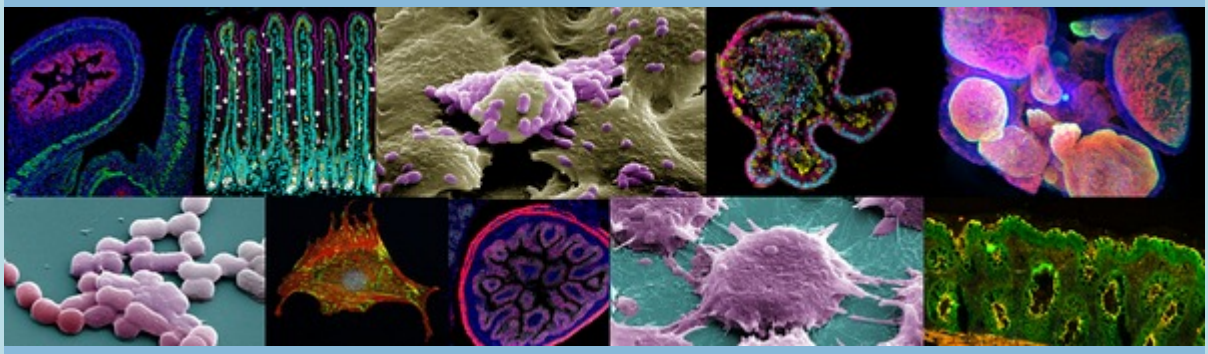
# DDRC DIGEST

Digestive Disease Research Center
Medical University of South Carolina

**Volume 2, Issue 1** **April 1, 2021**



**GI research at MUSC:** Data montage courtesy of Mindy Engevik, PhD and Jorge Munera, PhD, from the DDRCC, CDLD and Department of Regenerative Medicine and Cell Biology at MUSC.

## On the Inside



## A Note from the Directors

**Don C. Rockey**
DDRCC Director

**First of all, a big note of thanks** to all of our Digestive Disease Research Center members and our hardworking program and core directors and staff, for working together smoothly towards the successful submission of our Year 1 Research Performance Progress Report (RPPR) to NIDDK. As we reviewed our accomplishments for the somewhat shortened year, we cannot

**Stephen Duncan**
CDLD Director

help but feel encouraged and elated at the thriving state of our program.

As we begin Year 2, we are excited about sharing MUSC's research progress at our **Second Annual Digestive Disease Research Center Retreat and Symposium** on **April 23, 2021** (see below). We will feature a stellar lineup of short talks, focusing on work by of our junior faculty PIs, as well as Pilot & Feasibility Project awardees. We will look forward to viewing the broad scope of clinical, translational and basic GI and hepatology research being presented through our **virtual poster format**, which will feature chatting and as much interaction as possible. We anticipate a fabulous keynote research presentation by **Robert Schwabe** from Columbia University. It will be a great opportunity for us to "show our stuff" to members of our advisory board members, who have been invited to attend. Don't miss out! If you haven't already, please visit our **symposium website**, and register to be part of the all of the excitement!

## April 23rd, 2021

## Annual MUSC DDRC Retreat

**8:30 am - 1:00PM**

**REGISTER NOW!**

## Meet our Symposium Keynote Speaker: Robert F. Schwabe, MD

Dr. Schwabe received his MD and residency training and doctoral degree in medicine/immunology at Ruprecht-Karls-University Heidelberg and Ludwig-Maximilians-University Munich in Germany. He joined the Division of Digestive and Liver Diseases at Columbia University following a postdoctoral fellowship at the University of North Carolina Chapel Hill. Research in Dr. Schwabe's lab focuses on the basic mechanisms underlying the liver's response to injury, and how microbial and inflammatory inputs interact with innate liver cell functional pathways in the genesis of liver fibrosis and enhanced risk for liver cancer. His laboratory utilizes cutting edge cellular and animal model technologies to this end.

# Research Focus

# Quantitating Mitochondrial Functional Variability

Advanced Imaging Core

**Metabolic variation between normal and pathological cells** has been an area of keen interest for many disease researchers. Such differences represent novel correlates to differences in host susceptibility, disease severity, or response to treatment. A major example is the linkage between mitochondrial function and bioenergetics vs. cancer cell growth and resistance to chemotherapy. The **Warburg hypothesis** posits that an upregulation of glycolysis relative to oxidative metabolism endows cancer cells with key advantages such as resistance to hypoxia, and increased biosynthetic capacity that enables high cell proliferation and growth rates. This hypothesis has been recently challenged by findings that the hypoxia faced by tumor cells is highly variable in vivo, and that both normal and cancer cell populations exhibit broad ranges of mitochondrial function and oxidative metabolism. Current hypotheses have thus sought to link mitochondrial function to disease severity and susceptibility to treatment in more nuanced ways, particularly with regard to linkage to disease pathophysiology.

A major challenge for testing these hypotheses has been the lack of a method for precisely measure absolute levels of mitochondrial function. For the most part, contemporary methods seek to discern relative differences in function between cells, and are often performed under conditions that fail to address the relative dependence upon cell culture and environmental conditions. In order to solve this problem, and to begin to define a reference set of techniques, DDRCC member **Eduardo Maldonado** began lengthy discussions with other mitochondrial investigators, including Dr. Martin Brand at the Buck Institute for Research on Aging in Novato, CA. With their help, and through the efforts of AIC manager Monika Gooz, the Maldonado Lab was able to establish techniques to obtain consistent quantitative and absolute measurements of mitochondrial membrane potential as a key indicator of mitochondrial activity, and accurately assess its inter- and intracellular variability in both normal liver and cancer cells.Their findings, reported in *Rovini et al., FASEB J. 2021 Jan;35(1):e21148*, represent a gratifying validation of the overall hypothesis that differences in mitochondrial activity truly exist that correlate with cancerous states. For the Maldonado Lab, next steps include testing the effect of mitochondrial channel modulators on membrane potential and mitochondrial activity, and the ability of such modulation to kill tumor cells,or render them more sensitive to anti-cancer treatments.

**Contact Dr. Maldonado**
for more details

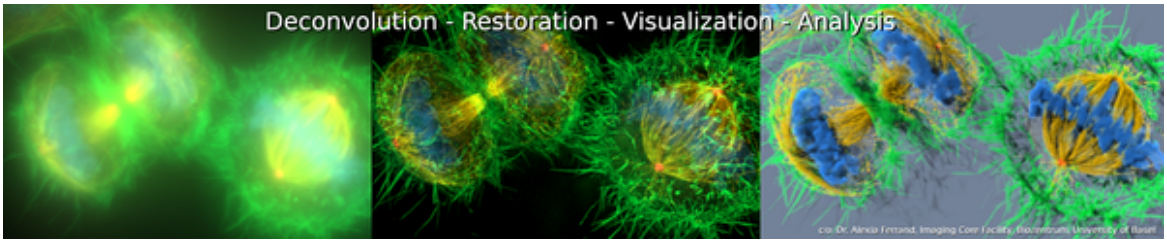
**Transcript available here**

More importantly, this effort represent their initial contribution to a broad collaboration with like-minded investigators to seeking to fundamentally advance the field of mitochondrial metabolism and its role in cancer, an experience they have found highly gratifying. Going forward, these techniques and capabilities will also be available to the MUSC DDRC community at large through the ongoing support of the Advanced Imaging Core (AIC).

April 14th and 15th, 2021

## Virtual SVI Huygens workshop

Advanced Imaging Core




The **Advanced Imaging Core** recently purchased the SVI Huygens deconvolution software package as an upgrade to their image processing capabilities. In conjunction with SVI, the AIC is offering an interactive virtual workshop on the features of this software and its capabilities. More details and a preliminary schedule are available at the SVI workshop **website**. The workshop is free, but registration is required. For further details, contact the AIC manager **Monika Gooz**.

**Register for the Workshop**

## 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 **Monika Gooz**.

## 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:

- The DDRCC provides **full members** with a **25% 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**.

# New Grants Funded

Antonis Kourtidis, PhD
Regenerative Medicine

DDRCC member **Antonis Kourtidis**, Assistant Professor in the Regenerative Medicine and Cell Biology Department, and Associate Director of the DDRCC Enrichment Series, recently received his notice award for his R01 application, **1R01DK124553-01A1,** "Epithelial adherens junctions regulate colon cell behavior through RNAi and lncRNAs." This project is an extension of his COBRE JI project, and its award marks his successful graduation from the COBRE program. **Congratulations and well done!**

CDLD Director and DDRCC co-Director **Steve Duncan** received a notice of award for the funding of his proposed **MUSC Digestive Disease Training Program (DDTP)**, which will support eligible US Citizen or permanent resident PhD pre-doctoral graduate students at MUSC. Interested applicants should contact Dr. Duncan for further information.

**Congratulations to Dr. Duncan and the CDLD!**

Steve Duncan, PhD
Regenerative Medicine

Hongjun Wang, PhD
Surgery

DDRCC full member **Hongjun Wang**, Professor in the Department of Surgery, and Associate Director of the DDRCC Enrichment Series, recently received her notice award for her R01 application, **5R01DK120394-02,** "Novel Gene and Stem Cell Therapy for Type 1 Diabetes." This award follows the successful completion of a Year 1 patient recruitment feasibility trial. This study was highlighted in the last issue of the DDRC Digest. **Congratulations Dr. Wang!**

# New Position Announcement

## COBRE IN DIGESTIVE AND LIVER DISEASE (CDLD)

## REQUEST FOR JUNIOR INVESTIGATOR AWARD APPLICATIONS

**KEY DATES**

Letter of Intent Due: **April 30, 2021**

Invitation to Submit Full Application: **May 3, 2021**

Full Application Due: **May 31, 2021**

Earliest Award Start Date: **July 1, 2021**

## OVERVIEW:

The **MUSC Center of Biomedical Research Excellence (COBRE) in Digestive and Liver Disease (CDLD)** is requesting applications for a Junior Investigator award. **The award provides approximately $150,000 in annual direct costs for up to three years, access to biostatisticians, and free use of the CDLD Core Resources.** In addition, CDLD Junior Investigators are provided mentoring and career development support to ensure a smooth transition to independence and to secure R01 funding. Project leaders must annually contribute a minimum of 6 calendar months to the CDLD project.

The overarching objective of the CDLD is to enhance the research capacity and competitiveness of CDLD members and Junior Investigators by expanding available infrastructure, access to quality training, and opportunities to collaborate, thereby enabling outstanding basic research in digestive and liver disease. It is also expected that the CDLD will facilitate collaboration and integration of our Junior Investigators with other members of the digestive and liver disease community, as the Junior Investigator transitions to independence.

## ELIGIBILITY:

Applicants must hold a tenure-track faculty appointment at the time the application is submitted and must meet the criteria of junior investigator. A Junior Investigator is an individual who does not have and has not previously had an external, peer-reviewed Research Project Grant (RPG), Program Project Grant (PPG), or PPG subproject, or equivalent awards from either a Federal or non-Federal source that names that investigator as the PD/PI. Grants that name an individual as a co-investigator, collaborator, consultant, or to a position other than PD/PI or PD/PI on research grants that allow multiple PD(s)/PIs, do not disqualify that investigator from Junior Investigator status. Academic Research Enhancement Award grants, exploratory/pilot project grants (such as NIH R03 and R21 awards), mentored career development awards (such as NIH K01 and K08 awards) do not disqualify the investigator. Junior Investigators that are also K awardees can serve as COBRE Junior Investigators only during the last two years of the K award when the effort

commitment is allowed to be reduced to six person-months per NIH policy. Investigators who have obtained significant support in the form of an RPG or PPG (e.g., NIH R01, K99/R00, or P01, NSF, or other Federal or non-Federal agency awards) would not be considered Junior Investigators. All Junior Investigators must submit an investigator-initiated RPG application by the end of two years of COBRE support and commit to contributing to all CDLD activities.

### APPLICATION PROCESS:

• **PART 1:** Applicants should submit a letter of intent that includes an NIH Biosketch and Specific Aims Page that describes the goal of the project, summarized approach, and the expected use of CDLD Core Resources. **Deadline for letter of intent submission is April 30, 2021.**

• **PART 2:** After review of the letter of intent, successful applicants will be asked to submit a full application. The full application will follow the format and guidelines for a R21 application including compliance sections and a budget justification. **Deadline for full application submission is May 31, 2021.**

Application materials should be submitted to **Caroline Westwater, PhD**. Applications will be reviewed by the CDLD Executive Committee using NIH-style criteria and scoring processes and those deemed most competitive will be assessed by the CDLD External Advisory Committee. The applicant that 1) is perceived to have the highest likelihood of transitioning to NIH R01 funding within three years, 2) is most likely to benefit from CDLD core resources and mentoring, and 3) whose project most closely aligns with the CDLD goals, will be awarded a Junior Investigator position within the CDLD.

**MUSC CDLD**

## Notes from the DDRCC

## DDRCC Investigator Spotlight

**Denis Guttridge, PhD**
**Pediatrics**

**Denis C. Guttridge**, Professor of Pediatrics and the Hollings Cancer Institute, and Director of the Darby Children's Research Institute, was the featured speaker for the March, 2021 MUSC "Science Never Sleeps" podcast series.

His topic: **"The War on Cancer: are we winning?"**

## Enrichment Series Seminars

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

#### April 7

**Guido Costamagna, MD** Università Cattolica del Sacro Cuore, Rome, Italy

Management of benign biliary strictures

#### April 14

**Erin Forster, MD, MPH** MUSC

Quality improvement in IBD

#### April 28

**Gregory Cotê, MD** MUSC

ERCP quality

#### May 5

**Alan Barkun, MD, CM, MSc** McGill University

Non-variceal upper GI bleeding

#### May 12

**Frank Anania, MD** US Food and Drug Administration

An FDA perspective on drug development in NASH

#### May 19

**Michael Wallace, MD, MPH** Sheikh Shakhbout Medical City, Abu Dhabi, UAE

Artificial intelligence in endoscopy

### May 26

**Jacques Devière, MD, PhD** Erasme University Hospital, Brussels, Belgium

Endoscopic anti-reflux procedures

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

### April 7

**Danijela Matic Vignjevic, PhD** Institut Curie

Cell migration in gut homeostasis and cancer invasion

### April 14

**Roeland Nusse, PhD** Stanford University School of Medicine

Food Cycles and Cell Cycles

### April 28

**Brent Stockwell, PhD** Columbia University

TBA

### May 5

**Janet Rossant, PhD** University of Toronto

TBA

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

## Selected GI Publications by our Members

## February, 2021 - March, 2021

Roh KH, Lee Y, **Yoon JH**, Lee D, Kim E, Park E, Lee IY, Kim TS, Song HK, Shin J, Lim DS, Choi EJ. TRAF6-mediated ubiquitination of MST1/STK4 attenuates the TLR4-NF-κB signaling pathway in macrophages. Cell Mol Life Sci. 2021 Mar;78(5):2315-2328. PubMed PMID: 32975614.

Sarangdhar M, Yacyshyn MB, Gruenzel AR, **Engevik MA**, Harris NL, Aronow BJ, Yacyshyn BR. Therapeutic Opportunities for Intestinal Angioectasia- Targeting PPARγ and Oxidative Stress. Clin Transl Sci. 2021 Mar;14(2):518-528. PubMed PMID: 33048460; PubMed Central PMCID: PMC7993272.

Barzilay JI, Younes N, Pop-Busui R, **Florez H**, Seaquist E, Falck-Ytter C, Luchsinger JA. The cross-sectional association of renal dysfunction with tests of cognition in middle-aged adults with early type 2 diabetes: The GRADE Study. J Diabetes Complications. 2021 Mar;35(3):107805. PubMed PMID: 33288412; PubMed Central PMCID: PMC7870547.

**Engevik MA**, Danhof HA, Auchtung J, Endres BT, Ruan W, Bassères E, Engevik AC, Wu Q, Nicholson M, Luna RA, Garey KW, Crawford SE, Estes MK, Lux R, Yacyshyn MB, Yacyshyn B, Savidge T, Britton RA, Versalovic J. Fusobacteriumnucleatum Adheres to Clostridioides difficile via the RadD Adhesin to Enhance Biofilm Formation in Intestinal Mucus. Gastroenterology. 2021 Mar;160(4):1301-1314.e8. PubMed PMID: 33227279; PubMed Central PMCID: PMC7956072.

Curran T, Sun Z, Gerry B, Findlay VJ, **Wallace K**, Li Z, Paulos C, Ford M, Rubinstein MP, Chung D, Camp ER. Differential immune signatures in the tumor microenvironment are associated with colon cancer racial disparities. Cancer Med. 2021 Mar;10(5):1805-1814. PubMed PMID: 33560598; PubMed Central PMCID: PMC7940243.

**Meissner EG,** Chung D, Tsao B, Haas DW, Utay NS. IFNL4 Genotype Does Not Associate with CD4 T-Cell Recovery in People Living with Human Immunodeficiency Virus. AIDS Res Hum Retroviruses. 2021 Mar;37(3):184-188. PubMed PMID: 33066718.

Qayed E, Deshpande AR, **Elmunzer BJ**. Low Incidence of Severe Gastrointestinal Complications in COVID-19 Patients Admitted to the Intensive Care Unit: A Large, Multicenter Study. Gastroenterology. 2021 Mar;160(4):1403-1405. PubMed PMID: 33188804; PubMed Central PMCID: PMC7657870.

**Hartman JH**, Widmayer SJ, Bergemann CM, King DE, Morton KS, Romersi RF, Jameson LE, Leung MCK, Andersen EC, Taubert S, Meyer JN. Xenobiotic metabolism and transport in Caenorhabditis elegans. J Toxicol Environ Health B Crit Rev. 2021 Feb 17;24(2):51-94. PubMed PMID: 33616007; PubMed Central PMCID: PMC7958427.

Paragomi P, Tuft M, Pothoulakis I, Singh VK, Stevens T, Nawaz H, Easler JJ, Thakkar S, **Cote GA**, Lee PJ, Akshintala V, Kamal A, Gougol A, Phillips AE, Machicado JD, Whitcomb DC, Greer PJ, Buxbaum JL, Hart P, Conwell D, Tang G, Wu BU, Papachristou GI. Dynamic changes in the pancreatitis activity scoring system during hospital course in a multicenter, prospective cohort. J Gastroenterol Hepatol. 2021 Feb 18. PubMed PMID: 33604947.

Sofi MH, Wu Y, Ticer T, Schutt S, Bastian D, Choi HJ, Tian L, Mealer C, Liu C, **Westwater C**, Armeson KE, Alekseyenko AV, Yu XZ. A single strain of Bacteroides fragilis protects gut integrity and reduces GVHD. JCI Insight. 2021 Feb 8;6(3). PubMed Central PMCID: PMC7934839.

Song L, Gou W, Wang J, Wei H, Lee J, Strange C, **Wang H**. Overexpression of alpha-1 antitrypsin in mesenchymal stromal cells improves their intrinsic biological properties and therapeutic effects in nonobese diabetic mice. Stem Cells Transl Med. 2021 Feb;10(2):320-331. PubMed PMID: 32945622; PubMed Central PMCID: PMC7848369.

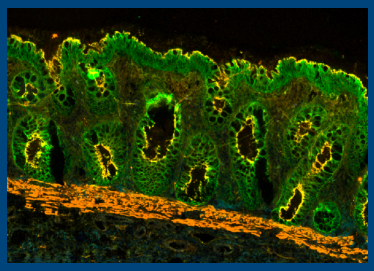
Qi X, Liu Y, Wang J, Fallowfield JA, Wang J, Li X, Shi J, Pan H, Zou S, Zhang H, Chen Z, Li F, Luo Y, Mei M, Liu H, Wang Z, Li J, Yang H, Xiang H, Li X, Liu T, Zheng MH, Liu C, Huang Y, Xu D, Li X, Kang N, He Q, Gu Y, Zhang G, Shao C, Liu D, Zhang L, Li X, Kawada N, Jiang Z, Wang F, Xiong B, Takehara T, **Rockey DC**. Clinical course and risk factors for mortality of COVID-19 patients with pre-existing cirrhosis: a multicentre cohort study. Gut. 2021 Feb;70(2):433-436. PubMed PMID: 32434831; PubMed Central PMCID: PMC7815629.

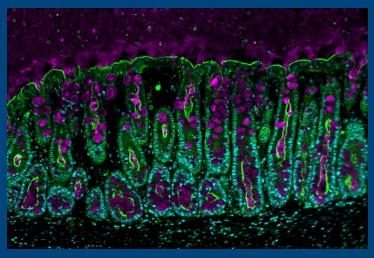
Blanding DP, Moran WP, Bian J, Zhang J, Marsden J, **Mauldin PD**, **Rockey DC**, **Schreiner AD**. Linkage to specialty care in the hepatitis C care cascade. J Investig Med. 2021 Feb;69(2):324-332. PubMed PMID: 33203787; PubMed Central PMCID: PMC7863626.

**A complete listing of DDRCC publications may be found on NCBI.**

## DDRCC Website Renovations

We are currently updating our DDRCC webpages, and would like contributions from our members. In addition to news items and open position notifications, please submit photos of lab groups or lab activities, journal covers images, or interesting data images, published or unpublished, to the **Center Manager** for consideration.





## CITE OUR GRANTS

### FOR THE DDRCC:
### P30 DK123704

**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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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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Regenerative Medicine and Cell Biology
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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