PITTSBURGH LIVER RESEARCH CENTER

A partnership of University of Pittsburgh & UPMC

Weekly Update – January 24, 2019

www.livercenter.pitt.edu

In this email:

Upcoming Seminars

For a complete list of upcoming PLRC events, please visit our website: www.livercenter.pitt.edu/events

PLRC Seminar Series

Tuesday, January 29, 2019

12:00-1:00 p.m.

S123 BST

Yanqiao Zhang, MD

Professor of Integrative Medical Sciences

Northeast Ohio Medical University

"NAFLD: Novel Pathogenic Mechanisms and Potential Therapeutics"

This activity has been approved for AMA PRA Category 1 Credit. #6242 Liver Center Seminars.

Pizza will be provided.

**This seminar will not be available via webcast.

Liver Seminar

Wednesday, January 30, 2019
12:00-1:00 p.m.
1104 Scaife

Chandrashekhar R. Gandhi, Ph.D., FAASLD
Professor, Gastroenterology, Hepatology and Nutrition
Cincinnati Children's Hospital Medical Center

"Critical Importance of Augmenter of Liver Regeneration Protein in Steatohepatitis"

PLRC SIG - Tumorigenesis

Tuesday, February 5, 2019
12:00-1:00 p.m.
S123 BST

Dr. Sarangarajan Ranganathan - Histology and Molecular Classification of Hepatoblastoma

Dr. Edward Prochownik - Predicting Hepatoblastoma Phenotypes

Pizza will be provided.

Liver Seminar

Monday, February 11, 2019
10:00-11:00 am
W995 BST (DDI conference room)

Ashutosh Agarwal, PhD

Assistant Professor, Biomedical Engineering Department
University of Miami College of Engineering

Expertise: Cardiovascular Tissue engineering, Microfluidics, Hydrogels, Organs on Chips

PLRC Seminar Series

Tuesday, February 26, 2019

12:00-1:00 pm

S123 BST

Kirsten Sadler, PhD

Associate Professor, Department of Biology

New York University in Abu Dhabi

Title TBA

This activity has been approved for AMA PRA Category 1 Credit. #6242 Liver Center Seminars.

Pizza will be provided.

Liver Seminar

Wednesday, February 27, 2019

12:00-1:00 pm

1104 Scaife

Bin Gao, MD, PhD

National Institute of Health

"Interleukin-22: A Magic Potion for Epithelial Cell Repair from Bench to Bedside"

Liver Cancer Conference

Community Liver Allicance
Liver Cancer Conference

Saturday, March 9, 2019 | 7:30 a.m. - 3:00 p.m.

Wyndham Grand Hotel, Pittsburgh, PA

CME Accredited (see flyer for details)

Please see attached brochure for schedule, speakers, and details.

To register, please visit the CLA website: **http://www.communityliveralliance.org/liver-cancer-conference**

Liver-Themed Gut Club May 2, 2019

Dr. Fasiha Kanwal, the division chief at Baylor, will speak at the May 2, 2019 Pittsburgh Gut Club accredited dinner/lecture series on "The Changing Epidemiology of Liver Cancer."

Liver-related clinical and research trainees are invited to attend the lecture with fee-waived registration. All faculty are invited to attend as well but are required to pay to attend. But, they welcome your trainees as fee-waived participants.

To register for this event, please complete the registration form found in the attached brochure (trainees mark "fee waived" in the payment section), and scan (joj2@pitt.edu) or fax (412-578-9537) it to Joy Merusi by April 15th.

Faculty Highlights – Grants, Publications, Awards

Dr. **Ramon Bataller** and Dr. **Gavin Arteel** are two of the editors of Journal of Hepatology special issue on Alcoholic Hepatitis

Journal of Hepatology, February 2019, Volume 70, Issue 2, p221-334
Current Trends in Alcohol-Related Liver Disease
Edited by **Ramon Bataller, Gavin Arteel**, Christophe Moreno, Vijay Shah

CONTENTS

EDITORIAL

- **Alcohol-related liver disease: Time for action**
  R. Bataller, G.E. Arteel, C. Moreno and V. Shah

REVIEWS

- **Treating alcohol-related liver disease from a public health perspective**
  T. Hydes, W. Gilmore, N. Sheron and I. Gilmore
- **Effect of ethanol on lipid metabolism**
  M. You and G.E. Arteel
- **Inflammatory pathways in alcoholic steatohepatitis**
  B. Gao, M.F. Ahmad, L.E. Nagy and H. Tsukamoto
- **Microbiome as a therapeutic target in alcohol-related disease**
  S.K. Sarin, A. Pande and B. Schnabl
- **Non-invasive diagnosis and biomarkers in alcohol- related liver disease**
  C. Moreno, S. Mueller and G. Szabo
- **Hepatocellular carcinoma in the setting of alcohol- related liver disease**
  N. Ganne-Carrie´ and P. Nahon
- **Fibrosis and alcohol-related liver disease**
  C. Lackner and D. Tiniakos
- **Current trials and novel therapeutic targets for alcoholic hepatitis**
  A.K. Singal and V.H. Shah
- **Endpoints and patient stratification in clinical trials for alcoholic hepatitis**
  P. Mathurin and M. Thursz
- **Acute-on-chronic liver failure in patients with alcohol- related liver disease**
  T. Gustot and R. Jalan
- **Liver transplantation for alcoholic hepatitis**
  G.Y. Im, A.M. Cameron and M.R. Lucey

To access the issue and all articles, please **click here**.

ORIGINAL ARTICLE

Dharendra Thapa, Kaiyuan Wu, Michael W. Stoner, Bingxian Xie, Manling Zhang, Janet R. Manning, Zhongping Lu, Jian H. Li, Yong Chen, Marjan Gucek, Martin P. Playford, Nehal N. Mehta, Daniel Harmon, **Robert M. O'Doherty, Michael J. Jurczak**, Michael N. Sack and Iain Scott. The protein acetylase GCN5L1 modulates hepatic fatty acid oxidation activity via acetylation of the mitochondrial β-oxidation enzyme HADHA. J Biol Chem. 2018 Oct 15. pii: jbc.AC118.005462. doi: 10.1074/jbc.AC118.005462. [Epub ahead of print] PubMed PMID: 30323061.

ABSTRACT

Sirtuin 3 (SIRT3) deacetylates and activates several mitochondrial fatty acid oxidation enzymes in the liver. Here, we investigated whether the protein acetylase GCN5 general control of amino acid synthesis 5-like 1 (GCN5L1), previously shown to oppose SIRT3 activity, is involved in the regulation of hepatic fatty

acid oxidation. We show that GCN5L1 abundance is significantly up-regulated in response to an acute high-fat diet (HFD). Transgenic GCN5L1 overexpression in the mouse liver increased protein acetylation levels, and proteomic detection of specific lysine residues identified numerous sites that are co-regulated by GCN5L1 and SIRT3. We analyzed several fatty acid oxidation proteins identified by the proteomic screen and found that hyperacetylation of hydroxyacyl-CoA dehydrogenase trifunctional multienzyme complex subunit α (HADHA) correlates with increased GCN5L1 levels. Stable GCN5L1 knockdown in HepG2 cells reduced HADHA acetylation and increased activities of fatty acid oxidation enzymes. Mice with a liver-specific deletion of GCN5L1 were protected from hepatic lipid accumulation following a chronic HFD and did not exhibit hyperacetylation of HADHA compared with WT controls. Finally, we found that GCN5L1-knockout mice lack HADHA that is hyperacetylated at three specific lysine residues (Lys-350, Lys-383, and Lys-406) and that acetylation at these sites is significantly associated with increased HADHA activity. We conclude that GCN5L1-mediated regulation of mitochondrial protein acetylation plays a role in hepatic metabolic homeostasis.

For full text, please **click here**.

PLRC Pilot & Feasibility RFA

The Pittsburgh Liver Research Center is pleased to announce the 2015 Request for Applications for Pilot/Feasibility Grants. The grants will fund new initiatives and/or support new investigators who are pursuing liver-related research that should lead to R01-type funding or other extramural support at a later date. For more information, please visit the website: **http://www.livercenter.pitt.edu/plrc-grants**

Funding Opportunities

Judith Graham Pool (JGP) Postdoctoral Research Fellowship
National Hemophilia Foundation (NHF)

Coulter – PLRC joint award
Please see attached flyer for details on this opportunity.

Pittsburgh Liver Research Center
200 Lothrop St. | Pittsburgh, PA 15261