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

11.025

TUMOR NECROSIS FACTOR ALPHA (TNF-α), INTERLEUKIN-1ß (IL-1ß) AND INTERLEUKIN-6 (IL-6) SYNTHESIS IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMNC) STIMULATED IN VITRO AND IN VIVO BY PROTEOLYTIC ENZYMES.

L. Desser, M. Macheiner, C. Oismüller, E. Kokron and A. Rehberger.

Proteolytic enzymes (Bromelain and Papain) stimulate in vitro the synthesis of TNF-α, IL-6 and IL-1ß in PBMNC isolated from blood of healthy donors.

TNF-α was determined in the cell-supernatant by a bioassay with the cell line L929 by a radioimmunoassay (RIA) and by Westernblot. I1-1ß and IL-6 concentration in the supernatants were measured by RIA.

The synthesis of these cytokines depends on time of culture and on enzyme concentration. The enzyme-induced TNF-α production as well as the IL-6 and IL-1 production in PBMNC can be synergistically stimulated by IFN-α and -gamma; yet, IFNs alone do not induce TNF-α production in vitro. However, TNF-α, IL-1 and IL-6 synthesis is inducible by IFN-gamma when PBMNC are obtained from donors to whom the proteolytic enzymes had been administered 1-3 hrs before.

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11.026

Variations in serum alkaline DNase activity have preditive value in the monitoring of clinical response to cancer therapy, B.Dewez, A.Karaoglou, M.Lans, H.Taper, M.Roberfroid. UCL 7369-1200 Bruxelles.

Numerous histochemical studies have shown that alkaline DNase ativity is inhibited in cancer cells and reactivated by active chemotherapy. Alkaline DNase is present in human serum. When measured at 50 C, a temperature which inactivates a thermolabile serum inhibitor, its activity (SADA) varies largely from person to person but is stable in time. In patients with miscellaneous cancer, an efficient tumor treatment produces a decrease in SADA (5-10 days), whereas SADA level remains unchanged if therapy is inactive. Furthermore, the regression of tumors is accompanied by an increase of SADA level and patients with complete remission have an increased SADA level which stays stable during months and years of follow-up. In such patients, a significant decrease in SADA indicates the reappearance of the disease a few weeks or a few months before clinical signs are recorded. The mechanisms of modulation of SADA are at present unknown. Our present hypothesis is that actin, the major component of cytoskeleton could be one modulator of SADA during cancer pathology.

11.027

QUANTITATIVE ANALYSIS OF MITOTIC CELLS BY ANTI-AF-2 MOABS.

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A novel protein related to cell cycle dependent alterations of chromatin structure, denominated AF-2, has been recently described (Pfeffer and Vidali (1991) Exp. Cell Res. 193: 411-419). We have further characterized this protein on a cell by cell analysis during the cell cycle by list mode flow cytometry (FCM). We could confirm and unambiguously prove that AF-2 antigen is accessible to specific monoclonal antibodies only in mitotic and post-mitotic G1 phase cells. Using AF-2/DNA FCM, M-phase cells were clear cut separated from G2-phase cells. This suggests that anti-AF-2 monoclonal antibodies may be used to quantitate the mitotic index and isolate mitotic cells by FCM. This hypothesis was confirmed using different human cell types, after treating the cells for different doses and times with colcemid, and comparing the results obtained by the AF-2/DNA FCM methodology with those obtained by two other independent methodologies, i.e., microscopic counting of M phases according to morphology and to scattering properties by FCM (Giaretti et al. (1989) Exp. Cell Res. 182: 290-295).
Using mixed cell populations, we have correctly detected as few as 0.08% mitotic cells. Data obtained by using anti-AF-2 and anti-Keratin monoclonal antibodies and counterstaining with propidium iodide indicate that the selective evaluation of the mitotic index of epithelial cells in a heterogeneous cell population is feasible. Work is in progress using human tumor biopsies.

11.028

Anti-tumour Immune Responses Induced in Colorectal Cancer Patients by Immunization with Human Monoclonal Anti-idiotypic Antibody.

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A human monoclonal anti-idiotypic antibody which mimics a colorectal tumour associated antigen, gp72 has been developed. It is currently being tested for its potential in stimulating cellular anti-tumour immune response in a phase I trial of advanced colorectal cancer patients. 5/6 patients showed a blastogenic response to gp72 positive tumour cells and 4/6 showed peak values of IL-2 of at least 5 units/ml in their serum. An autologous blastogenesis immune responses was observed in the one patient in whom it was possible to obtain tumour tissue. Clinical and laboratory investigations have revealed no evidence of antibody related toxicity. These results suggest that cellular anti-tumour immunity can be induced in patients by a human monoclonal anti-idiotypic antibody without exogenous carrier determinants.

11.029

Influence cellular DNA content on survival in advanced ovarian cancer

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Our research of the prognostic value of influence cellular DNA is based on 24 pacients with advanced ovarian cancer. The flow cytometric analysis of cellular DNA showed 12 pacients with diploid tumor and 10 with aneuploid tumor. The 3-years survival of pacients with diploid tumor is 27,27 %, of pacients with aneploid tumor - 23,07 %. The survival of pacient with diploid tumor is higher than survival of patient with aneploid tumor.

11.030

Diagnostic method with marked Ca-125 for detecting metastasis in advanced ovarian carcinoma

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Detection of metastasis in patients with advanced ovarian cancer by noninvasiv methods is possible with markers Ca-125 in serum and more exactly by marking the Ca-125 due to visuality of metastasis. The 8 patients are scanned. By 3 of them it was not necessary to effect second surgery because metastasis ad portam hepatis were discovered.
This contemporary diagnostic method has an important role in diagnostics of ovarian carcinoma.