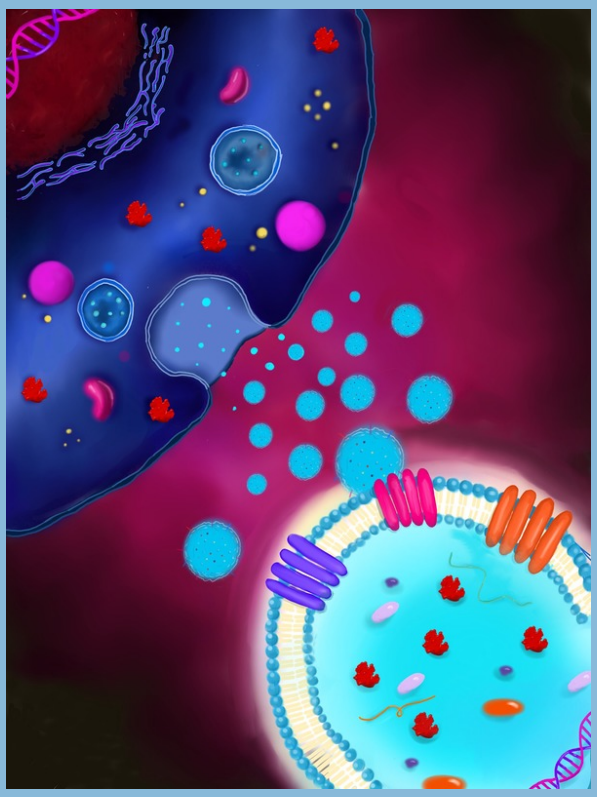
DDRC DIGEST
Digestive Disease Research Center
Medical University of South Carolina

Volume 2, Issue 6 **February 1, 2022**

On the Inside



Cover art illustrating extracellular vesicle release from mesenchymal stem cells, from a joint publication from the **Hongkuan Fan** and **Hongjun Wang** Labs. *Wei et l. Biology (Basel). 2021 Dec 21;11(1). PubMed PMID: 35053007; PubMed Central PMCID: PMC8773149.*

A Note from the Directors

Don C. Rockey
DDRCC Director

As we begin Year 3, we are looking forward to our **3rd Annual Digestive Disease Research Center (DDRC) Retreat and Symposium** on **April 8, 2022**. Please mark your calendars to block this day. As of now, we hope that we will be able to hold this meeting "in person." Our symposium website is up, and will be updated with detailed agenda and other news. This

Stephen Duncan
CDLD Director

year, we're excited to announce that University of Pittsburgh DDRCC Director and MUSC DDRCC External Advisory Board member **Paul Monga, MD, PhD** will be our keynote speaker. Registration and abstract submission are now available: please use the links in the announcement below. We are excited to hear all the research updates from our members and community from the past year.

Our center continues to grow with the addition of new faculty investigators from various departments. Please take a moment to read about our two latest additions so that you may welcome them at your next opportunity.

Over the next several months there will be exchange visits within the **Eastern DDRCC Alliance network.** We are in the process of making arrangements for our own exchange visitors, with updates to follow.

Our **7 am Clinical / Translational** and **11 am Basic Science** virtual enrichment series still have some available slots in 2022 so, as always, please let us know if you'd like to hear from a particular guest speaker (**email Antonis** or **Don**).

Best wishes for the current new year,

Don and Steve

Research Focus

The Digestive Disease Research Core Center continues to welcome new members to our ranks. As part of our goal to build community and collaboration, we are profiling these investigators to increase awareness of the increasing richness of scientific effort and thought in digestive disease here at MUSC. A list of the current DDRCC Full Membership may be found on the **Member Directory** page of the **DDRCC Website**.

Welcome to our New DDRCC Investigators

p53 Variants and Chaperone Function in Cancer Risk

Tim Barnoud, PhD

Department of Biochemistry & Molecular Biology

Tim Barnoud, PhD, joined the MUSC faculty in November of 2021, and currently serves as an Assistant Professor in the Department of Biochemistry and Molecular Biology at MUSC. He received his PhD in Biochemistry and Molecular Genetics from the University of Louisville. He continued his studies at the Wistar Institute by completing a postdoctoral fellowship in the Molecular and Cellular Oncogenesis Program.

Contact Dr. Barnoud

Dr. Barnoud's laboratory uses genetically engineered mouse models (GEMMs) to study the p53 tumor suppressor, the most frequently mutated gene in human cancer. The main goal of the Barnoud Lab is to study the impact of p53 variants on cancer risk and response to therapy. A second major research focus is to understand the role of heat shock proteins (HSPs) on the initiation and progression of cancer. The Barnoud Lab employs a series of inhibitors that target HSPs with the hopes of developing effective cancer therapies, with a focus on gastrointestinal (GI) cancers. As well, his laboratory has an interest in personalized medicine approaches based on p53 status and the activity of specific p53 variants.

For additional details about the Barnoud Lab and opportunities for collaboration, please contact Dr. Barnoud.

Ischemia-Reperfusion Injury in Liver Transplantation

Yuan Zhai, MD, PhD

Department of Surgery

Yuan Zhai, PhD was recently appointed as Professor in the Department of Surgery at MUSC. He received his MD from Beijing Medical University, and his PhD from the University of Wisconsin (Madison). Following post-doctoral training at the Dumont-UCLA Transplantation Center, and the Dunn School of Pathology at Oxford University, he was appointed faculty in the Department of Surgery at the David Geffen School of Medicine at UCLA, and was a member of the UCLA DDRCC.

Contact Dr. Zhai

Dr. Zhai's research interests include cellular and molecular mechanisms of tissue injury, inflammation, repair in liver transplantation, with a focus on innate-adaptive immune interactions. His laboratory has been studying liver ischemia and reperfusion injury (IRI) in mouse models for over 15 years. Major contributions to the field include demonstrations of novel mechanisms and pathways of inflammatory immune activation and regulation in liver IRI, such as Toll-Like-Receptor 4 (TLR4) and its endogenous ligands, type 1 interferon and CXCL10-CXCR3, and glycogen synthase kinase 3 beta. Additionally, his lab has found that the effector memory subset of adaptive CD4 T cells promotes liver inflammation in an Ag-non-specific manner.

His current research projects aim to (1) identify how distinctive liver macrophage subsets, resident vs. infiltrating, are involved in the activation and resolution of liver IRI; and, (2) dissect the roles of glycogen synthase kinase 3 beta (GSK3B), a serine/threonine kinase originally associated with insulin signaling, in liver macrophages in the context of their heterogenicity and functional complexity in inflammation and tissue repair.

For additional details about the Zhai Lab and opportunities for collaboration, please contact Dr. Zhai.

Notes from the DDRCC

REGISTRATION AND ABSTRACT SUBMISSION OPEN

4rd Annual MUSC Digestive Disease Research Center

RETREAT AND SYMPOSIUM

Friday, April 8, 2022

Register Here

Visit our Symposium webpage for more information

Click here for updates

DDRCC Members in the Top 2%

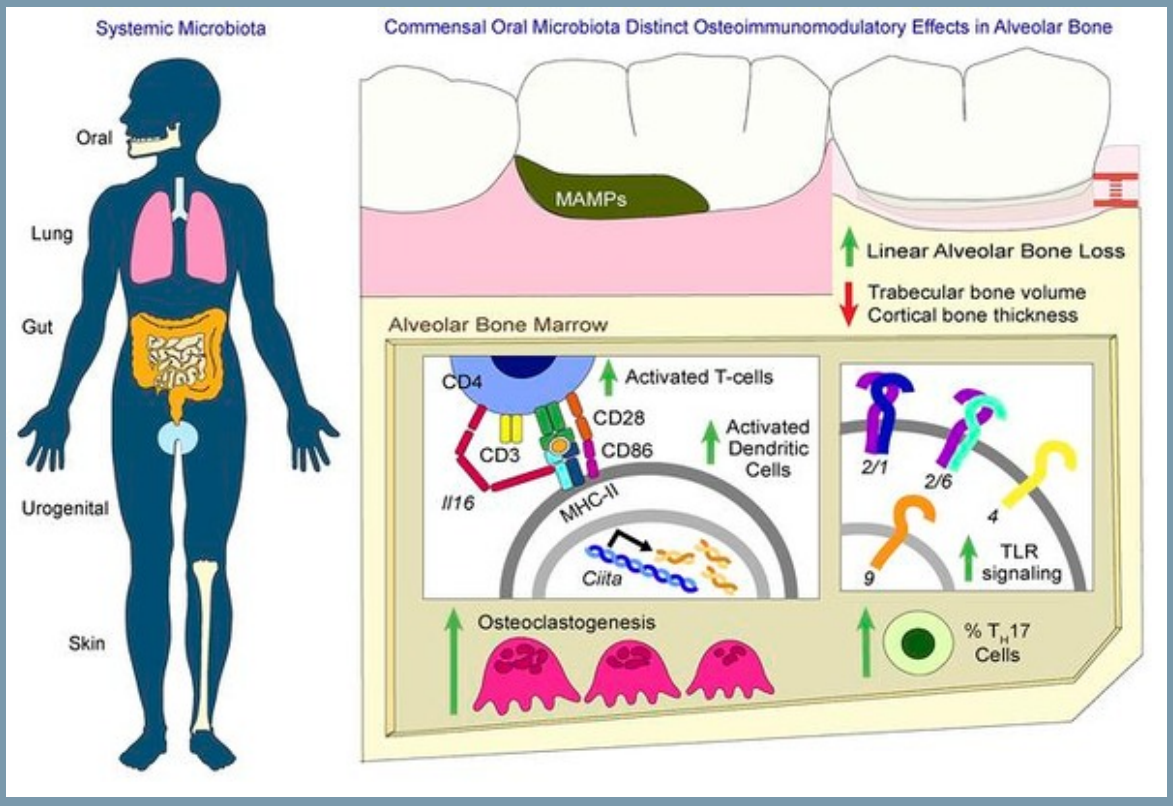
Raymond DuBois, MD, PhD

John Lemasters, PhD

Don Rockey, MD

Several MUSC DDRCC reseearch faculty were recently recognized as being on "the 2% list" of the most referenced researchers in the world, as tabulated by Stanford University. Among those additionally recognized as being among the top 2% cited investigators across all fields included Drs. **Raymond DuBois**, **John Lemasters**, and **Don Rockey**. Congratulations to these investigators for their outstanding science, and for representing our center and our institution! See the full **press release** from MUSC.

COBRE Publication Highlight



Chad Novince PhD, DDS

The laboratory of **COBRE Junior Investigator Chad Novince** recently published a notable paper in *JCI Insight*, with the support of the **Gnotobiotic Mouse Core** (Caroline Westwater, PhD, Director) in the **COBRE for Digestive and Liver Disease (CDLD)**. with the help of the core, the Novince group, led by postdoctoral fellow Jessica Hathaway-Schraeder, were able to discern distinct osteoimmunomodulatory effects on alveolar bone exerted by oral, but not gut microbiota. These effects were also specific to alveolar, but not long bones. These effects were further modulated by treatment with oral antiseptics. Congratulations to the team for representing the CDLD!

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.

Updates from Our Cores

Proteomics

Leadership

Rick Drake, PhD
Director

Lauren Ball, PhD
Assistant Director

Peggi Angel, PhD
MALDI Imaging

Proteomics Collaborations

The MUSC Proteomics Center focuses on clinical and translational proteomics and the development of centralized diagnostics. Two DDRCC-sponsored cores include the established Mass Spectrometry Facility for proteomic services, and a new core established for biomolecular mass spectrometry imaging, the Mass Spectrometry Imaging Research Center. Mass spectrometry (MS) is the key analytical method for proteomics research, and the Center has a comprehensive, complementary suite of instrumentation for proteomic analyses.

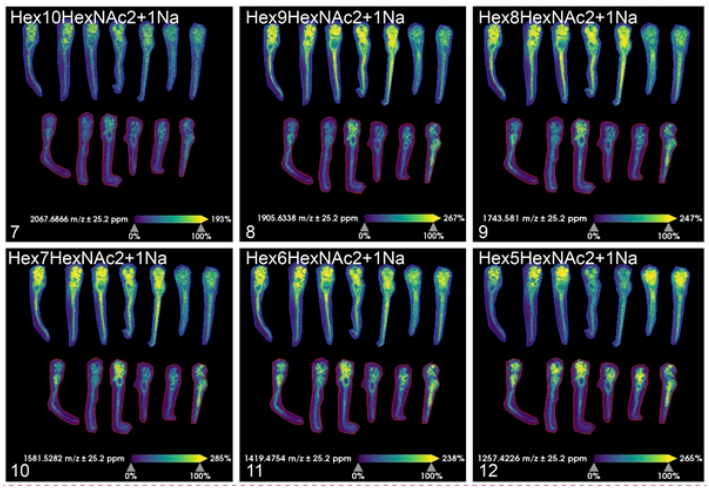
In the clinical setting, MS-driven qualitative and quantitative proteomics can be used to profile disease and/or patient-specific proteins, protein modifications, and small molecules and monitor biomarker changes in response to therapy or disease progression. Extension of MS profiling to two- or three-dimensions using tissue scanning technologies on histology specimens enables biomarker-driven disease profiling and staging in greater depth. As well, the ability to monitor molecular changes at the cell and tissue level facilitates the more insightful development of hypotheses regarding disease mechanisms.

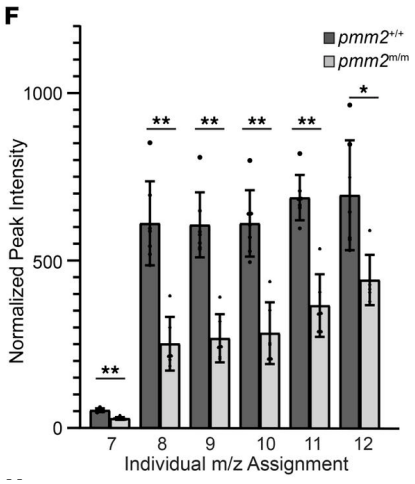
Quantitative proteomics can provide unbiased insights into pathophysiological mechanisms and the response to therapeutics. Available approaches include, but are not limited to, mapping of drug-, RNA-, or protein-protein interactions, and global or targeted measurements of changes in protein abundance, cellular phosphorylation, glycosylation and other post translational modifications in response to genetic or signal perturbations.

Mass spectrometry tissue imaging approaches are performed on tissue sections to localize lipids, glycans, and collagens to the tissue pathology. The MUSC Proteomics Center offers unique capabilities for multiplexed 'Omics, whereby multiple classes of analytes can be profiled within the same specimen. Imaging mass spectrometry approaches can also be applied to cultured cells for profiling of certain metabolites, lipids and N-glycans.

The Center leverages high-performance computing resources with modern protein search algorithms, mass spectrometry-based quantitative analysis, statistical analysis (frequentist or Bayesian techniques), data-driven systems biology, -omic integration techniques, and classifier development (machine learning based) to generate actionable and hypothesis driven results for investigators.

Proteomics Core Publication Highlight: MS Imaging





The Proteomics core collaborated with investigators at UGA and the Greenwood Genetics Center to link alterations in N-cadherin processing to craniofacial and motility defects in a mutant zebrafish novel. The figure above demonstrates the ability of MS imaging to quantitate differences in specific high-mannose oligosaccharides in sections of whole wild-type (top rows) and mutant (bottom rows) zebrafish embryos. This study demonstrated application of this technology for the characterization of congenital disorders of glycosylation. *Klaver et al, JCI Insight. 2021 Dec 22;6(24): e153474. doi: 10.1172/jci.insight.153474.*

To initiate a collaboration with the Proteomics Core:

For LC-MS/MS-based proteomics:

Please contact **Lauren Ball** for initial consultation. Further details about instrumentation, services and fees, facility descriptions to support grant writing and publication efforts, and details for acknowledging the core can be found on the **Mass Spectrophotometry Facility** webpage.

For MS Imaging:

Please contact **Peggi Angel** for initial consultation.

DDRCC Full Members receive a 50% discount on services

Contact Lauren **Contact Peggi** **MS Facility**

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)

February 2

GI & Hepatology Fellows MUSC

Case Conference

February 9

Thomas Werth, MD MUSC

HepatoRenal syndrome and the never-ending promise of Terlipressin

February 16

Shyam Varadarajulou Orlando Health Institute

Endoscopic management of pancreatic fluid collections

February 23

Field F. Willingham, MD, MPH

Early esophageal cancer

March 2

GI & Hepatology Fellows MUSC

Clinical case presentations

March 9

Thomas Rösch, MD University of Hamburg, Hamburg, Germany

Endotherapy of early gastric cancer: expanding the limits

March 16

Shiv Kumar Sarin, MD, DM, DSc Jawarahal Nehru University

Acute on chronic liver failure: terminology and management in 2022

March 30

Peter Draganov, MD University of Florida

What is new in our endoscopy armamentarium

DDRCC/CDLD/ RMCB Virtual Seminar Series:

Wednesday, 11 am EST (Zoom)

February 2

Silvia Guglietta, PhD MUSC - Works in Progress

COMPLEMENTing innate immunity to achieve gut health in intestinal diseases and beyond

February 9

Marino Zerial, PhD Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

Mechanisms of hepatocyte polarization and liver tissue morphogenesis

February 16

Gabriel Núñez, MD University of Michigan

Host-Microbiota Interactions in Health and Disease

February 23

Mahmood Hussain, PhD NYU Long Island School of Medicine

Role of MTP and lipid metabolism

March 2

Silvia Vilarinho, MD, PhD Yale School of Medicine

Genes, genomes and liver disease

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**.

December, 2021 - January, 2022

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 Jan 19. PubMed PMID: 35048297.

Liu X, Taylor SA, Gromer KD, Zhang D, Hubchak SC, LeCuyer BE, Iwawaki T, **Shi Z**, **Rockey DC**, Green RM. Mechanisms of liver injury in high fat sugar diet fed mice that lack hepatocyte X-box binding protein 1. PLoS One. 2022 Jan 14;17(1):e0261789. PubMed PMID: 35030194; PubMed Central PMCID: PMC8759640.

Chakrabarti J, Dua-Awereh M, Schumacher M, **Engevik A**, Hawkins J, Helmrath MA, Zavros Y. Sonic Hedgehog acts as a macrophage chemoattractant during regeneration of the gastric epithelium. NPJ Regen Med. 2022 Jan 12;7(1):3. PubMed PMID: 35022438; PubMed Central PMCID: PMC8755719.

Prakash S, **Elmunzer BJ**, **Forster EM**, **Cote GA**, Moran RA. Endoscopic ultrasound-directed transgastric ERCP (EDGE): a systematic review describing the outcomes, adverse events, and knowledge gaps. Endoscopy. 2022 Jan;54(1):52-61. PubMed PMID: 33506456.

Frey LJ. Informatics Ecosystems to Advance the Biology of Glycans. Methods Mol Biol. 2022;2303:655-673. PubMed PMID: 34626414.

Lauzon SD, Zhao W, **Nietert PJ**, Ciolino JD, Hill MD, **Ramakrishnan V**. Impact of minimal sufficient balance, minimization, and stratified permuted blocks on bias and power in the estimation of treatment effect in sequential clinical trials with a binary endpoint. Stat Methods Med Res. 2022 Jan;31(1):184-204. PubMed PMID: 34841963.

Hathaway-Schrader JD, Carson MD, Gerasco JE, Warner AJ, Swanson BA, Aguirre JI, **Westwater C**, Liu B, **Novince CM**. Commensal gut bacterium critically regulates alveolar bone homeostasis. Lab Invest. 2021 Dec 21. PubMed PMID: 34934182.

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.

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. Suzanne Craig**.
- For gnotobiotic mouse models, please contact **Dr. Caroline Westwater**.
- For transgenic and CRISPR/Cas9 projects, please contact the TGE 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:

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

FOR THE COBRE CDLD:

P20 GM120457

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

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

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Email Dr. Lee

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

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Regenerative Medicine and Cell Biology
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Charleston, SC 29425
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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