

MINI-REVIEW

Seeing the whole elephant: From fragmented findings to integrative oncology

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Abstract

Cancer research has long faced the “Blind Men and the Elephant” dilemma, a metaphor derived from an ancient Indian parable. In the story, several blind men each touch a different part of an elephant—its trunk, leg, ear, or tail—and conclude that the creature resembles a snake, tree, fan, or rope. Each perception is valid within its narrow scope but incomplete when viewed in isolation. Similarly, cancer research has often been fragmented, with investigators focusing on isolated molecular pathways, cellular behaviors, or clinical outcomes without fully connecting these pieces into a unified picture of the disease. This systematic review explores how integrative and multidisciplinary approaches are overcoming that fragmentation to reshape our understanding of cancer. Drawing on advances in systems biology, multi-omics technologies, artificial intelligence, and collaborative research frameworks, we illustrate how convergence across disciplines enables a more comprehensive view of tumor biology and therapeutic response. Major initiatives such as The Cancer Genome Atlas, pan-cancer analyses, and emerging computational platforms exemplify how data integration can reveal patterns invisible to single-dimension studies. By highlighting both the transformative potential and persistent challenges of such integration—ranging from data harmonization to interdisciplinary communication—we propose a roadmap toward a holistic, collaborative, and patient-centered paradigm in oncology. In doing so, we aim to move beyond the limitations of partial understanding toward a collective vision that more accurately reflects the complexity of cancer.

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Citation: Wu L. Seeing the whole elephant: From fragmented findings to integrative oncology. *Tumor Discov.* 2026;5(2):025270059. doi: 10.36922/TD025270059

Received: June 30, 2025

Revised: October 11, 2025

Accepted: November 7, 2025

Published online: November 21, 2025

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Keywords: Cancer research; Multi-omics; Interdisciplinary integration; Pan-cancer analysis; Computational oncology; Translational medicine

1. Introduction

The parable of the blind men and the elephant aptly illustrates the present state of cancer research: Each discipline—whether genomics, immunology, pathology, or clinical oncology—often perceives only a fragment of the disease, leading to incomplete or even conflicting interpretations. Despite substantial advances in diagnostics, targeted therapies, and immuno-oncology, cancer remains a leading cause of death worldwide, responsible for nearly 10 million deaths annually.¹ One of the major barriers to durable treatment success lies in the intrinsic complexity of cancer, including inter- and intra-

tumor heterogeneity,² adaptive resistance mechanisms,³ and the multifaceted tumor microenvironment that fosters immune evasion and therapeutic failure.⁴

This review explores how integrative and multidisciplinary strategies are being deployed to overcome these limitations. Systems biology approaches model cancer as a dynamic network rather than a linear pathway, enabling prediction of emergent behaviors under therapeutic perturbation.⁵ Multi-omics platforms, including genomics, transcriptomics, proteomics, and metabolomics, permit comprehensive characterization of tumors at multiple biological levels, yielding insights into regulatory crosstalk and therapeutic vulnerabilities.⁶ Artificial intelligence (AI) and machine learning are increasingly used to integrate these high-dimensional datasets to uncover patterns predictive of prognosis or treatment response.⁷

Landmark initiatives, such as The Cancer Genome Atlas (TCGA) and the Pan-Cancer Analysis of Whole Genomes (PCAWG), have laid the foundation for integrative efforts by cataloguing molecular alterations across diverse tumor types.^{8,9} Emerging platforms, such as the Human Tumor Atlas Network and Cancer Grand Challenges, further emphasize collaborative, multi-institutional approaches to dissect the spatial and temporal dynamics of cancer.¹⁰

By synthesizing advances across disciplines, this review proposes a roadmap for a more holistic, patient-centered paradigm in oncology—one that transcends reductionist silos and embraces the complexity of cancer as a systems-level disease. This review, “Seeing the Whole Elephant: From Fragmented Findings to Integrative Oncology,” provides a broad conceptual and evidence-based framework for integrative cancer research. The metaphor “Seeing the Whole Elephant” conveys the idea of understanding a complex system—such as cancer or integrative oncology—in its entirety, rather than focusing on isolated parts, emphasizing holistic insight over reductionist views (Figure 1).

2. From reductionism to integration: The rise of systems thinking

Traditional cancer research has long relied on a reductionist framework, dissecting individual genes, proteins, or pathways in isolation. This approach has yielded critical insights, such as the discovery of oncogenes and tumor suppressors, but falls short when confronted with the non-linear, adaptive, and context-dependent nature of cancer.¹¹ Tumors are not merely aggregates of malignant cells but complex ecosystems involving stromal components, immune cells, metabolic cues, and dynamic feedback loops.¹² The failure of many targeted therapies can be partly

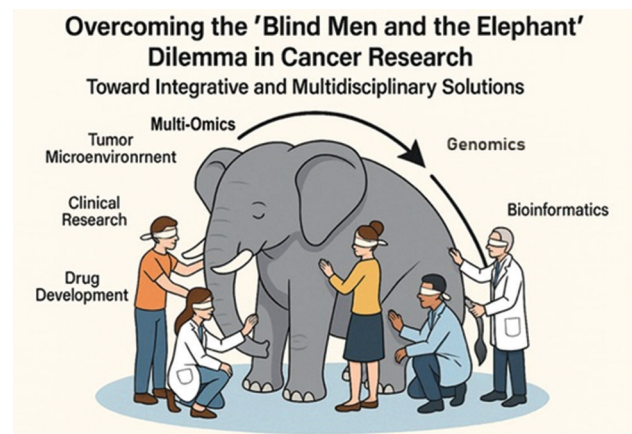


Figure 1. Toward integrative oncology: Systems thinking, multi-omics, and cross-disciplinary insights. This conceptual illustration represents the “Blind Men and the Elephant” dilemma in cancer research, highlighting the limitations of isolated disciplinary perspectives and the need for integrative, multidisciplinary approaches. The central elephant symbolizes the complexity and heterogeneity of cancer as a disease. Surrounding the elephant are five blindfolded researchers, each representing a distinct field: Tumor microenvironment, clinical research, drug development, genomics, and bioinformatics. Each investigator touches a different part of the elephant, metaphorically illustrating the partial understanding derived from siloed expertise. Arrows connecting their efforts converge toward a unified direction, signifying the integration of diverse knowledge domains into a cohesive framework for cancer discovery and therapy. This figure emphasizes the necessity of collaborative models that synthesize molecular, cellular, clinical, and computational insights to advance precision oncology and overcome fragmentation in cancer research. It underscores a paradigm shift toward systems-level thinking and cross-disciplinary synergy to resolve the complex biological landscape of cancer. This figure was generated using the ChatGPT platform.

attributed to this fragmented view, which often overlooks compensatory mechanisms and network-level resilience.¹³

In response, systems biology has emerged as a transformative paradigm, integrating data across multiple omics layers, including genomics, transcriptomics, proteomics, epigenomics, and metabolomics, to model cancer as a dynamic, interconnected system.¹⁴ Rather than studying single variables in isolation, systems approaches aim to understand interactions, feedback loops, and emergent behaviors that drive tumor progression or therapeutic resistance.¹⁵ High-throughput technologies and computational tools now enable the reconstruction of gene regulatory networks, signaling cascades, and cellular states with unprecedented resolution.¹⁶

Importantly, this systems perspective supports a shift from static snapshots to dynamic modeling. Time-series data and perturbation experiments are increasingly used to map the trajectories of tumor evolution and drug response.¹⁷ For example, dynamic network biomarkers can predict critical transitions in tumor progression before

phenotypic changes become apparent.¹⁸ These insights offer new opportunities for early detection, combination therapy design, and precision medicine.

Ultimately, systems thinking represents more than a technological upgrade, which is a conceptual shift that embraces cancer's complexity and seeks holistic understanding. By transcending reductionism, systems biology provides a framework to decode the emergent properties of malignancy and guide more effective interventions (Table 1).

3. Multi-omics integration: Decoding cancer complexity

Cancer is a multifactorial disease characterized by alterations across multiple biological layers, including DNA mutations, RNA expression changes, protein modifications, and metabolic reprogramming. Traditional single-omics studies provide valuable but limited snapshots of these alterations. In contrast, multi-omics approaches integrate data from genomics, transcriptomics, proteomics, epigenomics, and metabolomics to construct a more holistic and mechanistic view of tumor biology.¹⁹ This integrative strategy enables researchers to uncover cross-talk between molecular layers, identify converging pathways, and reveal emergent properties that would remain hidden in isolated datasets.²⁰

Notably, multi-omics integration has transformed cancer subtyping and biomarker discovery. Studies from TCGA and the Clinical Proteomic Tumor Analysis Consortium have shown that combining genomic and proteomic data refines tumor classification and improves prognostic accuracy.^{21,22} For example, in breast and ovarian cancers, proteogenomic analyses revealed protein expression patterns that are not always concordant with messenger ribonucleic acid levels, pointing to post-transcriptional regulation as a key determinant of phenotype.²³ Such insights provide novel targets for therapeutic intervention.

Moreover, multi-omics data support the development of personalized cancer therapies by identifying patient-specific molecular vulnerabilities.²⁴ Integration of metabolomic profiles with genomic mutations has uncovered distinct metabolic signatures linked to oncogenic drivers, offering potential biomarkers for diagnosis and response prediction.²⁵ Machine learning techniques further enhance the utility of these datasets, enabling the stratification of patients based on integrative molecular signatures and improving clinical outcome prediction.²⁶

Ultimately, multi-omics approaches represent a paradigm shift from linear to network-based models of cancer. By embracing the complexity of the disease, these methods enable more accurate characterization of tumor heterogeneity, deeper biological insights, and more effective, individualized treatment strategies

4. Pan-cancer and functional genomics: Cross-tumor insights

Large-scale genomics initiatives such as TCGA and the PCAWG have fundamentally reshaped the landscape of cancer biology. By compiling and harmonizing multi-omics data across dozens of tumor types, these efforts have enabled researchers to identify both cancer-specific and pan-cancer molecular features.^{7,27} Shared alterations in oncogenes, tumor suppressors, epigenetic regulators, and non-coding regions suggest that many cancers converge on common pathways of dysregulation, despite originating in different tissues.²⁸ This cross-tumor perspective has illuminated universal hallmarks of tumorigenesis, including disruptions in cell cycle regulation, DNA repair, and immune evasion.²⁹

Pan-cancer analyses have also improved tumor classification by uncovering molecular subtypes that transcend traditional histological boundaries. For instance, molecular subtyping based on RNA expression, mutation

Table 1. A comparison of different aspects between reductionism view and systems thinking in oncology

Dimension	Reductionist view	Systems thinking/integrative view
Focus	Single gene/protein/pathway	Networks, pathways, feedback loops
Scale	Molecular/cellular	Multi-scale (molecular to organismal to societal)
Approach	Linear causality	Complex interactions
Tools	PCR, Western blot, IHC	Multi-omics, AI, network modeling
Diagnosis	Biomarkers	Multi-modal signatures (e.g., radiogenomics)
Treatment	Targeted monotherapy	Combination, immunotherapy, adaptive strategies
Outcome prediction	Single variable-based	Integrated risk models
Clinical decision- making	Based on histology/genetics	Data-driven, real-time personalized models

Abbreviations: AI: Artificial intelligence; IHC: Immunohistochemistry; PCR: Polymerase chain reaction.

profiles, and methylation patterns has revealed that tumors from anatomically distinct sites can share similar oncogenic programs.³⁰ Such insights are increasingly guiding basket trials and tissue-agnostic therapeutic strategies, exemplified by food and drug administration (FDA) approvals of neurotrophic tyrosine receptor kinase (NTRK) and microsatellite instability-high (MSI-H) inhibitors across cancer types.³¹

In parallel, functional genomics approaches such as genome-wide CRISPR-Cas9 screens and *in vivo* perturbation studies have been critical in identifying essential genes, synthetic lethal interactions, and resistance mechanisms.³² These studies help distinguish driver mutations from passenger alterations and prioritize therapeutic targets. For example, systematic loss-of-function screening has revealed cancer-specific dependencies, such as the reliance of SMARCA4-deficient tumors on SMARCA2.³³

Together, pan-cancer and functional genomics offer a powerful synergy: While pan-cancer data map the common genomic architecture of tumors, functional studies validate the biological relevance of these findings in diverse cellular and *in vivo* contexts. This integrative framework accelerates the translation of genomic insights into precision therapies and fosters a deeper, more unified understanding of cancer biology. [Figure 2](#) provides a comprehensive pan-cancer analysis of copy number variations and single-nucleotide variations across selected cancer types (*e.g.*, colon cancer, breast cancer, and lung cancer), illustrating gene amplifications, deletions, mutation types, and their functional implications (<https://guolab.wchscu.cn/GSCA/>).

5. AI and computational modeling in oncology

The rapid expansion of multi-omics data, imaging, and clinical records in oncology has created unprecedented opportunities and challenges for data interpretation. AI and machine learning (ML) have emerged as transformative tools capable of processing high-dimensional datasets, uncovering hidden patterns, and generating clinically actionable insights.³⁴ These technologies are increasingly applied across the cancer research continuum, from biomarker discovery to drug development and patient stratification.³⁵

In particular, AI algorithms have demonstrated remarkable success in integrating heterogeneous data modalities, such as genomics, transcriptomics, radiomics, and electronic health records, to improve cancer diagnosis, prognosis, and therapy selection.³⁶ For instance, deep learning models trained on histopathological images

can accurately predict molecular subtypes and mutation status, outperforming conventional pathology.³⁷ Similarly, ML classifiers using multi-omics profiles have been used to identify responders to immune checkpoint inhibitors, guiding precision immunotherapy.³⁸

Beyond predictive analytics, computational modeling plays a vital role in simulating tumor dynamics, drug responses, and resistance evolution. Mechanistic and data-driven models help elucidate how molecular perturbations propagate through signaling networks and influence tumor behavior.³⁹ Agent-based models, for example, have been employed to study spatial heterogeneity, clonal competition, and tumor-immune interactions *in silico*.⁴⁰ These simulations support hypothesis generation, treatment optimization, and adaptive therapy design.

Importantly, AI-driven approaches also accelerate drug discovery by predicting compound-target interactions and optimizing drug combinations.⁴¹ Integrative platforms, such as DeepChem and AlphaFold2, are redefining structural biology and molecular docking, further expanding the scope of computational oncology.

While challenges such as data standardization, interpretability, and clinical integration remain, AI and computational modeling represent a powerful frontier in cancer research. By bridging biological complexity and clinical application, these tools enhance our ability to decode cancer and deliver more personalized, effective treatments.

6. Multidisciplinary collaboration: Bridging disciplines for holistic care

Cancer is not merely a genetic or cellular disease, which is a multifaceted challenge that spans molecular biology, clinical oncology, engineering, data science, behavioral medicine, and public health. Addressing this complexity requires a multidisciplinary approach that fosters integration of diverse perspectives and expertise. Unlike siloed research paradigms, collaborative models enable the co-development of technologies, therapies, and clinical frameworks that are more comprehensive and patient-centered.⁴²

Successful examples include multidisciplinary tumor boards, where oncologists, pathologists, radiologists, surgeons, and bioinformaticians collectively assess patient data to guide personalized treatment decisions.⁴³ On a larger scale, institutions such as the Parker Institute for Cancer Immunotherapy and the Stand Up To Cancer consortia have demonstrated the power of structured collaboration.^{44,45} These initiatives promote shared

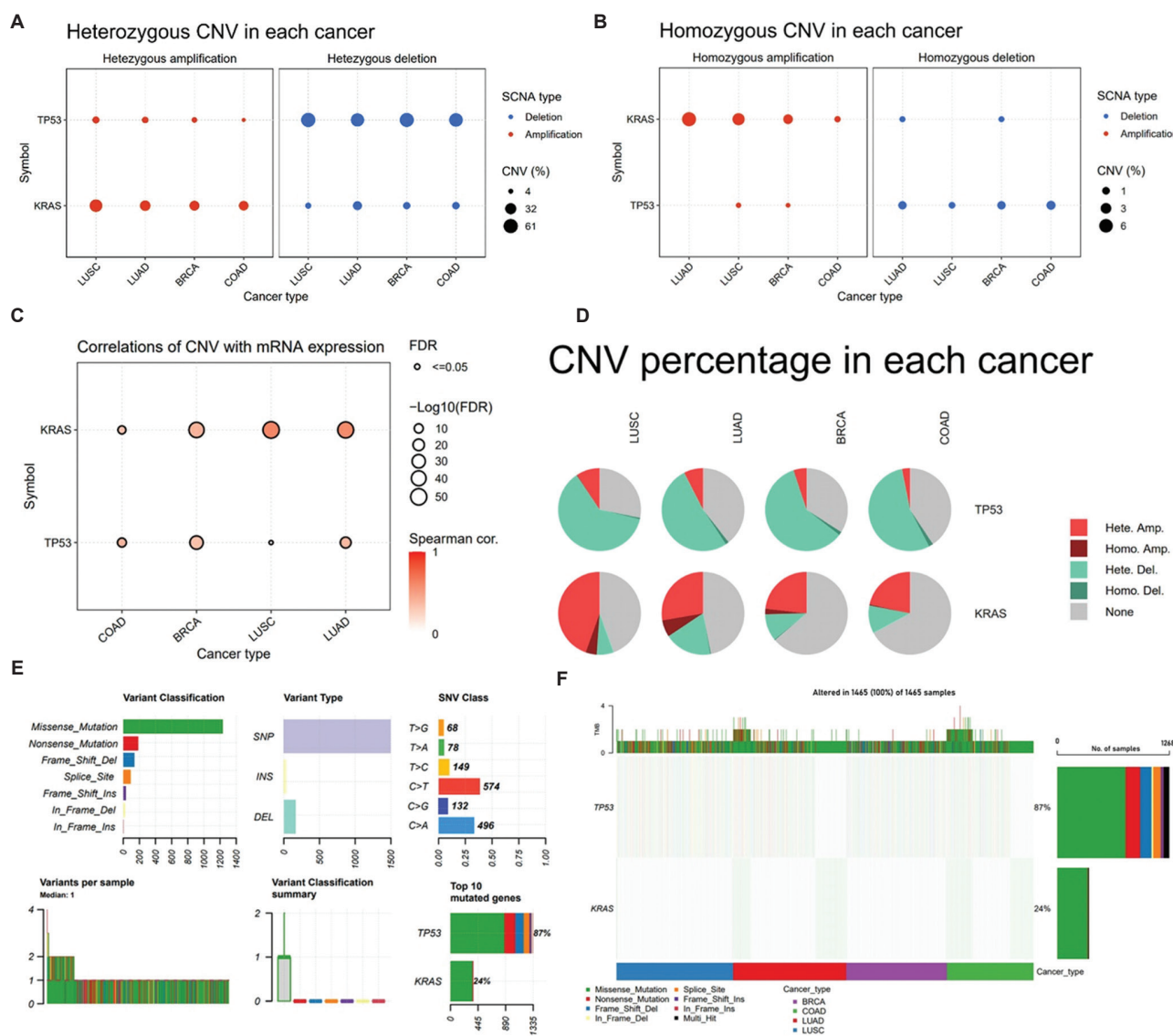


Figure 2. Pan-cancer and functional genomics: Cross-tumor insights. This multi-panel figure presents a comprehensive analysis of copy number variation (CNV) and single-nucleotide variation (SNV) profiles across selected cancer types for a given gene set (*TP53*, *KRAS*). (A) The heterozygous CNV landscape, highlighting gene amplifications and deletions across cancers. (B) The homozygous CNV profile, indicating complete gene losses or gains with potential functional impact. (C) The correlation between CNV and corresponding messenger ribonucleic acid expression, reflecting potential gene dosage effects. (D) The proportion and distribution of CNV types across the cancer types analyzed, offering a comparative overview. (E) The classification and frequency of SNVs within the gene set, categorized by mutation types (e.g., missense, nonsense, frameshift). (F) An oncoplot visualizes the top 10 most frequently mutated genes within the input gene set, across the selected tumors, enabling identification of mutation hotspots and co-occurring variants. Together, these panels provide a pan-cancer view of genomic alterations with functional implications. Colon adenocarcinoma, breast cancer, lung squamous cell cancer, and lung adenocarcinoma are all the standard tumor type codes used in The Cancer Genome Atlas (TCGA). The figure was generated based on TCGA databases using online platforms (<https://www.cbiportal.org/>; <https://guolab.wchscu.cn/GSCA/#/>).

infrastructure, real-time data exchange, and joint problem-solving across academia, industry, and clinical settings.

Multidisciplinary research has been particularly impactful in the development of immunotherapies, where insights from immunology, genomics, and systems biology have converged to produce checkpoint inhibitors and CAR-T cell therapies.⁴⁶ Collaborative frameworks also

drive translational research, accelerating the bench-to-bedside pipeline. For instance, engineers and clinicians working together have developed microfluidic tumor-on-a-chip models that better replicate *in vivo* conditions, improving pre-clinical drug screening.⁴⁷

Moreover, the integration of data science and clinical care is enhancing real-time decision-making through

digital dashboards, predictive models, and AI-driven diagnostics.³¹ Such synergies can help close the gap between research innovation and clinical application.

Ultimately, fostering a culture of multidisciplinary collaboration is not only beneficial but essential for overcoming the complexity of cancer. By dissolving traditional disciplinary boundaries, the oncology community can more effectively translate discoveries into interventions that improve survival, quality of life, and equity in cancer care.

7. Challenges and future directions

Despite significant progress, numerous challenges hinder the full realization of integrative and multidisciplinary approaches in cancer research. A major barrier is the lack of data standardization and interoperability, which complicates the integration of diverse datasets across genomic, proteomic, imaging, and clinical domains.⁴⁸ Variations in data formats, nomenclatures, and metadata limit reproducibility and scalability, especially across institutions and research platforms.⁴⁹

Privacy concerns and data governance further restrict data sharing, particularly in multinational collaborations. While frameworks, such as the Global Alliance for Genomics and Health advocate for responsible data sharing, discrepancies in ethical regulations and legal infrastructures remain.⁵⁰ Institutional silos, disciplinary boundaries, and funding mechanisms that favor single-domain research exacerbate these problems by disincentivizing collaboration.⁵¹

To overcome these barriers, future efforts must focus on developing unified data standards, secure and federated data-sharing infrastructures, and clear guidelines for ethical AI use in biomedical research.⁵² The findable, accessible, interoperable, and reusable data principles represent a foundational step toward harmonized and transparent data integration.⁵³

Additionally, incentivizing cross-disciplinary collaboration is critical. This includes restructuring academic reward systems to value team science, supporting joint appointments, and fostering environments that promote co-creation across biology, medicine, computation, and engineering.⁵⁴ Funding bodies such as the National Institutes of Health and Horizon Europe are increasingly supporting transdisciplinary initiatives, signaling a cultural shift toward collaboration-driven innovation.

Looking ahead, integrated platforms that combine multi-omics data, computational models, and clinical decision support tools will be pivotal in bridging the gap between bench and bedside. Efforts, such as the Cancer

Research Data Commons aim to provide centralized, interoperable infrastructures for collaborative oncology research.⁵⁵

Addressing these challenges will be essential not only to unlock the full potential of integrative cancer research but also to ensure equitable, efficient, and patient-centered advances in oncology.

8. Critical reflections and research implications

While integrative oncology offers a compelling vision for unifying cancer research, the field continues to face both conceptual and operational barriers. A clear distinction between theoretical gaps and practical challenges is essential to prioritize future efforts and optimize limited research resources.^{15,56}

8.1. Theoretical gaps and practical challenges

Despite rapid technological advances, significant conceptual voids persist. The prevailing reductionist paradigm still dominates cancer biology, emphasizing discrete molecular lesions rather than emergent systems-level behaviors.^{56,57} The absence of a unified theoretical framework linking genomic alterations, signaling dynamics, microenvironmental feedback, and clinical phenotypes limits predictive accuracy.^{15,58} Moreover, most computational or mathematical models remain static abstractions, failing to capture temporal, spatial, and stochastic dimensions of tumor evolution and therapy resistance.⁵⁷⁻⁵⁹ These theoretical shortcomings highlight the need for dynamic, multi-scale models that integrate molecular, cellular, and systemic processes within a single explanatory architecture.^{59,60}

In contrast, practical challenges stem from implementation and governance. Data fragmentation, incompatible file formats, and inconsistent metadata continue to impede cross-study integration.^{61,62} Ethical and regulatory heterogeneity constrains international data exchange,⁶² while unequal computational capacity across institutions perpetuates inequities in research participation.^{62,63} Funding and academic reward systems still favor individual achievements and siloed discoveries, creating disincentives for collaborative, interdisciplinary work.^{64,65} Translational bottlenecks further arise when computational findings lack standardized validation pipelines or clinical interpretability.^{62,66} These operational hurdles underscore the importance of robust infrastructures, federated data platforms, and policy mechanisms that promote collaboration without compromising patient privacy or data integrity.^{6,63}

8.2. Differentiating forms of evidence

Integrative oncology is distinguished by the coexistence of diverse forms of evidence, with each serving a distinct epistemic function.^{67,68}

Computational evidence, derived from AI models, network simulations, and predictive algorithms, offers hypothesis generation and mechanistic inference, but often lacks empirical validation.^{59,69}

Empirical evidence from multi-omics profiling, CRISPR screens, or single-cell analyses, provides causal or correlative insights grounded in direct measurement, though frequently limited by context dependence.^{66,68}

Clinical evidence, emerging from basket trials, real-world data, and translational consortia, demonstrates the applicability of integrative findings to patient outcomes.^{67,70} Recognizing the interplay and hierarchy among these evidence types is vital for translating theoretical predictions into therapeutic practice. Computational models must be iteratively refined through experimental feedback, while empirical results require clinical contextualization to achieve translational relevance.⁶⁷⁻⁶⁹

8.3. Resource economics and opportunity costs

Integrative research, while scientifically compelling, demands substantial investment in infrastructure, data curation, and interdisciplinary training.^{6,64,65} The cost-effectiveness of such endeavors depends on long-term efficiency gains—reducing redundant experimentation, improving trial design, and accelerating biomarker discovery.^{6,71} However, the opportunity costs of large-scale projects such as TCGA and PCAWG include potential diversion of funds from smaller, hypothesis-driven studies or underrepresented disease contexts.^{71,72} Given finite research resources, strategic prioritization is required: Shared infrastructures, open-data policies, and distributed computing networks can democratize access while minimizing duplication.^{6,62,73} Ultimately, embracing “team science” principles and collaborative funding models represents the most sustainable path toward a cost-efficient and equitable integrative oncology ecosystem.^{6,64,65}

9. Conclusion

To overcome the “Blind Men and the Elephant” dilemma in cancer research, a transition from fragmented, reductionist approaches to integrated, systems-level thinking is essential. This shift involves the convergence of multi-omics data, AI, and systems biology within multidisciplinary frameworks. Initiatives such as TCGA and the Pan-Cancer Atlas exemplify the power of these integrative strategies, revealing novel biomarkers and informing more effective treatment paradigms. However, persistent challenges—including data

silos, lack of standardization, and institutional boundaries—continue to hinder the full potential of such efforts. Addressing these barriers will require the development of shared infrastructures, robust data governance, and the widespread adoption of team science. By connecting molecular insights with clinical phenotypes, this unified approach enables the design of more precise, adaptive therapies. Ultimately, moving from isolated observations to holistic understanding promises to transform cancer care, shifting from generalized interventions to personalized, dynamic strategies that bring us closer to durable cures.

Acknowledgments

None.

Funding

None.

Conflict of interest

The author declares no conflict of interest.

Author contributions

This is a single-authored article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

Further disclosure

During the preparation of this review article, large language models (e.g., OpenAI's ChatGPT, DeepSeek, and Grok) were used to assist with language editing, conceptual organization, and figure outline drafting. All scientific content, interpretations, and references were developed, curated, and verified by the authors. No AI-generated text or figures were used without substantial modification and author oversight. The authors remain solely responsible for the accuracy and integrity of the content.

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