

Genetic correlations between inguinal, umbilical, and diaphragmatic hernias and identification of shared pathogenic genes

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Aim

Umbilical hernia (UH), inguinal hernia (IH), and diaphragmatic hernia (DH) are three common types of hernia, frequently associated with impaired collagen synthesis in connective tissue. Although they share a similar pathophysiological basis, the genetic relationships among these hernia subtypes remain insufficiently explored.

Material & Methods

We analyzed genome-wide association study (GWAS) data from the FinnGen cohort, which included 43,066 IH cases, 11,934 UH cases, 16,034 DH cases, and 426,666 controls. Linkage disequilibrium score regression was employed to estimate genetic correlations among the hernia types. To further investigate shared genetic mechanisms, we conducted multi-omics Mendelian randomization (MR) analyses, using cis-eQTLs from the eQTLGen consortium as exposures and the three hernia types as outcomes. Common risk genes were identified and validated through Bayesian co-localization analysis.

Results

A significant genetic correlation was observed among IH, UH, and DH (IH-UH: $r_g = 0.44$, $P < 0.001$; IH-DH: $r_g = 0.34$, $P < 0.001$; UH-DH: $r_g = 0.26$, $P < 0.001$). While no single gene was found to be causally associated with all three hernia types, MR and Bayesian co-localization analyses revealed six shared risk genes between IH and UH, reflecting their strong genetic correlation.

Conclusions

This study demonstrates significant genetic correlations among IH, UH, and DH, and identifies shared genetic risk factors between IH and UH. These findings provide new insights into the molecular basis of hernia development and may contribute to improved risk stratification and therapeutic strategies.

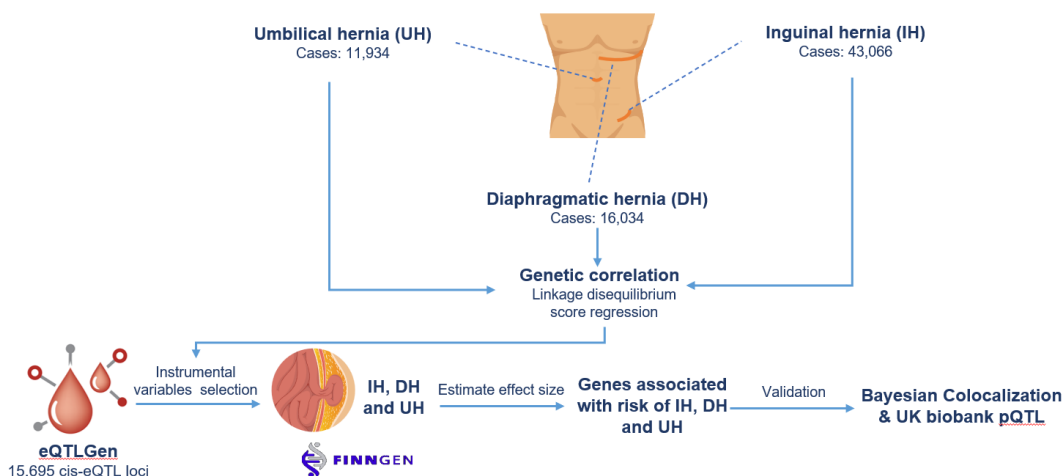


Fig. 1 Flow chart of study design.

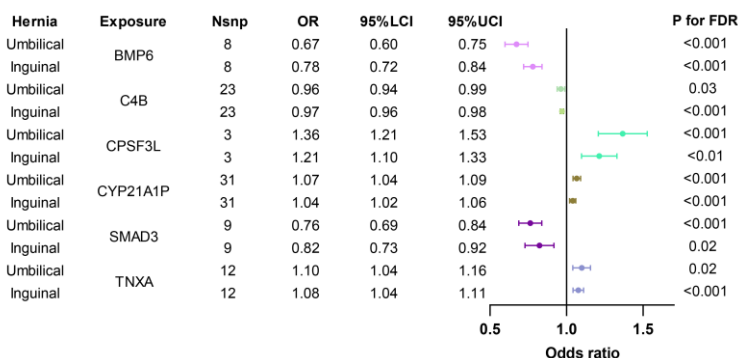


Fig. 2 The forest plot presents the results of the Mendelian randomization analysis of shared risk loci for inguinal and umbilical hernias.