Mapping rheumatoid arthritis susceptibility through integrative bioinformatics and genomics

ABSTRACT

Rheumatoid arthritis (RA) is an autoimmune disease that influences several organs and tissues, especially the synovial joints, and is associated with multiple genetic and environmental factors. Numerous databases provide information on the relationship between a specific gene and the disease pathogenesis. However, it is important to further prioritize biological risk genes for downstream development and validation. This study aims to map RA-association genetic variation using genome-wide association study (GWAS) databases and prioritize influential genes in RA pathogenesis based on functional annotations. These functional annotations include missense/nonsense mutations, cis-expression quantitative trait locus (cis-eQTL), overlap knockout mouse phenotype (KMP), protein-protein interaction (PPI), molecular pathway analysis (MPA), and primary immunodeficiency (PID). 119 genetic variants mapped had a potential high risk for RA based on functional scoring. The top eight risk genes of RA are TYK2 and IFNGR2, followed by TNFRSF1A, IL12RB1 and CD40, C5, NCF2, and IL6R. These candidate genes are potential biomarkers for RA that can aid drug discovery and disease diagnosis.