Symposium no. 1: Effector Cells against Cancer

1.013

HOMOTYPIC INTERACTIONS REGULATE THE LYTIC ABILITY OF CD3+ AND CD3- LAK EFFECTORS

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Adhesion molecule-mediated interactions are known to promote T-cell proliferation. Here we show that the cytolytic functions of CD3+ or CD3- cells can be regulated by adhesion molecule-mediated homotypic interactions. Pretreatment of effectors with Ab to LFA1 and LFA3, or to ICAM1, downregulated or, respectively, upregulated the cytolytic ability of CD3- LAK cells or CD3+/CD8+ cytolytic clones against tumor targets. To avoid interference on the effector to target cell adhesion, targets were selected according to their negativity for the complementary ligands, e.g. anti-LFA1-treated effectors were tested against ICAM1- targets. Therefore, interactions occurring among cytolytic effectors are able to modulate the lytic ability of the effectors. AIRC fellowship to R.G. and AIRC grants to C.E.G. and A.V.

1.014

GENERATION OF TUMOR SPECIFIC T-LYMPHOCYTES FOLLOWING INTRASPLENIC IMMUNIZATION WITH AN ALTERED MURINE LEUKEMIA VIRUS ANTIGEN DEFINED BY SYNGENEIC ANTIBODY

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Treatment of murine tumor cells with mutagens, such as the triazene derivative DTIC, generates cell variants expressing new, highly immunogenic antigens not present on the parental tumor. Using specific antibodies, we have recently identified an abnormal MuLV gp70 antigen in one such "xenogenized" lymphoma (L5178Y/DTIC). In the present study, we found that the intrasplenic immunizazion of syngeneic mice with nitrocellulose paper strips containing the abnormal gp70 protein determined an L5178Y/DTIC tumor specific T-cell mediated response. In particular, we observed a) an increase of $CD8^+$ precursors expressing cytotoxic activity in vitro and b) the development of a delayed type hypersensitivity response in vivo to L5178Y/DTIC cells. This indicates that both $CD4^+$ and $CD8^+$ cells are induced by immunization with a tumor transplantation antigen induced by chemical mutagenesis.

1.015

MITOGENIC STIMULATION OF HUMAN PBMC BY PHA INCREASES THEIR SUSCEPTIBILITY TOWARD KILLING BY SPERMINE-FCS

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We investigated the effect of polyamine spermine on viability of human peripheral blood mononuclear cells, PBMC, grown in RPMI 1640 medium (supplemented with L-glutamine and antibiotics) in the presence of: a) heat inactivated 10% FCS; b) 10% FCS and 1% of phytohemagglutinin, PHA; c) 10% of human serum, HS; d) 10% of HS and 1% of PHA. Results obtained indicate that spermine (100 μM) in the presence of 10% FCS decreases PBMC viability to 62%, and that stimulation of PBMC by PHA changed the PBMC viability to 32%. In the presence of human serum [c-d] the viability of PBMC was slightly affected (85% and 81%). In the presence of FCS [a-b] the lower PBMC mitogenic response to PHA stimulation correlates with the reduced viability of PBMC.

When spermine was lacking from the growing medium the mitogenic response of PBMC stimulated by PHA in the presence of 10% FCS is more than twice higher than in the presence of 10% HS. This indicates that an additional PHA-FCS PBMC stimulation occurs which could be particularly sensitive toward spermine-FCS product action.

1.016

STUDIES OF EFFECTOR CELL-MEDIATED ANTITUMOR IMMUNITY IN SQUAMOUS CELL LUNG CANCER

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The studies of parenchymal tumor lymphocytes (PTL) in cryostat sections give valuable insight into the notion of effector links of immunity in lung cancer.To evaluate PTL subpopulations in 56 patients with squamous cell lung cancer MoAbs to antigens of T-, B-lymphocytes, monocytes, epithelial and non-lineage antigens (CD1,4,5, 7,8,19,22, 11a,11b, 15,10,45,38,RFB-1,HLA-1,HLA-DR,CEA, Egp-34, etc.) were used. PTL included T-cells CD-7+ and CD8+ in 100% of cases, CD4+ cells in 55%, and CD11b- in 80%. Activation antigens HLA-DR and CD38 were frequently identified. In 30% of cases PTL expressed CD-10 antigen. The subpopulation ofCD-10+ lymphocytes in blood of lung cancer patients was usually negative (about or below 1%: T cells in double staining). T-cell infiltration grade of a tumor was related to HLA-1 or CEA expression on lung cancer cells, but not to the morphological form of disease.

1.017

LGL and NKA levels in patients with malignant lymphomas during diagnosis and treatment

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We studied changes in peipheral blood LGL in 100/3 patients with non-Hodgkin's disease during diagnosis and treatment.We revealed regularities in changes of theses parameters depending on morphologic type of pathology under the influence of cytostatic therapy. Findings were obtained as to the relation between peripheral blood lymphocytes and EKA of lymphomas grade in primaries and in patients following completion of treatment and in remission.The study revealed that in healthy individuals(110 pers.)LGL content was $5.2\pm0.3\%$ and $0.354\pm0.014\cdot10^9$ absolute units/litre. Evaluation of LGL and NKA in patients with lymphoproliferative disorders can be used as an additional diagnostic criterion.

1.018

MODULATION OF THE ACTIVITY OF CYTOTOXIC CELLS

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NK cells and CTL are the main cytotoxic cells against tumors. Our findings show decreased NK cell activity in breast cancer patients. Investigation of the effect of sera on NK cell activity of these patients indicates that autologous serum inhibits NK activity when compared to FCS but less than healthy sera while sera of breast cancer patients with advanced disease and metastases gives the most profound inhibition of NK cell activity of patients and healthy controls. However, in vitro treatment, especially with IL 2 potentiates NK cell activity. As cytotoxic cells kill their targets mainly by perforin we investigated in healthy human PBL the presence of the actual protein perforin with a novel mAb delta G9 synthesized against human perforin and found that in vitro treatment especially with IL 2 doubles the number of perforin positive cells. As perforin synthesis in NK cells seems to be IL 2 independent, we consider alternate mechanisms of NK cell activation by IL 2.