

FOUNDATION AI MODELS FOR PRECISION IMMUNOTHERAPY: PREDICTING RESPONSE, RESISTANCE, AND CLINICAL OUTCOMES

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Abstract: Immunotherapy has revolutionized modern oncology by enabling the immune system to recognize and eliminate malignant cells through immune checkpoint inhibitors, adoptive cellular therapies, cancer vaccines, bispecific antibodies, and emerging immunomodulatory strategies. Despite remarkable clinical success, therapeutic responses remain highly heterogeneous because of the extraordinary complexity of tumor-immune interactions, intratumoral heterogeneity, and dynamic evolution of the tumor microenvironment. Foundation artificial intelligence (AI) models have emerged as transformative computational frameworks capable of integrating heterogeneous biomedical information across radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, immunomics, spatial biology, laboratory biomarkers, liquid biopsy, wearable physiological monitoring, electronic health records, and longitudinal clinical outcomes into unified patient-specific representations. These intelligent systems enable comprehensive prediction of immunotherapy response, resistance mechanisms, toxicity, recurrence, and survival while supporting biomarker discovery, digital twin simulation, adaptive treatment planning, and intelligent clinical decision support. Recent advances in multimodal transformer architectures, graph neural networks, self-supervised learning, multimodal large language models, federated learning, reinforcement learning, retrieval-augmented generation, explainable artificial intelligence, and agentic AI further strengthen precision immunotherapy by enabling collaborative, privacy-preserving, and continuously adaptive computational medicine. Despite remarkable technological progress, significant scientific, technical, ethical, and regulatory challenges remain regarding multimodal data harmonization, computational scalability, interoperability, interpretability, cybersecurity, clinical validation, and equitable implementation. This review provides a comprehensive overview of foundation AI models for precision immunotherapy, emphasizing prediction of therapeutic response, resistance, and clinical outcomes as a transformative paradigm in personalized oncology.[1]

Keywords: Precision immunotherapy, Foundation models, Artificial intelligence, Immuno-oncology, Tumor microenvironment, Digital twins, Multi-omics, Clinical decision support, Personalized medicine, Computational oncology.

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1. Introduction

Immunotherapy has fundamentally transformed cancer treatment by harnessing the immune system to recognize and eliminate malignant cells through diverse therapeutic strategies including immune checkpoint inhibition, adoptive cellular

therapy, cancer vaccines, bispecific antibodies, and engineered immune-cell therapies. Nevertheless, only a subset of patients experiences durable clinical benefit because therapeutic response depends upon highly dynamic interactions among malignant cells, immune

populations, stromal components, molecular signaling pathways, and host physiology.[2]

Modern immuno-oncology generates enormous quantities of heterogeneous biomedical information through radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, immunomics, spatial biology, laboratory investigations, liquid biopsy, wearable physiological monitoring, electronic health records, and patient-reported outcomes. Although each modality provides valuable biological insight, isolated interpretation frequently fails to capture the systems-level mechanisms governing immune response and therapeutic resistance.[3]

Foundation artificial intelligence models have emerged as transformative computational frameworks capable of integrating these diverse biomedical modalities into unified patient-centered representations supporting precision immunotherapy. Through generalized multimodal learning, these models enable comprehensive prediction of therapeutic response while continuously adapting to evolving patient biology and clinical evidence.[4]

The convergence of foundation AI models with immuno-oncology therefore represents a major paradigm shift toward intelligent computational ecosystems capable of transforming personalized cancer immunotherapy.[5]

2. Evolution of Artificial Intelligence in Immunotherapy

Early computational approaches in immuno-oncology primarily relied upon statistical analyses of individual biomarkers such as PD-L1 expression, tumor mutational burden, microsatellite instability, or immune-cell infiltration. Although these biomarkers significantly improved patient stratification, they frequently demonstrated insufficient predictive accuracy because therapeutic response depends upon numerous interacting biological mechanisms.[6]

Deep learning subsequently enabled automated representation learning from radiological imaging, digital pathology, and molecular diagnostics, while transformer architectures introduced sophisticated multimodal reasoning capable of

integrating heterogeneous biomedical datasets. Foundation AI models further transformed computational immunotherapy by acquiring generalized biomedical knowledge through large-scale self-supervised learning before adaptation to specialized oncology applications.

Integration of graph neural networks, multimodal large language models, reinforcement learning, digital twins, and federated learning has now established intelligent computational ecosystems capable of supporting adaptive precision immunotherapy throughout the cancer care continuum.[7]

3. Principles of Foundation AI Models for Precision Immunotherapy

Foundation AI models differ fundamentally from conventional machine learning algorithms because they acquire generalized biomedical representations from massive multimodal datasets before specialization for individual clinical applications. Rather than learning isolated prediction tasks, these models develop transferable computational knowledge applicable across diagnosis, biomarker discovery, immunotherapy prediction, toxicity assessment, disease monitoring, and intelligent clinical decision support.[8]

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, immunomics, laboratory biomarkers, physician documentation, and longitudinal clinical trajectories within unified computational embedding spaces.

Graph neural networks complement transformer architectures by modeling interactions among genes, proteins, immune populations, signaling pathways, imaging phenotypes, tissue architecture, therapeutic targets, physiological variables, and clinical outcomes, thereby enabling systems-level computational reasoning supporting precision immunotherapy.[9]

4. Computational Architecture

Modern precision immunotherapy platforms consist of interconnected computational layers responsible for multimodal biomedical data acquisition, preprocessing, representation learning, immune ecosystem modeling, predictive analytics, adaptive learning, digital twin simulation, and intelligent clinical decision support.[10]

The acquisition layer continuously integrates radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, immunomics, spatial biology, laboratory investigations, circulating tumor DNA, wearable physiological monitoring, medication history, 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, immune ecosystem dynamics, physiological status, and longitudinal clinical trajectories. These unified computational representations support downstream prediction of immunotherapy response, resistance mechanisms, toxicity, recurrence, and survival.[11]

5. Foundation Models for Immune Ecosystem Intelligence

Foundation AI models represent the computational intelligence underlying precision immunotherapy because they acquire generalized biomedical knowledge from large-scale multimodal datasets before adaptation to specialized oncology applications. Unlike conventional task-specific algorithms, foundation models develop transferable computational representations applicable across diagnosis, biomarker discovery, immune profiling, therapeutic prediction, computational pathology, radiomics, and intelligent clinical decision support.[12]

Transformer architectures enable multimodal attention across imaging, pathology, molecular biology, immunomics, laboratory investigations,

wearable monitoring, and clinical documentation, while graph neural networks characterize biological interactions among immune cells, signaling pathways, cytokines, imaging phenotypes, therapeutic targets, physiological variables, and longitudinal clinical outcomes.

These generalized computational capabilities establish foundation AI models as continuously evolving immune intelligence systems supporting adaptive personalized immunotherapy.[13]

6. Multimodal Immune Profiling

Comprehensive precision immunotherapy requires seamless integration of heterogeneous biomedical modalities into unified patient-specific computational representations. Radiological imaging provides anatomical and functional characterization of tumors, whereas digital pathology contributes microscopic assessment of immune infiltration, stromal remodeling, angiogenesis, fibrosis, necrosis, and tissue architecture. Multi-omics technologies—including genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, and spatial biology—provide detailed molecular characterization of immune ecosystem dynamics.[14]

Wearable biosensors continuously monitor physiological parameters including physical activity, heart rate, sleep quality, treatment-related symptoms, medication adherence, and quality-of-life indicators. Laboratory biomarkers, physician documentation, environmental exposures, and electronic health records contribute longitudinal clinical context extending beyond conventional hospital-based assessments.

Artificial intelligence harmonizes these diverse modalities using multimodal transformers, graph neural networks, biological knowledge graphs, and cross-modal attention mechanisms capable of generating adaptive computational embeddings representing continuously evolving immune biology.[15]

7. Predicting Immunotherapy Response

One of the most important clinical applications of foundation AI models is prediction of responsiveness to immunotherapy through comprehensive modeling of tumor-immune

interactions. Artificial intelligence simultaneously analyzes imaging phenotypes, histopathological characteristics, immune-cell composition, genomic alterations, transcriptomic signatures, proteomic profiles, laboratory biomarkers, and longitudinal clinical trajectories to generate individualized predictions regarding responsiveness to immune checkpoint inhibitors, adoptive cellular therapies, cancer vaccines, bispecific antibodies, and combination immunotherapeutic strategies.[16]

Unlike conventional prediction based primarily on isolated biomarkers, adaptive foundation models continuously refine immune response predictions as new biomedical information becomes available, enabling clinicians to optimize treatment strategies according to evolving tumor biology and immune dynamics.

These predictive capabilities substantially improve patient selection while reducing unnecessary toxicity and improving long-term therapeutic outcomes.[17]

8. Artificial Intelligence for Resistance Mechanisms

Therapeutic resistance remains one of the principal challenges limiting durable responses to cancer immunotherapy. Foundation AI models integrate serial radiological imaging, computational pathology, spatial biology, multi-omics, liquid biopsy, laboratory biomarkers, wearable physiological monitoring, and longitudinal clinical outcomes into adaptive computational frameworks capable of identifying emerging mechanisms of immune escape, clonal evolution, stromal remodeling, metabolic adaptation, checkpoint pathway activation, and treatment resistance.[18]

Artificial intelligence continuously updates biological representations as tumors evolve under therapeutic pressure, thereby enabling earlier identification of resistance mechanisms and supporting adaptive modification of immunotherapeutic strategies before irreversible disease progression occurs.

These computational capabilities establish adaptive resistance modeling as a cornerstone of future precision immunotherapy.[19]

9. Predicting Clinical Outcomes

Foundation AI models extend beyond prediction of therapeutic response by estimating clinically meaningful outcomes including treatment-related toxicity, immune-related adverse events, recurrence probability, progression-free survival, overall survival, quality of life, and long-term survivorship. These adaptive computational models integrate imaging, pathology, immunomics, laboratory biomarkers, wearable physiological monitoring, medication history, and longitudinal clinical trajectories into comprehensive predictive frameworks supporting individualized outcome forecasting throughout the entire cancer care continuum.[20]

10. Digital Twins for Precision Immunotherapy

Digital twin technology represents one of the most advanced applications of foundation AI models in precision immunotherapy by creating continuously evolving virtual representations of individual cancer patients that integrate radiological imaging, digital pathology, immunomics, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, medication history, and longitudinal clinical records into adaptive computational ecosystems.[21]

These virtual immune patients continuously synchronize with newly acquired biomedical information, enabling simulation of tumor evolution, immune activation, immune escape, therapeutic response, immune-related adverse events, recurrence, metastatic dissemination, and survival under multiple therapeutic scenarios. Unlike conventional predictive models, digital twins evolve alongside biological patients while continuously updating immune ecosystem dynamics according to changing molecular and physiological conditions.

These adaptive computational ecosystems enable clinicians to evaluate alternative immunotherapeutic strategies before implementation while supporting individualized precision oncology based on continuously evolving patient biology.

11. Intelligent Clinical Decision Support

Foundation AI models provide the computational foundation for next-generation clinical decision-support systems capable of integrating heterogeneous biomedical information into comprehensive patient-centered recommendations for immunotherapy. Radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based immunotherapy guidelines are synthesized into unified computational environments supporting multidisciplinary oncology practice.[22]

Interactive clinical dashboards generate individualized immune biomarker analyses, diagnostic summaries, digital twin simulations, therapeutic recommendations, toxicity estimates, recurrence probabilities, survival forecasts, and adaptive treatment pathways while facilitating collaboration among oncologists, radiologists, pathologists, immunologists, surgeons, molecular biologists, pharmacists, nurses, and computational scientists.

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

12. Continuous Learning and Adaptive Immunotherapy

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

Continual learning algorithms enable incremental refinement of computational knowledge without catastrophic forgetting of previously acquired information, while reinforcement learning

optimizes immunotherapeutic recommendations through iterative evaluation of clinical outcomes. Consequently, adaptive foundation models remain synchronized with evolving tumor biology, immune dynamics, emerging scientific discoveries, changing clinical guidelines, and diverse patient trajectories.

This continuous learning paradigm transforms immunotherapy from static treatment selection toward adaptive precision medicine capable of responding dynamically to evolving immune biology.

13. Federated Foundation Models for Global Immuno-Oncology

Development of highly generalizable immunotherapy 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 immunotherapy models using radiological imaging, digital pathology, immune profiling, molecular diagnostics, laboratory investigations, wearable monitoring, 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 immuno-oncology therefore establishes an international computational ecosystem capable of accelerating scientific discovery, improving equitable access to precision immunotherapy, and supporting global cancer research while maintaining responsible data stewardship.

14. Explainability, Validation, and Ethical Governance

Successful implementation of foundation AI models for precision immunotherapy 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, immunological, 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 adaptive immunotherapy systems into routine oncology practice.

15. Future Perspectives

Future precision immunotherapy platforms 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) technologies, robotics, cloud-native healthcare infrastructure, and autonomous clinical reasoning systems into unified intelligent immuno-oncology ecosystems.[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 immunotherapeutic strategies, supporting adaptive clinical trials, generating

personalized patient communication, and continuously synthesizing biomedical evidence. Such intelligent ecosystems are expected to transform immunotherapy from reactive treatment selection toward predictive, preventive, adaptive, continuously learning, and precision-guided cancer care.

16. Discussion

Foundation AI models represent one of the most significant paradigm shifts in precision immunotherapy by integrating multimodal biomedical intelligence into comprehensive computational ecosystems capable of predicting therapeutic response, resistance mechanisms, and long-term clinical outcomes. Unlike conventional artificial intelligence systems developed for isolated predictive tasks, these intelligent frameworks simultaneously analyze molecular biology, immune ecosystem dynamics, tissue architecture, radiological imaging, laboratory biomarkers, physiological monitoring, environmental influences, and longitudinal clinical trajectories to generate holistic representations of evolving tumor-immune interactions.[27]

Applications spanning computational pathology, radiogenomics, immune biomarker discovery, digital twins, adaptive therapeutics, continuous learning, federated collaboration, digital health, survivorship management, and intelligent clinical decision support demonstrate the extraordinary potential of foundation AI models to redefine future immuno-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, adaptive foundation AI models are expected to become the central computational infrastructure supporting intelligent precision immunotherapy worldwide.

17. Conclusion

Foundation AI models are transforming precision immunotherapy by integrating radiological imaging, digital pathology, immunomics, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, digital twins, and longitudinal clinical intelligence into unified computational ecosystems capable of supporting accurate prediction of therapeutic response, resistance mechanisms, toxicity, disease progression, and personalized clinical outcomes throughout the cancer care 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 immune biomarker discovery, adaptive therapeutic optimization, continuous disease surveillance, predictive clinical decision-making, and continuously personalized immunotherapy.[29]

Although important scientific, technical, ethical, regulatory, and implementation challenges remain, sustained collaboration among oncologists, immunologists, 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 for precision immunotherapy. These innovations have the potential to improve patient outcomes, enhance healthcare efficiency, reduce disparities in cancer care, accelerate translational immuno-oncology research, and establish a new era of intelligent, adaptive, and continuously learning precision cancer immunotherapy worldwide.[30]

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