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A continuous cell lines has been established from a dog with leukaemia. The cells are regarded as members of the T-lymphocyte line in origin, because they did not produce immunoglobulins, did not phagocytize but did agglutinate with concanavalin A, phytohaemagglutinin and pokeweed mitogen and showed reactivity only in the lymphocyte acid phosphatase test. Their ability to grow on semi-solid agar as well as the clinical findings confirm that they are malignant.

The cells showed variability in chromosome number and extensive formation of centric fusions. Every cell was unique in chromosomal constitution and in addition, the prevalence of a nullisomy applying to many chromosomes in each cell was detected.

AFFINITY LABELLING OF THE MOUSE LIVER PROLACTIN RECEPTOR

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To detrmine the molecular weight of the prolactin receptor in the liver of lactating mice we covalently bound [125]I-iodinated human prolactin to its receptor in liver membranes using dimethyl suberimidate as a bifunctional cross-linker. SDS-PAGE and autoradiography reveals a single hormone rceptor complex at a MW of 60 kD that is competed wth an excess of cold ovine prolactin (oPRL) or human growth hormone (hGH). This suggests that the prolactin receptor has a binding subunit of about 36 kD (MW of prolactin: 24 kD). A cross-linked complex of the same molecular weight can be detected using [125]I-hGH and is competed wth cold hGH or oPRL, suggesting the use of the same binding subunit by both hormones. Immunoaffinity purification of the cross-linked ligand receptor complexes with anti-prolactin antibody is under investigation.

REGRESSION ANALYSIS OF EXPRESSION PATTERNS OF ANTIGENS IN COLORECTAL CANCER

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In addition to conventional pathological parameters in colon cancer, such as shape and size of the primary tumour, central node involvement, venous invasion, grade and stage, new variables, such as the immunoreactivity patterns at a cellular level of CEA, Ca 19-9, mucin, serotonin, secretory component and the DNA-index were tested for their potential prognostic values. A regrssion analysis was performed of the pathology data of 350 patients with primary colorectal cancer. These data were prospectively collected in a multicentre study with a follow-up of five years. All specimens were centrally reviewed.

In the multivariate analysis, stage was the predictive factor with the highest hazard ratios, but absence of central node involvement, tumours with diameters between 3,5 and 6 cm, exophytic growth, well differentiated tumours, tumours with CEA immunoreactivity, absence for staining with serotonin and diploid tumours had a favourable prognosis.

The aforementioned variables may be included in a prognostic index. Routine application of some variables is hampered by small numbers in the subgroups of hazard ratios.

MAPPING OF PAI-1 TO A REGION OF ABNORMALITIES OF CHROMOSOME 7 IN CANCER

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Alterations of chromosome 7 are frequently found in metaphases of patients with myelodysplasia or leukaemia. Dysfunction of one or more genes located in 7q21-q35 could be involved in these malignancies. Recently, several genes have been localized to this region of chromosome 7. In haematological cancers possible malfunctions of COL1A2, OI4, EPO, KIT, MET and TCRB are particularly interesting.

We have mapped the gene for plasminogen activator inhibitor, type 1 (PAI-1) by chromosomal in situ hybridization analysis to 7q21.3-q22. Interestingly, studies of genetic recombination between PAI-1 and other genes previously mapped to this region showed that it was closely linked to both

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.

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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