

Member: Sari Acra, MD, MPH
Rank: Professor, Director of the Division of Pediatric Gastroenterology
Department: Pediatrics
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

My major research focus is in the area of nutrition, and recent clinical nutrition research in our group has focused on measuring energy expenditure in chronic disease states. We are also defining the molecular mechanisms underpinning chronic diarrhea in children. A representative publication is: Gaibee Z, Warner N, Bugda Gwilt K, Li W, Guan R, Yourshaw M, Whittaker Hawkins R, Zorbas C, St-Germain J, Tabatabaie M, Mao S, Pinsk V, Yerushalmi B, Wang LK, Nelson SF, Wozniak L, Shouval DS, Matar M, Assa A, Frost N, Jimenez L, **Acra S**, Walters T, Mouat S, Li M, Lafontaine DLJ, Tyska M, Raught B, Avitzur Y, Lencer WI, Goldenring JR, Martin MG, Thiagarajah JR, Muise AM. The genetic architecture of congenital diarrhea and enteropathy. *N Engl J Med*. 2025;392(13):1297-1309. PMID: PMC11968080

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5RC2DK118640-07	Congenital diarrhea and enteropathy (PediCODE) consortium and biorepository	09/15/2019-08/31/2029	Listed under Contact PI

Summary of Digestive Disease Research

My research relates to measurement of energy metabolism in children using whole-room indirect calorimeters (metabolic chambers). This system is coupled with movement sensors to provide a similar-to-free-living environment where a study subject or patient's energy expenditure, substrate oxidation, physical activity, and body composition are accurately measured on a minute-by-minute basis. Through this approach, we are investigating the physiological regulation of energy metabolism in children with inflammatory bowel disease and other chronic disease states, as well as improving the technologies for measuring body composition and physical activity. I have also collaborated with other VDDRC members to study the etiology of chronic diarrhea in children.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient

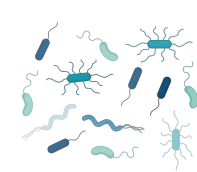
VDDRC Collaborations

Supported by my preliminary VDDRC Pilot-funded work in conjunction with VDDRC member Dr. Goldenring, we hypothesized that identification of specific cellular abnormalities in children with Undiagnosed Neonatal Diarrhea (UDND) syndrome, whole-genome sequencing of affected neonates and their parents, and studying the disease by recapitulating it in defined biologic systems would lead to insights into the causes of UDND cases, and potentially lead to individualized treatments. This work is now funded as a U2C NIDDK grant with Dr. Goldenring serving as Co-Principal Investigator. We have also collaborated with Drs. Choksi, Goettel, Kaji, Peek, Washington, Yan, and many other VDDRC investigators. A collaborative VDDRC publication is: Kaur H, Ali SA, Short SP, Williams CS, Goettel JA, Washington MK, Peek RM Jr, **Acra SA**, Yan F. Identification of a functional peptide of a probiotic bacterium-derived protein for the sustained effect on preventing colitis. *Gut Microbes*. 2023;15(2):2264456. PMID: PMC10566403.

Future VDDRC Core Use

We will utilize the services of the Cell Imaging and Flow Cytometry Cores for detailed examination of samples from children with UDND syndrome. We will also utilize the Biostatistical Component for database development, statistical analysis, and interpretation of whole-exome findings, and collaboration on the presentation of results.

Member: Holly M. Scott Algood, PhD
Rank: Associate Professor
Department: Medicine and Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

My research is grounded in the study of digestive diseases with an emphasis on *H. pylori* immunopathogenesis. The VDDRC previously supported one of my projects with a Pilot grant focused on T cells and *H. pylori*. My expertise in animal models, flow cytometry, tissue culture-based immune cell activation assays, and eukaryotic gene expression-based assays, in conjunction with access to a human tissue microarray, provides an opportunity to translate our findings into *H. pylori*-induced carcinogenesis. An example of a publication supported by the VDDRC is: Brackman LC, Jung MS, Green EH, Joshi N, Revetta F, McClain MS, Markham NO, Piazuelo MB, **Algood HMS**. IL-17 signaling protects against *Helicobacter pylori*-induced gastric cancer. *Gut Microbes*. 2024 Jan-Dec;16(1):2430421. PMID: PMC11639209.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
2I01BX000915	The role of T cell derived cytokines in <i>H. pylori</i> and other gastrointestinal infections	06/01/2025-05/31/2031	\$321,000

Summary of Digestive Disease Research

The overarching theme for my research is the delineation of the roles of T cell-derived cytokines in the immunopathogenesis of *H. pylori* infection and carcinogenesis. Specific projects in my laboratory focus on pathogen-host interactions in chronic infections, in the context of pathologic inflammation, and on how T cell-derived cytokines influence gastric epithelial cells and fibroblasts during infection.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Poster Judge
Retreat Speaker

VDDRC Collaborations

We collaborate with numerous VDDRC members, including Drs. Cover, Goldenring, Lacy, Markham, Olivares-Villagomez, Peek, Piazuelo, Skaar, Washington, Wilson, among others, for various aspects of our research focused on *H. pylori* pathogenesis. We have published numerous publications in collaboration with other VDDRC members in the last five years. An example is: Brackman LC, Jung MS, Ogaga EI, Joshi N, Wroblewski LE, Piazuelo MB, Peek RM Jr, Choksi YA, **Algood HMS**. IL-17RA-mediated epithelial cell activity prevents severe inflammatory response to *Helicobacter pylori* infection. *Immunohorizons*. 2024; 8(4):339-353. PMID: PMC11066722.

Future VDDRC Core Use

Our core usage is expected to increase in the future, particularly in the use of the Cell Imaging, Translational Analysis, MS/Omics, and Flow Cytometry Cores, as our funded projects propose to utilize tissue imaging by 2-photon confocal microscopy, cellular phenotyping using flow cytometry and single-cell transcriptomics methods, and antigen identification using mass spectrometry.

Member: Rafael Arrojo e Drigo, PhD
Rank: Assistant Professor
Department: Medicine and Molecular Physiology & Biophysics
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My laboratory's goal is to understand the basic mechanisms regulating cellular longevity in health and disease. My laboratory uses the islets of Langerhans in the pancreas as a platform to understand post-mitotic cell biology and relies on transcriptomic and multi-scale imaging pipelines such as confocal, electron and isotope microscopy to study cell biology at the single-cell level. One of my VDDRC publications is: Habashy A, Acree C, Kim KY, Zahraei A, Dufresne M, Phan S, Cutler M, Patterson E, Mulligan AG, Burkewitz K, Flynn CR, Lantier L, Deerinck T, McGuinness OP, Spraggins JM, Ellisman MH, **Arrojo E Drigo R.** (2025) Spatial patterns of hepatocyte glucose flux revealed by stable isotope tracing and multi-scale microscopy. *Nat Commun.* 16(1):5850. PMCID: PMC12219532.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK129340-05	Molecular mechanisms regulating pancreatic delta cell function and dysfunction	04/01/2022-01/31/2027	Listed under Contact PI

Summary of Digestive Disease Research

To understand pancreatic cell homeostasis regulation over long periods of time, our laboratory developed a pipeline that incorporates electron and isotope microscopy in an integrated manner, which has revealed that aging of these organs is cell-type and tissue-type specific.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member

VDDRC Collaborations

Through my involvement in the Academy of Investigators, I established new collaborations with other VDDRC members focused on pancreatic dysfunction, including Drs. Ayala, Burkewitz, Dean, DelGiorno, Flynn, and Tan. A representative collaborative publication is: Dos Santos C, Cambraia A, Shrestha S, Cutler M, Cottam M, Perkins G, Lev-Ram V, Roy B, Acree C, Kim KY, Deerinck T, Dean D, Cartailier JP, MacDonald PE, Hetzer M, Ellisman M, **Arrojo E Drigo R.** (2024) Calorie restriction increases insulin sensitivity to promote beta cell homeostasis and longevity in mice. *Nat Commun.* 115(1):9063. PMCID: PMC11493975.

Future VDDRC Core Use

We plan to utilize the VDDRC Cell Imaging and Translational Analysis Cores in the next funding cycle for our studies focused on pancreatic cellular longevity and to continue to use the Biostatistical Component for data analysis.

Member: Julio Ayala, PhD
Rank: Associate Professor
Department: Molecular Physiology & Biophysics
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

Research in my laboratory focuses on non-pancreatic roles for glucagon-like peptide-1 (Glp1) and Glp1 receptor (Glp1r) agonists in the maintenance of nutrient homeostasis. Initial studies during my postdoctoral training focused on the regulation of hepatic glucose fluxes by the Glp1r, independent of insulin secretion. The focus of the current research in my lab has since transitioned to identifying brain regions that mediate the food intake-suppressive and body weight-lowering effects of Glp1r agonists and elucidating the molecular mechanisms mediating such effects. A representative publication is: Shah H and **Ayala JE**. (2026) Prolonged semaglutide treatment reveals stage-dependent changes to feeding behavior and metabolic adaptations in male mice. *Diabetes* 75(2): 288-300. PMCID: PMC1282338.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK132852-04	Molecular mechanisms mediating metabolic benefits of glucagon-like peptide-1 receptor agonists	01/01/2023-11/30/2026	\$336,457

Summary of Digestive Disease Research

My interest in non-pancreatic, metabolic effects of Glp1r agonists began with several published observations demonstrating changes in nutrient flux in the absence of Glp1r expression. These data suggested a non-pancreatic mechanism for the modulation of tissue glucose fluxes. We have now shown that pharmacological manipulation of the Glp1r in the central nervous system can phenocopy the effects we have previously observed in whole-body Glp1r knockout mice. This proposes a role for the central Glp1r in the maintenance of nutrient homeostasis.

VDDRC-Related Training and Activities

Co-Leader, VDDRC Obesity, Metabolism and Nutrition (OMN) Research Interest Group
Pilot & Feasibility Project Reviewer
Retreat Speaker

VDDRC Collaborations

We have active collaborations with VDDRC members Drs. Arrojo e Drigo, Collins, and Winn. One example of a collaborative publication is: Ceddia RP, Zurawski Z, Thompson Gray A, Adegboye F, McDonald-Boyer A, Shi F, Liu D, Maldonado J, Feng J, Li Y, Alford S, **Ayala JE**, McGuinness OP, Collins S, Hamm HE. (2023) G β γ -SNAP25 exocytotic brake removal enhances insulin action, promotes adipocyte browning, and protects against diet-induced obesity. *J Clin Invest*. 2023;133(19):e160617. PMCID: PMC10541194.

Future VDDRC Core Use

We will continue to utilize the Cell Imaging, Flow Cytometry, and MS/Omics Core, but also anticipate utilizing services in the Translational Analysis Core.

Member: Samuel Bailin, MD, MSCI
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

I am a new Associate Member of the VDDRC. I completed my Internal Medicine residency and Infectious Diseases fellowship at VUMC and joined as faculty in 2021. My work specializes in caring for persons living with HIV, and my translational research program focuses on understanding the pathophysiology of metabolic diseases in persons living with HIV. A representative publication is: **Bailin SS**, Kropski JA, Gangula RD, Hannah L, Simmons JD, Mashayekhi M, Ye F, Fan R, Mallal S, Warren CM, Kalams SA, Gabriel CL, Wanjalla CN, Koethe JR. Changes in subcutaneous white adipose tissue cellular composition and molecular programs underlie glucose intolerance in persons with HIV. *Front Immunol*. 2023;14:1152003. PMCID: PMC10499182.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5K23DK135414-04	Adipose tissue T cell polarization and metabolic health in persons living with HIV	04/01/2023-01/31/2027	\$171,700

Summary of Digestive Disease Research

Adipose tissue is a critical regulator of systemic metabolic processes, and changes in adipose tissue immune cell populations that modulate adipose tissue function may, in part, contribute to the risk of metabolic disease in persons with HIV (PWH). Defining the mechanisms through which adipose tissue innate and adaptive immune cells contribute to metabolic diseases is critical for identifying preventative and therapeutic strategies that reduce morbidity and mortality in PWH. I leveraged single-cell RNA sequencing (scRNA-seq) to define adipose tissue compositional and transcriptional changes in PWH using cross-sectional data, and compared these changes to diabetic HIV-negative adipose tissue. I found that a higher proportion of CD4⁺ and CD8⁺ T effector memory (TEM) cells and lipid-associated macrophages (LAMs) was associated with glucose intolerance in PWH and a higher CD4⁺ and CD8⁺ TEM proportion was associated with greater fibroblastic cells in PWH only. Our overall hypothesis is that proinflammatory TEM cells expressing interferon- γ and tumor necrosis factor α are increased in PWH on ART, infiltrate adipose tissue and promote macrophage polarization, are associated with the adipose tissue viral reservoir, and contribute to the development of metabolic disease.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

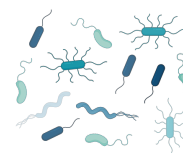
VDDRC Collaborations

Although I am a new member of the VDDRC, I have already developed productive collaborations with other VDDRC members, including Drs. Gabriel, Koethe, Mashayekhi, and Wanjalla. A representative VDDRC collaborative publication is: **Bailin SS**, Gabriel CL, Gangula RD, Hannah L, Nair S, Carr JJ, Terry JG, Silver HJ, Simmons JD, Mashayekhi M, Kalams SA, Mallal S, Kropski JA, Wanjalla CN, Koethe JR. Single-cell analysis of subcutaneous fat reveals profibrotic cells that correlate with visceral adiposity in HIV. *J Clin Endocrinol Metab*. 2024;110(1):238-253. PMCID: PMC11651702.

Future VDDRC Core Use

I will utilize the Cell Imaging Core, the Flow Cytometry Core, and the Biostatistical Component for data analysis.

Member: Megan Behringer, PhD
Rank: Assistant Professor
Department: Biological Sciences
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

My laboratory employs experimental evolution combined with genomic analysis to study how environmental factors affect the creation of genetic variation and influence how microbes adapt and diversify in novel complex environments. Among other environmental factors, these changes may be influenced by nutrient availability or limitation, spatial homogenization or structure, and the presence or absence of community members. My laboratory also applies these concepts to pathogen/microbiome interactions, investigating eco-evolutionary feedback between disease-causing and disease-preventing organisms. A representative publication from my laboratory is: Worthan SB, McCarthy RDP, Delaleau M, Stikeleather R, Bratton BP, Boudvillain M, **Behringer MG**. (2024) Evolution of pH-sensitive transcription termination in *Escherichia coli* during adaptation to repeated long-term starvation. *Proc Natl Acad Sci U S A* 121(39):e2405546121. PMCID: PMC11441560.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R35GM150625-03	Using experimental evolution to evaluate environmental effects on microbial mutation and adaptation	08/08/2023-07/31/2028	\$250,000

Summary of Digestive Disease Research

Research in my lab focuses on how microbes adapt and diversify in novel complex environments by applying multi-omic, systems microbiology approaches to experimental evolution. We investigate how oxygen availability shapes microbial evolution through feast-and-famine cycles by conducting an adaptive laboratory evolution experiment with two bacterial species: the facultative anaerobe *Escherichia coli* and the fastidious aerotolerant anaerobe *Lactobacillus crispatus*. Studies of microbial evolution have historically neglected fastidious microorganisms and anaerobic environments due to the challenges associated with their culture. Our research provides fundamental knowledge about evolutionary processes in a neglected fraction of the microbial tree of life that accounts for a significant proportion of the human intestinal microbiome.

VDDRC-Related Training and Activities

Retreat Speaker

VDDRC Collaborations

My laboratory collaborates with VDDRC members Drs. Olivares-Villagomez, Peek, Washington, and Zhu. One representative collaborative publication is: Spiga L, Fansler RT, Grote A, Langford-Butler M, Miller AK, Neal M, Hale OF, Wu Y, Singla D, Calcutt MW, Rose AE, Bresson MM, Schrimpe-Rutledge AC, Berdy B, Codreanu SG, Washington MK, Bratton BP, Sherrod SD, McLean JA, Zengler K, Sears CL, **Behringer MG**, Gnirke A, Livny J, Olivares-Villagómez D, Earl AM, Zhu W. (2025) An anaerobic pathogen rewires host metabolism to fuel oxidative growth in the inflamed gut. *bioRxiv* 31:2025.05.31.657111. PMCID: PMC12258715.

Future VDDRC Core Use

We plan to use the VDDRC Cell Imaging Core for our *in vivo* co-culture experiments and the MS/Omics Core to identify differentially abundant proteins during co-infections.

Member: Jennifer Below, PhD
Rank: Professor
Department: Medicine and Clinical Pharmacology
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My lab develops and applies computational methods to further understanding of the genetic and epigenetic basis of human disease, specifically, the development of novel strategies for identifying and confirming genetic risk factors to a wide range of familial and complex traits, including metabolic diseases and infectious diseases via the ascertainment of dense genetic, transcriptomic, and phenotypic data. A representative publication from this work is: Palmer AB, Lee KH, Roshani R, Frankel E, Lee M, Anwar MY, Highland HM, Young KL, Graff M, McCormick JB, Fisher-Hoch SP, Samuel JP, **Below JE**, North KE, Gordon-Larsen P. Prevalence of obesity with confirmed excess adiposity in US children and adolescents. *JAMA Pediatr.* 2025 Nov 1;179(11):1227-1229. PMID: PMC12418218.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5U01CA288325-03	Multi-omics for obesity-associated liver disease in a high-risk population cohort	09/01/2023-08/31/2028	\$108,273
5R01HL142302-07	Hispanic Latino lipid consortium	08/10/2018-03/31/2027	\$589,789
5R01DK139598-02	Leveraging metabolic pathways and gene expression data to propel understanding of severe obesity	08/01/2024-05/31/2029	\$98,047
Amgen Inc.	Obesity subtypes and risk of obesity-related conditions	07/14/2025-01/14/2027	\$259,259

Summary of Digestive Disease Research:

My lab works with numerous large-scale datasets. For example, we lead international efforts to meta-analyze all lipids GWAS data available from Hispanic populations (>60,000 samples) as part of the DIAMANTE and the Hispanic/Latino Lipids Consortium, respectively, and collaborate with the Cameron County Hispanic Cohort to explore the effects of gene expression and genetic variation on multiple metabolic traits in Hispanics.

VDDRC-Related Training and Activities

Retreat Poster Judge

VDDRC Collaborations

We collaborate with VDDRC members Drs. Brittain, Byndloss, Collins, Flynn, Lu, and Zhu. A representative collaborative publication is: Petty LE, Chen HH, Frankel EG, Zhu W, Downie CG, Graff M, Lin P, Sharma P, Zhang X, Scartozzi AC, Roshani R, Landman JM, Boehnke M, Bowden DW, Chambers JC, Mahajan A, McCarthy MI, Ng MCY, Sim X, Spracklen CN, Zhang W, Preuss M, Bottinger EP, Nadkarni GN, Loos RJJ, Chen YI, Tan J, Ipp E, Genter P, Emery LS, Louie T, Sofer T, Stilp AM, Taylor KD, Xiang AH, Buchanan TA, Roll K, Gao C, Palmer ND, Norris JM, Wagenknecht LE, Noursome D, Varma R, McKean-Cowdin R, Guo X, Hai Y, Hsueh W, Sadow K, Parra EJ, Cruz M, Valladares-Salgado A, Wachter-Rodarte N, Rotter JI, Goodarzi MO, Rich SS, Bertoni A, Raffel LJ, Nadler JL, Kandeel FR, Duggirala R, Blangero J, Lehman DM, DeFronzo RA, Thameem F, Wang Y, Gahagan S, Blanco E, Burrows R, Huerta-Chagoya A, Florez JC, Tusie-Luna T, González-Villalpando C, Orozco L, Haiman CA, Hanis CL, Rohde R, Whitsel EA, Reiner AP, Kooperberg C, Li Y, Duan Q, Lee M, Correa-Burrows P, Fried SK, North KE, McCormick JB, Fisher-Hoch SP, Gamazon ER, Morris AP, Mercader JM, Highland HM, **Below JE**; DIAMANTE Hispanic/Latino Consortium; Global Hispanic Lipids Consortium. Large-scale multi-omics analyses in Hispanic/Latino populations identify genes for cardiometabolic traits. *Nat Commun.* 2025 Apr 11;16(1):3438. PMID: PMC11985957.

Future VDDRC Core Use

We will use the Biostatistical Component for our GWAS data.

Member: Raymond Blind, PhD
Rank: Associate Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My laboratory explores second messenger signaling in the nucleus. Specifically, we seek to understand the structure, function, and signaling properties of nuclear inositide lipids and inositol phosphates, asking how these molecules directly participate in controlling gene expression. We utilize functional genomics, structural biology, and chemical genetics to query how these second messengers operate. We then apply that information to develop drug discovery platforms with the potential to treat metabolic and digestive diseases, including identifying endogenous ligands like bilirubin for liver nuclear receptors and characterizing mechanisms for intestinal crypt repair. A representative publication is: Wang H, Shears SB, **Blind RD**. Structural rationalization of IPMK inhibitor potency. *J Med Chem*. 2025;68(22):24316-24325. PMID: PMC12670395.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK141801-02	Liver and kidney responses to bilirubin as a nuclear receptor hormone	01/01/2025-12/31/2028	\$217,500

Summary of Digestive Disease Research

Nuclear inositide signaling is particularly interesting because the nucleus contains unique pools of lipids that do not exist in any membrane structure but are instead complexed with soluble proteins. We have discovered that certain pools of nuclear inositides can be directly remodeled by lipid signaling enzymes, with remarkable kinetic properties, providing a new framework to explain how nuclear second messenger signaling works. Current research in our laboratory is focused on determining what role phosphorylated inositols, phosphoinositide lipids, and their signaling enzymes play in chromatin biology, determining how nuclear phosphoinositide complexes are structured, identifying rapid nuclear signaling events using chemical genetics, and understanding how nuclear receptors (such as LXR-1) acquire lipid and hormone ligands (such as bilirubin) to regulate liver and intestinal metabolic homeostasis. We are also utilizing wet-lab validated artificial neural networks to predict compound library binding to full-length nuclear receptors to expand our drug discovery capabilities.

VDDRC-Related Training and Activities

Retreat Poster Judge

VDDRC Collaborations

We plan to collaborate with VDDRC members, Drs. Flynn, Iverson, and Singh in the coming years.

Future VDDRC Core Use

We plan to use the Flow Cytometry and the MS/Omics Cores to analyze the phosphorylation status of nuclear complexes.

Member: Evan L. Brittain, MD, MSCI
Rank: Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My research program focuses on the intersection of metabolism and cardiometabolic disease using translational human studies, clinical trials, molecular phenotyping, wearable technologies, and large-scale electronic health record-linked cohorts. A major focus of this work is adipose biology and metabolic dysfunction, including studies examining the effects of PDE5 inhibition on adipose metabolism and cardiometabolic disease in humans. These efforts align closely with the mission of the VDDRC through shared interests in obesity, metabolism, inflammation, liver disease, and systems biology. One representative publication is: **Brittain EL**, Han L, Annis J, Master H, Hughes A, Roden DM, Harris PA, Ruderfer DM. Physical activity and incident obesity across the spectrum of genetic risk for obesity. *JAMA Netw Open*. 2024;7(3):e243821. PMID: PMC10973894.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK124845-05	Effect of PDE5 inhibition on adipose metabolism in humans	02/01/2021-01/31/2027	\$444,292

Summary of Digestive Disease Research

My laboratory studies the metabolic and molecular mechanisms linking obesity, adipose dysfunction, and inflammation. Current work includes mechanistic human clinical trials examining adipose tissue biology, mitochondrial metabolism, lipid handling, and cardiometabolic dysfunction. We also use large-scale wearable and EHR-linked cohorts to study physical activity, sleep, obesity, diabetes, and chronic disease risk. A major area of interest is identifying molecular pathways that distinguish susceptibility from resilience in metabolic disease. This includes integrating metabolomics, genomics, imaging, and physiologic phenotyping to better understand disease progression and heterogeneity. These studies have implications for obesity-related digestive and liver disease, metabolic dysfunction, and systemic inflammatory disorders.

VDDRC-Related Training and Activities

Retreat Speaker

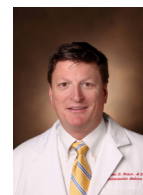
VDDRC Collaborations

I have established collaborations with VDDRC members Drs. Below, Brown, Collins, Izzy, Koethe, Spann, Vickers, and Zaganjor. A representative collaborative publication is: Ying X, Oje AO, De Witte AJ, Slaughter JC, Spann AL, Jesudian AB, Rosenblatt R, Ng C, Sholle E, Reidy D, Pan Y, Annis J, Gupta DK, **Brittain EL**, Fortune BE, Izzy M. Severity of liver disease is associated with cirrhotic cardiomyopathy: A multicenter study. *Liver Transpl*. 2025. PMID: 41378871.

Future VDDRC Core Use

We will use the MS/Omics Core for metabolomics studies in the future and the Biostatistical Component for data analysis.

Member: Jonathan D. Brown, MD
Rank: Associate Professor
Department: Medicine and Molecular Physiology & Biophysics
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

I have leveraged functional genomics approaches to examine dynamic remodeling of enhancers during proinflammatory activation in endothelial cells, macrophages, adipocytes, and hepatocytes, and these studies were initially funded by a VDDRC Pilot Award. A representative publication is: Steinhauser S, Estoppey D, Buehler DP, Xiong Y, Pizzato N, Rietsch A, Wu F, Leroy N, Wunderlin T, Claerr I, Tropberger P, Müller M, Vissieres A, Davison LM, Farber-Eger E, Wells QS, Sheng Q, Bergling S, Wild S, Moulin P, Liang J, English WJ, Williams B, Knehr J, Altorfer M, Reyes A, Voshol J, Mickanin C, Hoepfner D, Nigsch F, Frederiksen M, Flynn CR, Fodor BD, **Brown JD**, Kolter C. The transcription factor ZNF469 regulates collagen production in liver fibrosis. *JCI Insight*. 2025;10(7):e182232. PMCID: PMC11981625.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Novartis Pharmaceuticals	Long term chromatin changes in chronic liver disease	11/18/2019-11/18/2026	\$555,274
1R01DK141978-01A1	Investigating transcriptional mechanisms of fibrosis in the liver	06/01/2026-02/28/2030	Listed under Contact PI

Summary of Digestive Disease Research

I have a background in gene regulation with specific training in the mechanisms of transcription factor activation and chromatin-dependent signal transduction. In my postdoctoral fellowship, I studied nuclear receptor activation (PPARs) in metabolism in the liver. As an independent investigator, my group employs genome-wide sequencing techniques, including chromatin immunoprecipitation (ChIP), assay for accessible chromatin (ATAC-seq), global RNA profiling, and single-cell RNA sequencing techniques to study how abnormal gene expression programs are regulated in metabolic disease. We have an ongoing interest in using these tools to discover the core regulatory circuitry in fatty liver disease.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

I have formed collaborations with VDDRC members Drs. Ayala, Brittain, Collins, Flynn, Koethe, Niswender, Vickers, and Zaganjor. A collaborative publication is: Mashayekhi M, Beckman JA, Nian H, Garner EM, Mayfield D, Devin JK, Koethe JR, **Brown JD**, Cahill KN, Yu C, Silver H, Niswender K, Luther JM, Brown NJ. Comparative effects of weight loss and incretin-based therapies on vascular endothelial function, fibrinolysis and inflammation in individuals with obesity and prediabetes: A randomized controlled trial. *Diabetes Obes Metab*. 2023; 25(2):570-580. PMCID: PMC10306232.

Future VDDRC Core Use

I will continue to use the Flow Cytometry and the Cell Imaging Cores and will begin to use the Translational Analysis Core in the next funding cycle.

Member: Kristopher Burkewitz, PhD
Rank: Assistant Professor
Department: Cell and Developmental Biology
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My research occurs at the interface of cell biology, metabolism, and genetics to break the link between aging and disease. We are interested in combating age-onset diseases, such as metabolic dysfunction, by understanding and targeting their common risk factor: the aging process itself. A representative publication is: Donahue EKF, Hepowit NL, Ruark EM, Mulligan AG, Keuchel B, Urban ND, Peng L, Stephens S, Johnson DJ, Wallace NS, Jackson LP, Ellisman MH, Arrojo E Drigo R, Folkmann AW, Truttmann MC, MacGurn JA, **Burkewitz K**. ER remodeling is a feature of ageing and depends on ER-phagy. *Nat Cell Biol.* 2026;28(3):449-464. PMID: 41629400.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R21AG100967-01	Defining characteristics of a resilient organelle interactome during aging	05/15/2026-04/30/2028	\$275,000

Summary of Digestive Disease Research

We are currently mapping the spatial rearrangement of organelles in enterocytes that occurs during the aging process. By defining how the inner architecture of young vs. aged cells differs, we are identifying a cell biological basis for the reduced metabolic and functional plasticity observed during aging.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient

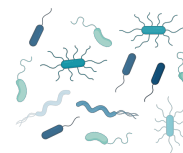
VDDRC Collaborations

We have active collaborations with VDDRC members Drs. Arrojo e Drigo and Flynn. A representative collaborative publication is: Habashy A, Acree C, Kim KY, Zahraei A, Dufresne M, Phan S, Cutler M, Patterson E, Mulligan AG, **Burkewitz K**, Flynn CR, Lantier L, Deerinck T, McGuinness OP, Spraggins JM, Ellisman MH, Arrojo E Drigo R. Spatial patterns of hepatocyte glucose flux revealed by stable isotope tracing and multi-scale microscopy. *Nat Commun.* 2025 Jul 1;16(1):5850. PMCID: PMC12219532.

Future VDDRC Core Use

I plan to utilize the Cell Imaging and MS/Omics Core for future studies.

Member: Mariana Xavier Byndloss, PhD
Rank: Assistant Professor
Department: Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

My research focuses on establishing novel molecular mechanisms responsible for the imbalance in microbial communities. We are particularly interested in how inflammation-mediated gut epithelial metabolism changes lead to gut dysbiosis and increased risk of chronic inflammatory disorders, namely obesity, IBD, and colorectal cancer. Another arm of my research examines how *Salmonella* Typhimurium-mediated intestinal inflammation changes host physiology and how these changes disrupt the microbial ecosystem in the large intestine to promote disease. A representative publication is: Yoo W, Shealy NG, Zieba JK, Torres TP, Baltagulov M, Thomas JD, Shelton CD, McGovern AG, Foegeding NJ, Olsan EE, **Byndloss MX**. *Salmonella* Typhimurium expansion in the inflamed murine gut is dependent on aspartate derived from ROS-mediated microbiota lysis. *Cell Host Microbe*. 2024; 32(6):887-899. PMID: PMC11189616.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Howard Hughes Medical Institute	Uncovering host-microbiota metabolic interactions in health and disease	09/01/2023-08/31/2028	\$400,000
5R01DK131104	Obesogenic diet-induced intestinal epithelium repair responses link dysbiosis and cardiovascular disease	01/12/2022-12/31/2026	\$283,609
5R01AI168302	Mechanisms of <i>Salmonella</i> -mediated disruption of colonization resistance in the inflamed gut	09/19/2022-07/31/2027	\$282,963
Burroughs Wellcome Foundation 1022792	Role of diet-microbiota interactions during <i>Salmonella</i> gastroenteritis	07/01/2023-06/30/2028	\$100,000
Pew Charitable Trusts 00036037	Role of microbiota and intestinal epithelial interactions in childhood obesity	07/12/2022-07/31/2027	\$69,444
The Obesity Society	Perturbation to the infant small intestine microbiota increases intestinal lipid absorption and the risk for childhood obesity	01/01/2026-12/31/2026	\$25,000

Summary of Digestive Disease Research

Intestinal inflammation can be caused by infection with an enteric pathogen, diet changes, antibiotic consumption, and/or other insults. These episodes are accompanied by a substantial alteration of the gut microbiota, termed bacterial dysbiosis. My work has demonstrated that *Enterobacteriaceae* and the pathogen *Salmonella enterica* serotype Typhimurium can bloom in the gut after antibiotic therapy and during colitis by taking advantage of increased nitrate, oxygen, and oxidized sugars availability. This work has established the concept that the host maintains gut homeostasis by limiting the availability of electron acceptors in the colon, which has important implications for the development of approaches to rebalance the gut microbiota during dysbiosis.

VDDRC-Related Training and Activities

Co-Leader, Gastrointestinal Infection and Injury (GII) Research Interest Group
 Academy of Investigators, Former Member
 Pilot & Feasibility Award Recipient
 Young Investigator Award
 Retreat Speaker

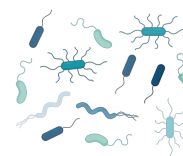
VDDRC Collaborations

I have established collaborations with VDDRC members Drs. Below, Cassat, Choksi, Collins, Flynn, Goettel, Lau, Markham, Markle, Nicholson, Peek, Skaar, Williams, Wilson, and Zhu. A representative collaborative publication is: Spiga L, Fansler RT, Perera YR, Shealy NG, Munneke MJ, David HE, Torres TP, Lemoff A, Ran X, Richardson KL, Pudlo N, Martens EC, Folta-Stogniew E, Yang ZJ, Skaar EP, **Byndloss MX**, Chazin WJ, Zhu W. Iron acquisition by a commensal bacterium modifies host nutritional immunity during *Salmonella* infection. *Cell Host Microbe*. 2023; 31(10):1639-1654. PMCID: PMC10599249.

Future Core Use

We will continue to use the Cell Imaging Core, Flow Cytometry Core, and MS/Omics Core for our discovery-based metabolomics studies, as well as the Translational Analysis Core.

Member: James Cassat, MD
Rank: Associate Professor
Department: Pediatrics and Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

My long-term objective is to lead a discovery-based team focused on understanding how infectious diseases and inflammation alter tissue homeostasis. To this end, one major focus of our laboratory is understanding how inflammatory bowel disease and dysbiosis trigger changes in bone remodeling. A representative publication is: Peek CT, Ford CA, Eichelberger KR, Jacobse J, Torres TP, Maseda D, Latour YL, Piazuelo MB, Johnson JR, Byndloss MX, Wilson KT, Rathmell JC, Goettel JA, **Cassat JE**. Intestinal inflammation promotes MDL-1+ osteoclast precursor expansion to trigger osteoclastogenesis and bone loss. *Cell Mol Gastroenterol Hepatol*. 2022; 14(4): 10:731-750. PMCID: PMC9420375.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01AI177615-02	Fungal-bacterial dynamics driving dysregulated host responses and lethal synergism	07/15/2024-06/30/2029	\$164,557

Summary of Digestive Disease Research

A major focus of our research is to understand the interaction between host and pathogen during invasive bacterial infections. We were funded by the VDDRC in a pilot project to investigate the mechanisms of bone loss during IBD. Our studies employ novel imaging techniques, skeletal cell culture models, and multi-parameter flow cytometry. The initial VDDRC pilot led to our acquisition of a CCF Senior Research Award and an award from the G. Harold and Leila Y. Mathers Foundation. We also study the host-pathogen interactions during invasive *Staphylococcal* disease in work supported by the NIH.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

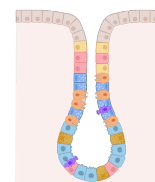
VDDRC Collaborations

We collaborate with VDDRC members Drs. Byndloss, Choksi, Flynn, Goettel, Lau, Williams, Wilson, and Zhu for studies of IBD. We also collaborate with Dr. Skaar for studies of bacterial pathogenesis. A representative collaborative publication is: Jacobse J, Brown RE, Li J, Pilat JM, Pham L, Short SP, Peek CT, Rolong A, Washington MK, Martinez-Barricarte R, Byndloss MX, Shelton C, Markle JG, Latour YL, Allaman MM, **Cassat JE**, Wilson KT, Choksi YA, Williams CS, Lau KS, Flynn CR, Casanova JL, Rings EHHM, Samsom JN, Goettel JA. Interleukin-23 receptor signaling impairs the stability and function of colonic regulatory T cells. *Cell Rep*. 2023; 42(2):112128. PMCID: PMC10432575.

Future VDDRC Core Use

We will rely heavily on the Cell Imaging and the Translational Analysis Cores for assessing intestinal damage and bone loss in our model. We will also heavily utilize the Flow Cytometry and the MS/Omics Cores to analyze immune cells and tissues in our NIH-funded experiments.

Member: Eunyong Choi, PhD
Rank: Associate Professor and Naji N. Abumrad Chair in Surgical Sciences
Department: Surgery
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am an Associate Professor and Inaugural Naji N. Abumrad Chair in Surgical Sciences. My research is multidisciplinary by integrating stem cell biology and gastric carcinogenesis. My research group seeks to not only define the cells of origin for gastric carcinogenesis but also determine the oncogenic potential and regulatory mechanisms during disease development. A recent VDDRC-related publication is: Kim H, Jang B, Zhang C, Caldwell B, Park DJ, Kong SH, Lee HJ, Yang HK, Goldenring JR, **Choi E**. Targeting stem cells and dysplastic features with dual MEK/ERK and STAT3 suppression in gastric carcinogenesis. *Gastroenterology*. 2024;166(1):117-131. PMCID: PMC10841458.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
4R01CA272687-04	Cell plasticity in the origin of gastric carcinogenesis	09/01/2025-08/31/2027	\$600,000
4R37CA244970-06	Drivers of gastric pre-neoplasia	08/01/2025-07/31/2027	\$448,305
5R01DK101332-12	Induction and evolution of metaplasia in the stomach	07/19/2022-05/31/2027	Listed under Contact PI
Congressionally Directed Medical Research Programs HT94252410383	Therapeutic intervention to reverse gastric precancer	06/01/2024-05/31/2028	Listed under Contact PI

Summary of Digestive Disease Research

Our overarching research goal is to define key features of high-risk pre-cancer cells critical for early diagnosis and treatment design for gastric cancer. Using advanced mouse models and human organoids, my research group investigates lineage heterogeneity, plasticity, and oncogenic transitions during gastric carcinogenesis. We have identified dysplastic stem cells in pre-cancerous lesions as cancer-initiating cells that are responsible for adenocarcinoma development. Current efforts extend to molecular and epigenetic mechanisms in pre-cancer cell lineage evolution and plasticity, and roles of fatty acid metabolism in disease progression.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Retreat Speaker

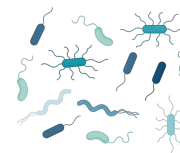
VDDRC Collaborations

We have ongoing collaborations with numerous VDDRC members, including Drs. Coffey, Goldenring, Lau, Peek, Piazuelo, and Washington. An example of a VDDRC collaborative publication is: Lee SH, Won Y, Gibbs D, Caldwell B, Goldstein A, **Choi E**, Goldenring JR. Amphiregulin switches progenitor cell fate for lineage commitment during gastric mucosal regeneration. *Gastroenterology*. 2024;167(3):469-484. PMCID: PMC11260537.

Future VDDRC Core Use

We will continue to utilize the VDDRC Biostatistical Component, Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores in the next funding cycle. We will also implement a new approach by using metabolomics.

Member: Yash Choksi, MD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

My research interests, previously funded by a VDDRC Pilot Award, are related to understanding esophageal inflammation and tumorigenesis, particularly (1) the role of eosinophils in esophageal squamous cell carcinogenesis and (2) the mechanisms by which oxidative stress can perturb esophageal epithelial homeostasis in EoE. One VDDRC-related publication is: Jacobse J, Brown R, Revetta F, Vaezi M, Buendia MA, Williams CS, Higginbotham T, Washington MK, Goettel J, Hiremath G, **Choksi YA**. A synthesis and subgroup analysis of the eosinophilic esophagitis tissue transcriptome. *J Allergy Clin Immunol*. 2024 ;153(3):759-771. PMID: PMC10939980.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK141803-02	Defining the role of GPX3 in eosinophilic esophagitis	03/15/2025-01/31/2030	\$387,338
Veterans Administration 1I01BX006820-01A1	Defining the role of eosinophils in the development of esophageal malignancy	04/01/2026-03/31/2030	\$380,000

Summary of Digestive Disease Research

My research program focuses on the intersection of epithelial biology and mucosal immunology in esophageal inflammation and disease. Specifically, I am interested in how oxidative stress modifies epithelial-stromal and epithelial-immune interactions. Our lab accomplishes this by utilizing human samples, organoid culturing, air-liquid interface culturing, and mouse modeling. Our significant experience in biobanking helps us achieve these goals and discovering how these pathways can deepen our understanding of EoE and esophageal carcinogenesis is the fundamental question my lab seeks to answer.

VDDRC-Related Training and Activities

Assistant Director, VDDRC
Co-Director, Pilot & Feasibility Program
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

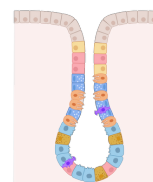
VDDRC Collaborations

I have ongoing collaborations with numerous VDDRC members, including Drs. Acra, Algood, Coburn, Coffey, Collins, Goettel, Goldenring, Hiremath, Kaji, Lau, Lee, Mahadevan-Jansen, Markham, Peek, Piazuelo, Washington, Williams, Wilson, and Yan. A representative collaborative publication is: Li J, Simmons AJ, Hawkins CV, Chiron S, Ramirez-Solano MA, Tasneem N, Kaur H, Xu Y, Revetta F, Vega PN, Bao S, Cui C, Tyree RN, Raber LW, Conner AN, Pilat JM, Jacobse J, McNamara KM, Allaman MM, Raffa GA, Gobert AP, Asim M, Goettel JA, **Choksi YA**, Beaulieu DB, Dalal RL, Horst SN, Pabla BS, Huo Y, Landman BA, Roland JT, Scoville EA, Schwartz DA, Washington MK, Shyr Y, Wilson KT, Coburn LA, Lau KS, Liu Q. Identification and multimodal characterization of a specialized epithelial cell type associated with Crohn's disease. *Nat Commun*. 2024 Aug 22;15(1):7204. PMID: PMC11339313.

Future VDDRC Core Use

Our group will continue to use the Translational Analysis Core to evaluate our models of disease, as well as the Cell Imaging, Flow Cytometry, and MS/Omics Cores to investigate our organoid models.

Member: Lori A. Coburn, MD
Rank: Associate Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am a Full Member of the VDDRC and will serve as Assistant Director of the Center and Director of the VDDRC Academy of Investigators. My research is focused on inflammatory bowel disease (IBD) and colon cancer pathogenesis and identification of potential biomarkers and/or therapeutic targets for these diseases, and a representative publication is: Raffa GA, Tyree RN, Carson K, Allaman MM, Beaulieu DB, Dalal RL, Pabla BS, Scoville EA, Horst SN, Schwartz DA, Washington MK, Wilson KT, **Coburn LA**. Non-invasive determination of disease activity in Crohn's disease by serum luminex profiling. *Sci Rep*. 2026 Mar 9;16(1):8867. PMID: PMC12988101.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Veterans Administration, 5I01CX002662-02	The role of CCL11 in inflammatory and sporadic colorectal cancer	07/11/2024-06/30/2028	\$300,000

Summary of Digestive Disease Research

Our studies, originally supported by a VDDRC Pilot and Feasibility Grant and now by a VA Merit, have shown by hierarchical clustering in metabolomic profiles that UC and CD patients were distinctly different from control subjects and from each other. The pathways most significantly altered between the 3 groups involved lipid metabolism and carbohydrate/energy metabolism. Furthermore, we showed that multiple serum cytokines/chemokines and adipokines were altered in UC and CD patients versus controls, as well as between UC and CD patients. Our ongoing work focuses on the chemokine CCL11 in IBD and colon cancer. Collaborations within the VDDRC between me, Ken Lau, and Keith Wilson also led to the acquisition of a Helmsley Trust Grant to generate a single-cell atlas for Crohn's disease.

VDDRC-Related Training and Activities

Assistant Director, VDDRC
Director, Academy of Investigators
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

VDDRC Collaborations

We collaborate extensively with VDDRC members, including Drs. Goettel, Lau, Piazuelo, Washington, Williams, and Wilson, for both our mouse models of colitis and human IBD samples. A collaborative publication is: Li J, Simmons AJ, Hawkins CV, Chiron S, Ramirez-Solano MA, Tasneem N, Kaur H, Xu Y, Revetta F, Vega PN, Bao S, Cui C, Tyree RN, Raber LW, Conner AN, Pilat JM, Jacobse J, McNamara KM, Allaman MM, Raffa GA, Gobert AP, Asim M, Goettel JA, Choksi YA, Beaulieu DB, Dalal RL, Horst SN, Pabla BS, Huo Y, Landman BA, Roland JT, Scoville EA, Schwartz DA, Washington MK, Shyr Y, Wilson KT, **Coburn LA**, Lau KS, Liu Q. Identification and multimodal characterization of a specialized epithelial cell type associated with Crohn's disease. *Nat Commun*. 2024 Aug 22;15(1):7204. PMID: PMC11339313.

Future VDDRC Core Use

We will increase our core usage, specifically the Translational Analysis Core and the Biostatistics Component, as we now have large datasets from metabolomic profiling of patients with IBD. We will use the Flow Cytometry Core to isolate cells for single-cell RNAseq. We also plan to use the Tissue Morphology Service in the Translational Analysis Core and the Cell Imaging Core to define the topography of identified biomarkers *in vivo*.

Member: Robert Coffey, MD
Rank: Professor
Department: Medicine and Cell and Developmental Biology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

Our group has contributed to the understanding of development and disease along the entire GI tract. I am also the PI of the NIH-funded GI SPORE and the Vanderbilt Epithelial Biology Center. We have worked closely with the VDDRC to leverage our resources in order to maximize funding of junior investigators in digestive diseases research and co-sponsor visiting researchers of mutual interest. One VDDRC publication is: Tutanov OS, Massick C, Ramirez M, Higginbotham JN, Jimenez L, Castleberry M, Cao Z, John E, Hamilton MS, Zhang Q, Jeppesen DK, Michell DL, Glass SE, Patel P, Rose KL, Krystofiak E, Chen HC, Sheng Q, Liu Q, Patton JG, Weaver AM, Franklin JL, Vickers KC, **Coffey RJ**. A comprehensive analysis of supermere, exomere, and extracellular vesicle isolation and cargo in colorectal cancer. *Cell Rep.* 2025; 44(10):116287. PMCID: PMC12632813.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R35CA197570-09	Early to late events in colorectal neoplasia: basic biology to clinical implementation	08/05/2024-07/31/2031	\$529,789
HT94252510915	Targeting the DPEP1-neutrophil axis in microsatellite stable colorectal cancer	08/15/2025-08/14/2027	\$400,000
2P01CA229123-06A1	Roles for supermeres in CRC progression	01/20/2020-05/31/2031	\$390,988
4U01CA294527-02	A multimodal 3D atlas of colorectal cancer across ages of onset	09/01/2024-08/31/2029	Listed under Contact PI

Summary of Digestive Disease Research

One area of research focus in our group is the study of the role of the EGF receptor (EGFR) and its ligands in GI diseases. We have a particular interest in investigating the trafficking of EGFR ligands in polarizing colonic epithelial cells. Naked2 has been identified as a critical regulator of basolateral trafficking of TGF- α , a major EGFR ligand, and provides a point of convergence between EGFR and Wnt signaling pathways. This work has led to the identification of a new mode of EGFR ligand signaling via exosomes and the development of FAVS (fluorescent-activated vesicle sorting) to isolate and characterize cellular organelles. An important clinical advance has been that cetuximab, a monoclonal antibody that blocks EGFR signaling, provides the first effective medical treatment for Ménétrier's disease, a premalignant overgrowth state of the stomach.

VDDRC-Related Training and Activities

Co-Director of the collaborating Epithelial Biology Center (EBC)
 Retreat Speaker

VDDRC Collaborations

I have collaborated extensively with multiple members within the VDDRC. I have worked closely with Drs. Crowe, Goldenring, Lau, Lee, Markham, Peek, Singh, Southard-Smith, Vickers, Washington, and Zhu on multiple projects that have subsequently led to over 30 co-authored papers published in journals such as the *Journal of Clinical Investigation*, *Gastroenterology*, *PNAS*, and *Science Translational Medicine*. A representative collaborative publication is: Heiser CN, Simmons AJ, Revetta F, McKinley ET, Ramirez-Solano MA, Wang J, Kaur H, Shao J, Ayers GD, Wang Y, Glass SE, Tasneem N, Chen Z, Qin Y, Kim W, Rolong A, Chen B, Vega PN, Drewes JL, Markham NO, Saleh N, Nikolos F, Vandekar S, Jones AL, Washington MK, Roland JT, Chan KS, Schürpf T, Sears CL, Liu Q, Shrubsole MJ, **Coffey RJ**, Lau KS. Molecular cartography uncovers evolutionary and microenvironmental dynamics in sporadic colorectal tumors. *Cell.* 2023; 186(25):5620-5637. PMCID: PMC10756562.

Future VDDRC Core Use

We will continue to rely heavily on the Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores for our studies of EGFR trafficking in novel *ex vivo* organoid models and mouse models of disease.

Member: Sheila Collins, PhD
Rank: Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My laboratory studies metabolic disease, and we have extensive expertise in signal transduction and transcriptional regulation with a focus on adipocyte biology. One of our VDDRC-related publication is: Liu D, Ceddia RP, Zhang W, Shi F, Fang H, **Collins S**. Discovery of another mechanism for the inhibition of particulate guanylyl cyclases by the natriuretic peptide clearance receptor. *Proc Natl Acad Sci USA*. 2023; 120(28):e2307882120. PMCID: PMC10334801.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK132236-03	Role of SIK3 in PKA/mTORC1 regulation of adipose browning	09/06/2023-08/31/2028	\$309,000
5R01DK126890-04	Natriuretic peptide and cGMP signaling in adipose tissue and energy metabolism	04/15/2022-02/28/2027	\$293,000

Summary of Digestive Disease Research

We have worked for many years on the regulation of brown and white adipocyte metabolism, with a strong emphasis on dissecting the signaling pathways initiated by activation of G-protein-coupled β -adrenergic receptors. This work has been extended to include how cardiac natriuretic peptides modulate fat cell metabolism through a parallel and complementary signaling cascade, to promote 'browning' and energy expenditure, and we have mapped much of the pathway.

VDDRC-Related Training and Activities

Retreat Speaker

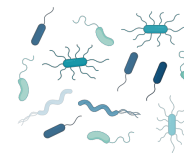
VDDRC Collaborations

We currently collaborate with several VDDRC investigators focused on adipocyte pathobiology, including Drs. Ayala, Below, Brittain, Brown, Koethe, Vickers, and Zaganjor. A representative VDDRC collaborative publication is: Ceddia RP, Zurawski Z, Thompson Gray A, Adegboye F, McDonald-Boyer A, Shi F, Liu D, Maldonado J, Feng J, Li Y, Alford S, Ayala JE, McGuinness OP, **Collins S**, Hamm HE. G β γ -SNAP25 exocytotic brake removal enhances insulin action, promotes adipocyte browning, and protects against diet-induced obesity. *J Clin Invest*. 2023;133(19):e160617. PMCID: PMC10541194.

Future VDDRC Core Use

We plan to utilize the Flow Cytometry Core for single-cell isolation for single-cell RNA-seq, the Translational Analysis Core for our mouse models, and continue to use the MS/Omics Core to identify signaling molecules within adipocytes.

Member: Timothy L. Cover, MD
Rank: Professor
Department: Medicine and Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I am Co-Leader of the VDDRC Gastrointestinal Infections and Injury (GII) Research Interest Group. My research focuses on *H. pylori* pathobiology, disorders of the stomach, and bacteria that colonize the gastrointestinal tract of humans. A VDDRC publication is: Bryant KN, Frick-Cheng AE, Solecki LE, Kroh HK, McDonald WH, Lacy DB, McClain MS, Ohi MD, **Cover TL**. Species-specific components of the *Helicobacter pylori* Cag type IV secretion system. *Infect Immun*. 2025;93(5):e0049324. PMCID: PMC12070742.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01AI118932-11	Type IV protein secretion in <i>Helicobacter pylori</i>	04/09/2021-03/31/2027	\$507,833
5I01BX004447-06	Pathogenesis of <i>Helicobacter pylori</i> infection	07/01/2024-06/30/2028	\$165,000
2R01AI039657-26	Structure and function of <i>Helicobacter pylori</i> VacA	04/07/2026-03/30/2031	\$432,862
5P01CA116087-19	Regulation of <i>Helicobacter pylori</i> virulence by dietary factors that impact gastric cancer	01/02/2009-02/28/2029	Listed under Contact PI

Summary of Digestive Disease Research

Longstanding themes of my laboratory's research include studies of *H. pylori* genetic diversity and studies of *H. pylori* proteins that cause alterations in host cells. Recently, we have isolated and analyzed the structure of a membrane-spanning protein complex within the *H. pylori* cag type IV secretion system. We also actively investigate the role of dietary constituents such as salt in modifying the pathogenic potential of bacteria.

VDDRC-Related Training and Activities

Co-Leader, VDDRC Gastrointestinal Infections and Injury (GII) Research Interest Group
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

VDDRC Collaborations

We collaborate with numerous VDDRC members, including Drs. Algood, Lacy, Peek, Piazuelo, Washington, and Wilson, on various projects related to our studies of *H. pylori*. A recent publication resulting from our VDDRC collaborations is: Shuman JHB, Lin AS, Westland MD, Bryant KN, Fortier GE, Piazuelo MB, Reyzer ML, Judd AM, Tsui T, McDonald WH, McClain MS, Schey KL, Algood HM, **Cover TL**. *Helicobacter pylori* CagA and Cag type IV secretion system activity have key roles in triggering gastric transcriptional and proteomic alterations. *Infect Immun*. 2025;93(4):e0059524. PMCID: PMC11977315.

Future VDDRC Core Use

We will continue using multiple DDRC cores. Specifically, we will continue using the MS/Omics Core to analyze *H. pylori* proteins and protein complexes, the MS/Small Molecule Core to analyze *H. pylori* effects on gastric epithelial cell metabolism, the Cell Imaging Core to study *H. pylori* effects on gastric epithelial cells, as well as Imaging Mass Spectrometry services and the Translational Analysis Core to detect *H. pylori*-induced alterations in lipids and metabolites in gastric tissue.

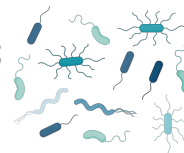
Member: James E. Crowe, Jr., MD

Rank: Ann Scott Carell Chair; Director, Vanderbilt Center for Antibody Therapeutics; Professor

Department: Pediatrics, Pathology, Microbiology and Immunology

VDDRC Status: Full Member

Research Group: GII



Rationale for VDDRC Membership

Our research interests related to the VDDRC lie in the broad fields of vaccine biology and immunology, and we have a particular expertise in studying the molecular and genetic basis for the development of human antibodies to rotavirus and norovirus. A representative VDDRC publication is: Alvarado G, Salmen W, Ettayebi K, Hu L, Sankaran B, Estes MK, Venkataram Prasad BV, **Crowe JE Jr.** Broadly cross-reactive human antibodies that inhibit genogroup I and II noroviruses. *Nat Commun.* 2021;12(1):4320. PMCID: PMC8280134.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
75N93024C00071	B cell epitope discovery and mechanisms of antibody protection for Enterovirus and Bunyavirus proteins	09/16/2024-09/15/2029	Not PI or MPI

Summary of Digestive Disease Research

I have over 30 years of experience in basic research of virology and immunology, especially antiviral antibodies, and we have made seminal contributions in the development of human neutralizing antibodies to microbial pathogens. We have been one of the leading groups in the development of innovative technologies for isolation and study of human monoclonal antibodies. Our work on rotaviruses was originally initiated by a VDDRC Pilot Project Award, and we have performed extensive norovirus work. Now we are engaged in enterovirus antibody and B cell studies.

VDDRC-Related Training and Activities

Former Scientific Director, VDDRC Flow Cytometry Core

Pilot & Feasibility Award Recipient

Retreat Speaker

VDDRC Collaborations

I will continue to collaborate with VDDRC members, Drs. Algoood, Lacy, Peek, Piazuolo, Washington, Wilson.

Future VDDRC Core Use

We will continue to use the Cell Imaging, Flow Cytometry, and the MS/Omics Cores for our studies of B and T cell repertoires that regulate immune responses.

Member: Kathleen DelGiorno, PhD
Rank: Assistant Professor
Department: Cell and Developmental Biology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My laboratory leverages histological and ultrastructural microscopy, small cell number sequencing techniques, and genetically engineered mouse models to study the physiological role of rare secretory cell populations in the pancreas and gastrointestinal tract. I was the previous recipient of a VDDRC Pilot and Feasibility Award to study epithelial heterogeneity in pancreatic injury and regeneration. A representative VDDRC publication is: Ankenbauer KE, Yang Y, Chung CY, Andrade LR, Novak SW, Jarvis B, Ali Hanel WH, Liu J, Sarkisian V, Dani N, Krystofiak E, Hu G, Ebrahim S, Kachar B, Gong Q, Wahl GM, Lau KS, Brown JW, Manor U, **DelGiorno KE**. Protocadherin 20 is a POU class 2 homeobox 3 target gene required for proper tuft cell microvillus organization. *Cell Mol Gastroenterol Hepatol*. 2026;101742. PMID: 41619969.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK145538	Tuft cells resolve pancreatic injury through a type 2 immune circuit	Pending	Pending
Adele Braun Charitable Foundation	IP agonism as a novel treatment for pancreatic cancer	03/01/2026-02/28/2029	\$300,000
American Cancer Society ACS 1433470	Modulating eicosanoids for the treatment and prevention of pancreatic cancer	09/01/2025-08/31/2029	\$215,000
4U01CA294527-02	A multimodal 3D atlas of colorectal cancer across ages of onset	09/01/2024-08/31/2029	Listed under Contact PI

Summary of Digestive Disease Research:

The goals of our laboratory are to generate tools to understand the process of pancreatic acinar-to-ductal metaplasia (ADM), to identify the consortium of ADM cell types that emerge, and to determine their physiological role in tissue injury, regeneration, and tumorigenesis. Identification of transdifferentiation intermediate cell states will provide a deeper understanding of this non-stem cell transition event.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I have established collaborations with other VDDRC members focused on pancreatic disease, including Drs. Arrojo e Drigo, Goldenring, Kaji, Lau, and Tan. A representative VDDRC collaborative publication is: Ma Z, Lytle NK, Chen B, Jyotsana N, Novak SW, Cho CJ, Caplan L, Ben-Levy O, Neiningner AC, Burnette DT, Trinh VQ, Tan MCB, Patterson EA, Arrojo E Drigo R, Giraddi RR, Ramos C, Means AL, Matsumoto I, Manor U, Mills JC, Goldenring JR, Lau KS, Wahl GM, **DelGiorno KE**. Single-cell transcriptomics reveals a conserved metaplasia program in pancreatic injury. *Gastroenterology*. 2022;162(2):604-620. PMCID: PMC8792222.

Future VDDRC Core Use

Our laboratory will utilize the Flow Cytometry, MS/Omics, and Translational Analysis Cores.

Member: Charles R. Flynn, PhD
Rank: Associate Professor
Department: Surgery
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

I have an active research program with an emphasis on metabolic derangements and metabolic improvements following bariatric procedures. One VDDRC publication from my research is: Cheung-Flynn J, Rathmacher JA, Pitchford LM, Xiong Y, **Flynn CR**. Reactive dicarbonyl scavenging with 2-hydroxybenzylamine improves MASH. *Nutrients*. 2025;17(4):610. PMCID: PMC11858443.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK141978-01A1	Investigating transcriptional mechanisms of fibrosis in the liver	06/01/2026-02/28/2030	\$499,852
R01DK143216-01A1	Intrinsic primary afferent neurons in regulation of intestinal nutrient sensing and obesity	04/01/2026-01/31/2030	\$580,252
R01CA275864-01A1	Gut microbiota-related mechanisms that impact colorectal cancer risk after bariatric surgery	09/07/2023-08/31/2028	Listed under Contact PI
R01DK145937-01A1	Assessment of metabolic flux dysregulation in patients with MASLD pre- and post-bariatric surgery	Pending	Pending

Summary of Digestive Disease Research

Our research program aims to delineate gastrointestinal molecular, cellular, and neural pathways governing metabolic disease progression and oncogenic risk. We utilize high-throughput CRISPR genetic screens and enteroid-neuronal co-cultures to dissect aberrant transcriptional regulation of collagen synthesis and neural mechanisms controlling nutrient absorption. Complementary rodent models incorporating targeted *in vivo* protein degradation, implantable microelectrode arrays, and engineered cell lineages determine how chronic sensory neuron hyperactivity and anatomical alterations drive obesity and adenoma formation. Finally, we translate these findings into human populations using multi-omic biopsy biorepositories and prospective surgical cohorts to examine long-term interactions between microbial remodeling, bile acid profiles, and systemic inflammation in high-risk patients.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient
Young Investigator Award
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

I am currently collaborating with VDDRC members Drs. Yu, Peek, Spann, Washington, Wilson, Arrojo e Drigo, Goettel, Choksi, Lau, Williams, Samuels, and Brown. A representative VDDRC collaborative publication is: Wang Z, Wang L, Zhang X, Lowery BD, Shaffer LL, Chen Y, Wells QS, **Flynn CR**, Williams B, Spann M, Srivastava G, Samuels JM, Yu D. Body composition changes after bariatric surgery or treatment with GLP-1 receptor agonists. *JAMA Netw Open*. 2026;9(1):e2553323. PMCID: PMC12789952.

Future VDDRC Core Use

Our core usage will increase in the future, specifically in the use of the Translational Analysis, MS/Omics, and Flow Cytometry Cores due to several ongoing studies examining bile acid flux in the mouse and the implementation of new high-dimensional spectral capabilities, respectively.

Member: Curtis Gabriel, MD, PhD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

I am a new member of the VDDRC and currently an Assistant Professor of Medicine in the Division of Gastroenterology, Hepatology and Nutrition. During graduate school, I worked with Amy S. Major, investigating the pathogenesis of fatty liver disease in a mouse model of systemic lupus erythematosus. After medical school, I completed my internal medicine residency and gastroenterology fellowship in the PSTP program at Vanderbilt. My current research focuses on the mechanisms that give rise to steatotic liver disease in people with HIV. A representative publication is: Bailin SS, Ma S, Perry AS, Terry JG, Carr JJ, Nair S, Silver HJ, Shi M, Mashayekhi M, Kropski JA, Ferguson JF, Wanjalla CN, Das SR, Shah R, Koethe JR, **Gabriel CL**. The primacy of adipose tissue gene expression and plasma lipidome in cardiometabolic disease in persons with HIV. *J Infect Dis*. 2025;231(2):e407-e418. PMID: PMC11841643.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5K23DK135420-03	The gut-liver axis in HIV-related non-alcoholic fatty liver disease	09/01/2023-05/31/2027	\$169,813
VDDRC P&F Award	Fecal lipidomics in HIV-related MASLD	06/01/2026-05/31/2027	\$40,000

Summary of Digestive Disease Research

Liver disease is a leading cause of mortality in persons with HIV (PWH), and PWH suffer a disproportionate burden of metabolic dysfunction-associated steatotic liver disease (MASLD). While the underlying mechanisms are not well understood, intestinal dysbiosis and intestinal barrier dysfunction may contribute to the pathogenesis of MASLD in PWH. HIV infection has been shown to alter the intestinal microbiome, change the plasma metabolome, and impair intestinal barrier function; however, there are few data on the microbiome and metabolome among PWH with MASLD. My research has demonstrated that hepatic steatosis is associated with differences in the levels of the key phospholipid phosphatidylcholine in PWH with MASLD. My ongoing research is focused on elucidating the links between the intestinal microbiome and plasma lipidome in PWH with MASLD.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Retreat Speaker

VDDRC Collaborations

Although I am a new member of the VDDRC, I have already developed fruitful collaborations with other VDDRC members, including Drs. Bailin, Brown, Koethe, Mashayekhi, and Wanjalla. A representative VDDRC collaborative publication is: Wanjalla CN, **Gabriel CL**, Fuseini H, Bailin SS, Mashayekhi M, Simmons J, Warren CM, Glass DR, Oakes J, Gangula R, Wilfong E, Priest S, Temu T, Newell EW, Pakala S, Kalams SA, Gianella S, Smith D, Harrison DG, Mallal SA, Koethe JR. CD4+ T cells expressing CX3CR1, GPR56, with variable CD57 are associated with cardiometabolic diseases in persons with HIV. *Front Immunol*. 2023;14:1099356. PMID: PMC9971959.

Future VDDRC Core Use

Future research projects will utilize the Cell Imaging and MS/Omics Cores to define the pathogenesis of MASLD in PWH at a molecular and cellular level.

Member: Jeremy Goettel, PhD
Rank: Associate Professor
Department: Medicine and Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My research interests are aimed at defining the mechanisms by which mucosal immune cells promote health and how immune dysfunction contributes to chronic inflammatory diseases, particularly those of the intestine. One representative publication is: Li J, Jacobse J, Pilat JM, Kaur H, Gu W, Kang SW, Rusznak M, Huang HI, Barrera J, Oloo PA, Roland JT, Hawkins CV, Pahnke AP, Khalil M, Washington MK, Wilson KT, Williams CS, Peebles RS Jr, Konnikova L, Choksi YA, Hammer GE, Lau KS, **Goettel JA**. Interleukin-10 production by innate lymphoid cells restricts intestinal inflammation in mice. *Mucosal Immunol.* 2025;18(3):643-655. PMCID: PMC12167137.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01DK149122-01	Bile acid-nuclear receptor crosstalk in Tregs: A new axis in IBD pathogenesis and therapy	Pending	Pending
5R01AI176521-04	Characterizing antibody responses to HIV-1 vaccination in next-generation immune humanized mice	03/21/2023-02/28/2027	\$244,719

Summary of Digestive Disease Research

Our group focuses on understanding mechanisms of immune homeostasis at mucosal surfaces. We have developed and utilized several models to target relevant IBD-related genes in a cell-specific manner to better understand their role in regulating intestinal immune tolerance. These insights are funneled into our translational immune humanized mouse platform that can be leveraged to study human immunobiology in a tractable *in vivo* setting.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

I have ongoing collaborations with other members of the VDDRC, including Drs. Cassat, Choksi, Coburn, Coffey, Flynn, Hiremath, Lau, Markham, Markle, Peek, Piazuelo, Washington, Williams, Wilson, and Zhu. One collaborative VDDRC publication is: Jacobse J, Brown RE, Li J, Pilat JM, Pham L, Short SP, Peek CT, Rolong A, Washington MK, Martinez-Barricarte R, Byndloss MX, Shelton C, Markle JG, Latour YL, Allaman MM, Cassat JE, Wilson KT, Choksi YA, Williams CS, Lau KS, Flynn CR, Casanova JL, Rings EHHM, Samsom JN, **Goettel JA**. Interleukin-23 receptor signaling impairs the stability and function of colonic regulatory T cells. *Cell Rep.* 2023;42(2):112128. PMCID: PMC10432575.

Future VDDRC Core Use

We plan to continue utilizing the Cell Imaging, Flow Cytometry, and Translational Analysis Cores for our work in humanized mouse models of IBD.

PI Name: James R. Goldenring, MD, PhD
Rank: Vice Chair of Surgical Research, Professor, Paul W. Sanger Professor
Department: Surgery and Cell and Developmental Biology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am Co-Leader for the Homeostasis, Regeneration, and Pathophysiology (HRP) Research Interest Group of the VDDRC and Director of the Digital Histomorphology Service within the Translational Analysis Core of the VDDRC. My research group studies 1) the cellular basis of the development of metaplasia in the stomach and 2) the role of vesicle trafficking in the establishment of enterocyte polarity and the characterization of defects in congenital neonatal diarrheal disease. A representative VDDRC-supported publication is: **Goldenring JR**, Jang B, Gotoda T, Yamaguchi N, Choi E, Nomura S; Gastric Precancer Working Group. Safety and efficacy of MEK inhibitor treatment for gastric precancerous lesions. *Gastroenterology*. 2025 Sep;169(4):722-725. PMID: PMC12981957.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK048370-30	Small GTP binding proteins in gastrointestinal mucosa	08/01/1997-07/31/2027	\$418,115
5RC2DK118640-07	Congenital diarrhea and enteropathy (PediCODE) consortium and biorepository	09/15/2019-08/31/2029	\$316,621
5R01DK101332-12	Induction and evolution of metaplasia in the stomach	05/01/2014-05/31/2027	\$309,430
Veterans Administration 2I01BX000930-14	Oxyntic atrophy and novel gastric lineages	04/01/2011-09/30/2029	\$300,000
Congressionally Directed Medical Research Programs HT94252410383	Therapeutic intervention to reverse gastric precancer	06/01/2024-05/31/2028	\$173,067
4R01CA272687-04	Cell plasticity in the origin of gastric carcinogenesis	09/01/2025-08/31/2027	Listed under Contact PI

Summary of Digestive Disease Research

My laboratory studies a number of subjects that apply broadly to epithelial biology and we have had a long-standing interest in gastritis, oxyntic atrophy, and premalignant lesions. We have identified a previously unrecognized metaplastic lineage associated with loss of gastric parietal cells. This lineage, designated Spasmolytic polypeptide expressing metaplasia (SPEM), is associated with gastric cancer in both humans and in mouse models of *Helicobacter* infection. We are also focusing on identification of genetic congenital causes of undiagnosed neonatal diarrheas and approaches to treatment of congenital diarrheal diseases, including Microvillus Inclusion Disease.

VDDRC-Related Training and Activities

Co-Leader, Homeostasis, Regeneration, and Pathophysiology (HRP) Research Interest Group
 Director, Digital Histomorphology Service
 Co-Director, collaborating Epithelial Biology Center (EBC)
 Pilot & Feasibility Award Recipient
 Pilot & Feasibility Project Reviewer

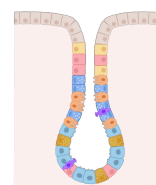
VDDRC Collaborations

We collaborate with numerous VDDRC members, including Drs. Choi, Coffey, Kaji, Lacy, Meenderink, Peek, Piazzuelo, Tyska, and Washington. An example of a paper resulting from these collaborations is: Bowman DM, Meenderink LM, Thomas KS, Manning EH, Tyska MJ, **Goldenring JR**. Microvillus inclusion disease-causing MYO5B point mutations exert differential effects on motor function. *J Biol Chem*. 2025 Apr;301(4):108328. PMID: PMC11964754.

Future VDDRC Core Use

We will heavily utilize the Cell Imaging Core for studies on intracellular trafficking in intestinal epithelial cells as well as for analysis of metaplastic lineages in the stomach. Additionally, we will use the Flow Cytometry, MS/Omics, and Translational Analysis Cores in this coming cycle.

Member: Xingyi Guo, PhD
Rank: Associate Professor
Department: Medicine and Biomedical Informatics
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My laboratory's broad research interest is centered in gastrointestinal disease etiology, prevention, and precision medicine through developing bioinformatics, statistical, and AI approaches and integrating multi-omics data (including single-cell-based omics data), with a major goal of identifying susceptibility variants and genes for human diseases. A representative VDDRC publication is: Holowatyj AN, Wen W, Gibbs T, Seagle HM, Keller SR, Edwards DRV, Washington MK, Eng C, Perea J, Zheng W, **Guo X**. Racial/ethnic and sex differences in somatic cancer gene mutations among patients with early-onset colorectal cancer. *Cancer Discov.* 2023; 13(3):570-579. PMCID: PMC10436779.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01CA297582-01A1	Leveraging omics and electronic health records data to study colorectal adenoma genetics and drug repurposing	09/10/2025-08/31/2029	\$749,332
5R01CA269589-04	Uncovering colorectal cancer etiology and biology by integrating proteomics with other omics data	04/11/2023-03/31/2028	\$430,884

Summary of Digestive Disease Research

Our digestive disease research program focuses on advancing the understanding of gastrointestinal disease etiology, prevention, and precision medicine through the development and application of integrative bioinformatics, statistical, and artificial intelligence approaches. We develop and apply computational tools and analytical pipelines for large-scale multi-omics data, including whole-genome sequencing (WGS), whole-exome sequencing (WES), RNA-seq, genotype and epigenetic profiling, metabolomics, single-cell and spatial omics, and electronic health records (EHRs). Leveraging high-performance computing platforms, including ACCRE, Terra and Amazon Web Services (AWS), we analyze population-scale genomic and clinical datasets to identify genetic susceptibility factors, somatic alterations, regulatory variants, and therapeutic targets associated with digestive diseases. Our research is particularly focused on inflammatory bowel disease (IBD), colorectal adenoma, and colorectal carcinogenesis. We integrate GWAS, TWAS, epigenomics, and single-cell/spatial omics data to characterize disease-associated genes, pathways, and cell type-specific regulatory mechanisms underlying disease initiation and progression. In parallel, we develop statistical and machine learning/deep learning models to investigate the interplay among germline susceptibility, somatic alterations, environmental exposures, and clinical outcomes. A major goal of our work is to facilitate precision prevention and intervention by identifying actionable therapeutic targets and candidate drugs for digestive diseases and gastrointestinal cancers.

VDDRC-Related Training and Activities

Retreat Speaker

VDDRC Collaborations

My lab collaborates with several VDDRC members, including Drs. Coffey, Lau, Shrubsole, Singh, Washington, and Zheng. A representative collaborative publication is: Chen Z, Song W, Li Q, Li C, Wen W, Huyghe JR, Law PJ, Fernandez-Rozadilla C, Timofeeva MN, Thomas M, Schmit SL, Martin V, Devall M, Dampier C, Moratalla-Navarro F, Cai Q, Wang J, Shi J, Kweon SS, Tanikawa C, Jia WH, Shu X, Long J, Gao J, Kim J, Shin A, Matsuo K, Jee SH, Jung KJ, Wang N, Kim DH, Ping J, Yang G, Shin MH, Ren Z, Oh JH, Oze I, Ahn YO, Gao YT, Pan ZZ, Kamatani Y, Van Kaer L, Wu L, Li B, Matsuda K, Shu XO, Hsu L, Dunlop MG, Gruber SB, Houlston R, Tomlinson I, Li L, Lau KS, Moreno V, Casey G, Peters U, Zheng W, **Guo X**. Mixed-model and transcriptome-wide association analyses identify transcription factors and genes associated with colorectal cancer susceptibility. *Nat Commun.* 2026;17(1):1377. PMCID: PMC12877115.

Future VDDRC Core Use

I will utilize the Translational Analysis Core and the Biostatistics Component for analysis of multi-omic data sets.

Member: Clint M. Hasenour, PhD
Rank: Assistant Research Professor
Department: Chemical and Biomolecular Engineering
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

The liver is the major organ where glucose biosynthesis is coupled to mitochondrial metabolism. Previous studies demonstrate that overnutrition accelerates whole-body gluconeogenesis (GNG) and citric acid cycle (CAC) activity *in vivo*. A limitation of prior research is that the unique contributions of the liver to whole-body GNG and CAC fluxes have been difficult to disentangle *in vivo*. The inability to discern hepatic from renal metabolic fluxes represents a significant knowledge gap, as obesity may not only cause an ectopic accumulation of lipid but also an “ectopic redistribution” of gluconeogenic function. A representative publication is: Bednarski TK, Rahim M, **Hasenour CM**, Banerjee DR, Trenary IA, Wasserman DH, Young JD. Pharmacological SERCA activation limits diet-induced steatohepatitis and restores liver metabolic function in mice. *J Lipid Res.* 2024 Jun;65(6):100558. PMID: PMC11179628.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5K01DK135924-04	<i>In vivo</i> hepato-renal metabolic flux dysregulation in obesity	04/01/2023-02/28/2027	\$111,658
1R03DK147764-01	Factors controlling metabolic plasticity in the kidney during obesity and injury	05/14/2026-03/31/2028	\$75,000

Summary of Digestive Disease Research

Our research group investigates the etiology and treatment of metabolic disease through the lens of multi-organ fluxomics while focusing on an understudied aspect of gluco(dys)regulation. It is significant because it will identify organ-specific metabolic nodes that may be better targeted to improve glycemic control and reduce damage in the liver.

VDDRC-Related Training and Activities

Academy of Investigators Member

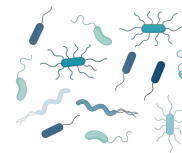
VDDRC Collaborations

I am a new member of the VDDRC, and our group has begun to establish collaborations with VDDRC members, including Drs. Bailin, Gabriel, and Winn.

Future VDDRC Core Use

I will utilize the Cell Imaging, MS/Omics Core, and the Biostatistical Component for data analysis.

Member: Girish Hiremath, MD, MPH
Rank: Associate Professor
Department: Pediatrics
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I am a recognized leader in eosinophilic gastrointestinal diseases (EGIDs), bringing nearly fifteen years of clinical and research experience to advance patient care and scientific discovery. I direct the multidisciplinary Pediatric EGID program, a leading referral center for EGID patients across the Southern region, and my clinic is dedicated to delivering evidence-based, compassionate care while addressing unique challenges faced by the children and families living with these complex conditions. My interdisciplinary translational research integrates pathology, allergy and immunology, biomedical engineering, computer science, industry partners, and patient care. As an active member of the NIH-funded Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR), I collaborate with global leaders in the field. A representative publication is: **Hiremath G**, Codreanu SG, Sherrod SD, Tyree R, Correa H, Choksi Y, McLean JA, Locke A. Salivary metabolomic signatures in pediatric eosinophilic esophagitis. *Allergy*. 2025;80(1):354-358. PMCID: PMC11724226.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01DK144385-01A1	Towards multi-modal biomarker and personalized medicine: Integrating esophageal biochemical, structural, and molecular alterations in pediatric eosinophilic esophagitis	06/15/2026-02/28/2031	\$493,692
5R01DK132338-04	Dual-wavelength endoscopic Raman probe for eosinophilic esophagitis	07/01/2022-05/31/2027	Listed under Contact PI

Summary of Digestive Disease Research

Our understanding of the pathogenesis of EoE is incomplete, and this has contributed to burdensome approaches to treating EoE patients. There is a critical unmet need to understand all factors related to the development of EoE, including determining the biochemical changes in the esophagus that lead to the transformation of an unaffected esophagus to an inflamed esophagus in EoE. Thus, my research proposes to fill this important knowledge gap by building on his published work through: 1) Validating the esophageal biochemical changes in EoE using Raman spectroscopy (a uniquely suited, highly sensitive, laser-based technique) and machine learning, 2) Determining the correlation between the Raman peaks and the disease activity, and the operating characteristics of the key Raman peaks in distinguishing EoE activity states, and 3) Determining if a combination of the baseline Raman, histologic, endoscopic, and clinical features can predict response to EoE therapy. By defining the key esophageal biochemical alterations, this work will offer novel insights into the pathogenesis of EoE, and by identifying the baseline predictors of the treatment response, it will lay a framework for personalized care of EoE patients.

VDDRC-Related Training and Activities

Retreat Speaker

VDDRC Collaborations

Although I am a new member of the VDDRC, I have already established collaborations with several VDDRC members, including Drs. Mahadevan-Jansen, Williams, Coburn, Washington, Goettel, and Choksi. A representative collaborative publication is: **Hiremath G**, Choksi Y, Correa H, Jacobse J, Das SR, Ma S, Goettel JA, Rajagopala SV. Children with eosinophilic esophagitis non-responsive to combination therapy have distinct esophageal transcriptomic and microbiome profile. *Allergy*. 2024;79(10):2798-2811. PMCID: PMC11528550.

Future VDDRC Core Use

Future research projects will utilize the Cell Imaging and Translational Analysis Cores.

Member: Tae Hyun Hwang, PhD
Rank: Professor, Director of Molecular AI Initiative, Director of AI Research
Department: Surgery
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

Our main research objective is to improve patient outcomes by integrating artificial intelligence (AI), machine learning, computational methods, and experimental approaches. Our interdisciplinary research spans spatial biology, single-cell analysis, digital pathology, biomarker discovery, spatial microbiome analysis, and therapeutic development, including immunotherapy and cellular therapies. A representative VDDRC publication is: Cheong JH, Wang SC, Park S, Porembka MR, Christie AL, Kim H, Kim HS, Zhu H, Hyung WJ, Noh SH, Hu B, Hong C, Karalis JD, Kim IH, Lee SH, **Hwang TH**. Development and validation of a prognostic and predictive 32-gene signature for gastric cancer. *Nat Commun*. 2022;13(1):774. PMCID: PMC8828873.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01CA276690-02	Using artificial intelligence to discover spatial, genomic, and pathologic biomarkers to guide and augment immune checkpoint inhibitor therapy for gastric cancer	04/01/2025-03/31/2029	\$141,541
4U01CA294518-02	Center for gastric pre-cancer atlas of multidimensional evolution in 3D (GAME3D)	01/01/2024-08/31/2029	\$95,562

Summary of Digestive Disease Research

We develop AI-driven 3D and 4D tumor models to investigate the complex interactions between cellular, molecular, and microbiome components. This approach enables the identification of novel biomarkers, therapeutic targets, and personalized treatment strategies. By integrating advanced technologies, our group advances personalized medicine, with a focus on the tumor immune microenvironment (TIME), ultimately benefiting patients.

VDDRC-Related Training and Activities

Co-Director, VDDRC Digital Histomorphology Service
Retreat Poster Judge

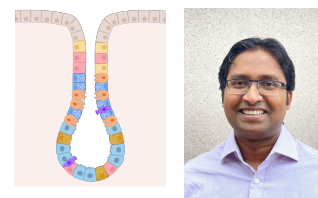
VDDRC Collaborations

As a new member of the VDDRC, I plan to continue collaborations with VDDRC member Dr. Goldenring, as well as initiate new collaborations with Drs. Coffey and Peek.

Future VDDRC Core Use

As a new member of the VDDRC, I plan to utilize the Translational Analysis Core in the upcoming funding cycle.

Member: Mirazul Islam, PhD
Rank: Postdoctoral Fellow
Department: Medicine and Cell and Developmental Biology
VDDRC Status: Associate Member
Research Group: HRP



Rationale for VDDRC Membership

I am a postdoctoral fellow in the laboratory of Dr. Robert Coffey. Our group has contributed to the understanding of development and disease along the entire GI tract. One VDDRC publication is: **Islam M**, Yang Y, Simmons AJ, Shah VM, Musale KP, Xu Y, Tasneem N, Chen Z, Trinh LT, Molina P, Ramirez-Solano MA, Sadien ID, Dou J, Rolong A, Chen K, Magnuson MA, Rathmell JC, Macara IG, Winton DJ, Liu Q, Zafar H, Kalhor R, Church GM, Shrubsole MJ, Coffey RJ, Lau KS. Temporal recording of mammalian development and precancer. *Nature*. 2024;634(8036):1187-1195. PMID: PMC11525190.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
VDDRC P&F Award	Role of BTG2 in maintaining quiescence of human LGR5 ⁺ colonic stem cells	07/30/2026-06/30/2027	\$40,000
GI SPORE Pilot Project Award	Role of BTG2 and LGR5 ⁺ stem cells in colorectal cancer	01/14/2026-07/31/2027	\$40,000
GI SPORE Career Enhancement Award	Development of a TOB2 reporter platform for investigating dormant cell states in colorectal cancer	07/01/2026-06/30/2027	\$75,000

Summary of Digestive Disease Research

Our group is focused on the study of the role of the EGF receptor (EGFR) and its ligands in GI diseases. We have a particular interest in investigating the trafficking of EGFR ligands in polarizing colonic epithelial cells as well as stem cells within the context of the development of colorectal diseases.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I have collaborated extensively with multiple members within the VDDRC. I have worked closely with Drs. Coffey, Lau, Magnuson, Markham, and Shrubsole. A representative collaborative publication is: **Islam M**, Bechard ME, Yang Y, Simmons AJ, Xu Y, Higginbotham JN, Zhao P, Cao Z, Tasneem N, Glass SE, Markham NO, Revetta F, Ramirez-Solano MA, Liu Q, Franklin JL, Lau KS, Coffey RJ. Unbiased recording of clonal potency reveals species-specific regulation of mammalian intestine. *bioRxiv*. 2025:2025.06.10.658707. PMID: PMC12259079.

Future VDDRC Core Use

We will continue to rely heavily on the Cell Imaging, Flow Cytometry, MS/Omics, and the Translational Analysis Cores for our studies in novel *ex vivo* human models (organoids) and mouse models of disease.

Member: Tina Iverson, PhD
Rank: Professor and Louise B. McGavock Chair
Department: Pharmacology and Biochemistry
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My research centers on the global question of how information is coded and transferred in biological systems by integrating basic chemical principles with biochemical, structural and cellular approaches. We investigate both bacterial and mammalian systems, which allows us to transcend biases associated with individual fields and our studies have been funded by a VDDRC Pilot Award. One representative VDDRC publication is: Sharma P, Maklashina E, Voehler M, Balintova S, Dvorakova S, Kraus M, Hadrava Vanova K, Nahacka Z, Zobalova R, Boukalova S, Cunatova K, Mracek T, Ghayee HK, Pacak K, Rohlena J, Neuzil J, Cecchini G, **Iverson TM**. Disordered-to-ordered transitions in assembly factors allow the complex II catalytic subunit to switch binding partners. *Nat Commun*. 2024;15(1):473. PMCID: PMC10784507.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
2R01GM120569-05	Molecular basis for arrestin-mediated signaling	08/01/2016-03/31/2029	\$215,000

Summary of Digestive Disease Research

My background is in the study of the stabilization, crystallization, and structure determination of proteins, and I have utilized this to study the mechanisms of cellular signaling and transmembrane transport during host-pathogen interactions. I bring a “molecules up” approach to the field by using crystal structures as a basis for developing testable hypotheses that tease apart biological mechanisms of mucosal immunity, which may lead to the identification of new therapeutic agents. To perform the structural aspects of these experiments, my laboratory houses a Mosquito high-throughput nano-liter drop setting robot, a Hamilton liquid handler, an Xantus lipid cubic phase drop-setting robot, and a Formulatrix Rock Imager. These tools are ideal for testing large numbers of crystallization conditions for proteins and have resulted in a dramatic improvement in our success rate in protein crystallization. We have now focused our R01-funded studies on the role of host-microbial interactions within the context of mucosal inflammation and cancer in the GI tract.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I have developed collaborations with Drs. Cover, Lacy, and Tyska in the field of gastrointestinal function and pathogenesis.

Future VDDRC Core Use

We will continue to use the Cell Imaging and MS/Omics Cores for our studies on membrane structure-function.

Member: Manhal Izzy, MD
Rank: Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

I am the Director of the Transplant Hepatology Fellowship Program and Director of Hepatology Research within the Division of Gastroenterology, Hepatology, and Nutrition. My clinical and research focus centers on complications of advanced liver disease, particularly portal hypertension and its systemic manifestations, with a specific emphasis on cirrhotic cardiomyopathy (CCM), an underrecognized yet clinically significant complication of cirrhosis that adversely impacts clinical outcomes. A representative publication is: Ying X, Oje AO, De Witte AJ, Slaughter JC, Spann AL, Jesudian AB, Rosenblatt R, Ng C, Sholle E, Reidy D, Pan Y, Annis J, Gupta DK, Brittain EL, Fortune BE, **Izzy M**. Severity of liver disease is associated with cirrhotic cardiomyopathy: A multicenter study. *Liver Transpl.* 2026;32(4):539-548. PMID: 41378871.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01HL181174-01	Prospective investigation of cirrhotic cardiomyopathy in humans	09/16/2025-06/30/2030	\$542,144

Summary of Digestive Disease Research

The overarching goal of my research is to elucidate the clinical significance, mechanistic basis, and prognostic implications of cirrhotic cardiomyopathy (CCM) in patients with advanced liver disease. My group is currently leading the first prospective U.S.-based study of CCM in patients with decompensated cirrhosis across two high-volume hepatology and liver transplant centers. Through this work, we aim to:

- Determine whether incorporation of CCM into MELD-based models enhances prediction of mortality
- Identify the clinical and biochemical determinants associated with CCM
- Define the mechanistic drivers of CCM, with particular emphasis on alterations in bile acid composition

By integrating comprehensive clinical phenotyping with biomarker and mechanistic analyses, our research seeks to advance understanding of cardiohepatic interactions and uncover novel therapeutic targets for patients with end-stage liver disease.

VDDRC-Related Training and Activities

Retreat Poster Judge

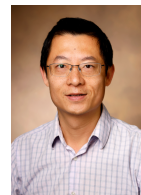
VDDRC Collaborations

We maintain close collaborations with VDDRC members, including Drs. Flynn, Washington, Spann, and Washington, on investigations focused on complications of advanced liver disease and their impact on clinical outcomes. A representative collaborative publication is: Brown S, Richardson B, Bouquet E, Reid E, Mercer E, Goncalves M, Spann A, Annis J, Brittain E, Dreher A, Alexopoulos S, Slaughter JC, Silver HJ, **Izzy M**. Cirrhosis-related sarcopenia may not resolve after liver transplantation. *JHEP Rep.* 2023;5(11):100881. PMCID: PMC10522892.

Future VDDRC Core Use

We will continue to utilize the Biostatistics Component for advanced clinical data analysis. We are also expanding into the MS/Omics Core to support biomarker characterization, including bile acid profiling relevant to mechanistic studies in cirrhotic cardiomyopathy.

Member: Xiaoyu Jiang, PhD
Rank: Research Assistant Professor
Department: Radiology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I completed my postdoctoral training at Vanderbilt University Institute of Imaging Science (VUIIS), which focused on the development, validation, and evaluation of advanced MRI techniques, including temporal diffusion spectroscopy imaging and quantitative magnetic transfer imaging, in preclinical and translational imaging. A representative publication is: **Jiang X**, Jin C, Kang H, Piantek G, Zu Z, Gore JC, Xu J. Repeatability of in vivo MR cytometry for measuring cell size and density in healthy human livers. *Magn Reson Imaging*. 2026;126:110563. PMCID: PMC12784474.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK135950-03	<i>In vivo</i> MR characterization of pathological changes in liver microstructures	02/01/2024-01/31/2028	\$221,461

Summary of Digestive Disease Research

Noninvasive tests and imaging techniques for the diagnosis and management of liver diseases have gained significant interest due to the limitations of liver biopsy, particularly for identifying nonalcoholic steatohepatitis (NASH), the most severe form of Nonalcoholic fatty liver disease (NAFLD). The ability to differentiate NASH from simple steatosis is critically important for the clinical management of NAFLD patients. Currently, NASH is exclusively diagnosed invasively through liver biopsy to assess steatosis, inflammation, ballooning, and fibrosis. While MRI-based PDFF and elastography have been shown to reliably quantify steatosis and fibrosis, respectively, the lack of a non-invasive tool to assess inflammation in NASH remains a significant gap in the daily clinical care of this common disease. Our group has developed a novel concept that cell size and cell density could serve as indicators of hepatic inflammation and has developed a multi-compartment diffusion MRI-based method called *in vivo* quantitative Temporal Diffusion Spectroscopy (qTDS), which quantifies cell size and cell density by fitting multi-b value- multi-diffusion time fat-suppressed diffusion-weighted MRI signals to a three-compartment (blood, intra, and extracellular water) signal model. Recently, qTDS has shown promising results in *in vivo* NASH patients and *ex vivo* human liver specimens with different pathologies, including normal liver tissues, cirrhosis, steatosis, and cirrhotic regenerative nodules (CRN). My group is currently establishing the relationship between qTDS-derived parameters and histology values in a mouse model of NASH, optimizing a clinical qTDS protocol for reliable *in vivo* quantification of cell size and cell density in human livers within a short period (less than 12 minutes), and demonstrating the efficacy of qTDS in characterizing hepatic inflammation, a key diagnostic component for differentiating NASH from simple steatosis. These findings will provide a critical foundation for a large-scale clinical trial to develop a noninvasive diagnostic metric for NASH, offer a standard qTDS imaging protocol that can be implemented on clinical 3T MR scanners, provide a qTDS data processing toolbox that can be downloaded online, and collectively will advance the use of noninvasive microstructure imaging in the diagnosis and management of liver diseases.

VDDRC-Related Training and Activities

Pilot & Feasibility Project Reviewer

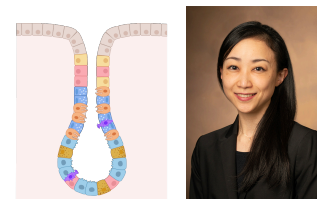
VDDRC Collaborations

We currently collaborate with VDDRC members Drs. Izzy and Washington. A representative VDDRC collaborative publication is: **Jiang X**, Washington MK, Izzy MJ, Lu M, Yan X, Zu Z, Gore JC, Xu J. Distinguishing hepatocellular carcinoma from cirrhotic regenerative nodules using MR cytometry. *Cancers (Basel)*. 2025;17(7):1204. PMCID: PMC11987932.

Future VDDRC Core Use

We will utilize the Cell Imaging Core for analysis of our *ex vivo* data and the Biostatistical Component to analyze our clinical data.

Member: Izumi Kaji, PhD
Rank: Assistant Professor
Department: Surgery
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My research focuses on defining how luminal chemosensing is involved in epithelial cell differentiation and mature cell functions under health and disease conditions. My recent efforts seek to delineate the cell signaling pathways underpinning nutrient transporter trafficking regulation with an ultimate goal of improving malnutrition and congenital diarrheal disorders, such as microvillus inclusion disease. A recent VDDRC publication is: Burman A, Brown ME, Yang Y, Momoh M, Adeniran F, Ramos C, Lau KS, Samuelson LC, Shub MD, Roland JT, **Kaji I**. Myosin VB is critical for progenitor cell identity and function in the intestine. *Stem Cell Reports*. 2026; 21(4):102862. PMCID: PMC13083783.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK128190-05	Impacting the pathophysiology of malabsorption induced by Myosin Vb inactivating mutations	09/25/2021-07/31/2026	\$220,000
5RC2DK118640-07	Pediatric congenital diarrhea consortium and bioRepository	09/15/2019-08/31/2029	Listed under Contact PI

Summary of Digestive Disease Research

We have recently developed novel mouse models to investigate the stem cell-specific impact of MYO5B loss. Our *ex vivo* electrophysiological methods have been extended with a pH-stat module for evaluating activity of epithelial nutrient transporters in murine tissues from a variety of diseases, including *C. difficile* infection. This method is able to quantify gastric acid secretion, intestinal sodium absorption, and colonic bicarbonate secretion in various tissues and monolayer organoids. In addition, I am identifying potential therapeutics for congenital diarrhea in mice and patient-derived organoids with MYO5B mutations, which target epithelial progenitor cell signals to upregulate nutrient absorption.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I have ongoing collaborations with VDDRC members Drs. Acra, Algood, Choi, Coffey, Goldenring, Lacy, Lau, Tyska, and Washington. One publication resulting from these VDDRC collaborations is: Peritore-Galve FC, **Kaji I**, Smith A, Walker LM, Shupe JA, Washington MK, Algood HMS, Dudeja PK, Goldenring JR, Lacy DB. Increased intestinal permeability and downregulation of absorptive ion transporters Nhe3, Dra, and Sglt1 contribute to diarrhea during *Clostridioides difficile* infection. *Gut Microbes*. 2023 Jan-Dec;15(1):2225841. PMCID: PMC10291935.

Future VDDRC Core Use

We will utilize the Translational Analysis Core for evaluation of our mouse models and the Cell Imaging Core to identify subcellular localization of proteins involved in microvillus inclusion disease, as well as the Biostatistical Component for data analysis.

Member: John Koethe, MD
Rank: Associate Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My research focuses on HIV-related metabolic diseases, immunometabolism, and the physiology of ectopic lipid accumulation in people with HIV, and I have led several large studies to characterize the health consequences of obesity among people with HIV and how HIV-related changes in the subcutaneous adipose tissue immune environment contribute to fat deposition in muscle, the viscera, liver and other organs. An example of a publication supported by the VDDRC is: Zhao OS, Silver HJ, Fan R, Ye F, Liu Q, Nair S, Terry JG, Carr JJ, Wanjalla C, Mashayekhi M, Bailin S, Gabriel C, **Koethe JR**. Subcutaneous adipose tissue gene transcripts associated with progressive myosteatosis in persons with HIV. *AIDS*. 2025;39(12):1739-1748. PMCID: PMC12279079.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK131529-05	Pathophysiology of metabolically detrimental changes in adipose distribution, adipocyte function, and adipose immune environment on antiretroviral therapy	02/10/2022-01/31/2027	\$494,826
5R01DK141455-03	Defining cellular and molecular processes underlying adipose tissue dysfunction on INSTI-based antiretroviral therapy	09/10/2024-06/30/2029	\$29,382
Veterans Administration 2101CX001930-06A1	A randomized trial to optimize skeletal muscle while reducing adiposity in veterans with HIV	01/01/2020-03/31/2029	\$400,000
Merck Sharp & Dohme Corp.	Effect of suppressing CMV replication on adipose tissue inflammation and metabolic outcomes in persons with HIV: A substudy to AIDS clinical trials group A5383 ELICIT	08/23/2024-08/22/2029	\$113,035

Summary of Digestive Disease Research

I have led several studies to understand how excess adiposity and HIV interact to affect metabolic parameters. In addition, I studied the role of serum phosphate as a contributor to early mortality among low-BMI persons starting antiretroviral therapy in sub-Saharan Africa. Our collaborative research group of US, UK, Zambian, and Tanzanian investigators hypothesized that malnourished HIV⁺ adults initiating treatment undergo a rapid increase in metabolic activity, which can lead to a variant of the 'refeeding syndrome' characterized by a depletion of bioavailable phosphate and other cellular energy metabolism intermediates.

VDDRC-Related Training and Activities

Retreat Speaker

VDDRC Collaborations

I have collaborated with Drs. Bailin, Brittain, Brown, Collins, Gabriel, Izzy, Mashayekhi, Niswender, Wanjalla, and Zaganjor. One resulting VDDRC collaborative publication is: Bailin SS, Gabriel CL, Gangula RD, Hannah L, Nair S, Carr JJ, Terry JG, Silver HJ, Simmons JD, Mashayekhi M, Kalams SA, Mallal S, Kropski JA, Wanjalla CN, **Koethe JR**. Single-cell analysis of subcutaneous fat reveals profibrotic cells that correlate with visceral adiposity in HIV. *J Clin Endocrinol Metab*. 2024;110(1):238-253. PMCID: PMC11651702.

Future VDDRC Core Use

Our laboratory will continue to use the Flow Cytometry Core for discovery-based single-cell studies of human adipose tissue, as well as future use of the MS/Omics Core.

Member: Shannon Kordus, PhD
Rank: Research Instructor
Department: Pathology, Microbiology and Immunology, and Biochemistry
VDDRC Status: Associate Member
Research Group: GII



Rationale for VDDRC Membership

I am a Research Instructor in the laboratory of Borden Lacy. Our laboratory focuses on understanding the molecular mechanisms by which bacterial protein toxins contribute to human disease. Specific interests include defining the virulence properties of the *C. difficile* toxins and the development of novel strategies for *C. difficile* infection prevention and therapy. A recent VDDRC-supported publication is: **Kordus SL**, Kroh HK, Rodríguez RC, Shrem RA, Peritore-Galve FC, Shupe JA, Wadzinski BE, Lacy DB, Spiller BW. Nanobodies against *C. difficile* TcdA and TcdB reveal unexpected neutralizing epitopes and provide a toolkit for toxin quantitation *in vivo*. *PLoS Pathog.* 2023;19(10):e1011496. PMID: PMC10621975.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
VDDRC P&F Award	Determining host signals that trigger toxin release in <i>Clostridioides difficile</i>	07/30/2026-06/30/2027	\$40,000

Summary of Digestive Disease Research

The primary focus of our laboratory has been to understand the structural biology of the three toxins produced by *C. difficile* and the roles these toxins play in pathogenesis. Most of this work has been focused on TcdA and TcdB, two homologous glucosyltransferase toxins that are considered the major virulence factors in *C. difficile* infection. We have more recently studied the *C. difficile* transferase (CDT) toxin, a third toxin that can impact disease severity.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Young Investigator Award

VDDRC Collaborations

We collaborate with Drs. Lacy, Washington, and Markham on projects related to human tissue, cell, and animal models of *C. difficile* toxin function. A recently published collaborative paper is: Nabukhotna K, **Kordus SL**, Shupe JA, Cano Rodríguez R, Smith A, Bohannon JK, Washington MK, Lacy DB. Purified CDT toxins and a clean deletion within the CDT locus provide novel insights into the contribution of binary toxin in cellular inflammation and *Clostridioides difficile* infection. *PLoS Pathog.* 2024;20(9):e1012568. PMID: PMC11444381.

Future VDDRC Core Use

We will continue to use the MS/Proteomics, Cell Imaging, and Flow Cytometry Cores to support our independent and collaborative projects on elucidating and defining the structural basis for gastrointestinal microbial toxins, as well as the Translational Analysis Core to evaluate our models of infection.

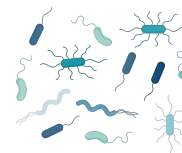
Member: D. Borden Lacy, PhD

Rank: Professor

Department: Pathology, Microbiology and Immunology, and Biochemistry

VDDRC Status: Full Member

Research Group: GII



Rationale for VDDRC Membership

I am an Associate Director of the VDDRC, and my laboratory focuses on understanding the molecular mechanisms by which bacterial protein toxins contribute to human disease. Particular interests include the virulence properties of the *C. difficile* toxins and the development of novel strategies for *C. difficile* infection prevention and therapy. Our most recent VDDRC-supported publication is: Thomas AK, Peritore-Galve FC, Ehni AG, Lança BBC, Coggin J, Brady EJ, Yoder SM, Shrem R, Rodríguez RC, Kroh HK, Gibson-Corley KN, Washington MK, Olivares-Villagómez D, Creech CB, Nicholson MR, Spiller BW, **Lacy DB**. Mucosal vaccination clears *Clostridioides difficile* colonization. *Nature*. 2026; 652,1289–1297. PMID: 41708852.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R37AI095755-16	Structural mechanisms of <i>Clostridioides difficile</i> pathogenesis	05/01/2021-04/30/2026	\$360,000

Summary of Digestive Disease Research

The primary focus in my laboratory has been to understand the three toxins produced by *C. difficile* and the roles these toxins play in pathogenesis, and this was initially funded as a VDDRC Pilot Project. Most of this work has been focused on TcdA and TcdB, two homologous glucosyltransferase toxins that are considered the major virulence factors in *C. difficile* infection. We have more recently studied the *C. difficile* transferase (CDT) toxin, a third toxin that can impact disease severity. In addition, we have maintained a 20-year collaboration with Dr. Tim Cover studying the mechanistic basis of virulence in *Helicobacter pylori*. Specifically, we study the vacuolating toxin VacA and the Cag Type Four Secretion System.

VDDRC-Related Training and Activities

Associate Director, VDDRC

Pilot & Feasibility Award Recipient

Retreat Speaker

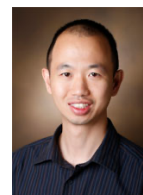
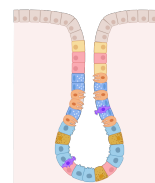
VDDRC Collaborations

We collaborate with Drs. Algood, Byndloss, Cover, Goldenring, Kaji, Markham, Nicholson, Olivares-Villagomez, Skaar, Tyska, and Washington on projects related to human tissue, cell, and animal models of *C. difficile* toxin function. We also collaborate with Dr. Cover on projects in *H. pylori* pathogenesis. A recently published collaborative paper is: Peritore-Galve FC, Kaji I, Smith A, Walker LM, Shupe JA, Washington MK, Algood HMS, Dudeja PK, Goldenring JR, **Lacy DB**. Increased intestinal permeability and downregulation of absorptive ion transporters Nhe3, Dra, and SglT1 contribute to diarrhea during *Clostridioides difficile* infection. *Gut Microbes*. 2023;15(1):2225841. PMCID: PMC10291935.

Future VDDRC Core Use

We will continue to use the MS/Omics, Cell Imaging, and Flow Cytometry Cores to support our independent and collaborative projects on elucidating and defining the structural basis for gastrointestinal microbial toxins, as well as the Translational Analysis Core to evaluate our mouse models of infection.

Member: Ken S. Lau, PhD
Rank: Professor, Director of Center for Computational Systems Biology
Department: Cell and Developmental Biology, Surgery
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

Our major research focus is to understand how communication between the gut microenvironment and epithelial cells orchestrates transitions between inflammatory states and precancerous states. I have previously been funded by a VDDRC Pilot Project. A VDDRC representative publication is: Islam M, Yang Y, Simmons AJ, Shah VM, Musale KP, Xu Y, Tasneem N, Chen Z, Trinh LT, Molina P, Ramirez-Solano MA, Sadien ID, Dou J, Rolong A, Chen K, Magnuson MA, Rathmell JC, Macara IG, Winton DJ, Liu Q, Zafar H, Kalhor R, Church GM, Shrubsole MJ, Coffey RJ, **Lau KS**. Temporal recording of mammalian development and precancer. *Nature*. 2024;634(8036):1187-1195. PMCID: PMC11525190.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
4U01CA294527-02	A multimodal 3D atlas of colorectal cancer across ages of onset	09/01/2024-08/31/2029	\$408,112

Summary of Digestive Disease Research

Currently, my laboratory is applying single-cell, spatial-omics, AI-based analyses to investigate cell-type-specific signaling and behaviors, for instance, in tuft cells and stem cells, in disease contexts such as inflammatory bowel disease and colorectal carcinogenesis. To accomplish this, we leverage mouse models, organoid cultures, and human patient samples.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

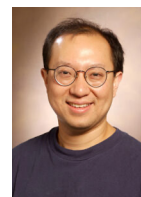
VDDRC Collaborations

I collaborate extensively with Dr. Coffey on stem cell studies, Dr. Goldenring on organoid co-cultures, Dr. Southard-Smith on single-nucleus RNA-seq, and Drs. Wilson and Coburn on cell-specific signaling in IBD. I have additional collaborations with Drs. Brown, Choi, Cover, DelGiorno, Goettel, Guo, Kaji, Markham, Peek, Shrubsole, Singh, Tan, Tyska, Wanjalla, Washington, Williams, Zheng, and Zhu. A publication resulting from a collaborative study is: Heiser CN, Simmons AJ, Revetta F, McKinley ET, Ramirez-Solano MA, Wang J, Kaur H, Shao J, Ayers GD, Wang Y, Glass SE, Tasneem N, Chen Z, Qin Y, Kim W, Rolong A, Chen B, Vega PN, Drewes JL, Markham NO, Saleh N, Nikolos F, Vandekar S, Jones AL, Washington MK, Roland JT, Chan KS, Schürpf T, Sears CL, Liu Q, Shrubsole MJ, Coffey RJ, **Lau KS**. Molecular cartography uncovers evolutionary and microenvironmental dynamics in sporadic colorectal tumors. *Cell*. 2023 Dec 7;186(25):5620-5637. PMCID: PMC10756562.

Future VDDRC Core Use

Our core usage will increase in the future, specifically in the use of the MS/Omics and Flow Cytometry Cores, due to larger sample influxes. We will also use the Translational Analysis Core for our histological analysis and longitudinal imaging of inflammation. The Cell Imaging Core will be continually used for super-resolution microscopy and multiphoton imaging of our samples.

Member: Ethan Lee, MD, PhD
Rank: Professor
Department: Cell and Developmental Biology, Pharmacology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My laboratory is interested in understanding the basic mechanism by which a Wnt signal is propagated and how this information can be used in regenerative medicine and in the treatment of GI diseases. A representative publication is: Kassel S, Yuan K, Bunnag N, Neitzel LR, Lu W, Schwarzkopf A, Maines B, Loberg MA, Xu G, Adams A, McCray AD, Cho A, Rockouski M, Orton G, Goldsmith L, Aronno MMA, Spencer ZT, Khan OM, Ye F, Williams C, Lebensohn AM, Rohatgi R, Wang X, Weiss VL, Hong CC, Kettenbach AN, Robbins DJ, Ahmed Y, **Lee E**. The TRIP12 E3 ligase induces SWI/SNF component BRG1- β -catenin interaction to promote Wnt signaling. *Nat Commun*. 2025;16(1):5248. PMCID: PMC12141612.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R35GM122516-09	Mechanism of Wnt signaling	04/01/2017-03/31/2027	\$355,000
5R01CA281002-04	A Cereblon signaling network in Wnt-driven cancers	03/10/2023-02/29/2028	\$578,221

Summary of Digestive Disease Research

My work focuses on studying the mechanism of action of the Wnt pathway and its misregulation in human disease. The Wnt pathway is a major driver of intestinal renewal in the adult gastrointestinal epithelium. Activating mutations of the Wnt pathway are found in over 90% of all colorectal cancer cases, and mutations in a component of the Wnt pathway, adenomatous polyposis coli, are responsible for the precancerous syndrome, Familial Adenomatous Polyposis. We have identified a gene that encodes a deubiquitinase that functions with R-Spondin to promote Wnt signaling in the intestine. We have also identified a new mechanism (degron) for regulating Notch1 signaling, another major regulator of intestinal homeostasis.

VDDRC-Related Training and Activities

Retreat Speaker

VDDRC Collaborations

We actively collaborate with Drs. Coffey and Peek to define the role of β -catenin signaling in *H. pylori* infections and colon cancer, respectively, as well as VDDRC members Drs. Choksi, Goettel, Goldenring, Lau, Washington, and Williams. A collaborative VDDRC publication is: Pilat JM, Brown RE, Chen Z, Berle NJ, Othon AP, Washington MK, Anant SA, Kurokawa S, Ng VH, Thompson JJ, Jacobse J, Goettel JA, **Lee E**, Choksi YA, Lau KS, Short SP, Williams CS. SELENOP modifies sporadic colorectal carcinogenesis and WNT signaling activity through LRP5/6 interactions. *J Clin Invest*. 2023;133(13):e165988. PMCID: PMC10313376.

Future VDDRC Core Use

We anticipate increased usage of the Cell Imaging, Flow Cytometry, and MS/Omics Cores to identify novel regulators of Wnt signaling in our *in vitro*, *ex vivo*, and *Xenopus* screens.

Member: Youngmin Lee, MD, PhD
Rank: Assistant Professor
Department: Surgery
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am a physician-scientist trained in hepatology with extensive experience in liver cell biology, particularly in mechanisms of liver injury and fibrosis. I was also a former VDDRC Pilot and Feasibility Award Recipient based on our work focused on hepatic stellate cells in disease. A representative publication is: Sugimoto A, Saito Y, Wang G, Sun Q, Yin C, Lee KH, Geng Y, Rajbhandari P, Hernandez C, Steffani M, Qie J, Savage T, Goyal DM, Ray KC, Neelakantan TV, Yin D, Melms J, Lehrich BM, Yasaka TM, Liu S, Oertel M, Lan T, Guillot A, Peiseler M, Filliol A, Kanzaki H, Fujiwara N, Ravi S, Izar B, Brosch M, Hampe J, Remotti H, Argemi J, Sun Z, Kendall TJ, Hoshida Y, Tacke F, Fallowfield JA, Blockley-Powell SK, Haeusler RA, Steinman JB, Pajvani UB, Monga SP, Bataller R, Masoodi M, Arpaia N, **Lee YA**, Stockwell BR, Augustin HG, Schwabe RF. Hepatic stellate cells control liver zonation, size and functions via R-spondin 3. *Nature*. 2025;640(8059):752-761. PMID: PMC12003176.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK133512-03	Hepatic stellate cells in liver homeostasis and regeneration	12/15/2023-11/30/2028	\$361,018

Summary of Digestive Disease Research

Hepatic stellate cells express a wide range of hepatic mitogens and growth factors; however, their contribution to liver regeneration has not been characterized. We established a novel murine mouse model (Gfap-Thymidine kinase) in which proliferating hepatic stellate cells, which would express the herpes simplex virus thymidine kinase under the mouse Gfap (glial fibrillary acidic protein) promoter could be depleted by treatment with Ganciclovir. We demonstrated that this mouse model was effective in depleting hepatic stellate cells and that they amplify liver injury, which formed the basis for our original VDDRC Pilot Project.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Young Investigator Award
Pilot & Feasibility Project Reviewer

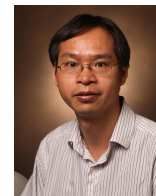
VDDRC Collaborations

I have developed productive collaborations with VDDRC members, Drs. Coffey, Dean, Flynn, Philip, and Washington. A collaborative VDDRC publication is: Chiusa M, **Lee YA**, Zhang MZ, Harris RC, Sherrill T, Lindner V, Brooks CR, Yu G, Fogo AB, Flynn CR, Zienkiewicz J, Hawiger J, Zent R, Pozzi A. Cytoplasmic retention of the DNA/RNA-binding protein FUS ameliorates organ fibrosis in mice. *J Clin Invest*. 2024;134(6):e175158. PMID: PMC10940094.

Future VDDRC Core Use

We will continue to utilize the Flow Cytometry Core to immunophenotype our mouse models, the Translational Analysis Core to analyze liver tissue histopathology, the Cell Imaging Core, and the Biostatistical Component for data analysis.

Member: Yingchang (Kevin) Lu, MD, PhD
Rank: Research Associate Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

I have extensive research experience in the genetics of complex traits, including autoimmune, metabolic traits, and disease. I have also developed extensive skills to design, implement, and analyze genetic data from genome-wide association and exome sequencing studies, as well as transcriptomic and metabolomic data. A representative VDDRC publication is: Park W, Kasi A, Spira AI, Paz-Ares Rodríguez L, Herzberg BO, Pelster MS, Tolcher AW, Kuboki Y, Kitano S, Shoji H, Wang JS, Berlin JD, Hollebecque A, LoRusso P, Fountzilas C, Cassier PA, Nishina T, Sakai D, Inagaki C, Morgensztern D, Ueno M, Jung M, Kim SW, Jänne PA, Italiano A, You B, Macarulla T, Fujii H, Shetty A, **Lu Y**, Cui D, Kadam S, Gill SC, Toyoshima J, Saito T, Goldman JW. Setidegrasib in advanced non-small-cell lung cancer and pancreatic cancer. *N Engl J Med*. 2026;394(14):1409-1420. PMID: 41879829. OR Chen Z, Guo X, Tao R, Huyghe JR, Law PJ, Fernandez-Rozadilla C, Ping J, Jia G, Long J, Li C, Shen Q, Xie Y, Timofeeva MN, Thomas M, Schmit SL, Díez-Obrero V, Devall M, Moratalla-Navarro F, Fernandez-Tajes J, Palles C, Sherwood K, Briggs SEW, Svinti V, Donnelly K, Farrington SM, Blackmur J, Vaughan-Shaw PG, Shu XO, **Lu Y**, Broderick P, Studd J, Harrison TA, Conti DV, Schumacher FR, Melas M, Rennert G, Obón-Santacana M, Martín-Sánchez V, Oh JH, Kim J, Jee SH, Jung KJ, Kweon SS, Shin MH, Shin A, Ahn YO, Kim DH, Oze I, Wen W, Matsuo K, Matsuda K, Tanikawa C, Ren Z, Gao YT, Jia WH, Hopper JL, Jenkins MA, Win AK, Pai RK, Figueiredo JC, Haile RW, Gallinger S, Woods MO, Newcomb PA, Duggan D, Cheadle JP, Kaplan R, Kerr R, Kerr D, Kirac I, Böhm J, Mecklin JP, Jousilahti P, Knekt P, Aaltonen LA, Rissanen H, Pukkala E, Eriksson JG, Cajuso T, Hänninen U, Kondelin J, Palin K, Tanskanen T, Renkonen-Sinisalo L, Männistö S, Albanes D, Weinstein SJ, Ruiz-Narvaez E, Palmer JR, Buchanan DD, Platz EA, Visvanathan K, Ulrich CM, Siegel E, Brezina S, Gsur A, Campbell PT, Chang-Claude J, Hoffmeister M, Brenner H, Slattery ML, Potter JD, Tsilidis KK, Schulze MB, Gunter MJ, Murphy N, Castells A, *et al*. Fine-mapping analysis including over 254,000 East Asian and European descendants identifies 136 putative colorectal cancer susceptibility genes. *Nat Commun*. 2024;15(1):3557. PMCID: PMC11053150.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK135938-04	Virtual systemic identification of drug targets of obesity candidate genes	04/01/2023-01/31/2027	\$557,687

Summary of Digestive Disease Research

I have a robust understanding of medicine, metabolism, and genetics. I have been involved in genetic studies of cardiometabolic traits and diseases for >10 years and have accumulated extensive experience in working with large-scale epidemiological, genotype, transcriptome, and metabolomic data. I have been actively involved in GWAS consortia for body adiposity (GIANT), CAD (CARDIoGRAM), blood lipids (GLGC), and genetic studies of rural populations. I have been leading national and international large-scale genetic studies of complex traits and diseases on adiposity, lipids, autoimmune diseases, and carcinogenesis.

VDDRC-Related Training and Activities

Retreat Poster Judge

VDDRC Collaborations

I am a new member of the VDDRC and have started establishing collaborations with several VDDRC members, including Drs. Below and Coffey. A VDDRC collaborative publication is: Liu H, Li D, Sun L, Qin H, Fan A, Meng L, Graves-Deal R, Glass SE, Franklin JL, Liu Q, Wang J, Yeatman TJ, Guo H, Zong H, Jin S, Chen Z, Deng T, Fang Y, Li C, Karijovich J, Patton JG, Wang X, Nie Y, Fan D, Coffey RJ, Zhao X, **Lu Y**. Interaction of lncRNA MIR100HG with hnRNPA2B1 facilitates m6A-dependent stabilization of TCF7L2 mRNA and colorectal cancer progression. *Mol Cancer*. 2022;21(1):74. PMCID: PMC8917698.

Future VDDRC Core Use

We will utilize the Biostatistical Component for our large-scale genomic, transcriptomic, and metabolomic data analysis.

Member: Mark Magnuson, MD
Rank: Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: HRP



Rationale for VDDRC Membership

My laboratory uses genetically altered mice, next-generation sequencing, and bioinformatics to study the regulation and function of genes that play critical roles in development and cell function. A representative publication is: Trinh LT, Osipovich AB, Liu B, Shrestha S, Cartailier JP, Wright CVE, **Magnuson MA**. Single-cell RNA sequencing of Sox17-expressing lineages reveals distinct gene regulatory networks and dynamic developmental trajectories. *Stem Cells*. 2023;41(6):643-657. PMID: PMC10465087.

Summary of Digestive Disease Research

The transcription factor SOX17 contributes to hepatopancreatic-biliary system formation and vascular-hematopoietic emergence. To better understand Sox17 function in the developing endoderm and endothelium, we developed a dual-color temporal lineage-tracing strategy in mice combined with single-cell RNA sequencing to analyze 6934 cells from Sox17-expressing lineages at embryonic days 9.0-9.5. Our analyses showed 19 distinct cellular clusters combined from all 3 germ layers. Differential gene expression, trajectory, and RNA-velocity analyses of endothelial cells revealed a heterogeneous population of uncommitted and specialized endothelial subtypes, including 2 hemogenic populations that arise from different origins. Similarly, analyses of posterior foregut endoderm revealed subsets of hepatic, pancreatic, and biliary progenitors with overlapping developmental potency. Calculated gene-regulatory networks predict gene regulons that are dominated by cell-type-specific transcription factors unique to each lineage. Vastly different Sox17 regulons found in endoderm versus endothelial cells support the differential interactions of SOX17 with other regulatory factors, thereby enabling lineage-specific regulatory actions.

VDDRC-Related Training and Activities

Director, Complementary Awards Program-Supported Genome Editing Core
Pilot & Feasibility Award Recipient

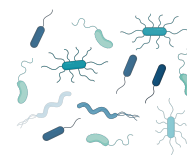
VDDRC Collaborations

My laboratory has developed collaborations with other VDDRC members, including Drs. Coffey, Lau, and Shrubsole. A representative collaborative publication is: Islam M, Yang Y, Simmons AJ, Shah VM, Musale KP, Xu Y, Tasneem N, Chen Z, Trinh LT, Molina P, Ramirez-Solano MA, Sadien ID, Dou J, Rolong A, Chen K, **Magnuson MA**, Rathmell JC, Macara IG, Winton DJ, Liu Q, Zafar H, Kalhor R, Church GM, Shrubsole MJ, Coffey RJ, Lau KS. Temporal recording of mammalian development and precancer. *Nature*. 2024;634(8036):1187-1195. PMID: PMC11525190.

Future VDDRC Core Use

I will use the Flow Cytometry Core, the MS/Proteomics Core, and the Biostatistical Component for data analysis.

Member: Anita Mahadevan-Jansen, PhD
Rank: Professor
Department: Neurological Surgery and Biomedical Engineering
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I am an internationally recognized biomedical engineer, particularly in the arena of Biomedical Photonics. My research focuses on the application of optical techniques for the diagnosis of pathology and neuromodulation in a variety of diseases. The primary research areas include optical diagnostics, neurophotonics, and image-guided surgical techniques. Specifically, I have pioneered the use of *in vivo* Raman spectroscopy for non-invasive diagnosis of dysplasia. I have now applied this technology for *in vivo* discrimination between Crohn's and Ulcerative Colitis and eosinophilic esophagitis (EoE). My work focuses on translational research to positively impact patient care and outcomes. A representative publication is: Haugen EJ, Locke AK, Dao LH, Walter AB, Rasiah PK, Baba JS, Buendia MA, Correa H, Hiremath G, **Mahadevan-Jansen A**. Biochemical detection of pediatric eosinophilic esophagitis using high wavenumber Raman endoscopy and stimulated Raman microscopy. *Sci Rep*. 2025;15(1):22471. PMCID: PMC12217470.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK132338-04	Dual-wavelength endoscopic Raman probe for eosinophilic esophagitis	07/01/2022-05/31/2026	\$288,637

Summary of Digestive Disease Research

EoE is difficult to diagnose and distinguish from other common esophageal diseases in real-time using white light endoscopic imaging of the esophagus conducted via an esophagogastroduodenoscopy (EGD) procedure. Therefore, clinicians rely on multiple random esophageal biopsies, which is obtained during this procedure for histologic confirmation (gold standard). However, since EoE is a patchy disease, even multiple biopsies may not yield accurate results. As such, there is an urgent need to develop alternative diagnostic tools that can quickly survey more regions of the esophagus, *in situ*, and provide tissue-specific inflammatory biomarker information for real-time identification of EoE. Raman spectroscopy (RS) is one such technology that can provide a solution as it relies on light interaction with molecules to provide a unique "fingerprint" of the biochemical and molecular composition of a specimen within seconds. Therefore, RS via an endoscope is uniquely suited for real-time biochemical assessment of active EoE. Thus, my research focus on the development and assessment of a depth-specific dual-wavelength Raman endoscope to characterize both biochemical and water changes within the esophagus as it relates to active EoE.

VDDRC-Related Training and Activities

Pilot & Feasibility Project Reviewer

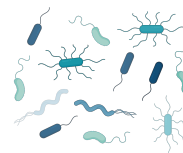
VDDRC Collaborations

As a new member of the VDDRC, I have already established collaborations with VDDRC members Drs. Hiremath and Acra and will continue to expand upon this collaborative network. A representative collaborative publication is: Locke A, Haugen E, Thomas G, Correa H, Dellon ES, **Mahadevan-Jansen A**, Hiremath G. *In vivo* Raman spectroscopy reveals biochemical composition of the esophageal tissue in pediatric eosinophilic esophagitis. *Clin Transl Gastroenterol*. 2024;15(2):e00665. PMCID: PMC10887437.

Future VDDRC Core Use

We will utilize the Cell Imaging and Translational Analysis Cores as well as the Biostatistical Component for data analyses.

Member: Nicholas O. Markham, MD, PhD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: GII



Rationale for VDDRC Membership

I am a previous Pilot and Feasibility Award recipient and a former member of the Academy of Investigators within the VDDRC. My interests include understanding how gastrointestinal epithelial cells interact with microbial toxins and how changes in the gut microbiome affect human diseases, such as colon carcinogenesis. One representative VDDRC publication is: Lunnemann HM, Shealy NG, Reyzer ML, Shupe JA, Green EH, Siddiqi U, Lacy DB, Byndloss MX, **Markham NO**. Cecum axis (CecAx) preservation reveals physiological and pathological gradients in mouse gastrointestinal epithelium. *Gut Microbes*. 2023;15(1):2185029. PMID: PMC10012889.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Veterans Administration 5IK2BX005699-05	Gastrointestinal cell type-specific signaling and <i>C. difficile</i> toxin pathogenesis	10/01/2021-09/30/2026	\$315,450
1R01DK149160-01	Gastrointestinal epithelial responses to recurrent <i>C. difficile</i> infection and asymptomatic colonization	07/01/2026-06/30/2031	Pending

Summary of Digestive Disease Research

Data from my VDDRC Pilot indicate that the *C. difficile* toxin TcdB transactivates EGFR, which is essential for stem cell function. I have now optimized a murine intrarectal model of toxin instillation, allowing our group to study the effect of TcdB on EGFR and stem cell functions. In a separate but related project, we have used spatial transcriptomics and multiplex immunofluorescence to show that early-stage colorectal cancers contain rich bacterial niches filled with species, like *C. difficile*, that are relatively low-abundance but disproportionately strong effectors of tumor transcriptional programming.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Poster Judge

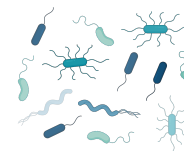
VDDRC Collaborations

I have ongoing collaborations with numerous VDDRC members, including Drs. Algood, Byndloss, Choksi, Coburn, Coffey, Goettel, Goldenring, Kaji, Lacy, Lau, Nicholson, Piazuelo, Shrubsole, Skaar, Singh, Washington, Williams, and K. Wilson. A recent VDDRC collaborative publication is: Green EH, Kotrannavar SR, Rutherford ME, Lunnemann HM, Kaur H, Heiser CN, Ding H, Simmons AJ, Liu X, Lacy DB, Washington MK, Shrubsole MJ, Liu Q, Lau KS, Sears CL, Coffey RJ, Drewes JL, **Markham NO**. Multiomic spatial atlas shows deleted in malignant brain tumors 1 (DMBT1) glycoprotein is lost in colonic dysplasia. *J Pathol*. 2025;266(1):51-65. PMID: PMC11985286.

Future VDDRC Core Use

I will continue using the Translational Analysis, Flow Cytometry, and the MS/Omics Core to analyze host responses to *C. difficile* toxin.

Member: Janet Markle, PhD
Rank: Assistant Professor
Department: Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

My work focuses on leveraging my skills in human genetics and immunology to define the causes and mechanisms of genetically mediated infectious immunological diseases, especially severe auto-inflammatory and autoimmune diseases affecting children, such as inflammatory bowel diseases. A VDDRC-related publication is: Bhattad S, Gil HM, Ruchinskas A, Stinson JR, Staines Boone AT, Mohite RS, Janardhanan J, Singh N, Mariskanish C, Choi JM, Basaria S, Ye X, Snow AL, **Markle JG**. B-cell lymphocytosis and reprogramming due to biallelic CARD11 mutations. *J Allergy Clin Immunol*. 2025:S0091-6749. PMID: 41456721.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R35GM155339-02	From genetic variants to mechanisms: Understanding drivers of inflammation	06/05/2024-04/30/2029	\$250,000

Summary of Digestive Disease Research

Next-generation sequencing data have been pivotal to my research across many projects, even bridging mouse and human studies. I have been involved in several efforts to develop and freely share tools for the analysis and interpretation of next-generation sequencing data, ranging from single-nucleotide variants in human whole-exome sequencing data to transcriptomics data from complex microbial communities. I am also actively working on the generation and analysis of mass cytometry data, which provides single-cell insight into the expression of 40+ proteins on hundreds of thousands of cells from a heterogeneous blood sample.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Young Investigator Award
Pilot & Feasibility Project Reviewer
Retreat Speaker

VDDRC Collaborations

I have established collaborations with VDDRC members, Drs. Byndloss, Skaar, and Nicholson regarding the microbiome and Drs. Cassat, Choksi, Flynn, Goettel, Lau, Williams, and K. Wilson on studies of the immunology of IBD. One resulting collaborative VDDRC publication is: Kvitne KE, Zuffa S, Charron-Lamoureux V, Mohanty I, Patan A, Mannocho-Russo H, Zemlin J, Burnett LA, Zhang LS, Cecala MC, Ersoz C, Connelly JA, Halasa N, Nicholson M, Dorrestein PC, Tsunoda SM, **Markle J**. Fecal microbial and metabolic signatures in children with very early onset inflammatory bowel disease. *NPJ Biofilms Microbiomes*. 2025;12(1):33. PMCID: PMC12864830.

Future VDDRC Core Use

I will utilize the Flow Cytometry Core for single-cell RNAseq, as well as the services in the MS/Omics and Translational Analysis Cores.

Member: Mona Mashayekhi, MD, PhD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

My laboratory research is focused on the contribution of chronic inflammation in individuals with obesity to cardiometabolic diseases. A representative publication is: **Mashayekhi M**, Beckman JA, Nian H, Garner EM, Mayfield D, Devin JK, Koethe JR, Brown JD, Cahill KN, Yu C, Silver H, Niswender K, Luther JM, Brown NJ. Comparative effects of weight loss and incretin-based therapies on vascular endothelial function, fibrinolysis and inflammation in individuals with obesity and prediabetes: A randomized controlled trial. *Diabetes Obes Metab.* 2023;25(2):570-580. PMCID: PMC10306232.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5K23HL159351-03	The effect of SGLT2 inhibition on adipose tissue inflammation and endothelial function	7/1/2023-6/30/2028	\$171,700

Summary of Digestive Disease Research

Obesity contributes to heightened chronic inflammation, which promotes the development of cardiometabolic diseases. No current therapies specifically target inflammatory pathways activated in obesity to improve these outcomes. Glucagon-like peptide-1 receptor agonists (GLP1-RAs) are a newer weight loss class of medications that reduce cardiometabolic diseases beyond what is expected from their glucose and weight reduction benefits alone. GLP-1RAs reduce inflammation in animals, but this has not been defined in humans. Our research program aims to characterize whether and how GLP1-RAs reduce obesity-associated inflammation in humans by altering the immune metabolic profile.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Young Investigator Award
Retreat Speaker

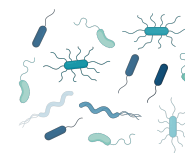
VDDRC Collaborations

I have established productive collaborations with several VDDRC members, including Drs. Bailin, Gabriel, Koethe, Niswender, Samuels, and Wanjalla. A representative VDDRC collaborative publication is: **Mashayekhi M**, Safa BI, Nian H, Devin JK, Gamboa JL, Yu C, Chen R, Beckman JA, Koethe JR, Silver HJ, Niswender K, Luther JM, Brown NJ. RISING STARS: Effects of a GLP-1 receptor polymorphism on responses to liraglutide. *J Endocrinol.* 2025;267(1):e250174. PMCID: PMC12556785.

Future VDDRC Core Use

I will utilize the Flow Cytometry and Cell Imaging Cores as well as the Biostatistical Component for data analysis.

Member: Leslie Meenderink, MD, PhD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: GII



Rationale for VDDRC Membership

I am a new VDDRC member. My undergraduate research at Yale University was in the laboratory of Dr. Paul Forscher, investigating cytoskeleton dynamics in neuronal growth cones. During the completion of my MD/PhD at Vanderbilt University, my PhD research in the lab of Dr. Steve Hanks focused on the role of p130Cas signaling in focal adhesion dynamics and cellular motility. While completing my internal medicine residency, infectious disease fellowship, and post-doctoral research, my research in the laboratory of Dr. Matthew Tyska utilized live-cell imaging to understand the mechanisms underlying assembly of the intestinal brush border. Since starting my own laboratory at VUMC, my research focus has investigated how the intestinal epithelium establishes and maintains a barrier against intestinal microbes. Using a combination of human tissue samples, mouse models, and cell culture in combination with advanced light and electron microscopy techniques, our research seeks to understand how the intestinal epithelium maintains balance with commensal bacteria and defends against pathogenic microbes. A representative publication is: Cowell RP, Bickart AC, Shashi SR, Vasquez A Jr, Brackman LC, Abdel-Dayem MA, Chen W, Bowman DM, Krystofiak ES, Essalki Y, Gross I, Harrison DG, Wanjalla CN, Algood HMS, Tyska MJ, **Meenderink LM**. Brush border intermicrovillar adhesion limits bacteria attachment to the small intestine brush border. *bioRxiv*. 2025:2025.11.25.690363. PMCID: PMC12772999.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01DK150197-01	The role of enterocyte apical structure in dysbiosis and inflammatory bowel disease	12/01/2026-11/31/2031	Pending

Summary of Digestive Disease Research

My current research aims to understand how the microscopic surface architecture of the gut is disrupted in and contributes to IBD pathogenesis and bacterial infection. Microvilli (MV) are the initial site of contact between intestinal epithelial cells and luminal bacteria. Perturbations in MV structure and density result in nutrient malabsorption and osmotic diarrhea as seen in IBD and infection with pathogenic bacteria. A recent study showed that even in uninfamed tissue, patients with Crohn's disease have lower levels of MV structural proteins. These findings imply MV defects are not only present in IBD during active inflammation but also persist despite therapy and may contribute to relapse. Interestingly, our data demonstrate that mice lacking the MV structural protein CDHR2 recapitulate several of the epithelial defects seen in Crohn's patients, providing a unique *in vivo* model system. Our laboratory is now addressing the hypothesis that defects in normal enterocyte apical surface structure and function persist in the absence of active inflammation and provide a path for microbial entry, driving inflammation, infection, and disease relapse. Through this work, we will identify defects in enterocyte structure in Crohn's patients and characterize how these defects contribute to persistent changes in the microbial content. These epithelial structural defects may provide a new target for therapeutic intervention.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Retreat Speaker

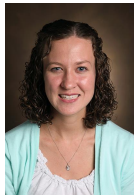
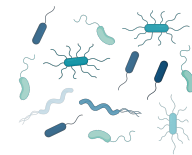
VDDRC Collaborations

I have established productive collaborations with several VDDRC members, including Drs. Algood, Choksi, Gabriel, Goettel, Goldenring, Koethe, Lau, Piazuelo, Tyska, Wanjalla, Washington, and Williams. A representative VDDRC collaborative publication is: Short SP, Brown RE, Chen Z, Pilat JM, McElligott BA, **Meenderink LM**, Bickart AC, Blunt KM, Jacobse J, Wang J, Simmons AJ, Xu Y, Yang Y, Parang B, Choksi YA, Goettel JA, Lau KS, Hiebert SW, Williams CS. MTGR1 is required to maintain small intestinal stem cell populations. *Cell Death Differ*. 2024;31(9):1170-1183. PMCID: PMC11369156.

Future VDDRC Core Use

I will utilize the Cell Imaging, Flow Cytometry, MS/Omics, and the Translational Analysis Cores.

Member: Maribeth R. Nicholson, MD, MPH
Rank: Associate Professor
Department: Pediatrics
VDDRC Status: Associate Member
Research Group: GI



Rationale for VDDRC Membership

My research program focuses on the clinical and translational evaluation of *C. difficile* infections (CDI) in children and adults, with a focus on the role of the intestinal microbiome, diagnostic challenges, and vaccine development. A representative publication is: **Nicholson MR**, Donskey CJ. Multistep testing algorithms for *Clostridioides difficile* infection. *JAMA*. 2023;330(10):966-967. PMID: PMC10528531.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Vedanta Biosciences	A randomized, double-blind, placebo-controlled phase 3 study of VE303 for prevention of recurrent <i>Clostridioides difficile</i> infection: The restorative303 study	05/29/2024-05/28/2029	\$161,496

Summary of Digestive Disease Research

I have established a translational research program centered on *C. difficile* infections in children and adults. Our studies have prospectively enrolled pediatric and adult patients with a collection of serum and fecal samples to interrogate the intestinal microbiome, anti-toxin antibody responses, and the prevalence/immune reactions to *C. difficile* colonization in patients with additional comorbidities. We have then used these human observations to inform *C. difficile* vaccine development through collaborations within the VDDRC.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient

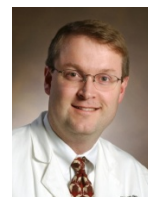
VDDRC Collaborations

I have ongoing collaborations with VDDRC members Drs. Acra, Byndloss, Lacy, Markham, Markle, Olivares-Villagomez, Skaar, and Washington. An example collaborative VDDRC publication is: Thomas AK, Peritore-Galve FC, Ehni AG, Lança BBC, Coggin J, Brady EJ, Yoder SM, Shrem R, Rodríguez RC, Kroh HK, Gibson-Corley KN, Kay Washington M, Olivares-Villagómez D, Creech CB, **Nicholson MR**, Spiller BW, Lacy DB. Mucosal vaccination clears *Clostridioides difficile* colonization. *Nature*. 2026. Online ahead of print. PMID: 41708852.

Future VDDRC Core Use

I will continue to use the Biostatistical Component and the MS/Omics Core for our clinical and translational work and have applied for a competitive extension of my VDDRC Pilot & Feasibility Award.

Member: Kevin D. Niswender, MD, PhD
Rank: Associate Professor
Department: Medicine and Molecular Physiology and Biophysics
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

I am the Co-Director of the Obesity, Metabolism, and Nutrition (OMN) Research Group for this application. My research interests include studying the pathophysiology of obesity and metabolic syndrome and novel mechanisms by which obesity contributes to morbidity and mortality. One representative publication is: Gu C, Olszewski T, King KL, Vaezi MF, **Niswender KD**, Silver HJ. The effects of modifying amount and type of dietary carbohydrate on esophageal acid exposure time and esophageal reflux symptoms: A randomized controlled trial. *Am J Gastroenterol.* 2022;117(10):1655-1667. PMCID: PMC9531994.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1K23DK143312-01	Use of adjuvant anti-obesity medications to enhance surgical weight loss	09/09/2025-07/31/2030	Not PI or MPI

Summary of Digestive Disease Research

Our research focuses on integrated *in vivo* metabolism, including energy and lipid homeostasis. We have studied rodent models of obesity and have identified pathogenic mechanisms by which tissues become resistant to the effects of hormonal action. We have translated several of our rodent findings into human studies, where we are interested in the impact of macronutrient-based dietary approaches to weight, body composition, and cardiometabolic risk management. We have also conducted similar, therapeutically based studies to assess the impact on weight, body composition, and metabolic outcomes in humans.

VDDRC-Related Training and Activities

Co-Leader, Obesity, Metabolism and Nutrition (OMN) Research Interest Group
Retreat Speaker

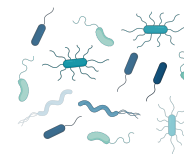
VDDRC Collaborations

I have a wide range of collaborators in obesity and metabolism, including VDDRC members Drs. Brittain, Brown, Dean, Flynn, Gabriel, Goldenring, Koethe, Peek, Samuels, and Spann. A collaborative VDDRC publication is: Samuels JM, Patel MB, Roumie CL, Self W, Funk L, Spann MD, **Niswender KD**. Patients experience with preoperative use of anti-obesity medications and associations with bariatric surgery expectations. *Surg Obes Relat Dis.* 2025;21(2):109-114. PMCID: PMC12288039.

Future VDDRC Core Use

We will utilize the Biostatistical Component as well as the Flow Cytometry and Translational Analysis Cores in the future as we identify novel biomarkers that regulate neural control of feeding and metabolic dysfunction.

Member: Kristen M. Ogden, PhD
Rank: Associate Professor
Department: Pediatrics and Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GI



Rationale for VDDRC Membership

A long-term goal of my laboratory is to make discoveries that enable rational engineering of improved therapeutics. Combined with an active engagement in mentoring and teaching, my commitment to collaborative research and my expertise in molecular virology in the context of enteric infections will contribute to the continued success of the VDDRC. An example of a publication supported by the VDDRC is: Sartalamacchia K, Veletanlic V, Diller JR, **Ogden KM**. Multiple rotavirus species encode fusion-associated small transmembrane (FAST) proteins with cell type-specific activity. *Journal of Virology*. 2025; 99(12):e0158725. PMID: PMC12724187.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01AI155646-05	Effects of Reoviridae assembly and transmission processes on viral genetic diversity	07/01/2021-06/30/2026	\$322,278
1R21AI190445-01	Human Rotavirus egress and infection in association with extracellular vesicles	07/16/2025-06/30/2027	\$275,000

Summary of Digestive Disease Research

Our work is focused on using molecular virology and culture models to understand how enteric viruses acquire genetic diversity and how such diversity impacts virus and host populations. Rotavirus is an important cause of diarrheal disease that results in the deaths of hundreds of thousands of infants and young children worldwide each year. Reovirus is an enteric virus that is largely asymptomatic in humans but efficiently kills some cancer cells and has potential as an oncolytic therapeutic. Our work encompasses studies of viral outer-capsid protein functions, viral tropism determinants, how viral functions regulate viral genetic diversity, and the outcomes of virus transport as free particles or in association with extracellular vesicles.

VDDRC-Related Training and Activities

Retreat Speaker

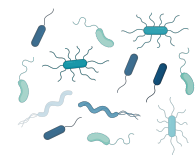
VDDRC Collaborations

We actively collaborate with VDDRC member Drs. Crowe and Zachos to investigate outcomes of enteric virus infection of human intestinal enteroids, including egress and infection of human enteroids when virus particles are packaged within extracellular vesicles. Dr. Zachos is a co-investigator on a funded NIH R21 grant studying the enteric virus rotavirus.

Future VDDRC Core Use

We will continue to utilize the Cell Imaging, MS/Omics, and Flow Cytometry Cores for our studies focused on viral pathogenesis to elucidate virus-host protein interactions, visualize and evaluate the composition of extracellular vesicles released from virus-infected cells, and determine extracellular vesicle-induced immune responses.

Member: Danyvid Olivares-Villagómez, PhD
Rank: Senior Research Scientist
Department: Medicine
VDDRC Status: Associate Member
Research Group: GII



Rationale for VDDRC Membership

My research focuses on the role of osteopontin, a ubiquitous protein present in many tissues and organs. This protein is also present in breast milk. Our group is studying the importance of breast milk-derived osteopontin in intestinal homeostasis. We also study the importance of a commensal, *Turicibacter sanguinis*, during intestinal inflammation. One example of VDDRC-sponsored publications: 1) Hoek KL, McClanahan KG, Latour YL, Shealy N, Piazuelo MB, Vallance BA, Byndloss MX, Wilson KT, **Olivares-Villagómez D**. *Turicibacterales* protect mice from severe *Citrobacter rodentium* infection. *Infect Immun*. 2023;91(11):e0032223. PMID: PMC10652940.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R21AI187749-01A1	<i>Turicibacter</i> modifies intestinal infection severity by modulating intestinal metabolites	08/01/2025-07/31/2027	Not PI or MPI

Summary of Digestive Disease Research

My research focuses on the immune responses mediated by cells associated with the intestinal epithelium, in particular intraepithelial lymphocytes (IEL). I am particularly interested in the interactions between different IEL populations and the protein osteopontin. Also, I am interested in the response of these cells during intestinal bacterial infections.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Retreat Poster Judge

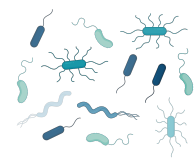
VDDRC Collaborations

We collaborate with many VDDRC members, including Drs. Wilson, Weitkamp, Piazuelo, Van Kaer, Washington, Cover, Algood, Gaddy, Lacy, Nicholson, Byndloss, Behringer, and Zhu, for various aspects of our research focused on IEL biology. An example of these VDDRC collaborations is represented in the following publication: Thomas AK, Peritore-Galve FC, Ehni AG, Lança BBC, Coggin J, Brady EJ, Yoder SM, Shrem R, Rodríguez RC, Kroh HK, Gibson-Corley KN, Kay Washington M, **Olivares-Villagómez D**, Creech CB, Nicholson MR, Spiller BW, Lacy DB. Mucosal vaccination clears *Clostridioides difficile* colonization. *Nature*. 2026. Online ahead of print. PMID: 41708852.

Future VDDRC Core Use

We will continue to rely significantly on the Flow Cytometry Core for enriching subsets of immune cell populations by flow sorting, as well as the Translational Analysis Core.

Member: Kristin L. Patrick, PhD
Rank: Associate Professor
Department: Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

My lab works to elucidate the molecular mechanisms of innate immune regulation in macrophages. While a rapid and robust innate immune response is needed to limit infection, a response that is too strong confers risks, including cytokine storms. Therefore, macrophage gene expression needs to be tightly regulated. My laboratory works to implicate post-transcriptional regulatory mechanisms (e.g., pre-mRNA splicing, mRNA export, RNA decay/turnover, RNA localization, etc.) in shaping inflammatory gene expression. We employ a multidisciplinary toolbox of protein and RNA biochemistry, transcriptomics, and microscopy-based approaches to dissect pathways of interest in mechanistic detail. By highlighting new and unexpected ways that RNA-binding proteins (RBPs) balance innate immune responses, our work furthers our understanding of how inflammation can be dysregulated during infection and in a variety of human diseases. A representative publication is: Azam S, Armijo KS, Weindel CG, Chapman MJ, Devigne A, Nakagawa S, Hirose T, Carpenter S, Watson RO, **Patrick KL**. The early macrophage response to pathogens requires dynamic regulation of the nuclear paraspeckle. *Proc Natl Acad Sci USA*. 2024;121(9):e2312587121. PMID: PMC10907238.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R35GM133720-07	Exploring the role of RNA binding proteins in post-transcriptional regulation of macrophage activation	09/01/2024-08/31/2029	\$275,000

Summary of Digestive Disease Research

My laboratory is working to implicate new RNA-binding proteins (RBPs) in the macrophage innate immune response and to define new paradigms through which macrophages reorganize their nuclei to activate innate gene expression. We have identified a cohort of RBPs in the SR/hnRNP families of splicing regulatory factors that are differentially phosphorylated in macrophages in response to PAMP/DAMP sensing. Our data demonstrate that the paraspeckle is dynamically up- and down-regulated over the course of early macrophage activation, can sequester specific RBPs in response to PAMP sensing, and is required for proper amplification of key inflammatory transcripts, including *Il6*, *Cxcl1*, and *Cxcl9*. We found that the RNA exosome can control paraspeckle dynamics and is required to maintain normal homeostatic levels of antiviral transcripts in macrophages. Pursuing these lines of investigation will provide fundamental insights into how specific RBPs and ribonucleoprotein complexes control the ability of macrophages to sense and respond to pathogens. By furthering our understanding of cellular stress responses and identifying novel nodes that control innate immune gene expression outcomes, our work may contribute to efforts to develop therapeutics to help patients battling immune disorders and infection.

VDDRC-Related Training and Activities

Retreat Poster Judge

VDDRC Collaborations

As a new member of the VDDRC, we plan to initiate collaborations with VDDRC members Drs. Byndloss, Lacy, and Skaar.

Future VDDRC Core Use

We plan to use the Cell Imaging Core and the Biostatistical Component for data analysis.

Member: Richard M. Peek, Jr., MD
Rank: Mina Cobb Wallace Professor
Department: Medicine, Pathology, Microbiology and Immunology, and Cancer Biology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I am the PI and Director of the VDDRC and my research is grounded in the study of digestive diseases with an emphasis on *H. pylori*-induced gastric inflammation and injury. An example of a publication supported by the VDDRC is: Noto JM, Piazuolo MB, Romero-Gallo J, Delgado AG, Suarez G, Akritidou K, Girod Hoffman M, Roa JC, Taylor CT, **Peek RM, Jr.** Targeting hypoxia-inducible factor-1 alpha suppresses *Helicobacter pylori*-induced gastric injury via attenuation of both cag-mediated microbial virulence and proinflammatory host responses. *Gut Microbes.* 2023;15(2):2263936. PMCID: PMC10578190.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK058587-24	<i>Helicobacter pylori</i> and gastrointestinal biology	09/15/2020-06/30/2026	\$221,671
5R01CA077955-29	<i>H. pylori</i> relationship to digestive diseases and cancer	05/01/2023-04/30/2028	\$306,703
5R01CA281732-03	Interactions between the microbiota and <i>Helicobacter pylori</i> in gastric carcinogenesis	06/01/2023-05/31/2028	\$530,921
5P01CA116087-18	<i>H. pylori</i> -induced inflammation and gastric cancer	04/02/2024-02/28/2029	\$1,049,836

Summary of Digestive Disease Research

The overarching theme for our research has been the delineation of the signaling events initiated by bacterial:epithelial cell contact that regulate gastric disease phenotypes using innovative and complementary model systems. We utilize *ex vivo* gastric organoid systems that closely recapitulate cellular organization in the stomach to examine aberrant responses to oncogenic *H. pylori* strains. We also developed robust and reproducible rodent models of *H. pylori*-induced gastric cancer. We have continually extended our observations into human populations, and have previously examined interactions between host and pathogen genetic ancestry that influence disease development in persons at high or low risk for disease.

VDDRC-Related Training and Activities

PI, VDDRC
Director, Administrative Core
Pilot & Feasibility Award Recipient
Retreat Poster Judge
Retreat Speaker

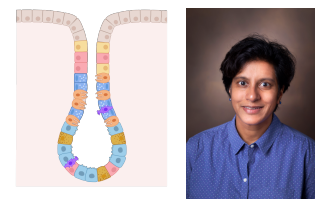
VDDRC Collaborations

We collaborate extensively with numerous VDDRC members, including Drs. Acra, Algood, Choksi, Choi, Coffey, Cover, Flynn, Goldenring, E. Lee, Piazuolo, Washington, K. Wilson, J. Wilson, and Yan, among many others, for various aspects of our *H. pylori*-related research. An example of a collaborative publication supported by the VDDRC is: Kaur H, Ali SA, Short SP, Williams CS, Goettel JA, Washington MK, **Peek RM Jr**, Acra SA, Yan F. Identification of a functional peptide of a probiotic bacterium-derived protein for the sustained effect on preventing colitis. *Gut Microbes.* 2023;15(2):2264456. PMCID: PMC10566403.

Future VDDRC Core Use

Our usage of the Cell Imaging, Flow Cytometry, and MS/Omics Cores will increase due to the implementation of new technology, such as metabolomics and live-cell imaging. In addition, we will continue to use the Translational Analysis Core for the evaluation of our animal models of infection, with extension into human disease states.

Member: Mary Philip, MD, PhD
Rank: Assistant Professor, Associate Director VI4
Department: Medicine
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am a former recipient of the VDDRC Young Investigator Award and a VDDRC Pilot and Feasibility Award, and my laboratory research program focuses on understanding the epigenetic and transcriptional mechanisms driving CD8 T cell dysfunction in pre-malignant liver lesions. A representative publication is: Rudloff MW, Zumbo P, Favret NR, Roetman JJ, Detrés Román CR, Erwin MM, Murray KA, Jonnakuti ST, Dünder F, Betel D, **Philip M**. Hallmarks of CD8+ T cell dysfunction are established within hours of tumor antigen encounter before cell division. *Nat Immunol.* 2023;24(9):1527-1539. PMID: PMC10878719.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R37CA263614-05	TCR signaling and cell cycle regulation in tumor-specific CD8 T cell dysfunction	04/01/2022-03/31/2027	\$322,037

Summary of Digestive Disease Research

To understand the epigenetic programs mediating T cell non-responsiveness, our laboratory has carried out whole-genome chromatin accessibility analyses (ATAC-Seq) on lymphocytes harvested from premalignant liver lesions in mice. We identified novel cell-surface markers associated with each chromatin state that can now be used to identify programmable from non-reprogrammable T cells from bulk populations. We have extended our research to study human CD8 T cells isolated from fresh hepatocellular tumor samples, and we have recently demonstrated that tumor-reactive CD8 T cells from human and mouse liver tumors increase expression of efflux transporters, such as MDR1, that promote T cell survival.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Young Investigator Award
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

My involvement in the Academy led to a robust collaboration with Dr. Y. Lee to establish an *in vitro* model to investigate hepatocyte-CD8 T-cell interactions, and I also collaborate with Dr. Washington. A representative VDDRC collaborative publication is: Detrés Román CR, Erwin MM, Rudloff MW, Revetta F, Murray KA, Favret NR, Roetman JJ, Roland JT, Washington MK, **Philip M**. Vaccination generates functional progenitor tumor-specific CD8 T cells and long-term tumor control. *J Immunother Cancer.* 2024;12(10):e009129. PMID: PMC11459355.

Future VDDRC Core Use

I will continue to utilize the Cell Imaging Core and the Flow Cytometry Core for single-cell isolation of immune cells from our animal models, the MS/Omics Core for proteomic analysis, and the Biostatistical Component for data analysis.

Member: Maria Blanca Piazuelo, MD
Rank: Research Associate Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: HRP



Rationale for VDDRC Membership

I serve as Associate Director of the Translational Analysis Core of the VDDRC, and I will provide expertise in GI pathology. I also have a primary research interest in pre-malignant lesion development in the stomach and the colon. A representative VDDRC publication is: Gobert AP, Hawkins CV, Williams KJ, Snyder LA, Barry DP, Asim M, Allaman MM, McNamara KM, Delgado AG, Wang Y, Zhao S, Rose KL, **Piazuelo MB**, Wilson KT. Hypusination in intestinal epithelial cells protects mice from infectious colitis. *Gut Microbes*. 2024;16(1):2438828. PMID: PMC11649231.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5P01CA116087-19	Gastric Histopathology Core	01/01/2009-02/28/2029	Listed under Contact PI

Summary of Digestive Disease Research

My research interests are focused on the morphological alterations of inflammatory and precancerous processes in the gastrointestinal tract in human tissues and in animal models. Our group has conducted studies in Colombia comparing the population in a high gastric cancer risk area (in the Andes Mountains) with an area of low gastric cancer risk on the Pacific coast. Both populations have a very high prevalence of *H. pylori* infection. With the collaboration of a multidisciplinary team, we found that the phylogeographic origin of *H. pylori* strains infecting the participants was associated with the severity of the gastric histopathological lesions as well as with the oxidative damage of the gastric mucosa. Additional studies concluded that *H. pylori* strains from the high-risk area have increased ability to induce oxidative stress and DNA damage compared with the low-risk area strains.

VDDRC-Related Training and Activities

Director, Histopathology Service in the Translational Analysis Core
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

I collaborate extensively with multiple VDDRC investigators, serving as a pathologist on numerous studies evaluating gastrointestinal inflammatory response and precancerous lesions in human subjects and in rodent models. Specifically, I have ongoing collaborations with Drs. Algood, Coburn, Cover, Markham, Peek, Washington, Williams, and K. Wilson, among many others. One VDDRC collaborative publication is: Brackman LC, Jung MS, Green EH, Joshi N, Revetta FL, McClain MS, Markham NO, **Piazuelo MB**, Scott Algood HM. IL-17 signaling protects against *Helicobacter pylori*-induced gastric cancer. *Gut Microbes*. 2024;16(1):2430421. PMID: PMC11639209.

Future VDDRC Core Use

I will continue to use the Translational Analysis Core for evaluation of GI inflammation and injury in rodent models and human samples.

Member: Jason Samuels, MD
Rank: Assistant Professor
Department: Surgery
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

I am a leader in clinical trials investigating multimodal treatment strategies for obesity and have a robust background in caring for over 500 bariatric surgery patients. Given the wide-ranging impact of obesity on health outcomes, a critical need exists to explore the efficacy of adjuvant weight loss therapies after gastric bypass surgery. Tirzepatide (TRZ), a type of glucagon-like peptide-1 receptor agonist, shows remarkable effectiveness in medical obesity with 25% weight loss after sustained therapy. However, nearly two-thirds of patients taking medications like TRZ have mild to moderate gastrointestinal (GI) symptoms, including nausea, vomiting, and abdominal pain. These medication side effects could be a consequence of gastroparesis via vagal stimulation of the stomach and may represent a major driver of weight loss. Limited data exist regarding the use of these newer agents, such as TRZ, in patients who have undergone gastric bypass, which disrupts vagal nerves responsible for managing food transit and gastric emptying. The focus of my research is this major and timely scientific gap in understanding whether gastric bypass surgery might mitigate these GI symptoms while allowing for enhanced weight loss with adjuvant TRZ use in the post-operative period. A representative publication is: **Samuels JM, Ye F, Irlmeier R, Silver H, Srivastava G, Spann M. Real-world titration, persistence & weight loss of semaglutide and tirzepatide in an academic obesity clinic. *Diabetes Obes Metab.* 2025;27(11):6200-6209. PMID: PMC12515774.**

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1K23DK143312-01	Use of adjuvant anti-obesity medications to enhance surgical weight loss	09/09/2025-07/31/2030	\$163,800
Intuitive Foundation 2024-4335	Comparative analysis of skeletal muscle adaptations and gastrointestinal adverse effects following bariatric surgery versus GLP-1 receptor agonist therapy	07/01/2025-06/30/2026	\$60,000
American College of Surgeons	Use of adjuvant anti-obesity medications to enhance surgical weight loss	07/01/2025-06/30/2027	\$40,000

Summary of Digestive Disease Research

My clinical and translational research is focused on the use of adjuvant anti-obesity medication to enhance surgical weight loss. The aims of this research are to 1) determine the impact of adjuvant TRZ administration on weight, total fat mass, and lean body mass in patients with a history of gastric bypass, 2) investigate the frequency and severity of GI discomfort associated with TRZ, and 3) investigate the impact of TRZ on GI motility in patients with prior Gastric Bypass.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Retreat Speaker

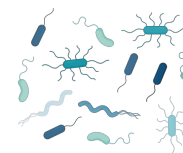
VDDRC Collaborations

Although I am a new member of the VDDRC, I have established collaborations with numerous VDDRC members, including Drs. Flynn, Mashayekhi, and Niswender. A representative VDDRC collaborative publication is: **Samuels JM, Niswender KD, Roumie CL, Spann MD, Flynn CR, Ye F, Blankush J, Irlmeier R, Funk LM, Patel MB. Adverse event comparison between glucagon-like peptide-1 receptor agonists and other antiobesity medications following bariatric surgery. *Diabetes Obes Metab.* 2024;26(9):3906-3913. PMID: PMC12223922.**

Future VDDRC Core Use

I will utilize the Biostatistical Component for data analysis.

PI Name: Claus Schneider, PhD
Rank: Professor
Department: Pharmacology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I am an analytical biochemist by training with a special emphasis on food analysis. The research interests in my laboratory are the structural and functional elucidation of novel metabolites of the COX-2 pathway and elucidating the molecular targets and functions of bioactive natural (dietary) products. My membership in the VDDRC began with a Pilot grant I received for our initial work on curcumin. An example of a VDDRC publication is: Luis PB, **Schneider C**. Large variability in the alkaloid content of *Corydalis yanhusuo* dietary supplements. *Front Pharmacol*. 2025;15:1518750. PMCID: PMC11774941.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R35GM144091-04	Novel pathways in eicosanoid biosynthesis and metabolism	08/01/2022-07/31/2027	\$300,000

Summary of Digestive Disease Research

For my NIH-funded projects, we use LC-MS methodology for metabolite quantification (stable isotope dilution assays), and structural identification of novel enzymatic or non-enzymatic metabolites is accomplished by NMR techniques and synthesis. For example, using LC-MS services provided by the VDDRC MS/Proteomics Core, we have established and quantified the *in vivo* formation of novel hemiketal eicosanoids and 5-hydroxy-prostaglandins that are formed by the cross-over of the 5-LOX and COX-2 pathways. We have developed LC-MS-based isotope dilution methods for the quantification of polyamines and, most recently, for the quantification of monoamines such as TMA, TMAO, choline, and carnitine.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

VDDRC Collaborations

We are performing quantitative analyses of polyamines in cell and tissue samples provided by Dr. Wilson's research group to determine the mechanism of inhibition of *H. pylori*-induced gastric disease. We also have ongoing collaborations with several additional VDDRC members, including Drs. Choksi, Coburn, Goettel, Piazzuelo, Singh, Washington, and Weitkamp, focused on the role of curcumin in suppressing colitis and gastritis. A representative publication is: Latour YL, Sierra JC, Finley JL, Asim M, Barry DP, Allaman MM, Smith TM, McNamara KM, Luis PB, **Schneider C**, Jacobse J, Goettel JA, Calcutt MW, Rose KL, Schey KL, Milne GL, Delgado AG, Piazzuelo MB, Paul BD, Snyder SH, Gobert AP, Wilson KT. Cystathionine γ -lyase exacerbates *Helicobacter pylori* immunopathogenesis by promoting macrophage metabolic remodeling and activation. *JCI Insight*. 2022;7(12):e155338. PMCID: PMC9309056.

Future VDDRC Core Use

We will continue our usage of the MS/Omics Core, which will increase as we further develop and define assays to determine the biological activities of dietary metabolites, as well as increased utilization of the Cell Imaging and Flow Cytometry Cores.

Member: Elizabeth A. Scoville, MD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: HRP



Rationale for VDDRC Membership

I am currently an Assistant Professor of Medicine in the Division of Gastroenterology at Vanderbilt University Medical Center. My research interests are related to understanding mechanisms of non-response to treatment in inflammatory bowel disease (IBD) as it relates to genetics and inflammatory pathways. I am a former VDDRC Pilot Award recipient. A representative publication is: Raffa GA, Tyree RN, Carson K, Allaman MM, Beaulieu DB, Dalal RL, Pabla BS, **Scoville EA**, Horst SN, Schwartz DA, Washington MK, Wilson KT, Coburn LA. Non-invasive determination of disease activity in Crohn's disease by serum luminex profiling. *Sci Rep.* 2026;16(1):8867. PMID: PMC12988101.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Takeda Pharmaceuticals North America, Inc.	A phase 4 study evaluating real-world use of CDPATH, a Crohns disease risk prediction tool COMPASS-CD study	09/15/2022-09/14/2027	\$54,393

Summary of Digestive Disease Research

My research has focused on defining inflammatory mediators in IBD predominantly related to adipose tissue-related signaling pathways and metabolic changes, and this was funded by a VDDRC Pilot and Feasibility Award. Our work has shown that non-targeted serum metabolomic profiling can differentiate between Crohn's disease, ulcerative colitis, and control patients.

VDDRC-Related Training and Activities

Academy of Investigator, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

I have several ongoing collaborations with VDDRC members, such as Drs. Coburn, Coffey, Goettel, Lau, Piazzuelo, Washington, Williams, and K. Wilson. One publication resulting from these VDDRC collaborations is: Li J, Simmons AJ, Hawkins CV, Chiron S, Ramirez-Solano MA, Tasneem N, Kaur H, Xu Y, Revetta F, Vega PN, Bao S, Cui C, Tyree RN, Raber LW, Conner AN, Pilat JM, Jacobse J, McNamara KM, Allaman MM, Raffa GA, Gobert AP, Asim M, Goettel JA, Choksi YA, Beaulieu DB, Dalal RL, Horst SN, Pabla BS, Huo Y, Landman BA, Roland JT, **Scoville EA**, Schwartz DA, Washington MK, Shyr Y, Wilson KT, Coburn LA, Lau KS, Liu Q. Identification and multimodal characterization of a specialized epithelial cell type associated with Crohn's disease. *Nat Commun.* 2024;15(1):7204. PMID: PMC11339313.

Future VDDRC Core Use

I will continue to use the Biostatistics Component of the VDDRC for statistical analysis of clinical data.

Member: Martha J. Shrubsole, PhD
Rank: Research Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

A major focus of my research is to identify modifiable risk factors and biomarkers of disease. These include one-carbon metabolism, genetic, epigenetic, microbial, and inflammation biomarkers, as well as large-scale cohort studies to identify risk factors for gastrointestinal carcinogenesis in the US South. A VDDRC-related publication is: Siddiqui ST, Munro HM, Yu D, Zheng W, Blot WJ, **Shrubsole MJ**. Cancer incidence and mortality risk: associations with diet quality scores in a predominantly low-income and Black cohort study. *Am J Clin Nutr*. 2025;122(5):1174-1184. PMID: PMC12799364.

Digestive Diseases-Related Grants:

Grant Number	Title	Project Period	Annual Direct Costs
Janssen Pharmaceuticals	Assessment of the role of the microbiome in the progression of colorectal adenoma to colorectal cancer	06/18/2015-06/17/2027	\$91,479

Summary of Digestive Disease Research:

My research centers on how dietary factors and other modifiable lifestyle factors affect and interact with genetic, microbial, epigenetic, and protein biomarkers in the risk of colorectal carcinogenesis. Additionally, I lead work seeking to identify molecular and etiologic differences between conventional adenomas and sessile serrated lesions. I also lead large-scale population studies evaluating the internal and external exposome in risk of GI carcinogenesis and other diseases.

VDDRC-Related Training and Activities

Retreat Speaker

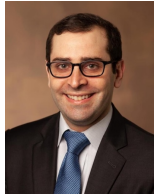
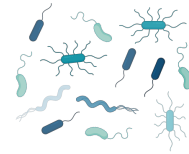
VDDRC Collaborations

I collaborate with VDDRC members Drs. Coffey, Goettel, Goldenring, Izzy, Lacy, Lau, Magnuson, Markham, Peek, Yu, Washington, and Zheng to study the effects of micronutrient-host interactions on the development of colorectal adenomas. A collaborative VDDRC publication is: Islam M, Yang Y, Simmons AJ, Shah VM, Musale KP, Xu Y, Tasneem N, Chen Z, Trinh LT, Molina P, Ramirez-Solano MA, Sadien ID, Dou J, Rolong A, Chen K, Magnuson MA, Rathmell JC, Macara IG, Winton DJ, Liu Q, Zafar H, Kalhor R, Church GM, **Shrubsole MJ**, Coffey RJ, Lau KS. Temporal recording of mammalian development and precancer. *Nature*. 2024;634(8036):1187-1195. PMID: PMC11525190.

Future VDDRC Core Use

We will continue to use the Translational Analysis Core for histologic analysis and the Biostatistical Component for our data analysis.

Member: Jeffrey Singer, MD, PhD
Rank: Postdoctoral Fellow
Department: Medicine
VDDRC Status: Associate Member
Research Group: GII



Rationale for VDDRC Membership

I am a Postdoctoral Fellow in the laboratory of Eric Skaar. My research focuses on mucosal immunology and host/microbe biology in the intestine and liver. One recent VDDRC-supported publication is: Yarosz EL, Kumar A, **Singer JD**, Chang CH. Cullin 3-mediated regulation of intracellular iron homeostasis promotes thymic invariant NKT cell maturation. *Immunohorizons*. 2023;7(3):235-242. PMID: PMC10122431

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
VDDRC P&F Award	Role of nutritional immunity in chronic liver disease	07/30/2026-06/30/2027	\$40,000

Summary of Digestive Disease Research

The primary focus of my research has been to understand why patients with decompensated liver disease are highly susceptible to infections, with particular interest in metal acquisition by *Klebsiella pneumoniae*.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I collaborate with Drs. Peek, Skaar, and Washington on projects related to metal acquisition and human gastrointestinal infections.

Future VDDRC Core Use

We will utilize the Cell Imaging and the Translational Analysis Cores to monitor and quantify inflammation in our animal models of infection, the MS/Omics Core for Imaging Mass Spectrometry, and the Flow Cytometry Core.

Member: Bhuminder Singh, PhD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My research is focused on receptor tyrosine kinase (RTK) signaling in human health and disease, with an emphasis on epidermal growth factor receptor (EGFR) signaling in colorectal carcinogenesis. We study response and resistance to anti-EGFR-directed therapies, including cetuximab. A recent VDDRC-related publication is: Jones VT, Graves-Deal R, Cao Z, Bogatcheva G, Ramirez MA, Harmych SJ, Higginbotham JN, Sharma V, Damalanka VC, Wahoski CC, Joshi N, Irudayam MJ, Roland JT, Ayers GD, Liu Q, Coffey RJ, Janetka JW, **Singh B**. Inhibition of autocrine HGF maturation overcomes cetuximab resistance in colorectal cancer. *Cell Mol Life Sci*. 2024 Jan 12;81(1):28. PMCID: PMC10784391.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
RSG-20-130-01-DDC	Overcoming a new mode of cetuximab resistance in colorectal cancer	02/01/2021-01/31/2027	\$165,000
5R01CA248505-05	Role of receptor tyrosine kinase cross-talk in colorectal cancer	05/12/2021-04/30/2027	\$251,496

Summary of Digestive Disease Research

Our laboratory has undertaken a comprehensive systematic analysis of trafficking for three of the seven EGFR ligands in polarized epithelial cells, which has opened up new areas of cell biological investigation. We have shown that spatial cues that regulate EGFR signaling are best appreciated in Transwell cultures and three-dimensional (3D) cultures (e.g., type I collagen and Matrigel™) compared with conventional 2D plastic cultures. Another key area of investigation in the laboratory is to study the mechanism of drug resistance using 3D culture systems of colorectal cancer (CRC) cells. Leveraging these models, our recent work published in *Communications Biology* utilizes 3D high-throughput screening to identify drugs that induce epithelial polarity and enhance chemotherapy response. Furthermore, we are actively expanding on novel mechanisms of targeted therapy resistance, with a manuscript currently under revision detailing how EGFR ectodomain mutations and ERBB2 signaling dynamics impact therapeutic efficacy of cetuximab in CRC.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Poster Judge
Retreat Speaker

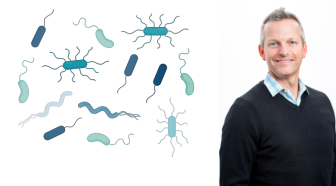
VDDRC Collaborations

I have ongoing collaborations with Drs. Coffey, Goldenring, Guo, Lau, Markham, Washington, and Williams. A representative collaborative publication is: Harmych SJ, Hasaka TP, Sievers CK, Kang SW, Ramirez MA, Jones VT, Zhao Z, Kovtun O, Wahoski CC, Liu Q, Lau KS, Coffey RJ, Bauer JA, **Singh B**. 3D collagen high-throughput screen identifies drugs that induce epithelial polarity and enhance chemotherapy response in colorectal cancer. *Commun Biol*. 2025;8(1):1261. PMCID: PMC12373842.

Future VDDRC Core Use

I will continue using the Cell Imaging, MS/Omics, and Translational Analysis Cores to analyze our novel 3D culture system of colorectal cancer cells, as well as the Biostatistical Component for data analysis.

Member: Eric P. Skaar, PhD, MPH
Rank: University Distinguished Professor, Vice Chair for Research,
 Director of the Division of Molecular Pathogenesis
Department: Pathology, Microbiology & Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I will serve as a VDDRC Member and Director of the VDDRC Flow Cytometry Core. My research program is focused on the battle for nutrients at the host-pathogen interface during infection. Research in my laboratory focuses on microbiology, immunity, and metal biology. More specifically, we are interested in the molecular intersection of nutrition and infectious diseases. An example of a VDDRC-related publication is: Pi H, Sun R, McBride JR, Kruse ARS, Gibson-Corley KN, Krystofiak ES, Nicholson MR, Spraggins JM, Zhou Q, **Skaar EP**. *Clostridioides difficile* ferrosome organelles combat nutritional immunity. *Nature*. 2023;623(7989):1009-1016. PMID: PMC10822667.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01AI073843-16	Pathobiology of heme inducible transporters in Gram positive pathogens	05/19/2021-04/30/2026	\$286,937
5R01AI178929-03	The role of the ZNG1 metallochaperone in the host response to infection	07/05/2023-06/30/2028	\$383,142
5R01AI138581-07	Molecular mapping of microbial communities at the host-pathogen interface by multi-modal 3-dimensional imaging mass spectrometry	07/02/2024-05/31/2029	\$526,889
4R01AI164587-04	Nutritional immunity and microbial competition during <i>Clostridioides difficile</i> infection	06/01/2025-05/31/2027	\$272,490

Summary of Digestive Disease Research

We have built a productive research program focused on the importance of nutrient metal to the pathogenesis of *C. difficile*, highlighted by the publication of several manuscripts on this topic. We have uncovered factors involved in nutrient metal acquisition in this organism, defined the impact of dietary metals on the outcome of *C. difficile* infection, and described factors that *C. difficile* employs to deal with metal stress. These recent discoveries underscore the impact of our research on digestive diseases and highlight our relevance to the Center application. We also focus on the pathogenesis of invasive *Staphylococcal* infections leading to abscesses in the liver and *Bacillus* infections, which lead to dysentery within the context of iron utilization, and this work is funded by the NIH.

VDDRC-Related Training and Activities

Director, VDDRC Flow Cytometry Core
 Director, collaborating VI4 Institute
 Pilot & Feasibility Award Recipient
 Retreat Speaker

VDDRC Collaborations

We collaborate extensively with numerous VDDRC members, including Drs. Algood, Gaddy, Lacy, Washington, Piazuelo, Peek, Cassat, Nicholson, and Byndloss, among many others. A collaborative VDDRC publication is: Munneke MJ, Yuan Y, Preisner EC, Shelton CD, Carroll DT, Kirchoff NS, Dickson KP, Cantu JO, Douglass MV, Calcutt MW, Gibson-Corley KN, Nicholson MR, Byndloss MX, Britton RA, de Crécy-Lagard V, **Skaar EP**. A thiouracil desulfurase protects *Clostridioides difficile* RNA from 4-thiouracil incorporation, providing a competitive advantage in the gut. *Cell Host Microbe*. 2025;33(4):573-588. PMID: PMC11985272.

Future VDDRC Core Use

We will utilize the Cell Imaging Core and the Translational Analysis Core to monitor and quantify inflammation in our animal models of *C. difficile* infection, the MS/Proteomics Core for Imaging Mass Spectrometry, and the Flow Cytometry Core.

Member: Nadia “Markie” Sneed, PhD, APRN, FPN-BC
Rank: Director, Whole Foods Research Lab
Department: Nursing
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

I have extensive clinical, academic, and research training in nutrition science, nursing, public health, and patient-centered outcomes research. My research focuses on identifying non-pharmacological nutritional interventions that utilize food as medicine to treat metabolic diseases such as obesity in at-risk families. I am also interested in studying the underlying mechanisms of how ultra-processed foods (UPFs) drive metabolic conditions like obesity by exploring their effects on the gut microbiome using omics-based approaches (e.g., metagenomics, metabolomics). A representative publication is: **Sneed NM**, Ukwuani S, Sommer EC, Samuels LR, Truesdale KP, Matheson D, Noerper TE, Barkin SL, Heerman WJ. Reliability and validity of assigning ultraprocessed food categories to 24-h dietary recall data. *Am J Clin Nutr.* 2023;117(1):182-190. PMID: PMC10196599.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
P30DK020593	Whole foods for teens: A pilot dietary intervention to reduce body adiposity in adolescents with obesity.	04/01/2025-03/30/2027	\$158,500

Summary of Digestive Disease Research:

The overarching theme of my research is the evaluation of whole foods–based dietary strategies to improve metabolic health across the lifespan without caloric restriction. Our lab conducts randomized controlled trials in adults and adolescents to examine how diet composition influences metabolic outcomes—specifically obesity. Through the *Whole Foods for Families* and *Whole Foods for Teens* programs, we integrate clinical, behavioral, and biologic measures—including body composition and gut microbiome profiling—to identify mechanisms linking diet to metabolic health. This work generates critical data to support the development of scalable, family-centered dietary interventions for obesity prevention.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I am a new member of the VDDRC and am currently working to establish collaborations with other VDDRC members, including Drs. Mashayekhi, Niswender, and Samuels.

Future VDDRC Core Use

I will utilize the Biostatistical Component for data analysis.

Member: Michelle Southard-Smith, PhD
Rank: Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My research focuses on visceral organ innervation with an emphasis on the enteric nervous system (ENS) that controls gastrointestinal motility, vascular perfusion, and release of neuroendocrine peptides in the gut. The overall theme of my research has been to define genes and developmental processes that contribute to GI dysmotility syndromes such as Hirschsprung disease and chronic intestinal pseudo-obstruction. A representative VDDRC publication is: Benthall JT, Avila JA, Smith JR, **Southard-Smith EM**. Combinatorial multiomic analysis from a pedigree of *Sox10^{Dom}* Hirschsprung mice implicates *Dach1* as a modifier of enteric nervous system development. *bioRxiv*. 2025:2025.11.02.686123. PMCID: PMC12637471.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK127178-04 A1	Mechanisms of enteric neuron diversification	07/01/2026-06/30/2031	Pending

Summary of Digestive Disease Research

My group investigates developmental processes that regulate lineage divergence of neural crest derivatives in visceral organs, focusing primarily on the enteric nervous system (ENS). We have demonstrated that ENS mutations, which produce aganglionosis of the hindgut, also alter the balance of neuronal subtypes in the proximal small intestine. These findings led clinical gastroenterologists to recognize that continued GI dysmotility in Hirschsprung patients after surgery is due to abnormal enteric ganglia in the proximal ganglionated small intestine and provide the incentive for our team's interest in defining processes that regulate the diversity of discrete neuron types in the ENS. We have used cutting-edge single-nucleus RNA-seq to map the spectrum and spatial distribution of enteric neuron subtypes in both mouse and human tissue.

VDDRC-Related Training and Activities

Co-leader, VDDRC Homeostasis, Regeneration, and Pathophysiology (HRP) Research Interest Group
Pilot & Feasibility Award Recipient
Retreat Speaker

VDDRC Collaborations

We collaborate with several VDDRC members, including Drs. Goldenring, Coffey, and Lau, Core Leader Dave Flaherty, and Core Leader Jenny Schafer. A representative VDDRC collaborative publication is: Avila JA, Benthall JT, Schafer JC, Flaherty DK, **Southard-Smith EM**. Single-cell profiling in the *Sox10Dom* Hirschsprung mouse implicates *hox* genes in enteric neuron trajectory allocation. *Cell Mol Gastroenterol Hepatol*. 2025;19(12):101590. PMCID: PMC12494863.

Future VDDRC Core Use

We will use the Cell Imaging Core frequently to track migrating neural crest cells in fetal bowel, as well as for analysis of specific lineages in the postnatal ENS by multispectral immunohistochemical labeling and confocal microscopy. The Flow Cytometry Core will be used routinely to isolate wild-type and mutant enteric neural crest cells at multiple stages of development as well as for capture of enteric neuronal nuclei for single-nucleus RNA-seq, ATAC-Seq, and integrated multiomics analysis.

Member: Ashley Spann, MD, MSACI
Rank: Assistant Professor
Department: Medicine and Biomedical Informatics
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

I am currently a board-certified internal medicine physician pursuing combined fellowship training in Clinical Informatics and Gastroenterology, Hepatology and Nutrition at Vanderbilt. My goals are to become dually equipped in the application of technology for patients affected by GI illness and liver disease and to impact patient care and clinical research within the field in a novel way that has yet to be done. Particular informatics interests include the use of predictive modeling for improving outcomes and management of patients with end-stage liver disease, and the integration of these models for use in clinical care through clinical decision support tools. A representative publication is: **Spann A**, Bishop KM, Weitkamp AO, Stenner SP, Nelson SD, Izzy M. Clinical decision support automates care gap detection among primary care patients with nonalcoholic fatty liver disease. *Hepatol Commun.* 2023;7(3):e0035. PMCID: PMC9915945.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
American Association for the Study of Liver Diseases	Harold Amos Medical Faculty Development Program Award	07/01/2024-06/30/2028	\$105,000
PCORI Award	Comparing low-touch and high-touch multimodal interventions for chronic pain in patients with cirrhosis	04/01/2026-03/31/2032	\$75,000

Summary of Digestive Disease Research

I am an academic hepatologist with particular interests in transplant hepatology within an active, practical research program focused on using machine learning methods and health system tools to not only advance care for the treatment of patients with end-stage liver disease, but also to be able to identify patients at risk of disease progression to trigger preventative measures for these patients. Other informatics interests include large-scale data assessment for modeling that could be potentially impactful for liver transplantation and organ allocation.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

Although I am a new VDDRC member, I actively collaborate with several VDDRC members, including Drs. Brittian, Hawkins, and Izzy. A representative collaborative publication is: **Spann A**, Bishop K, Marbach S, Ji X, Slaughter J, Weitkamp A, Stenner S, Nelson S, Lopez C, Theobald C, Izzy M. Electronic decision aids enhance management of primary care patients with steatotic liver disease: Proof of concept pilot study. *Hepatol Commun.* 2025;9(9):e0794. PMCID: PMC12412744.

Future VDDRC Core Use

I will utilize the Biostatistical Component for data analysis.

PI Name: Marcus C.B. Tan, MBBS, FACS
Rank: Associate Professor
Department: Surgery
VDDRC Status: Associate Member
Research Group: HRP



Rationale for VDDRC Membership

My long-term interest is centered on the mechanistic understanding and treatment of pancreatic lesions. Specifically, my research is focused on the biology of pre-malignant pancreatic cysts, which was funded as a VDDRC Pilot and Feasibility Project. A representative VDDRC publication is: Quoc-Huy Trinh V, Ankenbauer KE, Torbit SM, Taranto CP, Liu J, Batardiere M, Kumar B, Maurer HC, Revetta F, Chen Z, Kruse ARS, Judd AM, Copeland C, Wong J, Ben-Levy O, Jarvis B, Brown M, Brown JW, Das K, Makino Y, Spraggins JM, Lau KS, Azadi P, Maitra A, **Tan MCB**, DelGiorno KE. Mutant GNAS drives a pyloric metaplasia with tumor suppressive glycans in intraductal papillary mucinous neoplasia. *Cell Rep.* 2025;44(12):116684. PMID: PMC12860476.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
UG1CA189828	Comparing the clinical impact of pancreatic cyst surveillance programs	08/31/2020-12/31/2028	Not PI or MPI
R01DK145538-01A1	Tuft cells resolve pancreatic injury through a Type 2 Immune circuit	07/01/2026-06/30/2031	Pending

Summary of Digestive Disease Research

Our group believes that a better understanding of the mechanisms underlying the differentiation and growth of pancreatic cysts will improve identification of lesions at higher risk of malignant transformation, thereby improving the selection of patients for curative surgery. Towards this end, we are currently defining tumor-nerve interactions that drive the development of pancreatic cystic lesions, work that was funded by the VDDRC Pilot and Feasibility Component.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

Although I am a relatively new member of the VDDRC, my previous participation in the Academy of Investigators sparked several new collaborations with, among others, Drs. Arrojo e Drigo, Choi, DelGiorno, and Lau. An example of a collaborative VDDRC publication is: Won Y, Jang B, Lee SH, Reyzer ML, Presentation KS, Kim H, Caldwell B, Zhang C, Lee HS, Lee C, Trinh VQ, **Tan MCB**, Kim K, Caprioli RM, Choi E. Oncogenic fatty acid metabolism rewires energy supply chain in gastric carcinogenesis. *Gastroenterology.* 2024;166(5):772-786. PMID: PMC11040571.

Future VDDRC Core Use

We will use the Translational Analysis Core, Cell Imaging Core, and the Biostatistics Component for our VDDRC Pilot-initiated work.

Member: Matthew J. Tyska, PhD
Rank: Professor
Department: Cell and Developmental Biology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am the Director of the VDDRC Cell Imaging Core and a VDDRC member. The goal of my laboratory is to understand how transporting intestinal epithelial cells assemble a functional apical surface. An example of a VDDRC-supported publication is: Fitz GN, Weck ML, Bodnya C, Perkins OL, **Tyska MJ**. Protrusion growth driven by myosin-generated force. *Dev Cell*. 2023;58(1):18-33. PMCID: PMC9940483.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK095811-11	Molecular basis of brush border assembly	09/01/2013-11/30/2028	\$296,249
5R01DK111949-09	Role of actin bundlers during enterocyte differentiation	02/01/2017-05/31/2027	\$284,364
5R01DK125546-04	Myosin-2 function in the enterocyte terminal web	03/15/2021-02/28/2026	\$211,200

Summary of Digestive Disease Research

Our current studies are investigating how enterocytes assemble an apical surface, how the brush border contributes to maintaining physiological homeostasis, and how perturbation of this interface by inherited or infectious causes leads to human disease. Over the past decade, our laboratory has made several fundamental and field-leading discoveries on the assembly and function of the brush border interface. During this time, our research program has evolved an approach that combines elements of biochemistry, physiology, biophysics, and cell biology. Although light and electron microscopy serve as our principal discovery tools, our investigations are decidedly broad in scope, ranging from physiological experiments in mouse model systems to optical trap-based measurements on single cells to single-molecule imaging in live cells. Importantly, the critical physiological significance of the brush border indicates that many of our findings hold direct relevance for understanding human intestinal disease.

VDDRC-Related Training and Activities

Director, VDDRC Cell Imaging Core
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

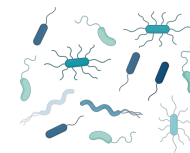
VDDRC Collaborations

We maintain active and ongoing collaborations with VDDRC members, including Drs. Algood, Coffey, Goldenring, Iverson, Kaji, Koethe, Lacy, Lau, Mahadevan-Jansen, Meenderink, Wanjalla, and J. Wilson. One example of a VDDRC collaborative publication is: Cencer CS, Silverman JB, Meenderink LM, Krystofiak ES, Millis BA, **Tyska MJ**. Adhesion-based capture stabilizes nascent microvilli at epithelial cell junctions. *Dev Cell*. 2023;58(20):2048-2062. PMCID: PMC10615885.

Future VDDRC Core Use

We will continue to use the Cell Imaging, Flow Cytometry, MS/Omics Core, and the Translational Analysis Cores for these studies to define molecular mechanisms underpinning the development of intestinal epithelial apical surfaces.

PI Name: Kasey C. Vickers, PhD
Rank: Associate Professor
Department: Medicine, Molecular Physiology and Biophysics, and Pathology, Microbiology and Immunology
VDDRC Status: Associate Member
Research Group: HRP



Rationale for VDDRC Membership

The global focus of my research program is to investigate the role(s) of cell-free RNA in intercellular communication and gene regulation in inflammation and lipid metabolism. We have made major contributions to fundamental understanding of extracellular RNA carriers, including lipoproteins, ribonucleoproteins, and non-vesicle extracellular particles. One recent VDDRC-related publication is: Michell DL, Massick C, Koya KS, Cavnar AB, Semler EM, Raby C, Gibson BHY, Moore-Lotridge SN, Zhu W, Ramirez-Solano M, Sheng Q, Allen RM, Linton MF, Schoenecker JG, **Vickers KC**. Plasminogen as a ribonucleoprotein: regulatory small RNA cargo modulates fibrinolysis and inflammation. *Blood*. 2025;146(15):1850-1861. PMID: PMC12978156.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
2P01CA229123-06A1	Roles for supermeres in CRC progression	01/20/2020-05/31/2031	Not PI or MPI
5R35CA197570-09	Early to late events in colorectal neoplasia: Basic biology to clinical implementation	04/01/2017-07/31/2031	Not PI or MPI

Summary of Digestive Disease Research

We aim to gain a fundamental understanding of cell-free small RNAs (sRNAs) and their regulators within cell-to-cell communication networks to predict, prevent, and treat metabolic disease. Our laboratory studies the mechanisms and consequences of cell-free sRNA secretion, transport, and biological functions in intestinal inflammation and colorectal carcinogenesis. We have made major contributions to understanding the impact of sRNAs on cholesterol and lipid metabolism. Early career activities in the laboratory were focused on alternative functions of lipoproteins, microRNAs, and gene regulatory modules in intestinal inflammation and lipid metabolism. As an independent investigator, my team has demonstrated that lipoproteins and other protein carriers deliver functional host and microbial small RNAs (sRNA) to recipient cells where they regulate target gene expression and inflammation. In the last decade, we also defined how this novel endocrine-like pathway is altered in colorectal cancer (CRC), inflammatory bowel disease, and other diseases. Recently, we discovered that bacterial sRNA cargo on circulating LDL particles collects microbial sRNAs at the intestinal mucosa and induces inflammatory macrophages and cytokine secretion within atherosclerotic lesions. Currently, our group is interested in defining the functional role of post-transcriptional RNA modifications on cell-free sRNAs in disease, specifically related to immunological memory of past insults (innate immune training) and intestinal inflammation. Our laboratory is well-suited for both wet and dry work, as we routinely perform and analyze high-end omics studies, including demethylation-based high-throughput sRNA sequencing (sRNA seq), bulk RNA sequencing, single-cell RNA sequencing, whole genome DNA sequencing, direct nanopore sequencing, and mass spectrometry-based proteomics, lipidomics, and epitranscriptomics. Our research program has opened new fields of study for cell-free sRNA research, and in the course, developed new tools and concepts that can be extended to other inflammatory diseases, including intestinal inflammation and carcinogenesis.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

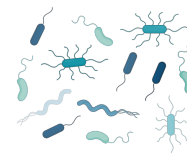
I have active collaborations with numerous VDDRC members, including Drs. Algood, Brown, Coffey, Philip, and J. Wilson. A recent representative publication of our collaboration within the VDDRC is: Tutanov OS, Massick C, Ramirez M, Higginbotham JN, Jimenez L, Castleberry M, Cao Z, John E, Hamilton MS, Zhang Q, Jeppesen DK,

Michell DL, Glass SE, Patel P, Rose KL, Krystofiak E, Chen HC, Sheng Q, Liu Q, Patton JG, Weaver AM, Franklin JL, **Vickers KC**, Coffey RJ. A comprehensive analysis of supermere, exomere, and extracellular vesicle isolation and cargo in colorectal cancer. *Cell Rep.* 2025;44(10):116287. PMCID: PMC12632813.

Future VDDRC Core Use

We anticipate using the MS/Omics, Cell Imaging, and Flow Cytometry Cores for comprehensive analysis of extracellular vesicles, lipoproteins, ribonucleoproteins, and NVEPs within digestive disease research projects.

Member: Celestine Wanjalla, MD, PhD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: GII



Rationale for VDDRC Membership

Persistent exposure to HIV antigens and co-infection with chronic herpes viruses such as CMV or hepatitis B/C contribute to chronic inflammation in persons living with HIV (PLWH) and appear to be important in metabolic dysfunction. My laboratory has adopted a multidisciplinary approach to 1) define virus-specific innate and adaptive immune cells in the peripheral blood of persons with metabolic dysfunction using existing multiparameter flow cytometry and single-cell techniques, 2) optimize techniques to better understand the antigenic drivers of the adaptive immune response at the tissue level, and 3) apply/implement changes in metabolic disease risk assessment and therapeutic approaches to improve outcomes in patients. A representative VDDRC publication is: Obare LM, Simmons J, Oakes J, Zhang X, Nochowicz C, Priest S, Bailin SS, Warren CM, Mashayekhi M, Beasley HK, Shao J, Meenderink LM, Sheng Q, Stolze J, Gangula R, Absi T, Ru Su Y, Neikirk K, Chopra A, Gabriel CL, Temu T, Pakala S, Wilfong EM, Gianella S, Phillips EJ, Harrison DG, Hinton A, Kalams SA, Kirabo A, Mallal SA, Koethe JR, **Wanjalla CN**. CD3+ T-cell: CD14+ monocyte complexes are dynamic and increased with HIV and glucose intolerance. *J Immunol*. 2025;214(3):516-531. PMID: PMC11952877.

Summary of Digestive Disease Research

The HIV reservoir and other co-infections, such as cytomegalovirus (CMV), promote chronic inflammation, which further contributes to accelerated aging. Our overarching hypothesis is that chronic inflammation accelerates aging-related diseases such as metabolic dysfunction in people living with HIV, even in the absence of detectable viral load. Overall, our research aims to identify mechanisms driving aging in people living with HIV, ultimately paving the way for targeted therapies that could slow down aging and reduce comorbidities in this population. Our findings will inform the development of targeted anti-inflammatory therapies, potentially transforming the management of aging-related comorbidities.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Retreat Speaker

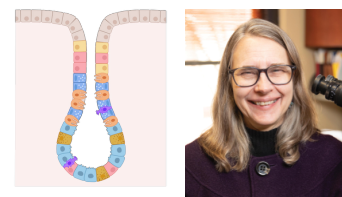
VDDRC Collaborations

I have established collaborations with several VDDRC members, including Drs. Algoood, Bailin, Gabriel, Koethe, Lau, Mashayekhi, Meenderink, and Tyska. A representative collaborative publication is: Obare LM, Priest S, Ismail A, Mashayekhi M, Zhang X, Stolze LK, Sheng Q, Nthenge K, Vue Z, Neikirk K, Beasley HK, Gabriel C, Temu T, Gianella S, Mallal SA, Koethe JR, Hinton A Jr, Bailin SS, **Wanjalla CN**. Cytokine and chemokine receptor profiles in adipose tissue vasculature unravel endothelial cell responses in HIV. *J Cell Physiol*. 2024;239(11):e31415. PMID: PMC12694733.

Future VDDRC Core Use

I will utilize the Flow Cytometry Core and the Biostatistical Component for data analysis.

PI Name: Mary Kay Washington, MD, PhD
Rank: Professor
Department: Pathology, Microbiology and Immunology
VDDRC Status: Associate Member
Research Group: HRP



Rationale for VDDRC Membership

My role in the VDDRC is to serve as the Director of the Translational Analysis Core. My research is focused on the pathology of inflammatory and pre-malignant diseases in the GI tract and the histopathologic assessment of mouse models of GI disease. One of my VDDRC-related publications is: Spiga L, Fansler RT, Wu Y, Grote A, Langford-Butler M, Miller AK, Neal M, Hale OF, Singla D, Calcutt MW, Rose AE, Bresson MM, Schrimpe-Rutledge AC, Berdy B, Codreanu SG, Washington MK, Bratton BP, Sherrod SD, McLean JA, Zengler K, Sears CL, Behringer MG, Gnirke A, Tao L, Livny J, Olivares-Villagómez D, Earl AM, Zhu W. An anaerobic pathogen rewires host metabolism to fuel oxidative growth in the inflamed gut. *Cell*. 2026 Apr 30:S0092-8674(26)00401-0. Online ahead of print. PMID: PMC13185528.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5P01CA116087-19	<i>H. pylori</i> -induced inflammation and gastric cancer	01/01/2009-02/28/2029	Not PI or MPI
5R01DK135950-03	<i>In vivo</i> MR characterization of pathological changes in liver microstructures	02/01/2024-01/31/2028	Not PI or MPI
5R35CA197570-09	Early to late events in colorectal neoplasia: Basic biology to clinical implementation	04/01/2017-07/31/2031	Not PI or MPI
4U01CA294527-02	A multimodal 3D atlas of colorectal cancer across ages of onset	09/01/2024-08/31/2029	Not PI or MPI
Congressionally Directed Medical Research Programs HT94252510915	Targeting the DPEP1-neutrophil axis in microsatellite stable colorectal cancer	08/15/2025-08/14/2027	Not PI or MPI

Summary of Digestive Disease Research

I am an experienced diagnostic gastrointestinal pathologist with extensive expertise in collaborative projects, administration of tissue resources, and interpretation of histopathology of animal models of human disease. I have led several consortia designed to define nomenclature, features, and characteristics of pre-malignant lesions that develop in the GI tract of rodent models.

VDDRC-Related Training and Activities

Director, VDDRC Translational Analysis Core
Retreat Poster Judge
Retreat Speaker

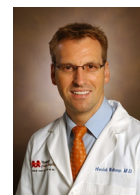
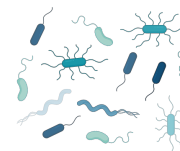
VDDRC Collaborations

I have long-standing collaborative projects with numerous VDDRC members (>40), including Drs. Algood, Choksi, Coburn, Coffey, Cover, Flynn, Goettel, Lacy, Lau, E. Lee, Y. Lee, Markham, Olivares-Villagomez, Peek, Piazuelo, Williams, K. Wilson, Yan, and Zhu. One collaborative VDDRC publication is Heiser CN, Simmons AJ, Revetta F, McKinley ET, Ramirez-Solano MA, Wang J, Kaur H, Shao J, Ayers GD, Wang Y, Glass SE, Tasneem N, Chen Z, Qin Y, Kim W, Rolong A, Chen B, Vega PN, Drewes JL, Markham NO, Saleh N, Nikolos F, Vandekar S, Jones AL, **Washington MK**, Roland JT, Chan KS, Schürpf T, Sears CL, Liu Q, Shrubsole MJ, Coffey RJ, Lau KS. Molecular cartography uncovers evolutionary and microenvironmental dynamics in sporadic colorectal tumors. *Cell*. 2023;186(25):5620-5637. PMID: PMC10756562.

Future VDDRC Core Use

I will continue to use the Translational Analysis and Cell Imaging Cores for our collaborative studies using rodent models of pre-neoplasia and Imaging Mass Spectrometry within the MS/Omics Core.

Member: Jörn-Hendrik Weitkamp, MD
Rank: Professor
Department: Pediatrics
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

As the Director for Patient-Oriented Research in Neonatology, I oversee numerous NIH-funded and industry-sponsored clinical trials and translational studies in neonatal gut and liver health. My research focuses on the development of mucosal immune regulation in preterm infants and the pathogenesis of necrotizing enterocolitis (NEC), and I am well-versed in the specific infectious and inflammatory complications of the human intestine. One VDDRC-supported publication is: Ocampo-Chih C, Hendricks H, Weitkamp S, Gowda NS, Singh H, Banerjee R, Rajagopala SV, **Weitkamp JH**. Impact of donor human milk pasteurization methods on the gut microbiome of preterm infants. *Pediatr Res*. 2025. doi: 10.1038/s41390-025-04386-2. PMID: 40957978.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01DK135567-03	Assessing variation in fecal bile acids as a novel early indicator of necrotizing enterocolitis	03/15/2024-01/31/2029	\$92,506

Summary of Digestive Disease Research

I have conducted several translational research studies that involved fresh intestinal tissue samples. These studies have focused on the phenotype and function of (1) intestinal FOXP3⁺ T regulatory cells, (2) small intestinal intraepithelial TCR $\gamma\delta$ lymphocytes, (3) CD8 $\alpha\alpha$ ⁺ innate-type lymphocytes in the intestinal epithelium, and (4) Osteopontin and iCD8 α cells which promote intestinal intraepithelial lymphocyte homeostasis. I am conducting several clinical trials focused on (1) non-invasive detection of neonatal jaundice, (2) management of neonatal cholestasis, and (3) biomarker for necrotizing enterocolitis.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

I have ongoing collaborations with Drs. Algood, Markham, Olivares-Villagómez, Piazuelo, Schneider, Washington, Williams, K. Wilson, and Yan. One publication resulting from VDDRC collaborations is: McClanahan KG, Reese J, **Weitkamp JH**, Olivares-Villagómez D. Effects of pasteurization on osteopontin concentrations in human breastmilk. *Pediatr Res*. 2024;95(3):641-646. PMID: 37833533.

Future VDDRC Core Use

We will continue to use the Biostatistical Component in our ongoing research projects focused on defining the role of the microbiome in NEC.

Member: Chris Williams, MD, PhD
Rank: Professor and Associate Dean for Physician Scientist Education and Training
Department: Medicine
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am an Associate Dean for Physician-Scientist Education and Training and Professor of Medicine, Gastroenterology, and current Director of the Medical Scientist Training Program (MSTP) at Vanderbilt University. My thesis work was focused on inflammatory carcinogenesis under the mentorship of Dr. Raymond DuBois, and my postdoctoral fellowship in Gastroenterology provided me with training in epigenetic and chromosomal mechanisms of transcriptional regulation under the mentoring of previous VDDRC member Dr. Scott Hiebert. My research program was initially funded by a VDDRC Pilot and Feasibility Award and is focused on intestinal injury response/repair programs to understand how these epithelial integrity programs are perturbed in the pathogenesis of IBD and, more importantly, in the progression to carcinogenesis, with the goal of identifying novel therapeutic targets or biomarkers. A representative publication is: Short SP, Brown RE, Chen Z, Pilat JM, McElligott BA, Meenderink LM, Bickart AC, Blunt KM, Jacobse J, Wang J, Simmons AJ, Xu Y, Yang Y, Parang B, Choksi YA, Goettel JA, Lau KS, Hiebert SW, **Williams CS**. MTGR1 is required to maintain small intestinal stem cell populations. *Cell Death Differ.* 2024;31(9):1170-1183. PMID: PMC11369156.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK131810-02	MTGs in intestinal biology and injury responses	07/01/2024-05/31/2028	\$402,759
GI SPORE in Gastrointestinal Cancer Development Research Program	Role of secreted Selenoprotein P in colon cancer	07/31/2026-06/30/2027	GI SPORE

Summary of Digestive Disease Research

My research program is focused on intestinal injury response/repair programs with the goal of understanding how these epithelial integrity programs are perturbed in the pathogenesis of IBD and colitis-associated carcinoma in order to identify novel therapeutic targets. I have expertise in animal models of colitis, inflammation, and signal transduction.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

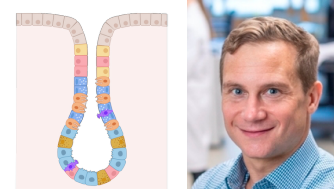
VDDRC Collaborations

With Drs. Coburn, Piazuolo, and K. Wilson, I have demonstrated increased expression of spermine oxidase in patients with ulcerative colitis. In collaboration with Drs. Wilson and Washington, we demonstrated that selenoprotein P (SEPP1) influences inflammatory tumorigenesis by affecting genomic stability, the inflammatory microenvironment, and epithelial stem cell functions. I have several additional collaborations with Drs. Cassat, Choksi, Goettel, Lau, E. Lee, Meenderink, Peek, Singh, Yan, and Zhu. A representative VDDRC collaborative publication is: Pilat JM, Brown RE, Chen Z, Berle NJ, Othon AP, Washington MK, Anant SA, Kurokawa S, Ng VH, Thompson JJ, Jacobse J, Goettel JA, Lee E, Choksi YA, Lau KS, Short SP, **Williams CS**. SELENOP modifies sporadic colorectal carcinogenesis and WNT signaling activity through LRP5/6 interactions. *J Clin Invest.* 2023 Jul 3;133(13):e165988. PMID: PMC10313376.

Future VDDRC Core Use

We have and will continue to use the Flow Cytometry, Cell Imaging, MS/Omics, and Translational Analysis Cores in our research projects, specifically to isolate and localize progenitor cells that influence the phenotypes we have observed to be regulated by BVES and SEPP1.

Member: John T. Wilson, PhD
Rank: Professor
Department: Chemical and Biomolecular Engineering;
Pathology, Microbiology and Immunology; Biomedical Engineering
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My laboratory works at the interface of engineering and immunology to improve human health. Our mission is to cure, detect, treat, and prevent a myriad of diseases through the design of novel molecularly engineered materials that interrogate the immune system in defined and specific manners. We are guided by the principle that the immune system must dictate therapeutic design requirements, and we turn to nature for inspiration to engineer highly modular and tunable materials to accommodate these criteria. By bringing together expertise in colloid and surface engineering, advanced polymerization techniques, cellular engineering, and drug delivery, we are developing innovative therapeutic approaches that specifically target and tightly regulate the delivery of immunomodulatory cues to the organs, cells, and intracellular pathways of the immune system. By doing so, we are working towards advancement in the following areas: molecularly engineered materials for biomedical applications, intracellular delivery of antigens and molecular adjuvants, engineering of vaccine colloids and surfaces and immunotherapy. A representative publication is: Kimmel BR, Arora K, Chada NC, Bharti V, Kwiatkowski AJ, Finkelstein JE, Hanna A, Arner EN, Sheehy TL, Pastora LE, Yang J, Pagendarm HM, Stone PT, Hargrove-Wiley E, Taylor BC, Hubert LA, Fingleton BM, Gibson-Corley KN, May JC, McLean JA, Rathmell JC, Richmond A, Rathmell WK, Balko JM, **Wilson JT**. Potentiating cancer immunotherapies with modular albumin-hitchhiking nanobody-STING agonist conjugates. *Nat Biomed Eng*. 2025;9(10):1719-1739. PMCID: PMC12532571.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01EB033822-04	RIG-I activating nanoparticles for immunopotential	09/30/2022-06/30/2027	\$423,738

Summary of Digestive Disease Research

We have several projects of relevance to digestive disease research. First, a goal of many of our projects is to develop new platforms for immunotherapy, including systems for more efficient delivery of innate immune agonists of the STING and RIG-I pathways, as well as next-generation vaccines. This work is highly relevant to GI-related diseases, and we have tested many of our platforms in colorectal carcinogenesis models. Second, we are investigating the role of physiological heat on T cells, with a particular emphasis on regulatory T cells (Tregs), finding that elevated temperatures activate DNA-sensing pathways that destabilize Treg function and immunosuppressive capacity. This project has potential implications for understanding immune dysfunction and homeostasis in the setting of digestive diseases. Finally, we have several projects focused on inhibiting inflammatory or autoimmune responses, including the use of stem cell-derived extracellular vesicles to induce antigen-specific tolerance, with potential applications for the treatment of Crohn's disease.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient

VDDRC Collaborations

Although I am a new member of the VDDRC, we have already established collaborations with VDDRC members, including Drs. Peek, Tyska, and Vickers. A representative VDDRC collaborative publication is: Arora K, Sheehy TL, Schulman JA, Loken JR, Lehmann Z, Kimmel BR, McAtee C, Bharti V, Stone PT, Weaver AM, Tyska M, Pathak RK, **Wilson JT**. Macromolecular diamidobenzimidazole conjugates can activate stimulator of interferon genes. *J Am Chem Soc*. 2025;147(38):35149-35163. PMCID: PMC12464991.

Future VDDRC Core Use

I will utilize the Cell Imaging, Flow Cytometry, MS/Omics Core, and the Biostatistical Component for data analysis.

Member: Keith T. Wilson, MD
Rank: Professor
Department: Medicine, Pathology, Microbiology and Immunology, and Cancer Biology
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

I am an Associate Director of the VDDRC and Director of the Pilot and Feasibility Program. I have investigated GI immunology, inflammation, and associated carcinogenesis for 30 years. A representative publication is: Gobert AP, Smith TM, Latour YL, Asim M, Barry DP, Allaman MM, Williams KJ, McNamara KM, Delgado AG, Short SP, Mirmira RG, Rose KL, Schey KL, Zagol-Ikapitte I, Coleman JS, Boutaud O, Zhao S, Piazuelo MB, Washington MK, Coburn LA, **Wilson KT**. Hypusination maintains intestinal homeostasis and prevents colitis and carcinogenesis by enhancing aldehyde detoxification. *Gastroenterology*. 2023;165(3):656-669. PMID: PMC10527201.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5I01CX002473-03	BCCMA: Targeting gut-microbiome in Veterans deployment related gastrointestinal and liver diseases: Dysbiosis, PTSD, and epithelial and immune biology in inflammatory bowel disease in Veterans	07/01/2023-06/30/2027	\$299,417
2I01CX002171-06	Dysregulated polyamine metabolism in <i>H. pylori</i> -associated gastric inflammation and disease progression	04/01/2025-03/31/2029	\$300,000
1R21AI196953-01	Inhibitors of the reverse transsulfuration pathway as a new treatment for <i>Helicobacter pylori</i> infection	04/01/2026-03/31/2028	\$275,000
5P01CA116087-19	Polyamines and electrophiles in gastric cancer	01/01/2009-02/28/2029	Listed under Contact PI

Summary of Digestive Disease Research

My laboratory has expertise in the assessment of inflammatory processes and oxidative stress-induced DNA damage; this includes molecular events in the inflammation-to-cancer sequence. We have focused extensively on gastric and colorectal carcinogenesis using a variety of innovative models with human validation.

VDDRC-Related Training and Activities

Associate Director, VDDRC
Director, Pilot & Feasibility Program
Retreat Speaker

VDDRC Collaborations

I have collaborated extensively with many members of the VDDRC, including Drs. Peek, Coburn, Schneider, Olivares-Villagomez, Byndloss, Cassat, Piazuelo, Washington, Yan, Algood, Goettel, Choksi, Markham, and Lau. A recent collaborative publication is: Latour YL, Allaman MM, Barry DP, Smith TM, Williams KJ, McNamara KM, Jacobse J, Goettel JA, Delgado AG, Piazuelo MB, Zhao S, Gobert AP, **Wilson KT**. Epithelial talin-1 protects mice from *Citrobacter rodentium*-induced colitis by restricting bacterial crypt intrusion and enhancing t cell immunity. *Gut Microbes*. 2023;15(1):2192623. PMID: PMC10038039.

Future VDDRC Core Use

We will continue to use the MS/Omics Core to conduct metabolomics and iTRAQ experiments on *H. pylori*-infected tissues; the Cell Imaging Core for *H. pylori* imaging, for assessing the interaction of *C. rodentium* with colonic epithelial cells and for multi-color analysis of macrophage markers; the Flow Cytometry Core for isolation of single cells; and the Tissue Morphology Service within the Translational Analysis Core for our mouse colitis models.

Member: Nathan Winn, PhD
Rank: Assistant Professor
Department: Medicine
VDDRC Status: Associate Member
Research Group: OMN



Rationale for VDDRC Membership

My research has focused on understanding the physiological and molecular links between immunometabolism in adipose tissue and metabolic disease. We leverage a combination of transgenic mouse models and surgical manipulations to obtain vascular access for determination of glucose and lipid fluxes. We have developed novel mouse models of yo-yo dietary or 'weight cycling' to study adaptive mechanisms of weight regain on metabolism. Indeed, the objective of my current research is to define the underlying mechanisms resulting in diminished capacity to adapt to weight regain. A representative VDDRC publication is: Cottam MA, Caslin HL, **Winn NC**, Hasty AH. Multiomics reveals persistence of obesity-associated immune cell phenotypes in adipose tissue during weight loss and weight regain in mice. *Nat Commun.* 2022 May 26;13(1):2950. PMCID: PMC9135744.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5K01DK136926-04	Uncovering mechanisms of pancreatic adaptability to weight cycling	04/28/2025-07/31/2028	\$135,518
1R03DK149527-01	Integrin regulation of metabolism	07/01/2026-06/30/2027	Pending

Summary of Digestive Disease Research

The majority of individuals who lose weight regain the weight within 1-5 years. This 'weight cycling' further increases the risk of metabolic disease compared to weight maintenance. Our group developed a mouse model of weight cycling to uncover mechanisms by which weight regain poses additional risk of metabolic disease. We demonstrated that weight-cycled diet-induced obese (WC-DIO) animals have worse metabolism than equally obese mice that have not been weight-cycled. The study of weight cycling is practical and clinically relevant. Despite the success of contemporary weight loss medicines, adherence to these drugs is <50% after a year of treatment, resulting in rapid weight regain. These clinical and real-world findings of weight rebound underscore the impetus for unraveling the mechanisms by which weight cycling increases metabolic disease risk.

VDDRC-Related Training and Activities

Academy of Investigators Member
Pilot & Feasibility Award Recipient
Young Investigator Award
Retreat Speaker

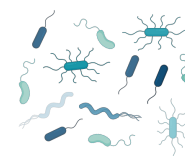
VDDRC Collaborations

I have established collaborations with other VDDRC members, including Drs. Arrojo e Drigo, Ayala, Flynn, Mashayekhi, Skaar, and Wanjalla. A representative collaborative publication is: Murdoch CC, Weiss A, Enriquez KT, Traina KA, Drury SL, **Winn NC**, Lantier LL, Skaar EP. Severe dietary zinc deficiency does not significantly alter energy balance in adult mice. *J Nutr Metab.* 2025;2025:6911386. PMCID: PMC12401606.

Future VDDRC Core Use

Our usage of the Translational Analysis, Cell Imaging, and the MS/Omics Core will increase due to the integrative nature of our studies.

Member: Fang Yan, MD, PhD
Rank: Professor
Department: Pediatrics
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I have a career-long research interest in investigating signaling mechanisms in intestinal epithelial cells and in macrophages as a means toward understanding the pathogenesis of inflammatory bowel disease and seeking potential treatment approaches. One VDDRC-supported publication is: Schlich KM, Buendia MA, Kaur H, Choksi YA, Washington MK, Codreanu GS, Sherrod SD, McLean JA, Peek RM Jr, Acra SA, Townsend SD, **Yan F**. A human milk oligosaccharide prevents intestinal inflammation in adulthood via modulating gut microbial metabolism. *mBio*. 2024;15(4):e0029824. PMID: PMC11005405.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01DK136893-02	Mechanisms by which human milk-derived oligosaccharides protect intestinal barrier and attenuate inflammation	05/15/2024-03/31/2028	\$317,759
1R01DK141070-01A1	Mechanisms underlying the functional regulation of the gut microbiota by intestinal epithelial cells to maintaining intestinal homeostasis	09/01/2025-06/30/2030	\$249,752

Summary of Digestive Disease Research

Our research goal to develop novel therapeutic strategies for inflammatory bowel disease has been fulfilled by several aspects of research. We study the mutualism between the gut microbiota and the host for developing potential microbiota-targeting therapy. We have identified a functional factor of probiotic bacteria, p40, that regulates intestinal homeostasis. Regarding the impact of the host on the function of the gut microbiota, our research has elucidated a previously unrecognized function of intestinal epithelial cells: intestinal epithelial cell-secreted extracellular vesicles that participate in communication between intestinal epithelial cells and commensal bacteria and up-regulate the beneficial effects of bacteria on the host. We also investigate the mechanisms through which human milk oligosaccharides (HMOs) maintain intestinal barrier function and prevent intestinal inflammation beyond early life. We have demonstrated that 2'-fucosyllactose, an abundant oligosaccharide in human milk, protects the intestinal barrier and ameliorates colitis in adulthood. These findings support the development of 2'-fucosyllactose as an approach for prevention of intestinal inflammation.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient
Retreat Speaker

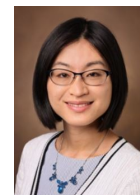
VDDRC Collaborations

We have ongoing collaborations with Drs. Acra, Choksi, Goettel, Peek, Washington, Williams, and Wilson on colitis-related projects. One collaborative publication is: Kaur H, Ali SA, Short SP, Williams CS, Goettel JA, Washington MK, Peek RM Jr, Acra SA, **Yan F**. Identification of a functional peptide of a probiotic bacterium-derived protein for the sustained effect on preventing colitis. *Gut Microbes*. 2023;15(2):2264456. PMID: PMC10566403.

Future VDDRC Core Use

We will use the Cell Imaging, MS/Omics, and Flow Cytometry Cores, especially to apply their new technologies, such as metabolomics, for our research.

Member: Danxia Yu, PhD
Rank: Associate Professor
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

I am a former VDDRC Pilot and Feasibility Award recipient and a former member of the Academy of Investigators. My research focuses on the nutritional and molecular epidemiology of metabolic diseases. A representative publication is: Deng K, Wang L, Nguyen SM, Shrubsole MJ, Cai Q, Lipworth L, Gupta DK, Zheng W, Shu XO, **Yu D**. A dietary pattern promoting gut sulfur metabolism is associated with increased mortality and altered circulating metabolites in low-income American adults. *EBioMedicine*. 2025;115:105690. PMID: PMC12001102.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01DK151797-01	Enhancing nutrition and lifestyle for incretin-based therapies (ENLIT) study	04/01/2027-03/31/2027	Pending
5R01CA275864-03	Gut microbiota-related mechanisms that impact colorectal cancer risk after bariatric surgery	09/07/2023-08/31/2028	\$414,224
5R01DK126721-05	The gut microbiota in metabolic surgery: A multi-ethnic, multi-omic, longitudinal study	02/05/2021-01/31/2027	\$229,067
U.S. Department of Agriculture 024-38821-42214	An in-depth elucidation of the correlation between dietary fiber and gut microbiota	04/15/2024-04/14/2027	\$67,854
5U01CA272541-04	Determining the contribution of microbial-derived metabolites to protective immunity in obesity-driven cancer risk	09/01/2022-08/31/2027	Not PI or MPI

Summary of Digestive Disease Research

I am committed to advancing science at the intersection of diet, lifestyle, and other modifiable risk factors, particularly the gut microbiota, in the etiology and prevention of metabolic disorders, including digestive diseases such as colorectal cancer and metabolic dysfunction-associated steatotic liver disease. My research projects leverage large prospective cohorts of demographically and geographically diverse populations, longitudinal electronic health records, and multi-omics technologies, such as metabolomics, metagenomics, and proteomics.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I have ongoing collaborations with Drs. Flynn, Samuels, Shrubsole, Spann, and Zheng. One collaborative VDDRC publication is: Wang Z, Wang L, Zhang X, Lowery BD, Shaffer LL, Chen Y, Wells QS, Flynn CR, Williams B, Spann M, Srivastava G, Samuels JM, **Yu D**. Body composition changes after bariatric surgery or treatment with GLP-1 receptor agonists. *JAMA Netw Open*. 2026;9(1):e2553323. PMID: PMC12789952.

Future VDDRC Core Use

I will continue to utilize resources provided by the VDDRC MS/Omics Core for metabolomic studies and the Biostatistical Component for data analysis.

Member: Nicholas Zachos, PhD
Rank: Associate Professor
Department: Surgery
VDDRC Status: Full Member
Research Group: HRP



Rationale for VDDRC Membership

My research program investigates stem cell responses to enteric pathogen infections in the gut using patient stem-cell-derived organoids. We have advanced these models by developing co-culture systems that incorporate primary human immune cells with organoids. We expose these co-culture models to bacteria, viruses, or fungi to identify and characterize which microbe- and innate immune-derived factors influence intestinal stem cell maintenance, proliferation, lineage differentiation, and repair/regeneration post-infection/injury. A representative publication is: **Zachos NC**, Vaughan H, Sarker R, Est-Witte S, Chakraborty M, Baetz NW, Yu H, Yarov-Yarovoy V, McNamara G, Green JJ, Tse CM, Donowitz M. A novel peptide prevents enterotoxin- and inflammation-induced intestinal fluid secretion by stimulating sodium-hydrogen exchanger 3 activity. *Gastroenterology*. 2023;165(4):986-998. PMCID: PMC11283679.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R01AI180038-03	Human M cells require Coronin 1a	11/20/2023-10/31/2028	\$403,647
Eli Lilly and Company	Human IBD organoid culture to evaluate epithelial barrier function	06/03/2025-06/02/2027	\$151,429

Summary of Digestive Disease Research

Patient stem-cell-derived organoids functionally recapitulate normal intestinal physiology and pathophysiology of GI disorders, including Inflammatory Bowel Disease and metabolic diseases, suggesting that disease-associated pathologies are imprinted in stem cells. The long-term goal is to use these multicellular co-culture models to compare organoids from healthy subjects or patients with GI disorders associated with inflammation to provide insights into disease etiology and progression, ultimately leading to the development of novel treatment strategies and drug discovery to target intestinal stem cells.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Poster Judge
Retreat Speaker

VDDRC Collaborations

Although I am a new member of the VDDRC, we have already established productive collaborations with VDDRC members, Drs. Coffey, Goldenring, Ogden, Peek, and Washington. A representative collaborative publication is: Holowatyj AN, Overman MJ, Votanopoulos KI, Lowy AM, Wagner P, Washington MK, Eng C, Foo WC, Goldberg RM, Hosseini M, Idrees K, Johnson DB, Shergill A, Ward E, **Zachos NC**, Shelton D; Appendix Cancer Pseudomyxoma Peritonei (ACPP) Research Foundation. Defining a 'cells to society' research framework for appendiceal tumours. *Nat Rev Cancer*. 2025;25(4):293-315. PMCID: PMC12427072.

Future VDDRC Core Use

I will utilize the Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores, as well as the Biostatistical Component for data analysis.

Member: Elma Zaganjor, PhD
Rank: Assistant Professor
Department: Molecular Physiology and Biophysics
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My research focuses on the role of metabolism in age-related diseases and metabolic disorders. We previously showed that the mitochondrial sirtuin SIRT4 regulates adipogenesis and protects against adipocyte hypertrophy, work that was initially supported by a VDDRC Pilot and Feasibility Project. VDDRC funding also enabled our discovery that nucleotide biosynthesis regulates adipogenesis by modulating mitochondrial fuel usage. Together, these findings provided key preliminary data for our current R35 award. A representative VDDRC publication is: Pinette JA, Myers JW, Park WY, Bryant HG, Eddie AM, Wilson GA, Montufar C, Shaikh Z, Vue Z, Nunn ER, Bessho R, Cottam MA, Haase VH, Hinton AO, Spinelli JB, Cartiailler JP, **Zaganjor E**. Disruption of nucleotide biosynthesis reprograms mitochondrial metabolism to inhibit adipogenesis. *J Lipid Res*. 2024;65(10):100641. PMID: PMC11913791.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R35GM154684-02	Reprogramming cell fate through nucleotide metabolism	06/15/2024-04/30/2029	\$250,000

Summary of Digestive Disease Research

My laboratory uses metabolomics, small-molecule and genetic perturbations, cell biology, and mouse models to define how metabolism is altered in obesity to drive obesity-mediated diseases. Building on our long-standing interest in mitochondrial sirtuins and adipocyte metabolism, we found that SIRT4 promotes the activity of methylcrotonyl-CoA carboxylase (MCCC1), a key enzyme in BCAA catabolism, thereby stimulating PPAR γ transcriptional activity and promoting adipogenesis. This work led us to investigate how broader metabolic pathways regulate adipocyte function and systemic physiology. My recent research centers on nucleotide metabolism as a critical regulator of adipocyte biology and whole-body metabolic health. We recently showed that disruption of nucleotide biosynthesis reprograms mitochondrial metabolism to inhibit adipogenesis, and that systemic inhibition of de novo purine biosynthesis prevents weight gain and improves metabolic health by increasing thermogenesis. Our ongoing work will determine how nucleotide availability and mitochondrial signaling in adipocytes influence adipocyte expansion, energy expenditure, inflammation, and physiology, to identify metabolic nodes that can be targeted to prevent obesity-mediated disease

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient

VDDRC Collaborations

I have established collaborations with Drs. Ayala, Choksi, and Winn focused on the pathobiology of adipocytes and the immune system. A representative collaborative VDDRC publication is: Myers JW, Park WY, Eddie AM, Shinde AB, Prasad P, Murphy AC, Leonard MZ, Pinette JA, Rampy JJ, Montufar C, Shaikh Z, Hickman TT, Reynolds GN, Winn NC, Lantier L, Peck SH, Coate KC, Stein RW, Carrasco N, Calipari ES, McReynolds MR, **Zaganjor E**. Systemic inhibition of de novo purine biosynthesis prevents weight gain and improves metabolic health by increasing thermogenesis and decreasing food intake. *bioRxiv*. 2024:2024.10.28.620705. PMID: PMC11566042.

Future VDDRC Core Use

We will continue to utilize the Cell Imaging and Flow Cytometry Cores and the Biostatistical Component for data analysis.

Member: Wei Zheng, MD, PhD, MPH
Rank: Anne Potter Wilson Professor, Director of Vanderbilt Epidemiology Center
Department: Medicine
VDDRC Status: Full Member
Research Group: OMN



Rationale for VDDRC Membership

My major research focus is investigating environmental exposures, biomarkers, and genetic risk factors for gastrointestinal and liver diseases, an important research domain within the VDDRC. A representative VDDRC publication is: Guo X, Ping J, Yang Y, Su X, Shu XO, Wen W, Chen Z, Zhang Y, Tao R, Jia G, He J, Cai Q, Zhang Q, Giles GG, Pearlman R, Rennert G, Vodicka P, Phipps A, Gruber SB, Casey G, Peters U, Long J, Lin W, **Zheng W**. Large-scale alternative polyadenylation-wide association studies to identify putative cancer susceptibility genes. *Cancer Res.* 2024;84(16):2707-2719. PMCID: PMC11326986.

Digestive Diseases Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
American Association for the Study of Liver Diseases Foundation CTORA24-179910	The influence of diet and lifestyle on metabolic profiles and cirrhosis risk	06/01/2025-10/31/2027	\$24,979
5R01CA269589-03	Uncovering colorectal cancer etiology and biology by integrating proteomics with other omics data	04/11/2023-03/31/2028	Not PI or MPI

Summary of Digestive Disease Research

The primary interest of my research is to identify risk factors for premalignant and malignant lesions. I am the PI, MPI, or key investigator for three large prospective cohort studies, including the Southern Community Cohort Study (SCCS), for which I have been a key founding investigator/MPI for nearly 10 years. Much of our work has centered on the pathobiology of colorectal carcinogenesis.

VDDRC-Related Training and Activities

Retreat Poster Judge
Retreat Speaker

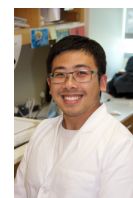
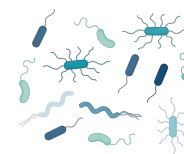
VDDRC Collaborations

We collaborate with numerous VDDRC investigators, including Drs. Coffey, Guo, Lau, Peek, Shrubsole, Washington, K. Wilson, and Yu. One resulting collaborative VDDRC publication is: Chen Z, Song W, Li Q, Li C, Wen W, Huyghe JR, Law PJ, Fernandez-Rozadilla C, Timofeeva MN, Thomas M, Schmit SL, Martin V, Devall M, Dampier C, Moratalla-Navarro F, Cai Q, Wang J, Shi J, Kweon SS, Tanikawa C, Jia WH, Shu X, Long J, Gao J, Kim J, Shin A, Matsuo K, Jee SH, Jung KJ, Wang N, Kim DH, Ping J, Yang G, Shin MH, Ren Z, Oh JH, Oze I, Ahn YO, Gao YT, Pan ZZ, Kamatani Y, Van Kaer L, Wu L, Li B, Matsuda K, Shu XO, Hsu L, Dunlop MG, Gruber SB, Houlston R, Tomlinson I, Li L, Lau KS, Moreno V, Casey G, Peters U, **Zheng W**, Guo X. Mixed-model and transcriptome-wide association analyses identify transcription factors and genes associated with colorectal cancer susceptibility. *Nat Commun.* 2026;17(1):1377. PMCID: PMC12877115.

Future VDDRC Core Use

We will continue to collaborate with the Biostatistical Component for assistance with experimental design and data analysis, and with the Translational Analysis Core for validation of biomarkers for our studies in the future.

Member: Wenhan Zhu, PhD
Rank: Assistant Professor
Department: Pathology, Microbiology, and Immunology
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I am a full member of the VDDRC and the recipient of a VDDRC Pilot and Feasibility Award. The focus of my research program is on defining the mechanisms that govern metabolic interactions between host and microbes in the inflamed intestine. A recent publication is: Spiga L, Fansler RT, Wu Y, Grote A, Langford-Butler M, Miller AK, Neal M, Hale OF, Singla D, Calcutt MW, Rose AE, Bresson MM, Schrimpe-Rutledge AC, Berdy B, Codreanu SG, Washington MK, Bratton BP, Sherrod SD, McLean JA, Zengler K, Sears CL, Behringer MG, Gnirke A, Tao L, Livny J, Olivares-Villagómez D, Earl AM, **Zhu W**. An anaerobic pathogen rewires host metabolism to fuel oxidative growth in the inflamed gut. *Cell*. 2026;189(13):3968-3990.e38. PMID: PMC13185528.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
1R01DK146015-01A1	Phase separation sustains commensal fitness in the inflamed gut	04/01/2026-03/31/2031	Pending
5R35GM147470-04	Commensal resilience mechanisms in the inflamed intestine	07/15/2022-05/31/2027	\$250,000
1R21AI199418-01	Bacterial membrane fusion sustains commensal resilience during enteric pathogen infection	05/08/2026-04/30/2028	\$170,438
Colorectal Cancer Alliance 10065978	A carcinogenic microbe rewires colonocyte metabolism to drive colorectal cancer development	01/01/2025-12/31/2026	\$104,762
1R21AI187749-01A1	<i>Turicibacter</i> modifies intestinal infection severity by modulating intestinal metabolites	08/01/2025-07/31/2027	\$150,000
Pew Charitable Trusts CID 00036885	Rational engineering of obligate anaerobes to grow in oxygen	07/09/2023-07/31/2028	\$69,444
5R01DK134692-03	Commensal bacteria resilience mechanisms in the inflamed intestine	04/07/2023-02/28/2027	\$233,137
GI SPORE Pilot Project Award	Collapsing a diet-microbe metabolic niche that drives early-onset colorectal cancer	01/14/2026-07/31/2027	GI SPORE

Summary of Digestive Disease Research

The overarching research interests in my laboratory revolve around defining the mechanisms that drive microbiota changes during health and disease, and leveraging the gained knowledge to strategically modify the microbiota to improve disease outcomes. I developed a multidisciplinary pipeline to obtain mechanistic insights on key metabolic interactions. This pipeline consists of next-generation sequencing, bacterial and host genetics, a mechanistic understanding of bacterial physiology *in vivo*, and high-throughput chemical screens. This pipeline allows for the generation of testable hypotheses, the discovery of druggable targets, and the subsequent translation into intervening compounds.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient
Retreat Speaker

VDDRC Collaborations

I am currently collaborating with VDDRC members Drs. Below, Byndloss, Coburn, Coffey, Goettel, Lau, Markham, Peek, Skaar, Washington, Williams, and K. Wilson to investigate the role of the microbiome in inflammation and IBD. One collaborative publication is: Spencer PN, Brown ME, Smith EP, Wang J, Kim W, Spiga L, Tasneem N, Simmons AJ, Kim T, Yang Y, Xu Y, Zheng L, Ro J, Kaur H, Kang SW, Helou MD, Lee MA,

Arceneaux D, Mueller KD, Kuddar OS, Harned MH, Li J, Banerjee A, Markham NO, Wilson KT, Coburn LA, Goettel JA, Liu Q, Washington MK, Valdivia RH, **Zhu W**, Lau KS. Pathobiont-triggered induction of goblet cell response drives regional susceptibility to inflammatory bowel disease. *J Clin Invest*. 2026:e201729. PMID: 41701533.

Future VDDRC Core Use

I will continue to utilize the Translational Analysis and MS/Omics Cores to define the metabolome in microbial-associated colorectal carcinogenesis, as well as the Biostatistical Component, for data analysis.