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FOUNDATION AI MODELS FOR SYSTEMS ONCOLOGY: INTEGRATING MULTI-OMICS, IMAGING, AND CLINICAL INTELLIGENCE FOR PRECISION CANCER CARE

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Abstract: Systems oncology is emerging as a transformative paradigm in precision cancer medicine through the integration of artificial intelligence (AI), multi-omics, medical imaging, digital pathology, and longitudinal clinical intelligence into comprehensive computational ecosystems capable of modeling cancer as a dynamic biological system. Conventional oncology often relies on fragmented analysis of individual diagnostic modalities, limiting the understanding of complex interactions among molecular pathways, tumor microenvironments, host immunity, and clinical outcomes. Recent advances in foundation AI models, multimodal transformer architectures, graph neural networks, self-supervised learning, and generative artificial intelligence have enabled unified analysis of radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, liquid biopsy, wearable physiological monitoring, electronic health records, and real-world clinical evidence. These intelligent systems support precision diagnosis, molecular characterization, biomarker discovery, prognostic prediction, therapeutic optimization, immunotherapy selection, digital twin simulation, adaptive disease monitoring, and evidence-based clinical decision support. Emerging technologies including multimodal large language models, federated learning, reinforcement learning, retrieval-augmented generation, explainable artificial intelligence, and agentic AI further strengthen systems oncology by enabling collaborative, privacy-preserving, and continuously adaptive biomedical intelligence. Despite remarkable technological advances, important scientific, technical, ethical, and regulatory challenges remain regarding multimodal data harmonization, computational scalability, interpretability, interoperability, cybersecurity, clinical validation, and equitable implementation. This review provides a comprehensive overview of foundation AI models for systems oncology, emphasizing the integration of multi-omics, imaging, and clinical intelligence as a transformative framework for precision cancer care.[1]

Keywords: *Systems oncology, Foundation models, Artificial intelligence, Precision oncology, Multi-omics, Digital pathology, Radiomics, Clinical intelligence, Computational oncology, Personalized medicine.*

1. Introduction

Cancer is a highly complex systems-level disease characterized by continuous genomic evolution, epigenetic remodeling, immune adaptation, metabolic reprogramming, angiogenesis, tissue remodeling, and dynamic interactions among malignant cells, stromal components, immune populations, and host physiology. These interconnected biological processes evolve throughout diagnosis, treatment, recurrence,

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metastasis, and survivorship, making precision oncology increasingly dependent upon computational systems capable of integrating heterogeneous biomedical information across multiple organizational scales.[2]

Modern healthcare generates unprecedented quantities of biomedical data through radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, liquid biopsy, wearable physiological monitoring, electronic health records, physician documentation, and patient-reported outcomes. Although each modality contributes valuable biological insight, isolated interpretation frequently overlooks systems-level relationships governing disease progression, therapeutic response, resistance mechanisms, and long-term clinical outcomes.[3]

Artificial intelligence has emerged as a transformative computational technology capable of integrating these heterogeneous biomedical datasets into unified patient-centered representations. Foundation AI models extend these capabilities through generalized multimodal learning that enables transfer of computational knowledge across numerous oncology applications while continuously adapting to evolving biomedical evidence.

The convergence of systems biology and foundation AI therefore establishes a new paradigm for precision cancer care capable of transforming oncology into an intelligent, continuously learning healthcare ecosystem.[4]

2. Evolution of Systems Oncology and Foundation AI

Systems oncology has evolved from reductionist analyses of isolated molecular pathways toward comprehensive computational frameworks capable of modeling cancer as an interconnected biological ecosystem. Early computational oncology relied primarily on statistical analyses and conventional machine learning algorithms developed for individual diagnostic or prognostic applications. Although these systems demonstrated clinical utility, they remained constrained by handcrafted feature engineering, limited adaptability, and fragmented biomedical information.[5]

Deep learning substantially advanced computational oncology through automated representation learning from radiological imaging, digital pathology, genomic sequencing, and electronic health records. Transformer architectures further revolutionized biomedical artificial intelligence by enabling generalized contextual learning across heterogeneous biomedical datasets.

Foundation AI models have now transformed computational oncology through large-scale self-supervised learning that develops transferable biomedical knowledge applicable across diagnosis, prognosis, biomarker discovery, therapeutic prediction, disease monitoring, computational pathology, radiomics, and intelligent clinical decision support. These advances establish the computational basis for next-generation systems oncology.[6]

3. Principles of Foundation AI Models in Systems Oncology

Foundation AI models differ fundamentally from conventional artificial intelligence because they acquire generalized biomedical representations from massive multimodal datasets before specialization for individual oncology applications. Rather than learning isolated predictive tasks, these models develop transferable computational knowledge applicable across diagnosis, prognosis, molecular characterization, biomarker discovery, therapeutic optimization, disease monitoring, digital pathology, radiomics, immunotherapy, and clinical decision support.[7]

Self-supervised learning enables discovery of latent biological relationships without requiring extensive manual annotation, while multimodal transformer architectures align radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable physiological monitoring, physician documentation, patient-reported outcomes, and longitudinal clinical trajectories within unified computational embedding spaces.

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Graph neural networks further characterize interactions among genes, proteins, signaling pathways, immune populations, imaging phenotypes, tissue architecture, therapeutic targets, physiological variables, and clinical outcomes, thereby enabling systems-level computational reasoning supporting precision oncology.[8]

4. Computational Architecture

Modern systems oncology platforms consist of interconnected computational layers responsible for multimodal biomedical data acquisition, preprocessing, representation learning, multimodal fusion, adaptive learning, predictive analytics, digital twin simulation, and intelligent clinical decision support.[9]

The acquisition layer continuously incorporates radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and electronic health records. Advanced preprocessing pipelines normalize imaging studies, harmonize molecular datasets, encode clinical narratives using natural language processing, and synchronize temporal patient information.

Foundation AI models subsequently generate generalized multimodal embeddings representing molecular biology, tissue architecture, imaging phenotypes, physiological function, and longitudinal clinical trajectories. These unified computational representations support downstream applications including diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, adaptive learning, and systems oncology.[10]

5. Multi-Omics Intelligence

Comprehensive molecular characterization represents one of the greatest strengths of foundation AI models within systems oncology. Artificial intelligence integrates genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, spatial biology, and single-cell sequencing into generalized molecular representations capable of characterizing evolving tumor biology across multiple organizational scales.[11]

Transformer architectures identify latent biological relationships among genes, proteins, signaling pathways, metabolites, immune responses, and therapeutic targets, while graph neural networks model complex biological interaction networks supporting systems-level computational reasoning. Foundation AI models thereby enable discovery of molecular subtypes, therapeutic biomarkers, resistance mechanisms, prognostic signatures, and novel drug targets while substantially improving individualized precision medicine.

These generalized molecular representations establish foundation AI models as intelligent computational engines supporting systems biology and translational oncology.[12]

6. Imaging Intelligence

Radiological imaging and digital pathology provide complementary information describing cancer biology across macroscopic and microscopic organizational scales. Foundation AI models automatically extract generalized imaging representations from computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, whole-slide pathology images, and multimodal imaging platforms without requiring handcrafted feature engineering.[13]

Artificial intelligence identifies latent imaging biomarkers associated with molecular alterations, immune infiltration, angiogenesis, fibrosis, hypoxia, therapeutic responsiveness, treatment resistance, and disease progression. Integration of imaging intelligence with molecular biology substantially improves diagnosis, prognostic prediction, biomarker discovery, therapeutic optimization, and longitudinal disease monitoring.

These imaging representations provide a non-invasive computational window into evolving tumor biology while strengthening precision oncology throughout the patient journey.[14]

7. Clinical Intelligence

Clinical intelligence represents the integration of structured and unstructured clinical information

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into continuously evolving computational representations supporting multidisciplinary oncology practice. Electronic health records, laboratory investigations, medication history, physician documentation, patient-reported outcomes, wearable physiological monitoring, and longitudinal clinical trajectories collectively provide comprehensive patient-level information extending beyond molecular diagnostics.[15]

Foundation AI models integrate these diverse clinical datasets with imaging and molecular biology using natural language processing, temporal transformers, and multimodal reasoning architectures. These unified computational representations enable adaptive prediction of disease progression, therapeutic response, recurrence, hospitalization, survivorship outcomes, and overall survival while supporting evidence-based clinical decision-making throughout diagnosis, treatment, follow-up, and survivorship.[16]

8. Systems-Level Multimodal Integration

The defining capability of foundation AI models in systems oncology is multimodal integration, whereby radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable physiological monitoring, physician documentation, environmental exposures, and longitudinal clinical trajectories are integrated into unified patient-specific computational representations. Artificial intelligence employs multimodal transformers, cross-modal attention mechanisms, graph neural networks, and biological knowledge graphs to identify latent biological relationships spanning molecular, cellular, tissue, organ, physiological, and clinical scales.[17]

These comprehensive multimodal representations substantially improve diagnostic classification, biomarker discovery, prognostic prediction, therapeutic optimization, digital twin simulation, and adaptive precision oncology while enabling systems-level computational understanding of cancer biology.[18]

9. Precision Diagnosis and Therapeutic Prediction

One of the most clinically important applications of foundation AI models in systems oncology is precision diagnosis and therapeutic prediction through comprehensive integration of molecular, imaging, and clinical intelligence. Foundation AI models simultaneously analyze heterogeneous biomedical information to predict responsiveness to chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations while estimating treatment-related toxicity, recurrence probability, progression-free survival, overall survival, and mechanisms of therapeutic resistance. These adaptive computational systems support individualized therapeutic planning while continuously refining predictive accuracy using newly acquired biomedical evidence throughout the cancer care continuum.[19][20]

10. Digital Twins and Systems-Level Patient Modeling

Digital twin technology represents one of the most transformative applications of foundation AI models within systems oncology by creating continuously evolving virtual representations of individual cancer patients synchronized with their biological counterparts. Foundation AI models integrate serial radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, medication history, patient-reported outcomes, and longitudinal clinical information into adaptive computational patient models capable of simulating disease progression, therapeutic response, treatment-related toxicity, recurrence, metastatic dissemination, and survival.[21]

Unlike conventional predictive models, digital twins continuously update their computational representations as new biomedical information becomes available. These intelligent virtual patients enable clinicians to evaluate multiple therapeutic strategies before implementation, optimize treatment sequencing, anticipate mechanisms of therapeutic resistance, and personalize supportive care according to evolving patient biology.

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By combining multimodal biomedical intelligence with predictive simulation, digital twins transform systems oncology from retrospective analysis toward proactive precision medicine supported by continuously adaptive virtual patient ecosystems.

11. Intelligent Clinical Decision Support

Foundation AI models provide the computational infrastructure for next-generation clinical decision-support systems capable of integrating heterogeneous biomedical information into comprehensive patient-centered recommendations. Rather than interpreting radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based clinical guidelines independently, these models synthesize diverse biomedical information into unified computational representations supporting multidisciplinary oncology practice.[22]

Interactive clinical dashboards generate individualized diagnostic summaries, multimodal biomarker analyses, digital twin simulations, therapeutic recommendations, toxicity estimates, recurrence probabilities, disease progression forecasts, and survival predictions while facilitating collaboration among oncologists, radiologists, pathologists, surgeons, radiation oncologists, molecular biologists, pharmacists, nurses, genetic counselors, and computational scientists.

These intelligent systems improve workflow efficiency, strengthen multidisciplinary communication, reduce information fragmentation, and promote evidence-based personalized cancer management throughout the cancer care continuum.

12. Continuous Learning and Adaptive Systems Oncology

A defining characteristic of foundation AI models is their ability to continuously evolve as new biomedical information becomes available. Artificial intelligence incorporates serial imaging examinations, computational pathology, circulating tumor DNA, laboratory biomarkers, wearable physiological monitoring, medication adherence, patient-reported outcomes, and real-world clinical evidence into adaptive computational frameworks capable of continuously refining predictive accuracy.[23]

Continual learning algorithms enable incremental refinement of computational knowledge without catastrophic forgetting of previously acquired information, while reinforcement learning optimizes therapeutic recommendations through iterative evaluation of treatment outcomes. Consequently, systems oncology platforms remain synchronized with evolving tumor biology, emerging scientific discoveries, changing clinical guidelines, and diverse patient trajectories.

This adaptive computational paradigm transforms oncology into a continuously learning healthcare ecosystem capable of supporting real-time personalized precision medicine.

13. Federated Foundation Model Networks

Development of highly generalizable foundation AI models requires access to diverse biomedical datasets representing multiple healthcare systems, imaging platforms, molecular technologies, treatment protocols, and patient populations. Federated learning enables collaborative development of foundation AI models while preserving patient privacy and institutional governance through decentralized computational training.[24]

Participating healthcare institutions independently train local models using radiological imaging, digital pathology, genomic sequencing, multi-omics, laboratory investigations, wearable monitoring, liquid biopsy, and longitudinal clinical records while securely exchanging encrypted model parameters rather than identifiable patient information. This collaborative learning strategy substantially improves algorithm robustness, fairness, external validity, and generalizability across diverse healthcare environments.

Federated systems oncology ecosystems therefore establish an international computational oncology network capable of accelerating scientific discovery, improving equitable access to precision medicine, and supporting global cancer research while maintaining responsible data stewardship.

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14. Explainability, Validation, and Ethical Governance

Successful implementation of foundation AI models in systems oncology requires transparent, interpretable, reproducible, and rigorously validated computational systems capable of supporting clinician confidence, patient trust, and regulatory approval. Explainable artificial intelligence (XAI) enables clinicians to understand computational reasoning through attention visualization, saliency maps, SHAP (Shapley Additive Explanations), feature attribution analysis, uncertainty estimation, and counterfactual explanations identifying the imaging, molecular, pathological, physiological, and clinical variables responsible for predictive outputs.[25]

Clinical deployment additionally requires standardized multimodal datasets, interoperable computational infrastructure, prospective multicenter validation, external benchmarking, cybersecurity safeguards, continuous monitoring for algorithmic bias, and compliance with evolving international regulatory frameworks governing AI-enabled healthcare technologies.

Responsible implementation further depends upon protection of patient privacy, informed consent, transparency, accountability, equitable access, responsible data governance, and continuous post-deployment surveillance to ensure trustworthy integration of intelligent computational systems into routine oncology practice.

15. Future Perspectives

Future systems oncology will increasingly integrate multimodal foundation models, multimodal large language models, agentic artificial intelligence, graph neural networks, reinforcement learning, federated learning, digital twins, spatial multi-omics, liquid biopsy, quantum computing, Internet of Medical Things (IoMT), robotics, and cloud-native healthcare infrastructure into unified precision oncology platforms.[26]

These next-generation computational ecosystems will continuously integrate molecular biology, imaging, pathology, laboratory medicine, wearable physiological monitoring, environmental exposures, electronic health records, biomedical literature, and real-world clinical outcomes while autonomously coordinating diagnostic workflows, optimizing therapeutic strategies, supporting adaptive clinical trials, generating personalized patient communication, and continuously synthesizing biomedical evidence.

Such intelligent ecosystems are expected to transform oncology from fragmented and reactive disease management toward predictive, preventive, adaptive, continuously learning, and precision-guided healthcare across the global cancer community.

16. Discussion

Foundation AI models represent one of the most significant paradigm shifts in systems oncology by integrating multi-omics, imaging intelligence, digital pathology, clinical reasoning, and longitudinal patient information into unified computational ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional artificial intelligence systems developed for isolated predictive tasks, these intelligent frameworks simultaneously analyze molecular biology, tissue architecture, radiological imaging, laboratory biomarkers, physiological monitoring, environmental influences, and longitudinal clinical trajectories to generate holistic representations of evolving cancer biology.[27]

Applications spanning computational pathology, radiogenomics, biomarker discovery, digital twins, precision immunotherapy, adaptive therapeutics, continuous learning, federated collaboration, digital health, survivorship management, and intelligent clinical decision support demonstrate the extraordinary potential of systems-level artificial intelligence to redefine future oncology. Nevertheless, successful implementation requires continued advances in multimodal data harmonization, explainable artificial intelligence, interoperability, computational infrastructure, cybersecurity, regulatory science, ethical governance, and sustained multidisciplinary collaboration.

As biomedical knowledge and healthcare data continue to expand exponentially, foundation AI models are expected to become the central

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computational infrastructure supporting systems oncology worldwide.

17. Conclusion

Foundation AI models are transforming systems oncology by integrating multi-omics, radiological imaging, digital pathology, laboratory biomarkers, wearable technologies, electronic health records, digital twins, and longitudinal clinical intelligence into unified computational ecosystems capable of supporting accurate diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, adaptive disease monitoring, and personalized cancer care throughout the disease continuum.[28]

Advances in transformer architectures, multimodal learning, graph neural networks, self-supervised learning, federated learning, reinforcement learning, digital twins, multimodal large language models, agentic AI, and generative artificial intelligence are expected to further strengthen these intelligent ecosystems, enabling increasingly accurate molecular characterization, predictive clinical decision-making, adaptive therapeutics, continuous disease surveillance, and continuously personalized oncology care.[29]

Although important scientific, technical, ethical, regulatory, and implementation challenges remain, sustained collaboration among oncologists, radiologists, pathologists, molecular biologists, biomedical engineers, computer scientists, healthcare organizations, policymakers, industry partners, and regulatory agencies will accelerate the responsible implementation of foundation AI models in systems oncology. These innovations have the potential to improve patient outcomes, enhance healthcare efficiency, reduce disparities in cancer care, accelerate translational research, and establish a new era of intelligent, adaptive, and continuously learning precision oncology worldwide.[30]

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