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1.043

Tumorigenicity of Ad12 transformed cells is independent of class I MHC protein expression.

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The tumorigenicity of adenovirus 12 (Ad12) transformed cells has been attributed to the low levels of class I MHC proteins they express. These levels might be below the threshold critical for recognition by cytotoxic T lymphocytes which are believed to be involved in tumor-cell immunosurveillance. We used a quantal assay of tumorigenicity to define the role played by class I protein expression in the tumorigenicity of Ad12 transformed BALB/c mouse cells. Cells expressing either low (endogenous) or high (transfected) levels of class I proteins were injected in syngeneic BALB/c or allogeneic adult mice, or in mice expressing the same BALB/c MHC haplotype but different genetic background (DBA-2, BIO.D2). Low class I protein expressing cells were highly immunogeneic in tumor protection assays and were rejected as allografts. High class I protein expression increased rather than abrogate tumorigenicity. In contrast, tumorigenicity was markedly reduced in DBA-2 and BIO.D2 mice. These data demonstrate that tumorigenicity of Ad12 transformed BALB/c cells is dependent on factors other than class I MHC protein expression.

1.044

IL-3 DEPENDENT, NON NK-ASIALO-GM-1 POSITIVE CELL LINE WITH IN VIVO ANTITUMOR ACTIVITY. L. Strzadala, E. Ziolo, Inst. Immunology Experimental Therapy, 53-114 Wroclaw, Czerska 12, Poland

In previous studies, we found that antimetastatic activity can be exerted by splenic adherent $ASGM1^+$ cells that do not exert NK cytotoxicity. We attempted to develop $ASGM1^+$ cell line from adherent spleen cells (B6C3F1 mice). Heterogenous adherent spleen cell population can grow on collagen covered plates in 20% FCS Iscove medium, but $ASGM1^+$ cells isolated from whole adherent population by panning method do not grow. Isolated $ASGM1^+$ cells were cultivated with the addition of: Il-1, Il-2, Il-3, Il-4 and GM-CSF. It appeared that with addition of Il-3 (A-3 line) isolated $ASGM1^+$ cells could be cultivated for more than 3 months and could be frozen and refrozen. FACs analysis revealed that A-3 cells are: $ASGM1^+$ (90-96%), FcR^+ (60-80%), Ia^{R+} (43-60%), Ig^-, $Mac\text{-}1^-$, $THY1.2^-$, $CD3^-$, $CD4^-$, $CD8^-$. A-3 cells are not endowed with NK cytotoxicity. In preliminary exeriments we found that s.c. injection of 10^5 A-3 cells + 10^6 LL_2 Lewis lung carcinoma cells results only in 44% of tumor takes (4 out of 9 mice) comparing to 100% in control.

1.045

EVALUATION OF THE SAFETY OF rIL-2 AND rIL-2 PLUS 5-FU IN THE ADJUVANT TREATMENT OF GASTRIC CANCER.

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Eight patients recieved either rIL-2 (Eurocetus BV, Amsterdam) alone or rIL-2 plus 5-FU within 28 days of undergoing potentially curative surgery for stage II and III gastric cancer.

Patients received rIL-2 at 18 x 10^6 IU/m²/24 hours for 5 days, after 6 days rest, patients then received either an additional rIL-2 infusion for 4½ days or 5-FU infusion at 12.5mg/kg/24 hours for 4½ days. This one treatment cycle was repeated after a 3 week rest.

All patients displayed rIL-2 related toxicities, including fever, nausea, anorexia and transient disturbances of renal and hepatic function. Only two episodes of WHO grade 3 toxicity occurred, both of which promptly responded to temporary interruption of rIL-2 infusion.

The rebound lymphocytosis usually seen 48 hours following completion of rIL-2 infusion was not significantly modified by the 5-FU infusions.

This pilot study has demonstrated that the administration of rIL-2 and rIL-2 plus 5-FU to cancer patients recovering from major surgery setting is safely tolerated and may provide the basis for larger studies of adjuvant immunotherapy for patients with cancer.

1.046

CHARACTERISATION OF LYMPHOCYTIC INFILTRATE IN SKIN BIOPSIES FOLLOWING rIL-2 THERAPY. **S.S. Ubhi, S. Spicer, T. Horsburgh, P.S. Veitch, P.R.F. Bell**
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To determine the significance of rIL-2 induced skin changes 3mm punch biopsies were taken from the skin of 9 cancer patients before and on the last day of constant infusion rIL-2. Skin infiltrate was characterised with a panel of monoclonal antibodies using an APAAP technique. Skin from normal healthy volunteers was used as controls. Results are expressed as mean number of positively staining cells per unit area.

	Leu Common	CD3(%)	CD4(%)	CD8(%)
Controls (n=8)	21	10(48)	13(62)	5(24)
Patients pre rIL-2				
≥Stable Disease (n=3)	31	13(42)	16(52)	3(10)
Progressive Disease (n=6)	11	6(55)	9(82)	4(36)
Patients post rIL-2				
≥Stable Disease	22	19(86)	15(68)	2(9)
Progressive Disease	10	6(60)	8(80)	3(30)

Patients with ≥SD had a heavier cellular infiltrate than controls and patients with PD. Following rIL-2, in patients with ≥SD the proportion of CD3+ve cells and CD4/CD8 ratio increased. However, in patients with PD rIL-2 therapy did not alter the number of CD3+ve cells or the CD4/CD8 ratio. This work suggests that the ability of CD3+ lymphocytes to infiltrate a solid organ may be an important factor in patients who develop tumour responses to rIL-2.

1.047

DISTRIBUTION AND PHENOTYPE OF POTENTIALLY CYTOTOXIC TIL IN LUNG CARCINOMA

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Tumor infiltrating lymphocytes(TIL) constitute host reaction to growing tumor. The aim of this study was to examine the distribution of TIL, their phenotype linked to Ag recognition and effector function in lung carcinoma. Cryosections of 20 surgical samples of the tumor in question were subjected to sensitive APAAP immunohistochemi- stry, using a panel of monoclonal antibodies vs. several lymphocyte epitopes. Positive cells were evaluated in relation to tumor area, its vicinity, blood vessels and to tumor stroma. It was found that the most common phenotype of TIL in lung cancer was CD2+,CD16+, followed by CD3+ CD8+. Few cells expressed TCR-1. Positive cells were mostly accumulated in the tumor stroma and relatively few penetrated tumor itself. It is concluded that potentially cytotoxic cells are present at tumor site, but their ability to invade tumor is limited.

1.048

TUMOR REGRESSION UNDER THE INFLUENCE OF IL-1 PRODUCED BY ONCOGENE-TRANSFORMED FIBROBLASTS.

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Anti-tumor immune responses are rarely efficient, supposedly due to a deficit in the activation of helper T cells. Supply of helper factors by the tumor itself may be a strategy to circumvent this deficiency. Oncogene-transformed fibroblasts (oFB) which spontaneously or after activation with conditioned medium and lipopolysaccharide expressed IL-1, regressed in the syngeneic, immune-competent host. Frequencies and proliferation rates of helper T cells were significantly increased after in vivo immunization with IL-1-expressing oFB, oFB-associated IL-1 delivering the costimulatory signal. As a consequence of activation of helper T cells, maturation / expansion of CTL has been observed. In addition, tumor-associated IL-1 initiated maturation of antigen-presenting cells. It is concluded that IL-1 expression by oFB significantly improved an efficient activation of helper T cells and supported activation of antigen presenting cells.