BIOGRAPHICAL SKETCH

NAME: Sandra A. Founds

POSITION TITLE: Associate Professor, Department of Health Promotion and Development, University of Pittsburgh, School of Nursing; Member, Magee-Womens Research Institute

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
State University of New York Geneseo	BA	05/1976	Psychology
Cornell University-New York Hospital	BS	05/1979	Nursing
Frontier Nursing Service, Hyden, KY	Certifications	05/1985	CNM, FNP
Case Western Reserve University, Cleveland	MSN	08/1996	Nursing
University of Massachusetts Amherst-Worcester	PhD	09/2002	Nursing
University of Pennsylvania, Philadelphia	Postdoctoral	08/2005	Nursing
NIH/NINR and Georgetown University, DC	Postgrad	08/2005	Molecular Genetics
Advanced Microarray Analysis and Pathways, NIH	Bio-trac	08/2006	Statistics/Bioinformatics
Placenta Workshop, Queens University, Ontario	IFPA	08/2007	Wetlabs/Conference
Nurse-Midwifery Intrapartum Update, Case-Western Reserve University	Clinical Course	08/2015	Evidence-based clinical nurse-midwifery
Big Data and Healthcare Analytics, University of Pittsburgh	Certificate	05/2016	Big Data in Healthcare

A. Personal Statement

My research focus is the prevention of adverse pregnancy outcomes through better understanding of molecular genomic aspects of the maternal-fetal interface. The long term goal is to inform precision care for improved health outcomes of mothers and offspring. My postdoctoral training in Research for Vulnerable Women, Children and Families and the NIH/NINR Summer Genetics Institute led to conducting the first global gene expression microarray analysis of chorionic villi and decidual tissues in the first trimester of women who subsequently developed preeclampsia versus uncomplicated pregnancies (A1). This seminal study was conducted at the Magee-Womens Research Institute and Magee-Womens Hospital of the University of Pittsburgh Medical Center. The International Federation of Placenta Associations (IFPA) Placenta Workshop provided me with training in methods to investigate placentation tissues/cells. In R03NR013961, I have developed expertise with image cytometry through collaborations with the Center for Biologic Imaging at the University of Pittsburgh. Clinically, I specialize in women's health and pregnancy care, practicing at the Magee-Womens Outpatient Clinics. I have published 31 peer-reviewed articles and presented my research internationally and nationally. I have been funded by the Preeclampsia Foundation and the NINR. My leadership in science includes reviewing manuscripts for over 30 journals in multiple disciplines. I was an Editorial Board member for the *Journal of Obstetric, Gynecologic, and Neonatal Nursing* (*JOGNN*) over two terms and was nominated to guest edit an "In Focus" section on Pregnancy Genomics and Nursing (A2, A3). I was an executive board member of the International Society of Nurses in Genetics (ISONG) and received the 2012 ISONG Research Award.

A1. Founds, S. A., Conley, Y. P., Lyons-Weiler, J. F., Jeyabalan, A., Hogge, W. A., & Conrad, K. P. (2009). Altered global gene expression in first trimester placentas of women destined to develop preeclampsia. *Placenta*, *30*(1), 15-24.

A2. Founds, S. A. (2013). Genomics in pregnancy. *JOGNN, 42*(6), 716-7. doi:10.1111/1552-6909.12245

A3. Allen, C. M., **Founds, S. A.** (2013). Genetics and preterm birth. *JOGNN, 42*(6), 730-6. doi: 10.1111/1552-6909.12246

B. Positions and Honors

1972 – 1976	BA Psychology, Summa Cum Laude; Dean's List all semesters
1977 – 1979	BSN Cornell University Dean's List all semesters
1979	Sigma Theta Tau International Honor Society of Nursing
1979	Who's Who in American Colleges and Universities
1999 – 2002	Nurses' Education Fund for Dissertation research
2000	Beta Zeta Chapter of Sigma Theta Tau Scholarship
2000	Beta Zeta Chapter of Sigma Theta Tau Research Award
1996 – 2003	Clinical Assistant Professor, University of Massachusetts Amherst, School of Nursing
1996 – 2004	Coordinator Transcultural Nursing Experience Jamaica, West Indies through University of Massachusetts Amherst
2003 – 2004	Fellow of the Summer Nursing Research Institute, University of Pennsylvania
2003 – 2005	Postdoctoral Fellow, Research for Vulnerable Women, Children and Families University of Pennsylvania, School of Nursing
2005	Xi Chapter of Sigma Theta Tau Research Award
2005	NIH Fellow, Summer Genetics Institute, National Institute of Nursing Research
2005 – 2014	Assistant Professor, University of Pittsburgh, School of Nursing
2006 – present	Research Faculty, T32 NR009759 Targeted Research and Academic Training of Nurses in Genomics, University of Pittsburgh School of Nursing
2007 – present	Member, Magee-Womens Research Institute, University of Pittsburgh
2007	American Nurses Foundation Eastern Nurses Research Society Grant & Rita Chow & Yaye Togaski-Breitenback Scholar
2008	NIH Oral Poster and Travel Award, 6th Symposium on Functional Genomics of Critical Illness and Injury
2009 – 2015	Editorial Board, *Journal of Obstetric, Gynecologic, and Neonatal Nursing (JOGNN)*
2010 – present	Family Nurse Practitioner Magee-Womens Hospital Outpatient Clinics, Pittsburgh, PA
2012	International Society of Nurses in Genetics Founders Award in Research
2012 – 2013	Nominated Guest Editor In Focus section Genomics of Pregnancy *JOGNN*
2014 – present	Associate Professor with tenure, University of Pittsburgh
2014 – present	Interim Program Director, Nurse-Midwife Doctor of Nursing Practice, University of Pittsburgh; Assistant Director since July 2016
2016	*JOGNN* Reviewer of the Year 2015

C. Contributions to Science

C.1 Developing predictive biomarkers of preeclamspia outcomes

The molecular etiology of preeclampsia remains to be elucidated, which hinders prevention, early detection and treatment. The placenta is involved, based on "cure" of the disease by removal of placental tissues; however, mothers and offspring who survive preeclampsia are at lifelong risk of cardiovascular disease. There is epidemiological evidence that preeclampsia is a complex genetic disorder with early and late onset subtypes. I was PI for the global gene expression analysis of first trimester placental/decidual tissues which aimed to identify novel biomarkers of placentation pathophysiology that might predict preeclampsia versus uncomplicated outcomes months before onset of clinical signs or symptoms (A1). The paper has been cited by 132 publications in high-ranking peer reviewed journals and in 2012 was among the top 10 cited papers in five years of the journal *Placenta*. A subset of the novel panel of 36 candidate genes was confirmed by quantitative real time polymerase chain reaction (1a). Follow up of the 36 candidates has led to molecular insights to maternal and fetoplacental aspects of preeclampsia and uncomplicated pregnancies. Through these studies, I have gained experience in gene expression (A1, 1a), genotyping, epi-genomic methods (1b), and protein assays (1c, 1d). Genetic and epi-genomic differences were demonstrated in candidate genes of preeclampsia versus controls (1b), but when investigating proteins encoded by the candidates, we did not find a sufficiently robust panel of peptides in maternal circulation to develop a noninvasive screening test (1c). On the other hand, cytokine protein of candidate gene *FSTL3* was associated with over 3-fold increase in preeclampsia outcomes when elevated at mid-gestation (1d).

1a. Founds, S. A., Terhorst, L. A., Conrad, K. P., Hogge, W. A., Jeyabalan, A., Conley, Y. P. Gene expression of eight candidates in first trimester preeclampsia placenta (2011). *Biological Research for Nursing*, *13*(2), 134-9.

1b. Founds, S. A., Shi, H., Conley, Y. P., Jeyabalan, A., Roberts, J. M., Lyons-Weiler, J. (2012). Variations in discovery-based preeclampsia candidate genes. *Clinical and Translational Science, 5*(4):333-9.

1c. Founds, S. A., Zeng, X., Lykins, D., & Roberts, J. M. (2015). Developing potential candidates of preclinical preeclampsia. *International Journal of Molecular Sciences*, *16*(11), 27208-27. doi: 10.3390/ijms161126023

1d. Founds, S. A., Ren, D., Roberts, J. M., Jeyabalan, A., & Powers, R. W. (2015). Follistatin-like 3 across gestation in preeclampsia and uncomplicated pregnancies among lean and obese women. *Reproductive Sciences, 22*(4):402-9. doi: 10.1177/1933719114529372.

C2. Localizing the preeclampsia candidate genes

With limited access to additional chorionic villus sampling surplus tissues, I followed up the preeclampsia candidate genes in archived first trimester termination tissues of healthy women. Localization studies of mRNA and proteins allow for determining maternal or fetal expression, as well as inferences about function. I was PI on localization studies of the most down-regulated candidate, *LAIR2*, demonstrating this gene is expressed by extravillous trophoblast invading maternal decidua (2a) and remodeling maternal spiral arteries, a critical physiologic process in placental development for maternal-fetal adaptation (2b). If *LAIR2* is down regulated in the first trimester, impaired placentation may lead to preeclampsia and other adverse outcomes. This study (2b) is cited by the seminal research monograph in placental pathology by Benirschke and by the NCBI *Gene* database (https://www.ncbi.nlm.nih.gov/gene/3904) to characterize *LAIR2*. My R03 to localize and semi-quantitate expression patterns of the candidate genes in first trimester decidua versus trophoblast continues in progress. Preliminary findings for the R03 were presented internationally in 2015 (2c) and a manuscript is in progress.

2a. Founds, S. A., Fallert-Junecko, B., Reinhart, T. A., Conley, Y. P., Parks, W. T. (2010). LAIR2 localizes specifically to sites of extravillous trophoblast invasion. *Placenta, 31*(10), 880-5.

2b. Founds, S. A., Fallert-Junecko, B., Reinhart, T. A., Parks, W. T. (2013). LAIR2-expressing extravillous trophoblasts associate with maternal spiral arterioles undergoing physiologic conversion. *Placenta, 34*(3), 248-55.

2c. Founds, S. A. (November 6, 2015.) Developing Genomic Biomarkers of Preeclampsia. Podium presentation. International Society of Nurses in Genetics 28th Annual Congress. Pittsburgh, PA.

C3. Pregnancy phenotype by molecular variability

We investigate phenotypic characteristics of pregnancy and its outcomes related to molecular variability, toward the goal of identifying risk factors that may be modifiable through nursing and midwifery interventions. For example, obesity increases risk of preeclampsia and gestational diabetes. The inflammatory cytokine TNF-α is elevated in both adiposity and in preeclampsia. We hypothesized that TNF-α would be highest in obese women with preeclampsia. Although we found no difference in circulating TNF-α between lean and obese cases and controls, TNF-α concentration predicted preeclampsia (3a). In line with the systems biology framework, we then hypothesized that groups of cytokines differentially predict subtypes of preeclampsia. We found that cytokines in insulin resistance correlated with inflammation, but did not distinguish a metabolic subtype of preeclampsia (3b). In a recent collaboration with the Preeclampsia Foundation funded by the School of Nursing, we examined whether symptom phenotype in preeclampsia and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) associated with genotype in some of the preeclampsia candidate genes. Examining 17 symptoms in preeclampsia and HELLP pregnancies in relation to 8 single nucleotide polymorphisms (SNPs) in 4 candidate genes, we found associations with 4 SNPs, including multiple symptoms associating with the same SNP (3c). We plan larger studies based on this feasibility study. I recently mentored a doctoral student who successfully defended her dissertation on effects of maternal blood phenotype on preeclampsia subtype and I am the senior author on the manuscript reporting her findings (3d).

3a. Founds, S. A., Powers, R. W., Patrick, T. E., Ren, D, Harger, G. F., Markovic, N., Roberts, J. M. (2008). A comparison of circulating TNF-alpha in obese and lean women with and without preeclampsia. *Hypertension in Pregnancy, 27*(1), 39-48.

3b. Founds, S. A., Catov, J. M., Gallaher, M. J., Harger, G. F., Markovic, N., Roberts, J. M. (2011) Is there evidence of separate inflammatory or metabolic forms of preeclampsia? *Hypertension in Pregnancy*, *30*(1), 1-10.

3c. Founds, S. (presenter), Tsigas, E., & Barmada, M. (September 16, 2016.) Piloting Symptom Phenotype and Genotype in Preeclampsia. Council for the Advancement of Nursing Science/American Academy of Nursing, 2016 State of the Science Congress on Nursing Research. Washington, DC.

3d. Founds, S. A., Tsigas, E., Ren, D., & Barmada, M. M. (In press). Associating symptom phenotype and genotype in preeclampsia. *Biological Research for Nursing*. Special Issue on Genomics in Nursing, March 2018.

3e. Burgess, A., Johnson, T., Simanek, A., Bell, T., & **Founds, S.** (Manuscript in progress). Maternal ABO blood phenotype and preeclampsia subtype.

C4. Systems biology for nursing science

Theoretical underpinnings are essential to scientific development. My orientation to understanding maternal-fetal interactions in pregnancy outcomes is a paradigm that contrasts with focus on either maternal *or* fetal/neonatal factors. I published the first discussion of systems biology synthesized with the nursing metaparadigm (4a), and a recent update for nursing with concepts in systems biology related to big data and precision health initiatives (4b).

4a. Founds, S. A. (2009). Introducing systems biology for nursing science. *Biological Research for Nursing, 11*(1), 73-80.

4b. Founds, S. (2017). Systems biology for nursing in the era of big data and precision health. *Nursing Outlook*. https://doi.org/10.1016/j.outlook.2017.11.006

D. Research Support

Center for Research and Evaluation 12/2012 – 5/31/2015
University of Pittsburgh School of Nursing
Role: PI
Feasibility Study of Preeclampsia Symptom Phenotype-Genotype in a Developing Collaborative Partnership
Collaborating with the Preeclampsia Foundation, we investigated associations of symptoms in preeclampsia with SNPs in some of the PI's candidate genes.

Preeclampsia Foundation 1/1/2012-12/31/2016
2011 Vision Grant
Role: PI
Biomarker Assay Development for Translation of Discovery-based Placental mRNA Candidates to Serum Protein Concentrations in Early Pregnancy to Predict Preeclampsia
We investigated whether proteins encoded by the preeclampsia candidate genes could comprise a noninvasive screening panel in early pregnancy to predict pregnancy outcomes.

NIH/NINR 1 R03 NR013961-01 5/15/2013 – 3/31/2016
Role: PI
Localizing Maternal and Fetal Message in Translation of Preeclampsia Candidate Gene
We examined mRNA and protein localizations to determine whether the candidates are expressed by maternal or fetal placentation tissues.