

Highlights from this issue

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Luminal GI

Bowel cancer screening in England: the first million

In April 2006 the Department of Health in England agreed funding for a national programme of biennial gFOBt screening of 60–69-year-olds. Roll out of the programme started in July 2006 and was complete by January 2010. In this issue of *Gut*, Logan *et al* report the uptake and early outcomes of the first million people screened. Almost 2.1 million were invited to participate, and as expected, women had a higher return of tests than men (54.4% vs 49.6%). Of the 1.08 million returning tests 2.5% of men and 1.5% of women had an abnormal test. Seventeen thousand five hundred and eighteen (10 608 M, 6910 F) underwent investigation, with 98% having a colonoscopy as their first investigation. Cancer (n=1772) and higher risk adenomas (n=6543) were found in 11.6% and 43% of men and 7.8% and 29% of women investigated, respectively. Seventy one percent of cancers were 'early' (10% polyp cancer, 32% Dukes A, 30% Dukes B; see table 1) and 77% were left-sided (29% rectal, 45% sigmoid) with only 14% being right-sided compared with expected figures of 67% and 24% for left and right side from UK cancer registration. These early data are encouraging and suggest that the intended target of 16% reduction in overall bowel cancer mortality is achievable (see page 1439).

The promise of microRNA's as biomarkers for colorectal cancer

MicroRNAs (miRNA) are short (approximately 20 basepairs in length)

Table 1 Duke's stage of bowel cancers detected after first investigation of first million people screened in England

Cancer stage	Males	Females	Total	%		Found in English pilot
Polyp cancer	114	41	155	9.8	71.3%	72%
Dukes A	349	154	503	32.0		
Dukes B	316	148	464	29.5		
Dukes C	272	133	405	25.7	28.7%	28%
Dukes D	37	10	47	3.0		
Total	1088	486	1574			

*In 198 staging data not available.

non-coding RNA's that affect the expression of genes. They have considerable potential as prognostic biomarkers and therapeutic targets in cancer, but that potential still remains to be realised. Yanlei and colleagues have profiled the miRNAs in human colorectal cancers and found that miR-150 is a promising tissue-based predictive and prognostic marker (see figure 1). They carried out a series of carefully done studies that validated their results. This study opens the possibility that miR-150 will be a molecular marker that will enhance our ability to precisely treat patients with colorectal cancer (see page 1447).

Identifying driver genes in colorectal cancer

Colorectal cancer arises as the consequence of mutations in colon epithelial cells that deregulate signalling pathways in these cells. One of the most common signalling pathways that is activated in colorectal cancer is the Wnt signalling pathway. This pathway induces the expression of a variety of genes that appear to be important promoters of tumour cell growth,

including *CYCLIND1*, *CMYC*, *CDK4*, etc. Expression of one of these genes, *ASCL2*, is present in almost 80% of colorectal tumours suggesting it helps drive tumour formation in the colon. Reed *et al* have now created a sophisticated mouse model to demonstrate that *Ascl2* is not of likely importance in mediating the effects of increased Wnt signalling, which provides valuable information regarding the search for 'druggable' targets for novel therapies for colorectal cancer (see figure 2). Studies such as these are critical for sorting out the relevant effects of gene mutations on the biology of cancers (see page 1435).

Hepatology

Does the role of insulin resistance change in HCV genotype 1 patients?

Insulin resistance is a negative predictive factor for sustained viral response (SVR) to treatment with interferon and ribavirin in patients with chronic hepatitis C virus infection. Direct antiviral agents may improve insulin sensitivity together with a decrease of viral load as recently reported in this journal (Moucarri R, *et al*. *Gut*

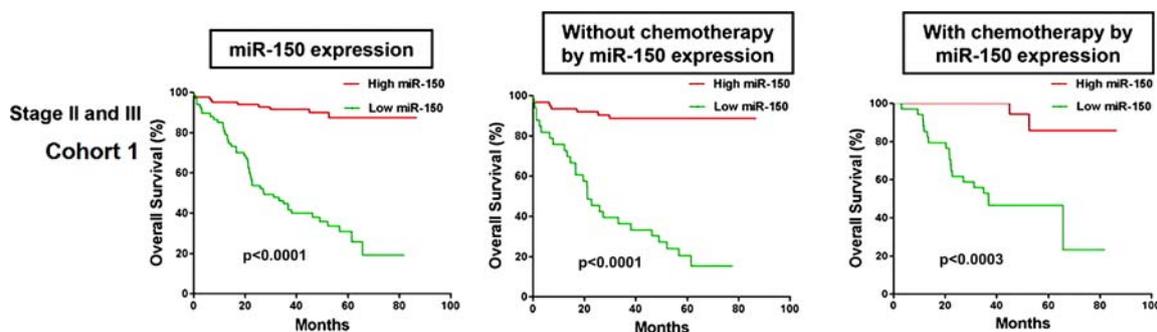


Figure 1 Association of miR-150 expression levels with chemotherapy outcome in the CRC patients with TNM stage II or III in the cohort 1 and cohort 2. A. For the 195 CRC patients with stage II or III, low miR-150 expression was associated with poor survival for those who received chemotherapy in the cohort 1.

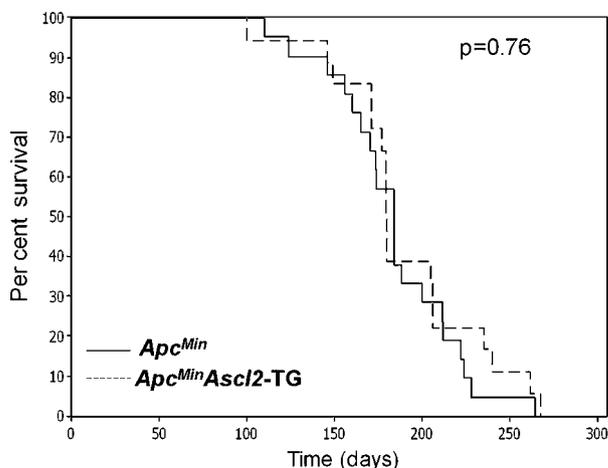


Figure 2 *Ascl2-TG* mice were interbred with *Apc^{Min}* mice to generate the required *Apc^{Min}* and *Apc^{Min}Ascl2-TG* cohorts. (A) Kaplan-Meier survival curve of aged cohorts of *Apc^{Min}* (n=21) and *Apc^{Min}Ascl2-TG* (n=18) mice, demonstrating that no significant differences in survival of the two cohorts.

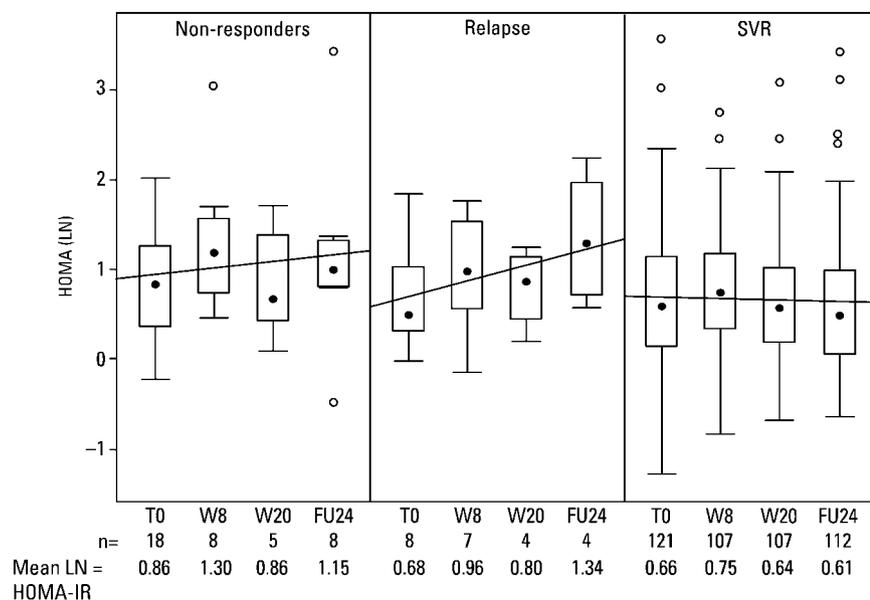


Figure 3 Association between log HOMA-IR and virological response during telaprevir-based treatment. HOMA-IR, homoeostatic model assessment-insulin resistance; LN, natural logarithm; SVR, sustained virological response; T0, baseline; W, week; FU24, follow-up week 24.

Table 2 Diagnostic accuracy for detection of hepatocellular carcinoma using one, two or three of the markers under study

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-
One marker						
GPC3	57.5	95.0	95.8	52.8	11.500	0.447
HSP70	57.5	85.0	88.5	50.0	3.833	0.500
GS	50.0	90.0	90.9	47.4	5.000	0.556
Two markers						
GPC3+HSP70	40.0	100	100	45.5	Inf	0.600
GPC3+GS	35.0	100	100	43.5	Inf	0.650
HSP70+GS	35.0	100	100	43.5	Inf	0.650
Three markers						
At least 1 positive	80.0	70.0	84.2	63.6	2.667	0.285
At least 2 positive	60.0	100	100	55.6	Inf	0.400
All 3 positive	25.0	100	100	40.0	Inf	0.750

GPC3, glypican 3; GS, glutamine synthetase; HSP70, heat shock protein 70; Inf, Infinite; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

2010;**59**:1694–8). The interesting paper by Serfaty *et al* (page xxxx) investigates the predictive role of metabolic factors in patients receiving a triple therapy with telaprevir in addition to interferon and ribavirin. This subanalysis of an international phase II trial found that insulin resistance was not a predictor of SVR and moreover, that at 24 weeks follow-up insulin resistance was significantly lower in SVR patients (figure 3). Thus, telaprevir may overcome insulin resistance and an as yet important predictive factor of response seems irrelevant for treatment with triple therapy. These results were obtained in young patients without advanced liver disease and thus need to be confirmed in further trials (see page 1473).

The role of immunohistochemical markers for the diagnosis of small hepatocellular carcinoma

The early diagnosis of hepatocellular carcinoma (HCC) is crucial for the success of treatment and for patient survival. Unfortunately, imaging often fails to detect very small HCC in a cirrhotic liver and therefore biopsy is considered the gold standard for nodules smaller than 2 cm. Histology can be flawed by false negative results. Therefore, some immunohistochemical markers have been proposed to improve the accuracy of histology. Several studies investigated the value of such markers in tissues known to be HCC but prospective analysis as demanded in this journal (Lamerz R. *Gut* 2011;**60**:881–2) has not been performed so far. This important study from Bruix *et al* for the first time prospectively evaluated a panel of three recently proposed immunohistochemical markers of HCC. They found a sensitivity of 60% and a specificity of 100% when at least two markers were positive (table 2). However, since the expert pathologists involved in this study performed extremely well with only 7.5% false negative results the additional value of the marker panel was poor. The conclusion may be that immunohistochemical markers could be valuable particularly for scarce biopsy material, difficult cases and less experienced pathologists (see page 1481).