drug Celladam (DCM) and a simple cancer diagnostic method (MTA) have been developed by Kovacs and his group. In animal experiments, including various immune diagnostic methods, therapeutic effect of CDM was as follows: 0.025 mg/kg CDM pretreatments administered 5 and 1 days before the tansplantation of Ehrlich tumours had increased the survival time of mice by 70%. CDM treatment in doses of 0.025 to 0.1 mg/kg twice a week inhibited the growth of subcutaneously transplanted Ehrlich and S180 tumours, increased survival time and stimulated PHA-induced blastogenesis. In the Ehrlich tumour bearing animals we found elevated transferrin, -glycoprotein and -lipoprotein levels in serum and ascitic fluid. On CDM treatment, the level of these plasma proteins, as well as the results of MTA diagnoses had approached the control levels: these results may be attributed to the mechanism of action of CDM.

CLONAL SENSITIVITY TO DIFFERENTIATION INDUCERS AND TO CYTOSTATIC DRUGS OF HETEROGENEOUS TUMOUR CELL POPULATIONS

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Heterogeneous responses of individual cells of tumour cell populations to inducers of differentiation, e.g. phorbol myristate acetate (TPA), were observed using various human tumour cell lines including HL-60 promyelocytic, K562 erythrocytic leukaemia, and A 2058 and BHM-97 melanomas of human origin. Clonal lines were isolated from the A 2058 melanoma line, which showed different cell morphology, kinetic parameters and different sensitivity against inducers of differentiation. The sensitivity to various cytostatic drugs of these clones was studied and compared with their sensitivity to the inducers. Evaluation of the effects was made with clonogenic assay, morphological alterations such as dendrite formation, cytotoxic effects, change in melanin production. The importance in the therapy of tumours of the correlation existing between the sensitivity to inducers of differentiation and to cytostatic drugs of cell clones has been evaluated.

UTILIZATION OF THE QUANTITATIVE COMPONENT OF THE INFORMATION OBTAINED FROM SHORT TERM TESTS: INTEGRATED USE OF POSITIVE AND NEGATIVE RESULTS

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Carcinogenicity in small rodents and short term test results are to some extent correlated phenomena, but at the same time profoundly different in their biological significance. For this reason usually only qualitative correlations between the two phenomena are investigated. In the perspective of risk assessment studies, we have attempted to establish a logical and mathematical bridge between the two formalisms of studying qualitative or quantitative correlations. We have shown that, as expected, the two formalisms are completely compatible and interchangeable. However, we have found that a not completely negligible amount of information is discarded using only the qualitative component of the information. Under certain reasonable hypotheses it is possible to transform coherently in a quantitative value of very low potency even negative results. This allows for a homogeneous treatment of the globality of the data. Using the quantitative component of the information a multiple correlation approach can be applied to batteries of tests, obtaining a more straightforward gain in predictivity than using the qualitative approach.

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BEN, AGE AND SCE

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Balkan endemic nephropathy (BEN) is a chronic renal disease often combined with uroepithelial tumours. It occurs in some regions of Bulgaria, Yugoslavia and Romania. The cause of the disease is unknown. One of the most likely explanations is the presence of genetic predisposition combined with some environmental agent.

Here are reported data from a study on the level of sister chromatid exchanges (SCE) in patients with BEN, matched controls with other kidney diseases living in non-endemic regions, children from endemic families and matched controls. It was found that the level of spontaneous SCE in peripheral lymphocytes was not higher in the patients with BEN and children from BEN families. However, it nearly doubled the control frequency following <u>in vitro</u> treatment with mitomycin C.

INDUCTION OF THE CYTOCHROME P-450c GENE AND THE METABOLISM OF BENZO(a)PYRENE-7,8-DIOL (BP7,8-DIOL) IN