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Analysis of Genetic Alterations in Primary Nasopharyngeal Carcinoma by Comparative Genomic Hybridization (CGH). *L. Sun[1], Y. Fong[2], J.S.T. Sham[3], Y. Guo[2], M. Deng[2], Q. Liang[2], H. Zhang[4], H. Zhou[4], H. Tideman[1], J.M. Trent[4], X.-Y. Guan[3].* 1) Oral Maxillofacial Surgery, The University of Hong Kong, Hong Kong, PR China; 2) Cancer Center, Sun Yat-sen University of Medical Sciences, China; 3) Department of Clinical Oncology, The University of Hong Kong, Hong Kong; 4) Cancer Genetics Branch, NHGRI, NIH, Bethesda, MD.

To identify genetic alterations associated with the development and progression of human nasopharyngeal carcinoma (NPC), 57 tumors were analyzed using comparative genomic hybridization (CGH). In 47 cases chromosomal imbalances were found. Several recurrent chromosomal abnormalities were identified in the present study. The most frequently detected chromosomal gains involved chromosomes 12q (24 cases, 51%), 4q (17 cases, 36%), 3q (16 cases, 34%), 1q (15 cases, 32%), and 18q (15 cases, 32%). Common regions of gain involved 12q13-q15, 4q12-q21, and 3q21-q26. High copy number increases of chromosomal materials were detected in 4 chromosomal regions, 3q21-q26.2, 4p12-q21, 8p, and 12q14-q15. The most frequently detected loss of chromosomal materials involved chromosomes 16q (26 cases, 55%), 14q (21 cases, 45%), 1p (20 cases, 43%), 3p (20 cases, 43%), 16p (19 cases, 40%) 11q (17 cases, 36%) and 19p (16 cases, 34%). The most common regions of loss involved 14q24-qter, 1pter-p36.1, 3p22-p21.3, 11q21-qter, and the distal region of 19p respectively. Genomic alterations detected using CGH were compared and found to be largely consistent with those identified using banding analysis and loss of heterozygosity studies. However, several previously unrecognized recurrent alterations were also identified in the present study including: gain of 4q and 18q, and loss of 16q, 14q, and 19p. In addition, gain of 1q, 8q, 18q, and loss of 9q showed statistically significant association with advanced clinical stage ($p<0.05$). Identification of recurrent sites of chromosomal gain and loss identify regions of the genome that may contain oncogenes or tumor suppressor genes respectively which maybe involved in the tumorigenesis of NPC.

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Recurrent Chromosome Changes in 31 Primary Ovarian Carcinomas Detected by Comparative Genomic Hybridization. *T.C.M. Tang[1], J.S.T. Sham[1], Y. Fong[2], L. Sun[3], L.X. Qin[4], X.-Y. Guan[1].* 1) Clinical Oncology, The University of Hong Kong, Hong Kong, China; 2) Cancer Center, Sun Yat-sen University of Medical Sciences, Guangzhou, China; 3) Oral Maxillofacial Surgery, The University of Hong Kong, Hong Kong; 4) Liver Cancer Institute, Zhongshan Hospital, Shanghai Medical University, Shanghai, China.

Ovarian cancer is one of the most frequent gynecological malignancies worldwide with poor prognosis. The development of new diagnostic, preventive, and treatment approaches requires good understanding of the mechanisms of the complex multi-step process of tumor pathogenesis in the ovarian cancer. Comparative genomic hybridization (CGH) has been applied to detect recurrent chromosome alterations in 31 primary ovarian carcinomas. Several nonrandom chromosomal changes including gains of 3q (17 cases, 55%) with a minimum gain region at 3q25-q26, 8q (16 cases, 52%), 19q (12 cases, 39%), Xq (11 cases, 35%), 1q (10 cases, 32%), 17q (10 cases, 32%), 12q (9 cases, 29%) with a minimum gain region at 12q12, and 20q (9 cases, 29%). High copy number gain (DNA sequence amplification) was detected in 10 cases. Amplification of 3q25-q26 and 12p11.2-q12 were detected in 4 and 3 cases, respectively. The regions most frequently lost included: 16q (9 cases, 29%), 1p (7 cases, 23%), 18q (7 cases, 23%), and 22 (7 cases, 23%). The recurrent gain and loss of chromosomal regions identified in this study provide candidate regions that may contain oncogenes or tumor suppressor genes respectively involved in the development and progression of ovarian cancer.

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Cytogenetic analyses of six neuroblastoma cell lines with cross-species color banding. *S.Y. Park[1], G.J. Kim[2], K.B. Lee[2], Y.H Kang[1], H. Kim[1,2], Y.H. Chun[1], S.H. Park[1,2].* 1) Institute of Human Genetics, Dept. of Anatomy, Korea University College of Medicine, Seoul, Korea; 2) Graduate School of Biotechnology, Korea University, Seoul, Korea.

The cytogenetic analyses of chromosomal aberrations became an essential method to identify the genes involved in the pathogenesis of cancers. Recently, the chromosome painting and cross-species color banding (RxFISH) in identifying marker chromosomes became useful techniques. Neuroblastoma is a pediatric malignant neoplasm of neural crest origin. The mechanisms contributing to the development of neuroblastoma are largely unclear, but non-random chromosomal changes, such as deletion of chromosome band 1p36, aberrations of 17q, and amplification of the *MYCN* oncogene, have identified over the past years. The purpose of this study was to establish, in detail, karyotypes of six neuroblastoma cell lines (SK-N-AS, SMS-KCNR, SK-N-MC, SK-N-SH, SH-SY5Y, and IMR 32) by G-banding, RxFISH, and FISH with chromosome painting probes. Each cell line had a variable number of numerical and structural aberrations. Deletion of 1p36 and a partial gain of chromosome 17 with the breakpoint on 17q21 were observed in four cell lines each. Chromosome 6, 15, 16, and 22 were commonly involved in structural abnormalities. Homogeneously staining regions or double minute chromosomes were confirmed in three cell lines, all of which were turned out to be amplification of *MYCN*. The chromosomal aberrations of the six neuroblastoma cell lines were effectively analyzed by RxFISH and multiple chromosome painting probes. The nonrandom rearrangements suggest candidate regions for isolation of genes related to neuroblastoma.

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BRCA1 copy number in paraffin embedded cancer tissue samples of known BRCA1 and BRCA2 mutation carriers using a BRCA1 FISH probe. *S.R. Young[1], N. Kataoka[1,2], Z. Wang[1], H. Kato[1,3], W.T. Loging[1], J.R. Marks[4], N. Lehman[5].* 1) Dept OB/GYN, Univ South Carolina Sch Med, Columbia, SC; 2) Dept GYN/OB, Kyoto Univ JAPAN; 3) Dept OB/GYN, Nagoya City Univ Hosp, JAPAN; 4) Dept Surgery, Duke Univ Durham, NC; 5) Dept Pathology, Creighton Univ, Omaha, NE.

BRCA1 and BRCA2 genes, located on 17q and 13q, respectively, have been linked to hereditary breast cancer. Women inheriting a mutant form of either gene have up to a 70-80%; lifetime risk of developing breast cancer. Both BRCA1 and BRCA2 are thought to function as tumor suppressor genes. LOH studies have shown that loss of the corresponding wild-type allele in a BRCA1 or BRCA2 mutation-carrying individuals is associated with the development of malignancy. We have developed a FISH probe for the BRCA1 gene to study allele loss in archived, paraffin-embedded, tissue samples. Studies of five normal breast tissue samples, obtained during reduction mammoplasty, showed 5.8 to 11.8% of interphase cells having one BRCA1 signal. Four known BRCA1 mutation carrying malignant breast cancer tissue samples showed 30.8 to 51.4% of cells having one BRCA1 signal present in the interphase cells. In comparison, four known BRCA2 mutation carrying malignant breast cancer tissue sections revealed 25 to 30% of interphase cells as having one BRCA1 signal present. While there appears to be greater allelic loss of BRCA1 in BRCA1 cases compared to BRCA2 cases, the difference appears too small to confidently differentiate the two. A BRCA2 probe FISH study may be helpful in this regard. Numerous Southern blot studies have reported LOH at 17q in sporadic breast cancer. Our current FISH results support the concept that the BRCA1 gene, or the loss of the BRCA1 gene, is important in both hereditary and non-hereditary breast cancers. The use of FISH technology to evaluate allelic loss of BRCA1 and other tumor suppressors may prove of value in the study of other forms of cancer. It remains to be seen if FISH probes can differentiate BRCA1 and BRCA2 mutation bearing tissue samples.

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Chromosomal abnormalities in colorectal polyps. *A.E. Rojas-Atencio, K. Urdaneta, P. Estrada, M. Soto-Alvarez, L. Borjas-Fajardo.* Unidad de Genetica, Universidad del Zulia, Maracaibo, Zulia, Venezuela.

The colorectal cancer is the second cause of death for cancer in the world, they usually begin as a benign polyp and many of them are never developed in cancer. The development of the cancer starting from a polyp you happens when it happens a mutation in the genetic code that controls the growth and repair of the cells. The objective of this work is to report the chromosomal anomalies found in 15 colorectales polyps The chromosome analysis was carried out through technical of short culture. A numeric anomaly was considered if this repeated at least 3 times and a structural one if it repeated at least 2 times. The chromosome analysis of the 15 polyps histology reported as benign adenoma, they revealed clonal chromosome aberrations in 11 of the 15 cases, seven of them presented specially lost numeric type anomalies of the chromosomes 8 and 22, other recurrent numerical change were +11 and +18, alone in a case an anomaly of structural type was observed that corresponded to a deletion of the short arm of the chromosome 7 [(del7p)]. The chromosome analysis of the polyps adenoma has been correlated by some authors with clinical and pathological parameters and the same ones could serve as a parameter suggestive presage of progression of the illness toward the metastasis.

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Karyotypic analysis of non-tumorigenic and tumorigenic, human prostatic epithelial cell lines representing a tumor progression model. *P.D. Storto[1], G. Bice[1], D. Bello-DeOcampo[2], S. Quader[2], M.M. Webber[2].* 1) Dept Pediatrics/Human Develop, Michigan State Univ, East Lansing, MI; 2) Dept Zoology Michigan State Univ, East Lansing, MI.

RWPE-1, a human prostate epithelial cell line, has been transformed with MNU (N-methyl-N-nitrosourea) to generate four new cell lines (referred to as the MNU cell lines). The four MNU cell lines have been designated WPE1-2A22, WPE1-NB14, WPE1-NB11, and WPE1-NB26, in increasing order of their malignancy. The cell lines represent different stages of tumor progression, from non-invasive to invasive, and will serve as an interesting in vitro model of prostatic neoplasia formation.

We have studied the four MNU cell lines in regards to their cytogenetic makeup, i.e. we have analyzed the specific chromosomal abnormalities present in the cell lines. The cell lines contained both common and unique aberrations; all four MNU lines had lost copies of chromosomes Y and 22, and gained entire copies of chromosomes 5 and 20. Breaks occurred at chromosomal regions 7q22, 9q11, 11q13, 11q23, 11q25, and 18q12.2. All cells lines revealed loss of material from chromosomes 7 and 18 long arms, and duplication of material from chromosomes 9 and 11 long arms.

Abnormalities not common to all cell lines were a deletion of chromosome 2 long arm material and a 13q isochromosome in cell line WPE1-2A22, a deletion of chromosome 1 long arm material and loss of chromosome 13 in cell lines WPE1-NB14 and WPE1-NB26, a duplication of chromosome 19 material in cell line WPE1-NB11, a break at region 19q21 and duplication of material from the long arm of chromosome 13 in cell line WPE1-NB26, and small unidentifiable markers in cell lines WPE1-NB11 and WPE1-NB26. Overall, the more tumorigenic cell lines appeared to contain a greater number of cytogenetic rearrangements. We discuss the significance of these cytogenetic abnormalities in terms of their prevalence in prostate cancer, and in regards to the locations of tumor-suppressor genes that may be involved in the chromosomal rearrangements.