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IN BRIEF

LIVER

Linking abnormal bile acid homeostasis and endocrine component of intrahepatic cholestasis of pregnancy

Abu-Hayyeh *et al.* have shown that levels of epiallopregnanolone sulphate—a sulphated progesterone metabolite—are above normal in patients with intrahepatic cholestasis of pregnancy. At these levels, epiallopregnanolone sulphate acted as a partial agonist for the farnesoid X receptor (FXR), mediating expression of bile acid homeostasis genes. Bile acid mediated recruitment of co-factor motifs to the FXR ligand binding domain was competitively inhibited by epiallopregnanolone sulphate.

Original article Abu-Hayyeh, S. *et al*. Intrahepatic cholestasis of pregnancy levels of sulfated progesterone metabolites inhibit FXR resulting in a pro-cholestatic phenotype. *Hepatology* doi:10.1002/hep.26055

BARRETT OESOPHAGUS

Genome-wide association study uncovers contributors to genetic susceptibility to Barrett oesophagus

Variants at two loci are associated with risk of Barrett oesophagus, as shown by a genome-wide association study (1,852 cases and 5,172 controls, with replication in 5,986 cases and 12,825 controls). 6p21 is within the MHC locus; *FOXF1*, the nearest protein-coding gene to 16q24, is thought to have a role in oesophageal development and structure. The authors also say that SNP alleles predisposing to obesity increase the risk of Barrett oesophagus.

Original article The Esophageal Adenocarcinoma Genetics Consortium *et al*. Common variants at the MHC locus and at chromosome 16q24.1 predispose to Barrett's esophagus. *Nat. Genet.* doi:10.1038/ng.2408

OESOPHAGEAL CANCER

Genetic contribution to risk of oesophageal squamous cell carcinoma and interaction with alcohol use confirmed

Wu *et al.* identified nine new oesophageal squamous cell carcinoma susceptibility loci in their genome-wide association study (2,031 cases and 2,044 controls, with validation in 8,092 cases and 8,620 controls). Seven loci had a significant but marginal effect; risk associated with variants at the 4q23 locus also had a significant interaction with alcohol use. Two loci (at 2q22 and 13q33) had a significant association only in a gene–alcohol drinking interaction.

Original article Wu, C. *et al.* Genome-wide association analyses of esophageal squamous cell carcinoma in Chinese identify multiple susceptibility loci and gene–environment interactions. *Nat. Genet.* doi:10.1038/ng.2411

LIVER

Essential role for IL-1 receptor in the pathogenesis of alcoholic liver disease via inflammasome activation

Inhibition of type I IL-1 receptor (IL-1R1) could have potential as a treatment for alcoholic liver disease, according to the findings of Petrasek *et al*. Their work in mice has shown that the development of liver steatosis, inflammation and injury induced by alcohol requires proinflammatory cytokine IL-1β and signalling by IL-1R1 to be upregulated via caspase 1, a component of the inflammasome. *In vivo*, a recombinant IL-1R antagonist blocked IL-1 signalling and ameliorated alcohol-induced liver steatosis, inflammation and injury.

Original article Petrasek J. *et al.* IL-1 receptor antagonist ameliorates inflammasome-dependent alcoholic steatohepatitis in mice. *J. Clin. Invest.* doi:10.1172/JCI60777