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1.001

METHOXIBUTROPATE-INDUCED RESISTANCE TO YOSHIDA ASCITES TUMOR CELLS.

Ainis T., Cavallaro A., Bottari C., Fimiani V.
Inst. of General Pathology, University of Messina, Italy

Sprague-Dawley rats i.p.-administered with 20/mg/Kg/day of Methoxibutropate for two weeks 24 hours after i.p. implantation of 10^3 Yoshida ascites sarcoma cells, showed a highly significant survival (90%) compared to control animals (0%). Since the drug has not any antitumor effect itself, we observed its action on some peritoneal macrophage activities of rats i.p.-treated with the drug. The following parameters were evaluated: phagocytosis and phagocytic index of zymosan particles, O_2^- production. Results show that after 3 days of drug administration there is a significant effect on macrophage recruiting in the peritoneal cavity , on the O_2^- production, on the phagocytosis and phagocytic index. The increased resistance to the tumor cells can be due to the action of Methoxybutropate that induces simultaneously the numerical and metabolic increase of peritoneal macrophages, thus hinding the inhibiting activity of tumor cells.

1.002

Cellular immunotherapy in ovarian cancer: Effect of multiple epitopes of 14C1 antigen recognised by human antibodies derived from ovarian cancer patients

F. Al-Azzawi, Senior lecturer and consultant in Obstetrics and Gynaecology, University of Leicester, Leicester Royal Infirmary, Leicester, U.K.
G. Gallagher, Lecturer, Department of Surgery, University of Glasgow, Glasgow Royal Infirmary, Glasgow, U.K.

EBV-transformed B-cells derived from enlarged lymph nodes of ovarian cancer patients produced human antibodies which bind a membrane associated antigen 14C1. These antibodies recognised three discernible epitopes of the ovarian cancer associated antigen. Evidence show that this antigen possess a transmembrane signalling function. These antibodies, IgG1k were deployed in an immunotherapy protocol, in ovarian cancer model, using an effector cell (U-937) and found to promote the in vitro killing of ovarian cancer cell lines.

1.003

MONOCLONAL ANTIBODY ENGINEERED T LYMPHOCYTE SELECTIVITY FOR HUMAN OVARIAN CANCER: PRECLINICAL AND CLINICAL RESULTS. R.L.H. Bolhuis[1], S.H. Goey[2], J.W. Gratama[1], G. Stoter[2]. Department of Immunology[1] and Medical Oncology[2], Dr. Daniel den Hoed Cancer Center, Groene Hilledijk 301, Rotterdam, The Netherlands. T lymphocytes can be triggered for cytokine production and cytolysis by mAbs, specific for lymphocyte activation sites. Bispecific mAbs (bs-mAbs) have been produced which recognize the T cell receptor complex (CD3) on the one hand and ovarian carcinoma tumor associated antigens (TAA) on the other. This bridging and complexing of the lymphocytes and cancer cells and their cell surface structures respectively result in tumor cell kill. After the lymphocytes detach from the lysed tumor cell they become inactivated. The mechanisms of inactivation as well as reactivation will be discussed. Patients with lesions of less than 2 cm (after surgical debulking) are eligible for a Phase I-II study. Lymphocytes retargeted with bs-mAbs + IL2 are administered daily for 5 days after which a restperiod of 2 weeks is followed by a second cycle of treatment. Meanwhile 7 patients have been treated. Our preliminary laboratory and clinical results will be presented.

1.004

Transforming growth factor-beta-1 and interferon-beta are secreted by 3LL tumor cells and are chemotactic for lymphokine-activated killer (LAK) cells in vitro .

L. Bouwens, N. Delens, P. De Baetselier [1] , E. Wisse , Laboratory of Cell Biology and Histology, and Laboratory of Cellular Immunology (1), Free University Brussels (V.U.B.), Brussels, Belgium.

LAK cells, generated by culturing C57Bl6 murine lymphocytes with interleukin-2, were tested for their in vitro migratory capacity in a modified Boyden chambre assay. Between 15 and 30% of the LAK cells migrated into the bottom compartment in this assay within 4 hr, across polycarbonate membranes with pore size of 3 µm. This migration was strongly enhanced , with up to 75% of the cells that migrated (average 1.5x more), when serum-free conditioned medium (CM) from 3LL carcinoma cells was added to the bottom compartment. Checkerboard analysis revealed that this effect from the CM was due to chemotaxis and not chemokinesis. A monoclonal antibody (mAb) neutralizing TGF-b1 was found to inhibit about 60% of the chemotactic effect of the 3LL-CM. A mAb neutralizing IFN-b inhibited about 40% of the chemotactic effect. A cocktail of both antibodies completely inhibited the chemotactic effect of 3LL-CM on LAK cells.

1.005

EFFECTS OF MITOMYCIN C ON CIRCULATING LYMPHOCYTES IN PATIENTS WITH MALIGNANCY. Cartei G*, Ceschia V*, Bardus P*, Vigevani E*, Cartei F^, Sanzari M', Sibau A*, Clocchiatti L*, Sala PG°. *Div Medical Oncology Cancer Center, °Clinical Chemistry-Biology (CCB), Udine General Hosp; 'CCB Geriatric Hosp Padova; ^Radiotherapy Inst Univ Pisa; Italy.

43 pts aged 40 to 82 yrs ($\bar{x}$=62, median (m)=62), 20 M, 23 F, 36 pretreated, received 10 (50 % cases) to 20 mg/mq i.v. MMC every 3 weeks. After 2nd cycle MMC was continued unless toxicity or progression. Cycles were 130, $\bar{x}$=3, m=2 per pt. Full blood counts, CD3, CD4, CD8, CD24, CD16, Leu11+, Leu7+ cells tested on blood samples taken 08 to 09.30. Progressive mild anaemia and leukopenia were observed during cycles; Δ % (fall) at the 5th cycle was: lymphocytes 29*, CD3 34*, CD4 38*, CD8 8**, CD4/CD8 19^, CD16 42*, Leu7+ 17, CD24 8 (*P< 0.001, **P< 0.025, ^P< 0.0125). MMC exerts a significative depression on some lymphocytes subsets.

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KATE CRANNAGE, J. LAWRY, R. C. REES, B.W.HANCOCK, C.W.POTTER. Institute for Cancer studies, University of Sheffield Medical School, Sheffield U.K.

Phenotypic and Cell cycle analysis of activated Peripheral blood mononuclear cells (PBMC).

Previous reports have detailed enhanced expansion and mediation of non-MHC-restricted cytotoxicity by PBMC activated in the presence of IL2 and OKT3.

Phenotypic and cell cycle analysis of short-term cultured PBMC was determined by flow cytometry (FACS). Results indicate that when PBMC are activated by IL2 alone, the $CD16^+$ and $CD56^+$ cells proliferate and move to the G2/M part of the cell cycle. The T-cells progress slowly, if at all through the cell cycle. In contrast, when cells PBMC are stimulated with IL2 and OKT3 in combination, the T-cells progress through the cell cycle as do the $CD16^+$ and $CD56^+$ cells, but the latter decrease in cell number. Expression of CD25 (IL2 R-α subunit), is greatly enhanced when PBMC are activated in the presence of IL2 and OKT3 in combination as compared with IL2 alone. These results indicate that IL2 activation stimulates LAK cells. IL2 and OKT3 activation stimulates T cells, which are not the mediators of non-MHC-restricted cytotoxicity.