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A Review on Immunopharmacology: Emerging Current therapies involved in targeting Autoimmune Disease and future perspectives

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ABSTRACT

Autoimmune diseases represent a diverse group of disorders characterized by immune-mediated attacks on the body's own tissues and organs. This review provides a comprehensive overview of autoimmune diseases, covering their definition, epidemiology, mechanistic approach, clinical manifestations, current treatments, and future research directions. Autoimmune diseases can be categorized into organ-specific (e.g., type 1 diabetes, Hashimoto's thyroiditis) and systemic (e.g., systemic lupus erythematosus, rheumatoid arthritis) conditions, each with distinct clinical presentations and underlying mechanisms. Genetic predisposition, environmental triggers, and immunological dysregulation play critical roles in disease development. Common symptoms include fatigue, joint pain, skin manifestations, and organ-specific dysfunction, contributing to significant morbidity and impaired quality of life. Traditional treatments often involve broad immunosuppression, which can compromise host defense. Recent advances in immune-pharmacology have introduced targeted therapies aiming to modulate specific immune pathways, offering improved efficacy and safety profiles. This review explores current trends in immunopharmacological interventions for Autoimmune diseases, including biologics, small molecule inhibitors, and innovative approaches like inverse vaccines and tolerogenic therapies. We also discuss emerging strategies such as CAR-T cell therapy, mRNA-based treatments, and the role of epigenetics and artificial intelligence in personalizing therapy. These developments herald a new era in the management of AIDs, emphasizing precision medicine and long-term disease control.

Keywords: *Biologics, Inverse vaccines, Tolerogenic therapy, CAR-T cells and mRNA therapy.*

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1. INTRODUCTION

Autoimmune diseases a diverse group of conditions characterized by aberrant B cell and T cell reactivity to normal constituents of the host.[1] These diseases occur widely and affect individuals of all ages, especially women. Autoimmune diseases encompass a diverse group of disorders characterized by immune-mediated destruction of self-tissues.[2] Conditions such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), multiple sclerosis (MS), and type 1 diabetes mellitus (T1DM) significantly impact patient quality of life and pose substantial healthcare burdens.[3] Traditional therapeutic approaches primarily involve non-specific immunosuppression, which, while alleviating symptoms, can lead to increased susceptibility to infections and other adverse effects.[4] Advancements in immunopharmacology have shifted the therapeutic paradigm towards targeted interventions that modulate specific components of the immune system.[5] This review delivers current and emerging immunopharmacological strategies for AIDs, highlighting their mechanisms, clinical applications, and future prospects.[6]

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2. EPIDEMIOLOGY

Although autoimmune illnesses are often considered to be relatively rare, they have a substantial impact on both mortality and morbidity. About 3–5% of people in the general community have autoimmunity overall.[7] Ironically, however, little is known about the aetiological processes that result in clinical pathology, particularly in spite of significant advancements in the detection and treatment of autoimmune illnesses.[8] The prevalence and incidence of autoimmune illnesses differ from one another. Taking into account differences in age, gender, ethnicity, and other demographic characteristics complicates the geoepidemiology.[9] Although autoimmune disorders can strike at any age, each disease has a distinctive age at which it first manifests.[10] First-degree relatives have a higher prevalence in practically all patients, and monozygotic twins have an even higher prevalence. With a female-to-male ratio ranging from 10:1 to 1:1, autoimmune disorders are more common in women [with the exception of Crohn's disease, which has a ratio of 1:1.2].[11] Despite receiving a lot of attention, the sex bias in autoimmunity has not been addressed.

3. CLINICAL MANIFESTATIONS

Autoimmune diseases can present with a wide range of symptoms and signs, depending on the specific disease and organs affected.[12] Some common manifestations for autoimmune disease are shown in table 1.

TABLE:1. Clinical manifestation of autoimmune diseases

Symptoms	Description
Fatigue	A symptom for many autoimmune diseases
Joint pain and Swelling	Arthralgia and arthritis
Skin Manifestations	Such as rashes, ulcers and photosensitivity
Fever	Fever Occur in systemic autoimmune diseases
Muscle Weakness	Muscle weakness Such as dermatomyositis and polymyositis
Neurological symptoms	Such as cognitive impairment and neuropathies
Gastrointestinal issues	Abdominal pain, diarrhea, and malabsorption
Endocrine dysfunction	Leading to symptoms like weight changes

4. MECHANISTIC APPROACH FOR AUTOIMMUNE DISEASES

This is especially true of the complement of B and T cells,[13] which have membrane-bound, antigen-specific recognition molecules.[14] some innate immune system components which are always present but nonspecific-also contribute to the pathophysiology of AIDx.[14] The first line of defense against external assaults and the first responders responsible for healing damaged tissue are innate immune mechanisms.[15] The main constituents are soluble mediators (e.g., complement and cytokines) and cells (e.g., macrophages, natural killer [NK] lymphocytes, and polymorphonuclear granulocytes).[16] Cellular components typically absorb foreign substances and/or release potent enzymes to break them down, but soluble substances work to speed up the preparedness and make the more specialized acquired defenses easier to use.[17] The main responsibility for breaking down and eliminating damaged cells falls on members of the myeloid lineage, particularly circulating and tissue-based macrophages.[18]

Mononuclear leukocytes, especially lymphocytes, are the primary source of signals that drive the acquired immune system, including responses in AIDx.[19] The conventional wisdom holds that T-lymphocytes are the primary initiators and maintainers of both spontaneous and induced AIDx.[20] Particularly powerful in this respect are cells belonging to the CD4+ T-helper (Th) class, which release a wide range of cytokines that support the activities of other immune effector cells. There are several distinct classes of Th-lymphocytes.[21] The Th1 class, which increases immune cell activity the Th2 class, which enhances the humoral (antibody) response; and the Th17 class, which secretes molecules that attract and excite neutrophils, seem to have made the most significant contributions to AIDx.[22] Immediate contact with APCs (mostly dendritic cells, but occasionally also mitogen-stimulated B-cells) that express major histocompatibility complex (MHC) type II and a co-stimulatory protein (e.g., B7 CD80/86) activates these master Th-cell phenotypes.[21] Only when the T-cell and an APC form an immune synapse using three signals simultaneously the primary T-cell receptor (TCR) binding to MHC II, the T-cell co-stimulatory receptor (such as CD28) connecting with the APC's co-stimulatory molecule, and the APC-secreted cytokines interacting paracrinely with T-cell receptors does lymphocyte activation take place.[22] One receptor-ligand stimulation method is insufficient to activate the cell. B-cell activation requires a similar receptor-mediated

process where the B cell receptor is surface-anchored immunoglobulin (Ig).[23] In AIDx, autoreactive T- and B-lymphocytes engage in mutually assisted positive feedback to perpetuate the disease over time. The range of the global antigenic pool that the whole complement of lymphocytes will recognize is altered by extensive recombination within the genes encoding the T- and B-cell receptor proteins (TCR and Ig, respectively).[24] Combinations that result in antigen-binding domains that can react with endogenous self-molecules are a reasonably common occurrence since the numerous gene elements for TCR and Ig mix randomly.[25]Therefore, AIDx must be prevented by teaching immune cells to ignore endogenous substances (self-tolerance) during development and then convincing them to actively maintain their quiescence throughout life.[26]

5. CURRENT THERAPIES IN AUTOIMMUNE DISEASES

5.1 Biologic Agents

Biologic agents have transformed the treatment landscape of autoimmune diseases. Unlike traditional immunosuppressants that affect broad components of the immune system, biologics are precision-engineered molecules-mostly monoclonal antibodies or fusion proteins-that target specific immune pathways.[27] They offer enhanced efficacy, reduced systemic toxicity, and are now central to immunopharmacological strategies in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), multiple sclerosis (MS), inflammatory bowel disease (IBD), and psoriasis.[28] Biologics have transformed AID management by targeting specific cytokines and immune cells. Tumor necrosis factor-alpha (TNF-α) inhibitors, such as infliximab and etanercept, have shown efficacy in RA and inflammatory bowel disease shown in (figure-1). Interleukin (IL)-6 receptor antagonists (e.g., tocilizumab) and IL-17 inhibitors (e.g., secukinumab) are effective in RA and psoriasis, respectively.[29] B-cell depletion therapies, notably rituximab, have been beneficial in SLE and MS.

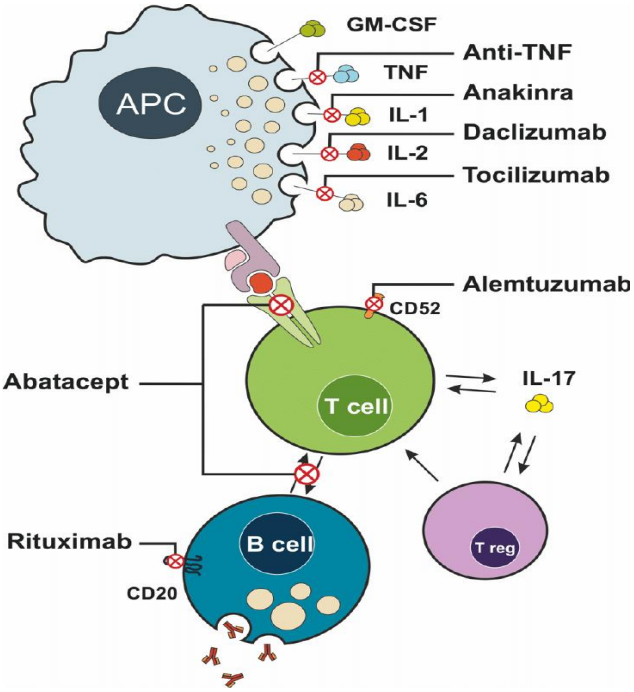

FIGURE-1: Common biological agents and their targets on immune cells and molecules.

5.2 Janus Kinase (JAK) Inhibitors: JAK inhibitors are a novel class of targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) that have reshaped the therapeutic landscape for various autoimmune and inflammatory diseases.[30] Unlike biologics that act extracellularly, JAK inhibitors target intracellular signal transduction pathways, specifically the JAK/STAT pathway, which is essential for the signal relay of numerous cytokines implicated in autoimmunity.[31] Small molecule inhibitors targeting the JAK-STAT pathway, such as tofacitinib and baricitinib, offer oral administration options and have demonstrated efficacy in RA and other AIDs.[32] JAK3 inhibitors, with lymphocyte-specific activity, present a promising avenue for selective immunomodulation.[33] Janus kinases (JAKs) are tyrosine kinases (JAK1, JAK2, JAK3, TYK2) associated with cytokine receptors. Upon cytokine binding, JAKs phosphorylate Signal Transducers and Activators of Transcription (STATs), shown in (figure-2) which then translocate to the nucleus to regulate gene transcription.[34] JAK inhibitors block these pathways, suppressing pro-inflammatory cytokine signaling (e.g., IL-2, IL-6, IFN-γ, GM-CSF), thereby modulating immune responses. [35] by increasing use of drugs notably found the new therapy drugs shown in (table-2)

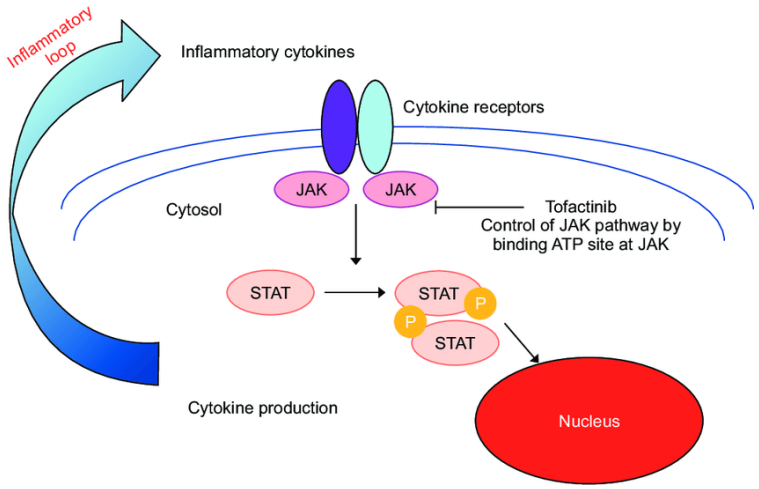

FIGURE-2: Mechanism of Janus kinase (JAK) inhibitors. STAT, signal transducer and activator of transcription.

TABLE:-2. Approved and Investigational JAK Inhibitors

Drug	Selectivity	Indications
Tofacitinib	JAK1/3 > JAK2	RA, PsA, UC
Baricitinib	JAK1/2	RA, alopecia areata
Upadacitinib	JAK1	RA, AS, Crohn's
Filgotinib	JAK1	RA, IBD (EU-approved)
Deucravacitinib	TYK2	Psoriasis (FDA-approved, 2022)

5.3 Inverse Vaccines

Inverse vaccines also referred to as tolerogenic vaccines represent an innovative immunopharmacological strategy that aims to induce antigen-specific immune tolerance, rather than stimulate immunity.[36] They are designed to suppress autoimmunity without impairing the body's defense against pathogens.[37] This approach is particularly promising for autoimmune diseases like type 1 diabetes (T1D), multiple sclerosis (MS), systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA).[38] Inverse vaccines aim to induce immune tolerance by eliminating pathogenic immune memory. Unlike traditional vaccines, they retrain the immune system to ignore specific self-antigens. Preclinical studies have shown that inverse vaccines can prevent autoimmune responses in models of MS and celiac disease.[39] Early human trials have indicated potential benefits in modulating disease activity with minimal systemic immunosuppression.

Cellular Target	Mechanism	Outcome
Naïve $CD4^+$ T cells	Treg Induction	Suppression of effector responses
Autoreactive T cells	Clonal Deletion/Energy	Elimination/inactivation of T cells
Dendritic cells	Tolerogenic DC Activation	Bias toward Treg induction
Th1/Th17 vs Treg cells	Cytokine Modulation	Shift to anti-inflammatory profile
Memory T/B cells	Memory Cell Reprogramming	Decreased recall autoimmunity
All immune cell types	Epigenetic Rewiring	Sustained tolerance at gene level

TABLE:-3. Cellular Targets and possible mechanism

5.4 Tolerogenic Therapies

Tolerogenic therapies are designed to re-establish immune tolerance to self-antigens, reversing the pathological immune response seen in autoimmune diseases.[40] This approach contrasts with broad immunosuppression by aiming to selectively suppress autoantigen-specific immune cells while preserving protective immunity.[41] Tolerogenic dendritic cells are engineered to promote immune tolerance by presenting antigens in a non-inflammatory context.[42] Many tolerogenic vaccination platforms have been created to deliver autoantigens to specific APC subtypes because APCs coordinate immunological tolerance.[43] These tolerogenic vaccination platforms include vaccines based on proteins or peptides, nanoparticles, or DNA or RNA.[44] Additionally, ex vivo manipulation and expansion of immunosuppressive cell types, including tDCs, has led to their reintroduction as cell-based tolerogenic vaccines. All of these substances can be summed up as tolerogenic vaccinations that are specific to antigens with specifically targeting immune cells Shown in (table-3)

TABLE:-4. Immune targets with possible outcomes

Mechanism	Immune Target	Immunological Outcome
Regulatory T cell induction	Naive $CD4^+$ T cells	Suppression of autoreactive effectors
Tolerogenic DC presentation	APCs + $CD4^+$ T cells	T cell anergy, deletion, or Treg conversion
Clonal deletion/anergy	Autoreactive T cells	Elimination or inactivation
Cytokine modulation	Th1/Th17 vs Treg balance	Shift to immune regulation
Tissue-specific targeting	Local DCs, T cells	Regional immune tolerance
Nanoparticle-based delivery	Antigen-specific T/B	Long-term antigen-specific tolerance

6. EMERGING THERAPEUTIC STRATEGIES

6.1 CAR-T Cell Therapy

Chimeric Antigen Receptor (CAR)-T cell therapy, originally developed for cancer immunotherapy, is emerging as a precision immune-reset tool for treating severe, refractory autoimmune diseases.[46] The therapy involves reprogramming patient-derived T cells to express engineered receptors that recognize specific immune cell targets,(table-4) such as autoreactive B cells, leading to their selective destruction.[47] (Figure-3) CAR-T therapy has induced remission in refractory SLE cases.[48] Challenges include potential cytokine release syndrome and the need for precise antigen targeting to avoid off-target effects. And finding a newly based target to a particular diseases.[49] (table-5)

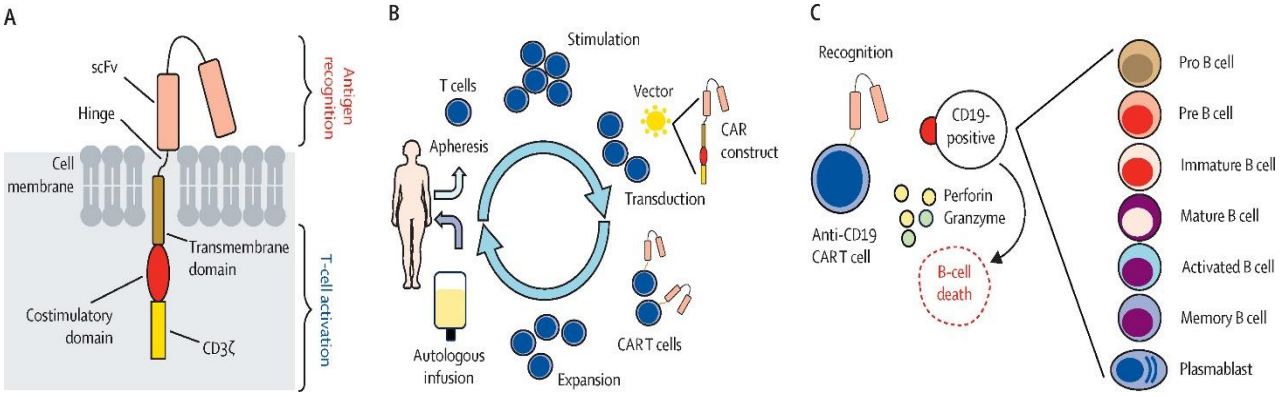

FIGURE-3: Design, production, and mode of action of CAR T cells

Mechanism	Target/Pathway Affected	Immunological Outcome
CD19 CAR-T cell-mediated cytotoxicity	B cells (CD19+)	Autoantibody and APC depletion
Immune reset	Entire B-cell compartment	Immune reprogramming and tolerance re-induction
Disruption of antigen presentation	APC-T cell interactions	Inhibition of autoreactive T-cell activation

CAR-Treg therapy	Inflammatory APCs, autoantigen	Site-specific suppression of immune responses
Cytokine dampening	IL-6, TNF-α, IFN-γ	Inflammatory circuit collapse

TABLE:-5. Target mechanism of CAR-t cells

TABLE: - 6. Ongoing Trials and Diseases Targeted (CD19)

Disease	Target	Status
Systemic lupus erythematosus (SLE)	CD19	Ongoing clinical trials, promising remission data
Multiple sclerosis (MS)	CD19 / Tregs	Preclinical/early-phase trials
Type 1 diabetes	CD19 / Tregs	Preclinical
Rheumatoid arthritis	CD19	Experimental, compassionate use cases

6.2 mRNA-Based Therapies

Messenger RNA (mRNA)-based therapies have emerged as a versatile and highly programmable platform in immunopharmacology, offering novel therapeutic approaches for autoimmune diseases.(figure-4)[50] Originally developed for infectious disease vaccines and oncology, the adaptability of mRNA technology has made it increasingly relevant in reprogramming immune responses to restore self-tolerance in autoimmune settings.[51] mRNA technology, propelled into prominence by COVID-19 vaccines, is being adapted for AIDs. mRNA vaccines encoding autoantigens aim to induce regulatory T cells and immune tolerance.[52] Preclinical models have shown promise in MS and T1DM, with ongoing research focused on optimizing delivery systems and minimizing unintended immune activation.[53] mRNA-based therapies operate by delivering synthetic mRNA molecules encoding specific antigens, immunomodulatory proteins, or regulatory elements into host cells-typically via lipid nanoparticles (LNPs).[54] Once inside the cytoplasm, these mRNAs are translated into functional proteins that can exert immune-modifying effects.[55] mRNA can be engineered to encode self-antigens implicated in autoimmune pathology.[56] When expressed in a tolerogenic context-e.g. via hepatic delivery or co-expression with immunosuppressive signals-these antigens promote T cell energy or regulatory T cell (Treg) expansion rather than effector activation. Example: mRNA encoding myelin oligodendrocyte glycoprotein (MOG) in models of multiple sclerosis has shown to reduce autoimmune demyelination via induction of antigen-specific Tregs. (table- 6)[57]

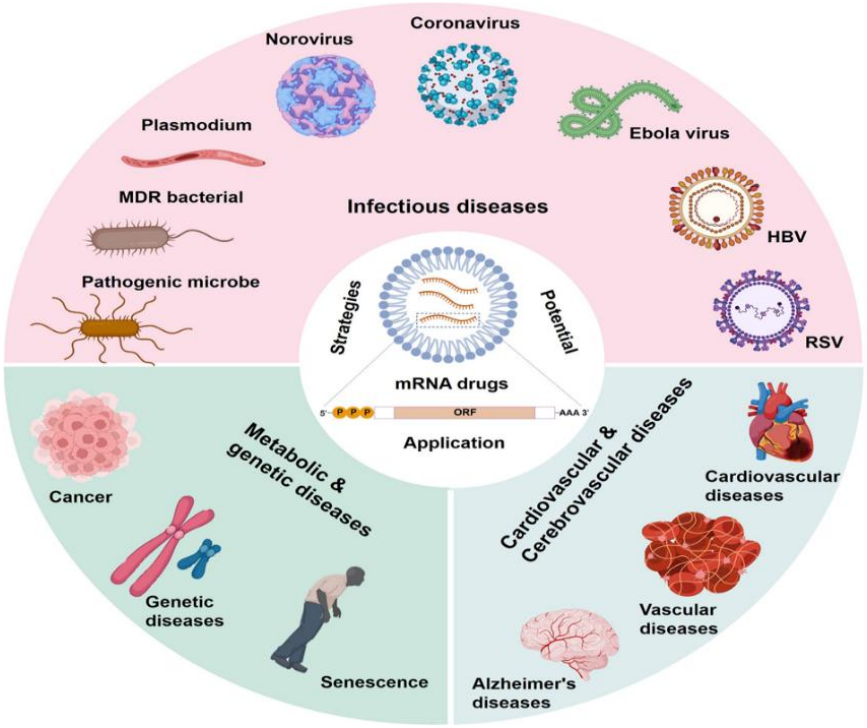

FIGURE:4 Strategies and potential application of mRNA-based therapeutics

TABLE:-6. Therapeutic Applications in Autoimmune Diseases

Disease	Target Antigen	mRNA Strategy	Outcome
Multiple Sclerosis (MS)	Myelin Oligodendrocyte Glycoprotein (MOG)	Tolerogenic mRNA in LNPs	Reduced EAE scores; increased Tregs
Type 1 Diabetes (T1D)	Insulin, GAD65	Antigen-specific tolerance	Delayed disease onset in NOD mice
Rheumatoid Arthritis (RA)	Citrullinated Peptides	DC targeting with tolerogenic payload	Reduced joint inflammation
Systemic Lupus Erythematosus (SLE)	IFN-regulated pathways	IL-10 or PD-L1 mRNA	Amelioration of nephritis, reduced IFN signature

6.3 Epigenetic Modulation

Recent advances in immunopharmacology have focused on targeting the epigenome to re-establish immune homeostasis.[58] Epigenetic drugs, or epidrugs, include inhibitors of histone-modifying enzymes, DNA methylation modulators, and non-coding RNA-based therapeutics. Epigenetic regulation-heritable yet reversible changes in gene expression without alterations to the DNA sequence-has emerged as a pivotal player in the pathogenesis and treatment of autoimmune diseases.[59] Epigenetic dysregulation affects immune cell differentiation, cytokine expression, and tolerance mechanisms, contributing to the chronic inflammation and autoantigen reactivity observed in conditions like systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and multiple sclerosis (MS).[60] shown in (table-7) Epigenetic alterations, such as DNA methylation and histone modifications, contribute to AID pathogenesis. Agents targeting these modifications, including histone deacetylase inhibitors, are under investigation for their potential to restore immune homeostasis.[61] Understanding individual epigenetic landscapes may facilitate personalized therapeutic approaches.[62]

TABLE:-7 Epigenetic targets for Autoimmune diseases

Epigenetic Target	Agent	Autoimmune Disease	Mechanism of Action	Stage
DNMT	Decitabine	SLE, RA	Reactivates Treg-promoting genes	Preclinical
HDAC	Vorinostat	MS, RA	Suppresses proinflammatory cytokines	Clinical trials (Phase I/II)
HDAC	Entinostat	Lupus	Enhances Foxp3+ Tregs	Preclinical
miR-155	Antagomir	RA, SLE	Reduces Th17 cell differentiation	Preclinical
BET Proteins (BRD4)	JQ1	Lupus, IBD	Inhibits inflammatory gene transcription	Preclinical

6.4 Artificial Intelligence in Precision Medicine

The large and complicated category of conditions known as autoimmune diseases is defined by an aberrant immune response directed against the body's own tissues.[63] Protecting the body from foreign invaders like bacteria, viruses, and other diseases is the main job of the immune system in a healthy person.[65] It accomplishes this by differentiating between self and non-self-antigens, a function that depends on a finely synchronized cell and signaling molecule network.[66] This self-recognition process malfunctions in people with autoimmune illnesses, though, and the immune system unintentionally targets its own cells, tissues, or organs.[67] Chronic inflammation, tissue damage, and reduced organ function are all possible outcomes of this abnormal immune response, which can lead to serious morbidity and, in extreme situations, death.[68] Artificial intelligence (AI) and machine learning algorithms are increasingly utilized to analyze complex immunological data, predict disease trajectories, and identify optimal therapeutic regimens.[69] AI-driven models can integrate genomic,

transcriptomic, and clinical data to tailor treatments, enhancing efficacy and reducing adverse effects.[70] The field of precision medicine is similarly experiencing rapid growth.(figure-5)[71] Precision medicine is perhaps best described as a health care movement involving what the National Research Council initially called the development of "a New Taxonomy of human disease based on molecular biology,"[72] or a revolution in health care triggered by knowledge gained from sequencing the human genome.[73] The field has since evolved to recognize how the intersection of multiomic data combined with medical history, social/behavioural determinants, and environmental knowledge precisely characterizes health states, disease states, and therapeutic options for affected individuals.[74] For the remainder of this paper, we will use the term precision medicine to describe the health care philosophy and research agenda described above, and the term personalized care to reflect the impact of that philosophy on the individual receiving care.[75] Precision medicine offers healthcare providers the ability to discover and present information that either validates or alters the trajectory of a medical decision from one that is based on the evidence for the average patient, to one that is based upon individual's unique characteristics.[76] It facilitates a clinician's delivery of care personalized for each patient.[77] Precision medicine discovery empowers possibilities that would otherwise have been unrealized.[78] AI can find patterns and correlations in these intricate datasets that are difficult for human therapists or conventional statistical techniques to detect.[79]AI algorithms can combine many kinds of data to create predictive models that improve the accuracy of autoimmune disease detection.[80] For example, based on minor variations in clinical, serological, and genetic data, machine learning models can be trained on sizable patient data sets to distinguish between autoimmune conditions that exhibit comparable symptoms,[81] such as rheumatoid arthritis and systemic lupus erythematosus.[82] This may improve patient outcomes by enabling prompt action and drastically cutting down on diagnostic delays.[83]AI is essential for finding biomarkers for autoimmune disorders. For the diagnosis, prognosis, and tracking of treatment response, biomarkers are essential.[84] However, because of the intricate pathophysiology and wide range of disease manifestations, it has been difficult to find trustworthy biomarkers for autoimmune diseases.[85]

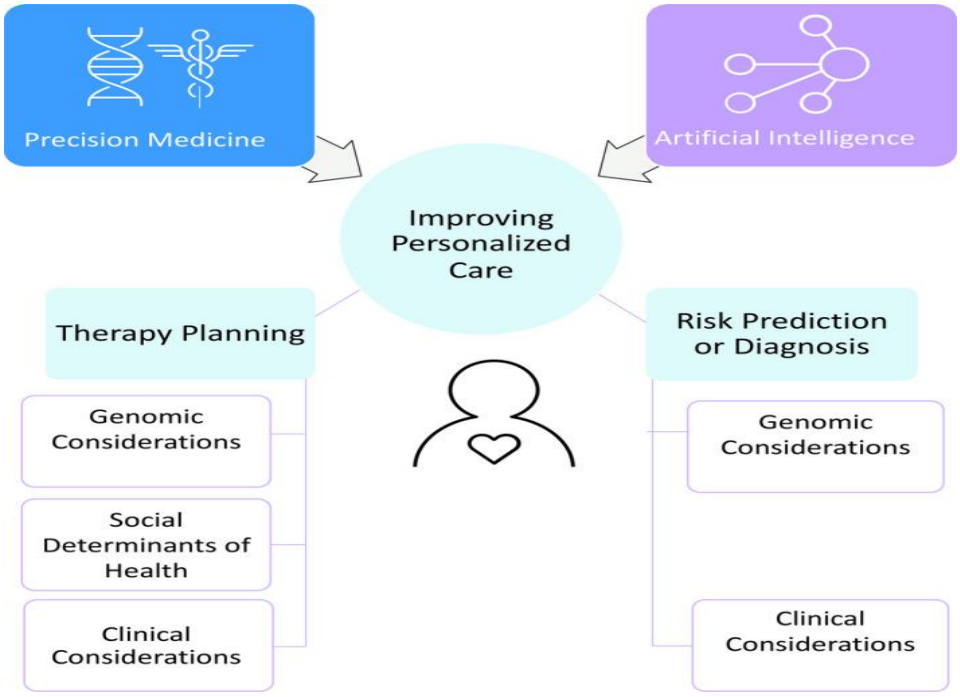

FIGURE:- 5 Dimensions of synergy between AI and precision medicine.

7. FUTURE PERSPECTIVES

Precision immunomodulation, nanomedicine, and systems biology integration are likely to influence it. According to predictions, drug targeting will be improved and off-target toxicity will be decreased by deep phenotyping of autoimmune profiles using multi-omics and AI-guided analytics. Furthermore, by enabling localized release and fewer systemic adverse effects, nanocarrier-based delivery methods have the potential to enhance the pharmacokinetics of immunotherapeutics. These are being investigated to deliver immunosuppressants, siRNAs, or antigens straight to inflammatory organs or lymphoid tissues. Using computational epitope mapping to create peptide-based immunotherapies that restore immunological homeostasis without widespread immunosuppression of autoreactive immune cells is another crucial step in the development of reverse vaccinology platforms for autoimmune tolerance induction. A new era in AID treatment is being ushered in by the combination of customized medicine, targeted immunotherapies, and cutting-edge technologies. Ongoing research aims to refine these approaches, ensuring sustained efficacy, safety, and accessibility. Collaborative efforts between clinicians, researchers, and technologists are essential to translate these innovations into clinical practice.

8. CONCLUSION

In this review of autoimmune diseases, several key points have emerged: autoimmune diseases involve the immune system mistakenly attacking the body's own tissues, Broad-spectrum immunosuppression is giving way to focused immunomodulatory approaches, marking a significant shift in the field of immunopharmacology for autoimmune disorders. In order to restablish immunological tolerance and reduce systemic toxicity, recent developments point to a critical shift toward the use of cell-based treatments, precision biologics, and metabolic pathway modification. Remarkably, adoptive cellular therapies-like CAR-T cells-that were first created for cancer are now being modified for autoimmune reasons while showing encouraging preclinical and early clinical results. A new paradigm in the treatment of autoimmune diseases is represented by these approaches in conjunction with innovative small-molecule drugs that specifically block important inflammatory signaling pathways, such as BTK and JAK/STAT inhibitors. Additionally, a growing focus on immunometabolism and metabolic reprogramming has created new opportunities for context-specific immune response modulation. These revelations highlight how crucial it is to integrate immunology, pharmacology, and metabolism at the systems level when developing new drugs. Not with standing these developments, there are still obstacles in getting these treatments from the lab to the patient's bedside. Disease etiology heterogeneity, the requirement for reliable biomarkers. the field of immunopharmacology is poised at the frontier of precision medicine, with promising therapeutic modalities that are increasingly mechanism-specific and patient-centric. Continued interdisciplinary collaboration will be critical to refine these therapies and ensure equitable access for patients suffering from autoimmune diseases. Immunopharmacology has significantly advanced the treatment landscape of autoimmune diseases, moving from broad immunosuppression to targeted, personalized interventions. Emerging therapies, including inverse vaccines, tolDCs, CAR-T cells, and mRNA-based treatments, offer the potential for durable remission with minimal systemic toxicity. Continued research and clinical trials are imperative to validate these strategies and integrate them into standard care, ultimately improving outcomes for patients with AIDs.

Conflicts of Interest

The authors declare no conflicts of interest

REFERENCES

[1] Tan L, Akahane K, McNally R, Development of Selective Covalent Janus Kinase 3 Inhibitors. J Med Chem. 2015;58(17):6589-6603.

[2] Maia M, Martinez D, Swaminathan S.J., Inverse-Vaccines for Rheumatoid Arthritis Re-establish Metabolic and Immunological Homeostasis in Joint Tissues. Adv Healthca Mater. 2024;13(6): e2301234.

[3] Mansilla M.J., Selles-Moreno C, Fabregas-Puig S, Vitamin D3-Induced Tolerogenic Dendritic Cells Combined with Interferon-β Treatment Induce Regulatory T Cells in Multiple Sclerosis Patients. Clin Immunol. 2015;160(2):70-79.

[4] Paech J, Schett G. CAR T-Cell Therapy Offers 'Single Shot' Hope to Autoimmune Disease Patients. Financial Times. 2024.

[5] Thumsi A, Martínez D, Swaminathan S.J., Inverse-Vaccines for Rheumatoid Arthritis Re-establish Metabolic and Immunological Homeostasis in Joint Tissues. Adv Healthc Mater. 2024;13(6): e2301234.

[6] Tang A, Wei M, Haemel A, et al. Artificial Intelligence-Enabled Precision Medicine for Inflammatory Skin Diseases.2025

[7] Altmann D. M., Sansom D., Marsh S. G., What is the basis for HLA-DQ associations with autoimmune disease? Immunol Today 1991; 12:267–270.

[8] Kong Y. M., Waldmann H., Cobbold S., Giraldo A. A., Fuller B. E., Simon L. L., Pathogenic mechanisms in murine autoimmune thyroiditis: Short- and long-term effects of in vivo depletion of CD4+ and CD8+ cells. Clin Exp Immunol 1989;77: 428–433.

[9] Singer P. A., Theofilopoulos A. N., T-cell receptor Vβ repertoire expression in murine models of SLE. Immunol Rev 1990; 118:103–102

[10] Waldor M. K., Sriram S., Hardy R., Herzenberg L. A., Lanier L., Lim M., Steinman L. Reversal of experimental allergic encephalomyelitis with monoclonal antibody to a T-cell subset marker. Science 1985; 227:415–417.

[11] Gutcher I., Becher B., APC-derived cytokines and T cell polarization in autoimmune inflammation. J Clin Invest 2007; 117:1119–1127.

[12] Samuels H, Malov M, Saha Detroja T, et al. Autoimmune Disease Classification Based on PubMed Text Mining. J Clin

[13] Med. 2022;11(15):4345. doi:10.3390/jcm11154345

[14] Shlomchik M. J., Activating systemic autoimmunity: B's, T's, and Tolls. Curr Opin Immunol 2009; 21:626–633.

[15] shii M. Immunology proves a great success for treating systemic autoimmune diseases - a perspective on immunopharmacology: Br J Pharmacol. 2017;174(13):1875-1880. doi: 10.1111/bph.13784

[16] Her, M., Kavanaugh, A. Advances in use of immunomodulatory agents-a rheumatology perspective. Nat Rev Gastroenterol Hepatol 2015;12:363–368 https://doi.org/10.1038/nrgastro.2015.65

[17] Geering B, Fussenegger M. Synthetic Immunology: Modulating the Human Immune System. Trends Biotechnol. 2015;33(2):65-73.

[18] Owen K.L., Brockwell N.K., Parker B.S., JAK-STAT Signaling: A Double-Edged Sword of Immune Regulation and Cancer Progression. Cancers (Basel). 2019;11(12):2002. doi: 10.3390/cancers11122002.

[19] Aaronson D.S., Horvath C.M., A road map for those who don't know JAK-STAT. Science. 2002. 296;5573:1653-1655. doi: 10.1126/science.1071545.

[20] Fu XY. A direct signaling pathway through tyrosine kinase activation of SH2 domain-containing transcription factors. J Leukoc Biol. 1995;57(4):529-535. doi: 10.1002/jlb.57.4.529

[21] Bagnoli, F., Galgani, I., Vadivelu, V.K., Reverse development of vaccines against antimicrobial-resistant pathogens. npj Vaccines 2024:9;71. https://doi.org/10.1038/s41541-024-00858-4

[22] Farmer L.J., Ledeboer M.W., Hoock T, Discovery of VX-509 (Decernotinib): A Potent and Selective Janus Kinase 3 Inhibitor for the Treatment of Autoimmune Diseases. J Med Chem. 2015;58(5):2073-2080.

[23] Zhang C, Liu J, Zhong J.F., Zhang X. Engineering CAR-T cells. Biomark Res. 2017 24;5:22. doi: 10.1186/s40364-017-0102-y

[24] Ramos CA, Dotti G. Chimeric antigen receptor (CAR)-engineered lymphocytes for cancer therapy. Expert Opin Biol Ther. 2011;11(7):855–873. doi: 10.1517/14712598.2011.573476

[25] ipowska-Bhalla G, Gilham D.E., Hawkins R.E., Rothwell D.G., Targeted immunotherapy of cancer with CAR T cells: achievements and challenges. Cancer Immunol Immunother. 2012;61(7):953–962. doi: 10.1007/s00262-012-1254-0

[26] Ozdemir C, Kucuksezer UC, Akdis M, Akdis CA. Mechanisms of immunotherapy to wasp and bee venom. Clin Exp Allergy. 2011; 41:1226–1234. doi: 10.1111/j.1365-2222.2011.03812. x.

[27] Rolland J.M., Gardner L.M., O'Hehir RE. Functional regulatory T cells and allergen immunotherapy. Curr Opin Allergy Clin Immunol. 2010; 10:559–566. doi: 10.1097/ACI.0b013e32833ff2b2

[28] Ozdemir C, Kucuksezer U.C., Akdis M, Akdis C.A., Specific immunotherapy and turning off the T cell: How does it work? Ann Allergy Asthma Immunol. 2011; 107:381–392. doi: 10.1016/j.anai.2011.05.017

[29] Liu J, Zhong J.F., Zhang X, Zhang C. Allogeneic CD19-CAR-T cell infusion after allogeneic hematopoietic stem cell transplantation in B cell malignancies. J Hematol Oncol. 2017;10(1):35. doi: 10.1186/s13045-017-0405-3

[30] Tasian S.K., Gardner R.A., CD19-redirected chimeric antigen receptor-modified T cells: a promising immunotherapy for children and adults with B-cell acute lymphoblastic leukemia (ALL) Ther Adv Hematol. 2015;6(5):228–241. doi: 10.1177/2040620715588916

[31] Miller S.D., Turley D.M., Podojil J.R., Antigen-Specific Tolerance Strategies for the Prevention and Treatment of Autoimmune Disease. Nat Rev Immunol. 2007;7(9):665-677.

[32] Putnam AL, Brusko T.M., Lee M.R., Liu W, Szot G.L., Ghosh T, Atkinson M.A., Bluestone J.A., Expansion of human regulatory T-cells from patients with type 1 diabetes. Diabetes. 2009; 58:652–662. doi: 10.2337/db08-1168.

[33] Dominguez-Villar M, Baecher-Allan C.M., Hafler D.A., Identification of T helper type 1–like, Foxp3+ regulatory T cells in human autoimmune disease. Nat Med. 2011; 17:673–675. doi: 10.1038/nm.2389

[34] Spiegel D.A., Grand Challenge Commentary: Synthetic Immunology to Engineer Human Immunity. Nat Chem Biol. 2010;6(12):871-873.

[35] Voo K.S., Wang Y.H., Santori F.R., Boggiano C, Wang Y.H., Arima K, Bover L, Hanabuchi S, Khalili J, Marinova E, Zheng B, Littman DR, Liu YJ. Identification of IL-17-producing FOXP3+ regulatory T cells in humans. Proc Natl Acad Sci USA. 2009; 106:4793–4798. doi: 10.1073/pnas.0900408106

[36] Johnson, Kevin & Wei, Wei-Qi & Weeraratne, Dilhan & Frisse, Mark & Misulis, Karl & Rhee, Kyu & Zhao, Juan & Snowdon, Jane. (2020). Precision Medicine, AI, and the Future of Personalized Health Care. Clinical and translational science. 14. 10.1111/cts.12884.

[37] Putnam A.L., Brusko T.M., Lee M.R., Liu W, Szot G.L., Ghosh T, Atkinson M.A., Bluestone J.A., Expansion

of human regulatory T-cells from patients with type 1 diabetes. Diabetes. 2009; 58:652–662. doi: 10.2337/db08-1168

[38] Mougiakakos D, Kronke G, Volkl S, CD19-Targeted CAR T Cells in Refractory Systemic Lupus Erythematosus. N Engl J Med. 2021;385(6):567-569.

[39] Mackensen A, Müller F, Mougiakakos D, Anti-CD19 CAR T Cell Therapy for Refractory Systemic Lupus Erythematosus. Nat Med. 2022;28(10):2124-2132.

[40] Passeri L, Marta F, Bassi V, Gregori S. Tolerogenic Dendritic Cell-Based Approaches in Autoimmunity. Int J Mol Sci. 2021;22(16):8732.

[41] Garcia-Gonzalez P, Ubilla-Olguin G, Catalan D, Tolerogenic Dendritic Cells for Reprogramming of Lymphocyte Responses in Autoimmune Diseases. Autoimmun Rev. 2016;15(11):1071–1080.

[42] Rosman Z, Shoenfeld Y, Zandman-Goddard G. Biologic therapy for autoimmune diseases: an update. BMC Med. 2013 Apr 4; 11:88. doi: 10.1186/1741-7015-11-88.

[43] Schiff M.H., Kremer J.M., Jahreis A, Vernon E, Isaacs J.D., Van Vollenhoven R.F., Integrated safety in tocilizumab clinical trials. Arthritis Res Ther. 2011;13: R141. doi: 10.1186/ar3455.

[44] Hashizume M, Mihara M. The roles of interleukin-6 in the pathogenesis of rheumatoid arthritis. Arthritis. 2011; 2011:765624. doi: 10.1155/2011/765624

[45] Nisar M.K., Ostor J.K.A., The role of tocilizumab monotherapy in the management of rheumatoid arthritis: a review. Int J Clin Rheumatol. 2012; 7:9–19. doi: 10.2217/ijr.11.66

[46] Tak P.P., Kalden J.R., Advances in rheumatology: new targeted therapeutics. Arthritis Res Ther. 2011;13:S5. doi: 10.1186/1478-6354-13-S1-S5

[47] Hilkens C.M., Isaacs J.D., Tolerogenic Dendritic Cell Therapy for Rheumatoid Arthritis: Clin Exp Immunol. 2013;172(2):148–157.

[48] Rad F, Ghorbani M, Roushandeh A.M., Habibi Roudkenar M. Mesenchymal Stem Cell-Based Therapy for Autoimmune Diseases: Emerging Roles of Extracellular Vesicles. Mol Biol Rep. 2019;46(1):1533–1549.

[49] Pittenger M.F., Discher D.E., Peault B.M., Mesenchymal Stem Cell Perspective: Cell Biology to Clinical Progress. NPJ Regen Med. 2019; 4:22.

[50] Jasim S.A., Yumashev A.V., Abdelbasset W.K., Clinical Application of Mesenchymal Stem Cell Therapy in Autoimmune Diseases. Stem Cell Res Ther. 2022;13(1):101.

[51] Sun Y, Yuan Y, Zhang B, Zhang X. CARs: A New Approach for the Treatment of Autoimmune Diseases. Sci China Life Sci. 2023; 66:711–728.

[52] Serra P, Santamaria P. Antigen-Specific Therapeutic Approaches for Autoimmunity. Nat Biotechnol. 2019; 37:238–251.

[53] Zhao Z, Hua Z, Luo X, Application and Pharmacological Mechanism of Methotrexate in Rheumatoid Arthritis. Biomed Pharmacother. 2022; 150:113074.

[54] Morand E.F., Furie R, Tanaka Y, Trial of Anifrolumab in Active Systemic Lupus Erythematosus. N Engl J Med. 2020; 382:211–221.

[55] Gladman D, Rigby W, Azevedo V.F., Tofacitinib for Psoriatic Arthritis in Patients with an Inadequate Response to TNF Inhibitors. N Engl J Med. 2017; 377:1525–1536.

[56] Wang J.L., Olsen N, Zheng S.G., Therapeutic Role of GMSC in Autoimmune Diseases. Acta Pharmacol Sin. 2017;38(6):733–740.

[57] Webb C. Treating Human Autoimmunity: Current Practice and Future Prospects. Sci Transl Med. 2012;4(125):125sr1.

[58] Jin Q, Liu Z, Chen Q. Controlled Release of Immunotherapeutics for Enhanced Cancer Immunotherapy After Local Delivery. J Control Release. 2021; 329:882–893.

[59] Li Z, Wang Y, Ding Y, Cell-Based Delivery Systems: Emerging Carriers for Immunotherapy. Adv Funct Mater. 2021;31(23):2100088.

[60] Vishnu Balaji R, Shaath H, Elango R, Alajez N.M., Noncoding RNAs as Potential Mediators of Resistance to Cancer Immunotherapy. Semin Cancer Biol. 2020; 65:65–79.

[61] Bar-Or A, Pender M.P., Khanna R, Epstein–Barr Virus in Multiple Sclerosis: Theory and Emerging Immunotherapies. Trends Mol Med. 2020;26(3):296–310.

[62] Aibara N, Ohyama K. Revisiting Immune Complexes: Key to Understanding Immune-Related Diseases. Adv Clin Chem. 2020; 93:1–17.

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[63] Tabrizi M, Zhang D, Ganti V, Azadi G. Integrative Pharmacology: Advancing Development of Effective Immunotherapies. AAPS J. 2018;20(4):85.

[64] Devarapu S.K., Rupanagudi K.V.R., Kulkarni O.P., Dual Blockade of the Pro-Inflammatory Chemokine CCL2 and the Homeostatic Chemokine CXCL12 in Murine Proliferative Lupus Nephritis. Clin Immunol. 2017; 185:119–127.

[65] Benizri S, Gissot A, Martin A, Bioconjugated Oligonucleotides: Recent Developments and Therapeutic Applications. arXiv preprint arXiv:2002.11532. 2020.

[66] Ataeinia B, Heidari P. Artificial Intelligence and the Future of Diagnostic and Therapeutic Radiopharmaceutical Development: In Silico Smart Molecular Design. arXiv preprint arXiv: 2021;2108.02354.

[67] Blyuss K.B., Nicholson L.B., The Role of Tunable Activation Thresholds in the Dynamics of Autoimmunity. arXiv preprint arXiv:1209.4487. 2012.

[68] Brzezicka K.A., Paulson J.C., Impact of Siglecs on Autoimmune Diseases. Mol Aspects Med. 2023; 90:101140.

[69] Porter, D. L., Levine, B. L., Kalos, M., Bagg, A.J., C. H., Chimeric antigen receptor-modified T-cells in chronic lymphoid leukemia. N. Engl. J. Med. 365, 725–733 (2011).

[70] June, C. H., O'Connor, R. S., Kawalekar, O. U., Ghassemi, S. & Milone, M. C. CAR-T-cell immunotherapy for human cancer. Science 2018:359; 1361–1365

[71] Boyiadzis, M. M., Chimeric antigen receptor (CAR) T therapies for the treatment of hematologic malignancies: clinical perspective and significance. J. Immunother. Cancer 2018; 6:137

[72] Del Bufalo, F. GD2-CART01 for relapsed or refractory high-risk neuroblastoma. reply. N. Engl. J. Med. 2023:388 ;1284–1295

[73] Richardson, B. DNA methylation and autoimmune disease. Clinical Immunology, 2021;226:108705. https://doi.org/10.1016/j.clim.2021.108705

[74] Liu, Y., Pan, Q., Zhao, Y., Epigenetic regulation of autoimmune diseases. Current Pharmaceutical Design, 2019;25(27):2906–2915. https://doi.org/10.2174/1381612825666191001152546

[75] Grabiec, A. M., Reedquist, K. A., HDAC inhibitors in immune-mediated diseases. Immunological Reviews, 2020;296(1):111–125. https://doi.org/10.1111/imr.12861

[76] Zhou, X., Zhang, L., MicroRNA-146a regulates type I interferon signaling in systemic lupus erythematosus. Arthritis Research & Therapy,2022;24(1):19. https://doi.org/10.1186/s13075-022-02636-4

[77] Khan, A. A., Targeted epigenetic therapies for immune modulation. Nature Reviews Drug Discovery, 2023;22(3):172–188. https://doi.org/10.1038/s41573-022-00631-0

[78] Angiolilli, C., Epigenetic biomarkers in autoimmune diseases: promise and challenges. Frontiers in Immunology, 2023;14:1124893. https://doi.org/10.3389/fimmu.2023.1124893

[79] Lin, S.Y., Ten ways artificial intelligence will transform primary care. J. Gen. Intern. Med. 2019; 34:1626–1630

[80] Akselrod-Ballin, A. Predicting breast cancer by applying deep learning to linked health records and mammograms. Radiology 2019; 292:331–342

[81] Ziegelstein, R.C., Personomics and precision medicine. Trans. Am. Clin. Climatol. Assoc. 2017; 128:160–168

[82] van der Schee, M. Breath biopsy for early detection and precision medicine in cancer. Ecancermedicalscience 2018;12: ed84

[83] Mascola, J.R., & Fauci, A.S., Novel vaccine technologies for the 21st century. Nat. Rev. Immunol. 2020; 20:87–88

[84] Sahin, U., Kariko, K. & Tureci, O. mRNA-based therapeutics–developing a new class of drugs. Nat. Rev. Drug Discov. 2014; 13:759–780

[85] Boczkowski, D., Nair, S. K., Snyder, D. & Gilboa, E. Dendritic cells pulsed with RNA are potent antigen-presenting cells in vitro and in vivo. J. Exp. Med. 1996:184:465–472.

[86] Sahin, U., Kariko, K. & Tureci, O. mRNA-based therapeutics–developing a new class of drugs. Nat. Rev. Drug Discov. 2014:13;759–780