Highlights from this issue

doi:10.1136/gutjnl-2012-302547

Emad El-Omar, William Grady and Alexander Gerbes, *Editor and Deputy Editors*

The Gut supplement on viral hepatitis

This month Gut offers its readers an exciting bonus! We are delighted to welcome our guest editors Professor David Thomas (USA), Masashi Mizokami (Japan) and Fabien Zoulim (France) who have put together an outstanding supplement on viral hepatitis. They have invited the world's leading authorities on viral hepatitis to summarise state-of-the-art knowledge on the pathogenesis and management of this disease. The authoritative reviews offer a unique insight into a disease that affects millions of patients worldwide and offer a window on future developments in the field.

Luminal GI

Maastricht Guidelines IV for *Helicobacter pylori* infection

Ever since *H pylori* was discovered and transformed our clinical practice, there has been a huge demand for guidance on how to manage this infection and its associated clinical sequelae. The European Helicobacter Study Group has been at the forefront of generating the necessary guidance. Through the so called Maastricht Consensus Reports of which there have been three since 1997, the best available evidence base has been presented and followed by large sections of our clinical community. In this issue of Gut, we are delighted to publish the latest consensus report on the subject. The report is titled Maastricht IV/Florence Consensus Report, to reflect the historical background of the original set (Maastricht) and the latest venue for the consensus meeting (Florence). The report presents a comprehensive assessment of all relevant questions relating to *H pylori* and is a valuable resource for clinicians and scientists alike ***(see page 646)***.

Biological therapy for IBD in developing countries

The incidence of IBD is rising in developing countries with an anticipated increase in complicated disease that would benefit from biological therapy. The problem of the limited availability of anti-TNF in developing countries has never been discussed in detail. If, as anticipated, the need for biological therapy rises in the developing world, then all relevant players including pharmaceutical industry, healthcare providers, patient advocate groups, governments and non-governmental organisations will have to discuss how to handle this. In this issue of Gut, Rogler *et al* present an international vision of how this could be achieved. They propose that this dialogue should begin now with regard to (1) the major needs of patients with complicated IBD in developing countries, (2) the potential need for biological therapy in developing countries to treat IBD, (3) the necessary infrastructure for selecting patients with IBD who need biological therapy, and (4) medical/ethical issues limiting the use of biological therapy. Our journal encourages and welcomes this essential dialogue and looks forward to aiding the implementation of its outcomes ***(see page 706)***.

A new generation of early detection biomarker assays for colon cancer and polyps

MicroRNA's are small RNA molecules (usually around 20 nucleotides long) that play an important role in regulating the expression of genes in cells. Many microRNA's (miRNA's) are over- or under-expressed in cancers, including colon cancer. The over-expressed miRNA's have the potential to be used as screening biomarkers for colorectal cancer. Sung and colleagues have assessed the feasibility of using two miRNA's that are over-expressed in colonic neoplasia, miR-21 and miR-92a, as stool-based early detection markers for colon polyps and cancer. They collected stool samples from 88 patients with colorectal cancer, 57 patients with colorectal polyps, and 101 healthy controls. They found that patients with CRC had significantly higher stool miR-21 level ($p<0.01$) and miR-92a level ($p<0.0001$) compared to normal controls. Stool miR-92a, but not miR-21, was significantly higher in patients with polyps than in controls ($p<0.0001$). At a cut-off value of 435 copies/ng of stool RNA, miR-92a had a sensitivity of 71.6% and 56.1% for cancer and polyps, respectively, and a specificity of 73.3% (see figure 1). These results suggest miRNA's have the potential to be an effective molecular version of the guaiac test ***(see page 739)***.

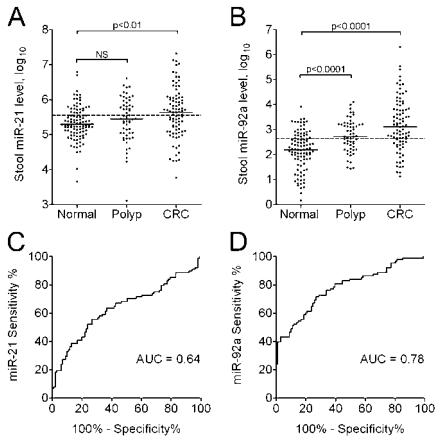

Figure 1 Comparison on levels of (a) miR-21 and (b) miR-92a in stool samples from CRC patients, polyp patients and normal controls. miRNA level is expressed in number of copies per ng of extracted RNA. The lines denote the medians. The dotted lines on the y-axis denote cut-off values. Receiver operating characteristics (ROC) curves based on using (c) miR-21 and (d) miR-92a were plotted to discriminate normal and CRC patients. miR-21 and miR-92a yield an area under the curve (AUC) value of 0.64 and 0.78 respectively.

New insights into the behaviour of colon cancer—new therapies?

Deregulation of the Wnt signalling pathway is central to colon cancer formation. The orphan nuclear receptor TR3 plays an important role in proliferation and apoptosis. Chen and colleagues have made a novel connection between TR3 and Wnt signalling. Using state-of-the-art mouse models, they have found that TR3 can suppress the formation of intestinal tumours by regulating Wnt signalling. They found that TR3 inhibited Wnt signalling through a variety of mechanisms that ultimately suppressed the cancer causing genes that are induced by the Wnt pathway in colon cancer. They also found that TR3 was phosphorylated in most primary human colorectal cancers, which attenuated the inhibitory activity of TR3 towards Wnt signalling. Most importantly, they showed that an agonist for TR3, Csn-B, can inhibit tumour formation in the

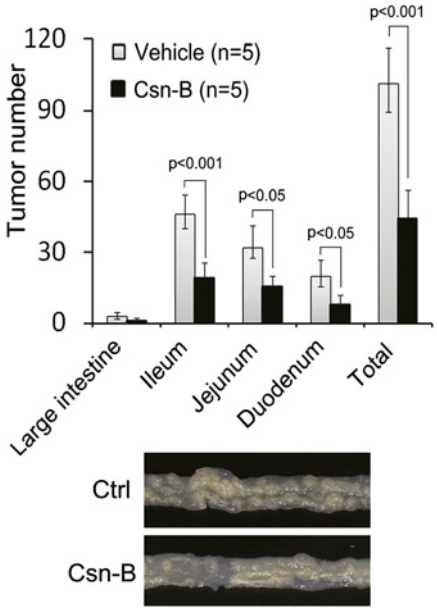

Figure 2 Csn-B inhibits intestinal tumorigenesis in *Apc*$^{min/+}$ mice. Four-week-old *Apc*$^{min/+}$ mice were intragastrically administered Csn-B (10 μg/g body weight) every other day for 12 weeks. The frequency of tumour formation in their intestine was then determined. Representative images of jejunal tissues are also shown.

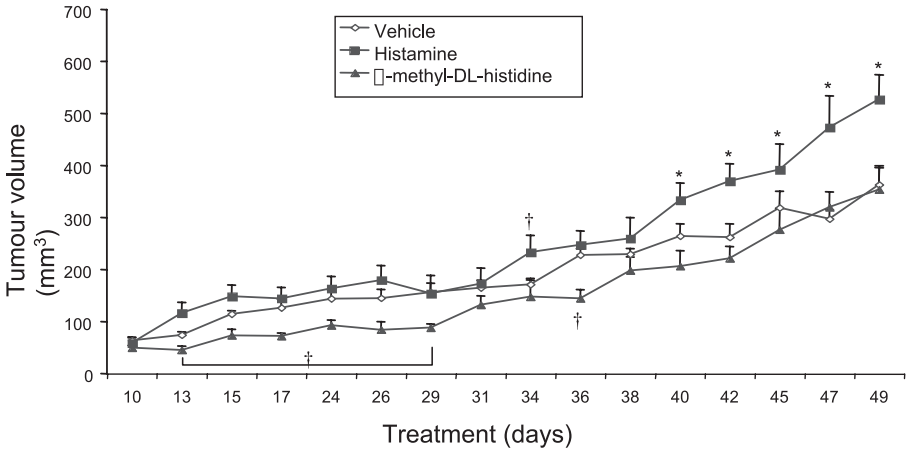

Figure 3 Histamine increases whereas the HDC inhibitor significantly decreases tumour volume compared to vehicle.

intestines. This new insight into the molecular mechanisms that cause colorectal cancer has provided the potential for new therapeutic approaches for this common form of cancer ***(see page 714)***.

Hepatology

A novel pharmacological approach for the treatment of cholangiocellular carcinoma (CCC)

Histamine promotes progression of various tumours. This exciting study from the group of Gianfranco Alpini elucidates the role of histamine in CCC, a biliary cancer with very poor treatment options. The authors demonstrate that CCC cells express higher levels of histidine decarboxylase and secrete greater amounts of histamine. Moreover, pharmacological and molecular down regulation of histidine decarboxylase in mouse models reduces CCC growth (figure 3). These findings have great translational potential. Targeting the histamine autocrine loop may be an exciting new option to address the challenge of CCC treatment. ***(see page 753)***.

Acute viral hepatitis B in Japan—new insights

HBV is sexually transmitted, a fact unfortunately unknown to many. This interesting prospective cohort study from Japan suggests sexual transmission of HBV genotype A spreading from Tokyo to other parts of Japan. Selective vaccination of babies of HBV carrying mothers starting in 1986 has markedly decreased HBsAg prevalence in young Japanese. However, acute viral hepatitis B has not decreased mainly due to an increase of infections with genotype A. Genotype A infections started to increase in the capital region and have been spreading towards other regions over time. Among this group the authors found a high proportion of males, homosexuals and HIV positive subjects, respectively. HBV persisted only in genotype A patients. This study supports the need for universal vaccination of babies regardless of the HBsAg status of the mother—a strategy introduced by several countries several years ago ***(see page 765)***.