

Topology of the associative cytokine gene network in primary open-angle glaucoma

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Motivation and Aim: Primary open-angle glaucoma (POAG) is one of the leading causes of global irreversible blindness. Therefore, it remains a serious medical and social problem throughout the world [1]. There is an assumption that the predisposition to the development of glaucoma is due to polymorphism of the regulatory regions of coding genes that determine the individual level of production of cytokines, chemokines, and growth factors [2, 3]. The aim of our study was to conduct a comprehensive bioinformatics analysis of polymorphic regions of the cytokine network genes to identify the relationship between the features of the topology of this network with the development of POAG.

Methods and Algorithms: A genetic study was performed on 199 subjects, including 99 patients with POAG and 100 patients without glaucoma of similar gender and age as a comparison control group. Polymorphisms of the regulatory regions of 10 cytokine genes (*IL1B* -31 C/T, *IL4* -590 C/T, *IL6* -174 C/G, *IL8* -251 T/A, *IL10* -592 C/A, *IL10*-1082 A/G, *IL17A* -197 G/A, *MMP2*-1306 C/T, *MMP3*-1171 5A/6A, *MMP9*-1562 C/T) were examined. To graphically visualize the stable gene compositions of the cytokine network, we performed a computer simulation of the network interactions of various cytokine genotypes involved in the formation of susceptibility to POAG using the Cytoscape bioinformatics platform.

Results: Analysis of the topology of the associative gene network of cytokines allowed us to identify the main genes and main intergenic interactions that make the greatest contribution to the development of primary open-angle glaucoma. In our opinion, six polymorphisms (*MMP2*-1306CT, *IL17*-197GG, *IL1B*-31TT, *IL8*-251TA, *MMP9*-1562CC and *IL6*-174GC) can act as the main genes, which account for 80 % of all involved genes. These genes form the main nodes ("hubs") in the gene network, since they have the largest number of interactions with other genes. These polymorphisms form the main intergenic interactions, which account for 50 % of all interactions in the gene network.

Conclusion: The construction of gene networks of transcriptional regulation and their topological analysis makes it possible to build and study the structural and functional organization of gene-gene interactions in relation to the study of the pathogenesis of primary open-angle glaucoma for the subsequent development of approaches to personalized prevention and therapy.

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References

1. Tham Y.C., Li X., Wong T.Y., Quigley H.A., Aung T., Cheng C.Y. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014;121(11):2081-2090. doi: 10.1016/j.ophtha.2014.05.013.
2. Zhang Y.H., Xing Y.Q., Chen Z., Ma X.C., Lu Q. Association between interleukin-10 genetic polymorphisms and risk of primary open angle glaucoma in a Chinese Han population: a case-control study. *Intl J Ophthalmol*. 2019;12(10):1605-1611. doi: 10.18240/ijo.2019.10.13.
3. Shevchenko A.V., Prokof'ev V.F., Konenkov V.I., Chernykh V.V., Ermakova O.V., Trunov A.N. Analysis of IL1B (rs1143627), IL4 (rs2243250), IL6 (rs1800795), IL8 (rs4073), IL10 (rs1800896, rs1800872), IL17A (rs227593) cytokines genes polymorphism and its complex genotypes among Caucasian patients of Western Siberia with primary open-angle glaucoma. *Immunologiya*. 2021;42(3):211-221. doi: 10.33029/0206-4952-2021-42-3-211-221 (in Russian).