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A Comprehensive Exploration of Molecular Cytogenetic Methods in Chromosomal and Genomic Analysis

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Opinion Article

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ABOUT THE STUDY

Beginning with the theory put forth by von Hansemann and Boveri that cancer is a chromosomal disease, cytogenetic analysis was applied to cancer cells, including mouse models of human cancer. However, for over 50 years, this method was unable to definitively demonstrate that chromosomal aberrations are the cause of tumorigenesis. Technical constraints came first, followed by unbreakable stereotypes that even stopped the accurate count of human chromosomes until Tijo and Levan's 1956 report.

The creation of this baseline stimulated cytogenetic research, and soon afterward it was shown that certain chromosomal aneuploidies were linked to disease syndromes like Patau syndrome, Edward syndrome, and down syndrome. The discovery by Nowell and Hungerford of a non-random, specific aberration in patients with chronic myelogenous leukemia the so-called Philadelphia chromosome was a seminal event in the field of cancer cytogenetics. Later research by Janet Rowley revealed that this aberration was a balanced translocation between chromosomes 9 and 22, which established the paradigm of oncogene activation associated with translocations.

Giemsa banding provided chromosome analysis with a crucial technological advancement. These accomplishments allowed for the accurate counting of chromosomes as well as the evaluation of their structural integrity. Catalogs of chromosomal abnormalities in leukemia, lymphoma, and sloid tumors provide compelling evidence of the significance of this discovery, which cannot be overstated. According to the recently released third edition of Heim and Mitelman's compendium Cancer Cytogenetics, chromosome banding techniques have been used to study approximately 50,000 cases. Banding analysis has allowed for the identification of numerous fusion genes at the site of chromosomal translocations, including well-known oncogenes like MYC in Burkitt's lymphoma.

However, the field of molecular cytogenetics emerged, offering previously unheard-of flexibility to experimental design and significantly enhancing resolution, with the development of molecular biology techniques like DNA cloning and hybridization-the first *in situ* hybridization was reported by Gall and Pardue in 1969. This article will provide a detailed review of four of the most important molecular cytogenetic methods for analyzing Cancer Chromosomes and Genomes: Comparative Genomic Hybridization (CCG), Spectral Karyotyping (SKY) and M-FISH, Fluorescene *in situ* Hybridization (FISH), and interphase cytogenetics.

FISH is the process of hybridizing fluorescently tagged DNA probes to interphase nuclei or metaphase chromosomes in tissue sections or cytological preparations. DNA probes can target entire chromosomes, specific DNA sequences, centromeres, or other regions. Various monographs contain complete instructions for the preparation, labeling, hybridization, and detection of probes. Strong signals are produced by centromere-targeting probes, but their applicability may be restricted by the presence of minor binding sites on other chromosomes.

These probes are mainly employed as reference probes to count particular clones that target particular genes. Nowadays, BAC clones or BAC clone contigs are the most common source of gene-specific probes. A large number of the known human tumor suppressor genes and oncogenes are offered for sale as FISH probes and are useful resources for researching genomic amplification, gain, and deletion in diagnostic material. FISH probes that target specific chromosomal translocations and have sophisticated probe designs are useful tools for diagnosing and differentiating hematological malignancies, tracking the effectiveness of treatment, and identifying minimal residual disease and relapse.