OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: K. Leigh Greathouse

eRA COMMONS USER NAME (credential, e.g., agency login): Leigh\_Greathouse

POSITION TITLE: Assistant Professor of Nutrition Science

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Stephen F. Austin State University, Nacogdoches, TX | B.S. | 05/1997 | Nutrition and Food Sci. |
| Texas Woman’s University, Denton, TX  University of Texas Houston Health Science Center and M.D. Anderson Cancer Center, TX  Johns Hopkins Bloomberg School of Public Health, Baltimore, MD  National Cancer Institute, Cancer Prevention Fellowship Program, Bethesda, MD | M.S.  Ph.D.  M.P.H.  Post-doc | 08/2001  05/2010  05/2011  06/2014 | Sports Nutrition  Molecular Carcinogenesis  Epidemiology and Biostatistics  Molecular Epidemiology of Lung Cancer |
|  |  |  |  |

**A. Personal Statement**

My role in this project is that of Co-PI. As a cancer biologist the main focus of my research group is to identify biomarkers and elucidate molecular mechanisms that can be used to define the relationship between diet, the microbiome and colon cancer pathogenesis. Using big data and machine learning techniques, we seek to define the relationship between diet, the microbiome and cancer. Our goal is to 1) delineate the dietary factors that modify the microbiome and its function, 2) develop microbial predictors that improve stratification of patients for obesity treatment, and 3) identify key functional pathways and mechanisms of the microbiota-host communication. Ultimately, our goal is to discover microbial and metabolic targets for the development of clinical tools to improve the treatment of and reduce mortality from colon cancer. Currently our laboratory is assessing the microbiome-host relationship by asking whether sRNA, contained in outer membrane vesicles (OMVs) shed by bacteria, can activate the Toll-like receptors (TLRs) on epithelial or immune cells, and thus trigger inflammation. This project is profiling the sRNAs (RNA-seq) contained in colon-cancer associated bacteria (*B. fragilis*) and those associated with the TLRs to identify mechanisms of immune evasion and activation

**B. Positions and Honors**

**Positions and Employment:**

2010- 2014 **Postdoctoral Fellow***,* Cancer Prevention Fellowship Program, NCI, Bethesda, MD

2014- 2015 **Research Fellow**, National Cancer Institute, NIH, Bethesda, MD

2015-present **Assistant Professor** of Nutrition Sciences, Baylor University, Waco, TX; Adjunct Professor of

Biology, Baylor University, Waco, TX

## Other Experience and Professional Memberships:

2015-present Active Member of the American Association for Cancer Research

2015-present Editorial Board Member – *Carcinogenesis*

2018-present Editorial Board Member – *Genetic Testing and Molecular Biomarkers*

**Honors:**

2008 R.W. Butcher Award, Graduate School of Biomedical Science, University of Texas M.D. Anderson Cancer Center, Houston, TX

2008 Schissler Foundation Fellowship in Human Genetics of Disease, Graduate School of Biomedical Science, University of Texas, M.D. Anderson Cancer Center, Houston, TX

2010 Cancer Prevention Fellowship, National Cancer Institute

2012 National Institutes of Health Merit Award

2013 Aspen Cancer Conference Fellow

2016 Rising Star Young Investigator, Baylor University

**2017 Fellow of the Texas Hunger Institute, Waco, TX**

**C. Contributions to Science**

Biomarker identification and microbiome profiling in cancer:

Following my research in mechanisms of cancer susceptibility during my PhD, I pursued early stage biomarker identification of cancer risk and treatment in human studies. This work included genetic and microbial analysis. In collaboration with colleagues, identification of genetic polymorphisms that may explain the relationship between secondhand smoke exposure and lung cancer risk was achieved. In research conducted during my postdoctoral fellowship at the National Cancer Institute, I identified for the first time, distinct bacteria that differentiate cancer from controls, and lung adenocarcinoma from squamous cell carcinomas. Moreover, this was the first time a gene-microbiome associated was identified in lung cancer. This work supports the use of the microbiome as biomarkers in early detection of lung cancer, in addition to demonstrating alterations in diversity between normal and cancerous lung. Most recently, I conducted a meta-analysis of the microbiome in colon cancer, which demonstrated that BMI was independent of the dysbiosis seen in colon cancer. It also illustrated a high variability between studies in the ability of the microbiome to predict colon cancer. I have also contributed to the microbiome field of study through publication of previews, one review and a book chapter that is currently in press.

**K. Leigh Greathouse**, James R White, R. Noah Padgett, Brittany G Perrotta, Gregory D Jenkins, Nicholas

Chia, Jun Chen. Gut microbiome meta-analysis reveals dysbiosis is independent of body mass index in predicting risk of obesity-associated CRC. *BMJ Open Gastroenterology.* 2019

**K. Leigh Greathouse**, J. White, V. Bliskovsky, A. Vargas, E. Polley, E. Bowman, M. Khan, A. Robles, B. Ryan,

A. Dzutsev, G. Trinchieri, M. Pineda, S. Bilke, P. Meltzer, C. Deming, S. Conlan, J. Oh, J.A. Segre, C.C. Harris. Microbiome-TP53 Gene Interaction in Human Lung Cancer. *Genome Biology*. 2018.

Daquigan N, Seekatz AM, **Greathouse KL**, Young VB, White JR. High-resolution profiling of the gut

microbiome reveals the extent of *Clostridium difficile* burden. *NPJ Biofilms Microbiomes*. 2017 Dec 5;3:35. doi: 10.1038/s41522-017-0043-0. eCollection 2017. PubMed PMID: 29214047; PubMed Central PMCID: PMC5717231.

Bríd M Ryan, PhD, Jin Jen, MD, Ana I Robles, PhD, Cain McClary, MD, Kara Calhouna, BS, Elise D Bowmana, M.Sc., Kirsi Vähäkangas, MD, **K. Leigh Greathouse**, PhD, Wang, Yie, MD, Susan Olivo Marston, PhD, Angela S. Wenzlaff, MPH, Bo Dengb, MD, Ping Yang, MD, Ann G. Schwartz, PhD, Curtis C Harris, MD. A DRD1 Polymorphism Predisposes to Lung Cancer among those Exposed to Secondhand smoke during Childhood. *Cancer Prevention Research.* 2014 Oct 3.

**Greathouse, K. L.**, Faucher, M. A., & Hastings-Tolsma, M. (2017). The Gut Microbiome, Obesity, and Weight Control in Women's Reproductive Health. *West J Nurs Res, 39*(8), 1094-1119.

**K.L. Greathouse,** C.C. Harris, S. Bultman. Dysfunctional families: Clostridium scindens and secondary bile acids inhibit the growth of Clostridium difficile. *Cell Metabolism.* 21(1): 9- 10, 2015.

Falana K, Knight R, Martin CR, Goldszmid R, **Greathouse KL**, Gere J, Young H, Kuo WP. Short Course in the

Microbiome. *J Circ Biomark*. 2015 Jul 27;4:8. doi: 10.5772/61257. eCollection 2015 Jan-Dec. PubMed PMID:

28936244; PubMed Central PMCID: PMC5572982.

Developmental reprogramming of the female reproductive tract

We found several genes specific to uterine leiomyomas that were reprogrammed by exposure to xenoestrogen. In addition, we also found that either estradiol or xenoestrogen resulted in estrogen receptor (ER) signaling via phosphatidylinositol 3-kinase/protein kinase B and phosphorylation the histone methyltransferase enhancer of zeste homolog 2 (EZH2). In turn, this modification of EZH2 reduced levels of trimethylation of lysine 27 on histone H3 (H3K27me3). Using an animal model of uterine leiomyoma, which contained a tumor suppressor gene defect in Tsc2, I sought to determine if neonatal exposure to either xenoestrogen could alter susceptibility to tumor formation in adult animals and the mechanism by which developmental reprogramming occurred. In my research, I used several molecular techniques to identify developmentally reprogrammed genes, nongenomic signaling patterns and histone modifications. I was also involved with dosing animals, necropsy and estrous staging. From this work I identified the pathway activated by early exposure to genistein, phosphoinositide 3-kinase PI3K/AKT, which I found lead to estrogen receptor signaling to the EZH2. This early signaling to EZH2 lead to aberrant decrease in the levels of the repressive chromatin mark H3K27me3 and resulted in hyperresponsive estrogen-activated genes in the adult uterus. However, this response was not seen with bisphenol A. Together these results demonstrated not only could early exposure to dietary estrogens lead to a gene-environment interaction that resulted in increased tumor formation, but also demonstrated a mechanism by which this reprogramming occurs.

**Greathouse, K. L.** *et al.* Identification of uterine leiomyoma genes developmentally reprogrammed by neonatal exposure to diethylstilbestrol. *Reproductive sciences* **15**, 765-778, doi:10.1177/1933719108322440 (2008).

Bredfeldt, T. G., **Greathouse, K.L** *et al.* Xenoestrogen-induced regulation of EZH2 and histone methylation via

estrogen receptor signaling to PI3K/AKT. *Molecular endocrinology* **24**, 993-1006, doi:10.1210/me.2009-0438 (2010).

**Greathouse, K. L.** *et al.* Environmental estrogens differentially engage the histone methyltransferase EZH2 to increase risk of uterine tumorigenesis. *Molecular cancer research: MCR* **10**, 546-557, doi:10.1158/1541- 7786.MCR-11-0605 (2012).

**Complete List of Published Works in MyBibliography:**

https://www.ncbi.nlm.nih.gov/sites/myncbi/1RGAUfG1s69Q8/bibliography/53509358/public/?sort=date&direction=ascending.

**D. Additional Information: Research Support and/or Scholastic Performance**

**Ongoing Research Support**

**Faculty Research Investment Program (FRIP)** Funding: $50,000 (2019-2020)

Project title: *Mediation of Host-Pathogen Interaction by Bacterial Outer Membrane Vesicle Small RNAs in Colon Cancer*

Investigators: K. Leigh Greathouse, PI; Robert Britton, Co-PI, Ramon Lavado, Co-PI, Noah Shroyer, Co-PI

The goal of this project is to determine the effect of bacterial outer membrane vesicles and their small RNA cargo on TLR activation and inflammation in 3D colon organoids.

**University Research Committee (URC)**  Funding: $7318 (2018-2019)

Project title: *A fiber intervention to prevent weight gain and reduce stress levels for physicians in training.*

Investigators: LesLee Funderburk, PI, Leigh Greathouse, Co-PI.

The goal of this RCT is to determine the effects of increased dietary fiber on weight gain, adiposity and reduce perceived stress levels in residents at the Family Health Clinic as the result of changes in distal gut microbiota composition and function.

**Undergraduate Research Student Award (URSA)** Funding: $4946 (2019-2020)

Project title: *Characterization of Outer Membrane Vesicle RNA During the Phases of Growth of B. fragilis.* The goal of this study is to characterize the size and concentration outer membrane vesicles secreted at each phase of growth, as well as, sequence their RNAs to analyze the differences in gene expression.

Role: PI