Symposium no. 4: Biology of Tumour Invasion and Metastasis

4.007

EGF RECEPTOR AND C-ERBB-2 ONCOPROTEIN IN HUMAN TUMORS OF THE CENTRAL NERVOUS SYSTEM.

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The expression of the EGF receptor and c-erbB-2 oncoprotein has been studied in several types of human brain tumors. The EGF-R levels were measured by specific ligand binding and the EGF-R associated phosphotyrosine kinase activity, by immunoprecipitation followed by autophosphorylation. The amount of c-erbB-2 (Neu p185) was evaluated by Western Blot. A micromethod, based on sandwich ELISA, was developed for the evaluation of p185 in small tumor specimens. Significant amounts of EGF-R and c-erbB-2 were expressed in >90% of the meningiomas (tot. n = 85), primarily benign, but often invasive tumors, irrespective of their histological type. In glial tumors (tot. n = 67), the expression of EGF-R is significantly correlated (p = 0.015) with the degree of malignancy. Small, but significant amounts of c-erbB-2 were observed in 3 out of 6 astrocytomas gr. 1-2 and in 8 out of 11 high grade astrocytomas and glioblastomas.

4.008

IMMUNOHISTOCHEMICAL PARAMETERS USEFUL IN THE PROGNOSIS OF CANINE MAMMARY NEOPLASMS

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Over 30% of the neoplastic lesions collected in the Animal Tumor Registry concern the mammary gland. In dogs, around half of the 2073 mammary tumors recorded in the Registry are malignant. Given the importance of the tumor-host interaction likely to modulate the clinical evolution of these neoplasms, we have undertaken a study on canine specimens to reveal the presence of specific antigens (TGF - β, fibronectin, citokeratins, k and λ light chains, UCHL1, lysozime, chymotripsin) in the peritumoral regions of the affected glands. Particular emphasis was given to the histologically defined "complex and mixed" forms of mammary tumors as compared to the "simple and solid" ones. The first group has a slower evolution and a better prognosis than the second one. Preliminary results suggest that the two groups are distinguishable by the expression of different levels of the tested markers. This difference might have prognostic value as well as provide useful indications in advancing therapeutic approaches. (Min. San. P.F. ' 87).

4.009

Histopathologic control of laser cordectomy

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It is difficult to evaluate histologically the surgical margin of the vocal cord specimen from laser cordectomy because of biological effects of the laser beam. Twenty-one T_1 vocal cord carcinoma were treated by CO_2 laser at 25-30 W in superpulsation mode attached to an operating microscope. The lesions were all excised and submitted for pathologic examination. Frozen sections were made from resection margins. If the margins of tumors approximated the edges of the surgical resection, standard biopsies were taken at several sites in the excision bed. Altough incomplet resection was observed only in one case, the local tumor recurrence rate was 14 per cent for 4 years.

The damaged tissue area was wider where connective tissue fibers and muscle bands were in a right angle situation to the resection surface. The thickness of histologically hardly evaluable damaged margin was less than 1 mm in every cases.

4.010

INHIBITION OF HUMAN MAMMARY CARCINOMA CELL INVASION IN VITRO BY INSULIN

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Two variants of MCF-7 human mammary carcinoma cells were detected that behave differently when confronted with embryonic chick heart fragments in organotypic suspension culture. MCF-7/6 cells were invasive, while MCF-7/AZ cells were not. Invasion of MCF-7/6 cells could be inhibited by insulin (1 to 100 μg/ml) in the culture medium during the incubation period.

These differences in invasiveness are presumably related to differences in cell-cell adhesion : MCF-7/AZ cells possess a cell-cell adhesion system that can be activated in MCF-7/6 cells via insulin. Homogenous expression at high level of E-cadherin has been implicated in the maintenance of the non-invasive phenotype in a number of cell families. However, immunodetection on Western blots, immunocytochemistry and the lack of inhibition of cell-cell adhesion by adding anti-E-cadherin antibodies to MCF-7/AZ cells indicated that homotypic cell-cell adhesion in these cells depends upon other molecules than E-cadherin.

4.011

STEROID RECEPTOR QUANTITIES IN DIFFERENT MALIGNANT LESIONS OF BREAST CANCER PATIENTS

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Estrogen and progesterone receptor quantitative values in primary tumors (n=69) were compared with receptors in the following lesions : a) regional lymph node metastases (n=28) as the sites which were usually first invaded during the disease progression , b) distant malignant deposits from patients with advanced disease (n=65). The groups composed with receptors of the same patients in primaries and regional lymph node metastases (n=15) as well as in primaries and distant metastatic lesions (n=16) were also analyzed. The obtained results indicated relative stability of both receptors in loco regional disease, but loss of the receptors in lesions from advanced disease.

4.012

Expression of tenascin in cultured normal and transformed human cells. B. Carnemolla, A. Leprini, M. Saginati, E. Balza, M.-Z. Sun, L. Borsi and L. Zardi Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy

Tenascin (TN) is a polymorphic high molecular mass extracellular matrix glycoprotein composed of six similar subunits joined together at their NH_2-terminal by disulfide bonds. Human TN is mainly made up of 14 and half epidermal growth factor like repeats (EGF-L), 15 units similar to fibronectin type III repeats (FN-L), and, at the C-terminal, by a sequence with 40% homology to the globular domain of the β-and γ-chain of fibrinogen. It has been shown that TN displays a restricted distribution in normal adult tissues and that its expression is ontogenically programmed. In fact, TN is transiently expressed in many developing organs and it has been proposed that TN could modulate epithelial-mesenchymal and neuronal-glial interactions. However, neoexpression, or a dramatically increased expression, of TN has been documented in a variety of tumors, thus suggesting that this glycoprotein may play a role in tumor cell-stroma interdependence. We have studied the expression of TN in cultured cells. We found that human fibroblasts produce large amounts of TN and retain from 60 to 90% of the produced TN in the extracellular matrix while the remaining is released into the cultured media. On the contrary, SV-40 transformed fibroblasts produce very low amounts of TN and less than 5% is incorporated in the extracellular matrix (ECM). Cultured melanoma cell lines produce very high amounts of TN, but also in this case, less than 5% is retained in the extracellular matrix. Thus, TN behaves as fibronectin (FN) which, in general, is present in large amounts in tumors but is not retained in the ECM of transformed or tumor derived cultured cells even when these latter produce large amounts of FN.