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Digital Immunology: Integrating AI into Immune Profiling

Chrysoula I. Liakou[1] ✉ **Marios Papadakis**[2] **and Markos Plytas**[3]
[1]*Chief Executive Officer, LK Connect LLC. 30N Gould St. Sheridan - WY 82801. USA*
[2]*Department of Surgery II. University of Witten-Herdecke. Wuppertal, Germany*
[3]*Academic Director. Epsilon College. Athens, Greece.*
Corresponding Author: Chrysoula I. Liakou, **E-mail**: mail@cliakou.gr

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ABSTRACT

As the rapid expansion of immunological data with diverse modalities in both dimensions through high throughput sequencing, single-cell technology, spatial omics, digital pathology and immunogenomics, immune profiling has emerged as a data-rich science that heavily relies on computational approaches as well as multi-dimensional multi-modal data integration to extract meaningful biological knowledge. Artificial intelligence (AI) has become one of the most powerful approaches in the integration and interpretation of these multi-dimensional data for complex immune heterogeneity, biomarker discovery, disease classification and therapy prediction. Here, we review the applications of AI in the evolution of digital immunology and translate how AI integrates with immune profiling. The paper also discusses the data-driven AI-powered frameworks used for immune cell profiling and multimodal integration for immune classification. Last but not least, the clinical implementations of AI-assisted immune profiling in various fields such as cancer, autoimmunity, transplantation, allergy and clinic immunology as well as the emerging digital immune twins are discussed. Challenges and limitations in AI-assisted immune profiling, such as need for standardized datasets, model transparency, interoperability, clinical validation and ethical concerns, are systematically discussed. Our findings highlight that the future of AI-powered immune profiling has positively contributed to the advance of digital immunology, thus fulfilling its promise in personalized immune diagnosis and therapy.

1. Introduction

In recent years, the explosion of high dimensional immunological data has revolutionized our understanding of immune system functions, providing unprecedented opportunities for precision diagnosis and customized treatment. The emergence of next-generation sequencing (NGS), single-cell genomics, spatial omics, and digital pathology has facilitated large-scale characterization of immune cell compositions, functions, and spatial architectures in numerous physiological and pathological settings. Yet, an ever expanding size and intricate nature of these omics datasets pose increasing challenge to apply naive computational approaches and to distill them into clinically effective information (Xu et al., 2021; Lei & Tsang, 2025; Ravi et al., 2025).

Artificial intelligence (AI), a highly flexible computational approach for extracting biologically important information from multidimensional immune data, has been heavily employed in this context. Due to its capacity to identify complex molecular signatures, to combine diverse data types and sources and to create predictive models, enabling biomarker discovery, disease classification and prediction of response to therapy, AI has become an essential part of contemporary immunology, where classical statistical approaches do not allow investigation of the extent of immune regulation (Curion & Theis, 2024; Kumar, 2024; Jariwala, 2025).

The capabilities provided by tools enabled by AI, are propelling the transition from population-based assessment of an immune system to personalized definitions of an individual immune profile. The high dimensional data generated by the synthesis of

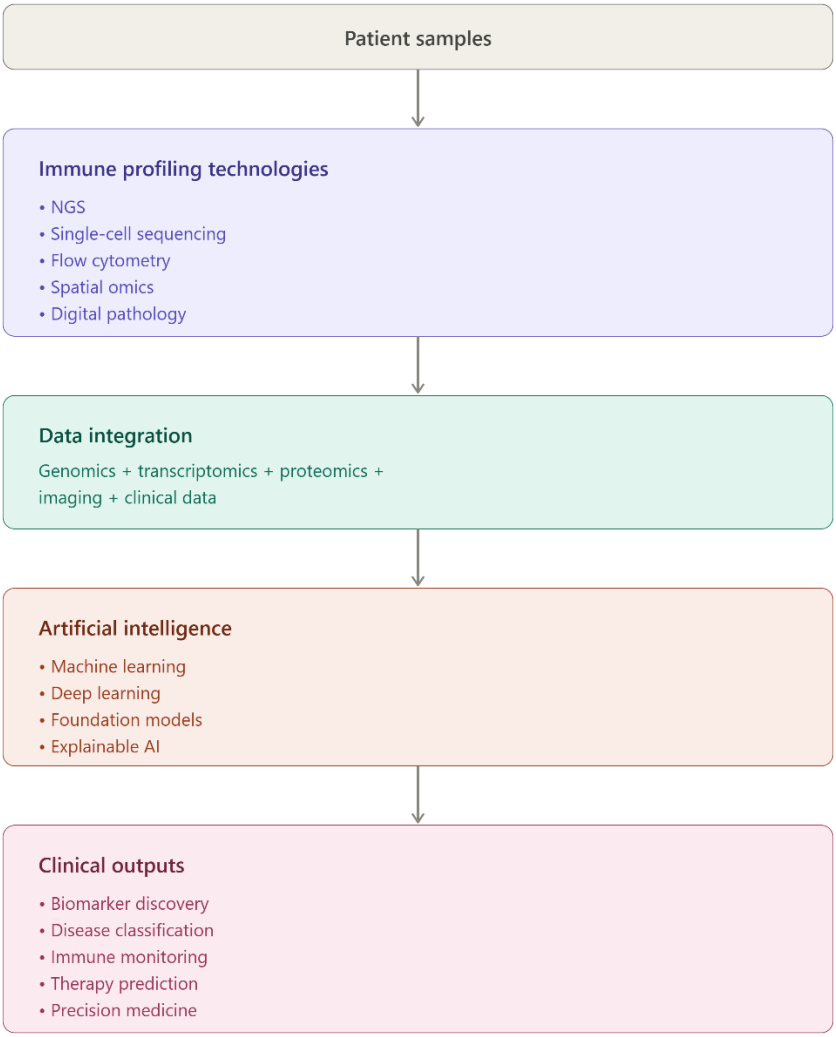
clinical reports with genomic, transcriptomic, proteomic and immunological parameters, can be intersected to identify immune correlates that may refine diagnosis and inform personalized treatment (Chen et al., 2025; Alshorman et al., 2026; Goktas & Damadoglu, 2025; Shin et al., 2026). Such an integrated approach to understanding immune alteration is of increasing clinical utility in oncology, autoimmune disease, transplantation and allergy, where immune variation has considerable impact on the disease course (Chen et al., 2025; Alshorman et al., 2026; Goktas & Damadoglu, 2025; Shin et al., 2026).

More recently, advances in technology have further refined the landscape of digital immunology by adding single-cell sequencing, spatial transcriptomics, immunogenomics and AI-driven digital pathology to the arsenal. These techniques are complementary to traditional laboratory methods, enabling unprecedented understanding of immune cell heterogeneity, tissue architecture and cell–cell interactions, thereby improving the performance of clinically relevant biomarker discovery and strengthening prognostic models of immunotherapy and disease progression (Dratva et al., 2026; Chang et al., 2025; Koelzer et al., 2019; Rigamonti et al., 2024; Shen et al., 2025).

Nevertheless, these advances have yet to be implemented on a routine basis in the clinic in part due to limitations such as lack of reproducibility, differences in data quality, limited interoperability in multi-omic platforms as well as lack of transparency of algorithms and a need for extensive clinical validation that remain obstacles before these strategies can offer clinical guidance in a safe manner (Negut & Visan, 2025; Dhar, 2025; Stensballe, 2026).

In this review, we consider how AI can be integrated with immune profiling by evaluating the computational methods that form the basis of digital immunology and their implications for precision diagnostics, biomarker discovery and personalized immunotherapy. In particular, we focus on the state-of-the-art in AI-supported immune profiling methods, their clinical potential and the hurdles that need to be overcome for their widespread adoption into precision immunology (Lei & Tsang, 2025; Curion & Theis, 2024; Chen et al., 2025).

Figure 1. Overview of the Digital Immunology Framework



2. Literature Review

2.1 Evolution of Digital Immunology

Throughout the years, molecular and cellular profiling of immune responses was revolutionized by advances in high-throughput technologies. The earliest immune studies used immunoassays or flow cytometry, which allow quantifying a few key immune cell populations while having limited resolution to study cellular heterogeneity or complex inter-cellular interactions. The development of next-generation sequencing, single-cell genomics, spatial transcriptomics and high-dimensional imaging dramatically broadened the analytic power of immune profiling, since multiple immune components can be profiled at the same time in different biological settings (Xu et al., 2021, Ravi et al., 2025).

The increasing complexities of these highly-dimensional datasets have also led to the emergence of digital immunology as a utility of computational approaches and immunological research to produce integrated knowledge towards immune function. By unifying various types of molecular, imaging, and clinical data, digital immunology has enabled systems-wide analytics for assessing immune signatures linked to disease susceptibility, treatment efficacy, and lifelong immune health. The transition from single-parameter studies to integrated computational models has enhanced the paradigm of precision immunology and personalized medicine (Lei & Tsang, 2025; Chen et al., 2025).

Recent advances in computational immunology have speeded up this transition by providing machine learning approaches that analyze heterogeneous data with large dimensionality, thus facilitating the discovery of biologically relevant patterns and enabling the predictive modeling of immune responses across many disease conditions. Digital immunology, therefore,

transitioned from a data collection platform into a predictive science that contributes to clinical decision making through AI-supported interpretation of immunological data. (Curion & Theis, 2024; Jariwala, 2025; Kumar, 2024).

2.2 Immune Profiling Technologies

However, immune profiling has been dramatically enhanced by the implementation of various high-throughput technologies allowing for detailed profiling of immune cell types and signaling pathways as well as cellular functions and interactions. In contrast to immunological measurements of a few biomarkers using traditional assays, current immune profiling employs a combination of systems approaches that enable precise consideration of cellular heterogeneity, functional states and cell location in both normal physiology and disease pathogenesis. This progress has broadened the clinical perspective of immune heterogeneity in addition to providing much needed data for disease diagnoses and prognostication (Ravi et al., 2025; Lei & Tsang, 2025).

Next-generation sequencing (NGS) has emerged as the gold standard for immune profiling allowing high-throughput analysis for immune genes, antigen receptor repertoires and immune-related germline variants. The combination of NGS with single cell sequencing has further improved the resolution of immune analyses by identifying immune cell subsets, trajectory maps of lineages and transcriptional landscapes that may be hidden in bulk sequencing analyses (Xu et al., 2021; Dratva et al., 2026; Shin et al., 2026).

With the advent of spatial omics and digital pathology, immune spatial data is available to complement molecular-based genomic technologies. Advanced high dimensional imaging platforms (including imaging mass cytometry and AI-based digital pathology) allow for simultaneous assessment of immune cell localization, tumor architecture and cellular interactions. This spatial data has been used to refine descriptions of the tumor-immune microenvironment and to identify prognostic and predictive biomarkers for precision immunotherapy (Koelzer et al., 2019; Rigamonti et al., 2024; Bilal et al., 2023; Huss et al., 2023).

The convergence of immunogenomics, proteomics, transcriptomics and spatial imaging has created a multimodal approach toward immune profiling that offers a broader representation of immune functionality than any one technique alone. These intersecting platforms yield high-dimensional information on molecular, cellular and tissue levels, laying the groundwork for AI-based approaches to enable promising advancements in biomarker discovery, patient selection, and tailored therapeutic decisions (Chang et al., 2025; Farzan, 2024; Chen et al., 2025).

2.3 Artificial Intelligence in Immune Profiling

Artificial intelligence has revolutionized immune profiling by unlocking the potential of protein, cell, and clinical datasets of unprecedented scale and complexity derived from genomics, transcriptomics, proteomics and imaging. Conventional approaches to data analysis are limited in their capacity to detect nonlinear effects and interactions among multiple immune variables, whereas the application of AI algorithms has uncovered underlying structures and generated predictive models that increased biological insight and clinical utility (Curion & Theis, 2024; Jariwala, 2025).

Machine learning algorithms are extensively used to delineate immune cell populations, identify prognostic and diagnostic biomarkers and predict response to therapies from multidimensional data (Kumar, 2024; Chen et al., 2025; Chang et al., 2025). Supervised learning methods are valuable in disease classification and response prediction while unsupervised learning has been employed for the discovery of novel immune cell subsets and molecular signatures. More recently, use of deep learning and foundational models have performed imaging and multi-omic analysis with arguably less manual feature engineering to achieve better predictive performance supportive of precision immunotherapy (Kumar, 2024; Chen et al., 2025; Chang et al., 2025).

The convergence of AI and digital pathology has greatly enhanced immune profiling through an automated, high throughput analysis of histopathology images. Deep learning algorithms can, for example, predict immune cell infiltration levels, define spatial organization of immune and tumor cells and find tissue features correlating with therapy response and prognosis. These approaches increase objectivity, are reproductive, and provide quantified biomarkers for clinical support, complementing traditional pathological assessment, especially in cancer (Koelzer et al., 2019; Bilal et al., 2023; Rigamonti et al., 2024; Shen et al., 2025).

In addition to image analysis, AI has also enabled the integration of multimodal data to produce a more holistic picture of immune function. The integration of molecular, clinical, and image data by AI algorithms can be used to enhance patient stratification, biomarker development, and personalized treatment optimization. Such integrative ability has made AI the dominant analytical paradigm in digital immunology with its application enabling the transition from descriptive to predictive and precision medicine approaches (Lei & Tsang, 2025; Curion & Theis, 2024; Alshorman et al., 2026).

2.4 AI-Driven Multi-Omics Integration

Multi-omic integration is now a key approach to unravel the intricacies of immune regulation as no one platform can encompass all mechanisms. Data from genomics, transcriptomics, proteomics, metabolomics and epigenomics are complementary and combined data offers a more holistic picture of immunology than any single dataset. However, the heterogeneity and high-dimension of the systems complicates and introduces variables into the analysis of these approaches (Chen et al. 2025; Curion et al. 2024).

Artificial intelligence has contributed greatly to the integration and cross-interpretation of multi-omic datasets by defined intricate relationships across various layers. Machine learning approaches can discern molecular and clinical data at the same time to capture immune signature in relation to disease risks, outcomes, and responses to treatment. Such integrative platforms have improved biomarker discoveries while enabling patient stratification for precision medicine in cancers and immune-mediated conditions (Jariwala, 2025; Chang et al., 2025; Alshorman et al., 2026).

Systems immunology has added to the multi-omic approach by integrating artificial intelligence with longitudinal immune systems data enabling the characterization of the immune health of a subject and defining their individual immune setpoint. This avoids the use of a single biomarker and relies on the detection of interconnected molecular/cellular interactions that determine immune response. These new models unveil the underpinnings of immune differences among individuals and facilitate the prediction of disease progression and treatment response (Lei & Tsang, 2025).

More recently, innovations have pushed multi-omic integration further to adopt the data types of spatial omics, single-cell sequencing and digital pathology, providing a means to analyze cellular molecular phenotypes and tissue architecture concurrently. The addition of these complementary data has revealed novel interactions between immune cells in complex tumor microenvironments, thus leading to improved identification of meaningful biomarkers for clinical practice. Such innovations are progressing digital immunology toward future breakthroughs of truly personalized medicine (Dratva et al., 2026; Rigamonti et al., 2024; Stensballe, 2026).

2.5 Clinical Applications of AI-Based Immune Profiling

The incorporation of AI in immune profiling has further widened its clinical application in a great spectrum of immune-mediated diseases by facilitating more accurate diagnosis, better prognostication and better therapeutic monitoring. AI-powered analysis algorithms are able to assimilate clinical, molecular and radiological information to delineate patient-centered immune profile, thus enabling precision medicine. This approach of personalized treatment demonstrated the potential to improve disease classification and disease-specific treatments in oncology, autoimmune diseases, transplantation and allergy (Chen et al., 2025; Alshorman et al., 2026; Goktas & Damadoglu, 2025).

In cancer, AI-enhanced immune profiling has been firmly established to support phenotyping of tumor immune microenvironment as well as predicting cancer patients' responsiveness to immunotherapy. Based on machine learning models, immune cell infiltration, spatial cellular interactions, as well as molecular biomarkers can be qualified or quantified to help clinicians distinguish those cancer patients who are more likely to respond to immune checkpoint blockade and other forms of immunotherapy (Ravi et al., 2025; Bilal et al., 2023; Rigamonti et al., 2024; Shen et al., 2025). The combination of digital pathology with AI has benefited the prediction of response rate (Ravi et al., 2025; Bilal et al., 2023; Shen et al., 2025).

AI has proven to be promising in the management of autoimmune diseases, aiding early diagnosis, disease monitoring, and treatment management. Multi-omic biomarkers driven by clinical data allows the application of computational models to distinguish disease subtypes, prognose disease progression, and identify patients likely to respond to immunomodulatory therapies. This approach has shown similar benefits in allergy and clinical immunology, assisting risk prediction and individualized treatment planning. (Negut & Visan, 2025; Alshorman et al., 2026; Goktas & Damadoglu, 2025; Stensballe, 2026).

In the fields of transplantation and immunogenetics AI has elevated the analysis of HLA and non-HLA genetic markers aiding the evaluation of donorselectronic benefits found following the participation of good HLA matches to improve the assessment of early post-transplant immune function. The fusion of next-generation sequencing with AI-powered predictive algorithms have demonstrated an increase in precision for histocompatibility calculations and agent specific approaches for transplantation (Joo et al., 2017) while inventive concepts such as digital immune Twin, which combines longitudinal clinical and multiomic data to generate a personalized simulation of immune function represents the future of immune prediction (Farzan, 2024; Sonmez et al., 2026; Shin et al., 2026; Abuhassan et al., 2026).

2.6 Challenges and Research Gaps

Nonetheless, although appropriate immune profiling using AI are well developed, many barriers still need to be overcome before its integration into daily practice. Among others, high-quality data with standardized protocols are crucial barriers. The immune profiling datasets were generated using multiple experimental platforms, protocols, sequencing technologies, leading to heterogenous immune profiling, which causess integrity and reproducibility of the model across independent cohorts. Developing the harmonized multimodal dataset is crucial for the AI models (Curion & Theis, 2024; Chen et al., 2025).

Another significant obstacle is the interpretability of models of artificial intelligence. Though the predictive accuracy of deep learning models is often quite high, their function remains difficult to articulate, making clinicians reluctant to trust them and regulatory agencies unwilling to approve them. Thus, fostering model transparency and creating artificial intelligence models that can be explained clearly are of utmost importance in reliably integrating these models into healthcare settings (Jariwala, 2025; Negut & Visan, 2025).

Furthermore, integrating various heterogeneous data sources introduces additional computational and technical hurdles. The integration of diverse data types such as genomic, transcriptomic, proteomic, spatial, imaging, and clinical data demands complex analytical frameworks that can account for variations in data formats, scale, and reliability. While recent progress in systems immunology and multimodal data integration has alleviated certain obstacles, more methodological development is essential to facilitate efficient data interoperability for clinical applications (Lei & Tsang, 2025; Stensballe, 2026; Dratva et al., 2026).

In addition to technical challenges, there are a variety of ethical and regulatory barriers to widespread adoption of AI into digital immunology. Despite its accuracy, the sensitive nature of genomic and clinical data on which many AI models are trained raises increasing concerns over data governance and patient privacy, as well as regulatory approval as frameworks adapt to new technologies (Goktas & Damadoglu, 2025). Furthermore, the presence of algorithmic bias in poor performance across under-represented populations threatens its widespread implementation due to limitations of generalizability, which is reliant on rigorous external validation of diverse datasets (Dhar, 2025).

Ongoing efforts are centered around the creation of explainable, interoperable and clinically validated AI frameworks that can seamlessly incorporate multimodal immune information instantaneously, while identifying the correct data to be incorporated at any given time. In the future, further investigation in the area should focus on collective data-generating standardized methodology, prospective multicenter validation, and libraries of shared data to enhance the robustness and clinical applicability of digital immunology. Only through tackling these areas of research can the true potential of AI-driven immune profiling reach the future of precision medicine (Curion & Theis, 2024; Lei & Tsang, 2025; Chen et al., 2025).

Following the Literature Review, the next important section should move onto the important subject of the paper. An acceptable structure in Elsevier style will be:

3. Artificial Intelligence Technologies Driving Digital Immunology

3.1 Machine Learning in Immune Profiling

In digital immunology, machine learning (ML) has been the most frequently employed AI method because of its utility in discovering detailed relationships in high-dimensional immune data. Most often, supervised learning approaches such as classification algorithms are used on labeled molecular and clinical data to delineate immune phenotypes, make disease trajectory predictions, and venture to determine therapy responses (Curion & Theis, 2024; Jariwala, 2025). Unsupervised learning, on the other hand, can be applied to identify novel immune cell populations as well as molecular features without precursor grouping to reveal detailed immune variability (Curion & Theis, 2024; Jariwala, 2025).

The growing number of multimodal immune data sets has only enabled further applications of ML algorithms for biomarker discovery and patient stratification. ML algorithms can, by combining genomic, transcriptomic, proteomic, and clinical data, determine predictive immune signatures for precision diagnosis and tailored treatments. Such computational tools have proven to be highly useful in cancers, autoimmune conditions, and other immune-mediated diseases where progression involves intricate biological networks (Chen et al., 2025; Chang et al., 2025; Alshorman et al., 2026).

3.2 Deep Learning for High-Dimensional Immune Data Analysis

Deep learning has greatly advanced the analysis of complicated immunological data by automating the extraction of hierarchical features from high-throughput biological data. Deep neural networks circumvent the need for pre-specified features in traditional machine learning algorithms and learn complex non-linear interactions directly from genome sequence, single-cell transcriptome data, histopathological images, and other high-dimensional data (Kumar et al., 2024; Curion & Theis, 2024).

CNNs have also proven to be very effective in digital pathology, including immune cell infiltration identification, spatial cellular interactions quantification, and tumor microenvironment characterizations based on whole-slide images (WSI) (Koelzer et al., 2019; Bilal et al., 2023; Rigamonti et al., 2024; Shen et al., 2025). They provide reproducible quantitative biomarkers, that make prognosis and therapy decision possible. This is especially true in immuno-oncology, where immune cell composition and distribution can highly impact the treatment efficiency.

3.3 Foundation Models and Large-Scale AI Frameworks

Foundation models are a significant development in computational immunology as they offer AI systems the ability to learn generalbiological representations across large volume of multimodal data, which can then be applied to many different immunological tasks (such as immune response prediction, biomarker detection, therapeutic outcomes prediction) without retraining from scratch for each task. Their scalability enables the multi-faceted simultaneous interpretation of molecular, imaging, and clinical data, resulting in increase efficiency andaccuracy (Kumar, 2024).

In the realm of precision immunology, foundation models have exhibited potential in harmonizing the diverse data outputs from sequencing platforms, digital pathology tools and electronic health records. Their ability to capture intricate biological relationships enables greater depth in immune profiling along with providing a key avenue toward personalized approaches for a range of autoimmune and cancer indications. As foundation models advance in scope and depth, they are poised to become integral elements of next-generation digital immunology frameworks (Chen et al., 2025; Kumar, 2024; Lei & Tsang, 2025).

3.4 Explainable Artificial Intelligence in Clinical Immunology

The increase of complexity of AI algorithms has led to a surge of interest in explainable artificial intelligence (XAI) in clinical settings, where the reasons behind specific outputs are crucial for medicine. Although such algorithms are often prone to high predictive performance, this is often at the expense of being difficult to interpret and understand which can lead to skepticism from clinicians and difficulties from regulators. XAI allows models to output understandable explanations for individual variables and their relationships to the model prediction, aiding clinical acceptance and enabling responsible use (Negut & Visan, 2025; Jariwala, 2025).

In digital immunology, explainable AI also aids in understanding immune biomarkers, disease risk estimates, and treatment choices by connecting results to understandable biological processes. This feature facilitates clinician-AI collaboration, as well as reproducibility, accountability, and patient-focused deliberation. As AI continues to be adopted in standard immunology operations, explainability will continue to be a necessary part of safe and accurate precision medicine (Dhar, 2025; Goktas & Damadoglu, 2025).

4. Applications of AI-Driven Immune Profiling

4.1 AI in Cancer Immunotherapy and Immuno-Oncology

Cancer immunotherapy has revolutionized cancer treatment by utilizing the immune system to detect and destroy tumor cells. Despite this, clinical responses to immunotherapeutic agents are diverse, owing to varying tumor biology, immune cell populations and local tumor microenvironment. AI based immune profiling has proven to be a successful method for immunocharacterisation, allowing biomarkers to be found so that patients can be stratified and personalized treatments administered (Ravi et al., 2025; Alshorman et al., 2026).

Machine learning algorithms have been utilized to integrate immunogenomic, transcriptomic, radiomic, and clinical information in order to predict responses to therapy and clinical outcomes. By extracting patterns of cellular and molecular expression that are indicative of response, successful models are able to select patients who are more likely to respond to immune checkpoint blockade or other immunotherapies, alleviating the burden of unnecessary therapies while maximizing clinical benefit (Chang et al., 2025; Kumar, 2024; Chen et al., 2025).

Intelligent digital pathology aided by artificial intelligence has already broadened immune profiling in the cancer field through the automatized analysis of histopathological images. Deep learning models can reliably quantify the level and composition of tumor infiltrating lymphocytes, identify immune cell spatial distribution, describe immune cell/malignant cell interactions and cell type distributions. Based on these quantitative assessments, reproducible biomarkers for prognosis are created, representing a useful adjunct to traditional pathological analysis (Koelzer et al., 2019; Bilal et al., 2023; Huss et al., 2023).

Recent work has shown the usefulness of combining digital pathology with other sophisticated imaging techniques to gain a more comprehensive characterization of the tumor immune microenvironment. The combination of AI image analysis and imaging mass cytometry, for example, allows analyst to assess tumor cells, stroma, and various immune cell populations simultaneously, enhancing the ability to identify clinically relevant classifiers (Rigamonti et al., 2024).

However, in addition to using tissue-based models, others have utilized AI to predict treatment response directly from regular tissue slides, Extracting higher-order morphological and immune-related features that are not visibly obvious but can accurately predict clinical PR to chemoradiotherapy and help guide personalized treatment. These successful demonstrations point towards the increasing uptake of AI-driven immune profiling in enhancing precision oncology and attaining personalized cancer immunotherapy (Shen et al., 2025; Ravi et al., 2025).

4.2 AI in Autoimmune Disease Diagnosis and Management

Autoimmune diseases (AID) are failures of the immune system, marked by improper immune response to self-antigens and long-term inflammation, tissue destruction and remodelling. The high variability in both clinical presentation and immune behavior in AID pose a great challenge for accurate phenotyping, diagnosis, disease classification and personalized treatment. AI-enabled immune profiling has proven to be a powerful platform for a comprehensive integration of clinical and molecular multi-omics data for disease identification and optimization of precision care (Alshorman et al., 2026; Negut & Visan, 2025).

Machine learning algorithms have been used to discover disease-specific immune signatures by combining clinical data with genomic, transcriptomic and proteomic data. These calculations predict disease and aid diagnosis by prescripting the pattern of groups of cells that is complementary to identifying them individually, provide us with the potential to differentiate between clinically similar autoimmune diseases and provide us with early indicators of disease progression enabling better management (Jariwala 2025, Chen et al 2025, Negut & Visan 2025).

The application of spatial omics and multimodal data has provided an additional protective layer for immune profiling to autoimmune diseases by systematizing a holistic perspective on immune cell coexistence within diseased tissue. AI-enabled analytical approaches allow concurrent analysis across molecular, spatial, and clinical components, allowing enhanced detection of predictive markers for disease activity, prediction of treatment responses and prediction of immune-related adverse effects (Stensballe, 2026; Lei & Tsang, 2025).

Another promising area where artificial intelligence has been shown to advance in immunology is over the therapeutic strategies for autoimmune diseases. AI-based predictive models have been generated to estimate the responses to immunotherapy and adverse immune effects. AI can also be used to decrease the empiricism of therapies by integrating various immune signatures over longitudinal immunoprofiles and assisting in choosing treatment strategies while patients are being monitored over time (Alshorman et al., 2026; Dhar, 2025; Goktas & Damadoglu, 2025).

4.3 AI in Immunogenetics and Transplantation

Immunogenetics is crucial in immune compatibility, disease predisposition and treatments especially with respect to transplantation. Proper identification of genetic factors that influence immune response such as HLA alleles as well as other immunogenic genes allows for more precise match between donor and recipient that reduces the likelihood for graft rejection. The implementation of AI in immunogenetic analysis allows for more efficient interpretation of large amounts of genomic data (Farzan, 2024; Sonmez et al., 2026).

With the progression of next-generation sequencing (NGS) technology, Immunogenetic information can now be obtained at an unprecedented scale with large genomic datasets. AI-driven algorithms can make uses of such high-dimensional genetic information to delineate complex immunogenetic patterns that cannot be identified by traditional methods. Examples include genotyping of HLA alleles (Shin et al., 2026), prediction of antigen presentation potential (Sonmez et al., 2026), and measuring immunological compatibility during HCT. Such functions would allow for a more optimal donor selection and individualized approaches to transplantation.

In addition to HLA typing AI has also been implicated in the amalgamation of genomic, transcriptomic and clinical data to aid in the immune surveillance of post-transplant patients. Dynamic monitoring of specific immune biomarker changes of patients over time can be used to build predictive models to determine those more likely to suffer graft rejection or immune mediated events, supporting earlier intervention, and potentially enabling personalized immunosuppressive regimens (Shin et al., 2026; Chen et al., 2025).

The ongoing integration of AI, immunogenetics, and precision medicine is anticipated to further structure transplant by expanding immune profiling and predictive algorithms. As AI models evolve and clinicaltested, they are expected to better predict outcomes, guide donor-recipient matching, and promote transplant long-term survival, consolidating digital immunology's role in the future of transplantation medicine (Farzan, 2024; Sonmez et al., 2026; Lei & Tsang, 2025).

4.4 AI in Allergy and Clinical Immunology

As allergy and immune-related diseases have become more common the demand for more accurate diagnostic and treatment options has been elevated. Traditional methods of diagnosis mainly involve clinical history, laboratory testing and allergy testing which may lack the specificity required to differentiate the available immune phenotypes. AI-based immune profiling allows for a broader analysis by evaluating clinical, molecular and immunological information to enhance disease classification, severity prediction, and therapy selection (Goktas & Damadoglu, 2025; Dhar, 2025).

Machine learning algorithms have been extremely useful in pinpointing immune biomarkers related to allergic disease as well as disease severity prediction using diverse datasets. The combination of genomic, proteomic and clinical information allows for AI algorithms to detect combinations of complex immune signatures that allow for pre-mature disease diagnosis and offer precise patient stratification. Such predication allows to starting individualized treatments and to optimize monitoring and long-term management of allergic diseases (Chen et al, 2025; Jariwala, 2025; Goktas & Damadoglu, 2025).

Moreover, the AI initiatives have been enhancing clinical decision support systems in immunology, by helping doctors understand detailed immune characterization and proposing personalized treatment plans. As they are given permanent individualized data, then they could predict the response to the medication, keep track of the disease development and selecting the proper clinical actions at the right moment. These AI tools have a significant impact in the treatment of chronic allergy diseases and immune defects, which need skills in chronic monitoring and flexible treatments administration (Negut & Visan, 2025; Dhar, 2025).

With the continual growth of multimodal immune dataset by AI, in the future, further integration of molecular biomarkers and routine clinical features by AI in allergy and clinical immunology will be valuable in achieving more accurate diagnosis, better benefit from targeted therapy and enhanced personalized care in a digital immunology context which will become an integral and critical part of future clinical practice (Chen et al., 2025; Goktas & Damadoglu, 2025; Lei & Tsang, 2025).

4.5 Digital Immune Twins and Predictive Immunology

Digital immune twinning is an innovative approach in digital immunology, whereby models of a person's immune system are created to emulate the real person by analysis of their longitudinal clinical, immunological, and molecular data. Combining the information extract from genomics, transcriptomics, proteomics, imaging, and electronic health records into virtual immune twins facilitates dynamic personalized prediction and optimization of immune responses and therapy (Abuhassan et al., 2026; Lei & Tsang, 2025).

AI the analytical backbone of digital immune twins, that would constantly analyze multidimensional data from various modes to simulate immune response to a spectrum of physiological and pathological conditions. These AI-enabled models could forecast disease progression, gauge potential benefits of a particular therapy and project immune adverse event risks, so that physicians could customize intervention strategy based on immune status. This prediction skill would find great utility in malignant diseases where 'precision' immunotherapy is steered by prognostication of the tumor–immune microenvironment (Abuhassan et al., 2026; Alshorman et al., 2026).

The combination of spatial omics and systems immunology improves digital immune twins' predictive accuracy by adding spatial information of immune cell populations, include molecular interactions between immune cell populations, as well as dynamic updates of immune activities over time. Such a comprehensive view of immune functionality allows real-time tracking of immune health status, and aids in defining personal immune path that may remain hidden to standard clinical observation. Therefore, digital immune twins hold great potential for the pursuit of precision immunology and long-term patient planning. (Lei & Tsang, 2025; Stensballe, 2026)

While still at nascent stages of clinical translation, digital immune twins may revolutionize immune profiling by redefining healthcare to preemptive and predictive measures in disease management. As the models gradually continue to develop, advancements in AI algorithms, a more robust integration of multimodal data sources and continued clinical validation will continue to increase the accuracy, scalability and implementation of these models in day-to-day precision medicine and personalized immunotherapy (Abuhassan et al., 2026; Chen et al., 2025; Lei & Tsang, 2025).

Figure 2. Clinical Applications of AI-Driven Immune Profiling

5. Future Perspectives of AI-Driven Digital Immunology

5.1 Advancing Precision Immunology Through AI

As it has been an ongoing process, the ongoing development of AI is promising for further refinement of immunology with more specific profiling of the immune function per person, and the design of individual therapies. AI regimes of the future will couple clinical records longitudinally with highly detailed multi-omic profiles, imaging data, and environmental information to create models that track immune health throughout life. These 'residents' may offer the potential to identify disease before symptoms emerge, select the optimal treatment, and monitor the response to therapy as it occurs (Lei & Tsang, 2025; Chen et al., 2025).

Further utilization of foundation models with large-scale machine learning algorithms is expected to enhance scalability and adaptability of immune profiling platforms. Drawing insights from a wide range of biomedical data sources, the next-generation of foundation models could facilitate biomarker discovery, impart robust predictive power over multiple immune-mediated conditions, and minimize the reliance on disease-specific computational models. As these methods are further developed, there is hope that clinical value will be increasingly realized in chemotherapy, autoimmune disease, transplant, and allergy (Kumar, 2024; Curion & Theis, 2024).

5.2 Integration of Emerging Multi-Omic Technologies

Because each innovative technique offers unique advantages and faces specific technical challenges, innovative applications of digital immunology are likely to require the integration of single-cell sequencing, spatial transcriptomics, imaging mass cytometry, and immunogenomics into a common powerful AI-analyse platforms. As all valuable digital datasets will be analyzed at the same time, undoubtedly, these integrated approaches will facilitate determination of immune cell interactions and tissue architecture, leading to identification of better biomarkers and personalized treatment regimens (Dratva et al., 2026; Chang et al., 2025; Rigamonti et al., 2024).

AI platforms containing multifaceted datasets can in addition empower clinicians with the ability to monitor immune status dynamically. This on-line information could provide further immune status as a basis for dynamic treatment guidance (Stensballe, 2026; Lei & Tsang, 2025).

5.3 Clinical Translation and Implementation

Even though technology has advanced at lightning speed, implementing AI based immune profiling in clinical setting on a daily basis will need enhancements in model validation, interoperability and adherence to regulatory policies. Future would focus on multi-center validation studies, standardized data collection methodology and explainable AI models that clinicians will understand. This will help generate more confidence among clinicians on data-driven AI supported clinical decision making (Negut & Visan, 2025; Dhar, 2025).

Multi-stakeholder collaborations involving immunologists, clinicians, computational scientists and regulatory bodies will be key for driving the establishment of standardized protocols for AI use in digital immunology. Multidisciplinary working groups will likely expedite the translation of clinically impactful AI tools that also regulate for patient privacy, algorithmic bias and reproducibility between populations (Goktas and Damadoglu, 2025; Alshorman et al., 2026; Chen et al., 2025).

6. Conclusion

Digital immunology has become a revolutionizing arm of immunology that harnesses the combined expertise of artificial intelligence and high-dimensional immune profiling technology to gain a deeper understanding of immune function in health and disease. The fusion of AI with high-throughput sequencing (single cell genomics, spatial omics), digital pathology, and immunogenomics has led to more holistic identification of immune reponses, allowing for better biomarker identification, disease classification, and decision making in personalized medicine.

These examples of AI-enabled immune profiling across oncology, autoimmune disease, transplantation and clinical immunology, demonstrate how computational approaches can enable to refine diagnosis and improve therapeutic success. Upcoming technological development, such as multimodal data learning, foundation AI model and digital immune twin, have exemplified the ability of computational approach to propel future precision immunology.

Yet despite these advances, issues regarding data standardization, model interpretability, interoperability, clinical validation and ethical governance remain significant barriers to adoption of AI-driven immune profiling into clinical care. Eliminating these barriers through ongoing technological advancement and interdisciplinary synergies will be key to translating AI immune profiling into a sustainable clinical paradigm.

In conclusion, the utilization of artificial intelligence approaches in immune profiling is an important advance in the field of precision medicine. As further advancements are made in computational and biomedical technologies, digital immunology will become more robust and enable more accurate prediction, prevention, and management of immune-mediated diseases, and in this way improve patient care.

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