DEG MULTIFACTORIAL PROTOCOLS OF RAT HEPATOCARCINOGENESIS; THEIR INFLUENCE ON THE MALIGNANT TUMOUR INCIDENCE AND LAG PERIOD

J.de Gerlache, M.Lans, H.Taper, V.Préat, K-O.Vo and M.Roberfroid
Laboratoire de Biochimie Toxicologique et Cancerologique-U.C.L. 73.69/1200
Brussels, Belgium.

In the triphasic protocol of hepatocarcinogenesis, the promoting effect of a selective differential growth stimulus adapted according to the Solt-Farber recipe (administered after initiation by a single dose of nitrosamine) is combined with the promoting effect of the chronic administration of phenobarbital (PB). This combination reduces the lag period for malignant tumour development in most treated animals to 6-7 months whereas in the absence of PB treatment the lag period is of 13 months. The effect of PB is reversible up to the third month of administration.

If a second phase of "Solt-Farber" selective proliferation is applied after one month of PB treatment, the disorganisation of the tissue is increased as evidenced by the nodular aspect of the liver. However, the lag period for tumour development is not shortened as in the case of prolonged PB administration. Furthermore, a second dose of the carcinogen used as initiator that is administered one month after the end of the selective procedure reduces effectively the lag period for tumour development, even in the absence of PB promoting treatment. It seems thus that these triphasic protocols reconstitute more closely the sequence of processes induced by a complete carcinogen during chronic intoxication.

DEL CHANGES OF NUCLEOLAR GENE EXPRESSION DURING RAT HEPATOCARCINOGENESIS

A.Deleener and Ph.Castelain
Laboratorium voor anthropogenetica, V.U.B. Brussels, Belgium.

Since changes in gene expression might play an important role in the carcinogenic process and since it is known that nucleolar size, morphology and number alter greatly with modification in growth and metabolic conditions, it is our aim to analyse the changes of the nucleolar gene expression (or rRNA synthesis) during rat hepatocarcinogenesis. Moreover there is a good correspondence of the rate of rRNA synthesis and silver staining, and the quantitative cytophotometrical analysis of silver staining seems to be a simple tool for the estimation of the nucleolar gene expression. To induce a hepatocarcinogenic process, male Wistar rats were treated chronically for 4-6 weeks with diethylnitrosamine (80 mg/l in drinking water) followed or not by a chronic treatment with phenobarbital for 7-9 months. The hepatocytes were enzymatically isolated. Cytological preparations were obtained by routine processing in hypotonic solution, fixation and spreading of isolated cells. Finally, these preparations were stained using a $AgNO_3$ (50%) solution and the staining intensity was measured by a SERVOGER XY-scanner, combined with a Hewlett-Packard 9874A calculator. Considering the average silver staining intensity per cell the increase of the nucleolar gene expression becomes statistically significant with time and more in particular at 9 months of phenobarbital treatment.

DEN TREATMENT OF ONC-GENE TRANSFECTED RODENT FIBROBLASTS WITH CHEMICAL CARCINOGENS

J.Denner, I.Ehm, B.Jandrig and D. Friese
Central Institute for Cancer Research, 1115 Berlin, G.D.R.

Transformation of normal rodent embryo fibroblasts requires the action of at least two co-operating onc-genes. Gene transfer of ras and myc, prototypes of these two complementary groups, in embryonic and established rodent fibroblasts was performed. Calcium phosphate co-precipitation and the polycation-dimethyl sulfoxide methods were used. Recipient cells after the gene transfer and control cells were treated with the carcinogens 3-methylcholanthrene (MC) and N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) and characterized in soft agar cultures.
