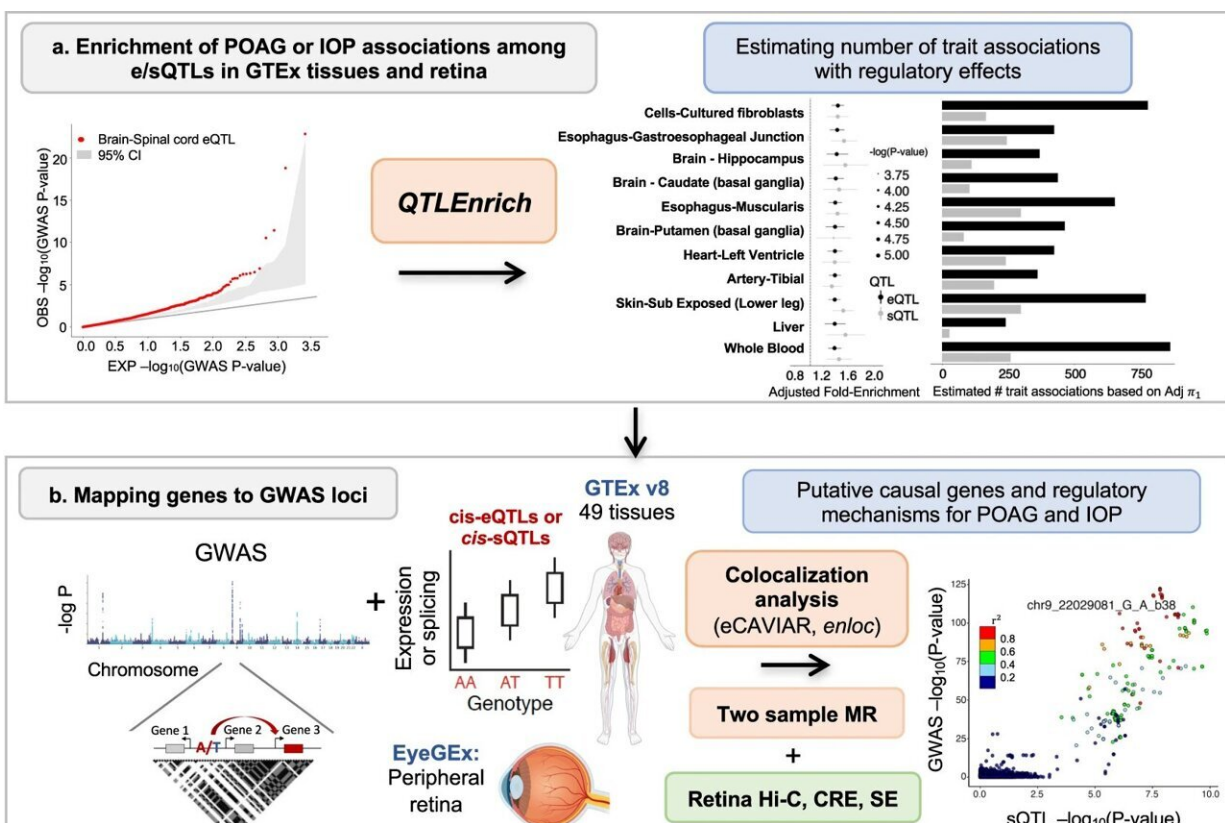


Researchers identify genes and cell types that may have causal role in primary open-angle glaucoma formation

February 16 2024, by Ryan Jaslow



Analysis workflow from POAG and IOP GWAS to causal regulatory mechanisms, genes, pathways, and cell types. **a** POAG and IOP associations genome-wide (known and modest associations) were tested for enrichment among expression and splicing quantitative trait loci (e/sQTLs) in GTEx tissues and retina compared to permuted null sets of variants matched on confounding factors, using *QTLEnrich* (one-sided). In cases where enrichment was found, the

lower bound number of e/sQTLs in a given tissue, likely to be true trait associations, was estimated using an empirically derived, true positive rate $((\pi_1)(\{\pi\}_{-1}))$ approach. **b** Putative causal genes were prioritized per known POAG and IOP genome-wide association study (GWAS) locus by applying two colocalization methods (eCAVIAR, *enloc*) to all e/sQTLs from 49 GTEx tissues and retina eQTLs that overlapped each locus, followed by two-sample Mendelian Randomization (MR). Overlap of the colocalizing GWAS loci and e/sQTLs with Hi-C (3D chromosome conformation capture), *cis*-regulatory element (CRE), and super-enhancer (SE) regions from the human retina was utilized to prioritize causal genes further. The human and eye images were created with BioRender.com. **c** All target genes of significantly colocalizing e/sQTLs (e/sGenes) or cell type-specific genes per trait were tested for enrichment in signaling and metabolic pathways (Reactome, KEGG), gene ontologies, and mouse phenotype ontologies using *GeneEnrich* (one-sided). The POAG cross-ancestry GWAS meta-analysis Manhattan plot was generated using QMplot (<https://github.com/ShujiaHuang/qmplot>). **d** Significantly colocalizing e/sGenes were tested for enrichment in specific cell types in single-nucleus RNA-seq data of glaucoma-relevant eye tissues, using ECLIPSER (one-sided). Cell type-specific genes were defined with cell type fold-change>1.3 and FDR

Citation: Researchers identify genes and cell types that may have causal role in primary open-angle glaucoma formation (2024, February 16) retrieved 13 May 2024 from <https://medicalxpress.com/news/2024-02-genes-cell-causal-role-primary.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.