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Degree Objective: Ph.D. Endocrinology and Reproductive Physiology

Background: BS Biochemistry San Francisco State University, San Francisco, CA

Current Research Project:

Pregnancy-induced elevations in uterine blood flow are closely correlated with concurrent increases in plasma estradiol-17 β levels and the expression/activity of eNOS. Indeed a physiologic cause and effect relationship has been established in vivo in that unilateral blockade of estrogen receptors (w/ICI 182,780) or nitric oxide synthase (w/L-NAME) locally reduces uteroplacental blood flow during late ovine gestation. Interestingly, numerous proteins that are involved in the estradiol-17 β -induced rapid eNOS activation and nitric oxide production are located in specialized membrane domains called the caveolae of uterine artery endothelial cells (UAECs). Further, eNOS activation is accompanied by alterations in its multi-site phosphorylation state which are dose-dependent (I will get initial data for this tomorrow – P-eNOS 635 only). **HYPOTHESIS:** We hypothesized that estradiol-17 β induces eNOS activation via the non-classical ER receptor and initiates the sequential and coordinated re-partitioning and activation of eNOS with altered multi-site phosphorylation. **METHODS:** UAECs were isolated from uterine arteries of pregnant ewes (gestational day 120-130; term 147d). First, confluent passage 4 UAECs were treated with increasing concentration of estradiol-17 β (0.01nM – 100nM). Second, UAECs were treated with vehicle (Control) or estradiol-17 β (10 nM) for 10 minutes from which caveolae were enriched in sucrose density gradient. Immunoblotting was utilized to study the multi-site phosphorylation state of eNOS and ERs from these sets of experiments. **RESULTS:** In control UAECs, total eNOS was predominantly located in the caveolar domain whereas it was detectable both in the caveolar and non-caveolar domains in 17 β -estradiol-treated cells. In control UAECs, stimulatory P635eNOS and P1177eNOS were both not detected in any of the fractions whereas inhibitory P114eNOS was detected strictly in the non-caveolar domain. In response to estradiol-17 β , stimulatory P635eNOS was detected in all cellular domains whereas stimulatory P1177eNOS was detected mainly in the caveolar domain. The inhibitory P114eNOS was decreased by estrogen to low levels in the non-caveolar domain and was not detected in the caveolar domain. In control UAECs, ERs were detected in a higher abundance in the non-caveolar domain and distribution was not altered. **CONCLUSIONS:** Estradiol-17 β produces temporal and spatial re-partitioning of eNOS from the caveolar to non-caveolar domains and alters its multi-site phosphorylation state in UAECs. These findings are critical to understand estradiol-17 β -induced gestational vascular adaptations.

Honors:

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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; June 2008-present

Publications:

National Presentations:

Oral presentation. Mayra B. Pastore, Jayanth Ramadoss, Wu-Xiang Liao, Dong-bao Chen, Ronald R. Magness Estradiol 17- β -induced post-translational modification of eNOS in ovine uterine artery endothelium cells from late pregnant sheep. Aspen Perinatal Biology Conference. August 29-31, 2010.

Mayra B. Pastore, Jayanth Ramadoss, Wu-xiang Liao, Dong-baoChen, and Ronald R. Magness. Estradiol-17 β -Induced Temporal and Spatial Partitioning of eNOS and Estrogen Receptors in Ovine Uterine Artery Endothelial Cells from Pregnant Sheep. Annual meeting SSR 2010.

Benjamin C. Hofeld, Jayanth Ramadoss, Mayra Pastore, Wu-Xiang Liao, DongbaoChen, and Ronald R. Magness. Uterine Artery Endothelial Cell Caveolar Proteomics Underscores Subcellular Compartmentalization of Estrogen Receptors Alpha and Beta. Annual meeting SSR 2010.

Other Presentations:

Mayra B. Pastore, Jayanth Ramadoss, Wu xiang Liao, Dong-bao Chen, Ronald R. Magness. 17 β estradiol induced Temporal and Spatial Partitioning of eNOS and Estrogen Receptors in Ovine Uterine Artery Endothelial Cells from Pregnant Sheep. ERP Annual Symposium 2010.

Mayra B. Pastore, Jayanth Ramadoss, Wu-Xiang Liao, Dong-bao Chen, Ronald R. Magness Estradiol 17- β -induced post-translational modification of eNOS in ovine uterine artery endothelium cells from late pregnant sheep. UW Cardiovascular Research Center 16th Annual Scientific Poster Fair, 2010.

ERP Service: