Name: Sheikh O Jobe

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Major Professor: Ronald Magness

Degree Objective: Ph.D. Endocrinology and Reproductive Physiology

Background: BS Biology andBiochemistry - Eastern Washington University, Cheney WA

Current Research Project:

Preeclampsia is a hypertensive disorder of pregnancy characterized by widespread maternal endothelial dysfunction that affects over 5- 10 % of all pregnancies, thus remaining a leading cause of maternal and fetal morbidity and mortality and greater risk and earlier onset of cardiovascular disease in both mother and infant according to the developmental origins of adult health and disease (DoHAD). Impaired pregnancy vascular adaptations such as vasodilation and angiogenesis are attributed with preeclampsia. Vascular adaptations during pregnancy are mediated in part by estrogens. Endogenous estradiol-17β (E2β) levels are significantly elevated during gestation and low E2β levels are associated with hypertensive pregnancies. E2β induces vasodilation via estrogen receptors (ERs) during pregnancy. E2β also promotes angiogenesis in human umbilical vein and uterine artery endothelial cells. Therefore, estrogen appears to be a primary regulator of uteroplacental vasodilation and angiogenesis. However, the mechanisms by which estradiol regulates these adaptations remain unclear. The effects of estrogen on vascular adaptations may be further modulated by its metabolites. The metabolism of estradiol to catecholestradiols and methoxyestradiols is catalyzed by the sequential actions of CYP450s and catechol-O-methyltransferase (COMT). Deficiency in 2-ME2 and COMT are associated with preeclampsia and COMT knockout mice exhibit a preeclampsia-like phenotype. It is conceivable that the vascular effects of E2β may be mediated in part by local conversion to its metabolites. Therefore, we propose a thesis study designed to test the vascular physiology and pharmacology of E2β and its metabolites in pregnancy vascular adaptation especially angiogenesis and vasodilator production, both adaptations impaired in preeclampsia.

Honors:

FASEB-MARC Travel Award Winner for poster presented at the 42nd Annual meeting for the Society for the Study of Reproduction, July 18-22, 2009. Pittsburgh, PA

USDA Travel Award Winner for the 2010 Aspen Perinatal Biology Conference; August 2010

USDA NRI CSREES Merit Award Fellow Winner for platform presentation at the 43rd SSR Annual Meeting, July 30 - August 3, 2010. Milwaukee, Wisconsin.

FASEB-MARC Merit Award Fellow Winner for platform presentation at the 43rd SSR Annual Meeting, July 30 - August 3, 2010. Milwaukee, Wisconsin.

Grants Received:

NIH R25 Scholar; National Institute of General Medical Sciences, IMSD Institutional Research Education Grant, "Training & Education to Advance Minorities in Science" (TEAM-Science) NIH R25 GM083252; September 2008-August 2010.

NIH T32 Trainee; NIH Ruth L. Kirschstein National Research Service Award NIH T32-HD041921-07; September 1, 2010 - August 31, 2011.

Publications:

Jayanth Ramadoss, Sheikh O. Jobe, Ronald R Magness. Alcohol and Maternal Uterine Vascular Adaptations during Pregnancy - Part I: Effects of chronic Binge-like Alcohol on Uterine Endothelial Nitric Oxide System and Function. Alcohol: Clin. Exp. Res., 2010 in Review.

Sheikh O. Jobe, Jayanth Ramadoss, Jill M. Koch, Yizhou Jiang, Jing Zheng, Ronald R Magness (2009. Estradiol-17β and Its Cytochrome P450- and Catechol-O-Methyltransferase–Derived Metabolites Stimulate Proliferation in Uterine Artery Endothelial Cells: Role of Estrogen Receptor-α Versus Estrogen Receptor-β. Hypertension, Apr 2010; 55: 1005 - 1011.

National Presentations:

Sheikh O. Jobe, Jayanth Ramadoss, Jing Zheng, Ronald R Magness. Role of ER-α versus ER-β in Estradiol-17β & CYP450- & COMT–Derived Metabolites-Stimulated COX-1- & PGI2 Synthase-Mediated PGI2 Production in Uterine Artery Endothelial Cells. Abstract submitted for the 58th annual meeting for the Society for Gynecologic Investigation, March 16-19, 2011. Miami, FL.

Sheikh O. Jobe, Jayanth Ramadoss, Yizhou Jiang, Jing Zheng, Ronald R Magness. Uterine Artery Endothelial Cell (UAEC) β-Adrenergic System Modulates Pregnancy-Specific Catecholestradiol-Mediated Proliferation: Interactions of Catecholamines, β-Adrenergic Receptors, cAMP & MAPKs. Abstract submitted for the 58th annual meeting for the Society for Gynecologic Investigation, March 16-19, 2011. Miami, FL

Sheikh O. Jobe, Jayanth Ramadoss, Jing Zheng, Ronald R Magness. 2-hydroxyestradiol and 4-hydroxyestradiol induce proliferation of uterine artery endothelial cells: role of β-adrenergic receptors, p38 and p42/44 mitogen-activated protein kinases. Pediatrics Research, 68 (2); 176, 2010.

Sean Fling, Sheikh O Jobe, Jill Koch, Jing Zheng, Ronald R. Magness. β-Adrenergic Receptors and Catecholamines Modulate Pregnancy-Specific Catecholestradiol-Mediated Proliferation of Uterine Artery Endothelial Cells. Poster presented at the 43rd SSR Annual Meeting, July 30 - August 3, 2010. Milwaukee, Wisconsin.

Sheikh O. Jobe, Jill M. Koch, Jayanth Ramadoss, Yizhou Jiang, Jing Zheng, Ronald R Magness (2010).Pregnancy Specific Estradiol-17β-Mediated Proliferation in Uterine Artery Endothelial Cells:

Role of ER-α vs. ER-β in Angiogenesis (2010). Poster presented at the 57th Annual meeting for the Society for Gynecologic Investigation, March 24-27, 2010. Orlando, FL.

Oral Presentation: Sheikh O Jobe, Jing Zheng, Ronald R. Magness. Estradiol-17β and Its Cytochrome P450- and Catechol-O-Methyltransferase–Derived Metabolites Stimulate Proliferation in Uterine Artery Endothelial Cells via Activation of ERK-1/2 and p38 MAPK Signaling Pathways. Platform presentation at the 43rd SSR Annual Meeting, July 30 - August 3, 2010. Milwaukee, Wisconsin.

Other Presentations:

Sheikh O. Jobe, Jill M. Koch, Jayanth Ramadoss, Yizhou Jiang, Jing Zheng, Ronald R Magness Estradiol-17β, its Hydroxylated, and Methoxylated Metabolites Stimulate Proliferation of Uterine Artery Endothelial Cells from Pregnant Sheep. ERP Annual Symposium 2009.

Sheikh O. Jobe, Jayanth Ramadoss, Jill M. Koch, Yizhou Jiang, J Zheng, R Magness Pregnancy Specific Estradiol 17β Mediated Proliferation in Uterine Artery Endothelial Cells: Role of ERα vs. ERβ in Angiogenesis. ERP Annual Symposium 2010.

Ronald R. Magness and Sheikh O Jobe. Uterine blood flow in pregnancy: Role of estrogen and its metabolites on regulating angiogenesis. Vascular Biology Research Colloquium. November 2010.

ERP Service: 2010/2011 ERP Seminar and Symposium Committee.