

# Pulmonary genetics: Susceptibility, treatment, and outcomes.

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## Introduction

Understanding the genetic underpinnings of pulmonary diseases and transplantation outcomes provides a crucial foundation for advancing diagnostics, therapeutics, and personalized medical approaches. This review compiles recent research emphasizing the significant and diverse roles genetics play across several major respiratory conditions, from infectious diseases like tuberculosis to chronic degenerative conditions such as Chronic Obstructive Pulmonary Disease (COPD), and the complex immunological challenges in lung transplantation.

A systematic review and meta-analysis explores the genetic factors influencing susceptibility to tuberculosis in African populations, highlighting specific gene polymorphisms associated with increased or decreased risk, emphasizing the complex interplay between host genetics and TB development [1]. This work suggests that understanding these genetic markers could aid in identifying high-risk individuals and developing targeted interventions [1]. Further building on the understanding of tuberculosis, another review summarizes recent progress in understanding the host genetic factors that influence susceptibility and resistance to pulmonary tuberculosis [10]. It discusses various genes involved in immune responses and their clinical implications, providing insights into potential biomarkers for disease risk and severity, and opening avenues for host-directed therapies [10]. Complementing these findings, genetic mutations in *Mycobacterium tuberculosis* that confer resistance to various anti-tuberculosis drugs are also explored [4]. Understanding these genetic determinants is crucial for rapid diagnosis of drug-resistant TB, guiding effective treatment regimens, and developing new drugs to combat the growing challenge of multidrug and extensively drug-resistant TB [4]. Moreover, genetic factors that predispose individuals to the co-occurrence of pulmonary tuberculosis and COPD are explored through a systematic review [7]. This research identifies several shared genetic pathways and specific gene variants that might explain why some individuals are more vulnerable to both conditions, offering insights into common pathogenic mechanisms and potential targets for combined management strategies [7].

The field of Chronic Obstructive Pulmonary Disease (COPD) also heavily benefits from genetic research. One review discusses how

genetic factors influence COPD susceptibility, progression, and treatment response [2]. It emphasizes the potential of precision medicine, where genetic insights can personalize therapeutic strategies, moving beyond a one-size-fits-all approach to better manage this heterogeneous disease [2]. Identifying genetic markers could guide optimal pharmacotherapy and risk stratification [2]. Similarly, the genetic predispositions and environmental interactions that contribute to COPD exacerbations, which are critical events impacting disease progression and patient quality of life, are investigated [5]. This highlights specific genetic variants and how they modulate individual responses to environmental triggers, offering insights for identifying high-risk patients and developing preventative strategies [5]. In a specific population context, a study investigated genetic and environmental factors contributing to COPD susceptibility in a Han Chinese population, identifying specific gene polymorphisms and environmental exposures that significantly increase risk [9]. The findings from this study suggest a complex interplay where particular genetic backgrounds, combined with factors like smoking, predispose individuals to COPD, supporting personalized prevention strategies [9].

Beyond infectious and chronic lung diseases, genetic factors profoundly influence outcomes in critical medical interventions like lung transplantation. One review delves into how genetic variations in both donors and recipients influence the success and complications of lung transplantation, particularly focusing on acute and chronic rejection [3]. It highlights the importance of genetic matching and the role of immune-related genes in predicting outcomes, suggesting avenues for improving post-transplant survival and quality of life [3]. The critical role of Human Leukocyte Antigen (HLA) in determining outcomes following lung transplantation is specifically highlighted in another review [8]. It explains how HLA mismatches can trigger immune responses leading to rejection and discusses strategies for optimal donor-recipient matching [8]. Understanding HLA genetics is fundamental for improving graft survival and minimizing post-transplant complications [8]. Finally, the genetic and epigenetic influences on Chronic Lung Allograft Dysfunction (CLAD), the primary cause of late mortality after lung transplantation, are examined [6]. This discusses specific genetic polymorphisms and epigenetic modifications that contribute to CLAD development, suggesting potential biomarkers for early detection

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Received: 04-Apr-2025, Manuscript No. AARRP-25-187; Editor assigned: 08-Apr-2025, Pre QC No. AARRP-25-187 (PQ); Reviewed: 28-Apr-2025, QC No. AARRP-25-187; Revised: 07-May-2025, Manuscript No. AARRP-25-187 (R); Published: 16-May-2025, DOI: 10.35841/aarrp-6.2.187

and therapeutic targets to improve long-term graft survival [6]. Together, these studies underscore the pervasive and intricate role of genetics in shaping pulmonary health and disease, offering promising pathways for future medical advancements.

## Conclusion

This compilation of research explores the critical role of genetic factors in various pulmonary conditions, focusing on susceptibility, progression, treatment, and outcomes. Several studies delve into tuberculosis, examining host genetic influences on susceptibility in diverse populations, including African groups, and identifying gene polymorphisms that modulate risk. This body of work also addresses the genetic determinants of drug resistance in *Mycobacterium tuberculosis*, which is vital for diagnosing and treating multidrug-resistant forms of the disease. Furthermore, the research extensively covers Chronic Obstructive Pulmonary Disease (COPD), highlighting how genetic factors influence its development, exacerbations, and response to treatment. The potential of precision medicine, guided by genetic insights, is emphasized for tailoring therapeutic strategies and identifying high-risk individuals for COPD. A unique aspect discussed is the genetic susceptibility to the co-occurrence of tuberculosis and COPD, pointing to shared pathogenic pathways. The collection also thoroughly investigates the impact of genetics on lung transplantation, detailing how donor and recipient genetic variations, particularly Human Leukocyte Antigen (HLA) matching, affect acute and chronic rejection, as well as the long-term success and complications like Chronic Lung Allograft Dysfunction (CLAD). Understanding these genetic and epigenetic influences is crucial for improving graft survival and quality of life post-transplant, alongside informing biomarker development and targeted therapies across these complex pulmonary

disorders.

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**Citation:** Zhang ML. *Pulmonary genetics: Susceptibility, treatment, and outcomes.* *Res Rep Pulmonol.* 2025;06(02):187.