Symposium no. 4: Biology of Tumour Invasion and Metastasis

4.019

Reduced adhesion to endothelial cells and reduced metastatic ability of H-2K^b transfectants

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Transfection of murine metastatic cells (derived from B16 melanoma) with a syngeneic H-2K^b gene strongly impaired their experimental metastatic ability. Two properties of H-2K^b transfectants correlated with their lower metastatic ability: they were slightly more immunogenic than control clones (transfected with pSV$_2$Neo alone) and they showed a decreased homotypic adhesion (De Giovanni *et al.*, Int. J. Cancer., 48: 270).

To investigate whether other non-immunological phenomena involved in the metastatic process were influenced by H-2 gene transfection, we studied the adhesion of H-2K^b transfectants to endothelial cells *in vitro* and the expression of integrin molecules.

The adhesion of H-2K^b transfectants to murine endotheliomas and to human HUVEC cells was significantly lower than that of control clones. Antibodies directed against VCAM-1 and the integrin subunit β_1 inhibited the adhesion of control clones to endothelial cells, thus suggesting that VLA-4 and VCAM-1 molecules could be involved in the adhesion of these cells to the endothelium.

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4.020

DECREASED ACIDITY OF THE VACUOLAR APPARATUS IN EHRLICH ASCITES TUMOUR CELLS. Paolo Dell'Antone+, Marcello Cantini+, Gianni Miotto* and Rina Venerando*, Institute of General Pathology+ and Department of Biochemistry*, University of Padova, Italy.

Acidic cytoplasmc vesicles were investigated in Ehrlich ascites tumour cells, and for comparison in rat hepatocytes and thymocytes, by spectrophotometry and fluorescence microscopy, using as probe the weak base acridine orange (1). A lower pH gradient-driven dye uptake was recorded with the Ehrlich cells, when assayed shortly after cell harvesting; the uptake increased (2-3-fold) in cells incubated for 3-4 hours in a simplified saline. As previously suggested (2), the present results indicate that in proliferating Ehrlich cells the average vacuolar pH is higher than in the quiescent cells, in agreement with recent findings (3) concerning the lysosomal pH of transformed fibroblasts. 1) P. Dell'Antone, J.of Cell Physiology (1989) 139, 78-82. 2) P. Dell'Antone and M.Cantini, Third European Congress of Cell Biology (1990) Florence, Italy. 3) L.W. Jiang et al. J. Biol. Chem. 265, 4775-4777 (1990).

4.021

TEST-SYSTEM FOR INVESTIGATION HUMORAL FACTORS (HF) OF TUMOR ACTION IN VIVO.

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We have developed a test-system for studying of action HF of tumors in vivo. It has been shown that HF can increase or decrease rate of tumor growth and cause growth of metastasis in vivo. It has been shown that HF can protect tumor cells from defence system of host. HF increase the number of animals with tumors from 8% in control group up to 100% in experimental group after transplantation i.m. $20 \cdot 10^5$ Ehrlich tumor cells into mice. HF decrease the life span from 54,9 ± 3,4 to 12,0 ± 1,4 days ($p < 0,05$) after i.m. transplantation $1 \cdot 10^6$ Ehrlich tumor cells into mice. HF of Ehrlich tumor cells decrease rate tumor growth Lewis carcinoma on 30% during 3 weeks. It can be suggested that this test-system modelise phenomen of concomitant immunity too. This test-system is usefull to study mechanisms of tumor growth in vivo.

4.022

FACTORS INFLUENCING MONOCLONAL ANTIBODY LOCALISATION IN TUMOUR METASTASES.

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To investigate critical factors influencing monoclonal antibody localisation, we have adapted a single rat sarcoma, HSN, for preferential growth in 3 major sites of metastasis; lung, liver and lymph nodes, and have raised a panel of syngeneic rat monoclonal antibodies to overlapping epitopes on a stable cell surface antigen. Using this model, we have determined that monoclonal antibody localisation is limited by increasing tumour mass (due to decreased blood flow), and is far less in lung metastases than liver tumour deposits due to significant differences in vascular permeability at these two sites. Strategies to optimise monoclonal antibody localisation in metastases must therefore take into account these topographical and physiological idiosyncracies.

4.023

INHIBITION OF LOCAL AND DISSEMINATED TUMOR GROWTH BY IL-2

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We have investigated the ability of endogenously secreted (following retroviral transfer and expression) or exogenously administered human IL-2 to induce effective immune responses against marginally immunogenic, highly malignant rodent tumors. Clones of HSN rat sarcoma secreting varying levels of IL-2 were rejected at a rate proportional to their cytokine production at s.c. sites and in lungs and liver; spontaneous haematogenous and lymphatic metastatis was also inhibited. The cells were shown to be susceptible to IL-2 stimulated LAK and NK activity in vitro, and to moderate doses of IL-2 administered in vivo.
Similar results were obtained in a mouse tumor system, and no systemic toxicity was encountered.

4.024

EFFECT OF LOCAL TUMOR IRRADIATION AND r-IL-2 ON LUNG METASTASES IN THE RAT

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The effect of local tumor irradiation and multiple doses of recombinant IL-2(r-IL-2)given systemically on metastases formation in the lung of an anaplastic carcinoma (ACA) in the rat Y59 was studied. Animals receiving single therapies(local irradiation or r-IL-2) developed much less metastases than their respective control. However, in those receiving combination of local tumor radiotherapy and r-IL-2 either after or before irradiation, tumor metastases formation in the lung was more reduced. The number of leukocytes as well as lymphocytes in this treated group was elevated. Lymphocytes from animals receiving combined therapy were more tumorocidal than cells from control group as tested in ^{51}Cr releasing test. In conclusion, combined radioimmunotherapy used in this tumor system was more benefitial in controling metastasis formation than any therapy alone.