Gastroenterology and Hepatology From Bed to Bench.

SHORT CUT

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Andersen V, Halfvarson J, Vogel U. ***Colorectal cancer in patients with inflammatory bowel disease: can we predict risk?*** *World J Gastroenterol 2012;18:4091-94.*

This article reviewed recent studies investigating the risk of developing inflammatory bowel disease (IBD)-associated CRC, a major potential complication of IBD. In patients with ulcerative colitis (UC) the risk of CRC increases with a younger age of diagnosis (age 0-19 years), longerdisease duration and concomitant primary sclerosing cholangitis. Of note, an underlying genetic predisposition in IBD-associated CRC remains unestablished. Contrary to previous studies, a new population-based cohort study observing 47,347 Danish patients with IBD over 30 years found that CRC risk in patients with crohn's disease was similar to the non-IBD population.
Current understanding of the pathophysiology of IBD-associated CRC, predominantly investigated in the mouse model, was explored. Inflammatory mediators driving IBD, including tumour necrosis factor-α and toll-like receptors, may induce the transcription of genes involved in tumorigenesis through activation of nuclear factor κβ. Co-existing dysfunctional p53 signalling may lead to defective apoptosis of these dysplastic cells and progression to CRC. The authors suggest that future research should aim to develop a model topredict the patient-specific risk of developing IBD-associated CRC. This would aid decision makingand assist the targeting of preventative strategies.

Mann KM et al. ***Sleeping beauty mutagenesis reveals cooperating mutations and pathways in pancreatic adenocarcinoma.*** *PNAS;109:5934-41.*

Pancreatic cancer, often diagnosed at an advanced stage once metastasised, has a devastating mortality rate. Identification of molecular cancer drivers are important to better understand disease pathogenesis and aid the development of diagnostic and therapeutic modalities. This study, an insertional mutagenesis screen conducted in mice using the inducible sleeping beauty (SB) transposon system in combination with an oncogenic Kras pancreatic cancer model, identified new candidate cancer genes (CCGs) responsible for driving pancreatic adenocarcinoma. Overall, 681 statistically significant common insertion sites including 543CCGs were identified of which 75 CCGs have known mutations in human pancreatic cancer. Point mutations in human pancreatic patient samples were identified for a further 11 CCGs. CCGs involved in chromatin remodelling and poor patient survival were uncovered. This study highlighted a large number of mutations that may drive the development of pancreatic adenocarcinoma. The significant overlap between this SB-driven mouse model and data from human pancreatic adenocarcinoma may help to inform on going genetic sequencing studies in human pancreatic cancer.

Saffar MJ et al. ***Age-specific seroprevalence of anti-hepatitis A antibody among 1-30 years old population of Savadkuh, Mazandaran, Iran with literature review.*** *Hepat Mon 2012;12(5)326-332*

The current region-specific health burden of hepatitis A virus (HAV) infection, an important cause of acute hepatitis in Iran, requires characterisation so that health resources can be better allocated. This cross-sectional study investigated the age-specific seroprevalence of anti-HAV antibody in 984 randomly sampled individuals aged 1- to 30-years old in Savadkuh, Mazandaran province, Iran. The mean anti-HAV antibody seroprevalence rate increased from 5.7% to 34.8% and 68.4% in age groups 1-2.9, 11-17.9 and 18-30 years respectively ($p<0.0001$). The overall anti-HAV antibody seroprevalence rate was 19.2%. Seroprevalence rates were not significantly influenced by place of residence, educational level, water supply and waste water/sewage disposal systems. Compared with

previous similar studies, the results suggest an epidemiological shift towards lower rates of anti-HAV antibody prevalence that may reflect improvements in several socioeconomic factors including sanitation, access to clean drinking water and health education. The authors recommend periodic nationwide seroprevalence studies to determine the ongoing burden of HAV infection and guide preventative strategies including immunisation.

Emami MH et al. ***Frequency of celiac disease in adult patients with typical or atypical malabsorption symptoms in Isfahan, Iran.*** *Gastroenterol Res Pract 2012;2012:106965:1-6*

The prompt diagnosis of celiac disease (CD) and introduction of a gluten-free diet is important to minimise the risk of associated malignancy and mortality. This interesting prospective study evaluated 151 and 173 adult patients with typical or atypical symptoms of CD respectively, referred to two outpatient clinics in Isfahan, Iran between 2004 and 2005. All patients with typical symptoms of CD (chronic diarrhoea, steatorrhoea and weight loss) underwent immunoglobulin (Ig)A anti-tissue transglutaminase (tTG) testing(8.6% positive) and were offered upper gastrointestinal endoscopy (completed in45%). Patients with atypical symptoms (unexplained abdominal pain, excessive gas passing, malodouress stool or gas, constipation, intermittent diarrhoea, bloating and unexplained nausea or vomiting) were offered upper gastrointestinal endoscopy (completed in 39%) in cases of IgA anti-tTG positivity (2.8%), IgA deficiency (4.6%) and where symptoms were prolonged and unexplained (97.1%).In patients with typical and atypical symptoms of CD respectively, the prevalence of CD, determined by positive serology with confirmatory pathology, was 5.9% and 1.25% however when seronegative patients were considered in addition, the overall CD prevalence was estimated as at least 9.2% and 4.0%. The authors recommend that patients with typical symptoms of malabsorption should undergo endoscopic biopsy irrespective of serology however serology should guide biopsy in patients with atypical symptoms. Routine duodenal biopsy is recommended when endoscopy is indicated based on symptoms.

Rafiei A et al. ***Inducible nitric oxide synthetase genotype and Helicobacter pylori infection affect gastric cancer risk.*** *World J Gastroenterol 2012 September 21;18(35):4917-4924*

Although gastric cancer (GC) is a major cause of cancer-related morbidity and mortality, the impact of genotype on GC risk is poorly understood, particularly in patients from Iran. This case-control study investigated the association of the inducible nitric oxide synthetase (iNOS) C150T polymorphism with *Helicobacter pylori (H. pylori)* infection and GC in 329 individuals (159 with endoscopically diagnosed GC, 170 controls) in Iran between April 2008 and March 2011. The study found that smoking, hot beverage consumption, a familial history of GC and *H. pylori* infection significantly increased the risk of GC ($p=0.015$, $p<0.001$, $p=0.0034$ and $p<0.015$ respectively). Carrying either a heterozygous allele or a homozygous allele at position 150 of exon 16 of the iNOS gene combined with *H. pylori* infection resulted in a significantly increased risk of developing GC (OR=2.1, $p=0.03$ and OR=5.0, $p=0.029$ respectively). The iNOS gene was not independently associated with development of GC. The authors postulate that in patients with iNOS allele expression and *H. pylori* infection, pathological and carcinogenic events may be perpetuated by increased levels of nitric oxide. By helping to stratify patients at high risk of developing GC, these findings may aid in screening and treatment targeting.

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