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REVIEW

Artificial intelligence in immunotherapy: revolutionizing diagnostic and therapeutic applications in cancer and autoimmune diseases

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Abstract

Artificial intelligence (AI) is increasingly advancing precision immunotherapy by integrating high-dimensional biomedical data to support diagnosis, treatment selection, and longitudinal monitoring in both cancer and autoimmune diseases. This review summarizes AI applications in biomarker discovery, prediction of immune checkpoint inhibitor (ICI) response and toxicity, neoantigen prioritization, CAR-T cell optimization, and therapeutic antibody engineering. In oncology, multimodal models combining multi-omics, medical imaging, and clinical variables improve patient stratification and non-invasive response assessment, with several imaging- and pathology-based prediction tasks reporting clinically meaningful performance (frequently AUC ~ 0.70–0.95 across tumor types and endpoints). In autoimmune diseases, AI enables earlier diagnosis, molecular subtyping, treatment-response prediction, and real-time disease activity tracking using EHR, laboratory, imaging, and wearable data—supporting precision management in conditions such as rheumatoid arthritis and type 1 diabetes. Key challenges include data heterogeneity, model interpretability, and governance; however, explainable AI, federated learning, and digital twin frameworks offer practical routes toward trustworthy clinical translation. Overall, AI

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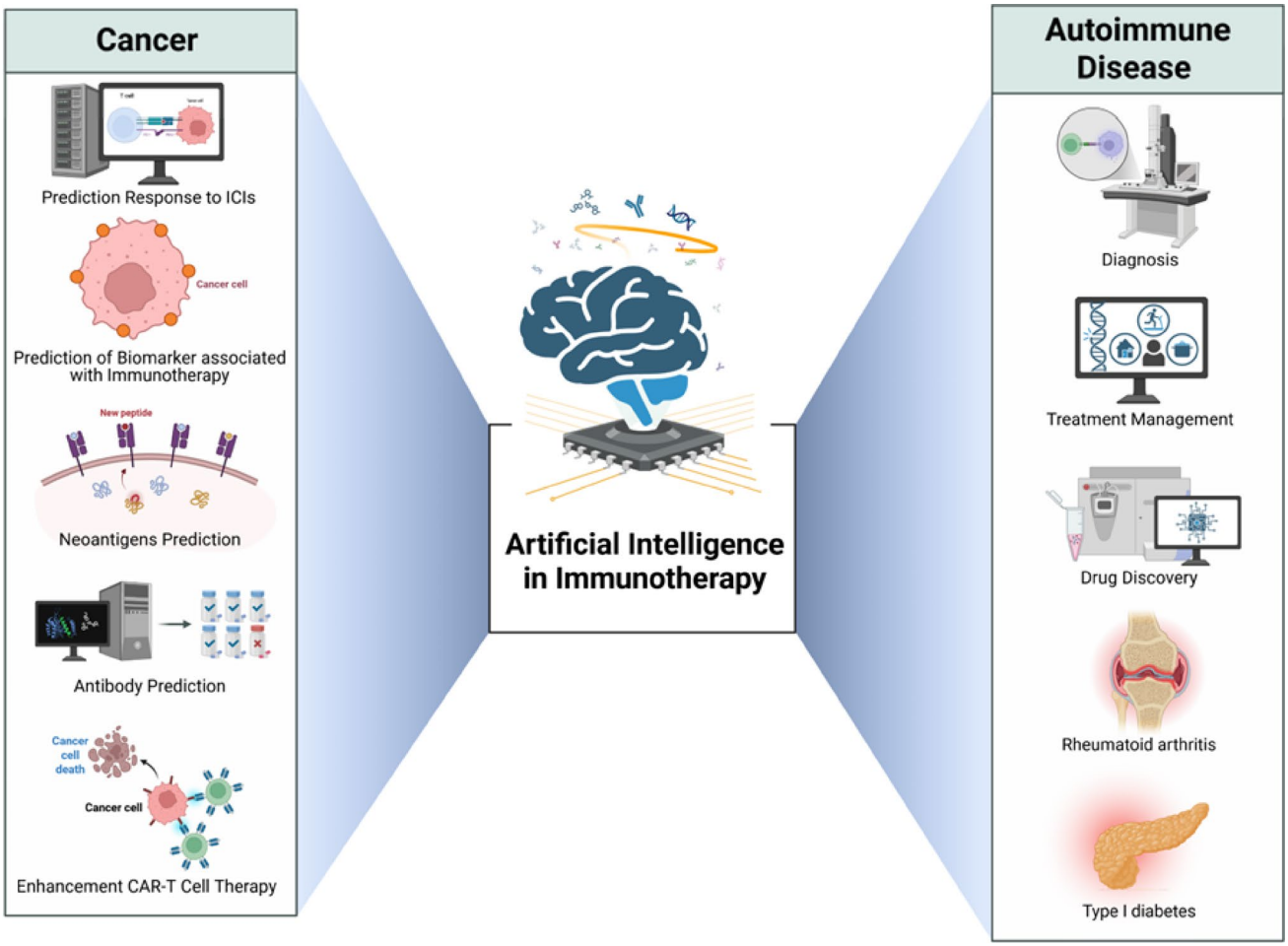
is emerging as a foundational technology for next-generation, patient-specific immunotherapy across oncology and autoimmune medicine.

Graphical abstract



Artificial intelligence enhances cancer and autoimmune disease immunotherapy through biomarker discovery, response prediction, neoantigen and antibody optimization, and real-time treatment management, enabling precision medicine across clinical applications.

Keywords Artificial Intelligence · Immunotherapy · Cancer · Autoimmune Diseases · Precision Medicine · Machine Learning

Introduction

Immunotherapy encompasses a wide range of strategies that harness components of the immune system, such as antibodies, immune cells, and cytokines, to treat cancers and autoimmune conditions. It also includes immunomodulation through vaccines aimed at preventing and managing infectious and allergic diseases(1). In this review, "precision immunotherapy" refers to the biomarker-informed selection and dynamic adaptation of immune-based interventions for an individual patient, integrating tumor/immune characteristics, microenvironmental context, and longitudinal monitoring of response and toxicity(2). Accordingly, we cover representative AI approaches ranging from classical machine learning (e.g., regularized regression, random forests, support vector machines) to deep learning architectures—including convolutional neural networks (CNNs) for radiology and whole-slide pathology, and transformer-based models/protein language models for sequence- and structure-informed prediction—applied across multi-omics (including single-cell RNA-seq), immunopeptidomics, medical imaging, digital pathology, and real-world clinical

data such as electronic health records (EHRs) and wearable-derived signals.

Cancer remains a major global health concern, causing nearly 10 million deaths each year and ranking as the second leading cause of mortality worldwide. This burden is influenced by aging populations, lifestyle changes, and exposure to risk factors such as tobacco use, obesity, and physical inactivity(3). Conventional cancer treatments, including surgery, chemotherapy, and radiotherapy, remain the foundation of care but face significant limitations. Chemotherapy, although effective against rapidly dividing tumor cells, lacks specificity and harms healthy tissues, leading to adverse effects and a reduced quality of life. Resistance to chemotherapeutic agents, whether intrinsic or acquired, further compromises long-term outcomes. Radiotherapy provides greater precision but can still damage adjacent tissues, causing complications such as skin injury and fatigue. These drawbacks underscore the urgent need for more innovative, targeted, and less toxic therapeutic alternatives(4, 5).

Cancer immunotherapy, which activates the host immune system to recognize and eliminate malignant cells, has emerged as one of the most promising therapeutic strategies.

Tumors frequently evade immune surveillance by exploiting immune checkpoint pathways, which suppress T-cell activation. Clinically relevant checkpoint molecules include programmed death-1 (PD-1), its ligand PD-L1, and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4)(6, 7). Significant clinical advances in immunotherapy include immune checkpoint inhibitors (ICIs), chimeric antigen receptor (CAR) T cell therapies, therapeutic cancer vaccines, and adoptive cell transfer techniques(8, 9). Conceptually, AI supports immunotherapy along two complementary axes: (i) target discovery and therapeutic engineering (e.g., antigen/neoantigen prioritization, CAR construct optimization, and antibody design), and (ii) clinical decision support (e.g., integrating multimodal patient data to predict ICI response/toxicity, guide treatment selection and sequencing, and enable monitoring and adaptive management)(10).

AI is increasingly integral to advancing cancer immunotherapy by refining target discovery, predicting treatment outcomes, and enabling personalized therapeutic strategies (11). For instance, researchers at the Cleveland Clinic and IBM demonstrated that AI models simulating peptide antigen dynamics can identify viable immunotherapy targets more efficiently than conventional trial-and-error approaches, particularly by capturing antigen structural changes in influencing immune recognition(12). AI-driven platforms now integrate diverse datasets, including genomic, proteomic, and imaging data, to predict patient responses to ICIs and optimize combination strategies(13). These approaches improve diagnostic accuracy by identifying biomarkers, such as PD-L1 expression and tumor mutational burden (TMB), and facilitate the discovery of novel therapeutic targets, like neoantigens(14, 15). Such tools support the design of personalized treatment regimens, enhancing efficacy while reducing adverse effects. Nonetheless, challenges persist in data standardization, model interpretation, and clinical integration, which must be addressed to fully realize AI's transformative potential in precision oncology(16).

AI also plays a critical role in the diagnosis and management of autoimmune diseases through precise risk assessment and individualized therapeutic planning(17). Autoimmune disorders result from the immune system's failure to distinguish between self and non-self, leading to chronic inflammation, tissue damage, and diverse clinical manifestations(18). These conditions can affect nearly any organ system. Notable examples include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), multiple sclerosis (MS), and type 1 diabetes mellitus (T1DM), all of which share immune dysregulation as a core mechanism despite differing clinical features(18, 19).

Cutting-edge AI algorithms are increasingly applied to analyze high-dimensional genetic and molecular data, uncovering new gene-disease associations and immune pathways implicated in autoimmune pathogenesis. For example, AI has improved risk prediction and treatment stratification in SLE and RA by integrating omics data with ML models(20). These tools facilitate early diagnosis, enable patient stratification based on molecular signatures, and predict therapeutic efficacy, thus supporting precision treatment strategies(21).

Drug repurposing is also being explored in immune-mediated diseases; for example, metformin has been evaluated as adjunct therapy in T1DM, with outcomes that can vary by cohort and clinical context(22, 23).While challenges such as data heterogeneity and algorithmic bias remain, AI continues to drive innovation in precision medicine for autoimmune disorders, ultimately improving clinical outcomes and quality of life(20, 21, 24). This review examines recent advances in AI applications in immunotherapy, with a focus on their growing role in cancer treatment and autoimmune diseases management.

Statement of significance.

Heading	Summary
Problem or Issue	Immunotherapy has transformed treatments for cancer and autoimmune diseases, yet major challenges remain in predicting therapeutic response, optimizing drug delivery, and ensuring patient safety, largely due to biological heterogeneity and the complexity of integrating multi-source biomedical data.
What is Already Known	AI has been applied separately in oncology and autoimmune disorders, showing promise in biomarker discovery, patient stratification, drug design, and outcome prediction. However, most reviews address one disease area in isolation, limiting cross-disciplinary insights.

Heading	Summary
What This Paper Adds	This work bridges oncology and autoimmune immunotherapy, offering a translational and pharmaceutical informatics perspective on AI-driven solutions — including explainable AI, federated learning, and digital twins — to address shared therapeutic challenges and accelerate precision medicine.
Who Would Benefit from the New Knowledge in This Paper	Biomedical informatics researchers, clinical immunologists, pharmaceutical scientists, and healthcare decision-makers involved in developing AI-enabled immunotherapies or optimizing targeted drug delivery for complex immune-mediated diseases.

AI advances in immunotherapy

AI-powered imaging biomarkers increasingly enable non-invasive tumor characterization and evaluation of the tumor microenvironment (TME), thereby enhancing patient selection for immunotherapy(25, 26). For instance, in non-small cell lung cancer (NSCLC) and melanoma, AI-derived radiomic features extracted from pre-treatment contrast-enhanced computed tomography (CT) scans have distinguished responders from non-responders. Radiographic heterogeneity- including irregular tumor borders and variable internal density-has been associated with favorable response to immune checkpoint inhibitors (ICIs) in multiple cohorts (25, 27, 28). In digital pathology, AI has revolutionized histological image analysis by enabling automated, high-throughput examination of tumor tissue samples. Generative Adversarial Networks (GANs), have shown remarkable ability to synthesize high-resolution histological images and capture latent image features through unsupervised learning. These advances have improved nuclear segmentation, detection, and domain adaptation, ultimately deepening our understanding of immune cell distribution and tumor architecture within the TME(29, 30). The conceptual framework for applying AI in immunotherapy, including data acquisition, preprocessing, model development, and translational applications, is summarized in Fig. 1.

AI has also played a key role in predicting TMB, a pivotal biomarker associated with responsiveness to immunotherapy. ML algorithms trained to classify TMB levels have enabled more accurate stratification of patients into groups with distinct survival outcomes following ICI treatment(31). Similarly, radiomic signatures derived from CT imaging

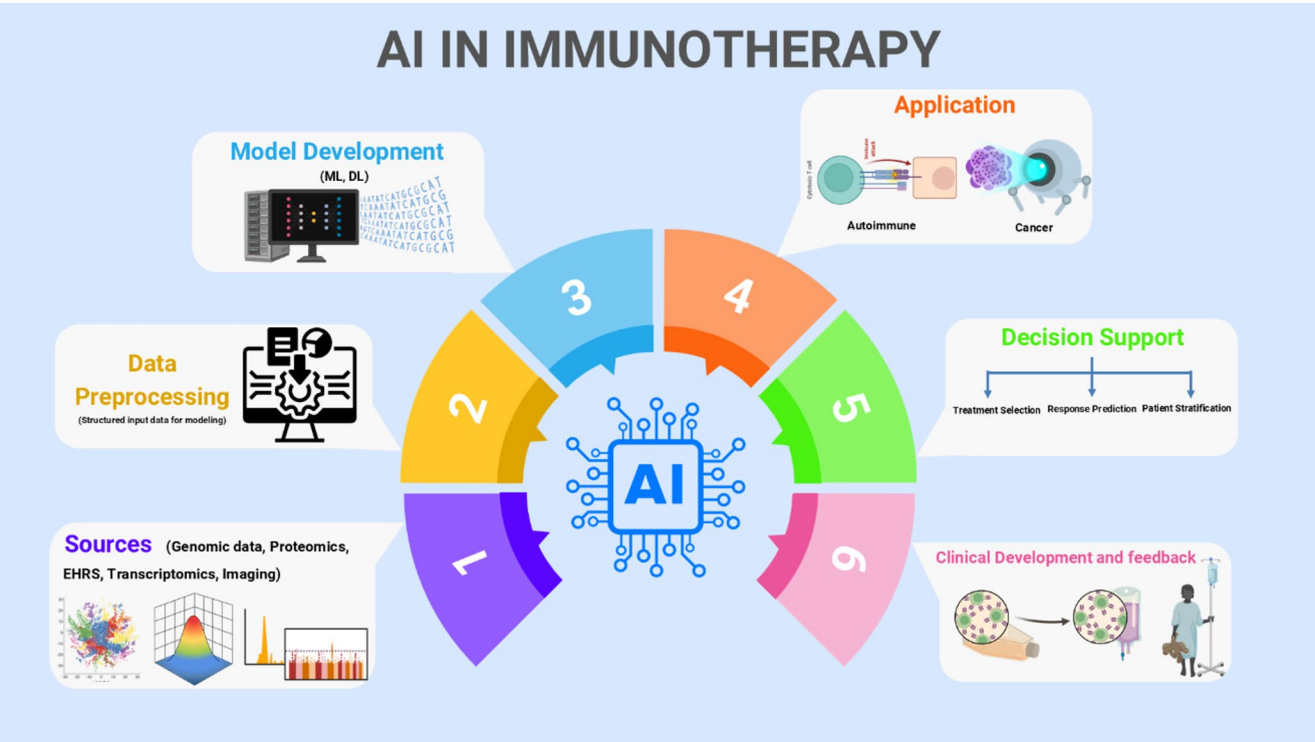


Fig. 1 Schematic representation of AI applications in immunotherapy. AI workflows typically begin with the integration of diverse data sources, including genomics, proteomics, transcriptomics, EHRs, and medical imaging. These are subjected to preprocessing to create structured datasets suitable for ML or DL model development. The resulting predictive models are applied to clinical scenarios involving cancer and autoimmune diseases, supporting key tasks including treatment response prediction, biomarker identification, and patient stratification. The feedback loop from clinical deployment informs model refinement and guides ongoing development—**Abbreviations**: *EHR, electronic health record; ML, machine learning; DL, deep learning*

Table 1 AI Applications in Cancer Immunotherapy

AI/ML Model or Algorithm Type	Cancer Type(s)	Data Modalities Used	AI Application Purpose	Performance Metrics	Clinical or Translational Impact	References
Deep Learning (CNNs, RNNs, Transformers)	Non-small cell lung cancer(NSCLC)	Radiomics (CT), histopathology, genomics	PD-L1 prediction, TMB prediction, and ICIs response classification	AUC 0.80–0.95, Sensitivity >85%	Enhanced patient stratification, non-invasive biomarker analysis	(51, 52, 107, 108)
	melanoma	Radiomics, Whole-slide imaging, Genomics	Overall survival prediction, neoantigen discovery, and immune phenotype classification	Accuracy >90%, AUC 0.92	Improved immunotherapy targeting and survival stratification	(56, 65, 135)
	colorectal cancer	Histopathology, Clinical data, Genomics	MSI/dMMR status prediction, TMB prediction	Clinical-grade accuracy, AUC >0.85	Supports FDA biomarker-based therapies	(124, 125, 130)
	Head and Neck Squamous Cell Carcinoma	Transcriptomics, Genomics	Neoantigen prioritization, immune receptor profiling	High precision in immune target selection	Precision targeting of immune checkpoint blockade	(307)
	Bladder Cancer	Histopathology, Clinical Data	Immune landscape profiling, TILs prediction	Accuracy >88%	Better immune characterization for ICIs	(308, 309)
Random Forest/ Gradient Boosting Machines	Melanoma	Radiomics (CT), clinical data, and immune profiling	Predict ICI response; classify tumor immune phenotypes	AUC: 0.85–0.90; Accuracy: ~85%	Improves ICI eligibility prediction and patient stratification	(57)
	Breast Cancer	Genomics, proteomics, imaging (radiology)	Drug response prediction; immune subtype classification	Accuracy: ~88%; AUC: 0.91	Optimizes biologics and targeted therapy selection	(310)
	Gastric Cancer	Clinical variables, radiological data, multi-omics	Biomarker discovery, survival outcome modeling	AUC ~0.86, precision ~83%	Enhances prognosis and therapy planning	(311–314)
Support Vector Machines (SVMs)	NSCLC	Radiomics (CT/MRI), histopathology, clinical parameters	Immune phenotype classification, TME analysis, biomarker prediction	Sensitivity >85%, Specificity >80%	Improves immunotherapy stratification; guides biomarker validation	(315, 318)
Reinforcement Learning	CAR-T applicable cancers (hematologic malignancies, solid tumors)	Clinical data, CAR cell characteristics, treatment parameters	Optimization of CAR infusion dosing and scheduling protocols	Early-stage development showing promise for therapy optimization	Potential for improved CAR-T production efficiency and personalized treatment adaptation	(65)
Deep Neural Networks (DNNs)	Melanoma	Peptide sequences, Protein language models (ProtTrans), Multi-window CNN	Neoantigen prediction without requiring specific MHC allele information	AUC: ~0.93; MCC: ~0.53; Accuracy: ~92%	Facilitates accurate neoantigen identification for personalized cancer vaccines and immunotherapies	(319)
	NSCLC	Genomics Clinical Data, PET/CT imaging	Gene mutation prediction (EGFR, KRAS, ALK)	AUC: 0.94	Enables precise targeted therapies and improved mutation-driven treatment planning	(320)
Transformers (BERT, BioBERT)	Head and Neck Cancer, Melanoma	Genomic sequences, transcriptomics	Neoantigen prioritization, immune repertoire profiling	High precision in antigen prediction	Enhanced immune receptor mapping; improved selection of immunotherapy targets	(321)
Multi-omics Integration Models	Lung, Breast, Colorectal Cancers	Genomics, transcriptomics, proteomics, metabolomics, clinical data	Integrated biomarker discovery, response prediction, and TME characterization	AUC >0.90	Comprehensive tumor profiling, precision immunotherapy, and identification of novel therapeutic targets	(322)
Graph Neural Networks (GNNs)	NSCLC	PET/CT radiomics and transcriptomic data	Predict lymph node metastasis; integrate genomic and imaging features	AUC = 0.85	Supports prognosis modeling; enhances multimodal integration for clinical risk assessment	(323)

Table 1 (continued)

AI/ML Model or Algorithm Type	Cancer Type(s)	Data Modalities Used	AI Application Purpose	Performance Metrics	Clinical or Translational Impact	References
Convolutional Autoencoders	Melanoma	Dermoscopic images	Skin lesion classification via dimensionality reduction and deep learning	Accuracy ~98–99%	Enhances early diagnosis and classification of melanoma and other skin cancers	(324)
Transfer Learning	Rare Cancers, Heterogeneous Tumors	Imaging	Adapt models to small datasets; improve classification and reduce training time	Accuracy up to 94.2% with small datasets	Enables AI application to rare cancers; improves generalizability with limited data	(325)
Attention-based Multi-task DL	NSCLC	Imaging (CT)	Subtype classification and staging; highlights discriminative features	AUC ~0.96	Improves interpretability and supports clinical decision-making	(326)
Explainable AI (XAI) Methods	All Cancer Types	Multi-omics, imaging, and clinical data	Model interpretability, biomarker importance elucidation	Improved clinical trust; diagnostic accuracy >90%	Enhances clinician acceptance; reveals novel biomarker roles; supports precision treatment	(327–329)
Capsule Networks	NSCLC (Lung), Colon	Histopathology images	Spatial and morphological feature extraction	Accuracy ~92–99%	Captures hierarchical features; improves diagnostic performance; aids in tumor grading	(330–332)
Hybrid Models (ML + DL Ensembles)	Lung, Colon, Breast Cancers	Histopathological images, clinical records, multimodal data	Tumor subtype classification, biomarker discovery, patient stratification	Accuracy up to 98.9%, AUC ~0.95	Integrates imaging and clinical features; enhances diagnostic accuracy; supports personalized therapy decisions	(333–336)

have been used to characterize immune phenotypes, distinguishing tumor-inflamed and tumor-desert subtypes. High signature scores, reflecting elevated $CD8^+$ T-cell infiltration, correlate with improved objective response rates and survival(32, 33). In addition, AI has contributed significantly to post-treatment evaluation. Radiomic-based models comparing baseline and on-treatment imaging, can identify patients with poor therapeutic sensitivity and shortened overall survival. These models quantify dynamic tumor changes, such as alteration in volume, boundary invasion, and spatial heterogeneity, providing early indicators of resistance (31, 34).

Clinical translation is progressing. Although most radiomic signatures for ICI response remain investigational, deep-learning radiomic biomarkers have undergone large, multi-institution validation in real-world cohorts and have also been evaluated using prospective clinical-trial datasets in advanced NSCLC, illustrating movement toward clinically testable decision support for immunotherapy selection(35). In parallel, peer-reviewed regulatory analyses indicate that regulators (including the FDA) have authorized a growing number of AI-enabled medical imaging devices and are refining oversight frameworks for AI software as a medical device, emphasizing clinical validation, generalizability across sites, bias mitigation, and lifecycle/post-deployment monitoring(36). Despite these advances, challenges remain in integrating AI into routine immunotherapy practice. Variability in data quality, limited model interpretability, and the need for large-scale, multicenter validation hinder clinical translation. Addressing these barriers will be essential. Future research should emphasize advanced frameworks such as reinforcement learning for adaptive treatment strategies and federated learning to support secure, privacy-preserving collaboration across institutions(29, 37).

AI in cancer immunotherapy

AI is redefining the landscape of cancer immunotherapy by processing large-scale, multidimensional biological datasets and discover predictive biomarkers that inform patient-specific responses to treatments, such as immune checkpoint inhibitors (ICIs)(38). One key advancement is the development of platforms such as SCORPIO (Standard Clinical and laboratory featuRes for Prognostication of Immunotherapy Outcomes), a machine-learning model that predicts ICI benefit using widely available clinical variables, including routine blood tests (e.g., complete blood count and standard chemistry panels) and basic patient characteristics. In a large multi-cohort study including 9,745 ICI-treated patients across 21 cancer types, SCORPIO was trained on an internal cohort and validated across independent datasets, showing

AUCs in the ~0.7–0.76 range for survival/clinical benefit prediction(39). Additionally, AI-based integrative models that combine genomic, proteomic, and imaging data have substantially improved the accuracy of therapeutic outcome predictions. These models not only facilitate the optimization of treatment strategies but also enable the identification of novel immunogenic targets, such as neoantigens. These advancements help address the limitations of conventional biomarkers like PD-L1, which often fail to capture tumor heterogeneity or the dynamics of the immune microenvironment(16, 40). AI has made significant progress in refining predictive biomarker discovery, which is pivotal in enhancing the personalization of cancer care. Furthermore, AI is instrumental in individualizing immunotherapy by evaluating patient response profiles and enabling real-time adjustments to treatment. ML algorithms, particularly those trained on histopathological images and molecular features, have proven effective in predicting immunotherapy responses across various solid tumors(41, 42). For instance, models developed using mass spectrometry-based human leukocyte antigen (HLA) datasets have greatly enhanced the identification of tumor-specific neoantigens, thereby improving immune targeting and overall therapeutic efficacy. Moreover, AI systems enable continuous monitoring of patient responses throughout the treatment course, offering clinicians actionable insights that support early intervention and adaptive therapy planning(33, 43). Despite its transformative potential, the full integration of AI into clinical oncology faces challenges that must be addressed for widespread adoption. These include issues related to data privacy, algorithmic transparency, and the interpretability of complex ML models. As AI models become more advanced, they will require robust regulatory frameworks and transparent standards to ensure their ethical use in clinical practice. Overcoming these barriers will be essential for the successful implementation of AI in routine oncological care. As these challenges are progressively addressed, AI is poised to play an increasingly central role in modern immuno-oncology, supporting precision and personalized cancer treatment(44). An overview of key AI applications in cancer immunotherapy is presented in Table 1.

AI in predicting response to immune checkpoint inhibitors

ICIs are among the most thoroughly studied and widely utilized immunotherapeutic agents in oncology. They have received FDA approval for treating a variety of cancers, demonstrating significant efficacy in clinical trials(45). In normal physiology, immune checkpoints regulate the immune system by balancing activation and suppression, maintaining immune homeostasis and preventing autoimmunity or excessive inflammation(46). However, cancer cells frequently exploit these regulatory pathways to evade immune surveillance, thereby fostering an immunosuppressive TME that hinders effective immune responses(47). AI plays a crucial role in predicting by learning outcomes-associated patterns from large, heterogenous datasets spanning genomics, transcriptomics, epigenomics, radiomics, and digital pathology, enabling the construction of composite predictive signatures that reflect both tumor-intrinsic features and the immune contexture(33, 48).

PD-L1 remains a critical component of response assessment, and AI-based pipelines—particularly deep learning applied to whole-slide images and ML-based radiomic frameworks—have improved the consistency and scalability of PD-L1-related evaluation across tumor types(49, 50). In NSCLC, AI-assisted whole-slide image analysis has demonstrated improved concordance among pathologists, reaching 90.2% agreement, surpassing traditional manual evaluations. Moreover, multimodal AI systems that integrate pathological and CT-derived features have achieved a validation AUC of 0.80 for predicting response to ICIs, illustrating the value of combining complementary data sources for outcome prediction(51, 52).

Beyond PD-L1, AI models incorporate additional determinants of ICI benefit, including HLA-related features and TMB. ML frameworks that combine transcriptomic, radiogenomic, and digital pathology data have can improve predictive performance by capturing interactions between antigen presentation capacity, tumor heterogeneity and immune infiltration (53, 54). For instances, ML analyses, have linked loss of heterozygosity in HLA genes and intratumoral heterogeneity with ICI efficacy in NSCLC(55, 56). Epigenomic signals, including DNA methylation patterns, have also been explored as predictors of immunotherapy response in solid tumors. In parallel, radiomic features reflecting tumor volume, spatial heterogeneity, and edge characteristics, have been associated with clinical outcomes, in melanoma, such features have correlated strongly with overall survival in ICI-treated patients, with AUC values reaching 0.92, supporting non-invasive prediction strategies(56, 57).

The TME is a complex and dynamic ecosystem composed of diverse immune and stromal cell populations, soluble mediators, and extracellular matrix components that collectively shape immunotherapy responsiveness(58). AI enables systematic characterization of this environment and supports response prediction using immune-related variables such as tumor-infiltrating lymphocytes, systemic inflammatory indices (e.g., neutrophil-to-lymphocyte ratio), and tumor stemness-associated patterns (59, 60). These computational approaches facilitate immune-phenotype classification and help contextualize mechanisms such as

T-cell exhaustion and immune evasion. Additionally, integrating emerging platforms (e.g., Raman spectroscopy) with ML has shown promise for assessing treatment effects and refining response prediction in selected settings(61, 62). A schematic overview of the AI-powered workflow for ICI biomarker prediction and treatment optimization is presented in Fig. 2.

Enhancing CAR-T cell therapy

CAR-T cell therapy is a revolutionary approach that utilizes genetically engineered immune cells designed to recognize and destroy cancer cells. CAR-T cell therapies have achieved remarkable clinical success, particularly in treating hematologic cancers such as B-cell acute lymphoblastic leukemia (ALL), non-Hodgkin B-cell lymphomas, and multiple myeloma, resulting in regulatory approval of several products worldwide(63). However, despite these successes, challenges such as complex manufacturing processes, safety concerns, the difficulty of identifying precise tumor targets, and the regulation of CAR-T cell differentiation and persistence remain substantial barriers to wider adoption(64). AI is transforming CAR-T cell therapy by optimizing each stage, from target discovery to clinical decision-making. By integrating ML and DL, AI addresses manufacturing challenges, enhances therapeutic efficacy, ensures safety, and facilitates personalized treatment strategies. Key applications include optimizing CAR construct designs using structural prediction tools, such as AlphaFold, streamlining manufacturing through predictive algorithms, and identifying biomarkers that predict clinical outcomes and adverse events, such as cytokine release syndrome (CRS)(64, 65). Importantly, AlphaFold was trained primarily on experimentally determined structures of naturally occurring proteins(66); thus, when applied to engineered CAR domains, its outputs should be interpreted as hypothesis-generating structural models that require experimental validation rather than as CAR-specific ground truth(64).These advancements aim to extend CAR-T therapy beyond hematologic malignancies into solid tumors and increase accessibility by lowering production costs(67).

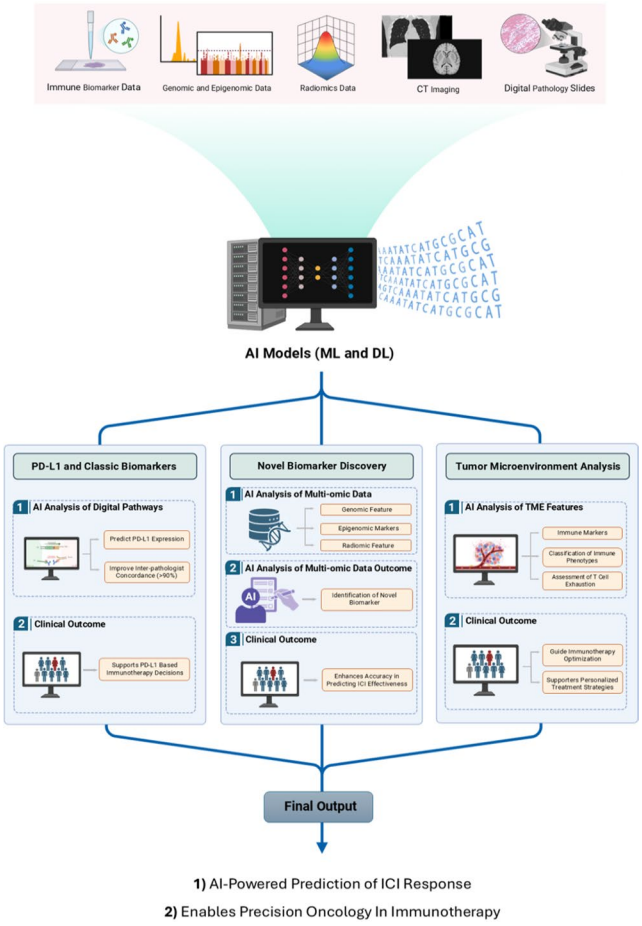


Fig. 2 AI-powered framework for predicting immune checkpoint inhibitor (ICI) response and supporting precision immunotherapy. Diverse data types—including immune biomarker profiles, genomic and epigenomic features, radiomic signatures, CT scans, and digital pathology slides—are integrated into ML and DL models. These models facilitate the prediction of PD-L1 expression, the discovery of novel biomarkers, and the characterization of tumor microenvironment (TME) features. Clinical outcomes derived from these analyses include improved PD-L1-based decision-making, enhanced accuracy in forecasting ICI effectiveness, and optimized treatment strategies through immune phenotype classification and T-cell exhaustion profiling. This pipeline supports the broader goal of precision oncology by enabling tailored and timely interventions in immunotherapy

AI plays a vital role in antigen target selection and CAR design by leveraging single-cell RNA sequencing data to identify tumor-specific markers while minimizing off-target effects. For instance, deep generative models have identified myeloid cell targets such as CD86 and CSF1R for acute myeloid leukemia(59, 64). Structural prediction tools optimize the stability and signaling domains of CAR proteins, utilizing ML models trained on thousands of synthetic costimulatory motifs to enhance T-cell activation and longevity. Concurrently, AI-assisted CRISPR-Cas9 genome editing improves precision and reduces off-target mutations, enabling the creation of CAR-T cells tailored for the challenging microenvironment of solid tumors(68, 69). Manufacturing optimization constitutes another critical frontier, where AI predicts ideal culture conditions and monitors cell proliferation via real-time “soft sensors.” Initiatives like AIDPATH utilize digital twin simulations of bioreactor processes, while scheduling algorithms coordinate parallel manufacturing cycles for multiple patients. ML models analyzing multi-omics data from CyTOF and single-cell RNA sequencing predict optimal CD4/CD8 ratios and memory cell proportions in final products, potentially reducing manufacturing failures by up to 30%. These innovations aim

to standardize production while preserving flexibility for patient-specific customization(63, 70, 71).

In clinical applications, AI enhances the prediction of treatment responses and the identification of adverse events. Multivariate logistic regression models incorporating lactate dehydrogenase levels and proportions of CAR^+ regulatory T cells achieve approximately 85% accuracy in forecasting six-month clinical outcomes(72, 73). For toxicity management, ML algorithms analyzing cytokine profiles, including interferon-gamma (IFN-γ) and macrophage inflammatory protein-1 alpha (MIP-1α), demonstrate over 85% sensitivity in predicting severe CRS. Additionally, models trained on PET/CT imaging data facilitate the early detection of relapse. Wearable AI systems enable the remote monitoring of physiological parameters, allowing for timely intervention in cases of side effects such as neurotoxicity(74). As these technologies mature, they hold promise to transform CAR-T therapy into a broadly accessible precision oncology modality capable of treating diverse cancer types with improved safety and efficacy profiles(75).

AI for neoantigen prediction

Neoantigens, the tumor-specific antigens generated by somatic mutations, represent a promising frontier in cancer immunotherapy. These antigens are expressed exclusively on cancer cells, making them ideal targets for immune-based therapies. However, only a fraction of these neoantigens elicit effective immune responses, necessitating accurate identification of the most immunogenic candidates(76).

AI is a vital tool in neoantigen prediction by addressing the limitations of traditional experimental methods through modeling peptide presentation by the major histocompatibility complex (MHC) and downstream T-cell receptor (TCR) recognition of the resulting peptide–MHC (pMHC) complexes (76, 77). Importantly, high MHC binding affinity mainly reflects antigen presentation likelihood and does not necessarily equate to true immunogenicity, which also requires productive TCR recognition and functional T-cell activation(78). AI-based strategies are revolutionizing neoantigen discovery by integrating multi-omics datasets to identify high-confidence targets. For example, platforms like EasyFuse utilize transcriptomic data to detect cancer-related gene fusions. In contrast, NeoDisc combines genomic, transcriptomic, and proteomic information to pinpoint immunogenic neoantigens more effectively than conventional methods(79). By improving neoantigen prediction and validation, AI accelerates the translation of precision immunotherapies into clinical usage, offering new treatment opportunities for patients with heterogeneous or treatment-resistant cancers(80, 81).

MHC-peptide binding prediction models are generally divided into allele-specific and pan-specific categories. Allele-specific models are trained on peptides corresponding to particular MHC alleles, while pan-specific models predict peptide binding across multiple alleles. These models typically encode MHC and peptide sequences into fixed-length vectors using methods such as one-hot encoding or embeddings(77, 82). Deep neural networks (DNNs) and convolutional neural networks (CNNs) are frequently employed to capture intricate patterns in peptide binding data(83). Notable predictors include NetMHCpan, MHCflurry, and HLAthena, which have enhanced prediction accuracy by incorporating ligand data derived from mass spectrometry(84–86). Although substantial progress has been made in predicting MHC class I (MHC-I) binding, predicting MHC class II (MHC-II) remains challenging due to the heterogeneity in peptide length and binding motifs, compounded by the polymorphic nature of MHC-II molecules(78, 82). However, incorporating MS-derived ligand data has improved the performance of MHC-II predictors, such as CAPTAn and MARIA(87, 88). Additionally, NetMHCIIpan has increased its predictive accuracy by deconvoluting MS-eluted ligand (MS-EL) data and expanding its training dataset to cover a broader range of HLA-II specificities(89, 90). Continued research is needed further to enhance the performance of MHC-II binding prediction models.

Forecasting the recognition of pMHC complexes by TCRs is particularly complex due to the diversity of TCR rearrangements and the spatial complexity of TCR-pMHC interactions(91, 92). Experimental techniques such as multimeric pMHC assays and high-throughput library screens have been developed to study pMHC-TCR binding. Technologies, including lentiviral transfer assays and synthetic peptide display libraries, have expanded the capacity to identify paired pMHC-TCR interactions(93, 94). Despite these advances, accurately predicting neoantigens based on pMHC-TCR binding remains a challenging area that requires further methodological improvements. The identification of tumor antigens and the development of cancer vaccines constitute cutting-edge immunotherapeutic strategies. Neoantigens, derived from somatic mutations unique to individual patients' tumors, are ideal targets for T-cell-based therapies because they are absent in normal tissues and evade central immune tolerance, allowing for specific recognition by both $CD4^+$ and $CD8^+$ T-cells. The personalized immunotherapy approach leverages AI to model immune interactions, optimize vaccine design, and efficiently select promising neoantigen candidates(95).

Accordingly, AI-guided mRNA and peptide vaccines have already progressed to phase I clinical trials in various cancers, illustrating AI's role in accelerating therapeutic

development(96, 97). Notably, computational/AI-supported neoantigen ranking is already being translated into personalized neoantigen vaccine trials(98). For example, BioNTech's individualized mRNA neoantigen vaccine autogene cevumeran has been evaluated as adjuvant therapy in resected pancreatic ductal adenocarcinoma, including in combination with checkpoint blockade, demonstrating feasibility and induction of neoantigen-specific T-cell responses in a subset of patients(99). In parallel, Moderna's individualized neoantigen therapy mRNA-4359 has been tested clinically in combination regimens (e.g., with pembrolizumab), as evaluated in resected melanoma, providing a concrete example of personalized neoantigen vaccine development in trials(96). Adjuvants further enhance vaccine efficacy by amplifying immune responses, and AI facilitates their design through virtual screening, property prediction, and drug repurposing efforts. For example, AI has identified CXCL12 inhibitors with potential as potent adjuvants(100, 101). By integrating genomics, bioinformatics, and machine learning, these innovations enable the precise selection of neoantigens and the formulation of vaccines, offering tailored solutions for tumors resistant to conventional therapies while addressing challenges such as immune suppression and tumor heterogeneity(102).

AI for direct prediction of immunotherapy responses

AI in cancer immunotherapy enables the detection of subtle phenotypic differences and generates detailed data that augment human assessment (103). AI algorithms excel in processing complex medical information, including imaging and large-scale datasets, to accurately and consistently forecast patient responses to ICB therapies(104). This capability supports the implementation of personalized treatment plans, ultimately improving clinical outcomes for cancer patients. In the realm of medical imaging, AI enhances radiological workflows by integrating high-dimensional data from modalities such as CT and magnetic resonance imaging (MRI)(105). AI-powered radiomic models noninvasively analyze tumor morphology and TME features, offering insights that outperform traditional imaging interpretation(106). These models have been particularly effective in predicting immunotherapy responses in cancers such as NSCLC, melanoma, and esophageal carcinoma. Radiomic biomarkers identified by AI also show correlations with genomic indicators, such as TMB, refining response prediction accuracy(107, 108).

Histopathology, the gold standard for cancer diagnosis, has similarly been transformed by AI. ML and DL applied to whole-slide histological images enable the precise identification and classification of cellular structures and protein expression patterns(109, 110). These AI-enhanced histopathological analyses enhance the prediction of immunotherapy responses by identifying abnormal morphological features and immune-related molecular markers within the tumor microenvironment. Such techniques facilitate more efficient patient selection for immunotherapy, potentially extending benefits to a broader patient population(111, 112). Figure 3 summarizes the major AI-integrated data domains, including medical imaging, histopathology, and immune signatures, used to predict immunotherapy outcomes directly. Beyond imaging and pathology, AI integrates multi-omics data to construct comprehensive predictive models. These incorporate a variety of biomarkers such as PD-L1 expression, TMB, tumor-infiltrating lymphocytes (TILs), and specific genetic mutations, thereby enhancing the reliability of immunotherapy response predictions. The integration of diverse data types enables a more nuanced characterization of tumors, advancing precision medicine and individualized treatment planning(113, 114).

Recent innovations include AI platforms like SCORPIO, which leverage routine clinical data, i.e., blood laboratory results and patient demographics, to predict responses to ICIs. SCORPIO surpasses current FDA-approved biomarkers in predictive performance with a faster, cost-effective, and widely accessible tool for guiding immunotherapy decisions. These predictive capabilities hold promise for improving treatment equity and reducing healthcare costs globally(39, 115). Overall, AI's contributions to cancer immunotherapy encompass detailed phenotypic profiling, advanced image analysis, histopathological interpretation, and the integration of multi-omics datasets, collectively enhancing the therapeutic response prediction, optimizing patient stratification, and supporting personalized immunotherapy to ensure precision oncology(16).

Predictive biomarkers and immunotherapy

AI models, particularly those employing ML and DL techniques, have demonstrated robust discriminative performance (e.g., AUC and sensitivity/specificity profiles) in detecting key immunotherapy-related biomarkers, such as PD-L1 expression, TMB, and microsatellite instability (MSI). Methods like Random Forest algorithms improve patient stratification for ICIs, thereby enhancing the personalization of treatments(116, 117). DL architectures, including convolutional neural networks (CNNs) and recurrent neural networks (RNNs), effectively process large-scale spatial and sequential datasets, enabling the identification of complex biomarkers, such as gene expression profiles predictive of ICI responsiveness. These AI approaches exhibit strong reliability, with AUC values ranging from 0.70 to 0.95, outperforming traditional, manual biomarker

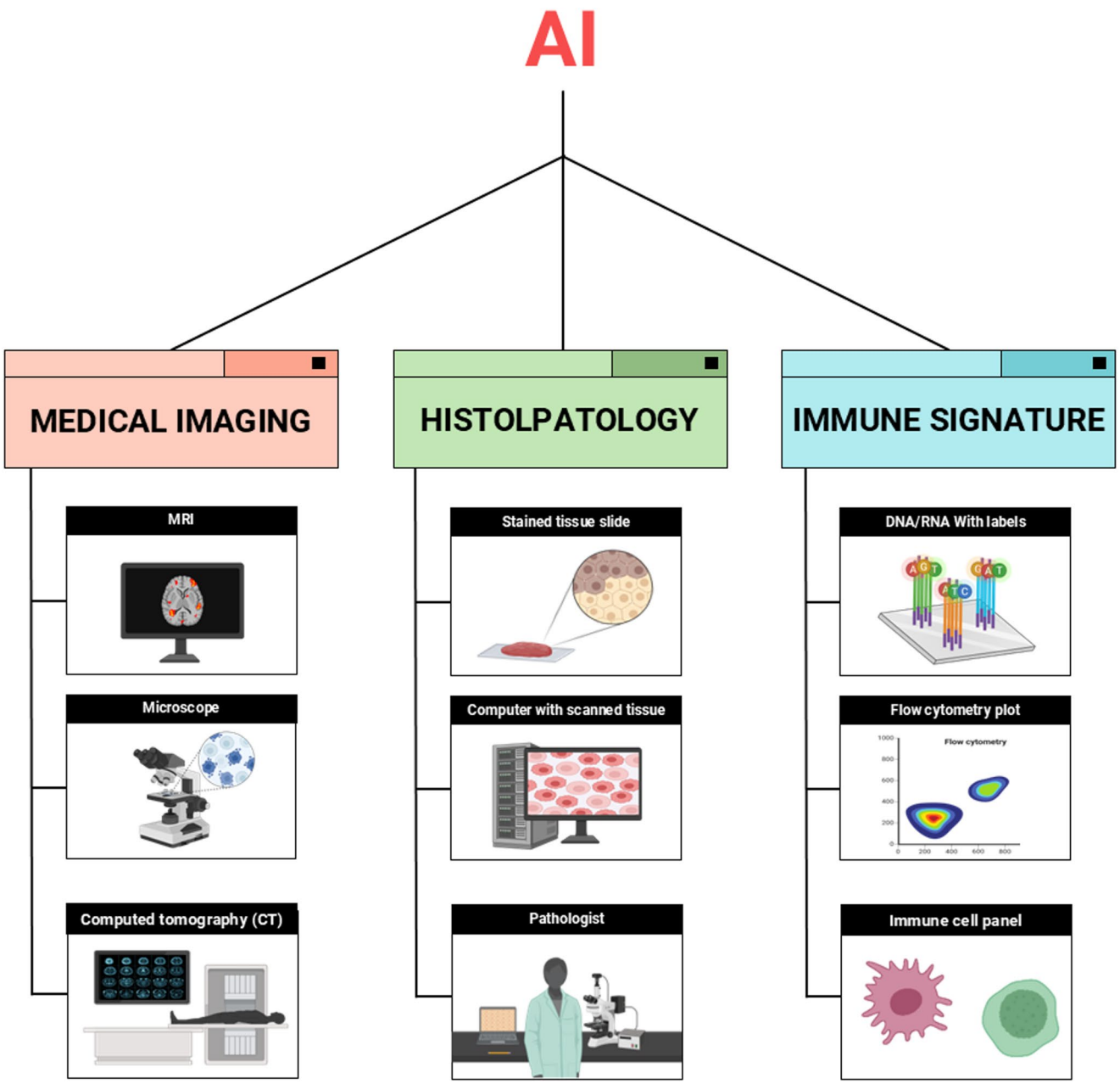


Fig. 3 Core data modalities integrated by AI for direct prediction of immunotherapy response. AI models utilize multimodal sources including (1) medical imaging (e.g., CT, MRI, microscopy) for radiomic feature extraction (2), histopathological analysis of whole-slide tissue sections to identify immune infiltration and morphological markers, and (3) immune profiling using genomic assays, flow cytometry, and immune cell panels. These datasets enable AI to detect clinically relevant tumor and immune signatures, enhancing the precision of response prediction in cancer immunotherapy

detection methods that tend to be slower, less precise, and less reproducible. Furthermore, AI's capacity to integrate multi-omics data has revolutionized biomarker identification by uncovering intricate patterns that conventional techniques often miss(118, 119).

Accurately detecting the expression status of tumor molecular pathological markers is essential before initiating clinical immunotherapy, as these markers guide treatment decisions and predict patient responses(120). For example, pembrolizumab (Keytruda) has gained FDA approval as a first-line treatment for patients with MSI-high (MSI-H) metastatic colorectal cancer, underscoring the clinical importance of such biomarkers. In addition to MSI, other genomic features, including TMB, homologous recombination deficiency (HRD), and whole-genome duplication carry significant predictive value(120–122). Consequently,

there is a growing demand for rapid and cost-effective biomarker detection methods, including approaches based on routine hematoxylin and eosin (H&E)-stained histopathology images, quantitative PCR (qPCR), immunohistochemistry (IHC), and next-generation sequencing (NGS), many of which do not require additional tissue samples(38).

While MSI testing is clinically valuable, it is not always performed due to the need for supplementary genetic or immunohistochemical assays. Advances in DL have enabled the direct prediction of MSI status from widely available H&E-stained histology slides, with model performance benchmarked against clinically determined MSI reference standards—typically PCR-based MSI testing and/or IHC-defined mismatch repair deficiency (dMMR)—and with formalin-fixed, paraffin-embedded (FFPE) slides demonstrating higher predictive accuracy than snap-frozen specimens(117, 123). Additionally, circulating tumor DNA (ctDNA) analysis has been used to predict MSI status in endometrial cancer patients, thereby supporting informed decision-making for immunotherapy. Large multicenter studies using DL models trained on whole-slide images of colorectal tumors have achieved clinical-grade accuracy in detecting MSI and mismatch repair deficiency (dMMR), surpassing even the accuracy of expert pathologists. Nevertheless, challenges remain in generalizing these models across diverse datasets, partly due to variability in slide preparation and scanning protocols(124, 125). AI has also been effectively used to predict PD-L1 expression. ML algorithms, including random forest classifiers and generative adversarial networks, have been used to quantitatively assess PD-L1 expression in tumor cells with high agreement compared to pathologists' manual scoring(126). Fully automated CNNs have further enhanced tumor cell detection and PD-L1 tumor proportion scoring (TPS), improving diagnostic consistency and efficiency, particularly among less experienced pathologists. These AI-enabled methods hold promise for standardizing and accelerating PD-L1 evaluation in clinical practice(127, 128).

TMB is another pivotal biomarker associated with immunotherapy response, as elevated TMB correlates with a higher neoantigen load and stronger immune recognition. DL models such as Image2TMB have been developed to predict TMB status directly from H&E slides, potentially replacing costly and time-intensive whole-exome sequencing(129, 130). Moreover, multimodal DL approaches that integrate histopathological images with clinical data have improved the accuracy of TMB prediction in cancers such as colorectal carcinoma. Clinical variables, such as tumor stage and patient age, have also been shown to have significant associations with TMB status, emphasizing the benefit of combining molecular and clinical information to tailor personalized immunotherapy strategies(130, 131).

AI for antibody prediction

AI is accelerating antibody discovery in cancer immunotherapy by enabling faster and more cost-efficient design of therapeutic antibodies(132). Advanced ML and DL models can predict antibody–antigen interactions, optimize binding affinity, and evaluate developability—key determinants of efficacy, safety, and manufacturability(133). For example, AI-driven platforms such as ADCNet integrate protein and small-molecule information to predict antibody–drug conjugate activity. Generative approaches, including variational autoencoders and language models, are increasingly used to propose novel antibody sequences, often with an emphasis on complementarity-determining regions (CDRs) that govern binding specificity(134, 135). In this review, "ImmunoNet" (mentioned later) is used as a hypothetical placeholder for a multimodal AI framework unless explicitly linked to a specific published model. Sequence design and affinity maturation. Recent progress in AI and DL has substantially advanced antibody discovery, particularly in target binding screening and affinity maturation. While high-throughput sequencing(HTS) and display libraries can explore vast antibody sequence spaces, much of the potential diversity remains experimentally inaccessible(136, 137).

AI approaches, including neural networks and generative algorithms, have therefore been integrated with experimental workflows to predict and enhance antibody sequences, improving affinity and specificity. For instance, ensemble neural networks can outperform individual models in predicting sequence enrichment during phage display panning, and gradient-based frameworks such as Ens-Grad propose sequence modifications that yield superior binding compared with training-set antibodies. Deep mutational scanning paired with CNNs further supports rational design of combinatorial libraries, reducing the search space and improving discovery of high-affinity binders(137, 138). AI-driven affinity maturation can also streamline iterative optimization by forecasting productive mutations and prioritizing candidates using confidence estimates, thereby improving efficiency early discovery efficiency(139).

Recent advances include LSTM-based deep generative models with downstream ranking (e.g., linear discriminant analysis) to generate and prioritize variants with progressively enhanced affinity and specificity, frequently surpassing frequency-only screening strategies(140). Despite these gains, distribution shift and limited negative/failed examples remain practical constraints, underscoring the importance of prospective, experiment-in-the-loop validation when deploying AI-guided sequence optimization(139). Structure prediction and antibody-antigen modeling. Recent advancements in DL have reduced reliance on labor-intensive and

expensive experimental structure determination (e.g., crystallography, NMR, and cryo-electron microscopy).

However, antibody structure prediction remains challenging because antibodies exhibit high conformational variability, particularly in the CDR H3 loop, and general protein structure predictors can underperform in these regions(66, 141). Moreover, the limited availability and diversity of high-quality experimentally resolved antibody structures (especially antibody–antigen complexes) remains a persistent bottleneck for training, benchmarking, and generalizing antibody-specific structural models. To address these challenges, antibody-focused models can be grouped by function. For CDR-focused loop modeling, DeepH3 uses deep residual neural networks with geometric features to improve prediction of CDR H3 conformations, outperforming earlier approaches in benchmark evaluations(142, 143). For full variable-domain modeling (including side chains), DeepAb integrates unsupervised representation learning and attention mechanisms to enhance interpretability and accuracy, while DeepSCAb incorporates side-chain geometry prediction, which further refines structural forecasts(144, 145).

However, some approaches remain multi-step and lack equivariance, which can limit speed and flexibility. For fast, end-to-end CDR loop prediction with scalable throughput, ABlooper applies E(n)-equivariant graph neural networks and provides reliable quality assessment, making it suitable for large-scale repertoire analyses(146, 147). For nanobody-specific modeling, NanoNet directly predicts 3D backbone coordinates, enabling rapid, high-throughput structure prediction useful for antibody–nanobody docking and epitope mapping(148). For integrated antibody–antigen pipelines, AbAdapt combines antibody and antigen modeling, epitope/paratope prediction, and rigid docking, leveraging state-of-the-art tools such as AlphaFold2 to accelerate antibody–antigen interaction studies((149, 150). AI and ML are also transforming prediction and optimization of key pharmaceutical properties in therapeutic antibodies, addressing specificity, immunogenicity, aggregation, solubility, viscosity, and pharmacokinetics. Traditional experimental approaches for developability screening are limited by material requirements and throughput, complicating early-stage triage(151, 152).

AI-driven techniques, including DL and protein language models, now support rapid prediction of these properties directly from antibody sequences. Examples include bidirectional LSTM networks and transformer-based tools such as BioPhi for evaluating antibody "nativeness" and humanization needs, as well as solPredict and DeepSCM for quantitative prediction of solubility and viscosity using transfer learning and CNN-based models(153–156). These approaches enable earlier elimination of candidates with unfavorable developability profiles, accelerating progression to downstream validation.

Beyond developability, AI models can support antibody optimization by simultaneously considering binding affinity and "naturalness"—which is associated with both key efficacy and safety. Deep contextual language models trained on affinity datasets can predict binding of novel variants and optimize functional and biophysical properties, outperforming purely random mutagenesis plus screening workflows(157, 158). AI can also integrate structural and in vitro assay data to predict pharmacokinetic behavior, identifying features such as isoelectric point and poly-specificity that influence antibody clearance. As more high-quality data becomes available, these ML methods are expected to continue improving, facilitating rational design of antibodies with superior therapeutic profiles and paving the way for safer, more effective biologic drugs (158, 159). A summary of AI applications in the diagnosis, treatment planning, and management of autoimmune diseases is provided in Table 2.

AI Applications in autoimmune disease diagnosis and therapy

The immune system is essential for protecting the body against foreign agents like bacteria, viruses and toxins. Upon detecting these invaders, the immune system mobilizes various defense cells to eliminate the threat. Normally, the immune system distinguishes between foreign entities and the body's own cells. However, when this balance is disrupted and the immune system attacks healthy self-cells, autoimmune disorders occur(18). These disorders can affect a wide range of organs and tissues, including blood vessels, connective tissue, endocrine glands (e.g., thyroid and pancreas), muscles, joints, skin, and red blood cells. To date, over 80 autoimmune diseases have been identified, with more likely undiscovered. Contributing factors include genetics, diet, infections, and chemical exposures. Diagnosing autoimmune diseases remains challenging due to the diversity of symptoms, which vary based on the affected organ or tissue and often include fatigue, redness, swelling, warmth, and pain(160).

Given the complexity of their clinical manifestations and underlying pathophysiology, autoimmune diseases present significant diagnostic and therapeutic challenges. AI has shown transformative potential in this area, particularly in improving diagnostic accuracy, enabling personalized treatment strategies, and providing real-time disease monitoring(161).

AI algorithms can process vast and diverse datasets, including EHRs, laboratory results, medical imaging, and genomic data(21). By identifying subtle patterns within

Table 2 AI Applications in Autoimmune Disease Management

AI/ML Model or Algorithm Type	Autoimmune Disease(s)	Data Sources	AI Application Purpose	Performance Metrics	Clinical or Translational Impact	References
CNNs	RA, Psoriasis, SLE	Radiographic (RA), Dermoscopic (Psoriasis), and Skin Images (SLE)	Automated diagnosis, lesion classification, inflammation assessment	AUC: 0.90–0.98; Accuracy: 91–96%	Enables early detection and image-based disease grading; supports differential diagnosis	(237, 337–339)
ANNs	RA, SLE	Clinical, lab, and serological data	Predict treatment outcomes, disease classification, and remission likelihood	AUC ~ 0.78–0.92; F1-score up to 0.91	Supports personalized therapy and disease severity stratification	(340, 341)
SVMs	MS	Blood biomarkers (Vit D3, B12, Se)	Diagnostic support	Sensitivity ~ 98.98%, Accuracy ~ 98.89%	Non-invasive, cost-effective diagnostic aid	(342)
XAI	RA, SLE	Multi-omics, HER, SNP	Biomarker discovery, transparent decision support	AUC > 90%	Enhances interpretability; enables personalized clinical decisions	(343, 344)
Random Forests & Gradient Boosting	RA	clinical/lab data	Predict biologic therapy response	AUC ~ 0.64–0.75	AUC ~ 0.64–0.75	(345, 346)
DL Models (DNNs, RNNs)	RA, MS, T1D Psoriasis	Imaging, genomics, clinical data	Diagnosis, disease progression prediction, patient stratification	AUC 0.80–0.92	Supports early detection and precision medicine; enables personalized interventions	(249, 347–352)
NLP	SLE, RA	EHR, clinical notes	Information extraction, risk assessment	Boosted diagnosis accuracy	Enhances structured data extraction from unstructured notes	(353–355)
Reinforcement Learning	MS	Force plate data (balance metrics)	Disease severity assessment and modeling	Qualitative improvement in balance modeling	Aids in quantifying MS progression and motor control	(356)
Decision Trees & Ensemble Methods	T1D, RA	EHR, biometrics, CGM glucose logs, cytokine data	Early diagnosis, complication prediction (e.g., hypoglycemia, RA activity)	Accuracy 78–93%	Supports timely diagnosis, predicts complications like hypoglycemia or disease flare	(357–359)
Transfer Learning	RA	Artificially augmented sparse datasets	Synovitis classification for disease monitoring	AUC 0.73–0.99	Enables AI application in data-scarce imaging scenarios	(360)
Digital Twin Models	T1D, MS	Multi-omics + clinical time series	In silico therapy simulation and precision dosing	Under validation; high simulation accuracy	Enables pre-trial prediction of individualized treatment responses and disease progression	(285, 361–363)

these datasets, AI supports earlier diagnosis, better disease prognosis and optimized therapeutic approaches(162).

For example, ML-based EHR phenotyping has been used to identify SLE cohorts using structured codes and laboratory data, with NLP-derived narrative features evaluated as additional signals(163). Similarly, AI analysis of OCT (including AS-OCT) can quantify intraocular inflammatory activity and assist uveitis grading, demonstrated correlation with Standardization of Uveitis Nomenclature (SUN) clinical grades and supporting earlier and more standardized assessment(164, 165). Despite its promise, challenges related to model development, data quality, and personalized treatment persist. Future progress is expected to rely on improved data integration and the refinement of AI algorithm, ultimately enhancing the diagnostic precision, treatment effectiveness, and disease monitoring. The application of AI in autoimmune disease research has grown considerably with advancements in AI technologies over the past two decades(162, 166). In the remainder of this section, we cover diagnostic applications, therapeutic applications (including drug discovery and treatment planning), and disease-specific examples in rheumatoid arthritis and type 1 diabetes.

Role of AI in diagnosing autoimmune disorders

AI, along with its associated models and algorithms, has become an invaluable asset in diagnosing autoimmune diseases, particularly in areas such as image analysis, laboratory data interpretation, and clinical decision support systems(167, 168). Furthermore, integrating AI with EHRs, wearable technologies, and patient-generated data has expanded the scope and precision of disease evaluation(169). AI-based image analysis has shown significant

promise in diagnosing autoimmune conditions, particularly RA and Immune-mediated dermatological diseases. In RA, ML and DL models can evaluate radiographs and ultrasound images to detect and quantify pathological features such as joint erosions and synovial hypertrophy, supporting earlier recognition and objective assessment of structural damage (170, 171). Similarly, AI models can analyze images of skin lesions in autoimmune dermatological diseases, recognizing characteristic patterns and estimating the prevalence of these diseases. DL models trained on large dermoscopic or histopathological image repositories facilitate automatic detection of disease-specific features, assisting dermatologists in diagnosis and personalized treatment planning(172). Representative performance has been reported for clinical image classification; for example, an EfficientNet-B4–based dermatology assistant achieved 91.4% sensitivity and 95.48% specificity for psoriasis when classifying clinical images among psoriasis, eczema/atopic dermatitis, and healthy skin in a labeled dataset(173). AI also plays a pivotal role in analyzing laboratory data for the diagnosis of autoimmune diseases, particularly neurological disorders such as MS and neuromyelitis optica (NMO). AI-driven models analyze MRI scans to detect and quantify lesions in the brain and spinal cord, utilizing ML to discern patterns and structural abnormalities that differentiate among autoimmune neurological conditions(174–177). Additionally, AI-based evaluation of serological markers, including autoantibody profiles, supports diagnosis and disease monitoring. For example, AI models that integrate patient-specific autoantibody data and clinical parameters can predict disease activity and risk of organ involvement in SLE, thereby assisting clinicians with personalized prognoses and decision-making(178, 179). AI-powered clinical decision support systems provide crucial assistance to healthcare providers in diagnosing autoimmune disorders. By synthesizing patient data, scientific literature, and AI-derived analyses, these systems generate evidence-based recommendations to improve diagnostic accuracy(180).

These systems process EHR information, which includes patient history, symptoms, and laboratory results, to propose diagnostic hypotheses and suggest appropriate tests. They also assist in differential diagnosis. Additionally, these AI systems analyze longitudinal patient data, which encompasses disease progression, treatment responses, and adverse effects, to improve and refine diagnostic workflows(181). Continuous learning from incoming data enables these platforms to dynamically update recommendations, contributing to the timely and individualized diagnosis of autoimmune diseases(182, 183).

The fusion of AI with EHRs, wearable devices, and patient-reported data enables a comprehensive assessment of autoimmune diseases. AI algorithms can extract hidden trends, correlations, and risk factors from EHR datasets(184, 185). Using natural language processing (NLP), AI can extract structured variables from unstructured clinical notes to support accurate diagnosis and prognosis. Wearable technologies, such as smartwatches and biosensors, continuously capture physiological data, including heart rate, temperature, and activity levels(186). AI analyzes these data streams in context to detect disease flares, predict symptom exacerbations, and optimize therapeutic interventions. Patient-generated inputs—such as symptom diaries and self-reported outcomes—can also be processed by AI to enhance disease monitoring and diagnostic accuracy(187, 188). Applications of AI in autoimmune disease diagnosis span image interpretation, laboratory data analysis, and clinical decision support systems(189). These applications demonstrate AI's potential to enhance diagnostic precision, promote personalized medical care, and facilitate comprehensive disease evaluation (190, 191). Algorithmic bias can arise when protected groups are underrepresented in training data (minority bias) or when deployment populations differ from training data (training–serving skew), reducing accuracy in those groups; therefore, subgroup performance reporting and equity-focused evaluation before and during deployment are essential(192). As AI technologies advance, their integration into healthcare systems is expected to improve the efficiency and effectiveness of autoimmune disease diagnosis, ultimately leading to better patient outcomes(191).

AI-driven drug discovery for autoimmune diseases

AI is reshaping drug development and precision medicine for autoimmune disorders, which are characterized by considerable heterogeneity in clinical symptoms and underlying biological mechanisms(193). While contemporary treatment strategies are effective for some patients, they often fail to address individual variability, resulting in inconsistent therapeutic outcomes and unmet patient needs. AI-powered approaches, leveraging extensive multi-omics datasets and sophisticated computational techniques, are enabling deeper mechanistic insight into these complex diseases and facilitating the design of more personalized treatment strategies(193, 194). By integrating high-throughput omics technologies with AI and ML, detailed molecular profiles can be generated from large patient cohorts. Analysis of these profiles using ML algorithms facilitates patient stratification into subgroups that share common biological signatures(195). Through clustering patients based on molecular and clinical characteristics, AI models can delineate distinct endotypes within autoimmune diseases, each characterized by specific dysregulated pathways (e.g., interferon signaling or acute-phase responses). This stratification is essential for

customizing treatments according to the unique pathophysiological features of patient subgroups, moving beyond the traditional one-size-fits-all approach(21, 195).

AI-driven modeling has also advanced the discovery of therapeutic targets in autoimmune diseases by mapping genes and proteins that are differentially expressed in specific patient clusters and applying pathway enrichment and network analyses, researchers can identify master regulators and driver mutations instrumental in disease progression. These insights facilitate the selection of highly relevant and druggable targets, accelerating the development of more effective and safer therapies(196–198). In the realm of drug development, AI is revolutionizing the design and optimization of novel drug candidates. Predictive models simulate interactions between millions of potential compounds and specific molecular targets, dramatically reducing the time and cost associated with conventional experimental methods(199, 200). A real-world illustration is AI-enabled drug repurposing, exemplified by BenevolentAI's knowledge-graph approach that prioritized baricitinib for immune-mediated indications, highlighting how AI can accelerate hypothesis generation and candidate prioritization for downstream validation(201, 202). Moreover, AI-enabled "virtual patient" models enable in-silico assessment of drug efficacy and safety, allowing researchers to predict responses in individual patients or subgroups prior to clinical trials. However, these "virtual patient"/digital-twin approaches remain an emerging capability; their predictive performance and clinical utility require iterative experimental and clinical validation and are still being established across autoimmune indications(203). This computational precision medicine approach holds great promise for delivering targeted therapies with improved benefit-risk profiles(204, 205). Importantly, the quality and interoperability of datasets used to train AI models are critical, alongside the need for standardized methodologies and well-characterized, sufficiently large patient cohorts. Ethical considerations—including data privacy, algorithmic bias, and transparency—must be rigorously addressed to ensure the equitable and trustworthy deployment of AI-based solutions(188, 206).

Looking forward, ongoing advancements in AI technologies, such as DL and digital twin modeling, are expected further to accelerate the transition to precision medicine in autoimmune disorders. These tools will enhance the monitoring of disease progression, prediction of treatment responses, and the real-time dynamic adjustment of therapeutic regimens(207, 208). The identification and validation of strong molecular and digital biomarkers will be crucial for enabling more precise patient stratification and disease monitoring, ultimately improving outcomes and quality of life for those affected by autoimmune diseases(162).

AI in treatment planning and management

AI is rapidly reshaping treatment planning and management for autoimmune diseases, which are characterized by complex pathophysiology and substantial variability in clinical presentation and therapeutic response(209). Conventional treatment approaches have primarily relied on empirical methods, often resulting in suboptimal outcomes, delayed interventions, and an increased risk of irreversible organ damage. AI-driven techniques, especially those employing ML and DL, can integrate and analyze extensive multidimensional datasets—spanning genetic, proteomic, imaging, and clinical data—to uncover novel biomarkers, stratify patients by risk, and predict disease progression with unprecedented precision(161, 193). For instance, ImmunoNet (a published DL framework) utilizes CNNs and multi-layer perceptrons (MLPs) to synthesize multi-omics and clinical information for disease classification, with up to 98% accuracy reported in the original study; however, this performance should be interpreted in the context of the study's validation design and cohort characteristics, and independent external validation in diverse populations is needed to confirm generalizability (210).

One of AI's most impactful contributions in autoimmune disorders lies in facilitating personalized treatment planning. By leveraging patient-specific data such as genetic profiles, molecular signatures, and longitudinal clinical records, AI algorithms like ImmunoNet can predict individual responses to therapies, including biologics, corticosteroids, and disease-modifying antirheumatic drugs (DMARDs), thereby reducing reliance on trial-and-error approaches(211, 212). In diseases such as RA and SLE, AI models can analyze immune cell phenotypes and genetic polymorphisms to stratify patients for targeted biologic therapies, enhancing efficacy while minimizing adverse effects. These systems also incorporate real-time data from wearable devices and EHRs to adjust treatment regimens, as exemplified in MS management dynamically. Such innovations are shifting clinical practice away from one-size-fits-all care toward truly individualized care(213–215).

Computational intelligence methods have become indispensable tools for biomarker discovery, especially in complex autoimmune diseases. These techniques employ advanced algorithms, including fuzzy logic, genetic algorithms, artificial neural networks (ANNs), support vector machines (SVMs), and clustering methods, to analyze large, heterogeneous biological datasets derived from genomics, proteomics, metabolomics, and clinical records(216). By integrating diverse data sources, computational intelligence can reveal hidden patterns and associations that may identify potential biomarkers linked to disease onset and progression. These approaches also support candidate biomarker

validation through cross-validation and the development of predictive models to inform personalized medicine, treatment, and prevention strategies(217).

In addition, modern deep-learning architectures—particularly transformer-based multimodal models that integrate medical imaging with routinely collected EHR variables (e.g., diagnostic codes, medications, and laboratory tests)—are increasingly used to capture complex temporal dependencies and improve representation learning in biomedical prediction tasks(218).

AI is revolutionizing disease monitoring and clinical decision support through continuous analysis of clinical, laboratory, and imaging data. Platforms such as ImmunoNet utilize XAI techniques to provide transparent insights into disease activity, enabling early detection of flares and complications. Remote monitoring tools combined with AI algorithms analyze data streams from wearable devices to assess disease status outside clinical settings, thereby enhancing patient engagement and facilitating proactive interventions. This capability is particularly vital for relapsing-remitting diseases, such as SLE, where timely adjustments to immunomodulatory therapies or corticosteroids can prevent irreversible damage(219, 220).

Despite these advances, challenges remain, including data privacy concerns, algorithmic bias, and the opaque "black box" nature of some AI models. Federated learning approaches, implemented in frameworks such as ImmunoNet, help address privacy issues by decentralizing data processing, while XAI methods enhance transparency to support clinical adoption(221). Interdisciplinary collaboration among clinicians, data scientists, and regulatory bodies is crucial for establishing ethical guidelines and robust validation frameworks. As these hurdles are overcome, AI is poised to transform autoimmune disease management, delivering precise, patient-centered care that enhances long-term outcomes and quality of life(219, 222, 223).

AI in rheumatoid arthritis

RA is a chronic autoimmune condition primarily targeting synovial joints, resulting in inflammation and potential joint damage(224). Affecting about 1% of the global population, RA is more common among women than men. Over the past five years, AI has made significant advancements in the field of rheumatology(225). AI has rapidly become a transformative tool in managing RA, a complex autoimmune disease characterized by wide variability in clinical symptoms and treatment responses(226). The inconsistent outcomes seen with advanced therapies, such as bDMARDs, highlight the urgent need for precision medicine approaches(227). Leveraging large and diverse datasets, AI methodologies now provide the capability to move beyond empirical treatment decisions, offering personalized and more effective interventions that can enhance patient prognosis and quality of life. AI also facilitates the identification and modeling of factors influencing treatment response. By integrating extensive clinical datasets, electronic health records, and multi-omics data, AI algorithms uncover subtle patterns and associations often missed by conventional analyses(193, 226, 227). For example, XAI methods, such as Shapley additive explanations (SHAP), have clarified the relative impact of clinical features on predicting remission among RA patients treated with biologics(228). These insights support individualized treatment planning and facilitate the discovery of novel biomarkers and therapeutic targets, thereby advancing rheumatology research(229). As illustrated in Fig. 4, multimodal data—including clinical, imaging, histopathological, and molecular profiles—are integrated through AI methodologies such as ML, DL, and NLP. These models facilitate early diagnosis, optimize therapeutic strategies, and enable personalized RA care through accurate risk prediction and outcome modeling. The integration of AI in rheumatology is part of a broader digital transformation in healthcare, including electronic health records, telemedicine, wearable devices, and mobile health applications(230). AI's strength lies in processing and interpreting complex, large-scale data, enabling the identification of intricate patterns and relationships that exceed human capacity(231). In RA, this capability is invaluable for modeling the complex interactions among genetic, clinical, and environmental factors influencing disease progression and treatment response (232). ML and DL algorithms have played a pivotal role in developing predictive models that inform risk stratification, prognosis, and therapeutic decisions(233).

One of AI's key applications in RA involves enhancing diagnostic accuracy and disease classification. Traditional diagnosis relies on clinical assessment, laboratory tests, and imaging; however, AI models, such as ANNs and CNNs, have automated and improved these processes(234, 235). For instance, ANNs trained on demographic and serological data have achieved high accuracy in identifying RA patients. At the same time, CNNs applied to hand radiographs automate the detection of typical joint abnormalities, enabling earlier and more cost-effective diagnosis. These AI tools reduce human error and facilitate timely referral and intervention, which are critical to preventing disease progression(236–238). AI also shows promise in predicting the response to methotrexate (MTX), a cornerstone of RA treatment(239). One study used a penalized logistic regression model based on gene expression ratios before and after four weeks of MTX therapy, achieving an AUC of 0.78 in forecasting six-month treatment response(240). Comparisons of ML methods—including Lasso regression, random forest, and XGBoost—indicate that although advanced algorithms

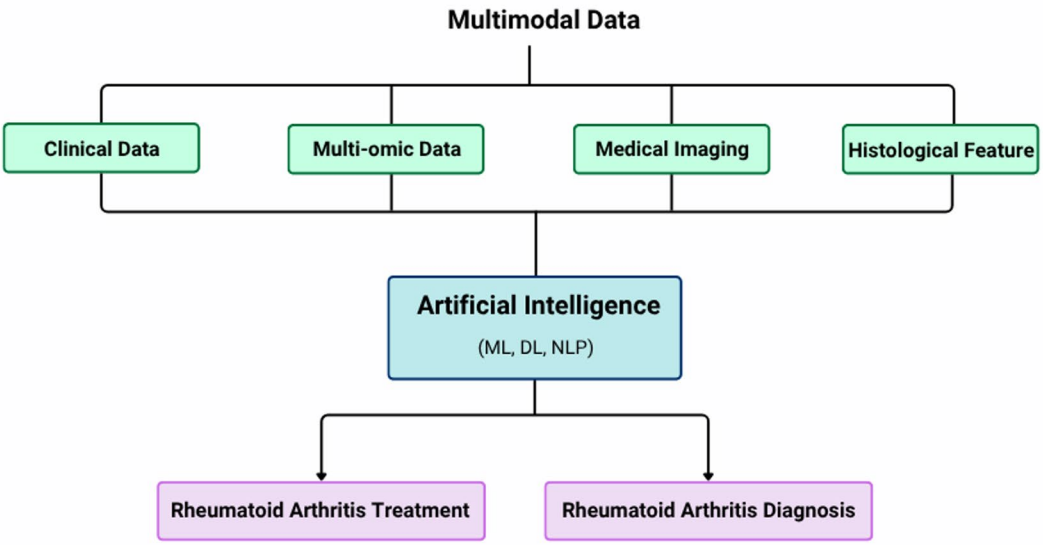


Fig. 4 Schematic representation of the AI-enabled pipeline for rheumatoid arthritis (RA) management. Multimodal data, including clinical records, multi-omics profiles, medical imaging, and histopathological features, are processed using ML, DL, and natural language processing (NLP) algorithms. These AI models support both diagnosis and personalized treatment planning, thereby contributing to the advancement of precision medicine in RA

may provide slight improvements, traditional logistic regression remains competitive, with AUCs ranging from 0.77 to 0.78(241, 242).

Beyond predicting pharmacologic response, AI helps identify important prognostic biomarkers and risk factors in RA(209). For example, they are strong predictors of early response to tumor necrosis factor inhibitors (TNFi). These findings enhance patient stratification and facilitate clinicians in selecting the most optimal therapies, thereby reducing the reliance on trial-and-error approaches that have been historically common in RA treatment(243, 244).

AI is also poised to transform research in RA and drug development(245). By mining clinical trial data, biomedical literature, and real-world evidence, AI models can identify new therapeutic targets, optimize trial designs, and predict treatment outcomes, thereby accelerating the development of novel therapies. The multi-omics integration of genetic, proteomic, and clinical data has shown promise in predicting responses to biologics and Janus kinase (JAK) inhibitors. However, challenges remain regarding data heterogeneity and integration(246–248). Despite these advances, several challenges limit the full potential of AI in RA. The disease's polygenic and multifactorial nature demands large and diverse datasets to develop robust, generalizable models. Variability in defining and measuring treatment responses, along with differing prediction timeframes across studies, complicates model comparison and clinical application. Moreover, issues of data quality, privacy, and ethics must be addressed to ensure the safe and effective deployment of AI in clinical practice(193, 249, 250).

AI in type 1 diabetes

T1DM is a multifaceted autoimmune disease characterized by the infiltration of immune cells into pancreatic islets, resulting in the selective destruction of insulin-producing β-cells. This β-cell loss causes insulin deficiency and hyperglycemia, necessitating lifelong insulin replacement therapy(251). AI has significantly advanced diabetes care by enabling earlier and more precise diagnoses, optimizing treatment approaches, and supporting real-time disease management(252). AI and ML offer new avenues

for early detection and prediction of diabetes, facilitating personalized interventions and improved outcomes. One critical application involves analyzing EHRs, which contain extensive patient data, including demographics, laboratory results, and medical history. AI/ML algorithms can detect patterns within this data that indicate diabetes or pre-diabetic conditions. Diabetes risk prediction models have been widely studied, with Schwarz et al. providing comprehensive analyses of their sensitivity and specificity(253, 254).

Accurate complication prediction is vital for targeted intervention to prevent or delay adverse outcomes(255). AI-powered predictive analytics hold great promise for enhancing management of chronic conditions by supporting patients in maintaining healthy lifestyles, adhering to medications, and effectively monitoring glycemic control(256, 257). Various AI algorithms, such as support vector machines, logistic regression, neural networks, and decision trees, are utilized in diabetes prediction(258).

These algorithms use diverse mathematical frameworks to recognize patterns and generate predictions. For example, Rajendra and Latifi applied logistic regression to the PIMA Indians Diabetes dataset (which primarily reflects T2DM risk rather than autoimmune T1DM) and a Vanderbilt dataset involving rural African Americans, achieving accuracies of 78% and 93%, respectively. Accordingly, predictive approaches based on PIMA (T2DM-oriented) should be distinguished from T1DM prediction models, which typically incorporate autoimmune/genetic markers (e.g., islet autoantibodies, HLA risk) and/or longitudinal glycemic trajectories. In addition, these accuracy values should be interpreted alongside sensitivity/specificity and AUC, and in the context of cohort characteristics (e.g., sample size, class balance, and population composition), which influence clinical utility and generalizability (259). Their findings highlight that factors beyond algorithm choice, such as thorough data preprocessing, removal of redundancies and missing values, normalization, cross-validation, feature selection, and ensemble methods, significantly impact model performance and efficiency(259, 260). Effective lifestyle management is a cornerstone of diabetes treatment, crucial for preventing complications and related health issues. Upon diagnosis, patients are encouraged to adopt healthier behaviors. Leveraging current technologies and extensive datasets, data-driven tools like Decision Support Systems (DSS) have been developed to empower patients and clinicians in diabetes management. These systems monitor diet, physical activity, medication adherence, glucose levels, and other relevant factors, thereby facilitating improved therapeutic outcomes(261). As illustrated in Fig. 5, AI technologies are revolutionizing T1DM care by enabling a comprehensive approach to disease prediction, real-time monitoring, and management. These systems support predictive modeling, guide individualized insulin therapy, inform lifestyle adjustments, and enhance clinical decision-making—ultimately driving more precise and responsive care tailored to each patient's unique profile.

Drug discovery and development for T1DM increasingly rely on repurposing immunotherapies initially designed for other autoimmune diseases, transplantation, and cancer(262). These therapies target immunological pathways, including the depletion of T- and B-cells, inhibition of cytokines, and enhancement of regulatory T-cells. While some drugs are guided by T1DM-specific genetic risk loci (e.g., CTLA4, IL2RA), others act on broader mechanisms, such as polyclonal anti-thymocyte globulin and JAK inhibitors(263–265). Although these interventions have met primary clinical endpoints, they typically only transiently preserve endogenous C-peptide, underscoring the need for earlier, continuous, or combination therapies, as well as the development of agents with more durable effects. Advanced computational methods, particularly AI and ML, are being employed to identify promising drug candidates and predict off-target effects; however, few have progressed to clinical trials in T1DM to date(266, 267). Antigen-specific immunotherapies offer another promising strategy, with preliminary evidence indicating preservation of C-peptide levels in select T1DM subgroups(268, 269). The effectiveness of these therapies often depends on genetic factors such as HLA haplotypes, which influence immune responses. AI/ML tools are being integrated into quantitative trait locus analyses to model complex genetic effects on therapy response and predict peptides most likely presented by specific HLA molecules(270, 271). Unbiased immunopeptidome studies and advanced sequencing are identifying novel antigenic targets, while AI-driven databases and algorithms assist in discovering new immune receptor sequences and their antigen specificities. These advancements promise more precise immune tolerance induction strategies tailored to patient subpopulations(272–274).

Combination therapies are gaining interest for prolonging therapeutic efficacy in T1D. Clinical trials combining agents with different mechanisms, such as anti-IL-21 with liraglutide, have shown potential by addressing both inflammation and β-cell function. In this specific setting, AI/ML can support anti-IL-21 + liraglutide combination trials by integrating immunologic and metabolic biomarkers (e.g., inflammatory signatures together with C-peptide and glycemic trajectories) to identify responder subgroups, enable biomarker-guided monitoring, and evaluate treatment interactions/synergy(275–277). AI/ML-driven in silico models are increasingly used to predict drug interactions, toxicity, and synergistic effects, informing the design of safer and more effective combination treatments(278). These computational approaches are also applied to optimize β-cell

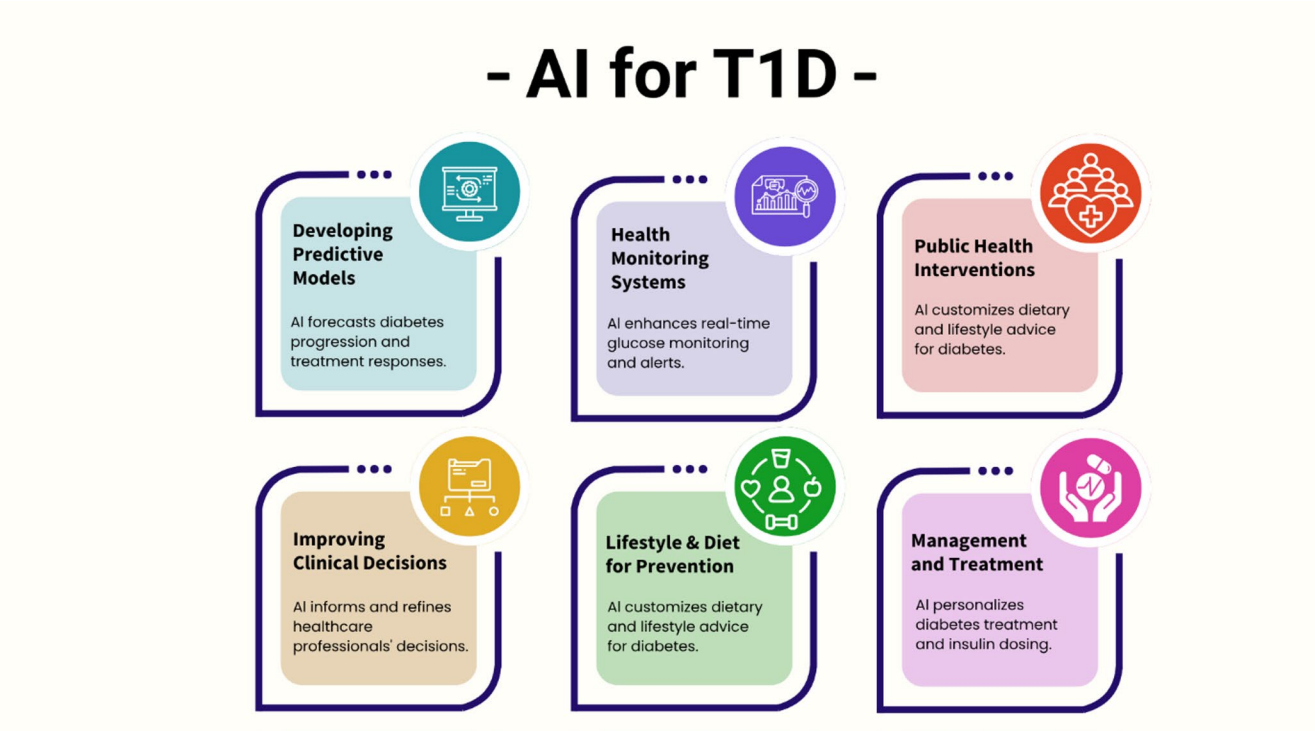


Fig. 5 Schematic overview of AI applications in T1D. AI models are utilized across various domains, including predictive modeling of disease progression, real-time health monitoring, clinical decision-making, and personalized patient management. Additional roles include optimizing treatment strategies, supporting public health interventions, and tailoring lifestyle and dietary recommendations to enhance patient outcomes and enable precision diabetes care

regeneration and immune modulation, leveraging insights from cancer and transplantation research. Future studies will likely integrate both in vitro and in silico methods to guide therapy selection and dosing, minimizing adverse effects while maximizing benefit(279, 280). Precision medicine in T1DM advances through identifying responder subgroups and customizing therapies based on patient-specific features. While conventional statistics have identified immune signatures of responders' post-treatment, predictive markers guiding therapy selection before initiation are needed(263, 281). Demographic (age, ethnicity), genetic (HLA, pharmacogenetic markers), and environmental factors contribute to variable drug responses(281–283). AI/ML models are being developed to integrate these factors, enabling the prediction of individual responses and the optimization of dosing regimens. The concept of "digital twins"—virtual patient models that incorporate genetic, immunological, and clinical data—holds promise for simulating therapeutic responses and refining precision medicine in T1D(284, 285).

Despite progress, challenges remain in clinically applying AI/ML to T1D therapy discovery. Ensuring model interpretability, generalizability, and actionability demands rigorous data management, interdisciplinary collaboration, and continuous expert engagement. The "black box" nature of many AI/ML approaches, DL, limits explainability, which is crucial for establishing clinical trust and adoption. Efforts to develop explainable AI (XAI) techniques aim to produce transparent outputs that clinicians and researchers can understand and validate. Bridging the gap between computational innovation and clinical relevance is essential to fully realize AI/ML's potential in advancing T1D treatment(286–288).

Algorithmic bias and equity in ai-driven immunotherapy

AI-enabled immunotherapy pipelines—spanning biomarker inference (e.g., PD-L1/TMB/MSI surrogates), response prediction, and immune-related adverse event (irAE) risk modeling—can amplify inequities when training and validation datasets do not reflect the populations intended for deployment(289). A central driver is the uneven composition and documentation of health datasets ("health data poverty"), which may result from structural barriers to research participation and persistent underrepresentation of certain demographic groups; consequently, model performance can degrade in precisely those settings where access to specialist oncology/immunology care is already limited, widening disparities in treatment selection and outcomes (290).

Bias can be introduced across the full AI lifecycle. Sampling bias occurs when genomic resources, clinical cohorts, trial-linked biobanks underrepresent specific ancestries/ethnicities, geographic regions, socioeconomic strata, or comorbidity profiles, undermining generalizability. Measurement and label bias arise when reference standards ("ground truth") are inconsistently defined or measured across institutions—for example, variability in PD-L1 staining/scoring practices or sequencing/variant-calling pipelines—leading models to learn site- or subgroup-specific artifacts rather than biology. In parallel, dataset (distribution) shift across scanners, staining protocols, and clinical workflows can produce subgroup-specific degradation even when overall headline performance appears acceptable(290–292). In immuno-oncology, these concerns are particularly consequential because model outputs can influence high-stakes decisions such as ICI initiation, combination selection, and toxicity surveillance. When diversity in training/validation cohorts is limited or demographic reporting is incomplete, fairness and transportability become difficult to establish, increasing the risk of uneven benefit and harm across patient subgroups(289, 290). Equity risks also extend upstream: AI-enabled drug discovery and development workflows (including candidate prioritization and trial enrichment) can inherit biases from incomplete or unbalanced real-world and experimental datasets, which may distort discovery signals and limit downstream clinical applicability(290, 293). Mitigation therefore requires treating equity as a core performance dimension. Practical steps include documenting dataset composition and missingness, reporting stratified performance (e.g., calibration and AUC/sensitivity/specificity across relevant demographic and clinical subgroups), conducting external validation across institutions and workflows, and implementing post-deployment monitoring to detect drift and emergent subgroup harm. While fairness-aware learning and reweighting can help, they cannot substitute for representative data and consistent reference standards; governance and transparency are essential for equitable clinical translation(290, 292).

Future Perspective

The integration of AI into immunotherapy marks a transformative shift in precision medicine for both cancer and autoimmune diseases(16). Looking ahead, several emerging directions are poised to reshape AI-driven Immunotherapeutics. In the near term, advancing explainable and interpretable AI will be essential for translating predictive models into clinically actionable tools. By making algorithmic outputs transparent and interpretable, AI will foster greater trust among clinicians, accelerate regulatory approval, and facilitate real-time decision-making in diverse clinical settings(39, 294).

However, routine clinical adoption remains limited not by model capability alone, but by translation barriers, most notably insufficient external validation across institutions and scanners/platforms, vulnerability to dataset shift, limited prospective and impact-focused clinical trials, and unresolved regulatory and clinical-evaluation requirements for AI deployed as software-as-a-medical-device (SaMD). These include a clear definition of intended use, clinically appropriate reference standards ("ground truth"), robust strategies for model updating and post-deployment performance monitoring, and ongoing surveillance for drift and safety(295, 296).

In parallel, immunotherapy relies on diverse datasets, including multi-omics, high-resolution imaging, and longitudinal clinical records, which must be integrated and harmonized across platforms and institutions(52). The rise of federated learning and privacy-preserving computation offers promising solutions, enabling collaborative model training without compromising patient privacy(297).

Yet, even with federated approaches, clinical-grade deployment requires standardized pre-analytic and analytic pipelines (e.g., acquisition/scanning protocols, sequencing batch correction, and complete metadata capture), rigorous quality control, and interoperable data governance to ensure that "real-world" inputs remain reliable enough for decision support (298, 299).

Over the longer term, digital twin technologies and in silico clinical trials are emerging as next-generation tools for therapy simulation(300). These patient-specific virtual models can dynamically predict disease trajectories and treatment responses, enabling preemptive optimization of dosing, safety, and efficacy before real-world administration(301). For example, in autoimmune disease, digital-twin ('virtual patient') models have been proposed for type 1 diabetes to simulate patient-specific glucose–insulin dynamics and immune–metabolic trajectories, supporting individualized insulin optimization and the in silico evaluation of immunomodulatory strategies; however, prospective clinical validation remains necessary before routine use(285).

This paradigm holds particular promise in reducing clinical trial costs and timelines(302), but its clinical translation will depend on demonstrating reproducible benefit against clinically meaningful endpoints in prospective evaluations, and meeting expectations for transparent verification/validation and safety monitoring (e.g., clearly defined intended use and reference standards, reporting algorithm versioning and input-data handling, systematic error analysis, and post-deployment surveillance for performance drift)(303). Additionally, the convergence of AI with next-generation biomedical technologies, such as

single-cell transcriptomics, spatial omics, and 3D imaging, will uncover new layers of immune complexity. These integrative approaches are expected to reveal novel biomarkers, resistance mechanisms, and combinatorial therapeutic strategies, thereby expanding the therapeutic arsenal available to clinicians(304).

Ethical, legal, and societal considerations must evolve in harmony with technical advancements. Addressing algorithmic bias, ensuring data representativeness across populations, and developing transparent regulatory pathways will be essential for equitable AI deployment. Multidisciplinary collaboration among clinicians, data scientists, policymakers, and patient communities will be critical to ensuring responsible and inclusive innovation. In summary, the future of AI in immunotherapy will be defined not only by methodological advances, but also by robust validation, regulatory readiness, and implementation science that enable safe, effective, and scalable deployment across real-world clinical systems.

Conclusion

AI is catalyzing a paradigm shift in immunotherapy, transforming the diagnosis, treatment, and monitoring of cancer and autoimmune diseases(16). By leveraging advanced ML and DL algorithms, AI enables the integration of complex biomedical data, including multi-omics, imaging, and real-world clinical records, into cohesive, clinically actionable insights(305). This data-driven transformation is propelling immunotherapy toward unprecedented levels of personalized treatment and efficacy(119).

AI has accelerated the identification of predictive biomarkers, including PD-L1, TMB, MSI, and neoantigen profiles in oncology(16, 33). These advances have improved patient stratification and enabled more precise deployment of ICIs(306). AI has also enhanced the design and monitoring of CAR-T cell therapies and antibody-based biopharmaceuticals by simulating molecular interactions, predicting toxicity, and optimizing dosing strategies, thereby shortening development timelines and improving safety profiles(65). In the realm of autoimmune disease, AI has deepened our understanding of disease heterogeneity, facilitated early diagnosis, and enabled personalized treatment(166). Through multi-omic analysis, wearable data integration, and EHR mining, AI supports longitudinal disease monitoring and drug repurposing in conditions such as RA, SLE, MS, and T1DM(21). These capabilities not only improve treatment outcomes but also open avenues for preventive and predictive care.

Despite these advancements, critical barriers remain. Data quality limitations, such as noise in single-cell RNA sequencing, batch effects in imaging, and inconsistencies in digital pathology staining, can compromise model performance. Inadequate quality control and dataset shifts across platforms exacerbate these issues, making model validation across institutions challenging. Equally important are interoperability challenges, insufficient standardization, and lack of regulatory frameworks for AI models, which remain significant hurdles to clinical adoption. Additionally, ethical considerations—including patient privacy, informed consent, accountability, and equitable access—must be embedded in the development and deployment of AI systems to ensure responsible translation into practice.

In conclusion, AI is a transformative force in immunotherapy, enhancing diagnostic accuracy, optimizing therapeutic efficacy, and advancing precision medicine. However, to fully realize its potential in clinical practice, continued investment in data infrastructure, model validation, and interdisciplinary collaboration will be essential. Ultimately, the goal is not just smarter algorithms—but more equitable, accessible, and human-centered care for all patients, everywhere.

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