



UNIVERSITY OF LEEDS

This is a repository copy of *Addressing the interplay between apoptosis and glucose metabolism in liver cirrhosis and HCC*.

White Rose Research Online URL for this paper:
<http://eprints.whiterose.ac.uk/105751/>

Version: Accepted Version

Proceedings Paper:

Iansante, V, Choy, PM, Chokshi, S et al. (4 more authors) (2015) Addressing the interplay between apoptosis and glucose metabolism in liver cirrhosis and HCC. In: Gut. 2nd Digestive Disorders Federation Conference, 22-25 Jun 2015, London, UK. BMJ Publishing Group , A12-A12.

<https://doi.org/10.1136/gutjnl-2015-309861.22>

© 2015 BMJ Publishing Group Ltd and British Society of Gastroenterology. This is an author produced version of an abstract published in Gut. Uploaded in accordance with the publisher's self-archiving policy.

Reuse

Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk
<https://eprints.whiterose.ac.uk/>

Addressing the interplay between apoptosis and glucose metabolism in liver cirrhosis and HCC

Valeria Iansante¹, Pui Man Choy¹, Shilpa Chokshi², Roger Williams^{1,2}, Robert A. Anders³, Concetta Bubici⁴ and Salvatore Papa¹

Email: s.papa@researchinliver.org.uk

¹Cell signaling and Cancer Laboratory and ²Viral Hepatitis Laboratory, Institute of Hepatology, Foundation for Liver Research, London, UK. ³Division of Gastrointestinal and Liver Pathology, The Johns Hopkins University School of Medicine, Baltimore, USA. ⁴Division of Biosciences, Brunel University London, UK.

Background and Aims: Pro-inflammatory signalling in the liver promotes the appearance of a metabolic phenotype that involves the transition from mitochondrial respiration to aerobic glycolysis. It was demonstrated that this metabolic shift occurs during the transition from healthy and early stage of liver injury (NAFLD/NASH, ALD to late stage of disease (i.e. cirrhosis), and further escalates during HCC development [1,2]. This metabolic signature enables dividing cells to satisfy anabolic and energetic needs for biomass production and to suppress apoptotic signalling, which is consistent with increased compensatory hepatic cell proliferation typical of cirrhotic and HCC livers. However other studies in contrast have suggested that hepatocytes are unable to sustain glycolysis during late stage of chronic liver disease [3].

Methods: We used unbiased gene expression analyses of microarray datasets to investigate the expression of glycolytic genes in cirrhotic and HCC livers and correlated their expression with patient outcome. Furthermore, by using a combination of *in vitro* and *in vivo* analyses we have characterized the abilities of a novel anti-apoptotic gene to regulate aerobic glycolysis in liver cirrhosis and HCC.

Results: mRNA profiling showed significantly higher expression of glycolytic transcripts in cirrhotic and HCC livers compared to normal quiescent livers ($P < 0.05$). Up regulation of *Glut1*, *Hk1*, *Hk2*, *G6PI*, and *PFKL* was seen in HCC livers compared to their adjacent non-tumor tissues ($P < 0.001$). Notably, expression of enzymes regulating mitochondrial activity (*Pdha*, *Pdk*) was unchanged between non-tumor tissues and late stage of HCC. Moreover, up regulation of a novel anti-apoptotic gene positively correlated with increased expression of glycolytic transcripts in a group of cirrhotic patients prospectively classified as poor prognosis based on HCC development, and promotes the aerobic glycolysis of hepatoma cells.

Conclusions: In summary, our findings delineate a putative link between aerobic glycolysis and suppression of apoptosis that is an important part of the progression of cirrhosis to HCC. The identification of the mechanism regulating this link may lead to design new therapeutic strategies for human liver disease.

Reference:

- [1] Beyoğlu D, Idle JR. *J Hepatol.* 59: 842-858 (2013).
- [2] Kakazu E, *et al. Sci. Rep.* 3:3459 (2013).
- [3] Nishikawa T, *et al. J Hepatol.* 60: 1203-1211 (2014).