Human melanoma variants and clones with increased metastatic abilities were obtained from melanoma cell lines in nude mice and in immunosuppressed new-born rats. Subcutaneous transplantation in a nude mouse of a human melanoma metastatic nodule resulted in a subcutaneous tumour (NTT) and in spontaneous lung (NTP) and lymph node (NTG) metastases (Neulat-Duga et al., Invasion and Metastasis, 4: 209-224, 1984) which were first maintained in vivo by subcutaneous passages in nude mice and then cultured in vitro as cell lines. Cytogenetic studies showed that all three tumour lines have a common origin and that metastases resulted from a population selection. After 15 in vitro passages, NTP cells were injected s.c. in nude mice : serial transplantation was accompanied by an increase in metastatic abilities of tumour cells. Melanoma cell lines, tumourigenic but non metastatic in nude mice, were xenografted to ATS-treated new-born rats. 3 weeks after s.c. injection of 10^6 cells, nearly all rats developed tumours and a proportion of them had lung and lymph node metastases. Agar cloning of M4Beu line showed that it is heterogeneous and contains poorly tumourigenic, but highly metastatic cells.

DETECTION OF AFLATOXIN-LIKE SUBSTANCES IN THE GENERAL DANISH POPULATION

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A competitive ELISA assay for detection of Aflatoxin B1 (AFB) in urine has been developed using a monoclonal anti-AFB antibody. The assay has been characterized with respect to sensitivity towards a range of aflatoxins and derivatives. The aromatic structures of AFB with the anisole group as well as the lactone region are required for competitive action in the assay. AFB concentrations down to 0.1 ng/ml could be detected.

Most urine samples from 80 normal Danish volunteers were positive in this assay, containing 0.1 to 10 ng-eqv. AFB per ml. The structure of the urinary aflatoxin-like antigenic substance (ALAS) is presently unknown. ALAS is a true competitor with AFB for the antibody and can be concentrated by affinity chromatography. We are presently attempting to identify the chemical structure of ALAS.

LOSS OF HETEROZYGOSITY ON CHROMOSOME 22 IN PRIMARY TUMOUR MATERIAL FROM MENINGIOMA

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Cytogenetic analyses have shown that monosomy 22 is common in primary cultures of meningioma. A small fraction of these tumours have also shown deletions on chromosome 22. We have analysed restriction fragment length alleles at eleven loci on chromosome 22 in primary tumour material and the corresponding constitutional tissue from 20 patients with meningiomas, using polymorphic DNA markers. Loss of constitutional alleles along the whole chromosome 22 were found in 6 cases, consistent with a non-disjunction event. In addition, 5 meningiomas showed loss of alleles on part of chromosome 22 while at least one other locus on chromosome 22 showed retained heterozygosity. Analysis of polymorphic loci on 15 other chromosomes revealed only a few tumours with single losses. A more extensive analysis of cases with deletions may help to localise a recessive meningioma gene regionally on chromosome 22.

DNA DAMAGE AND THIOL DEPLETION CAUSED BY FECAPENTAENE-12 IN HUMAN FIBROBLASTS

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Fecapentaene-12 (fec-12) is a fecal mutagen that also is genotoxic in cultured human fibroblasts (Plummer et al, Carcinogenesis 7, 1607-1609, 1986). Further studies indicate that survival of fibroblasts measured as colony forming efficiency or trypan blue exclusion was decreased to approximately 50% between 0.5 to 1.0 µm fec-12 after either 1, 3 or 24 hr exposure times. The cellular content of total thiols (mainly glutathione) was decreased in a dose dependent manner up to 1.0 µM fec-12 which decreased thiol content to 60% of control. Higher doses of fec-12 did not cause further thiol depletion. Because depletion of GSH was not coupled with formation of GSSG, these results indicate that fec-12 depletes cellular thiols by direct conjugation. As analyzed by alkaline elution, fec-12 also caused several types of DNA damage. Primarily DNA