PE 224

UNRAVELING THE GENETIC ARCHITECTURE OF SUSCEPTIBILITY TO *HELICOBACTER PYLORI*: AN INTEGRATED META-ANALYSIS AND COMPUTATIONAL APPROACH

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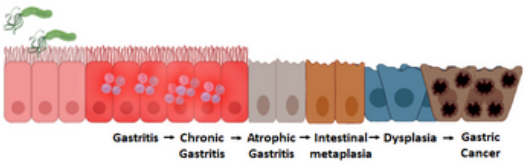
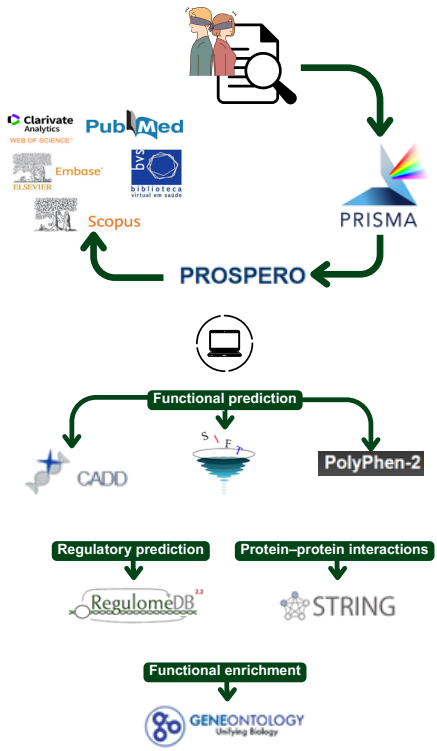
BACKGROUND AND OBJECTIVES

Host genetic variations can modulate the immune response to infections. *Helicobacter pylori* is a highly immunogenic bacterium whose presence is associated with several gastric alterations, including gastritis, metaplasia, atrophy, and, ultimately, gastric cancer. Identifying genetic polymorphisms associated with susceptibility to infection may support the development of personalized prevention and treatment strategies, in line with the principles of precision medicine. This study aimed to characterize host molecular biomarkers associated with susceptibility to *Helicobacter pylori* infection through a systematic review with meta-analysis and in silico analyses.



MATERIAL AND METHODS



RESULTS

A total of 43 polymorphisms were identified across 30 genes, six of which were included in the meta-analysis: rs1143627, rs16944 (*IL1B*), rs4833095 (*TLR1*), rs4986790 (TLR4), rs10004195 (*TLR10*), and rs1800629 (*TNF*).

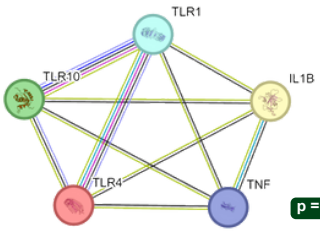
The meta-analysis showed that rs16944 and rs4986790 were associated with increased susceptibility to *Helicobacter pylori* infection

rs4833095 and rs10004195 conferred a protective effect

Coding variants → **CADD <15**

Coding variants → **SIFT Tolerated**

Variants in regulatory regions → **Strong evidence of functional impact (RegulomeDB)**



p = 0.00068

Functional enrichment → **Toll-like receptor signaling and the regulation of IL-6 and IL-8 production.**

DISCUSSION AND CONCLUSION

The integration of meta-analyses with in silico approaches demonstrates that susceptibility to *H. pylori* infection arises not only from gene sequence alterations but also from regulatory mechanisms that modulate host–pathogen interactions. The identification of variants with strong regulatory evidence, together with the involvement of genes in functional networks and critical inflammatory pathways, reveals a complex genetic architecture that goes beyond the isolated effect of individual variants. These findings broaden the understanding of the interplay between the genome and the immune response, highlighting new opportunities for personalized medicine strategies that consider not only the presence of variants but also their capacity to modulate biological processes.

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