BIOGRAPHICAL SKETCH

Senior Trainer

NAME: Dinesh M Shah, MD

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

POSITION TITLE: Professor (Tenured)

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
Elphinstone College, University of Bombay	Int. Sc.	1968	Biology
T. National Medical College, University of Bombay	MB, BS	1973	
T. National Medical College, University of Bombay	MD	1976	Medicine
B.Y.L Nair Hospital, T. National Medical College, Bombay, India	Intern	1972-1973	Obstetrics/Gynecology
B.Y.L. Nair Hospital, Bombay, India	Resident	1973-1975	Obstetrics/Gynecology
Rajawadi Municipal General Hospital, Bombay, India	Resident	1975-1976	Obstetrics/Gynecology
St. Joseph's Hospital, Northwestern University, Chicago, IL	Resident	1977-1981	Obstetrics/Gynecology
SUNY Upstate Medical Center, Syracuse, NY	Fellow	1981-1982	Maternal-Fetal Medicine
University of South Florida, Tampa, FL	Fellow	1982-1983	Maternal-Fetal Medicine

A. Personal Statement

I am an obstetrician with Maternal-Fetal Medicine (MFM) training with more than 30 years of clinical experience at several major medical centers. I have long-standing research and clinical interest and expertise in the pathogenesis of preeclampsia, a disorder well recognized to have origin in deficiency of utero-placental blood-flow and perfusion. I have collaborated with several scientists over my career. Most relevant in this context is collaboration with the internationally-recognized perinatal scientists at UW. Most notably, my collaboration with Dr. Bird has resulted in several scientific publications (1-3). More importantly, this has provided me with a unique perspective as a physician scientist curious about pathogenic mechanisms of preeclampsia. Most recently, there has been a convergence of our understanding of the mechanistic basis of endothelial cell injury and glomerular endothelial cell injury in preeclampsia. I have successfully established the transgenic animal model of preeclampsia at UW. The investigation of the renal pathogenesis in this model resulted in a manuscript, recently published in AJP-Renal (4). The novel findings we discovered are the basis of an NIH application to investigate the mechanism of renal injury in preeclampsia, with multidisciplinary collaboration. The scientific environment at the UW-School of Medicine and Public Health is very robust to allow multidisciplinary collaboration. I have recently (2015) relinquished administrative responsibilities as MFM-division director, and most recently (2016) relinquished responsibilities as MFM fellowship director, allowing me to have more time for research pursuits. I am currently PI, with Wieben, Oliver, PhD (UW- Medical Physics and Radiology) as Co-PI, on a U01 Human Placenta Project funded by NICHD to investigate and establish normative data on total utero-placental blood flow (TUBF), perfusion, oxygenation and cellular imaging using the most advanced ultrasound (US) and MRI techniques and to examine circulating inflammatory markers. Dr. Bird is named alternate PI in U01 in the event it becomes necessary, which exemplifies that our collaboration is very tight. The theme of our HPP project is to develop methods for the normative placental function as a prelude to applying these methods for identifying early who will develop preeclampsia and fetal growth restriction. Our U01 primate methods development has been a tremendous asset for its application to our current human investigation. We have established the 4D imaging

method for computing TUBF in a non-human primate model and we have developed the ultrasound (US) approach for TUBF for the human investigations. We thus have novel US method, and robust preliminary MRI data from the primate model, lessons of which are incorporated in the study design of a novel cutting edge R01 that includes application of our US and MRI techniques with targeted approach to identify who will develop preeclampsia with or without fetal growth restriction amongst clinically high-risk subjects. I am a named Co-PI in the R01 application spearheaded by Dr. Bird (PI). I have a serious passion for this research. My background in Obstetrics and in Maternal-Fetal Medicine functioning as a physician-scientist in a clinical department gives me a unique perspective on training of clinicians and physician-scientists in a clinical department. It was also during my tenure at Case Western Reserve University that I was invited by NICHD to be a member of a regular panel in Obstetrics and Maternal-Fetal Biology. Through this experience, I developed a healthy understanding of the intent and structure of training programs, specifically the K awards and T32 applications that were reviewed by this study section. My experiences so far have provided me exceptional insights regarding the need for infrastructure, scientific environment, and supportive mentors necessary for developing a training program. My discussions regarding these aspects began with Dr. Ian Bird well before I accepted the position at the University of Wisconsin. After arriving at the University of Wisconsin, I focused on development of a maternal-fetal medicine fellowship. This was structured as a training program patterned after phase 1 of a K-type award from the NIH and developed in a healthy partnership with the Director of the ERP, Dr. Ian Bird. Several of the Fellows trained in ERP published substantial papers and they are listed underlined here.

1. Krupp J, Boeldt DS, Yi FX, Grummer M, Bankowski-Anaya H, Shah DM, Bird IM. The Loss of Sustained Ca2+ Signaling Underlies Suppressed Endothelial Nitric Oxide Production in Preeclamptic Pregnancies: Implications for New Therapy. Am J Physiol Heart Circ Physiol. 2013 Oct 1 305(7): H969–H979 [Epub ahead of print 2013 Jul 26] PMID:23893163.
2. Anaya HA, Yi FX, Boeldt DS, Krupp J, Grummer MA, Shah DM, Bird IM. Changes in Ca2+ Signaling and Nitric Oxide Output by Human Umbilical Vein Endothelium in Diabetic and Gestational Diabetic Pregnancies. Biol Reprod. 2015 Sep;93(3):60. doi: 10.1095/biolreprod.115.128645. Epub 2015 Jul 22. PMID: 26203178
3. Boeldt D, Krupp J, Yi FX, Khurshid N, Shah D, Bird I. "Positive versus negative effects of VEGF165 on Ca2+ signaling and NO production in human endothelial cells". Accepted for publication in AJP-Heart and Circulatory Physiology.
4. Denney JM, Bird C, Gendron-Fitzpatrick A, Bird IM, Shah DM. Renin-Angiotensin System Transgenic Mouse Model Recapitulates Pathophysiology Similar to Human Preeclampsia with Renal Injury that may be Mediated through VEGF. In press AJP-Renal.

B. Positions and Honors

Professional Experience

1983-1990	Assistant Professor, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Vanderbilt University, School of Medicine, Nashville, Tennessee
1990-1993	Assistant Professor, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas
1993-1997	Associate Professor, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas
1996	Eleventh Annual New England Biolabs Molecular Biology Summer Workshop, Clark Science Center, Smith College, Northampton, Massachusetts
1997-2002	Associate Professor, Department of Reproductive Biology, Case Western Reserve University School of Medicine, and Tenure granted effective July 1, 2002
2002-2004	Marie Louise Woodson Professor (Tenured), Department of Obstetrics, Gynecology & Women's Health, University of Louisville School of Medicine, Louisville, Kentucky
2004-present	Professor (Tenured), Department of Obstetrics & Gynecology, and Director, Division of Maternal Fetal Medicine, University of Wisconsin-Madison, Madison, WI
2005-2016	Director, Maternal Fetal Medicine Fellowship, Dept. of Obstetrics & Gynecology, University of Wisconsin-Madison, Madison, WI

Honors and Awards

1968	L.H. Hiranandani Scholarship, T. National Medical College, Bombay, India
1990	Best Teacher Award for Vanderbilt University OB/GYN full-time Faculty, Nashville, Tennessee

1990 Italian Perinatal Society and Italian So. Hypertension in Pregnancy, 5th Prize, Perugia, Italy
1993 Outstanding Achievement in Resident Education, The University of Texas Health Science Center
2002 National Faculty Excellence Award (Teaching), Council on Resident Education in Obstetrics and Gynecology
2001 Member, National Institute of Child Health and Human Development Special Emphasis Panel, Study Section (NICHD) RFA: ZHD1 MCHG-B (21), Fetal Origins of Adult Disease
2001 Invited Member, Maternal-Fetal Medicine Units Network Committee, National Institute of Child Health and Human Development, (NICHD)
2001 Member, National Institute of Child Health and Human Development Panel RFP-NICHD-2001-11 "Services in Support of the Perinatology Research Branch (PRB) of the NICHD" Study Section (NICHD)
2001 Member, National Institute of Child Health and Human Development Special Emphasis Panel, Study Section ZHD1 DSR-H 05 1, RFA (HD-01-005): Health Disparity in Preterm Birth: The Role of Infectious and Inflammatory Processes"
2001 Member, National Institute of Child Health and Human Development, ZHD1-DRG-A (C3)
2001 Member, National Institute of Child Health and Human Development Special Emphasis Panel, Study Section ZHD1 DSR-H (05)
2002 Member, Maternal and Child Health Research Subcommittee, Study Section: MCHG-B National Institute of Child Health and Human Development, (NICHD)
2002 Member, Special Emphasis Panel, ZHD1 DSR-A 20R, Women's Reproductive Health Research Career Development Centers. NICHD
2003 Member, National Institute of Child Health and Human Development; Special Emphasis Panel, ZHD1 MCHG-B (25), Research on the Scope and Causes of Stillbirths in the United States.
2003-2007 Member, Obstetrics and Maternal-Fetal Biology Subcommittee, Study Section: MCHG-B, National Institute of Child Health and Human Development (NICHD)
2003 Member, Special Emphasis Panel, ZHD1 MCHG-B MC 1, Initiation of Human Labor: Prevention of Prematurity. NICHD
2004 Member, Special Emphasis Panel, ZHD1 MCHG-B (MW), Program Projects: Molecular Mechanisms of Fetal Growth Restriction, NICHD
2004 Member, Special Emphasis Panel for WRHR Programs, ZHD1 MCGH-B (14)
2004 Member, Special Emphasis Panel, ZDH1 MCHG-B LL, Program Projects: Mechanisms of Acclimatization: Fetus and Adult
2005 Member, Special Emphasis Panel, ZHD1-MCHG-B 15R
2007 Chairperson, NICHD Special Emphasis Panel, ZHD1 DSR-L (CH), Mechanisms of Preeclampsia: Impact of Obesity
2009, July 20 Member, NICHD Scientific Review Panel, ZHD1 DSR-K (29) "Preterm Birth in Nulliparous Women: An Understudied Population at Great Risk"
2009, Sept 30 Member, NICHD Scientific Review Panel, Special Emphasis Panel (SEP) ZRG1 PSE-E 02.
2012, April Member, NICHD Scientific Review Panel, Special Emphasis Panel (SEP) ZHD1-DSR-Z54.
2014, July Member, NICHD Scientific Review Panel, Special Emphasis Panel (SEP) to review P20 (COBRE: Center of Biomedical Research Excellence) ZGM1 TWD-6 (CI)
2016 Member, NICHD Human Placenta Project Investigator Group, U01-Funded Investigators, including 11 institutions around the world.
2016, May Member NICHD Scientific Review Panel, Special Emphasis Panel (SEP) ZHD1 DSR-Z(50) 1, to review "Using Omics to Define Human Placental Development and Function Across Pregnancy (R01/R21)
2016, July Member NIH/NIGMS Centers of Biomedical Research Excellence (COBRE) Award Program for COBRE-Phase 1 Special Emphasis Panel/Scientific Review Group 2016/10 ZGM1 RCB-9 (CI)
2016, August Member NIH Conflict Study Section on Pregnancy and Neonatology Topics- ZRG1-EMNR-B (02) M
2016, October Member NIH/National Institute of Biomedical Imaging and Bioengineering SEP ZEB1 OSR-F (J2), Health Disparity SBIR Review.
2016, December Member NIH/National Institute of Child Health and Human Development SEP ZHD1 DSR-Z(52), Assessing Human Placental Development and Function Using Existing Data
2017, Member Conflict SEP for Pregnancy and Neonatology, 2017/05 ZRG1 EMNR-S (02) M Meeting, Center for Scientific Review Internet Assisted Meeting
2017, Reviewer, National Science Center-Poland, Preeclampsia Application

C. Contribution to Science

I began my career as clinician scientist examining the perinatal implications of hypertensive disorders of pregnancy. The major findings included the observations that the hypertensive state itself had adverse effects on the fetus and it would be therefore important for me to explore underlying mechanisms of this aspect of the disease process. It is this exploration that led me to identify endometrial stromal cell as the origin of reproductive tissue renin on the maternal side and to begin examining the regulation of renin secretion. (4) This then led to my investigations of role of Renin Angiotensin System (RAS) *in pathogenesis of preeclampsia*. The major findings allowed us to propose a conceptualization that like renal injury leads to hypertension, utero-placental ischemic injury may lead to preeclamptic hypertension. This provided the impetus to establish a transgenic mouse model for investigation of mechanism of renal injury in preeclampsia. I have also collaborated with a well-known placental pathologist which provided me with additional insights in understanding placental biology. The importance of this clinical and scientific background is that I have depth of understanding of placental biology in context of disorder of pregnancy commonly seen by specialists well beyond an academic clinician. This background provided me with a broad perspective on how to think about clinical disorders, their origins and subsequent events. This then allowed me, with robust scientific input from multidisciplinary scientists (proposed Co-Is) to propose these investigations and research strategy, which then resulted in this robust scientific team. Even though all of us have not previously pursued collaborative scientific adventure, I hope review panel will agree with us that this is a scientifically formidable team!

1. Hypertension and Preeclampsia:

1. Diamond MP, **Shah DM**, Hester RA, Vaughn WK, Cotton RB, Boehm FH. Complication of insulin dependent diabetic pregnancies by pre-eclampsia and/or chronic hypertension: An analysis of outcome. Am J Perinatol 2:263-267, 1985. PMID: 4052175
2. **Shah DM**, Shenai JP, Vaughn WK. Neonatal outcome of premature infants of preeclamptic mothers. J Perinatol 15(4):264-267, 1995.
3. **Shah DM**, Reed G. Parameters associated with adverse perinatal outcome in hypertensive pregnancies. J Hum Hypertens 10:511-515, 1996. PMID: 8895034.
4. **Shah DM**, Higuchi K, Inagami T, Osteen KG. Effect of progesterone on renin secretion in endometrial stromal, chorionic trophoblast, and mesenchymal monolayer cultures. Am J Obstet Gynecol 164:1145-1150, 1991. PMID: 2014841.

2. Renin-angiotensin System in Preeclampsia:

1. **Shah DM**, Banu JM, Chirgwin JM, Tekmal RR. Reproductive tissue renin gene expression in preeclampsia. Hypertens in Preg. 19 (3): 341-351, 2000. PMID: 11118408.
2. Grant WM, **Shah DM**. Decidual renin secretion is modulated by vascular endothelial cells. J Matern Fetal Med 5:58-63, 1996. PMID: 8796769.
3. Li C, Ansari R, Yu Z, **Shah DM**. Definitive molecular evidence of RAS in human uterine decidual cells. Hypertension 36 (2): 159-164, 2000. PMID:10948071.
4. **Shah DM**. The Role of Renin Angiotensin System in the Pathogenesis of Preeclampsia. Am J Physiol Renal Physiol 2005;288(4):F614-25. PMID: 15753325.

3. Placental Function and Pathology:

1. Degner K, Magness R, Shah D. Establishment of the Human Uteroplacental Circulation: A Historical Perspective. J Repro Sci Accepted for Publication. 2016
2. Redline RW, **Shah DM**, Saker H, Schluchter M, Salvator A. Placental Lesions Associated with Abnormal Growth in Twins. Pediatr Dev Path 2001;4(5):473-81.
3. Redline RW, Jiang J, **Shah DM**. Discordancy for maternal floor infarction in dizygotic twin placentas. Hum Path 2003;34(8):822-4. PMID: 14506648.
4. Degner K, Magness R, Shah D. Establishment of the Human Uteroplacental Circulation: A Historical Perspective. J Repro Sci Accepted for Publication. 2016

D. Research Support

Current Grant Support

U01 HD087216 (DM Shah, O Wieben – MPI) 09/17/15-08/31/19
NIH-NICHD
Advanced MRI FOR Uteroplacental Flow, Perfusion, Oxygenation & Inflammation
The overall goal of the project is to adopt innovative imaging modalities to measure human placental function in normal and obese pregnancy.
Role: PI

R01 HL063174 (R Wakai) 08/09/13-05/31/17
NIH-NHLBI
Optimized Signal Processing of Fetal MCG
The goal of this project is to evaluate the novel magnetocardiography technology for accurate diagnosis of fetal arrhythmia and assess its potential clinical impact.
Role: Co-Investigator

5U01 HL120338-03 (A Tita) 12/01/16-11/30/19
NIH-NHLBI
Chronic Hypertension and Pregnancy (CHAP) Project
Collaborative Project - Clinical Coordinating Center (University of Alabama-Birmingham)
Role: Site PI
This project is to determine if antihypertensive therapy to a standard BP goal <140/90, compared with ACOG recommendations (no treatment) for mild CHTN will reduce the frequency of key adverse maternal and newborn outcomes associated with CHTN.

Recently Completed

R21 HD069181 (IM Bird) 07/01/11-06/30/13
NIH-NICHD
Vascular Endothelial Dysfunction in Preeclampsia
Role: Co-Investigator

133-PRJ84UB (DM Shah) 07/01/14-06/30/15
Meriter Foundation
Meriter Foundation Research & Education Grant
Supplemental Support for Maternal-Fetal Medicine Fellowship Research Training
Role: PI

Protocol # HPC-PK-005 (DM Shah) 12/06/13-12/31/15
KV Pharmaceuticals
A Multi-Center, Non-Randomized Pharmacokinetic Study of Makena® (Hydroxyprogesterone Caproate Injection, 250 mg/mL) and its Metabolites in Blood of Women with a Singleton Pregnancy and a Previous Singleton Spontaneous Preterm Delivery
Role: PI

F09-01998 (DM Shah) 08/01/09-12/31/15
University of British Columbia
Control of Hypertension In Pregnancy Study (CHIPS)
Role: Site PI

Pending

R01 (Bird-PI) 07/01/2017-06/30/2022
NICHD
Dissecting the Origins of Preeclampsia using MRI and Computational Biology.
We thus have novel US method, and robust preliminary MRI data from the primate model, lessons of which are incorporated in the study design of a novel cutting edge R01 that includes application of our US and MRI

techniques with targeted approach to identify who will develop preeclampsia with or without fetal growth restriction amongst clinically high-risk subjects.
Role: Co-I