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ISOFLAVONIC PHYTOESTROGENS IN HUMANS, -IDENTIFICATION AND METABOLISM

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Naturally occurring isoflavonic phytoestrogens and metabolites thereof have been investigated in connection with breast cancer and other estrogen dependent diseases because of their possible role as estrogens and/or antiestrogens. Human subjects, particularly vegetarians, excrete in comparison with estrogens high amounts of phytoestrogens in urine. The lowest amount of phytoestrogens were found in urine of postmenopausal breast cancer patients. During the course of the present investigation on the influence of diet on estrogen metabolism we identified by combined gas chromatography-mass spectrometry the following isoflavonic compounds in human urine: Formononetin (For), Daidzein (Da), Intermediate-E (I-E), Intermediate-O (I-O), O-desmethylangolensin (ODma), Equol (Eq), Methylequol (Meq) and Genistein (Ge). Naturally occurring For is metabolized by intestinal bacteria to either Da or in smaller amounts to Meq. Da which also occurs in foodplants is metabolized either via I-E to Eq (70%) or via I-O to ODma (5 to 20%). Ge is known to occur in plants but may also be a metabolic product of naturally occurring Biochanin A. It is concluded that the metabolism of isoflavonic phytoestrogens in human subjects is similar to that in animals.

CONTRIBUTION OF ras ONCOGENES TO NEOPLASTIC DEVELOPMENT

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Chemical and physical carcinogens have been implicated in the etiology of human cancer. Most of these carcinogens interact with DNA and have mutagenic properties. Whereas the majority of carcinogen-induced mutations have no serious consequences to the host, a small number of them are thought to be responsible for neoplastic development. The recent discovery that oncogenes, in particular those of the ras gene family, are reproducibly activated in carcinogen-induced tumours has made it possible to establish a correlation between those mutations responsible for the malignant activation of these oncogenes and the known mutagenic properties of the initiating carcinogens. These studies have indicated that initiation of neoplasia may involve the activation of oncogene(s) by the direct mutagenic action of certain carcinogens. In the present study, the contribution of normal developmental programmes to the phenotypic expression of oncogenes and the involvement of additional genetic events in the development of the full enoplastic phenotype has been investigated.

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ASSOCIATION IN THE EXPRESSION OF Ki-ras ONCOGENE AND MHC CLASS I ANTIGENS IN FIBROSARCOMA TUMOUR CELL VARIANTS EXHIBITING DIFFERENT METASTATIC CAPABILITIES

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The present study is aimed to investigate the expression of proto-oncogenes in the T-10 fibrosarcoma lines that exhibit distinct metastatic properties in correlation with the expressed H-2 antigens. The major oncogene which showed differential expression in the T-10 clones is the Ki-ras. The amounts of specific Ki-ras M-RNA and the Ki-ras p21 protein are expressed in elevated levels in the H-2D^{k} negative non-metastatic clones in comparison with low level of expression in the H-2D^{k} positive highly metastatic clones. Expression of H-2K antigens following transfection with cloned H-2K genes had no effect on the expressed Ki-ras oncogene in the T-10 clones. However, transfection of the non-metastatic cells with cloned H-2D^{k} gene resulted in shifting the cells to highly metastatic phenotype and in reduction of the expressed c-Ki-ras oncogens.

HISTOLOGICAL MARKERS USED TO FOLLOW-UP THE PROGRESSION OF SOFT TISSUE SARCOMAS

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Some histopathological factors (tumour differentiation, degree of cellularity, nuclear polymorphism, mitosis count, tumour