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 have 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.

GWAS have identified numerous genetic variants associated with susceptibility to auto-inflammatory diseases. GWAS have identified variants in genes encoding components of the innate immune system, such...
as NLRP3, TNFAIP3, and IL1RN, which are implicated in disorders like cryopyrin-associated periodic syndromes (CAPS) and familial Mediterranean fever (FMF) (Xavier and Rioux 2008; Jain et al. 2021). Moreover, NGS technologies, including whole genome sequencing (WGS) and whole exome sequencing (WES), have revolutionized the ability to uncover rare genetic variants and mutations underlying auto-inflammatory diseases (Satam et al. 2023; Fernandez-Marmiesse et al. 2018). NGS has been instrumental in identifying mutations in TNFRSF1A responsible for TNF receptor-associated periodic syndrome (TRAPS). GWAS and NGS have transformed our understanding of auto-inflammatory diseases by discovery of genetic variants, disease stratification, and personalized medicines. Over all, GWAS and NGS have revolutionized the field of auto-inflammatory diseases through the enhancing genetic discovery, enabling precise disease stratification, and paving the way for personalized therapeutic strategies based on individual genetic profiles.

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-α) 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 advancement are illustrated (Table 1).

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 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 (Ramadossand 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 from 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-α) 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 (Műzes and Sipos 2023).

**TABLE 1. Biotechnological advancements and their impact on the diagnosis of rheumatic and immunological disease**

<table>
<thead>
<tr>
<th>Biotechnological advancement</th>
<th>Impact on diagnosis</th>
<th>Examples</th>
<th>References</th>
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<tbody>
<tr>
<td>Multiplex Immunoassays</td>
<td>Simultaneous detection of autoantibodies and biomarkers</td>
<td>Detection of anti-cyclic citrullinated peptide (anti-CCP) antibodies in rheumatoid arthritis</td>
<td>Laborde et al. 2020</td>
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<tr>
<td>Next-Generation Sequencing (NGS)</td>
<td>Profiling of immune cell receptor repertoire</td>
<td>Characterization of T-cell receptor (TCR) and B-cell receptor (BCR) diversity in autoimmune diseases</td>
<td>Schultheiß et al. 2020</td>
</tr>
<tr>
<td>Point-of-Care Diagnostics</td>
<td>Rapid and decentralized testing</td>
<td>Detection of anti-nuclear antibodies (ANA) in Sjögren’s syndrome</td>
<td>Lei et al. 2016</td>
</tr>
<tr>
<td>High-Throughput Flow Cytometry</td>
<td>Quantitative analysis of immune cell subsets</td>
<td>Characterization of lymphocyte populations in autoimmune diseases</td>
<td>Goronzy et al. 2019</td>
</tr>
<tr>
<td>Genome-Wide Association Studies (GWAS)</td>
<td>Identification of genetic risk factors</td>
<td>Discovery of HLA alleles associated with rheumatoid arthritis susceptibility</td>
<td>Okada et al. 2014</td>
</tr>
<tr>
<td>Microarray Technology</td>
<td>Profiling gene expression patterns</td>
<td>Identification of molecular subtypes in systemic sclerosis</td>
<td>Milano et al. 2008</td>
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<tr>
<td>Digital Imaging Techniques</td>
<td>Visualization of disease manifestations</td>
<td>Ultrasound imaging of synovitis in juvenile idiopathic arthritis</td>
<td>Collado et al. 2017</td>
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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 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).

**CONCLUSION**

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.

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.

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**REFERENCES**


