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Emerging Trends in Drug Discovery for Respiratory Disorders: Innovations and Future Prospects

Roshmi Ray[1*], Nutan Sharma[2], Manish Kumar[3], Shikha Rathi[4], Mukesh Sharma[5]

[1*]Associate Professor, Sri Sukhmani Institute of Pharmacy, Dera Bassi
[2]Associate Professor, Sri Sukhmani Institute of Pharmacy, Dera Bassi
[3]Assistant Professor, Sri Sukhmani Institute of Pharmacy, Dera Bassi
[4]Associate Professor, Sri Sukhmani Institute of Pharmacy, Dera Bassi
[5]Assistant Professor, Sri Sukhmani Institute of Pharmacy, Dera Bassi

ABSTRACT
The field of respiratory medicine has seen significant advancements in drug discovery, leading to more targeted and effective treatment options for conditions such as asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), and pneumonia. Traditional therapies, including corticosteroids and bronchodilators, primarily focus on symptom management rather than addressing the underlying causes of these diseases. However, emerging trends such as precision medicine, biologic therapies, regenerative medicine, microbiome-based interventions, and artificial intelligence (AI)-driven drug discovery are revolutionizing respiratory disease management by offering personalized and disease-specific treatments.Precision medicine utilizes biomarkers to tailor therapies according to an individual's genetic and molecular profile, improving treatment efficacy and minimizing side effects. Biologic therapies, particularly monoclonal antibodies, have shown great promise in modulating immune responses and targeting specific inflammatory pathways, leading to improved disease control. Regenerative medicine, including stem cell-based therapies, aims to repair lung tissue damage, offering potential breakthroughs for chronic and progressive respiratory diseases. The microbiome has emerged as a critical factor in respiratory health, with microbiome-targeted therapies such as probiotics, prebiotics, and fecal microbiota transplantation (FMT) being explored to restore microbial balance and enhance immune function.AI-driven drug discovery is accelerating the identification of novel therapeutic agents and repurposing existing drugs for respiratory conditions. AI technologies, including machine learning and big data analytics, streamline drug screening, predict treatment responses, and optimize clinical trials, reducing the time and cost associated with drug development. Despite these advances, challenges such as treatment costs, long-term safety concerns, regulatory hurdles, and patient variability must be addressed before widespread clinical adoption. As research continues to advance, these innovations hold the potential to transform respiratory medicine, providing more effective, personalized, and accessible treatment options that improve patient outcomes and quality of life.

Keywords: Precision medicine, biologic therapies, regenerative medicine, microbiome-based interventions, AI-driven drug discovery.

INTRODUCTION

The field of respiratory medicine has witnessed significant progress in recent years, driven by advances in drug discovery techniques and a deeper understanding of the underlying pathophysiology of various respiratory disorders. Respiratory diseases, including asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), and lung cancer, affect millions globally. Despite significant therapeutic progress, many of these conditions still present unmet medical needs. New trends in drug discovery are now addressing these gaps, with innovations focused on precision medicine, biologics, and novel drug delivery systems.

A. Precision Medicine and Biomarker-Driven Approaches

Respiratory disorders such as asthma, chronic obstructive pulmonary disease (COPD), and idiopathic pulmonary fibrosis (IPF) pose significant global health challenges. Traditional treatments often follow a one-size-fits-all approach, which may not be effective for all patients due to variations in disease mechanisms and genetic factors. Precision medicine, which tailors therapies based on an individual's genetic profile, biomarkers, and disease pathways, is emerging as a transformative approach in respiratory care.Biomarkers serve as measurable indicators for disease diagnosis, progression, and treatment response. In respiratory diseases, they are categorized into genetic, molecular, cellular, and imaging-based markers, allowing for more precise patient stratification and therapy selection.[1,2]

Asthma: Biomarker-Guided Therapies

Asthma is a heterogeneous condition with multiple subtypes, such as eosinophilic and non-eosinophilic asthma. Biomarkers like fractional exhaled nitric oxide (FeNO), blood eosinophil count, and periostin levels help identify patients with type 2 (T2) inflammation, who respond well to biologic therapies targeting interleukins (IL-4, IL-5, and IL-13). Monoclonal antibodies like mepolizumab (anti-IL-5) and dupilumab (anti-IL-4/IL-13) have shown significant benefits in

managing severe eosinophilic asthma.For non-T2 asthma, alternative biomarkers such as sputum neutrophil counts and volatile organic compounds in breath analysis are being investigated to guide treatment strategies.[3]

COPD: Personalized Treatment Approaches
COPD is a progressive inflammatory disease characterized by airflow limitation. Biomarker-based approaches have improved patient classification and treatment selection. Blood eosinophil count is a key predictor of response to inhaled corticosteroids (ICS), with higher eosinophil levels indicating better responsiveness.Genetic biomarkers, such as alpha-1 antitrypsin (AAT) deficiency, have led to targeted augmentation therapy. Imaging biomarkers, including CT-derived lung density measurements, provide additional insights into disease progression and treatment response, aiding in personalized management.[4]

Idiopathic Pulmonary Fibrosis (IPF): Molecular Targets
IPF is a progressive fibrotic lung disease with limited treatment options. Biomarkers such as matrix metalloproteinases (MMP-7), Krebs von den Lungen-6 (KL-6), and surfactant proteins (SP-A, SP-D) have been explored for their role in disease progression and response to antifibrotic therapies like pirfenidone and nintedanib.Genomic studies have identified mutations in genes such as MUC5B, which influence disease susceptibility and progression, paving the way for targeted therapies.[5]

B. Biologics and Monoclonal Antibodies
Respiratory disorders such as asthma, chronic obstructive pulmonary disease (COPD), and idiopathic pulmonary fibrosis (IPF) are complex conditions driven by immune-mediated inflammation and fibrosis. Traditional treatments, including corticosteroids and bronchodilators, provide symptomatic relief but may not address the underlying disease mechanisms. In recent years, biologic therapies, particularly monoclonal antibodies (mAbs), have emerged as targeted treatments that modulate specific molecular pathways involved in these diseases.Biologics are protein-based drugs derived from living organisms that target specific immune components. Monoclonal antibodies neutralize key cytokines or immune cells, reducing inflammation and disease progression in respiratory conditions. Their precision allows for improved efficacy and reduced side effects compared to broad-spectrum therapies.[6,7]

Biologics in Asthma
Asthma is a heterogeneous disease with various inflammatory subtypes. Biologics have transformed the management of severe asthma by targeting key inflammatory mediators:[8]
- **Anti-IgE Therapy:***Omalizumab (Xolair)* binds to immunoglobulin E (IgE), preventing allergic inflammation and reducing asthma exacerbations in patients with elevated IgE levels.
- **Anti-IL-5 and IL-5R Therapy:***Mepolizumab* and *Reslizumab* target IL-5, reducing eosinophilic inflammation.*Benralizumab* binds to the IL-5 receptor, depleting eosinophils and improving lung function.
- **Anti-IL-4/IL-13 Therapy:***Dupilumab* inhibits IL-4 and IL-13 signaling, effectively managing severe type 2 (T2) asthma.

Biologics in COPD
COPD is a progressive disease characterized by persistent inflammation and airflow limitation. Although biologics have been less effective in COPD than in asthma, research continues to explore their potential:[9]
- *Benralizumab* and *Mepolizumab* are being investigated for eosinophilic COPD, showing potential in reducing exacerbations in patients with high eosinophil counts.
- *Infliximab* and *Etanercept*, TNF-α inhibitors, were tested but did not demonstrate significant benefits, highlighting the need for more targeted therapies.

Biologics in Idiopathic Pulmonary Fibrosis (IPF)
IPF is a chronic fibrotic lung disease with limited treatment options. Biologics are being developed to target fibrosis-related pathways:[10]
- *Pamrevlumab* inhibits connective tissue growth factor (CTGF), a regulator of fibrosis, and may slow lung function decline.
- *Simtuzumab* targets lysyl oxidase-like 2 (LOXL2), involved in collagen crosslinking, but has shown limited efficacy in trials.

C. Regenerative Medicine and Stem Cell Therapies
Chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), and acute respiratory distress syndrome (ARDS) cause progressive lung damage with limited treatment options. Conventional therapies focus on symptom management and slowing disease progression rather than reversing tissue damage. Regenerative medicine, particularly stem cell therapy, offers a novel approach by promoting lung tissue repair

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and regeneration.[11] Regenerative medicine utilizes biological therapies, including stem cells, gene therapy, and tissue engineering, to repair or replace damaged lung tissue. Its primary goals in respiratory disorders include:[12]

- **Restoring Lung Function** – It involves promoting the regeneration of alveoli, bronchioles, and lung vasculature to enhance respiratory efficiency. By supporting tissue repair and reducing inflammation, targeted therapies can help improve oxygen exchange, airway function, and overall lung health, offering new hope for patients with chronic respiratory conditions.
- **Reducing Inflammation and Fibrosis** – involves modulating immune responses to prevent excessive tissue scarring in the lungs. By regulating inflammatory pathways and promoting tissue repair, targeted interventions can help maintain lung elasticity, improve respiratory function, and slow the progression of chronic lung diseases.
- **Enhancing Tissue Repair** – This focuses on promoting the recovery of damaged epithelial and endothelial cells in the lungs. By supporting cellular regeneration and strengthening barrier function, targeted therapies can aid in restoring lung integrity, improving oxygen exchange, and reducing the risk of further complications in respiratory diseases.

Types of Stem Cells in Respiratory Medicine

Several stem cell types are being explored for lung regeneration:

Sr. No.	Stem cell types	Description	Potential Applications
1.	Mesenchymal Stem Cells (MSCs)	Have immunomodulatory and anti-inflammatory properties which are derived from bone marrow, adipose tissue, umbilical cord blood and placenta. Secrete anti-inflammatory cytokines. Promote epithelial and endothelial repair. Modulate fibroblast activity to prevent fibrosis.[13]	Potential to reduce lung inflammation in ARDS and COPD. Preclinical studies indicate MSCs may slow fibrosis in IPF.[13]
2.	Induced pluripotent stem cells (iPSCs)	These are programmed adult cells capable of differentiating into lung cell types.[14]	Potential in generating lung epithelial cells for transplantation. Modeling genetic lung disorders like cystic fibrosis. Developing personalized treatments.[14]
3.	Embryonic stem cells (ESCs)	ESCs can differentiate into any cell type, including lung cells. However, ethical concerns and tumor risks limit their clinical use.[15]	Potential in generating lung progenitor cells. Studying lung development and disease mechanisms.[15]
4.	Lung Progenitor cells	These specialized stem cells found within the lung contribute to alveolar and bronchiolar regeneration.[16]	Potential to repair and regenerate alveoli, bronchioles, and lung vasculature (in COPD, IPF, etc.). Restoring lung function and improving respiratory capacity. Promotes epithelial and endothelial cell repair, reducing inflammation.[16]

Stem Cell Therapy in Specific Respiratory Diseases

Sr. No.	Respiratory Diseases	Description	Current Research
1.	Chronic Obstructive Pulmonary Disease (COPD)	It involves chronic inflammation and alveolar destruction. MSC therapy has shown promise in reducing exacerbations and promoting lung repair.[17]	Clinical trials suggest MSCs may improve lung function and reduce inflammation. Also, the research is ongoing into optimal delivery methods, such as intravenous infusion and inhalation.[17]
2.	Idiopathic Pulmonary Fibrosis (IPF)	Characterized by excessive fibrosis. Stem cell therapy aims to slow disease progression and enhance lung regeneration.[18]	MSCs exhibit anti-fibrotic effects in preclinical methods. Early clinical trials show potential, but larger studies are needed.[18]
3.	Acute Respiratory Distress Syndrome (ARDS)	It involves severe lung inflammation and fluid accumulation. Stem cells may mitigate lung injury and improve oxygen exchange.[19]	MSCs have shown promise in reducing inflammation and improving survival rates. Further

			studies are required to establish long-term benefits.[19]
4.	Cystic Fibrosis (CF)	It is a genetic disorder affecting lung function. iPSC-based therapies are being explored for personalized treatment.[20]	Gene-edited iPSCs could generate healthy lung cells for transplantation. Stem cell-derived lung organoids are being used for drug testing.[20]

D. Targeting the Microbiome

The human microbiome, a diverse community of microorganisms living in and on the body, plays a crucial role in respiratory health. The lung microbiome, in particular, influences conditions like asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), and pneumonia. Microbial imbalances, or dysbiosis, can exacerbate inflammation, increase susceptibility to infections, and contribute to disease progression.Recent research highlights the gut-lung axis—interactions between gut and lung microbiota—suggesting that gut health can impact respiratory disease outcomes. This has led to growing interest in microbiome-targeted therapies, including probiotics, prebiotics, antibiotics, and novel microbiome-based treatments.[21]

Microbiome Alterations in Respiratory Disorders

Sr. No.	Respiratory disorders	Microbiome alterations
1.	Asthma	• Reduced gut microbial diversity in infancy, particularly a lack of of*Bifidobacterium* and *Lactobacillus*, is linked to a higher asthma risk. • Overgrowth of pro-inflammatory bacteria such as *Haemophilus influenzae* and *Moraxella catarrhalis* worsens airway inflammation.[22]
2.	COPD	• Increased levels of pathogens like *Pseudomonas aeruginosa* and *Streptococcus pneumoniae* contribute to frequent exacerbations. • A decline in beneficial bacteria such as *Prevotella* may impair immune regulation.[23]
3.	Cystic Fibrosis	• Persistent bacterial infections, particularly with *Pseudomonas aeruginosa* and *Staphylococcus aureus*, are common. • Long-term antibiotic use alters the microbiome, leading to resistant strains and heightened inflammation.[24]
4.	Pneumonia & Respiratory Infections	• Disruptions in the lung microbiome due to antibiotics or hospitalization increase infection risks.[25]

Microbiome-Based Therapeutic Strategies

1. Probiotics & Prebiotics

Probiotics and prebiotics play a crucial role in supporting respiratory health by promoting a balanced microbiome. Beneficial bacteria such as *Lactobacillus* and *Bifidobacterium* help regulate immune function and reduce airway inflammation, potentially mitigating symptoms in respiratory conditions like asthma and COPD. Research suggests that early probiotic supplementation may lower the risk of developing asthma and respiratory infections by enhancing immune resilience and maintaining microbial diversity.[26]

2. Targeted Antibiotics & Bacteriophage Therapy

Precision antibiotics are designed to target harmful bacteria while preserving beneficial microbes, reducing the risk of microbiome disruption and antibiotic resistance. Additionally, bacteriophage therapy, which uses viruses to selectively kill bacterial pathogens, is being explored as a potential treatment for cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD). This innovative approach offers a promising alternative to broad-spectrum antibiotics, potentially improving treatment outcomes while maintaining microbial balance in the lungs.[27]

3. Fecal Microbiota Transplantation (FMT)

While fecal microbiota transplantation (FMT) is primarily used to treat gut disorders, researchers are investigating its potential to restore immune balance and reduce lung inflammation. By transferring beneficial gut microbiota from a healthy donor to a patient, FMT may influence immune responses through the gut-lung axis, potentially benefiting conditions like asthma and chronic obstructive pulmonary disease (COPD). Although still in the early stages of research, FMT holds promise as a novel approach to modulating the microbiome for improved respiratory health.[28]

4. Personalized Microbiome-Based Therapies

Advances in metagenomic sequencing allow for personalized treatments based on an individual's unique microbial profile, paving the way for more targeted and effective therapies. By analyzing microbial composition, researchers can develop interventions that specifically restore balance and enhance immune function. Additionally, dietary modifications that

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influence the microbiome, such as prebiotic-rich foods or probiotic supplementation, may help improve respiratory health by reducing inflammation and strengthening immune defenses.[29]

E. Novel Drug Delivery Systems

The human microbiome, a diverse community of microorganisms residing in and on the body, significantly influences respiratory health. Recent research highlights its role in conditions such as asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), and pneumonia. Imbalances in the lung microbiome, known as dysbiosis, can contribute to inflammation, increased infection risk, and disease progression. Emerging therapies targeting the microbiome, including probiotics, prebiotics, antibiotics, and microbiome-based interventions, offer promising approaches for managing respiratory disorders.[30]

The Respiratory Microbiome and Disease Progression

The respiratory microbiome consists of bacteria, viruses, and fungi that interact with the immune system. A balanced microbiome helps maintain immune homeostasis, while dysbiosis can:

- **Increase Inflammation** – Excessive immune activation can disrupt the delicate balance of the respiratory system, triggering chronic lung inflammation. This persistent inflammatory response contributes to tissue damage, airway obstruction, and increased susceptibility to respiratory diseases, highlighting the need for therapies that restore immune balance and reduce inflammation.
- **Enhance Infection Susceptibility** – Disruptions in the microbial balance weaken the respiratory system's natural defenses, making individuals more vulnerable to infections. An imbalance in beneficial and harmful microorganisms can compromise immune responses, allowing pathogens to thrive and increasing the risk of respiratory diseases.
- **Alter Mucus Production** – Changes in microbial composition can influence mucus production, altering its viscosity and impairing clearance from the airways. An imbalance in the respiratory microbiome may lead to thicker, more adhesive mucus, making it difficult to expel pathogens and debris, thereby increasing the risk of respiratory infections and inflammation.[31]

Microbiome Alterations in Respiratory Disorders

1. Asthma

Asthma is influenced by genetic and environmental factors, including the gut-lung axis.

- **Early-Life Dysbiosis:** Reduced gut bacterial diversity (e.g., lower Bifidobacterium and Lactobacillus) is linked to higher asthma risk.
- **Respiratory Microbiome Changes:** Overgrowth of pro-inflammatory bacteria (e.g., *Haemophilus influenzae*, *Moraxella catarrhalis*) worsens airway inflammation.[32]

2. COPD

COPD is characterized by chronic lung inflammation and altered microbial composition.

- **Pathogen Dominance:** Increased *Pseudomonas aeruginosa* and *Streptococcus pneumoniae* contribute to exacerbations.
- **Loss of Beneficial Bacteria:** Decreased *Prevotella* and other commensals may impair immune regulation.[33]

3. Cystic Fibrosis (CF)

CF involves thick mucus accumulation and chronic infections.

- **Persistent Lung Infections:***Pseudomonas aeruginosa* and *Staphylococcus aureus* dominate the CF lung microbiome.
- **Antibiotic Resistance:** Prolonged antibiotic use disrupts microbial balance, leading to resistant strains.[34]

4. Pneumonia and Respiratory Infections

An imbalanced microbiome can increase susceptibility to bacterial and viral infections, especially in hospitalized patients or those on long-term antibiotics.

Microbiome-Based Therapeutic Strategies

1. Probiotics and Prebiotics

- **Modulating the Gut-Lung Axis:** Beneficial bacteria like *Lactobacillus* and *Bifidobacterium* support immune function and reduce lung inflammation.
- **Clinical Potential:** Probiotic supplementation may lower asthma and infection risks.

2. Targeted Antibiotics and Bacteriophage Therapy

- **Precision Antibiotics:** Designed to selectively eliminate harmful bacteria while preserving beneficial microbes.
- **Bacteriophage Therapy:** Utilizes viruses to target bacterial pathogens, showing promise in CF and COPD.

3. Fecal Microbiota Transplantation (FMT)

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Though primarily used for gut disorders, FMT is being investigated for its potential to restore immune balance in respiratory diseases.

4. Personalized Microbiome Therapies

- **Microbiome-Targeted Drugs:** Future treatments may regulate microbial composition to reduce inflammation and infection risks.
- **Dietary Interventions:** Nutrition-based strategies may help maintain a healthy microbiome.

F. Artificial Intelligence and Drug Repurposing

Artificial intelligence (AI) is transforming drug discovery, particularly in respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, and viral infections like COVID-19. AI accelerates drug repurposing by analyzing vast datasets, identifying novel therapeutic uses for existing drugs, and optimizing treatment strategies. This approach significantly reduces the time and cost associated with traditional drug development.AI employs machine learning, deep learning, and big data analytics to uncover drug-disease associations, predict drug efficacy, and streamline clinical trials. Its capabilities include:[35]

- **Identifying Hidden Drug-Disease Links:** AI-driven analysis uncovers hidden connections between drugs and diseases by examining genetic, proteomic, and metabolic interactions. By identifying previously unrecognized treatment potentials, AI accelerates drug discovery, enabling the repurposing of existing medications and the development of targeted therapies for various conditions.
- **Screening FDA-Approved Drugs:**AI efficiently screens FDA-approved drugs to assess their potential efficacy in treating respiratory diseases. By analyzing vast datasets, including clinical records and molecular interactions, AI accelerates drug repurposing, offering faster and cost-effective solutions for conditions like asthma, COPD, and pulmonary fibrosis.
- **Predicting Drug Safety and Side Effects:**Computational models leverage AI to predict drug safety and potential side effects before clinical trials, minimizing risks and improving patient outcomes. By analyzing vast biological and chemical datasets, these models help identify adverse reactions early, ensuring that only the safest and most effective treatments progress to human testing.

AI-Powered Strategies for Drug Repurposing

Sr. No.	Strategies	Description	Example
1.	Machine learning & big data analysis	AI algorithms process large datasets, including electronic health records and genomic studies, to identify repurposing opportunities.[36]	**Supervised learning:** Trains AI on known drug-disease relationships to predict new applications. **Unsupervised learning:** Clusters drugs and diseases based on molecular similarities to reveal unexpected therapeutic uses.[36]
2.	Network-based drug discovery	AI maps biological networks (e.g. protein interactions, gene expression) to find new drug candidates.[37]	AI identified *baricitinib*, an arthritis drug, as a COVID-19 treatment by targeting inflammatory pathways.[37]
3.	Molecular docking & virtual screening	AI simulates drug-target interactions to identify promising candidates for respiratory diseases.[38]	AI screened antiviral drugs for SARS-CoV-2, leading to potential COVID-19 treatments.[38]
4.	Natural Language Processing (NLP) for literature mining	AI scans scientific articles, patents, and clinical trials to uncover hidden drug-disease connections.[39]	AI-linked statins to potential anti-inflammatory benefits in COPD.[39]
5.	AI-optimized clinical trials	AI predicts patient responses to repurposed drugs, improving trial efficiency and success rates.[40]	

AI-Identified Drug Repurposing Candidates

1. COVID-19 & Viral Pneumonia

- *Baricitinib*: Originally for arthritis, repurposed to reduce lung inflammation in severe COVID-19.[41]
- *Remdesivir*: Initially developed for Ebola, AI identified its potential in inhibiting SARS-CoV-2 replication.[42]

2. COPD

- *Metformin*: A diabetes drug with anti-inflammatory properties that may reduce COPD exacerbations.[43]
- *Statins*: AI suggests their role in improving lung function and reducing inflammation.[44]

3. Pulmonary Fibrosis

- *Pirfenidone &Nintedanib*: Originally for idiopathic pulmonary fibrosis (IPF), AI suggests broader antifibrotic applications.[45]
- *Losartan*: AI indicates potential benefits in slowing lung fibrosis progression.[46]

4. Asthma & Allergic Respiratory Diseases

- *Montelukast*: AI refines its application for specific asthma subtypes.[47]
- *Azithromycin*: Identified as a potential anti-inflammatory agent for severe asthma.[48]

CHALLENGES AND FUTURE DIRECTIONS IN RESPIRATORY MEDICINE

Despite significant advancements, several challenges must be addressed before precision medicine, biologic therapies, stem cell treatments, microbiome-based interventions, and AI-driven drug discovery can be fully integrated into respiratory disease management.

Precision Medicine & Biologic Therapies: Variability in biomarker expression, high costs, and the need for large-scale validation studies limit widespread adoption. Identifying reliable biomarkers is crucial for optimizing biologic therapies, which have transformed severe respiratory disease treatment, particularly in asthma. Ongoing research in COPD and IPF aims to refine these therapies for broader applications.[49]

Stem Cell Therapy & Regenerative Medicine: While offering the potential for lung tissue repair and inflammation reduction, stem cell treatments face critical challenges, including risks of immune rejection, tumor formation, and unintended differentiation. Effective lung-targeted delivery methods, such as inhalation and direct administration, are under investigation. Long-term safety and efficacy require further research, alongside stringent regulatory and ethical considerations.[50]

Microbiome-Based Interventions: The respiratory microbiome influences inflammation, immune responses, and infection susceptibility. However, individual microbiome variability complicates treatment standardization, necessitating personalized approaches. Long-term safety concerns surrounding probiotics, fecal microbiota transplantation (FMT), and other microbiome-targeting therapies require further clinical validation. Establishing clear regulatory guidelines is essential to ensure their safe and effective implementation in respiratory disease management.[51]

AI in Drug Discovery & Repurposing: AI is revolutionizing respiratory medicine by predicting drug responses, integrating with CRISPR for genetic therapies, and designing novel treatments. However, challenges remain, including data quality and bias, regulatory hurdles, computational complexity, and ethical concerns surrounding patient data security. Overcoming these obstacles is key to leveraging AI's potential in accelerating drug discovery, reducing costs, and improving treatment outcomes.

As research continues, advancements in precision medicine, biologics, stem cell therapies, microbiome interventions, and AI-driven drug discovery are expected to transform respiratory disease management. These innovations will pave the way for more personalized, effective, and accessible treatments, offering new hope for patients with chronic lung conditions.[52]

CONCLUSION

The landscape of drug discovery for respiratory disorders is rapidly evolving, driven by advancements in precision medicine, biologic therapies, regenerative medicine, microbiome-based interventions, and AI-powered drug discovery. These innovations offer promising alternatives to traditional broad-spectrum treatments, providing more targeted and personalized therapeutic options. Precision medicine enables individualized treatment strategies based on biomarkers, while biologics such as monoclonal antibodies are revolutionizing the management of inflammatory lung diseases. Regenerative medicine, particularly stem cell therapy, holds the potential to repair damaged lung tissue and restore function in chronic respiratory diseases. Additionally, the growing understanding of the respiratory microbiome has paved the way for novel therapeutic strategies involving probiotics, prebiotics, and microbiome-targeted interventions.

Artificial intelligence is playing a crucial role in accelerating drug discovery by identifying novel drug candidates, optimizing clinical trials, and repurposing existing drugs for respiratory diseases. However, despite these advancements, challenges remain. Variability in patient responses, high treatment costs, regulatory barriers, and long-term safety concerns must be addressed before these therapies can be widely adopted. Moreover, ensuring equitable access to these cutting-edge treatments remains a critical consideration.

As research continues, integrating these emerging trends into clinical practice will be essential for transforming respiratory disease management. The future of respiratory medicine lies in the convergence of these innovative approaches, ultimately leading to more effective, personalized, and accessible treatments that improve patient outcomes and quality of life.

REFERENCES

1. Ho, D., Quake, S. R., McCabe, E. R., Chng, W. J., Chow, E. K., Ding, X., ... & Zarrinpar, A. (2020). Enabling technologies for personalized and precision medicine. *Trends in biotechnology*, *38*(5), 497-518.

2. Jain, P., Samantaray, S. S., Ayaz, A., & Aggarwal, S. (2024). Biomarkers of respiratory diseases. In *Biological Insights of Multi-Omics Technologies in Human Diseases* (pp. 363-387). Academic Press.
3. Mosbech, C. H., Godtfredsen, N. S., Ulrik, C. S., & Westergaard, C. G. (2023). Biomarker-guided withdrawal of inhaled corticosteroids in asthma patients with a non-T2 inflammatory phenotype–a randomized controlled trial study protocol. *BMC Pulmonary Medicine*, *23*(1), 372.
4. Franssen, F. M., Alter, P., Bar, N., Benedikter, B. J., Iurato, S., Maier, D., ... & Schmeck, B. (2019). Personalized medicine for patients with COPD: where are we?. *International journal of chronic obstructive pulmonary disease*, 1465-1484.
5. Ballester, B., Milara, J., & Cortijo, J. (2019). Idiopathic pulmonary fibrosis and lung cancer: mechanisms and molecular targets. *International journal of molecular sciences*, *20*(3), 593.
6. Lyly, A., Laulajainen-Hongisto, A., Gevaert, P., Kauppi, P., & Toppila-Salmi, S. (2020). Monoclonal antibodies and airway diseases. *International Journal of Molecular Sciences*, *21*(24), 9477.
7. Matera, M. G., Page, C., Rogliani, P., Calzetta, L., & Cazzola, M. (2016). Therapeutic monoclonal antibodies for the treatment of chronic obstructive pulmonary disease. *Drugs*, *76*(13), 1257-1270.
8. McGregor, M. C., Krings, J. G., Nair, P., & Castro, M. (2019). Role of biologics in asthma. *American journal of respiratory and critical care medicine*, *199*(4), 433-445.
9. Pavord, I. D. (2018). Biologics and chronic obstructive pulmonary disease. *Journal of Allergy and Clinical Immunology*, *141*(6), 1983-1991.
10. Chakraborty, A., & Royce, S. G. (2020). Use of biologics in the treatment of asthma, COPD, ACOS, and idiopathic pulmonary fibrosis. In *Targeting Chronic Inflammatory Lung Diseases Using Advanced Drug Delivery Systems* (pp. 97-115). Academic Press.
11. O'Brien, T., & Barry, F. P. (2009, October). Stem cell therapy and regenerative medicine. In *Mayo Clinic Proceedings* (Vol. 84, No. 10, pp. 859-861). Elsevier.
12. Adamič, N., & Vengust, M. (2023). Regenerative medicine in lung diseases: A systematic review. *Frontiers in veterinary science*, *10*, 1115708.
13. Harrell, C. R., Sadikot, R., Pascual, J., Fellabaum, C., Jankovic, M. G., Jovicic, N., ... & Volarevic, V. (2019). Mesenchymal stem cell-based therapy of inflammatory lung diseases: current understanding and future perspectives. *Stem cells international*, *2019*(1), 4236973.
14. Hawkins, F., & Kotton, D. N. (2015). Embryonic and induced pluripotent stem cells for lung regeneration. *Annals of the American Thoracic Society*, *12*(Supplement 1), S50-S53.
15. Tzouvelekis, A., Ntolios, P., & Bouros, D. (2013). Stem cell treatment for chronic lung diseases. *Respiration*, *85*(3), 179-192.
16. Kim, C. F. (2017). Intersections of lung progenitor cells, lung disease and lung cancer. *European Respiratory Review*, *26*(144).
17. Chen, Y. T., Miao, K., Zhou, L., & Xiong, W. N. (2021). Stem cell therapy for chronic obstructive pulmonary disease. *Chinese Medical Journal*, *134*(13), 1535-1545.
18. Barczyk, M., Schmidt, M., & Mattoli, S. (2015). Stem cell-based therapy in idiopathic pulmonary fibrosis. *Stem Cell Reviews and Reports*, *11*(4), 598-620.
19. Qin, H., & Zhao, A. (2020). Mesenchymal stem cell therapy for acute respiratory distress syndrome: from basic to clinics. *Protein & cell*, *11*(10), 707-722.
20. Hayes Jr, D., Kopp, B. T., Hill, C. L., Lallier, S. W., Schwartz, C. M., Tadesse, M., ... & Reynolds, S. D. (2019). Cell therapy for cystic fibrosis lung disease: regenerative basal cell amplification. *Stem cells translational medicine*, *8*(3), 225-235.
21. Chotirmall, S. H., Bogaert, D., Chalmers, J. D., Cox, M. J., Hansbro, P. M., Huang, Y. J., ... & Dickson, R. P. (2022). Therapeutic targeting of the respiratory microbiome. *American journal of respiratory and critical care medicine*, *206*(5), 535-544.
22. Wang, Z., Lai, Z., Zhang, X., Huang, P., Xie, J., Jiang, Q., ... & Chung, K. F. (2021). Altered gut microbiome compositions are associated with the severity of asthma. *Journal of Thoracic Disease*, *13*(7), 4322.
23. Tiew, P. Y., Jaggi, T. K., Chan, L. L., & Chotirmall, S. H. (2021). The airway microbiome in COPD, bronchiectasis and bronchiectasis-COPD overlap. *The Clinical Respiratory Journal*, *15*(2), 123-133.
24. Huang, Y. J., & LiPuma, J. J. (2015). The microbiome in cystic fibrosis. *Clinics in chest medicine*, *37*(1), 59.
25. Woodall, C. A., McGeoch, L. J., Hay, A. D., & Hammond, A. (2022). Respiratory tract infections and gut microbiome modifications: A systematic review. *PLoS One*, *17*(1), e0262057.
26. Hussain, M. S., Sharma, A., & Kumar, R. (2023). Prebiotics and probiotics: a focused review of applications in respiratory disorders.
27. Chan, B. K., Stanley, G., Modak, M., Koff, J. L., & Turner, P. E. (2021). Bacteriophage therapy for infections in CF. *Pediatric pulmonology*, *56*, S4-S9.
28. Li, N., Dai, Z., Wang, Z., Deng, Z., Zhang, J., Pu, J., ... & Ran, P. (2021). Gut microbiota dysbiosis contributes to the development of chronic obstructive pulmonary disease. *Respiratory Research*, *22*, 1-15.

29. Trivedi, R., & Barve, K. (2020). Gut microbiome a promising target for management of respiratory diseases. *Biochemical Journal*, *477*(14), 2679-2696.
30. Mishra, B., & Singh, J. (2020). Novel drug delivery systems and significance in respiratory diseases. In *Targeting chronic inflammatory lung diseases using advanced drug delivery systems* (pp. 57-95). Academic Press.
31. Li, R., Li, J., & Zhou, X. (2024). Lung microbiome: new insights into the pathogenesis of respiratory diseases. *Signal transduction and targeted therapy*, *9*(1), 19.
32. Wang, Z., Lai, Z., Zhang, X., Huang, P., Xie, J., Jiang, Q., ... & Chung, K. F. (2021). Altered gut microbiome compositions are associated with the severity of asthma. *Journal of Thoracic Disease*, *13*(7), 4322.
33. Tiew, P. Y., Jaggi, T. K., Chan, L. L., & Chotirmall, S. H. (2021). The airway microbiome in COPD, bronchiectasis and bronchiectasis-COPD overlap. *The Clinical Respiratory Journal*, *15*(2), 123-133.
34. Yi, B., Dalpke, A. H., & Boutin, S. (2021). Changes in the cystic fibrosis airway microbiome in response to CFTR modulator therapy. *Frontiers in cellular and infection microbiology*, *11*, 548613.
35. Zhou, Y., Wang, F., Tang, J., Nussinov, R., & Cheng, F. (2020). Artificial intelligence in COVID-19 drug repurposing. *The Lancet Digital Health*, *2*(12), e667-e676.
36. Kaplan, A., Cao, H., FitzGerald, J. M., Iannotti, N., Yang, E., Kocks, J. W., ... & Mastoridis, P. (2021). Artificial intelligence/machine learning in respiratory medicine and potential role in asthma and COPD diagnosis. *The Journal of Allergy and Clinical Immunology: In Practice*, *9*(6), 2255-2261.
37. Leung, E. L., Cao, Z. W., Jiang, Z. H., Zhou, H., & Liu, L. (2013). Network-based drug discovery by integrating systems biology and computational technologies. *Briefings in bioinformatics*, *14*(4), 491-505.
38. Azeem, M., Mustafa, G., & Mahrosh, H. S. (2022). Virtual screening of phytochemicals by targeting multiple proteins of severe acute respiratory syndrome coronavirus 2: Molecular docking and molecular dynamics simulation studies. *International Journal of Immunopathology and Pharmacology*, *36*, 03946320221142793.
39. Dreisbach, C., Koleck, T. A., Bourne, P. E., & Bakken, S. (2019). A systematic review of natural language processing and text mining of symptoms from electronic patient-authored text data. *International journal of medical informatics*, *125*, 37-46.
40. Mahmud, S. (2025). AI And Data Analytics For Enhancing Home Healthcare: Optimizing Patient Outcomes And Resource Allocation. *Frontiers in Applied Engineering and Technology*, *2*(01), 78-100.
41. Saber-Ayad, M., Hammoudeh, S., Abu-Gharbieh, E., Hamoudi, R., Tarazi, H., Al-Tel, T. H., & Hamid, Q. (2021). Current status of baricitinib as a repurposed therapy for COVID-19. *Pharmaceuticals*, *14*(7), 680.
42. Santoro, M. G., & Carafoli, E. (2021). Remdesivir: from Ebola to COVID-19. *Biochemical and biophysical research communications*, *538*, 145-150.
43. Ho, T. W., Huang, C. T., Tsai, Y. J., Lien, A. S. Y., Lai, F., & Yu, C. J. (2019). Metformin use mitigates the adverse prognostic effect of diabetes mellitus in chronic obstructive pulmonary disease. *Respiratory research*, *20*, 1-10.
44. Wygrecka, M., Alexopoulos, I., Potaczek, D. P., & Schaefer, L. (2023). Diverse functions of apolipoprotein AI in lung fibrosis. *American Journal of Physiology-Cell Physiology*, *324*(2), C438-C446.
45. Finnerty, J. P., Ponnuswamy, A., Dutta, P., Abdelaziz, A., & Kamil, H. (2021). Efficacy of antifibrotic drugs, nintedanib and pirfenidone, in treatment of progressive pulmonary fibrosis in both idiopathic pulmonary fibrosis (IPF) and non-IPF: a systematic review and meta-analysis. *BMC Pulmonary Medicine*, *21*(1), 411.
46. Lee, J. J., Galatioto, J., Rao, S., Ramirez, F., & Costa, K. D. (2016). Losartan attenuates degradation of aorta and lung tissue micromechanics in a mouse model of severe Marfan syndrome. *Annals of biomedical engineering*, *44*, 2994-3006.
47. Takemura, M., Niimi, A., Matsumoto, H., Ueda, T., Matsuoka, H., Yamaguchi, M., ... & Mishima, M. (2012). Clinical, physiological and anti-inflammatory effect of montelukast in patients with cough variant asthma. *Respiration*, *83*(4), 308-315.
48. Cramer, C. L., Patterson, A., Alchakaki, A., & Soubani, A. O. (2017). Immunomodulatory indications of azithromycin in respiratory disease: a concise review for the clinician. *Postgraduate medicine*, *129*(5), 493-499.
49. Cazzola, M., Calzetta, L., Rogliani, P., & Matera, M. G. (2017). The challenges of precision medicine in COPD. *Molecular diagnosis & therapy*, *21*, 345-355.
50. Jungebluth, P., & Macchiarini, P. (2011). Stem cell-based therapy and regenerative approaches to diseases of the respiratory system. *British medical bulletin*, *99*(1).
51. Gulliver, E. L., Young, R. B., Chonwerawong, M., D'Adamo, G. L., Thomason, T., Widdop, J. T., ... & Forster, S. C. (2022). the future of microbiome-based therapeutics. *Alimentary Pharmacology & Therapeutics*, *56*(2), 192-208.
52. Singh, A. (2024). Artificial intelligence for drug repurposing against infectious diseases. *Artificial Intelligence Chemistry*, *2*(2), 100071.