130

CYTOGENETICS OF TESTICULAR GERM CELL TUMORS.

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Testicular germ cell tumors (TGCT) of adults can be divided clinically and morphologically in two main entities: seminomas and nonseminomatous germ cell tumors (nonseminomas).

The cytogenetic studies of TGCT describe generally hyperdiploid to hypertriploid chromosome complements with higher modal chromosome numbers in seminomas as compared to nonseminomas.

An isochromosome of the short arm of chromosome 12 - i(12p) - has been found in more than 80% of all TGCT, as well as in some ovarian and extragonadal GCT, suggesting that this highly specific marker plays an important role in the oncogenesis of this group of tumors, irrespective of the histological subtype or location. However, molecular studies carried out on fresh TGCT and TGCT-derived cell lines have recently demonstrated that aneuploidization precedes the formation of this marker, indicating that the i(12p) is not the first genetic event in the pathogenetic pathway of these tumors.

Although the remaining 20% of TGCT have no evident i(12p), recent molecular cytogenetic studies have demonstrated that in virtually all cases markers composed of several copies of 12p are present. This leads to an over-representation of 12p sequences in this kind of tumors, similarly to what occurs in i(12p)-positive TGCT.

Preliminary molecular studies on the parental origin of the supernumerary copies of 12p provided evidence in favor of an uniparental origin of these copies, but no proof for genetic imprinting.

Isochromosome 12p-negative extragonadal germ cell tumors may represent a distinct subgroup, since no involvement of 12p has been demonstrated so far.

131

BREAST TUMOUR CYTOGENETICS

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Of the nearly 200 breast cancers with chromosome abnormalities that have been reported, many were analysed in direct preparations and several were incompletely karyotyped. The most common changes were of chromosome arms 1p, 1q, 3p, 6q, 11p, 11q, 16q, and 17p.

We have short-term cultured breast cancer cells and found clonal chromosome aberrations in 80% of the 60 tumours analysed completely until now. Cytogenetically unrelated clones were detected in half of the cases. Several recurring abnormalities were found, often as the only change, but sometimes together with evidence of clonal evolution. The defining characteristics of these cytogenetic subgroups were: 1. Gain of 1q material through der(1;16)(q10;p10), i(1)(q10), or unbalanced translocations. 2. Loss of 1q through deletions in 1qh. 3. Interstitial deletions in 3p, always including band 3p14. 4. Trisomy 18.

132

Cytogenetic alterations in benign and malignant colorectal tumors

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More than 200 human colorectal tumors, including 30 polyps were cytogenetically studied. Beside normal karyotypes, in 15 cases, recurrent anomalies were observed in polyps with various degrees of differenciation. In colorectal cancers, 7 % remained with normal karyotypes. They were observed in familial non polyposis patients principally. In about 20 % cases, few chromosomal rearrangements but gains of chromosomes, involving recurrently no. 7, X, 13, 20, 12 were observed. This group was called trisomic type (TT). In the remaing cases (70-75 %), chromosomes losses, involving 17p arm and no. 18, and less systematically other chromosomes (1p, 4, 8p, 14, 15) are very characteristic. This group was called monosomic type MT. TT tumors are preferentially located in the proximal and MT in the distal colon, but both types exist in the rectum. TT and MT tumors were also differentiated by the tendency for endoreduplication, limited to MT, and by their nucleotid metabolism. Most of the anomalies characterizing TT or MT tumors are observed in polyps, but with lower frequencies. Some benign polyps have, however, a typical "cancerous" karyotype. Except for the 17p arm deletion, none of the chromosomal anomalies is significantly correlated with pronostic factors or survival. This means that many chromosomal anomalies occur before cancerisation, as accident of preneoplastic tumor progression, and that their occurrence does not modify the severity of the desease, when malignancy has occurred. This conclusion does not apply to other epithelial tumors, since in breast cancer for instance, the rate of chromosome alterations is very strongly correlate with all pronostic factors.

133

CYTOGENETICS OF MESENCHYMAL TUMOURS

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Soft tissue tumours, particularly sarcomas, have been regarded as a difficult area of diagnostic histopathology. Cytogenetic analysis of both benign and malignant mesenchymal tumours reveals clonal chromosome aberrations in the majority of soft tissue tumours. Most commonly encountered chromosomal aberrations in malignant tumours are as follows: t(X;18) in synovial sarcoma, t(11;22) in Ewing's sarcoma, t(12;16) in myxoid liposarcoma, t(2;13) in alveolar rhabdomyosarcoma, t(12;22) in clear cell sarcoma and t(9;22) in extraskeletal myxoid chondrosarcoma. These clonal chromosome aberrations, particularly in small round-cell tumours in children and in spindle-cell soft tissue neoplasms, often have diagnostic significance.

134

SIGNIFICANCE OF TRISOMY 7 AND TRISOMY 10 IN KIDNEY TUMORS AND SURROUNDING PARENCHYMA

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During the last years several reports on chromosome alterations in renal cell carcinoma have been published or presented. Moreover some authors found clonal chromosomal alterations in the normal renal tissue of tumor bearing kidneys.

In order to identify the cells, carrying trisomy 7 and 10, conventional, cytogenetic analysis and in situ hybridization was performed on 17 kidney tumors and on healthy kidney tissue surrounding the tumor. Biopsies of 10 end stage nephropathy kidneys were used as controls.

Trisomy 7 and 10 in healthy parenchyma of tumor bearing kidneys was proved not to be a premalignant lesion, not a culture induced artifact and not an in vivo organ mosaicism. We demonstrated that trisomy 7 and 10 occurred indeed in kidney tumor but was much more prominent in the surrounding tissue, and was present, not in tubular cells but in mononuclear inflammatory cells. The latter were identified as tumor infiltrated lymphocytes which were very likely to originate in the fetal thymus.