



## LIVER SPOT–light: A weekly update of PLRC happenings

January 10, 2019

[www.livercenter.pitt.edu](http://www.livercenter.pitt.edu)

In this email:

[Upcoming Seminars](#)

[Faculty Highlights](#)

[PLRC Pilot & Feasibility RFA](#)

[NIH updating "Scientific Premise" phrasing](#)

Featured Faculty: [www.livercenter.pitt.edu](http://www.livercenter.pitt.edu)

### Upcoming Seminars

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

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#### PLRC Seminar Series

Tuesday, January 15, 2019

12:00-1:00 p.m.

S123 BST

**Samira Kiani, MD**

Assistant Professor

School of Biological and Health Systems Engineering  
Ira A. Fulton Schools of Engineering  
Arizona State University

**"CRISPR Tools for Controllable Gene Therapies *in Vivo*"**

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

*Pizza will be provided.*

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Registration URL: <https://attendee.gotowebinar.com/register/6607572696840938499>

For those viewing thru the webinar, please follow the directions below:

- Please Register for the live Webinar ASAP
- After registering, you will receive the confirmation email
- You will be prompt to download the CitrixOnline application and install on your PC or Laptop
- Please contact your local PC Support if you need help installing the application
- Feel free to email Ishtiaque Ahmed ([ahmedi@upmc.edu](mailto:ahmedi@upmc.edu)) if you have any questions

NOTE Webinar attendees -- use Telephone/Speakerphone and dial-in instead of using desktop/laptop speakers for better audio quality.

Telephone/Speakerphone Audio option is shown right at the Click to Join Webinar prompt.

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**PLRC Seminar Series**

Tuesday, January 22, 2019

12:00-1:00 p.m.

S123 BST

[Allison Formal, MBA](#), Director, Coulter Program

**"Implementing the Coulter Translational Research Model for Success"**

**&**

[Philip Brooks, MS, MBA](#), Entrepreneur in Residence, Innovation Institute

**"Inspiring Innovators in Translating their Research to the Marketplace"**

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

*Pizza will be provided.*

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**PLRC Seminar Series**

Tuesday, January 29, 2019

12:00-1:00 p.m.

S123 BST

**Yangiao 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.*

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Registration URL: <https://attendee.gotowebinar.com/register/6607572696840938499>

For those viewing thru the webinar, please follow the directions below:

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Telephone/Speakerphone Audio option is shown right at the Click to Join Webinar prompt.

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**Liver Seminar**

Wednesday, January 30, 2019

12:00-1:00 p.m.

1104 Scaife

**Chandrashekhar R. Gandhi, Ph.D., FAASLD**

Professor of Integrative Medical Sciences

Northeast Ohio Medical University

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

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## 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.*

## Faculty Highlights – Grants, Publications, Awards

**Dr. Michael Jurczak** has been awarded an R01 from the NIH for his proposal entitled "Role of Fbxo48-mediated AMPK proteostasis in the pathogenesis and treatment of NAFLD." **Dr. Paul Monga** and **Dr. Robert O'Doherty** are Co-Is on this grant. We wish Dr. Jurczak's team all the best in their research!

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Editorial: Grace L. Guo and **Wen Xie**. Metformin action through the microbiome and bile acids. Nat Med. 24: 1789-1790 (2018) PMID: 30523325.

SUMMARY: Metformin functions through a gut microbiome–bile acid–farnesoid X receptor axis to lower glucose in type 2 diabetes, revealing a new therapeutic target in this disease.

For full text, please [click here](#).

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**Dr. Paul Monga** has been awarded the 2019 APS Gastrointestinal and Liver Section Distinguished Research Award. This award recognizes an outstanding investigator who is internationally recognized for his/her contribution to research in areas represented by the Section. Candidates are judged based on their publication record, and the content of the nomination letter. Congratulations, Dr. Monga!

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Loomes KM, Spino C, Goodrich NP, Hangartner TN, Marker AE, Heubi JE, Kamath BM, Shneider BL, Rosenthal P, Hertel PM, Karpen SJ, Kerkar N, Molleston JP, Murray KF, Schwarz KB, **Squires RH**, Teckman J, Turmelle YP, Whittington PF, Sherker AH, Magee JC, Sokol RJ for the Childhood Liver Disease Research Network (ChiLDRen). Bone Density in Alagille Syndrome Correlates with Fracture

History and Severity of Cholestasis. Hepatology 2019;69:245-257. (PMID: 30063078)

#### ABSTRACT

Osteopenia and bone fractures are significant causes of morbidity in children with cholestatic liver disease. Dual-energy X-ray absorptiometry (DXA) analysis was performed in children with intrahepatic cholestatic diseases who were enrolled in the Longitudinal Study of Genetic Causes of Intrahepatic Cholestasis in the Childhood Liver Disease Research Network. DXA was performed on participants aged >5 years (with native liver) diagnosed with bile acid synthetic disorder (BASD), alpha-1 antitrypsin deficiency (A1AT), chronic intrahepatic cholestasis (CIC), and Alagille syndrome (ALGS). Weight, height, and body mass index Z scores were lowest in CIC and ALGS. Total bilirubin (TB) and serum bile acids (SBA) were highest in ALGS. Bone mineral density (BMD) and bone mineral content (BMC) Z scores were significantly lower in CIC and ALGS than in BASD and A1AT ( $P < 0.001$ ). After anthropometric adjustment, bone deficits persisted in CIC but were no longer noted in ALGS. In ALGS, height-adjusted and weight-adjusted subtotal BMD and BMC Z scores were negatively correlated with TB ( $P < 0.001$ ) and SBA ( $P = 0.02$ ). Mean height-adjusted and weight-adjusted subtotal BMC Z scores were lower in ALGS participants with a history of bone fractures. DXA measures did not correlate significantly with biliary diversion status. Conclusion: CIC patients had significant bone deficits that persisted after adjustment for height and weight and generally did not correlate with degree of cholestasis. In ALGS, low BMD and BMC reference Z scores were explained by poor growth. Anthropometrically adjusted DXA measures in ALGS correlate with markers of cholestasis and bone fracture history. Reduced bone density in this population is multifactorial and related to growth, degree of cholestasis, fracture vulnerability, and contribution of underlying genetic etiology.

For full text, please [click here](#).

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PLRC Pilot & Feasibility RFA

The Pittsburgh Liver Research Center is pleased to announce the 2019 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 see the attached RFA (also available at:

<https://www.livercenter.pitt.edu/plrc-grants>).

## NIH "Scientific Premise" Phrasing

Please note that the phrasing for "Scientific Premise" in NIH grants officially changes on January 25, 2019. Please see the announcement for more details: <https://nexus.od.nih.gov/all/2018/12/13/resources-for-rigorous-research/>



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

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## **Pilot / Feasibility Application Process**

### **Applications due March 15, 2019**

The Pittsburgh Liver Research Center is pleased to announce the 2019 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.

#### **Pilot/Feasibility grants:**

1. Are one-year awards for liver-related research. Funds can be used for reagents, animals, and core services, but not for equipment or travel. Under special circumstances and with proper justification, salary support may be considered. No indirects will be given. All funds must be used for the conduct of research. Funding will run from September 1, 2019 – August 31, 2020.
  - a. \$25,000 grant(s) will be awarded to individual applicants. The PLRC will fund between four and six (4-6) of these applications.
  - b. \$50,000 grant(s) will support a team of at least two investigators—a practicing physician and a basic scientist—working together to answer an important question pertaining to liver health and disease. The synergy and/or complementarity between the two investigators and their projects should be clearly visible. This award is intended to promote team science and/or translational science. The PLRC will fund one (1) of these applications.
2. Are for one year; in rare cases, awardees may apply for a second year of funding. Applicants applying for a second year of funding must provide a report of their progress to date and will be considered on a competitive basis with the entire pool of applicants.
3. Provide support for investigators to collect preliminary data sufficient to support a future extramural grant application for independent research and/or to test a novel hypothesis.
4. Encourage and support dissemination of research via peer-reviewed publication.
5. Are NOT intended for:
  - a. Bridge funding
  - b. Large projects by established investigators
  - c. Supporting or supplementing ongoing funded research of an investigator.

#### **Expected outcomes:**

1. The funds will be distributed in two disbursements. The first will be September 1, 2019. At the midpoint of the funding period, the PI(s) will submit a brief mid-year report; once the report has been approved, the second half of the funds will be disbursed.

2. At around the mid-point of the award, the PI(s) will present at a regularly scheduled PLRC seminar, and it will be expected that the PI(s) will discuss her/his work on the P/F project.
3. At the end of the funding period, it would be ideal for the PI(s) to have generated sufficient high-quality data to publish in a peer-reviewed scientific journal.
4. At the end of the funding period, it would be optimal for the PI(s) to have sufficient high-quality preliminary data to apply for extramural R01 (or similar) funding for the continuation of the project.
5. At the end of the funding period and using the data generated during the Pilot / Feasibility award period, the awardee(s) will submit to the PLRC one of the following: (1) a project completion report, or (2) a publication, or (3) a copy of the R01.
6. PLRC support shall be acknowledged in all relevant publications and presentations. A statement related to the acknowledgment can be obtained from the PLRC Administrator (Ann Vinski [vinskiam@upmc.edu](mailto:vinskiam@upmc.edu)).
7. The PLRC Director is available to discuss the progress of the project and offer other relevant scientific advice. The PLRC Director will be able to provide any supporting documents or letters necessary for the preparation of a successful R01 (or similar) application.
8. PIs will attend and participate in the PLRC Enrichment activities, including monthly seminars and relevant Special Interest Group roundtables.

### **Eligibility:**

All academic full-time faculty, including Instructors, Research Assistant Professors, and Assistant Professors, who are eligible to apply as PI for extramural NIH R01 funding and who are affiliated with the University of Pittsburgh and/or UPMC are eligible to apply. Projects will be considered on any aspect of fundamental or applied research relating to basic liver function, liver pathophysiology, or clinically relevant areas. Projects that will utilize the PLRC Scientific Cores will be given preference. Applicants must fall into one of the following categories of eligibility. Please note that this is a tiered priority scale, with preference being given to junior investigators.

- Track 1 (N). Junior investigators without independent grant support (excluding career development awards) seeking to establish independence in the field of liver research. *\*\*This category of applicant will be given preference.\*\**
- Track 2 (EN). Established investigators with independent grant support—past or present—who have not been involved in liver research and who wish to develop new research directions related to the liver.
- Track 3 (E). Established investigators working in liver-related research who wish to begin a new project representing a major departure from their previous NIH-funded research.

### **Application Process:**

1. PIs who intend to apply for the grant should send an email to Ann Vinski ([vinskiam@upmc.edu](mailto:vinskiam@upmc.edu)) no later than **February 15, 2019**. The email only needs to state the PI's name(s) and that they intend to apply for a grant.



2. Applications should follow the format of a new NIH R01 Grant, using NIH application forms ([PHS 398](#)) and must include the following:
  - a. Title and abstract
  - b. Detailed budget for the proposal. **\*\*Please be in contact with your departmental grant administrator for assistance in budget planning.\*\*** Effort is required of the principal investigator and must be reflected on the budget page. This effort should be cost shared by the department or other entity that will support such effort at the non-federal fringe rates.
  - c. NIH Biosketch for the PI (5 page limit); please use the [format that expires in 2020](#).
  - d. Specific Aims (1 page limit).
  - e. Research Strategy (6 page limit). The final section of the Research Strategy must be entitled "PLRC Core Use." This section will include a description of projected PLRC Core use during the project period. It is expected that each funded project will use at least one of the PLRC Research Cores. Please contact Ann Vinski ([vinskiam@upmc.edu](mailto:vinskiam@upmc.edu)) for details.
  - f. Bibliography (no page limit).
  - g. All institutional regulatory approvals for human, tissue, and animal use should be submitted with the application. If the relevant approvals have not yet been received, the applicant should indicate the date on which the approvals were requested.
3. Applications do not require institutional internal review or Dean's signature.
4. **All documents should be combined into a single pdf file and emailed to Ann Vinski ([vinskiam@upmc.edu](mailto:vinskiam@upmc.edu)) no later than March 15, 2019.**

#### **Review and Decision Process:**

1. Each application will be peer reviewed by at least two reviewers, one from the PLRC leadership, and one external reviewer.
2. Following initial review, a group of semi-finalists will be invited to present their proposals, in person, before the Executive Committee of the PLRC and a panel of external reviewers. **The PI is required to present in person to be considered for possible funding.** The presentations will be scheduled for the week of April 15, 2019.
3. The applications will be scored based on scientific merit and NIH fundability as deemed by the PLRC review panel. Emphasis will be placed on projects that have potential for NIDDK-supported liver research.
4. Applicants will be notified of award decisions no later than May 1, 2019. The Notice of Grant Award (NGA) will outline the expected outcomes (see above).
5. Grants begin September 1, 2019.