

# LIVER DIGEST

March 22, 2024

A monthly update of PLRC happenings



**PITTSBURGH LIVER  
RESEARCH CENTER**

A partnership of University of Pittsburgh & UPMC

## In this issue:

### • PLRC Faculty Highlights

- Dr. Sungjin Ko authors Editorial in Cellular & Molecular Gastroenterology and Hepatology
- Dr. Jaideep Behari authors a commentary in Digestive Diseases & Sciences
- Drs. Joe Locker, Ira Fox and Michael Oertel publish an article in Cellular & Molecular Gastroenterology and Hepatology
- Dr. Gavin Arteel publishes an article in the Journal of Leukocyte Biology

### • Upcoming Seminars & Meetings

- Mar 26th @ 12PM Dr. Stacey Huppert, S120 BST
- Apr 9th @ 12PM Dr. Jeff Albrecht, S120 BST
- Apr 16th @ 12PM Dr. Yulei Wang, S120 BST

### • Funding Opportunities

### • Announcements & Meetings

- Hepatic Sinusoid Meeting 4/24-26/2024
- UPMC/PITT Pathology Dept Retreat 5/29/24
- ASIP/SLAM Meeting 6/16-20/2024

### • Want Ads :

- Open positions
- Jobseekers CVs posted

Please acknowledge all support from the PLRC in your publications and presentations. Note the grant number and all CORES used. (NIH/NIDDK P30DK120531)

Please share your relevant accolades (grants, publications, awards and other news worthy items) with us, as it relates to the PLRC mission, so we can share with all of our members.

Visit the PLRC website ([www.livercenter.pitt.edu](http://www.livercenter.pitt.edu)) for up-to-date news, seminar and event information.

Contact Aaron Bell ([bellaaro@pitt.edu](mailto:bellaaro@pitt.edu)) if you have specific questions or suggestions.

## Our mailing address is:

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## FACULTY HIGHLIGHT

### Dr. Sungjin Ko, DVM, PhD

authored an editorial in the journal Cellular & Molecular Gastroenterology and Hepatology entitled "*Trailblazing TRAIL Therapy: Illuminating Pathways for Cholangiocarcinoma Treatment*"



Ko S. Trailblazing TRAIL Therapy: Illuminating Pathways for Cholangiocarcinoma Treatment. *Cell Mol Gastroenterol Hepatol.* 2024 Feb 28;S2352-345X(24)00036-5. doi: 10.1016/j.jcmgh.2024.02.008. Epub ahead of print. PMID: 38431266.

**Excerpt:** TNFSF10 (TRAIL), a member of the tumor necrosis factor  $\alpha$  superfamily, holds significant promise in the field of cancer research, particularly in immune modulation, implying potential synergism with personalized approaches, such as ICI and/or anti-angiogenic therapies. TRAIL signaling has garnered attention for its remarkable ability to selectively target cancer cells while sparing healthy tissue, a feature distinct from other tumor necrosis factor  $\alpha$  superfamily members such as FASLG. This selective cytotoxicity serves as the foundation of targeting the TRAIL–TRAIL-receptor pathway, and positioning it as a promising avenue for therapeutic intervention in various malignancies, including CCA. [READ MORE](#)

## FACULTY HIGHLIGHT

### Dr. Jaideep Behari, MD, PhD,

Associate Director of the PLRC, and Director of the UPMC FLOW clinic authored a commentary in the journal Digestive Diseases and Sciences on spleen stiffness measurement in MASLD and its potential utility in risk stratification of MASLD patients with cirrhosis, clinically significant portal hypertension and as an adjunct to liver stiffness measurements. The article is entitled, "Spleen Stiffness Measurement in Metabolic Dysfunction-Associated Steatotic Liver Disease-Value Added or Work in Progress?".



Behari J. Spleen Stiffness Measurement in Metabolic Dysfunction-Associated Steatotic Liver Disease-Value Added or Work in Progress? *Dig Dis Sci.* 2024 Feb 8. doi: 10.1007/s10620-024-08270-7. Epub ahead of print. PMID: 38332210.

[READ MORE](#)

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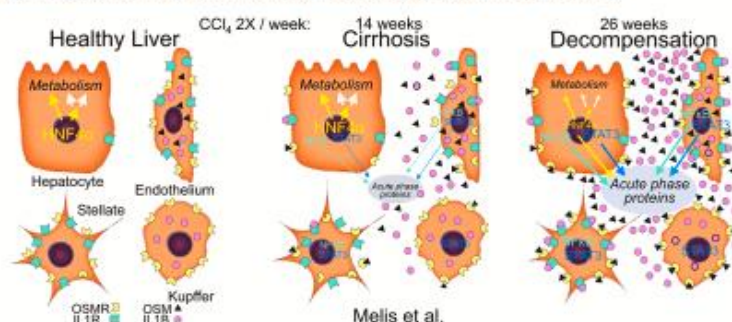
## FACULTY HIGHLIGHT

Dr. Joe Locker, MD, PhD along with Ira Fox, MD and Michael Oertel, PhD published an article in Cellular & Molecular Gastroenterology and Hepatology entitled “Mechanism and Effect of HNF4 $\alpha$  Decrease in a Rat Model of Cirrhosis and Liver Failure”.



### Mechanism and effect of HNF4 $\alpha$ decrease in a rat model of cirrhosis and liver failure

Reduced HNF4 $\alpha$  characterized end-stage livers. The reduction was caused by a multicellular response to inflammatory cytokines that affected HNF4 $\alpha$  and numerous other hepatocyte transcription factors. The reduced HNF4 $\alpha$  still provided extensive phenotypic regulation and stimulated expression of acute phase proteins.



cmgh CELLULAR AND MOLECULAR GASTROENTEROLOGY AND HEPATOLOGY

Melis M, Marino R, Tian J, Johnson C, Sethi R, Oertel M, Fox IJ, Locker J. Mechanism and Effect of HNF4 $\alpha$  Decrease in a Rat Model of Cirrhosis and Liver Failure. *Cell Mol Gastroenterol Hepatol.* 2024;17(3):453-479. doi: 10.1016/j.jcmgh.2023.11.009. Epub 2023 Nov 21. PMID: 37993018; PMCID: PMC10837635.

**Background & aims:** HNF4 $\alpha$ , a master regulator of liver development and the mature hepatocyte phenotype, is down-regulated in chronic and inflammatory liver disease. We used contemporary transcriptomics and epigenomics to study the cause and effects of this down-regulation and characterized a multicellular etiology.

**Methods:** Progressive changes in the rat carbon tetrachloride model were studied by deep RNA sequencing and genome-wide chromatin immunoprecipitation sequencing analysis of transcription factor (TF) binding and chromatin modification. Studies compared decompensated cirrhosis with liver failure after 26 weeks of treatment with earlier compensated cirrhosis and with additional rat models of chronic fibrosis. Finally, to resolve cell-specific responses and intercellular signaling, we compared transcriptomes of liver, nonparenchymal, and inflammatory cells.

**Results:** HNF4 $\alpha$  was significantly lower in 26-week cirrhosis, part of a general reduction of TFs that regulate metabolism. Nevertheless, increased binding of HNF4 $\alpha$  contributed to strong activation of major phenotypic genes, whereas reduced binding to other genes had a moderate phenotypic effect. Decreased Hnf4a expression was the combined effect of STAT3 and nuclear factor kappa B (NF $\kappa$ B) activation, which similarly reduced expression of other metabolic TFs. STAT/NF $\kappa$ B also induced de novo expression of Osmr by hepatocytes to complement induced expression of Osm by nonparenchymal cells.

**Conclusions:** Liver decompensation by inflammatory STAT3 and NF $\kappa$ B signaling was not a direct consequence of progressive cirrhosis. Despite significant reduction of Hnf4a expression, residual levels of this abundant TF still stimulated strong new gene expression. Reduction of HNF4 $\alpha$  was part of a broad hepatocyte transcriptional response to inflammation.

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## PLRC SEMINARS

Mar 26th @ 12:00 pm – 1:00 pm in S120 BST



**Stacey Huppert, PhD**

Associate Professor,  
Dept of Pediatrics  
Cincinnati Children's Hospital

Seminar Title: **Mechanisms regulating hepatic epithelial cell plasticity and identity**

April 9th @ 12:00 pm – 1:00 pm in S120 BST

**“George Michalopoulos Endowed  
Lectureship in Pathology”**



**Jeffrey Albrecht, MD**

Department of Medicine  
Division of Gastroenterology,  
Hepatology, and Nutrition  
University of Minnesota

Seminar Title: **Cyclin D1 at the nexus of cell cycle control and metabolism in the liver.**



**April 16th @ 12:00 pm – 1:00 pm  
in S120 BST**

**Yulei Wang, PhD**

Senior Fellow/Group Leader  
Department of Translational  
Medicine/Oncology

Genentech  
South San Francisco, CA

Seminar Title: **Hepatocellular Carcinoma: Biomarker Discovery, Disease Biology, and Clinical Translation**

## FUNDING OPPORTUNITIES

Notice of Participation of NIDDK in PAR-23-309 Health and Health Care Disparities Among Persons Living with Disabilities (R01 - Clinical Trials Optional) (NOT-DK-24-006) National Institute of Diabetes and Digestive and Kidney Diseases

NOT-DK-24-013: PAR-24-077: "Addressing Health and Health Care Disparities among Sexual and Gender Minority (SGM) Populations (R01 - Clinical Trials Optional)." For details, see <https://grants.nih.gov/grants/guide/notice-files/NOT-DK-24-013.html>

**Stephen I. Katz Early Stage Investigator Research Project Grant [PAR-24-075](#)** (innovative project that represents a change in research direction for an early stage investigator (ESI) and for which no preliminary data exist) 1/26 or 5/29 due dates

**Diabetes: JDRF Grant Opportunities [URL/LINK](#)**

**NOSI: Advancing Genomic Technology Development for Research and Clinical Application [NOT-HG-24-012](#)** (NHGRI) applications focused on developing novel laboratory-focused tools and technologies that enable new lines of scientific inquiry and advance research or clinical applications in human genomics

**To see all NIH Grants sorted by week, please visit: [NIH Guide](#)**

Or click below for recent weeks:

Week of: [Mar 1:](#) [Mar 8:](#) [Mar 15:](#)

[Click here](#) for all current **NIDDK** Funding opportunities

### NOTICE!

NIH GRANT SUBMISSION DEADLINES ARE **NOT AFFECTED** BY GOVERNMENT SHUTDOWN AS OF NOW.

Please submit by the standard dates

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## FACULTY HIGHLIGHT

Dr. Gavin Arteel, PhD published an article in the Journal of Leukocyte Biology entitled, “*When is a Kupffer cell not a Kupffer cell? Novel insight into macrophage fate and function in hepatic fibrosis*”.



Arteel GE. When is a Kupffer cell not a Kupffer cell? Novel insight into macrophage fate and function in hepatic fibrosis. J Leukoc Biol. 2024 Feb 23;115(3):415-416. doi: 10.1093/jleuko/qiae005. PMID: 38285520.

## ANNOUNCEMENTS & Meetings

- [Communityliveralliance.org](https://www.communityliveralliance.org)
- ASIP Annual Meeting “**Pathobiology: Mechanisms of Disease 2024**”: Baltimore, MD: **April 20-23, 2024**: [Registration](#): event [Program](#)
- **THE LIVER SINUSOID MEETING @ Chicago, IL April 24-26, 2024** [Program](#): Registration
- **Digestive Disease Week 2024**: Washington D.C May 18-21, 2024 [Registration](#): [Details](#)
- University of Pittsburgh Pathology Department Retreat- **May 29, 2024**
- The FASEB Liver Meeting is now the **Summer Liver Academy Meeting (SLAM)**.@ Cape Coral, FL **June 16-20, 2024** [Website](#)
- National Institute on Minority Health & Health Disparities (NIMHD) hosting “**Health Disparities Research Institute**” **August 5-9, 2024**: Bethesda, MD For ESI investigators/Application period open 2/8/24-3/14/24 [@ Application](#): [Learn More](#)



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## WANT ADS

This section is available for PLRC members to communicate wants or needs in your laboratories.

Available positions / Collaboration ideas / Equipment needs

Please send any "wants/needs" to be advertised to Aaron Bell ([bellaaro@pitt.edu](mailto:bellaaro@pitt.edu))

## **OPEN POSITIONS:**

### **JOB SEEKERS:**

- \* PhD, Senior Researcher at Hormel Institute, interested in Senior Lab role @ Pitt/UPMC. Experience with HCC, CCA, Mol. Biology, metabolism, signal transduction. [Link to CV](#) Email: [kpant@umn.edu](mailto:kpant@umn.edu)
- \* MD, PhD Researcher with extensive experience in cholangiocyte biology, strong PI references. [Link to CV](#). Email: [Qin.Li7@chp.edu](mailto:Qin.Li7@chp.edu)
- \* Res.Asst.Prof. Highly experienced researcher in many disciplines including bioinformatics, proteomics, genomics and molecular biology. [Link to CV](#) Email: [liz45@pitt.edu](mailto:liz45@pitt.edu)
- \* Sr. Postdoc from UPENN (Wells-Lab), Hepatobiliary toxicity, environmental toxins, organ-on-a-chip, mechanobiology and biomaterials. [Link to CV](#) Email: [Kapish.Gupta@Penmedicine.upenn.edu](mailto:Kapish.Gupta@Penmedicine.upenn.edu)
- \* Postdoc/Research Associate from Wash U with experience in Immunology & cytokine signaling of liver diseases and liver regeneration. Interest in gene editing research. [Link to CV](#) Email: [ramavathnareshnaik@gmail.com](mailto:ramavathnareshnaik@gmail.com)
- \* Res. Asst. Prof. Experience in hepatocyte-biliary trans-differentiation, Cholestatic liver diseases, gut-liver axis. [Link to CV](#) Email: [chhavi@pitt.edu](mailto:chhavi@pitt.edu)