Introduction

Glaucoma, an anterior optic neuropathy, is the second major cause of irreversible blindness worldwide. It is characterized by optic nerve head changes and corresponding visual field loss.[1] Primary open-angle glaucoma (POAG; OMIM 137760) is the most prevalent subtype of glaucoma, usually displaying asymptomatic developments until the late stages of the disease. The prevalence of POAG is predicted to increase to 76.0 million by 2020 and to 111.8 million by 2040 all over the world owing to population aging.[2] POAG was subdivided into two forms according to onset age: juvenile open-angle glaucoma (JOAG) and adult-onset POAG. JOAG develops clinical manifestation between 3 and 35 years of age[3] while adult-onset POAG often shows symptoms after 40 years.[4] Due to the suboptimal sensitivity of current diagnostic ability, the diagnosis of POAG is usually made after irreversible visual damage has already occurred. Thus, the early diagnosis of POAG is urgently required.[5,6] Genetically, POAG is considered as a complex disease with a substantial fraction showing complicated inheritance patterns, while...
JOAG typically follows an autosomal dominant inheritance. Identification of novel mutations provides opportunities for the understanding of etiology, realizing presymptomatic diagnosis, and improving the prognosis of POAG.

Up to date, several loci have been identified associated with POAG. Among them, four genes, including trabecular meshwork (TM) inducible glucocorticoid response (myocilin [MYOC], OMIM 601652), optineurin (OMIM 602432), human dioxin-inducible cytochrome P450 (CYP1B1, OMIM: 601771), and WD repeat-containing protein 36 (OMIM 609669), have been identified to be primarily responsible for POAG. As the most frequently mutated gene in POAG families, MYOC locates at GLC1A (OMIM 601652) locus on chromosome 1q23 [1,8]. Therefore, in a newly identified Chinese family with POAG, we screened for mutations at GLC1A locus to localize mutations that might be responsible for this pedigree.

Methods

Subjects and clinical examination

This POAG pedigree spans five generations with 23 members recruited. No consanguineous marriage was found in individuals of family. Then, all individuals underwent thorough ophthalmologic examinations including visual acuity, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement, gonioscopy, fundoscopy, and perimeter. The 200 controls only with no reported family history of hereditary eye diseases and normal ophthalmic examination findings could be recruited. This study was approved by the Medical Ethics Committee of Anhui Medical University. All participants were informed of the details and all of the procedures, and each individual provided informed consent in accordance with the Declaration of Helsinki. In this study, the diagnostic of criteria was defined by a normal anterior chamber angle and two of the following symptoms: (1) IOP >21 mmHg (no IOP lowering therapy); (2) characteristic visual field defects; (3) glaucomatous optic nerve head changes (cup-disc [C/D] ratio >0.6 or notches); JOAG was diagnosed when patients’ age at the time of POAG diagnosis was younger than 35 years.

DNA extraction

Genomic DNA was extracted from peripheral blood according to the standard procedures using FlexiGene DNA kits (TIANGEN, Beijing, China). DNA samples were stored at −20°C until used. The 1% agarose gel electrophoresis was used to evaluate DNA integrity.

Exome sequencing

Exome sequencing was employed to identify the POAG-associated genes. We performed exome sequencing on DNA samples of the three family members (IV: 1, IV: 9, and V: 4) by Axeq Technology Inc., Seoul, Korea, and prepared each sequenced sample according to the protocols provided by the Illumina Inc., San Diego, USA. In brief, we fragmented one microgram of genomic DNA by nebulization, repaired the fragmented DNA, ligated an “A” to the 3’ end, ligated Illumina adapters to the fragments, and the sample was size selected aiming for a 350–400 base pair product. The size-selected product was amplified using polymerase chain reaction (PCR). The Agilent Bioanalyzer (Agilent Technologies Inc., Santa Clara, USA) was used to identify the final product. Then, probes containing the targeted regions of interest were captured by streptavidin beads, and nonspecific binding was washed out. Next, the sequencing libraries were enriched for the desired target by the Illumina Exome Enrichment protocol and the enriched library validation for quality control analysis were performed using the Axeq Technology. For clustering and sequencing, the protein-coding regions of human genome DNA were collected by genomic DNA Illumina TruSeq Exome Capture System (Illumina Inc.). Every captured library was loaded onto the Illumina HiSeq2000 sequencer (Illumina Inc.) and performed by high-throughput sequencing to ensure that each sample met the desired average sequencing depth.

Reads, mapping, and variant detection

The high-quality sequencing reads were aligned to the human reference genome (NCBI build 37.1/ hg19) with SOAP aligner (soap2.21). Based on the SOAP alignment results, we assembled the consensus sequence and called genotypes in target regions using SOAPsnp v1.05. We collected data as lists of sequence variants (single nucleotide polymorphisms [SNPs] and short Indels) and filtered SOAPsnp results for SNP quality control as follows: (1) base quality >20; (2) depth is 4–200; (3) estimate copy number ≤2; (4) the distance between two SNPs longer than 4. BWA (version 0.5.9-r16, Sanger Institute, Cambridge, UK) was used to align all the high-quality reads to the human reference genome. Then, UnifiedGenotyper tool from GATK (version v1.0.4705) was used to perform small Indel detection. SNP and Indel detection were performed only on the targeted exome regions and flanking regions within 200 bp.

Filtering and annotation

The detected variants were annotated and filtered based on four databases including NCBI CCDS (http://www.ncbi.nlm.nih.gov/RefSeq (http://www.ncbi.nlm.nih.gov/RefSeq/),CCDS/CcdsBrowse.cgi), Ensembl (http://www.ensembl.org), and Encode(http://genome.ucsc.edu/ENCODE). Prioritized all the high-quality mutations including four major steps: (1) mutations including intronic, intergenic, untranslated regions and synonymous mutations were excluded from downstream analysis; (2) mutations in 1000 genome project (ftp://ftp.1000genomes.ebi.ac.uk/vol1-ftp/), dbSNP137 (http://www.ncbi.nlm.nih.gov/projects/SNP/), YH database (http://yh.genomics.org.cn/), and HapMap Project (ftp://ftp.ncbi.nlm.nih.gov/hapmap) were excluded; (3) SIFT (http://sift.bi.astar.edu.sg/) and Polyphen2 (http://genetics.bwh.harvard.edu/pph 2/) were used to predict possible damaging impacts of each variant on protein structure and function; (4) KEGG pathway annotations (http://www.ebi.ac.uk/kegg) and gene ontology (http://www.geneontology.org) were used to predict the biological function of each putative gene.
Variants validation
Sanger sequencing was used to determine if any of the potential mutations co-segregated with the disease phenotype in this pedigree. Primers flanking the candidate loci were designed on the basis of genomic sequences of human genome (hg19/build37.1) and synthesized by Invitrogen (USA): MYOC-F, 5’-GGGAGACAAACATCCGTAAGC-3’; MYOC-R, 5’-GTCTACGCCCCTCAGACTACA-3’; beta-1,4-galactosyltransferase 3 (B4GALT3)-F, 5’-AGAGAAGGCTAGGTAAGGATC-3’; B4GALT3-R, 5’-AAAGTGGAAGAGCAGTGC-3’. Genotyping for c.1456C<T in MYOC and c.322G<A in B4GALT3 in the members of family was then confirmed by direct PCR and analyzed on an ABI 3730XL Genetic Analyzer (ABI Inc., Foster City, USA). Sequencing data were compared with the human genome database.

RESULTS
Clinical findings
The POAG of this Chinese family in five generations showed an autosomal dominant inheritance [Figure 1]. Six members of this family were diagnosed as JOAG, and the glaucoma relevant characteristics of each affected member are illustrated in Table 1. The mean age at diagnosis was 26.3 years (range from 22.0 to 30.0 years). The proband (IV: 3, a 35-year-old woman) was diagnosed as JOAG 8 years ago (at the age of 27 years), with pretreatment IOPs of 42/36 mmHg (right eye/left eye [OD/OS]), open anterior chamber angle, and enlarged C/D ratio of 0.75/0.70 (OD/OS). Due to the poor efficacy of medical care, she underwent trabeculectomy on both eyes at the age of 27 years, and IOP was controlled (11–15 mmHg OU) until now. No visual field progression was found over the following years. The proband’s father (III: 2) recalled vision reduction (approximate 0.1) in his late twenties, had pretherapy IOPs of 40–50 mmHg, and accompanied with symptoms including painful eye bilges and headache. Because of his inactive hospitalized attitude and poor consciousness, POAG was diagnosed a decade later. Although undergoing surgery at the age of 39 years, he still became blind in his later forties. Funduscopy showed glaucomatous optic disc damage with C/D ratio of 1.0/1.0 in both eyes. In addition, he recalled that his grandfather and father (I: 1, II: 1), all became blind between the age of 40 and 50 years. III: 6 were diagnosed as POAG at the age of 39 years with high IOPs and dead 5 years later. Similar to the proband, her uncle (III: 4) recalled that his vision was reduced in his early twenties and performed trabeculectomy at the age of 25 years. The ophthalmologic examinations indicate his visual acuity of 0.04/perception of light, with IOPs of 17/11 mmHg and C/D ratio of 0.90/0.95 in both eyes. Moreover, patient IV: 1 was diagnosed as POAG at the age of 30 years with IOPs of 27/30 mmHg and achieved controlled IOPs after he underwent for trabeculectomy on both eyes. Proband’s younger brother and cousin (IV: 7, IV: 9) were diagnosed as POAG at the ages of 27 and 22 years, respectively, and only IV: 9 achieved controlled IOPs after received topical therapy (latanoprost and carteolol hydrochloride eye drops).

Mutations screening of myocilin and beta-1,4-galactosyltransferase 3 in primary open-angle glaucoma
In sequencing analysis, a heterozygous missense mutation, c.1456C>T (p.L486F), was found located at nucleotide 1456.

Figure 1: Pedigrees of the Chinese family with primary open-angle glaucoma. Arrow indicates the proband (IV: 3); Filled squares and circles indicate male and female members; solid symbols indicate the carrier; diagonal line indicates deceased subject.
in exon 3 of MYOC gene [Figure 2]. This mutation was present in all six affected and three asymptomatic members (IV: 11, V: 3, and V: 5). Meanwhile, sequencing analysis of B4GALT3 gene revealed a novel heterozygous missense mutation [Figure 3], c.322G<A (p.V108I) of all patients and three unaffected individuals (IV: 11, V: 2, and V: 5). No above-mentioned mutations were found in other asymptomatic individuals and all included controls. We did not find these two variants in public databases including dbSNP137, 1000 genome project, YH database, and HapMap project.

Bioinformatic analysis

The mutation, c.1456C<T, in the exon 3 of MYOC gene would lead to the replacement of leucine by phenylalanine. DNA sequence alignment in eight different species suggests that leucine 486 is a highly conserved residue in MYOC protein [Figure 4]. SIFT analysis predicts the p.L486F mutation of MYOC as “affecting protein function” with a score of 0.00 (score <0.05 means the protein function may be affected by the amino acid change). Similarly, valine 108 was highly conserved in B4GALT3 protein among different species. SIFT also predicts that the p.V108I mutation of B4GALT3 may affect its function by replacing valine to isoleucine at position 108 (a score of 0.00).

**Discussion**

MYOC gene locates at GLC1A locus on chromosome 1q23, includes three exons and encodes for 57kD MYOC protein, which is the first gene identified to be responsible for POAG. MYOC protein is expressed in various ocular tissues, including cornea, sclera, iris, ciliary body, retina, and optic nerve head, but most abundant in TM cells. Most glaucoma-causing MYOC mutants are misfolded, aggregation-prone, detergent-insoluble, and accumulated in the endoplasmic reticulum, which result in cytotoxicity in TM cells. It has been suggested that MYOC mutation is associated with the blockage of aqueous outflow through TM, and thus leads to elevated IOPs. There are more glaucoma risk mutations found in MYOC than any other glaucoma-associated genes. Over eighty different mutations have been identified in MYOC, and majority of them are clustered in exon 3, which constituted an important olfactomedin domain. Mutations of MYOC have been reported associated with POAG pedigrees.

| Member ID | Gender | Age at study (years) | Onset age (years) | OD/OS | Therapy |
|-----------|--------|----------------------|-------------------|-------|---------|
| III: 2    | Male   | 58                   | 28                | NPL/NPL | S/S     | Trabe   |
| III: 4    | Male   | 47                   | 23                | 0.04/PL | S/S     | Trabe   |
| III: 6    | Female | P                    | 39                | NR/NR  | NR/NR   | Trabe   |
| IV: 1     | Male   | 38                   | 30                | 0.5/0.6 | 0.80/0.65 | S/M     | Trabe   |
| IV: 3     | Female | 35                   | 27                | 0.5/0.8 | 0.75/0.70 | S/S     | Trabe   |
| IV: 7     | Male   | 30                   | 28                | 0.6/0.6 | 0.85/0.85 | S/S     | Med     |
| IV: 9     | Male   | 24                   | 22                | 1.0/0.8 | 0.50/0.65 | M/M     | Med     |

OD: Right eye; OS: Left eye; C/D: Cup-disc; PL: Perception of light; NPL: No perception of light; NR: No recordable; Trabe: Trabeculectomy; P: Pass away; S: Severe defect; M: Moderate defect; Med: Medical treatment; POAG: Primary open-angle glaucoma; IOP: Intraocular pressure.
Although the In vitro B4GALT3 gene The c.1456C<T (p.L486F) of B4GALT4 chains. The first and saccharide structures. The have distinct functions in the synthesis of glycoconjugates N‑linked glycosylation sites. The cytoplasmic domain of four residues, a stem region, a transmembrane glycoprotein which includes an N‑terminal segment. before a sequence encoding a hydrophobic transmembrane 1q23.3 and is one of seven (IV: 11, V: 2, and V: 5). Huang et al. evaluated mutations in several galectoma‑associated genes in 683 Chinese patients with primary glaucoma and also found c.1456C<T (p.L486F) mutation of MYOC in a sporadic POAG patient, which indicates that the c.1456C<T variants in MYOC are likely to be responsible for the pathogenesis of POAG in this family.[22] The majority of patients in this pedigree were JOAG as the onset of clinical manifestations occurs before the age of 30 years, and the average onset age was 26.3 years. This may explain why IV: 11, V: 3, and V: 5 (age of 19, 8, and 11 years, respectively) harbor the same mutation, yet without clinical manifestations. A careful follow‑up for these members may help us further clarify the onset age of disease and the pathological changes at the early stage.

Furthermore, sequencing analysis of B4GALT3 gene revealed a novel heterozygous missense mutation, c.322G<A (p.V108I) of all patients and three unaffected individuals (IV: 11, V: 2, and V: 5). B4GALT3 locates on chromosome 1q23.3 and is one of seven B4GALT genes. The coding region of B4GALT3 has a single initiation codon, immediately before a sequence encoding a hydrophobic transmembrane segment. B4GALT3’s coding sequence encodes Type II transmembrane glycoprotein which includes an N‑terminal cytoplasmic domain of four residues, a stem region, a transmembrane segment, and a catalytic domain with four N‑linked glycosylation sites.[23] All seven B4GALT proteins have distinct functions in the synthesis of glycoconjugates and saccharide structures. The B4GALT3 gene encodes an enzyme that may be mainly involved in the synthesis of the first N‑acetyllactosamine unit of poly‑N‑acetyllactosamine chains. In vitro assay predicted that B4GALT3 and B4GALT4 proteins exhibit similar kinetic properties and functions.[24] Recently, it has been reported that B4GALT3 protein plays an important role in invasion, proliferation, and metastasis in extravillose trophoblast, colorectal cancer, and neuroblastoma.[25‑27] The mutation of B4GALT3 gene was first identified in a POAG pedigree. POAG is a complex neurodegenerative disease which results in the stress in retinal ganglion cells and optic nerve axons. The outgrowth of an axon is critical for the regeneration of nerve fibers during wound healing. It has been suggested that B4GALT proteins play a role in maintaining the normal function of nerve cells, increasing neurite outgrowth, and promoting the regeneration of injured neurons.[28‑31] Although the association between the mutations in B4GALT gene/protein and the risk of POAG has not been reported, the p.V108I mutation of B4GALT3 protein may affect its function by replacing valine to isoleucine at position 108 and may also contribute to the pathogenesis and process of POAG in our reported kindred. Similar to the mutations of MYOC, the g.3322A mutation of B4GALT3 was also found in three asymptomatic members (IV: 11, V: 2, and V: 5).

Among these two reported mutations, we propose that c.1456C<T (p.L486F) mutation of MYOC plays a major role in the pathogenesis of POAG. The reasons are as follows: on one hand, the same mutation has been found and reported in a Chinese sporadic POAG patient; on the other hand, although the exact intraocular physiological functions of B4GALT protein are largely unknown, abnormal B4GALT protein may affect its function to maintain the normal activity of nerve cells, increase neurite outgrowth, and promote the regeneration of injured neurons. Considering its known functions, it may cooperate with the mutated MYOC to accelerate the progression of POAG after retinal ganglion cells and optic nerve axons being damaged, rather than being a main cause to initiate the onset of POAG. It is possible that c.1456C<T (p.L486F) mutation of MYOC leads to the pathogenesis of POAG in this family, in which c.3322A (p.V108I) variant of B4GALT3 accelerates its progression. The role of c.3322A (p.V108I) variant in this pedigree will be further clarified by the follow‑up studies of V: 2 and V: 3 who only possess c.1456C<T (p.L486F) mutation of MYOC and c.3322A (p.V108I) variant of B4GALT3, respectively.

In this pedigree, the majority of patients were JOAG. The onset symptoms occur before the age of 30 years. In addition, severe clinical manifestations, high IOPs, unstable to topical therapy, and most of the patients requiring surgery to avoid the progress of disease characterize this pedigree’s phenotype, which is different from the typical phenotypes of POAG. Thus, early diagnosis and proper interventions are very critical for protecting patients from the loss of visual acuity, and especially, preventing young members who harbor the same mutations in this family develop blindness at youth.

In conclusion, the mutations c.1456C<T (p.L486F) in MYOC and c.3322G>A (p.V108I) in B4GALT3 are likely responsible for the pathogenesis of POAG in this family. The new variants in these two genes provide a significant

| Human | LTIPTFRKRYKSSIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | p.L486F |
| Chimpanzee | LTIPTFRKRYKSSIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |
| Rhesus Monkey | LTIPTFRKRYKSSIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |
| Dog | LTIPTFRKRYKSSIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |
| Cattle | LTVFPTKRKKIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |
| House Mouse | LTVFPTKRKKIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |
| Marway Rat | LTVFPTKRKKIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |
| Chicken | LSVFPTKRKKIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |
| Zebrafish | LSVFPTKRKKIDWIVNPEKXXFAMDNLNMVTDYDIKLRSKNLQGKQ | |

**Figure 4:** The c.1456C<T (p.L486F) of MYOC involved a highly conserved residue. DNA sequence alignment in eight different species suggests that leucine 486 is a highly conserved residue in MYOC protein. MYOC: Myocilin.
opportunity to further clarify the etiology of POAG, as well as to improve the presymptomatic diagnosis and prognosis of POAG. Furthermore, the mechanisms of POAG could further be investigated in animal model using these two genetic mutations in the future.

Acknowledgments
We greatly thank all the family members and controls who participated in this study and also would like to thank Yi Liao for helpful comments.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006;90:262‑7. doi: 10.1136/bjo.2005.081224.
2. Abu‑Amero K, Kondkar AA, Chalam KV. An updated review on the genetics of primary open angle glaucoma. Int J Mol Sci 2015;16:28886‑911. doi: 10.3390/ijms161126135.
3. Morissette J, Côté G, Ancil JL, Plante M, Amyot M, Héon E, et al. A common gene for juvenile and adult‑onset primary open‑angle glaucomas confined on chromosome 1q. Am J Hum Genet 1995;56:1413‑2.
4. Quigley HA. Open‑angle glaucoma. N Engl J Med 1993;328:1097‑106. doi: 10.1056/NEJM199304153281507.
5. Fechtner RD, Weinreb RN. Mechanisms of optic nerve damage in primary open angle glaucoma. Surv Ophthalmol 1994;39:23‑42. doi: 10.1007/BF02985101.
6. Ritch R. Neuroprotection: Is it already applicable to glaucoma therapy? Curr Opin Ophthalmol 2000;11:78‑84. doi: 10.1097/00055735‑200004000‑00002.
7. Libby RT, Gould DB, Anderson MG, John SW. Complex genetics of glaucoma susceptibility. Annu Rev Genomics Hum Genet 2005;6:15‑44. doi: 10.1146/annurev.genom.6.080604.162209.
8. Stone EM, Fingert JH, Alward WL, Nguyen TD, Polansky JR, Sunden SL, et al. Identification of a gene that causes primary open angle glaucoma. Science 1997;275:668‑70. doi: 10.1126/science.275.5300.668.
9. Green CM, Kears LS, Wu J, Barbour JM, Wilkinson RM, Ring MA, et al. How significant is a family history of glaucoma? Experience from the glaucoma inheritance study in tasmania. Clin Exp Ophthalmol 2007;35:793‑9. doi: 10.1111/j.1442‑9071.2007.01612.x.
10. Ortego J, Escribano J, Coca‑Prados M. Cloning and characterization of subtracted cDNAs from a human ciliary body library encoding TIGR, a protein involved in juvenile open angle glaucoma with homology to myosin and oofactomedin. FEBS Lett 1997;413:349‑53. doi: 10.1016/S0014‑5793(97)00934‑4.
11. Joe MK, Sohn S, Har W, Moon Y, Choi YR, Kee C. Accumulation of mutant myocilins in ER leads to ER stress and potential cytotoxicity in human trabecular meshwork cells. Biochem Biophys Res Commun 2003;312:592‑600. doi: 10.1016/j.bbrc.2003.10.162.
12. Takamoto M, Araie M. Genetics of primary open angle glaucoma. Jpn J Ophthalmol 2014;58:1‑15. doi: 10.1007/s10384‑013‑0286‑0.
13. Kubota R, Kudoh J, Mashima Y, Asakawa S, Minoshima S, Hejtmancik JF, et al. Genomic organization of the human myocilin gene (MYOC) responsible for primary open angle glaucoma (GLC1A). Biochem Biophys Res Commun 1998;242:396‑400. doi: 10.1006/ bbrc.1997.7972.
14. Alward WL, Kwon YH, Khanna CL, Johnson AT, Hayreh SS, Zimmerman MB, et al. Variations in the myocilin gene in patients with open‑angle glaucoma. Arch Ophthalmol 2002;120:1189‑97. doi: 10.1001/archoph.120.9.1189.
15. Ge J, Zhuo Y, Guo Y, Ming W, Yin W. Gene mutation in patients with primary open‑angle glaucoma in a pedigree in China. Chin Med J 2000;113:195‑7.
16. Faucher M, Ancil JL, Rodrigue MA, Duchesne A, Bergeron D, Blondneau P, et al. Founder TIGR/myocilin mutations for glaucoma in the Québec population. Hum Mol Genet 2002;11:2077‑90. doi: 10.1093/hmg/11.18.2077.
17. Fingert JH, Héon E, Liebmann JM, Yamamoto T, Craig JE, Rait J, et al. Analysis of myocilin mutations in 1703 glaucoma patients from five different populations. Hum Mol Genet 1999;8:899‑905. doi: 10.1093/hmg/8.5.899.
18. Suzuki Y, Shirato S, Taniguchi F, Ohara K, Nishimaki K, Ohta S. Mutations in the TIGR gene in familial primary open‑angle glaucoma in Japan. Am J Hum Genet 1997;61:1202‑4. doi: 10.1086/301612.
19. Iliiev ME, Bodmer S, Gallati S, Lanz R, Sturmer J, Katsoulis K, et al. Glaucoma phenotype in a large Swiss pedigree with the myocilin G1367Arg mutation. Eye (Lond) 2008;22:880‑8. doi: 10.1038/ sj.eye.6702745.
20. Kanagavalli J, Krishnaswamy SR, Pandaranayaka E, Krishnaswamy S, Sundaresan P. Evaluation and understanding of myocilin mutations in Indian primary open angle glaucoma patients. Mol Vis 2003;9:606‑14.
21. Chen J, Cai SP, Yu W, Yan N, Tang L, Chen X, et al. Sequence analysis of MYOC and CYP1B1 in a Chinese pedigree of primary open‑angle glaucoma. Mol Vis 2011;17:1431‑5.
22. Huang X, Li M, Guo X, Li S, Xiao X, Jia X, et al. Mutation analysis of seven known glaucoma‑associated genes in Chinese patients with glaucoma. Invest Ophthalmol Vis Sci 2014;55:3594‑602. doi: 10.1167/iovs.14‑13927.
23. Amado M, Almeida R, Schwientek T, Clausen H. Identification and characterization of large galactosyltransferase gene families: Galactosyltransferases for all functions. Biochim Biophys Acta 1999;1473:35‑53. doi: 10.1016/S0034‑4146(99)00168‑3.
24. Almeida R, Amado M, David L, Lavery SB, Holmes EH, Merks G, et al. A family of human beta4‑galactosyltransferases. Cloning and expression of two novel UDP‑galactose: Beta‑n‑acetylgalcosaminide beta1,4‑galactosyltransferase in rat injured sciatic nerve. J Mol Chem 1997;272:31979‑91. doi: 10.1074/jbc.272.51.31979.
25. Liao WC, Liu CH, Chen CH, Hsa WM, Liao YY, Chang HM, et al. Beta1,4‑Galactosyltransferase III suppresses extravilous trophoblast invasion through modifying beta1‑integrin glycosylation. Placenta 2015;36:357‑64. doi: 10.1016/j.placenta.2015.01.008.
26. Chen CH, Wang SH, Liu CH, Wu YL, Wang WJ, Huang J, et al. Beta1,4‑Galactosyltransferase III suppresses beta1 integrin‑mediated invasive phenotypes and negatively correlates with metastasis in colorectal cancer. Carcinogenesis 2014;35:1258‑66. doi: 10.1093/carcin/bgu007.
27. Chang HH, Chen CH, Chou CH, Liao YF, Huang MJ, Chen YH, et al. Beta1,4‑Galactosyltransferase III enhances invasive phenotypes via beta1‑integrin and predicts poor prognosis in neuroblastoma. Clin Cancer Res 2013;19:1705‑16. doi: 10.1158/1078‑0432.CCR‑12‑2367.
28. Huang Q, Shur BD, Begovac PC. Overexpressing cell surface beta 1‑4‑galactosyltransferase in PC12 cells increases neurite outgrowth on laminin. J Cell Sci 1995;108(Pt 2):839‑47.
29. Shen A, Zhu D, Ding F, Zhu M, Gu X, Gu J. Increased gene expression of beta1‑4‑galactosyltransferase I in rat injured sciatic nerve. J Mol Neurosci 2003;21:103‑10. doi: 10.1385/JMN:21:2:103.
30. Hathaway HJ, Shur BD. Cell surface beta 1‑4‑galactosyltransferase functions during neural crest cell migration and neurulation in vivo. J Cell Biol 1992;117:369‑82. doi: 10.1083/jcb.117.2.369.
31. Shen A, Yan J, Ding F, Gu X, Zhu D, Gu J. Overexpression of beta1‑4‑galactosyltransferase I in rat Schwann cells promotes the growth of co‑cultured dorsal root ganglia. Neurosci Lett 2003;342:159‑62. doi: 10.1016/S0304‑3940(03)00271‑4.