5.

HUMAN COLORECTAL TUMOR XENOGRAFTS IN NUDE MICE : BEHAVIOR AND EXPRESSION OF MALIGNANCY. B. Sordat, W. R. Wang, J. F. Cajot and J. E. Testa. Swiss Institute for Experimental Cancer Research, 1066 Epalinges, Division of Hematology, CHUV 1011 Lausanne and Haerbin Medical College, 2nd Hospital Heilongjiang, China.

Athymic nude mice have proved to be a very useful tool for tumor biology studies including tumorigenicity assays, in vivo expression of the malignant phenotype and potential therapeutic responses. Over the past 3 years, 72 surgical specimens representing various types of human colorectal carcinomas have been grafted in nude mice using the subcutaneous (sc) implantation route. Approximately 70% of these tumors grew progressively in the mouse recipient. Advanced tumors in the patients (Duke's B and especially C grades) exhibited a higher take rate than less progressive lesions (no growth from Duke's A tumors in the present series). Mouse-passaged tumors generally maintained their individual characteristics but definite changes (kinetics, enzyme expression) have been described in relation to the new host environment and site. For instance, using the gut-implantation route and in contrast to the pseudo-benign behavior in sc situation, the colon xenografts could express marked micro- and macroinvasion. Using alternative hosts and a panel of representative tumors, it is hoped that this system will provide information not only on the sensitivity to therapies of individual tumors but also on tumoral invasive and metastatic processes.

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6.

COLORECTAL TUMOR MARKERS AND IMMUNOLOGICAL DIAGNOSIS. J.-P. Mach, F. Buchegger, J.-C. Volant, J.-Ph. Grob, V. von Fliedner, A. Bischof-Delaloye and B. Delaloye., Ludwig Institute for Cancer Research, CH-1066 Epalinges and the Division of Nuclear Medicine, CHUV CH-1010 Lausanne.

Three types of markers have been described in colorectal carcinoma, the CEA and two other markers defined by the monoclonal antibodies (Mab) : 19-9 and 17-1A. The CEA and 19-9 markers are released in the circulation and thus can be assayed in serum to determine the evolution of the tumor. Mab against the 3 markers have been radiolabeled and injected into patients to detect tumors by immunoscintigraphy with various degree of success : (Mach et al. Immunology Today 2 239, 1981 and Cancer Research 43 5593, 1983) (Chatal et al. J. Nucl. Med. 25 307 1984).

Following our results in nude mice indicating that $F(ab')_2$ and Fab fragments from anti-CEA Mab give earlier and higher relative concentration of radioactivity in tumors (Buchegger et al. J. Exp. Med. 158 413, 1983) we tested the fragments of Mab 35 anti-CEA clinically. The fragments were labeled with I-123 and detected 6, 24 and 48 h after injection by emission computerized tomography (ECT) using a dual head rotating camera.

The clinical results were the following : In 13 patients injected with $F(ab')_2$ we detected by ECT 23/28 tumour sites including 6/6 primary carcinomas, 3/8 liver metastases, 0/2 lung metastases and 12/12 bone metastases. In 15 patients injected with Fab fragments, we detected 6/7 primary carcinomas, 6/6 liver metastases and 18/18 bone metastases (Delaloye et al. Nuclear Med. Communication in press). The results should be confirmed in a prospective trial but the quality of the tumor images represents already a definite improvement over previously published results.

7.

EXPRESSION OF BRUSH BORDER HYDROLASES BY COLORECTAL ADENOCARCINOMAS. A.Zweibaum, N.Triadou, K.Haffen, H.P.Hauri, E.Stechi, J.Bamat, B.Sordat. INSERM, Paris & Strasbourg, France Biocenter of the University of Basel, University Children's Hospital, Berne & ISREC, Epalinges/Lausanne, Switzerland.

Brush border hydrolases are glycoproteins of high molecular weight (120 to 400 kd) which are normally restricted to the brush border of the small intestine and absent from the colon. The presence of six of them: sucrase-isomaltase (S), aminopeptidase N (APN), lactase (L), maltase-glucoamylase, dipeptidylpeptidase IV (DPP-IV) and alkaline phosphatase (was investigated in tumors developed in nude mice with six lon cell lines (HT-29, Caco-2, SW-480, HRT-18, HCT-8R, Co- in primary tumors from 27 patients and in normal adult and foetal colons. Four techniques were used: 1) indirect imm nofluorescence on tissue cryostat sections using monoclona or polyclonal antibodies against human small intestine enz 2) measurement of enzyme activities in tissue extracts, 3) immunoblotting, 4) transmission electron microscopy. Four zymes (SI, APN, DPP-IV, AP) were found to be concomitantly present in 2/6 tumors in nude mice (HT-29 and Caco-2) and 7/27 tumors from patients. The enzymes are located on api membranes and show activities which vary from one enzyme a from one tumor to another, reaching in some cases values s milar to those observed in the normal ileum. The presence the enzymes is associated, at the ultrastructural level, w that of well organized brush border microvilli. The same tumor-associated enzymes were also found to be present in lons from midgestation foetuses (16 to 30 weeks) whereas L and MGA, which were absent from the tumors, were also abse from foetal colons. No enzymes could be demonstrated in n mal adult colons. These data indicate that some colon tum exhibit a typical pattern of enterocytic differentiation w is of foetal type and which involves at least four brush b der associated hydrolases.

8.

CORRELATION BETWEEN TUMOR INVASIVENESS AND EXPRESSION OF FIBRINOLYTIC ACTIVITY. J.F. Cajot (1), B. Sordat (2) and F. Bachmann (1), Laboratoire central d'Hématologie, CHUV, CH-1011 Lausanne (1) and Swiss Institute for Experimental Cancer Research, CH-1066 Epalinges (2) Switzerland.

We have analyzed and quantitated the respective contribution to total fibrinolytic activity (FA) of urokinase-lik (u-PA) and of tissue-like (t-PA) plasminogen activators present in 0.125% Triton X-100 extracts of human primary colon carcinomas and of their respective serial subcutaneou (s.c.) xenografts in nude mice. A correlation between tumo invasiveness and plasminogen activator (PA) expression was observed in that primary tumors exhibiting clearly invasive growth patterns demonstrated high concentrations of PAs, while s.c. xenografts, exhibiting noninvasive pseudobenign growth, contained very low levels of PA activity. The decrease in fibrinolytic activity observed in s.c. xenografts was not due to an increase in inhibitors of fibrinolytic activity.

These results demonstrate a modulatory effect on tumoral PA expression by host tissue environment and suggest in this particular experimental system that tumor associated fibrinolysis may play a role in the invasive phenotype.

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