BIOGRAPHICAL SKETCH

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NAME: S. Ananth KARUMANCHI

eRA COMMONS USER NAME (credential, e.g., agency login): sananth

POSITION TITLE: Staff Physician, Cedars-Sinai Medical Center and Director, Center for Renovascular Research

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Kilpauk Medical College and University of Madras, Chennai, INDIA	M.D.	04/1992	Medicine
Henry Ford Hospital, Detroit, MI	Residency	06/1996	Internal Medicine
Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA	Fellowship	06/2000	Nephrology/Molecular Biology

A. Personal Statement

The Karumanchi laboratory is focused on understanding the role of angiogenesis and endothelial function in health and in disease with an emphasis on the pathogenesis of preeclampsia, a pregnancy disorder characterized by hypertension, proteinuria and glomerular endotheliosis. Novel angiogenic biomarkers for use in early diagnosis and prediction of preeclampsia and its related complications are being tested in prospective clinical studies. Dr. Karumanchi's research activities are vertically integrated, ranging from molecular and cell biological studies to animal models to first-in-class human clinical trials. His laboratory is also testing the pathogenesis of preeclampsia and chronic kidney disease- related cardiovascular diseases using both animal models and clinical studies. Dr. Karumanchi is on the editorial board of several medical journals (*Journal of Clinical Investigation*, *Hypertension*, *Journal of the American Society of Nephrology*, *Pregnancy Hypertension*, *and Hypertension in Pregnancy).* Dr. Karumanchi is recognized nationally and internationally for his seminal work on uncovering the critical importance of angiogenic factors in preeclampsia. He is a recipient of numerous awards and was inducted into the American Society for Clinical Investigation in 2007. In 2010, he won the highest recognitions from the International Society for the Study of Hypertension in Pregnancy – Chesley Award, and the American Federation for Medical Research – Outstanding Investigator Award. Dr. Karumanchi has supervised and mentored over 30 trainees during the last 10 years and his laboratory currently trains 7 post-doctoral/research fellows (2 out of 7 supported by T32 award), 1 medical student and 4 junior faculty members (2 out of 4 supported by K08 awards) in translational and basic research.

1. Maynard SE, Min J, Merchan J, Lim KH, Li J, Mondal S, Libermann T, Morgan JP, Sellke FW, Stillman IE, Epstein FH, Sukhatme VP, Karumanchi SA: Excess placental sFlt-1 may contribute to endothelial dysfunction, hypertension and proteinuria in preeclampsia. *Journal of Clinical Investigation 2003*, 111(5):649-658; PMCID: PMC151901 (Cited >3000 times)

2. Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, Schisterman EF, Thadhani R, Sachs BP, Epstein FH, Sibai BM, Sukhatme VP, Karumanchi SA: Circulating angiogenic proteins and the risk for preeclampsia *New England Journal of Medicine,* 2004, 350:672-8; PMID: 14764923 (Cited > 2000 times)

3. Venkatesha S, Toporsian M, Lam C, Hanai J, Mammoto, Kim YM, Bdolah Y, Lim KH, Yuan HT, Libermann TA, Stillman IE, Roberts D, D'Amore PA, Epstein FH, Sellke FW, Romero R, Sukhatme VP, Letarte M, Karumanchi SA: Soluble endoglin contributes to the pathogenesis of preeclampsia. *Nature Medicine*, 2006, 12:642-9; PMID: 16751767(Cited >1500 times)

4. Burke SD, Zsengellér ZK, Khankin EV, Lo AS, Rajakumar A, DuPont J, McCurley A, Moss ME, Zhang D, Clark CD, Wang A, Seely EW, Kang PM, Stillman IE, Jaffe, IZ, Karumanchi SA. Soluble fms-like tyrosine kinase 1 promotes angiotensin II sensitivity in preeclampsia. *Journal of Clinical Investigation.* 2016; 126(7):2561-74; PMCID: PMC4922717

B. Positions/Employment, Memberships and Honors

Professional Positions

2000-	Attending Physician (Nephrology)	Beth Israel Deaconess Med. Center (BIDMC), Boston, MA
2000-03	Instructor of Medicine	Harvard Medical School, Boston, MA
2003-06	Assistant Professor of Medicine	Harvard Medical School, Boston, MA
2004-07	Assistant Professor of OB/GYN.	Harvard Medical School, Boston, MA
2004-	Investigator	Center for Vascular Biology, BIDMC, Boston, MA
2006-14	Associate Professor of Medicine	Harvard Medical School, Boston, MA
2008-15	Investigator	Howard Hughes Medical Institute
2014-17	Professor of Medicine	Harvard Medical School, Boston, MA
2017-	Visiting Professor	Harvard Medical School, Boston, MA
2017-	Director, Ctr for Renovascular Res.	Cedars-Sinai Medical Center, Los Angeles, CA

Professional Memberships/Committees

1993-	American College of Physicians/American Society of Internal Medicine
1994-	American Medical Association
1996-	American Society of Nephrology
1996-	American Society for the Advancement of Science
2003-	Preeclampsia Foundation - Medical Science & Policy Advisory Board
2005-	Society for Gynecologic Investigation
2006-	Member, Institutional Review Board (IRB), Beth Israel Deaconess Med. Center
2008-	American Heart Association
2009-	American Federation for Medical Research
2012-	Member, Pregnancy and Neonatology Study Section, NIH
2012-13	Hypertension and Pregnancy Task Force, American College of Obstetrics and Gynecology

Honors and Awards

1991	Dr. Asirvada Nadar memorial prize - final MBBS degree exam – U of Madras, India
1999	NIH - Individual National Research Service Award (NRSA)
2000	NIH - Mentored Clinical Scientist Development Award (KO8)
2002	American Society of Nephrology – Carl W. Gottschalk Research Scholar Award
2006	Preeclampsia Foundation – Hope Award
2007	American Society of Hypertension, Young Scholar Award
2007	American Society for Clinical Investigation
2008	American Heart Association – Established Investigator Award
2008	American Society of Nephrology – Young Investigator Award
2008	Burroughs Wellcome Fund– Clinical Scientist Award
2008	Investigator, Howard Hughes Medical Institute
2009	La Renon TANKER foundation Award
2010	Outstanding Investigator Award, American Federation for Medical Research
2010	Chesley Award, International Society for the Study of Hypertension in Pregnancy
2010	Cunio-Richardson Memorial Award Lecture - National Kidney Foundation of Florida
2013	Serono Foundation Lecture – "Top 10 Breakthoughs in Reproductive Medicine"
2015	Association of American Physicians
2015	Arthur C. Corcoran Memorial Award, Council for Hypertension - American Heart Association
2016	Outstanding Contributions in Nephrology Research, International Society of Nephrology

C. Contributions to Science

1. Biomarkers in Hypertensive Disorders of Pregnancy: Dr. Karumanchi's seminal contribution has been the discovery from his laboratory that soluble vascular endothelial growth factor (VEGF) receptor (referred to as sFlt1) is a key pathogenic factor elaborated by the placenta that is responsible for the clinical signs/symptoms of preeclampsia, one of the most common medical complications of pregnancy. Dr. Karumanchi's laboratory also demonstrated that soluble endoglin is a second anti-angiogenic factor that contributes to the pathogenesis of severe preeclampsia and HELLP syndrome. Dr. Karumanchi's laboratory has led several clinical studies to evaluate angiogenic proteins as an aid in early detection of preeclampsia and its complications.

a. Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, Schisterman EF, Thadhani R, Sachs BP, Epstein FH, Sibai BM, Sukhatme VP, Karumanchi SA: Circulating angiogenic proteins and the risk for preeclampsia *New England Journal of Medicine,* 2004, 350:672-8; PMID: 14764923 (Cited > 2500 times)

b. Levine RJ, Thadhani R, Qian C, Lam C, Lim KH, Yu KF, Blink AL, Sachs BP, Epstein FH, Sibai, BM, Sukhatme VP, Karumanchi SA: Urinary PlGF and the risk of preeclampsia. *JAMA,* 2005, 293:77-85; PMID: 15632339 (Cited >350 times)

c. Levine RJ, Lam C, Qian C, Yu KF, Maynard SE, Sachs BP, Sibai BM, Epstein FH, Romero R, Thadhani R, Karumanchi SA: Soluble endoglin and other circulating anti-angiogenic factors in preeclampsia. *New England Journal of Medicine*, 2006, 355:992-1005; PMID: 16957146 (Cited >1500 times)

d. Rana S, Powe CE, Salahuddin S, Verlohren S, Perschel FH, Levine RJ, Lim KH, Wenger JB, Thadhani R, Karumanchi SA. Angiogenic Factors and the Risk of Adverse Outcomes in Women with Suspected Preeclampsia. *Circulation*, 2012, 125(7):911-9. PMCID: PMC3319742 (Cited >300 times)

2. Therapeutic Studies in Preeclampsia: Collaborating with Thadhani laboratory at Massachusetts General Hospital, we have developed a novel apheresis strategies to safely prolong pregnancies in women with preeclampsia. Dr. Karumanchi's laboratory is also evaluating growth factor replacement strategies and small molecules that promote vascular health in pre-clinical models of preeclampsia.

a. Thadhani R, Kisner T, Hagmann H, Bossung V, Noack S, Schaarschmidt W, Jank A, Kribs A, Cornely O, Kreyssig C, Hemphill L, Lindner TH, Mallmann P, Stepan H, Karumanchi SA, Benzing T. A Pilot Study of Extracorporeal Removal of Soluble Fms-like Tyrosine Kinase 1 (sflt-1) in Preeclampsia. *Circulation* 2011, 124:940-50. PMID: 21810665 (Cited >200 times)

b. Rana S, Rajakumar A, Geahchan C, Salahuddin S, Cerdeira AS, Burke SD, George E, Granger J, Karumanchi SA. Ouabain inhibits placental sFlt1 production by repressing HSP27 dependent HIF-1 alfa pathway. *FASEB Journal*, 2014, 28(10):4324-34. PMCID: PMC4202104

c. Makris A, Yeung KR , Lim SM, Sunderland N, Heffernan S, Thompson JF, Iliopoulos J, Killingsworth MC, Yong J, Xu B, Ogle RF, Thadhani R, Karumanchi SA, Hennessy A. Placental growth factor reduces blood pressure in a uteroplacental ischemia model of preeclampsia in non-human primates. *Hypertension* 2016, 67(6):1263-72. PMCID: PMC4867111

d. Li F, Fushima T, Oyanagi G, Townley-Tilson WHD, Sato E, Nakada H, Oe Y, Hagaman JR, Wilder J, Li M, Sekimoto A, Saigusa D, Sato H, Ito S, Jennette JC, Maeda N, Karumanchi SA, Smithies O, Takahashi N. Nicotinamide benefits both mothers and pups in two contrasting mouse models of pre-eclampsia. *Proceedings of the National Academy of Sciences, 2*016; 113:13450-13455. PMCID: PMC5127378

3. Preeclampsia and Cardiovascular Disease: Dr. Karumanchi's laboratory has also mechanistically linked preeclampsia to chronic maternal complications including hypertension, hypothyroidism, chronic renal disease, cardiomyopathy and cardiovascular disease.

a. Levine RJ, Vatten LJ, Horowitz GL, Qian C, Romundstad PR, Yu KF, Hollenberg AN, Hellevik AI, Asvold BO, Karumanchi SA. Preeclampsia, Soluble Fms-like Tyrosine Kinase 1, and the Risk of Reduced Thyroid Function. *British Medical Journal*, 2009, 339:b4336.doi:10.1136/bmj.b4336. PMCID: PMC2778749

b. Patten IS, Rana S, Shahul S, Rowe GC, Jang C, Liu L, Hacker MR, Rhee JS, Mitchell J, Mahmood F, Hess P, Farrell C, Koulisis N, Khankin EV, Burke SD, Tudorache I, Bauersachs J, del Monte F, Hilfiker-

Kleiner D, Karumanchi SA, Arany Z. Cardiac angiogenic imbalance leads to peripartum cardiomyopathy *Nature*, 2012; 485(7398):333-8. PMCID: PMC3356917

c. Pruthi D, Khankin EV, Blanton RM, Aronovitz M, Burke SD, McCurley A, Karumanchi SA, Jaffe IZ. Exposure to experimental preeclampsia in mice enhances the vascular response to future injury. *Hypertension*. 2015, 65(4):863-70. PMCID: PMC4359068

d. Goel A, Maski MR, Bajracharya S, Wenger JB, Zhang D, Salahuddin S, Shahul SS, Thadhani R, Seely EW, Karumanchi SA, Rana S. Epidemiology and Mechanisms of De Novo and Persistent Hypertension in the Postpartum Period. *Circulation*, 2015, 132(18):1726-33. PMCID: PMC 4816491

4. Uremia, Bone and Cardiovascular Disease: Another focus of research in Dr. Karumanchi's laboratory is to elucidate vascular mechanisms of uremia related complications. Using animal models, Dr. Karumanchi and his collaborators have identified novel factors that lead to bone and cardiovascular disease in patients with chronic kidney disease.

a. Bodyak N, Ayus JC, Achinger S, Shivalingappa V, Ke Q, Chen YS,. Rigor DL, Stillman I, Tamez H, Kroeger PE, Wu-Wong RR, Karumanchi SA, Thadhani R, Kang P. Activated vitamin D attenuates left ventricular abnormalities induced by dietary sodium in Dahl salt-sensitive animals. *Proceedings of the National Academy of Sciences, 2007,* 104(43):16810-5. PMCID: PMC2040477

b. Berg AH, Drechsler C, Wenger J, Buccafusca R, Hod T, Kalim S, Ramma W, Parikh SM, Steen H, Friedman DJ, Danziger J, Wanner C, Thadhani R, Karumanchi SA. Protein carbamylation resulting from urea-amino acid imbalance is associated with mortality in patients with kidney failure. *Science Translational Medicine* 2013, 5(175):175ra29. PMCID: PMC3697767

c. Powe CE, Evans MK, Wenger J, Zonderman AB, Berg AH, Nalls M, Tamez H, Bhan I, Karumanchi SA, Powe NR, Thadhani R. Vitamin D Binding Protein and Vitamin D Status of Community Dwelling Black and White Americans. *New England Journal of Medicine, 2013,* 369(21):1991-2000. PMCID: PMC4030388

d. Tran MT, Zsengeller Z, Berg AH, Khankin EV, Bhasin MK, Kim W, Clish CB, Stillman IE, Karumanchi SA, Rhee EP, Parikh SM. PGC1α drives NAD biosynthesis, linking oxidative metabolism to renal protection. *Nature* 2016, 531(7595):528-32. PMCID:PMC4909121

5 Collaborative Studies in the area of vascular leakage and sepsis-related complications: My laboratory actively collaborates with Aird laboratory and Parikh laboratory to evaluate the role of vascular factors in the sepsis-related morbidity in humans and in animal models.

a. Yano K, Law PC, Mulligton JM, Shih SC, Okada H, Bodyak N, Kang PM, Toltl L, Belikoff B, Buras J, Mizgerd JP, Karumanchi SA, Aird WC. Vascular endothelial growth factor is an important determinant of sepsis morbidity and mortality. *The Journal of Experimental Medicine,* 2006, 203:1447-58. PMCID: PMC2118329

b. Yano K, Okada Y, Beldi G, Shih SC, Bodyak N, Okada H, Kang PM, Luscinskas W, Robson SC, Carmeliet P, Karumanchi SA, Aird WC. Elevated levels of placental growth factor represent an adaptive host response in sepsis. *Journal of Experimental Medicine*, 2008, 205:2623-31. PMCID: PMC2571936

c. Parikh SM, Mammoto T, Schultz A, Yuan HT, Christiani D, Karumanchi SA, Sukhatme VP. Excess circulating angiopoietin-2 may contribute to pulmonary vascular leak in sepsis in humans. *PLoS Med.* 2006; 3(3):e46. PMCID: PMC1334221

d. David S, Mukherjee A, Ghosh CC, Yano M, Khankin EV, Wenger JB, Karumanchi SA, Shapiro NI, Parikh SM. Angiopoietin-2 may contribute to multi-organ dysfunction and death in sepsis. *Crit Care Med.* 2012. Nov; 40(11): 3034-41. PMID 22890252. PMCID: PMC3705559.

Total Publications: >250 publications and 25 book chapters; H index =80(google scholar)

http://www.ncbi.nlm.nih.gov/sites/myncbi/s.karumanchi.1/bibliograpahy/41154339/public/?sort=date&direction=descending

D. Research Support.

Ongoing Research Support

2R01DK094486-04 Thadhani (PI) 04/01/15 - 02/28/19
Redefining Vitamin D Deficiency: Role of Bioavailable Vitamin D
Aim of this grant is to understand the role of DBP mutations on Vitamin D metabolism using genetically modified mice.
Role: Dual PI with Dr. Thadhani

1RO1HL133399-01A1 Berg (PI) 04/01/2018- 01/31/2022
Protein Carbamylation and Uremic Cardiomyopathy in Chronic Kidney Disease
Evaluate the contribution of protein carbamylation and cardiovascular disease in mouse models and in patients with chronic kidney disease
Role: Co-I

1 RO1 HD 086111-01A1 Khvorova (PI) 07/01/16 – 06/30/21
Development of RNAi-based sFlt1 targeting therapeutic for treatment of preeclampsia
Evaluate the *in vivo* efficacy of siRNA products in preeclampsia mouse models. In addition, his laboratory will provide expertise in evaluating the potency of siRNA product in primary cytotrophoblasts.
Role: Co-I; Subcontract from University of Massachusetts

1RO1HL134371-01 Osol (PI) 07/15/16 -06/30/20
Shear-Stress induced Maternal Vascular Remodeling During Pregnancy
Evaluate the role of shear stress in pregnant rats with ultrasound imaging in uterine artery remodeling.
Role: Co-I; Subcontract from University of Vermont

Siemens Healthcare Diagnostics, Inc. Karumanchi (PI) 03/21/17-03/20/19
Angiogenic Markers in Preeclampsia
To evaluate use of Siemens' automated angiogenic factor assays as a prognostic tool prospectively among patients with suspected preeclampsia

Completed Support

Brahms Gmbh Karumanchi (PI) 4/11/14 – 4/10/15
Validation of Kryptor platform for angiogenic markers
To validate angiogenic factor assays in normal human pregnancy samples using Kryptor platform.
Role: PI

Howard Hughes Medical Institute Karumanchi (PI) 04/01/08 – 08/31/15
Pathogenesis of preeclampsia and related disorders
Aims are to characterize final common disease pathways for vascular disorders and to use this knowledge to develop novel therapeutic products

Phase II grant (Gates foundation) Moore (PI) 09/01/13 – 03/31/16
siRNA based therapeutics for preeclampsia
Aim of the sub-contract is to develop a delivery method for siRNAs targeting murine and baboon placenta.
Role: Co-PI

Pluristem Therapeutics Inc Karumanchi (PI) 03/20/15-03/19/17
Placental Stem Cells in an animal model of preeclampsia
To characterize the therapeutic efficacy of placental stem cells in an animal model of preeclampsia.

1R56HL133399-01 Berg (PI) 09/16/16 – 12/31/17
Protein Carbamylation and Uremic Kidney Disease
Evaluate contribution of urea to cardiac oxidative stress and myopathy in mouse models.
Role: Co-I

1 R21 HD088004-01 Karumanchi (PI) 03/01/16-02/28/18
Role of ADAMTS13 in maternal complications of Preeclampsia
Using genetically modified mice that are deficient in ADAMTS13, we will evaluate the biological role of ADAMTS13 and VWF in the maternal complications of preeclampsia.