EPO and COL1A2. However, direct evidence of the involvement of dysfunctioning PAI-1 in cancer has as yet not been shown.

A NOVEL SYSTEM FOR IN VIVO ANALYSIS OF THE EFFECT OF TUMOUR PROMOTERS ON DNA TUMOUR VIRUSES

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An animal system has been devloped that allows the analysis of the interaction of persisting hamster papovavirus (HaPV) genomes with the tumour-promoting phorbol ester, TPA. In a colony of HaPV-bearing Syrian hamsters developing spontaneously skin epitheliomas at higher ages, extrachromosomal HaPV-genomes were detected by Southern blot hybridization in skin DNA. Chronic topical treatment of young hamsters with TPA resulted in a dramatic increase of viral DNA in skin cells at the site of TPA application. After finishing the TPA treatment, the amount of extrachromosomal viral DNA declined but was still enhanced more than three months thereafter. This model offers the possibility of investigating effects of TPA and a variety of drugs on the activation of endogenous virus genomes.

VIRAL CARCINOGENESIS - ILLUSTRATED INTRODUCTORY THOUGHTS

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Virus infection of an animal may lead to neoplasia of uninfected cells (indirect mechanisms) or infected cells (direct mechanisms). In the latter case, neoplasia results from the activity of a viral gene or insertional mutagenesis by the viral genome. In either case, a restriction of virus expression in the host may modify pathogenesis. Experimental examples from our laboratory have been obtained that support different facets of this general scheme. In particular, a detailed dissection of the v-src oncogene and host-imposed restrictions on the transcription of retroviral proviruses has been considered and investigated.

ACTIVATION OF ONCOGENE EXPRESSION IN PSORIATIC LESIONS

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Psoriasis is characterized by hyperproliferation and alterations in differentiation programme of epidermal cells. The reason for abnormal behaviour of psoriatic keratinocytes is unknown. There are hypotheses connecting the nature of the disease with the genetic predisposition, with the involvement of retroviruses and mobile genetic elements. It is known now that cellular proliferation is accompanied or caused by expression of proto-oncogenes. We analysed by dot-blot (1) and Northern blot hybridization techniques the expression of proto-oncogenes in the epidermis of psoriatic patients. Cloned [32]P-labelled retroviral oncogenes were used as probes. Elevated levels of Ki-ras, myc, fos and abl specific were detected in RNAs from psoriatic lesions whereas expression of other oncogenes like src, yes, fes, sis, erbB and mos, was not observed. Southern analysis of DNAs isolated from leukocytes of psoriatic patients revealed structural alterations in some proto-oncogenes. These DNAs were tested in transfection assay of mouse fibroblasts NIH 3T3. One of two samples were active in transformation. All the data are consistent with the suggestion that genome of psoriatic cells is involved in pathogenesis of the disease. The resemblence of the neoplastic and psoriatic cells in oncogene expression opens new avenues in studying the etiology of this ancient desease and its cure.

(1)Zabarovsky, E.R., Starkov, I.V., Mordovtsev, V.N. and Kisselev, L.L., Biopolymery i Kletkam, 2: N4, 212-215, 1986.

EGF-DOWN REGULATION OF EGF-R IN TUMOUR CELL LINES OF GYNAECOLOGICAL CARCINOMAS

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EGF-receptor levels were assayed in two mammary (T47D and MDA-MB-231), one ovarian (SK-OV-3) and two endometrium (HEC-I-A and HEC-I-B) carcinoma cell lines by binding of [125]I labelled EGF (specified activity 160μCi/μg) and Scatchard plot analysis. Numbers of binding sites varied between 1.7

x 10^4 (T47D) and 1.9 x 10^5 (MD-MB-231) per cell. Ratios between binding at the cellular surface and intracellular binding were between 1 : 2 and 1 : 3 except for SK-OV-3 which exhibited similar binding for both locations. Down regulation was found for all cell lines with between 20 nM and 100 nM of EGF. The combined data suggest that EGF modulates proliferation of gynaecological carcinoma cells by affecting its own receptor.

DIVERGENT EFFECTS OF γ-INTERFRON ON ADAPTIVE AND NON-ADAPTIVE IMMUNE DEFENSE MODULATE METASTATIC SPREAD OF MELANOMA CELLS

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The correlation between γ-interferon (IFN) treatment, susceptibility to non-adaptive and adaptive immunity and metastatic spread was evaluated in the B16 melanoma system. Treatment of B16 with IFN abrogated lysability by NK cells and macrophages and metastaic capacity was increased (by 5 to 10 fold the number of lung nodules). On the other hand, IFN-induced enhancement of MHC antigen expression resulted in both an increased susceptibility towards cytotoxic T cells and an enhanced cytotoxic potential of T-cells stimulated by IFN-treated B16. This was reflected in a significant reduction of metastatic nodules and prolongation of survival time of mice immunized with IFN-treated B16 cells, regardless of whether they were challenged with treated or untreated cells. Thus, loss of NK cell- and macrophage-susceptibility of IFN-treated B16 led to increased metastasizing capacity, but IFN-treatment in combination with immunization significantly reduced metastatic spread, pointing to a dominance of the T cell effect.