Earlier studies indicate that dietary fiber intake correlates negatively and fat intake positively with plasma estrone and estradiol (E2) levels in young women. Decreasing fat intake lowers plasma testosterone (T), free T(FT) and percentage FT in men. We have studied 27 postmenopausal women [9 vegetarians (VG), 10 omnivores (OG) and 8 healthy women with surgically removed breast cancer (BC)] 4 times during one year, with intervals of about 18 weeks. Each time, diet was recorded during 3 days and blood samples were drawn on all 3 days. Analysis of variance showed statistically significant differenes between the groups for androstenedione (A), T, % FT, FT, % FE2 and sex hormone binding globulin binding capacity (SHBG). High protein and fat and low grain, carbohydrate, total and grain fiber intake were associated with high A, T, % FT, FT and % FE2 and low SHBG. All parameters showed this pattern in BC, but only two, SHBG and % FE2, differed significantly between BC, and OG and VG (non-paired t-test), the other differing significantly only from those of VG. It is concluded that a "Western type diet" is associated with high % FT and % FE2 and low SHBG and thus probably increases BC risk and risk for other sex hormone dependent cancers.

CORRELATIONS BETWEEN URINARY EXCRETION OF LIGNANS AND PHYTOESTROGENS AND PLASMA NON-PROTEIN BOUND SEX HORMONES AND SEX HORMONE BINDING GLOBULIN.

H.Adlercreutz(1), K.Hockerstedt(2), C.Bannwart(1), E.Hämäläinen(1) and T.Fotsis(1)

(1) Department of Clinical Chemistry and (2)IVth Department of Surgery, University of Helsinki, Helsinki, Finland.

During the last 7 years a number of biologically active compounds, belonging to the classes of lignans (Ligs) and isoflavonic phytoestrogens (Ph-ES), have been identified in human urine. These hormone-like compounds are products of intestinal bacterial action on dietary precursors. Urinary excretion of Ligs is particularly low in postmenopausal (pmp) breast cancer patients (BC) and correlates with fiber intake. It has been shown that the Ph-Es and Ligs are both estrogenic and antiestrogenic. Some are also moderate aromatase inhibitors. In the present study, the excretion of 2 Ligs and 3 Ph-Es was determined in the urine of 34 young women, including BC and in 20 pmp women. Preliminary results indicate that the lowest mean excretion of these compounds occur in BC and the highest in vegetarians. Positive correlations were found between urinary excretion of the lignan enterolactone, total Ligs and Ligs+Ph-Es, and fiber intake and plasma SHBG, and negative correlations with percentage free (F) estradiol (E2), FE2 and free testosterone ($p<0.05-<0.001$). It is concluded that intake of a fiber-rich food is associated with low non-protein bound sex hormone levels, probably due to stimulation of SHBG synthesis in the liver by these weak estrogens, entering portal circulation from the intestine.

ANTI-COLLAGENOLYTIC ACTIVITY OF TAMOXIFEN ON HUMAN K 562 CELLS

M.G.Akeli(1), P.Jeannesson(1), A.Rallet(1) and J.C.Jardillier(1,2)

(1)UER de Pharmacie, Reims and (2) Institut Jean Godinot, Reims, France.

Collagenolytic activity has been demonstrated in the human leukaemic cell line K 562 by employing Macartney's fluorescamine technique (FEBS Lett. 119: 327,1980) with fibrillar collagen I as substrate. The enzymes are either free or membrane bound and the total activity is 0.60 ± 0.06 mU/10^6 cells. Main enzymatic parameters including optimum pH, Ca-dependence, trypsin activation have been defined. Among various effectors studied, tamoxifen (Txf), a well-known antiestrogenic compound, exhibited a strong inhibitory effect. After 3 days of culture in the presence of 10^{-7}M of Txf, 75% of the collagenolytic activity was inhibited. Hydroxy-Txf and N-demethyl-Txf are equally potent inhibitors though devoid of any direct cytotoxic effect.

K 562 cells have no binding sites for estrogens but they possess high affinity membrane-bound binding sites for H-Txf (31 femtomoles/mg protein). These findings have been evaluated with respect to their significance in the prevention of metastases.

KINETICS OF HYDROLYSIS OF NORNITROGEN MUSTARD, A METABOLITE OF PHOSPHORAMIDE MUSTARD AND CYCLOPHOSPHAMIDE

A.Alhonen, K.Hemminki, E.Linkola and A.Hesso

Institute of Occupational Health, Helsinki, Finland.

Nornitrogen mustard (NOR) and phosphoramide mustard (PAM) are important metabolites of cyclophosphamide. A gas chromatographic (GC) method was developed

for the determination of NOR and its hydrolysis products. The method was based on derivatization by heptafluorobutyric anhydride. The structures of the derivatives were established by GCMS. The rate of disappearance of NOR at 37 degrees and pH 7.4 was about 20 min, and a similar rate was noted irrespective of whether NOR or PAM was used as starting material. N-(2-chloroethyl)-N-(2-hydroxyethyl)amine (NOR-OH) appeared with a half-life of 19 min when NOR was used, but with a half-life of 23 min when PAM was used as starting material. The main difference in product yields was the relatively higher amounts of NOR-OH and N,N-bis(2-hydroxyethyl)amine (NOR-OH-OH) formed when PAM instead of NOR was used as starting material. This suggests the formation of NOR-OH and NOR-OH-OH from NOR as well as from the hydroxylated derivatives of PAM.

REDUCTION TO HOMOZYGOSITY OF GENES ON CHROMOSOME 11 IN HUMAN BREAST NEOPLASIA

Iqbal U.Ali, Rosette Lidereau and Robert Callahan

There is increasing evidence that recessive genetic lesions might be involved in the genesis of several paediatric and adult tumours. These recessive mutations are unmasked when tumour cells attain hemi- or homozygosity for particular genes. In primary breast tumours an allelic loss of c-Ha-ras-1 locus (chromosome 11p) was detected in 27% of patients heterozygous for this proto-oncogene. Restriction fragment length polymorphism analysis of tumour DNAs provided evidence for reduction to homozygosity of not only c-Ha-ras-1 gene but also of several markers on the short arm of chromosome 11. This loss of normal cellular sequences was specific for chromosome 11 and had a significant correlation with the most aggressive form of the disease. Our analysis also suggested that the deletion of the region between the B-globin and PTH loci might be important in this subset of tumours.

A systematic study of the possible alterations in other proto-oncogenes strongly suggests that human breast neoplasia, a highly complex and genetically heterogeneous disease, might involve abnormalities of several proto-oncogenes.

GROWTH FACTOR AND ONCOGENE EXPRESSION DURING MEGAKARYOBLASTIC DIFFERENTIATION OF K562 LEUKAEMIA CELLS

R.Alitalo, T.P.Mäkelä and L.C.Andersson

Transplantation Laboratory, University of Helsinki, Helsinki, Finland

Platelets contain PDGF and TGF-beta, but their site of synthesis has not been proven since megakaryocytes are difficult to obtain for studies of this nature. Our results of studies with the chronic myeloid leukaemia (CML) cell line K562 suggest that the genes encoding the two PDGF chains and TGF-beta (1) and the synthesis of the corresponding proteins are induced during the megakaryoblastic differentiation process. The expression of the bcr-c-abl oncogene mRNA remained unaltered during the differentiation of K562 cells, but the kinase activity of the corresponding fusion protein is almost completely shut off suggesting that an active c-abl oncogene is incompatible with K562 cell differentiation.

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MONOCLONAL ANTIBODIES AGAINST NIH 3T3 CELLS TRANSFORMED BY HUMAN THYROID CARCINOMA DNA

R.Alzani, G.Della Torre(1), C.Traversari(2), M.Pierotti(1), S.Ménard, G.Della Porta(1) and M.I. Colnaghi

Experimental Oncology E, (1)Experimental Oncology A and (2)Experimental Oncology D, Istituto Nazionale Tumori, Milan, Italy.

First-cycle transfectants of NIH 3T3 transfected with human metastatic thyroid carcinoma DNA were used as an immunogen to obtain monoclonal antibodies against antigens induced by the transfected tumour DNA. The transfected cell line (M33) was shown to contain ALU sequences. Two monoclonal antibodies were selected on the basis of their differential reactivity toward NIH 3T3 or M33 cell lines. By biological and biochemical analysis, the first monoclonal antibody (MTr1) recognised an epitope on cytoskeletal filaments of proliferating murine fibroblasts. Similar filaments labelled by MTr1 were also found to accumulate into cytoplast-like structures produced by M33 cells.

Characterization by immunofluorescence of the second monoclonal antibody, MTr2 indicated that it recognizes a specific human antigen associated with normal thyroid tissues and differentiated thyroid tumours.

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