Abstract Form

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Project Title:	A Novel Method to Visualize Evolutionary Tradeoffs Underlying Vulnerability to the Development of Cataracts

Research Category (please check one):

☒	**Original Research**	☐	**Clinical Vignette**	☐	**Quality Improvement**	☐	**Medical Education Innovation**

Introduction:
Cataracts are the leading cause of blindness in the world and are associated with a lower quality of life and decreased life expectancy. There are few evolutionary explanations for our vulnerability to cataract development. Natural selection produces biologically beneficial phenotypes and vulnerability to disease may be a byproduct of this selection. We created a novel methodology to identify and quantify the biologically beneficial processes significantly linked to cataract development.

Methods:
We curated a gene set for cataracts from LifeMap Sciences' *MalaCards* (by the Weitzmann Institue of Science) and performed a gene enrichment analysis using *Gene Ontology,* a publicly available platform that identifies biological processes that contain/are enriched by the inputted cataract genes. We developed a novel index (*Smolens-Mazmanian Index*) to reorganize and rank the results, prioritizing the greatest percent overlapping of genes and the greatest number of overlapping genes to produce a relative score for each biological process. From the top 10 SMI-ranked biological processes, we compiled gene sets corresponding to each. We then ran the *Tidyr* Rpackage, to create a presence-absence matrix of the genes present in each biological process. We used *Flourish*, a publicly available platform to depict the overlapping sets of genes, to create an interactive visualization depicting the biological processes most congruent with cataract pathology

Results:
The interactive visualization (https://public.flourish.studio/story/2164103/) allows users to identify biological processes with the highest overlap with cataract development. Our findings suggest that selection for the biological processes: lens development in camera-type eye GO:0002088 (SMI: 637), lens fiber cell differentiation GO:0070306 (SMI: 279), and sensory perception of light stimulus GO:0050953 (SMI: 130), have contributed to the evolved vulnerability to cataracts as evolutionary trade-offs.

Conclusion:
The methodology we created positions vulnerability to cataracts as an evolutionary byproduct of selection for critical biological processes including lens development, lens fiber cell differentiation, and sensory perception. The rapid emergence of publicly available bioinformatics platforms creates an opportunity to leverage comparative genomics and evolutionary modeling to strengthen our understanding of high-impact pathology such as cataracts. Identifying the biologically beneficial pathways underlying vulnerability to disease holds promise to advance clinical research by strengthening our ability to identify therapeutic targets and reduce adverse clinical effects.