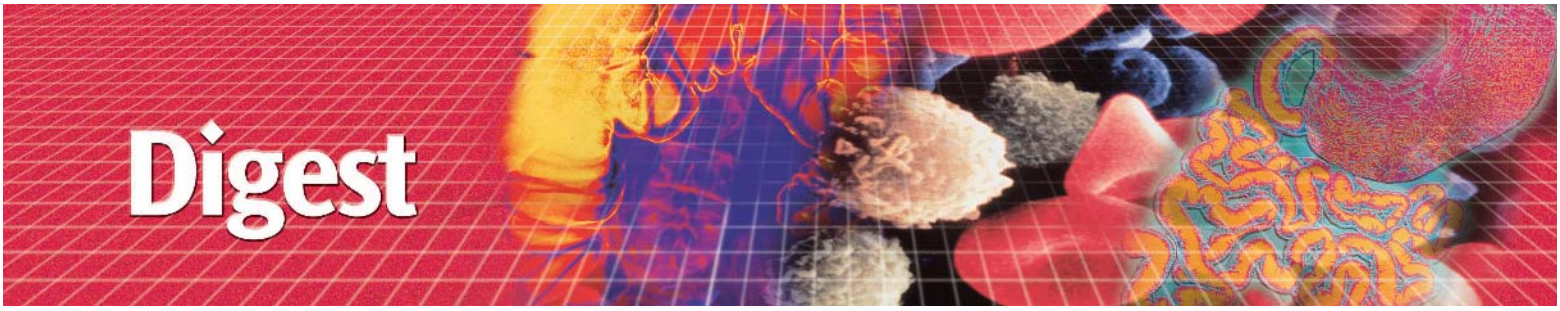

Robin Spiller, *Editor*

Enhancing chemotherapy responsiveness in gastric cancer by gene therapy

The late presentation and frequent chemotherapy resistance of gastric cancer makes this study of great interest. The authors used an elegant gene therapy approach targeting the insulin-like growth factor receptor (IGF-1r). They used an adenovirus vector to insert two types of defective receptors, which interfere with the function of the normal receptor, the so called "dominant negative" IGF receptors. The adenovirus treated cells failed to grow in response to IGF and also showed defective growth and enhanced apoptosis in response to alcohol, 5FU, and irradiation. Not only did the transduced cells fail to grow when implanted in vivo, but the adenovirus treatment also reduce the growth of established peritoneal metastases. This elegant work, which takes us from basic cell biology to cancer chemotherapy, offers new hope for the future treatment of this dreadful disease.

See p 591

Control of the innate immune response to commensal bacteria by adaptive immunity

Evidence from a range of murine models clearly show that chronic inflammation in the gut similar to human inflammatory bowel disease can arise from a dysregulation of the normally finely balanced innate and acquired immune responses to commensal bacteria. The present study examines how acquired immunity downregulates the innate response to gut commensals. The authors examined the effect of bacterial colonisation on two sorts of germ free mice, one (BALB/c) with an intact and the other (SCID) with a defective acquired immunity. They examined the expression of genes induced by colonisation and showed by gene array analysis that just eight genes were significantly (over twofold) upregulated in the SCID but not the BALB/c mice. The greatest effect was on the Reg III (β and γ) gene. This is found in the epithelial cells and is thought to be involved in epithelial repair during intestinal inflammation. Interferon γ, produced by intraepithelial natural killer T cells, was also shown to be significantly and independently increased. The lack of response seen in the intact animals shows how a normal immune response can inhibit the innate immune system. The paper demonstrates that both defective as well as over exuberant immune responses can lead to inflammation.

See p 623

Novel optics show increase local blood supply is an early event in colonic cancer

Angiogenesis and increased local blood flow is a key feature of carcinogenesis and a potential therapeutic target. Although it is known to be an early, preneoplastic event in non-gastrointestinal tumours, until now it has not been possible to say if this is true in colon cancer. The authors have applied a novel technique, 4-D elastic light scattering (4-D ELF) to measure blood flow in the colon of rats and men. A polarised beam of light is scattered by tissue and the various components of the scattered light measured, giving a fingerprint from each tissue dependent on its blood content. Using a rat model of chemically induced colon cancer (azoxymethane) and a mouse model of genetically determined colon cancer (MIN mouse) they show an increase in blood flow which preceded neoplastic changes. They also provide preliminary data showing that mucosal blood content is increased in patients at high risk from developing colorectal cancer. Provided the technology proves robust, increased mucosal blood supply could be an important marker of cancer risk, which might improve the effectiveness of colorectal cancer screening.

See p 654

Patients with occult hepatitis C could be infectious

Sadly, prior to the development of adequate screening tests, many cases of hepatitis C worldwide have been transmitted by well meaning medical staff. Screening and avoiding reuse of needles has substantially reduced this risk but as this paper shows our screening tests are still not perfect. Thus, rarely patients with occult hepatitis C infection can be found who have no evidence of infection as assessed by anti-hepatitis C virus (HCV) antibodies or serum viral RNA, and yet have viral RNA in their liver and circulating peripheral blood mononuclear cells (PBMC). The authors used strand specific RT-PCR to detect positive and negative strands of HCV RNA. This enabled them to show that some patients with occult hepatitis C infection had both positive and negative strands of RNA in PBMCs indicating the presence of replicating virus. These patients' blood could therefore be infectious, a risk which, albeit rare, could easily be missed.

See p 682

Patients over the age of 40 are at increased risk of fulminant hepatic failure after paracetamol overdose

Although previous studies have shown the age >40 years was a risk factor for mortality from non-paracetamol fulminant hepatic failure (FHF) this has not been show before for paracetamol overdoses. This study, which was based in a tertiary referral centre in Copenhagen, examined 1019 patients, 273 local patients, and 746 patients transferred from other hospitals because of clinical deterioration. The risk of liver failure was significantly greater in those >40 years with a relative risk of 3.2. Possible associated reasons for this poorer outcome included delayed administration of N-acetyl cysteine (median time from overdose 30 hours *v* 20 hours), a substantially greater incidence of chronic alcohol misuse (49 *v* 14%), and twice the incidence of co-overdose with benzodiazepines (22 *v* 10%). All these factors lead to an increased mortality, with 18% of the older group dying, versus just 3% of those <40 years.

See p 686