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

11.055

DETECTION OF TENASCIN USING LABELED BC-2 IN HUMAN TUMORS

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Evaluation of tenascin (TN) distribution in human tumors has made either in vivo or in vitro using a new MAb termed BC-2 (murine IgG1). I-131 labeled BC-2 (Sp. Act. 110-236 MBq/mg) has been injected in 14 pts. with intracranial malignancies, detecting 10 high-grade gliomas (T N +ve) while 2 astrocitomas, 1 meningioma and 1 melanoma metastasis were missed. Tumor uptake of BC-2 ranged from 0.002 to 0.007% of injected dose in positive tumors with tumor/non tumor ratios as high as 75-fold. 99mTc-BC-2 has been tested in 12 pts. with gliomas, depicting 90% of lesions. In vitro studies done by quantitative autoradiography, allowed to measure levels of TN in frozen biopsies of breast tumors, demostrating high concentrations (between 30 and 240 pmoles/g) in tumors and non detectable levels in normal breast.

These studies demostrated: a) levels of TN are expressed in large amount in tumors while normal tissues do not; b) BC-2 MAb uptake was correlated with tumor-size, blood-flow supply, histologic grading and was highly specific (TN-mediated); c) in vivo tumor-targeting using labeled BC-2 is related to specific binding; d) high tumor/non tumor ratios favor the use of BC-2 in therapy.

11.056

ADRENERGIC MODULATION OF HAEMOPOIESIS AFTER SYNGENEIC BONE MARROW TRANSPLANTATION IN MICE.

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Autologous or syngeneic and allogeneic bone marrow transplantation (BMT) are increasingly used in the therapy of lymphohaemopoietic and solid malignancies and in genetic or acquired haemopoietic diseases. Beside tumor eradication, the success of such procedures depends also on the rate and completeness of reconstitution of haemopoietic and immune functions after lethal irradiation and BMT. Here we demonstrate that lymphohaemopoietic reconstitution in mice is under an adrenergic regulation. Chemical sympathectomy by 6-hydroxydopamine (6-OHDA) significantly increased the number of peripheral blood leukocytes after syngeneic BMT. The alfa-1 adrenergic antagonist prazosin but not the beta-blocker propranolol mimicked and extended the effect of 6-OHDA inducing a rapid and significant increase also of platelets, granulocyte-macrophage colony forming units in the bone marrow and mononucleated spleen cells. Such enhancing effect was mainly exerted on myeloid cells. These findings open new perspectives in hematology and in the clinical management of BMT.

11.057

EFFECT OF II-CINAMYL-PIPERAZINIL RIFAMICIN SV (T-9) ON TUMOUR CELLS

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T-9 is a newly synthesized in Bulgaria semi synthetic antituberculosis antibiotic. It is determined that Rifamicin-cinamil-derivate T-9 has marked cytotoxic effect on Erlich ascite tumour, lymphoid leucosis L1210, Lymphocytic leucosis P388 and human T-leucosis cell line (CEM). As a representative of anzamicin group, T-9 possesses high antibacterial activity, esxpecialy as a tuberculostatic agent. It possesses an invaluable biological property - combined tuberculostatic and cytotoxic effect.

11.058

TISSUE POLYPEPTIDE SPECIFIC ANTIGEN in human breast cyst fluids.

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TPS is a new monoclonal antibody that recognised the essential M8 specific epitope of tissue polypeptide antigen, useful in the management of cancer patients and assessing prognosis by indicating the tumour proliferative rate rather than the tumour burden (*Bjerkhard B et al 7th Int Conf Human Tumour Markers, Kiev URSS, Sept 1988*).In present study TPS was evaluated in 62 breast cyst fluid needle-aspirated from breast gross cyst-affected patients.These women are at greater risk (3-4 fold higher) to develop breast adenocarcinoma than normal female population.Data analyses indicated a significant increase in the mean values of TPS in cysts with Na/K ratio <2 (*apocrine cysts*) when compared to *flattened epithelium cysts* with greater electrolyte ratios ($p<0.001$). The increased TPS levels in *apocrine cyst* could represent an altered expression of cell proliferation, providing a possible explanation of why women with apocrine cysts may be at greater risk of breast cancer. Our observations suggest that TPS assay could be an additional specific tumour-marker for early detection or clinical assessment of breast neoplastic diseases.

11.059

STUDY OF IL 2 RECEPTOR, p55 AND p75 CHAINS, ON PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH HAEMATOLOGICAL AND SOLID MALIGNANCIES

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The aim of the investigation was to directly study the IL 2 R, p55 and p75 chains, either membrane-bound or soluble, on PBMC of patients (pts) with haematological and with solid malignancies and,indirectly, the same pts' PBMC ability to produce IL 2. The final goal was to support the rationale for an immune manipulation approach aiming at the cure of malignancies. Forty-seven pts were studied: 30 males and 17 females. Eight had haematological malignancies (mean age: 51.5 years, range 15-75) and 39 solid tumors (mean age: 58.3 years, range 36-79), generally in advanced stages and in 19 cases metastatic. The following assays were performed: PBMC proliferative response to PHA in presence of anti-p55, anti-p75 mAb, or both, detection by flow cytometry of membrane-bound p55 and p75 chains on PHA-stimulated PBMC, serum levels of soluble IL 2 R (s IL 2 R), release of s IL 2 R by PHA-stimulated PBMC. Our results show that in malignancies: there is a lack of IL 2 production, the membrane-bound IL 2 R, both p55 and p75 chains, are expressed normally (except in HL), there is an high serum level of s IL 2 R, and there is a normal release of s IL 2 R in culture. Therefore, no primary impairment of IL 2 R was found in solid tumors. Moreover, in our study we found no difference in any parameter studied between pts with and pts without metastases. Therefore, our results may reinforce the rationale for an immunotherapy approach with IL 2, other IL 2-inducing cytokines, like IFN, and LAK cells/TIL in pts with solid malignancies.

11.060

INFLUENCE OF EXPERIMENTAL MODEL OF NEOANGIOGENESIS

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We have used an experimental model of neoangiogenesis in corneas of rabbits. Fix cauterization with 4% of sodium hydroxide was made on cornea of both eyes of white New Zeland rabbits. Farmorubicin (Farmitalia) was administered i.v. or was poured in the right eyes in the conjunctival sac. Vascolarization began after 4-5 days. It was accounted the inhibition of neoangiogenesis, a defect of the epithelium and the destroying of the corneal's stroma. We have demonstrated that Farmorubicin inhibit neoangiogenesis in this model.