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# Liver Digest

A weekly update of PLRC happenings

June 27, 2019

PITTSBURGH LIVER RESEARCH CENTER
A partnership of University of Pittsburgh & UPMC

www.livercenter.pitt.edu

Featured Faculty - Dr. Sadeesh Ramakrishnan

## In this issue

- Funding Opportunity

## New Faculty

We are delighted to announce that **Dr. Samira Kiani** and **Dr. Mo Ebrahimkhani** will be joining the faculty at the University of Pittsburgh. They will be members of the PLRC and the Department of Pathology.

**Dr. Kiani's** research focuses on developing safer and controllable genetic circuits by combining the technology with design principles of synthetic biology. In addition, she is co-producing a documentary film titled "Code of the Wild" about the future of humans in the era of genomics. She will arrive February 1, 2020, and her lab webpage is available here: **https://www.kianilab.com/**

**Dr. Ebrahimkhani** focuses his work on advancing regenerative medicine through integrating systems and synthetic biology. He will begin at Pitt on September 1, 2019, and his website is available here: **https://www.ebrahimkhanilab.com/**

We look forward to working with Dr. Kiani and Dr. Ebrahimkhani, and we welcome them to the PLRC family!

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## Faculty Highlights

Grant Award:

**Dr. Paul Monga** has been awarded an NIH Research Project Grant entitled "Role of Wnt/beta-catenin In Liver Regeneration." This grant is now in its 16th year

and is in the amount of around $2.14M for 5 years. The focus of the proposal is to elucidate the upstream mechanisms that activate the Wnt signaling pathway during the process of liver regeneration after partial hepatectomy. The proposal will also examine specific Wnt ligands and Frizzled receptors during the regeneration and zonation process in the liver.

Congratulations, Dr. Monga!

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Original Article:

Thapa D, Xie B, Manning JR, Zhang M, Stoner MW, Huckestein BR, Edmunds LR, Zhang X, Dedousis NL, **O'Doherty RM**, **Jurczak MJ**, Scott I. Adropin reduces blood glucose levels in mice by limiting hepatic glucose production. Physiol Rep. 2019 Apr;7(8):e14043. doi: 10.14814/phy2.14043. PubMed PMID: 31004398; PubMed Central PMCID: PMC6474842.

ABSTRACT

Adropin is a liver- and brain-secreted peptide hormone with striking effects on fuel metabolism regulation in a number of tissues. Previous studies demonstrated that adropin secretion is decreased in obese mice subjected to a long-term high-fat diet (HFD), and that whole-body loss of adropin expression resulted in systemic insulin resistance. Treatment of obese mice with adropin improves glucose tolerance, which has been linked to increased glucose oxidation and inhibition of fatty acid utilization in isolated skeletal muscle homogenates. In this study, we used in vivo physiological measurements to determine how treatment of obese mice with adropin affects whole-body glucose metabolism. Treatment with adropin reduced fasting blood glucose and, as shown previously, increased glucose tolerance in HFD mice during standard glucose tolerance tests. Under hyperinsulinemic-euglycemic clamp conditions, adropin treatment led to a nonsignificant increase in whole-body insulin sensitivity, and a significant reduction in whole-body glucose uptake. Finally, we show that adropin treatment suppressed hepatic glucose production and improved hepatic insulin sensitivity. This correlated with reduced expression of fatty acid import proteins and gluconeogenic regulatory enzymes in the liver, suggesting that adropin treatment may impact the pathways that drive vital aspects of hepatic glucose metabolism.

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

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Original Article:

Cannella R, **Borhani AA**, Tublin M, **Behari J**, **Furlan A**. Diagnostic value of MR-based texture analysis for the assessment of hepatic fibrosis in patients with nonalcoholic fatty liver disease (NAFLD). Abdom Radiol (NY). 2019 May;44(5):1816-1824. doi: 10.1007/s00261-019-01931-6. PubMed PMID: 30788556.

ABSTRACT

PURPOSE: To investigate the performance of MR-based texture analysis (TA) for the assessment of hepatic fibrosis in patients with nonalcoholic fatty liver disease (NAFLD).

METHODS: Fifty-four adult patients (33 females, 21 males, mean age 49.8 ± 13.5 years) with biopsy-proven NAFLD were enrolled and underwent MR imaging on a 1.5 T system. TA parameters were extracted on axial noncontrast 3D-GRE T1W images (slice thickness = 4.6 mm) using a commercially available research software (TexRAD). Receiver operating curves (ROC), areas under the ROC (AUROC) and 95% confidence intervals (CI) were calculated to assess the accuracy of each TA parameter for the diagnosis of significant ($F \geq 2$) and advanced fibrosis ($F \geq 3$). The correlation between TA and histopathological features of nonalcoholic steatohepatitis (NASH) was tested calculating the Spearman's rank correlation coefficient ($\rho$).

RESULTS: Thirty-seven (68%) subjects had significant fibrosis and 20 (37%) had advanced fibrosis. The TA parameters with the best performance were standard deviation (SD) and entropy, respectively, with AUROC 0.755 (95% CI 0.619-0.862, $p \leq 0.0002$) and 0.769 (95% CI 0.634-0.873, $p < 0.0001$) for significant fibrosis and AUROC 0.746 (95% CI 0.609-0.854, $p \leq 0.0004$) and 0.754 (95% CI 0.618-0.861, $p \leq 0.0002$) for advanced fibrosis. SD and entropy demonstrated a moderate correlation with the degree of fibrosis ($\rho = 0.457$ and 0.480; $p < 0.01$). No significant correlation was found between TA parameters and other histopathological features of NASH.

CONCLUSIONS: Entropy and SD extracted on T1-weighted MR images have fair accuracy for the diagnosis of significant and advanced hepatic fibrosis in patients with NAFLD.

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

Original Article:

Belmonte FR, Dedousis N, Sipula I, Desai NA, **Singhi AD**, Chu Y, Zhang Y, Bannwarth S, Paquis-Flucklinger V, Harrington L, Shiva S, **Jurczak MJ**, **O'Doherty RM**, Kaufman BA. Petite Integration Factor 1 (PIF1) helicase deficiency increases weight gain in Western diet-fed female mice without increased inflammatory markers or decreased glucose clearance. PLoS One. 2019 May 28;14(5):e0203101. doi: 10.1371/journal.pone.0203101. eCollection 2019. PubMed PMID: 31136580.

ABSTRACT

Petite Integration Factor 1 (PIF1) is a multifunctional helicase present in nuclei and mitochondria. PIF1 knock out (KO) mice exhibit accelerated weight gain and decreased wheel running on a normal chow diet. In the current study, we investigated whether Pif1 ablation alters whole body metabolism in response to weight gain. PIF1 KO and wild type (WT) C57BL/6J mice were fed a Western diet (WD) rich in fat and carbohydrates before evaluation of their metabolic phenotype. Compared with weight gain-resistant WT female mice, WD-fed PIF1 KO females, but not males, showed accelerated adipose deposition, decreased locomotor activity, and reduced whole-body energy expenditure without increased dietary intake. Surprisingly, PIF1 KO females did not show obesity-induced alterations in fasting blood glucose and glucose clearance. WD-fed PIF1 KO females developed mild hepatic steatosis and associated changes in liver gene expression that were absent in weight-matched, WD-fed female controls, linking hepatic steatosis to Pif1 ablation rather than increased body weight. WD-fed PIF1 KO females also showed decreased expression of inflammation-associated genes in adipose tissue. Collectively, these data separated weight gain from inflammation and impaired glucose homeostasis. They also support a role for Pif1 in weight gain resistance and liver metabolic dysregulation during nutrient stress.

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

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Research Award:

**Dr. James Squires** has received the Autoimmune Liver Disease Pilot Research Award from AASLD for his project titled, "A Learning Health System for Pediatric Autoimmune Liver Disease Through Partnership with ImproveCareNow." The AASLD announcement is available at the following site: **http://www.aasldfoundation.org/award-programs/2019-research-and-career-development-award-**

recipients

Congratulations, Dr. Squires!

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## Funding Opportunity

**AGA-Elsevier Pilot Research Award**

American Gastroenterological Association (AGA)

AGA Research Foundation

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