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Liver Digest

A weekly update of PLRC happenings

February 21, 2019

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

www.livercenter.pitt.edu

Featured Faculty - Dr. Ruben Zamora

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Next Week's Seminars

PLRC Seminar Series - Dr. Kirsten Sadler

Tues, February 26, noon-1:00 pm

1102 Scaife

Kirsten Sadler, PhD

Associate Professor, Department of Biology

New York University in Abu Dhabi

"Epigenetic compensation promotes liver regeneration"

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) 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.

Liver Seminar - Dr. Bin Gao

Wed, February 27, noon-1:00 pm

1104 Scaife

Bin Gao, MD, PhD

National Institute of Health

"Inflammatory pathways in steatohepatitis: Roles of neutrophils and adipose tissues"

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

Liver Cancer Conference - March 9

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

For schedule, speakers, and details, please visit the PLRC website: **http://www.livercenter.pitt.edu/livercancer-conference**

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

Liver-Themed Gut Club - May 2

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 brochure available on the here (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

Original Article:

Cannella R, Rangaswamy B, Minervini MI, **Borhani AA**, Tsung A, **Furlan A**. Value of Texture Analysis on Gadoxetic Acid-Enhanced MRI for Differentiating Hepatocellular Adenoma From Focal Nodular Hyperplasia. AJR Am J Roentgenol. 2018 Dec 17:1-9. doi: 10.2214/AJR.18.20182. [Epub ahead of print] PubMed PMID: 30557050.

ABSTRACT

OBJECTIVE: The objective of our study was to assess the diagnostic performance of texture analysis (TA) on gadoxetic acid-enhanced MR images for differentiation of hepatocellular adenoma (HCA) from focal nodular hyperplasia (FNH).

MATERIALS AND METHODS: This study included 40 patients (39 women and one man) with 51 HCAs and 28 patients (27 women and one man)

with 32 FNH lesions. All lesions were histologically proven with preoperative MRI performed with gadoxetic acid. Two readers reviewed all the imaging sequences to assess the qualitative MRI characteristics. The T2-weighted fast spin-echo, hepatic arterial phase (HAP), and hepatobiliary phase (HBP) sequences were used for TA. Textural features were extracted using commercially available software (TexRAD). The differences in distributions of TA parameters of FNHs and HCAs were assessed using the Mann-Whitney U test. Area under the ROC curve (AUROC) values were calculated for statistically significant features. A logistic regression analysis was conducted to explore the added value of TA. A p value < 0.002 was considered statistically significant after Bonferroni correction for multiple comparisons.

RESULTS: Multiple TA parameters showed a statistically different distribution in HCA and FNH including skewness on T2-weighted imaging, skewness on HAP imaging, skewness on HBP imaging, and entropy on HBP imaging ($p < 0.001$). Skewness on HBP imaging showed the largest AUROC (0.869; 95% CI, 0.777-0.933). A skewness value on HBP imaging of greater than -0.06 had a sensitivity of 72.5% and a specificity of 90.6% for the diagnosis of HCA. Six of 51 (11.8%) HCAs lacked hypointensity on HBP imaging. A binary logistic regression analysis including hypointensity on HBP imaging and the statistically significant TA parameters yielded an AUROC of 0.979 for the diagnosis of HCA and correctly predicted 96.4% of the lesions.

CONCLUSION: TA may be of added value for the diagnosis of atypical HCA presenting without hypointensity on HBP imaging.

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

Original Article:

Molina L, Yang H, Adebayo Michael AO, **Oertel M**, **Bell A**, Singh S, Chen X, Tao J, **Monga SP**. mTOR Inhibition affects Yap1-β-catenin-induced hepatoblastoma growth and development. Oncotarget. 2019; 10:1475-1490.

ABSTRACT

Hepatoblastoma (HB) is the most common pediatric liver malignancy. Around 80% of HB demonstrate simultaneous activation of β-catenin and Yes-associated protein 1 (Yap1). The mechanism by which these signaling pathways contribute to HB pathogenesis remain obscure. Recently, mTORC1 activation was reported in human HB cells and in a murine HB model driven by β-catenin and Yap1. Here, we directly investigate the therapeutic impact of mTOR inhibition following HB development in the Yap1-β-catenin model. HB were established by hydrodynamic tail vein injection of Sleeping Beauty transposase and plasmids coding for ΔN90-β-catenin and S127A-Yap1. Five weeks after injection, when HB were evident, mice were randomized into Rapamycin diet-fed or basal-diet-fed groups for 5-weeks. Tumor growth was monitored via ultrasound imaging and mice in both groups were euthanized after 5-weeks for molecular analysis. Transcriptomic analysis showed a strong correlation in gene expression between HB in the Yap1-β-catenin model and HB patient cohorts. Rapamycin treatment decreased HB burden, almost normalizing liver weight to body weight ratio. Ultrasound imaging showed reduction in tumor growth over the duration of Rapamycin treatment as compared to controls. Majority of HB in the controls exhibited crowded fetal or embryonal histology, while remnant tumors in the experimental group showed well-differentiated fetal morphology. Immunohistochemistry confirmed inhibition of mTORC1 in the Rapamycin group. Thus, Rapamycin reduces HB in a clinically relevant model driven by β-catenin and Yap1, supporting use of mTORC1 inhibitors in their therapy. We also show the utility of standard and 3D ultrasound imaging for monitoring liver tumors in

mice.

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

Funding Opportunities

Coulter - PLRC Joint Award

The University of Pittsburgh & UPMC Pittsburgh Liver Research Center (PLRC) is pleased to announce a new translational grant program in collaboration with the Coulter TPII Program (Coulter) at the University of Pittsburgh. In September of 2019, the PLRC/Coulter will award up to one $50,000 grant, aimed at developing the commercial potential of healthcare solutions that are based on innovative technologies related to liver health, including disease diagnosis, surgery, treatment, and public health. One-Page LOI Submission: Deadline - 5:00 p.m. Friday, March 15, 2019.

Our mailing address is:
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