnathambi V, Gao H, Yallampalli C. Temporal alterations in vascular angiotensin receptors and vasomotor responses in offspring of protein-restricted rat dams. Am J Obstet Gynecol. 2012 Jun;206(6):507.e1-10. PubMed PMID: 22537420; PubMed Central PMCID: PMC3361632.
c. **Sathishkumar K**, Balakrishnan MP, Yallampalli C. Enhanced mesenteric arterial responsiveness to angiotensin II is androgen receptor-dependent in prenatally protein-restricted adult female rat offspring. Biol Reprod. 2015 Feb;92(2):55. PubMed PMID: 25550341; PubMed Central PMCID: PMC4342791.
d. Blesson CS, Chinnathambi V, Hankins GD, Yallampalli C, **Sathishkumar K**. Prenatal testosterone exposure induces hypertension in adult females via androgen receptor-dependent protein kinase Cδ-mediated mechanism. Hypertension. 2015 Mar;65(3):683-90. PubMed PMID: 25489059; PubMed Central PMCID: PMC4326589.

Sex differences are often neglected when considering diagnosis or treatment. Dr. Sathish Kumar's studies provide seminal observations that there is distinct sex-specific hypertension signaling mechanisms in the endothelium. Dr. Sathish Kumar identified that the endothelial EDHF-mediated vasodilator pathway is selectively impaired in hypertensive males, whereas only the nitric oxide (NO)-mediated relaxation system is affected in hypertensive females. This information might be clinically relevant because sex differences in clinical responsiveness to antihypertensive therapies have been reported. Recently, Dr. Sathish Kumar demonstrated that the impaired EDHF relaxation in hypertensive males could be restored with the angiotensin converting enzyme inhibitor enalapril. These studies lay the ground work for identification of novel, sex-specific therapeutic strategies and new drug discovery paradigms for the treatment of hypertension.

a. **Sathishkumar K**, Elkins R, Yallampalli U, Yallampalli C. Protein restriction during pregnancy induces hypertension and impairs endothelium-dependent vascular function in adult female offspring. J Vasc Res. 2009;46(3):229-39. PubMed PMID: 18957856; PubMed Central PMCID: PMC2860528.

b. **Sathishkumar K**, Elkins R, Yallampalli U, Balakrishnan M, Yallampalli C. Fetal programming of adult hypertension in female rat offspring exposed to androgens in utero. Early Hum Dev. 2011 Jun;87(6):407-14. PubMed PMID: 21450421; PubMed Central PMCID: PMC3093104.

c. Chinnathambi V, Yallampalli C, **Sathishkumar K.** Prenatal testosterone induces sex-specific dysfunction in endothelium-dependent relaxation pathways in adult male and female rats. Biol Reprod. 2013 Oct;89(4):97. PubMed PMID: 23966325; PubMed Central PMCID: PMC4076398.

d. Chinnathambi V, More AS, Hankins GD, Yallampalli C, **Sathishkumar K.** Gestational exposure to elevated testosterone levels induces hypertension via heightened vascular angiotensin II type 1 receptor signaling in rats. Biol Reprod. 2014 Jul;91(1):6. PubMed PMID: 24855104.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/sathish.kumar.1/bibliography/41995480/public/?sort=date&direction=descending

D. RESEARCH SUPPORT

Ongoing Research Support

R01 HL119869 (Kumar) 2013/08/09–2019/05/31 (No Cost Extension)
NHLBI
Sex-specific fetal programming of adult vascular dysfunction and hypertension
The proposed studies, focusing on a molecular mechanistic link between adverse intrauterine environments and development of a hypertensive phenotype, will provide direct evidence that elevated androgen levels during pregnancy increases the risk of hypertension and cardiovascular disease in the offspring. This new evidence will provide several possible sex-specific approaches to improving vascular function and reducing high blood pressure.

R01 HL134779-01A1 (Kumar) 07/01/2017-06/30/2021
NHLBI
Vascular AT2R expression and function during pregnancy
The goal of this proposal is to examine molecular mechanism of vascular angiotensin type 2 receptor (AT2R) upregulation and its importance in normal pregnancy associated vascular function. Studies will also examine if activation of this receptor system can reverse preeclamptic vascular dysfunction and hypertension. The proposed study could lead to identification of targets to treat or prevent preeclampsia.

Completed Research Support

R03 HD069750 (Kumar) 2011/07/25–2014/06/30
NICHD
Maternal Androgen Excess: Vascular and Placental Function and Fetal Consequences
The main goal of this project is to examine the effect of elevated maternal testosterone levels on maternal cardiovascular adaptations to pregnancy and placental angiogenesis and nutrient transport capacity.

R01 HL102866 (Yallampalli) 12/01/2010–11/30/2014
NHLBI
Developmental Programming: Influence of Sex Steroids and Mechanisms
This project will assess the mechanisms underlying the developmental programming of adult health and disease and the influence of sex steroid hormones.
Role: Co-I

R01 HL058144 (Yallampalli) 07/01/2013–06/30/2017
NHLBI
Sex Steroid Hormones and Calcitonin Gene-Related Peptide
Our goal is to define the role of calcitonin gene-related peptide family peptides in the regulation of female vascular functions, and to examine their involvement of these peptides in uteroplacental function.
Role: Co-I