carcinoma; (2)HPV involvement in precancer and cancer lesions has been demonstrated by morphological, immunohistochemical and DNA hybridization techniques; (3)natural history of cervical HPV lesions is equivalent to that of CIN, being potentially progressive to carcinoma in situ; (4)latent HPV infections exist in both sexes; (5)PVs induce malignant transformation in animal models; (6)PV-induced malignant transformation seems to depend on virus type, and physical state of its DNA, i.e. whether or not integrated in the host cell genome; (7)malignant transformation most probably requires synergistic actions between the PVs and chemical or physical carcinogens, or other infectious agents; (8) genetic disposition (at least in animals) significantly contributes to malignant transformation; (9)immunological defence mechanisms of the host probably are capable of modifying the course of PV infections although efficacy in man remains to be elucidated.

HUMAN PAPILLOMAVIRUS (HPV) DAN DETECTED IN BRONCHIAL SQUAMOUS CELL CARCINOMAS

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The involvement of HPV in squamous cell carcinomas of the respiratory tract was recently suggested by the discovery of HPV 16 DNA sequences in carcinomas of the larynx, the nasal cavity/paranasal sinuses, and in an anaplastic lung cancer. In the present study, a systematic survey was made to assess the possibility that HPV could contribute to the development of bronchial cancer. Formalin-fixed, paraffin-embedded biopsies of 99 invasive bronchial squamous cell carcinomas were subjected to in situ DNA hybridization under stringent conditions (+42° C, 50% formamide; Tm -17), using a mixed probe of HPV types 6, 11, 16, 18, and 30 (provided by H.zur Hausen, DKFZ, Heidelberg, F.R.G.). HPV DNA sequences were disclosed in 5 (5.1%) of the 99 carcinomas, confined to nuclei of the squamous cells, both adjacent to and within the areas of frank invasion. This is the first occasion where HPV DNA sequences have been demonstrated in well characterized bronchial squamous cell carcinomas. The findings are in alignment with the recent theories emphasizing the mechanisms of potentiating and synergistic effects of physical and chemical agents (cigarette smoke among others) in HPV-induced carcinogenesis.

SPONTANEOUS AND SERUM-INDUCED CELLULAR REACTION IN RAT MAMMARY TUMOURS

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Mammary carcinomas were induced by a single MNU treatment in Buffalo rats. A strong mast-cell reaction was detected in the early phase of tumour growth in the connective tissue surrounding the tumour tissue nodules. After the tumours exceeded approximately one cm in diameter or one gram in weight a spontaneous inflammatory infiltration of the interstitial tissue appears parallel with the degranulation of the mast cells. The infiltration consists of neutrophil and eosinophil granulocytes, lymphocytes and in a low amount, plasma cells and macrophages.

A similar inflammatory reaction can be induced even in small tumours by the administration of rat serum absorbed against Protein A conjugated Sepharose. The absorbed serum contains products of the alternative pathway of complement degradation. It is supposed that both serum therapy and a factor released from the growing tumour can indicate mast cell degranulation leading to inflammatory reaction.

STRUCTURE AND EXPRESSION OF THE c-myc ONCOGENE IN MORTAL AND IMMORTAL, UNTRANSFORMED RODENT CELLS

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We have analysed the role of the cellular oncogene, c-myc in the process of cellular ageing and cellular immortalization using rodent fibroblasts. The steady-state level of c-myc mRNA of mouse and rat fibroblasts does not change significantly during cellular ageing in vitro. By contrast, the steady state level of c-myc mRNA increases 3 to 5 fold upon spontaneous establishment of these rodent fibroblasts. The increase in the steady-state level of mRNA has a contribution both from an increase in the transcriptional rate as well as from a change in the stability of the mature message. The mRNA levels of both c-fos and c-Ki-ras do not alter; the mRNA of non-muscle actin also does not increase. The changes in the steady-state level of c-myc mRNA are not due to gene

amplification nor to gross gene rearrangements or translocations. However, the response of the myc gene to growth factor stimulation is present apparently equally in both mortal (young and senescent) and immortal cells; a difference is seen in an increased survival of high c-myc mRNA levels after growth stimulation in established cell lines.

IN VITRO PRODUCTION AND LARGE SCALE PURIFICATION OF HUMAN ALPHA FOETOPROTEIN

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Alpha foetoprotein (AFO) purification is complicated by the problem that in most separation techniques the protein is contaminated with albumin, unless an immunoaffinity step is used. Also, the variability of the starting material affects the reproducibility of standardization of AFP in clinical assays. We investigated the possibility of obtaining considerable amounts of AFP from a constant and unlimited source. Human liver hepatoma cell line Hep G2 has been found to be a good source of human AFP. Various conditions have been assessed to obtain the highest yield of AFP with the minimum amount of protein contaminants and especially of albumin. By adapting these cells to grow in a serum free media we were able to avoid albumin, and separate AFP from foetal calf serum. This enhanced AFP secretion up to 25 to 35 ug/ml, in a total of 75 to 100 ug/ml protein. This enriched material allowed the development of a purification procedure using non-denaturing preparative PAGE. At least 98% pure ATP is obtained, as assessed by densitometric analysis, with no albumin detectable on Western blotting.

QUANTIFICATION OF AMPLIFIED ONCOGENES IN TUMOUR CELL LINES BY A NUCLEIC ACID SANDWICH HYBRIDIZATION TECHNIQUE

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The aggressiveness of some tumours correlates to the degree of genomic amplification of certain oncogenes. Detection and quantitation of specific oncogene amplifications can therefore be of clinical importance. In our laboratory we have developed the sandwich hybridization method (Ranki et al, Gene, 21: 77-85, 1983) for rapid detection of nucleic acids from crude specimens.

The method uses two non-overlapping DNA fragments as reagents. One is attached to a solid phase functioning as the capture probe and the other is the labelled probe. If the specimen contains sequences complementary to both probes it will mediate labelling of the solid carrier. Because the specimen is kept in solution it can be analysed in crude form without background problems. Sandwich hybridization has been applied to detection of a variety of viruses (Virtanen et al, J. Clin. Microbiol. 20: 1083-1088, 1984) and bacteria (Palva et al, FEMS Microbiol. Lett. 23: 83-89, 1984).

We have constructed reagents for measuring the number of N-myc genes in a human neuroblastoma cell line. The cell number in the assay was measured by a probe pair derived from the α-2(I) collagen gene present as single copy in haploid genome. The degree of N-myc gene amplification was calculated as number of N-myc genes per collagen gene. Quantification was done from a single undivided specimen by introducing the reagents for oncogene and the standard measurement into one assay. The method has also been applied to quantification of oncogene mRNA in the tumour cells.

ROLE OF CANCER REGISTRY IN CANCER EPIDEMIOLOGY

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One of the main functions of a cancer registry is to produce cancer incidence statistics by sex, site, age, subregion occupation, etc. This data base can be used in the identification of priorities (e.g. leading cancer sites), and in different kinds of descriptive and comparative studies including cancer trends and predictions, correlations, geographical analyses, etc. The cancer registry files contain data on individual cancer patients. This data set serves as a useful source of information in prospective follow-up studies (observed and expected numbers of cases), in case-control studies, in the evaluation of various preventive measures in the society (e.g. mass screenings), and as a starting point for clinical and clinico-pathological studies. If patients are followed-up for death, survival analyses can be conducted using country-wide unbiased patient series. Finally, the members of a cancer registry staff are often able to participate in health education in various ways.