

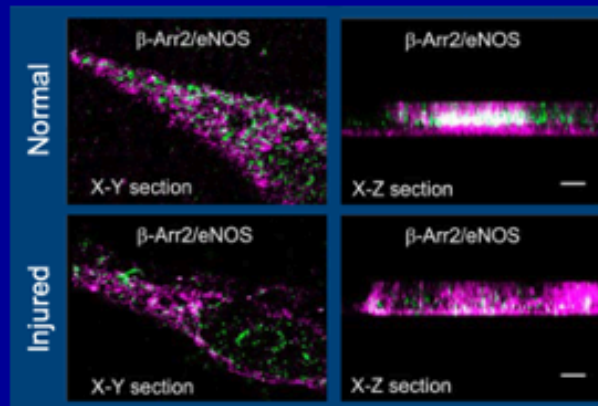


# DDRCC DIGEST

Digestive Disease Research Center  
Medical University of South Carolina

Volume 1, Issue 2

September 1, 2020



Altered co-localization of  $\beta$ -Arr2 and eNOS in injured sinusoidal endothelial cells. From Liu et al, (2020) PNAS 117:21:11483-92

## On the Inside

- **DDRCC New Full Members**
- **Profiles of two of our Cores:**
  - Clinical Component
  - Proteomics
- **Enrichment Series**
- **News from the DDRCC**

## Welcome New DDRCC Members

As we begin this funding cycle in 2020, the Digestive Disease Research Core Center welcomes our newest Full Members. They represent eight clinical and basic science departments across campus, and bring with them a diverse wealth of research interests and expertise. More detailed descriptions of their research interests, along with a complete listing of the current DDRCC Full Membership may be found on the [Member Directory](#) page of the [DDRCC Website](#).



### **Peggi Angel, PhD**

**Assistant Professor, Cell and Molecular Pharmacology and Experimental Therapeutics.** Modifications of extracellular matrix in liver inflammation, fibrosis, cirrhosis and hepatocellular carcinoma.



### **Hermes Florez, MD-PhD, MPH**

**Professor and Chair, Public Health Sciences.** Gene-environment interactions, prevention and management of chronic diseases and aging, diabetes, liver and cardiovascular disease, veteran's health.



### **Marvella E. Ford, PhD, MS, MSW**

**Professor and SmartState Endowed Chair in Prostate Cancer Disparities, SC State University.** Identification and intervention of factors driving disparities in cancer diagnosis and treatment.



### **Lewis J. Frey, PhD**

**Associate Professor, Public Health Sciences.** Artificial Intelligence (AI) approaches for predictive modeling of cirrhosis, hepatocellular carcinoma and nonalcoholic fatty liver disease progression.



### **Wenjian Gan, PhD**

**Assistant Professor, Biochemistry and Molecular Biology.** Kinase signaling pathways regulating liver development, fatty liver disease and cancer progression.



### **Denis C. Guttridge, PhD**

**Professor and Director, Darby Children's Research Institute, Department of Pediatrics.** NF- $\kappa$ B signaling modulation in pancreatic cancer and cancer cachexia.



### **Yan Huang, MD-PhD**

**Professor, Department of Medicine.** Sphingolipid and inflammatory signaling in diabetes, nonalcoholic fatty liver disease and periodontitis.



### **Jorge O. Munera, PhD**

**Assistant Professor, Regenerative Medicine and Cell Biology.** iPSC-derived human colonic organoids for modeling GI disease.



### **Anna-Liisa Nieminen, PhD**

**Associate Professor, Drug Discovery and Biomedical Sciences.** Mitochondrial iron homeostasis and pathophysiology in liver injury



### **Paul J. Nietert, PhD**

**Professor, Public Health Sciences.** Director, Clinical Component Core. Methodological research in hierarchical data analysis, truncated distributions, and randomization in clinical trials.



### **Andrew D. Schreiner, MD, MSCR**

**Associate Professor, Department of Medicine.** Developing Electronic Health Record (EHR)-based models for improving the diagnosis and management of chronic liver disease in primary care settings.



### **Özlem Yilmaz, DDS, PhD**

**Professor, Oral Health Sciences.** Microbial pro-inflammatory nucleotide signaling in chronic periodontitis and its linkage to oral cancer.



### **Je-Hyun Yoon, PhD**

**Assistant Professor, Biochemistry and Molecular Biology.** Non-coding RNA regulation and signaling linking alcohol-induced gut and chronic liver injury.



### **Zhi Zhong, MD-PhD**

**Professor, Drug Discovery & Biomedical Sciences.** Mitochondrial dysfunction in the genesis of alcoholic and nonalcoholic liver disease and steatohepatitis.

## **DDRCC Core Profile: PROTEOMICS**

### **Leadership**



**Rick Drake**  
Core Director



**Lauren Ball**  
Assistant Director



**Pegg Angel**  
MALDI Imaging



**Jennifer Bethard**  
MS Technician

**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.

Current instrumentation in the two core laboratories, the Mass Spectrometry Facility and Mass Spectrometry Imaging Research Center includes:



1. Two orbitrap mass spectrometers (ThermoScientific Orbitrap Fusion Lumos with ETD/UVPD and Orbitrap Elite with ETD) for LC-MS/MS analysis of post-translational modifications including phosphorylation, glycosylation, and redox-sensitive protein modifications.
2. Bruker instruments including a dual-source Tims-TOF FleX, a dual source SolariX 7T FT-ICR MS, a RapiFleX MALDI TissueTyper TOF, and an Autoflex MALDI-TOF MS for MALDI tissue imaging MS capabilities.

## To initiate a project with the Proteomics Core:

For **LC-MS/MS-based proteomics**, please email **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 email **Peggi Angel** for initial consultation. A separate webpage for the Mass Spectrometry Imaging Research Center services and fees is currently under construction.

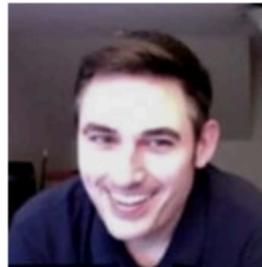
**Full members receive priority access and discounted services.**

## Core Profile: CLINICAL COMPONENT

### Leadership



**Paul Nietert**  
Director  
DDRCC



**Mat Gregoski**  
Biostatistician  
DDRCC



**Ramesh  
Ramakrishnan**  
Director, CDLD



**Abby Kelly**  
Biostatistician  
CDLD

### Biostatistics Collaborations

Successful research careers in clinical sciences invariably involve collaborations or consultations with biostatisticians. Our CDLD and DDRCC members will have access to high-quality, state-of-the-art service provided by two teams of biostatisticians, led respectively by Drs. **Paul Nietert** and **V. Ramakrishnan** (a.k.a. "Ramesh"), who will be assisted by Mat **Gregoski**, PhD, and Abby Kelley, MS.

Starting from simple data analysis for an abstract or sample size recommendations for your NIH grant, to complex designs of experiments or analyses of longitudinal clustered data or high-throughput data, Drs. [Nietert](#), Ramesh and their teams enthusiastically await your request for support. They share your goal of promoting research studies that seek to improve clinical outcomes for patients with digestive diseases.

The biostatistics team recommends consultation for all your research projects. Feel free to approach the team as early as when you are formulating the specific aims. Ultimately, the yardstick they'll use for measuring their success is the number of funded grants (from sources such as the NIH and VA) and quality publications from DDRCC and CDLD members that come about through collaborations with the biostatistics team.

The procedure for seeking help from them is just a few clicks away and is **free for CDLD and DDRCC members**. Soon after an inkling of an idea for research emerges, put in a SCTR SPARC request (please see below for 'how-to'), with Mat [Gregoski](#) as the point person. One of the team members (Abby, Paul, Ramesh Ramakrishnan, or Mat), will soon contact you and begin the collaborations with you.

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## To initiate a collaboration with the Biostatistics Core:

Go to [sparc.musc.edu](https://sparc.musc.edu)

Click on green SCTR button on left (middle of page).

Select: "Biostatistics, Design, & Epidemiology"

Put in any relevant study information, and make sure it gets "submitted"

## Enrichment Series: Upcoming Dates to Remember

**DDRCC / CDLD / GI and Hepatology Grand Rounds:**

**Wednesday, 7am EST**

**September 9: [Joseph Elmunzer](#)**

GI Manifestations of COVID-19: A Multi-center Study

**September 16: [Don Rockey](#)**

The Molecular Basis of Portal Hypertension

**September 23: David Whitcomb** - University of Pittsburgh

Genetics in Pancreatitis

**September 30: Peter Cotton**

How Flexible Endoscopy Began

**DDRCC / CDLD / RMCB Virtual Seminar Series:**

**Wednesday, 11am EST**

**September 2: Alejandro Adam** - Albany Medical Center

IL-6-induced Vascular Leakage and Multi-organ Dysfunction

**September 9: James Heslop** (Duncan Lab)

GATA6 Controls Endoderm Fate by Controlling Chromatin Assembly

**September 16: Hans Clevers** - University Medical Center, Utrecht

Organoids to Model Human Disease

**September 23: Stephan Huveneers** - University of Amsterdam

Endothelial adhesions sense forces for angiogenesis

## Notes from the DDRCC

### Meeting Presentations

**The 14th International Symposium on ALPD and Cirrhosis**

**Aug 13-14, 2020 in Seoul, Korea**

CYP2E1 Regulation of Ethanol-Induced Intestinal miRNAs in Liver Injury

**Je-Hyun Yoon** (Medical Univ. of South Carolina, USA)

**American Association for the Study of Liver Diseases SIG Virtual Seminar**

**Aug 11, 2020**



## Awards

### Department of Medicine Developing Scholar Award

**Eric G. Meissner, MD-PhD**

Read more  
about Dr.  
Meissner's  
research

## Selected Publications by our membership (April - June, 2020)

[Schreiner AD](#), [Rockey DC](#), Moran WP. The cost of hepatitis C testing strategies in primary care patients with abnormal transaminases. *J Gen Intern Med.* 2020 Apr;35(4):1340-1342. PubMed PMID: 31396811; PubMed Central PMCID: PMC7174443.

[Nair-Menon J](#), [Daulagala AC](#), Connor DM, Rutledge L, [Penix T](#), Bridges MC, [Wellslager B](#), [Spyropoulos DD](#), [Timmers CD](#), [Broome AM](#), [Kourtidis A](#). Predominant distribution of the RNAi machinery at apical adherens junctions in colonic epithelia is disrupted in cancer. *Int J Mol Sci.* 2020 Apr 7;21(7). PubMed PMID: 32272708; PubMed Central PMCID: PMC7177752.

[Engevik MA](#), Danhof HA, Chang-Graham AL, [Spinler JK](#), [Engevik KA](#), Herrmann B, Endres BT, [Garey KW](#), [Hyser JM](#), Britton RA, [Versalovic J](#). Human intestinal enteroids as a model of *Clostridioides difficile*-induced enteritis. *Am J Physiol Gastrointest Liver Physiol.* 2020 May 1;318(5):G870-G888. PubMed PMID: 32223302; PubMed Central PMCID: PMC7272722.

[Liu S](#), Luttrell LM, Premont RT, [Rockey DC](#).  $\beta$ -Arrestin2 is a critical component of the GPCR-eNOS signalosome. *Proc Natl Acad Sci U S A.* 2020 May 26;117(21):11483-11492. PubMed PMID: 32404425; PubMed Central PMCID: PMC7261012.

[Engevik AC](#), Coutts AW, [Kaji I](#), Rodriguez P, [Ongaratto F](#), [Saqui-Salces M](#), [Medida RL](#), Meyer AR, [Kolobova E](#), [Engevik MA](#), Williams JA, [Shub MD](#), Carlson DF, [Melkamu T](#), [Goldenring JR](#). Editing myosin VB gene to create porcine model of microvillus inclusion disease, with microvillus-lined inclusions and alterations in sodium transporters. *Gastroenterology.* 2020 Jun;158(8):2236-2249. PubMed PMID: 32112796; PubMed Central PMCID: PMC7282982.

[Wimborne HJ](#), Hu J, Takemoto K, Nguyen NT, [Jaeschke H](#), [Lemasters JJ](#), [Zhong Z](#). Aldehyde dehydrogenase-2 activation decreases acetaminophen hepatotoxicity by prevention of mitochondrial depolarization. *Toxicol Appl Pharmacol.* 2020 Jun 1;396:114982. PubMed PMID: 32240663.

# CITE OUR GRANTS

**FOR THE DDRCC:**  
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**FOR THE COBRE CDLD:**  
**P20GM120457**

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**This project was supported in part by NIH P20 GM120457 (core facility) at the MUSC COBRE in Digestive and Liver disease.**

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

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[leekh@musc.edu](mailto:leekh@musc.edu)

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

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**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>



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