BIOGRAPHICAL SKETCH
DO NOT EXCEED FIVE PAGES.

NAME: Claycombe-Larson, Kate J.

eRA COMMONS USER NAME (credential, e.g., agency login): CLAYCOMBE

POSITION TITLE: Research Scientist

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
Univ. of Tennessee at Knoxville	Ph.D.	1999	Nutritional Biochemistry
Tufts University	Post Doc	1999-2001	Nutritional Immunology
Michigan State University	Assistant Professor	2001-2010	Nutritional Biochem. & Immunology
USDA ARS	Lead Scientist and Acting Research Leader	2010-present 2016-present	Nutritional Epigenetics

A. Personal Statement

I have the extensive specific training and expertise in ***energy metabolism*** associated ***nutritional epigenetic regulation, particularly in the area of maternal diet and obesity and their effects on offspring obesity***. I received training as a graduate student in Nutritional Biochemistry Laboratory at the University of Tennessee where I studied transcriptional regulation of obesity genes. As a postdoctoral fellow at Tufts University in Boston, I studied molecular mechanism underlying macrophage-derived inflammation and immune dysfunction. As a faculty member at Michigan State University and in my current position at our USDA ARS GFHNRC located in Grand Forks ND, I have been studying maternal diet-induced epigenetic regulation responsible for obesity and metabolic function alterations in the offspring. Results from our laboratory have shown that key metabolic tissues such as adipose, skeletal muscle, brain, and placenta work together to induce offspring disease outcome.

B. Positions and Honors.

Positions and Employment

2020-present Research Leader, USDA ARS, Grand Forks Human Nutrition Research Center
2016-2019 Acting Research Leader, USDA ARS, Grand Forks Human Nutrition Research Center
2012-present Lead scientist, USDA ARS, Grand Forks Human Nutrition Research Center
2012-present Adjunct Associate Professor, University of North Dakota School of Medicine
2010-present Research Scientist, USDA ARS, Grand Forks Human Nutrition Research Center
Nov 2001- July 2010 Assistant Professor, Michigan State University, Department of Food Science and Human Nutrition, and Cell and Molecular Biology Program
1999-2001 Scientist III, Jean Mayer USDA/ Human Nutrition Research Center at Tufts University, Nutritional Immunology Laboratory
1996-2000 Graduate Research Assistant, Nutrition Department, University of Tennessee at Knoxville
1993-1995 Research Technician, Nutrition Department, University of Tennessee at Knoxville
1991-1993 Graduate Research Assistant, Biological Sciences Department, East Tenn. State University

Professional Positions, Awards, Honors, and Service

- 2019 USDA ARS PA Emerging Leaders Program Award
- 2018 Organizer & Chair, Am. Soc. for Nutr. Symposium on Immunometabolism and Obesity, Boston, MA.
- 2018 Session Chair, 5th Annual University of North Dakota Epigenetics and Epigenomics Symposium
- 2018 USDA ARS Merit Award for Annual Performance

- 2017 Organizer & Chair, Am. Soc. for Nutr. Symposium on Diet and Exercise on Adipocyte Epigenetics.
- 2017 USDA ARS, Merit Award for Annual Performance
- 2016 The Korean Nutrition Society Award
- 2016 Organizer & Chair, American Physiology Society Featured Topic Symposium, EB 2016
- 2016 USDA ARS, Merit Award for Annual Performance
- 2015 Co-Chair, USDA ARS GFHNRC-UND Med School, Nutritional Epigenetics, Grand Forks, ND
- 2015 Norman Kretchmer Memorial Award in Nutrition and Development, American Society of Nutrition
- 2013 Chair, Basic Science Section, The Obesity Society
- 2013 Session Co-Chair, 2013 Experimental Biology ASN Minsymposium "Obesity, Inflammation, and Nutrigenomics", Boston, M.A.
- 2012 Session co-chair and organizer, The American Society for Nutrition Symposium, Adipose Dysfunction Interaction of ROS and Inflammation, EB 2012, San Diego C.A., April 24.
- 2011 Chair, Nutrient and Gene Interaction Research Interest Section, Am. Society of Nutrition
- 2011 Chair, North Central Regional Multistate Research Project NC-1039 Group, n-3 Polyunsaturated Fatty acid and Human Health
- 2010 Chair, Molecular Mechanisms of Obesity Track, The Obesity Society Program Committee
- 2010 Session Chair, Symposium " Inflammatory and Molecular Links Between Obesity and Chronic Diseases "Symposium "Inflammation and Immune Dysfunction", 2010 Annual Obesity Society Meeting, San Diego, CA.
- 2009 Session Chair, Symposium "Inflammation and Immune Dysfunction", 2009 Annual Obesity Society Meeting, Washington D.C.
- 2009 Co-chair, "Cytokines and other Secreted Factors" session, 2009 Annual Obesity Society Meeting, Washington D.C.
- 2008 Chair, Symposium "Human adipose tissue as endocrine organ", 2008 Annual Obesity Society Meeting, New Orleans, LA
- 2007 Session Co-Chair and Organizer, 2007 Experimental Biology Symposium "Obesity-associated Inflammation, Immune Dysfunction, and Effects of Nutrient and Lifestyle Modification", Washington D.C.
- 2007 Expert Panel Member for the Life Science Research Office Special Meeting on Obesity, Inflammation and Nutrigenomics, FASEB office, Bethesda, MD.
- 2006 Session Co-chair of mini-symposiums, Nutrient Regulation of Immune function Session I and session II, 2006 Experimental Biology Meetings.
- 2005 Session Chair, Obesity Session for the "Creating Cardiovascular Innovations through Collaboration: Pfizer and MSU"
- 2005-2006, Chair, North Central regional Multistate Research Project, N-3 polyunsaturated fatty acid and Human Health
- 2004-2005, Secretary, North Central regional Multistate Research Project, N-3 polyunsaturated fatty acid and Human Health
- 2002 Chair of The 5th International Congress on Essential Fatty Acids and Eicosanoids, PUFAs/Eicosanoids, Inflammation and Immune Function Session
- 2000 The American Aging Association Paul E. Glenn Award for Postdoctoral Research
- 1998 North Am. Association of Obesity, Travel Award for the International Congress of Obesity

Professional and Committee Assignments and Memberships Assignments

- 2016-present Editorial board, Journal of Nutrition
- 2012-present Editorial board, Journal of Nutritional Biochemistry
- 2015-present Editorial board, Frontier in Immunology and Nutrition
- 2016 Editorial board, Scientific Reports
- 2012-2015 Editorial board, International Scholarly Research Network (ISRN) Nutrition Journal
- 2012-2015 Editorial board, Physiological Genomics
- 2013-2016 Member, American Nutrition Society, Program Committee
- 2012-present USDA ARS GF HNRC Animal Care and Use Committee member
- 2012 Working Group member, Inflammation and Nutritional Science for Programs/Policies and Interpretation of Research Evidence

(INSPIRE), Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH

- 2012-present USDA ARS GF HNRC The Biology of Obesity Prevention CRIS Research Project Unit group member
- 2012-2016 Member, American Heart Association Lipid II Peer Review Committee
- 2011 Search Committee Member, Research Leader Position at USDA ARS GF HNRC
- 2010-present University of North Dakota, Epigenetics Focus Group
- 2011 Member, NIH NCCAM P19 Study Section, 2011.
- 2007-2009 AHA Region IV Cardiorenal peer review committee)
- 2003-2004 American Society of Nutritional Science, Nutritional Immunology Research Interest Section, Steering Committee.

- Served on NIH study Section, PAR16-366, Research in Biomedicine and Agriculture Using Agriculturally Important Domestic Animal Species, April 2019
- Served on USDA NIFA National Needs Graduate Fellowship Program Peer Review Panel, May 2018
- Served on NIH Special Emphasis Panel, NCAM, 2010

C. Contribution to Science

1. My early publications directly addressed effects of **metabolic hormones** such as insulin and agouti on human fat cell synthesis of lipids. I postulated that increased insulin concentrations may have effects other than mediating glucose uptake, including inhibition of lipid oxidation and fat synthesis and demonstrated that cultured primary human fat cells are capable of making triglycerides by increasing lipid synthesizing fatty acid synthase enzyme activity and mRNA expression in response to insulin treatment. As a decades-long campaign of reducing fat consumption and increasing carbohydrate consumption by U.S. consumers coincided with an increased prevalence of obesity, this work shed important light that high sugar consumption that increases insulin secretion can increase fat cell synthesis of lipids. I served as the primary investigator or co-investigator in all of these studies.

a. **Claycombe, KJ**, Jones, BH, Standridge, MK, Guo, Y, Chun, JT, Taylor, JW, Moustaid-Moussa, N. Insulin increases fatty acid synthase gene transcription in human adipocytes. Am. J. Physiol. 274: R1253-R1259, 1998.
b. Jones, BH, Standridge, MK, **Claycombe, KJ**, Smith, PJ, Moustaid-Moussa, N. Glucose induces expression of stearoyl-CoA desaturase in 3T3-L1 adipocytes. Biochem. J. 335: 405-408, 1998.
c. Moustaid-Moussa, N, **Claycombe, KJ**. The yellow mouse obesity syndrome and mechanism of agouti-induced obesity. Obe. Res. 7:506-514, 1999.
d. **Claycombe, KJ**, Xue, B, Maynatte, RL, Zemel, MB, Moustaid- Moussa, N. Regulation of leptin by insulin and agouti. Physiol. Genom. 2: 101-105, 2000.
e. **Claycombe, KJ**, Jones, BH, Guo, Y, Wilkison, WO, Zemel, MB, Chun, J. Moustaid, N. Transcriptional regulation of the adipocyte fatty acid synthase gene by the agouti gene products: interaction with insulin. Physiol. Genom. 3: 157-162, 2000.

2. By applying knowledge from nutritional immunology and **adipose tissue biology**, I developed independent studies and demonstrated that stromal vascular cells (SVC) within adipose tissue are the primary source of pro-inflammatory cytokines and that SVC are responsible for the pervasive proinflammatory effects that occur with enlargement of adipose tissue in obese animals. I further discovered that inflammatory functions of immune cells from both innate and adaptive immunity are modulated by obesity, and particularly by metabolic hormone such as leptin. Moreover, I developed a cell-based bioassay to evaluate flavonoids isolated from tart cherries. These flavonoids proved effective in enhancing the efficacy of statins in reducing obesity-related inflammation, particularly in adipose tissue. I also showed that other nutrient such as n-3 polyunsaturated fatty acids (n-3 PUFA) have anti-inflammatory role by reducing IL-6 productions from adipose stem cells by a mechanism involving the down-regulation of Toll-Like Receptor-2 (TLR-2)-mediated signaling pathways in adipose stem cells.

a. Harkins, JM, Moustaid-Moussa, N, Penner, KM, Pestka, JJ, Chung, YJ, North, CM, **Claycombe, KJ**. Expression of interleukin-6 is greater in preadipocytes than in adipocytes of 3T3-L1 cells and C57BL/6J and ob/ob mice. J Nutr. 134: 2673-2677, 2004.
b. Zhou, HR, Kim, EK, Kim, H, **Claycombe, KJ**. Obesity -associated mouse adipose stem cell secretion of monocyte chemotactic protein-1 (MCP-1), Am. J. Physiol. 293: E1153-1158, 2007.
c. Chun, OK, Chung, SJ, **Claycombe, KJ**, Song, WO. Serum C-reactive protein concentrations are inversely associated with dietary flavonoid intake in U.S. adults, J. Nutr. 138: 753-760, 2008.
d. **Claycombe, K**. King, L. Fraker, P. A role for leptin in sustaining lymphopoiesis and myelopoiesis. PNAS. 105: 2017-2021, 2008.
e. Kalupahana NS, **Claycombe KJ**, Newman SJ, Stewart T, Siriwardhana N, Matthan N, Lichtenstein AH, Moustaid-Moussa N. Eicosapentaenoic acid prevents and reverses insulin resistance in high-fat diet-induced obese mice via modulation of adipose tissue inflammation. J Nutr. 140:1915-22, 2010.
f. Hsueh HW, Zhou Z, Whelan J, Allen KG, Moustaid-Moussa N, Kim H, **Claycombe KJ.** Stearidonic and eicosapentaenoic acids inhibit interleukin-6 expression in ob/ob mouse adipose stem cells via Toll-like receptor-2-mediated pathways. J Nutr. 141:1260-6, 2011.
g. Zhou Zhou, Muraleedharan Nair, and **K.J. Claycombe**, Synergistic inhibition of interleukin-6 production in adipose stem cells by tart cherry anthocyanins and atorvastatin, Phytomedicine, 19(10): 878-881, 2012.

3. I have conducted in vivo feeding studies to determine the ***nutritional epigenetic mechanism*** for maternal diet-induced adipose tissue catch-up growth, obesity, and insulin resistance. Results from these studies demonstrated that maternal low protein and postnatal diets result in lower birth weight followed by catch-up growth that is accompanied by obesity and glucose intolerance, and epigenetic changes that resulted in altered insulin-like growth factor 2 (Igf2) gene DNA methylation. This work provided the first evidence that adipose tissue growth rate is modulated by maternal low protein and postnatal high fat diets by increasing adipose tissue Igf2 gene methylation. These findings provide insight into how low maternal protein intake and postnatal high fat diets contribute to obesity and insulin resistance in offspring. I have also showed that other maternal diet-induced metabolic dysfunction in brain-BDNF, skeletal muscle, brown and beige brain, and adipocytes also contribute to offspring obesity.

a. **Claycombe KJ**, Uthus EO, Roemmich JN, Johnson LK, Johnson WT. Prenatal Low-Protein and Postnatal High-Fat Diets Induce Rapid Adipose Tissue Growth by Inducing Igf2 Expression in Sprague Dawley Rat Offspring. J Nutr. 143 (10): 1533-1539, 2013.
b. Martinez JA, Milagro FI, **Claycombe KJ,** Schalinske KL. Epigenetics in adipose tissue, obesity, weight loss, and diabetes. Adv Nutr. 2014;5:71-81.
c. **Claycombe. K.J.**, James N. Roemmich, LuAnn Johnson, Emilie E. Vomhof-DeKrey, and W. Thomas Johnson, Skeletal muscle Sirt3 expression and mitochondrial respiration are regulated by a prenatal low protein diet, 26(2):184-189, J Nutritional Biochem., 2015.
d. **Claycombe, K.J.**, Emilie E Vomhof-DeKrey; James N Roemmich; Turk Rhen; and Othman Ghribi, Maternal low protein diet causes body weight loss in male, neonate Sprague-Dawley rats involving UCP-1 mediated thermogenesis, J Nutritional Biochem., 26:729-35, 2015.
e. **Claycombe K.J.**, Brissette CA, Ghribi O. Epigenetics of inflammation, maternal infection, and nutrition. J Nutr. 2015;145:1109S-15S
f. **Claycombe, K.J.**, Emilie E. Vomhof-DeKrey, Rolando Garcia, William Thomas Johnson, Eric Uthus, and James N. Roemmich, Decreased beige adipocyte number and mitochondrial respiration coincide with reduced FGF21 gene expression in Sprague Dawley rats fed prenatal low protein and postnatal high fat diets, J Nutr. Biochem, 113: 113-121, 2016.
g. **Vomhof-DeKrey** E, Darland D, Ghribi O, Bundy A, Roemmich J, **Claycombe K**. Maternal low protein diet leads to ***placenta***l angiogenic compensation via dysregulated M1/M2 macrophages and TNFalpha expression in Sprague-Dawley rats. J Reprod Immunol. 2016;118:9-17
h. Dhasarathy A, Roemmich JN, **Claycombe KJ.** Influence of maternal obesity, diet and exercise on epigenetic regulation of adipocytes. Mol Aspects Med. In press, November 2016
i. Marwarha G, **Claycombe K**, Schommer J, Collins D, Ghribi O. Palmitate-induced Endoplasmic Reticulum stress and subsequent C/EBPalpha Homologous Protein activation attenuates leptin and Insulin-like growth factor 1 expression in the brain. Cell Signal. 2016;28:1789-805

j. Xie L, Zhang K, Rasmussen D, Wang J, Wu D, Roemmich JN, Bundy, A. Johnson, W. T., and **Claycombe, K**., Effects of prenatal low protein and postnatal high fat diets on visceral adipose tissue macrophage phenotypes and IL-6 expression in Sprague Dawley rat offspring. PloS one. 2017;12:e0169581.

k. Marwarha G, **Claycombe-Larson K**, Schommer J, Ghribi O: Maternal low-protein diet decreases brain-derived neurotrophic factor expression in the brains of the neonatal rat offspring. The Journal of nutritional biochemistry 2017, 45:54-66

l. Krout, D., Roemmich, J.N., Bundy, A., Garcia, R.A., Yan, L., and **Claycombe-Larson**, K.J. 2018. Paternal exercise protects mouse offspring from high-fat-diet-induced type 2 diabetes risk by increasing skeletal muscle insulin signaling. The Journal of nutritional biochemistry 57:35-44.

m. Krout, D., Schaar, A., Sun, Y., Sukumaran, P., Roemmich, J.N., Singh, B.B., and **Claycombe-Larson**, K.J. 2017. The TRPC1 Ca(2+)-permeable channel inhibits exercise-induced protection against high-fat diet-induced obesity and type II diabetes. The Journal of biological chemistry 292:20799-20807.

n. Marwarha G, **Claycombe-Larson K**, Lund J, Schommer J, Ghribi O. A Diet Enriched in Palmitate and Deficient in Linoleate Exacerbates Oxidative Stress and Amyloid-beta Burden in the Hippocampus of 3xTg-AD Mouse Model of Alzheimer's Disease. J Alzheimers Dis 2019;68(1):219-37. doi: 10.3233/JAD-180835

o. Marwarha G, **Claycombe-Larson K**, Lund J, Ghribi O. Palmitate-Induced SREBP1 Expression and Activation Underlies the Increased BACE 1 Activity and Amyloid Beta Genesis. Mol Neurobiol 2018. doi: 10.1007/s12035-018-1451-8.

p. Jayarathne S, Stull AJ, Miranda A, Scoggin S, **Claycombe-Larson K**, Kim JH, Moustaid-Moussa N. Tart Cherry Reduces Inflammation in Adipose Tissue of Zucker Fatty Rats and Cultured 3T3-L1 Adipocytes. Nutrients 2018;10(11). doi: 10.3390/nu10111576

q. Schaar, A., Sun, Y., Sukumaran, P., Rosenberger, T., Krout, D., Roemmich, J., Brinbaumer, L., **Claycombe-Larson, K.,** and Brij Singh, B., Calcium entry via TRPC1 is essential for cellular differentiation and modulates secretion via the SNARE complex, J Cell Science, In press, June 2019.

D. Research Support

Submitted and under review

- NIH COBRE Historical trauma and resilience as a biological state and its association with the effects of the traditional Indigenous food chokeberry, UND, 2019-2024, Co-Investigator
- NIH COBRE Stress and Health in American Indian Pregnancies, UND, 2019-2024, Co-Investigator

Ongoing Research Support

- USDA Agricultural Research Service Project #3062-51000-054-00D, 2019-2024, PI
- USDA NIFA, Maternal Nutrition, Epigenetic modifiers, and programming of fetal organ development in beef cattle, 2019-2014, Collaborator
- NIH COBRE Epigenomics of Development and Disease, UND, 2019-2024, Collaborator
- USDA NIFA, Synergistic effects of omega 3 polyunsaturated fatty acids and anthocyanins in inflammation-associated obesity and insulin resistance, 2018-2023, Consultant

Funded and completed:

- USDA Agricultural Research Service Project #3062-51000-052-00D, 2014-2019, PI
- 2016-2018, USDA ARS Research Associate Program Class of 2016, Maternal obesity, The placental microbiome and in utero short chain fatty acid-mediated offspring obesity, PI.
- USDA ARS Professional Activity Grant, For support of American Society of Nutrition Symposium at EB 2017, April-July 2017, PI.
- NIH COBRE Epigenomics of Development and Disease, UND, PI, Pilot Grant, 2014-15.
- 2015 USDA ARS professional activity Fund, The obesity Society, Basic Science Section Annual Meeting a nd graduate student and postdoc poster competition, PI
- 2014 USDA ARS professional activity Fund, American Society for Nutrition, Nutrient and Gene Interaction Research Interest Section Symposium, PI
- 2012, USDA ARS professional activity Fund
- 2007, Tekeda Pharmaceutical Company, Educational Grant Award for FASEB Summer Conference, Nutritional Immunology: Its Role in Health and Disease.

- Office of Vice President of Research and Graduate Studies at the Michigan State University, Intramural Research Grants Program for New Investigator, “Obesity-Associated Inflammation and Adipose Tissue”, 2005-2007, Role: PI.
- Office of Vice President of Research and Graduate Studies at the Michigan State University, Biomedical and Health Research Initiative, Cardiovascular Group, 2005-2007, Role: Co-investigator. 2006-2009, in postdoc salary support.
- 2007, Tekeda Pharmaceutical Company, Educational Grant Award for Experimental Biology Symposium.
- Project Green, Michigan State University Agricultural Experimental Station, Project Continuation Award “Preventive Effects of Tart Cherries on Cardiovascular Diseases Risk Biomarkers: C-Reactive Protein and Interleukin-6”, 2005-2006, Role: PI.
- Michigan Agricultural Experimental Station, Multistate Research Project Fund, #MICL02036, “N-3 Polyunsaturated Fatty Acid and Human Health and Disease”, 2002-2007, Role: PI.
- Cherry Marketing Institute, Research Grant, Preventive Effects of Tart Cherries on Cardiovascular Diseases Risk Biomarkers: C- Reactive Protein and Interleukin-6, 2004-2005, Role: PI.
- ROIP research seed grant, Michigan State University, College of Human Ecology, 2002-2003, “obesity-induced Cardiovascular Diseases: Inhibitory Effects of N-3 Fatty acid and vitamin E on Plasma C-reactive Protein (CRP) and interleukin-6 (IL-6) concentrations”, Role: PI.