2014 Final Report: Mark Santillan Vision Grant

"Utilizing Longitudinal microRNA Expression in Maternal Plasma to Understand and Predict Preeclampsia"

Our lab has made exciting progress with the assistance of the Vision Grant. We have made significant progress in our work to identify early biomarkers of preeclampsia.

In our first series of experiments, we used the Maternal Fetal Tissue Bank at the University of Iowa to identify normal changes that occur in microRNAs throughout pregnancy. MicroRNAs are critically important regulators of protein expression in our bodies. Though there is ample evidence that miRNAs are dysregulated in preeclampsia, these studies were carried out on placental tissues obtained after the patients had delivered. Methodologically, this clearly limits the use of miRNAs as a predictive tool. Our study is novel in that no previous studies have investigated this mechanism of genetic control of multiple pathways throughout all trimesters of pregnancy as a potential predictor of preeclampsia. Furthermore, the differentially expressed miRNA profiles will lead to further investigation of predicted mRNAs and protein targets. This will allow for the identification of novel pathways in the development of preeclampsia. We have prepared a manuscript detailing our results and hope to have it published soon.

In a separate project, we discovered a biomarker that could give expecting mothers and their doctors the first simple blood test to reliably predict that a pregnant woman may develop preeclampsia, at least as early as 6 weeks into the pregnancy. In our paper, "Vasopressin in Preeclampsia: A Novel Very-Early Human Pregnancy Biomarker and Clinically-Relevant Mouse Model," study authors Mark Santillan, M.D., assistant professor of Obstetrics and Gynecology and a Maternal Fetal Medicine specialist, Justin Grobe, Ph.D., assistant professor of Pharmacology and a Fellow of the American Heart Association (FAHA), and Donna Santillan, Ph.D., research assistant professor of Obstetrics and Gynecology, demonstrate that elevated secretion of arginine vasopressin (AVP) can be a very early biomarker of a preeclamptic pregnancy.

We found that maternal plasma copeptin, an inert, stable biomarker of vasopressin secretion with a substantially longer half-life in the blood than vasopressin, is a clinically useful biomarker that predicts preeclampsia. Using samples from the Maternal Fetal Tissue bank, a major part of the University of Iowa Women's Health Tissue Repository, copeptin levels were measured throughout pregnancy in maternal plasma from preeclamptic and control women. Copeptin levels were significantly higher throughout the preeclamptic pregnancies than in the control pregnancies.

Our group has also demonstrated that infusion of vasopressin into pregnant mice causes all of the major symptoms of preeclampsia. Until this discovery, there was no effective animal model of the early-pregnancy events that precipitate preeclampsia.

The paper was published online in July in the American Heart Association's journal, *Hypertension*. It will be published in print in October.

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