

The Pregnancy Foundation 2013 Garite Mini-Sabbatical Recipient

“Placental Biology and Advanced Research Techniques”

Meghan G. Hill, MBBS
Maternal-Fetal Medicine Fellow
Department of Obstetrics and Gynecology
University of Arizona

Mentor:

Kent Thornburg, PhD, Professor of Medicine,
Division of Cardiovascular Medicine,
Oregon Health & Science University



Recipient Statement and Summary:

The research question addressed during this sabbatical experience was the distribution of collagen in the human placenta. Specifically, the goal was to document the types of collagen present and their relative amounts in different areas of the placenta. Our goal during the sabbatical was to perform preliminary studies in controls. My ongoing plan is the continued collection of placentas from patients with medical comorbidities and to assess the collagen content of the placentas harvested as part of the thesis for my fellowship at the University of Arizona in Tucson.

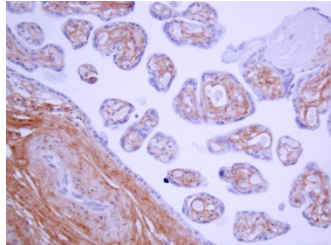
The sabbatical at Oregon Health & Science University In February 2014 allowed for 4 weeks of hands-on laboratory experience. I received mentoring from Prof. Kent Thornburg at regular meetings and worked closely with another researcher in the laboratory at all times until I was confident with a technique. I was taught how to fix tissue samples in formaldehyde or other reagents and learned the process of paraffin embedding. Additionally, I was instructed on the use of a microtome for slide production and the antibody staining of these slides. An important part of the work at the laboratory was the RNA analysis for collagen types. I was shown how to validate the primers and run the samples. By the end of my time in the laboratory, I was performing my own RNA analyses and Western Blot tests.

Prof. Thornburg scheduled meetings with me on a regular basis during the sabbatical. We discussed study progress and literature important to the scientific questions we were asking. In addition, we reviewed some of the work that he has performed on placental fibrillin location. An important part of my meetings with Prof. Thornburg was our discussions pertaining to study design to investigate causation in disease. Considering my clinical environment and his extensive laboratory experience, I was able to formulate questions more easily and he was able to advise me on how to best carry out future work. Not only was his teaching very valuable to me, but he also purchased antibodies for me at his own expense so that I could answer the questions I had asked. I had not expected that generosity and this was certainly above and beyond the commitment he made to me and The Pregnancy Foundation.

During my time spent in the Thornburg laboratory I was encouraged to attend teaching in other disciplines. Prof. Thornburg collaborates with several departments but has a special interest in cardiac disease. I was invited to several multidisciplinary meetings with basic science researchers and clinicians.

The opportunity to attend the laboratory meetings, journal clubs and teaching sessions was also important as these meetings exposed me to new ideas.

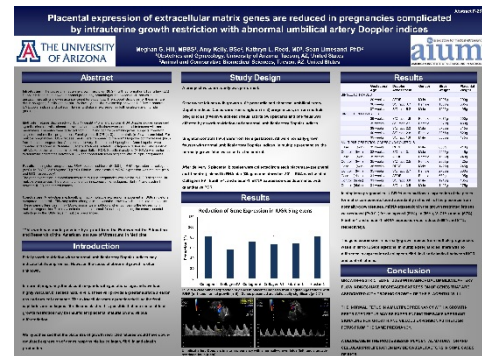
Prof. Thornburg organized meetings for me with other experts in placental morphology and pathology as well as other researchers with common interests to mine. These interactions were important in that they helped me to formulate plans for future research.



Our RNA analysis showed differences in the expression of collagen I and collagen IV between the center and periphery of the placentas we collected. Though this was a small series of patients, I am intrigued by these results. The reasoning is that collagen I and IV are laid down as a large proportion of the villous tree. Differences in collagen expression between areas of the placenta may be related to distinct growth patterns of these villous structures in the third trimester.

Clearly our work needs to be validated in more patients. Now that we have been able to identify the collagen composition of the controls, the work I am continuing involves the placentas from patients with comorbidities such as hypertension and diabetes in addition to the placentas I have already collected from pregnancies complicated by fetal growth restriction. Prof. Thornburg has generously arranged for transfer of the primers and antibodies to the laboratory here in Tucson so I can replicate our initial studies on samples from complicated pregnancies.

Since my return to Tucson, I have been mentored by Prof. Limesand at the Agricultural Research Center. We have developed a research protocol in which we store placental tissue and fetal blood for research. We bank samples from women with diabetes, hypertension and other medical conditions and are now entering the second year of recruitment for this project. Some of the inspiration from my sabbatical led to our testing collagen expression in the placentas of growth-restricted fetuses from singleton and multiple pregnancies. We found differences which supported the hypothesis of down-regulation of collagen expression in fetuses experiencing growth restriction. This work was presented at the Society for Reproductive Investigation meeting in 2015 as a poster “Placental expression of extracellular matrix genes are reduced in pregnancies complicated by intrauterine growth restriction with abnormal umbilical artery Doppler indices.” Though this particular project was not carried out as a part of my placement with Prof. Thornburg, the idea came from that experience.



The antibodies that Prof. Thornburg kindly purchased and transferred for us are being reserved for use on the specimens I have been storing in paraffin. The placental samples in our bank are now approaching a sufficient number to compare patients with comorbidities to controls. This will complete the work from the mini-sabbatical.

I would like to recognize Prof. Thornburg’s generosity in taking me on as a student. Though he is a very busy person, with many professional commitments, he always made time for me and encouraged me. I feel very thankful that I have had this experience. It has re-affirmed for me that research will continue to be an integral part of my career after the completion of my fellowship.