CANCER GENOMICS & PROTEOMICS *23*: 342-392 (2026)
doi: 10.21873/cgp.20580

Review

Cancer Cytogenetics: Deep Roots, New Branches in the Age of Omics

IOANNIS PANAGOPOULOS

Department of Molecular Oncology, Institute for Cancer Research, Oslo University Hospital-*Radiumhospitalet*, Oslo, Norway

Abstract

For decades, the "death of cancer cytogenetics" has been repeatedly proclaimed and has grown louder in the era of omics. However, cytogenetics continues to evolve, retaining its central role in the study of chromosomes. From the microscopic visualization of numerical and structural aberrations using staining and banding techniques, the field has steadily incorporated new methodologies, including fluorescence *in situ* hybridization, array comparative genomic hybridization, high-throughput sequencing, and, most recently, optical genome mapping. These approaches have revealed unprecedented details of chromosome structure and behavior, uncovered catastrophic genomic events in cancer, and given rise to new concepts such as cytogenomics and chromosomics. Although cytogenetics is sometimes viewed as synonymous with chromosome banding, its scope, namely the study of chromosome structure and behavior, extends far beyond any single method. Chromosomes remain indispensable for understanding genome architecture, chromosomal instability, and fusion-gene mechanisms in neoplasia, irrespective of the technologies applied. Rooted in its past yet continually branching outwards with each scientific advance, today's cytogenetics integrates classical and modern approaches, carrying forward the legacy of chromosome banding while adopting genome-wide technologies. These developments underscore the enduring importance of cytogenetics for interpreting the structural complexity of cancer genomes. This review aims to demonstrate that cytogenetics, far from being obsolete, remains a vital component of modern cancer research by highlighting essential insights into chromosome structure, genome architecture, and fusion-gene mechanisms in the era of *-omics*.

Keywords: Cancer cytogenetics, chromosomal instability, genome architecture, fusion genes, cytogenomics and chromosomics, review.

Ioannis Panagopoulos, Department of Molecular Oncology, Institute for Cancer Research, Oslo University Hospital-*Radiumhospitalet*, P.O. Box 4953 Nydalen, Oslo, NO-0424, Norway. E-mail: ioapan@ous-hf.no

Received December 22, 2025 | Revised February 10, 2026 | Accepted February 16, 2026

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.
©2026 The Author(s). Anticancer Research is published by the International Institute of Anticancer Research.

Introduction

For many years, at conferences, meetings, and in countless conversations with fellow scientists, the "death of cancer cytogenetics" has been repeatedly proclaimed. With the introduction of each new technology in cancer genetics, predictions emerged that cytogenetics would soon become obsolete. These forecasts have only grown louder over the past two decades, in the era of -*omics*, massively parallel sequencing (also known as next-generation or high-throughput sequencing), large-scale genomic data generation, and the rise of personalized medicine. Yassmine Akkari, Senior Director of the Clinical Laboratory at the Steve and Cindy Rasmussen Institute for Genomic Medicine, Nationwide Children's Hospital, and Professor of Pathology at The Ohio State University College of Medicine, described a similar situation. She wrote: "For decades, cytogenetics has been declared dead. But for as long as I can remember, I have never understood this statement. In my mind, cytogenetics is the science of chromosomes – and how can a science die?" (1).

Zhang and colleagues (2) similarly noted: "Between 1950 and 1970, cytogenetics was stagnant because there were few advances in new techniques. There were suggestions that 'cytogenetics is a dead science' and that it was no longer needed because of advances in other disciplines of biology."

Professor Thomas Liehr, founding editor and long-time Editor-in-Chief of Molecular Cytogenetics, has also encountered this notion. He recalls that when he entered the field in 1991, cytogenetics was already being dismissed as outdated and soon to be replaced by more modern approaches. He further noted that even his own supervisor, Professor Erich Gebhart (Erlangen, Germany), faced such skepticism when publishing his first articles in 1968 (3).

On the other hand, the College of American Pathologists, together with the American College of Medical Genetics and Genomics, provides and continues "to develop effective and timely proficiency testing in the practice of clinical cytogenetics, which includes both conventional and molecular cytogenetics and cytogenomics" (https://www.cap.org/member-resources/councils-committees/cap-acmg-cytogenetics-committee/). Likewise, the European Cytogeneticists Association continuous to organize courses in classical and molecular cytogenetics leading to a European diploma in clinical cytogenetics, which covers all aspects of the field in depth (https://www.e-c-a.eu/EN/default.asp). Such activities by these bodies clearly indicate the ongoing relevance of cytogenetics in both research and clinical practice.

This review aims to demonstrate that cytogenetics, far from being obsolete, remains a vital component of modern cancer research and diagnostics, and that chromosomal abnormalities still hold a central role in oncology, even in the era of omics and precision medicine.

Defining Cytogenetics: The Chromosomal Language of Life

In The Facts On File Dictionary of Biology, cytogenetics is defined as "the area of study that links the structure and behavior of chromosomes with inheritance" (4). In Henderson's Dictionary of Biological Terms, cytogenetics is defined as "genetics in relation to cytology; the cytological aspects of genetics" (from the Greek *kytos*, meaning hollow, and *genesis*, meaning descent) (5). The Bantam Medical Dictionary offers a slightly broader definition: "a science that links the study of inheritance (genetics) with that of cells (cytology); it is concerned mainly with the study of chromosomes, especially their origin, structure, and functions" (6). Stedman´s Medical Dictionary for the Health Professions and Nursing defines cytogenetics as "the branch of genetics concerned with structure and function of the cell, especially the chromosomes" (7). The online Merriam-Webster Dictionary describes cytogenetics as "a branch of biology that deals with the study of heredity and variation by the methods of both cytology and genetics." The National Human Genome Research Institute defines cytogenetics as "a branch of biology focused on the study of chromosomes and their inheritance, especially as applied to medical genetics."

It further explains in its glossary: "Cytogenetics is the study of chromosomes in any species" (https://www.genome.gov/genetics-glossary/Cytogenetics).

Many other dictionaries similarly describe cytogenetics as a branch of biology or genetics that merges cellular and hereditary perspectives. The term 'cytogenetics' emerged during the 1930s and 1940s, as the study of chromosome structure and behavior was increasingly integrated with the principles of Mendelian genetics. Although no single individual is credited with coining the term, it gained prominence through the work of early pioneers such as C.D. Darlington, who helped establish cytogenetics as a distinct scientific discipline (8). The field gained further significance in the late 1950s, following the discovery that the correct number of human chromosomes is 46 (9), and the subsequent identification of chromosomal abnormalities associated with human diseases, most notably, trisomy 21 in Down syndrome (10). Over time, cytogenetics has also become indispensable in other areas of biology, including evolutionary studies, developmental biology, and reproductive medicine. Its applications extend beyond human health to plant and animal breeding, species classification, and comparative genomics (11-13). Thus, while the term 'chromosome' belongs to the early, descriptive era of cell biology, 'cytogenetics' marks a conceptual shift toward understanding chromosomes as carriers of genetic function and as clinically relevant structures.

So, as Dr. Yassmine Akkari aptly asked: How can a science die?

Cytogenetic Methodologies and Periods: From Pre-banding to Cytogenomics and Chromosomics

Like every scientific discipline, cytogenetics relies on a range of methodologies that have evolved and expanded over time. These techniques have become increasingly sophisticated, largely due to advances in related technologies and adjacent fields. From the early use of basic staining techniques, the field progressed to chromosome banding methodologies, introduced in 1970-71, which became the gold standard techniques for several decades (14-17). These were followed by high-resolution banding, molecular cytogenetic tools such as fluorescence *in situ* hybridization and array comparative genomic hybridization, and, more recently, by high-throughput sequencing and optical genome mapping. Collectively, these advances have continually expanded the cytogenetic toolkit to meet evolving diagnostic and research challenges.

In 2002, Liehr and Claussen (18) proposed the division of cytogenetics into three historical periods, based on the central role of banding techniques: the pre-banding period, the pure banding period, and the molecular cytogenetics period. However, since then, major technological developments have transformed the field, enabling the investigation of chromosomes at submicroscopic resolution.

Recent advances, particularly high-throughput sequencing, single-cell analysis, and optical genome mapping, have led to the emergence of a fourth period, often referred to as the 'cytogenomics' or 'chromosomics' era (19-24). This phase is defined by the integration of cytogenetics with large-scale genomic and epigenomic data, enabling comprehensive analysis of structural chromosomal variations at unprecedented resolution. The term 'chromosomics' reflects this integrative approach, emphasizing not only the detailed characterization of chromosomal architecture, but also efforts to understand its functional implications in development, disease, and evolution (21, 22, 25). In this context, cytogenetics is no longer a stand-alone discipline, but a central component of multi-omics strategies, offering crucial insights into genome organization and its disruption in human disease.

The Pre-banding period. The pre-banding period of cytogenetics began, at least symbolically, in 1888, when the German anatomist Heinrich Wilhelm Gottfried von Waldeyer-Hartz coined the term *chromosome*, combining the Greek words *chroma* (χρώμα, meaning color) and *soma* (σώμα, meaning body) (26). This period continued until 1970, when chromosome banding techniques were introduced (27). During this time, chromosome

preparations were typically stained using simple dyes such as Orcein or Feulgen, which produced a uniform coloration across chromosomes (28-31). As a result, individual chromosomes were only distinguishable by their relative size and centromere position, a method known as karyotyping, a term derived from the Greek *karyon* (κάρυον), meaning nut or nucleus, and *typos* (τύπος), meaning form or impression. This morphology-based classification system made it extremely difficult to detect subtle structural abnormalities, balanced translocations, or small deletions and duplications.

These technical developments occurred in parallel with important theoretical breakthroughs. The Boveri–Sutton chromosome theory of inheritance, proposed independently by Walter Sutton (1902-1903) and Theodor Boveri (1902), identified chromosomes as the physical carriers of genetic material, a unifying framework that linked cytology with Mendelian genetics (32-34). This theory laid the groundwork for modern cytogenetics by establishing that the behavior of chromosomes during meiosis corresponded with the laws of inheritance.

Boveri later extended his insights into the field of oncology. In 1914, he published "Zur Frage der Entstehung maligner Tumouren" (Concerning the Origin of Malignant Tumours), in which he hypothesized that cancer could arise from chromosomal abnormalities, specifically, unbalanced chromosomal complements that disrupted normal cellular regulation (33, 35). Although speculative at the time, Boveri's ideas anticipated the chromosomal basis of cancer and are now recognized as visionary.

A key milestone of the pre-banding period was the correct determination of the human diploid chromosome number (9). Until the mid-1950s, it was widely believed that humans had 48 chromosomes, as unlit then, microscopes lacked the resolution to distinguish closely apposed chromosomes. In 1956, Joe Hin Tjio and Albert Levan, using improved techniques such as hypotonic treatment and better chromosome spreading, accurately established the human chromosome number as 46 (2n = 46), fundamentally revising our understanding of human genetics. This discovery laid the foundation for further standardization. In 1960, the Denver Conference proposed the first uniform system for naming and classifying human chromosomes (36). Chromosomes were grouped into seven categories (A-G) based on morphology, size and centromere position, and were assigned the now-standard numbering from 1 to 22, along with the X and Y chromosomes. This nomenclature system enabled more consistent karyotyping and interpretation, even in the absence of banding techniques.

Despite the technical limitations of the time, pioneering cytogeneticists were able to identify major numerical aberrations. Among the earliest and most significant discoveries were trisomy 21, responsible for Down syndrome (10), and abnormalities involving the sex chromosomes (37, 38). In 1959, Turner syndrome was described in individuals with a single X chromosome (45,X), and in the same year, Klinefelter syndrome was linked to the presence of an extra X chromosome in males (47,XXY). These findings not only demonstrated the relevance of chromosome number to human development and disease but also marked the beginning of clinical cytogenetics as a diagnostic field.

One of the most notable breakthroughs of this period was the discovery, in 1960, of a minute chromosome in the leukemia cells of patients with chronic granulocytic leukemia (now termed 'chronic myeloid leukemia') by Peter Nowell and David Hungerford (39, 40) (Figure 1A). They reported that this tiny chromosome replaced one of the four smallest autosomes in the chromosome complement of cultured peripheral blood cells and was absent from the normal chromosome constitution. This led them to propose a possible causal relationship between the observed abnormality and leukemia. This aberration, later designated the Philadelphia chromosome, represented the first cytogenetic link to cancer.

In addition to the Philadelphia chromosome, several other important tumor-associated chromosomal abnormalities were identified during the pre-banding period. In 1963, Lele, Penrose and Stallard reported a visible deletion on the long arm of chromosome 13 in a patient with retinoblastoma, marking one of the first cytogenetic links between a constitutional chromosomal

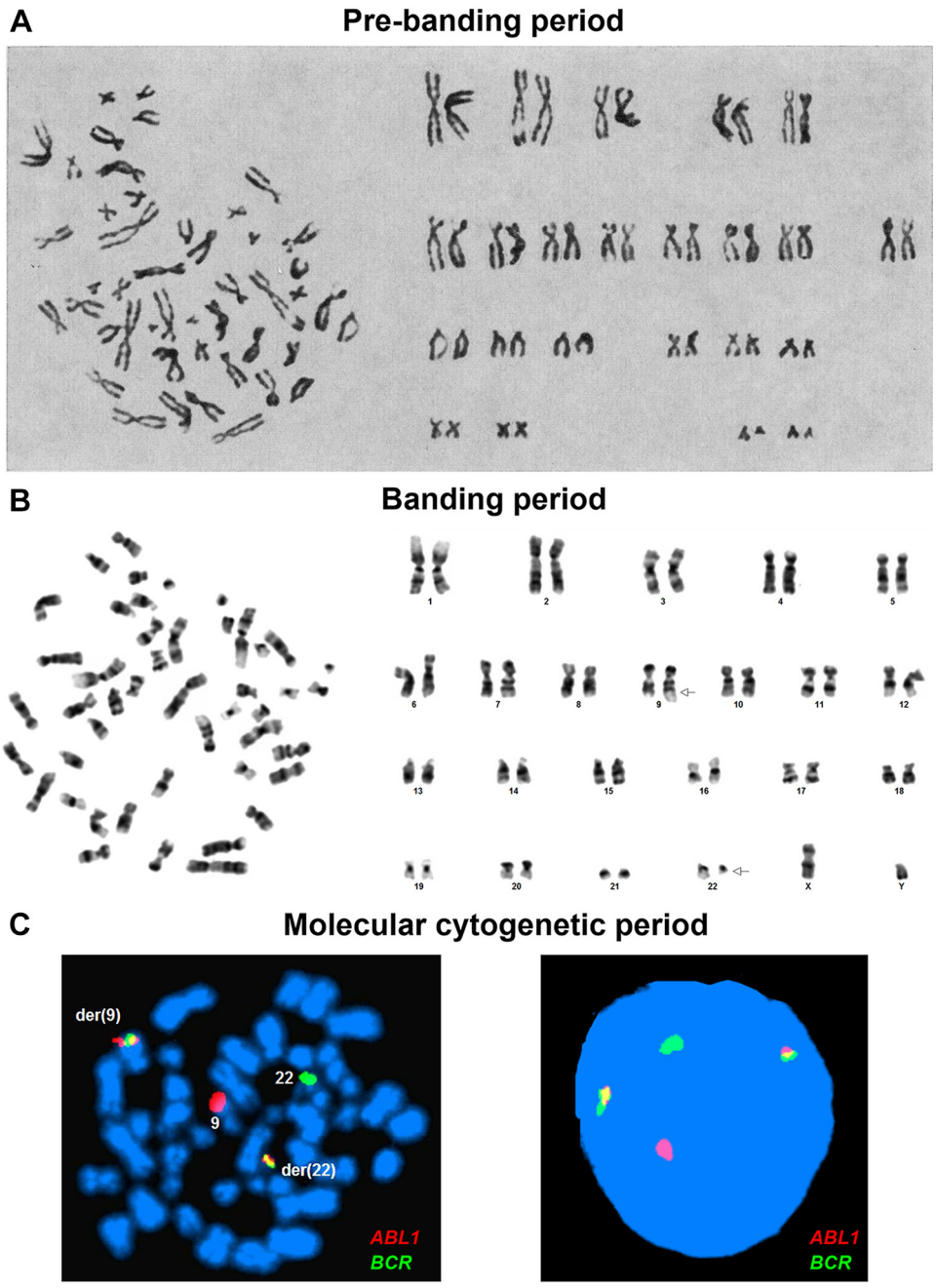


Figure 1. *Detection of the Philadelphia chromosome/BCR::ABL1 fusion gene in the pre-banding, banding, and molecular cytogenetic periods. (A) Pre-banding period: "Mitotic cell and karyotype from marrow examined without culture from a patient with chronic granulocytic leukemia to show the Ph[1] chromosome (small chromosome in the G group)" – original description by Conen. The left image corresponds to what is now referred to as a metaphase spread. Reproduced with permission from CMAJ Group. [Conen PE: Clinical conference on leukemia: Chromosome studies in leukemia. Can Med Assoc J 96: 1599-1605, 1967 (Figure 3)]. (B) Banding period: Philadelphia chromosome detected by G-banding. Left: metaphase spread. Right: corresponding karyogram. Courtesy of Kristin Andersen, Oslo University Hospital-Radiumhospitalet. (C) Molecular cytogenetic period: Detection of the Philadelphia chromosome/BCR::ABL1 fusion by fluorescence in situ hybridization (FISH) using the CytoCell BCR/ABL (ABL1) translocation, dual fusion FISH probe. Left: metaphase spread. Right: interphase nucleus. The ABL1 probe, red signal, hybridizes to chromosome 9, and the BCR probe, green signal, hybridizes to chromosome 22. Courtesy of Kristin Andersen, Oslo University Hospital-Radiumhospitalet.*

aberration and a solid tumor (41). That same year, Jacobs and colleagues published one of the earliest cytogenetic studies of Burkitt lymphoma, noting recurrent involvement of chromosome 8 in tumor cells (42). In 1965, Brewster and Garrett described chromosomal abnormalities in neuroblastoma, although the changes were nonspecific due to the limitations of the techniques available at the time (43).

These early findings, though limited in resolution, collectively demonstrated that both constitutional and acquired chromosomal abnormalities were involved in cancer biology. They provided initial insights into the cytogenetic basis of cancer development and diagnosis and laid the groundwork for the more detailed characterizations that would follow in the banding and molecular cytogenetics periods. In retrospect, these discoveries offered some of the first experimental support for Boveri's 1914 hypothesis that cancer could result from chromosomal imbalances that disrupt normal cellular regulation. What had once been a visionary theory was now gaining empirical footholds.

The pure banding period. The introduction of chromosome banding techniques in 1970 marked the beginning of what is often referred to as the pure banding period (3, 18), representing the second major phase in human cytogenetics. Banding refers to the alternating light and dark patterns visible along chromosomes under light or fluorescence microscopy. These reproducible patterns, unique to each chromosome, allow for their precise identification and help significantly to improve the detection of both numerical and structural abnormalities.

The period began with Lore Zech's introduction of Q-banding, a technique using quinacrine mustard that revealed reproducible fluorescence patterns along chromosomes under ultraviolet light (15, 27). In 1971, Seabright introduced a more practical and widely adopted alternative: trypsin-Giemsa staining for G-banding. This method produced comparable banding patterns, but could be visualized with standard light microscopy and did not require fluorescence (17). These innovations quickly became the gold standard in clinical cytogenetics, enabling consistent and accurate identification of chromosomal abnormalities with unprecedented resolution (44).

A major milestone of this period was the Paris Conference in 1971, which produced the influential document "Standardization in Human Cytogenetics" (45). This publication established a universal system for designating human chromosomes, chromosomal regions, and individual bands. It laid the foundation for the banding-based nomenclature that remains in use today and marked the beginning of what would become the International System for Human Cytogenetic/Cytogenomic Nomenclature (ISCN) (46) (*see below*, *Evolution of the International System for Human Cytogenetic/Cytogenomic Nomenclature*).

The pure banding period witnessed a surge in the discovery of recurrent chromosomal aberrations in cancer, many of which remain diagnostic and prognostic hallmarks today (47). One of the most groundbreaking findings came in 1973, when Janet Rowley demonstrated that the Philadelphia chromosome resulted from a reciprocal translocation between chromosomes 9 and 22, designated t(9;22)(q34;q11) (Figure 1B) (48). This built on Lore Zech's earlier identification of the small marker as chromosome 22 using Q-banding (14). Banding techniques soon led to the recognition of other recurrent translocations, including t(8;21)(q22;q22) in acute myeloid leukemia, t(15;17)(q24;q21) in acute promyelocytic leukemia, t(11;14)(q13;q32) in mantle cell lymphoma, and t(14;18)(q32;q21) in follicular lymphoma (49).

Recurrent cytogenetic abnormalities were also identified in solid tumors, such as t(11;22)(q24;q12) in Ewing sarcoma, t(X;18)(p11;q11) in synovial sarcoma, t(2;13)(q35;q14) in alveolar rhabdomyosarcoma, del(11)(p13) in Wilms tumor, del(13)(q14) in retinoblastoma, and monosomy 22 in meningiomas (49). These discoveries provided the first consistent cytogenetic links between specific chromosomal rearrangements and distinct tumor types.

To organize and disseminate this rapidly expanding body of knowledge, Felix Mitelman compiled the "Catalogue of Chromosome Aberrations in Cancer", first published in print during the banding period (50, 51). This pioneering reference systematically listed chromosomal rearrangements observed in human malignancies and became an essential resource for both researchers and clinicians. Over time, it evolved into the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer, which remains a key publicly available repository for cytogenetic and molecular data in oncology (52).

Concurrent advances in molecular genetics during the banding period laid the groundwork for molecular cytogenetics. Techniques such as restriction enzyme digestion (53), Southern blotting (54), and northern blotting (55) enabled the analysis of DNA structure and gene expression. Radioactive labeling of probes became routine in hybridization assays (56), and the introduction of Sanger sequencing in the late 1970s allowed for direct determination of nucleotide sequence (57). A pivotal resource was the 1982 publication of "Molecular Cloning: A Laboratory Manual" by Maniatis, Fritsch and Sambrook, which standardized and codified many of these protocols, quickly becoming the definitive reference for molecular biologists (58).

The application of these molecular tools to tumor samples with known cytogenetic abnormalities led to landmark discoveries, and by the end of 1987, eight unique fusion genes had been reported. In Burkitt lymphoma, rearrangements involving the *MYC* oncogene and immunoglobulin loci were identified, including *IGH::MYC* [t(8;14)(q24;q32)], *IGK::MYC* [t(2;8)(p12;q24)], and *IGL::MYC* [t(8;22)(q24;q11)] (59-62). In follicular lymphoma, the t(14;18)(q32;q21) translocation generated *IGH::BCL2* (63), while the t(11;14)(q13;q32) led to *IGH::CCND1* in B-cell chronic lymphocytic leukemia (64), a rearrangement that was later recognized as the genetic hallmark of mantle cell lymphoma. In chronic myeloid leukemia, the hallmark translocation t(9;22)(q34;q11) was shown to generate the *BCR::ABL1* fusion gene (65, 66). In T-cell acute lymphoblastic leukemia, the t(8;14)(q24;q11) gave rise to *TRA::MYC* (67-69), while in T-cell lymphoma, the inv(14)(q11q32) generated *IGH::TRA* (70). These discoveries revealed that chromosomal rearrangements were able to activate oncogenes or produce fusion genes, driving malignant transformation, and underscored the emerging synergy between cytogenetics and molecular biology (49).

The pure banding period remained dominant until the mid-1980s, when molecular techniques began to redefine the field. In 1982, Langer-Safer *et al.* demonstrated DNA hybridization on polytene chromosomes using fluorescently labeled antibodies, laying the groundwork for fluorescence *in situ* hybridization (71). In 1986, Pinkel *et al.* successfully applied high-sensitivity fluorescence *in situ* hybridization to human metaphase chromosomes, marking the transition from the pure banding era to the molecular cytogenetics period (72).

Collectively, the achievements of the pure banding period transformed cytogenetics from a largely descriptive discipline into a powerful diagnostic and investigative tool. By enabling precise chromosomal identification and linking specific rearrangements to distinct malignancies, this era laid the essential cytogenetic and molecular foundations for modern cancer genetics.

The molecular cytogenetics period. The third major phase in human cytogenetics, known as the molecular cytogenetics period, began in the mid 1980s as a natural progression from banding-based analysis. It was marked by the development of fluorescence *in situ* hybridization and its first high-sensitivity application to human chromosomes using directly labeled DNA probes (72). This transition was driven by the need for greater resolution and gene-level specificity than chromosome banding techniques offered. Fluorescence *in situ* hybridization enabled the precise localization of DNA sequences on both metaphase chromosomes and interphase nuclei (Figure 1C) using fluorescently labeled probes, eliminating the hazards and limitations associated with radioactive methods.

A decisive advance of the early 1990s was the introduction of bacterial artificial chromosome (BAC)

libraries (73). Compared with cosmids or yeast artificial chromosomes, BAC clones carry large human DNA inserts of up to 300 kb while remaining structurally stable, are easy to propagate in *Escherichia coli*, and avoid the frequent chimerism of yeast artificial chromosomes. These features made BAC clones highly reliable probes for fluorescence *in situ* hybridization, enabling precise chromosomal mapping and the detection of subtle aberrations undetectable by banding. BAC clones also provided the physical framework for the Human Genome Project and supported the development of locus-specific probes and whole-chromosome paints. Comprehensive BAC probe sets also provided the practical basis for the development of multiplex fluorescence *in situ* hybridization and spectral karyotyping (74, 75), which enables the simultaneous visualization of all chromosomes in distinct colors using combinatorial labeling and spectral imaging. Both methods significantly improved the detection of complex rearrangements, marker chromosomes, and cryptic structural aberrations, particularly in tumors with highly abnormal karyotypes (74, 76-78).

Another key development of the molecular cytogenetics period was the introduction of comparative genomic hybridization in 1992 (79). This technique enabled genome-wide detection of DNA copy-number changes without requiring specific probes for each locus or metaphase spreads from the test sample (79). In comparative genomic hybridization, differentially labeled tumor and reference DNA are co-hybridized to normal metaphase chromosomes, and gains or losses in tumor DNA are visualized as shifts in fluorescence intensity. Although limited by the resolution of metaphase spreads, this method represented a conceptual breakthrough, offering the first global approach to identifying chromosomal imbalances (80-82).

During the late 1980s and early 1990s, the adoption of new molecular genetic techniques played a pivotal role in accelerating the transition from the banding era to that of molecular cytogenetics (83). Among the most transformative innovations was the polymerase chain reaction (PCR), which enables rapid and specific amplification of DNA sequences from minimal amounts of genetic material (83-85). PCR quickly evolved into several powerful variations, including reverse transcription PCR for analyzing RNA, PCR-based Sanger sequencing, and rapid amplification of cDNA ends (RACE) for identifying unknown transcript termini (83-88). These methods provide a level of sensitivity and resolution far beyond that of chromosome banding or even early fluorescence *in situ* hybridization.

A landmark breakthrough during this period was the use of reverse transcription PCR to detect the *BCR::ABL1* fusion transcript in chronic myeloid leukemia (87). This was the first demonstration that it was possible to confirm a fusion gene, previously inferred from a chromosomal translocation, directly at the RNA level, representing a major conceptual advance in leukemia diagnostics. It established fusion transcript detection as a clinically relevant molecular tool and was soon extended to other oncogenic fusions in leukemias and sarcomas. By linking cytogenetic observations to gene-level events, these developments effectively bridged classical cytogenetics and molecular biology, solidifying the foundations of the molecular cytogenetics era.

Consequently, during the 1990s, the field of cancer cytogenetics advanced rapidly through the combined use of chromosome banding and molecular techniques, both established and newly emerging. The structural insights provided by chromosome banding laid the groundwork for interpreting chromosomal rearrangements, while methods such as reverse transcription PCR, fluorescence *in situ* hybridization, and PCR-based Sanger sequencing enabled the detection and molecular characterization of fusion genes at unprecedented resolution. This integrated approach led to the identification of numerous clinically significant fusion genes, many of which have become essential diagnostic and prognostic markers (47). According to the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer, 167 unique fusion partner genes were identified during the period 1988-1999, underscoring the remarkable impact of molecular cytogenetic and early molecular methods in cancer gene

discovery. Of these, 65 were discovered between 1988 and 1994, while 102 were identified in the subsequent five years (1995-1999), reflecting a marked acceleration in gene discovery during the latter half of the decade. This surge coincided with the broader utilization of emerging molecular technologies, including fluorescence *in situ* hybridization using BAC clones as probes, reverse transcription PCR, and Sanger sequencing, which enabled the detection and precise characterization of fusion genes at unprecedented resolution.

In leukemia, several discoveries during this period transformed classification and therapy. In acute myeloid leukemia, translocations such as t(8;21)(q22;q22)/*RUNX1::RUNX1T1* and inv(16)(p13q22)/*CBFB::MYH11* defined new cytogenetic subtypes (89-91), while the identification of *PML::RARA* from t(15;17)(q24;q21) in acute promyelocytic leukemia revolutionized therapy through the introduction of all-trans retinoic acid (92, 93). In acute lymphoblastic leukemia, the cryptic t(12;21)(p13;q22) remained invisible to chromosome banding and was first uncovered by fluorescence *in situ* hybridization, leading to the identification of the *ETV6::RUNX1* fusion, the most common genetic lesion in childhood acute lymphoblastic leukemia, associated with an excellent prognosis under current treatment protocols (47, 94-97). Another major advance was the identification of *KMT2A* at 11q23 as a central gene in leukemia pathogenesis (98, 99). Rearrangements of *KMT2A* involve more than 90 partner genes across acute myeloid leukemia, acute lymphoblastic leukemia, infant, and therapy-related leukemia (100-102). Together, these breakthroughs underscored how molecular cytogenetics not only expanded the catalog of fusion genes but also reshaped classification, prognosis, and treatment.

In sarcomas, cytogenetic–molecular correlations likewise transformed diagnosis and classification. The recurrent t(11;22)(q24;q12)/*EWSR1::FLI1* defined Ewing sarcoma (103), while t(12;16)(q13;p11)/*FUS::DDIT3* was recognized as the hallmark of myxoid liposarcoma (104). In alveolar rhabdomyosarcoma, t(2;13)(q35;q14)/*PAX3::FOXO1* and the variant t(1;13)(p36;q14)/*PAX7::FOXO1* emerged as critical diagnostic markers (105, 106). Synovial sarcoma was characterized by *SS18::SSX* fusions from t(X;18)(p11;q11), providing a unifying genetic signature for histologically variable cases (107-109). These discoveries not only clarified tumor classification but also established molecular criteria that remain central to the diagnosis of pediatric and soft tissue sarcomas (47).

A central insight of this period was the recognition that some genes appeared repeatedly as fusion partners, giving rise to the concept of 'promiscuous' partners in fusion genes in cancer (47). In hematological malignancies, prominent examples of 5′ fusion partners included *KMT2A* (formerly *MLL*), *ETV6*, and *NUP98*, as well as the immunoglobulin loci *(IGH*, *IGK*, and *IGL).* As 3′ fusion partners, recurrent examples included *BCL6*, *RARA*, and *ALK* together with T-cell receptor loci (*TRA*, *TRB*, and *TRD*). In solid tumors, *EWSR1* emerged as the paradigmatic promiscuous 5′ partner in mesenchymal tumors, and *RET* as a recurrent 3′ partner in thyroid carcinomas. These patterns revealed that certain genes were repeatedly involved in chromosome aberrations such as translocations, reflecting intrinsic features of their regulatory context or protein domains that predisposed them to recurrent involvement in oncogenic pathways. Several genes first identified in this period, including *ALK*, *KMT2A*, *RET*, *ETV6*, *RUNX1*, *EWSR1*, *NTRK1*, *PDGFRB, PLAG1*, and *NTRK3*, are now recognized as promiscuous fusion partners across many tumor types (47, 52). A systematic comparison of the genes found as fusion partners between the 1988-1999 period and the full dataset of the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (updated on July 10, 2025) illustrates the dramatic expansion of these genes, underscoring both their central role in the biology of fusion-driven neoplasia and the immense progress made in their identification and characterization (Table I).

A further important observation from this period was that it was possible to identify the same fusion gene and its associated cytogenetic aberration in different types of neoplasms. The recurrent *ETV6::NTRK3* fusion gene,

Table I. *Promiscuous fusion genes identified in the full dataset of the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (updated to July 2025). For each gene, the table lists the number (count) and distinct fusion partner genes. The Increase column indicates the net gain in unique fusion partners compared with those of 1988-1999 (underlined).*

Gene	Count at July 2025	Partner genes	Increase
ALK	188	*A2M, ABI2, ACTG2, ACYP2, ADGRV1, AK5, ALMS1, AP3D1, ARID2, ATIC, BIRC6, BUB1B, C2ORF42, CACNA1D, CAD, CAMKMT, CARS1, CCDC149, CCDC6, CCDC61, CCDC85A, CCDC88A, CDC42BPB, CDK14, CDK15, CDK2, CENPF, CEP44, CLIP1, CLIP4, CLTC, CLTCL1, COL1A2, CPE, CTNNA1, CTNNA2, CTNND1, CTSB, CUX1, DCTN1, DDX6, DES, DHX8, DIAPH2, DYSF, EEF1G, EHBP1, ELMOD3, EML4, EML6, ERC1, ETV6, FBXO11, FMR1, FN1, GALNT14, GCC2, GFPT1, GHR, GPC1, GTF2IRD1, HAO1, HIP1, HMBOX1, HNRNPA1, HNRNPH3, HOOK1, IAH1, IGFBP5, IKBKG, INPP5D, INTS10, ITGAV, ITPRID2, ITSN2, KANK1, KANK2, KCNQ5, KIAA1217, KIDINS220, KIF13A, KIF5B, KLC1, KTN1, LCLAT1, LIMS1, LMNA, LMO7, LRRC4C, LRRFIP2, LRRN2, LRRTM4, LTBP1, MAPRE3, MLPH, MPRIP, MSN, MYH10, MYH9, NBEA, NCOA1, NLRC4, NPM1, NRP2, NUMA1, PABPC1, PARD3, PHACTR1, PKNOX2, PLB1, PLCXD3, PLEKHA7, PLEKHH2, PLEKHM2, PNPT1, PON1, PPFIA1, PPFIBP1, PPP1CB, PPP1R21, PPP4R3B, PRKAR1A, PRKAR1B, PRKAR2A, PRKCB, PRKCE, PRRC2B, PTPN3, R3HDM1, RAB10, RAB5B, RANBP2, RBBP8, REG3A, RMDN2, RND3, RNF144A, RNF213, ROS1, RRBP1, RSRC1, SAP130, SCEL, SEC31A, SETD2, SETD3, SFPQ, SLC12A2, SLC20A1, SLC4A1AP, SLC8A1, SLMAP, SMPD3, SOX5, SP100, SPDYA, SPECC1L, SPTBN1, SQSTM1, SRBD1, SSH2, STK39, STPG4, STRN, SV2B, TCEAL2, TENM3, TFG, THBS1, THUMPD2, TIMP3, TMED2, TNS1, TP53I3, TPM1, TPM3, TPM4, TPR, TRAF1, TTC7A, VAX2, VCL, VIT, WDCP, WDPCP, XPO1, ZEB2, ZMYM1*	185
KMT2A	175	*ABI1, ABI2, ACACA, ACTN2, ACTN4, AFDN, AFF1, AFF3, AFF4, AHCYL2, AHDC1, AHNAK, AIP, AKAP13, AP2A2, ARHGAP26, ARHGEF12, ARHGEF17, ASXL2, ATG16L2, ATP5MG, BCAS4, BCL9L, BCOR, BTBD18, BTK, BTN3A1, BUD13, C2CD3, CASP8AP2, CBL, CCNJL, CD86, CDK19, CDK6, CENPK, CEP164, CEP170B, CIP2A, CLIC4, CLIP2, CLTA, CLTC, CPT1A, CREBBP, CT45A2, CT45A3, DAB2IP, DCP1A, DCP1B, DCPS, DIAPH2, DOCK10, DSCAML1, EDC4, EEFSEC, ELF2, ELL, ELP4, ENAH, EP300, EPS15, FER1L5, FLNA, FLNC, FNBP1, FOXO3, FOXO4, FOXR1, FRYL, FXYD6, FYN, GAS7, GIGYF2, GIMAP8, GMPS, GPHN, GRIK4, HABP4, IGHMBP2, INTS4, ITPR2, ITSN1, KIF2A, KNL1, KNTC1, KRAS, LAMC3, LASP1, LPP, MAML1, MAML2, MAP3K5, MAPRE1, MATR3, ME2, MEF2C, MLLT1, MLLT10, MLLT11, MLLT3, MLLT6, MON2, MRGPRF, MRTFA, MYH11, MYO18A, MYO1F, MYOM3, NCBP1, NCKIPSD, NEBL, NFKB1, NKD1, NOX4, NRIP3, NT5C2, NUP153, NUP98, NUTM2A, PBX1, PDS5A, PFDN4, PHLDB1, PICALM, PPP2R1B, PRPF19, PRRC1, RABGAP1L, RAD51B, RALGAPA2, RANBP3, RARA, RELT, RNF214, RUNDC3B, SARNP, SEC16A, SEPTIN11, SEPTIN14, SEPTIN2, SEPTIN3, SEPTIN5, SEPTIN6, SEPTIN9, SH3GL1, SIK3, SLC22A10, SLC25A24, SMAP1, SNX9, SORBS2, STK4, SUGP2, TCF12, TET1, TFE3, TIRAP, TMPRSS13, TNRC18, TOP3A, UBE4A, USO1, USP10, USP2, USP46, USP8, VAV1, VIM, YAP1, YJU2, YPEL4, ZC3H13, ZDHHC7, ZFYVE19*	156
IGH	138	*B2M, BACH2, BANK1, BCAS2, BCL10, BCL11A, BCL2, BCL2A1, BCL3, BCL6, BCL9, BMI1, BRAF, CALR, CBFA2T3, CCND1, CCND2, CCND3, CCNE1, CD274, CD44, CD74, CDK6, CDKN1A, CEBPA, CEBPB, CEBPD, CEBPE, CEBPG, CHST11, CIITA, CNN3, CRLF2, CXCR4, DCP2, DDX5, DDX6, BMI1, DUSP4, DUX4, EBF1, EGFR, EIF3A, EPOR, ERF, ERVW-1, ETV6, FCGR2B, FCRL4, FGFR3, FOS, FOSB, FOXP1, GANAB, GAS6, GNAS, GPR34, H1-10, HBB, HLA-C, HLA-E, ID4, IER2, IGF2BP1, IGL, IL3, IMMP2L, IRF4, IRF8, ITM2C, JAK2, JUN, JUNB, JUND, KDM4C, KLF2, KLF6, LHX2, LHX4, LMNB2, LRBA, LSP1, LTA4H, MAF, MAFB, MALT1, MRPL21, MTCP1, MUC1, MYC, MYCN, NECTIN2, NFKB2, NFKBIA, NOL4, NSD2, NT5DC2, OAZ1, P2RY8, PABPC4, PAFAH1B2, PAX5, PCSK7, PDIA4, PIM3, PLEC, PPIB, PPP1R15A, PPP4R3A, PSAP, PTMA, RAB29, RBM38, RHOB, RHOH, RND3, RPL8, SFMBT1, SOX4, SOX5, SPIB, SSR4, TENM2, TERT, THEMIS2, TNFRSF17, TNFSF13, TPM4, TRA, TRD, TRG, UBALD2, UBC, WDR6, WWOX, XBP1, YPEL5, ZEB2, ZFP36L1*	121
RET	137	*ABHD17C, ABI3BP, ACBD5, AFAP1L2, AGBL4, AKAP13, ANK3, ANKRD26, ARHGAP19, ARL9, ATP2B3, ATRNL1, BBIP1, BCR, BMS1, CCBE1, CCDC186, CCDC6, CCDC88C, CEP43, CHAT, CLIP1, CLIP2, CNTN1, CNTNAP2, CPEB3, CUX1, DCC, DLG5, DNER, DOCK1, DPP6, DSP, EEA1, ELMO1, EML4, ERC1, ETV6, FGD5, FKBP15, FRMD4A, FYCO1, GABRG3, GADL1, GAS2, GLI3, GOLGA5, GPHN, GPRC6A, GRB2, GRIPAP1, HOOK3, IKBKG, IL1RAPL2, ISOC1, ITGA8, ITIH2, KIAA1217, KIF13A, KIF5B, KTN1, LCOR, LDLR, LSM14A, MALRD1, MBIP, MGMT, MINPP1, MKX, MPRIP, MRLN, MYH10, MYH13, MYH9, NCOA4, NME8, NPAS3, OLFM4, OPALIN, OPTN, PARD3, PCGF5, PCM1, PHYHIPL, PIBF1, PICALM, PLCE1, PLXDC2, PPFIBP2, PRKAR1A, PRKG1, RAD1, RAI14, RASAL2, RASGEF1A, RBPMS, RELCH, ROBO1, RRBP1, RUFY2, SATB1, SEMA5A, SGIP1, SH2D3A, SHTN1, SLC12A2, SLC39A8, SNRNP70, SPECC1, SPECC1L, SQSTM1, TBC1D32, TBL1XR1, TET1, TFG, TIMM23B, TIMP3, TLN1, TNIP1, TNIP2, TPR, TRIM24, TRIM27, TRIM33, TRIM67, UBE2D1, UEVLD, UXS1, VCL, VIM, WAC, WWTR1, ZBTB41, ZMIZ1, ZNF239, ZNF33B, ZSWIM6*	130
IGK	105	*ACTB, ACTG1, ADA2, ARF1, ATP2A3, B2M, BCL10, BCL2, BCL3, BCL6, BTG2, CANX, CCL3, CCND1, CCND2, CD74, CDK6, CDKN1A, CDKN2A, CITED2, CXCL8, CYBA, DDOST, DHRS9, DPEP1, DUSP5, EEF1G, EEF2, EIF1, ETV6, EZR, FGFR3, FOS, FOSB, FRZB, FTL, GADD45A, GADD45B, GNAS, H1-10, HBA1, HBB, HDLBP, HERPUD1, HGS, HLA-A, HLA-B, HLA-C, HLA-E, HLA-F, HNRNPU, HSP90B1, HSPA5, IER2, IRF2BP2, ITM2C, JUN, JUNB, JUND, KDSR, KLF13, KLF6, KRBOX5, LMNA, MCL1, MEF2D, MYC, NFKBIA, NOP53, OAZ1, P4HB, PDIA4, PELI1, PPP1R15A, PRKCSH, PSAP, RACK1, RPL18, RPL28, RPL37A, RPL8, RPS23, RPS3, RRP12, S100A6, S100A8, SDC1, SEC61A1, SERF2, SSR4, ST6GAL1, ST6GALNAC4, SYVN1, THEMIS2, TLE3, TP53BP2, TPD52, TPT1, TRIB1, TSC22D3, TXNIP, UBALD2, VIM, ZC3H12D, ZFP36*	101

Table I. *Continued*

Table I. *Continued*

Gene	Count at July 2025	Partner genes	Increase
ETV6	104	*ABL1, ABL2, ACSL6, ACSL6, ADAMTS16, AIF1L, ALK, AMPH, ANLN, APOLD1, ARHGDIB, ARNT, BAZ2A, BCL2L14, BHMT, BMAL2, BORCS5, CACNA1C, CCND2, CDK2AP1, CDKN1B, CDX2, CHIC2, CIDEA, CIMAP2, CLEC2B, CREBBP, CTNNB1, CYP3A4, DUSP16, EBF1, EIF4B, ELK3, ELMO1, EMP1, EPB41L2, ERC1, ETS2, ETV6, EVX2, FAAP100, FGFR1, FGFR2, FGFR3, FLT3, FRK, GOT1, GSK3A, HIC1, HOXA11, IGH, IGK, IKZF1, INO80D, ITLN1, ITPR2, JAK2, LMBR1, LMBR1L, LPXN, LYN, MACROD2, MAML3, MECOM, MEIS2, MET, MN1, MNX1, MSH6, NCOA2, NCOA6, NID1, NIPBL, NOM1, NTRK2, NTRK3, NUFIP1, PAX5, PDE6H, PDGFRA, PDGFRB, PDZD7, PER1, PLEKHG6, PMEL, PRDM16, PRH2, PTPRO, PTPRR, QSOX1, RBFOX2, RET, RIMBP2, RNF217, RUNX1, SENP7, SMCO2, SNUPN, STK3, SYK, TMTC1, TNFRSF8, TOR1AIP2, YTHDF2, ZNF385A*	92
RUNX1	88	*CBFA2T2, CBFA2T3, CEP76, CHD1, CLCA2, CLDN14, CLIC6, CPNE8, CRYZL1, DDX47, DSCAM, DTD1, DYRK1A, EIF3E, ERG, ETS2, ETV6, EVX1, FAM117A, FBXO42, FNBP1, FOSL2, GRIK2, IFNAR1, KCNMA1, KIAA1549L, KIF2C, KMT2C, KRR1, LIPA, LPXN, MACROD1, MECOM, MLYCD, MRPL47, NDC1, NDST2, NOL4L, NTRK3, OPHN1, PCNT, PDCD6, PDZD7, PLAG1, PRDM16, PRDX4, PROS1, PRPF38A, PRRC1, PTGR3, PTHLH, RCAN1, RPL22, RUNX1T1, SEPTIN7, SH3D19, SIN3A, STK24, STX2, SV2B, TACC1, TCF12, THOC6, TMEM50B, TRIQK, TRPS1, TTC7B, UBE2G2, UBL7, UGGT2, URB1, USP16, USP42, WDR4, WSB2, YTHDF2, ZFPM2, ZMAT4, ZNF423, ZNF687*	84
FGFR1	71	*ADAM18, ADGRA2, AGAP1, ANK1, AZIN1, BAG4, BCR, BRF2, CEP43, CKAP5, CNTRL, CPSF6, CSMD1, CUX1, DNM1L, DOCK3, EBF2, ERLIN2, ERO1A, ETV6, FAM110B, FGFR1, FGFR1OP2, FN1, FOXO1, GSK3B, GTF2E2, HDLBP, HOOK3, HSPG2, IMMP2L, KAT6A, KIF5B, LETM2, LRRFIP1, MYO18A, MYO5A, NRG1, NSD3, NTM, NUDCD3, PARD6B, PCM1, PLAG1, PLPP5, PPFIA1, PSMG2, PTK7, RAB11FIP1, RBPMS, RHOT1, SCARA5, SLC20A2, SMIM19, SQSTM1, TACC1, TFG, TG, TIMP3, TLN1, TPR, TRIM24, TTLL1, TTLL4, USP33, USP6, ZMAT4, ZMYM2, ZNF577, ZNF791, ZNRF3*	69
EWSR1	69	*ABR, ATF1, BEND2, BRMS1L, CCDC157, CDADC1, CREB1, CREB3L1, CREB3L2, CREB3L3, CREM, CTBP1, DDIT3, ERG, ETV1, ETV4, EZHIP, FEV, FLI1, GAS2L1, GFI1B, GORASP2, HOXB13, HOXB8, KLF15, KLF17, LARP4, MYB, NACC1, NCAPH2, NF2, NFATC1, NFATC2, NR4A2, NR4A3, PATZ1, PBX1, PBX3, PLAG1, PLAGL1, POU2AF3, POU5F1, RORB, SELENOM, SMAD3, SMARCA5, SMR3B, SMTN, SP3, SSX1, SSX2, SSX3, STRADA, TCF7L2, TEF, TFCP2, TFE3, TFEB, TTC28, UBP1, VEZF1, VGLL1, WT1, YY1, ZBTB41, ZBTB44, ZNF384, ZNF444, ZNRF3*	60
RARA	62	*ACACA, ANKRD34C, BCOR, CA10, CCDC33, CDC6, CDK12, CERS4, COL10A1, FIP1L1, FNDC3B, GTF2I, HNRNPC, HOXB3, IGFBP4, IRF2BP1, IRF2BP2, KMT2A, LGALS16, LTBP1, LYRM9, MSL1, MUC16, MYO18A, MYO1D, NAB2, NABP1, NARS2, NHERF1, NPEPPS, NPM1, NUMA1, NUP98, PCTP, PGAP3, PKIA, PLEKHA6, PML, POLDIP2, PRKAR1A, PRR11, PSMD3, PSME3, RNF43, SGCD, SKAP1, SMARCE1, SNX15, SPOP, STAC2, STAT3, STAT5B, STRN3, TAOK1, TBL1XR1, TNRC18, TPCN2, TSPYL4, WIPF2, ZBTB16, ZBTB4, ZNF595*	57
NTRK1	62	*AFAP1, ARHGEF11, ARHGEF2, ATP1B1, BCAN, CACYBP, CD74, CEL, CHTOP, CLIP1, CPSF6, CTRC, DIAPH1, DYNC2H1, EPHB2, EPS15, F11, F11R, FMN2, FN1, GAS2L1, GPATCH4, GRIPAP1, GTF2I, IRF2BP2, KHDRBS1, KIF21B, KIF5B, LIPI, LMNA, LRRC71, MEF2D, METTL25B, MPRIP, NECTIN4, NFASC, NOS1AP, NUMA1, P2RY8, PEAR1, PHF20, PLEKHA6, PPL, PRDX1, RABGAP1L, SARM1, SCP2, SEL1L, SH3BP1, SQSTM1, SSBP2, STRN3, TFG, TP53, TPM3, TPR, TRG, TRIM33, TRIM63, TRO, ZBTB7B, ZKSCAN1*	59
HMGA2	59	*ACKR3, AICDA, AKAP9, ARFGAP2, BNC2, C12ORF42, C1orf87, CADM2, CCNB1IP1, CHMP1A, COG5, COL14A1, COX6C, DAB1, DYRK2, EBF1, EFCAB6, EGFR, FAM186B, FHIT, FRS2, GABRA3, GNS, GRIP1, GSN, HNRNPM, KALRN, KERA, KITLG, LEMD3, LHFPL6, LPP, LRMDA, NAA11, NCOR2, NEGR1, NELL2, NFIB, NR2C1, NUP107, PCBP2, PLPP3, PLXNC1, PPFIA2, PTGER3, RAB3IP, RAD51B, SARNP, SETBP1, SLC6A15, SNRPF, SOX5, STX5, TRAF3IP2, TSFM, TUBGCP6, UTRN, WIF1, YAP1*	55
PDGFRB	*57*	*AGGF1, ATF7IP, BCR, BIN2, CAPRIN1, CCDC6, CCDC88C, CD74, CEP85L, CPSF6, DIAPH1, DOCK2, DTD1, EBF1, ERC1, ETV6, FAR1, FN1, FOXO1, GCC2, GIT2, GOLGA4, GOLGB1, HIP1, KANK1, KAZN, MAP3K7, MPRIP, MRC1, MYO18A, NAB2, NDE1, NIN, PCM1, PDE4DIP, PRKG2, RABEP1, SART3, SATB1, SPARC, SPECC1, SPTBN1, SSBP2, STRN3, TBL1XR1, TERF2, TNIP1, TP53BP1, TPM3, TPR, TRIP11, TSC1, UBE2I, WDR48, WNK1, ZEB2, ZMYND8*	54
PLAG1	56	*ACTA2, ACTG2, BOC, CHCHD7, COL1A1, COL1A2, COL3A1, CRISPLD1, CSMD1, CTDSP2, CTNNB1, CTSB, EEF1A1, EIF4G2, EWSR1, FAM110B, FBXO32, FGFR1, FRMD6, GEM, H3-3B, HAS2, HNRNPA2B1, HNRNPC, ITGB1, LIFR, LYN, MYC, NCALD, NDRG1, NFIB, NTF3, OSR1, PCMTD1, PDE2A, PPP2R2A, PUM1, RAB2A, RAD51B, RBPMS, RUNX1, RUNX1T1, SDCBP, SNAI2, SOX10, SRSF3, TCEA1, TCF4, TGFBR3, TMEM68, TRIM13, TRPS1, VCAN, YWHAZ, ZEB2, ZFHX4*	53
NUP98	52	*ADD3, ANKRD28, ANO10, ASH1L, BPTF, BRWD3, CADM1, CCDC28A, CSTPP1, DDX10, DNHD1, EMX1, HHEX, HMGB3, HOXA9, HOXA11, HOXA13, HOXC11, HOXC13, HOXD11, HOXD13, IQCG, JADE2, KAT7, KDM5A, KMT2A, LNP1, MLLT1, MLXIP, NSD1, NSD3, PHF23, POU1F1, PRRX1, PRRX2, PSIP1, RAP1GDS1, RARA, RARG, RHOG, SET, SETBP1, STIM1, TMEM117, TNRC18, TOP1, TOP2B, VRK1, XRN1, ZFPL1, ZNF512B, ZNF91*	46
CREBBP	44	*ABCA3, ADCY9, ATG10, B2M, BCOR, BCORL1, CASKIN1, CIAO3, CIITA, CRAMP1, DEXI, DNAJA3, ELOB, ETV6, GLYR1, GOLGA6L2, HCN1, IFT140, KAT6A, KAT6B, KDM2B, KMT2A, LUC7L, MEFV, NAA60, NLRC3, NUBP1, PRSS22, PRSS33, RANBP3, RHBDF1, SLX4, SRCAP, SRGAP2B, SRL, SRRM2, TEDC2, TP53TG3, TRAP1, TRIM69, WRAP53, ZNF384, ZNF500, ZNF597*	42

Table I. *Continued*

Table I. *Continued*

Gene	Count at July 2025	Partner genes	Increase
BCL6	35	*C3, CBLB, CIITA, DMRT1, EIF4A2, FBH1, FNDC3B, GAPDH, GRHL1, GRHPR, H4C9, HSP90AA1, IGH, IGK, IGL, IKZF1, IL21R, IRAG2, LCP1, LPP, MBNL1, MYBL1, NAPA, PIM1, POU2AF1, RAB29, RAF1, RBM6, RCC1, RHOH, SPECC1L, SRSF3, ST6GAL1, TFRC, TP63*	23
TFE3	34	*ARID1B, ASPSCR1, CLTC, DVL2, EWSR1, FUBP1, GRIPAP1, HNRNPH3, KAT6A, KHSRP, KMT2A, LUC7L3, MATR3, MED15, NONO, PARP14, PHF1, PRCC, PSPC1, PUF60, RAI2, RBM10, RBMX, RREB1, SETD1B, SFPQ, U2AF2, UXT, VCP, WDR45, WWTR1, YAP1, ZC3H4, ZMYND8*	31
MLLT10	33	*ASCC1, BAZ2B, BUD13, CAPS2, CEP164, CLP1, CNTNAP3B, DDX3X, DNAJC1, DSCAML1, EED, FAM171A1, FDX1, FGFR3, HEATR3, HNRNPH1, KCNJ6, KMT2A, MAP2K2, MINPP1, NAP1L1, NAV1, PICALM, PPP2R1B, RNF169, SCN4B, SKIDA1, SLC16A1, SNTG1, TENT4B, UBE4A, WAC, XPO1*	30
ERG	33	*ABCC4, CDHR2, DUX4, DYRK1A, ELF4, ELK4, ETS2, EWSR1, FUS, GET1, GMPR, GRHL2, GUCA2A, HERPUD1, HNRNPH1, KCNJ6, LMBRD2, MAP3K7CL, MAPK11, MX1, NDRG1, PAK1, PLEKHH1, RPS18, RUNX1, SKOR2, SLC45A3, SON, SRPK2, TAF8, TCF4, TMPRSS2, ZNRF3*	31
KAT6A	28	*ADAM2, ANK1, ARID5B, ASXL2, CHD7, CREBBP, CSMD1, CYRIB, EP300, FGFR1, GOT1L1, GPAT4, IKBKB, KANSL1, KLK4, LEUTX, MSR1, NCOA2, NCOA3, NEFL, NRG1, RAB11FIP1, SLC20A2, SMIM19, TFE3, TRAPPC9, VDAC3, VPS13B*	26
IGL	27	*ADGRE5, AP1B1, BCL2, BCL3, BCL6, BCL9, CCL3, CCND1, CCND2, CCND3, CDK6, EEF2, FGFR3, HLA-B, HLA-C, HSPA5, IGH, IRF4, JUN, KLF6, MAF, MYC, PCBD2, PPP1R15A, PRDM16, REL, ZFP36*	21
TRB	26	*AHI1, CCND2, HOXA10, HOXA11, HOXA9, IL2RB, IRS4, KIF3B, LCK, LEF1, LMO1, LMO2, LYL1, MECOM, MTCP1, MYB, MYC, NOTCH1, PIM1, RIC3, TAL1, TAL2, TLX1, TLX3, TRA, TRG*	16
MYC	26	*ACP3, AICDA, ARHGEF17, BCL3, BCL7A, BTG1, CSMD3, DMD, IGH, IGK, IGL, IRAG2, LRATD2, NDRG1, NDUFAF6, PDLIM5, PLAG1, RFTN1, RNF213, SOCS1, SUPT3H, TRA, TRB, TRD, ZBTB5, ZCCHC7*	23
FUS	26	*ATF1, CHD1, CREB3L1, CREB3L2, CREM, DDIT3, ERG, ETV1, ETV4, FEV, FLI1, IL9R, KAT8, KLF17, MYB, NACC1, NFATC2, NFATC4, NR4A3, POU2AF3, POU5F1, PRSS36, PYCARD, SET, TFCP2, TMEM114*	24
MECOM	25	*ANKRD10, ARMC8, CD86, CDK6, CLDN11, EIF4A2, ETV6, FNDC3B, FRMD5, GATA2, GOLIM4, LMAN2L, LRRC31, LRRC34, MACROH2A1, MSL2, NCEH1, NRIP1, RPN1, RUNX1, SEC62, SLC7A14, SMC4, TPX2, TRB*	21
SS18	24	*ATP5F1A, CHST9, CRTC1, DOCK2, GREB1, KLF14, MEF2C, MEF2D, NEDD4, NPC1, OSBPL1A, POU5F1, PRKD2, SLC5A11, SSX1, SSX2, SSX4, SUPT3H, TRAPPC8, UBE2I, VGLL3, YAP1, ZBTB7A, ZNF521*	21
TRA	23	*CCND2, CDKN2A, CEP85L, IGH, IRF4, LMO1, LMO2, MDM4, MTCP1, MYC, NECTIN2, NKX2-1, NOTCH1, OLIG2, RHOH, SALL2, SFTA3, TAL1, TCL1A, TLX1, TRB, USP7, ZFP36L2*	19
TCF3	22	*ABHD17A, ADAMTSL5, AP3D1, APC2, BEND2, C19ORF25, CAPN10, DNAJC11, FLI1, HLF, MEX3D, NOP2, OAZ1, PBX1, PIK3R1, PLEKHJ1, REXO1, SYTL5, TEF, TFPT, TPM4, ZNF384*	19
NR4A3	19	*ACTB, AR, CITED2, ESR1, EWSR1, FUS, GREB1, HSPA8, LSM14A, NIPBL, OXR1, PGR, SEC24B, SLCO5A1, SMARCA2, STX17, TAF15, TCF12, TFG*	17
CCND1	16	*ANO1, B2M, CDC42BPA, DCPS, DDX5, FGF4, FSTL3, IGH, IGK, IGL, LTO1, MED16, OAZ1, PPM1D, TACSTD2, TPM4*	14
NUP214	16	*ABL1, AHDC1, AIF1L, BRAF, CACNA1B, DEK, GPSM1, NOTCH1, POMT1, PRRC2B, RAC1, SEC14L2, SET, SQSTM1, TOM1L2, XKR3*	14
TFG	14	*ADGRG7, ALK, CD46, FGFR1, MET, NR4A3, NTRK1, NTRK2, NTRK3, RET, ROS1, TFDP2, TMEM45A, ZBTB10*	12
TPM3	14	*ALK, ARHGEF11, B4GALT3, CFAP141, FAM193A, GPR37L1, JAK2, NTRK1, NUP210L, PDGFRB, RERE, ROS1, STAT3, TPR*	11
FOXO1	13	*ELF1, FGFR1, GATA6, MRPS31, NSD3, PAX3, PAX7, PDGFRB, PLAGL1, RUBCNL, SMARCA4, STK24, WDFY2*	11
TRD	13	*BCL11B, GNAQ, IGH, LMO1, LMO2, MYC, NKX2-1, NKX2-3, NKX2-5, RANBP17, TAL1, TLX1, TLX3*	8
NPM1	13	*ALK, BSPRY, CCDC28A, CLEC2D, FGFR2, MLF1, RAB4A, RARA, RARG, ROS1, TRIP12, TYK2, VIM*	10
BCL9	11	*BEST3, C1orf21, GOLPH3L, IGH, IGL, IVL, MEF2D, RASAL2, RGS17, SMCP, UAP1*	9
TAL1	11	*DHX9, GLUL, GNPAT, LRRC41, MBNL1, ST3GAL3, STIL, TCTA, TRA, TRB, TRD*	7
BCL3	11	*ATP9B, CEACAM16, GRIK4, HIPK4, IGH, IGK, IGL, IGSF23, MYC, PPP1R37, ZNF233*	9
TPR	10	*ALK, BRAF, FGFR1, JAK2, NTRK1, ODR4, PDGFRB, RET, ROS1, TPM3*	8
LMO2	9	*ABTB2, CD59, CSTF3, FOXJ3, MBNL1, STAG2, TRA, TRB, TRD*	7
BCL2	7	*AFF3, ATRX, IGH, IGK, IGL, NEDD4L, VPS4B*	5
TLX1	5	*CTRB2, RPP30, TRA, TRB, TRD*	3
DDIT3	4	*ERGIC2, EWSR1, FUS, GLI1*	2
MAF	4	*IGFBP7, IGH, IGL, KLHDC4*	2
TRG	4	*IGH, NTRK1, TCL1A, TRB*	2

resulting from t(12;15)(p13;q25), was first described in infantile fibrosarcoma (historically termed congenital fibrosarcoma) (110) and in congenital mesoblastic nephroma (111, 112), and subsequently in acute myeloid leukemia carrying complex chromosomal aberrations involving chromosome bands 12p13, 12q15, and 15q25 (113). Nowadays, the *ETV6::NTRK3* fusion gene is recognized across a wide spectrum of neoplasms, including acute lymphoblastic leukemia, adenocarcinomas arising in multiple organs, tumors of the central nervous system, melanoma, and many others (114). Over time, fusion-gene promiscuity has been documented for *EWSR1::ATF1/CREB1*, *YAP1::TFE3*, *ACTB/MALAT1/PTCH1::GLI1*, and others (114). This demonstrated that certain fusion genes are not confined to a single histogenetic tumor type but can act as versatile oncogenic drivers across mesenchymal, epithelial, and hematological tumors (114).

Another important realization of this period was the interchangeability of members of the same gene family as fusion partners, although not always within the same tumor type. This was exemplified by *FUS*, *EWSR1*, and *TAF15*, which together constitute the FET/TET gene family and show overlapping partnering patterns with certain oncogenes (47). For instance, *EWSR1::DDIT3* and *FUS::DDIT3* were both found in myxoid liposarcomas, whereas *EWSR1::NR4A3* and *TAF15::NR4A3* characterized extraskeletal myxoid chondrosarcomas. Similarly, *EWSR1* fused with *ERG* in Ewing sarcoma, while *FUS::ERG* was identified in acute myeloid leukemia and later also in Ewing sarcoma (115-117). These examples highlighted that related family members are able to substitute for one another in oncogenic fusion events, underscoring a broader principle of functional redundancy among certain RNA-binding proteins in tumorigenesis.

Beyond diagnostics and tumor classification, the association between chromosomal aberrations and fusion genes ushered in a therapeutic revolution. The culmination of this period was the development of imatinib, the first tyrosine kinase inhibitor in oncology (118). This landmark therapy was the direct harvest of decades of work that began with the discovery of the Philadelphia chromosome in 1960, advanced through the identification of t(9;22)(q34;q11) and the *BCR::ABL1* fusion, and ultimately led to the rational design of a drug that selectively inhibited the oncogenic kinase (118, 119). Imatinib transformed chronic myeloid leukemia from a rapidly fatal disease into a manageable condition with long-term survival, becoming the first true paradigm of targeted cancer therapy (120, 121). Its success not only validated the central role of fusion genes in cancer biology but also opened the door to the development of targeted therapies against other kinase fusions. The breakthrough of imatinib was so profound that, as Dan Longo later summarized in an editorial in the New England Journal of Medicine, "imatinib changed everything" (122).

The molecular cytogenetics period marked a turning point in the evolution of cancer cytogenetics. By integrating chromosome banding with emerging molecular techniques, researchers were finally able to investigate chromosomal rearrangements not only at the structural level but also at the gene and transcript level. This convergence enabled a deeper understanding of oncogenic mechanisms, more accurate tumor classification, and improved diagnostic precision, laying the groundwork for modern cancer diagnostics. The foundations established during this period set the stage for the genome-wide, high-resolution approaches that would characterize the next era: Cytogenomics. A new chapter was about to begin.

Cytogenetics in the New Millennium: A New Era for the Study of Chromosome Structure and Behavior

At the dawn of the 21st century, cytogenetics entered a transformative new phase, fundamentally redefining how scientists study chromosome structure, function, and behavior. This transition was catalyzed by the availability of the human genome sequence, the rise of advanced informatics tools, and the convergence of cytogenetics with genome-wide molecular technologies. No longer confined to the visible alterations captured by banding

techniques, the field embraced a sequence-informed framework that enabled the high-resolution detection and interpretation of chromosomal abnormalities. This integrated approach became known as cytogenomics.

The term cytogenomics (or cytogénomique, in its original French usage) was first introduced by Alain Bernheim in the context of cancer research in 1999 (123). It began appearing in English-language literature around 2008 (124, 125), gaining traction as an umbrella term for the integration of chromosome banding with genomic technologies such as fluorescence *in situ* hybridization, comparative genomic hybridization, DNA fiber analysis, high-throughput sequencing, and computational genomics. This approach enabled researchers and clinicians to study chromosome structure and function at both cytological and molecular levels, advancing precision diagnostics and targeted therapy. As Speicher and Carter noted, it "blurs the boundaries with molecular biology," earning it the designation 'new cytogenetics' (126).

Closely related, although conceptually broader, is the term 'chromosomics', introduced by Claussen in 2005 (25). Chromosomics expands the scope of cytogenetic investigation beyond sequence and structural analysis to include the dynamic plasticity of chromosomes within the interphase nucleus. It emphasizes the three-dimensional organization of the genome, chromatin remodeling, and epigenetic modifications that collectively shape gene regulation, cellular differentiation, and disease phenotypes. More recently, Liehr has emphasized chromosomics as the study of how nuclear organization and chromatin-mediated processes influence cellular function, disease susceptibility, and human evolution (21). In parallel, Deakin and colleagues proposed chromosomics to be a unifying framework that integrates genome sequencing, cytogenetics, cell biology, and bioinformatics, positioning it as a powerful approach to addressing unresolved questions in genome architecture and regulation (127).

Although cytogenomics has become the prevailing term for integrated genomic and cytogenetic analysis in both clinical and research settings, chromosomics offers a complementary perspective that unites the structural, spatial, and regulatory dimensions of chromosomes in both basic and translational research. Whether through the lens of cytogenomics or chromosomics, these frameworks have reshaped the field, laying the groundwork for modern precision diagnostics and ushering in a new era in the study of chromosomes.

These new conceptual frameworks, cytogenomics and chromosomics, were greatly accelerated by the release of the first draft of the human genome in 2001, a landmark event that transformed biomedical research (128, 129). For the first time, it became possible to explore the human genome at base-pair resolution, allowing chromosome bands, previously defined solely by cytological features, to be linked to precise DNA sequences and genomic coordinates (130). The emergence of freely available tools such as the University of California, Santa Cruz, Genome Browser (131), Ensembl (132), the database resources of the National Center for Biotechnology Information (133), and other public genomic databases has enabled researchers and clinicians worldwide to integrate cytogenetic findings with detailed molecular data. Genes were increasingly being identified and precisely mapped to chromosomal bands, assigned genomic positions, and annotated with their transcriptional orientation, indicating whether they are located on the plus or minus strand of the chromosome.

This period also saw widespread access to BAC clone libraries, which contained well-characterized, long DNA inserts (134-138). These BACs, often fully sequenced or end-sequenced, became essential tools in fluorescence *in situ* hybridization applications, enabling highly specific, sequence-anchored probe design (139). This development allowed researchers to map chromosomal breakpoints with greater precision, characterize copy-number changes at the molecular level, and build custom probe sets targeting specific genomic regions. It became possible for fluorescence *in situ* hybridization, which once relied on chromosomal morphology for probe positioning, to be anchored to genome sequence coordinates, further strengthening the fusion of cytogenetics and genomics.

Building on the availability of BAC clones anchored to the genome, the early 2000s saw the development

of array-based comparative genomic hybridization platforms, initially constructed with BAC clones spotted onto glass slides (140, 141). These BAC arrays enabled the first genome-wide assessment of DNA copy-number changes at submicroscopic resolution, representing a significant improvement over conventional karyotyping and metaphase comparative genomic hybridization. In cancer research, this approach proved particularly impactful. BAC array comparative genomic hybridization was instrumental in revealing segmental gains and losses in tumors that appeared karyotypically normal or highly complex, including in gliomas, breast cancer, neuroblastoma, and soft tissue sarcomas (142-146).

The use of tiling-path arrays, in which overlapping BAC clones covered entire chromosomal regions or even whole genomes, allowed for the fine-mapping of chromosomal breakpoints, the identification of recurrent minimal regions of gain or loss, and the detection of novel amplified oncogenes or deleted tumor suppressors. These tools led to a deeper understanding of genomic instability in cancer and established new diagnostic and prognostic biomarkers. Clinically significant findings, using BAC array comparative genomic hybridization, include amplification of *MYCN*, located on chromosome sub-band 2p24.3, in neuroblastoma; amplification of *ERBB2* (also known as *HER2*), located on 17q12, in breast cancer; and co-deletion of chromosome arms 1p and 19q (referred to as the 1p/19q co-deletion) in oligodendrogliomas (142, 144-149).

As the technology matured, BAC arrays were gradually replaced by oligonucleotide arrays with much higher probe density and resolution, enabling the detection of microdeletions, microduplications, and complex genomic rearrangements across the genome (150-153).

In parallel, single nucleotide polymorphism (SNP) arrays were developed to assess both copy-number variation and allelic imbalances that are not detectable by conventional array comparative genomic hybridization or G-banding (154-156). In acute myeloid leukemia and myelodysplastic syndrome, they revealed uniparental disomy with diagnostic and prognostic significance (153, 157). Similarly, in acute lymphoblastic leukemia, SNP arrays identified microdeletions as a common feature in adult and adolescent cases, highlighting unexpected similarities to the pediatric form of the disease (158).

These advancements culminated in the development of combined oligonucleotide/SNP array platforms, such as Affymetrix CytoScan HD, Oxford Gene Technology CytoSure Cancer+SNP arrays, and Illumina Infinium CytoSNP-850K, which enable the simultaneous detection of copy-number changes and copy-neutral genomic alterations on a single chip (159, 160). Their integration into routine diagnostics has provided high-resolution, genome-wide evaluation of structural variation at submicroscopic resolution, uncovering clinically relevant aberrations invisible to traditional karyotyping or array comparative genomic hybridization (153, 157, 158, 161).

Thus, at the beginning of the millennium, cytogenetics was no longer confined to the analysis of visible chromosomes under the microscope but had evolved into a sequence-informed discipline capable of interpreting genomic architecture at the kilobase scale and even at the nucleotide level. The combination of high-resolution array platforms with genome assembly data brought unprecedented precision to the detection and characterization of chromosomal abnormalities. This transformation laid the foundation for integrating array-based data with sequencing technologies, paving the way for the next phase in the field's evolution, the era of cytogenomics powered by high-throughput sequencing (162-164).

The emergence of high-throughput sequencing, also referred to as next-generation sequencing, massively parallel sequencing, or deep sequencing, extended chromosome analysis from the submicroscopic to the nucleotide level (Figure 2). This technology enabled comprehensive and unbiased interrogation of both the genome and transcriptome, expanding the scope of cytogenomic investigations beyond the capabilities of array-based methods. Pioneering efforts in cancer genomics demonstrated its power to detect somatic mutations, copy-number changes, structural variants, and fusion genes in tumor samples (162-164). It can reveal

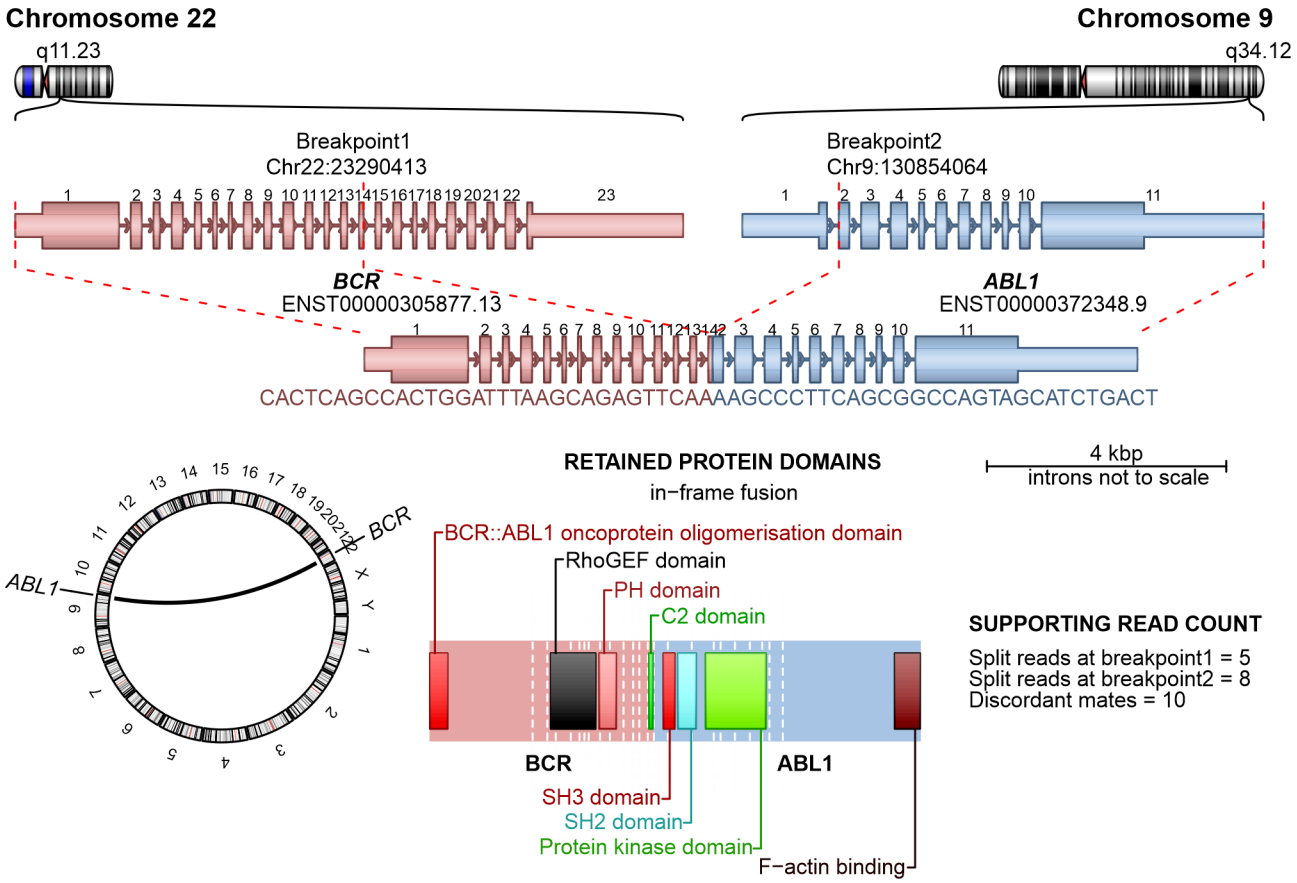


Figure 2. *Detection of the Philadelphia chromosome/BCR::ABL1 fusion gene in the new millennium using high-throughput sequencing. In this period, cytogenetics expanded into cytogenomics and chromosomics, extending analysis far beyond chromosome subbands such as 22q11.23 and 9q34.12 to provide nucleotide-level and functional insights. High-throughput sequencing analysis performed with the Arriba algorithm, using the test dataset included with the STAR-Fusion distribution, identified breakpoints at BCR (chr22: 23290413, ENST00000305877.13) and ABL1 (chr9: 130854064, ENST00000372348.9), generating an in-frame BCR::ABL1 transcript. The translocation is visualized in a circos plot as a connecting line between chromosomes 22 and 9. Retained protein domains include the BCR-ABL oligomerization, RhoGEF, PH, C2, F-actin binding, kinase, SH2, and SH3 domains. Supporting evidence comprised 5 split reads at breakpoint 1, 8 split reads at breakpoint 2, and 10 discordant read pairs.*

complex rearrangements, sub-clonal alterations, and cryptic events, all within a single assay, surpassing both the resolution and scope of prior technologies. Depending on whether DNA or RNA is used as template, high-throughput sequencing can be applied as whole-genome sequencing for unbiased structural variant detection, whole-exome sequencing for mutation analysis within coding regions, and whole-transcriptome sequencing (RNA sequencing or RNA-seq) for transcript-level profiling. The latter includes the detection of fusion transcripts, alternative splicing, gene expression patterns, and allele-specific expression (162, 164-168). High-throughput sequencing has been particularly impactful in oncology, enabling more accurate tumor classification, risk stratification, and identification of actionable genomic targets.

As sequencing costs declined and bioinformatic tools matured, high-throughput sequencing rapidly became integral to both cancer research and clinical diagnostics. Its implementation enabled a shift from targeted or karyotype-based assessments to genome-wide profiling, accelerating the discovery of novel driver events and refining the molecular classification of tumors. Today,

depending on the available material, a combination of chromosome banding, fluorescence *in situ* hybridization, array comparative genomic hybridization, and high-throughput sequencing methodologies is employed to comprehensively investigate the genetic landscape of cancer. In many tumor types, the combined use of chromosome banding and whole transcriptome sequencing is especially effective for identifying potential driver fusion genes (169). These two methodologies operate at different levels of genomic organization: Karyotyping visualizes large-scale chromosomal structure, while whole-transcriptome sequencing captures transcript-level changes. When a fusion transcript detected by whole transcriptome sequencing aligns with a cytogenetically visible breakpoint, it provides strong evidence of biological relevance. This approach was first used to identify the recurrent *WWTR1::CAMTA1* fusion gene in epithelioid hemangioendothelioma with the translocation t(1;3)(p36;q25) (170). A similar strategy was later applied to identify the *IRF2BP2::CDX1* fusion in mesenchymal chondrosarcoma carrying a t(1;5)(q42;q32) chromosome aberration (171), to demonstrate that *ZC3H7B::BCOR* is a recurrent chimera in endometrial stromal sarcomas with an X;22 translocation (172), and to identify the *SERPINE1::FOSB* fusion in pseudomyogenic hemangioendothelioma harboring a balanced t(7;19)(q22;q13) (173). This combinatorial strategy has since been widely adopted to uncover novel, clinically relevant fusion genes in tumors with simple karyotypic changes, including the identification of *NFIA::CBFA2T3* and *ZMYND8::RELA* in pediatric erythroid leukemias (174, 175).

High-throughput sequencing has also enabled the discovery of clinically significant fusion genes that were undetectable by chromosome banding. In leukemia, the *CBFA2T3::GLIS2* fusion, associated with a cryptic inversion of chromosome 16, inv(16)(p13.3q24.3), was identified solely through high-throughput sequencing (176). This fusion defines a distinct subtype of leukemia occurring exclusively in children and has never been reported in adults (177). The *IGH::DUX4* fusion, resulting from a translocation involving 14q32 and 4q or 10q that cannot be visualized by karyotyping, was readily identified by whole-transcriptome sequencing and defines a high-risk subtype of B-cell acute lymphoblastic leukemia with distinct gene expression and immunophenotypic features (178-180).

High-throughput sequencing revealed recurrent rearrangements of the *PRDM10* gene (11q24.3) in low-grade undifferentiated pleomorphic sarcomas. These tumors exhibit a distinct gene expression profile and indolent clinical behavior, supporting their recognition as a separate sarcoma subtype (181-184). In another group of sarcomas, sequencing revealed rare but recurrent fusion genes such as *YAP1::KMT2A::YAP1* and *VIM2::KMT2A* (185-188). These fusions expand the spectrum of *KMT2A*-driven neoplasia beyond hematological malignancies. Although infrequent, their recurrence suggests a pathogenetic role and underscores the power of high-throughput sequencing in uncovering cryptic oncogenic drivers in mesenchymal tumors.

An emerging addition to the cytogenomic toolbox is optical genome mapping, a high-resolution technique that enables genome-wide detection of structural variants without sequencing. Optical genome mapping works by labeling ultra-high-molecular-weight DNA and imaging individual molecules as they are linearized through nanochannels, generating detailed genome maps that identify insertions, deletions, duplications, inversions, and translocations at kilobase resolution (24). It has also proven to be a valuable tool for detecting catastrophic genomic events collectively referred to as chromoanagenesis (*see below*). These complex rearrangements often evade detection by conventional cytogenetic methods due to their localized and chaotic nature. Accordingly, optical genome mapping has been described as a next-generation cytogenetics or next-generation cytogenomic tool (189, 190).

Optical genome mapping has shown particular utility in hematological malignancies, where it can detect cryptic rearrangements, fusion genes, and complex structural variants that are not visible by traditional karyotyping (189, 191-197). It has already been applied to the diagnosis and risk stratification of both myeloid and lymphoid neoplasms (192, 194, 198, 199). In a recent study of 12

BCR::ABL1-positive cases, optical genome mapping was compared with chromosomal analysis, fluorescence *in situ* hybridization, and reverse transcription PCR (Figure 3). Optical genome mapping revealed additional abnormalities including chromoanagenesis and *IKZF1* deletion, leading the authors to conclude that "in scenarios where optical genome mapping is feasible, chromosomal analysis and reverse transcription polymerase chain reaction may not offer additional diagnostic value" (194).

To support clinical integration, an international consortium for optical genome mapping in hematological malignancies has issued expert recommendations for its implementation in routine diagnostics (200, 201). Furthermore, the standing committee for the ISCN recently recognized the need for a specific nomenclature tailored to genome mapping technologies. A standardized framework was proposed to accurately report structural and copy-number abnormalities detected by this technology in both research and clinical settings (202).

Optical genome mapping has also been applied to bone and soft-tissue tumors, despite challenges in obtaining high-quality DNA from these specimens (203-205). In one study, it succeeded in 38 out of 53 tumors (72%) and identified clinically relevant alterations in 91% of analyzable cases, including *POU2AF3::EWSR1* in a round cell sarcoma and t(1;5)(p22;p15) in a myxoinflammatory fibroblastic sarcoma, as well as complex genomic events (203). Another study reported successful analysis in 62% of cases (33 of 53 cases), detecting diagnostic alterations in 95.2% of evaluable samples, including novel oncogenic events and tumor-suppressor gene alterations (204). A third investigation successfully analyzed all 60 examined tumors, with optical genome mapping accurately identifying structural and copy-number variants previously detected by karyotyping and fluorescence *in situ* hybridization, while also revealing complex rearrangements and three- to six-way translocations that were not detectable by karyotyping (205). A combination of optical genome mapping and high-throughput sequencing identified diagnostic, disease-associated aberrations in 98% of cases.

The use of optical genome mapping has also been reported in carcinomas (206, 207). In metastatic lung squamous cell carcinoma, integration with whole-genome sequencing revealed intratumoral heterogeneity, with optical genome mapping detecting structural variants missed by sequencing and variants restricted to metastases (206). In clear-cell renal cell carcinoma, optical genome mapping combined with epigenome profiling enabled comprehensive characterization of tumor and adjacent tissue, uncovering both known and novel somatic aberrations (207).

Optical genome mapping has also been applied to brain tumors. In gliomas, it showed concordance with SNP array results while uncovering additional clinically significant aberrations that escape detection by SNP array (208). In pediatric *PATZ1*-rearranged gliomas, the combination of optical genome mapping and chromosome microarray analysis indicated that chromothripsis of chromosome 22 was responsible for generating the *PATZ1* fusion (209). In another pediatric brain tumor, optical genome mapping identified a rare *ZNF532::NUTM1* fusion (210).

Despite its strengths, optical genome mapping has some limitations. It may fail to detect certain abnormalities that are identifiable by other methods. For example, a near-tetraploid subclone was detected only by karyotyping (191). False-positive and false-negative results have also been reported, particularly when breakpoints fall within large repetitive regions or when inconsistencies arise between genome assemblies such as GRCh37 and GRCh38 (211).

Nevertheless, optical genome mapping is increasingly viewed as a valuable complement to traditional cytogenetic methods, such as karyotyping and fluorescence *in situ* hybridization. In some settings, it may even serve as an alternative, particularly when high-resolution structural analysis is required. Already in 2021, it was proposed as a promising substitute for standard cytogenetic approaches in acute lymphoblastic leukemia (191). More recently, concerns about a shrinking workforce and diminishing expertise in G-banding karyotyping have prompted the consideration of this method as a potential solution for the next generation of cytogenomic diagnostics (212).

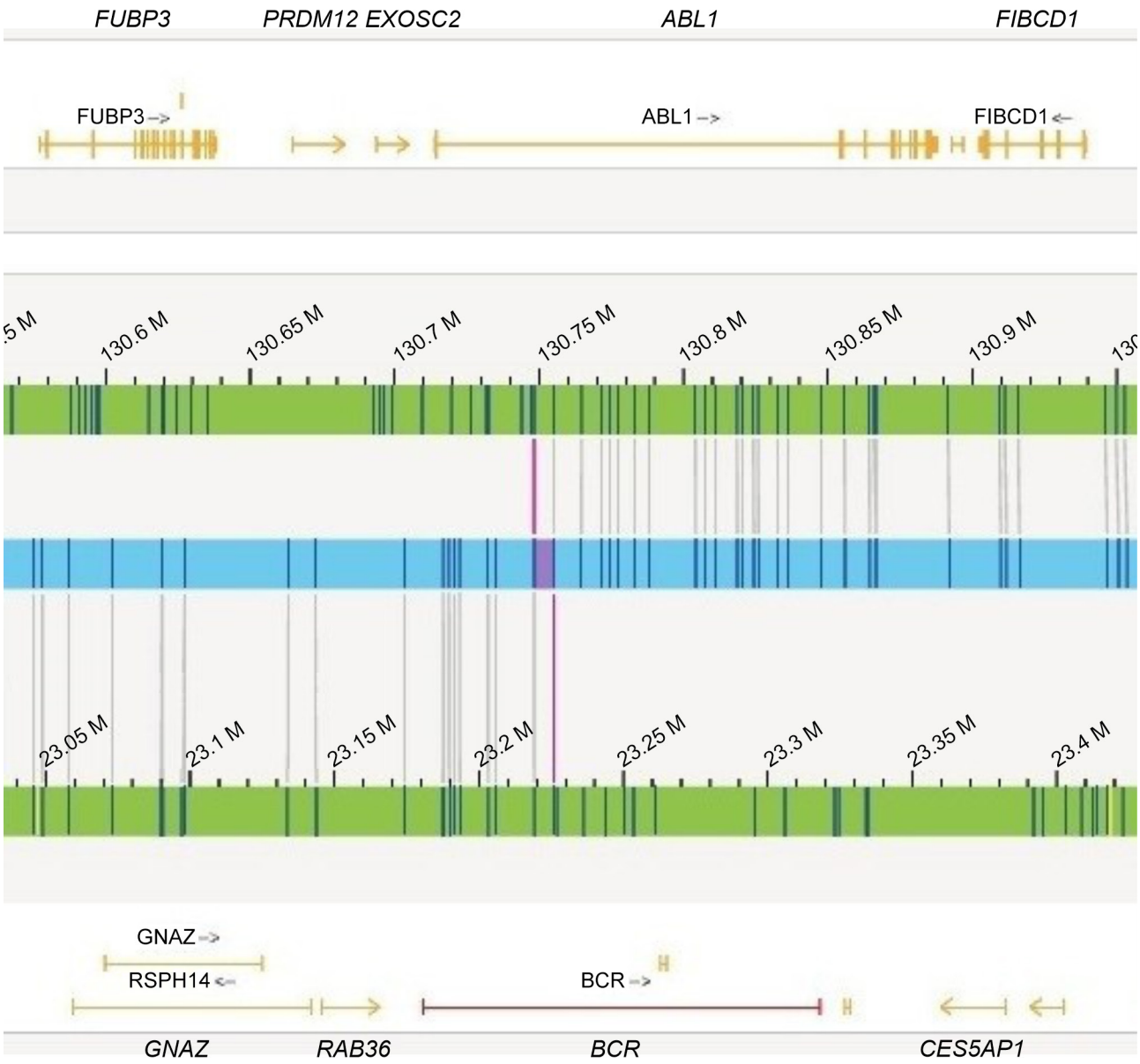


Figure 3. *Detection of the Philadelphia chromosome/BCR::ABL1 fusion gene using the latest cytogenomic tool, optical genome mapping (OGM), which enables direct visualization of structural variants across ultra-long DNA molecules. This technology complements sequencing-based approaches by providing genome-wide, high-resolution maps of chromosomal rearrangements. The molecule map from the sample (blue) aligns to chromosome 9 (Ref 9, top) and chromosome 22 (Ref 22, bottom), with vertical connections visualizing the translocation breakpoints. The fusion involves ABL1 on chr9q34.12 (~130.8 Mb, hg38) and BCR on chr22q11.23 (~23.2 Mb, hg38). Courtesy of Dr. Gokce A. Toruner, MD Anderson Cancer Center.*

Together, the technologies introduced in the New Millennium have not altered the core of cytogenetics, the science devoted to the study of chromosomes, their structure, origin, and function, but they have vastly expanded its methodological reach. By moving beyond the limitations of banding patterns and light microscopy, modern cytogenetic tools now permit the detection of rearrangements invisible to earlier techniques, the

reconstruction of derivative chromosomes shaped by complex or catastrophic events (*see below*), the identification of complete or partial gene alterations such as gains and losses, and even the mapping of nucleotide-level changes, such as insertions, deletions, or substitutions, onto chromosomal coordinates. Cytogenetics has thus evolved into a truly integrative discipline that lies at the intersection of chromosomal architecture, molecular function, and genomic sequence. It remains firmly rooted in its foundational principles yet has been redefined by the transformative power of contemporary genomic technologies.

More Greek Words in the Field of Cytogenetics

The explosive growth of genome analysis in cancer research over the past decade has led to the introduction of several striking new terms, all rooted in Greek, to describe complex genome rearrangements and mutational processes. All of these terms, with the exception of *kataegis* (see below), begin with the prefix *chromo*- underscoring their close association with chromosomes and cytogenetics.

These newer terms reflect a conceptual shift in cytogenetics from gradual models of genome evolution to sudden, catastrophic, and mosaic changes that shape cancer genomes and drive oncogenic processes, including the generation of fusion genes (213-218).

Chromothripsis. First described in 2011, chromothripsis, a compound of *chromo*- (chromosome) and the Greek *thripsis* (θρύψις, shattering), refers to a phenomenon in which chromosomes undergo massive fragmentation and chaotic reassembly in a single catastrophic event (213). In a seminal study of bone cancer and leukemia, localized clusters of tens to hundreds of chromosomal breakpoints suggested that entire chromosomes or chromosomal arms can shatter and subsequently be rejoined through error-prone repair mechanisms such as non-homologous end joining (213). Thus, a new paradigm in cancer genome evolution was introduced, challenging the traditional view of tumor progression as a gradual process: punctuated bursts of genomic chaos are capable of driving oncogenesis in a single step. Formal detection criteria were later established, including clustered breakpoints, oscillating copy-number states, and random fragment joins (219).

Large-scale analyses have identified chromothripsis in osteosarcomas, brain tumors, and certain leukemia types, often associated with *TP53* inactivation and poor prognosis, highlighting the vulnerability of cells with compromised genome surveillance (220-222). In prostate cancer, chromothripsis has generated complex multi-gene fusions (223). In leukemia, it contributes to recurrent fusions and complex karyotypes, facilitating rapid disease progression and resistance to treatment. The catastrophic restructuring of chromosomes can produce deletions, duplications, and gene fusions simultaneously, dramatically altering the cellular transcriptome in a single event (224-228). Chromothripsis has also been linked to the formation of extrachromosomal DNA, which amplifies oncogenes and promotes rapid tumor evolution and therapy resistance (229).

In pediatric cancer, chromothripsis is increasingly recognized as a major driver of genomic complexity and fusion-gene formation. In central nervous system tumors, it contributes to fusions such as *C11orf95::RELA* in ependymomas (230) and complex rearrangements involving *PATZ1* fusions (209, 231). In a pediatric undifferentiated small round cell neoplasm, an *HNRNPM::LEUTX* fusion arose through chromothripsis of chromosome 19 (232). Similar mechanisms have been implicated in lipoblastomas involving the *PLAG1* gene (233) and in the formation of *PAFAH1B1::USP6* fusions in periosteal solid aneurysmal bone cysts (234).

Overall, chromothripsis exemplifies a 'punctuated' model of genome evolution, contrasting with the gradualistic view that dominated classical cytogenetics. It highlights the dynamic and unpredictable nature of chromosomal instability, and the ability of cancer cells to acquire multiple oncogenic alterations in a single step. As sequencing and cytogenomic technologies continue to advance, our ability to detect and interpret chromothripsis will further elucidate its roles in cancer initiation, progression, and therapeutic resistance.

Chromoanasynthesis. First described in 2011, chromoanasynthesis, from chromo- (chromosome) and the Greek anasynthesis (ανασύνθεσις, meaning reconstitution or rebuilding), refers to a replication-based mechanism leading to complex chromosomal rearrangements (235). Chromoanasynthesis involves errors during DNA replication and repair, resulting in local duplications, triplications, and complex segmental rearrangements (236).

Accumulating data indicate that chromoanasynthesis occurs in human germline cells and during early embryonic development (236). It is characterized by clustered copy-number gains (including segmental duplications and triplications), microhomology at breakpoint junctions, and frequent complex chromosomal structures such as inverted duplications. These features reflect replication stress and errors in template switching rather than repair of double-strand breaks alone.

Replication stress can arise from various factors, including oncogene activation, DNA secondary structures, or difficult-to-replicate regions. Under such stress, the replication machinery may stall or collapse, forcing the cell to use alternative, error-prone pathways to complete DNA synthesis. During this process, segments of DNA may be aberrantly duplicated or rearranged through template switching, leading to chromoanasynthesis.

Righolt and Mai highlighted chromoanasynthesis alongside chromothripsis as a manifestations of 'chromosome crises' that contribute to cancer genome complexity (215). Multiple chromoanasynthesis events have been identified in a case of renal leiomyosarcoma, including in the 12q13.11-q21.2 region, which harbors crucial cell-cycle genes such as *MDM2* and *CDK4*. Rearrangements in this region was speculated to trigger further chromosomal instability, including events in 6q21-q27 and 7p22.3-p12.1 (237).

Chromoanasynthesis has also been reported as a common mechanism underlying *ERBB2* gene amplifications in early-stage *ERBB2*-positive breast cancers (238). Extensive local duplications and complex rearrangements can increase oncogene dosage, promoting tumor progression and potentially contributing to resistance to targeted therapies.

Chromoanasynthesis can be considered as a part of a broader spectrum of catastrophic events driving genome instability in both cancer and constitutional disorders (239). This 'chromosome chaos' model suggests that single, abrupt events may account for many complex rearrangements previously thought to accumulate gradually. Overall, chromoanasynthesis highlights the critical role of replication-based catastrophic events in shaping genome complexity and driving tumor evolution.

Chromoplexy. The term chromoplexy, consisting of chromo- and the Greek word plexis (πλέξις, meaning weaving or interweaving), was introduced in 2013 to describe a distinct class of complex structural rearrangements in cancer genomes (216). It refers to coordinated, interdependent chains of DNA rearrangements involving multiple chromosomes, typically occurring in a single catastrophic event.

In a seminal study of prostate cancer, whole-genome sequencing revealed intricate networks of balanced translocations, deletions, and inversions involving several chromosomes (216). These rearrangements often generated oncogenic fusions and disrupted tumor suppressor genes, suggesting that chromoplexy represents a punctuated mechanism accelerating tumor evolution. As a category of 'genomic catastrophes' distinct from chromothripsis, chromoplexy is thought to arise from the simultaneous breakage of spatially proximal chromatin regions, potentially facilitated by transcriptional activity or replication stress. The resulting DNA ends are aberrantly ligated in a coordinated yet tangled fashion, producing a 'weaving' of chromosomes rather than complete shattering (216, 217, 240).

Since its initial description, chromoplexy has been reported in a wide range of tumor types beyond prostate cancer. It has been identified in *EWSR1*-rearranged round cell sarcomas (241, 242), often giving rise to fusion oncogenes critical for sarcomagenesis, as well as in pediatric tumors such as Wilms tumor, rhabdomyosarcoma, and neuroblastoma (243).

Chromoplexy has also been observed in *NUT* midline carcinoma (244), esophageal adenocarcinomas (245), lung adenocarcinomas (246), mesotheliomas (247, 248), uterine leiomyosarcomas (249), myoepithelial carcinomas of soft tissue (250), acute myeloid leukemias (251), and multiple myelomas (252-254). Its diagnostic and therapeutic relevance is further illustrated by a case of acute promyelocytic leukemia lacking the canonical *PML::RARA*, in which chromoplexy, involving a complex 9-partner translocation, generated an *FNDC3B*::*RARB* fusion (255).

Chromoplexy embodies a shift from viewing chromosomal rearrangements as isolated, stepwise events to understanding them as complex, interconnected networks arising in single bursts. It complements concepts such as chromothripsis and kataegis (*see below*), contributing to a modern view of the cancer genomic landscape, characterized by punctuated, catastrophic changes that drive tumor heterogeneity, genomic instability, and promote the emergence of therapy-resistant clones. Chromoplexy highlights the importance of coordinated, multi-chromosome rearrangements in shaping tumor progression and genome complexity, and has been placed within the broader framework of chromoanagenesis (240).

Chromoanagenesis. From chromo- and the Greek anagenesis (ἀναγέννησις, meaning rebirth or regeneration), the term chromoanagenesis was introduced in 2012 to describe catastrophic one-step genomic events that result in complex, localized chromosomal rearrangements (214). It serves as an umbrella term encompassing chromothripsis, chromoplexy, and chromoanasynthesis. By integrating these diverse catastrophic rearrangements into a unifying concept of genomic chaos, chromoanagenesis captures events arising from defective mitosis, micronucleus formation, or failures in DNA repair, ultimately leading to abrupt chromosome shattering and reassembly (214, 256-258). Mechanistically, chromoanagenesis is tightly linked to mitotic errors and centrosome dysfunction. Abnormalities in centrosome number or structure promote chromosome instability by enabling multipolar mitoses and chromosome missegregation, conditions that favor sudden, catastrophic rearrangements. In other words, they create fertile ground for chromoanagenesis (259).

Chromoanagenesis has been described as a cataclysmic mechanism capable of driving macroevolution-like leaps in cancer cells. In sharp contrast to Darwinian gradualism, it embodies the idea that dramatic, large-scale remodeling can fundamentally reshape cancer genome architecture in a single event. Sudden, massive reorganizations may provide cancer cells with rapid adaptability, new oncogenic properties, and enhanced survival under selective pressure (256-258).

Analysis of more than 10,000 tumors from The Cancer Genome Atlas revealed that chromoanagenesis is a frequent event, affecting a broad spectrum of cancer types (260). Independent studies have also identified chromoanagenesis as a major driver of genome disruption in osteosarcoma, and as being strongly associated with highly abnormal karyotypes, extensive clonal diversity, and treatment resistance in acute myeloid leukemia (251, 261).

Case reports further illustrate the role of chromoanagenesis in diverse malignancies and highlight its clinical relevance. For example, in B-cell lymphoma, complex rearrangements consistent with chromoanagenesis have been described (262). In acute myeloid leukemia, a *KMT2A::ARHGEF12* fusion was generated through chromoanagenesis, demonstrating how such catastrophic rearrangements can directly give rise to oncogenic fusions (263). Together, these findings support the view that chromoanagenesis is a central contributor to cancer genome complexity and intratumoral heterogeneity.

Beyond cancer, chromoanagenesis has also been recognized as an underestimated cause of rare constitutional chromosomal disorders, contributing to complex rearrangements in patients with developmental syndromes and congenital anomalies (264-266).

Altogether, chromoanagenesis emerges as a unifying force behind both somatic and constitutional genomic complexity.

Kataegis. Kataegis (καταιγίς), the Greek word for thunderstorm, has been adopted into cancer genomics to

describe clusters of localized hypermutations observed in tumor genomes. This striking mutational pattern was first reported in 2012 in a whole-genome sequencing study of breast cancer, where mutation 'showers' appeared as clustered C>T and C>G substitutions at TpC dinucleotides (267). The term was chosen to reflect the visual and conceptual similarity to a genomic storm.

Kataegis is strongly associated with the activity of cytidine deaminases, particularly members of the apolipoprotein B mRNA-editing enzyme catalytic polypeptide-like family, such as APOBEC3A and APOBEC3B (268-270). These enzymes preferentially deaminate cytosines in single-stranded DNA regions, leading to localized hypermutation. DNA repair intermediates, such as those generated during double-strand break repair or break-induced replication, provide vulnerable single-stranded DNA substrates for APOBEC activity (271, 272). Studies have shown that telomere crisis, resulting in dicentric chromosomes and extensive DNA damage, can trigger both chromothripsis and kataegis, highlighting their interconnected nature (239, 273, 274). Bioinformatics tools such as the R packages kataegis and Katdetectr have been developed to systematically identify and visualize kataegis events in sequencing data (275, 276).

Kataegis has been detected across a wide range of cancer types, including breast, lung, pancreas, thyroid, and prostate, as well as pediatric leukemia (267, 277-283). In breast cancer, it is observed in approximately 55-60% of cases and has been associated with later onset, *ERBB2* amplification, and better prognosis (277, 282). The presence of kataegis is often linked to regions near genomic rearrangements, suggesting a role in structural genome instability and tumor heterogeneity, which may influence therapeutic responses (267). In a pan-cancer study involving 8,475 samples from 32 different cancer types, high kataegis activity was associated with increased expression of *CD274* (PD-L1) and *PDCD1LG2* (PD-L2), which encode ligands for the immune checkpoint receptor programmed cell death protein 1 PDCD1 (PD-1) (278, 284). The increased expression of *CD274* and *PDCD1LG2* may affect responses to immunotherapies and the use of Food and Drug Administration-approved immune checkpoint inhibitors (285).

In ovarian clear-cell carcinoma, APOBEC-mediated kataegis was found in the early phases of tumor pathogenesis. Tumors expressing APOBEC3B showed favorable prognosis and significant immunogenicity, as evidenced by marked cytotoxic T-cell infiltration (286, 287).

In lung adenocarcinomas, *APOBEC* mutational signatures are more frequent in receptor tyrosine kinase-driven cancer, such as those with *EGFR*, *ALK*, *RET*, and *ROS1* alterations (about 25%). These signatures became even more pronounced under the selective pressure of targeted therapy, such as osimertinib in *EGFR*-mutant tumors, and are strongly associated with kataegis and structural rearrangements, including duplications, deletions, inversions, and translocations (280).

In prostate cancer, kataegis has been linked to aggressive presentation, higher structural variant burden, and extensive copy number loss in high-risk tumors in African men. These tumors showed increased APOBEC3 activity and unique evolutionary trajectories, suggesting that kataegis may contribute to greater tumor heterogeneity and influence clinical outcomes (281).

In pediatric B-cell acute lymphoblastic leukemia, kataegis occurs at high frequency, especially in subtypes carrying *ETV6::RUNX1* and *ETV6::RUNX1*-like fusions, indicating a possible role for localized hypermutation in the pathogenesis of specific pediatric leukemia subgroups (283).

In summary, kataegis represents a distinct mutational phenomenon driven largely by APOBEC-mediated cytosine deamination during DNA repair processes. It has emerged as an important marker of genomic instability and tumor evolution, with potential implications for prognosis and treatment strategies across multiple cancer types.

Concluding Reflections on the Conceptual Shift in Cytogenetics through Modern Greek-derived Terms

Together, these modern Greek-derived terms represent more than just linguistic continuity. They encapsulate

major conceptual advances in our understanding of chromosomal instability and structural variation, and they now form an integral part of what can be considered modern cytogenetics.

While traditional methods such as chromosome banding, fluorescence *in situ* hybridization, and array comparative genomic hybridization have long focused on detecting visible abnormalities or copy-number alterations, terms like chromothripsis, chromoplexy, and chromoanasynthesis, all beginning with chromo-, show that chromosomes remain the central unit of study. However, their analysis has shifted from chromosome banding alone to a resolution enabled by genome-wide sequencing, optical genome mapping, and advanced cytogenomic approaches.

Chromoanagenesis unifies these catastrophic events under the broader concept of single-step genome remodeling, challenging the classical view that complex rearrangements arise through slow, stepwise accumulation. The incorporation of the terms chromothripsis (cth) and chromoanasynthesis (cha) in the International System for Human Cytogenomic Nomenclature (ISCN) reflects the growing recognition of these genomic catastrophes as legitimate cytogenetic entities, reinforcing their place within the science of studying chromosomes: cytogenetics.

Kataegis, though lacking the chromo- prefix, describes a parallel phenomenon involving localized hypermutation. It often occurs together with structural rearrangements and contributes to tumor heterogeneity and evolution. APOBEC-mediated kataegis, as well as ultramutated phenotypes arising from defects in DNA polymerases such as POLE and POLD1, illustrate how mutational bursts can shape tumor biology, immunogenicity, and treatment response (288, 289). Although kataegis operates primarily at the sequence level, its co-occurrence with chromosomal instability places it firmly within the expanding framework of cytogenetics and cytogenomics.

Collectively, chromothripsis, chromoplexy, chromoanasynthesis, chromoanagenesis, and kataegis can be seen as core components of the emerging field of chromosomics. This evolving discipline integrates chromosome structure, nuclear organization, gene regulation, and replication timing into a systems-level interpretation of genome function and dysfunction.

Overall, these modern Greek-derived terms mark a major transition in cytogenetics: from static, structural descriptions to dynamic, mechanistic, and genome-integrated models of chromosomal behavior in health and disease.

Evolution of the International System for Human Cytogenetic/Cytogenomic Nomenclature

The inclusion of new methodologies in the field of cytogenetics, and its transformation over recent decades into cytogenomics, is clearly reflected in the successive editions from 1995 to the current edition of the ISCN (290). Each edition has documented the gradual integration of novel technologies, expanding the field from the analysis of visible chromosome morphology to the detection of molecular and submicroscopic genomic alterations (46, 291-300).

A major turning point came with ISCN 1995, which introduced standardized nomenclature for fluorescence *in situ* hybridization (291). This inclusion reflected the growing importance of fluorescence *in situ* hybridization in both clinical diagnostics and research, as a methodology that complemented chromosome banding by enabling the identification of cryptic rearrangements and gene-level abnormalities. The incorporation of fluorescence *in situ* hybridization into ISCN marked the beginning of molecular cytogenetics, bridging banding-based analysis with DNA-based techniques. In ISCN 2005, fluorescence *in situ* hybridization nomenclature was further modernized, simplified, and expanded, and a basic nomenclature for recording the results of array comparative genomic hybridization was introduced (292). The ISCN 2009 edition formally integrated array-based technologies into the nomenclature system, reflecting their widespread adoption in clinical and research laboratories. The array nomenclature was revised and expanded to

accommodate all platform types, and the symbol 'arr' was introduced to denote copy-number variants detected by array comparative genomic hybridization and SNP arrays. Additional updates included expanded rules for describing mosaicism, marker chromosomes, and uniparental disomy, as well as updated idiograms based on refined banding resolution (293, 297).

During the preparation of ISCN 2013, the Committee emphasized that "the primary purpose of the ISCN is to foster communication among cytogeneticists using a standard nomenclature that can be used to describe any genomic rearrangement identified either by standard karyotyping or molecular methodologies." Reflecting this principle, ISCN 2013 incorporated genome build references into array-based results to ensure compatibility with genomic databases (294, 298). It introduced a standardized representation for complex genomic events such as chromothripsis and added the generic term 'region-specific assay' (rsa) for describing targeted methods, regardless of platform. This edition laid the groundwork for bridging chromosome banding with high-resolution molecular technologies and emphasized unified reporting principles across different methodologies.

The ISCN 2016 edition marked an important conceptual transition. To reflect technological advances and the integration of genome-wide data, the term 'Cytogenetic' in its title was replaced with 'Cytogenomic', formally renaming it the *International System for Human Cytogenomic Nomenclature* (295). In collaboration with the Human Genome Variation Society Sequence Variant Description Working Group, a unified nomenclature was developed that combined ISCN-like descriptions of chromosomal rearrangements with Human Genome Variation Society-like nucleotide variant descriptions. The term 'seq' was introduced to indicate that an abnormality had been detected using a sequence-based technology. This sequence-based nomenclature established a shared descriptive framework for both the molecular genetics and cytogenetics communities.

These conceptual and structural refinements paved the way for ISCN 2020, which further expanded sequence-based nomenclature to describe chromosomal abnormalities at nucleotide-level resolution (46, 299). The edition fully supported genome assembly–based reporting and harmonized descriptions across karyotyping, fluorescence *in situ* hybridization, array technology, genome mapping, and sequencing technologies. Clear annotations of all changes were included to facilitate transition from earlier editions, and the system promoted interoperability with genomic databases and clinical informatics tools.

The ISCN 2024 edition represents one of the most comprehensive revisions in the history of the system (296, 300). Building on the foundational changes introduced in 2016 and 2020, ISCN 2024 further consolidates general rules for clarity, resolved ambiguities from previous editions, and harmonized terminology across all cytogenomic platforms. New nomenclature was introduced for genome mapping technologies (including optical and electronic mapping) (202), shallow sequencing (sseq), and methylation-specific assays (rsa-ms). The representation of complex structural rearrangements was refined, nomenclature for fusion genes was clarified and standardized (301), and all examples were revised to promote consistent application in both clinical diagnostics and research. Overall, ISCN 2024 promotes platform-independent, integrative cytogenomic reporting, reflecting the continued evolution of chromosome analysis into high-resolution, genome-wide diagnostics.

The evolution of ISCN mirrors the transformation of cytogenetics, the science of studying chromosome structure and function, from its roots in chromosome banding methodology to a fully integrated scientific field that continuously embraces and incorporates new technologies while still utilizing established approaches. By harmonizing traditional and modern methods, ISCN enables comprehensive, precise, and universally interpretable reporting, supporting both research and clinical diagnostics in an era where genome-wide technologies are redefining the boundaries of modern medicine.

Digital Evolution of Cytogenetics: Software Solutions for Chromosome Analysis

In addition to general genome browsers such as the University of California, Santa Cruz, Genome Browser (131), Ensembl (132), and the National Center for Biotechnology Information Genome Data Viewer (302), which provide detailed genomic information alongside chromosomal positions and cytogenetic banding patterns, a wide range of specialized software tools and web-based databases have been developed for cytogenetic and cytogenomic analysis. These resources, which are reviewed elsewhere (303), play an essential role in storing, accessing, comparing, and visualizing chromosomal and genomic data. Software tools developed for array-comparative genomic hybridization have also illustrated how the digital evolution of cytogenetics has been driven by the need to interpret increasingly complex genomic data (304).

Regarding chromosome visualization, Cytogenetic Data Analysis System (CyDAS) stands out as a tool for analyzing and interpreting karyotypes, simulating chromosomal aberrations, and generating human chromosome ideograms in accordance with ISCN standards (305). RIdeogram, an R package, enables the generation of high-quality chromosome ideograms and allows users to overlay diverse genomic or transcriptomic data (306). Additional tools such as Idiographica and ChromDraw support the clear presentation of cytogenetic data and gene localization through customizable idiograms (307, 308). Several other R-based tools have further enriched chromosome visualization capabilities, including karyoploteR (309), chromoMap (310), shinyChromosome (311), and GenoPlotR (312), which enable flexible, customizable, and interactive rendering of chromosome structures and annotations.

Tools such as PhenoGram (313), Circos (314), and Circa (from OMGenomics Labs) are widely used to display genetic variants and complex structural rearrangements. Circos and Circa, in particular, represent chromosomes in a circular layout and are highly versatile, capable of displaying translocations, fusion genes, and other large-scale genomic events in human samples. Furthermore, fusion-gene detection software such as Arriba includes extensions that map genomic breakpoints onto chromosome ideograms, providing an integrated view of structural alterations (315). The tools FusionInspector and Chimeraviz also provide visualization of fusion events (316, 317). Chimeraviz, an R package, is particularly notable for its ability to generate chromosome ideograms and fusion diagrams from outputs of multiple callers, aiding in the interpretation of structural rearrangements (317).

Programs focused on copy-number and structural variant analysis, such as the Integrative Genomics Viewer (318), CNVkit (319), and Chromothripsis Explorer (320), offer also ideogram-based visualizations of chromosomal aberrations and help bridge molecular data with cytogenetic interpretation. In parallel, optical genome mapping has emerged as a next-generation cytogenetic technique that enables high-resolution visualization of structural variants using long DNA molecules, complementing digital karyotyping and sequence-based methods.

In clinical cytogenetic laboratories, digital karyotyping is undergoing a transformation through the integration of artificial intelligence (321). Several companies have introduced artificial intelligence-guided systems that automate key steps in chromosome analysis, including metaphase detection, chromosome segmentation, classification, and preliminary karyogram generation. Applied Spectral Imaging offers HiBand version 8.4, which uses convolutional neural networks to learn chromosome identification, pairing, and arrangement. BioView has developed an Artificial Intelligence Karyotyping Application Suite with real-time karyotype correction, high-definition imaging, and abnormality detection. Diagens, based in China, provides the AutoVision platform, also using convolutional neural networks, with an advertised classification accuracy of over 99%. Finally, MetaSystems' Ikaros version 6.3 employs deep neural networks and has demonstrated 97% accuracy across specimen types in clinical settings (321). These artificial intelligence-enabled systems significantly reduce analysis time and manual

workload, allowing cytogeneticists to focus more on interpretation and less on repetitive technical tasks. While still in the early stages of widespread adoption, artificial intelligence-guided karyotyping represents a promising and potentially transformative advancement in the practice of digital cytogenetics.

As the number of specialized tools and database interfaces continues to grow, standardizing data formats and enabling interoperability across platforms will be key to maximizing their utility in both research and clinical workflows.

All in all, the continued development and refinement of these specialized software tools underscore the dynamic and evolving nature of cytogenetics. The need to analyze, interpret, and visualize chromosomal data in increasingly detailed and integrative ways has driven the creation of these programs. This highlights that cytogenetics, as a branch of genetics dedicated to the study of chromosomes, remains an active field that continues to expand and adapt alongside advances in molecular and computational biology. Together, these developments illustrate how digital tools are not only supporting but actively shaping the future of cytogenetic research and diagnostics.

The Legacy of Chromosome Banding in Today's Oncology

Despite the emergence of powerful new technologies for studying chromosomes in cancer, chromosome banding analysis continues to play an indispensable and complementary role in both cancer diagnostics and research. New methods may challenge conventional approaches (322, 323), but chromosome banding remains especially valuable in hematological malignancies and in tumors of bone and soft tissue. In fact, the absence of chromosome banding results, whether due to technical failure or omission, has been associated with poor prognosis in acute myeloid leukemia (324-326). The fifth edition of the World Health Organization Classification of Hematolymphoid Tumors incorporates chromosomal aberrations, along with other genetic abnormalities, as key elements for defining disease entities (327, 328). Similarly, the fifth edition of the World Health Organization Classification of Bone and Soft Tissue Tumors includes chromosomal aberrations, fusion genes, and additional genetic features as integral components of tumor pathogenesis (329).

In cancer research, chromosome banding remains a valuable starting point for the discovery of novel fusion genes, which are subsequently characterized by high-throughput sequencing. Several studies published in 2024 and 2025 illustrate this approach and report fusion genes linked to specific chromosomal abnormalities (330-334).

Chromosomal abnormalities also continue to be reported at major scientific conferences such as the annual meetings of the American Society of Hematology (335, 336). Moreover, retrospective studies based on banding analysis, primarily in hematologic malignancies but also in bone and soft tissue tumors, remain a valuable source of data, providing biological and clinical insight. Recent large-scale retrospective analyses of chromosomal rearrangements in acute leukemia (337-341) and multiple myelomas (often in combination with fluorescence *in situ* hybridization) (342-345) have provided important insights into the patterns and the clinical implications of these aberrations.

A large retrospective study of gastrointestinal stromal tumors investigated chromosomal aberrations and the extent of intratumor cytogenetic heterogeneity (346). A subsequent study demonstrated that genomic complexity, defined by the number of chromosomal aberrations, may serve as a biomarker to guide de-escalation of adjuvant imatinib treatment in high-risk gastrointestinal stromal tumor (347).

In the context of this legacy, The Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer illustrates the remarkable evolution of cancer cytogenetics, transitioning from static documentation to dynamic, genome-informed analysis. First introduced in 1983 as a printed volume titled *Catalog of Chromosome Aberrations in Cancer*, and published in the journal *Cytogenetics and Cell Genetics*, it included 3,844 cases

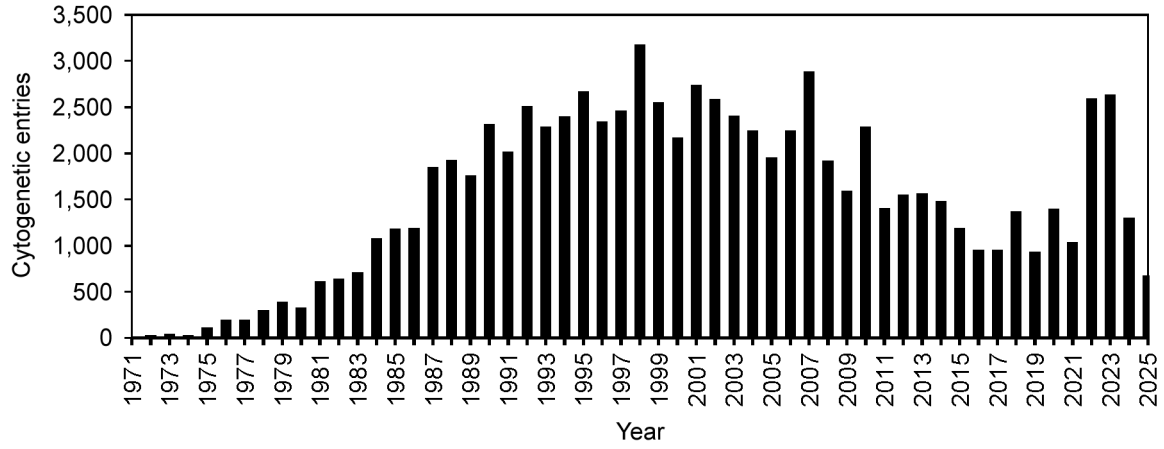


Figure 4. *Annual number of cytogenetic entries reported in the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (as of July 10, 2025). The diagram shows the number of newly registered cytogenetic entries per year from 1971 to 2025. The steep rise throughout the 1980s and 1990s mirrors the exponential expansion documented in the printed catalog editions published between 1983 and 1998, reflecting the intense activity in chromosome banding-based cancer cytogenetics. After this period of rapid growth, annual contributions became more variable, influenced by evolving diagnostic strategies, shifts in publication and reporting practices, and the growing impact of genome-wide technologies on cancer cytogenetics.*

(50). As knowledge rapidly expanded, updated editions of the catalog followed: the 1985 edition documented 5,345 cases; the 1988 edition included 9,069, the 1991 edition listed 14,141, the 1994 edition reached 22,076, and by 1998, the catalog had grown to 30,541 cases (348-351). Over the 15-year period from 1983 to 1998, a total of 26,697 new cases were added, corresponding to an average of approximately 1,780 cases per year. The growth was exponential, with an estimated compound annual growth rate of 14.8% in reported chromosomal aberrations (Figure 4).

In 2000, this growing body of work was transformed into a publicly accessible online database, hosted by the U.S. National Cancer Institute, enabling regular updates, advanced search capabilities, and global access (52). From that point forward, the database not only expanded in volume but also integrated emerging genomic data and tools, reflecting the shift from chromosome banding to modern sequence-based interpretation (52). The database now integrates CytoConverter, which translates conventional karyotype descriptions into genomic coordinates (352), and annotations from the Matched Annotation from the National Center for Biotechnology Information and EMBL-EBI (MANE) project, which provides a unified transcript set for clinical and research use (353). Additionally, through its incorporation into Google BigQuery, the dataset supports advanced, interactive analyses at scale (52).

Since the launch of the online version in 2000, the database has continued to grow, albeit at a slower pace. From 30,541 cases in 1998 to 80,008 by July 2025, the number of cytogenetically analyzed cancer cases has more than doubled, corresponding to an average of 1,832 new cases per year and a modest compound annual growth rate of 3.6% (Figure 4). Although modern technologies such as array-comparative genomic hybridization, genome-wide sequencing, and optical genome mapping are now widely used in cancer cytogenetics, new case studies based on chromosome banding continue to be documented and curated, underscoring the enduring clinical and research value of this foundational technique.

In contrast to cytogenetic case entries, which have accumulated steadily over decades from numerous studies worldwide, the fusion-gene data in the Mitelman Database reveal a striking imbalance (Figure 5A and B). As of the July 10, 2025, update, the database contains

52,669 fusion-gene entries in the standard *Gene1::Gene2* format, corresponding to 34,398 unique gene fusions and 14,105 genes involved in them. Remarkably, 41,749 of these entries (approximately 79%) originate from just five large-scale studies: Gao *et al*. 2018 (354) with 21,065 entries, Hu *et al*. 2018 (355) with 10,150 entries, Yoshihara *et al*. 2015 (356) with 7,700 entries, Calabrese *et al*. 2020 (357) with 2,309 entries, and Cleynen *et al*. 2017 (358) with 525 entries. The remaining 10,920 entries (approximately 21%) are derived from 3,266 other publications (52).

Likewise, this trend extends to the unique gene fusions, which also originate mainly from the same five large-scale studies. Analysis of the Mitelman Database (July 2025) shows that the number of newly reported fusion genes peaks sharply in years corresponding to the publication of these large-scale sequencing studies (Figure 5A and B).

For the purpose of this review, fusion genes appearing for the first time and never reported previously were identified for each year in the database (up to the July 10, 2025 update). Reciprocal *Gene1::Gene2* and *Gene2::Gene1* were considered as a single event, as both arise from the same underlying genomic aberration or its variants, and the format reported for the first time was retained.

Based on these criteria, 33,436 unique fusions were listed in the July 2025 version of the database. The years 2015, 2017, 2018, and 2020 account for 7,585, 884, 19,230, and 1,151 unique fusion genes, respectively, together representing 28,850 of the 33,436 unique fusions (≈86%). In 2015, the study by Yoshihara *et al.* (356) contributed 7,325 unique fusions; in 2017, Cleynen *et al.* (358) added 478; in 2018, the two studies by Gao *et al.* (354) and Hu *et al.* (355) contributed 9,263 and 9,794, respectively (jointly 19,057); and in 2020, Calabrese *et al.* (357) added 822. In total, 27,682 unique fusions (≈83%) originate from these five studies. These calculations confirm that the apparent expansion of fusion-gene diversity primarily reflects the influx of data from a few comprehensive transcriptome-wide studies rather than a continuous accumulation of independent cytogenetic discoveries (Figure 5A and B).

The Mitelman Database is extensive and widely regarded as the principal reference for chromosomal aberrations and gene fusions in cancer, but it does not include all published cases identified through chromosome banding analysis. Cases reported in conference abstracts (359), individual case reports (360, 361), smaller or larger case series (346, 362), and studies presenting cytogenetic data solely in supplementary materials (363-365) may be underrepresented. The database also excludes neoplasms carrying nonclonal chromosomal aberrations; for example, elastofibromas are characterized by chromosomal instability and predominantly nonclonal changes, whereas the few reported clonal aberrations in elastofibroma are believed to represent secondary rather than primary events (366-368). This biological nuance is not reflected in the database, which currently lists only two elastofibroma cases with clonal aberrations (52).

With regard to fusion genes, several of the most fusion-rich studies in the database draw upon overlapping The Cancer Genome Atlas tumor cohorts (354-357). As a result, the apparent diversity of fusion events in the database is partly inflated by multiple reports of the same underlying samples, underscoring the need for systematic curation, separating the wheat from the chaff, to accurately delineate the landscape of genuine, non-redundant fusion genes. Another limitation of the database is that it does not include fusions involving non-coding RNA or microRNAs. This omission may lead to misinterpretation of the frequency and distribution of certain fusion genes. Notable examples are the recurrent fusion gene *MALAT1::GLI1* reported in plexiform fibromyxoma, gastroblastoma, and epithelioid neoplasms (369-372), and the fusion of microRNA 143 with *NOTCH1* or *NOTCH2* in glomus tumor (373-376).

Nevertheless, the Mitelman Database remains an indispensable resource for both cancer research and diagnostics, providing a curated and continually updated view of the cytogenomic landscape in human malignancies. It is frequently used in combination with other major databases in cancer genomics, such as the

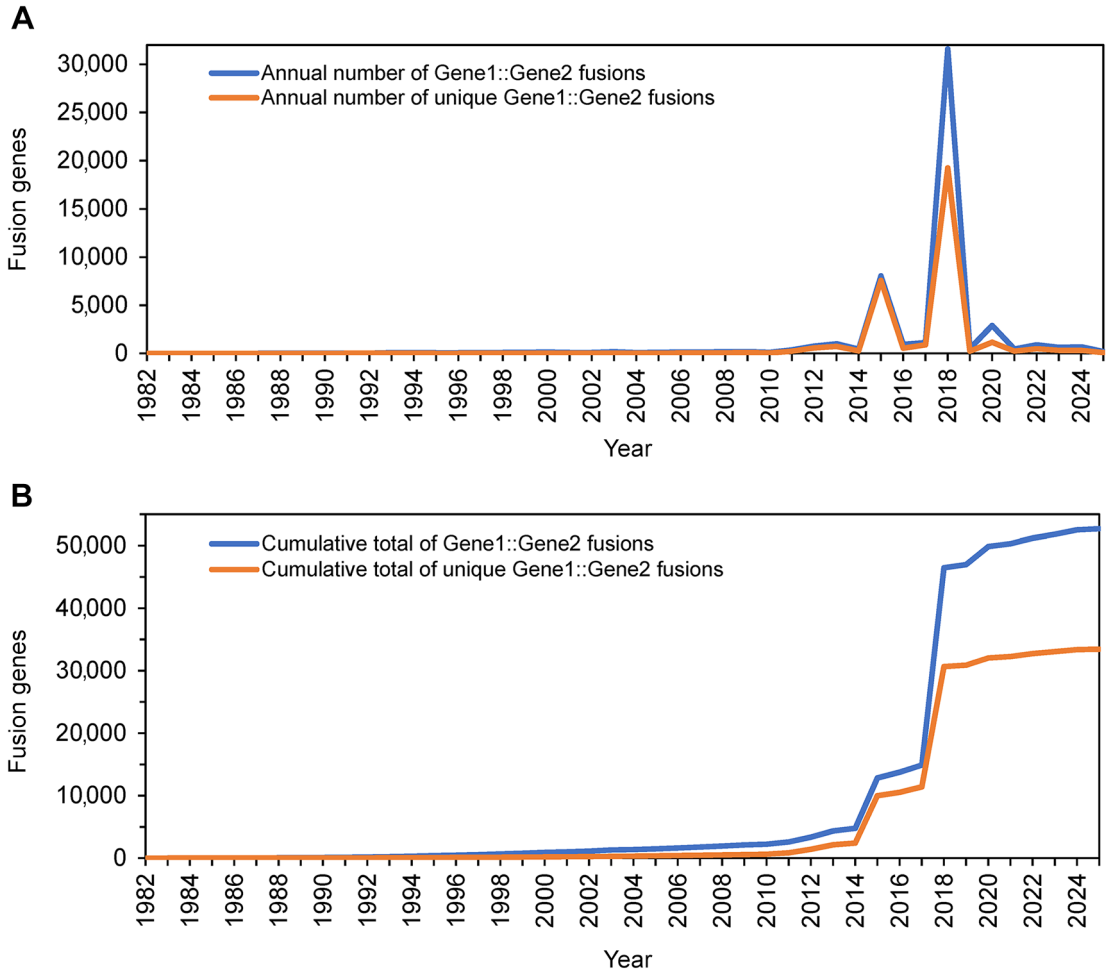


Figure 5. *Fusion-gene entries in the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (update of July 10, 2025). (A) Annual number of "Gene1::Gene2" fusions and unique Gene1::Gene2 fusions from 1982 to 2025. The sharp peaks in 2015, 2018, and 2020 correspond to a few large-scale transcriptome-wide studies, rather than a steady accumulation over time. (B) Cumulative totals of Gene1::Gene2 fusions and unique fusions over the same period. The near-vertical rises in 2015, 2018, and 2020 show that the apparent expansion of fusion-gene diversity is driven mainly by these large sequencing studies, with comparatively modest contributions from other years. 'Unique' Gene1::Gene2 fusions represent fusion pairs appearing for the first time in the database; reciprocal orientations (Gene1::Gene2 and Gene2::Gene1) are considered a single fusion event.*

Catalogue of Somatic Mutations in Cancer, which focuses on somatic mutations, and ChimerDB, which integrates experimentally validated as well as computationally predicted gene fusions (377, 378). Together, these resources offer a more comprehensive understanding of cancer-associated structural variants, supporting efforts in fusion-gene discovery, the classification and interpretation of novel aberrations, and the development of targeted therapeutic strategies.

An important aspect missing from curated resources, including the Mitelman Database, is the documentation of non-clonal chromosome aberrations (NCCAs). Traditionally dismissed as technical artifacts or background noise (379), NCCAs are now recognized as visible manifestations of chromosomal instability and a major source of karyotypic heterogeneity in both malignant and pre-malignant conditions (23, 379-381). Each NCCA represents a unique genomic cnfiguration that can drive macroevolutionary

changes in tumor cell populations, providing the diversity from which stable, disease-defining CCAs may arise (23, 379, 381). In inherited instability syndromes such as Fanconi anemia, NCCAs frequently appear years before the emergence of overt clonal evolution, and their burden may precede the development of complex karyotypes (382). Moreover, studies in cytopenic patients without hematologic malignancy have shown that the presence of NCCAs can be associated with adverse prognosis, in some cases exceeding the impact of CCAs (383). Systematically recording NCCAs in cytogenetic analyses, as proposed by Heng and colleagues (23, 379, 381), would improve our understanding of tumor heterogeneity and cancer evolution, and it could also strengthen the prognostic value of cytogenetic data. Furthermore, the development of a dedicated database capturing NCCA patterns across tumor types has been suggested as a potentially invaluable resource for both research and clinical practice (23, 379, 381).

In light of the above, despite the rise of high-throughput genomic technologies, chromosome banding retains its diagnostic and scientific value. It continues to serve not only as a complementary method but also as a foundational element in the legacy of cancer cytogenetics, supporting and informing modern genomic discovery. In the expanding territory of cytogenomics, chromosome banding remains a compass, guiding interpretation, anchoring discovery, and reminding us that even the most advanced journeys begin with a well-drawn map.

Is Cytogenetics Indeed a Dinosaur?

In a recent article published in the August 2025 issue of Prenatal Diagnosis, summarizing the International Society for Prenatal Diagnosis 2024 Debate 3, provocatively titled "Cytogenetics Is a Dinosaur and Should Be Replaced by Molecular Technologies", Michael E. Talkowski and Yassmine M. N. Akkari presented opposing views under the moderation of Amy M. Breman (384). Dr. Talkowski argued that whole-genome sequencing and related platforms such as exome sequencing now provide a far more comprehensive and higher-resolution genetic screen than karyotyping, chromosomal microarray, and fluorescence *in situ* hybridization, and should replace them as the first-line approach in prenatal diagnosis. He envisioned a future driven by unbiased, genome-wide, non-invasive sequencing capable of detecting nearly all clinically relevant variants. His position is "that with more training in sequencing technologies, clinicians and patients alike will demand the most comprehensive approaches available, and this is clearly ES/GS testing".

Dr. Akkari countered that cytogenetics is not merely a technique, but a science devoted to the study of chromosome behavior that continues to evolve with new tools such as optical genome mapping. She emphasized the enduring role of cytogenetics in education, in the interpretation of chromosomal structure, and in ensuring equitable access to diagnostics, noting that in many parts of the world, advanced sequencing remains a distant prospect: "In Lebanon, we can barely give Gleevec when a patient is diagnosed with chronic myeloid leukemia. Genome sequencing is not even on their radar." She further stated that "as much as we want people to understand next-generation sequencing, we also need them to understand the structure and behavior of chromosomes," and mentioned a discussion in which she was asked whether she would encourage her children to go into cytogenetics. Her answer was very genuinely "yes," because "the science of cytogenetics will make them understand chromosomes. Understanding chromosomes will make them understand behavior. Understanding everything about this science will make them able to fully understand the data that labs like Dr. Talkowski's are able to generate at large scale."

In the concluding remarks, Dr. Breman observed that both sides ultimately agreed on one central point: Understanding chromosomes remains fundamental to clinical genetics. The debate thus reflected not extinction but transformation and the continuing evolution of cytogenetics through and within the framework of modern technologies.

In considering the arguments presented in this debate, my perspective aligns more closely with that of Dr.

Akkari. Cytogenetics is the field of genetics studying the structure and behavior of chromosomes. So, paraphrasing Dr. Akkari's question "How can a science die?" I would ask: How can a methodology, such as whole-genome sequencing, replace a science? Cytogenetics is hardly a dinosaur as a scientific discipline; it is less than 150 years old, whereas many scientific fields are far older. The comparison in the debate was not truly about the science of cytogenetics but rather about chromosome banding *versus* high-throughput technologies.

Like Dr. Akkari, I remain acutely aware that access to high-throughput sequencing and other advanced genomic technologies is far from universal. In fact, gel electrophoresis together with ethidium bromide staining (now largely replaced by less toxic intercalating fluorescent dyes such as SYBR Green or GelRed), which is the methodological counterpart to chromosome banding in molecular biology, is still routinely used to visualize DNA fragments, for example after PCR amplification. Developed in the early 1970s by two independent research groups (385-388), gel electrophoresis/ethidium bromide staining is almost the same age as chromosome banding, and yet it remains widely used in many laboratories despite the availability of more advanced technologies. The continued use of these methods despite five decades of technological progress illustrates a broader truth: Methods do not become obsolete simply because newer ones exist but only when they cease to be informative.

In the same way that gel electrophoresis/ethidium bromide staining remains a basic structural tool in molecular biology, chromosome banding remains a basic structural tool in cytogenetics; each continues to support and guide the interpretation of high-throughput genomic data. In many regions, both methods, chromosome banding and gel electrophoresis/ethidium bromide staining continue to serve as practical and informative research and diagnostic approaches.

And even when using the most advanced genomic technologies and the most sophisticated genomic analyses, all genetic findings, whether indels, pathogenic variants, or complex rearrangements, are ultimately positioned within chromosomal coordinates. In the end, every layer of genomic information returns to the same foundational structure: the chromosome, which remains the enduring framework of genome organization and function and the unifying theme of cytogenetics.

Concluding Remarks

Cytogenetics has undergone successive methodological revolutions, from chromosome banding to high-resolution molecular and genomic technologies. Today, platforms such as array comparative genomic hybridization, next-generation sequencing, and optical genome mapping enable the interrogation of chromosomes with unprecedented precision. New terms like cytogenomics and chromosomics have emerged to reflect this evolution. Others, such as chromothripsis, chromoplexy, and chromoanasynthesis, now unified under the umbrella of chromoanagenesis, capture the notion that catastrophic genomic events can reshape cancer genomes in a single step. Likewise, the term kataegis describes clusters of localized hypermutations, revealing yet another layer of chromosomal complexity in cancer.

Yet despite these advances, the core mission of the field, the study of chromosomes, remains unchanged. Whether called cytogenetics or cytogenomics, the field broadly encompasses all efforts to understand chromosomes across species. Just as molecular genetics has embraced new tools over time, replacing Southern blotting and restriction enzymes with PCR and sequencing without losing its identity, so too has cytogenetics persisted, adapting to new methods while maintaining its core focus. For some, cytogenetics is synonymous with chromosome banding, yet its scope and spirit extend far beyond any single method.

Like a tree, it stands rooted in its past, branching outward with each scientific advance. It has been nourished, bent, and reshaped by successive methods, yet never losing its core identity. Today, cytogenetics is both graceful and strong, revealing the hidden architecture of life in ever-greater detail, and carrying the legacy of chromosome banding into the omics era.

The future may see the replacement of chromosome banding with genome-wide approaches, but this will not be the end of cytogenetics. It will simply be its natural evolution. The field will continue to thrive by integrating new technologies to deepen our understanding of chromosome structure, function, and pathology. As long as we seek to understand chromosomes, by any method, cytogenetics will endure.

Conflicts of Interest

The Author declares no competing interests.

Author's Contributions

I.P. conceived the topic, designed the structure of the review, performed the literature search, analyzed and synthesized the relevant scientific developments, wrote the manuscript, prepared all figures and tables, and approved the final version.

Acknowledgements

The Author thanks the CMAJ Group for kindly granting permission to reproduce Figure 1A. The Author also acknowledges the courtesy of Kristin Andersen (Oslo University Hospital – Norwegian Radium Hospital) for providing Figure 1B and C. Figure 2 was generated using the publicly available test dataset included with the STAR-Fusion distribution and analyzed with the Arriba algorithm. The Author gratefully acknowledges Professor Zhenya Tang for arranging access to the optical genome mapping image and Dr. Gokce A. Toruner (MD Anderson Cancer Center) for kindly providing it (Figure 3).

Funding

The Author's research is financially supported by Barnekreftforeningen (The Norwegian Childhood Cancer Society).

Artificial Intelligence (AI) Disclosure

The Author used the AI language model ChatGPT (OpenAI, San Francisco, CA, USA) for editorial assistance, limited to grammar correction and improvement of English readability. The AI tool had no role in study design, data collection, analysis, or interpretation. The Author takes full responsibility for the content of this manuscript.

References

1 Akkari Y: Science that lasts a lifetime. The Pathologist. June 2023. Available at: https://thepathologist.com/issues/2023/articles/jun/science-that-lasts-a-lifetime [Last accessed on January 28, 2026]
2 Zhang P, Friebe B, Gill B, Park RF: Cytogenetics in the age of molecular genetics. Aust J Agric Res 58(6): 498-506, 2007. DOI: 10.1071/AR07054
3 Liehr T: "Classical cytogenetics" is not equal to "banding cytogenetics". Mol Cytogenet 10: 3, 2017. DOI: 10.1186/s13039-017-0305-9
4 Tootill E: The Facts On File Dictionary of Biology. New York, NY, USA, Facts on File, 1981.
5 Holmes S: Henderson's Dictionary of Biological Terms (9th Edition). London, UK, Longman, 1985.
6 Market House Books Editors: The Bantam Medical Dictionary. New York, NY, USA, Bantam Books, 1990.
7 Stedman TL: Medical Dictionary for the Health Professions and Nursing (7th Edition). Philadelphia, PA, USA, Lippincott Williams & Wilkins, 2012.
8 Harman O: Darlington and the 'invention' of the chromosome. Endeavour 27(2): 69-74, 2003. DOI: 10.1016/s0160-9327(03)00054-1
9 Tjio JH, Levan A: The chromosome number of man. Hereditas 42(1-2): 1-6, 2010. DOI: 10.1111/j.1601-5223.1956.tb03010.x
10 Gautier M, Harper PS: Fiftieth anniversary of trisomy 21: returning to a discovery. Human Genetics 126(2): 317-324, 2009. DOI: 10.1007/s00439-009-0690-1
11 Guerra M: Chromosome numbers in plant cytotaxonomy: concepts and implications. Cytogenet Genome Res 120(3-4): 339-350, 2008. DOI: 10.1159/000121083
12 Schwarzacher T, Liu Q, Pat Heslop-Harrison JS: Plant cytogenetics: from chromosomes to cytogenomics. Methods Mol Biol 2672: 3-21, 2023. DOI: 10.1007/978-1-0716-3226-0_1
13 Switonski M, Szczerbal I, Nowacka-Woszuk J: From cytogenetics to cytogenomics: a new era in the diagnosis of chromosomal abnormalities in domestic animals. J Appl Genet 66(3): 661-673, 2025. DOI: 10.1007/s13353-025-00943-x

14 Caspersson T, Gahrton G, Lindsten J, Zech L: Identification of the Philadelphia chromosome as a number 22 by quinacrine mustard fluorescence analysis. Exp Cell Res 63(1): 238-240, 1970. DOI: 10.1016/0014-4827(70)90362-9

15 Caspersson T, Zech L, Johansson C: Differential binding of alkylating fluorochromes in human chromosomes. Exp Cell Res 60(3): 315-319, 1970. DOI: 10.1016/0014-4827(70)90523-9

16 Caspersson T, Zech L, Johansson C, Modest EJ: Identification of human chromosomes by DNA-binding fluorescent agents. Chromosoma 30(2): 215-227, 1970. DOI: 10.1007/BF00282002

17 Seabright M: A rapid banding technique for human chromosomes. Lancet 298(7731): 971-972, 1971. DOI: 10.1016/s0140-6736(71)90287-x

18 Liehr T, Claussen U: Current developments in human molecular cytogenetic techniques. Curr Mol Med 2(3): 283-297, 2002. DOI: 10.2174/1566524024605725

19 Bernheim A, Vagner-Capodano AM, Couturier J: From cytogenetics to cytogenomics of tumors. Medecine Sciences 16(4): 528-539, 2000.

20 Bernheim A: Cytogenomics of cancers: from chromosome to sequence. Mol Oncol 4(4): 309-322, 2010. DOI: 10.1016/j.molonc.2010.06.003

21 Liehr T: From human cytogenetics to human chromosomics. Int J Mol Sci 20(4): 826, 2019. DOI: 10.3390/ijms20040826

22 Liehr T: Molecular cytogenetics in the era of chromosomics and cytogenomic approaches. Front Genet 12: 720507, 2021. DOI: 10.3389/fgene.2021.720507

23 Ye JC, Heng HH: The new era of cancer cytogenetics and cytogenomics. Methods Mol Biol 2825: 3-37, 2024. DOI: 10.1007/978-1-0716-3946-7_1

24 Ye JC, Tang G: Optical genome mapping: a machine-based platform in cytogenomics. Methods Mol Biol 2825: 113-124, 2024. DOI: 10.1007/978-1-0716-3946-7_5

25 Claussen U: Chromosomics. Cytogenet Genome Res 111(2): 101-106, 2005. DOI: 10.1159/000086377

26 Cremer T, Cremer C: Centennial of Wilhelm Waldeyer's introduction of the term "chromosome" in 1888. Cytogenet Cell Genet 48(2): 65-67, 1988. DOI: 10.1159/000132590

27 Schlegelberger B: In memoriam: Prof. Dr. rer. nat. Dr. med. h.c. Lore Zech; 24.9.1923 - 13.3.2013: Honorary member of the European Society of Human Genetics, Honorary member of the German Society of Human Genetics, Doctor laureate, the University of Kiel, Germany. Mol Cytogenet 6(1): 20, 2013. DOI: 10.1186/1755-8166-6-20

28 Cour LL: Acettc-Orcein: a new stain-fixative for chromosomes. Stain Technol 16(4): 169-174, 1941. DOI: 10.3109/10520294109107302

29 Moorhead PS, Nowell PC, Mellman WJ, Battips DM, Hungerford DA: Chromosome preparations of leukocytes cultured from human peripheral blood. Exp Cell Res 20(3): 613-616, 1960. DOI: 10.1016/0014-4827(60)90138-5

30 Carr DH, Walker JE: Carbol Fuchsin as a stain for human chromosomes. Stain Technol 36(4): 233-236, 1961. DOI: 10.3109/10520296109113278

31 Rodman TC: Human chromosome banding by Feulgen stain aids in localizing classes of chromatin. Science 184(4133): 171-173, 1974. DOI: 10.1126/science.184.4133.171

32 Sutton WS: The chromosomes in heredity. Biol Bulletin 4: 231-251, 1903.

33 Boveri T: Concerning the origin of malignant tumours by Theodor Boveri. Translated and annotated by Henry Harris. J Cell Sci 121 Suppl 121(Supplement_1): 1-84, 2008. DOI: 10.1242/jcs.025742

34 Satzinger H: Theodor and Marcella Boveri: chromosomes and cytoplasm in heredity and development. Nat Rev Genet 9(3): 231-238, 2008. DOI: 10.1038/nrg2311

35 McKusick VA: Marcella O'Grady Boveri (1865-1950) and the chromosome theory of cancer. J Med Genet 22(6): 431-440, 1985. DOI: 10.1136/jmg.22.6.431

36 A proposed standard system of nomenclature of human mitotic chromosomes (Denver, Colorado). Ann Hum Genet 24(4): 319-326, 1960. DOI: 10.1111/j.1469-1809.1960.tb01744.x

37 Ford CE, Jones KW, Polani PE, De Almeida JC, Briggs JH: A sex-chromosome anomaly in a case of gonadal dysgenesis (Turner's syndrome). Lancet 273(7075): 711-713, 1959. DOI: 10.1016/s0140-6736(59)91893-8

38 Jacobs PA, Strong JA: A case of human intersexuality having a possible XXY sex-determining mechanism. Nature 183(4657): 302-303, 1959. DOI: 10.1038/183302a0

39 Nowell PC, Hungerford DA: Chromosome studies on normal and leukemic human leukocytes. J Natl Cancer Inst 25: 85-109, 1960.

40 Nowell PC, Hungerford DA: A minute chromosome in human chronic granulogytic leukemia. Science 132(3438): 1497, 1960.

41 Lele KP, Penrose LS, Stallard HB: Chromosome deletion in a case of retinoblastoma. Ann Hum Genet 27(2): 171-174, 1963. DOI: 10.1111/j.1469-1809.1963.tb00209.x

42 Jacobs PA, Tough IM, Wright DH: Cytogenetic studies in Burkitt's lymphoma. Lancet 282(7318): 1144-1146, 1963. DOI: 10.1016/s0140-6736(63)90795-5

43 Brewster DJ, Garrett JV: Chromosome abnormalities in neuroblastoma. J Clin Pathol 18(2): 167-169, 1965. DOI: 10.1136/jcp.18.2.167

44 Dolan M: The role of the Giemsa stain in cytogenetics. Biotech Histochem 86(2): 94-97, 2011. DOI: 10.3109/10520295.2010.515493

45 Paris Conference (1971): Standardization in human cytogenetics. Birth Defects Orig Artic Ser 8(7): 1-46, 1972.

46 McGowan-Jordan J, Hastings RJ, Moore S: ISCN 2020: An International System for Human Cytogenomic Nomenclature. Basel, Switzerland, Karger, 2020.

47 Heim S, Mitelman F: Cancer cytogenetics: Chromosomal and Molecular Genetic Abberations of Tumor Cells. Oxford, UK, Wiley-Blackwell, 2015.

48 Rowley JD: Letter: A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining. Nature 243(5405): 290-293, 1973. DOI: 10.1038/243290a0
49 Heim S, Mitelman F: Cancer cytogenetics. New York, NY, USA, Alan R. Liss, 1987.
50 Mitelman F: Catalogue of chromosome aberrations in cancer. Cytogenet Genome Res 36(1-2): 1-3, 1983. DOI: 10.1159/000131930
51 Mitelman F: Catalogue of Chromosome Aberrations in Cancer (2nd Edition). New York, NY, USA, Alan R. Liss, 1985.
52 Mitelman F, Johansson B, Mertens F: Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer. 2025. Available at: https://mitelmandatabase.isb-cgc.org/ [Last accessed on February 11, 2026]
53 Smith HO, Welcox K: A restriction enzyme from Hemophilus influenzae. I. Purification and general properties. J Mol Biol 51(2): 379-391, 1970. DOI: 10.1016/0022-2836(70)90149-x
54 Southern EM: Detection of specific sequences among DNA fragments separated by gel electrophoresis. J Mol Biol 98(3): 503-517, 1975. DOI: 10.1016/s0022-2836(75)80083-0
55 Alwine JC, Kemp DJ, Stark GR: Method for detection of specific RNAs in agarose gels by transfer to diazobenzyloxymethyl-paper and hybridization with DNA probes. Proc Natl Acad Sci U S A 74(12): 5350-5354, 1977. DOI: 10.1073/pnas.74.12.5350
56 Feinberg AP, Vogelstein B: A technique for radiolabeling DNA restriction endonuclease fragments to high specific activity. Anal Biochem 132(1): 6-13, 1983. DOI: 10.1016/0003-2697(83)90418-9
57 Sanger F, Nicklen S, Coulson AR: DNA sequencing with chain-terminating inhibitors. Proc Natl Acad Sci U S A 74(12): 5463-5467, 1977. DOI: 10.1073/pnas.74.12.5463
58 Maniatis T, Fritsch EF, Sambrook J: Molecular Cloning: A Laboratory Manual. Cold Spring Harbor, NY, USA, Cold Spring Harbor Laboratory Press, pp. 545, 1982.
59 Dalla-Favera R, Bregni M, Erikson J, Patterson D, Gallo RC, Croce CM: Human c-myc onc gene is located on the region of chromosome 8 that is translocated in Burkitt lymphoma cells. Proc Natl Acad Sci U S A 79(24): 7824-7827, 1982. DOI: 10.1073/pnas.79.24.7824
60 Taub R, Kirsch I, Morton C, Lenoir G, Swan D, Tronick S, Aaronson S, Leder P: Translocation of the c-myc gene into the immunoglobulin heavy chain locus in human Burkitt lymphoma and murine plasmacytoma cells. Proc Natl Acad Sci U S A 79(24): 7837-7841, 1982. DOI: 10.1073/pnas.79.24.7837
61 Erikson J, Nishikura K, ar-Rushdi A, Finan J, Emanuel B, Lenoir G, Nowell PC, Croce CM: Translocation of an immunoglobulin kappa locus to a region 3' of an unrearranged c-myc oncogene enhances c-myc transcription. Proc Natl Acad Sci U S A 80(24): 7581-7585, 1983. DOI: 10.1073/pnas.80.24.7581
62 Croce CM, Thierfelder W, Erikson J, Nishikura K, Finan J, Lenoir GM, Nowell PC: Transcriptional activation of an unrearranged and untranslocated c-myc oncogene by translocation of a C lambda locus in Burkitt. Proc Natl Acad Sci U S A 80(22): 6922-6926, 1983. DOI: 10.1073/pnas.80.22.6922
63 Tsujimoto Y, Finger LR, Yunis J, Nowell PC, Croce CM: Cloning of the chromosome breakpoint of neoplastic B cells with the t(14;18) chromosome translocation. Science 226(4678): 1097-1099, 1984. DOI: 10.1126/science.6093263
64 Tsujimoto Y, Yunis J, Onorato-Showe L, Erikson J, Nowell PC, Croce CM: Molecular cloning of the chromosomal breakpoint of B-cell lymphomas and leukemias with the t(11;14) chromosome translocation. Science 224(4656): 1403-1406, 1984. DOI: 10.1126/science.6610211
65 Heisterkamp N, Stam K, Groffen J, de Klein A, Grosveld G: Structural organization of the bcr gene and its role in the Ph' translocation. Nature 315(6022): 758-761, 1985. DOI: 10.1038/315758a0
66 Shtivelman E, Lifshitz B, Gale RP, Canaani E: Fused transcript of abl and bcr genes in chronic myelogenous leukaemia. Nature 315(6020): 550-554, 1985. DOI: 10.1038/315550a0
67 Erikson J, Finger L, Sun L, ar-Rushdi A, Nishikura K, Minowada J, Finan J, Emanuel BS, Nowell PC, Croce CM: Deregulation of c- myc by translocation of the α-Locus of the T-cell receptor in T-cell leukemias. Science 232(4752): 884-886, 1986. DOI: 10.1126/science.3486470
68 Hayashi Y, Yamamoto K, Kojima S: T-cell acute lymphoblastic leukemias with a t(8;14) possibly involving a c-myc locus and T-cell–receptor α-chain genes. N Engl J Med 314(10): 650-651, 1986. DOI: 10.1056/NEJM198603063141018
69 Mathieu-Mahul D, Sigaux F, Zhu C, Bernheim A, Mauchauffe M, Daniel MT, Berger R, Larsen CJ: A t(8;14)(q24;q11) translocation in a T-cell leukemia (L1-all) with c-myc and TcR-alpha chain locus rearrangements. Int J Cancer 38(6): 835-840, 1986. DOI: 10.1002/ijc.2910380609
70 Denny CT, Yoshikai Y, Mak TW, Smith SD, Hollis GF, Kirsch IR: A chromosome 14 inversion in a T-cell lymphoma is caused by site-specific recombination between immunoglobulin and T-cell receptor loci. Nature 320(6062): 549-551, 1986. DOI: 10.1038/320549a0
71 Langer-Safer PR, Levine M, Ward DC: Immunological method for mapping genes on Drosophila polytene chromosomes. Proc Natl Acad Sci U S A 79(14): 4381-4385, 1982. DOI: 10.1073/pnas.79.14.4381
72 Pinkel D, Straume T, Gray JW: Cytogenetic analysis using quantitative, high-sensitivity, fluorescence hybridization. Proc Natl Acad Sci U S A 83(9): 2934-2938, 1986. DOI: 10.1073/pnas.83.9.2934
73 Shizuya H, Birren B, Kim UJ, Mancino V, Slepak T, Tachiiri Y, Simon M: Cloning and stable maintenance of 300-kilobase-pair fragments of human DNA in Escherichia coli using an F-factor-based vector. Proc Natl Acad Sci U S A 89(18): 8794-8797, 1992. DOI: 10.1073/pnas.89.18.8794
74 Schröck E, du Manoir S, Veldman T, Schoell B, Wienberg J, Ferguson-Smith MA, Ning Y, Ledbetter DH, Bar-Am I,

Soenksen D, Garini Y, Ried T: Multicolor spectral karyotyping of human chromosomes. Science 273(5274): 494-497, 1996. DOI: 10.1126/science.273.5274.494

75 Speicher MR, Ballard SG, Ward DC: Karyotyping human chromosomes by combinatorial multi-fluor FISH. Nat Genet 12(4): 368-375, 1996. DOI: 10.1038/ng0496-368

76 Veldman T, Vignon C, Schröck E, Rowley JD, Ried T: Hidden chromosome abnormalities in haematological malignancies detected by multicolour spectral karyotyping. Nat Genet 15(4): 406-410, 1997. DOI: 10.1038/ng0497-406

77 Bayani JM, Squire JA: Applications of SKY in cancer cytogenetics. Cancer Invest 20(3): 373-386, 2002. DOI: 10.1081/cnv-120001183

78 Nordgren A: Hidden aberrations diagnosed by interphase fluorescence *in situ* hybridisation and spectral karyotyping in childhood acute lymphoblastic leukaemia. Leuk Lymphoma 44(12): 2039-2053, 2003. DOI: 10.1080/1042819031000083361

79 Kallioniemi A, Kallioniemi OP, Sudar D, Rutovitz D, Gray JW, Waldman F, Pinkel D: Comparative genomic hybridization for molecular cytogenetic analysis of solid tumors. Science 258(5083): 818-821, 1992. DOI: 10.1126/science.1359641

80 Hermsen MA, Meijer GA, Baak JP, Joenje H, Walboomers JJ: Comparative genomic hybridization: A new tool in cancer pathology. Hum Pathol 27(4): 342-349, 1996. DOI: 10.1016/s0046-8177(96)90106-9

81 Paszek-Vigier M, Talmant P, Méchinaud F, Garand R, Harousseau JL, Bataille R, Avet-Loiseau H: Comparative genomic hybridization is a powerful tool, complementary to cytogenetics, to identify chromosomal abnormalities in childhood acute lymphoblastic leukaemia. Br J Haematol 99(3): 589-596, 1997. DOI: 10.1046/j.1365-2141.1997.4243233.x

82 James LA: Comparative genomic hybridization as a tool in tumour cytogenetics. J Pathol 187(4): 385-395, 1999. DOI: 10.1002/(SICI)1096-9896(199903)187:4<385::AID-PATH290>3.0.CO;2-5

83 Innis MA, Gelfand DH, Sninsky JJ, White TJ: PCR Protocols: A guide to methods and applications. San Diego, CA, USA, Academic Press, 1990.

84 Saiki RK, Scharf S, Faloona F, Mullis KB, Horn GT, Erlich HA, Arnheim N: Enzymatic amplification of β-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia. Science 230(4732): 1350-1354, 1985. DOI: 10.1126/science.2999980

85 Saiki RK, Gelfand DH, Stoffel S, Scharf SJ, Higuchi R, Horn GT, Mullis KB, Erlich HA: Primer-directed enzymatic amplification of DNA with a thermostable DNA polymerase. Science 239(4839): 487-491, 1988. DOI: 10.1126/science.2448875

86 Frohman MA, Dush MK, Martin GR: Rapid production of full-length cDNAs from rare transcripts: amplification using a single gene-specific oligonucleotide primer. Proc Natl Acad Sci U S A 85(23): 8998-9002, 1988. DOI: 10.1073/pnas.85.23.8998

87 Kawasaki ES, Clark SS, Coyne MY, Smith SD, Champlin R, Witte ON, McCormick FP: Diagnosis of chronic myeloid and acute lymphocytic leukemias by detection of leukemia-specific mRNA sequences amplified *in vitro*. Proc Natl Acad Sci U S A 85(15): 5698-5702, 1988. DOI: 10.1073/pnas.85.15.5698

88 Gyllensten UB: PCR and DNA sequencing. Biotechniques 7(7): 700-708, 1989.

89 Erickson P, Gao J, Chang KS, Look T, Whisenant E, Raimondi S, Lasher R, Trujillo J, Rowley J, Drabkin H: Identification of breakpoints in t(8;21) acute myelogenous leukemia and isolation of a fusion transcript, AML1/ETO, with similarity to Drosophila segmentation gene, runt. Blood 80(7): 1825-1831, 1992. DOI: 10.1182/blood.V80.7.1825.1825

90 Miyoshi H, Kozu T, Shimizu K, Enomoto K, Maseki N, Kaneko Y, Kamada N, Ohki M: The t(8;21) translocation in acute myeloid leukemia results in production of an AML1-MTG8 fusion transcript. EMBO J 12(7): 2715-2721, 1993. DOI: 10.1002/j.1460-2075.1993.tb05933.x

91 Liu P, Tarlé SA, Hajra A, Claxton DF, Marlton P, Freedman M, Siciliano MJ, Collins FS: Fusion between transcription factor CBFβ/PEBP2β and a myosin heavy chain in acute myeloid leukemia. Science 261(5124): 1041-1044, 1993. DOI: 10.1126/science.8351518

92 de Thé H, Chomienne C, Lanotte M, Degos L, Dejean A: The t(15;17) translocation of acute promyelocytic leukaemia fuses the retinoic acid receptor α gene to a novel transcribed locus. Nature 347(6293): 558-561, 1990. DOI: 10.1038/347558a0

93 Sanz MA, Fenaux P, Tallman MS, Estey EH, Löwenberg B, Naoe T, Lengfelder E, Döhner H, Burnett AK, Chen SJ, Mathews V, Iland H, Rego E, Kantarjian H, Adès L, Avvisati G, Montesinos P, Platzbecker U, Ravandi F, Russell NH, Lo-Coco F: Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet. Blood 133(15): 1630-1643, 2019. DOI: 10.1182/blood-2019-01-894980

94 Romana SP, Le Coniat M, Berger R: t(12;21): A new recurrent translocation in acute lymphoblastic leukemia. Genes Chromosomes Cancer 9(3): 186-191, 1994. DOI: 10.1002/gcc.2870090307

95 Golub TR, Barker GF, Bohlander SK, Hiebert SW, Ward DC, Bray-Ward P, Morgan E, Raimondi SC, Rowley JD, Gilliland DG: Fusion of the TEL gene on 12p13 to the AML1 gene on 21q22 in acute lymphoblastic leukemia. Proc Natl Acad Sci U S A 92(11): 4917-4921, 1995. DOI: 10.1073/pnas.92.11.4917

96 Romana SP, Mauchauffe M, Le Coniat M, Chumakov I, Le Paslier D, Berger R, Bernard OA: The t(12;21) of acute lymphoblastic leukemia results in a tel-AML1 gene fusion. Blood 85(12): 3662-3670, 1995. DOI: 10.1182/blood.V85.12.3662.bloodjournal85123662

97 Shurtleff SA, Buijs A, Behm FG, Rubnitz JE, Raimondi SC, Hancock ML, Chan GC, Pui CH, Grosveld G, Downing JR: TEL/AML1 fusion resulting from a cryptic t(12;21) is the most

common genetic lesion in pediatric ALL and defines a subgroup of patients with an excellent prognosis. Leukemia 9(12): 1985-1989, 1995.

98 Rowley JD, Diaz MO, Espinosa R 3rd, Patel YD, van Melle E, Ziemin S, Taillon-Miller P, Lichter P, Evans GA, Kersey JH: Mapping chromosome band 11q23 in human acute leukemia with biotinylated probes: identification of 11q23 translocation breakpoints with a yeast artificial chromosome. Proc Natl Acad Sci U S A 87(23): 9358-9362, 1990. DOI: 10.1073/pnas.87.23.9358

99 Ziemin-van der Poel S, McCabe NR, Gill HJ, Espinosa R 3rd, Patel Y, Harden A, Rubinelli P, Smith SD, LeBeau MM, Rowley JD: Identification of a gene, MLL, that spans the breakpoint in 11q23 translocations associated with human leukemias. Proc Natl Acad Sci U S A 88(23): 10735-10739, 1991. DOI: 10.1073/pnas.88.23.10735

100 Rowley JD: The critical role of chromosome translocations in human leukemias. Annu Rev Genet 32(1): 495-519, 1998. DOI: 10.1146/annurev.genet.32.1.495

101 De Braekeleer M, Morel F, Le Bris MJ, Herry A, Douet-Guilbert N: The MLL gene and translocations involving chromosomal band 11q23 in acute leukemia. Anticancer Res 25(3B): 1931-1944, 2005.

102 Meyer C, Larghero P, Almeida Lopes B, Burmeister T, Gröger D, Sutton R, Venn NC, Cazzaniga G, Corral Abascal L, Tsaur G, Fechina L, Emerenciano M, Pombo-de-Oliveira MS, Lund-Aho T, Lundán T, Montonen M, Juvonen V, Zuna J, Trka J, Ballerini P, Lapillonne H, Van der Velden VHJ, Sonneveld E, Delabesse E, de Matos RRC, Silva MLM, Bomken S, Katsibardi K, Keernik M, Grardel N, Mason J, Price R, Kim J, Eckert C, Lo Nigro L, Bueno C, Menendez P, Zur Stadt U, Gameiro P, Sedék L, Szczepański T, Bidet A, Marcu V, Shichrur K, Izraeli S, Madsen HO, Schäfer BW, Kubetzko S, Kim R, Clappier E, Trautmann H, Brüggemann M, Archer P, Hancock J, Alten J, Möricke A, Stanulla M, Lentes J, Bergmann AK, Strehl S, Köhrer S, Nebral K, Dworzak MN, Haas OA, Arfeuille C, Caye-Eude A, Cavé H, Marschalek R: The KMT2A recombinome of acute leukemias in 2023. Leukemia 37(5): 988-1005, 2023. DOI: 10.1038/s41375-023-01877-1

103 Delattre O, Zucman J, Plougastel B, Desmaze C, Melot T, Peter M, Kovar H, Joubert I, de Jong P, Rouleau G, Aurias A, Thomas G: Gene fusion with an ETS DNA-binding domain caused by chromosome translocation in human tumours. Nature 359(6391): 162-165, 1992. DOI: 10.1038/359162a0

104 Crozat A, Åman P, Mandahl N, Ron D: Fusion of CHOP to a novel RNA-binding protein in human myxoid liposarcoma. Nature 363(6430): 640-644, 1993. DOI: 10.1038/363640a0

105 Galili N, Davis RJ, Fredericks WJ, Mukhopadhyay S, Rauscher FJ 3rd, Emanuel BS, Rovera G, Barr FG: Fusion of a fork head domain gene to PAX3 in the solid tumour alveolar rhabdomyosarcoma. Nat Genet 5(3): 230-235, 1993. DOI: 10.1038/ng1193-230

106 Davis RJ, D'Cruz CM, Lovell MA, Biegel JA, Barr FG: Fusion of PAX7 to FKHR by the variant t(1;13)(p36;q14) translocation in alveolar rhabdomyosarcoma. Cancer Res 54(11): 2869–2872, 1994.

107 Clark J, Rocques PJ, Crew AJ, Gill S, Shipley J, Chan AM, Gusterson BA, Cooper CS: Identification of novel genes, SYT and SSX, involved in the t(X;18)(p11.2;q11.2) translocation found in human synovial sarcoma. Nat Genet 7(4): 502-508, 1994. DOI: 10.1038/ng0894-502

108 Crew AJ, Clark J, Fisher C, Gill S, Grimer R, Chand A, Shipley J, Gusterson BA, Cooper CS: Fusion of SYT to two genes, SSX1 and SSX2, encoding proteins with homology to the Kruppel-associated box in human synovial sarcoma. EMBO J 14(10): 2333-2340, 1995. DOI: 10.1002/j.1460-2075.1995.tb07228.x

109 de Leeuw B, Balemans M, Olde Weghuis D, Geurts van Kessel A: Identification of two alternative fusion genes, SYT-SSX1 and SYT-SSX2, in t(X; 18)(p11.2;q11.2)-positive synoviaol sarcomas. Hum Mol Genet 4(6): 1097-1099, 1995. DOI: 10.1093/hmg/4.6.1097

110 Knezevich SR, McFadden DE, Tao W, Lim JF, Sorensen PH: A novel ETV6-NTRK3 gene fusion in congenital fibrosarcoma. Nat Genet 18(2): 184-187, 1998. DOI: 10.1038/ng0298-184

111 Knezevich SR, Garnett MJ, Pysher TJ, Beckwith JB, Grundy PE, Sorensen PH: ETV6-NTRK3 gene fusions and trisomy 11 establish a histogenetic link between mesoblastic nephroma and congenital fibrosarcoma. Cancer Res 58(22): 5046-5048, 1998.

112 Rubin BP, Chen CJ, Morgan TW, Xiao S, Grier HE, Kozakewich HP, Perez-Atayde AR, Fletcher JA: Congenital mesoblastic nephroma t(12;15) is associated with ETV6-NTRK3 gene fusion: cytogenetic and molecular relationship to congenital (infantile) fibrosarcoma. Am J Pathol 153(5): 1451-1458, 1998. DOI: 10.1016/S0002-9440(10)65732-X

113 Eguchi M, Eguchi-Ishimae M, Tojo A, Morishita K, Suzuki K, Sato Y, Kudoh S, Tanaka K, Setoyama M, Nagamura F, Asano S, Kamada N: Fusion of ETV6 to neurotrophin-3 receptor TRKC in acute myeloid leukemia with t(12;15)(p13;q25). Blood 93(4): 1355-1363, 1999. DOI: 10.1182/blood.V93.4.1355

114 Marcelis L, Folpe AL: "Putting the cart before the horse": an update on promiscuous gene fusions in soft tissue tumors. Virchows Arch 486(5): 905-921, 2025. DOI: 10.1007/s00428-025-04099-1

115 Ichikawa H, Shimizu K, Hayashi Y, Ohki M: An RNA-binding protein gene, TLS/FUS, is fused to ERG in human myeloid leukemia with t(16;21) chromosomal translocation. Cancer Res 54(11): 2865-2868, 1994.

116 Panagopoulos I, Åman P, Fioretos T, Höglund M, Johansson B, Mandahl N, Heim S, Behrendtz M, Mitelman F: Fusion of the FUS gene with ERG in acute myeloid leukemia with t(16;21)(p11;q22). Genes Chromosomes Cancer 11(4): 256-262, 1994. DOI: 10.1002/gcc.2870110408

117 Shing DC, McMullan DJ, Roberts P, Smith K, Chin SF, Nicholson J, Tillman RM, Ramani P, Cullinane C, Coleman N: FUS/ERG

gene fusions in Ewing's tumors. Cancer Res 63(15): 4568-4576, 2003.
118 Deininger MW, Goldman JM, Lydon N, Melo JV: The tyrosine kinase inhibitor CGP57148B selectively inhibits the growth of BCR-ABL–positive cells. Blood 90(9): 3691-3698, 1997. DOI: 10.1182/blood.V90.9.3691
119 Druker BJ, Tamura S, Buchdunger E, Ohno S, Segal GM, Fanning S, Zimmermann J, Lydon NB: Effects of a selective inhibitor of the Abl tyrosine kinase on the growth of Bcr–Abl positive cells. Nat Med 2(5): 561-566, 1996. DOI: 10.1038/nm0596-561
120 Goldman JM, Melo JV: Targeting the BCR-ABL tyrosine kinase in chronic myeloid leukemia. N Engl J Med 344(14): 1084-1086, 2001. DOI: 10.1056/NEJM200104053441409
121 Barnes DJ, Melo JV: Management of chronic myeloid leukemia: Targets for molecular therapy. Semin Hematol 40(1): 34-49, 2003. DOI: 10.1053/shem.2003.50002
122 Longo DL: Imatinib changed everything. N Engl J Med 376(10): 982-983, 2017. DOI: 10.1056/NEJMe1700833
123 Bernheim A: [Exploration of the genome and malignant proliferations: Cytogenetics and cytogenomics]. Ann Pathol 19(5 Suppl): S1-3, 1999.
124 Dobigny G, Yang F: Foreword. Comparative cytogenetics in the genomics era: cytogenomics comes of age. Chromosome Res 16(1): 1-4, 2008. DOI: 10.1007/s10577-008-1213-y
125 Iourov IY, Vorsanova SG, Yurov YB: Molecular cytogenetics and cytogenomics of brain diseases. Curr Genomics 9(7): 452-465, 2008. DOI: 10.2174/138920208786241216
126 Speicher MR, Carter NP: The new cytogenetics: blurring the boundaries with molecular biology. Nat Rev Genet 6(10): 782-792, 2005. DOI: 10.1038/nrg1692
127 Deakin JE, Potter S, O'Neill R, Ruiz-Herrera A, Cioffi MB, Eldridge MDB, Fukui K, Marshall Graves JA, Griffin D, Grutzner F, Kratochvíl L, Miura I, Rovatsos M, Srikulnath K, Wapstra E, Ezaz T: Chromosomics: bridging the gap between genomes and chromosomes. Genes (Basel) 10(8): 627, 2019. DOI: 10.3390/genes10080627
128 International Human Genome Sequencing Consortium: Initial sequencing and analysis of the human genome. Nature 409(6822): 860-921, 2001. DOI: 10.1038/35057062
129 International Human Genome Mapping Consortium: A physical map of the human genome. Nature 409(6822): 934-941, 2001. DOI: 10.1038/35057157
130 Jang W, Yonescu R, Knutsen T, Brown T, Reppert T, Sirotkin K, Schuler GD, Ried T, Kirsch IR: Linking the human cytogenetic map with nucleotide sequence: the CCAP clone set. Cancer Genet Cytogenet 168(2): 89-97, 2006. DOI: 10.1016/j.cancergencyto.2006.01.001
131 Kent WJ, Sugnet CW, Furey TS, Roskin KM, Pringle TH, Zahler AM, Haussler D: The human genome browser at UCSC. Genome Res 12(6): 996-1006, 2002. DOI: 10.1101/gr.229102
132 Hubbard T, Barker D, Birney E, Cameron G, Chen Y, Clark L, Cox T, Cuff J, Curwen V, Down T, Durbin R, Eyras E, Gilbert J, Hammond M, Huminiecki L, Kasprzyk A, Lehvaslaiho H, Lijnzaad P, Melsopp C, Mongin E, Pettett R, Pocock M, Potter S, Rust A, Schmidt E, Searle S, Slater G, Smith J, Spooner W, Stabenau A, Stalker J, Stupka E, Ureta-Vidal A, Vastrik I, Clamp M: The Ensembl genome database project. Nucleic Acids Res 30(1): 38-41, 2002. DOI: 10.1093/nar/30.1.38
133 Sayers EW, Beck J, Bolton EE, Brister JR, Chan J, Connor R, Feldgarden M, Fine AM, Funk K, Hoffman J, Kannan S, Kelly C, Klimke W, Kim S, Lathrop S, Marchler-Bauer A, Murphy TD, O'Sullivan C, Schmieder E, Skripchenko Y, Stine A, Thibaud-Nissen F, Wang J, Ye J, Zellers E, Schneider VA, Pruitt KD: Database resources of the National Center for Biotechnology Information in 2025. Nucleic Acids Res 53(D1): D20-D29, 2025. DOI: 10.1093/nar/gkae979
134 Zhao S: Human BAC ends. Nucleic Acids Res 28(1): 129-132, 2000. DOI: 10.1093/nar/28.1.129
135 Zhao S, Malek J, Mahairas G, Fu L, Nierman W, Venter JC, Adams MD: Human BAC ends quality assessment and sequence analyses. Genomics 63(3): 321-332, 2000. DOI: 10.1006/geno.1999.6082
136 Cheung VG, Nowak N, Jang W, Kirsch IR, Zhao S, Chen XN, Furey TS, Kim UJ, Kuo WL, Olivier M, Conroy J, Kasprzyk A, Massa H, Yonescu R, Sait S, Thoreen C, Snijders A, Lemyre E, Bailey JA, Bruzel A, Burrill WD, Clegg SM, Collins S, Dhami P, Friedman C, Han CS, Herrick S, Lee J, Ligon AH, Lowry S, Morley M, Narasimhan S, Osoegawa K, Peng Z, Plajzer-Frick I, Quade BJ, Scott D, Sirotkin K, Thorpe AA, Gray JW, Hudson J, Pinkel D, Ried T, Rowen L, Shen-Ong GL, Strausberg RL, Birney E, Callen DF, Cheng JF, Cox DR, Doggett NA, Carter NP, Eichler EE, Haussler D, Korenberg JR, Morton CC, Albertson D, Schuler G, de Jong PJ, Trask BJ, BAC Resource Consortium: Integration of cytogenetic landmarks into the draft sequence of the human genome. Nature 409(6822): 953-958, 2001. DOI: 10.1038/35057192
137 Osoegawa K, Mammoser AG, Wu C, Frengen E, Zeng C, Catanese JJ, de Jong PJ: A bacterial artificial chromosome library for sequencing the complete human genome. Genome Res 11(3): 483-496, 2001. DOI: 10.1101/gr.169601
138 Zhao S: A comprehensive BAC resource. Nucleic Acids Res 29(1): 141-143, 2001. DOI: 10.1093/nar/29.1.141
139 Roohi J, Cammer M, Montagna C, Hatchwell E: An improved method for generating BAC DNA suitable for FISH. Cytogenet Genome Res 121(1): 7-9, 2008. DOI: 10.1159/000124374
140 Snijders AM, Nowak N, Segraves R, Blackwood S, Brown N, Conroy J, Hamilton G, Hindle AK, Huey B, Kimura K, Law S, Myambo K, Palmer J, Ylstra B, Yue JP, Gray JW, Jain AN, Pinkel D, Albertson DG: Assembly of microarrays for genome-wide measurement of DNA copy number. Nat Genet 29(3): 263-264, 2001. DOI: 10.1038/ng754
141 Fiegler H, Carr P, Douglas EJ, Burford DC, Hunt S, Scott CE, Smith J, Vetrie D, Gorman P, Tomlinson IP, Carter NP: DNA microarrays for comparative genomic hybridization based on DOP-PCR amplification of BAC and PAC clones. Genes

Chromosomes Cancer 36(4): 361-374, 2003. DOI: 10.1002/gcc.10155

142 Hoebeeck J, Michels E, Menten B, Van Roy N, Eggert A, Schramm A, De Preter K, Yigit N, De Smet E, De Paepe A, Laureys G, Vandesompele J, Speleman F: High resolution tiling-path BAC array deletion mapping suggests commonly involved 3p21-p22 tumor suppressor genes in neuroblastoma and more frequent tumors. Int J Cancer 120(3): 533-538, 2007. DOI: 10.1002/ijc.22326

143 Nord H, Hartmann C, Andersson R, Menzel U, Pfeifer S, Piotrowski A, Bogdan A, Kloc W, Sandgren J, Olofsson T, Hesselager G, Blomquist E, Komorowski J, von Deimling A, Bruder CE, Dumanski JP, Díaz de Ståhl T: Characterization of novel and complex genomic aberrations in glioblastoma using a 32K BAC array. Neuro Oncol 11(6): 803-818, 2009. DOI: 10.1215/15228517-2009-013

144 Saito S, Morita K, Hirano T: High frequency of common DNA copy number abnormalities detected by bacterial artificial chromosome array comparative genomic hybridization in 24 breast cancer cell lines. Hum Cell 22(1): 1-10, 2009. DOI: 10.1111/j.1749-0774.2008.00061.x

145 Saito S, Morita K, Kohara A, Masui T, Sasao M, Ohgushi H, Hirano T: Use of BAC array CGH for evaluation of chromosomal stability of clinically used human mesenchymal stem cells and of cancer cell lines. Hum Cell 24(1): 2-8, 2011. DOI: 10.1007/s13577-010-0006-8

146 Robledo C, García JL, Hernández JM: Clinical applications of BAC array-CGH to the study of diffuse large B-cell lymphomas. Methods Mol Biol 973: 121-145, 2013. DOI: 10.1007/978-1-62703-281-0_8

147 Cowell JK, Barnett GH, Nowak NJ: Characterization of the 1p/19q chromosomal loss in oligodendrogliomas using comparative genomic hybridization arrays (CGHa). J Neuropathol Exp Neurol 63(2): 151-158, 2004. DOI: 10.1093/jnen/63.2.151

148 Natrajan R, Williams RD, Hing SN, Mackay A, Reis-Filho JS, Fenwick K, Iravani M, Valgeirsson H, Grigoriadis A, Langford CF, Dovey O, Gregory SG, Weber BL, Ashworth A, Grundy PE, Pritchard-Jones K, Jones C: Array CGH profiling of favourable histology Wilms tumours reveals novel gains and losses associated with relapse. J Pathol 210(1): 49-58, 2006. DOI: 10.1002/path.2021

149 Mosse YP, Diskin SJ, Wasserman N, Rinaldi K, Attiyeh EF, Cole K, Jagannathan J, Bhambhani K, Winter C, Maris JM: Neuroblastomas have distinct genomic DNA profiles that predict clinical phenotype and regional gene expression. Genes Chromosomes Cancer 46(10): 936-949, 2007. DOI: 10.1002/gcc.20477

150 Ylstra B, van den Ijssel P, Carvalho B, Brakenhoff RH, Meijer GA: BAC to the future! or oligonucleotides: a perspective for micro array comparative genomic hybridization (array CGH). Nucleic Acids Res 34(2): 445-450, 2006. DOI: 10.1093/nar/gkj456

151 Nowak NJ, Miecznikowski J, Moore SR, Gaile D, Bobadilla D, Smith DD, Kernstine K, Forman SJ, Mhawech-Fauceglia P, Reid M, Stoler D, Loree T, Rigual N, Sullivan M, Weiss LM, Hicks D, Slovak ML: Challenges in array comparative genomic hybridization for the analysis of cancer samples. Genet Med 9(9): 585-595, 2007. DOI: 10.1097/gim.0b013e3181461c4a

152 Wicker N, Carles A, Mills IG, Wolf M, Veerakumarasivam A, Edgren H, Boileau F, Wasylyk B, Schalken JA, Neal DE, Kallioniemi O, Poch O: A new look towards BAC-based array CGH through a comprehensive comparison with oligo-based array CGH. BMC Genomics 8: 84, 2007. DOI: 10.1186/1471-2164-8-84

153 Tyybäkinoja A, Elonen E, Vauhkonen H, Saarela J, Knuutila S: Single nucleotide polymorphism microarray analysis of karyotypically normal acute myeloid leukemia reveals frequent copy number neutral loss of heterozygosity. Haematologica 93(4): 631-632, 2008. DOI: 10.3324/haematol.12232

154 Heinrichs S, Look AT: Identification of structural aberrations in cancer by SNP array analysis. Genome Biol 8(7): 219, 2007. DOI: 10.1186/gb-2007-8-7-219

155 Nowak D, Hofmann WK, Koeffler HP: Genome-wide mapping of copy number variations using SNP arrays. Transfus Med Hemother 36(4): 246-251, 2009. DOI: 10.1159/000225372

156 Loo PV, Nilsen G, Nordgard SH, Vollan HKM, Børresen-Dale A, Kristensen VN, Lingjærde OC: Analyzing cancer samples with SNP arrays. Methods Mol Biol 802: 57-72, 2012. DOI: 10.1007/978-1-61779-400-1_4

157 Gondek LP, Tiu R, O'Keefe CL, Sekeres MA, Theil KS, Maciejewski JP: Chromosomal lesions and uniparental disomy detected by SNP arrays in MDS, MDS/MPD, and MDS-derived AML. Blood 111(3): 1534-1542, 2008. DOI: 10.1182/blood-2007-05-092304

158 Paulsson K, Cazier JB, Macdougall F, Stevens J, Stasevich I, Vrcelj N, Chaplin T, Lillington DM, Lister TA, Young BD: Microdeletions are a general feature of adult and adolescent acute lymphoblastic leukemia: Unexpected similarities with pediatric disease. Proc Natl Acad Sci U S A 105(18): 6708-6713, 2008. DOI: 10.1073/pnas.0800408105

159 Scionti F, Di Martino MT, Pensabene L, Bruni V, Concolino D: The cytoscan HD array in the diagnosis of neurodevelopmental disorders. High Throughput 7(3): 28, 2018. DOI: 10.3390/ht7030028

160 Cristescu R, Liu XQ, Arreaza G, Chen C, Albright A, Qiu P, Marton MJ: Concordance between single-nucleotide polymorphism-based genomic instability assays and a next-generation sequencing-based homologous recombination deficiency test. BMC Cancer 22(1): 1310, 2022. DOI: 10.1186/s12885-022-10197-z

161 Wiszniewska J, Bi W, Shaw C, Stankiewicz P, Kang SH, Pursley AN, Lalani S, Hixson P, Gambin T, Tsai CH, Bock HG, Descartes M, Probst FJ, Scaglia F, Beaudet AL, Lupski JR, Eng C, Cheung SW, Bacino C, Patel A: Combined array CGH plus SNP genome

analyses in a single assay for optimized clinical testing. Eur J Hum Genet 22(1): 79-87, 2014. DOI: 10.1038/ejhg.2013.77

162 Campbell PJ, Stephens PJ, Pleasance ED, O'Meara S, Li H, Santarius T, Stebbings LA, Leroy C, Edkins S, Hardy C, Teague JW, Menzies A, Goodhead I, Turner DJ, Clee CM, Quail MA, Cox A, Brown C, Durbin R, Hurles ME, Edwards PA, Bignell GR, Stratton MR, Futreal PA: Identification of somatically acquired rearrangements in cancer using genome-wide massively parallel paired-end sequencing. Nat Genet 40(6): 722-729, 2008. DOI: 10.1038/ng.128

163 Chen W, Kalscheuer V, Tzschach A, Menzel C, Ullmann R, Schulz MH, Erdogan F, Li N, Kijas Z, Arkesteijn G, Pajares IL, Goetz-Sothmann M, Heinrich U, Rost I, Dufke A, Grasshoff U, Glaeser B, Vingron M, Ropers HH: Mapping translocation breakpoints by next-generation sequencing. Genome Res 18(7): 1143-1149, 2008. DOI: 10.1101/gr.076166.108

164 Ley TJ, Mardis ER, Ding L, Fulton B, McLellan MD, Chen K, Dooling D, Dunford-Shore BH, McGrath S, Hickenbotham M, Cook L, Abbott R, Larson DE, Koboldt DC, Pohl C, Smith S, Hawkins A, Abbott S, Locke D, Hillier LW, Miner T, Fulton L, Magrini V, Wylie T, Glasscock J, Conyers J, Sander N, Shi X, Osborne JR, Minx P, Gordon D, Chinwalla A, Zhao Y, Ries RE, Payton JE, Westervelt P, Tomasson MH, Watson M, Baty J, Ivanovich J, Heath S, Shannon WD, Nagarajan R, Walter MJ, Link DC, Graubert TA, DiPersio JF, Wilson RK: DNA sequencing of a cytogenetically normal acute myeloid leukaemia genome. Nature 456(7218): 66-72, 2008. DOI: 10.1038/nature07485

165 Maher B: Exome sequencing takes centre stage in cancer profiling. Nature 459(7244): 146-147, 2009. DOI: 10.1038/459146b

166 Maher CA, Kumar-Sinha C, Cao X, Kalyana-Sundaram S, Han B, Jing X, Sam L, Barrette T, Palanisamy N, Chinnaiyan AM: Transcriptome sequencing to detect gene fusions in cancer. Nature 458(7234): 97-101, 2009. DOI: 10.1038/nature07638

167 Maher CA, Palanisamy N, Brenner JC, Cao X, Kalyana-Sundaram S, Luo S, Khrebtukova I, Barrette TR, Grasso C, Yu J, Lonigro RJ, Schroth G, Kumar-Sinha C, Chinnaiyan AM: Chimeric transcript discovery by paired-end transcriptome sequencing. Proc Natl Acad Sci U S A 106(30): 12353-12358, 2009. DOI: 10.1073/pnas.0904720106

168 Teer JK, Mullikin JC: Exome sequencing: the sweet spot before whole genomes. Hum Mol Genet 19(R2): R145-R151, 2010. DOI: 10.1093/hmg/ddq333

169 Panagopoulos I, Thorsen J, Gorunova L, Micci F, Heim S: Sequential combination of karyotyping and RNA-sequencing in the search for cancer-specific fusion genes. Int J Biochem Cell Biol 53: 462-465, 2014. DOI: 10.1016/j.biocel.2014.05.018

170 Tanas MR, Sboner A, Oliveira AM, Erickson-Johnson MR, Hespelt J, Hanwright PJ, Flanagan J, Luo Y, Fenwick K, Natrajan R, Mitsopoulos C, Zvelebil M, Hoch BL, Weiss SW, Debiec-Rychter M, Sciot R, West RB, Lazar AJ, Ashworth A, Reis-Filho JS, Lord CJ, Gerstein MB, Rubin MA, Rubin BP: Identification of a disease-defining gene fusion in epithelioid hemangioendothelioma. Sci Transl Med 3(98): 98ra82, 2011. DOI: 10.1126/scitranslmed.3002409

171 Nyquist KB, Panagopoulos I, Thorsen J, Haugom L, Gorunova L, Bjerkehagen B, Fosså A, Guriby M, Nome T, Lothe RA, Skotheim RI, Heim S, Micci F: Whole-transcriptome sequencing identifies novel IRF2BP2-CDX1 fusion gene brought about by translocation t(1;5)(q42;q32) in mesenchymal chondrosarcoma. PLoS One 7(11): e49705, 2012. DOI: 10.1371/journal.pone.0049705

172 Panagopoulos I, Thorsen J, Gorunova L, Haugom L, Bjerkehagen B, Davidson B, Heim S, Micci F: Fusion of the ZC3H7B and BCOR genes in endometrial stromal sarcomas carrying an X;22-translocation. Genes Chromosomes Cancer 52(7): 610-618, 2013. DOI: 10.1002/gcc.22057

173 Walther C, Tayebwa J, Lilljebjörn H, Magnusson L, Nilsson J, von Steyern FV, Øra I, Domanski HA, Fioretos T, Nord KH, Fletcher CD, Mertens F: A novel SERPINE1–FOSB fusion gene results in transcriptional up-regulation of FOSB in pseudomyogenic haemangioendothelioma. J Pathol 232(5): 534-540, 2014. DOI: 10.1002/path.4322

174 Micci F, Thorsen J, Panagopoulos I, Nyquist KB, Zeller B, Tierens A, Heim S: High-throughput sequencing identifies an NFIA/CBFA2T3 fusion gene in acute erythroid leukemia with t(1;16)(p31;q24). Leukemia 27(4): 980-982, 2013. DOI: 10.1038/leu.2012.266

175 Panagopoulos I, Micci F, Thorsen J, Haugom L, Buechner J, Kerndrup G, Tierens A, Zeller B, Heim S: Fusion of ZMYND8 and RELA genes in acute erythroid leukemia. PLoS One 8(5): e63663, 2013. DOI: 10.1371/journal.pone.0063663

176 Gruber TA, Larson Gedman A, Zhang J, Koss CS, Marada S, Ta HQ, Chen SC, Su X, Ogden SK, Dang J, Wu G, Gupta V, Andersson AK, Pounds S, Shi L, Easton J, Barbato MI, Mulder HL, Manne J, Wang J, Rusch M, Ranade S, Ganti R, Parker M, Ma J, Radtke I, Ding L, Cazzaniga G, Biondi A, Kornblau SM, Ravandi F, Kantarjian H, Nimer SD, Döhner K, Döhner H, Ley TJ, Ballerini P, Shurtleff S, Tomizawa D, Adachi S, Hayashi Y, Tawa A, Shih LY, Liang DC, Rubnitz JE, Pui CH, Mardis ER, Wilson RK, Downing JR: An Inv(16)(p13.3q24.3)-encoded CBFA2T3-GLIS2 fusion protein defines an aggressive subtype of pediatric acute megakaryoblastic leukemia. Cancer Cell 22(5): 683-697, 2012. DOI: 10.1016/j.ccr.2012.10.007

177 Masetti R, Bertuccio SN, Pession A, Locatelli F: CBFA2T3-GLIS2-positive acute myeloid leukaemia. A peculiar paediatric entity. Br J Haematol 184(3): 337-347, 2019. DOI: 10.1111/bjh.15725

178 Lilljebjörn H, Henningsson R, Hyrenius-Wittsten A, Olsson L, Orsmark-Pietras C, von Palffy S, Askmyr M, Rissler M, Schrappe M, Cario G, Castor A, Pronk CJ, Behrendtz M, Mitelman F, Johansson B, Paulsson K, Andersson AK, Fontes M, Fioretos T: Identification of ETV6-RUNX1-like and DUX4-rearranged subtypes in paediatric B-cell precursor acute

lymphoblastic leukaemia. Nat Commun 7: 11790, 2016. DOI: 10.1038/ncomms11790

179 Liu YF, Wang BY, Zhang WN, Huang JY, Li BS, Zhang M, Jiang L, Li JF, Wang MJ, Dai YJ, Zhang ZG, Wang Q, Kong J, Chen B, Zhu YM, Weng XQ, Shen ZX, Li JM, Wang J, Yan XJ, Li Y, Liang YM, Liu L, Chen XQ, Zhang WG, Yan JS, Hu JD, Shen SH, Chen J, Gu LJ, Pei D, Li Y, Wu G, Zhou X, Ren RB, Cheng C, Yang JJ, Wang KK, Wang SY, Zhang J, Mi JQ, Pui CH, Tang JY, Chen Z, Chen SJ: Genomic profiling of adult and pediatric B-cell acute lymphoblastic leukemia. EBioMedicine 8: 173-183, 2016. DOI: 10.1016/j.ebiom.2016.04.038

180 Yasuda T, Tsuzuki S, Kawazu M, Hayakawa F, Kojima S, Ueno T, Imoto N, Kohsaka S, Kunita A, Doi K, Sakura T, Yujiri T, Kondo E, Fujimaki K, Ueda Y, Aoyama Y, Ohtake S, Takita J, Sai E, Taniwaki M, Kurokawa M, Morishita S, Fukayama M, Kiyoi H, Miyazaki Y, Naoe T, Mano H: Recurrent DUX4 fusions in B cell acute lymphoblastic leukemia of adolescents and young adults. Nat Genet 48(5): 569-574, 2016. DOI: 10.1038/ng.3535

181 Hofvander J, Tayebwa J, Nilsson J, Magnusson L, Brosjö O, Larsson O, Vult von Steyern F, Mandahl N, Fletcher CD, Mertens F: Recurrent PRDM10 gene fusions in undifferentiated pleomorphic sarcoma. Clin Cancer Res 21(4): 864-869, 2015. DOI: 10.1158/1078-0432.CCR-14-2399

182 Hofvander J, Puls F, Pillay N, Steele CD, Flanagan AM, Magnusson L, Nilsson J, Mertens F: Undifferentiated pleomorphic sarcomas with PRDM10 fusions have a distinct gene expression profile. J Pathol 249(4): 425-434, 2019. DOI: 10.1002/path.5326

183 Puls F, Pillay N, Fagman H, Palin-Masreliez A, Amary F, Hansson M, Kindblom LG, McCulloch TA, Meligonis G, Muc R, Rissler P, Sumathi VP, Tirabosco R, Hofvander J, Magnusson L, Nilsson J, Flanagan AM, Mertens F: PRDM10-rearranged soft tissue tumor: a clinicopathologic study of 9 cases. Am J Surg Pathol 43(4): 504-513, 2019. DOI: 10.1097/PAS.0000000000001207

184 Perret R, Michal M, Carr RA, Velasco V, Švajdler M, Karanian M, Meurgey A, Paindavoine S, Soubeyran I, Coindre JM, Boidot R, Charon-Barra C, Geneste D, Weingertner N, Pissaloux D, Tirode F, Baud J, Le Loarer F: Superficial CD34-positive fibroblastic tumor and PRDM10-rearranged soft tissue tumor are overlapping entities: a comprehensive study of 20 cases. Histopathology 79(5): 810-825, 2021. DOI: 10.1111/his.14429

185 Yoshida A, Arai Y, Tanzawa Y, Wakai S, Hama N, Kawai A, Shibata T: KMT2A (MLL) fusions in aggressive sarcomas in young adults. Histopathology 75(4): 508-516, 2019. DOI: 10.1111/his.13926

186 Kao YC, Lee JC, Zhang L, Sung YS, Swanson D, Hsieh TH, Liu YR, Agaram NP, Huang HY, Dickson BC, Antonescu CR: Recurrent YAP1 and KMT2A gene rearrangements in a subset of MUC4-negative sclerosing epithelioid fibrosarcoma. Am J Surg Pathol 44(3): 368-377, 2020. DOI: 10.1097/PAS.0000000000001382

187 Massoth LR, Hung YP, Nardi V, Nielsen GP, Hasserjian RP, Louissaint A Jr, Fisch AS, Deshpande V, Zukerberg LR, Lennerz JK, Selig M, Glomski K, Patel PJ, Williams KJ, Sokol ES, Alexander BM, Vergilio JA, Ross JS, Pavlick DC, Chebib I, Williams EA: Pan-sarcoma genomic analysis of KMT2A rearrangements reveals distinct subtypes defined by YAP1-KMT2A-YAP1 and VIM-KMT2A fusions. Mod Pathol 33(11): 2307-2317, 2020. DOI: 10.1038/s41379-020-0582-4

188 Puls F, Agaimy A, Flucke U, Mentzel T, Sumathi VP, Ploegmakers M, Stoehr R, Kindblom L, Hansson M, Sydow S, Arbajian E, Mertens F: Recurrent fusions between YAP1 and KMT2A in morphologically distinct neoplasms within the spectrum of low-grade fibromyxoid sarcoma and sclerosing epithelioid fibrosarcoma. Am J Surg Pathol 44(5): 594-606, 2020. DOI: 10.1097/PAS.0000000000001423

189 Neveling K, Mantere T, Vermeulen S, Oorsprong M, van Beek R, Kater-Baats E, Pauper M, van der Zande G, Smeets D, Weghuis DO, Stevens-Kroef MJPL, Hoischen A: Next-generation cytogenetics: Comprehensive assessment of 52 hematological malignancy genomes by optical genome mapping. Am J Hum Genet 108(8): 1423-1435, 2021. DOI: 10.1016/j.ajhg.2021.06.001

190 Sahajpal NS, Barseghyan H, Kolhe R, Hastie A, Chaubey A: Optical genome mapping as a next-generation cytogenomic tool for detection of structural and copy number variations for prenatal genomic analyses. Genes (Basel) 12(3): 398, 2021. DOI: 10.3390/genes12030398

191 Lestringant V, Duployez N, Penther D, Luquet I, Derrieux C, Lutun A, Preudhomme C, West M, Ouled-Haddou H, Devoldere C, Marolleau JP, Garçon L, Jedraszak G, Ferret Y: Optical genome mapping, a promising alternative to gold standard cytogenetic approaches in a series of acute lymphoblastic leukemias. Genes Chromosomes Cancer 60(10): 657-667, 2021. DOI: 10.1002/gcc.22971

192 Gerding WM, Tembrink M, Nilius-Eliliwi V, Mika T, Dimopoulos F, Ladigan-Badura S, Eckhardt M, Pohl M, Wünnenberg M, Farshi P, Reimer P, Schroers R, Nguyen HP, Vangala DB: Optical genome mapping reveals additional prognostic information compared to conventional cytogenetics in AML/MDS patients. Int J Cancer 150(12): 1998-2011, 2022. DOI: 10.1002/ijc.33942

193 Vanjari N, Tang G, Toruner GA, Wang W, Thakral B, Zhao M, Dave BJ, Khoury JD, Medeiros LJ, Tang Z: Optical genome mapping helps to identify BCR::JAK2 rearrangement arising from cryptic complex chromosomal aberrations: a case report and literature review. Genes (Basel) 14(12): 2188, 2023. DOI: 10.3390/genes14122188

194 Tang Z, Wang W, Toruner GA, Hu S, Fang H, Xu J, You MJ, Medeiros LJ, Khoury JD, Tang G: Optical genome mapping for detection of BCR::ABL1-another tool in our toolbox. Genes (Basel) 15(11): 1357, 2024. DOI: 10.3390/genes15111357

195 Edelman Saul E, Urrutia S, Yang H, Montalban-Bravo G, Tang G, Toruner G, Patel K, Luthra R, Bueso-Ramos C, Wang SA, Chien K, Sasaki K, Atluri H, Goulart H, Thakral B, Garcia-Manero G, Kanagal-Shamanna R: A case of cryptic CBFB::MYH11 acute myeloid leukemia with noncanonical breakpoints detected by optical genome mapping. J Natl Compr Canc Netw 23(6): e257015, 2025. DOI: 10.6004/jnccn.2025.7015

196 Tsai MM, Kao HJ, Chen HH, Yu CH, Chien YH, Hwu WL, Kwok PY, Lee NC, Yang YL: Optical genome mapping with whole genome sequencing identifies complex chromosomal structural variations in acute leukemia. Front Genet 16: 1496847, 2025. DOI: 10.3389/fgene.2025.1496847

197 Vanhevel J, Rack K, Ameye G, Mokrani H, De Bie J, Michaux L, Dewaele B: The use of optical genome mapping for the detection of tyrosine kinase gene fusions in myeloid/lymphoid neoplasms. J Cell Mol Med 29(12): e70640, 2025. DOI: 10.1111/jcmm.70640

198 Loghavi S, Wei Q, Ravandi F, Quesada AE, Routbort MJ, Hu S, Toruner GA, Wang SA, Wang W, Miranda RN, Li S, Xu J, DiNardo CD, Daver N, Kadia TM, Issa GC, Kantarjian HM, Medeiros LJ, Tang G: Optical genome mapping improves the accuracy of classification, risk stratification, and personalized treatment strategies for patients with acute myeloid leukemia. Am J Hematol 99(10): 1959-1968, 2024. DOI: 10.1002/ajh.27435

199 Ballesta-Alcaraz L, Bernal M, Vilchez JR, Palacios JA, Jiménez P, Garrido P, Gutiérrez-Bautista JF, Ruiz-Cabello F: Application of optical genome mapping for the diagnosis and risk stratification of myeloid and lymphoid malignancies. Int J Mol Sci 26(12): 5763, 2025. DOI: 10.3390/ijms26125763

200 Levy B, Kanagal-Shamanna R, Sahajpal NS, Neveling K, Rack K, Dewaele B, Olde Weghuis D, Stevens-Kroef M, Puiggros A, Mallo M, Clifford B, Mantere T, Hoischen A, Espinet B, Kolhe R, Solé F, Raca G, Smith AC: A framework for the clinical implementation of optical genome mapping in hematologic malignancies. Am J Hematol 99(4): 642-661, 2024. DOI: 10.1002/ajh.27175

201 Kanagal-Shamanna R, Puiggros A, Granada I, Raca G, Rack K, Mallo M, Dewaele B, Smith AC, Akkari Y, Levy B, Hasserjian RP, Cisneros A, Salido M, Garcia-Manero G, Yang H, Iqbal MA, Kolhe R, Solé F, Espinet B: Integration of optical genome mapping in the cytogenomic and molecular work-up of hematological malignancies: expert recommendations from the International Consortium for Optical Genome Mapping. Am J Hematol 100(6): 1029-1048, 2025. DOI: 10.1002/ajh.27688

202 Moore S, McGowan-Jordan J, Smith AC, Rack K, Koehler U, Stevens-Kroef M, Barseghyan H, Kanagal-Shamanna R, Hastings R, ISCN Standing Committee: Genome mapping nomenclature. Cytogenet Genome Res 163(5-6): 236-246, 2023. DOI: 10.1159/000535684

203 Baelen J, Dewaele B, Debiec-Rychter M, Sciot R, Schöffski P, Hompes D, Sinnaeve F, Wafa H, Vanden Bempt I: Optical genome mapping for comprehensive cytogenetic analysis of soft-tissue and bone tumors for diagnostic purposes. J Mol Diagn 26(5): 374-386, 2024. DOI: 10.1016/j.jmoldx.2024.02.003

204 Berenguer-Rubio A, Such E, Hernández NT, González-Rojo P, Díaz-González Á, Avetisyan G, Gil-Aparicio C, González-López J, Pantoja-Borja N, Rubio-Martínez LA, Hernández-Girón S, Valera-Cuesta MS, Ramírez-Fuentes C, Simonet-Redondo M, Díaz-Beveridge R, de la Calva C, Amaya-Valero JV, Ballester-Ibáñez C, Liquori A, Giner F, Mayordomo-Aranda E: Exploring the potential of optical genome mapping in the diagnosis and prognosis of soft tissue and bone tumors. Int J Mol Sci 26(6): 2820, 2025. DOI: 10.3390/ijms26062820

205 Ghabrial J, Stinnett V, Ribeiro E, Klausner M, Morsberger L, Long P, Middlezong W, Xian R, Gocke C, Lin MT, Rooper L, Baraban E, Argani P, Pallavajjala A, Murry JB, Gross JM, Zou YS: Diagnostic and prognostic/therapeutic significance of comprehensive analysis of bone and soft tissue tumors using optical genome mapping and next-generation sequencing. Mod Pathol 38(4): 100684, 2025. DOI: 10.1016/j.modpat.2024.100684

206 Peng Y, Yuan C, Tao X, Zhao Y, Yao X, Zhuge L, Huang J, Zheng Q, Zhang Y, Hong H, Chen H, Sun Y: Integrated analysis of optical mapping and whole-genome sequencing reveals intratumoral genetic heterogeneity in metastatic lung squamous cell carcinoma. Transl Lung Cancer Res 9(3): 670-681, 2020. DOI: 10.21037/tlcr-19-401

207 Margalit S, Tulpová Z, Michaeli Y, Zur TD, Deek J, Louzoun-Zada S, Nifker G, Grunwald A, Scher Y, Schütz L, Weinhold E, Gnatek Y, Omer D, Dekel B, Friedman E, Ebenstein Y: Optical genome and epigenome mapping of clear cell renal cell carcinoma. NAR Cancer 7(1): zcaf008, 2025. DOI: 10.1093/narcan/zcaf008

208 Singh H, Sahajpal NS, Mondal AK, Burke SL, Farmaha J, Alptekin A, Vashisht A, Jones K, Vashisht V, Kolhe R: Clinical utility of optical genome mapping for improved cytogenomic analysis of gliomas. Biomedicines 12(8): 1659, 2024. DOI: 10.3390/biomedicines12081659

209 Rossi S, Barresi S, Colafati GS, Genovese S, Tancredi C, Costabile V, Patrizi S, Giovannoni I, Asioli S, Poliani PL, Gardiman MP, Cardoni A, Del Baldo G, Antonelli M, Gianno F, Piccirilli E, Catino G, Martucci L, Quacquarini D, Toni F, Melchionda F, Viscardi E, Zucchelli M, Dal Pos S, Gatti E, Liserre R, Schiavello E, Diomedi-Camassei F, Carai A, Mastronuzzi A, Gessi M, Giannini C, Novelli A, Onetti Muda A, Miele E, Alesi V, Alaggio R: PATZ1-rearranged tumors of the central nervous system: characterization of a pediatric series of seven cases. Mod Pathol 37(2): 100387, 2024. DOI: 10.1016/j.modpat.2023.100387

210 Bornhorst M, Eze A Jr, Bhattacharya S, Putnam E, Almira-Suarez MI, Rossi C, Kambhampati M, Almalvez M, Barseghyan M, Del Risco N, Dotson D, Turner J, Myseros JS, Vilain E, Packer RJ, Nazarian J, Rood B, Barseghyan H: Optical genome mapping identifies a novel pediatric embryonal tumor with

a ZNF532::NUTM1 fusion. J Pathol 260(3): 329-338, 2023. DOI: 10.1002/path.6085
211 Xu Y, Zhang Q, Wang Y, Zhou R, Ji X, Meng L, Luo C, Liu A, Jiao J, Chen H, Zeng H, Hu P, Xu Z: Optical genome mapping for chromosomal aberrations detection-false-negative results and contributing factors. Diagnostics (Basel) 14(2): 165, 2024. DOI: 10.3390/diagnostics14020165
212 Enjeti AK, Ashton K, Berry N, Chan E, Fodeades A, Ziolkowski A, Scott RJ: Next-generation karyotyping using optical genome mapping: a comparative study of genomic changes in haematological malignancies. Pathology 57(6): 775-777, 2025. DOI: 10.1016/j.pathol.2025.03.009
213 Stephens PJ, Greenman CD, Fu B, Yang F, Bignell GR, Mudie LJ, Pleasance ED, Lau KW, Beare D, Stebbings LA, McLaren S, Lin ML, McBride DJ, Varela I, Nik-Zainal S, Leroy C, Jia M, Menzies A, Butler AP, Teague JW, Quail MA, Burton J, Swerdlow H, Carter NP, Morsberger LA, Iacobuzio-Donahue C, Follows GA, Green AR, Flanagan AM, Stratton MR, Futreal PA, Campbell PJ: Massive genomic rearrangement acquired in a single catastrophic event during cancer development. Cell 144(1): 27-40, 2011. DOI: 10.1016/j.cell.2010.11.055
214 Holland AJ, Cleveland DW: Chromoanagenesis and cancer: mechanisms and consequences of localized, complex chromosomal rearrangements. Nat Med 18(11): 1630-1638, 2012. DOI: 10.1038/nm.2988
215 Righolt C, Mai S: Shattered and stitched chromosomes—chromothripsis and chromoanasynthesis—manifestations of a new chromosome crisis? Genes Chromosomes Cancer 51(11): 975-981, 2012. DOI: 10.1002/gcc.21981
216 Baca SC, Prandi D, Lawrence MS, Mosquera JM, Romanel A, Drier Y, Park K, Kitabayashi N, MacDonald TY, Ghandi M, Van Allen E, Kryukov GV, Sboner A, Theurillat JP, Soong TD, Nickerson E, Auclair D, Tewari A, Beltran H, Onofrio RC, Boysen G, Guiducci C, Barbieri CE, Cibulskis K, Sivachenko A, Carter SL, Saksena G, Voet D, Ramos AH, Winckler W, Cipicchio M, Ardlie K, Kantoff PW, Berger MF, Gabriel SB, Golub TR, Meyerson M, Lander ES, Elemento O, Getz G, Demichelis F, Rubin MA, Garraway LA: Punctuated evolution of prostate cancer genomes. Cell 153(3): 666-677, 2013. DOI: 10.1016/j.cell.2013.03.021
217 Shen MM: Chromoplexy: a new category of complex rearrangements in the cancer genome. Cancer Cell 23(5): 567-569, 2013. DOI: 10.1016/j.ccr.2013.04.025
218 Liu G, Stevens JB, Horne SD, Abdallah BY, Ye KJ, Bremer SW, Ye CJ, Chen DJ, Heng HH: Genome chaos: survival strategy during crisis. Cell Cycle 13(4): 528-537, 2014. DOI: 10.4161/cc.27378
219 Korbel JO, Campbell PJ: Criteria for inference of chromothripsis in cancer genomes. Cell 152(6): 1226-1236, 2013. DOI: 10.1016/j.cell.2013.02.023
220 Cortés-Ciriano I, Lee JJ, Xi R, Jain D, Jung YL, Yang L, Gordenin D, Klimczak LJ, Zhang CZ, Pellman DS, PCAWG Structural Variation Working Group, Park PJ, PCAWG Consortium: Comprehensive analysis of chromothripsis in 2,658 human cancers using whole-genome sequencing. Nat Genet 52(3): 331-341, 2020. DOI: 10.1038/s41588-019-0576-7
221 Voronina N, Wong JKL, Hübschmann D, Hlevnjak M, Uhrig S, Heilig CE, Horak P, Kreutzfeldt S, Mock A, Stenzinger A, Hutter B, Fröhlich M, Brors B, Jahn A, Klink B, Gieldon L, Sieverling L, Feuerbach L, Chudasama P, Beck K, Kroiss M, Heining C, Möhrmann L, Fischer A, Schröck E, Glimm H, Zapatka M, Lichter P, Fröhling S, Ernst A: The landscape of chromothripsis across adult cancer types. Nat Commun 11(1): 2320, 2020. DOI: 10.1038/s41467-020-16134-7
222 Espejo Valle-Inclan J, De Noon S, Trevers K, Elrick H, van Belzen IAEM, Zumalave S, Sauer CM, Tanguy M, Butters T, Muyas F, Rust AG, Amary F, Tirabosco R, Giess A, Sosinsky A, Elgar G, Flanagan AM, Cortés-Ciriano I: Ongoing chromothripsis underpins osteosarcoma genome complexity and clonal evolution. Cell 188(2): 352-370.e22, 2025. DOI: 10.1016/j.cell.2024.12.005
223 Wu C, Wyatt AW, McPherson A, Lin D, McConeghy BJ, Mo F, Shukin R, Lapuk AV, Jones SJ, Zhao Y, Marra MA, Gleave ME, Volik SV, Wang Y, Sahinalp SC, Collins CC: Poly-gene fusion transcripts and chromothripsis in prostate cancer. Genes Chromosomes Cancer 51(12): 1144-1153, 2012. DOI: 10.1002/gcc.21999
224 Harrison CJ: Blood Spotlight on iAMP21 acute lymphoblastic leukemia (ALL), a high-risk pediatric disease. Blood 125(9): 1383-1386, 2015. DOI: 10.1182/blood-2014-08-569228
225 Zavacka K, Plevova K: Chromothripsis in chronic lymphocytic leukemia: a driving force of genome instability. Front Oncol 11: 771664, 2021. DOI: 10.3389/fonc.2021.771664
226 Parry EM, Ten Hacken E, Wu CJ: Richter syndrome: novel insights into the biology of transformation. Blood 142(1): 11-22, 2023. DOI: 10.1182/blood.2022016502
227 Chen CY: Chromothripsis in myeloid malignancies. Ann Hematol 103(10): 3955-3962, 2024. DOI: 10.1007/s00277-024-05814-9
228 Lagunas-Rangel FA: Chromothripsis in hematologic malignancies. Exp Hematol 132: 104172, 2024. DOI: 10.1016/j.exphem.2024.104172
229 Shoshani O, Brunner SF, Yaeger R, Ly P, Nechemia-Arbely Y, Kim DH, Fang R, Castillon GA, Yu M, Li JSZ, Sun Y, Ellisman MH, Ren B, Campbell PJ, Cleveland DW: Chromothripsis drives the evolution of gene amplification in cancer. Nature 591(7848): 137-141, 2021. DOI: 10.1038/s41586-020-03064-z
230 Parker M, Mohankumar KM, Punchihewa C, Weinlich R, Dalton JD, Li Y, Lee R, Tatevossian RG, Phoenix TN, Thiruvenkatam R, White E, Tang B, Orisme W, Gupta K, Rusch M, Chen X, Li Y, Nagahawhatte P, Hedlund E, Finkelstein D, Wu G, Shurtleff S, Easton J, Boggs K, Yergeau D, Vadodaria B, Mulder HL, Becksfort J, Gupta P, Huether R, Ma J, Song G, Gajjar A, Merchant T, Boop F, Smith AA, Ding L, Lu C, Ochoa K, Zhao D, Fulton RS, Fulton LL, Mardis ER, Wilson RK, Downing JR, Green DR, Zhang J, Ellison DW, Gilbertson RJ: C11orf95-

RELA fusions drive oncogenic NF-κB signalling in ependymoma. Nature 506(7489): 451-455, 2014. DOI: 10.1038/nature13109

231 Tauziède-Espariat A, Dangouloff-Ros V, Sievers P, Duchesne M, Siegfried A, Nicaise Y, Boddaert N, Hasty L, Métais A, Ngo C, le Loarer F, Bouvier C, Fontaine A, Rousseau A, Marguet F, Beccaria K, Blauwblomme T, Uro-Coste E, Varlet P, RENOCLIP-LOC: Glioneuronal tumors PATZ1-fused: clinico-molecular and DNA methylation signatures for a variety of morphological and radiological profiles. Acta Neuropathol Commun 13(1): 114, 2025. DOI: 10.1186/s40478-025-02037-5

232 Furtado LV, Santiago T, Shi Z, Wang L, Liu YC, Gartrell J, Ruiz RE: Novel HNRNPM::LEUTX fusion resulting from chromothripsis of chromosome 19 in a pediatric undifferentiated small round cell neoplasm. Genes Chromosomes Cancer 62(12): 740-745, 2023. DOI: 10.1002/gcc.23187

233 Lanceta J, Tripodi J, Karp L, Shaham M, Mahmood N, Najfeld V, Edelman M, Cohen N: Chromothripsis in lipoblastoma: second reported case with complex PLAG1 rearrangement. Mol Cytogenet 16(1): 32, 2023. DOI: 10.1186/s13039-023-00665-x

234 Makise N, Lin J, Kageyama H, Kinoshita H, Kamoda H, Hagiwara Y, Oikawa M, Sugiyama T, Kawana H, Araki A, Yonemoto T, Kawazu M, Itami M: Nanopore DNA sequencing detected chromothripsis-induced PAFAH1B1::USP6 rearrangement in periosteal solid aneurysmal bone cyst initially diagnosed as osteosarcoma. Genes Chromosomes Cancer 63(7): e23254, 2024. DOI: 10.1002/gcc.23254

235 Liu P, Erez A, Nagamani SC, Dhar SU, Kołodziejska KE, Dharmadhikari AV, Cooper ML, Wiszniewska J, Zhang F, Withers MA, Bacino CA, Campos-Acevedo LD, Delgado MR, Freedenberg D, Garnica A, Grebe TA, Hernández-Almaguer D, Immken L, Lalani SR, McLean SD, Northrup H, Scaglia F, Strathearn L, Trapane P, Kang SH, Patel A, Cheung SW, Hastings PJ, Stankiewicz P, Lupski JR, Bi W: Chromosome catastrophes involve replication mechanisms generating complex genomic rearrangements. Cell 146(6): 889-903, 2011. DOI: 10.1016/j.cell.2011.07.042

236 Pellestor F, Gatinois V: Chromoanasynthesis: another way for the formation of complex chromosomal abnormalities in human reproduction. Hum Reprod 33(8): 1381-1387, 2018. DOI: 10.1093/humrep/dey231

237 Anoshkin KI, Karandasheva KO, Goryacheva KM, Pyankov DV, Koshkin PA, Pavlova TV, Bobin AN, Shpot EV, Chernov YN, Vinarov AZ, Zaletaev DV, Kutsev SI, Strelnikov VV: Multiple chromoanasynthesis in a rare case of sporadic renal leiomyosarcoma: a case report. Front Oncol 10: 1653, 2020. DOI: 10.3389/fonc.2020.01653

238 Vasmatzis G, Wang X, Smadbeck JB, Murphy SJ, Geiersbach KB, Johnson SH, Gaitatzes AG, Asmann YW, Kosari F, Borad MJ, Serie DJ, McLaughlin SA, Kachergus JM, Necela BM, Thompson EA: Chromoanasynthesis is a common mechanism that leads to ERBB2 amplifications in a cohort of early stage HER2(+) breast cancer samples. BMC Cancer 18(1): 738, 2018. DOI: 10.1186/s12885-018-4594-0

239 Poot M: Of simple and complex genome rearrangements, chromothripsis, chromoanasynthesis, and chromosome chaos. Mol Syndromol 8(3): 115-117, 2017. DOI: 10.1159/000454964

240 Pellestor F, Ganne B, Gaillard JB, Gatinois V: Chromoplexy: a pathway to genomic complexity and cancer development. Int J Mol Sci 26(8): 3826, 2025. DOI: 10.3390/ijms26083826

241 Anderson ND, de Borja R, Young MD, Fuligni F, Rosic A, Roberts ND, Hajjar S, Layeghifard M, Novokmet A, Kowalski PE, Anaka M, Davidson S, Zarrei M, Id Said B, Schreiner LC, Marchand R, Sitter J, Gokgoz N, Brunga L, Graham GT, Fullam A, Pillay N, Toretsky JA, Yoshida A, Shibata T, Metzler M, Somers GR, Scherer SW, Flanagan AM, Campbell PJ, Schiffman JD, Shago M, Alexandrov LB, Wunder JS, Andrulis IL, Malkin D, Behjati S, Shlien A: Rearrangement bursts generate canonical gene fusions in bone and soft tissue tumors. Science 361(6405): eaam8419, 2018. DOI: 10.1126/science.aam8419

242 Dermawan JK, Slotkin E, Tap WD, Meyers P, Wexler L, Healey J, Vanoli F, Vanderbilt CM, Antonescu CR: Chromoplexy is a frequent early clonal event in EWSR1-rearranged round cell sarcomas that can be detected using clinically validated targeted sequencing panels. Cancer Res 84(9): 1504-1516, 2024. DOI: 10.1158/0008-5472.CAN-23-2573

243 van Belzen IAEM, van Tuil M, Badloe S, Janse A, Verwiel ETP, Santoso M, de Vos S, Baker-Hernandez J, Kerstens HHD, Solleveld-Westerink N, Meister MT, Drost J, van den Heuvel-Eibrink MM, Merks JHM, Molenaar JJ, Peng WC, Tops BBJ, Holstege FCP, Kemmeren P, Hehir-Kwa JY: Complex structural variation is prevalent and highly pathogenic in pediatric solid tumors. Cell Genom 4(11): 100675, 2024. DOI: 10.1016/j.xgen.2024.100675

244 Lee JK, Louzada S, An Y, Kim SY, Kim S, Youk J, Park S, Koo SH, Keam B, Jeon YK, Ku JL, Yang F, Kim TM, Ju YS: Complex chromosomal rearrangements by single catastrophic pathogenesis in NUT midline carcinoma. Ann Oncol 28(4): 890-897, 2017. DOI: 10.1093/annonc/mdw686

245 Wang Z, Cheng Y, Abraham JM, Yan R, Liu X, Chen W, Ibrahim S, Schroth GP, Ke X, He Y, Meltzer SJ: RNA sequencing of esophageal adenocarcinomas identifies novel fusion transcripts, including NPC1-MELK, arising from a complex chromosomal rearrangement. Cancer 123(20): 3916-3924, 2017. DOI: 10.1002/cncr.30837

246 Lee JJ, Park S, Park H, Kim S, Lee J, Lee J, Youk J, Yi K, An Y, Park IK, Kang CH, Chung DH, Kim TM, Jeon YK, Hong D, Park PJ, Ju YS, Kim YT: Tracing oncogene rearrangements in the mutational history of lung adenocarcinoma. Cell 177(7): 1842-1857.e21, 2019. DOI: 10.1016/j.cell.2019.05.013

247 Mansfield AS, Peikert T, Smadbeck JB, Udell JBM, Garcia-Rivera E, Elsbernd L, Erskine CL, Van Keulen VP, Kosari F, Murphy SJ,

Ren H, Serla VV, Schaefer Klein JL, Karagouga G, Harris FR, Sosa C, Johnson SH, Nevala W, Markovic SN, Bungum AO, Edell ES, Dong H, Cheville JC, Aubry MC, Jen J, Vasmatzis G: Neoantigenic potential of complex chromosomal rearrangements in mesothelioma. J Thorac Oncol 14(2): 276-287, 2019. DOI: 10.1016/j.jtho.2018.10.001

248 Oey H, Daniels M, Relan V, Chee TM, Davidson MR, Yang IA, Ellis JJ, Fong KM, Krause L, Bowman RV: Whole-genome sequencing of human malignant mesothelioma tumours and cell lines. Carcinogenesis 40(6): 724-734, 2019. DOI: 10.1093/carcin/bgz066

249 Choi J, Manzano A, Dong W, Bellone S, Bonazzoli E, Zammataro L, Yao X, Deshpande A, Zaidi S, Guglielmi A, Gnutti B, Nagarkatti N, Tymon-Rosario JR, Harold J, Mauricio D, Zeybek B, Menderes G, Altwerger G, Jeong K, Zhao S, Buza N, Hui P, Ravaggi A, Bignotti E, Romani C, Todeschini P, Zanotti L, Odicino F, Pecorelli S, Ardighieri L, Bilguvar K, Quick CM, Silasi DA, Huang GS, Andikyan V, Clark M, Ratner E, Azodi M, Imielinski M, Schwartz PE, Alexandrov LB, Lifton RP, Schlessinger J, Santin AD: Integrated mutational landscape analysis of uterine leiomyosarcomas. Proc Natl Acad Sci U S A 118(15): e2025182118, 2021. DOI: 10.1073/pnas.2025182118

250 Cyrta J, Rosiene J, Bareja R, Kudman S, Al Zoughbi W, Motanagh S, Wilkes DC, Eng K, Zhang T, Sticca E, Mathew S, Rubin MA, Sboner A, Elemento O, Rubin BP, Imielinski M, Mosquera JM: Whole-genome characterization of myoepithelial carcinomas of the soft tissue. Cold Spring Harb Mol Case Stud 8(7): a006227, 2022. DOI: 10.1101/mcs.a006227

251 Wei Q, Hu S, Loghavi S, Toruner GA, Ravandi-Kashani F, Tang Z, Li S, Xu J, Daver N, Medeiros LJ, Tang G: Chromoanagenesis is frequently associated with highly complex karyotypes, extensive clonal heterogeneity, and treatment refractoriness in acute myeloid leukemia. Am J Hematol 100(3): 417-426, 2025. DOI: 10.1002/ajh.27575

252 Kaur G, Gupta R, Mathur N, Rani L, Kumar L, Sharma A, Singh V, Gupta A, Sharma OD: Clinical impact of chromothriptic complex chromosomal rearrangements in newly diagnosed multiple myeloma. Leuk Res 76: 58-64, 2019. DOI: 10.1016/j.leukres.2018.12.005

253 Maura F, Bolli N, Angelopoulos N, Dawson KJ, Leongamornlert D, Martincorena I, Mitchell TJ, Fullam A, Gonzalez S, Szalat R, Abascal F, Rodriguez-Martin B, Samur MK, Glodzik D, Roncador M, Fulciniti M, Tai YT, Minvielle S, Magrangeas F, Moreau P, Corradini P, Anderson KC, Tubio JMC, Wedge DC, Gerstung M, Avet-Loiseau H, Munshi N, Campbell PJ: Genomic landscape and chronological reconstruction of driver events in multiple myeloma. Nat Commun 10(1): 3835, 2019. DOI: 10.1038/s41467-019-11680-1

254 Rustad EH, Yellapantula VD, Glodzik D, Maclachlan KH, Diamond B, Boyle EM, Ashby C, Blaney P, Gundem G, Hultcrantz M, Leongamornlert D, Angelopoulos N, Agnelli L, Auclair D, Zhang Y, Dogan A, Bolli N, Papaemmanuil E, Anderson KC, Moreau P, Avet-Loiseau H, Munshi NC, Keats JJ, Campbell PJ, Morgan GJ, Landgren O, Maura F: Revealing the impact of structural variants in multiple myeloma. Blood Cancer Discov 1(3): 258-273, 2020. DOI: 10.1158/2643-3230.BCD-20-0132

255 Bidet A, Klein E: Chromoplexy and FNDC3B::RARB fusion: deciphering a rare case of PML::RARA-negative APL. Blood 145(14): 1588-1588, 2025. DOI: 10.1182/blood.2024027991

256 Pellestor F: Chromoanagenesis: cataclysms behind complex chromosomal rearrangements. Mol Cytogenet 12: 6, 2019. DOI: 10.1186/s13039-019-0415-7

257 Pellestor F, Gatinois V: Chromoanagenesis: a piece of the macroevolution scenario. Mol Cytogenet 13: 3, 2020. DOI: 10.1186/s13039-020-0470-0

258 Pellestor F, Gaillard JB, Schneider A, Puechberty J, Gatinois V: Chromoanagenesis, the mechanisms of a genomic chaos. Semin Cell Dev Biol 123: 90-99, 2022. DOI: 10.1016/j.semcdb.2021.01.004

259 Pihan GA: Centrosome dysfunction contributes to chromosome instability, chromoanagenesis, and genome reprograming in cancer. Front Oncol 3: 277, 2013. DOI: 10.3389/fonc.2013.00277

260 Rasnic R, Linial M: Chromoanagenesis landscape in 10,000 TCGA patients. Cancers (Basel) 13(16): 4197, 2021. DOI: 10.3390/cancers13164197

261 Li G, Wu N, Ghabrial J, Stinnett V, Klausner M, Morsberger L, Long P, Baraban E, Gross JM, Zou YS: Chromoanagenesis in osteosarcoma. Biomolecules 15(6): 833, 2025. DOI: 10.3390/biom15060833

262 Ortega V, Chaubey A, Mendiola C, Ehman W Jr, Vadlamudi K, Dupont B, Velagaleti G: Complex chromosomal rearrangements in B-cell lymphoma: evidence of chromoanagenesis? A case report. Neoplasia 18(4): 223-228, 2016. DOI: 10.1016/j.neo.2016.02.004

263 Klos C, Roynard P, Berthon C, Soenen V, Marceau A, Fournier E, Fenwarth L, Daudignon A, Roche C, Guermouche H: Unravelling a KMT2A::ARHGEF12 fusion within chromoanagenesis in acute myeloid leukemia using Optical Genome Mapping. Ann Hematol 103(11): 4793-4795, 2024. DOI: 10.1007/s00277-024-05948-w

264 Burnside RD, Harris A, Speyer D, Burgin WS, Rose DZ, Sanchez-Valle A: Constitutional chromoanagenesis of distal 13q in a young adult with recurrent strokes. Cytogenet Genome Res 150(1): 46-51, 2016. DOI: 10.1159/000452144

265 Zepeda-Mendoza CJ, Morton CC: The iceberg under water: unexplored complexity of chromoanagenesis in congenital disorders. Am J Hum Genet 104(4): 565-577, 2019. DOI: 10.1016/j.ajhg.2019.02.024

266 Villela D, Mazzonetto PC, Migliavacca MP, Perrone E, Guida G, Milanezi MFG, Jorge AAL, Ribeiro-Bicudo LA, Kok F, Campagnari F, de Rosso-Giuliani L, da Costa SS, Vianna-Morgante AM, Pearson PL, Krepischi ACV, Rosenberg C: Congenital chromoanagenesis in the routine postnatal

chromosomal microarray analyses. Am J Med Genet A 185(8): 2335-2344, 2021. DOI: 10.1002/ajmg.a.62237
267 Nik-Zainal S, Alexandrov LB, Wedge DC, Van Loo P, Greenman CD, Raine K, Jones D, Hinton J, Marshall J, Stebbings LA, Menzies A, Martin S, Leung K, Chen L, Leroy C, Ramakrishna M, Rance R, Lau KW, Mudie LJ, Varela I, McBride DJ, Bignell GR, Cooke SL, Shlien A, Gamble J, Whitmore I, Maddison M, Tarpey PS, Davies HR, Papaemmanuil E, Stephens PJ, McLaren S, Butler AP, Teague JW, Jönsson G, Garber JE, Silver D, Miron P, Fatima A, Boyault S, Langerød A, Tutt A, Martens JW, Aparicio SA, Borg Å, Salomon AV, Thomas G, Børresen-Dale AL, Richardson AL, Neuberger MS, Futreal PA, Campbell PJ, Stratton MR, Breast Cancer Working Group of the International Cancer Genome Consortium: Mutational processes molding the genomes of 21 breast cancers. Cell 149(5): 979-993, 2012. DOI: 10.1016/j.cell.2012.04.024
268 Lada AG, Dhar A, Boissy RJ, Hirano M, Rubel AA, Rogozin IB, Pavlov YI: AID/APOBEC cytosine deaminase induces genome-wide kataegis. Biol Direct 7: 47; discussion 47, 2012. DOI: 10.1186/1745-6150-7-47
269 Taylor BJ, Nik-Zainal S, Wu YL, Stebbings LA, Raine K, Campbell PJ, Rada C, Stratton MR, Neuberger MS: DNA deaminases induce break-associated mutation showers with implication of APOBEC3B and 3A in breast cancer kataegis. Elife 2: e00534, 2013. DOI: 10.7554/eLife.00534
270 Casellas R, Basu U, Yewdell WT, Chaudhuri J, Robbiani DF, Di Noia JM: Mutations, kataegis and translocations in B cells: understanding AID promiscuous activity. Nat Rev Immunol 16(3): 164-176, 2016. DOI: 10.1038/nri.2016.2
271 Sakofsky CJ, Roberts SA, Malc E, Mieczkowski PA, Resnick MA, Gordenin DA, Malkova A: Break-induced replication is a source of mutation clusters underlying kataegis. Cell Rep 7(5): 1640-1648, 2014. DOI: 10.1016/j.celrep.2014.04.053
272 Elango R, Osia B, Harcy V, Malc E, Mieczkowski PA, Roberts SA, Malkova A: Repair of base damage within break-induced replication intermediates promotes kataegis associated with chromosome rearrangements. Nucleic Acids Res 47(18): 9666-9684, 2019. DOI: 10.1093/nar/gkz651
273 Maciejowski J, Li Y, Bosco N, Campbell PJ, de Lange T: Chromothripsis and Kataegis Induced by Telomere Crisis. Cell 163(7): 1641-1654, 2015. DOI: 10.1016/j.cell.2015.11.054
274 Maciejowski J, Chatzipli A, Dananberg A, Chu K, Toufektchan E, Klimczak LJ, Gordenin DA, Campbell PJ, de Lange T: APOBEC3-dependent kataegis and TREX1-driven chromothripsis during telomere crisis. Nat Genet 52(9): 884-890, 2020. DOI: 10.1038/s41588-020-0667-5
275 Lin X, Hua Y, Gu S, Lv L, Li X, Chen P, Dai P, Hu Y, Liu A, Li J: kataegis: an R package for identification and visualization of the genomic localized hypermutation regions using high-throughput sequencing. BMC Genomics 22(1): 440, 2021. DOI: 10.1186/s12864-021-07696-x
276 Hazelaar DM, van Riet J, Hoogstrate Y, van de Werken HJG: Katdetectr: an R/bioconductor package utilizing unsupervised changepoint analysis for robust kataegis detection. Gigascience 12: giad081, 2022. DOI: 10.1093/gigascience/giad081
277 D'Antonio M, Tamayo P, Mesirov JP, Frazer KA: Kataegis expression signature in breast cancer is associated with late onset, better prognosis, and higher HER2 levels. Cell Rep 16(3): 672-683, 2016. DOI: 10.1016/j.celrep.2016.06.026
278 Boichard A, Tsigelny IF, Kurzrock R: High expression of PD-1 ligands is associated with kataegis mutational signature and APOBEC3 alterations. Oncoimmunology 6(3): e1284719, 2017. DOI: 10.1080/2162402X.2017.1284719
279 Stenman A, Yang M, Paulsson JO, Zedenius J, Paulsson K, Juhlin CC: Pan-genomic sequencing reveals actionable CDKN2A/2B deletions and kataegis in anaplastic thyroid carcinoma. Cancers (Basel) 13(24): 6340, 2021. DOI: 10.3390/cancers13246340
280 Selenica P, Marra A, Choudhury NJ, Gazzo A, Falcon CJ, Patel J, Pei X, Zhu Y, Ng CKY, Curry M, Heller G, Zhang YK, Berger MF, Ladanyi M, Rudin CM, Chandarlapaty S, Lovly CM, Reis-Filho JS, Yu HA: APOBEC mutagenesis, kataegis, chromothripsis in EGFR-mutant osimertinib-resistant lung adenocarcinomas. Ann Oncol 33(12): 1284-1295, 2022. DOI: 10.1016/j.annonc.2022.09.151
281 Hayes V, Jiang J, Tapinos A, Huang R, Bornman R, Stricker P, Mutambirwa S, Wedge D, Jaratlerdsiri W: Kataegis associated mutational processes linked to adverse prostate cancer presentation in African men. Res Sq, 2024. DOI: 10.21203/rs.3.rs-4597464/v1
282 Veerla S, Staaf J: Kataegis in clinical and molecular subgroups of primary breast cancer. NPJ Breast Cancer 10(1): 32, 2024. DOI: 10.1038/s41523-024-00640-8
283 Gunnarsson R, Yang M, Biloglav A, Lundin-Ström KB, Lilljebjörn H, Castor A, Fioretos T, Olsson-Arvidsson L, Paulsson K, Johansson B: Mutational signatures and kataegis in pediatric B-cell precursor acute lymphoblastic leukemia. Hemasphere 9(5): e70136, 2025. DOI: 10.1002/hem3.70136
284 Dong Y, Sun Q, Zhang X: PD-1 and its ligands are important immune checkpoints in cancer. Oncotarget 8(2): 2171-2186, 2017. DOI: 10.18632/oncotarget.13895
285 Vaddepally RK, Kharel P, Pandey R, Garje R, Chandra AB: Review of indications of FDA-approved immune checkpoint inhibitors per NCCN guidelines with the level of evidence. Cancers (Basel) 12(3): 738, 2020. DOI: 10.3390/cancers12030738
286 Yin X, Bi R, Ma P, Zhang S, Zhang Y, Sun Y, Zhang Y, Jing Y, Yu M, Wang W, Tan L, Di W, Zhuang G, Cai MC: Multiregion whole-genome sequencing depicts intratumour heterogeneity and punctuated evolution in ovarian clear cell carcinoma. J Med Genet 57(9): 605-609, 2020. DOI: 10.1136/jmedgenet-2019-106418
287 Long X, Lu H, Cai MC, Zang J, Zhang Z, Wu J, Liu X, Cheng L, Cheng J, Cheung LWT, Shen Z, Zhou Y, Di W, Zhuang G, Yin X: APOBEC3B stratifies ovarian clear cell carcinoma with distinct

immunophenotype and prognosis. Br J Cancer 128(11): 2054-2062, 2023. DOI: 10.1038/s41416-023-02239-5
288 Campbell BB, Light N, Fabrizio D, Zatzman M, Fuligni F, de Borja R, Davidson S, Edwards M, Elvin JA, Hodel KP, Zahurancik WJ, Suo Z, Lipman T, Wimmer K, Kratz CP, Bowers DC, Laetsch TW, Dunn GP, Johanns TM, Grimmer MR, Smirnov IV, Larouche V, Samuel D, Bronsema A, Osborn M, Stearns D, Raman P, Cole KA, Storm PB, Yalon M, Opocher E, Mason G, Thomas GA, Sabel M, George B, Ziegler DS, Lindhorst S, Issai VM, Constantini S, Toledano H, Elhasid R, Farah R, Dvir R, Dirks P, Huang A, Galati MA, Chung J, Ramaswamy V, Irwin MS, Aronson M, Durno C, Taylor MD, Rechavi G, Maris JM, Bouffet E, Hawkins C, Costello JF, Meyn MS, Pursell ZF, Malkin D, Tabori U, Shlien A: Comprehensive analysis of hypermutation in human cancer. Cell 171(5): 1042-1056. e10, 2017. DOI: 10.1016/j.cell.2017.09.048
289 Ma X, Dong L, Liu X, Ou K, Yang L: POLE/POLD1 mutation and tumor immunotherapy. J Exp Clin Cancer Res 41(1): 216, 2022. DOI: 10.1186/s13046-022-02422-1
290 Lindsten J, Klinger HP, Hamerton JL: An international system for human cytogenetic nomenclature. Cytogenet Cell Genet 21(6): 309-404, 1978. DOI: 10.1159/000130909
291 Mitelman F: ISCN 1995: An International System for Human Cytogenetic Nomenclature. Basel, Switzerland, Karger, 1995.
292 Shaffer LG, Tommerup N: ISCN 2005: An International System for Human Cytogenetic Nomenclature. Basel, Switzerland, Karger, 2005.
293 Shaffer LG, Slovak ML, Campbell LJ: ISCN 2009: An International System for Human Cytogenetic Nomenclature. Basel, Switzerland, Karger, 2009.
294 Shaffer LG, McGowan-Jordan J, Schmid M: ISCN 2013: An International System for Human Cytogenetic Nomenclature. Basel, Switzerland, Karger, 2013.
295 McGowan-Jordan J, Simons A, Schmid M: ISCN 2016: An International System for Human Cytogenomic Nomenclature. Basel, Switzerland, Karger, 2016.
296 Hastings RJ, Moore S, Chia N: ISCN 2024: An International System for Human Cytogenomic Nomenclature. Basel, Switzerland, Karger, 2024.
297 Brothman AR, Persons DL, Shaffer LG: Nomenclature evolution: changes in the ISCN from the 2005 to the 2009 edition. Cytogenet Genome Res 127(1): 1-4, 2009. DOI: 10.1159/000279442
298 Simons A, Shaffer LG, Hastings RJ: Cytogenetic nomenclature: changes in the ISCN 2013 compared to the 2009 edition. Cytogenet Genome Res 141(1): 1-6, 2013. DOI: 10.1159/000353118
299 Hastings R, McGowan-Jordan J, Moore S, ISCN Standing Committee: Addenda to ISCN 2020. Cytogenet Genome Res 163(1-2): 1-4, 2023. DOI: 10.1159/000533170
300 Chia NL, Moore S, Hastings RJ: ISCN 2024: Summary of revisions and new nomenclature. Cytogenet Genome Res 165(1): 1-8, 2025. DOI: 10.1159/000544969
301 Bruford EA, Antonescu CR, Carroll AJ, Chinnaiyan A, Cree IA, Cross NCP, Dalgleish R, Gale RP, Harrison CJ, Hastings RJ, Huret JL, Johansson B, Le Beau M, Mecucci C, Mertens F, Verhaak R, Mitelman F: HUGO Gene Nomenclature Committee (HGNC) recommendations for the designation of gene fusions. Leukemia 35(11): 3040-3043, 2021. DOI: 10.1038/s41375-021-01436-6
302 Rangwala SH, Kuznetsov A, Ananiev V, Asztalos A, Borodin E, Evgeniev V, Joukov V, Lotov V, Pannu R, Rudnev D, Shkeda A, Weitz EM, Schneider VA: Accessing NCBI data using the NCBI Sequence Viewer and Genome Data Viewer (GDV). Genome Res 31(1): 159-169, 2021. DOI: 10.1101/gr.266932.120
303 Kasperski A, Heng HH: The digital world of cytogenetic and cytogenomic web resources. Methods Mol Biol 2825: 361-391, 2024. DOI: 10.1007/978-1-0716-3946-7_21
304 Karimpour-Fard A, Dumas L, Phang T, Sikela JM, Hunter LE: A survey of analysis software for array-comparative genomic hybridisation studies to detect copy number variation. Hum Genomics 4(6): 421-427, 2010. DOI: 10.1186/1479-7364-4-6-421
305 Hiller B, Bradtke J, Balz H, Rieder H: CyDAS: a cytogenetic data analysis system. Bioinformatics 21(7): 1282-1283, 2005. DOI: 10.1093/bioinformatics/bti146
306 Hao Z, Lv D, Ge Y, Shi J, Weijers D, Yu G, Chen J: RIdeogram: drawing SVG graphics to visualize and map genome-wide data on the idiograms. PeerJ Comput Sci 6: e251, 2020. DOI: 10.7717/peerj-cs.251
307 Kin T, Ono Y: Idiographica: a general-purpose web application to build idiograms on-demand for human, mouse and rat. Bioinformatics 23(21): 2945-2946, 2007. DOI: 10.1093/bioinformatics/btm455
308 Janečka J, Lysak MA: chromDraw: an R package for visualization of linear and circular karyotypes. Chromosome Res 24(2): 217-223, 2016. DOI: 10.1007/s10577-015-9513-5
309 Gel B, Serra E: karyoploteR: an R/Bioconductor package to plot customizable genomes displaying arbitrary data. Bioinformatics 33(19): 3088-3090, 2017. DOI: 10.1093/bioinformatics/btx346
310 Anand L, Rodriguez Lopez CM: ChromoMap: an R package for interactive visualization of multi-omics data and annotation of chromosomes. BMC Bioinformatics 23(1): 33, 2022. DOI: 10.1186/s12859-021-04556-z
311 Yu Y, Yao W, Wang Y, Huang F: shinyChromosome: an R/Shiny application for interactive creation of non-circular plots of whole genomes. Genomics Proteomics Bioinformatics 17(5): 535-539, 2019. DOI: 10.1016/j.gpb.2019.07.003
312 Guy L, Kultima JR, Andersson SG: genoPlotR: comparative gene and genome visualization in R. Bioinformatics 26(18): 2334-2335, 2010. DOI: 10.1093/bioinformatics/btq413
313 Wolfe D, Dudek S, Ritchie MD, Pendergrass SA: Visualizing genomic information across chromosomes with PhenoGram. BioData Min 6(1): 18, 2013. DOI: 10.1186/1756-0381-6-18

314 Krzywinski M, Schein J, Birol I, Connors J, Gascoyne R, Horsman D, Jones SJ, Marra MA: Circos: an information aesthetic for comparative genomics. Genome Res 19(9): 1639-1645, 2009. DOI: 10.1101/gr.092759.109
315 Uhrig S, Ellermann J, Walther T, Burkhardt P, Fröhlich M, Hutter B, Toprak UH, Neumann O, Stenzinger A, Scholl C, Fröhling S, Brors B: Accurate and efficient detection of gene fusions from RNA sequencing data. Genome Res 31(3): 448-460, 2021. DOI: 10.1101/gr.257246.119
316 Haas BJ, Dobin A, Ghandi M, Van Arsdale A, Tickle T, Robinson JT, Gillani R, Kasif S, Regev A: Targeted in silico characterization of fusion transcripts in tumor and normal tissues *via* FusionInspector. Cell Rep Methods 3(5): 100467, 2023. DOI: 10.1016/j.crmeth.2023.100467
317 Lågstad S, Zhao S, Hoff AM, Johannessen B, Lingjærde OC, Skotheim RI: chimeraviz: a tool for visualizing chimeric RNA. Bioinformatics 33(18): 2954-2956, 2017. DOI: 10.1093/bioinformatics/btx329
318 Robinson JT, Thorvaldsdóttir H, Winckler W, Guttman M, Lander ES, Getz G, Mesirov JP: Integrative genomics viewer. Nat Biotechnol 29(1): 24-26, 2011. DOI: 10.1038/nbt.1754
319 Talevich E, Shain AH, Botton T, Bastian BC: CNVkit: Genome-wide copy number detection and visualization from targeted DNA sequencing. PLoS Comput Biol 12(4): e1004873, 2016. DOI: 10.1371/journal.pcbi.1004873
320 Goldman MJ, Zhang J, Fonseca NA, Cortés-Ciriano I, Xiang Q, Craft B, Piñeiro-Yáñez E, O'Connor BD, Bazant W, Barrera E, Muñoz-Pomer A, Petryszak R, Füllgrabe A, Al-Shahrour F, Keays M, Haussler D, Weinstein JN, Huber W, Valencia A, Park PJ, Papatheodorou I, Zhu J, Ferretti V, Vazquez M: A user guide for the online exploration and visualization of PCAWG data. Nat Commun 11(1): 3400, 2020. DOI: 10.1038/s41467-020-16785-6
321 Rosenblum LS, Holmes J, Taghiyev AF: The emergence of artificial intelligence-guided karyotyping: a review and reflection. Genes (Basel) 16(6): 685, 2025. DOI: 10.3390/genes16060685
322 Mareschal S, Palau A, Lindberg J, Ruminy P, Nilsson C, Bengtzén S, Engvall M, Eriksson A, Neddermeyer A, Marchand V, Jansson M, Björklund M, Jardin F, Rantalainen M, Lennartsson A, Cavelier L, Grönberg H, Lehmann S: Challenging conventional karyotyping by next-generation karyotyping in 281 intensively treated patients with AML. Blood Adv 5(4): 1003-1016, 2021. DOI: 10.1182/bloodadvances.2020002517
323 Boer JM, Koudijs MJ, Kester LA, Sonneveld E, Hehir-Kwa JY, Snijder S, Waanders E, Buijs A, de Haas V, van der Sluis IM, Pieters R, den Boer ML, Tops BBJ: Challenging conventional diagnostic methods by comprehensive molecular diagnostics: a nationwide prospective comparison in children with ALL. JCO Precis Oncol 9: e2400788, 2025. DOI: 10.1200/PO-24-00788
324 Medeiros BC, Othus M, Estey EH, Fang M, Appelbaum FR: Unsuccessful diagnostic cytogenetic analysis is a poor prognostic feature in acute myeloid leukaemia. Br J Haematol 164(2): 245-250, 2014. DOI: 10.1111/bjh.12625
325 Lazarevic V, Hörstedt A, Johansson B, Antunovic P, Billström R, Derolf Ã, Lehmann S, Möllgård L, Peterson S, Stockelberg D, Uggla B, Vennström L, Wahlin A, Höglund M, Juliusson G: Failure matters: unsuccessful cytogenetics and unperformed cytogenetics are associated with a poor prognosis in a population-based series of acute myeloid leukaemia. Eur J Haematol 94(5): 419-423, 2015. DOI: 10.1111/ejh.12446
326 Lazarevic VL, Johansson B: Why classical cytogenetics still matters in acute myeloid leukemia. Expert Rev Hematol 13(2): 95-97, 2020. DOI: 10.1080/17474086.2020.1711733
327 Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IBO, Berti E, Bhagat G, Borges AM, Boyer D, Calaminici M, Chadburn A, Chan JKC, Cheuk W, Chng WJ, Choi JK, Chuang SS, Coupland SE, Czader M, Dave SS, de Jong D, Du MQ, Elenitoba-Johnson KS, Ferry J, Geyer J, Gratzinger D, Guitart J, Gujral S, Harris M, Harrison CJ, Hartmann S, Hochhaus A, Jansen PM, Karube K, Kempf W, Khoury J, Kimura H, Klapper W, Kovach AE, Kumar S, Lazar AJ, Lazzi S, Leoncini L, Leung N, Leventaki V, Li XQ, Lim MS, Liu WP, Louissaint A Jr, Marcogliese A, Medeiros LJ, Michal M, Miranda RN, Mitteldorf C, Montes-Moreno S, Morice W, Nardi V, Naresh KN, Natkunam Y, Ng SB, Oschlies I, Ott G, Parrens M, Pulitzer M, Rajkumar SV, Rawstron AC, Rech K, Rosenwald A, Said J, Sarkozy C, Sayed S, Saygin C, Schuh A, Sewell W, Siebert R, Sohani AR, Tooze R, Traverse-Glehen A, Vega F, Vergier B, Wechalekar AD, Wood B, Xerri L, Xiao W: The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia 36(7): 1720-1748, 2022. DOI: 10.1038/s41375-022-01620-2
328 Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, Bejar R, Berti E, Busque L, Chan JKC, Chen W, Chen X, Chng WJ, Choi JK, Colmenero I, Coupland SE, Cross NCP, De Jong D, Elghetany MT, Takahashi E, Emile JF, Ferry J, Fogelstrand L, Fontenay M, Germing U, Gujral S, Haferlach T, Harrison C, Hodge JC, Hu S, Jansen JH, Kanagal-Shamanna R, Kantarjian HM, Kratz CP, Li XQ, Lim MS, Loeb K, Loghavi S, Marcogliese A, Meshinchi S, Michaels P, Naresh KN, Natkunam Y, Nejati R, Ott G, Padron E, Patel KP, Patkar N, Picarsic J, Platzbecker U, Roberts I, Schuh A, Sewell W, Siebert R, Tembhare P, Tyner J, Verstovsek S, Wang W, Wood B, Xiao W, Yeung C, Hochhaus A: The 5th edition of the World Health Organization Classification of haematolymphoid tumours: Myeloid and histiocytic/dendritic neoplasms. Leukemia 36(7): 1703-1719, 2022. DOI: 10.1038/s41375-022-01613-1
329 WHO Classification of Tumours Editorial Board: Soft Tissue and Bone Tumours. Vol. 3 in WHO Classification of Tumours series, 5th Edition. Lyon, France, International Agency for Research on Cancer, 2020.
330 Jayne S, López C, Put N, Nagel I, Lierman E, Penas EMM, Michaux L, Ahearne MJ, Walter HS, Bens S, Drewes C,

Szczepanowski M, Schlesner M, Rosenstiel P, Wlodarska I, Siebert R, Dyer MJS: The chromosomal translocation t(1;6)(p35.3;p25.2), recurrent in chronic lymphocytic leukaemia, leads to RCC1::IRF4 fusion. Br J Haematol 205(6): 2321-2326, 2024. DOI: 10.1111/bjh.19790

331 Panagopoulos I, Andersen K, Gorunova L, Lobmaier I: Fusion of platelet derived growth factor receptor alpha (PDGFRA) with ubiquitin specific peptidase 8 (USP8) in a calcified chondroid mesenchymal neoplasm harboring t(4;15)(q12;q21) as a sole aberration. Cancer Genomics Proteomics 21(3): 252-259, 2024. DOI: 10.21873/cgp.20444

332 Yang S, Sun M, Chen L, Zhang H, Sun L, Liu E, Tian X, Hou X, Lin Y, Lu M: WNT inhibitory factor 1 (WIF1) is a novel fusion partner of RUNX family transcription factor 1 (RUNX1) in acute myeloid leukemia with t(12;21)(q14;q22). J Hematop 17(4): 245-249, 2024. DOI: 10.1007/s12308-024-00597-4

333 Liu YZ, Zhang FH, Hou CX, Zhang ZY, Zhu YY, Wang Q, Chen Y, Chen SN: Identification of t(X;1)(q28;q21) generating a novel GATAD2B::MTCP1 gene fusion in CMML and its persistence during progression to AML. Hematology 30(1): 2439110, 2025. DOI: 10.1080/16078454.2024.2439110

334 Mikkilineni S, Pineda-Reyes JP, Wilde L, Ferber A, Wang ZX, Peiper S, Uppal G, Gong J, Liu J: Case Report: Myeloid neoplasms with the t(3;12)(q26.2;p13.1)/MECOM-ETV6 translocation: report of two new cases and review of the literature. Front Oncol 15: 1526044, 2025. DOI: 10.3389/fonc.2025.1526044

335 American Society of Hematology: 65th ASH Annual Meeting Abstracts. Blood 142(Supplement 1): 1-7445, 2023.

336 American Society of Hematology: 66th ASH Annual Meeting Abstracts. Blood 144(Supplement 1): 1-7964, 2024.

337 Thao LTT, Ha CT, Ha NTT, Beaupha SMC, Nghia H, Tung TT, Son NT, Binh NT, Dung PC, Vu HA, Xinh PT: Cytogenetic characteristics of de novo acute myeloid leukemia in Southern Vietnam. Asian Pac J Cancer Prev 24(5): 1789-1795, 2023. DOI: 10.31557/APJCP.2023.24.5.1789

338 Vundinti BR, Korgaonkar S, Dhangar S, Jijina F, Shanmukhaiah C: Frequency and pattern of chromosomal abnormalities in acute myeloid leukemia from Western India: A retrospective study. J Cancer Res Ther 19(2): 340-346, 2023. DOI: 10.4103/jcrt.jcrt_393_22

339 Brohi S, Shaikh IA, Tariq F, Tahir A, Iftikhar I, Siddiqui IA, Bokhari SW, Tariq Mahmood M, Qazi R, Ahmad U: Spectrum of cytogenetic abnormalities in adolescent and young adult patients of B-cell acute lymphoblastic leukemia in a tertiary care hospital in Pakistan. Cureus 17(4): e83122, 2025. DOI: 10.7759/cureus.83122

340 Rashidi AA, Kasaeian A, Alimoghadam K, Noori M, Alemi H, Seghatoleslami G, Salehi O, Ghavamzadeh A, Vaezi M, Mousavi SA, Kamranzadeh H, Babakhani D, Rad S, Barkhordar M, Shiraji ST, Yaghmaie M: Cytogenetic abnormalities and their impact on acute myeloid leukemia outcomes following allogeneic hematopoietic stem cell transplantation: a single-center retrospective study. Health Sci Rep 8(6): e70914, 2025. DOI: 10.1002/hsr2.70914

341 Son D, Jang HC, Lee YE, Choi YJ, Park JH, Lim HJ, Choi HJ, Baek HJ, Kook H, Kim M, Song GY, Ahn SY, Jung SH, Yang DH, Lee JJ, Kim HJ, Ahn JS, Shin MG: Chromosomal rearrangements in 1,787 cases of acute leukemia in Korea over 15 years. Ann Lab Med 45(4): 391-398, 2025. DOI: 10.3343/alm.2024.0570

342 Crabtree M, Cai J, Qing X: Conventional karyotyping and fluorescence *in situ* hybridization for detection of chromosomal abnormalities in multiple myeloma. J Hematol 11(3): 87-91, 2022. DOI: 10.14740/jh1007

343 Kadam Amare P, Nikalje Khasnis S, Hande P, Lele H, Wable N, Kaskar S, Nikam Gujar N, Gardi N, Prabhudesai A, Todi K, Waghole R, Roy P: Cytogenetic abnormalities in multiple myeloma: incidence, prognostic significance, and geographic heterogeneity in Indian and western populations. Cytogenet Genome Res 162(10): 529-540, 2022. DOI: 10.1159/000529191

344 Hamdaoui H, Nouadi B, Benlarroubia O, Chbel F, Saadoune C, Bennis F, Lamzouri A, Chegdani F: Cytogenetic abnormalities correlate with clinico-biological characteristics in 30 Moroccan multiple myeloma patients. Leuk Res Rep 20: 100392, 2023. DOI: 10.1016/j.lrr.2023.100392

345 Uryu H, Mishima Y, Ishihara Y, Shirouchi Y, Yamauchi N, Hirano M, Hirano K, Teramoto Y, Yoshida K, Maruyama D: Complex karyotype determined using conventional cytogenetic analysis is a poor prognostic factor in patients with multiple myeloma. J Clin Exp Hematop 64(1): 10-20, 2024. DOI: 10.3960/jslrt.23047

346 Gorunova L, Boye K, Panagopoulos I, Berner JM, Bjerkehagen B, Hompland I, Lobmaier I, Hølmebakk T, Hveem TS, Heim S, Micci F: Cytogenetic and molecular analyses of 291 gastrointestinal stromal tumors: site-specific cytogenetic evolution as evidence of pathogenetic heterogeneity. Oncotarget 13: 508-517, 2022. DOI: 10.18632/oncotarget.28209

347 Boye K, Gorunova L, Gunawan B, Hompland I, Sander B, Panagopoulos I, Langer C, Golas M, Heim S, Füzesi L, Hølmebakk T, Micci F: Genomic complexity as a biomarker to de-escalate adjuvant imatinib treatment in high-risk gastrointestinal stromal tumor. JCO Precis Oncol 7: e2200351, 2023. DOI: 10.1200/PO.22.00351

348 Mitelman F: Catalogue of Chromosome Aberrations in Cancer (3rd Edition). New York, NY, USA, Alan R. Liss, 1988.

349 Mitelman F: Catalogue of Chromosome Aberrations in Cancer (4th Edition). New York, NY, USA, Wiley-Liss, 1991.

350 Mitelman F: Catalogue of Chromosome Aberrations in Cancer (5th Edition). New York, NY, USA, Wiley-Liss, 1994.

351 Mitelman F: Catalogue of Chromosome Aberrations in Cancer '98 (6th Edition). New York, NY, USA, Wiley-Liss, 1998.

352 Wang J, LaFramboise T: CytoConverter: a web-based tool to convert karyotypes to genomic coordinates. BMC Bioinformatics 20(1): 467, 2019. DOI: 10.1186/s12859-019-3062-4

353 Morales J, Pujar S, Loveland JE, Astashyn A, Bennett R, Berry A, Cox E, Davidson C, Ermolaeva O, Farrell CM, Fatima R, Gil L, Goldfarb T, Gonzalez JM, Haddad D, Hardy M, Hunt T, Jackson J, Joardar VS, Kay M, Kodali VK, McGarvey KM, McMahon A, Mudge JM, Murphy DN, Murphy MR, Rajput B, Rangwala SH, Riddick LD, Thibaud-Nissen F, Threadgold G, Vatsan AR, Wallin C, Webb D, Flicek P, Birney E, Pruitt KD, Frankish A, Cunningham F, Murphy TD: A joint NCBI and EMBL-EBI transcript set for clinical genomics and research. Nature 604(7905): 310-315, 2022. DOI: 10.1038/s41586-022-04558-8

354 Gao Q, Liang WW, Foltz SM, Mutharasu G, Jayasinghe RG, Cao S, Liao WW, Reynolds SM, Wyczalkowski MA, Yao L, Yu L, Sun SQ, Fusion Analysis Working Group, Cancer Genome Atlas Research Network, Chen K, Lazar AJ, Fields RC, Wendl MC, Van Tine BA, Vij R, Chen F, Nykter M, Shmulevich I, Ding L: Driver fusions and their implications in the development and treatment of human cancers. Cell Rep 23(1): 227-238.e3, 2018. DOI: 10.1016/j.celrep.2018.03.050

355 Hu X, Wang Q, Tang M, Barthel F, Amin S, Yoshihara K, Lang FM, Martinez-Ledesma E, Lee SH, Zheng S, Verhaak RGW: TumorFusions: an integrative resource for cancer-associated transcript fusions. Nucleic Acids Res 46(D1): D1144-D1149, 2018. DOI: 10.1093/nar/gkx1018

356 Yoshihara K, Wang Q, Torres-Garcia W, Zheng S, Vegesna R, Kim H, Verhaak RG: The landscape and therapeutic relevance of cancer-associated transcript fusions. Oncogene 34(37): 4845-4854, 2015. DOI: 10.1038/onc.2014.406

357 PCAWG Transcriptome Core Group, Calabrese C, Davidson NR, Demircioğlu D, Fonseca NA, He Y, Kahles A, Lehmann KV, Liu F, Shiraishi Y, Soulette CM, Urban L, Greger L, Li S, Liu D, Perry MD, Xiang Q, Zhang F, Zhang J, Bailey P, Erkek S, Hoadley KA, Hou Y, Huska MR, Kilpinen H, Korbel JO, Marin MG, Markowski J, Nandi T, Pan-Hammarström Q, Pedamallu CS, Siebert R, Stark SG, Su H, Tan P, Waszak SM, Yung C, Zhu S, Awadalla P, Creighton CJ, Meyerson M, Ouellette BFF, Wu K, Yang H, PCAWG Transcriptome Working Group, Brazma A, Brooks AN, Göke J, Rätsch G, Schwarz RF, Stegle O, Zhang Z, PCAWG Consortium: Genomic basis for RNA alterations in cancer. Nature 578(7793): 129-136, 2020. DOI: 10.1038/s41586-020-1970-0

358 Cleynen A, Szalat R, Kemal Samur M, Robiou du Pont S, Buisson L, Boyle E, Chretien ML, Anderson K, Minvielle S, Moreau P, Attal M, Parmigiani G, Corre J, Munshi N, Avet-Loiseau H: Expressed fusion gene landscape and its impact in multiple myeloma. Nat Commun 8(1): 1893, 2017. DOI: 10.1038/s41467-017-00638-w

359 Sevov M, Bunikis I, Häggqvist S, Höglund M, Rosenquist R, Ameur A, Cavelier L: Targeted RNA sequencing assay efficiently identifies cryptic KMT2A (MLL)-fusions in acute leukemia patients. Blood 124(21): 2406-2406, 2014. DOI: 10.1182/blood.V124.21.2406.2406

360 Rubin BP, Hasserjian RP, Singer S, Janecka I, Fletcher JA, Fletcher CD: Spindle cell rhabdomyosarcoma (so-called) in adults: report of two cases with emphasis on differential diagnosis. Am J Surg Pathol 22(4): 459-464, 1998. DOI: 10.1097/00000478-199804000-00011

361 Zambrano E, Pérez-Atayde AR, Ahrens W, Reyes-Múgica M: Pediatric sclerosing rhabdomyosarcoma. Int J Surg Pathol 14(3): 193-199, 2006. DOI: 10.1177/1066896906290558

362 Panagopoulos I, Gorunova L, Lund-Iversen M, Andersen K, Andersen HK, Lobmaier I, Bjerkehagen B, Heim S: Cytogenetics of spindle cell/pleomorphic lipomas: karyotyping and FISH analysis of 31 tumors. Cancer Genomics Proteomics 15(3): 193-200, 2018. DOI: 10.21873/cgp.20077

363 Hmeljak J, Sanchez-Vega F, Hoadley KA, Shih J, Stewart C, Heiman D, Tarpey P, Danilova L, Drill E, Gibb EA, Bowlby R, Kanchi R, Osmanbeyoglu HU, Sekido Y, Takeshita J, Newton Y, Graim K, Gupta M, Gay CM, Diao L, Gibbs DL, Thorsson V, Iype L, Kantheti H, Severson DT, Ravegnini G, Desmeules P, Jungbluth AA, Travis WD, Dacic S, Chirieac LR, Galateau-Sallé F, Fujimoto J, Husain AN, Silveira HC, Rusch VW, Rintoul RC, Pass H, Kindler H, Zauderer MG, Kwiatkowski DJ, Bueno R, Tsao AS, Creaney J, Lichtenberg T, Leraas K, Bowen J, TCGA Research Network, Felau I, Zenklusen JC, Akbani R, Cherniack AD, Byers LA, Noble MS, Fletcher JA, Robertson AG, Shen R, Aburatani H, Robinson BW, Campbell P, Ladanyi M: Integrative molecular characterization of malignant pleural mesothelioma. Cancer Discov 8(12): 1548-1565, 2018. DOI: 10.1158/2159-8290.CD-18-0804

364 Iacobucci I, Wen J, Meggendorfer M, Choi JK, Shi L, Pounds SB, Carmichael CL, Masih KE, Morris SM, Lindsley RC, Janke LJ, Alexander TB, Song G, Qu C, Li Y, Payne-Turner D, Tomizawa D, Kiyokawa N, Valentine M, Valentine V, Basso G, Locatelli F, Enemark EJ, Kham SKY, Yeoh AEJ, Ma X, Zhou X, Sioson E, Rusch M, Ries RE, Stieglitz E, Hunger SP, Wei AH, To LB, Lewis ID, D'Andrea RJ, Kile BT, Brown AL, Scott HS, Hahn CN, Marlton P, Pei D, Cheng C, Loh ML, Ebert BL, Meshinchi S, Haferlach T, Mullighan CG: Genomic subtyping and therapeutic targeting of acute erythroleukemia. Nat Genet 51(4): 694-704, 2019. DOI: 10.1038/s41588-019-0375-1

365 Cheng WY, Li JF, Zhu YM, Lin XJ, Wen LJ, Zhang F, Zhang YL, Zhao M, Fang H, Wang SY, Lin XJ, Qiao N, Yin W, Zhang JN, Dai YT, Jiang L, Sun XJ, Xu Y, Zhang TT, Chen SN, Zhu HH, Chen Z, Jin J, Wu DP, Shen Y, Chen SJ: Transcriptome-based molecular subtypes and differentiation hierarchies improve the classification framework of acute myeloid leukemia. Proc Natl Acad Sci U S A 119(49): e2211429119, 2022. DOI: 10.1073/pnas.2211429119

366 Vanni R, Marras S, Faa G, Uccheddu A, Dal Cin P, Sciot R, Samson I, Van den Berghe H: Chromosome instability in elastofibroma. Cancer Genet Cytogenet 111(2): 182-183, 1999. DOI: 10.1016/s0165-4608(98)00243-x

367 Batstone P, Forsyth L, Goodlad J: Clonal chromosome aberrations secondary to chromosome instability in an elastofibroma. Cancer Genet Cytogenet 128(1): 46–47, 2001. DOI: 10.1016/s0165-4608(01)00394-6

368 McComb EN, Feely MG, Neff JR, Johansson SL, Nelson M, Bridge JA: Cytogenetic instability, predominantly involving chromosome 1, is characteristic of elastofibroma. Cancer Genet Cytogenet 126(1): 68-72, 2001. DOI: 10.1016/s0165-4608(00)00395-2

369 Spans L, Fletcher CD, Antonescu CR, Rouquette A, Coindre JM, Sciot R, Debiec-Rychter M: Recurrent MALAT1-GLI1 oncogenic fusion and GLI1 up-regulation define a subset of plexiform fibromyxoma. J Pathol 239(3): 335-343, 2016. DOI: 10.1002/path.4730

370 Graham RP, Nair AA, Davila JI, Jin L, Jen J, Sukov WR, Wu TT, Appelman HD, Torres-Mora J, Perry KD, Zhang L, Kloft-Nelson SM, Knudson RA, Greipp PT, Folpe AL: Gastroblastoma harbors a recurrent somatic MALAT1–GLI1 fusion gene. Mod Pathol 30(10): 1443-1452, 2017. DOI: 10.1038/modpathol.2017.68

371 Antonescu CR, Agaram NP, Sung YS, Zhang L, Swanson D, Dickson BC: A distinct malignant epithelioid neoplasm with GLI1 gene rearrangements, frequent S100 protein expression, and metastatic potential: expanding the spectrum of pathologic entities with ACTB/MALAT1/PTCH1-GLI1 fusions. Am J Surg Pathol 42(4): 553-560, 2018. DOI: 10.1097/PAS.0000000000001010

372 Higashi M, Hamada T, Sasaki K, Tsuruda Y, Shimonosono M, Kitazono I, Kirishima M, Tasaki T, Noguchi H, Tabata K, Hisaoka M, Fukukura Y, Ohtsuka T, Tanimoto A: Esophageal plexiform fibromyxoma: A case report with molecular analysis for MALAT1-GLI1 fusion. Pathol Res Pract 233: 153878, 2022. DOI: 10.1016/j.prp.2022.153878

373 Mosquera JM, Sboner A, Zhang L, Chen CL, Sung YS, Chen HW, Agaram NP, Briskin D, Basha BM, Singer S, Rubin MA, Tuschl T, Antonescu CR: Novel MIR143-NOTCH fusions in benign and malignant glomus tumors. Genes Chromosomes Cancer 52(11): 1075-1087, 2013. DOI: 10.1002/gcc.22102

374 Agaram NP, Zhang L, Jungbluth AA, Dickson BC, Antonescu CR: A molecular reappraisal of glomus tumors and related pericytic neoplasms with emphasis on NOTCH-gene fusions. Am J Surg Pathol 44(11): 1556-1562, 2020. DOI: 10.1097/PAS.0000000000001531

375 Miao R, Bui MM, Walko C, Mullinax JE, Brohl AS: A malignant glomus tumor of the liver harboring MIR143-NOTCH2 rearrangement: from diagnosis to management. Cureus 14(10): e30718, 2022. DOI: 10.7759/cureus.30718

376 Birkness-gartman JE, Wangsiricharoen S, Lazar AJ, Gross JM: Oesophageal glomus tumours: rare neoplasms with aggressive clinical behaviour. Histopathology 82(7): 1048-1055, 2023. DOI: 10.1111/his.14888

377 Sondka Z, Dhir NB, Carvalho-Silva D, Jupe S, Madhumita, McLaren K, Starkey M, Ward S, Wilding J, Ahmed M, Argasinska J, Beare D, Chawla MS, Duke S, Fasanella I, Neogi AG, Haller S, Hetenyi B, Hodges L, Holmes A, Lyne R, Maurel T, Nair S, Pedro H, Sangrador-Vegas A, Schuilenburg H, Sheard Z, Yong SY, Teague J: COSMIC: a curated database of somatic variants and clinical data for cancer. Nucleic Acids Res 52(D1): D1210-D1217, 2024. DOI: 10.1093/nar/gkad986

378 Jang YE, Jang I, Kim S, Cho S, Kim D, Kim K, Kim J, Hwang J, Kim S, Kim J, Kang J, Lee B, Lee S: ChimerDB 4.0: an updated and expanded database of fusion genes. Nucleic Acids Res 48(D1): D817-D824, 2020. DOI: 10.1093/nar/gkz1013

379 Heng HH, Regan SM, Liu G, Ye CJ: Why it is crucial to analyze non clonal chromosome aberrations or NCCAs? Mol Cytogenet 9: 15, 2016. DOI: 10.1186/s13039-016-0223-2

380 Rangel N, Forero-Castro M, Rondón-Lagos M: New insights in the cytogenetic practice: karyotypic chaos, non-clonal chromosomal alterations and chromosomal instability in human cancer and therapy response. Genes (Basel) 8(6): 155, 2017. DOI: 10.3390/genes8060155

381 Heng E, Thanedar S, Heng HH: The importance of monitoring non-clonal chromosome aberrations (NCCAs) in cancer research. Methods Mol Biol 2825: 79-111, 2024. DOI: 10.1007/978-1-0716-3946-7_4

382 Sánchez S, García-de-Teresa B, Mejía-Barrera MA, Reyes-Jiménez PV, Paz-Martínez A, Martínez MA, Fiesco-Roa MÓ, Monsiváis-Orozco A, Molina B, Torres L, Rodríguez A, Frias S: High burden of non-clonal chromosome aberrations before onset of detectable neoplasia in Fanconi anemia bone marrow. Cancers (Basel) 17(11): 1805, 2025. DOI: 10.3390/cancers17111805

383 Imataki O, Kubo H, Takeuchi A, Uemura M, Kadowaki N: Nonclonal chromosomal alterations and poor survival in cytopenic patients without hematological malignancies. Mol Cytogenet 12: 46, 2019. DOI: 10.1186/s13039-019-0458-9

384 Akkari YMN, Talkowski ME, Breman AM: International Society for Prenatal Diagnosis 2024 Debate 3-cytogenetics is a dinosaur and should be replaced by molecular technologies. Prenat Diagn 45(10): 1334-1342, 2025. DOI: 10.1002/pd.6847

385 Aaij C, Borst P: The gel electrophoresis of DNA. Biochim Biophys Acta 269(2): 192-200, 1972. DOI: 10.1016/0005-2787(72)90426-1

386 Sharp PA, Sugden B, Sambrook J: Detection of two restriction endonuclease activities in Haemophilus parainfluenzae using analytical agarose-ethidium bromide electrophoresis. Biochemistry 12(16): 3055-3063, 1973. DOI: 10.1021/bi00740a018

387 Borst P: Ethidium DNA agarose gel electrophoresis: How it started. IUBMB Life 57(11): 745-747, 2005. DOI: 10.1080/15216540500380855

388 Lalchhandama K: The making of modern biotechnology: How ethidium bromide made fame. Science Vision 16(1): 27-36, 2016.