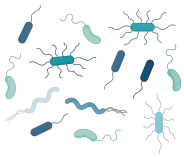
Member: Holly M. Scott Algood, PhD
Rank: Associate Professor
Department: Medicine and Pathology, Microbiology and Immunology
VDDRC Status: Full Member
Research Group: GII





Rationale for VDDRC Membership

My research focuses on 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. PMCID: PMC11639209.

Digestive Diseases-Related Grants

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

Summary of Digestive Disease Research

My overarching research theme is delineating the roles of T cell-derived cytokines in the immunopathogenesis of *H. pylori* infection and carcinogenesis. My laboratory's specific projects focus on pathogen-host interactions in chronic infections, pathologic inflammation, and how T cell-derived cytokines influence gastric epithelial cells and fibroblasts during infection.

VDDRC-Related Training and Activities

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

VDDRC Collaborations

We collaborate with numerous VDDRC members, including Drs. Choksi, Cover, Goldenring, Kaji, Lacy, Markham, Meenderink, Olivares-Villagomez, Peek, Piazuelo, Skaar, Washington, K. 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. PMCID: PMC11066722.

Future VDDRC Core Use

We will continue to use the Biostatistical Component, 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: Molecular Physiology & Biophysics
VDDRC Status: Full Member
Research Group: OMN





Rationale for VDDRC Membership

My laboratory aims to understand the basic mechanisms that regulate cellular longevity in health and disease. My laboratory uses the islets of Langerhans in the pancreas as a platform to study post-mitotic cell biology and relies on transcriptomic and multi-scale imaging pipelines, including confocal, electron, and isotope microscopy, to study cell biology at single-cell resolution. 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
R01DK129340	Molecular mechanisms regulating pancreatic delta cell function and dysfunction	04/01/2022-01/31/2027	Not PI or MPI

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

Promotion to VDDRC Full Member
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, Collins, Burkewitz, DelGiorno, Flynn, Tan, and Winn. 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**. (2025) Spatial patterns of hepatocyte glucose flux revealed by stable isotope tracing and multi-scale microscopy. *Nat Commun*. 16(1):5850. PMCID: PMC12219532.

Future VDDRC Core Use

We plan to continue utilizing the VDDRC Cell Imaging and MS/Omics Cores, as well as the 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

My laboratory focuses on non-pancreatic roles of glucagon-like peptide-1 (Glp1) and Glp1 receptor (Glp1r) agonists in maintaining nutrient homeostasis. Early in my postdoctoral training, I focused on Glp1r-mediated regulation of hepatic glucose fluxes, independent of insulin secretion. My lab's current research has since shifted to identifying brain regions that mediate the food intake-suppressive and body weight-lowering effects of Glp1r agonists and elucidating the molecular mechanisms underlying these 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: PMC12823338.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK132852	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 the 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

New Co-Leader, VDDRC Obesity, Metabolism and Nutrition (OMN) Research Interest Group
Promotion to VDDRC Full Member
Pilot & Feasibility Project Reviewer
Retreat Speaker
Retreat Poster Judge

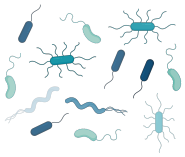
VDDRC Collaborations

We have active collaborations with VDDRC members Drs. Arrojo e Drigo, Collins, Mashayekhi, Samuels, 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) Gβγ-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 use the Cell Imaging and Flow Cytometry Cores, and we also anticipate using services in the MS/Omics and Translational Analysis Cores.

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





Rationale for VDDRC Membership

My laboratory uses experimental evolution and genomic analysis to study how environmental factors shape genetic variation and influence how microbes adapt and diversify in novel, complex environments. 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
R35GM150625	Using experimental evolution to evaluate environmental effects on microbial mutation and adaptation	08/08/2023-07/31/2028	$250,000
NSF 2540620	CAREER: Investigating the dynamic interplay between DNA methylation and bacterial evolution	08/01/2026-07/31/2031	$206,474

Summary of Digestive Disease Research

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 because of the challenges of culturing them. 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

New VDDRC Full Member
Retreat Speaker

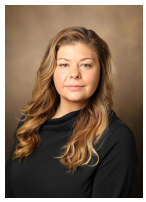
VDDRC Collaborations

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. *Cell*. 2026; 189(13):3968-3990. PMCID: PMC13185528.

Future VDDRC Core Use

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

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. PMCID: PMC12418218.

Digestive Diseases-Related Grants

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

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

New VDDRC Full Member
Retreat Poster Judge

VDDRC Collaborations

We collaborate with VDDRC members Drs. Bailin, Brittain, Byndloss, Collins, Flynn, Gabriel, Guo, Koethe, Lu, and Zhu. A representative collaborative publication is: Perry AS, Hadad N, Chatterjee E, Jimenez-Ramos M, Farber-Eger E, Roshani R, Stolze LK, Betti MJ, Zhao S, Huang S, Martens L, Kendall TJ, Thone T, Amancherla K, **Bailin S**, **Gabriel CL**, **Koethe J**, Carr JJ, Terry JG, Vaitinadin NS, Freedman JE, Tanriverdi K, Alsop E, Van Keuren-Jensen K, Sauld JFK, Mahajan G, Khan SS, Colangelo L, Nayor M, Fisher-Hoch S, McCormick JB, North KE, **Below JE**, Wells QS, Abel ED, Kalhan R, Scott C, Guilliams M, Gamazon ER, Fallowfield JA, Banovich NE, Das S, Shah R. A prognostic molecular signature of hepatic steatosis is spatially heterogeneous and dynamic in human liver. *Cell Rep Med*. 2024;5(12):101871. PMCID: PMC11722105.

Future VDDRC Core Use

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

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. PMCID: PMC12670395.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK141801	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 kinetics, providing a new framework for understanding nuclear second-messenger signaling. 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 LRH-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

New VDDRC Full Member
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 continue using 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 VDDRC mission 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. PMCID: PMC10973894.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK124845	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

Director, collaborating Physician Scientist Training Program (PSTP)
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 continue to use the MS/Omics and Translational Analysis Cores for our metabolomics studies and clinical research.

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
R01DK141978	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 transcription factor activation mechanisms and chromatin-dependent signal transduction. During my postdoctoral fellowship, I studied nuclear receptor activation (PPARs) in liver metabolism. 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 in the last 10 years
Pilot & Feasibility Project Reviewer

VDDRC Collaborations

I have formed collaborations with VDDRC members Drs. Ayala, Brittain, Collins, Flynn, Gabriel, Koethe, Mashayekhi, Niswender, Vickers, Yu, 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 using the Cell Imaging, Flow Cytometry, and Translational Analysis Cores 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 sits at the interface of cell biology, metabolism, and genetics, aiming 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
R21AG100967	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

New VDDRC Full Member
Pilot & Feasibility Award Recipient in the current funding cycle

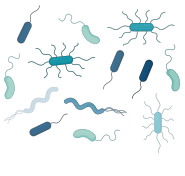
VDDRC Collaborations

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 continue using the Biostatistical Component and Cell Imaging Core, as well as the MS/Omics Core, for future studies.

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





Rationale for VDDRC Membership

My research focuses on identifying novel molecular mechanisms underlying imbalances 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 alters host physiology and disrupts the large-intestine microbial ecosystem, promoting 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. PMCID: PMC11189616.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Howard Hughes	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 *Salmonella*-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 *Salmonella* 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 shown that *Enterobacteriaceae* and the pathogen *Salmonella enterica* serotype Typhimurium can bloom in the gut after antibiotic therapy and during colitis by exploiting increased availability of nitrate, oxygen, and oxidized sugars. This work established that the host maintains gut homeostasis by limiting electron-acceptor availability in the colon, with important implications for developing approaches to rebalance the gut microbiota during dysbiosis.

VDDRC-Related Training and Activities

New Co-Leader, Gastrointestinal Infection and Injury (GII) Research Interest Group; Promotion to VDDRC Full Member; Academy of Investigators, Former Member; Pilot & Feasibility Award Recipient in the last 10 years; Named Supported Investigator; Retreat Poster Judge; Retreat Speaker; Seminar Speaker

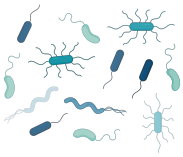
VDDRC Collaborations

I have established collaborations with VDDRC members Drs. Below, Cassat, Choksi, Collins, Flynn, Goettel, Lacy, Lau, Markham, Markle, Nicholson, Olivares-Villagomez, Peek, Piazuelo, Skaar, Williams, K. 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 Biostatistical Component, Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores for our discovery-based metabolomics studies.

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
R01AI177615	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 in the last 10 years
Pilot & Feasibility Project Reviewer
Retreat Speaker

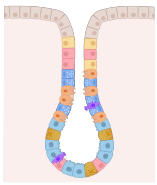
VDDRC Collaborations

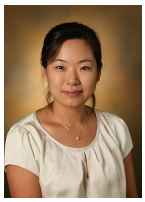
We collaborate with VDDRC members Drs. Byndloss, Choksi, Flynn, Goettel, Lau, Markle, Piazuelo, Washington, Williams, K. Wilson, and Zhu for studies of IBD. We also collaborate with Dr. Skaar for studies of bacterial pathogenesis. A representative collaborative publication is: Jacobse J, Brown RE, Li 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: Eunyoung 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, integrating stem cell biology and gastric carcinogenesis. My research group seeks not only to define the cells of origin for gastric carcinogenesis but also to 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
R01CA272687	Cell plasticity in the origin of gastric carcinogenesis	09/01/2025-08/31/2027	$600,000
R37CA244970	Drivers of gastric pre-neoplasia	08/01/2025-07/31/2027	$448,305
Congressionally Directed Medical Research Programs HT9425-24-1-0383	Therapeutic intervention to reverse gastric precancer	06/01/2024-05/31/2028	$188.147
R01DK101332	Induction and evolution of metaplasia in the stomach	07/19/2022-05/31/2027	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 precancerous lesions as cancer-initiating cells responsible for adenocarcinoma development. Current efforts extend to molecular and epigenetic mechanisms in pre-cancer cell lineage evolution and plasticity, and the roles of fatty acid metabolism in disease progression.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the last 10 years
Retreat Speaker
Seminar Speaker

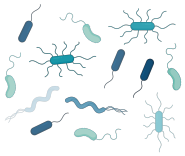
VDDRC Collaborations

We have ongoing collaborations with numerous VDDRC members, including Drs. Coffey, Goldenring, Kaji, Lau, Peek, Piazuelo, Tan, 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 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. PMCID: PMC10939980.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK141803	Defining the role of GPX3 in eosinophilic esophagitis	03/15/2025-01/31/2030	$387,338
VA I01BX006820	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 study how oxidative stress modifies epithelial-stromal and epithelial-immune interactions. Our lab accomplishes this using human samples, organoid culture, air-liquid interface culture, and mouse models. cant 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

New Assistant Director, VDDRC
New Co-Director, Pilot & Feasibility Program
Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the last 10 years
Pilot & Feasibility Project Reviewer
Retreat Speaker
Retreat Poster Judge
Seminar Speaker

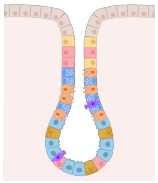
VDDRC Collaborations

I have ongoing collaborations with numerous VDDRC members, including Drs. Acra, Algood, Byndloss, Cassat, Coburn, Coffey, Collins, Flynn, Goettel, Goldenring, Hiremath, Kaji, Lau, E. Lee, Mahadevan-Jansen, Markham, Markle, Meenderink, Peek, Piazuelo, Schneider, Scoville, Washington, Williams, K. 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. PMCID: PMC11339313.

Future VDDRC Core Use

Our group will continue to use the Biostatistical Component, Translational Analysis Core to evaluate our disease models, and 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. PMCID: PMC12988101.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
Veterans Administration, I01CX002662	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 among Ken Lau, Keith Wilson, and me 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

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

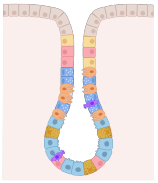
VDDRC Collaborations

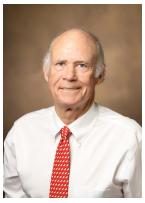
We collaborate extensively with VDDRC members, including Drs. Choksi, Goettel, Hiremath, Lau, Markham, Piazuelo, Schneider, Scoville, Washington, Williams, K. Wilson, and Zhu, for both our mouse models of colitis and human IBD samples. A collaborative publication is: Li J, Simmons AJ, Hawkins CV, Chiron 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. PMCID: PMC11339313.

Future VDDRC Core Use

We will continue to use and 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 also continue to use the Flow Cytometry Core to isolate cells for single-cell RNA-seq. 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
R35CA197570	Early to late events in colorectal neoplasia: basic biology to clinical implementation	08/05/2024-07/31/2031	$607,315
P01CA229123	exRNA in colorectal carcinoma: Biogenesis and function	01/20/2020-05/31/2031	$390,988
U01CA294527	A multimodal 3D atlas of colorectal cancer across ages of onset	09/01/2024-08/31/2029	Not PI or MPI

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, a major EGFR ligand, and provides a point of convergence between EGFR and Wnt signaling pathways. This work identified a new mode of EGFR ligand signaling via exosomes and led to the development of FAVS (fluorescent-activated vesicle sorting) to isolate and characterize cellular organelles. A major clinical advance is 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

Director, collaborating GI SPORE
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. Choi, Crowe, Goldenring, Guo, Islam, Kaji, Lacy, Lau, E. Lee, Y. Lee, Magnuson, Markham, Peek, Shrubsole, Singh, Southard-Smith, Tyska, Vickers, Washington, Zheng, 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 publications 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
R01DK132236	Role of SIK3 in PKA/mTORC1 regulation of adipose browning	09/06/2023-08/31/2028	$309,000
R01DK126890	Natriuretic peptide and cGMP signaling in adipose tissue and energy metabolism	04/15/2022-02/28/2027	$293,000
R01DK131529	Pathophysiology of metabolically detrimental changes in adipose distribution, adipocyte function, and adipose immune environment on antiretroviral therapy	02/10/2022-01/31/2027	Listed under Contact PI

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 Poster Judge
Retreat Speaker

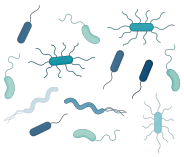
VDDRC Collaborations

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. Gβγ-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 in the next funding cycle and will continue to use the Translational Analysis Core for our mouse models and 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 human gastrointestinal tract. 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
R01AI118932	Type IV protein secretion in *Helicobacter pylori*	04/09/2021-03/31/2027	$507,833
R01AI039657	Structure and function of *Helicobacter pylori* VacA	04/07/2026-03/30/2031	$432,862
I01BX004447	Pathogenesis of *Helicobacter pylori* infection	07/01/2024-06/30/2028	$165,000
P01CA116087	Regulation of *Helicobacter pylori* 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 investigate how dietary constituents such as salt modify the pathogenicity of bacteria.

VDDRC-Related Training and Activities

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

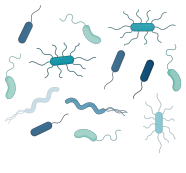
VDDRC Collaborations

We collaborate with numerous VDDRC members, including Drs. Algood, Lacy, Peek, Piazuelo, Skaar, Washington, and K. 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 VDDRC 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 in the last 10 years
Retreat Speaker

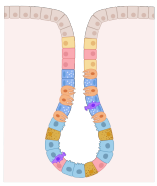
VDDRC Collaborations

I will continue to collaborate with VDDRC members, Drs. Algood, Lacy, Peek, Piazuelo, Washington, and K. Wilson.

Future VDDRC Core Use

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

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 uses 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 previously received 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	09/01/2026-05/31/2030	$532,258
American Cancer Society ACS 1433470	Modulating eicosanoids for the treatment and prevention of pancreatic cancer	09/01/2025-08/31/2029	$215,293

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

Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the current funding cycle
Seminar Speaker

VDDRC Collaborations

I have established collaborations with other VDDRC members focused on pancreatic disease, including Drs. Arrojo e Drigo, Goettel, 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, Neininger 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 Biostatistical Component, Cell Imaging, 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 focused 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	Investigating transcriptional mechanisms of fibrosis in the liver	06/01/2026-02/28/2030	$499,852
R01DK143216	Intrinsic primary afferent neurons in regulation of intestinal nutrient sensing and obesity	04/01/2026-01/31/2030	$92,654
R01CA275864	Gut microbiota-related mechanisms that impact colorectal cancer risk after bariatric surgery	09/07/2023-08/31/2028	Listed under Contact PI

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

Former Pilot & Feasibility Award Recipient
Named Supported Investigator
Pilot & Feasibility Project Reviewer

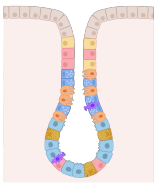
VDDRC Collaborations

I am currently collaborating with VDDRC members Drs. Arrojo e Drigo, Below, Brown, Burkewitz, Byndloss, Cassat, Choksi, Goettel, Lau, Y. Lee, Markle, Niswender, Peek, Samuels, Spann, Washington, Williams, Winn, K. Wilson, and Yu. 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

We will continue to utilize the Biostatistical Component, Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores. Our core usage will increase in the next funding cycle, particularly for 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.

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 focus on 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
R01DK145538	Tuft cells resolve pancreatic injury through a Type 2 immune circuit	09/01/2026-05/31/2030	Not PI or MPI
U01CA294527	A multimodal 3D atlas of colorectal cancer across ages of onset	09/01/2024-08/31/2029	Not PI or MPI
GI SPORE Pilot Project Award P50CA236733	Bile acid regulation of IL-23R+ Tregs in CRC	08/28/2026-07/31/2027	Pilot funding not listed

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

Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the last 10 years
Pilot & Feasibility Project Reviewer
Retreat Poster Judge
Seminar Speaker

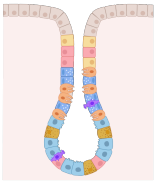
VDDRC Collaborations

I have ongoing collaborations with other VDDRC members, including Drs. Acra, Byndloss, Cassat, Choksi, Coburn, Coffey, DelGiorno, Flynn, Hiremath, Lau, E. Lee, Markham, Markle, Meenderink, Peek, Piazuelo, Scoville, Tan, Washington, Williams, K. Wilson, Yan, 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 Flow Cytometry, MS/Omics, and Translational Analysis Cores for our work in humanized mouse models of IBD. We will also utilize the Cell Imaging Core in the next funding cycle.

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. PMCID: PMC12981957.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK048370	Small GTP binding proteins in gastrointestinal mucosa	08/01/1997-07/31/2027	$418,115
RC2DK118640	Congenital diarrhea and enteropathy (PediCODE) consortium and biorepository	09/15/2019-08/31/2029	$316,621
R01DK101332	Induction and evolution of metaplasia in the stomach	05/01/2014-05/31/2027	$309,430
Veterans Administration I01BX000930	Oxyntic atrophy and novel gastric lineages	04/01/2011-09/30/2029	$300,000
Congressionally Directed Medical Research Programs HT9425-24-1-0382	Therapeutic intervention to reverse gastric precancer	06/01/2024-05/31/2028	$173,067
4R01CA272687	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 several subjects that broadly apply to epithelial biology, and we have long been interested 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); Former Pilot & Feasibility Award Recipient; Pilot & Feasibility Project Reviewer; Retreat Speaker; Retreat Poster Judge

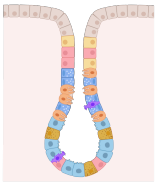
VDDRC Collaborations

We collaborate with numerous VDDRC members, including Drs. Acra, Algood, Choi, Coffey, Kaji, Lacy, Lau, E. Lee, Meenderink, Peek, Piazuelo, 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. PMCID: 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 continue to use the Flow Cytometry, MS/Omics, and Translational Analysis Cores in the 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 centers on gastrointestinal disease etiology, prevention, and precision medicine by 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
R01CA297582	Leveraging omics and electronic health records data to study colorectal adenoma genetics and drug repurposing	09/10/2025-08/31/2029	$749,332
R01CA269589	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

New VDDRC Full Member
Retreat Speaker

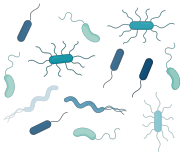
VDDRC Collaborations

My lab collaborates with several VDDRC members, including Drs. Below, Coffey, Lau, Lu, 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 continue to use the Translational Analysis Core to analyze multi-omic datasets.

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 delivers evidence-based, compassionate care while addressing the unique challenges children and families face 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
R01DK144385	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
R01DK132338	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 EoE pathogenesis is incomplete, which 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 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 key esophageal biochemical alterations, this work will offer novel insights into EoE pathogenesis, and by identifying baseline predictors of treatment response, it will lay a framework for personalized care for EoE patients.

VDDRC-Related Training and Activities

New VDDRC Full Member
Retreat Poster Judge

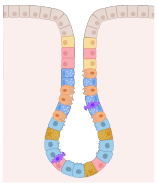
VDDRC Collaborations

Although I am a new VDDRC member, I have already established collaborations with several VDDRC members, including Drs. Acra, Choksi, Coburn, Goettel, Mahadevan-Jansen, Washington, and Williams. 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

I will continue using the Biostatistical Component, and future research projects will use 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
U01CA294518	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 us to identify 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 (TIidentify), ultimately benefiting patients.

VDDRC-Related Training and Activities

Co-Director, VDDRC Digital Histomorphology Service in the Translational Analysis Core
New VDDRC Full Member
Retreat Poster Judge

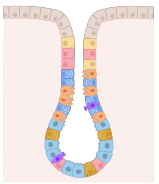
VDDRC Collaborations

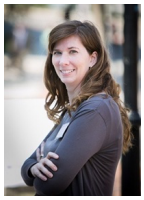
As a new VDDRC member, I plan to continue collaborating with VDDRC members Drs. Choi, Coffey, Goldenring, and Peek. A representative collaborative publication is: Rhodes JD, Hur S, Zhang C, Tamayo-Sarver I, Sha E, Manning EH, Clemenceau JR, Caldwell B, Jang B, Choi E, **Hwang TH**, Lee SH, **Goldenring JR**. Fibroblast-derived Spondin-2 promotes dysplastic transition in metaplastic gastric epithelial cells. *Gastroenterology*. 2026:S0016-5085. Online ahead of print. PMID: 42641992.

Future VDDRC Core Use

As a new VDDRC member, I plan to continue using the Translational Analysis Core.

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
R01GM120569	Molecular basis for arrestin-mediated signaling	08/01/2016-03/31/2029	$199,754

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
Former 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 MS/Omics Cores for our studies on membrane structure-function and use the Cell Imaging Core in the next funding cycle.

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



Rationale for VDDRC Membership

I direct the Transplant Hepatology Fellowship Program and 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
R01HL181174	Prospective investigation of cirrhotic cardiomyopathy in humans	09/16/2025-06/30/2030	$542,144
American Association for the Study of Liver Diseases	Harold Amos Medical Faculty Development Program Award	07/01/2024-06/30/2028	Listed under Contact PI

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

New VDDRC Full Member
Retreat Poster Judge

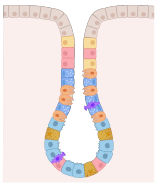
VDDRC Collaborations

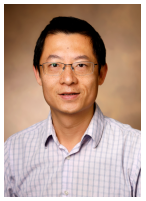
We maintain close collaborations with VDDRC members, including Drs. Brittain, Flynn, Jiang, Shrubsole, Spann, and Washington, on investigations focused on complications of advanced liver disease and their impact on clinical outcomes. A representative collaborative publication is: Brown S, Richardson 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), focusing on developing, validating, and evaluating advanced MRI techniques, including temporal diffusion spectroscopy imaging and quantitative magnetic transfer imaging, in preclinical and translational settings. 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
R01DK135950	*In vivo* 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 reliably quantify steatosis and fibrosis, respectively, the lack of a non-invasive tool to assess inflammation in NASH remains a significant challenge 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

New VDDRC Full Member
Retreat Poster Judge

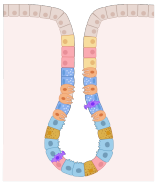
VDDRC Collaborations

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 continue to utilize the Translational Analysis Core to analyze our clinical data and will use the Cell Imaging Core for analysis of our *ex vivo* data in the next funding cycle.

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





Rationale for VDDRC Membership

My research focuses on how luminal chemosensing influences epithelial cell differentiation and mature cell functions under healthy and disease conditions. My recent efforts aim to delineate the cell signaling pathways that regulate nutrient transporter trafficking, with the 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
R01DK128190	Impacting the pathophysiology of malabsorption induced by Myosin Vb inactivating mutations	09/25/2021-07/31/2026	$220,000
RC2DK118640	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 the activity of epithelial nutrient transporters in murine tissues from a variety of diseases, including *C. difficile* infection. This method quantifies 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 by targeting epithelial progenitor cell signals to upregulate nutrient absorption.

VDDRC-Related Training and Activities

Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the current funding cycle
Retreat Poster Judge
Seminar Speaker

VDDRC Collaborations

I have ongoing collaborations with VDDRC members Drs. Acra, Algood, Choi, Coffey, DelGiorno, 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 continue to utilize the Translational Analysis Core for evaluation of our mouse models and the Cell Imaging and MS/Omics Cores 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: 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
R01DK131529	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
Veterans Administration I01CX001930	A randomized trial to optimize skeletal muscle while reducing adiposity in veterans with HIV	01/01/2020-03/31/2029	$400,000
R01DK141455	Defining cellular and molecular processes underlying adipose tissue dysfunction onINSTI-based antiretroviral therapy	09/10/2024-06/30/2029	$29,382
K23DK135414	Adipose tissue T cell polarization and metabolic health in persons living with HIV	04/01/2023-01/31/2027	Listed under Contact PI
K23DK135420	The gut-liver axis in HIV-related non-alcoholic fatty liver disease	09/01/2023-05/31/2027	Listed under Contact PI
K23HL159351	The effect of SGLT2 inhibition on adipose tissue inflammation and endothelial function	07/01/2023-06/30/2028	Listed under Contact PI

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 Poster Judge and Retreat Speaker

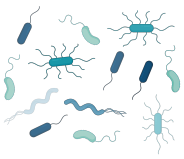
VDDRC Collaborations

I have collaborated with Drs. Bailin, Below, Brittain, Brown, Collins, Gabriel, Izzy, Mashayekhi, Meenderink, 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 and Translational Analysis Cores for discovery-based single-cell studies of human adipose tissue, as well as future use of the MS/Omics Core.

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
R37AI095755	Structural mechanisms of *Clostridioides difficile* pathogenesis	05/01/2021-04/30/2026	$360,000
Veterans Administration IK2BX005699	Gastrointestinal cell type-specific signaling and *C. difficile* toxin pathogenesis	10/01/2021-09/30/2026	Listed under Contact PI

Summary of Digestive Disease Research

My laboratory's primary focus has been understanding the three toxins produced by *C. difficile* and their roles in pathogenesis, 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. More recently, we have 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

New Associate Director, VDDRC
Co-Director, Scientific Catalyst Program
Strategic Planning Committee, collaborating VI4 Institute
Former Pilot & Feasibility Award Recipient
Retreat Speaker
Retreat Poster Judge

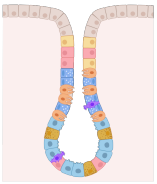
VDDRC Collaborations

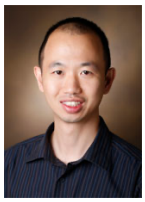
We collaborate with Drs. Algood, Byndloss, Coffey, Goldenring, Kaji, Kordus, Lau, Markham, Nicholson, Olivares-Villagomez, Shrubsole, Skaar, Tyska, and Washington on projects related to human tissue, cell, and animal models of *C. difficile* toxin function. We also collaborate with Dr. Cover on projects 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 Cell Imaging, Flow Cytometry, and MS/Omics 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 the 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
U01CA294527	A multimodal 3D atlas of colorectal cancer across ages of onset	09/01/2024-08/31/2029	$1,024,132
Roxanne and Henry Brandt Foundation	Tuft cell–derived Prostaglandin D2 as a target for chemoprevention in FAP	12/01/2025-11/30/2027	$45,454
R35CA197570	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

My laboratory currently applies single-cell, spatial-omics, and 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 in the current funding cycle
Pilot & Feasibility Project Reviewer
Retreat Speaker

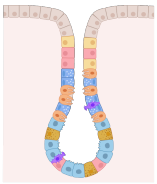
VDDRC Collaborations

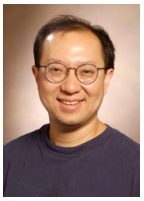
I collaborate extensively with Dr. Coffey on stem cell studies, Dr. Goldenring on organoid co-cultures, Dr. Southard-Smith on single-nucleus RNA-seq, and Drs. Wilson and Coburn on cell-specific signaling in IBD. I have additional collaborations with Drs. Brown, Byndloss, Cassat, Choi, Choksi, Cover, DelGiorno, Flynn, Goettel, Guo, Islam, Kaji, Lacy, E. Lee, Lu, Magnuson, Markham, Markle, Meenderink, Peek, Scoville, Shrubsole, Singh, Tan, Tyska, Wanjalla, Washington, Williams, K. Wilson, 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

We will continue using the Biostatistical Component, Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores, and our core usage will increase in the next funding cycle, particularly in the MS/Omics and Flow Cytometry Cores, due to larger sample influxes. We will also continue to use the Translational Analysis Core for our histological analysis and longitudinal imaging of inflammation. We will continue to use the Cell Imaging Core 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 Wnt signals are propagated and how this information can be used in regenerative medicine and to treat 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
R35GM122516	Mechanism of Wnt signaling	04/01/2017-03/31/2027	$355,000

Summary of Digestive Disease Research

My work focuses on studying the mechanism of action of the Wnt pathway and its dysregulation in human disease. The Wnt pathway is a major driver of intestinal renewal in the adult gastrointestinal epithelium. Activating mutations in the Wnt pathway occur in over 90% of colorectal cancer cases, and mutations in a Wnt pathway component, adenomatous polyposis coli, cause 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
Retreat Poster Judge

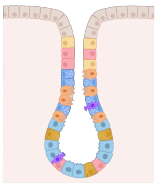
VDDRC Collaborations

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 will continue to use 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. PMCID: PMC12003176.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK133512	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 effectively depletes hepatic stellate cells and that they amplify liver injury, which formed the basis of our original VDDRC Pilot Project.

VDDRC-Related Training and Activities

Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the last 10 years
Named Supported Investigator
Pilot & Feasibility Project Reviewer
Seminar Speaker

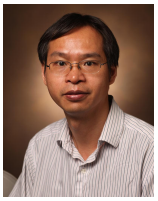
VDDRC Collaborations

I have developed productive collaborations with VDDRC members, Drs. Coffey, 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. PMCID: 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 autoimmunity, metabolic traits, and associated diseases. I have also developed strong skills in designing, implementing, and analyzing 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 a*l. 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
R01DK135938	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 led national and international large-scale genetic studies of complex traits and diseases related to adiposity, lipids, autoimmune diseases, and carcinogenesis.

VDDRC-Related Training and Activities

New VDDRC Full Member
Retreat Poster Judge

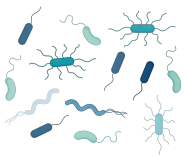
VDDRC Collaborations

As a new VDDRC member, I have begun establishing collaborations with several VDDRC members, including Drs. Below, Coffey, Guo, Lau, and Zheng. 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, Karijolich 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 continue to utilize the Biostatistical Component for our large-scale genomic, transcriptomic, and metabolomic 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 biomedical photonics. My research focuses on applying optical techniques to diagnose pathology and neuromodulate 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 disease, ulcerative colitis, and eosinophilic esophagitis (EoE). My work focuses on translational research that improves 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
R01DK132338	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 during esophagogastroduodenoscopy (EGD). Therefore, clinicians rely on multiple random esophageal biopsies obtained during this procedure for histologic confirmation (the gold standard). However, because EoE is a patchy disease, multiple biopsies may still 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, as it relies on light interacting with molecules to provide a unique "fingerprint" of a specimen's biochemical and molecular composition within seconds. Therefore, RS via an endoscope is uniquely suited for real-time biochemical assessment of active EoE. Thus, my research focuses on developing and assessing a depth-specific, dual-wavelength Raman endoscope to characterize biochemical and water changes within the esophagus as they relate to active EoE.

VDDRC-Related Training and Activities

New VDDRC Full Member
Retreat Poster Judge

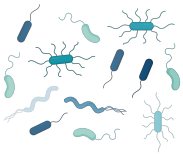
VDDRC Collaborations

As a new VDDRC member, I have already established collaborations with VDDRC members Drs. Acra, Choksi, and Hiremath, and I will continue to expand 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 continue to use the Cell Imaging, Flow Cytometry, and Translational Analysis Cores and implement use of the Biostatistical Component for data analysis.

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 leverages 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
R35GM155339	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 contributed to several efforts to develop and freely share tools for analyzing and interpreting next-generation sequencing data, from single-nucleotide variants in human whole-exome sequencing to transcriptomics data from complex microbial communities. I also actively work on generating and analyzing mass cytometry data, which provides single-cell insight into the expression of 40+ proteins across hundreds of thousands of cells from a heterogeneous blood sample.

VDDRC-Related Training and Activities

Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot &Feasibility Award Recipient in the current funding cycle
Named Supported Investigator
Pilot & Feasibility Project Reviewer
Retreat Speaker
Seminar 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, Washington, 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, Mannochio-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 continue to use the Biostatistical Component, Cell Imaging and Flow Cytometry Core. I will expand my usage of the MS/Omics and Translational Analysis Cores for single-cell RNA-seq in the next funding cycle.

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-Leader 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
K23DK143312	Use of adjuvant anti-obesity medications to enhance surgical weight loss	09/09/2025-07/31/2030	Listed under Contact PI

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
Retreat Poster Judge

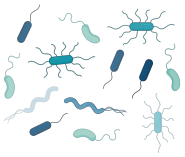
VDDRC Collaborations

I have a wide range of collaborators in obesity and metabolism, including VDDRC members Drs. Bailin, Brittain, Brown, Flynn, Gabriel, Goldenring, Koethe, Mashayekhi, Peek, Samuels, Spann, and Wanjalla. 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 continue to 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: GII





Rationale for VDDRC Membership

A long-term goal of my laboratory is to make discoveries that enable rational engineering of improved therapeutics. Combined with 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 VDDRC's continued success. 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. PMCID: PMC12724187.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01AI155646	Effects of Reoviridae assembly and transmission processes on viral genetic diversity	07/01/2021-06/30/2027	$322,278
R21AI190445	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 Poster Judge
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 use the Biostatistical Component, Cell Imaging, Flow Cytometry, and MS/Omics Cores for our viral pathogenesis studies 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: 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, robust innate immune response limits infection, an overly strong response poses 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. PMCID: PMC10907238.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R35GM133720	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

New VDDRC Full Member
Retreat Poster Judge

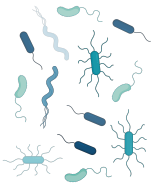
VDDRC Collaborations

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 continue to use the Cell Imaging, Flow Cytometry, and MS/Omics Cores in addition to the Biostatistical Component.

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 focuses on 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, Piazuelo 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
P01CA116087	*H. pylori*-induced inflammation and gastric cancer	04/02/2024-02/28/2029	$1,049,836
R01CA281732	Interactions between the microbiota and *Helicobacter pylori* in gastric carcinogenesis	06/01/2023-05/31/2028	$530,921
R01CA077955	*H. pylori* relationship to digestive diseases and cancer	05/01/2023-04/30/2028	$306,703
R01DK058587	*Helicobacter pylori* and gastrointestinal biology	09/15/2020-06/30/2026	$221,671

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

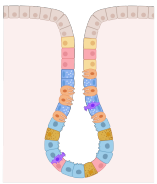
VDDRC Collaborations

We collaborate extensively with numerous VDDRC members, including Drs. Acra, Algood, Choksi, Choi, Coffey, Cover, Flynn, Goettel, Goldenring, E. Lee, Piazuelo, Washington, K. Wilson, J. Wilson, and Yan, among 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**, **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 use of the Cell Imaging, Flow Cytometry, and MS/Omics Cores will continue to increase as we implement new technologies, 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, Dündar 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. PMCID: 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

Associate Director, collaborating VI4 Institute
Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the last 10 years
Named Supported Investigator
Pilot & Feasibility Project Reviewer

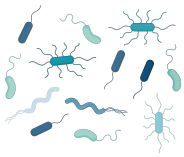
VDDRC Collaborations

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. PMCID: PMC11459355.

Future VDDRC Core Use

I will continue to use the Cell Imaging and Flow Cytometry Cores to isolate and visualize immune cells from our animal models. I will expand my use to the MS/Omics Core for proteomic analysis and the Translational Analysis Core for our human studies.

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. My laboratory's research interests include the structural and functional elucidation of novel metabolites in the COX-2 pathway and the molecular targets and functions of bioactive natural (dietary) products. I joined the VDDRC with a Pilot grant 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
R35GM144091	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

Former 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, Piazuelo, 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, **Piazuelo 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 using the MS/Omics Core as we further develop and define assays to determine the biological activities of dietary metabolites, and we will also expand our use of the Cell Imaging and Flow Cytometry Cores in the next funding cycle.

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



Rationale for VDDRC Membership

My research focuses on identifying modifiable risk factors and biomarkers of disease. These include one-carbon metabolism, genetic, epigenetic, microbial, and inflammatory 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. PMCID: 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 and other modifiable lifestyle factors affect and interact with genetic, microbial, epigenetic, and protein biomarkers that influence colorectal carcinogenesis risk. I also lead work 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

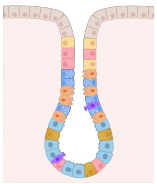
VDDRC Collaborations

I collaborate with VDDRC members Drs. Coffey, Goettel, Goldenring, Guo, Islam, Izzy, Lacy, Lau, Magnuson, Markham, Peek, Washington, Yu, and Zheng to study how micronutrient-host interactions affect 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. PMCID: PMC11525190.

Future VDDRC Core Use

We will continue to use the Biostatistical Component for our data analysis and the Flow Cytometry, MS/Omics, and Translational Analysis Core for histologic analyses.

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
R01CA248505	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 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^{TM}) 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 the therapeutic efficacy of cetuximab in CRC.

VDDRC-Related Training and Activities

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

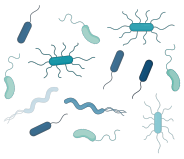
VDDRC Collaborations

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, Flow Cytometry, and Translational Analysis Cores to analyze our novel 3D culture system of colorectal cancer cells, and will extend our use of the MS/Omics Core in the next funding cycle.

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. 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. PMCID: PMC10822667.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01AI138581	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
R01AI178929	The role of the ZNG1 metallochaperone in the host response to infection	07/05/2023-06/30/2028	$383,142
R01AI073843	Pathobiology of heme inducible transporters in Gram positive pathogens	05/19/2021-04/30/2027	$286,937
R01AI164587	Nutritional immunity and microbial competition during *Clostridioides difficile* infection	06/13/2022-05/31/2027	$272,490

Summary of Digestive Disease Research

We have built a productive research program focused on the role of nutrient metals in *C. difficile* pathogenesis, as shown by several manuscripts on this topic. We have identified factors involved in nutrient metal acquisition in this organism, defined the impact of dietary metals on *C. difficile* infection outcomes, and described factors *C. difficile* uses to cope 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 that lead to liver abscesses and *Bacillus* infections that lead to dysentery, within the context of iron utilization; this work is funded by the NIH.

VDDRC-Related Training and Activities

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

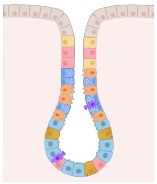
VDDRC Collaborations

We collaborate extensively with numerous VDDRC members, including Drs. Algood, Byndloss, Cassat, Cover, Lacy, Nicholson, Peek, Piazuelo, Washington, Winn, and Zhu, 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. PMCID: PMC11985272.

Future VDDRC Core Use

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

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), which controls gastrointestinal motility, vascular perfusion, and the release of neuroendocrine peptides in the gut. My research has focused on identifying genes and developmental processes that contribute to GI dysmotility syndromes such as Hirschsprung disease and chronic intestinal pseudo-obstruction. A representative VDDRC publication is Benthal 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	Mechanisms of enteric neuron diversification	07/01/2026-06/30/2031	$480,476

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 provided 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 in the last 10 years
Retreat Speaker
Retreat Poster Judge

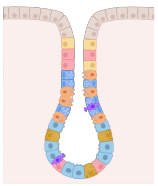
VDDRC Collaborations

We collaborate with several VDDRC members, including Drs. Coffey, Goldenring, and Lau; Core Leader Dave Flaherty; and Core Leader Jenny Schafer. A representative VDDRC collaborative publication is Avila JA, Benthal 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 continue to 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. We will also continue to use the Flow Cytometry Core to isolate wild-type and mutant enteric neural crest cells at multiple stages of development, as well as to capture enteric neuronal nuclei for single-nucleus RNA-seq, ATAC-seq, and integrated multi-omics analysis.

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





Rationale for VDDRC Membership

I direct the VDDRC Cell Imaging Core and am a VDDRC member. My laboratory aims 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
R01DK095811	Molecular basis of brush border assembly	09/01/2013-11/30/2028	$296,249
R01DK111949	Role of actin bundlers during enterocyte differentiation	02/01/2017-05/31/2027	$284,980

Summary of Digestive Disease Research

Our current studies investigate how enterocytes assemble an apical surface, how the brush border helps maintain physiological homeostasis, and how inherited or infectious perturbations of this interface lead to human disease. Over the past decade, our laboratory has made several fundamental, field-leading discoveries about the assembly and function of the brush border interface. During this time, our research program has evolved into an approach that combines 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
Former Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker
Retreat Poster Judge

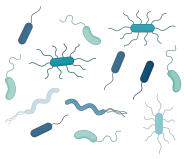
VDDRC Collaborations

We maintain active and ongoing collaborations with VDDRC members, including Drs. Acra, 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.

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





Rationale for VDDRC Membership

As Director of Patient-Oriented Research in Neonatology, I oversee numerous NIH-funded and industry-sponsored clinical trials and translational studies on neonatal gut and liver health. My research focuses on developing mucosal immune regulation in preterm infants and on the pathogenesis of necrotizing enterocolitis (NEC), and I am well-versed in the 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
R01DK135567	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) CD8αα+ innate-type lymphocytes in the intestinal epithelium, and (4) Osteopontin and iCD8α 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) biomarkers for necrotizing enterocolitis.

VDDRC-Related Training and Activities

Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer

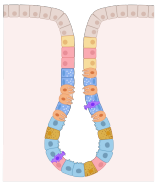
VDDRC Collaborations

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, Professor of Medicine, Gastroenterology, and Director of the Medical Scientist Training Program (MSTP) at Vanderbilt University. Under the mentorship of Dr. Raymond DuBois, I completed my thesis work on inflammatory carcinogenesis, and my postdoctoral fellowship in Gastroenterology provided training in epigenetic and chromosomal mechanisms of transcriptional regulation under the mentorship of former VDDRC member Dr. Scott Hiebert. My research program was initially funded by a VDDRC Pilot and Feasibility Award and focuses on intestinal injury response/repair programs to understand how these epithelial integrity programs are perturbed in IBD pathogenesis and, more importantly, in 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. PMCID: PMC11369156.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK131810	MTGs in intestinal biology and injury responses	07/01/2024-05/31/2028	$402,759
GI SPORE in Gastrointestinal Cancer Development Research Program P50CA236733	Role of secreted Selenoprotein P in colon cancer	07/31/2026-06/30/2027	GI SPORE

Summary of Digestive Disease Research

My research program focuses on intestinal injury response and repair programs to understand how these epithelial integrity programs are perturbed in the pathogenesis of IBD and colitis-associated carcinoma, and to identify novel therapeutic targets. I have expertise in animal models of colitis and inflammation, as well as signal transduction.

VDDRC-Related Training and Activities

Director, collaborating Medical Student Training Program (MSTP)
Former Pilot & Feasibility Award Recipient
Pilot & Feasibility Project Reviewer
Retreat Speaker

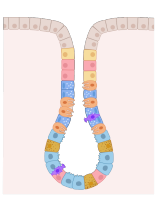
VDDRC Collaborations

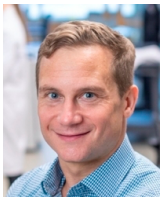
With Drs. Coburn, Piazuelo, and K. Wilson, I have demonstrated increased expression of spermine oxidase in patients with ulcerative colitis. In collaboration with Drs. K. Wilson and Washington, we demonstrated that selenoprotein P (SEPP1) influences inflammatory tumorigenesis by affecting genomic stability, the inflammatory microenvironment, and epithelial stem cell functions. I have several additional collaborations with Drs. Acra, Byndloss, Cassat, Choksi, Flynn, Goettel, Hiremath, Lau, E. Lee, Markhman, Markle, Meenderink, Peek, Singh, Washington, 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. PMCID: PMC10313376.

Future VDDRC Core Use

We have used and will continue to use the Cell Imaging, Flow Cytometry, 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 look to nature for inspiration to engineer highly modular, tunable materials that meet 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
R01EB033822	RIG-I activating nanoparticles for immunopotentiation	09/30/2022-06/30/2027	$317,016

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 using stem cell-derived extracellular vesicles to induce antigen-specific tolerance, with potential applications for treating Crohn's disease.

VDDRC-Related Training and Activities

New VDDRC Full Member
Pilot & Feasibility Award Recipient in the current funding cycle

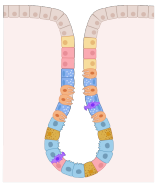
VDDRC Collaborations

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 continue to utilize the Biostatistical Component, Cell Imaging, Flow Cytometry, MS/Omics, and the Translational Analysis Cores to achieve our research goals and objectives.

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. PMCID: PMC10527201.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
I01CX002171	Dysregulated polyamine metabolism in *H. pylori*-associated gastric inflammation and disease progression	04/01/2025-03/31/2029	$300,000
I01CX002473	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
R21AI196953	Inhibitors of the reverse transsulfuration pathway as a new treatment for *Helicobacter pylori* infection	04/01/2026-03/31/2028	$275,000
P01CA116087	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 assessing inflammatory processes and oxidative stress-induced DNA damage, including 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, VDDRC Pilot & Feasibility Program
Retreat Speaker and Retreat Poster Judge

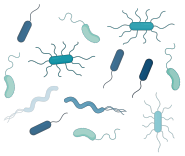
VDDRC Collaborations

I have collaborated extensively with many members of the VDDRC, including Drs. Acra, Algood, Byndloss, Cassat, Choksi, Coburn, Cover, Flynn, Goettel, Lau, Markham, Markle, Olivares-Villagomez, Peek, Piazuelo, Schneider, Scoville, Washington, Williams, Yan, and Zhu. 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. PMCID: 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: Fang Yan, MD, PhD
Rank: Research 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 macrophages to understand the pathogenesis of inflammatory bowel disease and identify potential treatment approaches. One VDDRC-supported publication is: Schalich 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. PMCID: PMC11005405.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01DK136893	Mechanisms by which human milk-derived oligosaccharides protect intestinal barrier and attenuate inflammation	05/15/2024-03/31/2028	$317,759
R01DK141070	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 of developing novel therapeutic strategies for inflammatory bowel disease has advanced through several research efforts. We study the mutualism between the gut microbiota and the host to develop potential microbiota-targeting therapy. We have identified a functional factor of probiotic bacteria, p40, that regulates intestinal homeostasis. Regarding the host's impact on gut microbiota function, our research has elucidated a previously unrecognized role of intestinal epithelial cells: intestinal epithelial cell-secreted extracellular vesicles that mediate communication between intestinal epithelial cells and commensal bacteria and amplify the bacteria's beneficial effects 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 developing 2'-fucosyllactose as an approach to prevent intestinal inflammation.

VDDRC-Related Training and Activities

Former Pilot & Feasibility Award Recipient
Retreat Speaker
Retreat Poster Judge

VDDRC Collaborations

We have ongoing collaborations with Drs. Acra, Choksi, Goettel, Peek, Washington, Williams, and K. Wilson on colitis-related projects. One collaborative publication is: Kaur H, Ali SA, Short SP, **Williams CS**, **Goettel JA**, **Washington MK**, **Peek RM**, **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

We will continue to use the Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores, especially to apply their new technologies, such as metabolomics, to 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. PMCID: PMC12001102.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R01CA275864	Gut microbiota-related mechanisms that impact colorectal cancer risk after bariatric surgery	09/07/2023-08/31/2028	$414,224
R01DK126721	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
U01CA272541	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 from demographically and geographically diverse populations, longitudinal electronic health records, and multi-omics technologies, including metabolomics, metagenomics, and proteomics.

VDDRC-Related Training and Activities

Academy of Investigators, Former Member
Pilot and Feasibility Award Recipient in the last 10 years

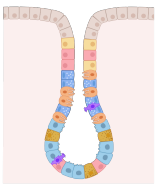
VDDRC Collaborations

I have ongoing collaborations with Drs. Brown, 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. PMCID: PMC12789952.

Future VDDRC Core Use

I will continue to use resources from the VDDRC Biostatistical Component and plan to use the MS/Omics Core for metabolomic studies in the next funding cycle.

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
R01AI180038	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 with those from patients with inflammation-associated GI disorders, providing insights into disease etiology and progression and ultimately enabling the development of novel treatment strategies and drug discovery to target intestinal stem cells.

VDDRC-Related Training and Activities

New VDDRC Full Member
Pilot & Feasibility Award Recipient in the current funding cycle
Pilot & Feasibility Project Reviewer
Retreat Poster Judge
Retreat Speaker
Seminar 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 (ACPMP) 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 continue to utilize the Biostatistical Component and Cell Imaging Core, and I plan to use the Flow Cytometry, MS/Omics, and Translational Analysis Cores in the next funding cycle.

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 metabolism's role 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, Cartailler JP, **Zaganjor E**. Disruption of nucleotide biosynthesis reprograms mitochondrial metabolism to inhibit adipogenesis. *J Lipid Res*. 2024;65(10):100641. PMCID: PMC11913791.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R35GM154684	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 PPARγ 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

Promotion to VDDRC Full Member
Academy of Investigators, Former Member
Pilot & Feasibility Award Recipient in the current funding cycle

VDDRC Collaborations

I have established collaborations with Drs. Ayala, Choksi, and Winn, focused on adipocyte pathobiology 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. PMCID: PMC11566042.

Future VDDRC Core Use

We will continue to utilize the Biostatistical Component, Cell Imaging, Flow Cytometry, and Translational Analysis Cores.

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
R01CA269589	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

My primary research interest is identifying 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), where I have served as 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

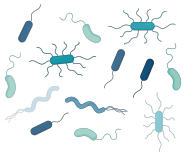
VDDRC Collaborations

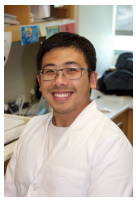
We collaborate with numerous VDDRC investigators, including Drs. Coffey, Guo, Lau, Lu, Peek, Shrubsole, Washington, K. Wilson, and Yu. One resulting collaborative VDDRC publication is: Chen Z, Song W, Li Q, Li C, Wen W, Huyghe JR, Law PJ, Fernandez-Rozadilla C, Timofeeva MN, Thomas M, Schmit SL, Martin 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 Translational Analysis Core to validate biomarkers for our future studies.

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. My research program focuses 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. PMCID: PMC13185528.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
R35GM147470	Commensal resilience mechanisms in the inflamed intestine	07/15/2022-05/31/2027	$250,000
R21AI199418	Bacterial membrane fusion sustains commensal resilience during enteric pathogen infection	05/08/2026-04/30/2028	$170,438
R21AI187749	*Turicibacter* modifies intestinal infection severity by modulating intestinal metabolites	08/01/2025-07/31/2027	$150,000
Colorectal Cancer Alliance 10065978	A carcinogenic microbe rewires colonocyte metabolism to drive colorectal cancer development	01/01/2025-12/31/2026	$104,762
Pew Charitable Trusts 00036885	Rational engineering of obligate anaerobes to grow in oxygen	07/09/2023-07/31/2028	$69,444
R01DK134692	Commensal bacteria resilience mechanisms in the inflamed intestine	04/07/2023-02/28/2027	$233,137
GI SPORE Pilot Project Award P50CA236733	Collapsing a diet–microbe metabolic niche that drives early-onset colorectal cancer	01/14/2026-07/31/2027	Pilot funding not listed

Summary of Digestive Disease Research

My laboratory's overarching research interests focus on defining the mechanisms that drive microbiota changes during health and disease and leveraging that 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 combines next-generation sequencing, bacterial and host genetics, mechanistic understanding of bacterial physiology *in vivo*, and high-throughput chemical screens. This pipeline generates testable hypotheses, discovers druggable targets, and translates them into intervening compounds.

VDDRC-Related Training and Activities

Promotion to VDDRC Full Member; Academy of Investigators, Former Member; Pilot & Feasibility Award Recipient in the current funding cycle; Retreat Speaker; Seminar Speaker

VDDRC Collaborations

I am currently collaborating with VDDRC members Drs. Behringer, Below, Byndloss, Coburn, Coffey, Goettel, Lau, Markham, Olivares-Villagomez, 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 Biostatistical Component, Cell Imaging, Flow Cytometry, MS/Omics, and Translational Analysis Cores to define and characterize the metabolome in microbial-associated colorectal carcinogenesis.