EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES

http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 2
297-306
Year: 2016

A REVIEW ON THE SNP'S AND RELATED CONCEPTS IN SOME OF THE KNOWN EYE DISEASES.

Jincy Anna Jomy and Rao Sethumadhavan*

Bioinformatics Division, School of Bio Sciences and Technology, VIT University, Vellore, Tamil Nadu.

***Author for Correspondence: Prof. Rao Sethumadhavan**
Bioinformatics Division, School of Bio Sciences and Technology, VIT University, Vellore, Tamil Nadu.

Article Received on 26/11/2015 **Article Revised on 17/12/2015** **Article Accepted on 08/01/2016**

ABSTRACT

The Genetics of human phenotype variation and especially, the genetic basis of human complex diseases could be understood by knowing the functions of Single Nucleotide Polymorphisms (SNPs). The primary objective of this work reported here is to foresee the pernicious nsSNPs, so that the quantity of SNPs screened for relationship with infections can be decreased to those that in all probability adjust quality capacity. In this work utilizing computational instruments, we have investigated the SNPs that can change the expression and capacity of 6 genes. To investigate conceivable connections between hereditary transformation and phenotypic variety, distinctive computational calculation instruments like Sorting Intolerant From Tolerant (sequence based methodology), Polymorphism Phenotyping (structure-based methodology) and I- Mutant 3.0 (bolster vector machine), were utilized for arrangement level examination. To further explore the conceivable reasons for infections at atomic level, we mapped the malicious nsSNPs to 3D protein structures of eight qualities to be specific RP2, OAT, CHN1, CRYGD, ARL6, and CYP1B1. An investigation of auxiliary structure and cooperation studies was likewise performed to comprehend the effect of a change on protein capacity and solidness. The computational building design proposed in this study is in light of coordinating significant biomedical data sources to give a precise investigation of straightforward and complex illnesses. We have demonstrated a "certifiable" utilization of some current bioinformatics devices for SNPs examination. Overall this is a review on the snp's and related concepts in some of these known eye diseases.

KEYWORDS: SNP, RP2, OAT, CHN1, CRYGD, ARL6, and CYP1B1.

1. INTRODUCTION

Understanding the genomic differences in the human population is one of the major challenges in the field of current genomics research.[1] The human genome contains many forms of genetic variation.[2] Single nucleotide polymorphisms are the simplest and most frequent type of DNA sequence variation among individuals.[3] Human genome is composed of more than three billion base pairs and ten million SNPs.[4]

SNPs in coding and regulatory regions may be implicated in disease themselves. Among the various types of SNPs, nonsynonymous SNPs (nsSNPs) are believed to have the greatest impact on protein function because they often lead to mutation of the encoded amino acids, which can have a deleterious effect on the structure and/or function of the proteins.[5-8]

Nonsynonymous SNPs that lead to an amino acid change in the protein product are of major interest because amino acid substitutions currently account for approximately half of the known gene lesions responsible for human inherited disease.[9] The aim of these studies is to map genetic factors underlying such phenotypes by comparing genetic information and phenotypes of individuals sampled from a population. Computational algorithms are a high priority for characterizing variants because they have the ability to be employed on a scale that is consistent with the large number of variants being identified in systematic screening of representatives of human populations for variation.

Henceforth, we have utilized the intense computational devices for anticipating the adverse amino acid substitutions in eye related proteins and further examined their consequences for protein 3D structures to comprehend structure-capacity associations with the assistance of the accompanying parameters specifically sequence conservation, structural environment, structural stability, cation-π interactions, protein-protein interaction and protein-drug interaction, which thusly is crucial to pick up bits of knowledge into disease sickness genotype-phenotype relationships.

2. Overview on the methods used

2.1 Overview on computational tools for predicting deleterious functional nssnps

Different computational tools have been created for foreseeing the huge missense mutaions taking into account succession and basic methodologies. Sequence based techniques can be subcategorized into sequence homology-based and single sequence based strategies. Sequence homology-based system approaches in this classification ascertain the likelihood of the substitutions in light of numerous grouping arrangements.[10] Single Sequence Based Predictions Single arrangement based examination construct its forecasts singularly with respect to single succession data.[11-12] By and large, these order the transformations into whether they have negative, unbiased or beneficial outcomes on the structure or capacity of the proteins.[13] To group whether a change will be endured, a preparation set is typically built of changes known not malicious proceeded with this collection of exploration by adding to a position particular estimation of non-moderate transformations with their strategy, Sorting Intolerant From Tolerant (SIFT) to find that 25 every penny of nsSNPs in dbSNP are liable to influence protein capacity.[14] The fuse of basic information enormously enhances the nature of the numerous grouping arrangement and the exactness of forecast. This is very much shown by PolyPhen[15] a various grouping arrangement server that adjusts successions utilizing basic data. I-Mutant 3.0 rank all the conceivable substitutions as indicated by a three state arrangement framework and demonstrate that the general precision of our indicator is as high as 56% when performed beginning from succession data and 61% when the protein structure is accessible, with a mean worth connection coefficient of 0.27 and 0.35, individually.[16]

2.2 Structure-based assessment of deleterious nssnps

Information of a protein's three-dimensional (3D) structure is key for a full comprehension of its usefulness.[17] To comprehend the relationship in the middle of hereditary and phenotypic variety, it is key to evaluate the basic outcomes of the separate non-synonymous transformations in proteins.[18] A few studies have set up that the coupling of an 'organic'cation of the sorts depicted underneath to the sweet-smelling amino acids phenylalanine, tyrosine or tryptophan contributes 2–4 kcal mol−1 to a generally tying cooperation[19] and a computational study shows that, in an uncovered watery environment, a commonplace cation–π collaboration is more grounded than an average salt bridge.[20] The samples examined underneath are not planned to be comprehensive; rather they underline cases for which solid backing for a part of cation–π collaborations is available.[21] An extraordinary arrangement of immediate and conditional confirmation demonstrates that cation-pi cooperations are imperative in a mixture of proteins that tie cationic ligands or substrates. In this connection, the amino acids phenylalanine (Phe), tyrosine (Tyr), and tryptophan (Trp) can be seen as polar, yet hydrophobic, buildups.[22] The cation-pi association is a vital, general power for atomic acknowledgment in natural receptors. Here we report here various counts on prototypical cation-pi frameworks, underscoring structures of significance to natural receptors and prototypical heterocycles of the sort regularly of significance in restorative science.[23]

2.3 Root mean square deviation (RMSD)

The relative examination of the structures of related proteins can uncover the impacts of the amino corrosive succession changes that have happened amid advancement.[24] Any of programming projects is utilized to make a 3D structure; a procedure called energy minimization ought to be completed once the structure is manufactured. This is on account of the development procedure may have brought about unfavorable bond lengths, bond points or torsion edges. The energy minimization procedure is normally done by an atomic mechanics program which figures the vitality of the beginning atom, then differs the bond lengths, bond points and torsion edges to make another structure. The docking procedure includes the forecast of ligand conformity and introduction inside of a focused on tying site.[24] In general, there are two points of docking studies: precise auxiliary demonstrating and right expectation of action.[25]

Moderately basic scoring capacities keep on being vigorously utilized, in any event amid the early phases of docking reenactments. Preselected conformers are regularly further assessed utilizing more unpredictable scoring plans with more itemized treatment of electrostatic and van der Waals collaborations, and incorporation of in any event some solvation or entropic impacts.[26]

3. Results of the experiment (Eye related diseases investigated in this study)

3.1 RP2 genes in retinitis pigmentosa

Retinitis pigmentosa (RP) includes an extensive gathering of heterogeneous illnesses that outcomes in dynamic retinal degeneration and is the main reason for innate difficulty seeing in populace.[27] In basic terms RP reveal to a collection of acquired issue in which variations from the norm of the photoreceptors (rods and cones) of the retina lead to dynamic visual misfortune.[28] The infection condition may isolate as an autosomal dominant, autosomal recessive or a X- linked recessive trait and it might likewise happen on a sporadic premise in up to 50% of cases.[29] The RP2 gene (NM_006915.2) is the gene in charge of Retinitis Pigmentosa. It is situated on the short (p) arm of the X chromosome at position 11.3.[30] RP2 gene is situated from base combine 46,696,346 to construct match 46,741,792 with respect to the X chromosome.[31] RP2 is a pervasively communicated 350-amino corrosive protein, which does not have all the earmarks of being advanced in retina. It is accordingly as of now indistinct why changes in the RP2 gene lead to a retina-particular phenotype. The RP2

gene gives directions to making a protein that is fundamental for typical vision.[32] In human retina, RP2 was confined to the plasma film of cells in both bar and cone photoreceptors, reaching out from the external fragment through the inward section to the synaptic terminals. To date, the main distinguished interfacing accomplice of RP2 is the ADP ribosylation variable (Arf)-like protein Arl3.[32] All things considered these information propose that one of the fundamental elements of RP2 may be to coordinate cooperations between the plasma layer and cytoskeleton. RP2 is anticipated to be a negative controller of Arl3. Arl3 is an omnipresent microtubule-related protein (MAP), which is restricted to the interfacing cilium in photoreceptors.[33] It was proposed RP2 works working together with Arl3 to connection the phone layer with the cytoskeleton in photoreceptors as a major aspect of the phone flagging or vesicular transport apparatus.[30] The protein XRP2 is in charge of the reason for retinitis pigmentosa, which actuates RP2 gene. It prompts degeneration of retinal photoreceptor cells. ADP-ribosylation element like protein 3 is a protein that in people is encoded by the ARL3 gene. ARL3 ties guanine nucleotides however needs ADP ribosylation component movement. XRP2 goes about as a guanine nucleotide separation inhibitor for ARL3.[34]

The gem structure of human retinitis pigmentosa 2 protein (RP2) comprises of a N-terminal beta helix and a C-terminal ferredoxin-like alpha/beta area. RP2 is a particular effector protein of Arl3. Arl3 is confined to microtubule structures all through the retina and is available at high focus in the joining cilium of photoreceptors. In similarity to the part of Arf proteins in cell transport responses, Arl3 and RP2 may be included in protein trafficking as a rule or photoreceptor support specifically. The collaborations in the middle of RP2 and Arl3 were quantitatively described with refined proteins. RP2 is a true blue effector of Arl3.[35] The N-terminal 34 deposits and b helix area of RP2 are needed for tying of Arl3. As RP characterizes a clinically and hereditarily various gathering of retinal dystrophies, which are described by dynamic photoreceptor cell degeneration, patients present with night lack of sight and loss of fringe vision as the pole photoreceptor cells brokenness and pass on, trailed by cone photoreceptor cell demise.[36] Retinal degeneration advances towards the focal retina, prompting trademark burrow vision and possible sightlessness.[37] The starting indication of RP is generally flawed dim adjustment (i.e., nyctalopia or "night visual deficiency"). Visual keenness, fundus appearance, Posterior subcapsular waterfalls, Dust-like particles in the vitreous, White specks somewhere down in the retina, Hyaline bodies (drusen) of the optic nerve head, Exudative vasculopathy regularly called Coats-like ailment are the side effects of RP.[38] The primary indication of the sickness is the vicinity of dull stores in the retina.[39]

3.2 OAT gene in gyrate atrophy

Ornithine aminotransferase (OAT) (MIM: 258870) is a mitochondrial framework protein that catalyzes the pyridoxal phosphate (PLP)-subordinate transamination of ornithine to glutamic γ-semialdehyde.[40] OAT gene is situated on the long (q) arm of chromosome 10 at position 26. All the more accurately, the OAT gene is situated from base match 126,085,871 to construct combine 126,107,544 in light of chromosome 10. OAT lack (EC 2.6.1.13) is an uncommon inborn metabolic issue portrayed by rotate decay of the choroid and retina bringing on an uncommon autosomal latent issue connected with two diverse clinical phenotypes.[41] Changes that outcome in lack of OAT protein causes autosomal passive eye malady called Gyrate Atrophy. The OAT gene encodes the mitochondrial catalyst ornithine aminotransferase, which is a key chemical in the pathway that changes over arginine and ornithine into the major excitatory and inhibitory neurotransmitters glutamate and GABA. Rotate decay of the choroid and retina is an autosomal latent chorioretinal dystrophy which prompts a gradually dynamic loss of vision.[42] This issue is described by night sightlessness, narrowing of the field of vision, dynamic fringe retinal degeneration, an at last stifled electroretinogram, and a stamped height of plasma ornithine.[43]

Different manifestations incorporate vision misfortune, neonatal hyperammonemia (overabundance smelling salts in the blood in the infant period), neurological variations from the norm, scholarly incapacity, fringe nerve issues, and muscle shortcoming may happen. This condition is acquired in an autosomal latent way. The level of OATase mRNA in the ordinary human retina is roughly equivalent to 1/100th the level of rhodopsin mRNA and 1/5th to 1/10th the level present in the retinoblastoma cells.[44] Ornithine aminotransferase (OAT) catalyzes a response in the pathway that interconvert ornithine and proline, furthermore serves to unite the urea and citrus extract cycles. Loss of OAT capacity brings about sickness in people, the catalyst is not a center for discerning inhibitor outline. OAT is in the same subgroup as some different aminotransferases that likewise have key metabolic parts. This subgroup incorporates γ-aminobutyric corrosive aminotransferase (GABA-AT), a catalyst whose substrate is the cerebrum's major inhibitory neurotransmitter, and glutamate-1-semialdehyde aminotransferase (GSA-AT), a key protein in the tetrapyrrole union pathway in plants.[45] Any data on the instrument of hindrance regarding OAT is pertinent to sane medication outline endeavors on these other more alluring targets. L-canaline is practically indistinguishable to ornithine.

The precious stone structure of OAT in complex with gabaculine gives the first basic proof that the intensity of the inhibitor is because of great aromatic–aromatic communications with dynamic site buildups. OATase is a pyridoxal phosphate-obliging catalyst that catalyzes the interconversion of ornithine, glutamate, and proline.

Taking into account the gem structure of human OAT, both substrate tying and response component of the chemical are surely known. OAT demonstrates an expansive auxiliary and unthinking likeness to different chemicals from the subgroup III of aminotransferases, which exchange an amino gathering from a carbon particle that does not convey a carboxyl capacity.[46] Rotate decay is commit heterozygotes indicate pretty nearly 50% of ordinary OAT action, and connection in folks of influenced people is normal. The instrument by which the OAT lack prompts the choroidal and retinal decay and waterfall arrangement stays vague.[47] It is realized that ornithine can be metabolized in three pathways (a) the transformation to glutamic corrosive y-semialdehyde by OAT and afterward to proline or glutamate, (b) the change to citrulline by ornithine transcarbamylase in urea cycle and (c) the transformation to putrescine by ornithine decarboxylase.[48] Ornithine delta aminotransferase controls the L-ornithine (Orn) level in tissues by catalyzing the exchange of the delta amino gathering of Orn to 2-oxoglutarate. The results of this response are L-glutamate gama semialdehyde and L-glutamate. Among the mixes known not (or inactivate) OAT, just L-canaline and (SS)-5-(fluoromethyl) ornithine [(SS)-5FMOrn] are particular for OAT.[49]

3.3 CHN1 genes in duane retraction syndrome 2

Duane's retraction disorder (DRS) is an innate eye development issue described by adduction insufficiency, kidnapping constraint, globe retraction, and palpebral gap narrowing on endeavored adduction.[50] DRS are the successive reason for strabismus in kids and may bring about amblyopia-related visual misfortune. A portion of the information recommends that DRS may come about because of anomalous advancement or nonattendance of the abducens nerve (cranial nerve VI).[51] As the six muscles help in eye development, the disgraceful development of these eye muscles causes Duane disorder i.e. the 6th cranial nerve that controls the horizontal rectus muscle (the muscle that pivots the eye out towards the ear) does not grow legitimately.[52] The issue happens with the eye muscles, as well as with nerves, that transmits the electrical driving forces to the muscle. The eye goes astray upward and descending is a primary indication of DRS.[53] Now and then the head position of patients regularly keep up a head stance or head swing to keep the eyes straight and sometimes the eye have all the earmarks of being littler than the other one. The protein N-chimaerin is in charge of the reason for DRS, which initiates CHN1.[54]

Duane retraction disorder 2 (DURS2; 604356) is brought about by change in the CHN1 gene (118423) on chromosome 2q31. CHN1 (chimerin 1) transformations can hyperactivate α2-chimaerin and bring about atypical cranial engine neuron advancement.[55] Mutational examination proposes that CHN1 interracts with RAC1. Ras-related C3 botulinum poison substrate 1 (Rac1) is a protein found in human cells which encodes RAC1 gene.[56]

3.4 CRYGD genes in cataract

Vision misfortune among the elderly is a real human services issue. The most well-known reasons for vision misfortune among the elderly are age-related macular degeneration, glaucoma, waterfall and diabetic retinopathy. Waterfall is a typical reason for vision weakness among the elderly, however surgery is frequently compelling in restoring vision.[57] Most waterfalls emerge on account of maturing of the crystalline lens. The straightforwardness of the lens is kept up by numerous reliant variables that are in charge of its optical homogeneity, including its tiny structure and compound constituents. With maturing, there is a slow aggregation of yellow-chestnut shade inside the lens, which diminishes light transmission. There are additionally basic changes to the lens strands, which bring about interruption of the standard construction modeling and plan of the filaments that are important to keep up optical clarity.[58]

Changes in the CRYGD gene have been found to bring about numerous sorts of waterfall. CRYGD (crystallin, gamma D) is a protein-coding gene. Sicknesses connected with CRYGD incorporate waterfall 4, numerous sorts, and waterfall 3, various sorts.[59] The predominant basic segment of vertebrate eye lens is crystallins. A percentage of the studies expresses that, gamma-crystallins have been included in waterfall development, because of maturing or transformations in particular qualities. Protein displaying proposed that the impact of gamma-D-crystallin change was an unpretentious one, influencing the surface properties of the crystallin particle as opposed to its tertiary structure, reliable with the way that the patients' lenses were typical during childbirth. This was the first gene imperfection indicated to be in charge of a noncongenital progressive cataract.[60] Typically SNPs are found in coding and non-coding areas. Among these, the non-synonymous SNPs (nsSNPs) reason changes in the amino corrosive deposits. These are liable to be an essential component adding to the utilitarian differing qualities of the encoded proteins in the human populace.[61] Likewise nsSNPs influence the practical part of proteins in sign transduction of visual, hormonal and different stimulants.[62]

3.5 ARL6 genes in bardet-biedl syndrome 3

Bardet- Biedl disorder (BBS) is an autosomal passive condition portrayed by bar cone dystrophy, postaxial polydactyly, focal corpulence, mental impediment, hypogonadism, and renal brokenness.[63] BBS is an issue that influences numerous parts of the body. The signs and indications of this condition shift among influenced people, even among individuals from the same gang. Vision misfortune is one of the significant highlights of BBS. Loss of vision happens as the light-detecting tissue at the back of the eye (the retina) steadily falls apart. Just about 12 qualities have been distinguished to be in charge of BBS so far.[64] In spite of the fact that the BBS proteins demonstrate minimal auxiliary likeness, an

arrangement of BBS proteins are situated in the area of cilia and are included in the ciliogenesis and/or cilia function.[65] ARL6 (ADP-ribosylation element like 6) is the protein-coding gene which fits in with the Arf/Arl-family GTPases has demonstrated to be a reason for BBS utilizing similar genomic investigation.[66]

Bardet-biedl disorder 1 and arl6-related retinitis pigmentosa are different illnesses that connected with ARL6. It includes in film protein trafficking at the base of the ciliary organelle and intercedes enlistment onto plasma layer of the BBSome complex which would constitute a coat complex needed for sorting of particular layer proteins to the essential cilia.[67] There is huge phenotypic and sub-atomic cover between Bardet-Biedl disorder and different cilopathies.[68] Changes in a few qualities that cause BBS can likewise prompt other particular ciliopathy disorders. The principle clinical highlights are cone-pole dystrophy, with adolescence onset vision misfortune went before by night difficulty seeing; postaxial polydactyly; truncal corpulence that shows amid early stages and stays tricky all through adulthood; scholarly inability; male hypogenitalism and complex female genitourinary mutations; and renal brokenness, which is a significant reason for dreariness and mortality. BBS declaration changes both inside and in the middle of families and analysis is regularly troublesome.[69]

3.6 CYP1B1 gene in glaucoma

Glaucoma is a term portraying a gathering of visual issue with multi-factorial etiology united by a clinically trademark intraocular weight related optic neuropathy.[70] It is described by the dynamic loss of retinal ganglion cells that is connected with a trademark optic neuropathy and visual field misfortune.[71] Essential open-angle glaucoma (POAG) and edge conclusion glaucoma (ACG) are the most common types of glaucoma and are the most well-known reasons for glaucoma-related visual impairment overall.[72] The sickness shows during childbirth or in the first year of life and typically prompts perpetual vision debilitation.[73] The CYP1B1 gene was the first quality in which changes were found to bring about essential innate glaucoma. It is situated on chromosome 2p22–p21.[74] Changes in CYP1b1 have a malicious impact on reactant movement, prompting loss of capacity.[75] CYP1B1 protein is incorporated in the absorption arrangement of steroids, retinol and retinal, arachidonate, and melatonin.[76] CYP1B1 protein imparts in distinctive human visual tissues including cornea, ciliary body, iris, and retina.[77] CYP1B1 includes two coding exons and encodes the cytochrome P450 superfamily, subfamily B, polypeptide 1, a 543 amino acids long protein. It is communicated in the trabecular meshwork and in the back fragment of the eye.[78]

Despite, different in vitro and in-silico studies have exhibited the pathogenic way of the distinguished changes. Despite the fact that the accurate capacity of CYP1B1 protein in the eye is still hazy yet as it is a mono-oxygenase, the accompanying situations may be normal for its part in the advancement of the eye.[79] Pernicious changes in the protein have been involved in the genuine youth ailment essential inherent glaucoma (PCG). The exact component by which this happens or the pathway that is influenced because of changes in CYP1b1 has not been portrayed.[80] Grouping and auxiliary examinations have so far uncovered a few transformations in the CYP1b1 quality, some of which are discovered just in PCG-influenced people.[81] It could therefore be derived that changes in CYP1b1 have a harmful impact on synergist action.[82]

4. CONCLUSION

It is assessed that around 90% of human hereditary varieties are a result of single nucleotide polymorphisms (SNPs) and non synonymous reason amino acid change in proteins have a potential influence on protein structure and function. The eventual fate of SNP examination enormously lies in the improvement of customized medications that can encourage the treatment of genomic varieties actuated issue at a higher degree. A percentage of the missense changes are not connected with any adjustments in phenotype and are viewed as practical unbiased, however others conveying malicious impacts to protein work and are in charge of numerous human hereditary maladies. Here we have concentrated on eye related infections. Various eye diseases have no early reactions. They may be easy, and one may see no adjustment in their vision until the sickness has turn out to be truly cutting-edge. The absolute most ideal approach to secure the vision is through customary expert eye examinations.

We have taken normal 6 eye related maladies viz, Retinitis pigmentosa (RP2), Gyrate Atropy (OAT), Duane retraction syndrome (CHN1), Cataract (CRYGD), Bardet-Biedl syndrome (ARL6), Glaucoma (CYP1B1) for computational investigation. There are number of studies and assets which have started to investigate the impacts of missense changes in eye related genes, including: SIFT, PolyPhen and I-Mutant. However, every one of these tools won't give the outcomes with same precision. Thusly it is rationale to coordinate the normal results with best score for the missense transformations from these computational projects and ought to further assessed by basic examination incorporates (i) in silico change displaying, (ii) discovering dependability of mutants by figuring aggregate vitality, (iii) understanding the auxiliary deviation and useful action by Root Mean Square Deviation (RMSD) and (iv) mimicking the mutant protein with their accomplice/medication to figure out the coupling effectiveness to present the potential and practically huge missense changes. Here we couldn’t find any significant role for cation-π interactions in both native and mutants. Thus, we recognized the most impeding missense changes for eye related issue genes (*RP2*, *OAT*, *CHN1*, *CRYGD*, *ARL6*, and *CYP1B1*).

We found that RP2 has 14 transformations, in that 7 transformation destinations demonstrate a harmful impact by SIFT, PolyPhen and I-Mutant 3.0 score and are likewise considered to practically noteworthy nsSNPs. Cation-π communications have no huge part in local and mutants. ADP-ribosylation variable like protein 3 is a protein in people is encoded by the ARL3 quality. ARL3 ties guanine nucleotides however needs ADP ribosylation component movement. XRP2 goes about as a Guanine Nucleotide separation inhibitor for ARL3. RP2 is a specific effector protein of Arl3. Here we have discovered C86Y, R118C and D338Y were anticipated to be malicious.[39]

Of 22 variations, 16 were generally discovered to be pernicious mutants by arrangement level investigation and basic level examination. The structures of these 16 mutants were demonstrated and the RMSD among the mutants and local structures extended from 1.29å to 2.47å. Local and mutant has been docked with 3BH6 and free vitality scores have been ascertained. H319Y, G353D and L402P were said to be damaged.[49]

Of the 7 variations that were recovered from Swissprot, 6 variations were discovered less steady by I-Mutant 3.0, 6 variations were discovered to be harmful by SIFT and 6 variations were viewed as harming by PolyPhen 2.0. Five variations were chosen as possibly negative point transformations on the grounds that they were regularly discovered to be less steady, injurious and harming by the I-Mutant 3.0, SIFT and Poly-Phen-2.0 servers, individually. The structures of these 5 variations were displayed and the RMSD between the mutants and local structures went from 0.39å to 2.58å. Docking examination somewhere around 1MH1 and the local and mutant demonstrated structures created Free Energy scores between -1009.37 and -1053.73. At long last, we inferred that the lower tying partiality of 5 mutants (L20FI, Y143H, G228S, P252Q and E313K) with RAC1 contrasted and CHN1 as far as their Free vitality and RMSD scores recognized them as harmful changes. Here we have found that the mutant L → I at buildup position 20 in CHN1 may be the fundamental cause for Duane retraction syndrome.[56]

Two nsSNPs were found to be essential in I-Mutant 3.0, SIFT and PolyPhen server. The cation-π uniting developments are found to settle both the general and non-standard discretionary assistant parts. We found that the lower tying favoritism of 2 mutants (R36S and W42R) of their free energy and RMSD scores remembered them as harmful changes. So we complete up from the general results got in this work that, both the changes should be seen as indispensable in bringing on Cataract by CRYGD quality. This information will help the scientists who are managing CRYGD gene in future.[62]

Of 5 varieties that were recouped from Swissprot, each one of the 5 were found unfriendly by SIFT and I-Mutant 3.0 independently and 4 varieties were found less steady by PolyPhen. As four varieties were conventionally found to be less enduring, vindictive and hurting by SIFT, PolyPhen and I-Mutant 3.0, they were picked as conceivably unfavorable point changes. The structures of these 4 varieties were shown and the RMSD between the mutants and nearby structures were discovered. The cation-π working together stores are found to settle both the steady and non-ordinary discretionary fundamental segments. Arginine-Tyrosine and Arginine- Tryptophan sets have most grounded cation-π associations. Finally we contemplated that the lower tying inclination of 4 mutants of their free energy and RMSD scores remembered them as harmful change. Here we have taken BBS1 only. T31R and L170W were anticipated to be lethal.[69]

Out of the 54 mutants in the alpha chain of CYP1B1 protein, 36 was found to be hurting by PolyPhen server, SIFT and I-Mutant 3.0. Docking examination in the middle of local and mutants with the accomplice CYP1B1 and AHR moreover, structures made Atomic Contact Energy scores -5.2 and -497.54 independently. L77P, Y81N, A115P, M132R, R145W, S206N, E229K, V320L, A330F and R444Q were discovered to be harmfull.[82]

REFERENCES

1. Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC, Baldwin J, Devon K, Dewar K, Doyle M, FitzHugh W, Funke R, Gage D, Harris K, Heaford A, Howland J, Kann L, Lehoczky J, LeVine R, McEwan P, McKernan K, Meldrim J, Mesirov JP, Miranda C, Morris W, Naylor J, Raymond C, Rosetti M, Santos R, Sheridan A, Sougnez C, Stange-Thomann Y, Stojanovic N, Subramanian A, Wyman D, Rogers J, Sulston J, Ainscough R, Beck S, Bentley D, Burton J, Clee C, Carter N, Coulson A, Deadman R, Deloukas P, Dunham A, Dunham I, Durbin R, French L, Grafham D, Gregory S, Hubbard T, Humphray S, Hunt A, Jones M, Lloyd C, McMurray A, Matthews L, Mercer S, Milne S, Mullikin JC, Mungall A, Plumb R, Ross M, Shownkeen R, Sims S, Waterston RH, Wilson RK, Hillier LW, McPherson JD, Marra MA, Mardis ER, Fulton LA, Chinwalla AT, Pepin KH, Gish WR, Chissoe SL, Wendl MC, Delehaunty KD, Miner TL, Delehaunty A, Kramer JB, Cook LL, Fulton RS, Johnson DL, Minx PJ, Clifton SW, Hawkins T, Branscomb E, Predki P, Richardson P, Wenning S, Slezak T, Doggett N, Cheng JF, Olsen A, Lucas S, Elkin C, Uberbacher E, Frazier M, Gibbs RA, Muzny DM, Scherer SE, Bouck JB, Sodergren EJ, Worley KC, Rives CM, Gorrell JH, Metzker ML, Naylor SL, Kucherlapati RS, Nelson DL, Weinstock GM, Sakaki Y, Fujiyama A, Hattori M, Yada T, Toyoda A, Itoh T, Kawagoe C, Watanabe H, Totoki Y, Taylor T, Weissenbach J, Heilig R, Saurin W, Artiguenave F, Brottier P, Bruls T, Pelletier E, Robert C, Wincker P, Smith DR, Doucette-Stamm L, Rubenfield M, Weinstock K, Lee HM, Dubois J,

Rosenthal A, Platzer M, Nyakatura G, Taudien S, Rump A, Yang H, Yu J, Wang J, Huang G, Gu J, Hood L, Rowen L, Madan A, Qin S, Davis RW, Federspiel NA, Abola AP, Proctor MJ, Myers RM, Schmutz J, Dickson M, Grimwood J, Cox DR, Olson MV, Kaul R, Raymond C, Shimizu N, Kawasaki K, Minoshima S, Evans GA, Athanasiou M, Schultz R, Roe BA, Chen F, Pan H, Ramser J, Lehrach H, Reinhardt R, McCombie WR, de la Bastide M, Dedhia N, Blöcker H, Hornischer K, Nordsiek G, Agarwala R, Aravind L, Bailey JA, Bateman A, Batzoglou S, Birney E, Bork P, Brown DG, Burge CB, Cerutti L, Chen HC, Church D, Clamp M, Copley RR, Doerks T, Eddy SR, Eichler EE, Furey TS, Galagan J, Gilbert JG, Harmon C, Hayashizaki Y, Haussler D, Hermjakob H, Hokamp K, Jang W, Johnson LS, Jones TA, Kasif S, Kaspryzk A, Kennedy S, Kent WJ, Kitts P, Koonin EV, Korf I, Kulp D, Lancet D, Lowe TM, McLysaght A, Mikkelsen T, Moran JV, Mulder N, Pollara VJ, Ponting CP, Schuler G, Schultz J, Slater G, Smit AF, Stupka E, Szustakowki J, Thierry-Mieg D, Thierry-Mieg J, Wagner L, Wallis J, Wheeler R, Williams A, Wolf YI, Wolfe KH, Yang SP, Yeh RF, Collins F, Guyer MS, Peterson J, Felsenfeld A, Wetterstrand KA, Patrinos A, Morgan MJ, de Jong P, Catanese JJ, Osoegawa K, Shizuya H, Choi S, Chen YJ, and Szustakowki J. Initial sequencing and analysis of the human genome. Nature., 2001; 409: 860-921.

2. Hinds DA, Stuve LL, Nilsen GB, Halperin E, Eskin E, Ballinger DG, Frazer KA, and Cox DR. Whole-genome patterns of common DNA variation in three human populations. Science., 2005; 307: 1072–1079.
3. Sachidanandam R, Weissman D, Schmidt SC, Kakol JM, Stein LD, Marth G, Sherry S, Mullikin JC, Mortimore BJ, Willey DL, Hunt SE, Cole CG, Coggill PC, Rice CM, Ning Z, Rogers J, Bentley DR, Kwok PY, Mardis ER, Yeh RT, Schultz B, Cook L, Davenport R, Dante M, Fulton L, Hillier L, Waterston RH, McPherson JD, Gilman B, Schaffner S, Van Etten WJ, Reich D, Higgins J, Daly MJ, Blumenstiel B, Baldwin J, Stange-Thomann N, Zody MC, Linton L, Lander ES, and Altshuler D. A map of human genome sequence variation containing 1.42 million single nucleotide polymorphisms, Nature., 2001; 409: 928–933.
4. Cargill M, Altshuler D, Ireland J, Sklar P, Ardlie K, Patil N, Shaw N, Lane CR, Lim EP, Kalyanaraman N, Nemesh J, Ziaugra L, Friedland L, Rolfe A, Warrington J, Lipshutz R, Daley GQ, and Lander ES. Characterization of single nucleotide polymorphisms in coding regions of human genes. Nat Genet., 1999; 22: 231–238.
5. Chasman D, and Adams RM Adams (2001). Predicting the functional consequences of non-synonymous single nucleotide polymorphisms: structure-based assessment of amino acid variation., J Mol Biol, 2001; 307(2): 683–706.
6. Dryja TP, McGee TL, Hahn LB, Cowley GS, Olsson JE, Reichel E, Sandberg MA, and Berson EL. Mutations within the rhodopsin gene in patients with autosomal dominant retinis pigmentosa. N Engl J Med, 1990; 323: 1302– 1307.
7. Smith EP, Boyd J, Frank GR, Takahashi H, Cohen RM, Specker B, Williams TC, Lubahn DB, and Korach KS. Estrogen resistance caused by a mutation in the estrogen-receptor gene in a man, N Engl J Med, 1994; 331: 1056– 1061.
8. Krawczak M, Ball EV, Fenton I, Stenson PD, Abeysinghe S, Thomas N, and Cooper DN. Human gene mutation database-a biomedical information and research resource, Hum Mutat, 2000; 15: 45–51.
9. Ferrer-Costa C, Gelpí JL, Zamakola L, Parraga I, de la Cruz X, and Orozco M. PMUT: a web-based tool for the annotation of pathological mutations on proteins, Bioinformatics., 2005; 21: 3176-3178.
10. Lappalainen I, Thusberg J, Shen B, and Vihinen M. Genome wide analysis of pathogenic SH2 domain mutations. Proteins., 2008; 72: 779-92.
11. Capriotti E, Fariselli P, and Casadio R. I-Mutant2.0: predicting stability changes upon mutation from the protein sequence or structure. Nucleic Acids Res., 2005; 1: 306-310.
12. Shen Y, Zhang Y, Ma T, Bao X, Du F, Zhuang G, and Qu Y. Simultaneous saccharification and fermentation of acid-pretreated corncobs with a recombinant Saccharomyces cerevisiae expressing beta-glucosidase. Bioresour Technol., 2008; 99: 5099-5103.
13. Ng PC, and Henikoff S. Predicting the effects of amino acid substitutions on protein function, Annu Rev Genomics Hum Genet., 2006; 7: 61-80.
14. Zilberman D, Gehring M, Tran RK, Ballinger T, and Henikoff S. Genome-wide analysis of Arabidopsis thaliana DNA methylation uncovers an interdependence between methylation and transcription. Nat Genet., 2007; 39: 61-69.
15. Ramensky V, Bork P, and Sunyaev S. Human non-synonymous SNPs: server and survey. Nucleic Acids Res., 2002; 1: 3894-3900.
16. Capriotti E, Arbiza L, Casadio R, Dopazo J, Dopazo H, and Marti-Renom MA. Use of estimated evolutionary strength at the codon level improves the prediction of disease-related protein mutations in humans. Hum Mutat., 2008; 29: 198-204.
17. Zhou F, Xue Y, Lu H, Chen G, and Yao X. A genome-wide analysis of sumoylation-related biological processes and functions in human nucleus, FEBS Lett., 2005; 576: 3369-3375.
18. Zhong H, Voll RE, and Ghosh S. Phosphorylation of NF-kappa B p65 by PKA stimulates transcriptional activity by promoting a novel bivalent interaction with the coactivator CBP/p300, Mol Cell., 1998; 1: 661-667.
19. Justin PG, and Dennis AD. A Computational Study of Cation−π Interactions vs Salt Bridges in Aqueous

Media: Implications for Protein Engineering. J. Am. Chem. Soc., 2000; 122: 870–874.
20. Zacharias N, and Dougherty DA. Cation-pi interactions in ligand recognition and catalysis. Trends Pharmacol Sci., 2002; 23: 281-287.
21. DA Dougherty. The Cation- π Interaction. Science., 1996; 271: 163-168.
22. Mecozzi S, West AP Jr, and Dougherty DA. (1996). A Cation-pi interactions in aromatics of biological and medicinal interest: electrostatic potential surfaces as a useful qualitative guide. Proc. Natl. Acad. Sci., 1996; 10566–10571.
23. Leanne MM, Kirk AM, and Brian JW. An assessment of grassland restoration success using species diversity components. J Appl Ecol., 2005; 42: 327-336.
24. Kitchen DB, Decornez H, Furr JR, and Bajorath J. Docking and scoring in virtual screening for drug discovery: methods and applications. Nat Rev Drug Discov., 2004; 3: 935-949.
25. Anish M, Gill NS, and Arora R. A Review on Molecular Docking. Int. J. Recent Adv. Pharm. Res., 2014; 4: 64-70.
26. Brooijmans N and Kuntz ID. Molecular recognition and docking algorithms. Annu. Rev. Biophys. Biomol. Struct., 2003; 32: 335-373.
27. Karin K, Veltel S, Schlichting I, and Wittinghofer A. Crystal structure of the human retinitis pigmentosa 2 protein and its interaction with Arl3. Structure, 2006; 14: 367-378.
28. Jane ER, Hardcastle JA, Michael, and Cheetham ME. Focus on Molecules: X-linked Retinitis Pigmentosa 2 protein, RP2. Exp. Eye. Res., 2006; 82: 543-544.
29. Humphries P, Farrar GJ, Kenna P, and McWilliam P. Retinitis pigmentosa: genetic mapping in X-linked and autosomal forms of the disease. Clin. Genet., 1990; 38: 1-13.
30. Evans RJ, Hardcastle AJ, and Cheetham ME. Focus on molecules: X-linked Retinitis Pigmentosa 2 protein, RP2. Exp. Eye. Res., 2006; 82: 543-544.
31. Schwahn U, Paland N, Techritz S, Lenzner S, and Berger W. Mutations in the X-linked RP2 gene cause intracellular misrouting and loss of the protein, Hum. Mol. Genet. 2001; 10: 1177-1183.
32. Schwarz N, Novoselova TV, Wait R, Hardcastle AJ, and Cheetham ME. The X-linked Retinitis Pigmentosa protein RP2 facilitates traffic of cilia target proteins. Hum. Mol. Genet., 2012; 21: 863-873.
33. Schwahn U, Lenzner S, Dong J, Feil S, Hinzmann B, Duijnhoven G, Kirschner R, Hemberger M, Bergen AA, Rosenberg T, Pinckers AJ, Fundele R, Rosenthal A, Cremers FP, Ropers HH and Berger W. Positional cloning of the gene for X-linked retinitis pigmentosa, Hum. Mol. Genet., 1998; 19: 327 – 332.
34. Bartolini F, Bhamidipati A, Thomas S, Schwahn U, Lewis SA and Cowan NJ. Functional overlap between retinitis pigmentosa 2 protein and the tubulin-specific chaperone cofactor. C. J. Biol. Chem., 2002; *277:* 14629-14634.
35. Grayson C, Bartolini F, Chapple JP, Willison KR, Bhamidipati A, Lewis SA, Luthert PJ, Hardcastle AJ, Cowan NJ, and Cheetham ME. Localization in the human retina of the X-linked retinitis pigmentosa protein RP2, its homologue cofactor C and the RP2 interacting protein Arl3. Hum. Mol. Genet., 2002; 11: 3065-3074.
36. Olitsky SE, Hug D, Plummer LS, Isern MS, Kliegman RM, Behrman RE, Jenson HB and Stanton BF. Disorders of the retina and vitreous. Nelson Textbook of Pediatrics, Philadelphia. PA: Saunders Elsevier., 2011; 622.
37. Evans RJ, Schwarz N, Nagel-Wolfrum K, Wolfrum U, Hardcastle AJ, and Cheetham ME. The retinitis pigmentosa protein RP2 links pericentriolar vesicle transport between the Golgi and the primary cilium. Hum. Mol. Genet., 2010; 19: 1358-1367.
38. Yanoff M, and Cameron D. Diseases of the visual system. J. Neuroophthalmol., 2011; 72: 302-327.
39. Jincy AJ, Rajasekaran R, Sethumadhavan R. Computational Analysis of Significant Missense Mutations in RP2 Gene That Cause Retinitis Pigmentosa. J. Bioinf. Intell. Control., 2013; 2: 228-236.
40. Doimo M, Desbats MA, Baldoin MC, Lenzini E, Basso G, Murphy E, Graziano C, Seri M, Burlina A, Sartori G, Trevisson E, and Salviati L. Functional analysis of missense mutations of OAT, causing gyrate atrophy of choroid and retina, Hum. Mutat., 2013; 34: 229–236.
41. Ohkubo Y, Ueta A, Ito T, Sumi S, Yamada M, Ozawa K, and Togari H. Vitamin B6-responsive ornithine aminotransferase deficiency with a novel mutation G237D, Tohoku J. Exp. Med., 2005; 205: 335-42.
42. Wang T, Steel G, Milam AH, Valle D. Correction of ornithine accumulation prevents retinal degeneration in a mouse model of gyrate atrophy of the choroid and retina, J. Inherit . Metab. Dis., 2004; 97: 187-196.
43. O'Donnell JJ, Vannas-Sulonen K, Shows TB, and Cox DR. Gyrate atrophy of the choroid and retina: assignment of the ornithine aminotransferase structural gene to human chromosome 10 and mouse chromosome 7, Am. J. Hum. Genet., 1988; 43: 922-928.
44. Inana G, Totsuka S, Redmond M, Dougherty T, Nagle J, Shiono T, Ohura T, Kominami E, and Katunuma N. Molecular cloning of human ornithine aminotransferase mRNA. Proc. Natl. Acad. Sci. U S A., 1986; 83: 1203-1207.
45. Shah SA, Shen BW, and Brünger AT. Human ornithine aminotransferase complexed with L-canaline and gabaculine: structural basis for substrate recognition, Structure, 1997; 5: 1067-1075.
46. Jana Stránská,David Kopečný, Martina Tylichová, Jacques Snégaroff, and Marek Šebela. Ornithine δ-

aminotransferase. Plant Signal Behav., 2008; 3: 929-935.
47. Barrett DJ, Bateman JB, Sparkes RS, Mohandas T, Klisak FI, and lnono G. Chromosomal localization of human ornithine aminotransferase gene sequences to 10q26 and Xp11.2. Invest. Ophth. Vis. Sci., 1987; 28: 1037-42.
48. Seiler N. Ornithine aminotransferase, a potential target for the treatment of hyperammonemias. Curr. Drug Targets., 2000; 1: 119-153.
49. Jincy AJ, and Rao S. Computational Analysis of Significant Missense Mutations in OAT gene that cause Gyrate Atrophy. Res. J. Pharm., Biol. Chem. Sci., 2014; 5: 1289-1299.
50. Miller NR, Kiel SM, Green WR, and Clark AW. Unilateral Duane's retraction syndrome (Type 1), Arch. Ophthalmol., 1982; 100: 1468-1472.
51. Appukuttan B, Elizabeth G, Suh-Hang J, Diana F, Sandra O, Raman S, Ann VA, Joan B, Xiaoguang W, Reshma JP, Christiane MR, Mina C, Geralyn A, Kenneth W, Mark SB, Jeffrey MT, Michael JB and Timothy S. Localization of a gene for Duane retraction syndrome to chromosome 2q31. Am. J. Hum. Genet., 1999; 65: 1639-46.
52. Azarmina M, and Azarmina H. The Six Syndromes of the Sixth Cranial Nerve, J. Ophthalmic. Vis. Res., 2013; 8: 160–171.
53. Chung M, Stout JT, and Borchert MS. Clinical diversity of hereditary Duane's retraction syndrome. Ophthalmology., 2000; 107: 500-503.
54. Miyake N, Chilton J, Psatha M, Cheng L, Andrews C, Chan W, Law K, Crosier M, Lindsay S, Cheung M, Allen J, Gutowski NJ, Ellard S, Young E, Iannaccone A, Appukuttan B, Stout JT, Christiansen S, Ciccarelli ML, Baldi A, Campioni M, Juan CZ, Davenport D, Mariani LE, Sahin M, Guthrie S, and Engle CE . Human CHN1 mutations hyperactivate α2-chimaerin and cause Duane's retraction syndrome, Science, 2008; 321: 839-843.
55. Evans JC, Frayling TM, Ellard S, and Gutowski NJ. Confirmation of linkage of Duane's syndrome and refinement of the disease locus to an 8.8-cM interval on chromosome 2q31. Hum. Genet., 2000; 106: 636-638.
56. Jincy AJ, and Rao S. Computational Identification and Structural Analysis of Deleterious Functional Snps in Chn1 Gene Causing Duane Retraction Syndrome. Int J Pharm Sci Rev Res, 2015; 2: 319-326.
57. David AQ. Common Causes of Vision Loss in Elderly Patients, Am. Fam. Physician. 1999; 60: 99-108.
58. David A, and Abhay V. Cataract and surgery for cataract, Brit. Med. J., 2006; 333: 128–132.
59. Deborah, KVV, Caroline A, Bharti RN, and Elizabeth CE. Crystalline cataract caused by a heterozygous missense mutation in γD-crystallin (CRYGD). Mol. Vis., 2011; 17: 3333–3338.
60. Dietrich AS, Elizabeth G, Deborah V, Diana F, Graeme W, Andreas DB, Christiane, Ann MR, Matthew V, Joan IQ, Suh-Hang B, Jeffrey HJ, Lois MT, and Michael JB. Progressive juvenile-onset punctate cataracts caused by mutation of the γD-crystallin gene. Proc .Natl. Acad. Sci. USA., 1999; 96: 1008-1012.
61. Lander ES. The new genomics: global views of biology. Science., 1996; 274: 536-539.
62. Jincy AJ, and Rao S. Insilico analysis of functional SNPs in crygd gene that cause cataract. Indian Pharmocology and Pharmacy Research., 2014; 1: 1-7.
63. Forsythe E, and Beales PL. Bardet-Biedl syndrome. Eur. J. Hum. Genet. 2013; 21: 8–13.
64. Slavotinek AM., Stone EM, Mykytyn K, Heckenlively JR, Green JS, Heon E, Musarella MA, Parfrey PS, and Sheffield VC. Mutations in MKKS cause Bardet-Biedl syndrome. Nat. Genet., 2000; 26: 15-16.
65. Shah AS, Farmen SL, Moninger OT, Businga RT, Andrews PM, Bugge K, Searby C, Nishimura D, Brogden AK, Kline JN, Sheffield VC, and Welsh MJ. Loss of Bardet-Biedl syndrome proteins alters the morphology and function of motile cilia in airway epithelia. Proc. Natl. Acad. Sci. USA., 2008; 105: 3380–3385.
66. Chiang PA, Nishimura D, Searby C, Elbedour K, Carmi R, Ferguson AL, Secrist J, Braun T, Casavant T, Stone EM, and Sheffield VC. Novel mutations in BBS5 highlight the importance of this gene in non-Caucasian Bardet–Biedl syndrome patients. Am. J. Hum. Genet., 2004; 75: 475–484.
67. Nachury MV, Loktev AV, Zhang Q, Westlake CJ, Peranen J, Merdes A, Slusarski DC, Scheller RH, Bazan FJ, Sheffield VC, and Jackson PK. A Core Complex of BBS Proteins Cooperates with the GTPase Rab8 to Promote Ciliary Membrane Biogenesis. Cell, 2007; 129: 1201–1213.
68. Bealesa PL, Elcioglub N, Woolfc AS, Parkerd D, and Flintera FA. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. J. Med. Genet., 1999; 36: 437-44.
69. Jincy AJ, and Rao S. Computational Identification and Structural Analysis of Deleterious Functional SNPs in ARL6 Gene Causing Bardet-Biedl Syndrome. Res. J. Pharm. Biol. Chem. Sci., 2014; 5: 1360-1368.
70. Casson RJ, Chidlow G, Wood JP, Crowston JG, and Goldberg I. Definition of glaucoma: clinical and experimental concepts. Clin. Experiment Ophthalmol., 2012; 40: 341-349.
71. Kuehn MH, Fingert JH, and Kwon YH. Retinal ganglion cell death in glaucoma: mechanisms and neuroprotective strategies. Ophthalmol. Clin. North Am., 2005; 18: 383-395.
72. Liu Y, and Allingham RR. Molecular genetics in glaucoma. Exp. Eye Res., 2011; 93: 331-339.
73. Gogate P, Gilbert C, and Zin A. Severe Visual Impairment and Blindness in Infants: Causes and Opportunities for Control. Middle East Afr. J. Ophthalmol., 2011; 18: 109-114.

74. Lim SH, Tran-Viet KN, Yanovitch TL, Freedman SF, Klemm T, Call W, Powell C, Ravichandran A, Metlapally R, Nading EB, Rozen S, and Young LT. CYP1B1, MYOC, and LTBP2 Mutations in Primary Congenital Glaucoma Patients in the United States. Am. J. Ophthalmol., 2013; 155: 508-517.
75. Achary MS, and Nagarajaram HA. Comparative docking studies of CYP1b1 and its PCG-associated mutant forms. J. Biosci., 2008; 33: 699-713.
76. Vasiliou V, and Gonzalez FJ. Role of CYP1B1 in glaucoma. Annu. Rev . Pharmacol. Toxicol., 2008; 48: 333-58.
77. Kaur K, Mandal AK, and Chakrabarti S. Primary Congenital Glaucoma and the Involvement of CYP1B1. Middle East Afr. J. Ophthalmol. 2011; 18: 7-16.
78. Sheikh SA, Waryah AM, Narsani AK, Shaikh H, Gilal IA, Shah K, Qasim M, Memon AI, Kewalramani P, and Shaikh N. Mutational spectrum of the CYP1B1 gene in Pakistani patients with primary congenital glaucoma: Novel variants and genotype-phenotype correlations. Mol. Vis., 2014; 20: 991-1001.
79. Guengerich FP, and Cheng Q. Orphans in the Human Cytochrome P450 Superfamily: Approaches to Discovering Functions and Relevance in Pharmacology. Pharmacol. Rev., 2011; 63: 684-699.
80. Achary MS, and Nagarajaram HA. Comparative docking studies of CYP1b1 and its PCG-associated mutant forms. J. Biosci., 2008; 33: 699-713.
81. Jones GE, Ostergaard P, Moore AT, Connell FC, Williams D, Quarrell O, Brady AF, Spier I, Hazan F, Moldovan O, Wieczorek D, Mikat B, Petit F, Coubes C, Saul RA, Brice G, Gordon K, Jeffery S, Mortimer PS, Vasudevan PC, and Mansour S. Microcephaly with or without chorioretinopathy, lymphoedema, or mental retardation (MCLMR): review of phenotype associated with KIF11 mutations. Eur. J. Hum. Genet., 2014; 22: 881-887.
82. Jincy AJ, and Rao S. Identification and Structural Comparison of Deleterious Mutations in Nssnps of Cyp1b1 Gene in Glaucoma. Int J Recent Sci Res., 2015; 6: 4644-4652.