STM JOURNALS

International Journal of
Cell Biology and Cellular Functions

ISSN: 3139-1834
Volume 4, Issue 1, 2026
January–June
DOI: 10.37591/IJCBCF

https://journals.stmjournals.com/ijcbcf/

Review IJCBCF

Structural–Epigenomic Atlas: CNV/SV-Driven Prognostic Refinement Across Cancers

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Abstract

Structural genomic alterations, including copy number variations (CNVs) and structural variants (SVs), play a central role in cancer initiation and progression. These alterations extend beyond gene dosage effects and interact dynamically with epigenomic mechanisms such as DNA methylation, histone modifications, and three-dimensional chromatin organization. Recent pan-cancer studies have demonstrated that CNV burden and SV signatures reflect key oncogenic processes including chromothripsis, homologous recombination deficiency, enhancer hijacking, and extrachromosomal DNA (ecDNA) amplification. These mechanisms alter transcriptional regulation through chromatin remodeling, neo-topologically associating domain formation, and enhancer–promoter interactions. Integration of multi-omics datasets, including CNV, SV, methylation, and transcriptomic data, has enabled identification of robust molecular subtypes with distinct clinical outcomes, immune microenvironments, and therapeutic responses. These integrated signatures outperform traditional single-layer biomarkers in prognostic prediction and treatment stratification. Furthermore, structural–epigenomic interactions provide insights into tumor heterogeneity, resistance mechanisms, and disease evolution. Clinical implementation of such integrative models can enhance personalized treatment strategies and improve survival outcomes. In conclusion, structural–epigenomic integration represents a transformative approach in oncology, offering improved prognostic accuracy and guiding precision medicine. Future research should focus on translating these findings into clinically applicable tools and validating them across diverse populations.

Keyword: Copy number variation, structural variants, epigenomics, cancer prognosis, multi-omics integration

INTRODUCTION

Genomic instability in cancer manifests as point mutations, arm-level and focal CNAs, and complex SVs such as chromothripsis, ecDNA, and breakage–fusion–bridge cycles. Early pan-cancer efforts (e.g., TCGA) established that copy-number alteration (CNA) patterns and burden are at least as prognostic as mutation profiles in several tumor types [1]. More recent work formalizes CNV/SV "signatures" analogous to mutational signatures, capturing specific patterns of gains, losses, and rearrangements linked to distinct oncogenic processes (e.g., HR deficiency, whole-genome doubling, ecDNA) [2].

Epigenomic states, defined by DNA methylation, histone marks, and 3-D chromatin topology, are both targets and mediators of these structural lesions. Integrative analyses demonstrate that CNV-correlated expression genes (CNVcor) and methylation-correlated expression genes (METcor) co-segregate into reproducible molecular subtypes

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Received Date: March 21, 2026
Accepted Date: March 25, 2026
Published Date: March 25, 2026

Citation: Atul Khajuria, Ashish Kumar. Structural–Epigenomic Atlas: CNV/SV-Driven Prognostic Refinement Across Cancers. International Journal of Cell Biology and Cellular Functions. 2026; 4(1): 35–43p.

with distinct outcomes, immune microenvironments, and therapeutic sensitivities [3, 4]. Thus, a pan-cancer atlas now links: (i) the type and topology of structural change, (ii) local chromatin state, and (iii) downstream transcriptional and clinical phenotypes.

LANDSCAPE OF STRUCTURAL AND COPY-NUMBER VARIATION ACROSS CANCERS

Systematic SV mapping across adult and pediatric cancers shows that SVs account for most driver events in many childhood tumors and a substantial fraction in adult solid cancers. These include canonical events (e.g., BCR ABL1, EWSR1 FLI1) and numerous non-coding rearrangements that reposition enhancers, create neo-TADs, or generate ecDNA carrying oncogenes [4, 5]. Deep whole-genome and 3-D connectome profiling in primary tumors reveals that inversions, translocations, and focal amplifications frequently rewire enhancer–promoter contacts, often without extreme copy-number changes at the target gene.

Copy-number landscapes show recurrent whole-chromosome and arm-level aneuploidies, recurrent focal amplifications (e.g., ERBB2, MYC, MDM2, CDK4), and deletions (e.g., CDKN2A/B, PTEN, TP53), as well as tumor-type-specific patterns of chromosomal instability. A conceptual CN signature framework decomposes these patterns into a limited set of recurrent "copy-number signatures" reflecting underlying biological processes such as breakage–fusion–bridge cycles, tandem duplication, and chromothripsis [6]. Clinically, global CNA burden (fraction of genome altered) is independently associated with recurrence and cancer-specific mortality across multiple TCGA and external cohorts, beyond conventional clinicopathologic factors and tumor mutation burden [7].

MECHANISTIC LINKS BETWEEN CNVS, SVS, AND THE CANCER EPIGENOME

Emerging data highlight bidirectional crosstalk between structural variation and epigenetic regulation.

Structural Variants as Epigenome Architects

Enhancer Hijacking and Neo-Tad Formation

Rearrangements that juxtapose strong enhancers with proto-oncogenes can activate transcription without point mutations, often through neo-TAD formation [8]. High-resolution 3-D genome mapping in primary cancers shows that inversions and translocations can reposition super-enhancers across hundreds of kilobases, driving activation of genes not obviously amplified by CNV analysis alone [9]. Such enhancer-driven oncogenes show binary expression patterns that correlate more strongly with enhancer connectivity than with copy-number.

ecDNA and Focal Amplification

ecDNA elements carrying oncogenes (e.g. MYC, EGFR, CDK4) create highly accessible chromatin hubs with dense enhancer contacts, extreme transcriptional output and poor prognosis [10]. These circular elements enable rapid copy-number escalation and can dynamically change abundance under therapeutic pressure, contributing to acquired resistance.

Fragile Sites and Chromatin Context

SV mapping in pediatric tumors shows that fragile sites and driver loci are preferentially disrupted by SVs, with intra-patient evolution revealing ongoing complex rearrangements during progression [11]. Regions with repressive histone marks and late replication are enriched for certain SV classes, suggesting that baseline chromatin state predisposes to specific structural lesions.

CNVs as Modulators of Enhancer Activity

CN gains can amplify both gene bodies and their associated enhancers, but integrative analyses indicate that many oncogenes are better explained by enhancer remodeling than by raw copy-number. Pan-cancer analyses show that while some top copy-driven oncogenes exhibit extreme CN changes, many enhancer-driven oncogenes have comparable CN distributions yet much higher expression, implicating local chromatin activation and 3-D rewiring. CNV-driven dosage effects on chromatin

modifiers (e.g. Histone methyltransferases, acetyltransferases, DNA methyltransferases) can globally remodel epigenomic landscapes, indirectly shaping gene expression programs and differentiation state.

Epigenetic State as a Determinant of Structural Vulnerability

Regions marked by active enhancers (H3K27ac, H3K4me1/3) and bivalent chromatin show enriched switching between active and inactive states across cancer cell lines, correlating with mutation density and DNA methylation changes. Such dynamic regions may be more permissive to SV-mediated enhancer hijacking, as they already reside in an accessible chromatin environment [12]. Conversely, hypermethylated or heterochromatic domains may suppress expression from structurally amplified loci, underlying some discordances between CN gains and mRNA levels that are resolved only by integrating methylation and transcriptomic data.

INTEGRATING CNVS WITH EPIGENOMIC STATES: MULTI-OMICS SUBTYPING

Multi-omics integration (CNV, DNA methylation, histone marks, gene expression) has been applied in several tumor types and pan-cancer settings to define molecular subtypes with prognostic relevance.

Organ-Specific Examples

Esophageal Carcinoma

Integrative analyses in esophageal cancer identified strong concordance between DNA copy-number variation and aberrant methylation, stratifying CNV-associated genes (CNV-Gs) and methylation-regulated genes (MET-Gs). ICluster-based integration of CNVs, methylation and expression defined three molecular subtypes (iC1–iC3) with distinct epigenetic traits, immune microenvironments and survival, and yielded a small panel of representative prognostic genes (e.g. CLDN3, FAM221A, GDF15, YBX2).

Hepatocellular Carcinoma

In liver cancer, joint modeling of CNVcor and METcor expression genes showed co-regulation of copy-number and methylation aberrancies, segregating tumors into three reproducible prognostic clusters. These subtypes correlate with etiologic background, chromosomal instability burden, and immune infiltration patterns, and can be validated in independent cohorts [13, 14].

NCI-60 and Diverse Cancer Cell Lines

Chromatin state maps across the NCI-60 panel revealed extensive switching between enhancer and repressed states along chromosomes, with histone mark density correlating with mutation rate, DNA methylation and gene activity. Integration with genetic mutation and CNV data underscores that combining epigenomic and structural information yields clearer functional interpretation of driver lesions than either layer alone [15].

Pan-Cancer Subtyping and Holistic Classification

Pan-cancer frameworks now classify tumors using multi-dimensional features that include CN signatures, CNA burden, SV classes, DNA methylation clusters and expression phenotypes. Holistic classification models built on large datasets (e.g. TCGA plus clinical sequencing cohorts) identify molecular groups that cut across histologic boundaries and better explain immunotherapy response variation and targeted-therapy sensitivity than single-omics taxonomies [16]. For pathologists, this implies future diagnostic reports may increasingly provide "structural–epigenomic class" labels alongside traditional histology and stage.

PROGNOSTIC CNV AND SV SIGNATURES IN A PAN-CANCER SETTING

CNA Burden and Size-Dependent Prognostic Value

Multiple studies confirm that global CNA burden (fraction of the genome with CN gains or losses) is prognostic for disease-free and overall survival across cancers such as breast, endometrial, renal clear cell, thyroid and colorectal carcinoma, independent of standard clinicopathologic variables [17, 18. Interestingly, the direction and magnitude of risk associated with CNA burden can vary by tumor type,

with colorectal and pancreatic cancers showing inverse relationships in some cohorts. Beyond global burden, pan-cancer CNV analyses in large datasets (e.g. >9, 000 TCGA tumors) demonstrate that the prognostic impact of CNVs depends on lesion size and chromosome context, leading to optimized tumor- and chromosome-specific size thresholds for risk stratification [19].

These models reveal that intermediate-size CNVs and specific co-occurrence patterns (e.g. Combined losses of key tumor suppressor regions plus gains of proliferation-promoting segments) carry strong prognostic information across diverse cancers. Incorporating such size-aware CNV signatures into clinical models refines individualized risk prediction beyond simple presence/absence of classical driver CNAs.

Copy-Number Signatures and Chromosomal Instability Phenotypes

Copy-number signature frameworks, developed using thousands of cancer genomes, deconvolute CNA profiles into a small set of recurrent patterns associated with specific etiologies (e.g. Homologous recombination deficiency, whole-genome duplication, ecDNA, breakage–fusion–bridge cycles) [20, 21]. These signatures are associated with therapeutic vulnerabilities, such as sensitivity to platinum, PARP inhibition or anti-mitotic agents, and with clinical outcomes, suggesting a role in prognostic and predictive biomarker panels. For example, tumors with high HR-deficiency-like CN signatures often show improved responses to DNA-damaging agents but may have variable long-term outcomes depending on concurrent epigenomic features and immune contexture.

Structural Variants and Enhancer-Centric Prognostic Features

High-resolution SV and 3-D genome mapping across primary cancers exposes recurrent enhancer rewiring events, including ecDNA-mediated amplifications and rearrangements that correlate with poor survival. Some enhancer-driven oncogenes remain highly expressed despite modest copy-number, with prognostic power rooted in enhancer activation patterns rather than CN amplitude [22]. Integrating SV classes, enhancer contact maps and gene expression enables derivation of prognostic signatures that capture “regulatory topology risk” rather than simply “gene dosage risk”.

CLINICAL TRANSLATION: REFINING PROGNOSTIC MOLECULAR SIGNATURES

Integrative Signatures Versus Single Layer Biomarkers

Multi-omics signatures that jointly model CNVs, epigenetic marks, and transcriptomic output generally outperform single-layer signatures in prognostic modeling. For instance, integrating CNV and methylation status of key loci with downstream expression improves risk stratification in esophageal and hepatocellular carcinoma compared with CNV-only or methylation-only models [2, 19, 22]. Similarly, adding CNA burden and CN signatures to mutation-based models increases concordance indices for survival prediction across several TCGA cohorts, and these findings have been validated in independent clinical sequencing cohorts such as MSK-IMPACT.

A pan-cancer CNV analysis demonstrates that co-occurrence patterns and optimized size thresholds add prognostic value over simply counting the number of altered chromosomes or focal events. These observations collectively argue that future prognostic signatures should explicitly encode: (i) structural context (SV class, CN signature, lesion size), (ii) epigenomic state (methylation, histone marks, 3D contacts), and (iii) resultant gene-expression modules.

Implications for Immuno-Oncology and Therapy Selection

Holistic tumor classification integrating structural and epigenomic data provides a cellular basis for variable responses to immunotherapy by mapping oncogenic programs to specific cell-of-origin and differentiation states. CNV burden and specific CN signatures may modulate neoantigen load, interferon signaling, and immune evasion pathways, influencing checkpoint inhibitor efficacy and toxicity profiles. Enhancer rewiring events in the tumor microenvironment can alter expression of immune-regulatory genes in non-cancer cells, suggesting that structural-epigenomic signatures must consider both malignant and stromal compartments for accurate prognostication [23].

Therapeutically, SV-shaped epigenomes (e.g., ecDNA-driven enhancer hubs) may be susceptible to bromodomain inhibitors, CDK7/9 inhibitors, or chromatin-targeting agents, whereas specific CN signatures may indicate sensitivity to PARP inhibitors or antimitotic regimens [15, 24]. Integrating such predictive signals into prognostic signatures will be critical for developing clinically actionable, therapy-informed risk scores.

In gliomas, structural variants (SVs) and copy-number variants (CNVs) interact with epigenomic states – particularly DNA methylation, histone modifications, and 3D chromatin architecture – to generate prognostic signatures that refine beyond IDH/1p19q/MGMT status, capturing tumor cell states, neuronal integration, and evolutionary dynamics. This integration reveals molecular subtypes with distinct survival outcomes, therapeutic vulnerabilities, and microenvironmental features, emphasizing enhancer hijacking, ecDNA, and neural-like epigenetic reprogramming [22, 25].

Glioma CNV/SV Landscape

Adult gliomas exhibit recurrent CNVs, including EGFR amplification (+7/–10), CDKN2A/B homozygous deletion (9p21), PTEN loss (10q), and PDGFRA amplification (4q12), often co-occurring with SVs that amplify enhancers or form ecDNA. In pediatric high-grade gliomas (pHGG), SVs recurrently target MYC enhancers (e.g., CCDC26 tandem duplications activating MYC via neural-specific H3K27ac peaks), RTKs (PDGFRA, EGFR, MET with enhancer-rich amplicons), and MYCN via ID2 enhancer hijacking on ecDNA. Lower-grade gliomas (LGG) show chr1q/7p/11q gains and chr2q/3p/9q/10q losses, with CNV burden correlating inversely with survival in IDH-mutant cases [16, 22, 26].

SV signatures classify gliomas into simple (deletions, duplications, translocations/inversions) versus complex (chromothripsis, BFB, chromoplexy), where complex patterns associate with TP53/RB1/CDKN2A alterations and ecDNA, driving rapid evolution.

Epigenomic Modulation in Glioma

DNA methylation classifiers (e.g., DKFZ) define glioma subtypes: IDH-mutant (G-CIMP-high), H3 K27-altered, RTK I/II (PDGFRA/EGFR-enriched), and mesenchymal. CNVs/SVs reshape epigenomes by disrupting TADs, amplifying enhancers (e.g., SEC61G for EGFR, CAPZA2 for MET), or creating neo-enhancer contacts, upregulating oncogenes without coding-sequence gains [4, 9].

Neural epigenetic signatures – hypomethylated CpGs in synaptic/invasivity genes (e.g., GRIN3A, SYT4, SNAP25) – define high-neural gliomas with OPC/NPC/astrocyte-like states, increased OLIG2+ cells, and stemness (28% vs. 17% in low-neural). These correlate with H3K27ac at SV-amplified loci and 3D rewiring promoting MYC/MYCN via enhancer-TAD loops [5, 27, 28].

PROGNOSTIC MULTI-OMICS SIGNATURES

Classical/RTK Subtypes

EGFR-amplified (+7/–10, often ecDNA) gliomas show classical signatures, with enhancer SVs (e.g., SEC61G) driving expression; high CNA burden predicts poor OS independent of MGMT. PDGFRA SVs incorporate KIT/KDR enhancers, associating with complex SVs and shorter survival in DMG (Table 1) [21].

Table 1. Prognostic significance of CNV/SV-driven classical and RTK-associated molecular subtypes in gliomas, highlighting key genomic alterations, epigenomic features, and survival outcomes.

Subtype	Key CNV/SV	Epigenomic feature	Prognosis (median OS)	References
Classical (EGFR+)	+7/–10, ecDNA	SEC61G enhancer amp, H3K27ac ↑	12–15 mo	[19]
PDGFRA/RTK I	4q12 amp, enhancer SV	KIT/KDR co-amp, TAD disruption	10–14 mo (DMG)	[12)]
MYC-driven	8q24 SV (CCDC26)	Neural enhancer amp, MYC loop ↑	Worse in H3K27M	[21, 24]

Neural-Epigenetic Signature

High-neural gliomas (neural score > 0.41 via deconvolution) exhibit synaptic proteome (PSD95/Synapsin colocalization ↑), neuron-glioma synapses, and functional connectivity (MEG/rs-fMRI), predicting shorter OS (14 vs. 21 mo) and PFS (6 vs. 10 mo) independent of resection/MGMT. Validated in TCGA (12 vs. 17 mo); associates with PIK3CA/TP53 mutations, stemness, low immunity [29].

IDH-Mutant/LGG Integration

In IDH-mutant gliomas, CNV-miR/methylation subtypes (CNV_C1/DNAmC2 overlap) show chr1q/7p/11q gains with miRNA dysregulation, outperforming grade/1p19q for prognosis; high CNA (BAF segments) links to better OS paradoxically via immune/TIL effects [30].

Breast cancer CNVs and SVs profoundly interact with epigenomic states, like H3K4 methylation and DNA methylation, to shape subtypes and prognostic signatures, particularly distinguishing aggressive triple-negative (TNBC) from luminal tumors. This multi-omics lens refines risk beyond ER/PR/HER2, revealing enhancer-driven oncogenesis, immune modulation, and therapy resistance via ecDNA and TAD disruptions [31].

BREAST CANCER CNV/SV LANDSCAPE

Recurrent CNVs include 1q/8q/16p/20q gains (MYC, MDM2, ZNF217) and 8p/11q/13q/16q/17p losses (RB1, BRCA1); SVs mediate 10–20% of drivers via fusions (e.g., ESR1-YAP1) and enhancer hijacking. TNBC shows highest SV burden (e.g., TP53 deletions, PIK3CA amps) and complex rearrangements (chromothripsis, BFB); luminal tumors favor arm-level CNAs. Long-read SV analysis in SKBR3 (HER2+) uncovers hundreds of missed variants in ERBB2, APOBEC3B, CDH1 [19, 32].

SVs cluster into simple (del/dup) vs. Complex (chromoplexy), with complex SVs enriching TP53/BRCA1 mutations and poor OS in early BC.

Epigenomic Crosstalk

H3K4me1/2 ↑ in TNBC sustains mesenchymal/stem-like states via enhancer activation; H3K27me3 ↓ enables oncogene derepression. CNV-correlated methylation (e.g., hypermethylated CpGs in CpG islands with del CNVs) drives subtype-specific profiles; SVs rewire TADs, amplifying distal enhancers for ESR1/MYC [33].

CNV-related DEGs (649 from TCGA) enrich PPAR/PI3K-Akt pathways; hypomethylation in SV-overlapping promoters correlates with immune evasion (Table 2).

PROGNOSTIC MULTI-OMICS SIGNATURES

Subtype-Specific Patterns

Nine-gene CNV signature (ANO6↑, CELSR3↑, CLDN7↑ protective; GPLD1↓, PPARG↓ risky) stratifies TCGA/GEO cohorts (AUC 0.7–0.8, 1–5 yr); high-risk: TP53↑/PIK3CA↓ mut, high immune/stromal score, advanced T/N. Eleven-gene (CNV/MSI/TMB-integrated) model independently predicts OS (HR > 2), validated ICGC [18, 21, 34].

Table 2. Integrated subtype-specific copy number and structural variation profiles in breast cancer, with corresponding epigenomic traits and 5-year overall survival estimates.

Subtype	Key CNV/SV	Epigenomic trait	Prognosis (5-yr OS)	References
Luminal A	16q loss, 1q gain	G-CIMP-like, H3K27me3 ↑	90–95%	[24]
TNBC	TP53 del, 5q amp, ecDNA	H3K4me ↑, hypoMe ↑	60–70%	[28]
HER2+ (SKBR3-like)	ERBB2 amp/ecDNA, SVs	Enhancer hijack, APOBEC ↑	75–85%	[35]

H3K4me2 ChIP-seq distinguishes TNBC (distal enhancer ↑) from LuA, linking CNV burden to immune-hot phenotypes but poor response.

HCC CNV/SV LANDSCAPE

HCC genomes feature 8q24 (MYC) gains, 1p/4q/8p/9p/13q/16q/17p losses (e.g., CDKN2A, AXIN1); SVs drive 20–30% of drivers via fusions (TERT, TP53) and chromothripsis. HBV integration amplifies CNVs (e.g., CCND1, FGF19); iC1 subtype shows chr1/11/14 CNV enrichment, complex SVs. CNV burden correlates with aggressive proliferation (cell cycle, p53 pathways).

Epigenomic Crosstalk

CNV gains associate with enhancer activation (H3K27ac ↑), hypomethylation at TSS; losses with hypermethylation silencing TS genes (e.g., IGF2 hyperMe despite gain). Aberrant enhancers (AE) drive six-gene signature; METcor genes (hypoMe ↑ expression) overlap CNVcor in iC1. Histone dysregulation (EZH2 ↑, H3K27me3 ↓) enables oncogene derepression; chr8 gains amplify EZH2 (Table 3) [18, 24, 35].

Prognostic Multi-Omics Signatures

Molecular Subtypes

8-gene CNV-driven signature (CDCA8↑, EZH2↑, CBX2↑ high-risk) predicts OS (AUC 0.70-0.77 TCGA/ICGC); high-risk: neutrophil ↑, CTLA4/TIM3 ↑. 6-AE-DEG model superior to clinical; ANXA2/CHAF1B (iC1 ↑, CNV gain/hypoMe) confirm poor OS (HR>2).

Table 3. Molecular subtypes of hepatocellular carcinoma defined by CNV/SV patterns and epigenomic alterations, and their association with clinical prognosis and median overall survival.

Subtype	CNV/SV pattern	Epigenomic trait	Prognosis (median OS)	References
iC1 (Proliferation/Immune-hot)	chr1/5/11 gains, complex SV	HypoMe ↑, H3K4me ↑, AE ↑	12–18 mo	[15]
iC2 (Metabolic/Differentiated)	chr9/17 losses	HyperMe ↑, H3K27me3 ↑	>30 mo	[28]

CONCLUSION

Structural–epigenomic integration represents a paradigm shift in understanding cancer biology. CNVs and SVs dynamically interact with epigenomic mechanisms to influence gene expression, tumor evolution, and clinical outcomes.

These interactions highlight the importance of moving beyond mutation-centric approaches toward integrative multi-omics models. Such models provide superior prognostic accuracy and enable personalized treatment strategies.

The incorporation of structural–epigenomic signatures into clinical workflows has the potential to improve risk stratification, guide therapeutic decision-making, and enhance patient outcomes. Future research should focus on validating these findings in diverse populations, developing cost-effective diagnostic tools, and translating complex multi-omics data into clinically actionable insights.

In conclusion, structural–epigenomic integration is essential for advancing precision oncology and represents a critical step toward improving cancer care worldwide.

REFERENCES

1. Weinstein JN, Collisson EA, Mills GB, Shaw KR, Ozenberger BA, Ellrott K, et al. The cancer genome atlas pan-cancer analysis project. Nat Genet. 2013 Oct;45(10):1113–1120.
2. Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, et al. Cell-of-origin patterns dominate the molecular classification of 10,000 tumors from 33 types of cancer. Cell. 2018 Apr 5;173 (2):291–304.
3. Hieronymus H, Murali R, Tin A, Yadav K, Abida W, Moller H, et al. Tumor copy number alteration burden is a pan-cancer prognostic factor associated with recurrence and death. eLife. 2018 Sep 4;7:e37294.

4. Steele CD, Abbasi A, Islam SA, Bowes AL, Khandekar A, Haase K, et al. Signatures of copy number alterations in human cancer. Nature. 2022 Jun 30;606(7916):984–991.
5. MacLennan S, Marra MA. How structural variation shapes the cancer epigenome. Trends Cancer. 2025 Sep 30.
6. Ma M, Chen Y, Chong X, Jiang F, Gao J, Shen L, et al. Integrative analysis of genomic, epigenomic and transcriptomic data identified molecular subtypes of esophageal carcinoma. Aging (Albany NY). 2021 Feb 26;13(5):6999.
7. Woo HG, Choi JH, Yoon S, Jee BA, Cho EJ, Lee JH, et al. Integrative analysis of genomic and epigenomic regulation of the transcriptome in liver cancer. Nat Commun. 2017 Oct 10;8:839.
8. Raleigh D, Nguyen M, Chen W, Zakimi N, Mirchia K, Lucas CH. Pan-cancer copy number variant analysis identifies optimized size thresholds and co-occurrence models for individualized risk-stratification. Res Sq. 2024 Jan 11:rs-3.
9. Gröbner SN, Worst BC, Weischenfeldt J, Buchhalter I, Kleinheinz K, Rudneva VA, et al. The landscape of genomic alterations across childhood cancers. Nature. 2018;555(7696):321–7. doi: 10.1038/nature25480.
10. Yost KE, Zhao Y, Hung KL, Zhu K, Xu D, Corces MR, et al. Three-dimensional genome landscape of primary human cancers. Nat Genet. 2025;57(5):1189–200.
11. Drexler R, Khatri R, Sauvigny T, Mohme M, Maire CL, Ryba A, et al. A prognostic neural epigenetic signature in high-grade glioma. Nat Med. 2024 Jun;30(6):1622–1635.
12. Dubois FP, Shapira O, Greenwald NF, Zack T, Wala J, Tsai JW, et al. Structural variants shape driver combinations and outcomes in pediatric high-grade glioma. Nat Cancer. 2022 Aug;3(8):994–1011.
13. Nik-Zainal S, Davies H, Staaf J, Ramakrishna M, Glodzik D, Zou X, et al. Landscape of somatic mutations in 560 breast cancer whole-genome sequences. Nature. 2016 Jun 2;534(7605):47–54.
14. Turner KM, Deshpande V, Beyter D, Koga T, Rusert J, Lee C, et al. Extrachromosomal oncogene amplification drives tumour evolution and genetic heterogeneity. Nature. 2017 Mar 2;543(7643):122–125.
15. Capper D, Jones DT, Sill M, Hovestadt V, Schrimpf D, Sturm D, et al. DNA methylation-based classification of central nervous system tumours. Nature. 2018 Mar 22;555(7697):469–474.
16. Hu W, Li M, Zhang Q, Liu C, Wang X, Li J, et al. Establishment of a novel CNV-related prognostic signature predicting prognosis in patients with breast cancer. J Ovarian Res. 2021 Aug 8;14(1):103.
17. Thorsson V, Gibbs DL, Brown SD, Wolf D, Bortone DS, Yang TH, et al. The immune landscape of cancer. Immunity. 2018 Apr 17;48(4):812–830.
18. Hnisz D, Abraham BJ, Lee TI, Lau A, Saint-André V, Sigova AA, et al. Super-enhancers in the control of cell identity and disease. Cell. 2013 Nov 7;155(4):934–947.
19. Fontebasso AM, Jabado N. Chromatin regulators shape the oncogenic epigenome in cancer. Cancer Cell. 2015;28(5):557–559.
20. Degasperi A, Amarante TD, Czarnecki J, Shooter S, Zou X, Glodzik D, et al. A practical framework and online tool for mutational signature analyses show intertissue variation and driver dependencies. Nat Cancer. 2020 Feb 14;1(2):249–263.
21. Verhaak RG, Hoadley KA, Purdom E, Wang V, Qi Y, Wilkerson MD, et al. Integrated genomic analysis identifies clinically relevant subtypes of glioblastoma characterized by abnormalities in PDGFRA, IDH1, EGFR, and NF1. Cancer Cell. 2010 Jan 19;17(1):98–110.
22. Cancer Genome Atlas Research Network. Comprehensive, integrative genomic analysis of diffuse lower-grade gliomas. N Engl J Med. 2015 Jun 25;372(26):2481–2498.
23. Shen Y, Xiong W, Gu Q, Zhang Q, Yue J, Liu C, et al. Multi-omics integrative analysis uncovers molecular subtypes and mRNAs as therapeutic targets for liver cancer. Front Med (Lausanne). 2021 May 24;8:654635.
24. Woo HG, Choi JH, Yoon S, Jee BA, Cho EJ, Lee JH, et al. Integrative analysis of genomic and epigenomic regulation of the transcriptome in liver cancer. Nat Commun. 2017 Oct 10;8:839.
25. Wang K, Lim HY, Shi S, Lee J, Deng S, Xie T, et al. Genomic landscape of copy number aberrations enables the identification of oncogenic drivers in hepatocellular carcinoma. Hepatology. 2013 Aug;58(2):706–717.

26. Guichard C, Amaddeo G, Imbeaud S, Ladeiro Y, Pelletier L, Maad IB, et al. Integrated analysis of somatic mutations and focal copy-number changes identifies key genes and pathways in hepatocellular carcinoma. Nat Genet. 2012 Jun;44(6):694–698.
27. Zack TI, Schumacher SE, Carter SL, Cherniack AD, Saksena G, Tabak B, et al. Pan-cancer patterns of somatic copy number alteration. Nat Genet. 2013 Oct;45(10):1134–1140.
28. Zack TI, Schumacher SE, Carter SL, Cherniack AD, Saksena G, Tabak B, et al. Pan-cancer patterns of somatic copy number alteration. Nat Genet. 2013 Oct;45(10):1134–1140.
29. Mermel CH, Schumacher SE, Hill B, Meyerson ML, Beroukhim R, Getz G. GISTIC2.0 facilitates sensitive and confident localization of the targets of focal somatic copy-number alteration in human cancers. Genome Biol. 2011 Apr 28;12(4):R41.
30. Yang J, Wang Q, Zhang ZY, Long L, Ezhilarasan R, Karp JM, et al. DNA methylation-based epigenetic signatures predict somatic genomic alterations in gliomas. Nat Commun. 2022 Jul 29;13(1):4410.
31. Yang Z, Liu X, Xu H, Teschendorff AE, Xu L, Li J, et al. Integrative analysis of genomic and epigenomic regulation reveals miRNA-mediated tumor heterogeneity and immune evasion in lower grade glioma. Commun Biol. 2024 Jul 6;7(1):824.
32. Aganezov S, Goodwin S, Sherman RM, Sedlazeck FJ, Arun G, Bhatia S, et al. Comprehensive analysis of structural variants in breast cancer genomes using single-molecule sequencing. Genome Res. 2020 Sep 1;30(9):1258–1273.
33. Jin X, Yan J, Chen C, Chen Y, Huang WK. Integrated analysis of copy number variation, microsatellite instability, and tumor mutation burden identifies an 11-gene signature predicting survival in breast cancer. Front Cell Dev Biol. 2021 Sep 28;9:721505.
34. Huang P, Zhang B, Zhao J, Li MD. Integrating the epigenome and transcriptome of hepatocellular carcinoma to identify systematic enhancer aberrations and establish an aberrant enhancer-related prognostic signature. Front Cell Dev Biol. 2022 Mar 1;10:827657.
35. Wang C, Yao C, Sun Y, Chen J, Ge Y, Wang Y, et al. Identification and verification of a novel epigenetic-related gene signature for predicting the prognosis of hepatocellular carcinoma. Front Genet. 2022 Nov 30;13:897123.

