Newsletter Summer 2022



NIDDK grant P30 DK120515

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Dear Colleagues,

We are delighted to circulate our newly developed SDDRC newsletter as part of our mission to facilitate and enhance research in digestive diseases by our Center members. We are planning to publish the newsletter twice a year with news about services, announcements, and achievements of our members.

The Center continues to thrive, expanding its members to now 45 full and 11 associate members. Members do fantastic work as illustrated by the list of recent publications in this newsletter. We are delighted to highlight these achievements.

> Best wishes, Bernd Schnabl and Lars Eckmann SDDRC Co-Directors



Core Service and Updates

Human Translational Core

The Core provides access to well-characterized human biospecimens for patients with Nonalcoholic Fatty Liver Disease (NAFLD) and Inflammatory Bowel Disease (IBD).

As a <u>new service</u>, the Core is now offering <u>access to archival clinical (GI/liver) tissue samples</u> (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.

If you are not sure how to get started, we can provide consultation in pathology, biostatistics, protocol design, and training. Contact us with any questions: sddrc@ucsd.edu.

Preclinical Model Core

The Core provides histological support through an arrangement with the Histology Core at the La Jolla Institute for Immunology. A wide range of technologies and services are available, including tissue preparation, fixation, routine and specialized staining, and state-of-the-art microscopy.

The Core also provides routine access to germ-free and gnotobiotic mice, and to various murine models of liver and gastrointestinal disease.

Direct any questions on the logistics of histological sample submission or the use of murine models to the Center administration: sddrc@ucsd.edu.

Microbiomics and Genomics Services

The Core provides access to all common sequencing-based assays, including 16S rRNA and metagenomic shotgun sequencing of microbial communities, and RNA-seq (including single-cell transcriptomics), ChIP-seq, miRNA-Seq, GRO-Seq, Ribo-Seq, ATAC-Seq, Whole Genome Sequencing, and Exome sequencing.

If you plan to use these services for the first time, we encourage you to contact Dr. Kristen Jepsen (kjepsen@health.ucsd.edu) for guidance on preparation and sample submission.

The Core also provides bioinformatics support, including analysis of sequencing-based assays and consultation and training in specific experimental and analytical techniques related to microbiomics and functional genomics.

Please contact Dr. Sara Brin Rosenthal (sbrosenthal@health.ucsd.edu) with any questions about the bioinformatics services of the Core.



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<u>Center News</u>

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

Lars Bode, PhD

P50 center grant from the NIH to establish a Center of Excellence in Therapeutics as part of the new NICHD MPRINT (Maternal and Pediatric Precision in Therapeutics) Hub. This Center has a focus on human milk, antibiotics, and microbiome, thus complementing the work done at SDDRC.



Network Grant from the Larry L. Hillblom Foundation to examine a molecular pathway that regulates blood sugar and fat independent of insulin.

The 2021 Asan Award in Basic Medicine by the Asan Foundation. The Asan Foundation is a Korean foundation that supports critical medical research as well as social and medical welfare programs. The award, which totals \$250,000, recognizes "medical scientists who have achieved remarkable accomplishments in the fields of basic and clinical medicine to promote human health," according to the Asan Foundation. Evans is the first international recipient of the Asan Award in Basic Medicine.



Hiutung Chu, PhD, SDDRC P&F Awardee

R01AI167860

"Bacterial adaptions in host-microbe interactions", 3/11/22 -2/28/27



Ronald Evans, PhD and Dannielle Engle, PhD (SDDRC P&F Awardee)

Granted a 2021 ASPIRE (Accelerating Scientific Platforms and Innovative Research) award to study the cellular and molecular drivers of pancreatic cancer, one of the deadliest cancers with few effective treatment options. The \$250,000 award, supported by the Mark Foundation for Cancer Research, enables innovative approaches to solving impactful problems in cancer research.





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<u>Center News</u>

Congratulations to the SDDRC members on obtaining the following awards:

Mamata Sivagnanam, MD, SDDRC P&F Awardee

Use of Human Enteroids to Understand Carbohydrate Malabsorption in Congenital Tufting Enteropathy NASPGHAN Foundation QOL Research Award For The Study Of Disorders Associated With Carbohydrate Maldigestion/ Malabsorption in Children

1/1/22-12/31/23



Cristina Llorente, PhD, SDDRC P&F Awardee

UC San Diego's Hispanic Center of Excellence 10/01/2020 – 11/30/22



Bernd Schnabl, MD

Received a Senior Clinician Scientist Investigator Award from the Department of Veterans Affairs. This provides an extension of 4 years on his recently renewed Merit Award entitled to a total of 8 years. The National Advisory Council on Alcohol Abuse and Alcoholism and Dr. Michael Lauer, the NIH Deputy Director for Extramural Research approved the recommendation of NIAAA Division of Metabolism and Health Effects to award him a NIH MERIT (Method to Extend Research In Time) Award (R37). This will allow to extend his recently renewed R01 application for another 5 years to a total of 10 years, without a need to submit a competing renewal. He also received the Harrington Scholar-Innovator Award 2022 from the Harrington Discovery Institute for his innovative work in the field of microbiome research.

Honors

Web of Science ranked 9 SDDRC members among the top 1% highly-cited researchers by citations in 2021. Drs. Brenner, Gilbert, Glass, Karin, Kaufman, Knight, Loomba, Schnabl and Sirlin are among the world's most influential researchers in their fields.



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Upcoming Center Events

SDDRC Seminar Series (Mondays, 12:00 - 1:00 pm): The Center invites nationally and internationally renowned speakers to facilitate and promote interactions among digestive diseases researchers in the San Diego area.

Date	Location	Speaker	Affiliation
8/29/22	Leichtag - 107	Rhonda F. Souza, MD	Baylor University Medical Center
9/26/22	Leichtag - 107	Jasmohan Bajaj, MD	Medical College of Virginia School of Medicine
10/24/22	Online only	Malin Johansson, PhD	University of Gothenburg
11/28/22	TBD	Guadalupe Garcia-Tsao, MD, FRCP	Yale School of Medicine
12/12/22	Leichtag - 107	Nicholas O. Davidson, MD, DSc.	Washington University

SDDRC Career Development Club (Thursdays, 12:00 - 1:00 pm): The meetings provide an opportunity for faculty, particularly early-stage faculty, to present and discuss projects that are at various stages of grant preparation from Career Development Awards and K-awards to full research grant at the R or U level. We encourage all interested faculty to join us at the meetings, which will be informal and provide excellent networking opportunities. If you would like to present at one of the upcoming meetings, please email the Center (sddrc@health.ucsd.edu) with a very brief description of the topic and goals.

Date	Time	Presenter	Location
8/25/22	12:00 – 1:00 PM	Cynthia Hsu, MD, PhD	ACTRI or Zoom
9/29/22	12:00 – 1:00 PM	Daniel Huang, MBBS	ACTRI or Zoom
10/27/22	12:00 – 1:00 PM	Jin Lee, PhD	ACTRI or Zoom
11/17/22	12:00 – 1:00 PM	Eric Low, MD	ACTRI or Zoom
12/15/22	12:00 – 1:00 PM	Marygorret Obonyo, PhD	ACTRI or Zoom



Upcoming Center Events

LIVER SYMPOSIUM COHOSTED BY SDDRC AND LCSD



FREE: Intended Audience is Liver Patients and Caregivers but All are Welcome!



Saturday, September 10, 2022 UC San Diego Altman Clinical and Translational Research Institute Building 9452 S Medical Center Drive La Jolla, CA 92037

Attendees may join in-person or virtually

The Liver Coalition of San Diego in partnership with UCSD's San Diego Digestive Diseases Research Center is proud to present the Liver Symposium for patients, caregivers and anyone interested in learning more about living with liver disease. Attendance is FREE to all registered guests. Learn from the experts and network with other patients and caregivers. For those attending in-person, registration includes complimentary parking in the Campus Point Patient & Visitor Parking Structure (located next door at 304 S Medical Ctr Dr, La Jolla, CA 92037), continental breakfast, and a box lunch at the conclusion of the conference.

To register, please visit: livercoalition.org/upcoming-events/



AGENDA:

8:00am – 9:00am: Registration and Continental Breakfast



9:00am – 9:30am: Session 1 - Mindfulness for those living with chronic health conditions. Hector Martinez, PsyD, Community Research Foundation

9:45am – 11:00am:

Session 2 - Reversing the trend, progress updates on these liver diseases: Alcohol Related, Viral Hepatitis, Non-alcohol Fatty Liver Disease/NASH, and Liver Cancer.



Heather Patton, MD, UC San Diego



Veeral Ajmera, MD, UC San Diego

Yuko Kono, MD, UC San Diego



11:15am – 12:15pm: Session 3 - Nutrition, followed by boxed lunch to go Eduardo Grunvald, MD, FACP, UC San Diego



Recent Publications by Center Members

SDDRC members and associate members have published 65 papers that acknowledge Center support in the first half of 2022. To recognize the excellence and breath 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 Kamioka M, Goto Y, Nakamura K, Yokoi Y, Sugimoto R, Ohira S, Kurashima Y, Umemoto S, Sato S, Kunisawa J, Takahashi Y, Domino SE, Renauld JC, Nakae S, Iwakura Y, Emst PB, Ayabe T and Kiyono H. Intestinal commensal microbiota and cytokines regulate Fut2(+) Paneth cells for gut defense. 2022. Proc Natl Acad Sci U S A 119: PMCID: PMC8784097
- Orecchioni M, Kobiyama K, Winkels H, Ghosheh Y, McArdle S, Mikulski Z, Kiosses WB, Fan Z, Wen L, Jung Y, Roy P, Ali AJ, Miyamoto Y, Mangan M, Makings J, Wang Z, Denn A, Vallejo J, Owens M, Durant CP, Braumann S, Mader N, Li L, Matsunami H, **Eckmann L**, Latz E, Hazen SL and Ley K. Olfactory receptor 2 in vascular macrophages drives atherosclerosis by NLRP3-dependent IL -1 production. 2022. *Science* 375:214-221.
- 3 Mills RH, Dulai PS, Vazquez-Baeza Y, Sauceda C, Daniel N, Gerner RR, Batachari LE, Malfavon M, Zhu Q, Weldon K, Humphrey G, Carrillo-Terrazas M, Goldasich LD, Bryant M, Raffatellu M, Quinn RA, Gewirtz AT, Chassaing B, Chu H, Sandborn WJ, Dorrestein PC, Knight R and Gonzalez DJ. Multi-omics analyses of the ulcerative colitis gut microbiome link Bacteroides vulgatus proteases with disease severity. 2022. Nat Microbiol 7:262-276. PMCID: PMC8852248
- 4 Peyrin-Biroulet L, Hart A, Bossuyt P, Long M, Allez M, Juillerat P, Armuzzi A, Loftus EV, Jr., Ostad-Saffari E, Scalori A, Oh YS, Tole S, Chai A, Pulley J, Lacey S and **Sandborn WJ**. Etrolizumab as induction and maintenance therapy for ulcerative colitis in patients previously treated with tumour necrosis factor inhibitors (HICKORY): a phase 3, randomised, controlled trial. 2022. *Lancet Gastroenterol Hepatol* 7:128-140.
- 5 Hartmann P, Duan Y, Miyamoto Y, Demir M, Lang S, Hasa E, Stern P, Yamashita D, Conrad M, **Eckmann L** and **Schnabl B**. Colesevelam ameliorates non-alcoholic steatohepatitis and obesity in mice. 2022. *Hepatol Int* 16:359-370. PMCID: PMC9013343
- Qin Y, Havulinna AS, Liu Y, Jousilahti P, Ritchie SC, Tokolyi A, Sanders JG, Valsta L, Brozynska M, Zhu Q, Tripathi A, Vazquez-Baeza Y, Loomba R, Cheng S, Jain M, Niiranen T, Lahti L, Knight R, Salomaa V, Inouye M and Meric G. Combined effects of host genetics and diet on human gut microbiota and incident disease in a single population cohort. 2022. Nat Genet 54:134-142.
- 7 Papamichael K, Afif W, Drobne D, Dubinsky MC, Ferrante M, Irving PM, Kamperidis N, Kobayashi T, Kotze PG, Lambert J, Noor NM, Roblin X, Roda G, **Vande Casteele N**, Yarur AJ, Arebi N, Danese S, Paul S, **Sandborn WJ**, Vermeire S, Cheifetz AS and Peyrin-Biroulet L. Therapeutic drug monitoring of biologics in inflammatory bowel disease: unmet needs and future perspectives. 2022. *Lancet Gastroenterol Hepatol* 7:171-185.
- 8 Zamani M, Alizadeh-Tabari S, **Singh S** and **Loomba R**. Meta-analysis: prevalence of, and risk factors for, non-alcoholic fatty liver disease in patients with inflammatory bowel disease. 2022. *Aliment Pharmacol Ther* 55:894-907. PMCID: PMC9297733
- 9 Ma S, Patel SA, Abe Y, Chen N, Patel PR, Cho BS, Abbasi N, Zeng S, **Schnabl B**, **Chang JT** and Huang WJM. RORgammat phosphorylation protects against T cell-mediated inflammation. 2022. *Cell Rep* 38:110520. PMCID: PMC8982147
- 10 Katkar GD, Sayed IM, Anandachar MS, Castillo V, Vidales E, Toobian D, Usmani F, Sawires JR, Leriche G, Yang J, **Sandborn WJ**, **Das S**, Sahoo D and Ghosh P. Artificial intelligence- rational ized balanced PPARalpha/gamma dual agonism resets dysregulated macrophage processes in I nflame matory bowel disease. 2022. *Commun Biol* 5:231. PMCID: PMC8921270



Recent Publications by Center Members

- The Zhu Q, Huang S, Gonzalez A, McGrath I, McDonald D, Haiminen N, Armstrong G, Vazquez-Baeza Y, Yu J, Kuczynski J, Sepich-Poore GD, Swafford AD, Das P, Shaffer JP, Lejzerowicz F, Belda-Ferre P, Havulinna AS, Meric G, Niiranen T, Lahti L, Salomaa V, Kim HC, Jain M, Inouye M, Gilbert JA and Knight R. Phylogeny-Aware Analysis of Metagenome Community Ecology Based on Matched Reference Genomes while Bypassing Taxonomy. 2022. *mSystems* 7:e0016722. PMCID: PMC9040630
- 12 Gonzalez CG, Mills RH, Kordahi MC, Carrillo-Terrazas M, Secaira-Morocho H, Widjaja CE, Tsai MS, Mittal Y, Yee BA, Vargas F, Weldon K, Gauglitz JM, Delaroque C, Sauceda C, Rossitto LA, Ackermann G, Humphrey G, Swafford AD, Siegel CA, Buckey JC, Jr., Raffals LE, Sadler C, Lindholm P, Fisch KM, Valaseck M, Suriawinata A, Yeo GW, Ghosh P, Chang JT, Chu H, Dorrestein P, Zhu Q, Chassaing B, Knight R, Gonzalez DJ and Dulai PS. The Host-Microbiome Response to Hyperbaric Oxygen Therapy in Ulcerative Colitis Patients. 2022. *Cell Mol Gastroenterol Hepatol* 14:35-53. PMCID: PMC9117812
- 13 Liu Y, Meric G, Havulinna AS, Teo SM, Aberg F, Ruuskanen M, Sanders J, Zhu Q, Tripathi A, Verspoor K, Cheng S, Jain M, Jousilahti P, Vazquez-Baeza Y, Loomba R, Lahti L, Niiranen T, Salomaa V, Knight R and Inouye M. Early prediction of incident liver disease using conventional risk factors and gut-microbiome-augmented gradient boosting. 2022. *Cell Metab* 34:719-730. PMCID: PMC9097589
- 14 **Ajmera V**, Nguyen K, Tamaki N, Sharpton S, Bettencourt R and **Loomba R**. Prognostic utility of magnetic resonance elastography and MEFIB index in predicting liver-related outcomes and mortality in individuals at risk of and with nonalcoholic fatty liver disease. 2022. *Therap Adv Gastroenterol* 15:17562848221093869. PMCID: PMC9058353
- 15 Moon JS, Riopel M, Seo JB, Herrero-Aguayo V, Isaac R and Lee YS. HIF-2alpha Preserves Mitochondrial Activity and Glucose Sensing in Compensating beta-Cells in Obesity. 2022. *Diabetes* 71:1508-1524. PMCID: PMC9233300
- 16 Hsu CL, Zhang X, Jiang L, Lang S, Hartmann P, **Pride D**, Fouts DE, Starkel P and **Schnabl B**. Intestinal virome in patients with alcohol use disorder and after abstinence. 2022. *Hepatol Commun* 6:2058-2069. PMCID: PMC9315129
- 17 Lumibao JC, Tremblay JR, Hsu J and **Engle DD**. Altered glycosylation in pancreatic cancer and beyond. 2022. *J Exp Med* 219:e20211505. PMCID: PMC9086500
- 18 Ihara S, Miyamoto Y, Le CHY, Tran VN, Hanson EM, Fischer M, Hanevik K and Eckmann L. Conserved metabolic enzymes as vaccine antigens for giardiasis. 2022. PLoS Negl Trop Dis 16:e0010323. PMCID: PMC9037923
- 19 Martino C, McDonald D, Cantrell K, Dilmore AH, Vazquez-Baeza Y, Shenhav L, Shaffer JP, Rahman G, Armstrong G, Allaband C, Song SJ and Knight R. Compositionally Aware Phylogenetic Beta-Diversity Measures Better Resolve Microbiomes Associated with Phenotype. 2022. mSystems 7:e0005022. PMCID: PMC9238373
- 20 Holmer AK, Boland BS, Singh S, Neill J, Le H, Miralles A, Collins AE, **Sandborn WJ** and **Dulai PS**. A Serum Biomarker Panel Can Accurately Identify Mucosal Ulcers in Patients With Crohn's Disease. 2022. *Inflamm Bowel Dis* Jun 15;izac117.
- 21 Kanbar JN, Ma S, Kim ES, Kurd NS, Tsai MS, Tysl T, Widjaja CE, Limary AE, Yee B, He Z, Hao Y, Fu XD, Yeo GW, Huang WJ and **Chang JT**. The long noncoding RNA Malat1 regulates CD8+ T cell differentiation by mediating epigenetic repression. 2022. *J Exp Med* 219:e20211756. PMCID: PMC9127983



Acknowledging 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 NIDDKfunded San Diego Digestive Diseases Research Center (P30 DK120515)."

Thank you!

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@ucsd.edu

NEW SDDRC PILOT/FEASIBILITY AWARDS

In a new partnership with the Moores Cancer Center, we are delighted to announce that a new round of pilot/ feasibility awards in digestive diseases is available.

It is planned to award a total of four to five \$40,000 grants for both early-stage and established investigators. The applications are short (4 pages maximum). Details and application form can be found on the <u>SDDRC website</u>.

The submission deadline is Monday, October 03, 2022, at 11:59 pm.

WE ENCOURAGE YOU TO APPLY!