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2024-2025 PILOT PROJECT AWARDS—CALL FOR APPLICATIONS

The NIH/NIDDK P30 Liver Center grant provides for the annual submission of pilot projects (up to \$40,000 direct costs each) from both Liver Center and non-Liver Center investigators.

The purposes of the pilots are to fund new initiatives, not ongoing research, and to support new investigators to pursue liver related research that should lead to future R01-type funding or other support. Projects utilizing Core Facilities and supporting young investigators or applying new methodologies or approaches to the study of liver pathophysiology are given priority.

Investigators should meet one of the following criteria, in order of priority:

1. Senior fellows or junior faculty at Yale, currently not funded by NIH grants and in need of funds to help prepare for R01-type applications.
2. Established University investigators not currently funded for work related to the Center's focus on liver related research, but who wish to apply their areas of expertise to subjects of Center interest.
3. Funded Center investigators who wish to pursue a project that is different from their current focus of interest, and who needs to develop preliminary data to apply for new R01-type funding.

DEADLINE FOR LETTER OF INTENT

Friday, August 18, 2023: Deadline for submission of Letter of Intent (one electronic copy) emailed to Christine Abu-Hanna at Christine.abu-hanna@yale.edu by 5:00pm.

The letter of intent **must include** the following:

1. Academic position, VISA status and future scientific plans regarding liver-related research
2. Title of pilot project and
3. A sentence as to the applicability of the pilot project to the Liver Center. **Projects must make use of the Center's facilities.**

For more information, please visit our [website](#).

2023 LIVER CENTER RETREAT—REGISTRATION OPEN

Our retreat is scheduled for Sunday, September 10th, 2023 at the Water's Edge Resort and Spa in Westbrook, CT. **This year, our Keynote Speaker is Dean Nancy J. Brown.** We would like to invite you and your lab to join us. The day will begin around 8:00am with registration, poster setup, and breakfast and then presentations will start at 8:30am. We very much hope that you will stay for the whole program, and also join us for dinner at 6:00pm.

Additionally, we invite you to submit one or more poster(s) from your lab related to the liver center activities. The poster session is the liveliest component of the program and a great opportunity to interact with the center members and get acquainted on their research. All Center members are encouraged to submit posters, as there will be a poster session prior to dinner.

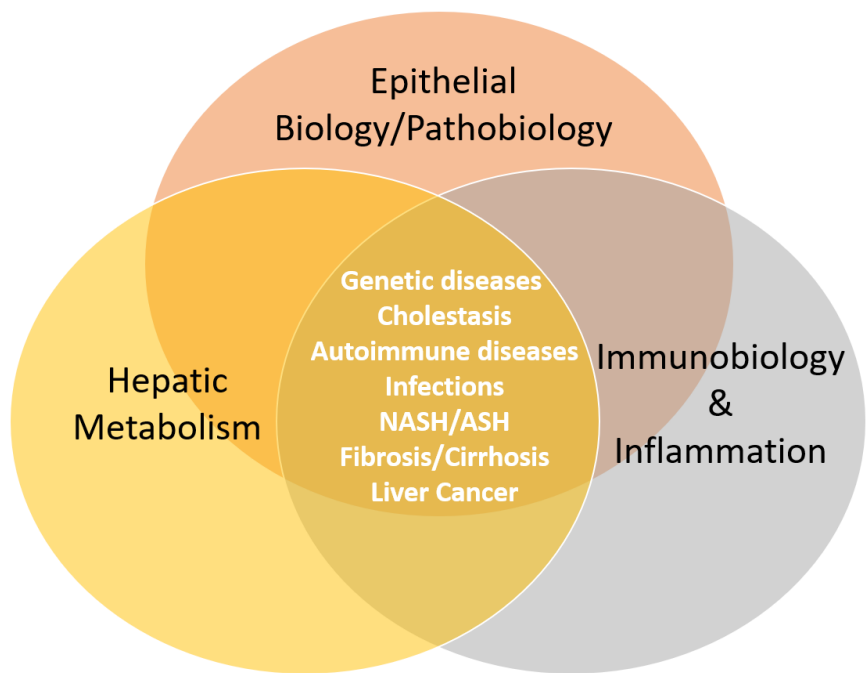
Please RSVP by clicking on this link: https://yalesurvey.ca1.qualtrics.com/jfe/form/SV_8GoZxiEqily0VOC

LIVER CENTER THEMES

The Research Base of the Liver Center focuses on three broad translational themes. These include:

- (1) Immunobiology and inflammation
- (2) Hepatic metabolism
- (3) Epithelial biology and pathobiology

The major areas of liver disease examined within these translational themes include autoimmune diseases, cholestasis, fibrosis/cirrhosis, genetic diseases, infections, liver cancer, and NASH/ASH. Many of our investigators have research interests that span multiple themes.



PERSONNEL UPDATE

Maria Ciarleglio has accepted a position outside of Yale University and is no longer our Liver Center Biostatistician.

This service will continue to be provided by the Clinical-Translational Core through Yanhong Deng and new biostatistician Yunshan Xu.

ADDITIONAL NEW CENTER SERVICES

IPSC/LIVER ORGANOIDS

On request, PBMCs are transferred to the Yale Stem Cell Center (YSCC) for reprogramming into iPSC. YSCC will generate at least 3 clones of iPSCs for each PBMC sample. iPSCs can be differentiated into liver cells (biliary cells or hepatocytes) and made available. Liver organoids available upon request. For more information, please contact Romina Fiorotto (Romina.fiorotto@yale.edu).

BIOINFORMATIC SUPPORT

We are pleased to announce the addition of free bioinformatics analysis support for Liver Center members through the Yale Center for Genome Analysis (YCGA) bioinformatics core. They specialize in next-generation sequencing analysis, including the full range of DNA and RNA sequence analysis, bulk and single-cell analysis, as well as ChIP-seq, CLIP-seq, ATAC-seq analysis, among others. They will also provide free consultation on experiment design, customization of analysis results reporting, and figure generation and manuscript writing for journal/grant submission or review. If you wish to utilize the service, please contact Dr. Dejian Zhao (dejian.zhao@yale.edu).

DATABASE ON LIVER CANCER AND PREDISPOSING CONDITIONS

This incorporates an expert-annotated, multi-parametric multi-time point imaging and clinical database including derived scores and survival outcomes. In collaboration with the Department of Radiology and Biomedical Imaging, the core offers access to data and advisory support for design of advanced data analysis research initiatives including with data-driven learning application. Contact James.duncan@yale.edu; Julius.chapiro@yale.edu; ariel.jaffe@yale.edu; tamar.taddei@yale.edu; mario.strazzabosco@yale.edu;

AVAILABLE CENTER CORE SERVICES

ADMINISTRATIVE

PROGRAM MANAGER: CHRISTINE.ABU-HANNA@YALE.EDU

PILOT FEASIBILITY PROGRAM

Pilot grants given annually to promote studies of liver disease

ENRICHMENT PROGRAM

Monthly seminar series, annual Klatskin/Boyer Lectureship, annual Center retreat, extended visiting professorship, research in progress series

CELLULAR-MOLECULAR

CORE DIRECTOR: MARIO.STRAZZABOSCO@YALE.EDU

ISOLATED CELL PREPARATIONS

Hepatocytes, cholangiocytes, endothelial cells, stellate cells, portal fibroblasts and hepatic lymphocytes, primarily from mice and rats. Human hepatocytes when available.

PROTEIN & GENE EXPRESSION

Quantitative real time PCR and infrared imaging detection. Altering gene expression in these cells using siRNA transfection and adenovirus infection technologies

IPSC/LIVER ORGANOID

On request, PBMCs are transferred to the Yale Stem Cell Center (YSCC) for reprogramming into iPSC. YSCC will generate at least 3 clones of iPSCs for each PBMC sample. iPSCs can be differentiated into liver cells (biliary cells or hepatocytes) and made available. Liver organoids available upon request.

CELL CULTURE FACILITIES

Available for short- and long- term cultures and cell lines.

MORPHOLOGY

CORE DIRECTOR: MICHAEL.NATHANSON@YALE.EDU

CONFOCAL, SUPER-RESOLUTION, MULTIPHOTON IMAGING

Leica SP5 Confocal Microscope
Stellaris 8 DIVE Multiphoton Microscope
Zeiss LSM 880 Airyscan Confocal Microscope
Leica SP8 Gated STED 3X Super Resolution
Bruker Opterra II Swept Field Microscope
Bruker Luxendo Light Sheet Microscope

BRUKER VUTARA 352 SUPER RESOLUTION MICROSCOPEELECTRON MICROSCOPY

Tecnai 12. biotwinFEI Tecnai TF20 FEG

OTHER MICROSCOPY TOOLS

Zeiss Axio Observer epifluorescence microscope
Olympus BX51 multi-headed brightfield microscope
Dissecting microscope
Zeiss Discovery 8 SteReo

IMAGE ANALYSIS WORKSTATIONS

4 PC workstations dedicated to image analysis. Software from Zeiss (ZEN blue), Leica (LAS X), Bitplane (Imaris), SVI (Huygens Deconvolution) and Perkin Elmer (Volocity) are available to users.

CLINICAL-TRANSLATIONAL

CORE DIRECTOR: GUADALUPE.GARCIA-TSAO@YALE.EDU

BIOSTATISTICAL SUPPORT

Two biostatisticians available for expertise in the design, conduct, and analysis of patient-oriented studies, as well as methodological development, education, and training

BIOSPECIMEN & LIVER BIOPSY REPOSITORY

Recruitment of patients and collection of blood samples

PATIENT REGISTRY

Patient databases on diagnoses including: chronic hepatitis C, cirrhosis, chronic hepatitis B, PBC, autoimmune hepatitis, PSC, hepatocellular carcinoma, NAFLD, and cholangiocarcinoma

BIOINFORMATICS

Bioinformatics analysis support for Liver Center members through the Yale Center for Genome Analysis (YCGA) bioinformatics core.

Members' Original Recent Publications

Above the legal limit: Alcohol brings ER and mitochondria too close together. Guerra MT, Nathanson MH. *Cell Calcium*. 2023 Jul;113:102763. doi: 10.1016/j.ceca.2023.102763. Epub 2023 May 22. PMID: 37235972

Gene and protein expression and metabolic flux analysis reveals metabolic scaling in liver ex vivo and in vivo. Akingbesote ND, Leitner BP, Jovin DG, Desrouleaux R, Owusu D, Zhu W, Li Z, Pollak MN, Perry RJ. *Elife*. 2023 May 23;12:e78335. doi: 10.7554/eLife.78335. PMID: 37219930

Cell-matrix interactions control biliary organoid polarity, architecture, and differentiation. Fiorotto R, Mariotti V, Taleb SA, Zehra SA, Nguyen M, Amenduni M, Strazzabosco M. *Hepatology*. 2023 Mar 24;77(4):e0094. doi: 10.1097/HCP.000000000000094. eCollection 2023 Apr 1. PMID: 36972396

HERV1-env Induces Unfolded Protein Response Activation in Autoimmune Liver Disease: A Potential Mechanism for Regulatory T Cell Dysfunction. Subramanian K, Paul S, Libby A, Patterson J, Arterbery A, Knight J, Castaldi C, Wang G, Avitzur Y, Martinez M, Lobritto S, Deng Y, Geliang G, Kroemer A, Fishbein T, Mason A, Dominguez-Villar M, Mariappan M, Ekong UD. *J Immunol*. 2023 Mar 15;210(6):732-744. doi: 10.4049/jimmunol.2100186. PMID: 36722941

Inhibition of HSD17B13 protects against liver fibrosis by inhibition of pyrimidine catabolism in nonalcoholic steatohepatitis. Luukkonen PK, Sakuma I, Gaspar RC, Mooring M, Nasiri A, Kahn M, Zhang XM, Zhang D, Sammalkorpi H, Penttilä AK, Orho-Melander M, Arola J, Juuti A, Zhang X, Yimlamai D, Yki-Järvinen H, Petersen KF, Shulman GI. *Proc Natl Acad Sci U S A*. 2023 Jan 24;120(4):e2217543120. doi: 10.1073/pnas.2217543120. Epub 2023 Jan 20. PMID: 36669104

Locoregional Therapy in the Management of Intrahepatic Cholangiocarcinoma: Is There Sufficient Evidence to Guide Current Clinical Practice? Wang Y, Strazzabosco M, Madoff DC. *Curr Oncol Rep*. 2022 Dec;24(12):1741-1750. doi: 10.1007/s11912-022-01338-5. Epub 2022 Oct 18. PMID: 36255606 Review.

Tick transmission of *Borrelia burgdorferi* to the murine host is not influenced by environmentally acquired midgut microbiota. Narasimhan S, Rajeevan N, Graham M, Wu MJ, DePonte K, Marion S, Masson O, O'Neal AJ, Pedra JHF, Sonenshine DE, Fikrig E. *Microbiome*. 2022 Oct 17;10(1):173. doi: 10.1186/s40168-022-01378-w. PMID: 36253842

Noninvasive predictors of clinically significant portal hypertension in NASH cirrhosis: Validation of ANTICIPATE models and development of a lab-based model. Rabiee A, Deng Y, Ciarleglio M, Chan JL, Pons M, Genesca J, Garcia-Tsao G. *Hepatology*. 2022 Dec;6(12):3324-3334. doi: 10.1002/hep4.2091. Epub 2022 Oct 10. PMID: 36214066 Free PMC article. Clinical Trial.

Holistic management of hepatocellular carcinoma: The hepatologist's comprehensive playbook. Jaffe A, Taddei TH, Giannini EG, Ilagan-Ying YC, Colombo M, Strazzabosco M. *Liver Int*. 2022 Dec;42(12):2607-2619. doi: 10.1111/liv.15432. Epub 2022 Oct 11. PMID: 36161463 Review.

Invasive Fungal Infections Are Underdiagnosed in Hospitalized Patients With Decompensated Cirrhosis: An Autopsy Study. Saffo S, Jain D, Sanchez H, Garcia-Tsao G. *Gastro Hep Adv*. 2022;1(5):803-806. doi: 10.1016/j.gastha.2022.05.015. Epub 2022 Jun 2. PMID: 36160304

Immune-mediated tubule atrophy promotes acute kidney injury to chronic kidney disease transition. Xu L, Guo J, Moledina DG, Cantley LG. *Nat Commun*. 2022 Aug 19;13(1):4892. doi: 10.1038/s41467-022-32634-0. PMID: 35986026

Early mechanical ventilation for grade IV hepatic encephalopathy is associated with increased mortality among patients with cirrhosis: an exploratory study. Saffo S, Garcia-Tsao G. *Acute Crit Care*. 2022 Aug;37(3):355-362. doi: 10.4266/acc.2022.00528. Epub 2022 Aug 18. PMID: 35977889