Symposium no. 3

Cytogenetics of Solid Tumours

3.001

INTERLEUKIN-2 INDUCED GROWTH SUPPRESSION OF OESTROGEN DEPENDENT BREAST TUMOUR GROWTH.

J.Byrne,K.Barry,D.Gough,P.G.Horgan,L.Hanrahan, H.F.Given.
NBCRI,Univ.Coll.Hosp.,Galway,Ireland.

Alterations in growth of an oestrogen dependent human mammary cell line (ZR-75-1) caused by Tamoxifen and the immunomodulator Interleukin-2 (IL-2) were examined.
ZR-75-1 cells (4 x 10^5/ml) were exposed to Tamoxifen and IL-2. Cell number and viability were assessed using acridine orange staining at 2,4,and 6 days and compared to standard growth curves.Addition of Tamoxifen (200,400, 600 and 800 ng/ml) significantly ($p<0.001$) reduced viability of cells after 4 days for each concentration of Tamoxifen compared to the standard growth curve. IL-2 at 10,50, and 100 units/ml also significantly ($p<0.001$) inhibited growth in a dose dependent manner with maximal inhibition occurring at 6 days for all IL-2 concentrations.
IL-2 and Tamoxifen inhibit oestrogen dependent growth in breast cancer cell lines suggesting a possible therapeutic role for IL-2.

3.002

DISSECTION OF MARKER CHROMOSOMES WITH INTERSTITIAL C-BANDS BY MEANS OF IN SITU HYBRIDIZATION WITH CHROMOSOME-SPECIFIC PROBES.

Doneda L., Larizza L.
Department of Biology and Genetics,Medical Faculty, University of Milan

Human melanoma was found to be a favourable tumor to study chromosome rearrangements involving C-heterochromatin transposition. The Me 14932 cell line was selected by C-banding screening of a large panel of human melanomas to investigate the origin of two marker chromosomes (m1 and m2) , unidentifiable by Q-banding , endowed with two closely-spaced interstitial C-bands .Non isotopic in situ hybridization with chromosome-specific probes hybridizing to highly repeated DNA located at the centromeres of human chromosomes is under way in order to identify the derivation of both the centromeres and the C-bands of m1 and m2. Scoring of interphase hybridization signals will also allow to quantify the dosage of different chromosomes in the Me 14932 cell line.
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3.003

CHROMOSOME CHANGES IN HUMAN MALIGNANT MELANOMA

I.Encuţ

Laboratory of Cellular Biology

Institute of Oncology Bucharest-ROMANIA

Chromosome aberrations were analyzed in 18 cases of human malignant melanoma (HMM).
The chromosomal analysis revealed:
1.- a steam-line of tumors ranging between 37-69 chromosomes;
2.- an increased incidence of the trisomy in groups 1, 6 and 7;
3.- chromosomes 1 and 6 were found to be the most involved in structural aberrations;
4.- each marker chromosome was unique for a given case;
5.- in six cases of HMM the frequency absence from tumoral cells of X heterochromatic chromosome.
The significance of these chromosomal changes is discussed related to the prognostic of the disease.

3.004

Füzesi,L[1], Jürgen,P.[1], Szücs,S.[2]
Institute of Pathology, Medical Faculty of Technical University of Aachen[1] and Munich[2], Germany

Evidence on bisomy, trisomy and tetrasomy 7 in solid tumors by using chromosomal in situ hybridization

Reliability of targeted interphase cytogenetics has been proved on formalin fixed and paraffin embedded tissue sections of cytogenetically analyzed human solid tumors (sarcomas and renal tumors as well as testicular). We used a centromeric,alpha satellite chromosome-7-specific DNA probe. In case of bisomy 7 nuclei of both normal and tumor cells exhibited one and two labelled spots in about 50%, irrespectively of the tumor type. The frequency of labelled spots per nuclei showed a statistically significant shift to higher labelling signals in nuclei of trisomic and tetrasomic nuclei. The main advantage of this technique is the morphological verification of cytogenetically different tumor clones for primary and secundary chromosomal aberrations.

3.005

EVOLUTION OF DNA PLOIDY DURING THE HUMAN COLORECTAL TUMOR PROGRESSION.

W. Giaretti, E. Geido, A. Di Vinci, H. Aste,S. Sciallero.
Istituto Nazionale per la Ricerca sul Cancro (I.S.T.), Genoa, Italy.

Colorectal lesions provide one of the most potentially informative systems for investigating human tumor progression, since they proceed through defined stages from benign towards invasive malignant tumors. We have examined 300 adenomas (AD), 150 carcinomas (CA) and the corresponding individual-specific mucosa using the technique of high resolution DNA flow cytometry of fresh/frozen material. This methodology provides information on the degree of DNA aneuploidy (DNA index, DI), which for colorectal tumors was shown to highly correlate with the cytogenetic index, and on the proliferation characteristics of the tumor (S-phase fraction).
We have found a high frequency (about 70%) of near-diploid clones (DI=0.8-1.2) in AD with mild-moderate dysplasia, their rare occurrence (about 10%) in CA with moderate-poor differentiation, and a high frequency of near-hypertriploid clones (DI=1.4-1.8) in AD with foci of CA and in CA. Near-hypertriploid stemlines exhibited twofold higher cell proliferation than near-diploid stemlines, and, when present in CA, were associated with an increased relative risk of death of the patients.
These data indicate that near-hypertriploid clones emerge later than near-diploid clones in the natural history of colorectal cancer, probably derive from near-diploid clones by tetraploidization, are associated to a proliferative advantage (perhaps due to a favorable oncogene/antioncogene balance), and may be corresponsible for a more aggressive biological behavior of the colorectal tumors.

3.006

CYTOGENETIC AND MOLECULAR STUDY OF 30 MALIGNANT MELANOMA PRIMARY CELL CULTURES.

P. Grammatico(1),L. Varesco(2),U. Bottoni(3),F. Roccella (1),L. Casarino(2),A. Heouaine(1),V. Gismondi(2),M. Roccella(1),L. De Benedetti(2),B. Grammatico(1),O.A. Carlesimo(3),G.B. Ferrara(2),G. Del Porto(1).
(1) Cattedra di Genetica Medica "La Sapienza" Roma
(2) Lab. Immunogenetica IST Genova
(3) Clinica Dermatologica "La Sapienza" Roma

A cytogenetic and molecular study was conducted on primary cell cultures obtained from malignant melanocitic lesions, clinically and histologically defined.

The authors refer the results about 30 different patients and the possible correlation with the clinical evolution.

In addition the authors present here preliminary data regarding the analysis of the short arm of chromosome 17 using the highly polimorfic probe YNZ22.No loss of heterozigosity was detected in the 14 cell lines examined. This suggest that the allele loss on chromosome 17p, reported in metastatic melanoma, is a late event.