DDRC DIGEST
Digestive Disease Research Center
Medical University of South Carolina

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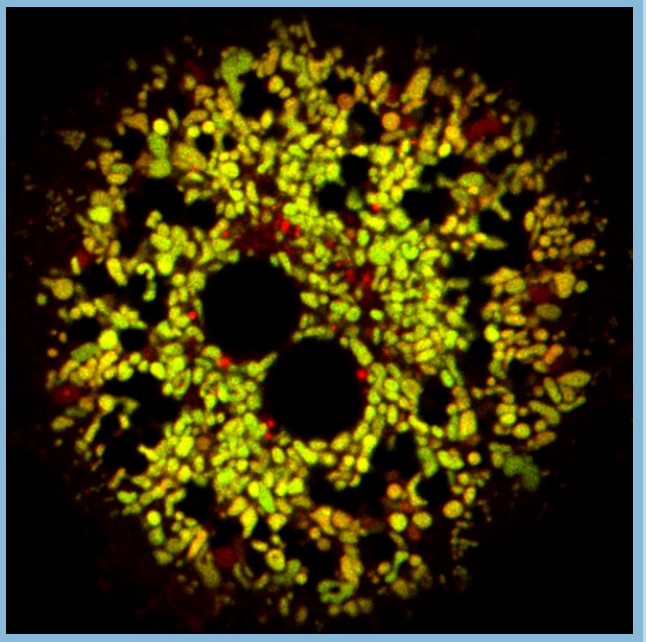
On the Inside



Overlay image of primary mouse hepatocyte mitochondria double-stained with Rh123 mitochondrial membrane potential indicator, and novel mitoferrofluor (MFF) dye detecting free or chelatable mitochondrial iron levels. From Kholmukhamedov et al., J. Biol. Chem 289(9): 102336 (courtesy of the Lemasters Lab)

A Note from the Directors

Don C. Rockey
DDRCC Director

Dear All: As the new academic year starts in earnest, and our centers are clearly running "on all cylinders." As a consistent finding, we continue to be gratified and amazed at all of our members' publication and grant funding achievements, several of which are highlighted in the news content below. We also continue to increase our presence and outreach

Stephen Duncan
CDLD Director

Welcome New Members!

A primary role of the MUSC Digestive Disease Research Core Center is to provide support for GI & liver disease researchers across the campus, and to foster communication and collaboration between our 41 full members, who represent a dozen basic science and clinical divisions at MUSC. As part of these functions, we are glad to provide the updates below on our steadily growing full member ranks, and on the associated GI and metabolic disease clinical, translational and basic research community.

Update: Division of Gastroenterology (Pediatrics)

Ben Kuhn, DO

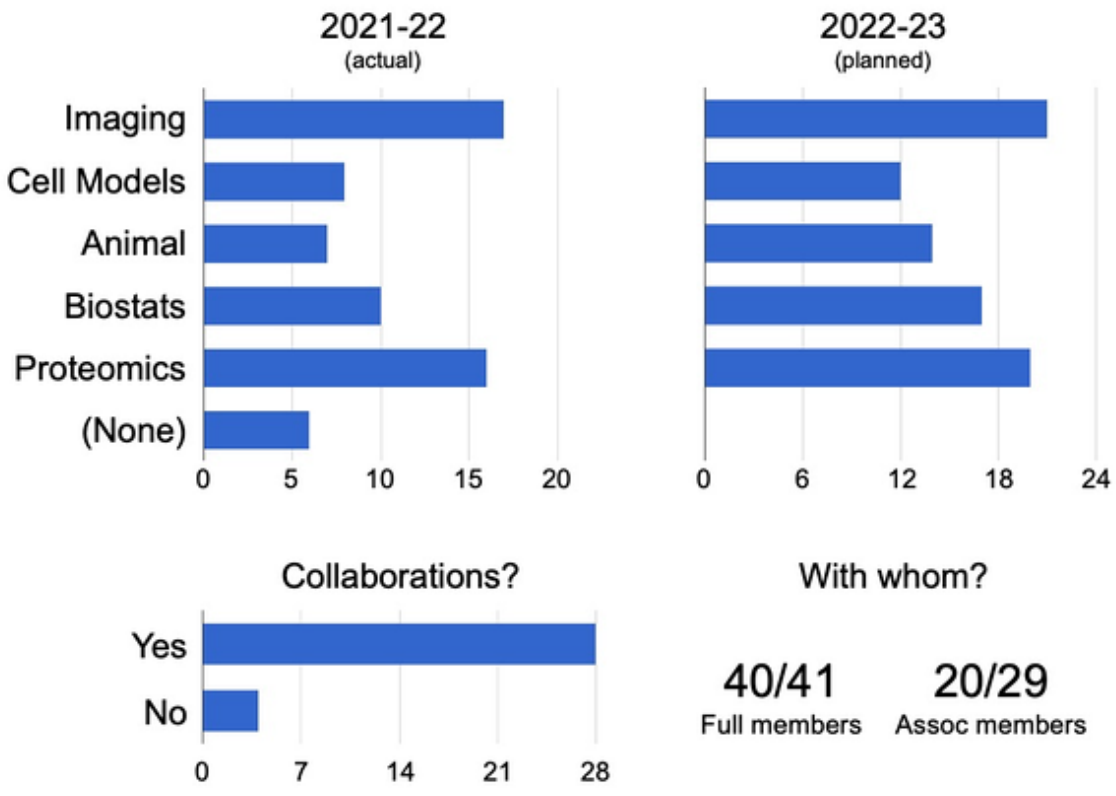
Benjamin Kuhn, DO, FAAP

Dr. Benjamin Kuhn arrived in August of this year to take on the position of Professor of Pediatrics and **Division Chief of Gastroenterology in the Department of Pediatrics** at Shawn Jenkins Children's Hospital at MUSC. He comes to Charleston following his tenure as faculty and Regional Director of Pediatrics at the Geisinger Commonwealth School of Medicine, and his fellowship training at the Cincinnati Children's Hospital Medical Center.

Dr Kuhn's research interests are focused on inflammatory bowel disease, with a particular interest in eosinophilic esophagitis. During his tenure in the Geisinger health system, he spearheaded regional system-wide patient-reported data integration efforts to optimize the management and medical treatment of EoE, as well as Next Generation GWAS and novel PheWAS initiatives for this disease. Going forward, he hopes to replicate these efforts in the Charleston region and the state. Welcome, Dr. Kuhn!

Contact Dr. Kuhn

Annual DDRC Cores & Collaborations Survey



Evaluation of core usage is a key measure for our center's ongoing success and viability: **Our research membership base will increasingly be defined by those investigators who utilize our cores, and demonstrate their value by citing their support in their publication and grant successes**. The very robust response to our Full Members cores and collaborations survey this year (>80%) therefore supplied key metrics toward a "snapshot" of our center.

As seen in the summary figures above, all of our cores provided services to a solid proportion of our 41 full members. As expected, those cores producing experimental models for more long-term use (Cell Models, Animal) show lower per-year usage, as compared to analytical cores (Imaging, Proteomics). Overall, users had few issues with the core services, which they overall described as completely satisfactory or mostly satisfactory, with scheduling issues being the predominant shortcoming (not shown here). As further evidence of user satisfaction, 100% of respondents stated they would definitely use the core again, which is also reflected across the board in planned usage for the coming year. This includes the Biostatistical core, which can provide valuable input for experimental planning and statistically robust evaluation of data resulting from clinical, translational and basic science efforts.

Also gratifying is the highly collaborative nature of our center: the vast majority of our full member base reported being involved with collaborations with at least one other member. Approximately two-thirds of our associate members were also cited as being involved with collaborations, a metric we hope will continually improve. Going forward, we the leadership would appreciate being kept apprised of particularly fruitful long-term collaborations enabling novel directions in digestive disease research.

PLEASE CITE OUR CORES!

Please help us to credit our centers for your publications successes by adding a statement like the samples below to the **Acknowledgements** section of your manuscript:

"This work was supported by the core resources of the Medical University of South Carolina Digestive Disease Research Core Center (P30 DK123704)"

"This work was supported by the ____ core of the

News from the DDRCC

New Grant: Jorge Munera, PhD

Jorge Munera, PhD

Jorge Munera, PhD, Assistant Professor in the Department of Regenerative Medicine & Cell Biology, was recently awarded a new grant from the NIDDK:

NIH/NIDDK
"*The Role of GATA3 and SATB2 in Early Colonic Patterning*"

R56 DK129575-01A1
September 16, 2022 - August 31, 2023 ($250,000)

Congratulations, Dr. Munera!

New Grant: Andrew Schreiner, MD, MSCR

Andrew Schreiner, MD

Andrew Schreiner, MD, Assistant Professor in the Department of Medicine (GI & Hepatology), was recently awarded a new grant from the NIDDK:

NIH/NIDDK
"*Improving the Diagnosis and Fibrosis Risk Assessment of Nonalcoholic Fatty Liver Disease in Primary Care Patients with Abnormal Liver Chemistries.*"

R03 DK129558-01A1
May 15, 2022 - April 30, 2024 ($150,000)

Congratulations, Dr. Schreiner!

New Grant: Mindy Engevik, PhD

Mindy Engevik, PhD

Mindy Engevik, PhD, Assistant Professor in the Department of Regenerative Medicine & Cell Biology, was recently awarded an American Gastroenterology Association - Pfizer Pilot Research Award in Inflammatory Bowel Disease:

"Exploring the contribution of intestinal microbes to intestinal inflammation and its... ."

June 1, 2022 - May 31, 2023 ($30,100)

Congratulations, Dr. Engevik!

New Grant: Aaron Hobbs, PhD

Aaron Hobbs, PhD

Aaron Hobbs, PhD, Assistant Professor in the Department of Cell and Molecular Pharmacology and Experimental Therapeutics, was recently awarded a research grant from the Concern Foundation titled:

"*KRASG12R Allele-specific Metabolic Reprogramming Alters Therapeutic Sensitivity.*"

October 1, 2022 - September 30, 2024 ($120,000)

Congratulations, Dr. Hobbs!

Promotion and Developing Scholar Recognition: Antonis Kourtidis, PhD

Antonis Kourtidis, PhD

DDRCC member Antonis Kourtidis, PhD, was recently promoted to **Associate Professor** in the Regenerative Medicine & Cell Biology Dept., effective January 1, 2023.

Additionally, Antonis's outstanding and novel research contributions toward the understanding of RNAi regulation of gene expression by cellular junctional complex machinery was recognized by the MUSC Foundation's **Developing Scholar Award** at the August, 2022 Faculty Convocation.

Congratulations, Dr. Kourtidis!

SEND US YOUR LOGO IDEAS!

We've had some interesting submissions so far, but the **MUSC DDRC Logo Design Contest** is still open to new submissions. Unleash your artistic instincts and leave your permanent mark on our center! Winning entries will receive free t-shirts for their research group.

DEADLINE: MONDAY, OCTOBER 31st, 2022

We like 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 were 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 (Zoom)

October 12th

Kevin S. Hughes, MD MUSC

Bringing cancer genetic testing into standard GI practice

October 19th

Nikhil Kumta, MD, MS Mt Sinai Health System

Endoscopic management of obesity

October 26th

Vivek Kaul, MD, University of Rochester

Early detection of pancreatic cancer

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

October 5th

Takako Makita, PhD MUSC

New insigts into enteric nervous system development and disease

October 19th

Kris DeMali, PhD University of Iowa

Mechanisms linking mechanotransduction and metabolism

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 particularly significant papers 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**.

August, 2022 - September, 2022

Kurz J, Weiss AC, Lüdtke TH, Deuper L, Trowe MO, Thiesler H, Hildebrandt H, Heineke J, **Duncan SA**, Kispert A. GATA6 is a crucial factor for Myocd expression in the visceral smooth muscle cell differentiation program of the murine ureter. Development. 2022 Aug 1;149(15). PubMed PMID: 35905011.

Nielsen EM, Anderson KP, Marsden J, Zhang J, **Schreiner AD**. Nonalcoholic Fatty Liver Disease Underdiagnosis in Primary Care: What Are We Missing?. J Gen Intern Med. 2022 Aug;37(10):2587-2590. PubMed PMID: 34816326; PubMed Central PMCID: PMC9360350.

Aroniadis OC, Wang X, Gong T, Forbes N, Yang JY, Canakis A, **Elmunzer BJ**, Yadav D. Factors Associated with the Development of Gastrointestinal Symptoms in Patients Hospitalized with Covid-19. Dig Dis Sci. 2022 Aug;67(8):3860-3871. PubMed PMID: 34751837; PubMed Central PMCID: PMC8575674.

Sobotka LA, Esteban J, Volk ML, **Elmunzer BJ**, **Rockey DC**. Acute Liver Injury in Patients Hospitalized with COVID-19. Dig Dis Sci. 2022 Aug;67(8):4204-4214. PubMed PMID: 34487314; PubMed Central PMCID: PMC8419385.

Qu N, Jeffcoat B, Maity P, Christensen RK, **Múnera JO**. Retinoic Acid Promotes the In Vitro Growth, Patterning and Improves the Cellular Composition of Human Pluripotent Stem-Cell-Derived Intestinal Organoids. Int J Mol Sci. 2022 Aug 3;23(15). PubMed PMID: 35955755; PubMed Central PMCID: PMC9368900.

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

Haslund-Gourley BS, Grauzam S, **Mehta AS**, Wigdahl B, Comunale MA. Acute lyme disease IgG N-linked glycans contrast the canonical inflammatory signature. Front Immunol. 2022;13:949118. PubMed PMID: 35990620; PubMed Central PMCID: PMC9389449.

Lei Y, Lethebe BC, Wishart E, Bazerbachi F, **Elmunzer BJ**, Thosani N, Buxbaum JL, Chen YI, Bass S, Cole MJ, Turbide C, Brenner DR, Heitman SJ, Mohamed R, Forbes N. Test Performance Characteristics of Dynamic Liver Enzyme Trends in the Prediction of Choledocholithiasis. J Clin Med. 2022 Aug 5;11(15). PubMed PMID: 35956191; PubMed Central PMCID: PMC9369577.

DelaCourt AT, Liang H, **Drake RR**, **Angel PM**, **Mehta AS**. Novel Combined Enzymatic Approach to Analyze Nonsialylated N-Linked Glycans through MALDI Imaging Mass Spectrometry. J Proteome Res. 2022 Aug 5;21(8):1930-1938. PubMed PMID: 35766466.

Brobbey C, Liu L, Yin S, **Gan W**. The Role of Protein Arginine Methyltransferases in DNA Damage Response. Int J Mol Sci. 2022 Aug 29;23(17). Review. PubMed PMID: 36077176; PubMed Central PMCID: PMC9456308.

Kholmukhamedov A, Li L, Lindsey CC, Hu J, **Nieminen AL**, Takemoto K, Beeson GC, Beneker CM, McInnes C, Beeson CC, **Lemasters JJ**. A new fluorescent sensor mitoferrofluor indicates the presence of chelatable iron in polarized and depolarized mitochondria. J Biol Chem. 2022 Sep;298(9):102336. PubMed PMID: 35931111; PubMed Central PMCID: PMC9460511.

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 Sep 5;:e16029. PubMed

Publication Highlights:

Je-Hyun Yoon, PhD

Je-Hyun Yoon, PhD, Assistant Professor in the Biochemistry & Molecular Biology Dept., was co-principal author on a manuscript published in the journal *Nature Communications*:

"***The nucleolus is the site for inflammatory RNA decay during infection***." *Nat Comm 13, 5203 (2022)*

In this article, Dr. Yoon and colleagues demonstrated that LPS-activated macrophages accumulated precursor mRNAs encoding pro-inflammatory cytokines in the nucleolus to facilitate their rapid degradation.

Congratulations, Dr. Yoon!

Anna Liese Nieminen, PhD

John Lemasters, MD, PhD

Anna-Liese Nieminen, PhD and **John Lemasters, MD, PhD** jointly co-authored a manuscript published in The Journal of Biological Chemistry describing their newly developed mitochondrial fluorescent indicator, mitoferrofluor (MFF). MFF fluorescence is strongly and selectively quenched by Fe2+, the predominant form of free or non-chelatable iron in the reductive mitochondrial environment. MFF accumulates in polarized mitochondria and is retained there even following loss of membrane potential. Because of its stable retention in failing mitochondria, MFF can be used to monitor Fe2+ levels during mitochondrial membrane potential loss as a mediator of mitochondrial permeability transition and cell death.

"Mitoferrofluor, a probe of mitochondrial chelatable Fe2+." *J. Biol. Chem. (2022) 298(9) 102236.*

Congratulations, Drs. Nieminen and Lemasters!

DDRC Core Update: Live Cell Imaging

The DDRC Imaging Core recently purchased a Tokai Hit tabletop stage incubator system for the **Leica Sp8** confocal microscope housed in the Regenerative Medicine & Cell Biology Department on BSB 6th floor. This system is able to provide a suitable environment (5% CO2, 37 deg C) for most live cell imaging needs. Currently, the unit has the ability to accommodate 35/50/60 mm dishes, chamber slides, and multiwell plates. For more specific details including the purchasing of appropriate culture vessels for use with this unit and the Sp8 confocal microscope, please contact Ray Deepe in the RMCB department.

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 THE COBRE CDLD:
P20 GM120457

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

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Charleston, SC 29425
(843) 792-1689
Email Dr. Lee

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

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

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

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