DDRC DIGEST
Digestive Disease Research Center
Medical University of South Carolina

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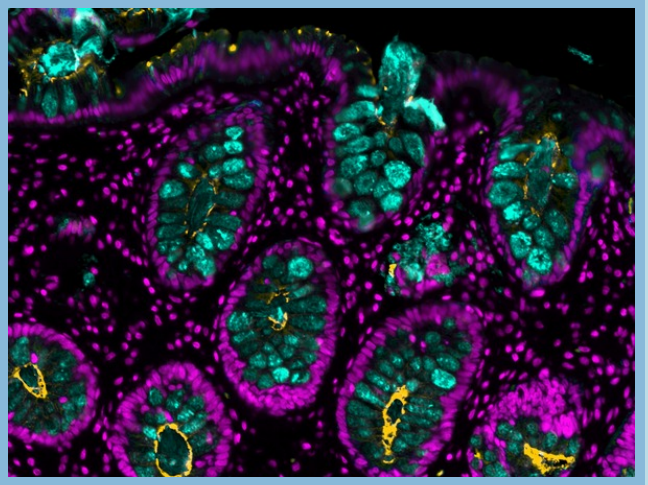
On the Inside



Human colon stained for MUC1 (green) and MUC2 (magenta). M. Engevik Lab (unpublished) @MicroMindy #FluorescenceFriday

A Note from the Directors

Don C. Rockey
DDRCC Director

Dear All: The start of the New Year and the submission of our annual progress report to NIDDK marks a time of reckoning for the progress of our Center so far. As we start Year 4, our ongoing self-assessment will be focused on our first competitive renewal application. Following our participation in the Annual Directors' Meeting last October, and based on

Stephen Duncan
CDLD Director

our growing experience in the DDRCC network, and feedback from our External Advisory Boards, we are enthusiastic about how far we have come in a relatively short time, especially for an institution of our size. We are extremely proud of the successes that our CDLD Junior Investigators have had, and that should help with renewal of the CDLD. Our Year 4 efforts will continue to be focused on continued growth of our cadre of digestive disease investigator base, and on the constant improvement of our ability to provide optimal core resources for our membership base. As you can see in the Year 3 core highlights in this issue, the hard work of our core directors and staff have begun to bear fruit in the successes of our supported members. Our feeling is that these highlights represent the leading edge of the enhanced productivity that will ultimately lead to renewal.

We hope that these successful examples will stimulate your thoughts about how our cores could help open new horizons on your research efforts. As a further stimulus to this re-imagining, we'd like to remind you of the educational opportunity afforded by the annual Charleston Workshop in Light Microscopy sponsored by our **Advanced Imaging Core** this coming Summer.

As part of our own ongoing work to optimize core services, we will soon be sending out another survey on Year 3 and anticipated Year 4 core usage. This year, we will include an open-ended query as to what other modified or novel core services you would find valuable going forward.

Our **7 am Clinical / Translational** and **11 am Basic Science** virtual enrichment series continue in the "back half" of the academic year. If you experience any difficulties with the switch, please contact our center manager **Kyu**. Let us know of any final suggestions you may have for the remainder of the 2022-23 Seminar Series (**email Antonis** or **Don**).

Best wishes for an exciting and productive Year 4,

Don and Steve

Cores Update: Year 3 Highlights

The main purpose of the DDRCC funded cores is to enhance the productivity and competitiveness of our funded members through technological support and consultations. This year, our DDRCC Cores supported numerous notable publications and several successful grant funding efforts. Several members benefited from the synergistic support of more than one core for their efforts. A short summary of some highlights follows.

ANALYTICAL CELL MODELS CORE

The Cell core generated genetically modified iPSC cells and cell lines that supported:

1) Successful funding of an R35 proposal by **Wenjian Gan, PhD** (Biochemistry and Molecular Biology Department) (**R35 GM146749: Regulatory Mechanisms of Arginine Methylation**) (*see also: Proteomics Core*).

2) Successful funding of an R56 by **Jorge Munera, PhD** (Regenerative Medicine and Cell Biology) (R56DK129575: The Role of GATA3 and SATB2 in Early Colonic Patterning), and a related R01 resubmission.

3) A recent publication on targeting the VDAC channel in mitochondria by the laboratory of **Eduardo Maldonado, DVM, PhD** (Drug Discovery & Biomedical Science) and related R01 and R21 applications (*see also: Imaging Core*).

4) Recent publications by the laboratory of **Don Rockey, MD** (Medicine) on the mechanistic roles of hepatic stellate and endothelial cells in fibrosis and cirrhosis:

Hijazi N, Rockey DC, Shi Z. *"The cellular microenvironment and cytoskeletal actin dynamics in liver fibrogenesis."* Biocell. 2022 May 19; 46(9):2003-2007. PMID: 35734751.

Liu S, Premont RT, Park KH, Rockey DC. *"B-PIX cooperates with GIT1 to regulate endothelial nitric oxide synthase in sinusoidal endothelial cells."* Am J Physiol Gastrointest Liver Physiol. 2022 Nov 1; 323(5):G511-G522. PMID: 36044673.

ADVANCED IMAGING CORE

The Advanced Imaging Core supported 24 DDRCC full and associate member users this year, contributing to several new and important scientific discoveries.

1) Successful screening of small molecules targeting the NADH binding region of the VDAC channel in mitochondria to induce mitochondrial dysfunction and inhibit cell proliferation, by the laboratory of **Eduardo Maldonado, DVM, PhD** (Drug Discovery & Biomedical Science);

Heslop, KA et al. *"Small molecules targeting the NADH-binding pocket of VDAC modulate mitochondrial metabolism in hepatocarcinoma cells,"* Biomed Pharmacother. (2022) Jun;150:112928. PMID: 35447542 PMC9400819, and related R01 and R21 applications (*see also: Cell Core*).

2) Characterization of GFP-LC3 autophagy marker dynamics in the presence or absence of agents affecting mitochodnrial dpolarization (mtDepo) following ethanol exposure, by the laboratory of **Zhi Zhong, PhD** (Drug Discovery & Biomedical Science);

Samuvel et al., *"Mitochodrial depolarzation after acute ethanol treatment drives mitophagy in living mice."* Y, Gooz M, Takemoto K, Woster PM, Lemasters JJ, Zhong Z. Autophagy. 2022 Nov;18(11):2671-2685. PMID: 35293288

PROTEOMICS CORE

The LC-MS/MS and MALDI Imaging proteomics core supported the following efforts:

1) Analysis of post-translational modifications: several years of collaboration with **Wenjian Gan, PhD** (Biochemistry and Molecular Biology Department) to idenfity novel sites of arginine mono- and di-methylation on multiple proteins of interest culminated in a recent publication:

Liu L, Lin B, Yin S, Ball LE, Delaney JR, Long DT, Gan W. *"Arginine methylation of BRD4 by PRMT2/4 governs transcription and DNA repair."* Sci Adv. 2022 Dec 9;8(49):eadd8928. PMID: 36475791, PMCID: PMC9728970.

This work also contributed a successful R35 application (*see also: Cell Core*).

2) A study evaluating extracellular matrix differences in human tissues with Hepatocellular Carcinoma was performed by the laboratory of **Peggi Angel, PhD** (Dept. of Pharmacology). The detection of multiple peptides distinguishing between differential clinical outcomes was presented at several scientific meetings:

10/17/2022 "*Fibroblasts: Promise and Challenge*" American Society for Matrix Biology, Charlottesville, VA.

09/27/2022 "*Uncovering the Hidden Fibrosis in Human Health and Disease by Imaging of Matrix Biology*", Department of Surgery, Baylor College of Medicine, Houston Texas, Surgical Departmental Seminar.

07/29/2022 Macdonald, J, Taylor, H., Edge, C., Delacourt, A., Lewin, D., Hoshida, Y., Drake, R. R., Mehta, AS, Angel, Angel, PM. "*Pathological Collagen Proteomic Variation in Subtypes of Hepatocellular Carcinoma Defined by Clinical Outcomes*." 2022 Workshop for the Society of Mass Spectrometry Imaging, Baltimore, MD.

3) A recent collaborative publication between **Peggi Angel, PhD** , **Richard Drake, PhD**, **Anand Mehta, PhD** (Pharmacology) and **Don Rockey, MD**, (Medicine) describing the identification of N-glycosylation patterns by imaging MS associated with histopathological changes in nonalcoholic steatohepatitis (NASH) and non-alcoholic fatty liver diseases (NAFLD) in mouse and human.

Ochoa-Rios S et al. *"Imaging Mass Spectrometry Reveals Alterations in N-Linked Glycosylation That Are Associated With Histopathological Changes in Nonalcoholic Steatohepatitis in Mouse and Human." Mol Cell Proteomics*. 2022 May;21(5):100225. PMID: 35331917, PMCID: PMC9092512.

CLINICAL COMPONENT CORE

The Clinical Component provided services to 11 full DDRCC members on 19 unique projects this year, as well as providing statistical support and consultation for Pilot & Feasibility Program applications.

1) The core provided statistical analysis support for publications from the laboratory of **Don Rockey, MD**, (Medicine) and a collaborative study with **Andrew Schreiner, MD** (Medicine):

Sullivan MK, Daher HB, Rockey DC. *"Normal or near normal aminotransferase levels in patients with alcoholic cirrhosis."* Am J Med Sci. 2022 Jun;363(6):484-489. PMID:34619146.

Schreiner AD, Zhang J, Durkalski-Mauldin V, Livingston S, Marsden J, Bian J, Mauldin PD, Moran WP, Rockey DC. *"Advanced liver fibrosis and the metabolic syndrome in a primary care setting."* 2021 Nov; 37(9):e3425. PMID: 33759300.

2) The core provided support for two targeted funding applications by DDRCC member **Hongjun Wang, PhD** (Dept. of Surgery)

- Mesenchymal Stromal Cells and their Extracellular Vesicles for Chronic Pain (NIH)
- Novel Cellular Therapy for Chronic Pain Caused by Chronic Pancreatitis (NIH)

These highlights are representative of many ongoing projects that were initiated and conducted through the course of Year 3. We look forward to highlighting the fruits of these efforts throughout Year 4.

News from the DDRCC

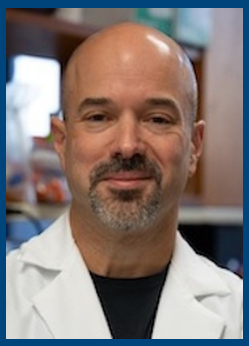
SOCIETY AWARD: MINDY ENGEVIK LAB

Mindy Engevik

Mindy Engevik, PhD (Regenerative Medicine & Cell Biology Dept.) is the recipient of a **2023 Lazaro J. Mandel Young Investigator Award** from the American Physiological Society. This award recognizes an individual demonstrating outstanding promise in the field of epithelial or renal physiology, and will be awarded at the American Physiology summit in April 20-23, 2023. ($10,000)

CONGRATULATIONS, DR. ENGEVIK!

NEW COLLABORATIVE FUNDING AWARD



Antonis Kourtidis

Chad Novince

Antonis Kourtidis, PhD (Regenerative Medicine & Cell Biology) was recently awarded a **2023 Discovery Award** from the MUSC SCTR Institute:

"An adherens junction associated RNAi machinery as a guardian of oral epithelial homeostasis."

2/1/23 - 1/31/24 ($25,000)

This research project will also include collaboration with fellow DDRCC Member **Chad Novince, DDS, PhD** (Oral Health Sciences), as well as Visu Palanisamy, PhD (Biochemistry & Molec Biol), and Angela Yoon, PhD (Stomatology, CDM).

CONGRATULATIONS DRS KOURTIDIS AND NOVINCE!

OUTSTANDING PUBLICATION: GUGLIETTA LAB

Silvia Guglietta, PhD (Regenerative Medicine & Cell Biology Dept.) received an **Excellence Award** from MUSC for a recent publication with outstanding scientific impact on her field:

"Complement downregulation promotes an inflammatory signature that renders colorectal cancer susceptible to immunotherapy" J Immunother Cancer. 2022; 10(9): e004717. PMID: 36137652, PMCID: PMC9511657

CONGRATULATIONS DR. GUGLIETTA!

NEW COLLABORATIVE FUNDING AWARD

Antonis Kourtidis

Mindy Engevik

Silvia Guglietta

Antonis Kourtidis, PhD is also the PI of a recently awarded **Pre-Clinical & Clinical Concepts Award** from the MUSC Hollings Cancer Center, along with collaborators **Mindy Engevik, PhD**, and **Silvia Guglietta, PhD**.

"Fusobacterium nucleatum promotes oncogenic signaling through disruption of the epithelial adherens junction - associated RNAi."

11/01/22 - 10/30/23 ($25,000)

CONGRATULATIONS TO ALL!

MUSC DISTINGUISHED ALUMNI AWARD

Paul J. Nietert, PhD

This month, Clinical Component Director **Paul J. Nietert, PhD** **('97)** (Dept. of Public Health Sciences) was honored with a **Distinguished Alumni Award** by the Medical University of South Carolina and the MUSC Office of Alumni Affairs for his many outstanding contributions to biomedical research and the MUSC research community at large.

CONGRATULATIONS, DR. NIETERT!

Our New DDRC Logo!

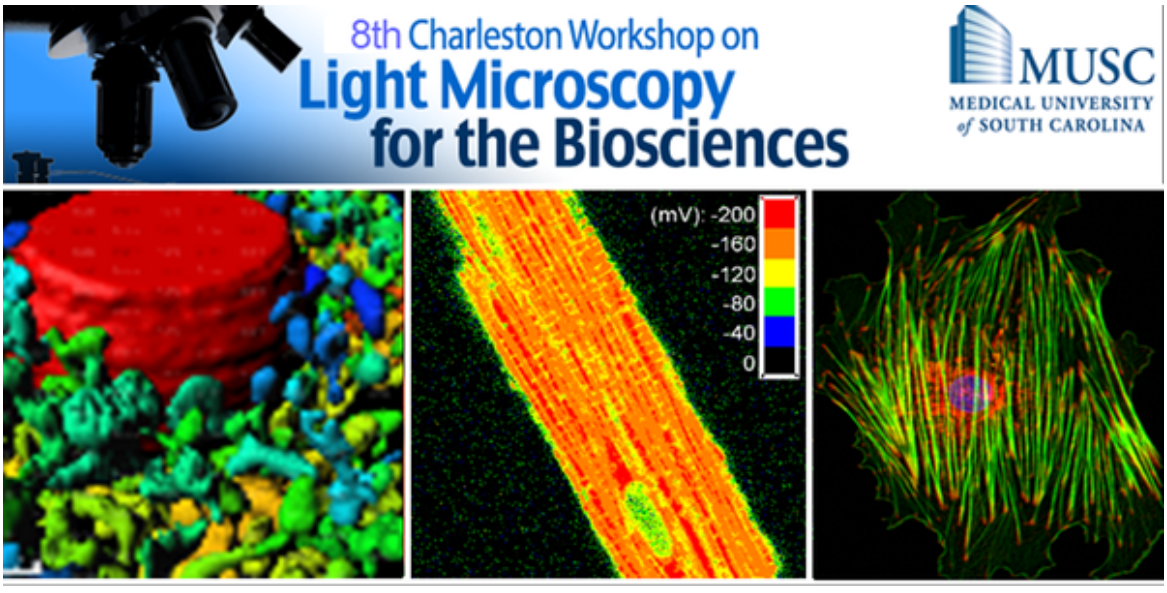
Many thanks to our members for the vigorous response we received asking for suggestions about a logo. The submissions were great, and we thank everyone for their ideas. Given such a great turnout, we asked you to choose, and based on the survey, the winner was this one:

Digestive Diseases Research Center

Medical University of South Carolina

Congratulations to **Elizabeth** and **Monica Ampollini** (**Hartman Lab**) for submitting the winning design! We are through our preliminary approvals by the MUSC Branding Office, and hope to settle on a final design in time for our Annual Retreat and Symposium this Spring.

CORE UPDATE: TRAINING/EDUCATIONAL OPPORTUNITY



Medical University of South Carolina (MUSC)
June 11-16, 2023

The **8th Charleston Workshop on LIGHT MICROSCOPY FOR THE BIOSCIENCES (LMB)** will provide a solid introduction to the concepts and practical applications of light microscopy relevant to modern cell and molecular biology under the direction of Dr. John J. Lemasters, GlaxoSmithKline Distinguished Endowed Professor at MUSC. Students will have opportunities for extensive hands-on experience with state-of-the-art equipment for optical imaging, digital image processing and deconvolution, fluorescence microscopy, confocal/multiphoton microscopy, and super-resolution microscopy guided by experienced academic and commercial faculty. Lectures and laboratory exercises will include: optics of image formation; microscope alignment; phase contrast and differential interference contrast microscopy; video and digital cameras; contrast enhancement by analog and digital image processing; principles of fluorescence and fluorescence microscopy; ion imaging and fluorescent probes, including fluorescent proteins; fluorescence resonance energy transfer; light-sheet imaging; laser scanning confocal and multiphoton microscopy; and super-resolution microscopy. Commercial faculty representing leading microscope manufacturers will make available for student use the latest and most advanced instrumentation for light microscopy, image detection, and computerized image analysis. **LMB** is designed for doctoral level scientists, pre-doctoral students, and high-level technical personnel. No prior experience with microscopy is required. All students will benefit from in-depth interaction with instructors. Students are encouraged to bring their own specimens for analysis.

The workshop qualifies for **1 course credit as DDBS 722, Light Microscopy for the Biosciences for students registered with the College of Graduate Studies**.

Course fee: $650.00

Application deadline: April 25, 2023

For further information contact: **Li Li, Ph.D.**, Manager, Cell & Molecular Imaging, 70 President Street, MSC 139, Charleston, SC 29425

We want to hear about your progress and achievements!

Please sent your news and announcements to the DDRC Digest via email to the Center Manager.

DDRCC and CDLD Enrichment Seminar Series

We are privileged to host an outstanding series of virtual seminars this year, featuring speakers of national and international renown. All of the GI & Hepatology 7am series were recorded, and are available through Box. A few notable highlights are mentioned below. The complete collection of recorded talks are available to DDRCC and CDLD members **here**.

DDRCC / CDLD / GI and Hepatology Grand Rounds:
Wednesday, 7am EST (Teams)

February 8th

Bernadette Marriott, PhD MUSC

Dietary supplements in the US: regulation, use and science

February 15th

Samir Gupta, MD Univ. of Calif. San Diego

Surveillance after colorectal polypectomy: past, present and future

February 22nd

Garth Swanson, MD, MS Rush University / MUSC

It's about time. Sleep and circadian rhythms in IBD

March 8th

Thomas Curran, MD, MPH MUSC

Diverticulitis. Role of antibiotics and when to consider surgery

March 15th

Hamed Khali, MD, MPH Harvard Medical School

Microscopic colitis

March 22nd

George Verne, MD Univ. of Tennessee

Intestinal hyperpermeability: a gateway to gastrointestinal dysfunction

March 29th

Katherine Morgan, MD MUSC

Surgery for chronic pancreatitis

DDRCC/CDLD/ RMCB Virtual Seminar Series:
Wednesday, 11 am EST (Zoom)

February 1st

Arianne Theiss, PhD Univ. of Colorado Anschutz Medical

Mitochondrial dysfunction as a driver of intestinal inflammation

February 8th

Eunyoung Choi, PhD Vanderbilt University School of Medicine

De novo cancer-initiating cells in gastric carcinogenesis

To receive notifications for our Enrichment series seminars, please contact the DDRCC Center Manager.

Selected GI Publications by our Members

Each newsletter, we highlight a subset of the many outstanding papers published and presented by our DDRC members. We strive to mention particularly significant primary research papers where our members were lead authors or key contributors, and to represent the broad scope of clinical, basic science and clinical-translational research interests across our membership. To assist us in these efforts, we continue to encourage you to **email Kyu**, our center manager, about your notable publications and presentations.

While space does not allow us to list a comprehensive month-to-month list of our member publications, such a list can be found on our DDRCC website **here**.

A complete listing of our DDRCC member publications since its inception can also be found through NCBI **here**.

December, 2022 - January, 2023

Carson MD, Warner AJ, **Hathaway-Schrader JD**, Geiser VL, Kim J, Gerasco JE, Hill WD, **Lemasters JJ**, Alekseyenko AV, Wu Y, Yao H, Aguirre JI, **Westwater C**, **Novince CM.** Minocycline-induced disruption of the intestinal FXR/FGF15 axis impairs osteogenesis in mice. JCI Insight. 2023 Jan 10;8(1). PubMed PMID: 36413391.

Obeid JS, Khalifa A, Xavier B, Bou-Daher H, **Rockey DC**. An AI Approach for Identifying Patients With Cirrhosis. J Clin Gastroenterol. 2023 Jan 1;57(1):82-88. PubMed PMID: 34238846, PubMed Central PMCID: PMC8741865.

Schreiner AD, Zhang J, Moran WP, Koch DG, Marsden J, Livingston S, Mauldin PD, Gebregziabher M. FIB-4 and incident severe liver outcomes in patients with undiagnosed chronic liver disease: A Fine-Gray competing risk analysis. Liver Int. 2023 Jan;43(1):170-179. PubMed PMID: 35567761; PubMed Central PMCID: PMC9659674.

Whyte SS, Karns R, Min KW, Cho JH, Lee S, Lake C, Bondoc A, **Yoon JH**, Shin S. Integrated analysis using ToppMiR uncovers altered miRNA-mRNA regulatory networks in pediatric hepatocellular carcinoma-A pilot study. Cancer Rep (Hoboken). 2023 Jan;6(1):e1685. PubMed PMID: 35859536; PubMed Central PMCID: PMC9875636.

Liu L, Lin B, Yin S, Ball LE, Delaney JR, Long DT, **Gan W**. Arginine methylation of BRD4 by PRMT2/4 governs transcription and DNA repair. Sci Adv. 2022 Dec 9;8(49). PubMed PMID: 36475791; PubMed Central PMCID: PMC9728970.

Gou W, Hua W, Swaby L, Cui W, Green E, Morgan KA, Strange C, **Wang H**. Stem Cell Therapy Improves Human Islet Graft Survival in Mice via Regulation of Macrophages. Diabetes. 2022 Dec 1;71(12):2642-2655. PubMed PMID: 36084289; PubMed Central PMCID: PMC9750955.

Whaby M, Wallon L, Mazzei M, Khan I, Teng KW, Koide S, **O'Bryan JP.** Mutations in the α4-α5 allosteric lobe of RAS do not significantly impair RAS signaling or self-association. J Biol Chem. 2022 Dec;298(12):102661. PubMed PMID: 36334633; PubMed Central PMCID: PMC9763690.

Accessing DDRC Cores

Quick Links for DDRCC and CDLD Core Use

A reminder that Full Members receive subsidized usage of our cores. Below are some summary details for accessing the cores and intiating projects.

This project was supported in part by NIH P30 DK123704 (*core facility*) at the MUSC Digestive Disease Research Core Center.

This project was supported in part by NIH P20 GM120475 (core facility) at the MUSC Digestive Disease Research Core Center.

Analytical Cell Models Core:

- The DDRCC and CDLD both **fully subsidize** the use of the ACC by its members.
- For iPSC projects, please contact the Core Director, **Dr. Steve Duncan**.
- For primary cell isolation, please contact **Dr. Don Rockey**.

Advanced Imaging Core:

- The DDRCC and CDLD both provide **full members** with a **25% discount** on facility fees.
- For imaging projects, please contact the Core Director, **Dr. John Lemasters** and Core Manager **Li Li**.

CDLD Animal Models Core:

- The CDLD **fully subsidizes** the use of the Animal Models Core for its **Junior Investigators**.
- Other **discounts** may currently apply for DDRCC members.
- For animal projects please contact the Core Director, **Dr. Kristi Helke**.
- For gnotobiotic mouse models, please contact **Dr. Caroline Westwater**.
- For transgenic and CRISPR/Cas9 projects, please contact the TGE Director, **Dr. Fulei Tang**, or Executive Director, **Dr. Alexander Awgulewitsch.**

DDRCC Proteomics Core:

- **DDRCC full members** will receive a 50% discount from facility fees.
- For MS projects, please contact the Core Co-Director, **Dr. Lauren Ball**.

Clinical Component Core:

- The DDRCC and CDLD **fully subsidize** biostatistical consultations with the Clinical Component Core by all of its members, including biostatistical support and mentoring for its Junior Investigators and Pilot & Feasibility applicants and awardees.
- To start a project, visit the SPARC website and submit a Biostatistics, Design & Epidemiology request, and contact:
  - DDRCC Core Director, **Dr. Paul Nietert**
  - CDLD Director **Dr. Ramesh Ramakrishnan**.

CITE OUR GRANTS

FOR THE DDRCC:
P30 DK123704

For queries regarding DDRCC news, membership and cores, please contact the Center Manager:

Kyu-Ho Lee, MD-PhD
Gastroenterology and Hepatology
Department of Medicine
CSB HE903B
96 Jonathan Lucas St
Charleston, SC 29425
(843) 792-1689
Email Dr. Lee

Visit the DDRCC Website:
https://medicine.musc.edu/departments/dom/divisions/gastroenterology/research/labs-and-centers/ddrcc

FOR THE COBRE CDLD:
P20 GM120457

For queries regarding the COBRE in Digestive and Liver Disease, please contact the COBRE PI:

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Charleston, SC 29425
(843) 792-9104
Email Dr. Duncan

Visit the CDLD Website:
https://medicine.musc.edu/departments/regenerative-medicine/cobre-digestive-liver-disease