Highlights from this issue

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LUMINAL

British society of gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus

Gut is very pleased to publish the first set of BSG guidelines prepared along the rigorous protocol of the National Institute for Heath and Care Excellence (NICE). This landmark document by Fitzgerald and her colleagues from the British Society of Gastroenterology provides a practical and evidence-based resource for the management of patients with Barrett's oesophagus and related early neoplasia. It is aimed at gastroenterologists, physicians and nurse practitioners, as well as members of multidisciplinary teams (surgeons, radiologists, pathologists), who take decisions on the management of such patients. The population covered by these guidelines includes: patients with gastro-oesophageal reflux disease or other risk factors for Barrett's (obesity, family history for Barrett's and oesophageal adenocarcinoma (OAC)); every patient with incident or prevalent Barrett's oesophagus regardless of their age, sex or comorbidities; patients with early OAC and patients with intestinal metaplasia at the gastro-oesophageal junction with no endoscopic evidence of Barrett's oesophagus. This valuable document will become the reference point for clinicians and researchers in this field and is essential reading for all. See also the podcast on the website.

Genome Wide Association Studies (GWAS) in IBD, Pancreatic cancer survival and tumour biomarkers

GWAS is a powerful tool for identifying important genetic contributions to disease risk. In this issue of *Gut*, we publish *three* important GWAS studies covering IBD from Korea, pancreatic cancer survival, and tumour biomarkers (see separate digest). Yang *et al* (***see page 80***) performed a GWAS and two validation studies in the Korean population comprising a total of 2311 patients with Crohn's Disease (CD) and 2442 controls. Three novel risk loci including *ATG16L2* were discovered of which two loci showed consistent patterns of association in the International Inflammatory Bowel Disease Genetics Consortium dataset. Twenty-one of the previously reported 140 CD risk loci showed consistent associations in the Korean population, in which four loci were validated at a genome-wide significant level. The data suggest that the risk loci for CD are partly shared between Caucasians and Asians, and that distinct therapeutic targets might be considered depending on ethnic groups. The genetic risk of *ATG16L2* for CD needs to be validated in other populations. Wu *et al* (***see page 152***) analysed overall survival in pancreatic adenocarcinoma in relation to single nucleotide polymorphisms among 1005 patients from two large GWAS datasets, PanScan I (European and US populations) and ChinaPC. They show that germline genetic variation in the *SBF2* locus was associated with overall survival in patients with pancreatic adenocarcinoma of European and Asian ancestry. These results implicate altered membrane trafficking of 3-phosphoinositides in pancreatic cancer growth and progression. The third GWAS by He *et al* is summarised below.

The effect of genetic variants, tumour related proteins, and the risk of cancer

There are a variety of tumour markers, including CA 19-9, CEA and AFP, which are commonly used to monitor the clinical course of individuals diagnosed with gastrointestinal cancer. However, they have been of limited value with regards to predicting the risk of cancer or for screening. He *et al* (***see page 143***) have now conducted a study to extend the clinical use of these markers by assessing genetic variants that associate with the expression of these markers and the risk oesophageal squamous-cell (ESCC), pancreatic, and hepatocellular cancers. They carried out a genome-wide association study and correlated these results with plasma CA19-9, CEA, and AFP levels in 3451 healthy Han Chinese. They also validated the results in 10 326 individuals as well as in independent case-control cohorts. They have found significant associations of several loci with CA19-9, CEA, and AFP concentrations. They also found ABO variants were associated with the risk for ESCC and pancreatic cancers and AFP variants with the risk for hepatocellular cancer. These results suggest that these traditional tumour markers may have a role in predicting risk for cancer in individuals with these genetic variants, providing another example of the future of personalised medicine.

HEPATOLOGY

Novel targets for the treatment of non-alcoholic fatty liver disease (NAFLD)

YY1 is a multifunctional zinc-finger transcription factor. This interesting study from Shanghai (***see page 170***) describes a novel role of YY1 for hepatic triglyceride metabolism in obesity. Hepatic YY1 was overexpressed in obese mice whereas ablation reduced hepatic triglycerides (figure 1A,C).

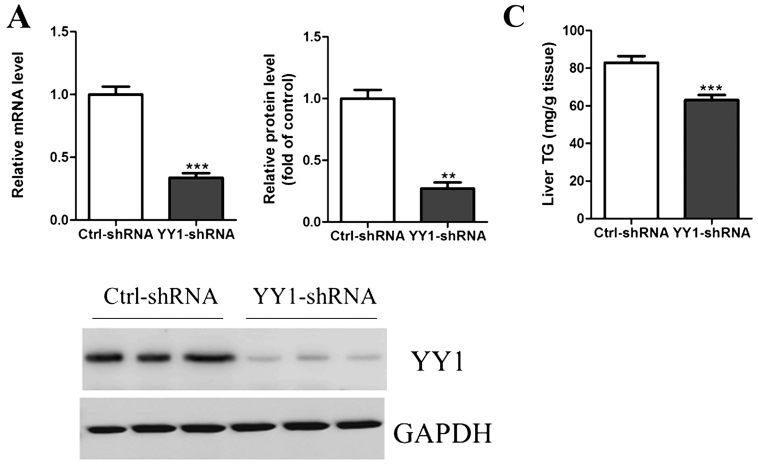

Figure 1 Reduction of hepatic YY1 expression (A) significantly reduces triglyceride content of the liver (C).

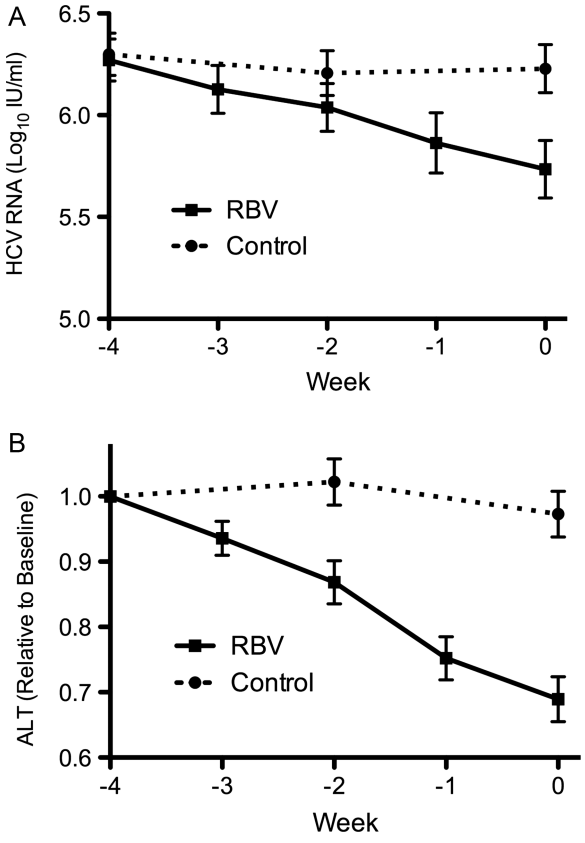

Figure 2 Effect of ribavirin (RBV) monotherapy for 4 weeks on serum levels of hepatitis C virus (HCV)-RNA (A) and ALT activity (B). Solid line—RBV treatment. Dotted line—untreated controls. Mean±SE.

Interestingly, YY1 suppressed the nuclear FXR receptor. Just recently it has been shown that FXR stimulation by obeticholic acid improves fatty livers of patients with diabetes mellitus and reduces their body weight. Therefore the current study supports therapeutic interventions targeting the YY1—FXR axis for the treatment of NAFLD. Please also read the commentary on ***page 1***.

How does ribavirin work in patients with chronic HCV?

Ribavirin (RBV) in combination with interferon has been the standard treatment for HCV and shall be a component of most future interferon-free regimens. Various modes of action have been proposed. This elegant study from the NIH (***see page 161***) shows that the marked ALT reduction (figure 2B), but not the modest antiviral effect of RBV monotherapy (figure 2A), predict the response to subsequent combination therapy with interferon. This introduces the intriguing concept that improvement of hepatic inflammation by RBV enhances the effects of immunomodulatory drugs. Please read the insightful commentary on ***page 3***.