Editorial Desk

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From the Editor's desk....

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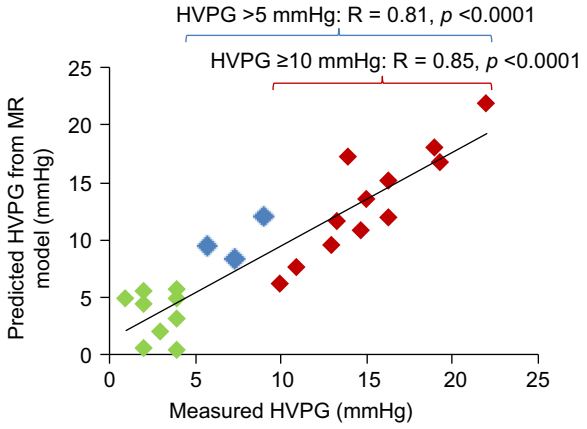
SELECTION OF THE MONTH

MRI may replace invasive portal pressure measurements

At present, the treatment of portal hypertension is seriously limited by the need to perform invasive portal pressure measurements because it requires special skill, and is both invasive and cumbersome to use routinely in clinical practice. An important paper in the present issue of *the Journal* by **Palaniyappan *et al.* describes very convincing data, suggesting that using novel algorithms to calculate splanchnic hemodynamics and hepatic architectural characteristics very closely reflects invasive measurements of hepatic venous pressure gradient.** This model was then validated in a small cohort. If the data generated in this paper can be reproduced accurately, it may be a game changer for the practicing hepatologist.

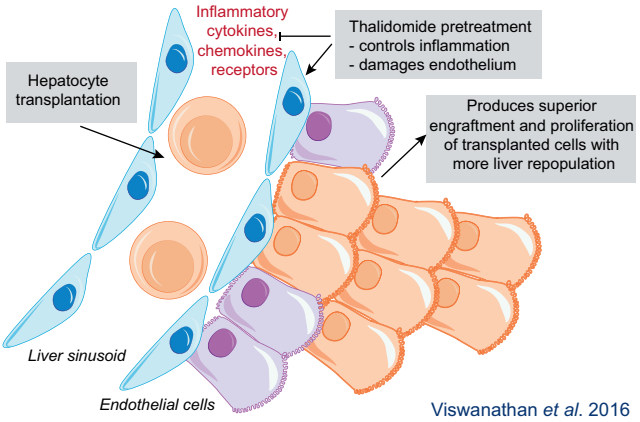


Palaniyappan *et al.* 2016

CELL TRANSPLANTATION

Thalidomide: an old drug for a new indication?

Cell transplantation has been proposed as an alternative to liver transplantation. However, efficient engraftment of transplanted cells is critical. Engraftment failure may be related to recruitment of neutrophils or Kupffer cells. Thalidomide is a drug that can reduce recruitment of these cells by inhibiting cytokine production and/or signaling. Here using an elegant animal model, Viswanathan *et al.* show that **thalidomide improves transplanted cell engraftment and liver repopulation**. Thalidomide effects were not fully recapitulated by repertaxin or etanercept suggesting an original mechanism of action.



Viswanathan *et al.* 2016

HEPATOCELLULAR ADENOMA (HCA)

Post-menopausal follow-up

Hepatocellular adenoma (HCA) is a rare benign liver tumor which develops in women in their reproductive phase and is associated with the use of oral contraceptives. It is uncertain whether or not follow-up should be terminated after the occurrence of menopause in women with HCA. Klompenhouwer *et al.* addressed this question in a cross-sectional cohort study in 48 post-menopausal women with HCA. They show important data: first, HCA-diameter becomes significantly smaller after the occurrence of menopause and as time progresses, this regression increases. **This suggests that routine follow-up of HCA <5 cm in post-menopausal women is not required**. Second, they found that patients' mental health-related quality of life was inferior to that of the general population.

HEPATOCELLULAR CARCINOMA (HCC)

Effectiveness of surveillance for HCC

From the Editor's desk

Little is known on the effectiveness of surveillance for HCC in reducing cancer-related mortality among patients with cirrhosis. Mittal *et al.* conducted a retrospective cohort study of patients with HCC during 2005–2010 by reviewing patients' medical records to determine receipt of HCC surveillance in the 2 years prior to HCC diagnosis. They now provide important results showing that **among patients with HCC, pre diagnosis HCC surveillance is associated with a significant 38% reduction in overall mortality**. The reduction in mortality risk with surveillance is mediated via stage migration and receipt of HCC specific treatment.

NON-ALCOHOLIC STEATOHEPATITIS (NAFLD)

BCL3 mediates inflammation in NASH, autophagy-related gene *IRGM* variations and risk for NAFLD, mechanisms of malnutrition-associated liver steatosis

The B-cell chronic lymphocytic leukemia/lymphoma 3 (*BCL3*) gene product regulates NFκB; a key inducer of inflammation. In this issue, Gehrke *et al.* investigated the role of this gene in experimental and human NAFLD. Hepatocyte-specific **overexpression of *Bcl3* led to hepatic steatosis, augmented inflammatory milieu and hepatocellular injury**. Moreover, Bcl-3 expression decreased insulin sensitivity. The authors identified the transcription factors PPARα, PPARγ and PGC-1α as critical regulators of hepatic metabolism and inflammation downstream of Bcl3. Remarkably, these findings were **recapitulated in human NASH**, which exhibited **increased expression and nuclear localization of BCL3**. This study reveals a role for *BCL3* as a novel regulator of steatosis, insulin sensitivity and inflammation in NASH.

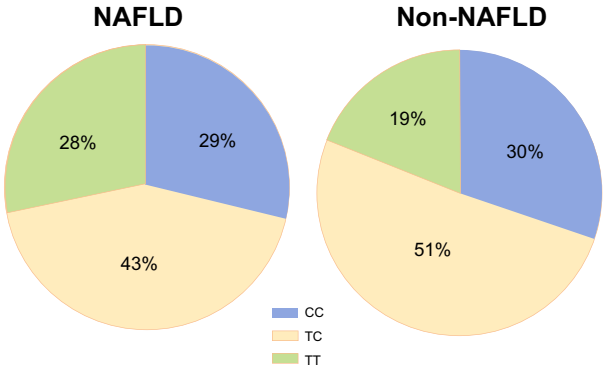
Autophagy regulates lipid stores in hepatocytes. Lin *et al.* studied whether the gene called immunity-related GTPase family M (*IRGM*) – an autophagy-related gene – variants confer the susceptibility to NAFLD. A total of 832 obese children and adolescents were recruited and NAFLD was determined by liver ultrasonography. Twenty-three percent of the obese children and adolescents had NAFLD. After controlling for age- and gender-adjusted body mass index, gender, *PNPLA3* and *TM6SF2* polymorphisms, a **variant in *IRGM* rs10065172 ([TT] genotype) independently increased the odds ratio of NAFLD by 2**. *In vitro* studies revealed that IRGM regulates autophagic flux and lipid droplet content in hepatocytes. This interesting study suggests that IRGM may contribute to the development of human NAFLD by altering hepatic lipid metabolism through the autophagy pathway.

Severe malnutrition is associated with steatosis and hypoalbuminemia, but its etiology is largely unknown. Van Zutphen *et al.* investigates the role of peroxisomes and mitochondria in a rat model of malnutrition. Low protein diet-fed rats developed hypoalbuminemia and hepatic steatosis, associated with **peroxisomal dysfunction**. This was followed by **structural and functional changes in mitochondria** and reduced hepatic ATP levels. Interestingly, **fenofibrate restored** hepatic peroxisome abundance and increased mitochondrial β-oxidation, resulting in **reduced steatosis and normalization of ATP and plasma albumin levels**. This study shows novel mechanisms of malnutrition-induced liver dysfunction and proposes a protective effect by fibrates.

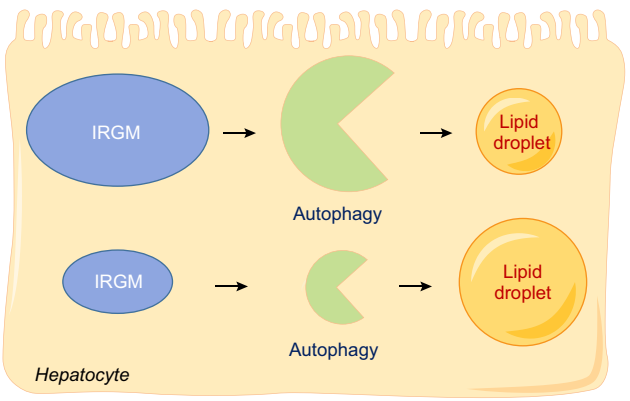
HEPATITIS C VIRUS (HCV) INFECTION

The global HCV genotype distribution in people who inject drugs (PWID), at the EDGE – Head-2-Head comparison of IFNα-free with IFNα-containing DAA regimens, decline in hepatocellular carcinoma trends among Australian people with HBV but not with HCV infection

PWID are a high risk population for transmitting HCV, contribute significantly to the current spreading of the virus, and are most likely to influence the future global burden of the HCV epidemiology. So far, no systematic review exists on the HCV genotype distribution in PWID. The knowledge thereof, however, is relevant as HCV genotype still determines treatment response, disease progression and vaccine development strategies. The study by Robaeys *et al.* is the first to investigate the distribution of the HCV genotypes in PWID globally, and compares the results with the distribution of HCV genotypes in the general population (see Gower *et. al.*, J Hepatol 2014; 61 (Supplementary material): S45-57). **The**



Distribution of *IRGM* rs10065172 genotypes in subjects with and without NAFLD. $p = 0.007$



Lin *et al.* 2016