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Zeroing-in-on breakpoint susceptibility regions on chromosomes in breast carcinoma. A. Mattoo and R S. Verma. Division of Molecular Medicine and Genetics, Wyckoff Heights Medical Center, Brooklyn-New York Hospital/Weill Medical College of Cornell University, New York, Institute of Molecular Biology and Genetics and SUNY Health Science Center at Brooklyn, NY.

Breast cancer is a complex disease in which numerous genetic aberrations occur whose causative effects on tumorigenesis remain illusive. It is becoming clearer that specific molecular alterations are required in the progression of this disease and have been implicated in the development of breast cancer. Therefore specific genetic changes have become critical factors towards understanding the development of this disease. At the chromosomal level, data of the least and most associated chromosomal sites, that may be relevant to breast tumorigenesis, are accumulating rapidly.

The most frequently involved sites are: 1p32, 1p34, 1q25-qter, del(1)(q11-q12), der(1;16)(q10p10), t(1;3)(p31;q24), t(1;7)(p22q32), t(1;10)(p22;q14); 2q; 3p14.2-21.1, 3p24.3-25, del(3)(p12-21), t(3;4)(p14;q21); 4q21; 5q; 6p, del(6)(q21.2); 8p11, 8p12, 8q24; 9p21-24, 9p; 11p11, 11p15, 11q13, 11q23.1, 11q24.1; 12p, 12q13; 13q12-24; 14q; 15q; 16q22, 16q24; 17p13.3, 17q11.2-21, 17q12; 18q21; 20q12-qter and 22q13.1.

Strikingly, the breaks on different chromosomes are highly variable. The recurrent gains of chromosomes were 1, 4, 5, 6, 7, 11, 12, 16, 17, 18, 19 and 20 while loss of chromosomes 6 and 7 were quite frequent. Some of these changes have been correlated with adverse prognosis in this disease. In addition, we present a detailed account of molecular markers and discuss their clinical relevance.

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Interphase Spectral FISH: Tailoring a diagnostic and minimal residual disease (MRD) assay for oncology. J.L. Murata-Collins, F. Zhang, L. Tcheurekdjian, and M.L. Slovak. City of Hope National Medical Center, Duarte, CA.

Spectral FISH is a powerful multiplex fluorescence *in situ* hybridization (FISH) technique requiring only a single hybridization to target disease-specific multiple chromosomal aberrations in interphase nuclei, using combinatorial fluorescence and digital imaging microscopy developed for the ASI™ Spectral Karyotyping System. In oncology, it becomes a particularly useful tool to diagnosis and monitor clonal aberrations not readily amenable to PCR technology, including aneuploidy or recurrent deletions of variable chromosomal regions, such as del(5q), del(6q), or del(7q). Multiple aneuploidies are common in both hematologic malignancies and solid tumors, with particularly frequent involvement of chromosomes 4, 5, 6, 7, 8, 9, 10, 11, 13, 14, 18, 21, X, and Y. To assess ploidy status in low or non-mitotic cells from various neoplastic disorders, including breast cancer, lymphoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia, and cells recovered from bladder washings suspicious for recurrence of bladder cancer, we developed an initial Spectral FISH oncology panel of six centromeric probes for chromosomes 7, 8, 9, 10, X, and Y, using unique two-dye combinations of four fluorophores: Cy5.5, Spectrum Green, Spectrum Orange, and Spectrum Red. Spectral FISH readily identified clonal aberrations in all recurrent bladder cancer cases tested and identified MRD in hyperdiploid ALL, providing proof of concept. Validations of the Spectral FISH assay were performed by classic cytogenetics, when mitotic cells were available, or by standard FISH analyses. Advantages of Spectral FISH include increased sensitivity by surveying multiple genetic targets in specimens with limited cell numbers for analysis, identifying aberrations in poor growth/no growth specimens, and the ability to detect specific genetic aberrations at the single cell level to assess MRD or early stages of recurrent disease. To obviate the limitations of low cell numbers, spectral FISH requires only a single hybridization, while allowing simultaneous detection of multiple numerical changes, with the ability to select combinations of informative probes highly associated with, or characteristic for a specific malignancy. Disadvantages include labor intensive screening, and interpretative challenges associated with signal overlap in highly polyploid samples, and focal plane distortions resulting in false positives or negatives. Spectral FISH, as a sensitive MRD assay, has significant potential clinical application, allowing early detection of new or re-emerging clones, and earlier therapeutic intervention.

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Ring Chromosome 14 Syndrome: Prenatal diagnosis of two cases with 45,XY,-14/46,XY,r(14)(p11.2q32). R.T. Schmidt[1], J.B. Ravnan[2], A.N. Lamb[2], and M.E. Weinstein[1]. [1]Genzyme Genetics, Yonkers NY, and [2]Genzyme Genetics, Santa Fe, NM.

Two prenatally detected cases of 45,XY,-14/46,XY,r(14) are described. The breakpoints of the ring chromosome 14 at bands p11.2q32 were confirmed using fluorescence in situ hybridization (FISH). These cases are added to a growing number of cases of ring chromosome 14 syndrome reported since 1971. The r(14) syndrome is reviewed with emphasis on the clinical features that set it apart from "general ring syndrome". Although individual cases show a variety of manifestations, the major clinical features include growth retardation, mental retardation, seizures, microcephaly and distinct dysmorphic facial features.

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Tandem duplication of bands q13.13q13.33 resulting in partial trisomy of long arm of chromosome 19. G.S. Sekhon and E.B. Johnson. University of Wisconsin, Madison.

A tandem duplication of the proximal long arm of chromosome 19 was identified in a 2 year old female infant with developmental delays. GTG technique revealed that the long arm region 19q13.13-q13.33 was tandemly duplicated. The karyotype is: 46,XX,dup(19)(q13.13q13.33) FISH technique using whole chromosome paint showed that the abnormal chromosome was composed entirely of chromosome 19 material. Parental chromosomes were normal.

To our knowledge, this is the first case of "pure" trisomy of 19q13.13-q13.33. Clinical follow up of our patient and a further molecular characterization of the breakpoints involved should shed light on the development effects of the duplicated genes in this region. These studies are in progress.