



**Name:** Dr. Chanel Tyler MD

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**Major Professor:** Dr. Manish Patankar

**Degree Objective:** Ph.D. Endocrinology and Reproductive Physiology

**Background:** Drexel University Medical School, MD, Residency: University of Massachusetts Medical School, UMass Memorial Medical Group. MFM Fellowship UW Madison SMPH, Dept OBGyn.

### **Current Research Project:**

MUC16 is expressed during pregnancy. Initial experiments conducted by the applicant demonstrate that MUC16 binds to NK cells from peripheral blood and decidua. In the case of preeclampsia, the binding pattern of MUC16 to NK cell subsets is distinct from that observed in healthy pregnant control. Our data indicates that MUC16 binds to NK cells via Siglec-9, an inhibitory receptor. In preeclamptic patients' higher siglec-9 expression and associated MUC16 binding is observed on the subset of NK cells that have previously been shown to facilitate angiogenesis in the decidua. We are therefore hypothesizing that aberrant MUC16 binding to this NK cell subset prevent sufficient trophoblastic invasion of the spiral arterioles and attenuates the blood supply to the growing fetus in preeclampsia. Here we will conduct specific studies to prove this hypothesis.

**Specific Aims:** Natural Killer (NK) cells are a major component of the innate immune system that lyse tumor cells and virally infected cells. Approximately 70-80% of the lymphocytes in the decidua are NK cells. The decidual NK cells have a distinct phenotype characterized by the lack of expression of CD16 and very high expression of CD56. These CD16neg/CD56bright decidual NK cells exhibit low cytotoxicity and instead expresses cytokines and other soluble factors that promote angiogenesis. The pro-angiogenic function of the decidual NK cells facilitates trophoblastic invasion of the spiral arterioles, thereby promoting fetal growth. Deficiency in this particular function of the decidual NK cells is associated with intrauterine growth restriction and preeclampsia. In our preliminary experiments we have demonstrated that NK cells from peripheral blood and decidua of pregnant women bind to the mucin MUC16 that is produced in the deciduas basalis. MUC16 is a potent inhibitor of NK cell function. Our experiments show aberrant expression of Siglec-9 on NK cells of patients with preeclampsia and likewise, an aberrant binding of MUC16 to the NK cells in preeclampsia patients. Based on these observations we are proposing the hypothesis that aberrant expression of Siglec-9 and the subsequent high level of binding of MUC16 to the CD16neg/CD56bright NK cells abrogates the ability of these cells to produce appropriate levels of the pro-angiogenic cytokines and soluble factors in preeclamptic women. As a result, the NK cells are unable to induce optimal invasion of the spiral arterioles by the trophoblasts. The goals of this proposal are to conclusively prove this hypothesis and delineate the exact role of MUC16-Siglec-9 interaction in NK cell mediated angiogenesis.



## **Honors:**

2002 Women's Health Scholar MCP Hahnemann School of Medicine

2005 Golden Apple Teaching Award University of Massachusetts Medical School

2006 Golden Apple Teaching Award University of Massachusetts Medical School

2008 The Scientific Committee of the 16th World Congress of International Society for the Study of Hypertension in Pregnancy (ISSHP) Young Investigator Travel Award

2010 NIH R13 - Perinatal Research Society Young Investigator Travel Award.

## **Grants Received:**

2007-2009 University of Wisconsin – Madison, Department of Obstetrics and Gynecology, Research and Development Grant. "Characterizing the Phenotype and Function of Natural Killer Cells in Preeclampsia," Chanel T. Tyler, MD, Award.

2009-2010 NIH T32 HD041921 Endocrine and Reproductive Physiology Program University of Wisconsin School of Medicine and Public Health Madison, Wisconsin, July 1 2009-June 30, 2010. (Eligible for predoctoral T32 since enrolled as PhD student but required to be paid predoctoral stipend).

2010-2011 University of Wisconsin School of Medicine and Public Health – Madison, Department of Obstetrics and Gynecology, Research and Development Grant. "Expression and Function of TH17 Cells in Preeclampsia,"

2010-2013 University of Wisconsin School of Medicine and Public Health – Madison, Centennial Scholar Faculty Development Program.

## **Publications:**

Tyler CT, Grady M, Rice G, Raca G. 2009 Mild Clinical Presentation in a Child with Prenatally Diagnosed 45,X/47,XX,+18 Mosaicism. American Journal of Medical Genetics A Nov;149A(11):2588-92. PMID: 19876897.

## **National Presentations:**

Tyler CT, Raca G, Rice G, Oxendine Kim, Thompson K, Miller C, Gurel E, Laffin J, Montgomery K, Stewart KS. 2007 Mild Clinical Presentation in a Child with Prenatally-Diagnosed Double Aneuploidy for Chromosomes 18 and X. American College of Medical Genetics 2007 Annual Clinical Genetics Meeting, March 21-25, 2007. Nashville, TN. Poster presentation.

Tyler CT, Trautman C, Belisle, JA, Shah D, Patankar MS. 2008 Phenotypic Expression of Decidual Natural Killer Cells: A Comparison of Normal Term Versus Preeclampsia. The International Society



for the Study of Hypertension in Pregnancy (ISSHP) 16th World Congress, September 21-24, 2008, Washington, DC. Oral presentation.

Dolan S, Moore Simas T, Tyler C, Delpapa E, Pechet L. 2008 Screening Tests for Disseminated Intravascular Coagulation (DIC): Clinical vs. Laboratory Diagnosis. *Obstet Gynecol* 111(4) (2008), 102S. American College of Obstetrics and Gynecology (ACOG) 2008 Annual Clinical Meeting, May 3-7, 2008, New Orleans, LA. Poster presentation.

Tyler CT, Belisle, JA, Arens J, Petrie Sarah, Shah D, Patankar MS. 2008 Phenotypic Expression of Decidual Natural Killer Cells. Society for Maternal Fetal Medicine 28th Annual Meeting, January 28 – February 2, 2008, Dallas, TX. Poster presentation.

### **Other Presentations:**

Chanel Tyler, Jennifer A. Belisle, Jennifer Arens, Sarah Petrie, Dinesh Shah, Manish S. Patankar. Phenotypic Expression of Decidual Natural Killer Cells. ERP Annual Symposium 2008.

Chanel Tyler, Christine Trautman, Jennifer Belisle, Dinesh Shah, MD, Manish Patankar, Phenotypic Expression of Natural Killer Cells: A Comparison of Normal Term Versus Preeclampsia. ERP Annual Symposium 2009. Oral Presentation.

Chanel Tyler, Arvinder Kapur, Jennifer A. Belisle, Joseph P. Connor, Manish S. Patankar. Studying the importance of MUC16 Siglec 9 binding on the function of NK cells in preeclampsia. ERP Annual Symposium 2010.

### **ERP Service:**

Symposium Committee 2010/11