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1.031

CYTOKINES ON PBL FROM COLON CANCER PATIENTS

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In order to determinate the efficiency of the biological response modifiers on the amplification of cytotoxic cells in colon cancer patients, the proliferative and cytotoxic effects of combinations of cytokines were assessed on PBL from colon cancer patients. IL-2, IL-2+IL-4, IL-2+antiCD3, IL-2+IL-4+antiCD3 were tested on proliferation and cytotoxic activity of PBL by chromium-51 release assay. The preliminary data shows that the stimolation with IL-2+anti-CD-3, with or without IL-4, seems the most effective both for having the maximal proliferation and for a better potentiation of the cytotoxic activity of MHC restricted populations.

1.032

ANALYSIS OF CELLULAR MECHANISMS OF IMMUNITY TO NATIVE TUMOR CELLS AND WITH THE PHENOTYPE OF MULTIDRUG RESISTANCE BEFORE AND AFTER THERAPY

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We have shown a stimulating effect of glucosomuramyldipeptide, lipopolysaccharide and their combination on the cytokine production and the cytotoxicity of various killer cells. We have detected differences in the individual sensitivity to the therapy of the organism and of tumors of different genesis. Those differences seemed to depend on the level of the endogenic production of cytokines, prostaglandins and on the proportoin of tumor-specific suppressors and killer cells subpopulation. Heterogenety of specific antitumor T-killers has been demonstrated expressed in the phenotype, sensitivity to suppressor and recombinant interleukin-2,as well as in the conditions for the in vivo and in vitro generation.

1.033

NATURAL CYTOTOXIC ACTIVITIES IN SELECTED RESISTANT OR SENSITIVE MICE TO TWO-STAGE SKIN CARCINOGENESIS.

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The aim of this study is to selecte a resistant (Car-R) and a sensitive (Car-S) line of mice to two-stage skin chemical carcinogenesis. DMBA (9,10-dimetil-1,2-benzoantracene) is the initiator and TPA (12-O-tetradecanoilforbolo-13-acetato) the promoter. The selective character chosen for the assortative mating is the number of tumors at the end of the promotion period. The progressive response to selection shows that the characters investigated are subject to polygenic control. At F5 the tumor incidence is the following: 5% Car-R, 83% Car-S. Preliminary results show that the cytotoxic activity of NK cells and macrophages is higher in the Car-R than Car-S mice suggesting a role of the immune system in the polygenic control of chemical carcinogenesis.

1.034

INVOLVEMENT OF THYROTROPIC/THYROID/THYMIC HORMONES IN THE SEQUENTIAL ACTIVATION OF NK CELLS.

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Natural Killer (NK) cells are sensitive to various lymphokines and hormonal factors. Recent studies of our laboratory were aimed to verify the reversibility of the low NK activity in cells from old mice by in vitro administration of thyrotropic (TSH)/thyroid (T3)/thymic (TH) hormones. In vitro administration of thymulin increases the basal activity of NK cells from old mice, whereas it does not modify IFN-boosted cytotoxicity. Administration of thyrotropic/thyroid hormones do not affect basal NK activity while they influence the responsiveness of old NK cells to lymphokines, being TSH and T3/T4 able to specifically increase the IL-2 boosted and the IFN-induced NK activity respectively. These findings indicate that thymic/thyrotropic/thyroid hormones act on different steps of NK differentiation and/or activation.

1.035

HUMAN AUTOLOGOUS MELANOMA-REACTIVE T HELPER LYMPHOCYTE CLONES. M. Radrizzani, P. Squarcina, A. Longo*, G.B. Ferrara*, G. Parmiani, G. Fossati. Istituto Nazionale Tumori of Milan - *Istituto Nazionale Tumori of Genoa, Italy.

CD3+ CD4+ clones derived from the infiltrate of a s.c. melanoma (Me) metastasis (Me9742/2) were analyzed for proliferative response to Me9742/2 and to a different autologous metastasis, Me9742/1, both expressing HLA-DR7. 26/82 clones were stimulated (SI > 10) by both Me9742/1 and Me9742/2, 5/82 clones by Me9742/2 only and 0/82 by PBL9742. The response of 12/12 clones to Me9742/2, but not to IL-2 (120 IU/ml), was significantly inhibited by anti-CD3 and anti-HLA-DR MAb. Specificity analysis showed that 4/12 clones (including clone #31) recognized Me9742/1, Me9742/2, 4/5 allogeneic HLA-DR7+ Me, 0/6 allogeneic Me expressing different HLA-DR alleles. Stimulation with Me9742/2, but not with Me10538 (HLA-DR4), significantly augmented the expression of IL-2 receptor (CD25) on the lymphocyte surface (clone #31: mean fluorescence intensity from 75 to 398 in 24h) and induced production of IL-2 (clone #31: 8.9 IU/ml at 4h). These data suggest that T helper clones such as #31 recognize through their TCR/CD3 complex, in an HLA-DR-restricted manner, a structure expressed on Me9742/1, Me9742/2 and some allogeneic Me.

1.036

INHIBITION OF NK AND LAK CELLS LYSIS *IN VITRO* AFTER EXPOSURE TO 50-Hz SINUSOIDAL MAGNETIC FIELDS.

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In recent years biological effects of extremely-low-frequency (ELF) electric and magnetic fields have become an important scientific issue, expecially for the reported possible links between exposures and increased cancer risk. Fresh human PBL were exposed to a 50-Hz sinusoidal magnetic flux density ranging from 0.1 to 10 mT. Cultures of PBL were also exposed to the same fields, both in media containing, or not, PHA, Con A, A23187, PMA, and rIL-2. NK and LAK activities were tested in a 3-h ^{51}Cr-release assay of several prelabelled NK- and/or LAK-sensitive allogeneic cell lines. The experimental findings suggest that exposures to 50-Hz magnetic fields do not affect fresh human PBL. On the contrary, a significant (up to 70%) inhibition of cytotoxic activity has been observed in activated PBL after 70-h exposures to magnetic flux density of 2.5 mT. These results suggest mechanisms by which 50-Hz magnetic fields could affect the function of NK and LAK cells.