Symposium no. 11: New Approaches to Cancer Diagnosis and Management

11.067

BIOCHEMICAL AND TOXIC PROPERTIES OF AN IMMUNOTOXIN COMPOSED OF AN ANTI EGFR MOUSE MAB AND THE RIP α-SARCIN.

S.M. Muñoz[1], E. Tosi[2], D. Mezzanzanica[2], E. Luison[2], S. Canevari[2], S.M. Salvarelli[1], F.P. Conde[1] and M.I. Colnaghi[2]. [1]Inmunoquímica, Investigación, Hospital "Ramón y Cajal" Madrid, Spain. [2]Oncologia Sperimentale E, Istituto Nazionale dei Tumori, Milan, Italy.

An immunotoxin was synthesized by the attachment of α-sarcin, a ribosome-inactivating protein (RIP) isolated from *Aspergillus giganteus* MDH 18894 fungi, to the MINT5 monoclonal antibody (MAb) which recognizes the epidermal growth factor receptor (EGFR). A disulfide protected bond was introduced between the MAb and the RIP by derivatization with SMPT and SPDP respectively. Gel filtration and stepwise elution trough a hydroxyapatite column totally removed the unconjugated toxin and MAb.
The MINT5-α-sarcin immunotoxin inhibited the protein synthesis in a cell-free rabbit reticulocyte lysate both in the presence and absence of 2-mercaptoethanol, thus suggesting that the RIP enzymic site was not sterically hindered by conjugation. In addition the conjugate inhibited protein synthesis of cells overexpressing EGFR with an IC_{50} ($5x10^{-10}$M) 5000 times lower than that of α-sarcin alone.

11.068

Correlated analysis of nuclear DNA content and nuclear morphological features in thyroid tumors

S. Murata, H. Itoi, Y. Urata and T. Ashihara
Dept. Path., Kyoto Prefectural University of Medicine, Japan

This study of 32 human thyroid tumors demonstrates the possibility of cytological malignancy determination by using a combined, quantitative analysis of DNA content and nuclear morphology of the same individual cells. We employed our test model of a computer aided autostaging cytofluorometer combined with an image processor. The cytocentrifuged smears from tumors were used after staining nuclear DNA with propidium iodide. A total of 13 morphometric parameters for DNA ploidy pattern, nuclear size and shape constants of diploid tumor cells as well as total tumor cells in each case were used for this study. By stepwise linear and canonical discriminant analyses of the diploid tumor cells, these nuclear morphometric parameters could separate carcinomas from the benign lesions with a high statistical significance. It therefore appears that multiparametric analysis using these diploid cell parameters obtained from the image cytometry would provide a useful means for differentiating between benign and malignant lesions of the thyroid.

11.069

Growth-inhibitory Effects of Epidermal Growth Factor on Carcinoma Transplanted into Nude Mice

Yoichi Murayama and Yoshio Mishima
School of Medicine,Tokyo Medical & Dental Univ

Various concentrations of recombinant EGF were injected locally into the subcutaneous tissue surrounding the tumor transplanted into nude mice.2ng of EGF did not inhibit tumor growth of human breast cancers(MX-1 & UM-1) and ES-4 esophageal cancer.However,20ng,200ng,and 2μg of EGF inhibited the growth of these tumors in a dose dependent manner.2ng,20ng,200ng,and 2μg of EGF also inhibited the tumor growth of MKN-28 human gastric carcinoma in a dose dependent manner.Tumor growth of Co-3 human colonic carcinoma was also inhibited by EGF injection. Response to EGF was associated with EGF receptor content.EGF injection caused the increase in EGF receptor content,the decrease in affinity of EGF receptor,and the decrease in biosynthesis of intra-cellular cAMP.EGF injection also caused a necrosis of the tumor in histological study.These results indicate a possibility in developing a new therapy using EGF.

11.070

Correlation between sonographic appearance of secondary hepatic lesions and corresponding oncologic type

Murolo C.,Pino G.,Schenone F.,Conzi G.F.,Garibaldi C., De Lorenzi M.
Istituto Nazionale per la Ricerca sul Cancro
V.le Benedetto XV° n° 10 Genova

Sonography evaluation of secondary hepatic lesions have been assessed in 201 patients(pts) among which 101 pts had a primitive breast cancer, 75 a colon cancer, 15 a gastric cancer and 10 had a melanoma. Sonographic appearance of lesion (US pattern) has been dynamically interpreted in all these cases with periodic check-up. Suspect reports in which the ultrasound examination was doubtful were tested with fine needle aspiration under echotomographic guide (22 G) and were examined cytologically. US patterns were: diffused heterogeneous areas, anechoic areas, hipoechoic areas, calcific areas and complex areas. These patterns were correlated with corresponding oncologic type.

11.071

EVOLUATION OF CA M26 WITH CEA, TPA AND CA 15-3 IN THE POST-OPERATIVE FOLLOW-UP OF BREAST CANCER PATIENTS.

A. Nicolini, C. Colombini, *M. Ferdeghini, **G. Meucci, **L. Giuliani.

Istituto di Clinica Medica II, *Istituto di Medicina Nucleare e Istituto di Clinica Chirurgica dell'Università di Pisa.

In the post-operative follow-up of breast cancer patients (pts) CEA-TPA-CA 15-3 association showed high sensitivity but low specificity which is mainly due to the many high TPA unspecific values. Recently we reported promising data as to CA M26 and CA M29 to replace TPA. In the present study in 311 of 321 breast cancer pts followed-up with CEA-TPA-CA 15-3 association CA M26 without CA M29 was evaluated to possibly define a high sensitivity and specificity combination. So far 50 pts showed certain signs of relapse. In 45 (90%) of them and in 266 (98%) of the remaining 271 non relapsed pts also CA M26 values were measured. In metastatic pts sensitivity of CEA-TPA-CA 15-3 association was 94% and when also serum CA M26 values were considered it slightly increased to 95.5%. Sensitivity of combinations with CA M26 but without TPA i.e. CEA-CA 15-3-CA M26, CEA-CA M26, CA 15-3-CA M26 was 84.4%, 77.7% and 84.4% respectively. In non metastatic pts specificity of CEA-TPA-CA 15-3 association was 58.6% and when also serum CA M26 values were considered it was 47.5%. Specificity of combinations with CA M26 but without TPA i.e. CEA-CA 15-3-CA M26, CEA-CA M26, CA 15-3-CA M26 was 65.8%, 68% and 75.2% respectively. These data suggest that CA M26 alone is unsuitable both in addition and to replace TPA in the CEA-TPA-CA 15-3 association. In fact in the former instance sensitivity does not significantly increase while specificity strongly decreases. In the latter instance sensitivity strongly decreases in spite of the high specificity.

11.072

EFFECTS OF AN ACUTE INJECTION OF IL-2 ON ATRIAL NATRIURETIC PEPTIDE(ANP)SECRETION IN CANCER PATIENTS.

F.Paolorossi,P.Lissoni,M.Perego,M.G.Grassi,A.Ardizzoia, S.Crispino,S.Barni,G.Tancini.Divisione di Radioterapia Oncologica,Ospedale S.Gerardo,Monza(Milan),Italy.

Our previous data showed important changes in the cardiac endocrine secretion of ANP during cancer immuno therapy with IL-2 given as a 24-hour i.v.infusion.At present,it is unknown if changes in ANP simply reflect the IL-2-induced hemodynamic variations,or if they may be due to a direct action of IL-2 on ANP secretion from the heart.To solve this problem,we have analyzed the acute effect of an acute subcutaneous injection of IL-2 at 9 million IU/m2 at 8.00 a.m. on ANP plasma levels in 4 metastatic renal cancer patients,by collecting blood samples at 0,2,6 and 8 hours after IL-2 injection.No important changes in blood pressure and in renal function was seen during the endocrine study.ANP progressively increased after IL-2 with a peak at 6 hours,and ANP values at peak were significantly higher than those seen before IL-2.This datum suggests a IL-2 control of ANP.