Host Susceptibility Genes for Pulmonary NTM Disease Identified by International Network

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Educational background

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Professional experience

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Pulmonary nontuberculous mycobacterial (NTM) disease is a chronic, progressive pulmonary infection caused by low-virulence environmental pathogens. The global incidence of NTM disease has been steadily rising, posing an increasing public health concern. Despite this trend, current antimicrobial therapies remain suboptimal due to limited efficacy, the difficulty of developing new drugs, and the risk of antimicrobial resistance resulting from prolonged treatment. These challenges underscore the urgent need for novel therapeutic strategies grounded in a deeper understanding of disease pathogenesis.

Given the ubiquitous presence of NTM in the environment and its relatively low pathogenicity, previous epidemiological findings—including familial clustering and a higher incidence among Asians compared to other ethnic groups in the United States—suggest that host genetic factors play a critical role in susceptibility. However, until recently, genetic research on pulmonary NTM disease has been limited.

To address this gap, we conducted the first genome-wide association study (GWAS) of pulmonary Mycobacterium avium complex (MAC) disease, comprising 1,066 patients and 1,135 controls. This study identified a significant association at the CHP2 locus on chromosome 16p21. The lead single nucleotide polymorphism (SNP), rs109592, was associated with decreased CHP2 expression in lung tissue and was particularly linked to the nodular bronchiectasis subtype. Notably, the risk allele demonstrated consistent effects across both Japanese and European populations, suggesting a shared genetic architecture. Since CHP2 encodes a protein involved in intracellular pH and ion homeostasis, this discovery provides novel insight into the molecular basis of host susceptibility to pulmonary MAC disease.

Building upon these findings, we plan to expand our international collaborative network and conduct transethnic meta-GWAS analyses, including additional cohorts from Korea and other Asia-Pacific regions.