

Spring 2024



**NIDDK grant P30 DK120515**

**In this issue:**

- Updates from SDDRC Cores
- Center News
- New Center Members
- SDDRC P&F Awards
- Upcoming Center Events
- Recent Center Publications



Dear Colleagues,

We are excited to present the latest edition of the SDDRC Newsletter.

In this newsletter, you will find a wealth of information, including updates on our services and Center events, announcement of the 2023-24 Pilot and Feasibility awardees, and remarkable achievements of our members as illustrated by the list of recent publications. We are pleased to start a new SDDRC Lunch & Networking seminar series offered on second Monday of each month. The networking seminars will be presented by a Center member to increase awareness of their work and possible collaboration with other members.

Furthermore, we are excited to share that our P30 renewal application submission to the National Institutes of Health (NIH) received an impressive priority score of 20, so we expect to obtain funding for a new 5-year period. This significant milestone demonstrates our commitment to the pursuit of excellence in digestive diseases research.

Thank you for your continued support and engagement. We hope that this newsletter serves as a source of inspiration, connection, and valuable information for all our Center members.

Best wishes and much research success,

Bernd Schnabl and Lars Eckmann





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## **Core Services and Updates**

### **Human Translational Core**

- Access to well-characterized human biospecimens for patients with Metabolic dysfunction-associated steatotic liver disease (MASLD) and Inflammatory Bowel Disease (IBD).
- Access to archival clinical (GI/liver) tissue samples (stained or unstained slides) from the Pathology Department. This service can be obtained by submitting the sample request form located on the Center website, or via email to the Center.
- Consultation in pathology, biostatistics, protocol design, and training.

### **Preclinical Model Core**

- Services in histology and microscopy including tissue preparation, help in establishing proper fixation, routine and specialized staining, slide scanning, multiplex immunofluorescence, state-of-the-art microscopy, second harmonic generation collagen imaging, intravital imaging, and image analysis. The SDDRC members are eligible for a subsidy which will be applied via cost transfer to your paid invoices to LJI.
- Access to germ-free and gnotobiotic mice, and various murine models of liver and gastrointestinal disease. SDDRC members are eligible for a subsidy for using this service.
- **Now offering** access to Human Liver Resource services.

### **Microbiomics and Genomics Services**

- Sample processing (with IGM and UCSD Microbiome Core)
  - ◊ DNA/RNA extraction for microbiomics (stool, tissues)
  - ◊ DNA/RNA extraction for functional genomics (tissues)
- Sequencing-based assays (with IGM), Microbiome sequencing (16S, ITS, shotgun), RNA-seq, Single-cell sequencing (RNA, ATAC, Multiome), Spatial transcriptomics, Other sequencing-based assays (e.g. miRNA-Seq, ChIP-Seq)
- Bioinformatics support
  - ◊ Microbiomics (e.g. OTU,  $\alpha/\beta$  diversity, shotgun metagenomics, archiving)
  - ◊ Functional genomics (e.g. transcript quantitation, systems biology interpretation)
- Consultation and training in specific experimental and analytical techniques related to microbiomics and functional genomics.
- SDDRC members are eligible for a subsidy for using the core services.

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## New SDDRC Members



**Li-Fan Lu, Ph.D.**

Professor, Department of Molecular Biology

Institution: UC San Diego

[lifanlu@ucsd.edu](mailto:lifanlu@ucsd.edu)

**Research Interests:** Dr. Lu's research interest is to study immune regulation in different tissue microenvironments under different physiological and pathological conditions. Particularly, in the past few years his research aims at exploring the cellular and molecular mechanisms underlying regulatory T (Treg) cell-mediated control of intestinal homeostasis in the presence or absence of commensal and pathogenic microbes.



**Debashis Sahoo, Ph.D.**

Associate Professor, Department of Pediatrics,

Department of Computer Science and Engineering

UC San Diego, San Diego

Institution: UC San Diego

[dsahoo@health.ucsd.edu](mailto:dsahoo@health.ucsd.edu)

**Research Interests:** Dr. Sahoo is a computer scientist with strong biology and translational medicine experience. He leads a group with broad expertise ranging from computer science and engineering, data science, and electrical engineering to bioinformatics, systems biology, to cellular and molecular biology. Dr. Sahoo's computational technique is focused on the mathematics of two values (Boolean logic), which has allowed him to make unique contributions in bioinformatics and systems biology including in the areas of biomarkers in colorectal cancer and inflammatory bowel disease.



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### **2023 Clarivate Highly Cited Researchers**

Clarivate provides analytics in scientific research and identifies researchers “who demonstrated significant influence in their chosen field or fields through the publication of multiple highly cited papers during the last decade.” Clarivate listed 7,125 Highly Cited Researcher designations in 2023, who rank in the top 1 percent by citations for field and publication year in the Web of Science citation index. Clarivate’s rankings are considered to be the “who’s who” of science.

Congratulations to the following Center members named in the prestigious 2023 Clarivate listing!





## Center News

**Congratulations to the SDDRC members on the following achievements and recognitions:**



**Kathleen "Kit" Curtius, PhD**

Awarded an R01 grant for Multiscale modeling of spatiotemporal evolution in Barrett's esophagus.



**Cristina Llorente, PhD**

Awarded an R21 grant for The role of intestinal gp130 in alcohol-associated liver disease.

Awarded a pilot grant for Role of goblet cell associated antigen passages in autoimmune spondylarthritis.



**John Carethers, MD**

Elected Fellow of the American Association for Cancer Research Academy 2024.

**Hilde Cheroutre, PhD**  
Named a Distinguished Fellow of the American Association of Immunologists class of 2024.



**Jesus Rivera-Nieves, MD**

Awarded a K26 grant for Enhancing Mentoring of Diverse Early Career Researchers.

**Ronald Evans, PhD**

Named the 2024 recipient of the Japan Prize in the field of Medical Science and Pharmaceutical Science.



**Siddharth Singh, MD**

Awarded an R01 for Comparative effectiveness research in Hispanic patients with inflammatory bowel diseases.

Awarded an R03 grant Predicting Short- and Long-term Risk of Serious Infections in Older Patients with Inflammatory Bowel Diseases.



**Nicolas Webster, PhD**

Awarded a Curebound Targeted Grant for a feasibility study for prolonged nightly fasting in patients treated for HCC.

Awarded a VA Merit Review grant for the role of IGF2 in DNA damage in liver disease and cancer.

Awarded a pilot grant from the Krupps Center for Integrative Research to test time-restricted eating in patients undergoing therapy for liver cancer.

Awarded a multi-PI NIH R01 grant on the role of house dust mite exposure in lung cancer in non- or never smokers.



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## **Congratulations to the 2023-24 Pilot & Feasibility Awardees**

The Pilot & Feasibility program has awarded a total of \$80,000 to the following investigators with promising research projects in digestive diseases:



**Thomas Riffelmacher, PhD, Instructor, Director of Immunometabolism Core, La Jolla Institute for Immunology**

Project Title: "Targeting metabolic dependencies of MAIT cells in fatty liver disease"

**Summary:** Metabolic syndrome and hepatic steatosis affects 30-40% of adults in the U.S and 1 in 5 progress to cirrhosis, a life-threatening condition. Mucosal-associated-invariant-T (MAIT) cells are an innate-like T cell subset that recognizes vitamin B metabolites and is highly enriched in liver (up to 40% of lymphocytes). We recently combined single cell (sc) RNA-seq with sc-metabolic analysis and identified an active, mitochondrial fatty acid oxidation metabolic program of MAIT cells was critical for IL-17A synthesis. The disturbed metabolic microenvironment present in steatotic liver likely shapes the functional state of MAIT cells and in turn impacts inflammation. My research will test if MAIT cell functional states may be uniquely tied to distinct metabolic programs impacted by metabolic dysbiosis, which could be exploited to tune innate-like T cell responses in the context of fatty liver disease.



**Karsten Zengler, PhD, Professor, Department of Pediatrics, UC San Diego**

Project Title: "Leveraging Microbial Competition to Fight Intestinal Multidrug-Resistant Infections"

**Summary:** Infectious diseases and intestinal inflammation are on the rise, but drug development struggles to keep up with antimicrobial resistance. In addition to acute infection, colonization by multi-drug resistant Gram-negative pathogens poses a significant, often undetected, threat. Here, we will apply a new method that aims to identify natural competitors of emerging pathogens and enhance these competitors to combat inflammation and infectious diseases.

Spring 2024



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## Upcoming Center Events

### 2024 Upcoming SDDRC Seminar Series

The Center invites nationally and internationally renowned speakers to facilitate and promote interactions among investigators in the San Diego area committed to digestive diseases research.

<i>Date</i>	<i>Location</i>	<i>Time</i>	<i>Speaker</i>	<i>Affiliation</i>
4/30/24	ECOB 1-001	7:30 - 8:30 AM	W. Ray Kim, MD	Stanford University
5/13/24	Leichtag- 107	12:00 - 1:00 PM	Jessica L Maiers, PhD	Indiana University
6/17/24	Leichtag- 107	12:00 - 1:00 PM	Juanita L Merchant, MD, PhD	University of Arizona
7/29/24	Leichtag- 107	12:00 - 1:00 PM	Yasuko Iwakiri, PhD	Yale School of Medicine
8/26/24	Leichtag- 107	12:00 - 1:00 PM	Gretchen Diehl, PhD	Memorial Sloan Kettering Cancer Center

### 2024 Upcoming SDDRC Workshop:

<i>Date</i>	<i>Location</i>	<i>Time</i>	<i>Presenter</i>	<i>Affiliation</i>
4/8/24	Online Only	12:00 - 1:15 PM	Frank Anania, MD, FACP, AGAF, FAASLD	U.S. Food & Drug Administration (FDA)

### 2024 Upcoming SDDRC Lunch & Network:

<i>Date</i>	<i>Location</i>	<i>Time</i>	<i>Speaker</i>	<i>Affiliation</i>
6/3/2024	BRF2 -5A03	12:00 - 1:00 PM	Li-Fan Lu, PhD	UC San Diego
8/12/24	BRF2 -5A03	12:00 - 1:00 PM	Hiroshi Kiyono, PhD	UC San Diego



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### Recent 2023 Publications by Center Members acknowledging SDDRC

To recognize the excellence and breadth of research done by our members, we highlight a number of representative papers (**members are shown in bold**). Reprints of these papers can be provided upon request.

1. Vasquez Ayala A, Hsu CY, Oles RE, Matsuo K, Loomis LR, Buzun E, Carrillo Terrazas M, Gerner RR, Lu HH, Kim S, Zhang Z, Park JH, Rivaud P, Thomson M, **Lu LF**, Min B, **Chu H**. Commensal bacteria promote type I interferon signaling to maintain immune tolerance in mice. *J Exp Med*. 2024 Jan; 221:e20230063. PMCID: PMC10716256.
2. Buzun E, Hsu CY, Sejane K, Oles RE, Vasquez Ayala A, Loomis LR, Zhao J, Rossitto LA, McGrosso DM, **Gonzalez DJ**, **Bode L**, **Chu H**. A bacterial sialidase mediates early-life colonization by a pioneering gut commensal. *Cell Host Microbe*. 2024 Feb ;32:181-190.e9. PMCID: PMC10922750.
3. Nouredin N, **Ajmera V**, Bergstrom J, Bettencourt R, Huang DQ, Siddiqi H, Majzoub AM, Nayfeh T, Tamaki N, Izumi N, Nakajima A, Idilman R, Gumussoy M, Oz DK, Erden A, **Loomba R**. MEFIB-Index and MAST-Score in the assessment of hepatic decompensation in metabolic dysfunction-associated steatosis liver disease-Individual participant data meta-analyses. *Aliment Pharmacol Ther*. 2023 Nov; 58:856-865. PMCID: PMC10901230.
4. Liu X, Lam K, Zhao H, Sakane S, Kim HY, Eguileor A, Diggle K, Wu S, Gontijo Weber RC, Soroosh P, Hosseini M, Mekeel K, **Brenner DA**, **Kisseleva T**. Isolation of primary human liver cells from normal and nonalcoholic steatohepatitis livers. *STAR Protoc*. 2023 Jul; 4:102391. PMCID: PMC10345194.
5. Umemoto S, Nakahashi-Ouchida R, Yuki Y, Kurokawa S, Machita T, Uchida Y, Mori H, Yamanoue T, Shibata T, Sawada SI, Ishige K, Hirano T, Fujihashi K, Akiyoshi K, Kurashima Y, Tokuhara D, **Ernst PB**, Suzuki M, **Kiyono H**. Cationic-nanogel nasal vaccine containing the ectodomain of RSV-small hydrophobic protein induces protective immunity in rodents. *NPJ Vaccines*. 2023 Jul; 8:106. PMCID: PMC10366164.
6. Brennan C, Salido RA, Belda-Ferre P, Bryant M, Cowart C, Tiu MD, González A, McDonald D, Tribelhorn C, **Zarrinpar A**, **Knight R**. Maximizing the potential of high-throughput next-generation sequencing through precise normalization based on read count distribution. *mSystems*. 2023 Aug; 8:e0000623. PMCID: PMC10469589.
7. Zamani M, Alizadeh-Tabari S, Chitkara P, **Singh S**, **Loomba R**. Prevalence of Nonalcoholic Fatty Liver Disease in Patients With Rheumatoid Arthritis: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol*. 2023 Oct; 21:2789-2796. PMCID: PMC10792512.
8. Takeda K, Koi M, Okita Y, Sajibu S, Keku TO, **Carethers JM**. Fusobacterium nucleatum Load Correlates with KRAS Mutation and Sessile Serrated Pathogenesis in Colorectal Adenocarcinoma. *Cancer Res Commun*. 2023 Sep; 3:1940-1951. PMCID: PMC10530411.
9. Lin CH, Wu CJ, Cho S, Patkar R, Huth WJ, Lin LL, Chen MC, Israelsson E, Betts J, Niedzielska M, Patel SA, Duong HG, Gerner RR, Hsu CY, Catley M, Maciewicz RA, **Chu H**, **Raffatellu M**, **Chang JT**, **Lu LF**. Selective IL-27 production by intestinal regulatory T cells permits gut-specific regulation of TH17 cell immunity. *Nat Immunol*. 2023 Dec; 24:2108-2120. PMID: 37932457.
10. Low EE, Demb J, **Shah SC**, Liu L, Bustamante R, **Yadlapati R**, **Gupta S**. Risk of Esophageal Cancer in Achalasia: A Matched Cohort Study Utilizing the Nationwide Veterans Affairs Achalasia Cohort (VA-AC). *Am J Gastroenterol*. 2023 Nov 17. PMID: 37975607
11. Bennett H, Troutman TD, Zhou E, Spann NJ, Link VM, Seidman JS, Nickl CK, Abe Y, Sakai M, Pasillas MP, Marlman JM, Guzman C, Hosseini M, **Schnabl B**, **Glass CK**. Discrimination of cell-intrinsic and environment-dependent effects of natural genetic variation on Kupffer cell epigenomes and transcriptomes. *Nat Immunol*. 2023 Nov; 24:1825-1838. PMCID: PMC10602851.



Spring 2024



**NIDDK grant P30 DK120515**

## Recent 2023 Publications by Center Members acknowledging SDDRC (cont'd)

12. Latorre G, Silva F, Montero I, Bustamante M, Dukes E, Uribe J, Corsi Sotelo O, Reyes D, Fuentes-López E, Pizarro M, Medel P, Torres J, Roa JC, Pizarro S, Achurra P, Donoso A, Wichmann I, Corvalán AH, Chahuan J, Candia R, Agüero C, Gonzalez R, Vargas JI, Espino A, Camargo MC, **Shah SC**, Riquelme A. Comparison of OLGA and OLGIM as predictors of gastric cancer in a Latin American population: the ECHOS Study. *Gut*. 2023 Dec: gutjnl-2023-331059.
13. Urrete J, Mitra T, **Boland BS**, Bertrand K, Chambers C, **Rivera-Nieves J**. Vedolizumab Does Not Affect Antibody Secreting Cell Recruitment to the Lactating Mammary Gland of Mothers With Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2024 Feb 9:izae023 PMID: 38334263.
14. Viebahn G, **Hartmann P**, Lang S, Demir M, Zhang X, Fouts DE, Stärkel P, **Schnabl B**. Fungal signature differentiates alcohol-associated liver disease from nonalcoholic fatty liver disease. *Gut Microbes*. 2024 Jan-Dec ;16:2307586. PMCID: PMC10841010.



## Highlights from the 2024 SDDRC Symposium





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## Letters of Support

We are here to help you conduct digestive diseases research projects. The Center can provide you with support for your grant application. If you need a letter of support, please contact us:

**[sddrc@health.ucsd.edu](mailto:sddrc@health.ucsd.edu)**



### Citing the Center



Have you used the services offered by the Center? Please remember to acknowledge the Center grant in your publication:

**“The study was supported by the NIDDK-funded San Diego Digestive Diseases Research Center (P30 DK120515).”**

Thank you!

## CONTACT US

If you have any questions , please send an email to the Center (**[sddrc@health.ucsd.edu](mailto:sddrc@health.ucsd.edu)**) or the Center Coordinator Victoria Shokrollah (**[vshokrollah@health.ucsd.edu](mailto:vshokrollah@health.ucsd.edu)**)

Center Website: **<http://sddrc.ucsd.edu>**

Follow us on X: **<https://twitter.com/SDDRC>**