

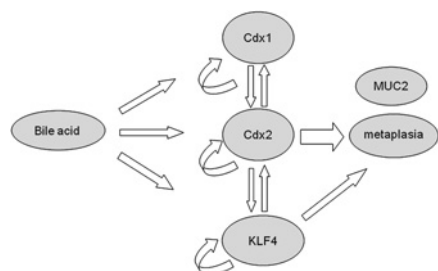
# Highlights from this issue

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## New insights into the factors that cause Barrett's oesophagus

The mechanisms responsible for the transformation of the normal oesophageal squamous epithelium into the metaplastic intestinal epithelium that characterises Barrett's oesophagus are poorly understood, but are essential to know in order to develop better ways for preventing Barrett's oesophagus. Prior work by the authors of this study and by others has shown that a transcription factor called CDX2 is one of the mechanisms involved in the formation of Barrett's oesophagus. Kazumori and colleagues now show that Kruppel-Like Factor 4 (KLF4), a key protein that regulates the differentiation of the epithelium of the gastrointestinal tract, is a second transcription factor strongly expressed in Barrett's epithelium that is induced by bile acids. Importantly, they have shown that KLF4 and CDX2 cooperate to induce each other's expression and that KLF4 induces the expression of the mucin protein MUC2, which is involved in intestinal metaplasia. Moreover, they also show that the inflammation related signalling pathway, NF- $\kappa$ B, is also involved in this process. This study advances our understanding of the transcriptional network related to KLF4 and CDX2 that affects the development of Barrett's oesophagus. KLF4 and CDX2 are possible molecular targets for the prevention of Barrett's oesophagus, and therapies directed at these proteins may yield a much-needed medical treatment for Barrett's oesophagus (*see page 608*).



Model of how KLF4 and the CDX2 transcription factors regulate Barrett's oesophagus.

## British society of gastroenterology guidelines on inflammatory bowel disease

This issue proudly presents the long awaited BSG guidelines on IBD. The authors are keen to maintain an interactive dialogue with readers and users of the guidelines and have imbedded links to a discussion forum within the new guidelines. We invite readers to utilise this interesting facility and this will provide an evolving and thorough peer review of the guidelines (*see page 571*).

## Dysbiosis in Crohn's patients and their relatives

A general dysbiosis of the intestinal microbiota has been described in Crohn's disease (CD) patients but the characterisation of this has remained superficial. There is also no data about the microbiota in relatives of

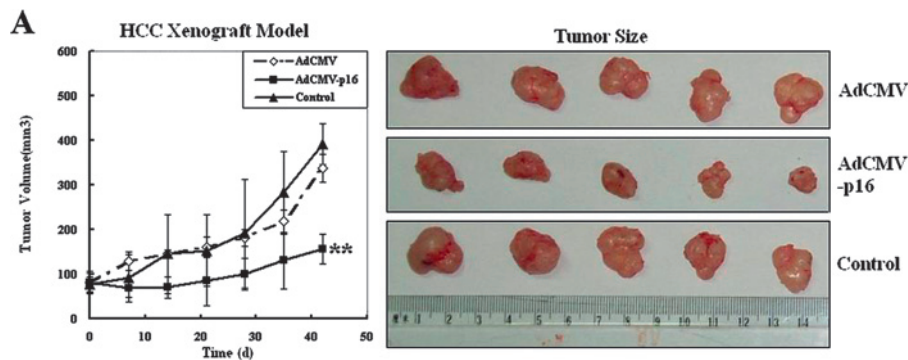
affected subjects. In this issue of *Gut*, Joossens *et al* provide some new insight. Focusing on families with at least three members affected with CD, faecal samples of 68 patients with CD, 84 of their unaffected relatives and 55 matched controls were subjected to community fingerprinting of the predominant microbiota using denaturing gradient gel electrophoresis (DGGE). They were able to describe a dysbiosis signature associated with CD, characterised by five bacterial species, namely *Dialister invisus*, an uncharacterised species of *Clostridium* cluster XIVa, *Faecalibacterium prausnitzii*, *Bifidobacterium adolescentis* and *Ruminococcus gnavus*. This dysbiosis signature was markedly characteristic for the disease as it was not observed in unaffected relatives despite a common genetic background and shared nutritional habits. Interestingly, the relatives had their own unique signature which was different from healthy controls. This first detailed

Sensitivity (per-patient) of radiologists in detection of lesions of different types and sizes at computed 632 tomographic colonoscopy 633 (CTC), according to performance at initial training, and subsequent experience

Variable of interest	Lesion group	Sensitivity of radiologists in lower half of distribution		Sensitivity of radiologists in upper half of distribution	
		%	95% CI	%	95% CI
Training performance: % detection of polyps of any size in training set (median was 49%)	Overall	52	44 to 60	58	51 to 65
	Polyps $\geq 6$ mm	62	50 to 74	76	65 to 85
	Polyps $\geq 10$ mm	68	48 to 84	86	71 to 95
	Adenomas $\geq 6$ mm	61*	47 to 74	80*	68 to 89
	Adenomas $\geq 10$ mm	68	47 to 85	87	72 to 96
Training performance: % detection of polyps $\geq 6$ mm in training set (median was 61%)	Overall	51	43 to 59	58	52 to 65
	Polyps $\geq 6$ mm	63	50 to 74	75	64 to 84
	Polyps $\geq 10$ mm	69	49 to 85	85	71 to 94
	Adenomas $\geq 6$ mm	60*	46 to 74	79*	67 to 88
	Adenomas $\geq 10$ mm	68	47 to 85	87	72 to 96
Case volume in the study (median number was 18)	Overall	55	40 to 69	55	50 to 61
	Polyps $\geq 6$ mm	56	31 to 78	71	63 to 79
	Polyps $\geq 10$ mm	50	12 to 88	81	70 to 90
	Adenomas $\geq 6$ mm	55	23 to 83	72	63 to 81
	Adenomas $\geq 10$ mm	25*	1 to 81	83*	71 to 92
Potential number of polyps for detection (median number was 19)	Overall	58	43 to 72	55	49 to 61
	Polyps $\geq 6$ mm	68	47 to 85	70	61 to 78
	Polyps $\geq 10$ mm	56	21 to 86	82	70 to 91
	Adenomas $\geq 6$ mm	70	46 to 88	71	61 to 80
	Adenomas $\geq 10$ mm	57	18 to 90	82	70 to 91

The radiologists were divided into two subgroups, according to the median of the distribution of the variable of interest, and the pooled sensitivity was found for each subgroup.

\* $p < 0.03$  ( $\chi^2$  test and Fisher exact test).



HCC xenograft models were established by subcutaneous injection of  $5.0 \times 10^6$  MHCC cells per mouse in three groups of nude mice ( $n=5/\text{group}$ ).

description of CD-associated dysbiosis will break new ground in unravelling the role of bacteria in CD (*see page 631*).

## A real-life assessment of the performance of CT colonography

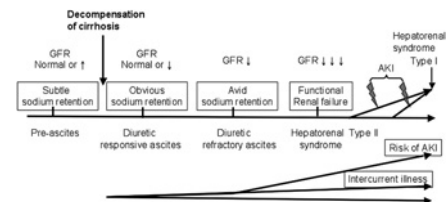
The assessment of the accuracy of computed tomographic colonography (CTC) has mainly come from studies involving expert radiologists at single academic centres. Heresbach *et al* have performed a more real-to-life study of CT colonography by investigating its performance in 26 academic clinical units by 28 radiologists. All the radiologists in this study attended a short training course and worked through a training set of 52 cases before beginning to read the CTC exams. In this study, 845 average or high-risk patients were assessed by both complete CTC and videocolonoscopy. Using videocolonoscopy as the gold standard, the positive and negative predictive values for polyps  $>6$  mm in size was 67% (59–74) and 92% (90–94), respectively. Surprisingly, the detection rate for polyps  $\geq 6$  mm was not linked to radiologist

case volume or to number of polyps, but was related to the sensitivity achieved by the radiologist in the training set. This study highlights the need for pre-certification of radiologists reading CT colonographic studies in order to ensure high quality CT colonography exams (*see page 658*).

## Hepatology

### Treatment of hepatocellular carcinoma (HCC)—yet another success of nanotechnology

Conventional chemotherapy is rather ineffective for the treatment of HCC. This interesting study investigates a novel approach in vitro and in an animal model of HCC. Ceramide is a very hydrophobic sphingolipid with remarkable pro-apoptotic properties. The authors constructed ceramide containing nanoliposomes suitable for intravenous application. Using this innovative tool they achieved a marked reduction of tumour size (*see figure*) and tumour vascularisation, possibly mediated by interference with akt signalling. Future clinical evalu-



Natural history of cirrhosis and acute kidney injury (AKI).

ation of this new therapeutic strategy is to be expected (*see page 710*).

### Renal dysfunction in cirrhosis—a never ending story?

Renal dysfunction is a major complication in patients with cirrhosis of the liver. The most severe forms of functional acute and chronic renal failure in cirrhosis have been defined as hepatorenal syndrome (HRS) type 1 and type 2, respectively (*Gut* 2007;**56**:1310–18). In recent years interest has focused on the functional nature of HRS (*see figure*) and an effective treatment with vasopressors in combination with albumin has been established. However, there is increasing recognition, gained for example by screening patients for HRS, that renal dysfunction in cirrhosis can also be due to organic renal diseases and structural changes of the kidney. As yet there is no classification system as used in nephrology for such patients. An international working group of outstanding nephrologists and hepatologists has now elaborated a classification system for acute kidney injury, chronic kidney disease and acute on chronic kidney disease in cirrhosis. The new classification should stimulate future studies of these subtypes of renal dysfunction and may help to elaborate treatment strategies (*see page 702*).