عنوان مقاله:

Another approach for identification of gene interactions relevant to pathogenesis of complex disorders

محل انتشار:

هشتمین همایش تحقیقات چشم پزشکی و علوم بینایی ایران (سال: 1397)

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خلاصه مقاله:

Genetic analyses are useful for deciphering molecular pathways and components therein involved in the etiology of complex diseases. Most importantly, bioinformatics approaches have created powerful publically available software that allow making optimal use of the vast amount of data, often genetic in nature, available in the literature and in the internet. Glaucoma is a complex disease and the leading cause of irreversible blindness worldwide. Although great advances have been made, knowledge of the etiology of glaucoma remains incomplete. Here, we made extensive use of data and various softwares for identification of genes involved in manifestation of glaucoma and potential interactions among the genes.Methods: The target tissue studied was the trabecular meshwork (TM) and regulatory molecules investigated were the transcription factors PITX2 and FOXC1 and also miR-204, NFKB, and MEIS2. The TM is a tissue within the anterior chamber of the eye that is very relevant to glaucoma pathology. PITX2 and FOXC1 are transcription factors, and mutations in the genes that encode these proteins cause Axenfeld-Rieger syndrome that is often accompanied with glaucoma. Micro-RNA mi-204, NFKB, and MEIS2 are also relevant to glaucoma pathology. TM transcription data was derived from whole genome microarray-based expression studies on TM cells in which PITX2 and FOXC1 were knocked down. Bioinformatics tools were used to identify PITX2 and FOXC1 binding sites in affected genes in order to predict direct effects of the transcription factors, and also to identify genes relevant to glaucoma and TM functions. Dual luciferase assays, real-time PCR, Western blot analysis, and flow cytometry in three cell types were performed to confirm results of in silico studies.Results: A complex gene regulatory network within TM was identified in which PITX2, FOXC1, and miR-204 are important components. The harmonized effects of these molecules are expected to affect processes including apoptosis and NFKB, NODAL, TGFB, and RHO pathways.Conclusion: The genetic/bioinformatic/wet lab approach used has enhanced understanding of gene regulatory interactions in the TM that are potentially relevant to glaucoma pathology. The vast amount of available in .silico data allows that the same approach can be applied to study of other complex disorders

کلمات کلیدی: