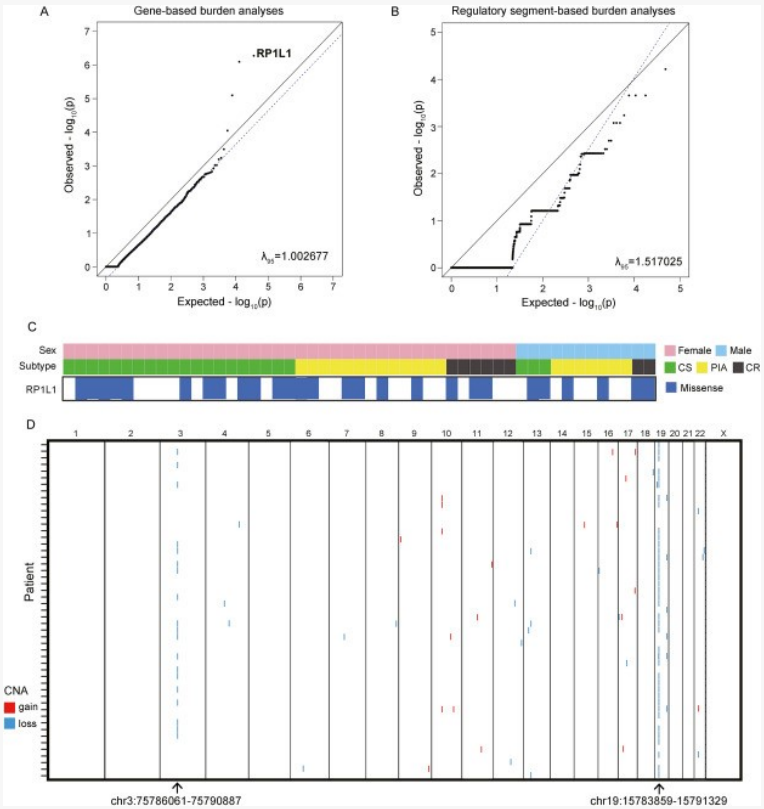
Comprehensive Genomic and Epigenomic Characterization of Iridocorneal Endothelial Syndrome

New Study Unravels The Underlying Mechanisms Of ICE Syndrome

CHINA, March 28, 2025 / EINPresswire.com/ -- Iridocorneal endothelial (ICE) syndrome is a rare, irreversibly blinding ocular disorder with an unknown etiology. Lack of targeted effective drugs, inadequate disease prognosis, and high relapse rates post-surgery are the current challenges of ICE. Therefore, understanding its genomic and epigenomic landscape could aid in developing etiology-based therapies.

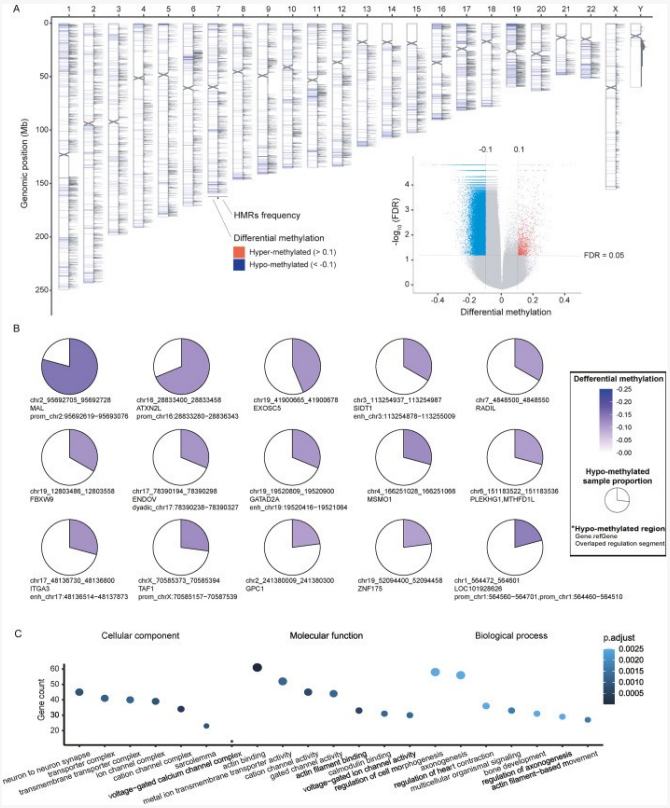


(A) Gene-based burden test of rare coding-altering mutations (max gnomAD AF ≤ 0.01). (B) Mutation burden analysis of rare pathogenic noncoding mutations (max gnomAD AF ≤ 0.001; predicted deleterious by all the 3 algorithms: GERP++, GWAVA, and CADD). (C) G

This research, published in the Genes & Diseases journal by a team from Sun Yat-sen University, Guangzhou Medical University, Fujian Medical University, Shandong First Medical University, Huazhong University of Science and Technology, Nanchang University, Nanjing Medical University, China Three Gorges University, Hebei Medical University, Central South University, Xiamen University, Zhejiang University, and the Macau University of Science and Technology, provides a comprehensive genomic and epigenomic landscape of ICE syndrome, with the potential to inform the development of etiology-based therapies.

The researchers recruited 99 ICE patients and performed whole-genome sequencing (WGS) on 51 and genome-wide DNA methylation profiling on 48. Mutational burden testing was conducted to compare the ICE cohort with control groups, revealing a significant association between the RP1L1 (retinitis pigmentosa 1-like 1) gene and ICE syndrome.

The researchers then investigated copy number variation (CNV) in ICE syndrome and identified 41 regions with significant CNVs, including three regions at chr19:15783859-15791329 (hg19), chr3:75786061-75790887 (hg19) and chr19: 55276166-55295820 (hg19), showing copy number loss in 39, 19 and 5 patients, respectively. Additionally, this study indicated that copy number loss of genes CYP4F12, ZNF717 and KIR2DL1 may induce dysfunction of corneal endothelial cells and viral infection-induced pathological conversion of corneal endothelial cells in ICE syndrome.



(A) Differentially methylated region (DMR) and hypomethylated region (HMR) frequency in ICE syndrome. The ideogram shows, for each chromosome, from left to right: DMR comparing ICE syndrome (n = 48) to normal Chinese (n = 45), and HMR frequency in 100-bp

This study also identified 2,717 differentially methylated regions (DMRs), with hypomethylation prevalent in ICE syndrome (91.9% of DMRs). Among these, 45 recurrent hypomethylated regions (HMRs) in more than 10% of ICE patients showed differential methylation compared to normal controls. Interestingly, the researchers found that Chr2_95692705_95692728 (hg19), the most frequently identified HMR in ICE patients, lies on the promotor of gene MAL. This indicates that promoter hypomethylation and elevated expression of MAL may contribute to epithelioid hyperplasia of corneal endothelial cells in ICE syndrome.

The key findings of this study include the identification of pathogenic genes in patients with ICE syndrome that are related to ocular diseases, viral immunity, and epithelioid hyperplasia. These findings suggest that viral infections may trigger the pathological transformation of corneal endothelial cells based on these genetic and epigenetic susceptibilities, leading to the development of ICE syndrome. In conclusion, this study represents the first comprehensive genomic and epigenomic analysis of ICE syndrome using unbiased next-generation sequencing.

Reference

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