the limited proteolysis of IGF Binding Protein-3 (IGFBP-3) increases the tissue bioavailability of IGFs, in response to a catabolic stress. The aim of this prospective study (2 years), in 14 colorectal cancer patients was to assess if postoperative induction of IGFBP-3 protease activity may be a prognostic marker of metastatic progression.

Methods: Serum samples were taken before (J0) and after (J6) surgery and analyzed by Western Blot.

Results: Before surgery, we observed a strong increase in IGFBP-2 (+340%) associated to a slight decrease in IGFBP-3 levels whereas IGFBP-3 protease activity was not significantly altered. After surgery, two different profiles were noted: a/ in 7/14 patients, we observed an expected catabolic profile with induction of IGFBP-3 protease activity associated to diminished IGFBP-3 and increased IGFBP-2 concentrations. No metastatic disease was observed in this group. b/ in 7/14 patients, no significant proteolytic mobilization of the IGF system was observed. 4/7 patients had a progression. We hypothesize that such a metabolic anergy could be related to the postoperative persistence of cancer cells that released an IGFBP-3 protease inhibitor. Such an inhibitor was indeed found in conditioned medium from HT29-D4 human colon cancer cells.

Conclusion: Assessment of IGFBP-3 protease activity in postoperative serum might be an useful early prognostic factor of metastatic progression in colorectal cancer patients.

749 POSTER

Diagnostic and prognostic significance of protein patterns in human epithelial cancer

M.A. Reymond[1], J.-C. Sanchez[2], C. Schneider[1], S. Tortola[3], M.A. Peinado[3], W. Hohenberger[1], T. Kirchner[1], D.F. Hochstrasser[2], F Köckerling[1]. [1]*Dpt of Surgery, University of Erlangen, Germany;* [2]*Central Chemistry Laboratory, University Hospital, Geneva, Switzerland;* [3]*Institut de Recerca Oncologica, Barcelona, Spain*

To improve results of surgical therapy of human epithelial tumors, new diagnostic, prognostic and therapeutic markers are necessary. Available staging systems (e.g. TNM-system) are clinically useful but show severe limitations in defining the prognosis of a particular patient. New approaches, close to the clinical reality, relying on phenotypic patterns are emerging. These markers can be searched by differential display techniques at DNA (PCR), RNA (RAP-PCR) or protein (high-resolution 2-dimensional polyacrylamide electrophoresis) level. The accuracy of such phenotypic comparisons between pathological and normal tissues depends on the purity of the samples.

We have developed techniques of preparation of pure epithelial cell samples from fresh operation specimens without any enzymatic digestion.

Using these techniques, followed by denaturation, gel running, protein microsequencing and immunoblotting, a protein map (master) of the normal colonic mucosa was defined with over 50 reference landmarks and will soon be available on the Internet (http://www.expasy.ch) and can be matched with pathological patterns obtained with these reproducible techniques.

750 POSTER

Safety of adjuvant mAb 17-1A in colorectal cancer (CRC)

H.J. Schmoll[1], D. Quietzsch[3], P. Börner[3], E. Kettner[3], R. Mennigen[3], M. Zingrebe[2], J Preiß[3,4]. [1]*Medical Oncology, University of Halle;* [2]*Medical University of Hannover;* [4]*Medical Oncology, Saarbrücken;* [3]*17-1A Surveillance Trial Group, Germany*

Purpose: Monoclonal antibody (mAb) 17-1A (edrecolomab) has reduced distant metastases and mortality as adjuvant treatment in CRC Stage III (Riethmüller et al , Lancet 343, 1994; Proc. ASCO 15, 1996). After German marketing authorization, a surveillance trial started in 1995 to monitor safety in clinical use.

Methods: 277 patients (52% male, 48% female; age 64 y [35–85]; Stage [I–IV]: 1.5, 19.4, 72.5, 6.6%) were treated with 17-1A.

Results: 142 pts (51.3%) showed no adverse effects. 103 pts (37.3%) developed toxic effects grade 1–2; 21 pts (7.6%) grade 3 and 11 pts (4%) grade 4, requiring discontinuation of 17-1A and symptomatic treatment with full recovery. No lethal toxicity was observed.

WHO-grades (% patients)	0	1	2	3	4
Nausea	79.8	12.3	6 1	1.8	–
Vomiting	92.1	4.7	2.5	0.7	–
Diarrhoea	69.3	13.7	12.3	2.9	1 8
Abdominal pain	81 2	11.9	3.6	2.5	0.7
Flush/Erythema	91.7	4.0	2.5	1.1	0.7
Anaphylactic reaction	97 1	0 7	1.1	0.4	0.7

Conclusion: Adverse effects were predominantly mild to moderate with the exception of a minority of pts (11.6%) developing grade 3–4 gastrointestinal or anaphylactic reactions. Toxicity observed in this large cohort is in accordance with previous reports and underlines the favourable safety profile of 17-1A.

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751 POSTER

Adjuvant chemotherapy of Dukes C colon carcinoma: Comparison of 5-FU + levamisole (LEV) 12 months vs. 5-FU + folinic acid (FA) 12 months VS 5-FU + FA 6 months

G. Hartung[1], K. Maas[1], L. Edler[4], P. Diezler[2], E. Hagmüller[3], L. Pasternak[1], W. Queißer[1]. [1]*III. Dept. of Medicine;* [2]*Dept. of Radiology;* [3]*Dept. of Surgery, Klinikum Mannheim, University Heidelberg;* [4]*Biostatistics, DKFZ, Heidelberg, Germany*

Purpose: Postoperative chemotherapy has been established for stage III (Dukes C) colon cancer. Currently, treatment with 5-FU and LEV for 12 months is still considered standard outside clinical studies. However, optimal duration of therapy and biomodulation of 5-FU with FA might improve adjuvant treatment.

Patients and Method: From 1993 until 1996 116 patients with surgically resected colon cancer (Dukes C) were randomly assigned to A) standard therapy with 5-FU + LEV for 12 months, B) FA 100 mg/m^2 + 5-FU 450 mg/m^2, day 1–5 every 4 weeks for 12 cycles and C) 5-FU + FA 6 cycles respectively.

Results: After a median follow-up of 3.2 years no significant difference concerning disease free survival (p = 0.7) and survival (p = 0.6) was observed. Toxicity among the 3 groups is similar. However, a trend for more pronounced gastrointestinal toxicity under treatment with 5-FU + FA is observed.

Conclusion: In accordance with recently presented results of other studies, the preliminary data of this trial indicate that adjuvant treatment with 5-FU + FA for 6 months may be as effective as treatment with 5-FU + LEV for 12 months.

752 POSTER

Brain metastases from colon- and rectumcarcinoma

C. Nieder, U. Nestle, M. Niewald, K. Walter, K. Schnabel. *Dept. of Radiotherapy, University Hospital Homburg/Saar, Germany*

Purpose: We analyzed 20 cases with respect to pattern of spread and prognosis after radiotherapy (RT) or neurosurgery plus radiotherapy.

Methods: 14 patients were treated with RT (30–60 Gy), 6 with neurosurgery plus radiotherapy (OP + RT, 30–40 Gy). All had advanced primary tumors (T3, T4), most of which were poorly differentiated; lymph node metastases were common. In 5 cases the brain was the first site of distant metastases. Ten patients had a solitary brain metastasis.

Results: Results of OP + RT were superior to those of RT, with respect to palliation of symptoms as well as to local tumor remission and survival. Overall median survival was only 51 days (1-year survival rate 6%). In 5 of 14 cases symptomatic improvement was observed after RT. Partial remission of the brain metastases occurred in 3 of 14 cases. The presence of extracerebral metastases was the most important prognostic factor.

Conclusion: Selected patients considered to have a favourable prognosis may profit from combined treatment (OP + RT). Despite the short survival time, stereotactic irradiation should be evaluated as an alternative to conventional RT in the remaining patients because the palliative effect of RT was relatively disappointing.

753 POSTER

Pseudocontinent perineal colostomy following abdominoperineal resection: Technique and findings in 40 patients

P. Dubé, J.M. Guillot, D. Elias, Ph. Lasser. *Of Surgery, Gustave-Roussy Institute, Villejuif, France*

Purpose: This prospective study was designed to evaluate the morbidity and the functional results of pseudocontinent perineal colostomy with free flap of colic muscle following abdominoperineal resection.

Methods: Forty patients (26 men and 14 women) averaging 50 of age were given this type of treatment between February 1989 and February 1997 at the Gustave-Roussy Institute. Thirty-four patients presented with