

# Biotechnology in Rheumatology and immunology for researchers: An overview

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### **ABSTRACT**

Biotechnology has revolutionized the fields of rheumatology and immunology, providing innovative solutions for understanding and treating autoimmune diseases. Traditionally, these fields relied on basic immunological techniques and limited therapeutic options. However, advancements in biotechnology have introduced novel diagnostic tools, targeted therapies, and personalized medicine approaches, significantly improving patient outcomes. The aim of this overview is to provide researchers with a comprehensive understanding of the current biotechnological advancements in rheumatology and immunology, highlighting their impact on disease diagnosis, management, and treatment. The primary objective is to explore the various biotechnological innovations that have transformed rheumatology and immunology. This includes the development of biologics, biomarkers, and genetic tools that have enabled precise diagnosis and tailored treatments. Additionally, the overview seeks to examine the ongoing research and future directions in these fields, emphasizing the potential for further breakthroughs. Biotechnology has significantly advanced the fields of rheumatology and immunology, offering new hope for patients with autoimmune diseases. The introduction of biologics has been a game-changer, allowing for targeted therapies that have improved disease management and patient quality of life. Biomarker discovery has enhanced diagnostic accuracy and enabled the monitoring of disease progression. Genetic and genomic tools have paved the way for personalized medicine,

tailoring treatments to individual patient profiles. As research continues to evolve, the integration of biotechnology in these fields promises to bring even more innovative solutions, ultimately transforming the landscape of autoimmune disease treatment and management. Researchers must stay abreast of these developments to continue driving progress and improving patient outcomes.

**Keywords:** rheumatic diseases, immunological disorders, genomics, proteomics, next-generation sequencing (NGS), multiplex immunoassays, autoimmune diseases, precision diagnostics

## INTRODUCTION

Rheumatology and immunology are fields of medicine focused on understanding and treating autoimmune and inflammatory conditions that affect the joints, connective tissues, and immune system. Biotechnological advancements have significantly enhanced our understanding of these diseases and expanded treatment options. Biotechnology has revolutionized the detection and management of rheumatic and immunological diseases, offering sophisticated tools and techniques for accurate diagnosis and personalized treatment. By harnessing advancements in genomics, proteomics, and immunology, biotechnology has enabled earlier detection, better understanding of disease mechanisms, and the development of targeted therapies. Here's an overview of how biotechnology has contributed to the detection of rheumatic and immunological diseases. There are several aspects of biotechnology which has helped in disease diagnosis in rheumatic and immunological diseases such as genomic biomarkers, biomarker panel, immunological assays, NGS, point care diagnostics, and precision medicine approaches.

Biotechnology has facilitated the identification of genetic markers associated with rheumatic diseases such as rheumatoid arthritis (RA) and lupus. Genome-wide association studies (GWAS) have uncovered specific genetic variations linked to susceptibility and disease progression. For instance, a study by Plenge et al. (2007) identified the association between certain genetic variants in the HLA region and RA susceptibility, providing insights into the disease's pathogenesis. Biotechnological advancements have led to the development of multiplex biomarker panels for rheumatic diseases. These panels detect a combination of biomarkers, including autoantibodies, cytokines, and acute-phase proteins, providing a more comprehensive assessment of disease activity and prognosis. The use of biomarker panels has been shown to improve diagnostic accuracy and guide treatment decisions (Ingegnoli et al., 2014). Biotechnology has

facilitated the development of highly sensitive immunological assays for detecting autoantibodies and immune complexes associated with rheumatic diseases. Techniques such as enzyme-linked immunosorbent assay (ELISA), immunoblotting, and multiplex bead-based assays allow for the simultaneous detection of multiple autoantibodies, aiding in the differential diagnosis of conditions like systemic lupus erythematosus (SLE) and Sjögren's syndrome (Agmon-Levin et al. 2014). NGS technologies have enabled comprehensive analysis of the immune repertoire in patients with immunological diseases. By sequencing the variable regions of T-cell receptors (TCRs) and B-cell receptors (BCRs), researchers can characterize the diversity and clonality of immune cell populations, providing valuable insights into disease pathogenesis and identifying potential therapeutic targets (Mazzotti et al. 2022). Biotechnology has facilitated the development of point-of-care diagnostic devices for rapid and decentralized testing of rheumatic and immunological diseases. These devices leverage miniaturized biosensors and microfluidic platforms to detect biomarkers in patient samples with high sensitivity and specificity, enabling early intervention and improved patient outcomes (Firestein et al. 2014). Biotechnology has paved the way for precision medicine approaches in the management of rheumatic and immunological diseases. By integrating genetic, molecular, and clinical data, researchers can stratify patients into subgroups with distinct disease phenotypes and treatment responses. This personalized approach allows for the selection of optimal therapies based on individual patient characteristics, maximizing efficacy and minimizing adverse effects (Kuret et al. 2022).

## REVIEW AND LITERATURE

A comprehensive review published in the Journal of Autoimmunity by Firestein GS highlights the pivotal role of biotechnological techniques in unraveling the complex pathogenesis of rheumatic diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Through techniques like genome-wide association studies (GWAS), researchers have identified numerous genetic variants associated with disease susceptibility and severity (Firestein, 2019). Furthermore, a study published in Nature Reviews Rheumatology by Smolen et al. discusses the transformative impact of biologic therapies on the management of rheumatic diseases. Biologics, including tumor necrosis factor-alpha (TNF- $\alpha$ ) inhibitors and interleukin-6 (IL-6) receptor antagonists, have revolutionized treatment by targeting specific inflammatory pathways with greater precision and efficacy than conventional therapies (Smolen et al., 2020). The biotechnical advancements and

the overview of impact on the diagnosis of rheumatic and immunological diseases, along with specific examples and citations supporting each advancements are illustrated (Table 1).

Table 1 Biotechnological advancements and their impact on the diagnosis of rheumatic and immunological disease

Biotechnological Advancement	Impact on Diagnosis	Examples <sup>9</sup>	References
Multiplex Immunoassays	Simultaneous detection of autoantibodies and biomarkers	Detection of anti-cyclic citrullinated peptide (anti-CCP) antibodies in rheumatoid arthritis <sup>10</sup>	Laborde et al. <sup>19</sup> 2020
Next-Generation Sequencing (NGS)	Profiling of immune cell receptor repertoire	Characterization of T-cell receptor (TCR) and B-cell receptor (BCR) diversity in autoimmune diseases	Schultheiß et al., 2020
Biomarker Panels	Identification of disease-specific biomarkers	Measurement of cytokine levels in systemic lupus erythematosus (SLE)	Liu et al.2013
Point-of-Care Diagnostics	Rapid and decentralized testing	Detection of anti-nuclear antibodies (ANA) in Sjögren's syndrome	Lei et al. 2016
High-Throughput Flow Cytometry <sup>15</sup>	Quantitative analysis of immune cell subsets	Characterization of lymphocyte populations in autoimmune diseases	Goronzy et al., 2019
Genome-Wide Association Studies (GWAS)	Identification of genetic risk factors	Discovery of HLA alleles associated with rheumatoid arthritis susceptibility	Okada et al., 2014
Microarray Technology	Profiling gene expression patterns	Identification of molecular subtypes in systemic sclerosis <sup>22</sup>	Milano et al., 2008
Digital Imaging Techniques	Visualization of disease manifestations	Ultrasound imaging of synovitis in juvenile idiopathic arthritis	Collado et al., 2017

Multiplex immunoassays enable the simultaneous detection of multiple antibodies, cytokines, and other immune markers in patient samples. These assays offer high sensitivity and specificity, allowing for comprehensive profiling of immune system activity. They are particularly useful in diagnosing autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and <sup>12</sup>

multiple sclerosis (Agmon-Levin N et al. 2014). NGS technologies allow for the comprehensive analysis of the immune repertoire, including T-cell receptors (TCRs) and B-cell receptors (BCRs). By sequencing the variable regions of these receptors, NGS facilitates the characterization of immune cell diversity and clonality, providing insights into disease pathogenesis and identifying potential therapeutic targets (Ramadoss and Robinson 2020)

GWAS identify genetic variants associated with susceptibility to immunological disorders. By analyzing the genomes of large patient cohorts, GWAS reveal novel disease-associated loci and provide insights into the genetic basis of autoimmune and immune-mediated diseases (Okada et al. 2014). High-throughput flow cytometry enables quantitative analysis of immune cell subsets in patient samples. By measuring surface markers and intracellular proteins, flow cytometry provides valuable information about immune cell populations, aiding in the diagnosis of immune deficiencies and monitoring of disease progression (Goronzy et al. 2019).

## **NOVELTY OF BIOTECHNIQUES IN RHEUMATOLOGY**

In recent decades, biotechnological advancements have catalyzed significant progress in understanding and managing rheumatic diseases, offering novel insights into disease mechanisms and therapeutic targets. These innovations have transformed the landscape of rheumatology, enabling more precise diagnosis, personalized treatment strategies, and improved patient outcomes. This essay explores the novelty of biotechniques in rheumatology, emphasizing their impact on various rheumatic diseases, supported by specific references from reputable journals such as Springer, Elsevier, and Scopus.

Rheumatoid arthritis (RA), a chronic autoimmune disorder characterized by joint inflammation and destruction, exemplifies the transformative role of biotechniques in rheumatology. Genome-wide association studies (GWAS) have identified numerous genetic variants associated with RA susceptibility and severity, shedding light on its complex pathogenesis. Notably, a study published in the journal Nature Reviews Rheumatology by Smolen et al. (2018) elucidates the genetic architecture of RA and its implications for personalized medicine, underscoring the significance of biotechnological approaches in unraveling disease mechanisms.

Furthermore, the advent of biologic therapies has revolutionized RA treatment by targeting specific inflammatory pathways with greater precision and efficacy. Biologics, such as tumor

necrosis factor-alpha (TNF- $\alpha$ ) inhibitors and interleukin-6 (IL-6) receptor antagonists, have demonstrated remarkable efficacy in reducing disease activity and halting joint damage. A comprehensive review published in the Journal of Autoimmunity discusses the transformative impact of biologics on RA management, highlighting their role in achieving clinical remission and improving patients' quality of life (Patel et al. 2023).

Beyond RA, biotechnological innovations have also advanced our understanding and treatment of other rheumatic diseases, including systemic lupus erythematosus (SLE) and psoriatic arthritis (PsA). In SLE, biomarker discovery using biotechniques has facilitated early diagnosis and prognostication, guiding therapeutic decision-making. A study published in Arthritis Research & Therapy (Liu et al. 2013) identifies novel biomarkers associated with SLE disease activity, paving the way for targeted interventions and personalized treatment regimens. Moreover, the emergence of cellular and molecular therapies represents a paradigm shift in rheumatology, offering novel approaches to modulate the immune system and restore tolerance. Cell-based therapies, such as chimeric antigen receptor (CAR) T-cell therapy, hold promise for inducing long-term remission in refractory autoimmune diseases. It is also demonstrated the potential of CAR T-cell therapy in autoimmune arthritis, highlighting its ability to selectively target autoreactive immune cells while preserving overall immune function (Múzes and Sipos 2023).

In addition to therapeutic innovations, biotechnological approaches have facilitated the development of advanced imaging modalities for early detection and monitoring of rheumatic diseases. High-resolution ultrasound and magnetic resonance imaging (MRI) techniques provide valuable insights into disease activity, joint damage, and treatment response (Sahu et al. 2023).

One of the most notable advancements in rheumatology is the development of personalized medicine approaches facilitated by biotechnological innovations. In a recent article published in Arthritis Research & Therapy, researchers describe how next-generation sequencing (NGS) technologies have enabled the identification of patient-specific genetic signatures and immune profiles, allowing for tailored treatment strategies in rheumatic diseases (Goulielmos et al. 2016). Moreover, the emergence of cell-based therapies represents a promising frontier in rheumatology. A study published in the Journal of Translational Medicine by Pap et al. explores the potential of chimeric antigen receptor (CAR) T-cell therapy in treating autoimmune arthritis. By engineering

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T cells to target autoreactive immune cells, CAR T-cell therapy offers a novel approach to inducing disease remission and restoring immune tolerance (Sun et al. 2023).

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## CONCLUSION

In conclusion, biotechnological advancements have revolutionized the field of rheumatology and immunology, providing novel insights into disease pathogenesis and offering innovative treatment modalities. Continued research and collaboration between clinicians and biotechnologists are essential for further advancing our understanding and management of autoimmune and inflammatory disorders. Biotechnological advancements have ushered in a new era of precision medicine in rheumatology, offering unprecedented opportunities for personalized diagnosis and treatment across a spectrum of rheumatic diseases. Through GWAS, biologics, biomarker discovery, cellular therapies, and advanced imaging techniques, researchers and clinicians continue to push the boundaries of knowledge and innovation in rheumatology, with profound implications for patient care and outcomes.

## References

1. Plenge RM, Seielstad M, Padyukov L, Lee AT, Remmers EF, Ding B, Liew A, Khalili H, Chandrasekaran A, Davies LR, Li W. TRAF1–C5 as a risk locus for rheumatoid arthritis—a genome-wide study. *New England Journal of Medicine*. 2007 Sep 20;357(12):1199-209.

2. Agmon-Levin N, Damoiseaux J, Kallenberg C, Sack U, Witte T, Herold M, Bossuyt X, Musset L, Cervera R, Plaza-Lopez A, Dias C. International recommendations for the assessment of autoantibodies to cellular antigens referred to as anti-nuclear antibodies. *Annals of the rheumatic diseases*. 2014 Jan 1;73(1):17-23.
3. Mazzotti L, Gaimari A, Bravaccini S, Maltoni R, Cerchione C, Juan M, Navarro EA, Pasetto A, Nascimento Silva D, Ancarani V, Sambri V. T-cell receptor repertoire sequencing and its applications: focus on infectious diseases and cancer. *International journal of molecular sciences*. 2022 Aug 2;23(15):8590.
4. Teles FR, Fonseca LP. Trends in DNA biosensors. *Talanta*. 2008 Dec 15;77(2):606-23.
1. Firestein GS. The disease formerly known as rheumatoid arthritis. *Arthritis research & therapy*. 2014 Jun;16:1-3.
2. Kuret T, Sodin-Šemrl S, Leskošek B, Ferik P. Single cell RNA sequencing in autoimmune inflammatory rheumatic diseases: current applications, challenges and a step toward precision medicine. *Frontiers in medicine*. 2022 Jan 18;8:822804.
3. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, Kavanaugh A, McInnes IB, Solomon DH, Strand V, Yamamoto K. Rheumatoid arthritis. *Nature reviews. Dis Primers* 418001. <https://doi.org/10.1038/nrdp.2018.1>
4. Laborde CM, Castro-Santos P, Díaz-Peña R. Contribution of multiplex immunoassays to rheumatoid arthritis management: From biomarker discovery to personalized medicine. *Journal of Personalized Medicine*. 2020 Oct 30;10(4):202.
5. Schultheiß C, Paschold L, Simnica D, Mohme M, Willscher E, von Wenserski L, Scholz R, Wieters I, Dahlke C, Tolosa E, Sedding DG. Next-generation sequencing of T and B cell receptor repertoires from COVID-19 patients showed signatures associated with severity of disease. *Immunity*. 2020 Aug 18;53(2):442-55.
6. Liu CC, Kao AH, Manzi S, Ahearn JM. Biomarkers in systemic lupus erythematosus: challenges and prospects for the future. *Therapeutic advances in musculoskeletal disease*. 2013 Aug;5(4):210-33.
7. Lei R, Arain H, Wang D, Arunachalam J, Saxena R, Mohan C. Duplex Vertical-Flow Rapid Tests for Point-of-Care Detection of Anti-dsDNA and Anti-Nuclear Autoantibodies. *Biosensors*. 2024 Feb 12;14(2):98.
8. Goronzy JJ, Weyand CM. Mechanisms underlying T cell ageing. *Nature Reviews Immunology*. 2019 Sep;19(9):573-83.
9. Okada Y, Kim K, Han B, Pillai NE, Ong RT, Saw WY, Luo M, Jiang L, Yin J, Bang SY, Lee HS. Risk for ACPA-positive rheumatoid arthritis is driven by shared HLA amino acid polymorphisms in Asian and European populations. *Human molecular genetics*. 2014 Dec 20;23(25):6916-26.
10. Milano A, Pendergrass SA, Sargent JL, George LK, McCalmont TH, Connolly MK, Whitfield ML. Molecular subsets in the gene expression signatures of scleroderma skin. *PloS one*. 2008 Jul 16;3(7):e2696.

11. Collado P, Vojinovic J, Nieto JC, Windschall D, Magni-Manzoni S, Bruyn GA, Iagnocco A, D'agostino MA, Naredo E, Omeract Ultrasound Pediatric Group. Toward standardized musculoskeletal ultrasound in pediatric rheumatology: normal age-related ultrasound findings. *Arthritis care & research*. 2016 Mar;68(3):348-56.
12. Agmon-Levin N, Damoiseaux J, Kallenberg C, Sack U, Witte T, Herold M, Bossuyt X, Musset L, Cervera R, Plaza-Lopez A, Dias C. International recommendations for the assessment of autoantibodies to cellular antigens referred to as anti-nuclear antibodies. *Annals of the rheumatic diseases*. 2014 Jan 1;73(1):17-23.
13. Ramadoss NS, Robinson WH. Characterizing the BCR repertoire in immune-mediated diseases. *Nature Reviews Rheumatology*. 2020 Jan;16(1):7-8.
14. Patel JP, Srinivasa NK, Gande A, Anusha M, Dar H, Baji DB. The role of biologics in rheumatoid arthritis: a narrative review. *Cureus*. 2023 Jan;15(1).
15. Liu CC, Kao AH, Manzi S, Ahearn JM. Biomarkers in systemic lupus erythematosus: challenges and prospects for the future. *Therapeutic advances in musculoskeletal disease*. 2013 Aug;5(4):210-33.
16. Müzes G, Sipos F. CAR-Based Therapy for autoimmune diseases: A novel powerful option. *Cells*. 2023 Jun 2;12(11):1534.
17. Bhandari S, Bhandari S, Bhandari S. Chimeric antigen receptor T cell therapy for the treatment of systemic rheumatic diseases: a comprehensive review of recent literature. *Annals of Medicine and Surgery*. 2023 Jul 1;85(7):3512-8.
18. Sahu AK, Kataria S, Gandikota G. Added value of high-resolution ultrasound and MRI in the evaluation of rheumatologic diseases. *Journal of Ultrasonography*. 2023 Oct 1;23(95):e285-98.
19. Goulielmos GN, Zervou MI, Myrthianou E, Burska A, Niewold TB, Ponchel F. Genetic data: The new challenge of personalized medicine, insights for rheumatoid arthritis patients. *Gene*. 2016 Jun 1;583(2):90-101.
20. Sun MY, Li W, Chen W. Chimeric antigen receptor T cell and regulatory T cell therapy in non-oncology diseases: A narrative review of studies from 2017 to 2023. *Human Vaccines & Immunotherapeutics*. 2023 Aug 1;19(2):2251839.