Symposium no. 3: Cytogenetics of Solid Tumours

3.007

ANALYSIS OF NON-HODGKIN'S LYMPHOMA CELL METAPHASES BY IN-SITU HYBRIDIZATION

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Chromosomal abnormalities are one of the most characteristic features of malignant cells, and have proved themselves to be powerful indicators of changes that have occurred at the molecular level. Microscopic analysis of such abnormalities however may not reveal changes that are too subtle or obscure. We have therefore been using a non-radioactive in-situ hybridization technique to map DNA probes to human chromosomes. This technique allows for a much finer analysis of chromosome structure and we have used it to study a number of abnormal karyotypes derived from non-Hodgkin lymphoma cells. In particular we have studied the presence of the MYB proto-oncogene on the 6q⁻ derivative chromosome that is present in 25% of our cases. These studies have demonstrated that MYB is not consistently deleted from the 6q⁻, and have also revealed interesting and unsuspected structural changes in some of the derivative chromosomes.

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3.008

Different histological types of stomach carcinomas have different cytogenetic aberrations.

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Stomach carcinomas of the diffuse and intestinal type of Lauren were investigated. Metaphases of 12 patients with signet ring cell carcinomas and of 11 patients with carcinomas of the intestinal type were won by in-situ-preparation or harvest of the primary culture. Lymphocytes of the spleen served as controls. Numerical aberrations, especially an age-independent loss of the Y-chromosome, could be found in signet ring cell carcinomas, whereas structural changes of chromosomes of the D-group as isochromosomes and translocations and a trisomy 20 can be detected in intestinal type gastric carcinoma. Therefore the cytogenetic investigation may be helpful for a further differentiation of stomach carcinomas and be of prognostic value.

3.009

REVERSION OF ANCHORAGE INDEPENDENCE INDUCED BY CHROMOSOMAL SEGREGATION IN CHINESE HAMSTER CELLS.

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In CHEF18 Chinese hamster cells, the cytogenetic analysis of anchorage independent clones isolated from transformed and from tumor derived cell lines has shown a high karyotype homogeneity, i.e. the presence of four marker chromosomes (4q+,7p+,8p- and 9q+). In order to identify which, if any, of the four markers were related to transformation,one tumor derived cell line was treated with Colcemid to disrupt the association of the marker chromosomes. Subclones presenting altered chromosomal distributions were challenged in soft agar. The pattern of loss of the markers suggested that only chromosomes 7p+ and 8p- may be involved in transformation events:subclones lacking one of these two chromosomes showed the reversion of anchorage-independent phenotype in that they had lost the soft agar colony forming ability, while both the presence or the absence of chromosomes 4q+ and 9q+ did not affect such trait.

3.010

CHROMOSOME STUDIES OF BREAST CARCINOMAS IN ICELAND.

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The study of karyotypic changes in malignant cells may give an indication of genetic changes that might be involved in carcinogensis. Analyses of chromosome abnormalities in breast carcinomas have been hampered by difficulties in culturing the malignant cells. By use of a specially developed serum-free medium we have cultured cells from 20 primary and metastatic breast carcinomas and control samples of normal tissue from the same individuals. Clonal chromosome abnormalities were found in 10 cases, 5 of 18 cases after direct harvesting and 5 of 17 successful cases after 3 to 6 days of cell culture. Cell cultures lasting more than 6 days yielded only single cell abnormalities. The chromosomes most frequently involved in aberrations, structural or numerical, were in descending order: 1, 17, 3, X and 8. HSR's were detected in two cases. DNA was extracted from all samples both directly and after culture and analysed for deletions and amplifications of oncogenes and antioncogenes on chromosome 17. Cell morphology and behaviour in culture will also be discussed in relation to the observed changes.

Chromosome analysis of breast carcinomas is possible both after direct harvesting and culture. Changes on chromosome 17 are of particular interest in the light of our previous results on loss of heterozygosity.

3.011

CHARACTERIZATION OF A NEW HUMAN RHABDOMYOSARCOMA CELL LINE

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A cell line, designed VK, was established from an embryonal type rhabdomyosarcoma of a 20 year old female patient. During 13 mo. in culture the cell line underwent 52 subcultures in ratio 1:3. The VK cells had a stable population doubling time of 38 hrs and plating efficiency of 0.02%. The VK cell line demonstrated morphologic and growth rate dependency on polar solvents and nutritional status. A clone (VK-C3) consists of less differentiated cells. DNA flow cytometry indicated euploid DNA content. Cytogenetic analysis of passages 3, 12 and 36 showed mainly pseudodiploid cells with 9 stable markers involving chromosomes 1, 2, 4, 9, 10, 11, 14, 17 and 19.

3.012

PHYSIOLOGICAL EXPRESSION OF A METASTASIS-ASSOCIATED VARIANT CD44 MOLECULE IS RESTRICTED TO PROLIFERATING CELLS IN A STAGE OF LOCOMOTION.

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The metastasizing subline of a rat adenocarcinoma expresses a splice variant of CD44 (vCD44), which is sufficient to transfer the metastatic phenotype on non-metastasizing tumor lines. In view of the importance of vCD44 for metastatic progression, its physiological expression appears to be of special interest. In contrast to CD44, vCD44 was not expressed on any lymphatic tissue in adult rats. Yet, it was expressed on activated lymphocytes and in the neonatal period on bone marrow cells. Variant CD44 was also detected on non-lymphatic tissue. Again, its expression differed markedly from that of CD44. Variant vCD44 was expressed only on cryptic cells of the gut, on the basal layer of hair follicles and epidermis and , in the newborn, on epithelial cells of pancreatic ducts. Hence, expression of metastasis-associated vCD44 is restricted to proliferating cells in a stage of directed locomotion, i.e. metastatic progression may be based on reactivation of developmentally expressed genes, which are responsible for tissue organization.