LETTERS TO THE EDITOR

Gastric cancer cell lines lack Fas ligand (FasL) expression but kill T cells via a FasL independent pathway

EDITOR,—Bennett et al (Gut 1999;44:156–162) reported that in each of 30 paraffin wax specimens of human gastric adenocarcinomas, FasL mRNA and protein co-localised to neoplastic epithelial cells. TUNEL staining revealed that a high number of tumour infiltrating lymphocytes (TIL) displayed apoptotic features. From these results and from their findings of Fas expression in human colon and oesophageal cancer, the authors propose that FasL might be a mediator of immune privilege in gastrointestinal cancers.

We studied intrinsic FasL expression in gastric cancer cell lines derived from primary (RF-1, SNU-1) or from metastatic sites (SNU-1-16, Kato-III, N-87, RF-48). We did not detect FasL mRNA or protein in any of the six cell lines analysed by RT-PCR and by flow cytometry (table 1).1 We then performed the JAM assay to rule out the presence of a functional FasL expression below the detection limit of our assays.2 Although we found that gastric cancer cells were able to induce DNA fragmentation in the Fas sensitive T-cell line CEM-C7H2 (fig 1A), blocking FasL on the effector cell site did not reduce the extent of cytotoxicity. This result was confirmed by replacing the target cell line by a subclone stably expressing the viral protein crmA, which inhibits activation of caspases 1 and 8 and thereby mediates resistance to Fas triggering (fig 1B).3

Owing to the discrepancy between our results (all cell lines were FasL negative) and those of Bennett et al (all 30 primary neoplasias were FasL positive), we wondered whether tissue derived factors such as tumour necrosis factor (TNF-α) and interferon (IFN-γ) might upregulate FasL in vivo, thus explaining the differences observed. In our setting, neither of the cytokines was able to modify FasL expression on gastric cancer cell lines (table 1). In addition, killing of T cell lines was not mediated via secretion of TNF-α as blocking the cytokine using a monoclonal antibody did not influence the result of the JAM assay (fig 1A).

How can the

Figure 1 CEM-C7H2 T-acute lymphocytic leukaemia cells are killed by gastric carcinoma cell lines via a FasL independent pathway. (A) CEM-C7H2 target cells were incubated with 10 µCi/ml [3H]-thymidine for 16 hours and co-cultivated with the gastric cancer cell lines at a target:effector ratio of 1:10. Cocultivation of cells was performed for 72 hours at 37°C. The reduction in radioactivity was used to calculate the percentage of gastric cell mediated target cell killing. The bars represent mean (SEM) specific killing (%). Statistical analysis of the blocking experiments showed the following: untreated v anti-FasL monoclonal antibody treated effectors (RF-1, p=0.5; RF-48, p=0.5; SNU-1, p=0.2); untreated v anti-tumour necrosis factor (TNF-α) treated effectors (RF-1, p>0.07; RF-48, p=0.15; SNU-1, p>0.5). (B) CrmA expressing CEM-C7H2 (C7H2/crmA) cells were used as target cells. Experimental conditions were as for (A). Statistical analysis did not reveal any significant reduction in mean specific killing of the crmA expressing C7H2 cells by the gastric cancer cell lines (RF-1, p>0.3; RF-48, p>0.8; SNU-1, p>0.5).

Table 1 Expression of FasL and Fas in gastric cancer cell lines and their sensitivity toward Fas triggering by the CH11 monoclonal antibody

<table>
<thead>
<tr>
<th>Cell line</th>
<th>FasL mRNA1</th>
<th>Constitutive expression NOK-1/1H1</th>
<th>+TNF-α (100 ng/ml)2</th>
<th>+IFN-γ (100ng/ml)2</th>
<th>Fas expression3</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF-1</td>
<td>Negative</td>
<td>1.1/1.0</td>
<td>1.0</td>
<td>0.8</td>
<td>8.3</td>
<td>1</td>
</tr>
<tr>
<td>RF-48</td>
<td>Negative</td>
<td>1.3/1.0</td>
<td>0.9</td>
<td>0.9</td>
<td>6.1</td>
<td>3</td>
</tr>
<tr>
<td>Kato-III</td>
<td>0.9/1.2</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
<td>1.4</td>
<td>7</td>
</tr>
<tr>
<td>SNU-1</td>
<td>Negative</td>
<td>1.1/1.0</td>
<td>0.9</td>
<td>0.9</td>
<td>4.9</td>
<td>8</td>
</tr>
<tr>
<td>SNU-1-16</td>
<td>Negative</td>
<td>1.0/1.2</td>
<td>Not done</td>
<td>Not done</td>
<td>1.1</td>
<td>21</td>
</tr>
<tr>
<td>N-87</td>
<td>Not done</td>
<td>1.0/1.2</td>
<td>Not done</td>
<td>Not done</td>
<td>2.2</td>
<td>Not done</td>
</tr>
</tbody>
</table>

1RT-PCR analysis was done as follows: total RNA from about 1 × 10⁶ cells was extracted by the acid guanidinium thiocyanate-phenol-chloroform protocol described by Chomczynski and Sacchi;1 1µg RNA together with 250 ng of oligo (dT)₁₅ primer was diluted in a d. to a final volume of 14 µl, denatured by heating up to 70°C for five minutes and immediately chilled on ice. To each reaction, 6 µl RT mixture containing 4 µl × buffer, 2 pmol each of dATP, dCTP, dGTP and dTTP, and 200 units Moloney-murine leukaemia virus reverse transcriptase, was added (all reagents from Promega, Wisconsin, USA). For cDNA synthesis all samples were incubated at 37°C for 60 minutes. The reaction was stopped by heating the sample to 80°C for two minutes; 100 ng cDNA obtained was amplified by 50 cycles with 1 µg RNA together with 250 ng of oligo (dT)₁₅, primer was diluted in a.d. to a final volume of 14 µl, denatured by heating up to 70°C for 60 minutes. The reaction was stopped by heating the sample to 80°C for two minutes; 100 ng cDNA obtained was amplified by 50 cycles with 1

2Statistical analysis of the blocking experiments showed the following: untreated v anti-FasL monoclonal antibody treated effectors (RF-1, p=0.5; RF-48, p=0.5; SNU-1, p=0.2); untreated v anti-tumour necrosis factor (TNF-α) treated effectors (RF-1, p>0.07; RF-48, p=0.15; SNU-1, p>0.5)

3Constitutive expression of FasL protein was determined using different two monoclonal antibodies, NOK-1 (Pharmingen, San Diego, California, USA) and HI1 (Alexis, Laufelfingen, Switzerland). For detection of FasL expression, 0.5 × 10⁶ cells were fixed with paraformaldehyde, permeabilised with a buffer containing 0.05% saponin and 1% bovine serum albumin and stained with 1 µg of the respective specific monoclonal antibody or a relevant isotype matched negative control antibody for 30 minutes at 4°C. In the case of staining with NOK-1, cells were incubated for 20 minutes at 4°C with a secondary fluorescein isothiocyanate (FITC) labelled rabbit anti-mouse antibody (Dako, Vienna, Austria; dilution 1 in 10). Cells were washed and immediately analysed by flow cytometry for their specific fluorescence signals. Mean specific fluorescence intensities (MFI) were calculated as the ratio of mean fluorescence intensity achieved with the specific antibody/isotype matched matched control antibody. A ratio > 1.5 was considered positive. The mean value of MFI for three independent experiments is given.

4Time kinetics (1-3 days' stimulation) were performed and values are given for day 3. Tumour necrosis factor (TNF-α) and interferon (IFN-γ) were purchased from R&D Systems (Minneapolis, Minnesota, USA). Flow cytometric analysis was performed using the NOK-1 monoclonal antibody.

5For detection of Fas expression, 0.5 × 10⁶ cells were stained with 1 µg of a specific FITC labelled anti-Fas monoclonal antibody (UB2, Immunotech, Marseille, France) or an isotype matched control. The mean value of MFI for three independent experiments is given.

6Cells were incubated with the CH11 monoclonal antibody (250 ng/ml) for 24 hours and the proportion of apoptotic cells was determined using the propidium iodide assay. Even after 72 hours' incubation, there was only a very small increase in the percentages of apoptotic cells (e.g. in the SNU-1 cell line the increase was from 3% (control) to 5% (CH11)).
differences between in situ and in vitro results be explained?”

Bennett et al mention that CD45+ TIL express FasL mRNA, but they did not analyse Fas expression and sensitivity, features that together characterise activation induced cell death. Although on morphologi-cal examination of slides the authors excluded the possibility of lymphocytes being killed by infiltrating neutrophils potentially attracted by the expression of FasL on the tumour cells, it is possible that lymphocytes succeeded to apoptosis owing to extracellular signals. This mechanism could well be under the (cytokine) control of the tumour as has been discussed for other diseases.2 Alternatively, lymphocytes could indeed be killed by the tumour cells but by a mechanism independent of the Fas system, a hypothesis supported by our data (fig 1).

Bennett et al did not use the standard Lauren classification system. It has been shown that gastric carcinomas of the intestinal and diffuse type (according to Lauren) differ in morphology, growth pattern and risk factors, and also in their expression of molecules involved in apoptosis such as Fas or p53.7 This evidence that at least in some tumour models Fas and FasL expression are under transcriptional control of p53.8 Loss-of-function mutations or deletions of p53 have been reported to be involved in gastric carcinogenesis9 and the frequency of these events differs between intestinal and diffuse gastric cancers.10 Also, a correlation between p53 mutation, Fas expression and gastric carcinoma cell differentiation has been demonstrated.11 Further studies of the impact of differentiation and p53 functional status on FasL expression are therefore mandatory in gastric carcinoma cells.

Innsensitivity towards Fas is usually an early step in tumour development, allowing tumour cells to resist the attack of the immune system and to avoid suicide when FasL expression is acquired.12 Furthermore, a sequence of Fas resistance and FasL expres-sion has been demonstrated for hepatocellular carcinoma.13 Secondary loss of the Fas gene or of its expression during continuous culture of gastric adenocarcinoma cells is unlikely for the following reasons: (I) FasL mRNA and FasL expression is an early event in hepatocellular carcinoma.14 (II) Loss of FasL expression does not seem to be a prerequisite for their survival, and (II) to our knowledge, no data are available from other cell (line) systems that tumour cells lose FasL expression during long term culture.

In conclusion, we think that Bennett et al’s data suggest that CD45+ lymphocytes die in the immediate proximity of neoplastic cells. Although their data are compatible with Fas induced TIL cell death, our functional data from cell line suggest that other tumour mediated mechanisms of killing immuno-competent cells might also exist in gastric cancer. Further work clarifying the sequence of Fas/FasL expression and function during the transformation and metastatic process is needed.1

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Reply

EVROV—We concur with the view expressed by Tinhofer et al that Fas ligand (Fasl) mediated “counterattack” against antitumour lymphocytes is not the sole mechanism of immune evasion in gastric, or indeed any other form of cancer. Tumours evolve multiple immune evasive strategies. However, there is ample in vitro and in vivo evidence that constitutive expression of FasL enables cancers to promote apoptosis of antitumour immune effector cells.1 For example, Fasl has been shown to be associated with apoptosis and loss of tumour infiltrating lymphocytes in human esophageal cancer and depletion of antitumour natural killer cells in a mouse model.2

In stomach cancer, apart from our finding of Fasl expression at the mRNA and protein level in vivo in all 30 gastric adenocarcinomas examined,3 Rudi and colleagues4 showed Fasl mRNA in all three gastric carcinoma cell lines examined—including one cell line, KATO III, in which Tinhofer et al failed to detect Fasl mRNA. This poses serious questions regarding the sensitivity of the Fasl RT-PCR performed by Tinhofer et al. In fact, appropriate positive controls have not been shown to verify that their negative findings are not merely owing to the insensitivity of their assays for detecting Fasl RNA and protein in adherent cells. Successful use of the JAM assay depends on using target cells that exhibit good sensitivity to Fasl mediated apoptosis. Even different cultures of cell lines that are regarded as Fas sensitive, such as Jurkat E6 cells, can vary in their Fas sensitivity for reasons which are unclear, and Fas resistant subtypes may be generated. Tinhofer et al need to demonstrate that their cultures of CEM-C7H2 target cells were indeed susceptible to apoptosis via Fas in order to validate their negative results.5 Authentic Fasl mediated killing of Fas sensitive target cells is normally detectable after eight hours of co-culture with Fas expressing effector cells.6 Tinhofer et al performed a prolonged co-culture of 72 hours. It is possible that the cell death detected in target cells at this late stage was from non-specific effects, such as exhaustion of nutrients or growth factors in the presence of proliferating effector cells rather than a specific killing event. We agree with Tinhofer et al that the sequence of Fas/Fasl expression and function during gastric carcinogenesis merits further investigation. Their suggestion that these molecules should also be investigated in metastases of gastric cancer is also pertinent as recent evidence suggests that Fasl contributes to the invasion of Fas sensitive organs, such as the liver, by colonic adenocarcinoma cells.7

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4 Rudi J, Kuck D, Strand S, et al. Involvement of the CD95 (APO-1/Fas) receptor and ligand system in Helicobacter pylori-induced gastric
Vector manometry and LOS dynamics

EDITOR,—We read with interest the recent paper by Kahrlas et al on the effect of hiatus hernia on gastro-oesophageal junction pressure (Gut 1999;44:476–482). These authors used a novel technique that combined vector manometry, fluoroscopy, and endoscopic tagging of anatomical landmarks to map the differences in pressure profile between patients with and without hiatus hernia. Analysis of the vector profiles, taken at end expiration, revealed two distinct high pressure zones in each of the seven patients with hiatus hernia. These were thought to represent an axial separation of the internal and external components of the lower oesophageal sphincter (LOS). When these high pressure zones were repositioned to represent a simulated reduction of the hernia, the vector profile took on the appearance of a normal sphincter.

This study drew some interesting conclusions regarding the effect of hiatal herniation on LOS pressure dynamics. We would like to raise two issues with the authors—the methodology of this study and the reproducibility of vector manometry.

With regard to the methodology of this paper, the numerical vector pressure analysis used was based on the assumption that the gastric fundus is stationary. We believe that three factors contribute to the poor reproducibility of vector manometry. Firstly, the point at which respiration is suspended is critical in defining vector volume. It is likely that the point at which respiration is suspended varies from patient to patient and from pull-through to pull-through—that is, not all patients suspend respiration at the end tidal point. Secondly, it is unlikely that the diaphragm is completely relaxed during a 15 second expiratory breath hold. It is speculated that crural activity would therefore be expected. Finally, there can be significant minute to minute variation in lower oesophageal sphincter tone.

The poor reproducibility of vector manometry has been described previously by Bemelman et al using rapid pull-through vector manometry (8 channel catheter, 0.7 ml/s pull-back speed). They showed that LOS pressure varied from 20 to 80 mm Hg in 20 pull-throughs performed in one hour in the same patient.1 Kahrlas et al did not mention the number of pull-throughs for each patient or the reproducibility of vector profiling. It is therefore difficult to draw accurate conclusions on the size and position of high pressure zones, particularly when the study population is limited to seven patients.

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Mycophenolate mofetil for Crohn’s disease

EDITOR,—On the basis of a study reported recently by Neurath et al (Gut 1999;44:625–628), commentators in Gut and the Lancet suggested that mycophenolate mofetil (MMF) should be used in patients with Crohn’s disease who have either not responded to or are intolerant of azathioprine or 6-mercaptopurine. This advice is premature: firstly, because the study was flawed and, secondly, because it examined only management of acute inflammation, not the place of MMF in maintaining remission and in steroid sparing (a fact acknowledged in both commentaries).

The study by Neurath et al compared the effect of MMF 15 mg/kg daily with azathioprine 2.5 mg/kg daily, both with high dose steroids, in the treatment of active chronic Crohn’s disease (six months’ follow up). The main conclusions were that activity, as measured by the Crohn’s disease activity index (CDAI), dropped further at one month in patients given MMF plus steroids than in those given azathioprine plus steroids, and that this was as a result of a faster effect in more severe disease. The major drawbacks of the study were as follows. As pointed out by the authors, neither patients nor investigators were blinded. Four (11%) of 35 patients in the MMF group were lost to follow up compared with none in the azathioprine group: thus results may have looked different if analysed on an intention to treat basis. The MMF group had higher starting CDAIs: if the levels of CDAI reached at one month were compared between groups, rather than the fall of CDAI, the groups may not have been significantly different. The division of patients into those with moderate and severe activity was retrospective: thus conclusions based on this division should be regarded as hypothesis generating only, especially as important differences between the groups do not reach formal statistical significance if adjustments for multiple comparisons are made. Finally, steroid usage in the two groups is not recorded: one can imagine that a poor early response would lead to more steroids being given and so to a better overall result.

I agree with the authors and commentators that alternatives to azathioprine/6-mercaptopurine are needed. I also agree that the therapeutic effect of MMF in chronic active Crohn’s disease should be assessed in properly performed trials, and perhaps importantly that its effect in maintaining remission and in steroid sparing should be assessed. However, until then, MMF should be considered to have no clear indications for use in Crohn’s disease.

J C ATHERTON
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Reply

EDITOR,—Mycophenolate mofetil (MMF) is an immunosuppressive drug that is often used in organ transplantation.1 It is an outer produg of mycophenolic acid that inhibits inosine monophosphate dehydrogenase and potently suppresses lymphocyte proliferation.2 Furthermore various clinical trials have shown its efficacy in suppressing autoimmune and chronic inflammatory disorders, such as rheumatoid arthritis,3 pemphigus vulgaris,4 and psoriasis.5 There are several case reports6 7 and also our controlled study indicating that MMF can be successfully used in patients with Crohn’s disease. In our study treatment of patients with moderately active Crohn’s disease with MMF/cortisone led to a significant reduction in clinical activity scores compared with treatment with azathioprine/cortisone. These data suggested that treatment of chronic active Crohn’s disease with MMF/cortisone would be effective in inducing remission. As corticosteroids were given to patients in addition to
MMF, the data available do not show unequivocally that MMF alone is effective in the maintenance of remission in Crohn’s disease. This question is currently under study in a double blind, randomised controlled trial in Europe and the USA, in which the effects of MMF on maintenance of remission will be analysed.

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Laboratory of Immunology, I. Medical Clinic, University of Mainz, Langenbeckstrasse, 55116 Mainz, Germany

5 Goldblum R. Therapy of rheumatoid arthritis with mycophenolate mofetil. Clin Exp Rheumato-

BOOK REVIEWS


The clear track record of success of Emerg

cy Abdominal Surgery is proved by the publication of a third edition. The authors, who are all from Aberdeen, classify them-

selves as general surgeons and the book is dedicated to the general surgeons of the future. As we enter the millennium, general surgery is still vital to the management of unclassified surgical emergencies, and sur-

geons of all disciplines need to be trained in triage. Yet, ultimately, it is probable that few of the subjects in this book will remain the province of the general surgeon and many will be within the auspices of specialist service groups. However, although the days of the general surgeon who dealt with ruptured aeurysms may be over, but there is still a role for a surgeon to identify the physical signs and to direct the patient along the right route.

This book tackles emergencies in children as well as adults. Furthermore, the emergency presentation of vascular disease, and gynaecological and urological disorders is also dis-

cussed and the entire spectrum of general sur-

gery as seen in the accident and emergency department of a district general hospital is comprehensively reviewed. Whether surgery in the future will follow the same pattern is open to speculation but there is currently a need for an up to date general surgical text for trainees and consultant surgeons.

The text is well illustrated and referenced, and I found the chapter devoted to the acute abdomen in pregnancy and the puerperium to be particularly valuable as this information is not readily available in other general surgical texts. The book achieves a good balance of guidance on when a generalist can tackle a problem safely and when it is best to stop; complex liver injuries are acknowledged as a problem best managed in a tertiary referral centre where all the available support facilities are operational.

I congratulate the authors of this book for bringing together a third edition of this text and they are to be applauded for using specialists in the areas that they no longer feel comfortable tackling themselves—that is, emergencies in children, urological emergen-

cies, vascular emergencies, gynaecological disorders, and medical aspects of the acute abdomen. They are also to be praised for acknowledging in their preface that, nowa-

days, vascular surgery should be performed by specialists as should colorectal emergency surgery. Nevertheless, the emphasis in this book is on the clarity of decision making, by generalists where appropriate, and by special-

ists when indicated, and to continue to be a valuable resource for surgeons in training as well as those in practice.

M R K EIGHLEY


The first edition of this handbook was a valu-

able resource to both junior hospital staff and family doctors for its practical coverage of basic gastroenterology. In the seven years since it was first published, there have been many advances in gastroenterology and these have been included in the new edition, which is a rapid reference book which the authors hope will be of interest to doctors and health professionals in clinics, accident and emer-

dency departments and to the general public.

Covering a wide range of topics, including the various aspects of hollow organ gastroen-

terology, liver, biliary, and pancreatic disease, the book would prove invaluable to surgeons on nutrition and the gut in systemic disease, areas of interest to the more experienced reader. There are also sections on essential proce-

dures for those involved in the preparation of patients, and a comprehensive chapter on gastroenterological emergencies which should prove invaluable in accident and emergency departments.

The breadth of coverage is impressive for such a small book although some parts lack depth. However, the authors live up to their promise to include recent advances in all areas and supply a comprehensive selection of further reading for those requiring more detailed information.

The style is dogmatic and didactic and, in conjunction with clear algorithms, presents infor-

mation in the clear, concise manner essential to a rapid reference text. There are few radiological or pathological illustrations but they are of good quality and are accompanied by line diagrams to aid their interpretation.

The book aims to be a rapid and compre-

hensive reference tool for a wide audience of health professionals. This new edition easily achieves this and will undoubtedly continue to be useful in surgeries and wards for those who work in gastroenterology but have limited practical experience of the specialty.

R A HARRY


While medical students can confidently hold forth on the mechanisms of the Zollinger-Ellison syndrome, a condition affecting one in a million of the population, they rarely have much to say about functional GI disorders (FGIDs), which can affect up to a quarter of the population at some stage in their life. Part of the reason is that the Rome process, which requires the integration of pathophysiology with psychology, and even sociology. FGIDs also suffer from having no objective measurable abnormalities, so that classifications must of necessity be symptom based. The Rome process is a valiant attempt to make this area of study less confused, more consistent, and scientifically respectable. As such, it undoubtedly has had a major impact, and some criteria are now used for the first time into most clinical trials and studies in this area. The senior chairman claims that this process has “done for functional gastroin-

testinal disorders what the Diagnostic and Statistical Manual of Mental Disorders (DSM III) has done for psychiatry”. While this may appear grandiose, I think it just might be true.

This book provides an overview of many years’ work, which has greatly contributed to our understanding of functional gastro-

intestinal disease (FGID). This is due in no small part to the “Rome” process, which is described in detail in the book. The challenge was to create order out of chaos by agreeing criteria for the diagnosis of FGIDs. The major advantage of such a classification is that studies using agreed definitions become comparable and the next study can build on the results of the last. The major disadvan-

tages, which the authors constantly remind the reader of, are that uncritical readers may accept these definitions as fixed in stone. This would of course stultify inquiry and progress. We need to be constantly reminded that the new Rome criteria (for example, for irritable bowel syndrome), in reality excludes as many as 60% of the patients diagnosed as having IBS in clinical practice. This has the advan-

tage of producing closely comparable patients for studies, but the disadvantage of reduced generalisability to normal clinical practice.

The excellent introductory chapter outlines the ideas behind the Rome process and emphasises the importance of the “bio-

psycho-social model for IBS” for understanding how sufferers become patients. I much enjoyed the next chapter on the basic science for functional gastroenterology, which is a much work and renders it in a form readily understandable to clinicians with only vague memories of neuroanatomy. There then follows a section on motility and sensation measurements, again comprehensive but suitably cautious. There are sections on psychological assessments, and a good account of the weaknesses and strengths of various psychological rating scales for non-physicians. Specific functional disor-
Inflammation, and Sepsis will be held in The 5th World Congress on Trauma, Shock, Inflammation, and Sepsis 5th World Congress on Trauma, Shock, Inflammation, and Sepsis Lauderdale, Florida 33309, USA. Tel: +1

Disease Symposium will be held at the Mar-

The 11th Annual International Colorectal Disease Symposium will be held at the University Hos-

Barrett 2000

The 6th World Congress on Barrett's Oesophagus will be held in Paris, France, on 1–6 September 2000. Further information from: Michele Liegeom, Academic Medical Centre, Amster-

The 11th World Congress on Trauma, Shock, Inflammation, and Sepsis will be held in Munich, Germany, from 29 February to 4 March 2000. Further information from: Prof Eugen Faist, Department of Surgery, Ludwig Maximilians University Munich, Klinikum Grosshadern, Marchioninistrasse 15, 81377 Munich, Germany. Tel: +49 89 7095 5461/ 2461; fax: +49 89 7095 2460; email: faist@gh.med.uni-muenchen.de

Second Annual Gastrointestinal Cancer Update: A Multidisciplinary Approach

The Second Annual Gastrointestinal Cancer Update conference will be held at the Yarrow Hotel and Conference Centre, Park City, Utah, USA, on 15–19 March 2000. Further information from: Rosalie Lammle. Tel: +1 801 581 8664; fax: +1 801 581 3647; email: rosalie.lammle@hsc.utah.edu

European Courses on Laparoscopic Surgery

The European Courses on Laparoscopic Surgery will be held at the University Hospital Saint Pierre, Brussels, Belgium, on 4–7 April 2000 and 21–24 November 2000. Fur-

Third Scandinavian Course on Inflammatory Bowel Diseases

The Third Scandinavian Course on Inflammatory Bowel Diseases will be held at the Wilanderselen, Örebro Medical Centre, Öre-

XVIIIth European Workshop on Gastroenterology and Endotherapy

The XVIIIth European Workshop on Gastroenterology and Endotherapy will be held in Brussels, Belgium, on 26–28 April 2000. Further information from: Administrative Secretariat, Ms Nancy Beaprez, Gastroen-

Digestive Disease Week

The Digestive Disease Week will be held at the San Diego Convention Centre, San Diego, California, USA, on 21–24 May 2000. Further information from: DDW Administra-

International Hepato-Pancreato-Biliary Association 4th World Congress

The International Hepato-Pancreato-Biliary Association 4th World Congress will be held in Brisbane, Australia, from 28 May to 1 June 2000. Further information from: Intermediate Convention and Event Management, PO Box 1280 (Intermediate House, 1197 Castlemaine Street), Mélton, Queensland 4064, Australia. Tel: +61 (0)7 3369 0477; fax: +61 (0)7 3369 1512; email: hpb2000@cim.com.au

7th Southeast European Symposium of Paediatric Surgery: Intestinal Motility Disorders

The 7th Southeast European Symposium of Paediatric Surgery will be held at the Univer-

Courses from the European Postgraduate Gastro-Surgical School

The Board of Directors of the European Postgraduate Gastro-Surgical School an-

NOTES

11th Annual International Colorectal Disease Symposium

The 11th Annual International Colorectal Disease Symposium will be held at the Mar-

5th World Congress on Trauma, Shock, Inflammation, and Sepsis

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Gastric cancer cell lines lack Fas ligand (FasL) expression but kill T cells via a FasL independent pathway
I TINHOFER, H WYKYPIEL, I MARSCHITZ, T HENN and R GREIL

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