The Role of Artificial Intelligence and Machine Learning in Autoimmune Disorders

Faizan Siddiqui, Danish Aslam, Khushnuma Tanveer, and Mohamed Soudy

Abstract The immune system of an organism responds to threats from outside the body. Autoimmunity in immunology is the system of an organism's immune responses against its healthy cells, tissues, and other typical body parts. Therefore, a disorder known as an autoimmune illness results from an inappropriate immune reaction to a healthy bodily function. The science of developing computers with intelligence that both mimics and exceeds that of humans is known as artificial intelligence (AI). Programs having AI capabilities can contextualize and analyze data to deliver information or automatically initiate operations without the need for human intervention. Furthermore, AI can be attained through machine learning. This branch of AI applies to learning to make ever-better judgments using algorithms to discover patterns and acquire insights from data automatically. In this chapter, we present the role of AI and machine learning to analyze how autoimmunity behaves in conditions like autoimmune diseases. Moreover, we also discussed the impact of employing machine learning techniques to optimize precision medicine for patients.

Keywords Autoimmunity · Artificial intelligence · Image analysis · Immune disorders · Precision medicine

F. Siddiqui
International Medical Faculty, Osh State University, Osh City, Kyrgyzstan

D. Aslam · K. Tanveer
Department of Computer Science, Jamia Millia Islamia, New Delhi, India
e-mail: danish2101125@st.jmi.ac.in

M. Soudy (✉)
Bioinformatics Program, Faculty of Computer Science and Information, Ain Shams University, Cairo, Egypt
e-mail: mohmedsoudy2009@gmail.com

K. Raza and S. Singh (eds.), *Artificial Intelligence and Autoimmune Diseases*, Studies in Computational Intelligence 1133, https://doi.org/10.1007/978-981-99-9029-0_3

1 Introduction

The use of machine learning and deep learning in autoimmune disorders is a rapidly growing field of research, as it has the potential to revolutionize the diagnosis and treatment of these conditions. Machine learning is a subfield of Artificial Intelligence (AI) that uses algorithms to learn from data and make predictions. Deep learning, on the other hand, is a subset of machine learning that uses neural networks to process data. Both methods have been used in various applications related to autoimmune disorders, such as diagnosis, prognosis, drug discovery, and treatment optimization [1]. In terms of diagnosis, machine learning algorithms are used to analyze medical images or patient data to identify patterns associated with autoimmune disorders. For example, researchers utilized deep learning algorithms to analyze Magnetic Resonance Imaging (MRI) scans for Multiple Sclerosis (MS) and Rheumatoid Arthritis (RA) [2, 3]. The results showed that deep learning was able to detect MS and RA with high accuracy. Similarly, machine learning algorithms have been used to diagnose Systemic Lupus Erythematosus (SLE) by analyzing patient data such as age, gender, race/ethnicity, laboratory test results, and medical history [4, 5].

In terms of prognosis, machine learning algorithms are used to predict the course of an autoimmune disorder over time. For example, researchers utilized machine learning algorithms to predict how RA patients will respond to certain treatments based on their clinical features. Similarly, deep learning algorithms have been used to predict which patients with SLE are at risk for developing complications such as organ damage or stroke [6].

In terms of drug discovery and treatment optimization for autoimmune disorders, both machine learning and deep learning were utilized to identify new drugs or optimize existing treatments. For example, researchers have applied machine learning techniques such as random forest to identify novel drugs for RA that could target specific pathways involved in the disease progression [7]. Similarly, deep neural networks have been used to optimize existing treatments for MS by predicting which drugs would be most effective at reducing disease symptoms [7].

Overall, the use of machine learning and deep learning in autoimmune disorders has great potential for improving diagnostic accuracy and optimizing treatments for these conditions. In this chapter, we will go through the AI approaches used for diagnosis, and prognosis, and AI in treatment and drug discovery. Moreover, we will discuss the main workflow of the prediction of drug-induced autoimmune diseases utilizing autoimmune drug data and research databases as shown in Fig. 1.

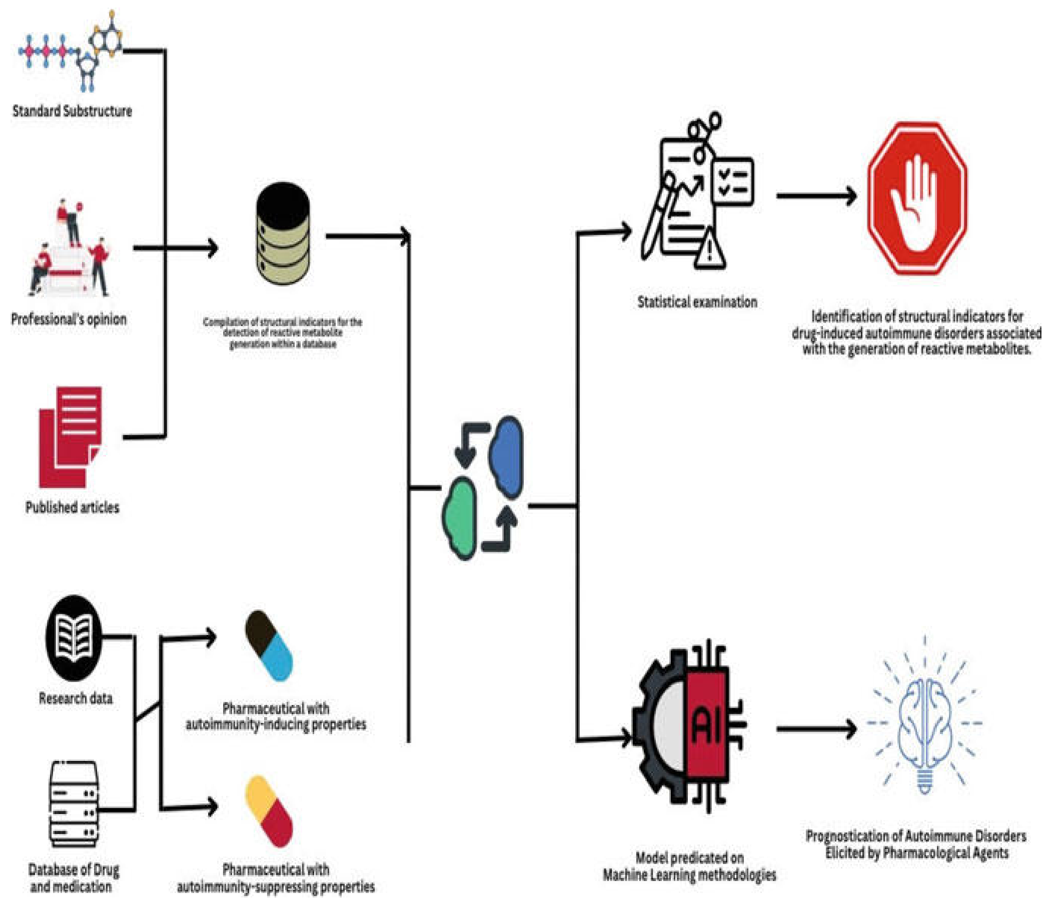

Fig. 1 Schematic representation of the methodology employed for the prediction of drug-induced autoimmune diseases utilizing autoimmune drug data and research databases

2 Literature Review

2.1 AI Approaches for the Diagnosis and Prognosis

In the diagnosis of autoimmune diseases, AI, models, and algorithms have emerged as extremely useful tools, particularly in the domains of image analysis, data from laboratory interpretation, and systems for clinical decision support [8]. In addition, the incorporation of AI with electronic health records (EHR), wearable devices, and patient-generated data has increased the scope of disease evaluation [9]. The following examples illustrate specific AI applications in the diagnosis of autoimmune diseases.

2.2 Image Analysis

AI-based assessment of images has shown great promise in making diagnoses of autoimmune diseases, especially rheumatoid arthritis and dermatological conditions such as psoriasis and systemic lupus erythematosus. In rheumatoid arthritis, AI algorithms are capable of analyzing radiographic images of afflicted joints to identify identifying indications such as joint erosions and synovial hypertrophy. Using methods such as deep learning and machine learning on huge amounts of radiographic image data, AI models may be trained to identify and measure these pathological features, thereby aiding in the precise diagnosis of RA [10]. Similarly, AI algorithms can analyze depictions of skin lesions in dermatological autoimmune diseases such as psoriasis and SLE to recognize particular patterns and evaluate disease prevalence. The training of deep learning models on vast databases of dermoscopic or histopathological images enables the automatic identification of disease-specific characteristics. This aids dermatologists in diagnosing these conditions and developing the most suitable treatment plans [11].

2.3 Laboratory Data Interpretation

AI algorithms play a crucial role in the analysis of laboratory data for the diagnosis of autoimmune disease, especially in conditions such as multiple sclerosis and neuromyelitis optica (NMO). AI models can analyze MRI images to detect and measure brain and spinal cord lesions in these diseases [12]. By employing machine learning techniques, these models can recognize patterns and structural abnormalities that aid in differentiating autoimmune neurological disorders [13]. In addition, AI-based evaluation of serological indicators such as autoantibodies aids in the diagnosis of autoimmune diseases. For instance, AI models can analyze patient-specific autoantibody profiles and clinical data to predict disease activity and assess the risk of organ involvement in systemic lupus erythematosus. Using machine learning algorithms, these models provide personalized predictions and facilitate clinical decision-making [14].

2.4 Clinical Decision Support Systems

AI-powered medical decision support systems help in the diagnosis of autoimmune disorders by providing essential support to doctors and nurses. By incorporating data from patients, scientific research, and AI algorithms, these systems provide suggestions based on evidence to enhance diagnostic precision [15]. It aids in processing

EHR data, such as patient history, symptoms, and laboratory results, to generate diagnostic hypotheses, recommend appropriate testing, and facilitate differential diagnosis. Moreover, clinical decision support systems powered by AI may analyze longitudinal patient data, such as the progression of the disease, response to treatment, and adverse reactions to refine and enhance the diagnostic procedure [16]. These systems continually gain insight from new data, enabling recommendations to be updated and contributing to the timely and individualized diagnosis of autoimmune diseases [17].

2.5 Integration of Electronic Health Records, Wearable Technologies, and Patient-Generated Data

The incorporation of AI with electronic health records, wearable devices, and patient-generated data enables a comprehensive evaluation of autoimmune diseases. Using EHR data, AI algorithms can uncover latent trends, connections, and risk factors associated with autoimmune diseases [18]. By utilizing Natural Language Processing (NLP) techniques, AI can extract pertinent information from unstructured clinical notes, thereby facilitating accurate diagnosis and prognosis. In addition, wearable devices, such as smartwatches and biosensors, acquire physiological data in real time, such as heart rate, temperature, and activity levels [19]. In conjunction with contextual information, AI algorithms can analyze this data to detect disease flares, predict symptom exacerbation, and optimize treatment. Using AI techniques, patient-generated data, such as symptom diaries and self-reported outcomes, can be analyzed to enhance disease monitoring and assist in diagnosis [20]. AI applications in the diagnosis of autoimmune diseases include image analysis, interpretation of laboratory data, and clinical decision support systems, among others [21]. These applications demonstrate the potential of AI to improve diagnostic accuracy, facilitate personalized medical care, and enable comprehensive disease assessment. As AI continues to advance, its integration with healthcare systems is likely to improve the efficiency and efficacy of diagnosing autoimmune diseases, ultimately leading to better patient outcomes [22]. AI has shown promise in medical diagnosis, but it should always be utilized alongside clinical experience. AI should be used to improve healthcare professionals' diagnoses while preserving human judgment and personalized patient care. The list of various AI-based applications for human disease is listed in Table 1.

3 AI Approaches in Treatment and Drug Discovery

In recent years, the role of AI in the treatment and drug discovery of autoimmune diseases has become increasingly prominent. Autoimmune diseases occur when the body's immune system mistakenly attacks its healthy cells and tissues. Through the

Table 1 A summary of current AI-based tools and their applications in autoimmune diseases

Disease	AI-Based tools	Application	References
Cancer diagnosis	ER APP, Breast Cancer (Visiopharm A/S); Kaiku Health (Kaiku Oy); Transpara (ScreenPoint Medical BV); ColonFlag (Medial EarlySign Inc.); GI Genius (Medtronic Inc. (parent company: Medtronic plc.))	AI was used to utilize the data of cancer biomarkers, scan multiple biopsies, uncover trends, and detect, classify, and forecast illnesses using sophisticated algorithms and machine learning	[23]
Cardiovascular disease assessment	Bay Labs, Caption HealthZebra Medical Vision, Arterys LLC, Aidoc	Medical pictures, ECGs, and genetic data may be used for AI to diagnose cardiovascular disorders. Risk factors, cardiac illnesses, including heart attacks and strokes may be predicted using machine learning algorithms	[24]
Neurological disorder diagnosis	Icometrix, BrainScope, Mindstrong Health, Aidlab, Synchron, Neural Analytics, Viz.ai	Alzheimer's, Parkinson's, and multiple sclerosis may be diagnosed using AI. AI systems are used to find biomarkers and trends in brain scans, genetic data, and patient complaints	[25]
Dermatological diagnosis	DermAI, MetaOptima, SkinVision, VUNO	AI-powered systems were used to detect skin cancers like melanoma. AI systems may help doctors detect skin lesions by analyzing photos and comparing them to large databases	[26]
Pulmonary disease detection	Subtle Medical, Quantib, RadLogics, Lunit, VIDA Diagnostics, Aidful, Enlitic, Butterfly Network	AI can diagnose asthma, COPD, and pneumonia. Lung function tests, medical pictures, and patient information may be used by machine learning algorithms to diagnose respiratory disorders	[27]
Genetic disease identification	FDNA, Sophia Genetics, Deep Genomics, Diploid, Genoox, Fabric Genomics, Blueprint Genetics	AI systems are used to discover genetic abnormalities and illness risks by analyzing DNA sequencing and genomic profiles. AI can diagnose hereditary disorders by comparing genome variants to genetic markers	[28]

(continued)

Table 1 (continued)

Disease	AI-Based tools	Application	References
Ophthalmic disease diagnosis	IDx-DR, RetinAI Medical, Visulytix, Eyenuk Inc, ZEISS, NovaSight, Google DeepMind	AI is used to identify diabetic retinopathy and age-related macular degeneration. AI algorithms may help ophthalmologists diagnose and treat anomalies in retinal pictures	[29]
Mental health assessment	Woebot, Ginger, Talkspace, SilverCloud Health, Lantern, Cogito Corporation, X2AI, Taliaz, AiCure, Cerebri	AI technologies were used to diagnose depression, anxiety, and bipolar illness by analyzing voice, text, and facial expressions. Natural language processing and sentiment analysis algorithms may identify mental health trends and indications for early intervention and personalized therapy	[30]
Rare disease diagnosis	FDNA (now part of Invitae corporation), Mendelian, RD-Connect, Deep 6 AI, SOPHiA Genetics, Congenica, Genomenon, Fabric Genomics, Diploid, N-of-One (part of Qiagen)	Patient symptoms, genetic data, and medical literature may help AI diagnose uncommon illnesses. Machine learning algorithms may help doctors detect rare diseases	[31]

integration of AI, significant advancements have been made in improving diagnosis, personalizing treatment plans, and accelerating the discovery of effective therapies for these complex conditions. Moreover, AI has the potential to significantly impact the treatment of autoimmune diseases in several ways. For Predictive Analytics, AI algorithms can be trained on patient data to develop predictive models that estimate disease progression, treatment response, and potential complications. These models can help healthcare providers make informed decisions regarding personalized treatment plans and identify high-risk patients who require closer monitoring. For Precision Medicine, AI can facilitate precision medicine approaches by analyzing individual patient characteristics, such as genetic profiles, lifestyle factors, and medical history, to develop personalized treatment strategies. This can lead to more targeted and effective interventions, minimizing adverse effects and optimizing outcomes. For Treatment Optimization, AI algorithms can continuously analyze patient data, treatment outcomes, and real-time monitoring data to optimize treatment protocols. By considering multiple variables and adjusting treatment plans in real time, AI can help healthcare providers make data-driven decisions and improve patient outcomes. It is important to note that while AI holds great promise, they are not meant to replace healthcare professionals. Instead, they are tools that can augment their capabilities, improve decision-making processes, and enhance patient care in the context of autoimmune diseases and other complex medical conditions.

3.1 Predictive Analytics for Disease Progression and Treatment Response

In several studies associated with inflammatory bowel diseases, machine learning-based methods such as Random Forest and Support Vector Machine (SVM) were implemented to predict response to treatment, disease risk, and disease severity [32]. Notably, in a study associated with Type 1 diabetes, a machine learning-based fTPM approach for the diagnosis and monitoring of Type 1 Diabetes Mellitus (T1DM) was presented. The study focused on assessing the physical state of Red Blood Cell (RBC) membranes, which undergo alterations in T1DM and serve as an indicator for disease progression. The researchers observed increasing fluidification of RBC membranes as the disease progressed, along with the formation of microdomains exhibiting different fluidity. Sub-micrometric fluidity maps showed a widening of the fluidity spectrum and a consistent increase in the fluid region. Based on these findings, a diagnostic system was developed to measure variations in a measurable quantity induced by the disease [33]. Additionally, various novel methods/hybrid models based on Neural Networks, and Support Vector Regression have been used for studying disease progression and autoimmune diseases.

3.2 Precision Medicine for Disease Progression and Treatment Response

In the case of rheumatoid arthritis, the treatment selection process primarily relies on trial and error, despite the availability of various targeted biological and conventional therapies. This highlights the existence of a “precision gap” in the field of rheumatic diseases, which indicates the factors hindering the advancement and adoption of precision medicine approaches [34]. Notably, in a study associated with Systemic Sclerosis, a machine learning approach was employed to identify pathways that were down-regulated by treatment. Genes demonstrating a significant decrease after treatment were utilized as positive examples in an SVM classifier, while genes exhibiting no evidence of differential expression served as negative examples. By learning the connectivity patterns of differentially expressed genes in a skin network, the classifier ranked all genes in the genome. The top-ranked genes held great relevance to treatment response, even if they were missed due to small sample sizes or undetectable changes at the mRNA level. In summary, the integration of machine learning in this framework enabled a more comprehensive and nuanced understanding of treatment response, allowing for the identification of key pathways, potential therapeutic targets, and the exploration of alternative therapies for patients who do not respond to initial treatments. This approach enhances the precision and individualization of treatment strategies, paving the way for more effective and tailored precision medicine interventions [35].

3.3 Treatment Optimization for Autoimmune Diseases

In autoimmune diseases, such as rheumatoid arthritis, personalized and precise medicine holds promise. Current treatment approaches often involve trial and error, leading to suboptimal outcomes and increased healthcare costs. Implementing a precision medicine approach based on patients' biological profiles could enhance treatment responsiveness [36]. Machine learning algorithms have demonstrated the ability to predict treatment response using demographic and clinical data, achieving high accuracy with Area Under the ROC Curve (AUC) up to 0.84 [37, 38]. Additionally, machine learning techniques have been employed to forecast the need for treatment escalation, identifying patients who may require more powerful medications. Omics data, including genetic and microbiome information, offer valuable insights for predicting treatment response. Random forest models utilizing gut microbiome data achieved an AUC of 0.84 in identifying methotrexate (MTX) responders while incorporating transcriptomics data reached an AUC of 0.78 for MTX response prediction [39, 40]. Notably, omics data appear more beneficial in predicting response to second or third-line biological disease-modifying antirheumatic drugs (bDMARDs) compared to MTX [41, 42].

Incorporating imaging data, such as ultrasound images, can further enhance response prediction. Scoring systems based on the severity of synovitis, tenosynovitis, and enthesitis on ultrasound images have been developed to assess treatment response, enabling the identification of patient clusters with significantly different treatment outcomes [43]. The use of virtual patient models and AI-enhanced Quantitative Systems Pharmacology (QSP) allows for the prediction of drug efficacy and optimization of treatment regimens for autoimmune and inflammatory diseases [44]. These models help in selecting dosing regimens, administration schemes, and clinical endpoints to improve the effectiveness of the drug. Additionally, the identification of biomarkers through machine learning analysis aids in patient stratification and monitoring during treatment, further optimizing the therapeutic approach. Overall, these methods contribute to the optimization of drug therapies in the context of autoimmune and inflammatory diseases [44].

3.4 AI Approaches for Target Identification

The identification of suitable therapeutic targets for autoimmune and inflammatory diseases (AIDs) can be enhanced through AID modeling combined with AI-powered computational analyses. By conducting comprehensive multi-omics molecular profiling of patients, these models facilitate patient stratification into homogeneous subgroups [45]. Moreover, they shed light on dysregulated pro-inflammatory pathways and generate hypotheses regarding potential therapeutic targets and candidate biomarkers, aiding in patient stratification and monitoring during treatment. AID models provide valuable insights into the rational design of combination therapies that target independent pro-inflammatory pathways associated with various immune compartments contributing to AID pathophysiology [46]. These immune compartments encompass pro-inflammatory signals originating from tissues, innate immune mechanisms, T lymphocyte activation, autoantibodies, and B cell activation, as well as soluble mediators involved in immune cross-talk.

By integrating multi-omics data and leveraging AI algorithms, AID modeling optimizes the identification of therapeutic targets for AIDs. This approach allows for a more personalized and precise treatment strategy by identifying combinations of therapies that effectively target distinct aspects of the disease pathology. Ultimately, AID modeling plays a vital role in advancing precision medicine for AIDs, leading to improved patient outcomes [47]. Despite significant investments and extensive preclinical research, there is a significant discrepancy between the number of promising lead compounds and the limited number of approved drugs. A major contributing factor to this issue is the inadequate predictive validity of animal models of multiple sclerosis (MS) in translating pathogenic mechanisms into safe and effective treatments for patients. This concerning situation has led to criticism regarding the relevance of current animal models used in preclinical research and has sparked a call for the enhancement of these models [48].

4 AI Approaches for Optimization of Drug Candidates and Repurposing Existing Drugs

Machine learning techniques were utilized to predict the risk of drug-induced autoimmune diseases [49]. Their approach involves analyzing structural alerts, which are specific molecular features associated with adverse drug reactions, as well as considering the daily dose of the drug. By training a machine learning model on a dataset of known drug-induced autoimmune diseases, the researchers aim to develop a predictive model that can assess the potential risk of these adverse events based on the structural properties of the drug and its dosage. This approach holds the potential to enhance the evaluation of the safety profile of new drugs and guide the drug development process, reducing the occurrence of autoimmune adverse reactions. In a study, a model was employed to identify potential drug candidates for repurposing [50]. The model utilized a methodology involving data collection and integration, followed by the evaluation and selection of candidate drugs based on predefined criteria. Through this approach, promising drug candidates were identified for treating these diseases. The findings of the study highlight the potential of drug repurposing as a strategy to enhance treatment options for rheumatic autoimmune inflammatory diseases, offering new avenues for improving patient outcomes in this challenging therapeutic area. The study utilizes machine learning approaches that capitalize on network medicine concepts. These approaches aim to replicate the intricate interactions between drugs and diseases. One specific tool mentioned is deepDR [51], which integrates various networks such as drug-side effect, drug-target, drug-disease, and multiple drug-drug networks. In this tool, an autoencoder is employed to learn drug features from these networks. These learned features are then utilized to predict approved drugs for neurodegenerative diseases. The study highlights the potential of machine learning in overcoming limitations associated with a lack of mechanistic understanding of complex diseases, as demonstrated in the context of neurodegenerative diseases.

5 Challenges and Future Directions

Despite the considerable promise shown by AI and machine learning in the realm of autoimmune disease research, some challenges require attention and resolution. To achieve optimal performance, AI models need the use of comprehensive and high-quality datasets, including both a substantial volume and superior standards. Ensuring the accessibility of databases related to rare autoimmune diseases is a significant challenge. The issue of interpretability becomes relevant when examining black-box AI models since their ability to provide predictions is hindered by the challenge of understanding the underlying biological processes. The significance of developing interpretable AI models lies in its contribution to the pursuit of comprehending disease processes. The incorporation of AI in the healthcare sector requires the development of ethical and regulatory structures to adequately address issues related to patient privacy, transparency, and accountability. The use of AI and machine learning techniques in the realm of autoimmune disease research has ushered in a new era of investigation and progress. The technologies listed above have the potential to significantly transform the detection, treatment, and management of autoimmune diseases, therefore improving the general health and well-being of many individuals worldwide. Despite the presence of enduring challenges, the field of AI holds promise for ongoing progress as a result of the relentless attempts undertaken by researchers, medical professionals, and individuals participating in research and cooperative initiatives.

6 Conclusion

The use of machine learning and deep learning in autoimmune disorders is a rapidly growing field of research, as it has the potential to revolutionize the diagnosis and treatment of these conditions. Incorporating different omics and clinical data may lead to better results in both prognosis and treatment of autoimmune diseases. AI has proven its potential in improving diagnosis, personalizing treatment plans, and accelerating the discovery of effective therapies. Through predictive analytics, precision medicine, and treatment optimization, AI empowers healthcare providers to make informed decisions, develop personalized treatment strategies, and optimize patient outcomes. Additionally, AI plays a crucial role in drug discovery by identifying potential targets, optimizing drug candidates, and uncovering repurposing opportunities. By leveraging AI's capabilities, the field of autoimmune diseases can benefit from enhanced precision medicine approaches and optimized drug therapies. AI serves as a powerful tool in the fight against autoimmune diseases, offering new possibilities for improved patient care and outcomes.

References

1. Stafford IS, Kellermann M, Mossotto E, Beattie RM, MacArthur BD, Ennis S (2020) A systematic review of the applications of artificial intelligence and machine learning in autoimmune diseases. NPJ Digital Med 3(1):30
2. Momtazmanesh S, Nowroozi A, Rezaei N (2022) Artificial intelligence in rheumatoid arthritis: current status and future perspectives: a state-of-the-art review. Rheumatol Therapy 9(5):1249–1304
3. Bonacchi R, Filippi M, Rocca MA (2022) Role of artificial intelligence in MS clinical practice. NeuroImage: Clinical 103065
4. Yaung KN, Yeo JG, Kumar P, Wasser M, Chew M, Ravelli A, Law AHN et al (2023) Artificial intelligence and high-dimensional technologies in the theragnosis of systemic lupus erythematous. Lancet Rheumatol 5(3):e151–e165
5. Zhou Y, Wang M, Zhao S, Yan Y (2022) Machine learning for diagnosis of systemic lupus erythematosus: a systematic review and meta-analysis. Computat Intell Neurosci (2022)
6. Vodencarevic A, Tascilar K, Hartmann F, Reiser M, Hueber AJ, Haschka J, Bayat S et al (2021) Advanced machine learning for predicting individual risk of flares in rheumatoid arthritis patients tapering biologic drugs. Arthritis Res Ther 23(1): 1–8
7. Kalweit M, Walker UA, Finckh A, Müller R, Kalweit G, Scherer A, Boedecker J, Hügle T (2021) Personalized prediction of disease activity in patients with rheumatoid arthritis using an adaptive deep neural network. PLoS ONE 16(6):e0252289
8. Raza K, Singh NK (2021) A tour of unsupervised deep learning for medical image analysis current medical imaging. Bentham Sci 17(9):1059–1077. https://doi.org/10.2174/1573405617666210127154257
9. Ahn JC, Connell A, Simonetto DA, Hughes C, Shah VH (2021) Application of artificial intelligence for the diagnosis and treatment of liver diseases. Hepatol Baltim Md 73(6):2546–2563. https://doi.org/10.1002/hep.31603
10. Chen H, Sung JJY (2021) Potentials of AI in medical image analysis in gastroenterology and hepatology. J Gastroenterol Hepatol 36(1):31–38. https://doi.org/10.1111/jgh.15327
11. Christou CD, Tsoulfas G (2021) Challenges and opportunities in the application of artificial intelligence in gastroenterology and hepatology. World J Gastroenterol 27(37):6191–6223. https://doi.org/10.3748/wjg.v27.i37.6191
12. Siddiqui MF et al (2022) Computational intelligence: a step forward in cancer biomarker discovery and therapeutic target prediction. In: Oncology KR (ed) Computational intelligence. Studies in computational intelligence, vol 1016. Singapore: Springer Singapore, pp 233–250. https://doi.org/10.1007/978-981-16-9221-5_14.
13. Khalifa A, Obeid JS, Erno J, Rockey DC (2023) The role of artificial intelligence in hepatology research and practice. Curr Opin Gastroenterol 39(3):175–180. https://doi.org/10.1097/MOG.0000000000000926
14. Krittanawong C, Zhang H, Wang Z, Aydar M, Kitai T (2017) Artificial intelligence in precision cardiovascular medicine. J Am Coll Cardiol 69(21):2657–2664. https://doi.org/10.1016/j.jacc.2017.03.571

15. Magrabi F et al (2019) Artificial intelligence in clinical decision support: challenges for evaluating AI and practical implications. Yearb Med Inform 28(1):128–134. https://doi.org/10.1055/s-0039-1677903
16. Garcia-Vidal C, Sanjuan G, Puerta-Alcalde P, Moreno-García E, Soriano A (2019) Artificial intelligence to support clinical decision-making processes. EBioMedicine 46:27–29. https://doi.org/10.1016/j.ebiom.2019.07.019
17. Shaikh F et al (2021) Artificial intelligence-based clinical decision support systems using advanced medical imaging and radiomics. Curr Probl Diagn Radiol 50(2):262–267. https://doi.org/10.1067/j.cpradiol.2020.05.006
18. Wong GL-H, Yuen P-C, Ma AJ, Chan AW-H, Leung HH-W, Wong VW-S (2021) Artificial intelligence in prediction of non-alcoholic fatty liver disease and fibrosis. J Gastroenterol Hepatol 36(3):543–550. https://doi.org/10.1111/jgh.15385
19. Siddiqui MF et al (2023) Leveraging healthcare system with nature-inspired computing techniques: an overview and future perspective. In: Raza K (ed) Nature-inspired intelligent computing techniques in bioinformatics. Studies in computational intelligence, vol 1066. Singapore: Springer Nature Singapore, pp 19–42. https://doi.org/10.1007/978-981-19-6379-7_2
20. Su T-H, Wu C-H, Kao J-H (2021) Artificial intelligence in precision medicine in hepatology. J Gastroenterol Hepatol 36(3):569–580. https://doi.org/10.1111/jgh.15415
21. Qazi, S, Iqbal N, Raza K (2022) Fuzzy logic-based hybrid models for clinical decision support systems in cancer. In: Computational intelligence in oncology. Studies in computational intelligence (SCI), vol 1016. Springer, pp 1–13. https://doi.org/10.1007/978-981-16-9221-5_12
22. Le Berre C et al (2020) Application of artificial intelligence to gastroenterology and hepatology. Gastroenterology 158(1):76-94.e2. https://doi.org/10.1053/j.gastro.2019.08.058
23. Mitsala A, Tsalikidis C, Pitiakoudis M, Simopoulos C, Tsaroucha AK (2021) Artificial intelligence in colorectal cancer screening, diagnosis and treatment. A new era. Curr. Oncol. Tor. Ont 28(3):1581–1607. https://doi.org/10.3390/curroncol28030149
24. Siontis KC, Noseworthy PA, Attia ZI, Friedman PA (2021) Artificial intelligence-enhanced electrocardiography in cardiovascular disease management. Nat Rev Cardiol 18(7):465–478. https://doi.org/10.1038/s41569-020-00503-2
25. Patel UK et al (2021) Artificial intelligence as an emerging technology in the current care of neurological disorders. J Neurol 268(5):1623–1642. https://doi.org/10.1007/s00415-019-09518-3
26. Young AT, Xiong M, Pfau J, Keiser MJ, Wei ML (2020) Artificial intelligence in dermatology: a primer. J Invest Dermatol 140(8):1504–1512. https://doi.org/10.1016/j.jid.2020.02.026
27. Hong L, Cheng X, Zheng D (2021) Application of artificial intelligence in emergency nursing of patients with chronic obstructive pulmonary disease. Contrast Media Mol Imaging 2021:6423398. https://doi.org/10.1155/2021/6423398
28. James KN, Phadke S, Wong TC, Chowdhury S (2023) Artificial intelligence in the genetic diagnosis of rare disease. Clin Lab Med 43(1):127–143. https://doi.org/10.1016/j.cll.2022.09.023
29. Li J-PO et al (2021) Digital technology, tele-medicine and artificial intelligence in ophthalmology: a global perspective. Prog Retin Eye Res 82:100900. https://doi.org/10.1016/j.preteyeres.2020.100900
30. Fiske A, Henningsen P, Buyx A (2019) Your robot therapist will see you now: ethical implications of embodied artificial intelligence in psychiatry, psychology, and psychotherapy. J Med Internet Res 21(5):e13216. https://doi.org/10.2196/13216
31. Noll R et al (2022) Conception, development and validation of classification methods for coding support of rare diseases using artificial intelligence. Stud Health Technol Inform 295:422–425. https://doi.org/10.3233/SHTI220755
32. Stafford IS, Kellermann M, Mossotto E et al (2020) A systematic review of the applications of artificial intelligence and machine learning in autoimmune diseases. npj Digit Med 3, 30. https://doi.org/10.1038/s41746-020-0229-3

33. Maulucci G et al (2017) Phase separation of the plasma membrane in human red blood cells as a potential tool for diagnosis and progression monitoring of type 1 diabetes mellitus. PLoS ONE 12
34. Lin CMA, Cooles FAH, Isaacs JD (2022) Precision medicine: the precision gap in rheumatic disease. Nat Rev Rheumatol 18:725–733. https://doi.org/10.1038/s41584-022-00845-w
35. Taroni JN, Martyanov V, Mahoney JM, Whitfield ML (2017) A functional genomic meta-analysis of clinical trials in systemic sclerosis: toward precision medicine and combination therapy. J Invest Dermatol 137:1033–1041
36. Momtazmanesh S, Nowroozi A, Rezaei N (2022) Artificial intelligence in rheumatoid arthritis: current status and future perspectives: a state-of-the-art review. Rheumatol Ther 9:1249–1304. https://doi.org/10.1007/s40744-022-00475-4
37. Amin Shipa MR, Yeoh SA, Embleton-Thirsk A, Mukerjee D, Ehrenstein MR (2022) The synergistic efficacy of hydroxychloroquine with methotrexate is accompanied by increased erythrocyte mean corpuscular volume. Rheumatology (Oxford) 61(2):787–793
38. Westerlind H, Maciejewski M, Frisell T, Jelinsky SA, Ziemek D, Askling J (2021) What is the persistence to methotrexate in rheumatoid arthritis, and does machine learning outperform hypothesis-based approaches to its prediction? ACR Open Rheumatol. 3:457–463
39. Artacho A, Isaac S, Nayak R, Flor-Duro A, Alexander M, Koo I, Manasson J, Smith PB, Rosenthal P, Homsi Y et al (2021) The pretreatment gut microbiome is associated with lack of response to methotrexate in new-onset rheumatoid arthritis. Arthritis Rheumatol 73:931–942
40. Plant D, Maciejewski M, Smith S, Nair N, Hyrich K, Ziemek D, Barton A, Verstappen S (2019) Maximising therapeutic utility in rheumatoid arthritis consortium tRSG. Profiling of gene expression biomarkers as a classifier of methotrexate nonresponse in patients with rheumatoid arthritis. Arthritis Rheumatol 71:678–84
41. Tao W, Concepcion AN, Vianen M, Marijnissen ACA, Lafeber F, Radstake T, Pandit A (2021) Multiomics and machine learning accurately predict clinical response to adalimumab and etanercept therapy in patients with rheumatoid arthritis. Arthritis Rheumatol 73:212–222
42. Kim KJ, Kim M, Adamopoulos IE, Tagkopoulos I (2019) Compendium of synovial signatures identifies pathologic characteristics for predicting treatment response in rheumatoid arthritis patients. Clin Immunol 202:1–10
43. Kato M, Ikeda K, Sugiyama T, Tanaka S, Iida K, Suga K, Nishimura N, Mimura N, Kasuya T, Kumagai T et al (2021) Associations of ultrasound-based inflammation patterns with peripheral innate lymphoid cell populations, serum cytokines/chemokines, and treatment response to methotrexate in rheumatoid arthritis and spondyloarthritis. PLoS ONE 16:e0252116
44. Moingeon P (2023) Artificial intelligence-driven drug development against autoimmune diseases. Trends Pharmacol Sci 31:S0165–6147(23)00088–3. https://doi.org/10.1016/j.tips.2023.04.005. Epub ahead of print. PMID: 37268540
45. Desvaux E, Aussy A, Hubert S, Keime-Guibert F, Blesius A, Soret P, Guedj M, Pers JO, Laigle L, Moingeon P (2022) Model-based computational precision medicine to develop combination therapies for autoimmune diseases. Expert Rev Clin Immunol. 18(1):47–56. https://doi.org/10.1080/1744666X.2022.2012452. Epub 2021 Dec 13. PMID: 34842494
46. Aghamiri SS, Amin R, Helikar T (2022) Recent applications of quantitative systems pharmacology and machine learning models across diseases. J Pharmacokinet Pharmacodyn 49(1):19–37. https://doi.org/10.1007/s10928-021-09790-9. Epub 2021 Oct 20. PMID: 34671863; PMCID: PMC8528185.
47. Zhang T, Androulakis IP, Bonate P, Cheng L, Helikar T, Parikh J, Rackauckas C, Subramanian K, Cho CR (2022) Working Group. Two heads are better than one: current landscape of integrating QSP and machine learning: An ISoP QSP SIG white paper by the working group on the integration of quantitative systems pharmacology and machine learning. J Pharmacokinet Pharmacodyn. 49(1):5–18. https://doi.org/10.1007/s10928-022-09805-z. Epub 2022 Feb 1. PMID: 35103884; PMCID: PMC8837505
48. Hart BA, Luchicchi A, Schenk GJ, Killestein J, Geurts JJG (2021) Multiple sclerosis and drug discovery: a work of translation. EBioMedicine. 68:103392. https://doi.org/10.1016/j.ebiom.2021.103392. Epub 2021 May 24. PMID: 34044219; PMCID: PMC8245896

49. Wu Y, Zhu J, Fu P, Tong W, Hong H, Chen M (2021) Machine learning for predicting risk of drug-induced autoimmune diseases by structural alerts and daily dose. Int J Environ Res Public Health 18(13):7139. https://doi.org/10.3390/ijerph18137139.PMID:34281077;PMCID:PMC8296890
50. Kingsmore KM, Grammer AC, Lipsky PE (2020) Drug repurposing to improve treatment of rheumatic autoimmune inflammatory diseases. Nat Rev Rheumatol 16:32–52. https://doi.org/10.1038/s41584-019-0337-0
51. Zeng X et al (2019) deepDR: a network-based deep learning approach to in silico drug repositioning, Bioinformatics 35(24):5191–5198. https://doi.org/10.1093/bioinformatics/btz418