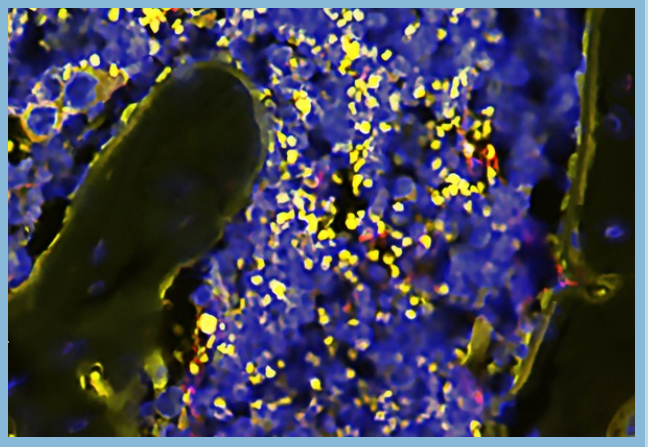
DDRC DIGEST
Digestive Disease Research Center
Medical University of South Carolina

Volume 3, Issue 5 **December 1, 2022**

On the Inside



*Minocycline effect on murine osteogenesis as assessed by expression of small heterodimer partner (SHP; FITC, green) and Osterix (rhodamine, red) in osteoblasts lining trabecular bone in mouse femurs (from Carson et al. (2022), JCI Insight, in press)(courtesy of the Novince Lab). Please see the collaboration and publication highlight in **News and Notes**.*

A Note from the Directors

Don C. Rockey
DDRCC Director

Dear All: As we enter the holiday season, we indeed have much to be thankful for. This October, we successfully hosted the DDRCC Directors Meeting in Charleston. We received rave reviews, both for the meeting and for our recently established and growing center. A strong showing from some of our Junior Investigators was a key part of

Stephen Duncan
CDLD Director

our success in projecting a positive image. Many thanks from us for those who contributed! Our role in hosting this meeting, as well as the DDRCC Eastern Alliance will go a long way toward increasing our presence and ties to the Silvio O. Conte DDRCC network, and to the digestive diseases research world at large.

We also received very positive reviews from our CDLD External Advisory Committee. This also mostly reflects the outstanding achievements of our COBRE Junior Investigators and Pilot & Feasibility awardees documented in the past issues of the *Digest*. These continued publication and grant funding successes bode well for our center's longevity, and for progress towards making digestive diseases research a cornerstone of institutional strength at MUSC.

To help us establish our identity as a unique and thriving presence at MUSC, we need to adopt a center logo. Please take a moment to review and vote on the several options that have been submitted to the Digest by some of our more creative and artistically talented center members. Decisions are made by those who show up!

A major goal of our combined CDLD and DDRCC programs is to provide optimal core resources for our membership base. To this end, we are indebted to the tireless efforts of our core directors and managers. Some recent upgrades to our **Proteomics Core** are described in this issue, as well as the educational opportunity afforded by the annual Charleston Workshop in Light Microscopy sponsored by our **Imaging Core** this coming Summer.

Our **7 am Clinical / Translational** and **11 am Basic Science** virtual enrichment series continue with an outstanding slate of speakers, with a recent change of platforms to Microsoft Teams for our 7am series. If you experience any difficulties with the switch, please contact our center manager **Kyu**. There are a few remaining seminar slots this year, so please let us know of any final suggestions for the remainder of the 2022-23 Seminar Series (**email Antonis** or **Don**).

Best wishes for an enjoyable holiday season,

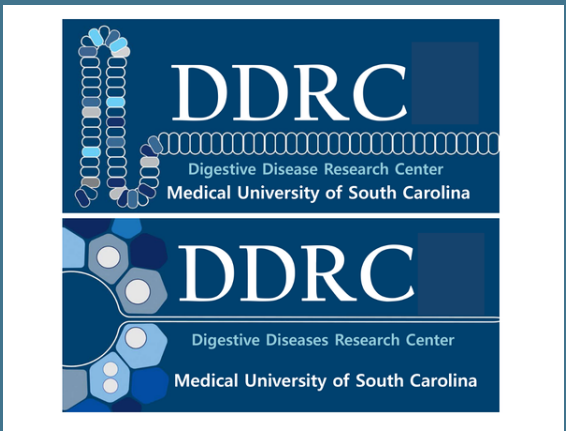
Don and Steve

Choose Our New DDRC Logo!

We received a number of striking and creative submissions to our Digestive Disease Research Center logo contest from our membership. We would like your input before choosing one to represent our center. To indicate your preference, please **rank** the entries below from **1 - 5**, **1 being your top choice and 5 being your last choice**, by clicking on the appropriate survey button below each entry. The finalized version of the logo may be modified to conform with relevant MUSC branding policies, and to facilitate transfer to various media; e.g. t-shirts, stationary or other branded "swag."

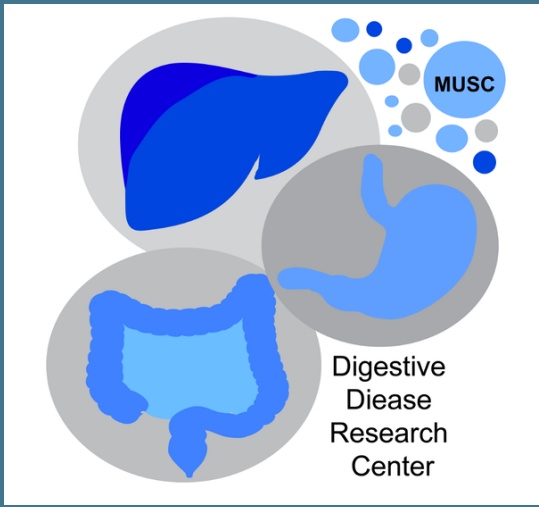
1 2 3 4 5

1 2 3 4 5



1 2 3 4 5

1 2 3 4 5



1 2 3 4 5

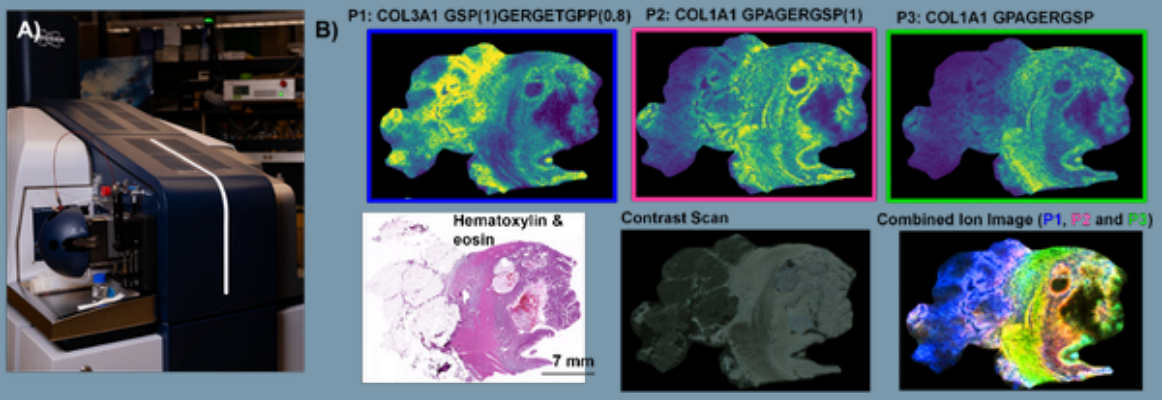
Please submit your choices no later than noon Friday, December 9. The individual submitting the winning entry will earn free t-shirts for all of their group members!

Cores Update: Proteomics

A state-of-the-art high mass resolution, high mass accuracy imaging mass spectrometer (Scimax, Bruker) was installed in May 2022, awarded to DDRCC member and Proteomics Core co-director, **Dr. Peggi Angel** (NIGMS/OD S10OD030212). This $1.7-million Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometer is capable of assaying a broad range of analytes and a wide dynamic range of detection for state-of-the art glycomic, lipidomic, and proteomic imaging work in clinical cohorts. The instrument has **double the acquisition speed, double the sensitivity, increased high mass accuracy, and improved mass resolving power in complex samples**.

For complex samples such as lipid imaging on tissue, algorithmic changes in data handling increase mass resolution by over 60% and improve mass accuracy calculation, allowing fine isotopic resolution. The instrument is ideal for spatial 'omics within the complex tissue microenvironment, reporting spatial distribution and localized concentrations of lipids, peptides, and glycans. Unique workflows at MUSC may be used for investigating the same sample including both imaging of extracellular matrix proteomics (collagen proteins and elastin) and glycomics. Software packages support visualization of data as peak intensity distribution and co-registration with multiplexed histology, pathology, or other imaging data.

The Scimax FT-ICR instrument is the only instrument of its kind in South Carolina and provides a unique resource that is being used at the state, national, and international levels. For more information, contact **Peggi Angel**.



New Spatial 'Omics capabilities within the DDRCC. A) A New high mass resolution high mass accuracy mass spectrometer (Scimax, Bruker) is located in CRI 305G. B) Example imaging of collagen peptides in colorectal cancer, courtesy Kristin Wallace. Post-translational modifications of hydroxylated proline are marked by site probabilities in parentheses. Site localization for post-translational modifications done with Lauren Ball, Mass Spectrometry Facility, DDRCC.

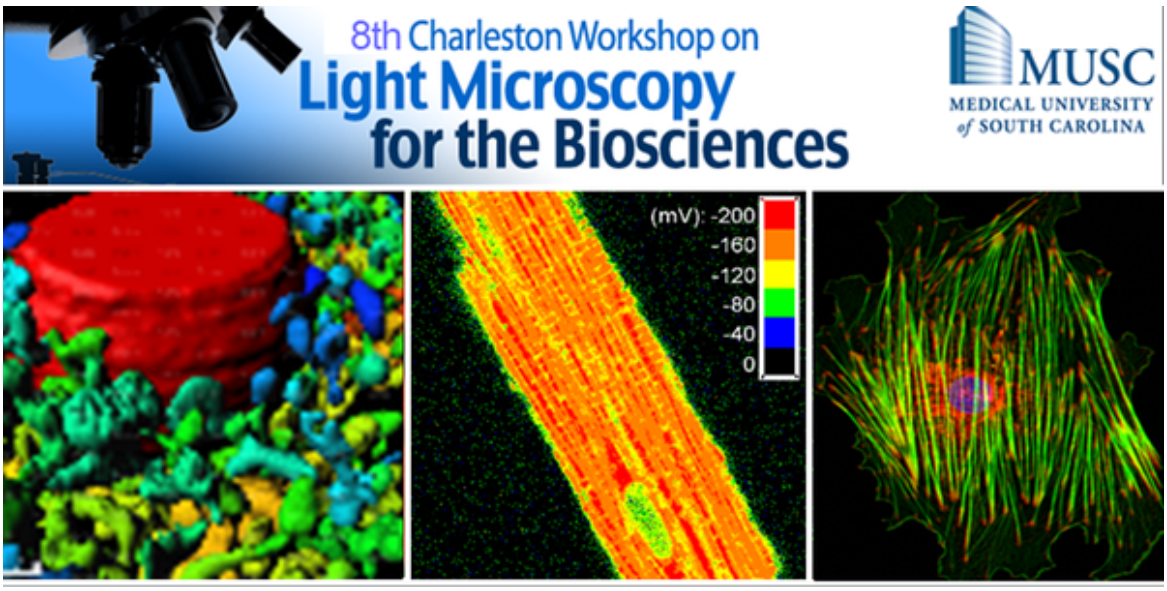
The Proteomics Core also acquired a state-of-the-art high mass accuracy, high resolution **Orbitrap Exploris 480 mass spectrometer** (ThermoScientific), awarded to **Dr. Lauren Ball** (NIGMS/OD S10 OD028692) for **quantitative proteomics**. With this LC-MS/MS system, installed in July 2022, we are providing investigators with next-generation, label free proteomics (DIA-MS) to identify differentially abundant proteins in samples from any source. As compared to label free quantitation (LFQ), DIA-MS provides more sensitive detection of proteins of low abundance with higher quantitative resolution and accuracy. In an ongoing study with Dr. Zhi Zhong aimed at identifying the mechanism of action of a novel drug to treat fatty liver disease and NASH, this alternative data acquisition mode, in combination with advances in instrumentation and new DIA-MS data analysis software, **yielded 40% more quantifiable hepatic proteins with half the material in half the time**.

For global identification of regulated sites of **post-translational modification**, the instrument can yield unparalleled depth of analysis at the protein, peptide, and modification site level. For our investigators who need to characterize modifications including glycosylation and disulfide linked modifications, or modifications that may occur on many amino acids such as methylation and oxidation, the **Orbitrap Fusion Lumos** with multiple complementary fragmentation modes (HCD, ETD, EThcD, UVPD, CID) is also available (NIGMS/OD S10 OD025126, PI Ball).

Following the discovery of a modification of interest, a newly available **data acquisition mode** can be used for absolute or relative quantification of the modified peptide in experimental sample sets. This highly sensitive, internal standard-triggered assay (SureQuant IS-PRM, ThermoScientific) is capable of quantifying analytes that remain undetected by conventional targeted proteomic assays. In ongoing studies we utilized this new capability to confirm the presence of novel modifications of a protein immunoprecipitated from minute, dissected tissue preparations of **limited quantity**.

For more information regarding the new instrument and proteomic experiments please contact **Lauren Ball**.

Cores Update: Imaging Workshop



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

News from the DDRCC

Center Collaboration Highlight and Publication EurekAlert: Novince Lab

Chad Novince, PhD, DDS

The laboratory of **Chad Novince, PhD, DDS**, spearheaded a multi-member, multi-core research effort whose results were accepted to JCI Insight, and that was highlighted via a recent MUSC EurekAlert notification. A joint effort between the Novince Lab, including new member **Jessica Hathaway-Schrader, PhD**, and the laboratories of **Caroline Westwater, PhD**, and **John Lemasters, MD, PhD**, delineated the distinct contributions of gut microbiota and host liver metabolism to the bone-modulating effects of the antibiotic minocycline.

The research utilized the CDLD-sponsored **Gnotobiotic Mouse Facility** and **Animal Core**, as well as the **Advanced Imaging Core** funded by the DDRCC.

CONGRATULATIONS TO ALL!

Meeting Presentation: Je-Hyun Yoon, PhD

Je-Hyun Yoon, PhD

Je-Hyun Yoon, PhD, Associate Professor in the Department of Biochemistry and Molecular Biology recently presented a platform session at the 2022 American Society for Exosomes & Microvesicles in Asilomar, CA (Sept 29 - Oct 3)

"*Mature microRNA-binding proteins and extracellular release*."

Congratulations, Dr. Yoon!

DDRCC Seminar: John Lemasters, PhD

John Lemasters, MD, PhD

John Lemasters, MD, PhD, Professor of Drug Discovery and Biomedical Sciences, was recently invited for a seminar at our sister DDRCC institution, the **Pittsburgh Liver Research Center** (PLRC) at the University of Pittsburgh Medical Center. His seminar:

"*Role of Mitochondria in Hepatic Pathobiology – Examples from Hepatotoxicity and Alcoholic and Non-alcoholic Steatohepatitis*." November 15, 2022

Core Innovation: Cancer Biomarker Imaging

Monika Gooz, MD, PhD

Eduardo Maldonado, DVM, PhD

Drug Discovery and Biomedical Sciences faculty members **Monika Gooz** and **Eduardo Maldonado**, in collaboration with Agilent scientist Brad Larson, PhD, recently published an application note highlighting the use of cancer biomarkers in high content fluorescence microscopy for anti-cancer drug development.

The paper entitled “Expression and Intracellular Translocation of Cancer Biomarkers in Hepatocarcinoma Cells Induced by Changes in Mitochondrial Metabolism” utilizes the capabilities of the BioTek Cytation 5 multimode imager/reader system purchased by the NIH S10 grant (OD028663) to Dr. Gooz.

CONGRATULATIONS, DRS. GOOZ AND MALDONADO!

DDRC at MUSC Research Day

The Digestive Disease Research Center was well-represented by our faculty, postdocs, students and staff at the **2022 Perry V. Halushka Research Day**, with several winning awards in their presentation category.

Congratulations to All!

Denys Ruchanagrong	Angel Lab	**2nd place: PhD II Poster**
Gray Evans	Meissner Lab	**1st Place PhD III/IV Poster**
Eva Allen	Ferreira Lab	**1st Place Undergrad/Master's Oral**
Caren Doueiry	Duncan Lab	**1st Place PhD II Oral**
Alexander Oles	Guttridge Lab	**1st Place PhD IV Oral**
Rob Robino	Ferreira Lab	**2nd Place Res. Spec. / Technician**

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)

December 14th

Zachary Henry, MD, MS University of Virginia

Managing gastric varices in the age of IR

January 11th

Benjamin Kuhn, DO MUSC, Shawn Jenkins Children's Hospital

Eosinophilic esophagitis: to know what you know and what you do not know, that is true knowledge

January 18th

Heather Simpson, MD, MUSC

Hepatitis C: epidemiology and management

January 25th

William P. Lancaster, MD, MUSC

Management of biliary obstruction in patients with cholangiocarcinoma

DDRCC/CDLD/ RMCB Virtual Seminar Series:

Wednesday, 11 am EST (Zoom)

December 7th

Jim Luyendyk, PhD Michigan State University

Mechanisms linking blood coagulation to liver regeneration: from mice to patients

January 11th

Joseph M. Miano PhD Medical College of Georgia at Augusta University

Regulation and function of the SRF-myocardin transcriptional switch

January 25th

Yuan Zhai, MD, PhD MUSC

The innate immune regulation of liver ischemia/reperfusion injury

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**.

October, 2022 - November, 2022

Hijazi N, Shi Z, **Rockey DC**. Characterization of focal adhesion proteins in rodent hepatic stellate cells. Histochem Cell Biol. 2022 Oct;158(4):325-334. PubMed PMID: 35960334.

Strand DS, Law RJ, Yang D, **Elmunzer BJ.** AGA Clinical Practice Update on the Endoscopic Approach to Recurrent Acute and Chronic Pancreatitis: Expert Review. Gastroenterology. 2022 Oct;163(4):1107-1114. Review. PubMed PMID: 36008176.

Schreiner AD, Moran WP, Zhang J, Livingston S, Marsden J, Mauldin PD, Koch D, Gebregziabher M. The Association of Fibrosis-4 Index Scores with Severe Liver Outcomes in Primary Care. J Gen Intern Med. 2022 Oct;37(13):3266-3274. PubMed PMID: 35048297; PubMed Central PMCID: PMC9550951.

Oezguen N, Yılmaz V, Horvath TD, Akbayir E, Haidacher SJ, Hoch KM, Thapa S, Palacio J, Türkoğlu R, Kürtüncü M, **Engevik MA**, Versalovic J, Haag AM, Tüzün E. Serum 3-phenyllactic acid level is reduced in benign multiple sclerosis and is associated with effector B cell ratios. Mult Scler Relat Disord. 2022 Oct 10;68:104239. PubMed PMID: 36279598.

Wallon L, Khan I, Teng KW, Koide A, Zuberi M, Li J, Ketavarapu G, Traaseth NJ, **O'Bryan JP**, Koide S. Inhibition of RAS-driven signaling and tumorigenesis with a pan-RAS monobody targeting the Switch I/II pocket. Proc Natl Acad Sci U S A. 2022 Oct 25;119(43):e2204481119. PubMed PMID: 36252024; PubMed Central PMCID: PMC9618066.

Liu S, Premont RT, Park KH, **Rockey DC**. β-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. PubMed PMID: 36044673; PubMed Central PMCID: PMC9639759.

Samuvel DJ, Li L, Krishnasamy Y, **Gooz M**, Takemoto K, Woster PM, **Lemasters JJ**, **Zhong Z**. Mitochondrial depolarization after acute ethanol treatment drives mitophagy in living mice. Autophagy. 2022 Nov;18(11):2671-2685. PubMed PMID: 35293288; PubMed Central PMCID: PMC9629059.

Lefler JE, MarElia-Bennett CB, Thies KA, Hildreth BE 3rd, Sharma SM, Pitarresi JR, Han L, Everett C, Koivisto C, Cuitino MC, Timmers CD, O'Quinn E, Parrish M, Romeo MJ, Linke AJ, **Hobbs GA**, Leone G, **Guttridge DC**, Zimmers TA, Lesinski GB, Ostrowski MC. STAT3 in tumor fibroblasts promotes an immunosuppressive microenvironment in pancreatic cancer. Life Sci Alliance. 2022 Nov;5(11). PubMed PMID: 35803738; PubMed Central PMCID: PMC9270499.

Young LEA, Conroy LR, Clarke HA, Hawkinson TR, Bolton KE, Sanders WC, Chang JE, Webb MB, Alilain WJ, Vander Kooi CW, **Drake RR**, Andres DA, Badgett TC, Wagner LM, Allison DB, Sun RC, Gentry MS. In situ mass spectrometry imaging reveals heterogeneous glycogen stores in human normal and cancerous tissues. EMBO Mol Med. 2022 Nov 8;14(11):e16029. PubMed PMID: 36059248; PubMed Central PMCID: PMC9641418.

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:

Stephen Duncan, DPhil
Department Chair
Regenerative Medicine and Cell Biology
BSB 657A MSC508
173 Ashley Ave
Charleston, SC 29425
(843) 792-9104
Email Dr. Duncan

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

© Medical University of South Carolina
173 Ashley Avenue
Charleston, SC 29425