cells with a single nucleus but not multinucleated or giant cells were determined. The DNA content and nucleus area showed a time dependent change 10 to 18 days after transplantation with hypotetra-to octaploidal pattern. The increasing DNA content and the behaviour of aneuploidy has been suggested as the result of endoreduplication or nuclear fusion in the environment of host defense.

IMMUNOMODULATING EFFECT OF COPOLYMERS OF METACRYLIC ACID

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The immunomodulatory effect of six copolymers of metacrylic acid (MA) were investigated in $BD2F_1$ mice. The copolymer of MA with acrylamide (MAA) was selected for further investigation. MAA applied i.p. was able to enhance (as compared to the control) by 147% the plaque-forming cell response, by 100% rosette-forming cells response, by 142% the delayed type hypersensitivity reaction, as well as 10 times the NK activity of spleen cells. Suppression of humoral immune response induced by some bacteria could be reduced by MAA pretreatments. In L1210 leukaemia-bearing mice MAA exhibited some synergistic therapeutic effect when combined with BCNU.

EFFECTS OF BETEL EXTRACT AND RELATED COMPOUNDS IN CULTURED HUMAN BUCCAL CELLS

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Effects of aqueous betel nut extract and several betel-specific alkaloids and N-nitroso compounds were investigated in cultured human buccal epithelial cells and fibroblasts. The extract decreased both colony forming efficiency and clonal growth rate of epithelial cells to less than 50% at 10 µg/ml. Exposure to higher concentrations also caused both dose-dependent depletion of thiols and formation of DNA single strand breaks. Of eight betel nut-associated compounds investigated, 3-(methyl-nitrosamino)propionaldehyde was the most potent on a molar basis and significantly decreased both cellular survival and thiol content and also caused DNA damage in buccal cells between 0.1 and 0.3 mM. More than 10-fold higher concentrations of arecoline, guvacoline or N-nitrosoguvacoline were required to cause similar effects. Arecaidine, guvacine, N-nitrosoguvacine or 3-(methylnitrosamino) propionitrile up to 6 mM did not affect the cells significantly. The induction of cyto- and genotoxic effects by extract and several betel nut-specific compounds may be of importance for understanding the relationship beteeen betel chewing and carcinogenesis in the human buccal epithelium.

POLY-L-LYSINE AS DIFFERENTIATION INDUCER IN FRIEND ERYTHROLEUKAEMIA: STUDIES IN VITRO AND IN VIVO

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The ability of the synthetic cationic polypeptide poly-L-lysine (PLL) to induce differentiation was examined in Friend murine erythroleukaemia cells. Like other membrane-interacting agents, PLLs of different molecular weights were found to be good inducers of differentiation. These polymers enhanced differentiation produced by suboptimal concentrations of dimethylsulphoxide (DMSO). Since PPL was inactive as an initiator of maturation of DMSO-resistant cells, it is likely that some events (presumably membrane-related effects) involved in the multistep stimulation process are common to polar-planar solvents and to this polycationic polymer. A PLL of 2,700 MW was selected to examine the induction of differentiation process in animals bearing Friend erythroleukaemia. Although no increase in the survival was observed, the pattern of differentiation in erythro- and granulocytopoietic series in the myelograms of treated animals showed evidence of some cell maturation.

HUMAN PAPILLOMAVIRUS (HPV) INFECTIONS AND CERVICAL SQUAMOUS CELL CANCER

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Current data implicating the role of HPV in squamous cell carcinogenesis of the uterine cervix can be summarized as follows: (1)cervical HPV infections are a sexually transmitted disease (STD), shown to represent an increased risk for cervical

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