Mid-Year Progress Report for Preeclampsia Foundation Vision Grant 2011

Date: August 22, 2010

Project Title: Elucidating the Effects of DNA Methylation on the Development of Preeclampsia

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I would like to thank the Preeclampsia Foundation for awarding me a Vision Grant in support of my research project "Elucidating the Effects of DNA Methylation on the Development of Preeclampsia." This research project was designed to investigate if the development of preeclampsia is caused by changes in placental gene expression due to alterations in DNA that are not directly regulated by the genetic code. Most commonly these alterations in DNA are associated with chemical modifications known as methylation. DNA Methylation that occurs at places within the genome that are associated with specific gene function can result in altered function of that gene. We believe that these epigenetic modifications cause genes within in the placenta to not work properly and thus could be contributing to the development of preeclampsia. For this research project we have chosen to focus on genes that are responsible for placental blood vessel growth (angiogenesis) since these genes have been previously identified to contribute to the development of preeclampsia. Additionally, we hope to identify new genes that could help us understand why preeclampsia occurs and possibly offer new therapeutic options or diagnostic tests. In order to determine if DNA methylation is associated with preeclampsia we are using an existing preeclampsia case-control study that was performed between March 2005 and December 2010. In this study, placental tissues were collected from 1) preeclamptic women delivering either at term (≥37 weeks) or preterm (≤ 37 weeks) or 2) term controls without hypertension-related complications.

DNA Isolation and Methylation Array:

In order to determine if alterations in methylation status are associated with preeclampsia, we performed a large methylation array which provides genome wide coverage of over 450,000 known DNA methylation sites per sample. To perform this array, we isolated genomic DNA from a total of 45 placental tissues from women enrolled in our study. We successfully completed this methylation array in June, 2011. We are now working on analyzing over 450,000 points of data for each sample. We have been working closely with the bioinformatics department at the University of Pennsylvania in order to determine the significant changes in gene methylation status for the angiogenic genes which have been previously identified as being involved in the development of preeclampsia. Additionally, we want to identify those genes that exhibited the largest and most significant changes in methylation status (either under methylated or over methylated). While these analyses are still on-going, we do have some preliminary data. The placentas from women with preterm preeclampsia show the biggest difference in overall methylation status when compared to both normal pregnant and term preeclamptic placentas. This would suggest that preterm preeclampsia, indicative of the most severe cases of preeclampsia, could be associated with significant changes in gene specific methylation status.

Future Work:

Over the next couple of months, we will be closely investigating gene specific methylation changes between normal pregnant and preeclamptic placentas. Once the genes with the most significant changes in methylation have been identified, we will also be able to focus on the function of these genes and how they might impact placental function. We are excited to be able to share our findings with you soon.