BIOGRAPHICAL SKETCH

Steering Committee, Senior Trainer

NAME: Dinesh M Shah, MD

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

POSITION TITLE: Professor (Tenured)

EDUCATION/TRAINING

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 am a faculty member of the Integratated Program in Endocrinology (iPEnd) and a Trainer in the Endocrinology, Reproductive Physiology UW Graduate School program, both of which provide exceptional opportunities to contribute to training of young scientists. I was instrumental in working with Dr Bird to set up the MS training track in ERP for Clinical Fellows. Several of my own Clinical fellows successfully defended Master's thesis as part of their MFM fellowship (see training tables).

My background is in the study of hypertension, and my collaborations with Dr. Ian Bird has given me insights into endothelial biology. I have pursued the application of tools of modern molecular biology, and have received relevant training in these techniques, so allowing me to incorporate them in to my own studies. 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 uteroplacental blood-flow and perfusion. I have collaborated with several scientists over my career. Most relevant in this context is collaboration with the perinatal scientists at UW. My collaboration with Dr. Bird has resulted in several scientific publications. (1) 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. We entered investigation of PE using animal model in a planned manner, carefully selecting the specific transgenic animals, established the colony at UW, successfully developed transgenic RAS model, and systematically investigated the pathogenesis. It is the results of these investigations that led us to pursuing the renal injury in PE and resulted in a manuscript on VEGF mediated renal injury in this model AJP-Renal. (2) The novel findings we discovered are basis of on-going applications to investigate the mechanism of renal injury in preeclampsia. The scientific environment at the UW-School of Medicine and Public Health is very robust to allow such multidisciplinary collaborations.

More recently (2015), I relinquished administrative responsibilities as MFM-division director, and (2016) relinquished responsibilities as fellowship director administrative responsibilities, in order to allow me to have

more time for research pursuits. I am currently PI (Multi-PI Wieben, Oliver, PhD) on a U01 project funded by NICHD on Advanced MRI FOR Uteroplacental Flow, Perfusion, Oxygenation & Inflammation, which examines total uteroplacental blood flow, perfusion, oxygenation, circulating inflammatory markers and cellular imaging, theme of which is to examine the placental basis of identifying who will develop preeclampsia and fetal growth restriction. Many of the people working on this project are proposed Trainers in this application.

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. 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. 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, (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"

2001 Member, National Institute of Child Health and Human Development Special Emphasis Panel, ZHD1 DSR-H 05 1, RFA (HD-01-005): Health Disparity in Preterm Birth: The Role of Infectious and Inflammatory Processes"

2002 Ad-Hoc Member, Maternal and Child Health Research Subcommittee, MCHG-B National Institute of Child Health and Human Development **(**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.

2003-07 Member, Obstetrics and Maternal-Fetal Biology Subcommittee, 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
2002 Member, Special Emphasis Panel, ZHD1 DSR-A 20R, Women's Reproductive Health Research Career Development Centers. 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
2007 Chairperson, NICHD Special Emphasis Panel, ZHD1 DSR-L (CH), Mechanisms of Preeclampsia: Impact of Obesity
2007 Member, NICHP Scientific Review Panel, RFA-HD—08-029 "Preterm 'Birth in Nulliparous Women: An Understudied Population at Great Risk"
2009 Member, NICHD Scientific Review Panel, ZHD1 DSR-K (29) "Preterm Birth in Nulliparous Women: An Understudied Population at Great Risk"
2009 Member, NICHD Scientific Review Panel, Special Emphasis Panel (SEP) ZRG1 PSE-E 02
2012 Member, NICHD Scientific Review Panel, Special Emphasis Panel (SEP) ZHD1-DSR-Z54
2014 Member, NICHD Scientific Review Panel, Special Emphasis Panel (SEP) to review P20 (COBRE: Center of Biomedical Research Excellence)
2016 Member, NICHD Human Placenta Project (HPP) Investigator Group, U01-Funded Investigators, including 11 institutions around the world.
2016 Member, NICHD Scientific Review Panel, Special Emphasis Panel (SEP) ZHD1 DSR-Z (50) 1 "Using Omics to define Human Placental Development and Function Across Pregnancy (R01/R21s)

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. This exploration 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 similar to renal injury leading to hypertension, utero-placental ischemic injury leads 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.

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. Endothelial Cell Biology:

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". Am J Physiol Heart Circ Physiol 2017 312(1):H173-H181. DOI 10.1152/ajpheart.00924.2015 PMCID 5283913

D. Research Support

Current Grant Support

U01 HD087216 (DM Shah, O Wieben – MPI) 09/17/15-08/31/19
NIH-NICHD No cost extension till 08/31/20
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
No cost extension:
Rhesus subproject: Non-contrast and contrast MRI to detect experimental placental lesions mimicking lesions in human FGR and Preeclampsia
Human subproject: Detection of placental lesions in on-going FGR pregnancies by non-contrast and contrast MRI using Ferumoxytpol.
Role: PI

R01 HL063174 (R Wakai PI) 07/01/17-06/30/22
NIH-NHLBI
Optimized Measurement and 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

HL120338-03 (A Tita) 12/01/16-11/30/19
NIH-NHLBI
Chronic Hypertension and Pregnancy (CHAP) Project; Collaborative Project-Clinical Coordinating Center (Univ of Alabama-Birmingham)
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.
Role: Site Co-I

1R01HL134779-01A1 (Sathish Kumar PI) 8/15/17-8/14/21
NIH-DHHS-PHS
Vascular AT2R expression and function during pregnancy
Goal: 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. Proposed study could lead to identification of targets to treat or prevent hypertension.
Role: Co-I

Recently Completed

R21 HD069181 (IM Bird) 07/01/11-06/30/13
NIH-NICHD
Vascular Endothelial Dysfunction in Preeclampsia
Goal: The aim of this project is support the preliminary data showing that mother's with PE that the cells lining the umbilical cord blood vessels have reduced function and may be readily available and a useful tool to screen drugs for therapy. This may allow for developing a drug-screening plan for future treatment.
Role: Co-Investigator

University of Wisconsin-Madison 03/01/12-04/30/14
Dept. of Obstetrics and Gynecology
Research and Development Grant
"Vascular maladaptation in preeclampsia mouse model".
Dinesh Shah

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 (University of British Columbia) Shah (PI) 08/01/09-12/31/15
Title: **Control of Hypertension In Pregnancy Study**
Goal: The CHIPS trail is a randomized, controlled trial with an intention-to-treat analysis. The trial is designed to reflect real clinical practice, rather than the tightly controlled circumstances of investigational trials.
Role: Site PI