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### Cancer Foundation Models: The Next Generation of Generalizable Artificial Intelligence for Precision Medicine

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#### ABSTRACT

Cancer remains one of the leading causes of morbidity and mortality worldwide despite remarkable advances in molecular diagnostics, targeted therapeutics, immunotherapy, and precision medicine. The rapid expansion of biomedical data generated from radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory investigations, wearable technologies, and electronic health records has created unprecedented opportunities for artificial intelligence (AI)-driven oncology while simultaneously presenting substantial computational challenges. Cancer foundation models have emerged as a transformative paradigm by enabling generalized representation learning across heterogeneous biomedical modalities using large-scale self-supervised pretraining. Unlike conventional machine learning systems designed for individual clinical tasks, foundation models learn transferable biomedical knowledge that can be adapted to diagnosis, molecular characterization, prognostic prediction, therapeutic optimization, radiogenomics, computational pathology, digital twins, clinical decision support, and precision therapeutics. Advances in transformer architectures, multimodal learning, contrastive learning, graph neural networks, retrieval-augmented generation, large language models, and generative AI have substantially accelerated development of oncology foundation models capable of integrating imaging, pathology, multi-omics, longitudinal clinical information, and real-world healthcare data into unified patient representations. These intelligent systems demonstrate remarkable generalizability across diverse cancer types while supporting increasingly personalized medicine. Nevertheless, important challenges remain regarding multimodal data harmonization, computational scalability, explainability, interoperability, cybersecurity, regulatory validation, and equitable clinical implementation. This review provides a comprehensive overview of cancer foundation models, highlighting computational principles, clinical applications, implementation challenges, and future perspectives for next-generation precision oncology.[1]

**Keywords:** Foundation models, Artificial intelligence, Precision oncology, Multimodal learning, Computational oncology, Digital pathology, Medical imaging, Large language models, Precision medicine, Clinical decision support.

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#### 1. Introduction

Cancer is a biologically heterogeneous disease characterized by genomic instability, epigenetic dysregulation, transcriptional diversity,

metabolic reprogramming, immune heterogeneity, and dynamic interactions within the tumor microenvironment. Although advances in molecular medicine and targeted therapeutics have significantly improved patient outcomes,

individuals with apparently similar pathological diagnoses frequently exhibit remarkably different therapeutic responses and long-term clinical outcomes because of complex biological variability that extends beyond individual biomarkers.[2]

Modern oncology continuously generates enormous quantities of heterogeneous biomedical information through computed tomography, magnetic resonance imaging, positron emission tomography, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory investigations, wearable biosensors, and electronic health records. Conventional artificial intelligence systems typically analyze these datasets independently, limiting comprehensive understanding of cancer biology and personalized patient management.[3]

Foundation models have emerged as one of the most important advances in artificial intelligence by learning generalized computational representations from large-scale biomedical datasets through self-supervised learning. Unlike traditional task-specific models, foundation models acquire transferable biomedical knowledge that can subsequently be adapted across multiple downstream oncology applications with minimal additional training.[4]

The emergence of cancer foundation models therefore represents a major paradigm shift toward generalized artificial intelligence capable of supporting comprehensive precision medicine through integrated analysis of multimodal biomedical information.[5]

## 2. Evolution of Artificial Intelligence Toward Foundation Models

Artificial intelligence within oncology has evolved through several major developmental stages. Early computational systems relied primarily on rule-based algorithms and handcrafted features that demonstrated limited adaptability and predictive capability. Machine learning subsequently introduced statistical prediction models capable of identifying nonlinear relationships among clinical variables, molecular biomarkers, imaging characteristics, and patient outcomes.[6]

Deep learning significantly expanded computational performance through automated extraction of hierarchical representations from radiological imaging, digital pathology, genomic sequencing, and physiological signals. Convolutional neural networks revolutionized medical image analysis, whereas recurrent neural networks improved interpretation of longitudinal clinical information.

Transformer architectures subsequently introduced self-attention mechanisms capable of efficiently modeling long-range contextual relationships across biomedical modalities. Foundation models further extended these advances through large-scale self-supervised pretraining on enormous biomedical datasets, enabling generalized knowledge transfer across diverse downstream oncology tasks.[7]

Today, cancer foundation models combine multimodal learning, transformer architectures, graph neural networks, large language models, and generative artificial intelligence into unified computational ecosystems capable of supporting comprehensive precision oncology.[8]

## 3. Principles of Cancer Foundation Models

Foundation models differ fundamentally from conventional artificial intelligence because they are pretrained on extremely large biomedical datasets before adaptation to specialized clinical applications. Rather than learning isolated diagnostic tasks, foundation models acquire generalized representations that capture fundamental biological, molecular, anatomical, and clinical relationships across multiple cancer domains.[9]

Self-supervised learning enables foundation models to discover latent biomedical structure without requiring extensive manual annotation. Contrastive learning aligns heterogeneous modalities including radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, and clinical documentation within shared computational embedding spaces.

Transformer architectures provide cross-modal attention mechanisms that integrate complementary biomedical information, whereas graph neural networks model interactions among

genes, proteins, signaling pathways, immune networks, and therapeutic targets.

These generalized computational representations substantially improve transfer learning, zero-shot learning, few-shot learning, and adaptability across multiple oncology applications while reducing dependence on manually labeled datasets.[10]

#### **4. Computational Architecture of Cancer Foundation Models**

Cancer foundation models consist of multiple computational layers responsible for multimodal biomedical data acquisition, preprocessing, representation learning, multimodal fusion, downstream adaptation, and clinical decision support.[11]

The data acquisition layer collects radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable sensor information, electronic health records, medication history, and longitudinal clinical documentation. Advanced preprocessing pipelines subsequently normalize imaging studies, harmonize molecular datasets, encode clinical narratives using natural language processing, and generate multimodal feature representations.

Large transformer architectures convert heterogeneous biomedical information into unified computational embeddings through self-supervised pretraining. Downstream adaptation modules subsequently fine-tune these generalized representations for specialized oncology applications including diagnosis, prognosis, biomarker discovery, therapeutic prediction, toxicity estimation, and survival analysis.

Continuous incorporation of longitudinal clinical information further enables adaptive precision medicine by allowing foundation models to evolve alongside individual patient trajectories.[12]

#### **5. Foundation Models in Medical Imaging**

Medical imaging represents one of the largest biomedical domains supporting foundation

model development. Computed tomography, magnetic resonance imaging, positron emission tomography, mammography, ultrasound, and hybrid imaging collectively generate enormous image repositories suitable for large-scale self-supervised representation learning.[13]

Foundation models pretrained on millions of medical images automatically learn generalized anatomical and pathological representations that can subsequently be adapted to tumor detection, lesion segmentation, disease classification, radiomics, treatment response assessment, and longitudinal disease monitoring.

Compared with conventional convolutional neural networks trained for individual tasks, foundation models demonstrate substantially improved transferability, robustness, zero-shot learning, and few-shot learning capabilities across multiple cancer types and healthcare environments while requiring significantly fewer annotated datasets.[14]

#### **6. Digital Pathology Foundation Models**

Digital pathology has become one of the most important domains for cancer foundation model development because whole-slide imaging generates extremely high-resolution tissue images containing millions of microscopic structures ideally suited for self-supervised learning.[15]

Transformer-based pathology foundation models automatically learn generalized histomorphological representations before adaptation to downstream tasks including tumor classification, grading, biomarker prediction, lymph node metastasis detection, recurrence estimation, immune-cell quantification, and survival prediction.

Recent computational studies have demonstrated accurate prediction of clinically important biomarkers including EGFR mutations, KRAS mutations, HER2 amplification, microsatellite instability, estrogen receptor status, progesterone receptor status, PD-L1 expression, and numerous therapeutic biomarkers directly from routine histopathological images.

Integration of pathology representations with imaging, genomics, laboratory investigations, and longitudinal clinical information further strengthens precision oncology while improving

diagnostic reproducibility across diverse pathology laboratories.[16]

## 7. Foundation Models for Multi-Omics

Multi-omics technologies—including genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, lipidomics, and single-cell sequencing—provide comprehensive characterization of cancer biology across multiple molecular layers. Foundation models enable generalized representation learning across these heterogeneous biological modalities through self-supervised transformer architectures and graph neural networks.[17]

Artificial intelligence identifies interactions among genes, proteins, metabolites, signaling pathways, immune responses, and therapeutic targets while supporting molecular subtype classification, biomarker discovery, systems biology research, drug response prediction, and personalized therapeutic planning.

These generalized molecular representations substantially improve biological understanding while enabling transfer learning across multiple cancer types, thereby strengthening precision medicine beyond isolated genomic analyses.[18]

## 8. Multimodal Foundation Models in Clinical Oncology

Modern precision oncology increasingly depends upon simultaneous interpretation of radiological imaging, digital pathology, multi-omics, laboratory investigations, electronic health records, wearable biosensors, and longitudinal clinical documentation. Cancer foundation models integrate these heterogeneous biomedical modalities into unified patient-specific computational representations capable of comprehensive clinical reasoning.[19]

Transformer-based multimodal learning enables artificial intelligence to capture complementary biological information across imaging, pathology, molecular biology, and temporal clinical data while preserving complex relationships among diverse biomedical modalities.

These integrated representations improve diagnosis, molecular characterization, prognostic

prediction, therapeutic optimization, toxicity assessment, recurrence estimation, and long-term patient management while supporting increasingly individualized precision oncology across the entire cancer care continuum.[20]

## 9. Foundation Models for Precision Cancer Diagnosis

One of the most significant clinical applications of cancer foundation models is precision diagnosis through integrated analysis of radiological imaging, digital pathology, multi-omics, laboratory biomarkers, and longitudinal clinical information. Unlike conventional artificial intelligence systems that analyze individual data modalities independently, foundation models generate unified patient-specific representations that improve diagnostic reasoning across multiple biomedical domains.[21]

Artificial intelligence combines imaging-derived radiomic features, histopathological characteristics, genomic alterations, transcriptomic signatures, proteomic profiles, laboratory investigations, and clinical documentation to improve tumor detection, disease classification, molecular subtype identification, cancer staging, and individualized risk stratification.

These generalized representations reduce diagnostic variability while supporting multidisciplinary oncology teams through evidence-based computational decision support and more consistent interpretation across diverse healthcare environments.

## 10. Personalized Therapeutics and Treatment Optimization

Personalized treatment planning represents one of the most promising applications of cancer foundation models. These intelligent systems integrate molecular biology, pathology, imaging, laboratory biomarkers, treatment history, and patient-specific clinical characteristics into comprehensive computational frameworks capable of supporting individualized therapeutic decisions.[22]

Machine learning algorithms estimate treatment response, recurrence probability, progression-free survival, overall survival, treatment-related toxicity, and mechanisms of therapeutic

resistance across chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations.

Because foundation models continuously learn generalized biomedical representations, they can rapidly adapt to emerging therapeutic strategies while providing increasingly accurate recommendations that evolve alongside changing patient conditions.

### **11. Immunotherapy and Tumor Microenvironment Modeling**

The tumor microenvironment exerts profound influence on cancer progression and responsiveness to immunotherapy. Foundation models integrate radiological imaging, computational pathology, transcriptomics, immunomics, spatial biology, laboratory biomarkers, and longitudinal clinical outcomes to generate comprehensive computational representations of tumor-immune interactions.[23]

Artificial intelligence evaluates tumor-infiltrating lymphocytes, immune checkpoint expression, cytokine signaling pathways, stromal organization, angiogenesis, and immune-cell spatial relationships to estimate responsiveness to immune checkpoint inhibitors, CAR-T cell therapies, cancer vaccines, bispecific antibodies, and adoptive cellular therapies.

By simultaneously integrating multiple biological modalities, foundation models improve prediction of immunotherapy outcomes while supporting development of increasingly individualized therapeutic strategies.

### **12. Drug Discovery and Clinical Research**

Cancer foundation models are transforming oncology drug discovery by integrating molecular biology, pharmacology, structural biology, systems biology, and clinical outcome data into generalized computational frameworks. Artificial intelligence identifies novel therapeutic targets, predicts drug-target interactions, estimates toxicity profiles, and models mechanisms of therapeutic resistance.[24]

Generative AI further strengthens pharmaceutical research by designing candidate molecules, predicting protein structures, simulating molecular interactions, and generating synthetic biomedical datasets for preclinical investigation.

Foundation models also improve clinical trial efficiency by automating molecular eligibility assessment, patient stratification, adaptive trial optimization, outcome prediction, and identification of patients most likely to benefit from investigational therapies.

### **13. Digital Twins and Clinical Decision Support**

The convergence of cancer foundation models with digital twin technology is creating continuously evolving virtual patient ecosystems capable of integrating imaging, pathology, genomics, laboratory investigations, wearable technologies, and longitudinal clinical information into adaptive computational models.[25]

Artificial intelligence continuously updates these digital twins as new patient information becomes available, allowing simulation of disease progression, therapeutic response, toxicity, recurrence, and survival before clinical intervention.

Within routine oncology practice, foundation model-powered clinical decision-support systems provide individualized diagnostic assessments, therapeutic recommendations, toxicity predictions, recurrence estimates, and survivorship planning through interactive multidisciplinary dashboards while maintaining physician oversight.

### **14. Explainability, Trustworthiness, and Clinical Translation**

Although cancer foundation models demonstrate exceptional predictive capabilities, successful clinical implementation requires transparency, interpretability, and clinician trust. Explainable artificial intelligence (XAI) enables healthcare professionals to understand computational reasoning through attention visualization, saliency maps, SHAP (Shapley Additive Explanations), feature attribution analysis, and counterfactual explanations that identify the

biological variables contributing most strongly to model predictions.[26]

Several additional challenges remain. Foundation models require extremely large computational resources, standardized multimodal datasets, secure computational infrastructure, robust validation across diverse healthcare systems, and continuous monitoring for algorithmic bias.

Regulatory approval, cybersecurity, patient privacy, interoperability, equitable access, and prospective multicenter clinical validation will remain essential prerequisites for responsible translation into routine oncology practice.

## 15. Future Perspectives

The future of precision oncology will likely be driven by increasingly sophisticated cancer foundation models capable of continuously learning from imaging, pathology, genomics, transcriptomics, proteomics, metabolomics, wearable biosensors, electronic health records, and real-world clinical outcomes.[27]

Emerging technologies including multimodal large language models, digital twins, federated learning, agentic artificial intelligence, reinforcement learning, spatial multi-omics, liquid biopsy, quantum computing, cloud-native healthcare infrastructure, and Internet of Medical Things (IoMT) technologies will further strengthen computational oncology ecosystems.

Future foundation models may function as comprehensive biomedical reasoning systems capable of adaptive clinical decision-making, personalized patient communication, autonomous knowledge synthesis, intelligent workflow optimization, and continuous learning across international healthcare networks.

## 16. Discussion

Cancer foundation models represent one of the most significant paradigm shifts in computational oncology by enabling generalized artificial intelligence capable of integrating multimodal biomedical information into unified patient-centered computational representations. Unlike conventional task-specific machine learning models, foundation models learn transferable biomedical knowledge that supports diagnosis,

molecular characterization, therapeutic optimization, digital twins, drug discovery, and intelligent clinical decision support across diverse cancer types.[28]

Their ability to generalize across multiple biomedical modalities substantially strengthens precision medicine while reducing dependence on extensive task-specific training datasets. Nevertheless, continued advances in explainable artificial intelligence, computational infrastructure, interoperability, cybersecurity, regulatory science, and ethical governance will be essential for widespread clinical implementation.

## 17. Conclusion

Cancer foundation models are redefining precision oncology by enabling generalized artificial intelligence that integrates radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, and longitudinal clinical information into unified computational frameworks supporting personalized cancer medicine.[29]

Advances in transformer architectures, multimodal learning, graph neural networks, large language models, digital twins, federated learning, generative artificial intelligence, and agentic AI are expected to further strengthen these intelligent systems, enabling increasingly accurate diagnosis, adaptive therapeutics, continuous disease monitoring, and evidence-based clinical decision-making.

Although important scientific, technical, ethical, and regulatory challenges remain, continued interdisciplinary collaboration among oncologists, computer scientists, molecular biologists, biomedical engineers, healthcare organizations, and regulatory agencies will accelerate responsible translation of cancer foundation models into routine clinical practice, ultimately improving patient outcomes and advancing the future of precision medicine worldwide.[30]

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