Am J Clin Exp Urol 2025;13(1):57-68
www.ajceu.us /ISSN:2330-1910/AJCEU0160492

Original Article

Genetic factors associated with erectile dysfunction- mendelian randomisation analysis

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Received September 12, 2024; Accepted February 10, 2025; Epub February 15, 2025; Published February 28, 2025

Abstract: Background: Studies have established a strong link between erectile dysfunction (ED) and genetic factors. However, the genetic protective genes associated with ED have yet to be identified. In this study, we used Mendelian randomization (MR) analysis to investigate potential genetic protective genes related to ED. Methods: We used ED-associated GWAS data and whole blood expression quantitative trait loci (eQTLs) data from the Finnish database, which included 1,154 cases and 94,024 controls, for our analysis, resulting in a total of 95,178 individuals for Mendelian randomization (MR) analysis. To further identify potential causative genes and explore their functional roles and relationship to phenotype, we conducted PPI and single-cell analysis using the GSE206528 dataset. Results: The MR analysis identified 263 genes associated with ED, with TRIP10 showing the highest degree, exhibiting an odds ratio (OR) of 0.58. Located on chromosome 7, TRIP10 plays a protective role in ED. Single-cell sequencing analysis revealed that TRIP10 is most highly expressed in endothelial cells and tissue stem cells, particularly in endothelial cells. Through PPI and single-cell analysis, we further identified potential causative genes, shedding light on their functions and their connection to the phenotype. Conclusions: Our study found that among the 263 genes associated with ED, TRIP10 was strongly linked to a decreased risk of ED. These findings offer valuable insights for the personalized treatment of ED from a genetic perspective.

Keywords: Erectile dysfunction, mendelian randomization, TRIP10 gene

Introduction

The Massachusetts Male Aging Study (MMAS) found that among 1,290 white men aged 40-70 years, the overall prevalence of erectile dysfunction (ED) was 52%, with prevalence rates for mild, moderate, and severe ED at 17.2%, 25.2%, and 9.6%, respectively [1, 2]. ED affects not only the individual but also the quality of life of their partner [3, 4]. Effective treatment options are crucial for improving patients' quality of life [3, 4]. Penile erection is a complex neurovascular-tissue process regulated by bioactive factors and hormones [3, 4]. Current studies have established that the main mechanisms and risk factors contributing to ED include vascular, neurogenic, anatomical, psychogenic, hormonal, pharmacological, and traumatic factors [3-5]. However, recent research indicates a significant genetic component in the pathogenesis of ED [6-8].

Scientists have identified a potential link between genetic factors and erectile dysfunction (ED). The relationship between genetic susceptibility and ED is becoming increasingly apparent, with family clustering studies indicating that individuals with a family history of ED are at a higher risk of developing the condition [7]. Genome-wide association studies (GWAS) and candidate gene studies have pinpointed several genetic loci associated with ED, offering insights into the underlying biological mechanisms and genetic risk factors related to erectile function [9]. However, the translation of these findings into clinical practice and therapeutic interventions remains limited, primarily due to the complexity of gene interactions and the challenges of establishing causality. Further screening of ED-associated genes and the development of targeted interventions would offer significant clinical value. In this context, Mendelian randomization (MR) has emerged as

https://doi.org/10.62347/BVHS3637

a powerful epidemiological tool, enabling the investigation of causal relationships between potentially modifiable risk factors and ED through the use of genetic variation as an instrumental variable [10, 11]. The key advantage of MR is its ability to minimize confounding and reverse causation, common issues in observational studies [12]. By utilizing randomly assigned genetic variation at conception, MR functions as a natural experiment, mimicking the randomness of a randomized controlled trial, and providing evidence that is less susceptible to confounding factors. In this paper, we apply MR methods to explore the causal effects of genetic variants associated with ED and identify potential therapeutic targets. Our study found that 263 genes were associated with ED, with TRIP10 playing a crucial role in its development. A comprehensive analysis of genetic factors using MR will contribute to personalized strategies for understanding ED genetics and advancing treatment options.

Materials and methods

eQTL data and single cell data collection

The Genotype-Tissue Expression (GTEx) project is an essential resource that collects tissue samples from various healthy individuals, including organs such as the heart, liver, kidney, lung, and brain, among others [13]. With contributions from thousands of donors, GTEx provides comprehensive Expression Quantitative Trait Loci (eQTL) data, helping to clarify the relationship between genotypes and gene expression levels. Our analysis focuses on the GTEx V8 whole blood eQTL summary statistics ($P < 1 \times 10^{-5}$) for Mendelian randomization (MR) analysis. Single-cell data were sourced from the public GEO dataset GSE206528 [14], which includes three standard tissue samples from tumor margins of cancer resections, all from patients reporting normal erections and morning erections. Additionally, five ED CC tissue samples were collected from biopsies of implanted penile prostheses. All ED patients in this study were diagnosed with organic ED, confirmed by nocturnal penile tumescence and intracavernous penile injection testing, rather than psychogenic ED.

MR analysis

We employed a pooled data Mendelian randomization (MR) approach to investigate whether the effects of single nucleotide polymorphisms (SNPs) on phenotype are mediated by gene expression. Pooled data from genome-wide association studies (GWAS) and expression quantitative trait loci (eQTL) studies were used to explore the relationship between gene expression and erectile dysfunction (ED). Additionally, we conducted the Heterogeneity in Dependent Instruments (HEIDI) test to evaluate whether the observed associations were confounded by linkage disequilibrium. An AP_HEIDI value of less than 0.05 suggests that the observed association may be driven by two independent genetic variants in linkage disequilibrium. A statistically significant association was indicated by an AP_MR value of less than 0.05. All analyses were performed using MR software tool version 1.3.1 [15].

Functional enrichment and pathway enrichment analysis

Gene Ontology (GO) analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis are two distinct bioinformatics approaches used to analyze and interpret biological data. GO analysis primarily focuses on the functions of individual genes, while KEGG analysis examines the interactions between genes within an organism's biological systems. Both GO and KEGG analyses were conducted using the R package clusterProfiler, and the results of the enrichment analysis were visualized. A significance threshold of $P < 0.05$ was applied.

PPI analysis

Following the Mendelian randomization (MR) analyses, protein-protein interaction (PPI) analyses were conducted for each of the three diseases. PPI refers to the physical or chemical interactions between different proteins, which can induce structural changes that may influence their function. The PPI analyses were performed using the online STRING database (string-db.org), with a confidence threshold of 0.15 to limit the number of target genes and ensure key genes were not overlooked. To validate the key genes, topological analysis methods, particularly the degree algorithm, were applied. The CytoHubba plugin integrated into Cytoscape 3.9.1 (University of California, San Diego) was used to analyze the topology of the PPI network and identify key nodes.

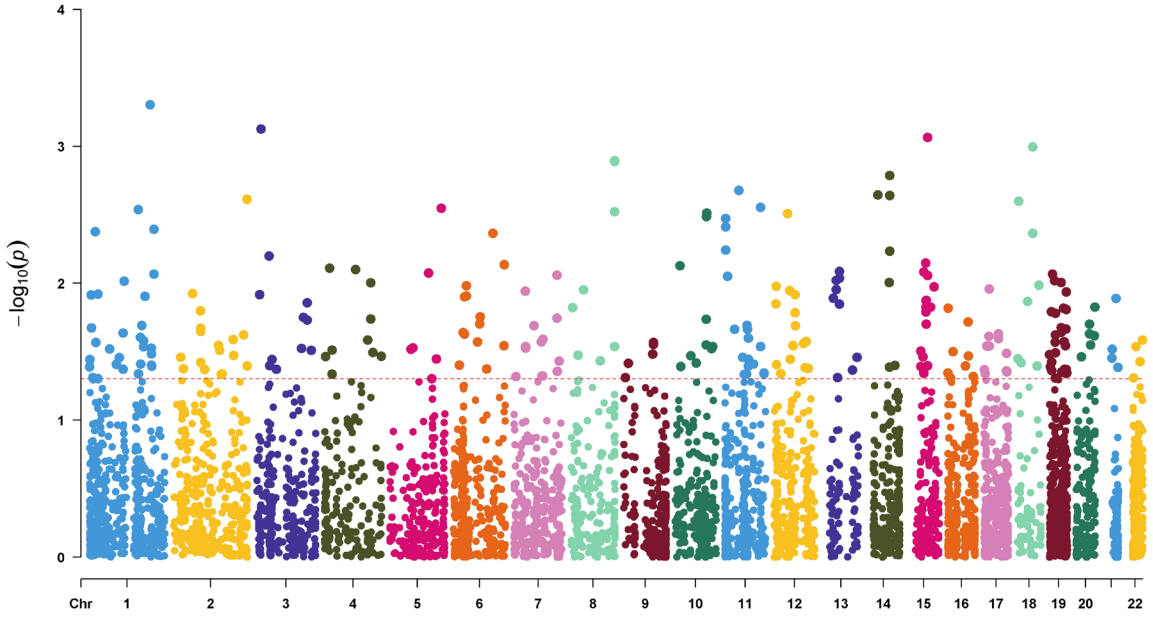

Figure 1. Manhattan plot of genes associated with erectile dysfunction analyzed by Mendelian randomization. The horizontal axis represents chromosome numbers, while the vertical axis represents the *P*-value of gene associations with ED. Red dots indicate disease-related target genes.

Genotype analysis and screening

The analysis and selection of genetic loci are based on two approaches in conjunction with Mendelian randomization (MR) analysis: (1) Selection of key loci in the disease: MR analysis identifies genetic loci that meet the criteria of FDR < 0.05 and HEIDI_P > 0.05. These loci are considered to influence the disease at the genetic level. (2) Single-cell sequencing analysis of gene expression at relevant loci in different cells: This method examines the changes in cell ratios within the ED group and analyzes their expression patterns through single-cell sequencing. This approach provides valuable insights that can inform drug design [16].

Statistical analysis

Statistical analyses were conducted using Mendelian randomization (MR) to investigate whether the effect of single nucleotide polymorphisms (SNPs) on phenotype is mediated by gene expression. We analyzed pooled data from genome-wide association studies (GWAS) and expression quantitative trait loci (eQTL) studies to explore the association between gene expression and erectile dysfunction (ED). The Heterogeneity of Dependent Instruments (HEIDI) test was also employed to evaluate whether association effects might confound the observed relationships. Disease-associated genes were identified using the criteria of *p*-values < 0.01 and HEIDI > 0.01. Single-cell analyses were performed using Principal Component Analysis (PCA) to reduce the dimensionality of the original dataset, followed by Unified Method of Apparent Approximation and Projection (UMAP) to map the high-dimensional data into a low-dimensional space for visualization and analysis. All statistical procedures were performed using R software (version 4.3.1).

Result

Screening of genes associated with ED

MR analysis produced a Manhattan plot of genes associated with erectile dysfunction (ED) (**Figure 1**), where the x-axis represents chromosome numbering and the y-axis represents the significance of each gene's association with ED, expressed as the negative logarithmic (decimal) value of the *p*-value (-log10(p)). Red dots on the plot highlight the disease-associated targets. To determine statistical significance, a *p*-value threshold of 0.05 was set, with genes having *p*-values below this threshold considered significantly associated with the disease. Additionally, to ensure consistency and minimize the likelihood of spurious results, gene heterogeneity was assessed. A heterogeneity

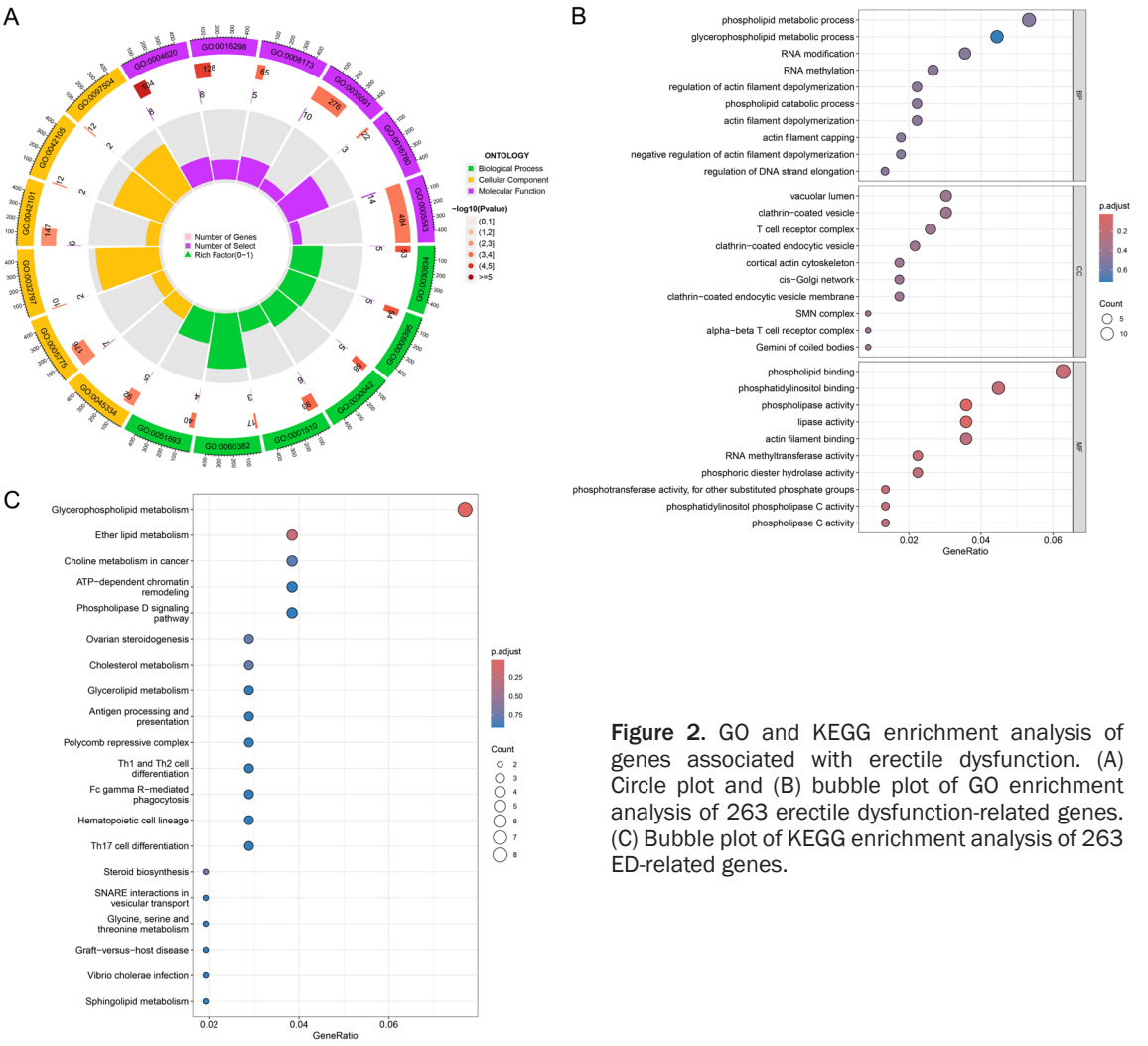

Figure 2. GO and KEGG enrichment analysis of genes associated with erectile dysfunction. (A) Circle plot and (B) bubble plot of GO enrichment analysis of 263 erectile dysfunction-related genes. (C) Bubble plot of KEGG enrichment analysis of 263 ED-related genes.

P-value greater than 0.05 indicates no significant inconsistency between the analyzed genes. Ultimately, 263 genes were identified as being associated with erectile dysfunction.

Enrichment analysis of genes associated with ED

To further investigate the impact of genes associated with erectile dysfunction (ED), we performed Gene Ontology (GO) enrichment analyses on the 263 ED-related genes. In **Figure 2A**, different colours represent various GO categories: biological processes (green), cellular components (yellow), and molecular functions (purple). The size and shade of each region indicate the degree of gene enrichment and statistical significance within that functional category. **Figure 2B** presents a bubble plot of these enrichment results, with the gene ratio shown on the x-axis and different GO terms on the y-axis. The size of the bubbles reflects the number of enriched genes, while the depth of the colour represents the *p*-value, with darker colours corresponding to lower *p*-values and greater statistical significance. Notably, several GO terms in **Figure 2B** are marked with larger, darker bubbles, indicating high gene enrichment and statistically significant associations with ED. Specifically, we observed significant enrichment of genes in pathways related to phospholipids, RNA, actin filaments, and immune mechanisms. The terms 'phospholipid metabolic processes', 'glycerophospholipid metabolic processes', and 'phospholipid catabolic processes' suggest that phospholipid pathways and muscle activity are involved in the pathological processes underlying ED. In the cellular component category, a significant number of genes were associated with structures such as

the 'T cell receptor complex', 'α-β T cell receptor complex', and 'vesicular lumen', indicating that ED-related genes play a critical role in cell structure and subcellular localisation.

In terms of molecular functions, we observed enrichment related to 'phospholipid binding', 'phosphatidylinositol binding', and 'phospholipase activity'. Notably, the enrichment analysis in the Biological Processes (BP) section of **Figure 2B** reveals that ED-related genes exhibit the highest enrichment in two molecular functions: phospholipid binding and phospholipase activity (represented by large bubbles). These genes show the highest gene ratios (around 0.05) and the most significant correlations (indicated by red bubbles). This suggests that the proteins encoded by these genes may be involved in crucial molecular interactions and biochemical processes.

We then extended our investigation to the enrichment of ED-associated genes in specific pathways and biological processes using KEGG (Kyoto Encyclopedia of Genes and Genomes) enrichment analysis. This approach helps to explore how important genes contribute to ED by influencing key pathways and biological processes. **Figure 2C** shows a bubble plot of KEGG enrichment analysis, revealing that ED-related genes were primarily enriched in signaling pathways and biological processes such as glycerophospholipid metabolism, ether lipid metabolism, choline metabolism in cancer, and the phospholipase D signaling pathway. Among these, glycerophospholipid metabolism displayed the highest gene enrichment, with significant gene ratios and strong correlations. This suggests that glycerophospholipids may play an essential role in the pathogenesis of ED, potentially involving the regulation of lipid levels.

PPI combined with MR results to further search for disease-associated genes

As shown in **Figure 3A**, protein-protein interaction (PPI) network analysis reveals that proteins such as CEPT1, CHPT1, and PLD2 exhibit larger nodes and darker colours, indicating extensive interactions with other proteins. These proteins have a high density of network connections, suggesting that they play crucial roles in biological processes and may act as key regulatory factors in the development of erectile dysfunction (ED).

Subsequently, we selected 24 genes associated with ED that exhibited high degree values for forest mapping and analysis.The results, presented in **Figure 3B**, show the odds ratio (OR) value, which indicates the likelihood of ED occurrence when a gene is present compared to when it is absent. An OR value greater than 1 suggests an increased risk of ED in the presence of the gene, whereas an OR value less than 1 indicates a decreased risk. The p_MR value reflects the statistical significance of the association between gene expression and ED, with a *p*-value of less than 0.05 considered statistically significant. As illustrated in **Figure 3B**, two genes were found to influence the risk of developing ED, as indicated by their OR values, aligning with the goal of this study to identify genes that contribute to ED development. The two genes with 95% confidence intervals (CIs) greater than 1 or less than 1 (TRIP10 and SLC41A1) were selected for further analysis. Among these, TRIP10 had the highest degree value and the most significant effect on ED (OR 0.58, 95% CI -0.27 to 0.93), indicating that TRIP10 is most strongly associated with a reduced risk of ED in this gene group.

The gene expression association analysis, depicted in the dot plot at the top of **Figure 3B**, illustrates the correlation between individual single nucleotide polymorphisms (SNPs) and TRIP10 gene expression. Higher dots in the graph indicate a stronger association between specific SNPs and TRIP10 expression levels. The scatter plot at the bottom of **Figure 3B** shows the effect of specific SNPs as expression quantitative trait loci (eQTLs) on TRIP10 gene expression. In this plot, the vertical position of the dots reflects the level of statistical significance, with higher positions indicating greater significance. **Figure 3B** further reveals that TRIP10 is located within the 204.4-204.5 Mb interval on chromosome 7. To investigate the effects of specific eQTLs on TRIP10 gene expression and ED (as assessed by GWAS effect size), we analyzed the eQTL and GWAS effect sizes of each cis-eQTL, as well as the top cis-eQTL for TRIP10. As shown in **Figure 3C**, the eQTL effect size and GWAS effect size of the top cis-eQTL were significantly positive, suggesting that this variant may confer a protective effect against ED by enhancing TRIP10 expression. Moreover, the top cis-eQTL (**Figure 3D**) lies precisely on the dashed line with a slope of 1, indicating that its effect on TRIP10 gene

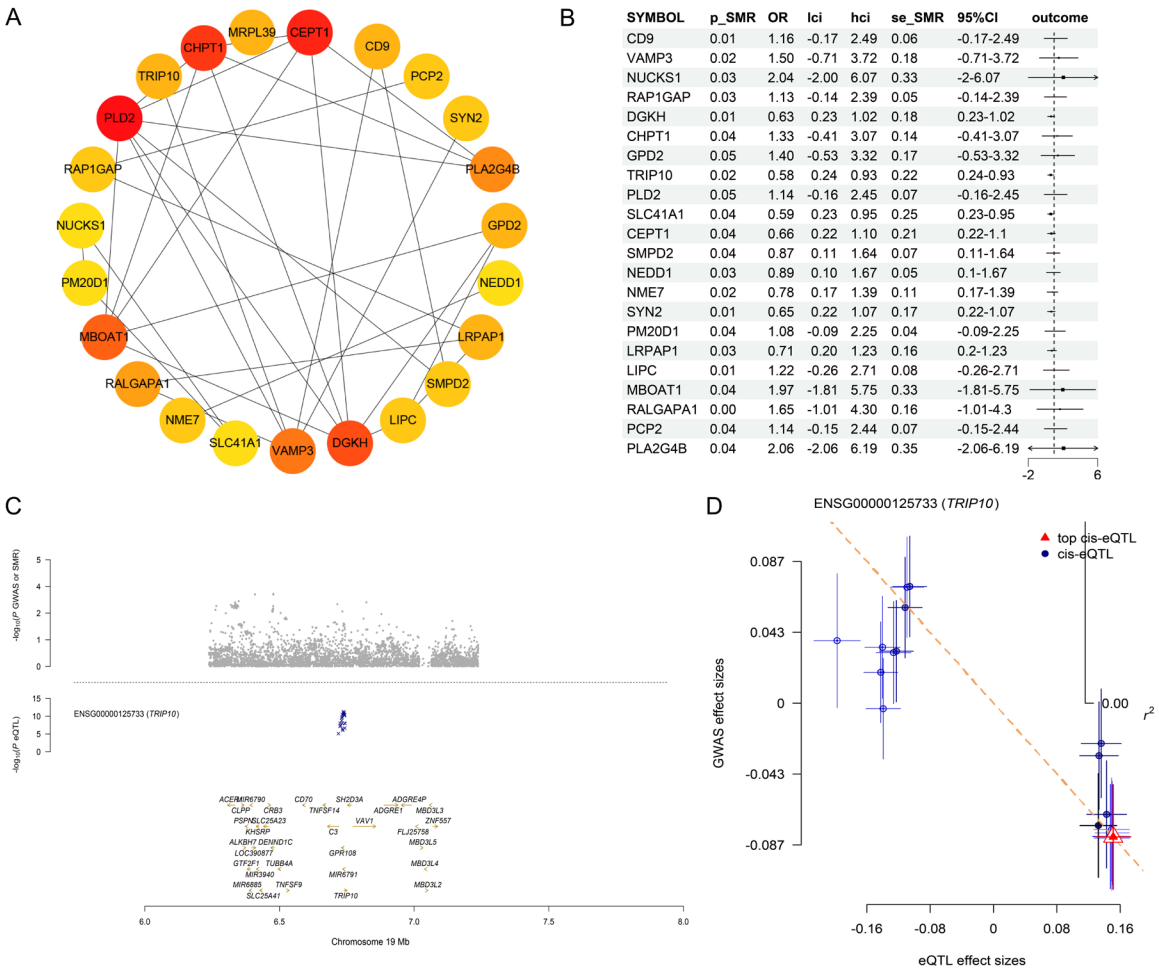

Figure 3. PPI combined with Mendelian randomization (MR) analysis of erectile dysfunction-associated genes. A. PPI network map of genes associated with erectile dysfunction (ED). B. Forest plot obtained by selecting high -degree nodes from the PPI network for analysis. C. Localized chromosomal regions, including the TRIP10 gene, as part of the GWAS and MR analyses. The upper part shows a scatterplot of SNPs indicating the strength of association with ED, while the lower part displays the -log10 *p*-value from the eQTL analysis, indicating the strength of the association between each SNP and TRIP10 gene expression. D. Distribution of GWAS and eQTL effect sizes in the TRIP10 gene, with dotted lines representing linear trends and red triangles marking sites with the largest eQTL effect.

expression (eQTL effect size) is consistent with its effect on ED traits (GWAS effect size).

Single-cell sequencing analysis

A comprehensive gene expression analysis in cells associated with erectile dysfunction (ED) was conducted using single-cell sequencing technology. As shown in **Figure 4A**, the cells from the entire sample were successfully classified into 25 distinct clusters, which were clearly mapped in two-dimensional space using Uniform Manifold Approximation and Projection (UMAP). The annotation of these clusters was achieved by analyzing the expression of marker genes across the 25 clusters, as illustrated in **Figure 4B** and **4C**. Subsequently, we examined the spatial distribution of five major cell types (endothelial cells, monocytes, fibroblasts, T cells, smooth muscle cells, and tissue stem cells) in both the ED group and the healthy control group. The UMAP method was used for this analysis (see **Figure 5A** and **5B**). In the ED group, the distribution of endothelial cells was significantly more widespread than in the normal group, indicating an increased number of phenotypic changes in these cells associated with ED. Additionally, the distribution of smooth muscle cells was more dispersed in the ED group, which may be linked to the pathophysiological processes of ED, such as alterations in

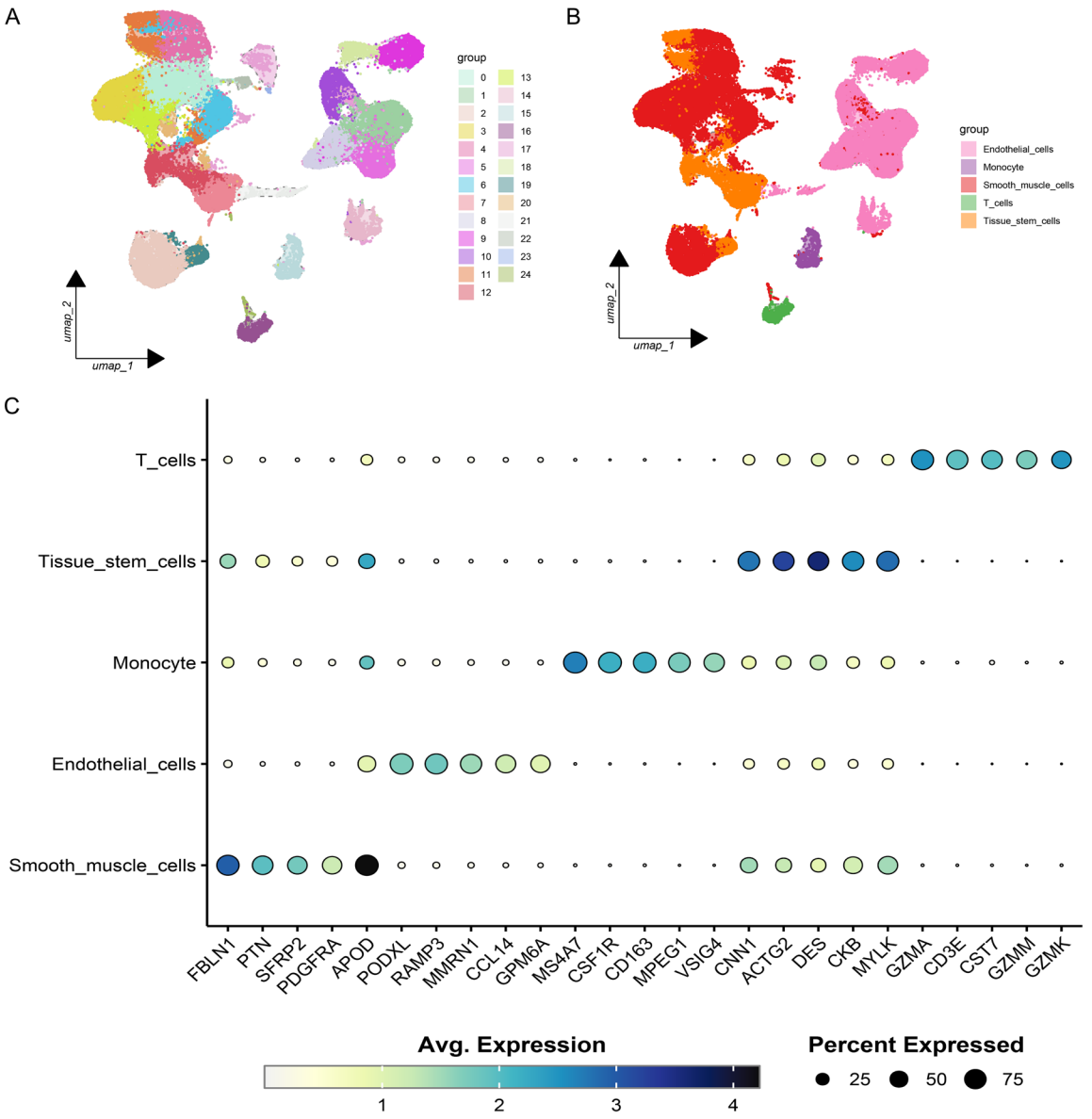

Figure 4. Ectile dysfunction (ED) related single-cell sequencing analysis. A. UMAP plot of multidimensional clustering results for cells in single-cell sequencing data. B. Annotated UMAP plots for 25 clusters. C. Dot plots of single-cell sequencing data showing expression levels and expression percentages of selected genes in different cell types.

vascular smooth muscle function. Conversely, the distribution of monocytes showed minimal differences between the two groups, although they were slightly more compact in the normal group. T cells were present in both groups, but their distribution was more scattered in the ED group, potentially reflecting altered immune responses or changes in the local microenvironment associated with ED.

A comparison of cell content between the ED group and the control group (**Figure 5C**) reveals that the ED group has a relatively higher proportion of endothelial cells, smooth muscle cells, T cells, and monocytes, with values exceeding 50%. In contrast, the control group predominantly consists of 100% chondrocytes. Additionally, the proportion of tissue stem cells in the ED group shows an inverse correlation with the other cell types, being significantly lower than in the control group.

To further investigate the function of TRIP10 in the context of erectile dysfunction (ED), we

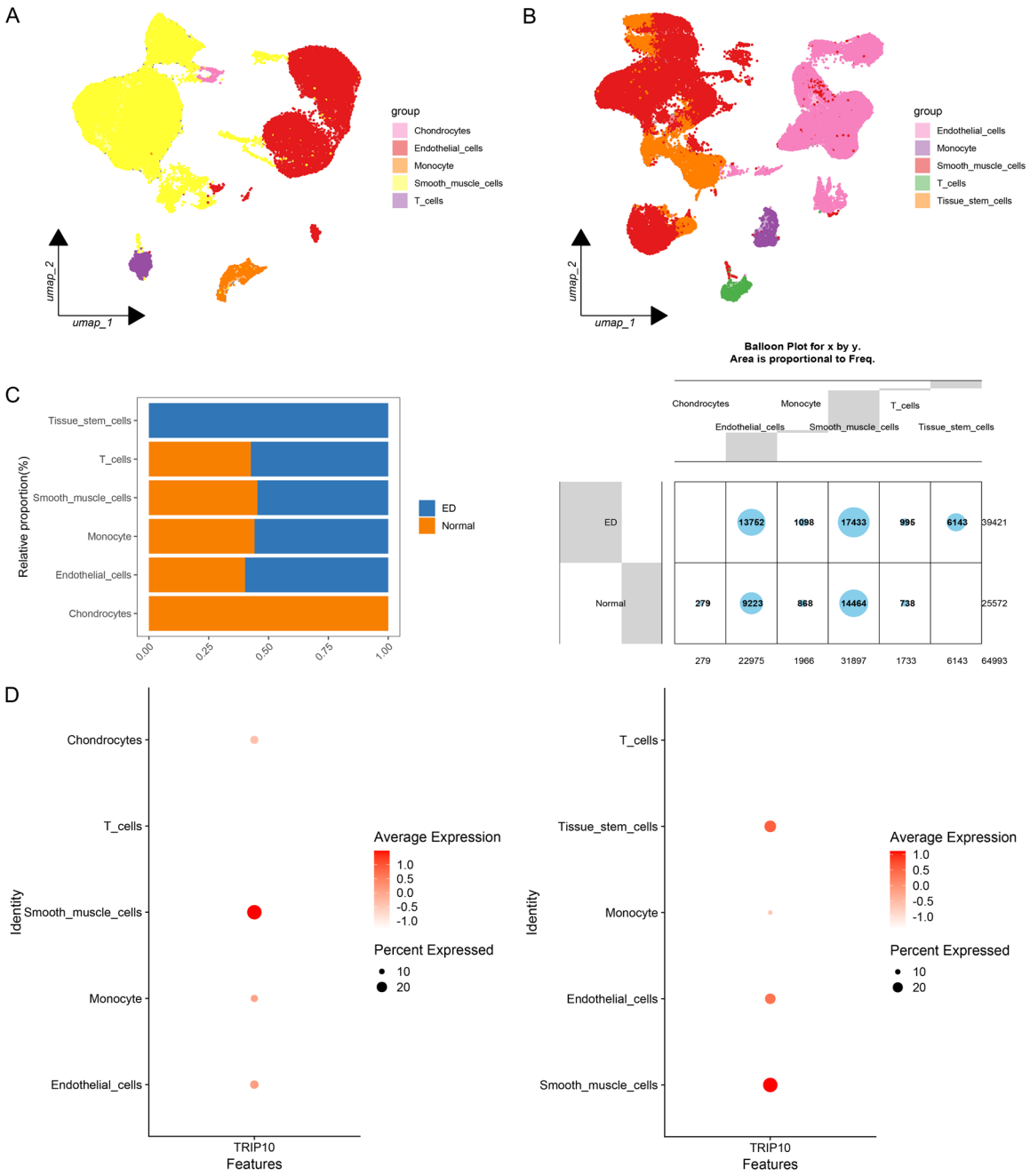

Figure 5. Cell ratio analysis and expression of disease-associated genes. A. UMAP plot of cell distribution differences between the erectile dysfunction (ED) group and the normal group. B. UMAP plot of cell distribution differences between the ED groups. C. Histogram of the proportions of the five cell types and details of the proportions table. D. A dot plot of the expression of selected genes in six different cell types in the ED patient group (right) versus the normal healthy group (left).

examined the expression of the ED-related genes identified earlier across six different cell types. As shown in **Figure 5D**, the expression of TRIP10 was significantly upregulated in endothelial cells and tissue stem cells within the ED group, with a notably higher average expression in endothelial cells. The expression levels of TRIP10 in the remaining four cell types were comparable to those observed in the normal group, suggesting a specific role for TRIP10 in endothelial cells and tissue stem cells in the pathophysiology of ED.

Discussion

Erectile dysfunction (ED) is a prevalent condition that significantly impacts a man's sexual well-being and overall physical and mental health [1, 2]. ED has been attributed to various causes, including psychological, endocrine, vascular, and neurological factors [1-3]. However, increasing evidence suggests that genetic factors also play a crucial role in the development of ED [6-9]. In this study, by integrating genome-wide association study (GWAS) data and gene expression databases, and performing Mendelian randomization (MR) analysis, we identified a total of 263 potential candidate genes associated with ED.

These findings offer deeper insights into the pathogenesis of ED and provide a foundation for future functional studies and the development of potential therapeutic targets. Notably, we observed a clear association between alterations in gene expression and susceptibility to ED, supporting the hypothesis that these genes are integral to the disease's development. This study provides valuable opportunities to further explore the complex genetic underpinnings of ED and paves the way for targeted interventions aimed at mitigating its impact.

In this study, GO enrichment analysis revealed that the identified genes are involved in both the physiological and pathological processes of erectile dysfunction (ED) through specific biological processes, cellular components, and molecular functions. First, we found that processes such as "phospholipid metabolism", "glycerophospholipid metabolism", and "phospholipid degradation metabolism" are significantly associated with ED. These processes are involved in the regulation of lipids and phospholipids, which can directly impact blood flow and vascular health, thereby affecting erectile function. For instance, parameters such as blood flow velocity and vessel diameter have been established as valid measures for assessing arterial erectile dysfunction. Additionally, the regulation of muscle hypertrophy plays a pivotal role in penile tissue dynamics, particularly the mass of trabecular smooth muscle, which is crucial for the veno-occlusive mechanism needed to maintain an erection [17]. An imbalance in the mechanisms controlling muscle growth could disrupt the structural and functional integrity of penile tissue, thereby impairing erectile function [18]. The analysis also highlighted significant enrichment in the cellular component category, particularly in relation to the "T cell receptor complex", "alpha-beta T cell receptor complex", and "vacuolar lumen". This suggests that the genes associated with ED may play a crucial role in immune regulation at the cellular level, influencing gene expression in response to physiological demands. Such regulatory mechanisms are essential for maintaining cellular function and may contribute to the development of ED by affecting cellular health and responses.

From a molecular functional perspective, our study identified significant enrichment of molecular functions such as 'phospholipid binding', 'phosphatidylinositol binding', and 'phospholipase activity' in the context of erectile dysfunction (ED). These molecular functions are involved in energy transfer and molecular signaling, both of which are critical for cellular signaling pathways. Lipid metabolism, in particular, plays a pivotal role in the pathophysiology of ED [16, 17]. Normal erectile function depends on the health of the vascular endothelium, and disturbances in lipid metabolism - especially hyperlipidemia - often lead to endothelial dysfunction, which is a key mechanism underlying ED [18]. Abnormal lipid metabolism contributes to the development of atherosclerosis, a condition that affects the blood supply to the penile arteries and corpora cavernosa. Atherosclerosis leads to narrowing of the arteries and reduced arterial elasticity, directly impairing the blood flow necessary for achieving and maintaining an erection. Furthermore, chronic inflammation and oxidative stress induced by hyperlipidemia accelerate endothelial cell damage, thereby reducing the production and release of nitric oxide (NO), a critical molecule for maintaining erectile function [19, 20]. This combination of effects exacerbates the impairment of erectile function in ED patients.

Therefore, understanding how lipid regulators control these processes offers promising avenues for developing novel treatments for ED. The KEGG enrichment analysis of ED-related genes further supported these findings, showing significant enrichment in several signaling pathways and biological processes, including glycerophospholipid metabolism, ether lipid metabolism, and choline metabolism. This aligns with the earlier GO enrichment analysis,

reinforcing the critical role of lipid metabolism abnormalities in the development and progression of ED.

In this study, we identified several key nodal proteins involved in the pathogenesis of erectile dysfunction (ED) through protein-protein interaction (PPI) network analysis, including CEPT1, CHPT1, and PLD2. The high linkage density of these proteins suggests that they may play critical regulatory roles in biological processes and could be key factors in the development of ED. However, forest plot analysis of the high -scoring ED-related genes revealed that these proteins did not significantly promote the ED process. Notably, TRIP10 stood out due to its high degree value in the PPI network and its strong correlation with an increased risk of ED. This suggests that TRIP10 may play a central role in the development of ED.

Further analysis through expression quantitative locus (eQTL) showed that specific single nucleotide polymorphisms (SNPs) in the TRIP10 gene significantly affected its expression, further confirming the gene's pivotal role in regulating ED-related biological processes. The effect size of the largest cis -eQTL and GWAS effect size analyses suggested that this variant could reduce the risk of ED by increasing TRIP10 expression. The TRIP10 gene, located on human chromosome 7q31.1 and also known as CIP4 (Cdc42 -interacting protein 4), plays a crucial role in cytoskeletal regulation and cellular signaling [21]. The protein encoded by TRIP10 primarily interacts with the GTPase Cdc42 and regulates cell membrane morphology, endocytosis, vesicle trafficking, and cell migration. Additionally, TRIP10 is involved in insulin signaling and lipid metabolism, particularly in regulating lipid droplet formation and degradation in adipocytes [23]. Its expression is found in various cell types and is associated with dynamic changes in cell structure, endocrine signaling, and tumor-related behaviors [24]. Studies have also suggested that TRIP10's interaction with the tumor suppressor protein p53 and the E3 ubiquitin ligase MDM2 may contribute to carcinogenesis by influencing cell proliferation and apoptosis [25, 26]. Furthermore, TRIP10's regulation of the cytoskeleton in the tumor microenvironment may promote cancer progression by affecting cell motility and invasiveness. Single-cell sequencing analysis of TRIP10 gene expression in five distinct cell types confirmed its involvement in ED. Notably, TRIP10 gene expression was significantly upregulated in endothelial cells and tissue stem cells in the ED group. These findings suggest that TRIP10 may help reduce the risk of ED by regulating lipid metabolism or modulating lipid-related pathways. Further investigation into how TRIP10, particularly its regulatory effects on lipid metabolism, contributes to the pathophysiology of ED could provide novel insights into the molecular mechanisms underlying ED. Such studies may identify new therapeutic targets within the lipid pathway, offering potential avenues for developing more effective treatments for ED.

This study has the following limitations: (1) The reliance on bioinformatics analysis and transcriptomic data from public databases may limit the comprehensiveness of the data and the depth of experimental validation. (2) Although our analyses highlighted TRIP10 as a potential key target for ED, the specific mechanism by which TRIP10 influences ED was not fully elucidated. (3) This study was primarily based on data analysis, and no clinical trial or patient cohort was involved. While the findings provide promising leads, clinical validation in a larger patient population is essential to confirm the role of TRIP10 in ED. Future studies should focus on validating the expression patterns of TRIP10 and assess its potential as a biomarker for ED diagnosis or as a therapeutic target in clinical settings.

Conclusion

Through MR analysis, we successfully identified 263 genes associated with erectile dysfunction (ED). Our findings highlight the significant role of lipid pathways in the pathophysiology of ED, suggesting that these pathways could serve as potential new targets for ED treatment. The TRIP10 gene may influence the pathophysiology of ED through its role in lipid control and apoptosis.

Acknowledgements

This work was supported by the Xinlicheng Jinyi Hospital of Chongqing and the Hechuan Hongren Hospital of Chongqing.

Disclosure of conflict of interest

None.

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