4.037

ANALYSIS OF B-LYMPHOMA GROWTH, STABILIZATION AND REGRESSION. A MATHEMATICAL MODELING FOR THE INTERACTION BETWEEN CYTOTOXIC LYMPHOCYTES AND TUMOUR CELLS.

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A mathemical model of the CTL response to the non-exponential growth of an immunogenic tumour has been presented. It has been shown that the model describes satisfactorily the kinetics of growth and regression of B-lymphoma BCL1 in the spleen of mice, which are chimeric with respect to the major histocompatibility complex (H-2b-->H-2d). Numerical estimation of the parameters describing processes which cannot be measured in vivo have been derived. It is predicted that the course of the tumour process and its clinical manifestation has a recurrent profile with a three-four-month cycle. According to the model the limited growth of the tumour BCL1 and its transition into dormant state is associated with a high rate of accumulation of the CTL in the tumour, rapid lysis of lymphoma cells and the inability of tumour cells to suppress the affector functions of cytotoxic lymphocytes.

4.038

Chromosomal mapping of the metastasis associated MTS1 gene by in situ hybridisation. M.S. Lakshmi, C. Parker and G.V. Sherbet, Cancer Research Unit, The Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne NE2 4HH, U.K.

The murine 18A2/MTS1 probe labelled with 5,6 ^{3}H-UTP was hybridised to human lymphocyte metaphase spreads. Hybridised sequences were visualised by dip emulsion autoradiography. The chromosomes with grains touching or on the chromatids were typed using the Joyce-Loebl Magiscan MD with the chromosome software. An analysis of the data has mapped the MTS1 gene to chromosome 7q22. There was significant hybridisation also to chromosome 13q21-q22, possibly by an MTS1 pseudogene or a processed pseudogene.

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4.039

Integrins and other cell adhesion molecules of human rhabdomyosarcoma cells - Correlations with myogenic differentiation and with experimental metastatic ability

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To investigate the involvement of adhesive interactions in the metastatic ability and the myogenic differentiation of human rhabdomyosarcoma cells, we studied the expression of integrin subunits and other cell adhesion molecules of three human cell lines (RMZ-RC2, RD/18, and CCA) endowed with different metastatic ability in nude mice, before and after culture in differentiation medium.

A correlation was found between the expression of the α_4 integrin subunit and experimental metastatic ability in nude mice. RD/18 cells express more α_4 molecules and are more metastatic than RMZ-RC2 or CCA cells. Moreover, after culture in differentiation medium, we observed a reduction in α_4 expression and in metastatic ability of RD/18 cells.

A study of the adhesion of RD/18 to endothelial cells and to matrix components *in vitro* will reveal whether a reduction in $\alpha_4\beta_1$ expression does indeed mediate alterations in the adhesive properties of human rhabdomyosarcoma cells.

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4.040

EPITOPE MAPPING OF THE COLON CARCINOMA-ASSOCIATED MUCIN DETECTABLE WITH AM-3 ANTIBODY

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Four mAbs AM-1,AM-3,AM-4 and AM-7, directed against different determinants of the same mucin molecule have been applied for comparison of the epitope distribution in the mucin isolated by gel chromatography and CsCl gradient from normal or malignant colonic mucosa.Immunohistochemistry by APAAP method showed that AM-3 and AM-7 epitopes are more strongly expressed in tumour than in the normal tissue while the expression of AM-1 and AM-4 epitopes was comparable in both tissues. MAbs AM-1 and AM-4 bind in ELISA with the same avidity and mAbs AM-3 and AM-7 with higher avidity to tumour- than to the normal tissue-derived mucin. Rotary shadowing and electron microscopy of the mucin-mAb complexes indicated that the higher binding avidity is due to a higher density of the epitopes on the carcinoma-associated mucin. This indicates that the increase of AM-3 and AM-7 epitopes in carcinoma is due to increased mucin glycosylation rather than biosynthesis.

4.041

IN VITRO PLATELET PROAGGREGATING ACTIVITY OF A431 HUMAN EPIDERMOID CARCINOMA CELL LINE IS ADP RELEASE DEPENDENT, COMPLEMENT MEDIATED.

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In a previous work we demonstrated that the differential in vitro platelet proaggregating activity of two Burkitt's lymphoma derived human B-cell lines, i.e. Daudi and Raji, was related to differential amount of ADP released from tumor cells after contact with serum. This was related to intracellular Ca^{2+} influx into tumor cells. Both ADP release and Ca^{2+} increase were absent when serum pretreated with anti-C3 antibody was used. The present experiments demonstrate that a human epidermoid carcinoma cell line, i.e. A431, also exhibits a marked platelet proaggregating activity, similarly related to ADP release (1.24 $\pm$ 0.36 μM/2 x 10^7 A431 cells), in the presence of serum. Serum was also able to enhance the cytoplasmic free Ca^{2+} levels, as analyzed by FURA 2 AM, in the range 737 $\pm$ 254 nM/2 x 10^7 A431 cells, when added to A431 cell suspensions. Anti-C3 treated serum failed to induce either ADP release or Ca^{2+} influx.

These data suggest that similar mechanisms are involved in the in vitro platelet proaggregating activity of A431 epidermoid carcinoma and Daudi and Raji EBV-transformed human B-cell lines.

4.042

A SOLUBLE MUTANT OF THE UROKINASE RECEPTOR ABLE TO BIND THE LIGAND

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A cooperation between urokinase (uPA) and uPA receptor (uPA-R) has been demonstrated in extra cellular matrix (ECM) degradation and invasion. In the presence of both uPA and uPA-R, ECM degradation increases of at least three fold,compared to uPA alone(Quax,Pedersen, Masucci,WeeningVerhoeff,Dano,Verheijen,Blasi;unpublished). A mutant of the human uPA-R lacking the region required for membrane attachment (s-uPA-R) has been constructed and stably transfected into mouse LB6 cells. s-uPA-R is secreted into the cell medium and is able to bind uPA and inhibit the binding of uPA to cells that express the wild type receptor.The ability of s-uPA-R to bind uPA can be exploited as a starting point for producing an anti-uPA-directed anti-invasive therapy.

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