Molecular Vision 2017; 23:1048-1080 <http://www.molvis.org/molvis/v23/1048>
Received 8 May 2017 | Accepted 29 December 2017 | Published 31 December 2017

Insight into the molecular genetics of myopia

Jiali Li, Qingjiong Zhang

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China

Myopia is the most common cause of visual impairment worldwide. Genetic and environmental factors contribute to the development of myopia. Studies on the molecular genetics of myopia are well established and have implicated the important role of genetic factors. With linkage analysis, association studies, sequencing analysis, and experimental myopia studies, many of the loci and genes associated with myopia have been identified. Thus far, there has been no systemic review of the loci and genes related to non-syndromic and syndromic myopia based on the different approaches. Such a systemic review of the molecular genetics of myopia will provide clues to identify additional plausible genes for myopia and help us to understand the molecular mechanisms underlying myopia. This paper reviews recent genetic studies on myopia, summarizes all possible reported genes and loci related to myopia, and suggests implications for future studies on the molecular genetics of myopia.

1. Introduction:

Myopia is the most common cause of visual impairment worldwide. Myopia is a condition in which parallel light passes through the eye and focuses in front of the retina. Myopia can be classified as common myopia with refractive error less than −6 diopters (D) and high myopia with refractive error equal or greater than −6 D. Myopia can sometimes be an accompanying symptom in other diseases. Thus, myopia can also be classified as non-syndromic myopia (if it occurs alone) and syndromic myopia (if it is an associated sign of another ocular or systemic disease). As common myopia is too common to be a sign of a specific disease, usually high myopia has been reported as a specific phenotype of a syndrome or other ocular or systemic diseases; thus, syndromic myopia usually means syndromic high myopia. Myopia may also be classified as physiologic myopia (usually low-grade myopia) and pathological myopia (mostly associated with degenerative changes in the retina). Sometimes, common or physiologic myopia in early childhood may develop as high myopia or pathological myopia in adult or older individuals. Most individuals with high myopia may not have pathological changes in the retina, especially in younger ages.

Genetic and environmental factors are well known components that contribute to the development of myopia. Common myopia is more likely to be a complex trait, resulting from the effects of genetic and environmental factors. High myopia may be transmitted as a complex trait (especially late-onset high myopia commonly seen in university students) or a Mendelian trait (such as most early-onset high myopia that is not related to extensive near work) [1]. Efforts to decipher the hereditary determinants of myopia began in the 1960s, and the important role of genetic factors has been implicated in several studies, including familial aggregation, pedigree analysis, twin studies, and population studies. Until now, many loci and genes associated with myopia have been identified with linkage analysis, association studies, whole exome sequencing, and experimental myopia studies. This paper reviews the genetic determinations of myopia and the molecular genetics of non-syndromic and syndromic myopia according to the different approaches.

Correspondence to: Qingjiong Zhang, State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, 54 Xianlie Road, Guangzhou 510060, China; Phone: (+86)-20-87333393; FAX: (+86)-20-87333271; email: zhangqji@mail.sysu.edu.cn or zhangqingjiong@gzzoc.com

2. Contribution of genetic factors to the development of human myopia:

2.1 Hereditability and familial aggregation of myopia—Familial aggregation has provided strong evidence to support the important role of genetic factors in causing the pathogenesis of myopia [2-6]. Studies on individuals with myopia from different populations have shown positive indications. For example, Yap et al. performed refraction examinations on 2,888 children in China to investigate the risks of passing myopia from parents to children [2]. This study showed that children with myopic parents tend to have a greater chance of developing myopia than those without myopic parents. Several subsequent studies also supported this finding. Ip et al. conducted a similar study on 2,353 children in Australia with a mean age of 7 years [4]. The results suggested that the prevalence of myopia increased statistically significantly with the number of myopic parents; the associated development risk rates are 7.6% for no myopic parents, 14.9% for one myopic parent, and 43.6% for two myopic

parents. In addition, the recurrence risks of myopia among siblings with myopia are also higher than siblings without myopia. A report based on 6,497 inhabitants in Tehran, Iran, confirmed that the heritability of refractive error is 61%, and the ratio of sibling recurrence odds for myopia is 2.25–3.00 [6]. Apart from refraction status, the impacts of myopia in parental history on children's ocular growth were also observed. Lam et al. followed up with 7,560 children in China for 1 year and reported the effects of myopia in parental history, including eye size and growth. The change in annual axial length increased with the number of myopic parents: 0.20 mm, 0.26 mm, and 0.37 mm for children with no, one, and two myopic parents, respectively [3]. This line of evidence suggests that the genetic risks are higher in families with myopia.

2.2 Genetic transmission traits of myopia—Pedigree analysis is widely used in myopia and high myopia studies. High myopia is often found to be transmitted through families in Mendelian patterns, including autosomal dominant (AD), autosomal recessive (AR), and X-linked recessive (XL) inheritance. Based on linkage analysis, 18 myopia and high myopia loci have been discovered and documented in the Online Mendelian Inheritance in Man database (OMIM), including nine high myopia loci in AD inheritance (*MYP2*: Gene ID 4658, OMIM 160700 [7], *MYP3*: Gene ID 8782, OMIM 603221 [8], *MYP5*: Gene ID 404682, OMIM 608474 [9], *MYP11*: Gene ID 594832, OMIM 609994 [10], *MYP12*: Gene ID 664780, OMIM 609995 [11], *MYP15*: Gene ID 100294716, OMIM 612717 [12], *MYP16*: Gene ID 100270641, OMIM 612554 [13], *MYP17*: Gene ID 100359401, OMIM 608367 [14], and *MYP19*: Gene ID 100653370, OMIM 613969 [15]), one high myopia locus in AR inheritance (*MYP18*, Gene ID 100359406, OMIM 255500 [16]), two XL recessive high myopia loci (*MYP1*: Gene ID 4657, OMIM 310460 [17] and *MYP13*: Gene ID 677764, OMIM 300613 [18]), and six myopia loci (*MYP6*: Gene ID 9997, OMIM 608908 [19], *MYP7*: Gene ID 553190, OMIM 609256 [20], *MYP8*: Gene ID 553192, OMIM 609257 [20], *MYP9*: Gene ID 553194, OMIM 609258 [20], *MYP10*: Gene ID 553195, OMIM 609259 [20], and *MYP14*: Gene ID 100359407, OMIM 610320 [21]). The identification of these 18 loci in the human genome through linkage studies not only indicates the contribution of genetic factors to myopia but also provides clues for further screening of candidate genes.

2.3 Twin study: Monozygotic twins have more similar refraction than dizygotic twins—A twin study is an ideal way to estimate the hereditary component of myopia. This study design provides cogent evidence for the important role of genetic factors in myopia. Monozygotic twins are identical in genetic material, while dizygotic twins share 50% of their genetic material. Therefore, monozygotic twins are considered to have more similarity in phenotype for genetic diseases. A comparison of similarity in refraction power between monozygotic and dizygotic twins can be used to evaluate the heritability of myopia. Karlsson et al. systemically reviewed a series of twin studies and found that 95% of monozygotic twins appear to have a similar refraction power, and only 29% of dizygotic twins have such similarity [22]. Subsequently, several large-scale twin studies from different countries confirmed this finding, and the heritability varied from 75% to 94% [23-25]. In addition, the impacts of genetic and environmental factors on myopia have been observed by analyzing refraction power in 1,152 monozygotic twins and 1,149 dizygotic twins: 77% of the difference in refraction power was explained by genetic components, while 7% of the difference was explained by environmental factors [26]. This result once again supports the importance of genetic factors in the development of myopia.

2.4 SNPs in myopia-related genes from population-based association studies—Population-based association studies include genome-wide association studies (GWASs) and case-control studies. Population-based association studies have identified that many single nucleotide polymorphisms (SNPs) are statistically significantly associated with myopia, suggesting the involvement of multiple gene effects. The traits used in an association study include spherical equivalent (SE), axial length, and corneal curvature. Although there are some controversial issues and arguments related to the results of association studies, some SNPs have been replicated and confirmed to be statistically significantly associated with myopia or high myopia in separate independent studies from different populations. The replication of significant SNPs is necessary before further analysis is conducted. Disease-associated SNPs would be more convincing if they could be replicated in different large-scale GWASs. For example, Kiefer et al. [27] and Verhoeven et al. [28] identified several significant associations of SNPs in 45,771 and 45,758 participants with myopia and refractive error, respectively. Twelve SNPs were discovered in these two different studies, which provided strong evidence that the 12 SNPs are statistically significantly associated with myopia. Association studies, similar to pedigree analysis, have indicated the importance of genetic factors in myopia and provided clues for discovering new causative genes.

3. Molecular genetic basis of non-syndromic myopia: The role of molecular genetics in myopia has been investigated mainly in population- and family-based studies. GWASs, as one of the major forms, have been widely used to identify

associations between the characteristics of myopia (i.e., refraction, axial length, or corneal curvature) and genetic variants across the whole genome. Meanwhile, linkage analysis was traditionally applied in family-based studies to exploit linkage regions within families, especially for Mendelian high myopia. Aside from the approaches above, whole exome sequencing and experimental myopia studies have also been applied to reveal the molecular genetic basis of myopia. Overall, molecular genetic studies on myopia have identified numerous loci and genes, which are of great importance in implicating the mechanisms underlying myopia.

3.1 Linkage analysis of the genetic loci for myopia— Myopia is generally heterogeneous. Through linkage analysis of families with myopia and high myopia, about 18 loci have been identified. The details of these 18 loci were mentioned above and are listed in Table 1. The candidate genes inside the linkage intervals have been screened based on their potential functions involved in the development of myopia.

3.1.1 Susceptibility loci for common myopia— Common myopia is usually considered a complex trait because genetic and environmental factors contribute to the susceptibility risk. The genetic mapping of complex traits has identified six susceptibility loci for myopia. Among them, four loci (*MYP7–MYP10*) were identified in a genome-wide scan with a multipoint linkage analysis in 226 monozygotic and 280 dizygotic twins, using refraction as a quantitative trait ranging from −12.12 D to + 7.25 D [20]. In these four loci, *MYP10* was replicated in a GWAS with high myopia (rs189798) [29], and *MYP7* was replicated in another genome-wide scan in dizygotic twins [20,30].

For two other loci, *MYP*6 and *MYP14*, *MYP6* was mapped in a genome-wide scan in 44 Ashkenazi Jewish families with mild to moderate myopia [19]. The scan was replicated in another genome-wide scan of 486 extended families with refractions ranging from −12.13 D to +8.38 D [31]. *MYP14* was identified in a genome-wide scan with multipoint regression-based quantitative trait locus (QTL) linkage in 49 Ashkenazi Jewish families (mean SE=−3.46 D

Table 1. Loci identified by linkage studies.

Phenotype	Location	MIM number	Size(Mb)	Lod Score	Study poplution	Reference
adHM						
MYP2	18p11.31	160,700	7.6-cM	9.59	USA	(Young TL et al., 2001)
MYP3	12q21-q23	603,221	30.1-Cm	3.85	German/Italian	(Young TL et al., 1998)
MYP5	17q21-q22	608,474	7.71-cM	3.17	English/Canadian	(Paluru P et al., 2003)
MYP11	4q22-q27	609,994	20.4-cM	3.11	Chinese	(Zhang Q et al., 2005)
MYP12	2q37.1	609,995	9.1 cM	4.75	Northern European	(Paluru PC et al., 2005)
MYP15	10q21.1	612,717	2.67 cM	3.22	Hutterite	(Nallasamy S, 2007)
MYP16	5p15.33-p15.2	612,554	17.45Mb	4.81	Chinese	(Lam CY et al., 2008)
MYP17	7p15	608,367	7.81 cM	NA	France	(Paget et al., 2008)
MYP19	5p15.1-p13.3	613,969	14.14-Mb	3.71	Chinese	(Ma et al., 2010)
arHM						
MYP18	14q22.1-q24.2	255,500	25.23-Mb	2.19	Chinese	(Yang et al., 2009)
X-linked HM						
MYP1	Xq28	310,460	6.1cM	3.59	Chinese	(Guo et al., 2010)
MYP13	Xq23-q27.2	300,613	25-cM	2.75	Chinese	(Zhang et al., 2006)
Complex myopia						
MYP6	22q12.3	608,908	4cM	3.54	Ashkenazi Jewish	(Stambolian et al., 2004)
MYP7	11p13	609,256	40cM	6.1	UK	(Hammond et al., 2004)
MYP8	3q26	609,257	185cM	3.7	UK	(Hammond et al., 2004)
MYP9	4q12 3.3	609,258	65cM	3.3	UK	(Hammond et al., 2004)
MYP10	8p23	609,259	NA	3.7	UK	(Hammond et al., 2004)
MYP14	1p36	610,320	49.1 Cm	9.5	Ashkenazi Jewish	(Wojciechowski et al., 2006)

Note: adHM, autosomal dominant high myopia; arHM, autosomal recessive high myopia; NA, not available

± 3.29 D) [21]. In a large international collaborative study of high myopia, *MYP14* (1p36.32) was replicated in a subset of 24 families from Denmark with a maximum logarithm (base 10) of odds (LOD) score of 1.8 at rs1870509 in a multipoint linkage analysis [32].

Candidate genes within these six myopia loci have been screened according to their related functions. *PAX6* (Gene ID: 5080, OMIM: 607108), located in the *MYP7* locus, has been of great concern and research interest. *PAX6* is an important transcriptional regulator involved in the development of the eye [33] from the surface ectoderm to the cornea and the lens [34,35] and from the neuroectoderm to the iris, ciliary body, and retina [36,37]. Mutations in *PAX6* are associated with a wide range of abnormalities in humans, including aniridia, Peter's anomaly, microcornea, cataract, coloboma of the optic nerve, microphthalmia, and nystagmus [38-43]. Studies have reported an association between *PAX6* and high myopia [44-49], but these results are not consistent with other studies [50-52]. Therefore, *PAX6* should be evaluated with caution as a candidate gene for myopia. *MYP8*, *MYP9*, and *MYP10* have not been investigated yet as candidate genes.

3.1.2 Genetic loci and genes identified in families with high myopia—In genetic analysis of non-syndromic high myopia, 12 loci have been identified using linkage studies, as mentioned above (Table 1). These loci were frequently observed in families with Mendelian high myopia, characterized by onset in early childhood (≤7 years old) and monogenic inheritance. Several loci have been replicated or refined in independent families using the same approach.

Of these 12 loci, *MYP1*, located at Xq28, is a locus for non-syndromic and syndromic high myopia (the latter will be discussed in the section on syndromic myopia). In studies on non-syndromic high myopia, *MYP1* was mapped in a Chinese family [17] with high myopia, and the finding was replicated in two Indian families [53]. *MYP3* was revealed by Young et al. in a large German–Italian family [8] and was further replicated in at least four independent studies involving different populations [32,54-56]. Moreover, a genome-wide scan in 254 families with high myopia also discovered the *MYP1*, *MYP3*, *MYP6*, *MYP11*, *MYP12*, and *MYP14* loci and identified a novel locus at chromosome 9q34.11 [32]. In addition, several loci have been replicated in association studies on myopia, including *MYP11*, *MYP15*, *MYP16*, and *MYP17*. However, compared with the high prevalence of high myopia in the general population, these 12 loci account for fewer than 5% of individuals with high myopia, suggesting that more loci and genes await to be identified.

Numerous candidate genes in these 12 loci have been screened in different kinds of studies, including direct sequencing, association analysis, and experimental animal analysis. Although several candidate genes or SNPs have been investigated frequently in association studies, inconsistent results were often noted. No mutations in candidate genes have been identified in mapped families using Sanger sequencing (Table 2) [10,11,13,15,17,53,57-59]. For example, *TGIF* (Gene ID 7050, OMIM 602630), located in the *MYP2* locus, is expressed strongly in the sclera, retina, and optic nerve. *TGIF* is involved in the regulation of the transforming growth factor (TGF)-beta pathway [60], which has a close relationship with the development of myopia [61,62]. However, screening mutations in *TGIF* among affected members in families mapped to *MYP2* did not identify any cosegregated mutations; no significant associations between SNPs in *TGIF* and high myopia were reported [3,63,64]. Although knockout of *LUM* (Gene ID 4060, OMIM 600616; located in *MYP3*) in mice showed a series of myopia-related phenotypes [65], Sanger sequencing of *LUM* in an *MYP3*-mapped family did not identify any mutations [57]. Other candidate genes within these loci are not listed here because of their undetermined relationship with myopia. The exact mutations among these genes need to be further studied. Especially with the method of whole exome sequencing, which fully screens all genes within linkage regions for mapped families, new genes are expected to be revealed in the future.

3.2 Genetic association studies on myopia—To investigate the genetic factors for myopia in the general population, GWASs and a series of replications in follow-up association studies have identified numerous associations with myopia, although some are uncertain. A literature search was conducted in PubMed (until 11/18/2016) using the following terms: (association) and myopia/genetics, myopia and gene and association, and (association) and refractive errors/genetics. Only association studies related to myopia are included and reviewed in this section. There were some controversial issues in the GWASs and case-control association studies, such as the level of the test and the sample sizes. Thus, this part of the review mainly focuses on genetic loci that were detected by GWASs and met the significance standard of $p<5 \times 10^{-8}$.

3.2.1 Evidence of associations between polymorphisms and common myopia—Thus far, around 82 loci for myopia have been examined in GWASs and case-control association studies using refractions between −0.50 D and −6.00 D as parameters (Appendix 1) [3,27,52,66-94]. Of these 82 loci, 41 loci were identified by seven GWAS and GWAS meta-analyses (Appendix 1) that met the requirement of $p<5 \times 10^{-8}$. An important principle for an association study is replication, replication, and replication. The 15q14 locus has

Table 2. Candidate genes within linkage region were screened in mapped-families using Sanger sequencing.

Position	Locus	Genes	Reference
2q37.1	MYP12	SAG	(Paluru et al., 2005)
2q37.1	MYP12	DGKD	(Paluru et al., 2005)
4q22-q27	MYP11	RRH	(Zhang et al., 2005)
5p15.33-p15.2	MYP16	IRX2	(Lam et al., 2008)
5p15.33-p15.2	MYP16	IRX1	(Lam et al., 2008)
5p15.33-p15.2	MYP16	POLS	(Lam et al., 2008)
5p15.33-p15.2	MYP16	CCT5	(Lam et al., 2008)
5p15.33-p15.2	MYP16	LOC442129	(Lam et al., 2008)
5p15.33-p15.2	MYP16	CTNND2	(Lam et al., 2008)
5p13.3-p15.1	MYP19	CDH6	(Ma et al., 2010)
5p13.3-p15.1	MYP19	CDH10	(Ma et al., 2010)
5p13.3-p15.1	MYP19	CDH12	(Ma et al., 2010)
5p13.3-p15.1	MYP19	PDZD2	(Ma et al., 2010)
5p13.3-p15.1	MYP19	GOLPH3	(Ma et al., 2010)
5p13.3-p15.1	MYP19	ZFR	(Ma et al., 2010)
12q21-q23	MYP3	LUM	(Paluru et al., 2004)
18p11.31	MYP2	TGIF	(Scavello et al., 2004; Young et al., 2004)
18p11.31	MYP2	EMLIN-2	(Young et al., 2004)
18p11.31	MYP2	MLCB	(Young et al., 2004)
18p11.31	MYP2	CLUL1	(Young et al., 2004)
Xq28	MYP1	GPR50	(Guo X et al., 2010)
Xq28	MYP1	PRRG3	(Guo X et al., 2010)
Xq28	MYP1	CNGA2	(Guo X et al., 2010)
Xq28	MYP1	BGN	(Guo X et al., 2010)
Xq28	MYP1	CTAG2	(Ratnamala et al., 2011)
Xq28	MYP1	GAB3	(Ratnamala et al., 2011)
Xq28	MYP1	MPP	(Ratnamala et al., 2011)
Xq28	MYP1	F8Bver	(Ratnamala et al., 2011)
Xq28	MYP1	FUNDC2	(Ratnamala et al., 2011)
Xq28	MYP1	VBP1	(Ratnamala et al., 2011)
Xq28	MYP1	RAB39B	(Ratnamala et al., 2011)
Xq28	MYP1	CLIC2	(Ratnamala et al., 2011)
Xq28	MYP1	TMLHE	(Ratnamala et al., 2011)
Xq28	MYP1	SYBL	(Ratnamala et al., 2011)
Xq28	MYP1	IL9R	(Ratnamala et al., 2011)
Xq28	MYP1	SPRY3	(Ratnamala et al., 2011)
Xq28	MYP1	CXYorf1	(Ratnamala et al., 2011)

been confirmed frequently in replication studies over the past few years (Table 3). Until now, about 20 association studies have aimed to test the relationship between the 15q14 locus and myopia in different populations, and only three showed no statistically significant association due to the small size of the samples. The SNP rs634990, reaching the greatest p value of 9.20×10^{-23}, was identified by a GWAS meta-analysis in 55,177 samples in Caucasian and Asian populations. Known genes near the 15q14 locus include *GJD2* (OMIM 607058), *ACTC1* (Gene ID 70, OMIM 102540), *GOLGA8B* (Gene ID 440270, OMIM 609619), *LPCAT4* (Gene ID 254531, OMIM 612039), and *CHRM5* (Gene ID 1133, OMIM 118496). Of

Table 3. Summary of studies which identified the 15q14 locus.

Locus	Best SNP	Best p value	Population	First author, year
15q14	rs634990	2.21E-14	Dutch	Solouki, 2010
15q14	rs634990	8.78E-07	Japanese	Hayashi, 2011
15q14	rs634990	9.20E-23	Caucasian and Asian	Verhoeven, 2012
15q14	rs560764	6.40E-04	Caucasian	Schache, 2013
15q14	rs634990	8.81E-07	Chinese	Jiao, 2012
15q14	rs1357179	1.69E-03	Caucasian	Simpson, 2013
15q14	rs524952	5.60E-19	European	Kiefer, 2013
15q14	rs11073060	9.11E-11	Multi-Ethnic	Simpson, 2014
15q14	rs11073058	2.70E-09	Japanese/Chinese/Caucasian	Miyake, 2015
15q14	rs524952	3.70E-06	Japanese	Yoshikawa, 2014
15q14	rs1370156	2.29E-07	European	Simpson, 2014
15q14	rs634990	p>0.05	Chinese	Qiang, 2014
15q14	rs2070664	p>0.05	Chinese	Chen, 2015
15q14	rs524952	1.11E-13	European/Asian	Verhoeven, 2013
15q14	rs634990	p>0.05	Chinese	Chen, 2012
15q14	rs524952	1.01E-25	European/Asian	Fan, 2016
15q14	rs11073058	2.90E-02	Chinese	Li, 2016
15q14	rs2277558	p>0.05	Chinese	Li, 2015
15q14	rs11073058	4.30E-11	European/Asian	Cheng, 2013
15q14	rs634990	1.80E-03	Various	Gong, 2016

these genes, *gap junction protein, delta 2* (*GJD2*), is located closest to the most significant SNP rs634900. *GJD2* was first screened in 47 individuals with refractive error, but no pathogenic variants were identified. Later in our previous study, a sequence analysis of *GJD2*, which had been detected in significant association with myopia in the 15q14 locus within the cohort, did not identify any causative variants. As for the other genes in the 15q14 locus, none have been reported in statistically significant association with myopia. Therefore, the mechanism underlying this significant p value needs to be studied further.

An important and often mentioned discovery is related to two recent large-scale GWASs, which identified 24 and 22 statistically significant associations from independent cohorts. One study was a GWAS meta-analysis involving 37,382 individuals from 27 studies of European ancestry and 8,376 individuals from five Asian cohorts. The other study was a GWAS of 45,771 participants in a USA population of European ancestry. The findings are remarkable for genetic studies on myopia. These two GWASs not only replicated the previously associated loci but also identified several novel significant associations. The findings, if replicated from each other, would lead to less controversial results. There were 12 overlapping statistically significant associations with myopia and refractive error ($p<5 \times 10^{-8}$), and the candidate genes nearby were shown as follows: protease, serine, 56 (*PRSS56*, OMIM 613858); bone morphogenetic protein 3 (*BMP3*, OMIM 112263); potassium voltage-gated channel, KQT-like subfamily, member 5 (*KCNQ5*, OMIM 607357); laminin, alpha 2 (*LAMA2*, OMIM 156225); thymocyte selection-associated high mobility group box (*TOX*, OMIM 606863); tight junction protein 2 (*TJP2*, OMIM 607709); retinol dehydrogenase 5 (11-cis/9-cis; *RDH5*, OMIM 601617); zinc family member 2 (*ZIC2*, OMIM 603073); Ras protein-specific guanine nucleotide-releasing factor 1 (*RASGRF1*, OMIM 606600); *GJD2*; RNA binding protein, fo×-1 homolog (*C. elegans*) *1* (*RBFOX1*, OMIM 605104); and *shisa family member 6* (*SHISA6*, Gene ID 388336, OMIM 617327). These genes are involved in neurotransmission, ion transport, retinoic acid metabolism, extracellular matrix remodeling, and eye development. They have common networks in the protein–protein interactions related to cell cycle and growth pathways, such as the well known molecular mechanisms of refractive error, which are the TGF-beta, mitogen-activated protein kinase (MAPK), and SMAD pathways. Overall, the findings of GWASs provide us with clues to discover more candidate genes and enrich our understanding of the pathogenesis of myopia.

Studies on the association of SNPs with myopia are generally based on refractive error after adjusting for age and gender. The association of SNPs with age at the onset of myopia or gender in myopia is not commonly seen but also provided us with new ideas to some extent. Association studies on SNPs with the age of myopia onset suggest that variants associated with myopia might have age-dependent genetic effects [27,95-98]. A study of the association between the age of myopia onset and 39 previously reported associated loci among 5,200 children ages 7–15 years provided evidence [95]. The results categorized the variants by ages into three groups: early-onset effect remaining stable, early-onset effect progressed with increasing age, and later-onset effect. The analysis of the genetic score for the 39 loci revealed a greater percentage of variants explained the phenotype at older age (2.3% at age 15 versus 0.6% at age 7), suggesting an increased genetic effect at older age. All of this evidence implies that the effects of the associated variants on the risk of myopia vary with age. This finding provided us with the new idea that association studies should be performed in a more specific sub-phenotype [95], and different biologic processes might contribute to the development of myopia at different ages. The gender association of SNPs with myopia was also observed in some studies [96-99]. For example, an association analysis of the GSTP1 Val/Val genotype with myopia identified this genotype as having a higher frequency in female probands [96], the CC genotype of TGF-beta 1 gene polymorphism (T869C) was statistically significantly associated with low myopia cases among male probands [97], and the DN genotype in endostatin gene polymorphism (D104N) increased the risk of myopia for women [98]. This evidence provided the information that gender is an important factor affecting the results and should be controlled in association analyses.

3.2.2 Identification of susceptibility loci for high myopia using association analysis—GWASs and case-control studies have tested at least 27 loci associated with non-syndromic high myopia based on a refraction of SEM < −6.00 D (Appendix 2) [16,29,44-48,50,63,64,66,68,72,75,99-178]. Of these studies, eight loci were identified by GWASs and GWAS meta-analyses in Chinese, French, and Japanese populations and met the requirement of $p<5 \times 10^{-8}$ (Appendix 2). These loci were 2q22.3, the best SNP (rs13382811) near the *ZFHX1B* (Gene ID 9839, OMIM 605802) gene; 4q25 (*MYPI1*), the best SNP (rs10034228); 7p36.3 (*MYP4*), the best SNP (rs2730260) near the *VIPR2* (Gene ID 7434, OMIM 601970) gene; 8q24.12, the best SNP (rs4455882) near the *SNTB1* (Gene ID 6641, OMIM 600026) gene; 8q23 (*MYPI0*), the best SNP (rs17155227) near the *MIR4660* (Gene ID 100616350) and *PPP1R3B* (Gene ID 79660, OMIM 610541) genes; 13q12.12 (*MYP20*), the best SNP (rs9318086) near the *MIPEP* (Gene ID 4285, OMIM 602241), *C1QTNF9B-AS1* (Gene ID 542767, OMIM 617122), and *C1QTNF9B* (Gene ID 387911, OMIM 614148) genes; 15q14, the best SNP (rs11073058) near the *GJD2* gene; and 22q13.31, the best SNP (rs10453441) near the *WNT7B* (Gene ID 7477, OMIM 601967) gene. Some were consistent with the findings in linkage studies, as seen in 7p36.3 (*MYP4*), 4q25 (*MYPI1*), 13q12.12 (*MYP20*), and 8q23 (*MYPI0*).

The SNP rs4455882 near *SNTB1* has been reported to be statistically significantly associated with high myopia in a Chinese population and reached a best p value of 2.13×10^{-11} using GWAS meta-analysis (665 high myopia cases and 960 controls) followed by replications in three additional cohorts (a total of 2,128 cases and 3,683 controls) [154]. Another SNP, rs6469937 in *SNTB1*, was also found to be statistically significantly associated with myopia in another meta-analysis study [179]. *SNTB1* is expressed in the human retina and sclera [179]. In mice with induced myopia, the expression of *SNTB1* was downregulated in the retina/RPE compared with that in control mice [179]. This line of evidence indicates that *SNTB1* might be the best candidate gene for high myopia as suggested by GWASs. Other loci were less replicated or replicated in controversial studies. None of the causative variants were detected in the myopia-associated genes.

3.2.3 Association studies of quantitative trait analysis—Axial length and corneal curvature are key determinants of the refractive power in the eye. Association studies on these quantitative traits have tested 21 susceptible loci for ocular axial length and corneal curvature (Table 4) [3,69,79,80,141,180-184]. Of these loci, 16 were identified as statistically significantly associated with phenotype by GWASs, reaching $p<5 \times 10^{-8}$.

3.2.3.1 The role of axial length in association studies on myopia—In a meta-analysis of three GWASs on axial length involving 1,118 cases and 5,433 controls from Chinese and Malay populations, SNP rs4373767 in *ZC3H11B* (Gene ID 643136) was found to be statistically significantly associated with axial length ($p=2.69 \times 10^{-10}$) and high myopia ($p=4.38 \times 10^{-7}$) [185]. *ZC3H11B* was also replicated to be associated with axial length and high myopia in another large meta-analysis with GWASs involving a total of 12,531 Europeans and 8,216 Asians [69]. Together with *ZC3H11B*, six other genes, *RSPO1* (Gene ID 284654, OMIM 609595), *C3orf26* (Gene ID 84319), *LAMA2*, *GJD2, CD55* (Gene ID 1604, OMIM 125240), and *ZNRF3* (Gene ID 81433, OMIM 612062), were found to be associated with axial length in this study [69]. The differential expression of these six genes has been observed between the induced myopic eyes and the control eyes in tissues, including the sclera, the RPE, and the neural retina. Among

Table 4. Loci or genes tested in association with quantitative trait analysis.

CHR	Loci/Location	Gene	Method	Population	Best SNP	Best p value	First author, year
1	1q32.2	CD55	GWAS-Meta	European/Asian	CD55	2.30E-07	Cheng, 2013
1	1p33	CMPK1	GWAS-Meta	Asian	rs17103186	3.30E-12	Chen, 2014
1	1p36.2	FRAP1	GWAS	European	NO	p>0.05	Guggenheim, 2013
1	1p36.2	FRAP1	Meta	Australian	NO	p>0.05	Mishra, 2012
1	1p36.22	MTOR	GWAS-Meta	Asian	rs74225573	4.00E-13	Chen, 2014
1	1p34.3	RSPO1	GWAS-Meta	European/Asian	rs4074961	9.60E-13	Cheng, 2013
1	1q41	ZC3H11B	GWAS-Meta	European/Asian	rs994767	9.60E-12	Cheng, 2013
2	2q37.1	ALPPL2	GWAS-Meta	European/Asian	ALPPL2	1.80E-06	Cheng, 2013
3	3q12.1	C3orf26	GWAS-Meta	European/Asian	rs9811920	4.90E-11	Cheng, 2013
4	4q12	PDGFRA	GWAS	European	rs6554163	2.80E-06	Guggenheim, 2013
4	4q12	PDGFRA	GWAS-Meta	Asian	rs1800813	3.30E-10	Chen, 2014
4	4q12	PDGFRA	Meta	Australian	rs2114039	4.50E-03	Mishra, 2012
4	4q12	PDGFRA	GWAS	Chinese and Malay	rs7677751	7.87E-09	Fan, 2011
6	MYP2/6q22.33	LAMA2	GWAS-Meta	European/Asian	rs12193446	1.20E-08	Cheng, 2013
7	7q21.11	HGF	A	Chinese	rs3735520	5.00E-02	Chen, 2012
7	7q31.2	MET	A	Caucasian	NO	p>0.05	Schache, 2009
10	10q11.22	RBP3	GWAS-Meta	Asian	rs11204213	1.10E-13	Chen, 2014
12	12q23.2	IGF1	A	Chinese	rs6214	3.40E-02	Chen, 2012
12	12q13.3	MIP	GWAS-Meta	European/Asian	MIP	2.80E-07	Cheng, 2013
15	15q14	GJD2	GWAS	Japanese/Chinese/Caucasian	rs11073058	2.70E-09	Miyake, 2015
15	15q14	GJD2	A	Chinese	rs634990	p>0.05	Chen, 2012
15	15q14	GJD2	GWAS-Meta	European/Asian	rs11073058	4.30E-11	Cheng, 2013
15	15q14	NA	A	Caucasian	rs560764	6.40E-04	Schache, 2013
15	15q25	NA	A	Caucasian	NO	p>0.05	Schache, 2013
18	MYP2/18p11.31	TGIF1	A	Caucasian	NO	p>0.05	Pertile, 2008
22	22q13.31	WNT7B	GWAS	Japanese/Chinese/Caucasian	rs10453441	2.90E-40	Miyake, 2015
22	22q12.1	ZNRF3	GWAS-Meta	European/Asian	rs12321	4.10E-08	Cheng, 2013

Note: A, association; Meta, Meta-analysis; GWAS-Meta, GWAS-Meta analysis; GWAS, genome-wide association; CHR, chromosome

these genes, *GJD2* and *CD55* were previously reported to be associated with refractive error. *GJD2* is a candidate gene in the 15q14 locus, which has been replicated in multiple studies. A statistically significant SNP near *CD55* (rs1652333; p combined=3.05 × 10^{-12}) was previously detected on a large scale in GWASs. These findings indicate that there is a close relationship between refractive error and axial length, which share about 50% of variants [186].

3.2.3.2 Association of variants with corneal curvature—GWASs in corneal curvature have identified several loci near four genes, including *PDGFRA* (Gene ID 5156, OMIM 173490; 4p12), *CMPK1* (Gene ID 51727, OMIM 191710; 1p32), *RBP3* (Gene ID 5949, OMIM 180290; 10q11.2), and *FRAP1* (Gene ID 2475, OMIM 601231; 1p36.2), that are statistically significantly associated with corneal curvature. *FRAP1* and *PDGFRA* were first identified in a GWAS in an Asian population from Singapore and were replicated in two subsequent GWASs. Together with *FRAP1* and *PDGFRA*, one of the subsequent GWAS discovered two other novel genes, *CMPK1* and *RBP3*, associated with corneal curvature. These studies have opened a new path for investigating the molecular genetic basis of myopia, although the relationship between myopia and the genes associated with corneal curvature is unclear. Thus, it might be of interest for further study in the future.

3.2.4 Association studies on myopia: Principles and directions for the future—More myopia loci have been identified by GWASs, but these loci account for a small proportion (less than 1%) of myopia in the general population. All of these significant associations tend to have a small effect due to their high allele frequencies. Thus, genotyping genomic regions near the significant locus in a larger cohort might detect variants with very rare frequencies and high penetrance, as seen in the discovery of highly penetrant variants in the *CFH* (Gene ID 3075, OMIM 134370) gene associated with age-related macular degeneration. Our previous study of 12 myopia-associated genes identified several rare variants in families with high myopia using whole exome sequencing [122]. Although the variant types and allele frequencies did not show statistically significant differences between the cases and controls, it opened up a new approach to analyze significant associations implicated by GWASs.

Most of the significant associations are located outside the protein-coding regions. Genes close to the significant regions are considered potential causative genes and chosen for further study. Even though no mutations in candidate genes have been identified, systemically reviewing genes near significant regions can enrich our understanding of pathways and gene–gene networks in the development of myopia.

In summary, all SNPs related to myopia, high myopia, axial length, and corneal curvature have been summarized according to their positions in the chromosome. SNPs identified by GWASs must be consistent with the principle of replication and reach the significant association level of p≤5 × 10^{-8}. Recruiting larger cohorts or conducting an international collaboration would be helpful to improve statistical power and enable the discovery of additional significant associations.

3.3 Unraveling causative genes for high myopia with whole exome sequencing—Whole exome sequencing has been widely used in studies on genetic defects for high myopia. With exome sequencing, ten genes in total have thus far been reported as associated with high myopia (Table 5), including four genes related to AD high myopia (*ZNF644*: Gene ID 84146, OMIM 614159, *SLC39A5*: Gene ID 283375, OMIM 608730, *SCO2*: Gene ID 9997, OMIM 604272, *P4HA2*: Gene ID 8974, OMIM 600608), three genes related to AR high myopia (*LRPAP1*: Gene ID 4043, OMIM 104225, *LEPREL1*: Gene ID 55214, OMIM 610341, *CTSH*: Gene ID 1512, OMIM 116820), two genes for XL high myopia (*OPN1LW*: Gene ID 5956, OMIM 300822 and *ARR3*: Gene ID 407, OMIM 301770), and one gene (*BSG*: Gene ID 682, OMIM 109480) inherited by de novo mutations [68,187-199].

Among these genes, mutations detected in genes with the AD trait were mostly missense, while those in genes with AR were mainly frameshift mutations. All of these genes are common in the expression spectrum in eye tissues, including the sclera, retina, and RPE; these genes also have a close relationship with the mechanism underlying the development of myopia. *LRPAP1* and *SCL39A5* were identified to be involved in the well known pathway TGF-beta/BMP. The mice that were homozygous deficient in *LRPAP1* had reduced expression of *LRP* in the liver and brain [200], which, in turn, caused the activation of TGF-beta [201]. *LRPAP1* was assumed to be associated with myopia through regulating the expression of TGF-beta. A loss of function in *SLC39A5* was detected as involved in the expression of Smad1, a key phosphate protein downstream of the TGF-beta/BMPs. Other genes were involved with collagen synthesis (*LERPEL1*), ATP metabolism in the retina (*SCO2*), the transcription factor (*ZNF644*), and the degradation of lysosomal proteins (*CTSH*). The exact mechanisms of these genes remain unclear, and functional studies are anticipated in the future.

A recent analysis of whole exome sequencing data from 298 probands with early-onset high myopia discovered that one-fourth of the probands carried mutations in the genes responsible for retinal diseases and myopia-related syndromes [202]. This finding provided further clues for candidate gene

screening using whole exome sequencing. Overall, in the era of whole exome sequencing, more genes are expected to be identified, which will provide more information on mechanisms of high myopia.

3.4 Gene analysis in the experimental animal models of myopia—Animal models of myopia are used to identify the altered expression of genes in the retina, RPE, choroid, and sclera or to observe the features of myopia after knocking out the targeted gene. Methods for establishing myopia models include the form deprivation myopia (FDM), lens-induced

Table 5. Genes suggested from exome sequencing studies.

Inheritance	Locus	Region	Gene	Mutation	Reference
AD	MYP21	1p22.2	ZNF644	p.S672G	(Shi et al., 2011; Jiang et al., 2014)
AD	MYP21	1p22.2	ZNF644	p.R680G	(Shi et al., 2011)
AD	MYP21	1p22.2	ZNF644	p.C699Y	(Shi et al., 2011)
AD	MYP21	1p22.2	ZNF644	p.T242M	(Tran-Viet et al., 2012)
AD	MYP21	1p22.2	ZNF644	p.E274V	(Tran-Viet et al., 2012)
AD	MYP21	1p22.2	ZNF644	p.T401A	(Xiang et al., 2014)
AD	MYP21	1p22.2	ZNF644	p.E1278G	(Xiang et al., 2014)
AD	MYP21	1p22.2	ZNF644	p.R683T	(Jiang et al., 2014)
AD	MYP21	1p22.2	ZNF644	p.D851H	(Jiang et al., 2014)
AD	MYP25	5q31.1	P4HA2	p.E291K	(Guo et al., 2015)
AD	MYP25	5q31.1	P4HA2	p.K443*	(Guo et al., 2015)
AD	MYP25	5q31.1	P4HA2	p.Q140R	(Guo et al., 2015)
AD	MYP25	5q31.1	P4HA2	p.I150V	(Guo et al., 2015)
AD	MYP25	5q31.1	P4HA2	p.R451Gfs*8	(Guo et al., 2015)
AD	MYP24	12q13.3	SLC39A5	p.Y47*	(Guo et al., 2015)
AD	MYP24	12q13.3	SLC39A5	p.M304T	(Guo et al., 2015)
AD	MYP24	12q13.3	SLC39A5	p.G413A	(Jiang et al., 2014)
AD	Unknown	22q13.33	SCO2	p.R112W	(Jiang et al., 2014)
AD	Unknown	22q13.33	SCO2	p.R120W	(Jiang et al., 2014)
AD	Unknown	22q13.33	SCO2	p.Q53*	(Yanovitch et al., 2013)
AD	Unknown	22q13.33	SCO2	p.R114H	(Yanovitch et al., 2013)
AD	Unknown	22q13.33	SCO2	p.E140K	(Yanovitch et al., 2013)
AD	Unknown	22q13.33	SCO2	p.A259V	(Yanovitch et al., 2013)
AR	Unknown	3q28	LEPREL1	p.G508V	(Mordechai et al., 2011)
AR	Unknown	3q28	LEPREL1	p.Q5*	(Guo et al., 2014)
AR	MYP23	4p16.3	LRPAP1	p.N202Tfs*8	(Aldahmesh et al., 2013)
AR	MYP23	4p16.3	LRPAP1	p.I288Rfs*118	(Aldahmesh et al., 2013)
AR	MYP23	4p16.3	LRPAP1	p.Q67Sfs*8	(Jiang et al., 2014)
AR	MYP23	15q25.1	CTSH	p.L162Pfs*66	(Aldahmesh et al., 2013)
X-linked	MYP1	Xq28	OPN1LW	LVAVA haplotype	(Li et al., 2015)
X-linked	Unknown	Xq13.1	ARR3	p.L80P	(Xiao et al., 2016)
X-linked	Unknown	Xq13.1	ARR3	p.R100*	(Xiao et al., 2016)
X-linked	Unknown	Xq13.1	ARR3	p.A298D	(Xiao et al., 2016)
De Novo	Unknown	19p13.3	BSG	p.G297S	(Jin et al., 2017)
De Novo	Unknown	19p13.3	BSG	p.P221S	(Jin et al., 2017)
De Novo	Unknown	19p13.3	BSG	p.Q69X	(Jin et al., 2017)
De Novo	Unknown	19p13.3	BSG	pc.415+1G>A	(Jin et al., 2017)

myopia (LIM), and knockout animal models. The animal models are varied and can include chicks, mice, guinea pigs, rabbits, monkeys, or tree shrews, as well as the recently used zebrafish.

Experimental studies on myopia have provided convincing evidence for the role of the RPE, choroid, and sclera in the regulation of ocular growth and the development of myopia [203-212]. Animal models established by FDM and LIM have been widely used to investigate the candidate genetic factors underlying ocular growth and myopia. Studies on RPE have revealed that BMPs (typically *BMP2*: Gene ID 650, OMIM 112261, *BMP4*: Gene ID 652, OMIM 112262, *BMP7*: Gene ID 655, OMIM 112267) have bidirectional regulation during ocular growth [203,211]. For example, the expression of *BMP2* was upregulated in a myopic defocus model (induced hyperopia) and downregulated in a hyperopic defocus model (induced myopia) [203]. BMPs encode secreted ligands of the TGF-beta superfamily of proteins involved in the TGF-beta/BMPs pathway. The expression of TGF-beta isoforms (TGF-beta 1, 2, and 3) in chick RPE was also found to be statistically significantly different in the LIM chick model [213]. All of this evidence indicates that TGF-beta superfamily members are involved in the regulation of ocular growth and suggests that the RPE plays a role as a signal relay. Studies on the choroid indicated its active role in conveying signals from the retina to the sclera [210]. Significant differences in gene expression in the choroid were observed between eyes with induced myopia and control eyes [205,206,210,213]. In addition, it is well accepted that the sclera plays a pivotal role in controlling ocular size. Sclera remodeling leads to decreased collage synthesis, scleral thinning, and loss of scleral tissue, all of which underlie the development of myopia [214].Thus, the alteration of scleral gene expression during the development and recovery of induced myopia in animal models has been widely investigated to explore the relationship between candidate genes and myopia [204,207,208,215-223]. Genes involved in scleral remodeling, such as *TGF-beta isoforms*, *BMPs*, *cAMP*: Gene ID 820, OMIM 600474, *COL1A1*: Gene ID 1277, OMIM 120150, *TIMPs*, and *GAGs*, were investigated mostly based on their functions as ocular growth factors, extracellular matrix (ECM) protein and enzymes, and their role in ECM and collagen synthesis. However, no specific mutations were detected among these genes associated with myopia in human beings. Most alterations in gene expression tend to be consistent during the development and recovery of induced myopia. This evidence not only indicates that scleral remodeling might involve the modulation of gene expression at the transcriptional level but also suggests that scleral remodeling is too complex to be explained by a single gene.

The genes identified in experimental myopia studies have features in common. First, they have expression in the sclera, retina, or choroid. Second, increased or decreased changes in expression can be observed in induced myopia models. Third, knockout animal models present with some related features of myopia, such as a thinner sclera, an elongated axial length, and the decreased synthesis of collagen fibers. Importantly, most of these genes are relevant to the signaling pathways possibly underlying myopia (Table 6) [121,203-207,211,217,224-246], although most have yet to be determined. The potential signaling pathways are TGF-beta signaling, scleral remodeling, Wnt signaling, Pax6 in early embryonic growth, Sonic hedgehog, retinoic acid, nitric oxide synthase, neurotransmitter, muscarinic receptor signaling, and retinal dopamine signaling. Among them, the well recognized signaling pathway is the TGF-beta/BMPs pathway, which has been implicated independently in different studies. The TGF-beta/BMPs pathway is considered to have a potential role in controlling ocular growth. Decreased expression of TGF-beta isoforms (the TGF-beta 1 to 3 isoforms) in the sclera of the FDM animal models was intended to reduce the synthesis of collagen, thus making a contribution to the sclera remodeling in the myopic eye. Additional candidate genes related to the TGF-beta/BMPs pathway will be of interest for future investigation.

In addition, animal model studies have provided further evidence to support the findings of association studies, whole exome sequencing, and linkage studies. In human beings, P3H2 is encoded by *LERPEL1*, in which mutations have been reported to be associated with autosomal recessive high myopia using whole exome sequencing [192]. *P3h2* null mice were further observed with altered collagen prolyl 3-hydroxylation [235], which is believed to cause abnormalities in the structure of the sclera, thus resulting in progressive myopia. A GWAS identified *ZFHX1B* as a susceptible locus for severe myopia [121]. The decreased expression of *Zfhx1b* was observed from the induced experimental mouse model for myopia, providing further evidence of the involvement of this locus in the development of myopia [121]. However, we still have little knowledge about the exact relationship between induced myopia in animals and physiologic myopia in humans, and the exact variants in most of the genes suggested by animal studies are still unclear.

4. Molecular genetic basis of syndromic high myopia: Myopia, usually high myopia, has been reported as a feature in a variety of ocular and systemic syndromes. These myopic syndromes are often shown in Mendelian inheritance patterns, and the genetic defects underlying these syndromes have been well clarified with certain protein-coding genes. A

Table 6. Genes analyzed in experimental myopia studies.

Potential pathway	Gene involved in animal models	Function related with myopia	Refs.
Environmental induced animal model studies:			
TGF-beta	TGF-beta 1–3, Zfhx1b, BMP2, BMP4, BMP5, and BMP7	Ocular growth	Jobling et al. (2004); Jobling et al. (2009); Mathis et al. (2010); Khor et al.(2013); Zhang et al. (2012); Zhang et al. (2013); Zhang et al. (2016); Wang et al. (2011); Li et al. (2015)
Scleral remodeling	GAGs, MMPs, TIMPs, BMP2, and TGF-β	Scleral remodeling	Mcbrien et al. (2000); Siegwart et al.(2005); Li et al.(2015)
Wnt signaling	Wnt2b, Fzd5, and β-catenin	Ocular growth	Ma et al.(2014)
Pax-6	Pax-6	Early embryonic growth	Bhat et al.(2004); Ashby et al. (2009); Zhong et al.(2004)
Sonic hedgehog	Shh	Ocular growth	Akamatsu et al.(2001); Escaño et al.(2000); Qian et al.(2009)
Retinoic acid receptor	Retinoic acid receptor	Ocular growth	Seko et al. (1996); Morgan et al.(2004); Wang et al.(2014)
Nitric oxide synthase	NOS isoform (iNOS, eNOS bNOS)	Nitric oxide synthase	Fujii et al. (1998)
Neurotransmitter/neuromodulator	Glucagon and its receptors	Increased the Camp	Feldkaemper et al. (2000);Feldkaemper et al.(2004)
Muscarinic receptor signaling	Muscarinic subtypes M1 to M5	Ocular growth	Liu et al. (2007)
Retinal dopamine	D2R	Light adaptation and retinal circadian rhythm	Huang et al. (2014)
Cell surface	EPHA1, SCUBE3, P2RY1, VIPR2, and NPR3	Ocular growth regulation	He et al. (2014) ; Lin et al. (2013)
Cytoskeleton related	ANXA2, CAPNS1, and NGEF	Axial elongation	Lin et al. (2013)
Intracellular signaling	BCO2, ZNF185, CYP26B1, RLBP1, and RPE65	Ocular growth regulation	He et al. (2014)
Transcription signaling	HIF1A and EGR1	Ocular growth regulation	He et al. (2014)
Secreted signaling	IGF2, NRG1, PT15, FAM180A, MEST, SOSTDC1,TGFBI, CILP, PENK, PTX3, ANGPTL7, BMP2, BMP4, TGFB2, TGFB3, and IL18	Ocular growth regulation	He et al. (2014) ; Lin et al. (2013)
Matricellular signaling	NOV, THBS1, CYR61, CTGF,and TNC	Ocular growth regulation	He et al. (2014) ; Lin et al. (2013)
MPs/TIMPs signaling	ADAMTSL3, TIMP1, TIMP3, ADAMTS5, and MMP14	Ocular growth regulation	He et al. (2014) ; Lin et al. (2013)
Extracellular matrix	COL6A6, COL12A1, OGN, MXRA5, and NYX	Ocular growth regulation	He et al. (2014)
Genetic induced animal model studies			
Collagen synthesis	P3h2	Related with the collagen synthesis in sclera	Hudson et al. (2015)
Soni hedgehog	Lrp2	An endocytic receptor	Veth et al.(2011); Collery et al.(2014)
Transcriptional regulatory	Egr-1	A transcription factor	Schippert et al. (2007)

total of 382 entries were obtained using "myopia" as a search word (until 3/18/2017) in OMIM. Entries associated with syndromic myopia were included and reviewed. A total of 115 genes were identified as the causes of the 131 syndromes accompanied by myopia (Appendix 3) [116,164,192,247-416]. These syndromes shown in Appendix 3 are congenital and inherited by defects in certain genes in a pattern of autosomal recessive, autosomal dominant, or X-linked inheritance.

Myopic syndromes have variable clinical manifestations, ranging from mild to severe, that affect patients' daily lives in various aspects. Some even lead to death after birth or in childhood. Myopia or high myopia is one of these variable features, and other clinical features involve many different systems, especially other segments of the ocular system, nervous system, or locomotor system. For example, some ocular abnormalities include astigmatism, nystagmus, night blindness, strabismus, microphthalmia, microcornea, brittle cornea, keratoconus, cataract, ectopia lentis, posterior staphyloma, glaucoma, vitreoretinopathy, retinitis pigmentosa, and retinal detachment. In association with the nervous system, mental retardation, microcephaly, cerebellar hypoplasia, special facial appearance, and hearing loss are often seen. In ophthalmology, myopic syndromes, such as Stickler syndrome, Marfan syndrome, congenital stable night blindness (CSNB), retinitis pigmentosa (RP) associated with *RP2* (Gene ID 6102, OMIM 312600) and *RPGR* (Gene ID 6103, OMIM 312610), Bornholm eye disease (BED), and cone-rod dystrophy (CORD), have been well established, and high myopia is their common feature. Others involving primarily non-ocular systems are rare and have not been thoroughly investigated.

Systematic reviews of myopia-related syndromes have great implications in diagnosis, prevention, and treatment. Two studies [417,418] revealed that most patients diagnosed with simple myopia showed other ocular or systemic symptoms after full assessment, especially children under 10 years of age. Stickler syndrome, Marfan syndrome, and retinal dystrophy were predominantly seen. If early diagnosis and early prevention were made available for patients with conditions such as Stickler syndrome, it would reduce their chances of developing retinal detachment using prophylactic cryotherapy. Practically, high myopia might be an earlier feature in some syndromes or a major complaint in a patient's first visit. In routine clinical practice, syndromic high myopia was generally considered to be rare and might be simply cosidered as high myopia alone due to unawareness or atypical manifestation of other major signs. This situation may not well recorgnized until recently. Sun et al. performed a systematic analysis of the genes associated with retinal dystrophy and myopia-related syndromes in 298 probands with early-onset high myopia (eoHM) [202]. Mutations were identified in one-fourth of the probands, of whom 62% have mutations in the genes that contribute to myopia-related syndromes. Mutations in genes *COL2A1* (Gene ID 1280, OMIM 120140) and *COL11A1* (Gene ID 1301, OMIM 120280) associated with Stickler syndrome, *CACNA1F* (Gene ID 778, OMIM 300110) associated with CSNB, and *RPGR* associated with XL-RP were predominantly discovered among these probands. Follow-up examination on some of the eoHM with the mutations revealed that: 1) some of the eoHM are still hardly recorgnized as related syndromes due to atypical or variable manifestation, and 2) a small portion of those eoHM should be syndromic high myopia if systemic examination of the eyes as well as other related organs could be thoroughly performed. The investigation of the genes associated with syndromic high myopia has also become an additional approach for the candidate gene screening of isolated high myopia based on a common molecular genetic function, such as involving the ECM and connective tissues. Mutations in *NYX* (Gene ID 60506, OMIM 300278) have been reported to cause high myopia without congenital stationary night blindness (CSNB1) [419]. A recent study conducted with seven families with BED, two of whom were previously mapped to the *MYP1* locus, discovered two rare haplotypes (*LIAVA* and *LVAVA*) underlying BED [334]. Li et al. later found that one of the haplotypes (LVAVA) also contributes to two large families with X-linked non-syndromic high myopia [191]. These observations suggest that there is a close relationship between the genetic basis for syndromic and non-syndromic high myopia, and thus, it is a good approach for investigating the genes implicated in studies of syndromic high myopia.

5. Conclusions: This review provides a comprehensive overview of studies on the molecular genetics of myopia. For the reported genetics factors associated with myopia listed in this review, some might be very preliminary while a few may already have contradictory evidence. Therefore, many of the myopia-related genes or loci need to be further validated. In addition, for most loci or associated SNPs, the exact genetic defects and their related functional consequence that contributes to myopia await disclosure. No specific pathways underlying myopia have been clarified that would impede our prioritization of candidate genes. Therefore, in conjunction with functional studies and a combination of different technologies will be helpful for enhancing our understanding of the genetic factors in myopia, ultimately leading to improvements in the prediction of onset, prevention, and treatment in the future.

APPENDIX 1. LOCI OR GENES TESTED IN ASSOCIATED WITH COMPLEX MYOPIA

AL, axial length; CC, corneal curvature, CHR, chromosome; A, association analysis; GWAS, genome-wide association study; SPE, spherical equivalent; NA, not available; GWAS-Meta: Genome-wide meta analysis. To access the data, click or select the words "Appendix 1"

APPENDIX 2. LOCI OR GENES TESTED IN ASSOCIATION WITH NONSYNDROMIC HIGH MYOPIA

Note: CHR, chromosome; A, association study; AL, axial length, CC, Corneal curvature; GWAS, genome-wide association study;Meta: Meta analysis; NA, not available. To access the data, click or select the words "Appendix 2"

APPENDIX 3. REPORTED GENES ASSOCIATED WITH SYNDROMIC HIGH MYOPIA.

Note: IC, isolated cases; AR, autosomal recessive; AD, autosomal domiant; NA, non-available; #, References only included the first published paper for clinical features report and genetic analysis. To access the data, click or select the words "Appendix 3"

ACKNOWLEDGMENTS

The authors acknowledge the grant support from the Natural Science Foundation of Guangdong (S2013030012978), the National Natural Science Foundation of China (81770965), the Science and Technology Planning Projects of Guangzhou (201607020013), and the Fundamental Research Funds of the State Key Laboratory of Ophthalmology

REFERENCES

1. Zhang Q. Genetics of Refraction and Myopia. Prog Mol Biol Transl Sci 2015; 134:269-79. [PMID: 26310160].
2. Yap M, Wu M, Liu ZM, Lee FL, Wang SH. Role of heredity in the genesis of myopia. Ophthalmic Physiol Opt 1993; 13:316-9. [PMID: 8265177].
3. Pertile KK, Schache M, Islam FM, Chen CY, Dirani M, Mitchell P, Baird PN. Assessment of TGIF as a candidate gene for myopia. Invest Ophthalmol Vis Sci 2008; 49:49-54. [PMID: 18172074].
4. Ip JM, Huynh SC, Robaei D, Rose KA, Morgan IG, Smith W, Kifley A, Mitchell P. Ethnic differences in the impact of parental myopia: findings from a population-based study of 12-year-old Australian children. Invest Ophthalmol Vis Sci 2007; 48:2520-8. [PMID: 17525179].
5. Farbrother JE, Kirov G, Owen MJ, Guggenheim JA. Family aggregation of high myopia: estimation of the sibling recurrence risk ratio. Invest Ophthalmol Vis Sci 2004; 45:2873-8. [PMID: 15326097].
6. Wojciechowski R, Congdon N, Bowie H, Munoz B, Gilbert D, West SK. Heritability of refractive error and familial aggregation of myopia in an elderly American population. Invest Ophthalmol Vis Sci 2005; 46:1588-92. [PMID: 15851555].
7. Young TL, Atwood LD, Ronan SM, Dewan AT, Alvear AB, Peterson J, Holleschau A, King RA. Further refinement of the MYP2 locus for autosomal dominant high myopia by linkage disequilibrium analysis. Ophthalmic Genet 2001; 22:69-75. [PMID: 11449316].
8. Young TL, Ronan SM, Alvear AB, Wildenberg SC, Oetting WS, Atwood LD, Wilkin DJ, King RA. A second locus for familial high myopia maps to chromosome 12q. Am J Hum Genet 1998; 63:1419-24. [PMID: 9792869].
9. Paluru P, Ronan SM, Heon E, Devoto M, Wildenberg SC, Scavello G, Holleschau A, Makitie O, Cole WG, King RA, Young TL. New locus for autosomal dominant high myopia maps to the long arm of chromosome 17. Invest Ophthalmol Vis Sci 2003; 44:1830-6. [PMID: 12714612].
10. Zhang Q, Guo X, Xiao X, Jia X, Li S, Hejtmancik JF. A new locus for autosomal dominant high myopia maps to 4q22-q27 between D4S1578 and D4S1612. Mol Vis 2005; 11:554-60. [PMID: 16052171].
11. Paluru PC, Nallasamy S, Devoto M, Rappaport EF, Young TL. Identification of a novel locus on 2q for autosomal dominant high-grade myopia. Invest Ophthalmol Vis Sci 2005; 46:2300-7. [PMID: 15980214].
12. Nallasamy S, Paluru PC, Devoto M, Wasserman NF, Zhou J, Young TL. Genetic linkage study of high-grade myopia in a Hutterite population from South Dakota. Mol Vis 2007; 13:229-36. [PMID: 17327828].
13. Lam CY, Tam PO, Fan DS, Fan BJ, Wang DY, Lee CW, Pang CP, Lam DS. A genome-wide scan maps a novel high myopia locus to 5p15. Invest Ophthalmol Vis Sci 2008; 49:3768-78. [PMID: 18421076].
14. Paget S, Julia S, Vitezica ZG, Soler V, Malecaze F, Calvas P. Linkage analysis of high myopia susceptibility locus in 26 families. Mol Vis 2008; 14:2566-74. [PMID: 19122830].
15. Ma JH, Shen SH, Zhang GW, Zhao DS, Xu C, Pan CM, Jiang H, Wang ZQ, Song HD. Identification of a locus for autosomal dominant high myopia on chromosome 5p13.3-p15.1 in a Chinese family. Mol Vis 2010; 16:2043-54. [PMID: 21042559].
16. Yang Z, Xiao X, Li S, Zhang Q. Clinical and linkage study on a consanguineous Chinese family with autosomal recessive high myopia. Mol Vis 2009; 15:312-8. [PMID: 19204786].
17. Guo X, Xiao X, Li S, Wang P, Jia X, Zhang Q. Nonsyndromic high myopia in a Chinese family mapped to MYP1: linkage confirmation and phenotypic characterization. Arch Ophthalmol 2010; 128:1473-9. [PMID: 21060050].
18. Zhang Q, Guo X, Xiao X, Jia X, Li S, Hejtmancik JF. Novel locus for X linked recessive high myopia maps to Xq23-q25

but outside MYP1. J Med Genet 2006; 43:e20-[PMID: 16648373].

19. Stambolian D, Ibay G, Reider L, Dana D, Moy C, Schlifka M, Holmes T, Ciner E, Bailey-Wilson JE. Genomewide linkage scan for myopia susceptibility loci among Ashkenazi Jewish families shows evidence of linkage on chromosome 22q12. Am J Hum Genet 2004; 75:448-59. [PMID: 15273935].

20. Hammond CJ, Andrew T, Mak YT, Spector TD. A susceptibility locus for myopia in the normal population is linked to the PAX6 gene region on chromosome 11: a genomewide scan of dizygotic twins. Am J Hum Genet 2004; 75:294-304. [PMID: 15307048].

21. Wojciechowski R, Moy C, Ciner E, Ibay G, Reider L, Bailey-Wilson JE, Stambolian D. Genomewide scan in Ashkenazi Jewish families demonstrates evidence of linkage of ocular refraction to a QTL on chromosome 1p36. Hum Genet 2006; 119:389-99. [PMID: 16501916].

22. Karlsson JI. Concordance rates for myopia in twins. Clin Genet 1974; 6:142-6. [PMID: 4430154].

23. Dirani M, Chamberlain M, Shekar SN, Islam AF, Garoufalis P, Chen CY, Guymer RH, Baird PN. Heritability of refractive error and ocular biometrics: the Genes in Myopia (GEM) twin study. Invest Ophthalmol Vis Sci 2006; 47:4756-61. [PMID: 17065484].

24. Hammond CJ, Snieder H, Gilbert CE, Spector TD. Genes and environment in refractive error: the twin eye study. Invest Ophthalmol Vis Sci 2001; 42:1232-6. [PMID: 11328732].

25. Lyhne N, Sjolie AK, Kyvik KO, Green A. The importance of genes and environment for ocular refraction and its determiners: a population based study among 20–45 year old twins. Br J Ophthalmol 2001; 85:1470-6. [PMID: 11734523].

26. Lopes MC, Andrew T, Carbonaro F, Spector TD, Hammond CJ. Estimating heritability and shared environmental effects for refractive error in twin and family studies. Invest Ophthalmol Vis Sci 2009; 50:126-31. [PMID: 18757506].

27. Kiefer AK, Tung JY, Do CB, Hinds DA, Mountain JL, Francke U, Eriksson N. Genome-wide analysis points to roles for extracellular matrix remodeling, the visual cycle, and neuronal development in myopia. PLoS Genet 2013; 9:e1003299-[PMID: 23468642].

28. Verhoeven VJ, Hysi PG, Wojciechowski R, Fan Q, Guggenheim JA, Hohn R, MacGregor S, Hewitt AW, Nag A, Cheng CY, Yonova-Doing E, Zhou X, Ikram MK, Buitendijk GH, McMahon G, Kemp JP, Pourcain BS, Simpson CL, Makela KM, Lehtimaki T. Genome-wide meta-analyses of multiancestry cohorts identify multiple new susceptibility loci for refractive error and myopia. Nat Genet 2013; 45:314-8. [PMID: 23396134].

29. Meng W, Butterworth J, Bradley DT, Hughes AE, Soler V, Calvas P, Malecaze F. A genome-wide association study provides evidence for association of chromosome 8p23 (MYP10) and 10q21.1 (MYP15) with high myopia in the French Population. Invest Ophthalmol Vis Sci 2012; 53:7983-8. [PMID: 23049088].

30. Schache M, Richardson AJ, Pertile KK, Dirani M, Scurrah K, Baird PN. Genetic mapping of myopia susceptibility loci. Invest Ophthalmol Vis Sci 2007; 48:4924-9. [PMID: 17962440].

31. Klein AP, Duggal P, Lee KE, Klein R, Bailey-Wilson JE, Klein BE. Confirmation of linkage to ocular refraction on chromosome 22q and identification of a novel linkage region on 1q. Arch Ophthalmol 2007; 125:80-5. [PMID: 17210856].

32. Li YJ, Guggenheim JA, Bulusu A, Metlapally R, Abbott D, Malecaze F, Calvas P, Rosenberg T, Paget S, Creer RC, Kirov G, Owen MJ, Zhao B, White T, Mackey DA, Young TL. An international collaborative family-based whole-genome linkage scan for high-grade myopia. Invest Ophthalmol Vis Sci 2009; 50:3116-27. [PMID: 19324860].

33. Gehring WJ, Ikeo K. Pax 6: mastering eye morphogenesis and eye evolution. Trends Genet 1999; 15:371-7. [PMID: 10461206].

34. Machon O, Kreslova J, Ruzickova J, Vacik T, Klimova L, Fujimura N, Lachova J, Kozmik Z. Lens morphogenesis is dependent on Pax6-mediated inhibition of the canonical Wnt/beta-catenin signaling in the lens surface ectoderm. Genesis 2010; 48:86-95. [PMID: 20027618].

35. Huang J, Rajagopal R, Liu Y, Dattilo LK, Shaham O, Ashery-Padan R, Beebe DC. The mechanism of lens placode formation: a case of matrix-mediated morphogenesis. Dev Biol 2011; 355:32-42. [PMID: 21540023].

36. Marquardt T, Ashery-Padan R, Andrejewski N, Scardigli R, Guillemot F, Gruss P. Pax6 is required for the multipotent state of retinal progenitor cells. Cell 2001; 105:43-55. [PMID: 11301001].

37. Hsieh YW, Yang XJ. Dynamic Pax6 expression during the neurogenic cell cycle influences proliferation and cell fate choices of retinal progenitors. Neural Dev 2009; 4:32-[PMID: 19686589].

38. Wang P, Sun W, Li S, Xiao X, Guo X, Zhang Q. PAX6 mutations identified in 4 of 35 families with microcornea. Invest Ophthalmol Vis Sci 2012; 53:6338-42. [PMID: 22893676].

39. Jia X, Guo X, Xiao X, Li S, Zhang Q. A novel mutation of PAX6 in Chinese patients with new clinical features of Peters' anomaly. Mol Vis 2010; 16:676-81. [PMID: 20405024].

40. Xiao X, Li S, Zhang Q. Microphthalmia, late onset keratitis, and iris coloboma/aniridia in a family with a novel PAX6 mutation. Ophthalmic Genet 2012; 33:119-21. [PMID: 22171686].

41. Bremond-Gignac D, Bitoun P, Reis LM, Copin H, Murray JC, Semina EV. Identification of dominant FOXE3 and PAX6 mutations in patients with congenital cataract and aniridia. Mol Vis 2010; 16:1705-11. [PMID: 20806047].

42. Hanson I, Churchill A, Love J, Axton R, Moore T, Clarke M, Meire F, van Heyningen V. Missense mutations in the most ancient residues of the PAX6 paired domain underlie a spectrum of human congenital eye malformations. Hum Mol Genet 1999; 8:165-72. [PMID: 9931324].

43. Dansault A, David G, Schwartz C, Jaliffa C, Vieira V, de la Houssaye G, Bigot K, Catin F, Tattu L, Chopin C, Halimi P, Roche O, Van Regemorter N, Munier F, Schorderet D, Dufier JL, Marsac C, Ricquier D, Menasche M, Penfornis A, Abitbol M. Three new PAX6 mutations including one causing an unusual ophthalmic phenotype associated with neurodevelopmental abnormalities. Mol Vis 2007; 13:511-23. [PMID: 17417613].

44. Han W, Leung KH, Fung WY, Mak JY, Li YM, Yap MK, Yip SP. Association of PAX6 polymorphisms with high myopia in Han Chinese nuclear families. Invest Ophthalmol Vis Sci 2009; 50:47-56. [PMID: 19124844].

45. Ng TK, Lam CY, Lam DS, Chiang SW, Tam PO, Wang DY, Fan BJ, Yam GH, Fan DS, Pang CP. AC. and AG dinucleotide repeats in the PAX6 P1 promoter are associated with high myopiaMol Vis 2009; 15:2239-48. [PMID: 19907666].

46. Jiang B, Yap MK, Leung KH, Ng PW, Fung WY, Lam WW, Gu YS, Yip SP. PAX6 haplotypes are associated with high myopia in Han chinese. PLoS One 2011; 6:e19587-[PMID: 21589860].

47. Miyake M, Yamashiro K, Nakanishi H, Nakata I, Akagi-Kurashige Y, Tsujikawa A, Moriyama M, Ohno-Matsui K, Mochizuki M, Yamada R, Matsuda F, Yoshimura N. Association of paired box 6 with high myopia in Japanese. Mol Vis 2012; 18:2726-35. [PMID: 23213273].

48. Liang CL, Hsi E, Chen KC, Pan YR, Wang YS, Juo SH. A functional polymorphism at 3′UTR of the PAX6 gene may confer risk for extreme myopia in the Chinese. Invest Ophthalmol Vis Sci 2011; 52:3500-5. [PMID: 21421876].

49. Tsai YY, Chiang CC, Lin HJ, Lin JM, Wan L, Tsai FJA. PAX6 gene polymorphism is associated with genetic predisposition to extreme myopia. Eye (Lond) 2008; 22:576-81. [PMID: 17948041].

50. Dai L, Li Y, Du CY, Gong LM, Han CC, Li XG, Fan P, Fu SB. Ten SNPs of PAX6, Lumican, and MYOC genes are not associated with high myopia in Han Chinese. Ophthalmic Genet 2012; 33:171-8. [PMID: 22809227].

51. Zayats T, Guggenheim JA, Hammond CJ, Young TL. Comment on 'A PAX6 gene polymorphism is associated with genetic predisposition to extreme myopia'. Eye (Lond) 2008; 22:598-9. , author reply 9. [PMID: 18219338].

52. Simpson CL, Hysi P, Bhattacharya SS, Hammond CJ, Webster A, Peckham CS, Sham PC, Rahi JS. The Roles of PAX6 and SOX2 in Myopia: lessons from the 1958 British Birth Cohort. Invest Ophthalmol Vis Sci 2007; 48:4421-5. [PMID: 17898260].

53. Ratnamala U, Lyle R, Rawal R, Singh R, Vishnupriya S, Himabindu P, Rao V, Aggarwal S, Paluru P, Bartoloni L, Young TL, Paoloni-Giacobino A, Morris MA, Nath SK, Antonarakis SE, Radhakrishna U. Refinement of the X-linked nonsyndromic high-grade myopia locus MYP1 on Xq28 and exclusion of 13 known positional candidate genes by direct sequencing. Invest Ophthalmol Vis Sci 2011; 52:6814-9. [PMID: 21357393].

54. Nurnberg G, Jacobi FK, Broghammer M, Becker C, Blin N, Nurnberg P, Stephani U, Pusch CM. Refinement of the MYP3 locus on human chromosome 12 in a German family with Mendelian autosomal dominant high-grade myopia by SNP array mapping. Int J Mol Med 2008; 21:429-38. [PMID: 18360688].

55. Farbrother JE, Kirov G, Owen MJ, Pong-Wong R, Haley CS, Guggenheim JA. Linkage analysis of the genetic loci for high myopia on 18p, 12q, and 17q in 51 U.K. families. Invest Ophthalmol Vis Sci 2004; 45:2879-85. [PMID: 15326098].

56. Abbott D, Li YJ, Guggenheim JA, Metlapally R, Malecaze F, Calvas P, Rosenberg T, Paget S, Zayats T, Mackey DA, Feng S, Young TL. An international collaborative family-based whole genome quantitative trait linkage scan for myopic refractive error. Mol Vis 2012; 18:720-9. [PMID: 22509102].

57. Paluru PC, Scavello GS, Ganter WR, Young TL. Exclusion of lumican and fibromodulin as candidate genes in MYP3 linked high grade myopia. Mol Vis 2004; 10:917-22. [PMID: 15592176].

58. Scavello GS, Paluru PC, Ganter WR, Young TL. Sequence variants in the transforming growth beta-induced factor (TGIF) gene are not associated with high myopia. Invest Ophthalmol Vis Sci 2004; 45:2091-7. [PMID: 15223781].

59. Young TL. Dissecting the genetics of human high myopia: a molecular biologic approach. Trans Am Ophthalmol Soc 2004; 102:423-45. [PMID: 15747770].

60. Bartholin L, Powers SE, Melhuish TA, Lasse S, Weinstein M, Wotton D. TGIF inhibits retinoid signaling. Mol Cell Biol 2006; 26:990-1001. [PMID: 16428452].

61. Honda S, Fujii S, Sekiya Y, Yamamoto M. Retinal control on the axial length mediated by transforming growth factor-beta in chick eye. Invest Ophthalmol Vis Sci 1996; 37:2519-26. [PMID: 8933768].

62. Seko Y, Shimokawa H, Tokoro T. Expression of bFGF and TGF-beta 2 in experimental myopia in chicks. Invest Ophthalmol Vis Sci 1995; 36:1183-7. [PMID: 7730028].

63. Hasumi Y, Inoko H, Mano S, Ota M, Okada E, Kulski JK, Nishizaki R, Mok J, Oka A, Kumagai N, Nishida T, Ohno S, Mizuki N. Analysis of single nucleotide polymorphisms at 13 loci within the transforming growth factor-induced factor gene shows no association with high myopia in Japanese subjects. Immunogenetics 2006; 58:947-53. [PMID: 17048038].

64. Wang P, Li S, Xiao X, Jia X, Jiao X, Guo X, Zhang Q. High myopia is not associated with the SNPs in the TGIF, lumican, TGFB1, and HGF genes. Invest Ophthalmol Vis Sci 2009; 50:1546-51. [PMID: 19060265].

65. Chakravarti S, Paul J, Roberts L, Chervoneva I, Oldberg A, Birk DE. Ocular and scleral alterations in gene-targeted lumican-fibromodulin double-null mice. Invest Ophthalmol Vis Sci 2003; 44:2422-32. [PMID: 12766039].

66. Fan QVV, Wojciechowski R, Barathi VA, Hysi PG, Guggenheim JA, Höhn R, Vitart V, Khawaja AP, Yamashiro K, Hosseini SM, Lehtimäki T, Lu Y, Haller T, Xie J, Delcourt C,

Pirastu M, Wedenoja J, Gharahkhani P, Venturini C, Miyake M, Hewitt AW, Guo X. Meta-analysis of gene-environment-wide association scans accounting for education level identifies additional loci for refractive error. Nat Commun 2016; 7:11008-[PMID: 27020472].

67. Gao Y, Wang P, Li S, Xiao X, Jia X, Guo X, Zhang Q. Common variants in chromosome 4q25 are associated with myopia in Chinese adults. Ophthalmic Physiol Opt 2012; 32:68-73. [PMID: 22150588].

68. Gong B, Qu C, Huang XF, Ye ZM, Zhang DD, Shi Y, Chen R, Liu YP, Shuai P. Genetic association of COL1A1 polymorphisms with high myopia in Asian population: a Meta-analysis. Int J Ophthalmol 2016; 9:1187-93. [PMID: 27588274].

69. Cheng CY, Schache M, Ikram MK, Young TL, Guggenheim JA, Vitart V, MacGregor S, Verhoeven VJ, Barathi VA, Liao J, Hysi PG, Bailey-Wilson JE, St Pourcain B, Kemp JP, McMahon G, Timpson NJ, Evans DM, Montgomery GW, Mishra A, Wang YX. Nine loci for ocular axial length identified through genome-wide association studies, including shared loci with refractive error. Am J Hum Genet 2013; 93:264-77. [PMID: 24144296].

70. Hysi PG, Simpson CL, Fok YK, Gerrelli D, Webster AR, Bhattacharya SS, Hammond CJ, Sham PC, Rahi JS. Common polymorphisms in the SERPINI2 gene are associated with refractive error in the 1958 British Birth Cohort. Invest Ophthalmol Vis Sci 2012; 53:440-7. [PMID: 22110064].

71. Hysi PG, Young TL, Mackey DA, Andrew T, Fernandez-Medarde A, Solouki AM, Hewitt AW, Macgregor S, Vingerling JR, Li YJ, Ikram MK, Fai LY, Sham PC, Manyes L, Porteros A, Lopes MC, Carbonaro F, Fahy SJ, Martin NG, van Duijn CM, Spector TD, Rahi JS, Santos E, Klaver CC, Hammond CJ. A genome-wide association study for myopia and refractive error identifies a susceptibility locus at 15q25. Nat Genet 2010; 42:902-5. [PMID: 20835236].

72. Khor CC, Fan Q, Goh L, Tan D, Young TL, Li YJ, Seielstad M, Goh DL, Saw SM. Support for TGFB1 as a susceptibility gene for high myopia in individuals of Chinese descent. Arch Ophthalmol 2010; 128:1081-4. [PMID: 20697017].

73. Li Q, Wojciechowski R, Simpson CL, Hysi PG, Verhoeven VJ, Ikram MK, Hohn R, Vitart V, Hewitt AW, Oexle K, Makela KM, MacGregor S, Pirastu M, Fan Q, Cheng CY, St Pourcain B, McMahon G, Kemp JP, Northstone K, Rahi JS, Cumberland PM, Martin NG. Genome-wide association study for refractive astigmatism reveals genetic co-determination with spherical equivalent refractive error: the CREAM consortium. Hum Genet 2015; 134:131-46. [PMID: 25367360].

74. Liu J, Zhang HX. Polymorphism in the 11q24.1 genomic region is associated with myopia: a comprehensive genetic study in Chinese and Japanese populations. Mol Vis 2014; 20:352-8. [PMID: 24672220].

75. Metlapally R, Ki CS, Li YJ, Tran-Viet KN, Abbott D, Malecaze F, Calvas P, Mackey DA, Rosenberg T, Paget S, Guggenheim JA, Young TL. Genetic association of insulin-like growth factor-1 polymorphisms with high-grade myopia in an international family cohort. Invest Ophthalmol Vis Sci 2010; 51:4476-9. [PMID: 20435602].

76. Metlapally R, Li YJ, Tran-Viet KN, Abbott D, Czaja GR, Malecaze F, Calvas P, Mackey D, Rosenberg T, Paget S, Zayats T, Owen MJ, Guggenheim JA, Young TL. COL1A1 and COL2A1 genes and myopia susceptibility: evidence of association and suggestive linkage to the COL2A1 locus. Invest Ophthalmol Vis Sci 2009; 50:4080-6. [PMID: 19387081].

77. Mutti DO, Cooper ME, O'Brien S, Jones LA, Marazita ML, Murray JC, Zadnik K. Candidate gene and locus analysis of myopia. Mol Vis 2007; 13:1012-9. [PMID: 17653045].

78. Schache M, Baird PN. Assessment of the association of matrix metalloproteinases with myopia, refractive error and ocular biometric measures in an Australian cohort. PLoS One 2012; 7:e47181-[PMID: 23077567].

79. Schache M, Chen CY, Dirani M, Baird PN. The hepatocyte growth factor receptor (MET) gene is not associated with refractive error and ocular biometrics in a Caucasian population. Mol Vis 2009; 15:2599-605. [PMID: 20011629].

80. Schache M, Richardson AJ, Mitchell P, Wang JJ, Rochtchina E, Viswanathan AC, Wong TY, Saw SM, Topouzis F, Xie J, Sim X, Holliday EG, Attia J, Scott RJ, Baird PN. Genetic association of refractive error and axial length with 15q14 but not 15q25 in the Blue Mountains Eye Study cohort. Ophthalmology 2013; 120:292-7. [PMID: 23131718].

81. Sharmila F. Abinayapriya, Ramprabhu K, Kumaramanickavel G, Sudhir RR, Sripriya S. Genetic analysis of axial length genes in high grade myopia from Indian population. Meta Gene 2014; 2:164-75. [PMID: 25606400].

82. Simpson CL, Wojciechowski R, Oexle K, Murgia F, Portas L, Li X, Verhoeven VJ, Vitart V, Schache M, Hosseini SM, Hysi PG, Raffel LJ, Cotch MF, Chew E, Klein BE, Klein R, Wong TY, van Duijn CM, Mitchell P, Saw SM, Fossarello M, Wang JJ, Polasek O, Campbell H, Rudan I, Oostra BA, Uitterlinden AG, Hofman A, Rivadeneira F, Amin N, Karssen LC, Vingerling JR, Doring A, Bettecken T, Bencic G, Gieger C, Wichmann HE, Wilson JF, Venturini C, Fleck B, Cumberland PM, Rahi JS, Hammond CJ, Hayward C, Wright AF, Paterson AD, Baird PN, Klaver CC, Rotter JI, Pirastu M, Meitinger T, Bailey-Wilson JE, Stambolian D. Genome-wide meta-analysis of myopia and hyperopia provides evidence for replication of 11 loci. PLoS One 2014; 9:e107110-[PMID: 25233373].

83. Simpson CL, Wojciechowski R, Yee SS, Soni P, Bailey-Wilson JE, Stambolian D. Regional replication of association with refractive error on 15q14 and 15q25 in the Age-Related Eye Disease Study cohort. Mol Vis 2013; 19:2173-86. [PMID: 24227913].

84. Solouki AM, Verhoeven VJ, van Duijn CM, Verkerk AJ, Ikram MK, Hysi PG, Despriet DD, van Koolwijk LM, Ho L, Ramdas WD, Czudowska M, Kuijpers RW, Amin N, Struchalin M, Aulchenko YS, van Rij G, Riemslag FC, Young TL, Mackey DA. A genome-wide association study identifies a susceptibility locus for refractive errors and myopia at 15q14. Nat Genet 2010; 42:897-901. [PMID: 20835239].

85. Teo YY, Mackey DA, Oexle K, Yoshimura N, Paterson AD, Pfeiffer N, Wong TY, Baird PN, Stambolian D, Wilson JE, Cheng CY, Hammond CJ, Klaver CC, Saw SM, Rahi JS,

Korobelnik JF, Kemp JP, Timpson NJ, Smith GD, Craig JE, Burdon KP. Correlation between polymorphisms in the MFN1 gene and myopia in Chinese population. Nat Commun 2015; 8:1126-30. [PMID: 26682159].

86. Veerappan S, Pertile KK, Islam AF, Schache M, Chen CY, Mitchell P, Dirani M, Baird PN. Role of the hepatocyte growth factor gene in refractive error. Ophthalmology 2010; 117(2):239–45.

87. Veerappan S, Schache M, Pertile KK, Islam FM, Chen CY, Mitchell P, Dirani M, Baird PN. The retinoic acid receptor alpha (RARA) gene is not associated with myopia, hypermetropia, and ocular biometric measures. Mol Vis 2009; 15:1390-7. [PMID: 19626135].

88. Verhoeven VJ, Hysi PG, Saw SM, Vitart V, Mirshahi A, Guggenheim JA, Cotch MF, Yamashiro K, Baird PN, Mackey DA, Wojciechowski R, Ikram MK, Hewitt AW, Duggal P, Janmahasatian S, Khor CC, Fan Q, Zhou X, Young TL, Tai ES, Goh LK, Li YJ, Aung T, Vithana E. Large scale international replication and meta-analysis study confirms association of the 15q14 locus with myopia. The CREAM consortium. Hum Genet 2012; 131:1467-80. [PMID: 22665138].

89. Verhoeven VJ, Hysi PG, Wojciechowski R, Fan Q, Guggenheim JA, Hohn R, MacGregor S, Hewitt AW, Nag A, Cheng CY, Yonova-Doing E, Zhou X, Ikram MK, Buitendijk GH, McMahon G, Kemp JP, Pourcain BS, Simpson CL, Makela KM, Lehtimaki T. Genome-wide meta-analyses of multiancestry cohorts identify multiple new susceptibility loci for refractive error and myopia. Nat Genet 2013; 45:314-8. [PMID: 23396134].

90. Wang Q, Gao Y, Wang P, Li S, Jia X, Xiao X, Guo X, Zhang Q. Replication study of significant single nucleotide polymorphisms associated with myopia from two genome-wide association studies. Mol Vis 2011; 17:3290-9. [PMID: 22194655].

91. Wojciechowski R, Bailey-Wilson JE, Stambolian D. Association of matrix metalloproteinase gene polymorphisms with refractive error in Amish and Ashkenazi families. Invest Ophthalmol Vis Sci 2010; 51:4989-95. [PMID: 20484597].

92. Wojciechowski R, Yee SS, Simpson CL, Bailey-Wilson JE, Stambolian D. Matrix metalloproteinases and educational attainment in refractive error: evidence of gene-environment interactions in the Age-Related Eye Disease Study. Ophthalmology 2013; 120:298-305. [PMID: 23098370].

93. Yoshikawa M, Yamashiro K, Miyake M, Oishi M, Akagi-Kurashige Y, Kumagai K, Nakata I, Nakanishi H, Oishi A, Gotoh N, Yamada R, Matsuda F, Yoshimura N. Comprehensive replication of the relationship between myopia-related genes and refractive errors in a large Japanese cohort. Invest Ophthalmol Vis Sci 2014; 55:7343-54. [PMID: 25335978].

94. Zidan HE, Rezk NA, Fouda SM, Mattout HK. Association of Insulin-Like Growth Factor-1 Gene Polymorphisms with Different Types of Myopia in Egyptian Patients. Genet Test Mol Biomarkers 2016; 20:291-6. [PMID: 27167306].

95. Fan Q, Guo X, Tideman JW, Williams KM, Yazar S, Hosseini SM, Howe LD, Pourcain BS, Evans DM, Timpson NJ, McMahon G, Hysi PG, Krapohl E, Wang YX, Jonas JB, Baird PN, Wang JJ, Cheng CY, Teo YY, Wong TY, Ding X, Wojciechowski R, Young TL, Parssinen O, Oexle K, Pfeiffer N, Bailey-Wilson JE, Paterson AD, Klaver CC, Plomin R, Hammond CJ, Mackey DA, He M, Saw SM, Williams C, Guggenheim JA, Consortium C. Childhood gene-environment interactions and age-dependent effects of genetic variants associated with refractive error and myopia: The CREAM Consortium. Sci Rep 2016; 6:25853-[PMID: 27174397].

96. Bindu CH. Sandhya, A.; Pavani, K. V.; Vishnupriya, S. Substantial Risk Factor of GSTP Gene Polymorphism with Myopia. IUP Journal of Genetics & Evolution 2011; 4:21-.

97. Sandhya A. TGFB1 codon 10 polymorphism and its association with the development of myopia: a case-control study. Biology & Medicine 2011; 418-24. .

98. . SANDHYA. VISHNUPRIYA, Bindu H, Reddy P. ROLE OF ENDOSTATIN GENE POLYMORPHISM IN THE DEVELOPMENT OF HIGH MYOPIA. J. Cell Tissue Res 2008; 8:1233-8. .

99. Annamaneni S, Bindu CH, Reddy KP, Vishnupriya S. Association of vitamin D receptor gene start codon (Fok1) polymorphism with high myopia. Oman J Ophthalmol 2011; 4:57-62. [PMID: 21897619].

100. Ahmed I, Rasool S, Jan T, Qureshi T, Naykoo NA, Andrabi KI. TGIF1 is a potential candidate gene for high myopia in ethnic Kashmiri population. Curr Eye Res 2014; 39:282-90. [PMID: 24215395].

101. Chen CD, Yu ZQ, Chen XL, Zhou JQ, Zhou XT, Sun XH, Chu RY. Evaluating the association between pathological myopia and SNPs in RASGRF1. ACTC1 and GJD2 genes at chromosome 15q14 and 15q25 in a Chinese population. Ophthalmic Genet 2015; 36:1-7. [PMID: 23834555].

102. Chen T, Shan G, Ma J, Zhong Y. Polymorphism in the RASGRF1 gene with high myopia: A meta-analysis. Mol Vis 2015; 21:1272-80. [PMID: 26644762].

103. Chen X, Xue A, Chen W, Ding Y, Yan D, Peng J, Zeng C, Qu J, Zhou X. Assessment of exonic single nucleotide polymorphisms in the adenosine A2A receptor gene to high myopia susceptibility in Chinese subjects. Mol Vis 2011; 17:486-91. [PMID: 22740769].

104. Chen ZT, Wang IJ, Liao YT, Shih YF, Lin LL. Polymorphisms in steroidogenesis genes, sex steroid levels, and high myopia in the Taiwanese population. Mol Vis 2011; 17:2297-310. [PMID: 21921981].

105. Chen ZT, Wang IJ, Shih YF, Lin LL. The association of haplotype at the lumican gene with high myopia susceptibility in Taiwanese patients. Ophthalmology 2009; 116:1920-7. [PMID: 19616852].

106. Deng ZJ, Shi KQ, Song YJ, Fang YX, Wu J, Li G, Tang KF, Qu J. Association between a lumican promoter polymorphism and high myopia in the Chinese population: a meta-analysis of case-control studies. Ophthalmologica 2014; 232:110-7. [PMID: 24516061].

107. Ding Y, Chen X, Yan D, Xue A, Lu F, Qu J, Zhou X. Association analysis of retinoic acid receptor beta (RARbeta) gene with high myopia in Chinese subjects. Mol Vis 2010; 16:855-61. [PMID: 20508731].

108. Fan Q, Barathi VA, Cheng CY, Zhou X, Meguro A, Nakata I, Khor CC, Goh LK, Li YJ, Lim W, Ho CE, Hawthorne F, Zheng Y, Chua D, Inoko H, Yamashiro K, Ohno-Matsui K, Matsuo K, Matsuda F, Vithana E, Seielstad M, Mizuki N, Beuerman RW, Tai ES, Yoshimura N, Aung T, Young TL, Wong TY, Teo YY, Saw SM. Genetic variants on chromosome 1q41 influence ocular axial length and high myopia. PLoS Genet 2012; 8:e1002753-[PMID: 22685421].

109. Feng YF, Zhang YL, Zha Y, Huang JH, Cai JQ. Association of Lumican gene polymorphism with high myopia: a meta-analysis. Optom Vis Sci 2013; 90:1321-6. [PMID: 24061151].

110. Gong B, Liu X, Zhang D, Wang P, Huang L, Lin Y, Lu F, Ma S, Cheng J, Chen R, Li X, Lin H, Zeng G, Zhu X, Hu J, Yang Z, Shi Y. Evaluation of MMP2 as a candidate gene for high myopia. Mol Vis 2013; 19:121-7. [PMID: 23378725].

111. Guo L, Du X, Lu C, Zhang WH. Association between Insulin-Like Growth Factor 1 Gene rs12423791 or rs6214 Polymorphisms and High Myopia: A Meta-Analysis. PLoS One 2015; 10:e0129707-[PMID: 26076017].

112. Han W, Yap MK, Wang J, Yip SP. Family-based association analysis of hepatocyte growth factor (HGF) gene polymorphisms in high myopia. Invest Ophthalmol Vis Sci 2006; 47:2291-9. [PMID: 16723436].

113. Hawthorne F, Feng S, Metlapally R, Li YJ, Tran-Viet KN, Guggenheim JA, Malecaze F, Calvas P, Rosenberg T, Mackey DA, Venturini C, Hysi PG, Hammond CJ, Young TL. Association mapping of the high-grade myopia MYP3 locus reveals novel candidates UHRF1BP1L, PTPRR, and PPFIA2. Invest Ophthalmol Vis Sci 2013; 54:2076-86. [PMID: 23422819].

114. Hayashi H, Yamashiro K, Nakanishi H, Nakata I, Kurashige Y, Tsujikawa A, Moriyama M, Ohno-Matsui K, Mochizuki M, Ozaki M, Yamada R, Matsuda F, Yoshimura N. Association of 15q14 and 15q25 with high myopia in Japanese. Invest Ophthalmol Vis Sci 2011; 52:4853-8. [PMID: 21436269].

115. He M, Wang W, Ragoonundun D, Huang W. Meta-analysis of the association between lumican gene polymorphisms and susceptibility to high Myopia. PLoS One 2014; 9:e98748-[PMID: 24956166].

116. Schuurs-Hoeijmakers JH, Oh EC, Vissers LE, Swinkels ME, Gilissen C, Willemsen MA, Holvoet M, Steehouwer M, Veltman JA, de Vries BB, van Bokhoven H, de Brouwer AP, Katsanis N, Devriendt K, Brunner HG. Recurrent de novo mutations in PACS1 cause defective cranial-neural-crest migration and define a recognizable intellectual-disability syndrome. Am J Hum Genet 2012; 91:1122-7. [PMID: 23159249].

117. Hsi E, Chen KC, Chang WS, Yu ML, Liang CL, Juo SH. A functional polymorphism at the FGF10 gene is associated with extreme myopia. Invest Ophthalmol Vis Sci 2013; 54:3265-71. [PMID: 23599340].

118. Inamori Y, Ota M, Inoko H, Okada E, Nishizaki R, Shiota T, Mok J, Oka A, Ohno S, Mizuki N. The COL1A1 gene and high myopia susceptibility in Japanese. Hum Genet 2007; 122:151-7. [PMID: 17557158].

119. Jiao X, Wang P, Li S, Li A, Guo X, Zhang Q, Hejtmancik JF. Association of markers at chromosome 15q14 in Chinese patients with moderate to high myopia. Mol Vis 2012; 18:2633-46. [PMID: 23170057].

120. Kanemaki N, Meguro A, Yamane T, Takeuchi M, Okada E, Iijima Y, Mizuki N. Study of association of PAX6 polymorphisms with susceptibility to high myopia in a Japanese population. Clin Ophthalmol 2015; 9:2005-11. [PMID: 26604670].

121. Khor CC, Miyake M, Chen LJ, Shi Y, Barathi VA, Qiao F, Nakata I, Yamashiro K, Zhou X, Tam PO, Cheng CY, Tai ES, Vithana EN, Aung T, Teo YY, Wong TY, Moriyama M, Ohno-Matsui K, Mochizuki M, Matsuda F, Yong RY, Yap EP, Yang Z, Pang CP, Saw SM, Yoshimura N. Genome-wide association study identifies ZFHX1B as a susceptibility locus for severe myopia. Hum Mol Genet 2013; 22:5288-94. [PMID: 23933737].

122. Li J, Jiang D, Xiao X, Li S, Jia X, Sun W, Guo X, Zhang Q. Evaluation of 12 myopia-associated genes in Chinese patients with high myopia. Invest Ophthalmol Vis Sci 2015; 56:722-9. [PMID: 25587058].

123. Li M, Zhai L, Zeng S, Peng Q, Wang J, Deng Y, Xie L, He Y, Li T. Lack of association between LUM rs3759223 polymorphism and high myopia. Optom Vis Sci 2014; 91:707-12. [PMID: 24927138].

124. Li YJ, Goh L, Khor CC, Fan Q, Yu M, Han S, Sim X, Ong RT, Wong TY, Vithana EN, Yap E, Nakanishi H, Matsuda F, Ohno-Matsui K, Yoshimura N, Seielstad M, Tai ES, Young TL, Saw SM. Genome-wide association studies reveal genetic variants in CTNND2 for high myopia in Singapore Chinese. Ophthalmology 2011; 118:368-75. [PMID: 21095009].

125. Li YT, Xie MK, Wu J. Association between Ocular Axial Length-Related Genes and High Myopia in a Han Chinese Population. Ophthalmologica 2016; 235:57-60. [PMID: 26485405].

126. Li Z, Qu J, Xu X, Zhou X, Zou H, Wang N, Li T, Hu X, Zhao Q, Chen P, Li W, Huang K, Yang J, He Z, Ji J, Wang T, Li J, Li Y, Liu J, Zeng Z, Feng G, He L, Shi Y. A genome-wide association study reveals association between common variants in an intergenic region of 4q25 and high-grade myopia in the Chinese Han population. Hum Mol Genet 2011; 20:2861-8. [PMID: 21505071].

127. Liang CL, Hung KS, Tsai YY, Chang W, Wang HS, Juo SH. Systematic assessment of the tagging polymorphisms of the COL1A1 gene for high myopia. J Hum Genet 2007; 52:374-7. [PMID: 17273809].

128. Liang CL, Wang HS, Hung KS, Hsi E, Sun A, Kuo YH, Juo SH. Evaluation of MMP3 and TIMP1 as candidate genes for high myopia in young Taiwanese men. Am J Ophthalmol 2006; 142:518-20. [PMID: 16935611].

129. Liao X, Yang XB, Liao M, Lan CJ, Liu LQ. Association between lumican gene −1554 T/C polymorphism and high myopia in Asian population: a meta-analysis. Int J Ophthalmol 2013; 6:696-701. [PMID: 24195052].

130. Lin HJ, Kung YJ, Lin YJ, Sheu JJ, Chen BH, Lan YC, Lai CH, Hsu YA, Wan L, Tsai FJ. Association of the lumican gene functional 3′-UTR polymorphism with high myopia. Invest Ophthalmol Vis Sci 2010; 51:96-102. [PMID: 19643966].

131. Lin HJ, Wan L, Chen WC, Lin JM, Lin CJ, Tsai FJ. Muscarinic acetylcholine receptor 3 is dominant in myopia progression. Invest Ophthalmol Vis Sci 2012; 53:6519-25. [PMID: 22899762].

132. Lin HJ, Wan L, Tsai Y, Chen WC, Tsai SW, Tsai FJ. Muscarinic acetylcholine receptor 1 gene polymorphisms associated with high myopia. Mol Vis 2009; 15:1774-80. [PMID: 19753311].

133. Lin HJ, Wan L, Tsai Y, Chen WC, Tsai SW, Tsai FJ. The association between lumican gene polymorphisms and high myopia. Eye (Lond) 2010; 24:1093-101. [PMID: 20010793].

134. Lin HJ, Wan L, Tsai Y, Liu SC, Chen WC, Tsai SW, Tsai FJ. Sclera-related gene polymorphisms in high myopia. Mol Vis 2009; 15:1655-63. [PMID: 19710942].

135. Lin HJ, Wan L, Tsai Y, Tsai YY, Fan SS, Tsai CH, Tsai FJ. The TGFbeta1 gene codon 10 polymorphism contributes to the genetic predisposition to high myopia. Mol Vis 2006; 12:698-703. [PMID: 16807529].

136. Liu X, Wang P, Qu C, Zheng H, Gong B, Ma S, Lin H, Cheng J, Yang Z, Lu F, Shi Y. Genetic association study between INSULIN pathway related genes and high myopia in a Han Chinese population. Mol Biol Rep 2015; 42:303-10. [PMID: 25266237].

137. Lu B, Jiang D, Wang P, Gao Y, Sun W, Xiao X, Li S, Jia X, Guo X, Zhang Q. Replication study supports CTNND2 as a susceptibility gene for high myopia. Invest Ophthalmol Vis Sci 2011; 52:8258-61. [PMID: 21911587].

138. Mak JY, Yap MK, Fung WY, Ng PW, Yip SP. Association of IGF1 gene haplotypes with high myopia in Chinese adults. Arch Ophthalmol 2012; 130:209-16. [PMID: 22332214].

139. Meng B, Li SM, Yang Y, Yang ZR, Sun F, Kang MT, Sun YY, Ran AR, Wang JN, Yan R, Ba IY, Wang NL, Zhan SY. The association of TGFB1 genetic polymorphisms with high myopia: a systematic review and meta-analysis. Int J Clin Exp Med 2015; 8:20355-67. [PMID: 26884952].

140. Metlapally R, Li YJ, Tran-Viet KN, Bulusu A, White TR, Ellis J, Kao D, Young TL. Common MFRP sequence variants are not associated with moderate to high hyperopia, isolated microphthalmia, and high myopia. Mol Vis 2008; 14:387-93. [PMID: 18334955].

141. Miyake M, Yamashiro K, Tabara Y, Suda K, Morooka S, Nakanishi H, Khor CC, Chen P, Qiao F, Nakata I, Akagi-Kurashige Y, Gotoh N, Tsujikawa A, Meguro A, Kusuhara S, Polasek O, Hayward C, Wright AF, Campbell H, Richardson AJ, Schache M, Takeuchi M, Mackey DA, Hewitt AW, Cuellar G, Shi Y, Huang L, Yang Z, Leung KH, Kao PY, Yap MK, Yip SP, Moriyama M, Ohno-Matsui K, Mizuki N, MacGregor S, Vitart V, Aung T, Saw SM, Tai ES, Wong TY, Cheng CY, Baird PN, Yamada R, Matsuda F. Nagahama Study Group. Yoshimura N. Identification of myopia-associated WNT7B polymorphisms provides insights into the mechanism underlying the development of myopia. Nat Commun 2015; 6:6689-[PMID: 25823570].

142. Miyake M, Yamashiro K, Nakanishi H, Nakata I, Akagi-Kurashige Y, Tsujikawa A, Moriyama M, Ohno-Matsui K, Mochizuki M, Yamada R, Matsuda F, Yoshimura N. Insulin-like growth factor 1 is not associated with high myopia in a large Japanese cohort. Mol Vis 2013; 19:1074-81. [PMID: 23734076].

143. Moriyama M, Ohno-Matsui K, Mizuki N, MacGregor S, Vitart V, Aung T, Saw SM, Tai ES, Wong TY, Cheng CY, Baird PN, Yamada R, Matsuda F, Yoshimura N, Ye Z, Luo H, Gong B, Lin Y, Shuai P, Wang P, Ye C, Yang Z, Wang W, Shi Y. Evaluation of four genetic variants in han chinese subjects with high myopia. Nat Commun 2015; 2015:729463-[PMID: 25628894].

144. Nakanishi H, Yamada R, Gotoh N, Hayashi H, Otani A, Tsujikawa A, Yamashiro K, Shimada N, Ohno-Matsui K, Mochizuki M, Saito M, Saito K, Iida T, Matsuda F, Yoshimura N. Absence of association between COL1A1 polymorphisms and high myopia in the Japanese population. Invest Ophthalmol Vis Sci 2009; 50:544-50. [PMID: 18836165].

145. Nakanishi H, Yamada R, Gotoh N, Hayashi H, Yamashiro K, Shimada N, Ohno-Matsui K, Mochizuki M, Saito M, Iida T, Matsuo K, Tajima K, Yoshimura N, Matsuda F. A genome-wide association analysis identified a novel susceptible locus for pathological myopia at 11q24.1. PLoS Genet 2009; 5:e1000660-[PMID: 19779542].

146. Nishizaki R, Ota M, Inoko H, Meguro A, Shiota T, Okada E, Mok J, Oka A, Ohno S, Mizuki N. New susceptibility locus for high myopia is linked to the uromodulin-like 1 (UMODL1) gene region on chromosome 21q22.3. Eye (Lond) 2009; 23:222-9. [PMID: 18535602].

147. Oishi M, Yamashiro K, Miyake M, Akagi-Kurashige Y, Kumagai K, Nakata I, Nakanishi H, Yoshikawa M, Oishi A, Gotoh N, Tsujikawa A, Yamada R, Matsuda F, Yoshimura N. Association between ZIC2, RASGRF1, and SHISA6 genes and high myopia in Japanese subjects. Invest Ophthalmol Vis Sci 2013; 54:7492-7. [PMID: 24150758].

148. Okui S, Meguro A, Takeuchi M, Yamane T, Okada E, Iijima Y, Mizuki N. Analysis of the association between the LUM rs3759223 variant and high myopia in a Japanese population. Clin Ophthalmol 2016; 10:2157-63. [PMID: 27826181].

149. Park SH, Mok J, Joo CK. Absence of an association between lumican promoter variants and high myopia in the Korean population. Ophthalmic Genet 2013; 34:43-7. [PMID: 23145541].

150. Qiang Y, Li W, Wang Q, He K, Li Z, Chen J, Song Z, Qu J, Zhou X, Qin S, Shen J, Wen Z, Ji J, Shi Y. Association study of 15q14 and 15q25 with high myopia in the Han Chinese population. BMC Genet 2014; 15:51-[PMID: 24767175].

151. Rasool S, Ahmed I, Dar R, Ayub SG, Rashid S, Jan T, Ahmed T, Naikoo NA, Andrabi KI. Contribution of TGFbeta1 codon 10 polymorphism to high myopia in an ethnic Kashmiri population from India. Biochem Genet 2013; 51:323-33. [PMID: 23325483].

152. Rydzanicz M, Nowak DM, Karolak JA, Frajdenberg A, Podfigurna-Musielak M, Mrugacz M, Gajecka M. IGF-1 gene polymorphisms in Polish families with high-grade myopia. Mol Vis 2011; 17:2428-39. [PMID: 21976954].

153. Sasaki S, Ota M, Meguro A, Nishizaki R, Okada E, Mok J, Kimura T, Oka A, Katsuyama Y, Ohno S, Inoko H, Mizuki N. A single nucleotide polymorphism analysis of the LAMA1 gene in Japanese patients with high myopia. Clin Ophthalmol 2007; 1:289-95. [PMID: 19668483].

154. Shi Y, Gong B, Chen L, Zuo X, Liu X, Tam PO, Zhou X, Zhao P, Lu F, Qu J, Sun L, Zhao F, Chen H, Zhang Y, Zhang D, Lin Y, Lin H, Ma S, Cheng J, Yang J, Huang L, Zhang M, Zhang X, Pang CP, Yang Z. A genome-wide meta-analysis identifies two novel loci associated with high myopia in the Han Chinese population. Hum Mol Genet 2013; 22:2325-33. [PMID: 23406873].

155. Shi Y, Qu J, Zhang D, Zhao P, Zhang Q, Tam PO, Sun L, Zuo X, Zhou X, Xiao X, Hu J, Li Y, Cai L, Liu X, Lu F, Liao S, Chen B, He F, Gong B, Lin H, Ma S, Cheng J, Zhang J, Chen Y, Zhao F, Yang X, Chen Y, Yang C, Lam DS, Li X, Shi F, Wu Z, Lin Y, Yang J, Li S, Ren Y, Xue A, Fan Y, Li D, Pang CP, Zhang X, Yang Z. Genetic variants at 13q12.12 are associated with high myopia in the Han Chinese population. Am J Hum Genet 2011; 88:805-13. [PMID: 21640322].

156. Tang SM, Rong SS, Young AL, Tam PO, Pang CP, Chen LJ. PAX6 gene associated with high myopia: a meta-analysis. Optom Vis Sci 2014; 91:419-29. [PMID: 24637479].

157. Tang WC, Yip SP, Lo KK, Ng PW, Choi PS, Lee SY, Yap MK. Linkage and association of myocilin (MYOC) polymorphisms with high myopia in a Chinese population. Mol Vis 2007; 13:534-44. [PMID: 17438518].

158. Vatavuk Z, Skunca Herman J, Bencic G, Andrijevic Derk B, Lacmanovic Loncar V, Petric Vickovic I, Bucan K, Mandic K, Mandic A, Skegro I, Pavicic Astalos J, Merc I, Martinovic M, Kralj P, Knezevic T, Barac-Juretic K, Zgaga L. Common variant in myocilin gene is associated with high myopia in isolated population of Korcula Island, Croatia. Croat Med J 2009; 50:17-22. [PMID: 19260140].

159. Wang H, Su S, Yang M, Hu N, Yao Y, Zhu R, Zhou J, Liang C, Guan H. Association of ZNF644, GRM6, and CTNND2 genes with high myopia in the Han Chinese population: Jiangsu Eye Study. Eye (Lond) 2016; 30:1017-22. [PMID: 27034204].

160. Wang IJ, Chiang TH, Shih YF, Hsiao CK, Lu SC, Hou YC, Lin LL. The association of single nucleotide polymorphisms in the 5′-regulatory region of the lumican gene with susceptibility to high myopia in Taiwan. Mol Vis 2006; 12:852-7. [PMID: 16902402].

161. Wang J, Wang P, Gao Y, Li S, Xiao X, Zhang Q. High myopia is not associated with single nucleotide polymorphisms in the COL2A1 gene in the Chinese population. Mol Med Rep 2012; 5:133-7. [PMID: 21993774].

162. Wang P, Liu X, Ye Z, Gong B, Yang Y, Zhang D, Wu X, Zheng H, Li Y, Yang Z, Shi Y. Association of IGF1 and IGF1R gene polymorphisms with high myopia in a Han Chinese population. Ophthalmic Genet 2016; •••:1-5. [PMID: 27044882].

163. Yang X, Liu X, Peng J, Zheng H, Lu F, Gong B, Zhao G, Meng Y, Guan H, Ning M, Yang Z, Shi Y. Evaluation of MYOC, ACAN, HGF, and MET as candidate genes for high myopia in a Han Chinese population. Genet Test Mol Biomarkers 2014; 18:446-52. [PMID: 24766640].

164. Yanovitch T, Li YJ, Metlapally R, Abbott D, Viet KN, Young TL. Hepatocyte growth factor and myopia: genetic association analyses in a Caucasian population. Mol Vis 2009; 15:1028-35. [PMID: 19471602].

165. Yip SP, Leung KH, Ng PW, Fung WY, Sham PC, Yap MK. Evaluation of proteoglycan gene polymorphisms as risk factors in the genetic susceptibility to high myopia. Invest Ophthalmol Vis Sci 2011; 52:6396-403. [PMID: 21743019].

166. Yiu WC, Yap MK, Fung WY, Ng PW, Yip SP. Genetic susceptibility to refractive error: association of vasoactive intestinal peptide receptor 2 (VIPR2) with high myopia in Chinese. PLoS One 2013; 8:e61805-[PMID: 23637909].

167. Yoshida M, Meguro A, Okada E, Nomura N, Mizuki N. Association study of fibroblast growth factor 10 (FGF10) polymorphisms with susceptibility to extreme myopia in a Japanese population. Mol Vis 2013; 19:2321-9. [PMID: 24265547].

168. Yoshida M, Meguro A, Yoshino A, Nomura N, Okada E, Mizuki N. Association study of IGF1 polymorphisms with susceptibility to high myopia in a Japanese population. Clin Ophthalmol 2013; 7:2057-62. [PMID: 24204106].

169. Yu YS, Wang LL, Shen Y, Yap MK, Yip SP, Han W. Investigation of the association between all-trans-retinol dehydrogenase (RDH8) polymorphisms and high myopia in Chinese. J Zhejiang Univ Sci B 2010; 11:836-41. [PMID: 21043051].

170. Yu Z, Zhou J, Chen X, Zhou X, Sun X, Chu R. Polymorphisms in the CTNND2 gene and 11q24.1 genomic region are associated with pathological myopia in a Chinese population. Ophthalmologica 2012; 228:123-9. [PMID: 22759899].

171. Zayats T, Yanovitch T, Creer RC, McMahon G, Li YJ, Young TL, Guggenheim JA. Myocilin polymorphisms and high myopia in subjects of European origin. Mol Vis 2009; 15:213-22. [PMID: 19180258].

172. Zha Y, Leung KH, Lo KK, Fung WY, Ng PW, Shi MG, Yap MK, Yip SP. TGFB1 as a susceptibility gene for high myopia: a replication study with new findings. Arch Ophthalmol 2009; 127:541-8. [PMID: 19365037].

173. Zhang D, Shi Y, Gong B, He F, Lu F, Lin H, Wu Z, Cheng J, Chen B, Liao S, Ma S, Hu J, Yang Z. An association study of the COL1A1 gene and high myopia in a Han Chinese population. Mol Vis 2011; 17:3379-83. [PMID: 22219633].

174. Zhang X, Zhou X, Qu X. The association between IGF-1 polymorphisms and high myopia. Int J Clin Exp Med 2015; 8:10158-67. [PMID: 26309715].

175. Zhao F, Bai J, Chen W, Xue A, Li C, Yan Z, Chen H, Lu F, Hu Y, Qu J, Zeng C, Zhou X. Evaluation of BLID and LOC399959 as candidate genes for high myopia in the Chinese Han population. Mol Vis 2010; 16:1920-7. [PMID: 21031016].

176. Zhao YY, Zhang FJ, Zhu SQ, Duan H, Li Y, Zhou ZJ, Ma WX, Li Wang N. The association of a single nucleotide polymorphism in the promoter region of the LAMA1 gene with susceptibility to Chinese high myopia. Mol Vis 2011; 17:1003-10. [PMID: 21541277].

177. Zhu MM, Yap MK, Ho DW, Fung WY, Ng PW, Gu YS, Yip SP. Investigating the relationship between UMODL1 gene polymorphisms and high myopia: a case-control study in Chinese. BMC Med Genet 2012; 13:64-[PMID: 22857148].

178. Zhuang W, Yang P, Li Z, Sheng X, Zhao J, Li S, Yang X, Xiang W, Rong W, Liu Y, Zhang F. Association of insulin-like growth factor-1 polymorphisms with high myopia in the Chinese population. Mol Vis 2012; 18:634-44. [PMID: 22509095].

179. Khor CCMM, Chen LJ, Shi Y, Barathi VA, Qiao F, Nakata I, Yamashiro K, Zhou X, Tam PO, Cheng CY, Tai ES, Vithana EN, Aung T, Teo YY, Wong TY, Moriyama M, Ohno-Matsui K, Mochizuki M, Matsuda F. Nagahama Study Group. Yong RY, Yap EP, Yang Z, Pang CP, Saw SM, Yoshimura N. Genome-wide association study identifies ZFHX1B as a susceptibility locus for severe myopia. Hum Mol Genet 2013; 22(25)5288-94. [PMID: 23933737].

180. Chen JH, Chen H, Huang S, Lin J, Zheng Y, Xie M, Lin W, Pang CP, Zhang M. Endophenotyping reveals differential phenotype-genotype correlations between myopia-associated polymorphisms and eye biometric parameters. Mol Vis 2012; 18:765-78. [PMID: 22509107].

181. Fan Q, Zhou X, Khor CC, Cheng CY, Goh LK, Sim X, Tay WT, Li YJ, Ong RT, Suo C, Cornes B, Ikram MK, Chia KS, Seielstad M, Liu J, Vithana E, Young TL, Tai ES, Wong TY, Aung T, Teo YY, Saw SM. Genome-wide meta-analysis of five Asian cohorts identifies PDGFRA as a susceptibility locus for corneal astigmatism. PLoS Genet 2011; 7:e1002402-[PMID: 22144915].

182. Guggenheim JA, McMahon G, Kemp JP, Akhtar S, St Pourcain B, Northstone K, Ring SM, Evans DM, Smith GD, Timpson NJ, Williams C. A genome-wide association study for corneal curvature identifies the platelet-derived growth factor receptor alpha gene as a quantitative trait locus for eye size in white Europeans. Mol Vis 2013; 19:243-53. [PMID: 23401653].

183. Mishra A, Yazar S, Hewitt AW, Mountain JA, Ang W, Pennell CE, Martin NG, Montgomery GW, Hammond CJ, Young TL, Macgregor S, Mackey DA. Genetic variants near PDGFRA are associated with corneal curvature in Australians. Invest Ophthalmol Vis Sci 2012; 53:7131-6. [PMID: 22969067].

184. Moriyama M, Ohno-Matsui K, Mizuki N, MacGregor S, Vitart V, Aung T, Saw SM, Tai ES, Wong TY, Cheng CY, Baird PN, Yamada R, Matsuda F, Yoshimura N, Chen P, Miyake M, Fan Q, Liao J, Yamashiro K, Ikram MK, Chew M, Vithana EN, Khor CC, Aung T, Tai ES, Wong TY, Teo YY, Yoshimura N, Saw SM, Cheng CY. CMPK1 and RBP3 are associated with corneal curvature in Asian populations. Nat Commun 2014; 23:6129-36. [PMID: 24963161].

185. Fan Q, Barathi VA, Cheng CY, Zhou X, Meguro A, Nakata I, Khor CC, Goh LK, Li YJ, Lim W, Ho CEH, Hawthorne F, Zheng YF, Chua D, Inoko H, Yamashiro K, Ohno-Matsui K, Matsuo K, Matsuda F, Vithana E, Seielstad M, Mizuki N, Beuerman RW, Tai ES, Yoshimura N, Aung T, Young TL, Wong TY, Teo YY, Saw SM. Genetic Variants on Chromosome 1q41 Influence Ocular Axial Length and High Myopia. PLoS Genet 2012; 8:[PMID: 22685421].

186. Dirani M, Shekar SN, Baird PN. Evidence of shared genes in refraction and axial length: the Genes in Myopia (GEM) twin study. Invest Ophthalmol Vis Sci 2008; 49:4336-9. [PMID: 18552384].

187. Aldahmesh MA, Khan AO, Alkuraya H, Adly N, Anazi S, Al-Saleh AA, Mohamed JY, Hijazi H, Prabakaran S, Tacke M, Al-Khrashi A, Hashem M, Reinheckel T, Assiri A, Alkuraya FS. Mutations in LRPAP1 are associated with severe myopia in humans. Am J Hum Genet 2013; 93:313-20. [PMID: 23830514].

188. Guo H, Jin X, Zhu T, Wang T, Tong P, Tian L, Peng Y, Sun L, Wan A, Chen J, Liu Y, Li Y, Tian Q, Xia L, Zhang L, Pan Y, Lu L, Liu Q, Shen L, Li Y, Xiong W, Li J, Tang B, Feng Y, Zhang X, Zhang Z, Pan Q, Hu Z, Xia K. SLC39A5 mutations interfering with the BMP/TGF-beta pathway in non-syndromic high myopia. J Med Genet 2014; 51:518-25. [PMID: 24891338].

189. Guo H, Tong P, Peng Y, Wang T, Liu Y, Chen J, Li Y, Tian Q, Hu Y, Zheng Y, Xiao L, Xiong W, Pan Q, Hu Z, Xia K. Homozygous loss-of-function mutation of the LEPREL1 gene causes severe non-syndromic high myopia with early-onset cataract. Clin Genet 2014; 86:575-9. [PMID: 24172257].

190. Jiang D, Li J, Xiao X, Li S, Jia X, Sun W, Guo X, Zhang Q. Detection of mutations in LRPAP1, CTSH, LEPREL1, ZNF644, SLC39A5, and SCO2 in 298 families with early-onset high myopia by exome sequencing. Invest Ophthalmol Vis Sci 2014; 56:339-45. [PMID: 25525168].

191. Li J, Gao B, Guan L, Xiao X, Zhang J, Li S, Jiang H, Jia X, Yang J, Guo X, Yin Y, Wang J, Zhang Q. Unique Variants in OPN1LW Cause Both Syndromic and Nonsyndromic X–Linked High Myopia Mapped to MYP1. Invest Ophthalmol Vis Sci 2015; 56:4150-5. [PMID: 26114493].

192. Mordechai S, Gradstein L, Pasanen A, Ofir R, El Amour K, Levy J, Belfair N, Lifshitz T, Joshua S, Narkis G, Elbedour K, Myllyharju J, Birk OS. High myopia caused by a mutation in LEPREL1, encoding prolyl 3-hydroxylase 2. Am J Hum Genet 2011; 89:438-45. [PMID: 21885030].

193. Shi Y, Li Y, Zhang D, Zhang H, Li Y, Lu F, Liu X, He F, Gong B, Cai L, Li R, Liao S, Ma S, Lin H, Cheng J, Zheng H, Shan Y, Chen B, Hu J, Jin X, Zhao P, Chen Y, Zhang Y, Lin Y, Li X, Fan Y, Yang H, Wang J, Yang Z. Exome sequencing identifies ZNF644 mutations in high myopia. PLoS Genet 2011; 7:e1002084-[PMID: 21695231].

194. Tran-Viet KN, Powell C, Barathi VA, Klemm T, Maurer-Stroh S, Limviphuvadh V, Soler V, Ho C, Yanovitch T, Schneider G, Li YJ, Nading E, Metlapally R, Saw SM, Goh L, Rozen S, Young TL. Mutations in SCO2 are associated with autosomal-dominant high-grade myopia. Am J Hum Genet 2013; 92:820-6. [PMID: 23643385].

195. Tran-Viet KN, St Germain E, Soler V, Powell C, Lim SH, Klemm T, Saw SM, Young TL. Study of a US cohort supports the role of ZNF644 and high-grade myopia susceptibility. Mol Vis 2012; 18:937-44. [PMID: 22539872].

196. Xiang X, Wang T, Tong P, Li Y, Guo H, Wan A, Xia L, Liu Y, Li Y, Tian Q, Shen L, Cai X, Tian L, Jin X, Xia K, Hu Z. New ZNF644 mutations identified in patients with high myopia. Mol Vis 2014; 20:939-46. [PMID: 24991186].

197. Xiao X, Li S, Jia X, Guo X, Zhang Q. X-linked heterozygous mutations in ARR3 cause female-limited early onset high myopia. Mol Vis 2016; 22:1257-66. [PMID: 27829781].

198. Guo H, Tong P, Liu Y, Xia L, Wang T, Tian Q, Li Y, Hu Y, Zheng Y, Jin X, Li Y, Xiong W, Tang B, Feng Y, Li J, Pan Q, Hu Z, Xia K. Mutations of P4HA2 encoding prolyl 4-hydroxylase 2 are associated with nonsyndromic high myopia. Genet Med 2015; 17:300-6. [PMID: 25741866].

199. Jin ZB, Wu J, Huang XF, Feng CY, Cai XB, Mao JY, Xiang L, Wu KC, Xiao X, Kloss BA, Li Z, Liu Z, Huang S, Shen M, Cheng FF, Cheng XW, Zheng ZL, Chen X, Zhuang W, Zhang Q, Young TL, Xie T, Lu F, Qu J. Trio-based exome sequencing arrests de novo mutations in early-onset high myopia. Proc Natl Acad Sci USA 2017; 114:4219-24. [PMID: 28373534].

200. Willnow TE, Armstrong SA, Hammer RE, Herz J. Functional expression of low density lipoprotein receptor-related protein is controlled by receptor-associated protein in vivo. Proc Natl Acad Sci USA 1995; 92:4537-41. [PMID: 7538675].

201. Boucher P, Li WP, Matz RL, Takayama Y, Auwerx J, Anderson RG, Herz J. LRP1 functions as an atheroprotective integrator of TGFbeta and PDFG signals in the vascular wall: implications for Marfan syndrome. PLoS One 2007; 2:e448-[PMID: 17505534].

202. Sun W, Huang L, Xu Y, Xiao X, Li S, Jia X, Gao B, Wang P, Guo X, Zhang Q. Exome Sequencing on 298 Probands With Early-Onset High Myopia: Approximately One-Fourth Show Potential Pathogenic Mutations in RetNet Genes. Invest Ophthalmol Vis Sci 2015; 56:8365-72. [PMID: 26747767].

203. Zhang Y, Liu Y, Wildsoet CF. Bidirectional, optical sign-dependent regulation of BMP2 gene expression in chick retinal pigment epithelium. Invest Ophthalmol Vis Sci 2012; 53:6072-80. [PMID: 22879416].

204. Guo L, Frost MR, He L, Siegwart JT Jr, Norton TT. Gene expression signatures in tree shrew sclera in response to three myopiagenic conditions. Invest Ophthalmol Vis Sci 2013; 54:6806-19. [PMID: 24045991].

205. He L, Frost MR, Siegwart JT Jr, Norton TT. Gene expression signatures in tree shrew choroid in response to three myopiagenic conditions. Vision Res 2014; 102:52-63. [PMID: 25072854].

206. He L, Frost MR, Siegwart JT Jr, Norton TT. Gene expression signatures in tree shrew choroid during lens-induced myopia and recovery. Exp Eye Res 2014; 123:56-71. [PMID: 24742494].

207. Li H, Cui D, Zhao F, Huo L, Hu J, Zeng J. BMP-2 Is Involved in Scleral Remodeling in Myopia Development. PLoS One 2015; 10:e0125219-[PMID: 25965995].

208. McBrien NA. Regulation of scleral metabolism in myopia and the role of transforming growth factor-beta. Exp Eye Res 2013; 114:128-40. [PMID: 23399866].

209. Rymer J, Wildsoet CF. The role of the retinal pigment epithelium in eye growth regulation and myopia: a review. Vis Neurosci 2005; 22:251-61. [PMID: 16079001].

210. Summers JA. The choroid as a sclera growth regulator. Exp Eye Res 2013; 114:120-7. [PMID: 23528534].

211. Zhang Y, Liu Y, Ho C, Wildsoet CF. Effects of imposed defocus of opposite sign on temporal gene expression patterns of BMP4 and BMP7 in chick RPE. Exp Eye Res 2013; 109:98-106. [PMID: 23428741].

212. Zhang Y, Wildsoet CF. RPE and Choroid Mechanisms Underlying Ocular Growth and Myopia. Prog Mol Biol Transl Sci 2015; 134:221-40. [PMID: 26310157].

213. Zhang Y, Raychaudhuri S, Wildsoet CF. Imposed Optical Defocus Induces Isoform-Specific Up-Regulation of TGFbeta Gene Expression in Chick Retinal Pigment Epithelium and Choroid but Not Neural Retina. PLoS One 2016; 11:e0155356-[PMID: 27214233].

214. McBrien NA, Gentle A. Role of the sclera in the development and pathological complications of myopia. Prog Retin Eye Res 2003; 22:307-38. [PMID: 12852489].

215. Gentle A, Liu Y, Martin JE, Conti GL, McBrien NA. Collagen gene expression and the altered accumulation of scleral collagen during the development of high myopia. J Biol Chem 2003; 278:16587-94. [PMID: 12606541].

216. Guo L, Frost MR, Siegwart JT Jr, Norton TT. Scleral gene expression during recovery from myopia compared with expression during myopia development in tree shrew. Mol Vis 2014; 20:1643-59. [PMID: 25540576].

217. Jobling AI, Nguyen M, Gentle A, McBrien NA. Isoform-specific changes in scleral transforming growth factor-beta expression and the regulation of collagen synthesis during myopia progression. J Biol Chem 2004; 279:18121-6. [PMID: 14752095].

218. Rada JA, Perry CA, Slover ML, Achen VR. Gelatinase A and TIMP-2 expression in the fibrous sclera of myopic and recovering chick eyes. Invest Ophthalmol Vis Sci 1999; 40:3091-9. [PMID: 10586929].

219. Schippert R, Brand C, Schaeffel F, Feldkaemper MP. Changes in scleral MMP-2, TIMP-2 and TGFbeta-2 mRNA expression after imposed myopic and hyperopic defocus in chickens. Exp Eye Res 2006; 82:710-9. [PMID: 16289164].

220. Siegwart JT Jr, Norton TT. Steady state mRNA levels in tree shrew sclera with form-deprivation myopia and during

recovery. Invest Ophthalmol Vis Sci 2001; 42:1153-9. [PMID: 11328721].

221. Siegwart JT Jr, Norton TT. The time course of changes in mRNA levels in tree shrew sclera during induced myopia and recovery. Invest Ophthalmol Vis Sci 2002; 43:2067-75. [PMID: 12091398].

222. Wang Q, Zhao G, Xing S, Zhang L, Yang X. Role of bone morphogenetic proteins in form-deprivation myopia sclera. Mol Vis 2011; 17:647-57. [PMID: 21403850].

223. Zhou X, Ji F, An J, Zhao F, Shi F, Huang F, Li Y, Jiao S, Yan D, Chen X, Chen J, Qu J. Experimental murine myopia induces collagen type Ialpha1 (COL1A1) DNA methylation and altered COL1A1 messenger RNA expression in sclera. Mol Vis 2012; 18:1312-24. [PMID: 22690110].

224. Jobling AI, Wan R, Gentle A, Bui BV, McBrien NA. Retinal and choroidal TGF-beta in the tree shrew model of myopia: isoform expression, activation and effects on function. Exp Eye Res 2009; 88:458-66. [PMID: 19046968].

225. Mathis U, Schaeffel F. Transforming growth factor-beta in the chicken fundal layers: an immunohistochemical study. Exp Eye Res 2010; 90:780-90. [PMID: 20350541].

226. Akamatsu S, Fujii S, Escano MF, Ishibashi K, Sekiya Y, Yamamoto M. Altered expression of genes in experimentally induced myopic chick eyes. Jpn J Ophthalmol 2001; 45:137-43. [PMID: 11313044].

227. Ashby RS, Megaw PL, Morgan IG. Changes in the expression of Pax6 RNA transcripts in the retina during periods of altered ocular growth in chickens. Exp Eye Res 2009; 89:392-7. [PMID: 19379739].

228. Bhat SP, Rayner SA, Chau SC, Ariyasu RG. Pax-6 expression in posthatch chick retina during and recovery from form-deprivation myopia. Dev Neurosci 2004; 26:328-35. [PMID: 15855761].

229. Collery RF, Veth KN, Dubis AM, Carroll J, Link BA. Rapid, accurate, and non-invasive measurement of zebrafish axial length and other eye dimensions using SD-OCT allows longitudinal analysis of myopia and emmetropization. PLoS One 2014; 9:e110699-[PMID: 25334040].

230. Escano MF, Fujii S, Sekiya Y, Yamamoto M, Negi A. Expression of Sonic hedgehog and retinal opsin genes in experimentally-induced myopic chick eyes. Exp Eye Res 2000; 71:459-67. [PMID: 11040081].

231. Feldkaemper MP, Burkhardt E, Schaeffel F. Localization and regulation of glucagon receptors in the chick eye and preproglucagon and glucagon receptor expression in the mouse eye. Exp Eye Res 2004; 79:321-9. [PMID: 15336494].

232. Feldkaemper MP, Wang HY, Schaeffel F. Changes in retinal and choroidal gene expression during development of refractive errors in chicks. Invest Ophthalmol Vis Sci 2000; 41:1623-8. [PMID: 10845578].

233. Fujii S, Honda S, Sekiya Y, Yamasaki M, Yamamoto M, Saijoh K. Differential expression of nitric oxide synthase isoforms in form-deprived chick eyes. Curr Eye Res 1998; 17:586-93. [PMID: 9663848].

234. Huang F, Yan T, Shi F, An J, Xie R, Zheng F, Li Y, Chen J, Qu J, Zhou X. Activation of dopamine D2 receptor is critical for the development of form-deprivation myopia in the C57BL/6 mouse. Invest Ophthalmol Vis Sci 2014; 55:5537-44. [PMID: 25097246].

235. Hudson DM, Joeng KS, Werther R, Rajagopal A, Weis M, Lee BH, Eyre DR. Post-translationally abnormal collagens of prolyl 3-hydroxylase-2 null mice offer a pathobiological mechanism for the high myopia linked to human LEPREL1 mutations. J Biol Chem 2015; 290:8613-22. [PMID: 25645914].

236. Liu Q, Wu J, Wang X, Zeng J. Changes in muscarinic acetylcholine receptor expression in form deprivation myopia in guinea pigs. Mol Vis 2007; 13:1234-44. [PMID: 17679952].

237. Ma M, Zhang Z, Du E, Zheng W, Gu Q, Xu X, Ke B. Wnt signaling in form deprivation myopia of the mice retina. PLoS One 2014; 9:e91086-[PMID: 24755605].

238. McBrien NA, Lawlor P, Gentle A. Scleral remodeling during the development of and recovery from axial myopia in the tree shrew. Invest Ophthalmol Vis Sci 2000; 41:3713-9. [PMID: 11053267].

239. Morgan I, Kucharski R, Krongkaew N, Firth SI, Megaw P, Maleszka R. Screening for differential gene expression during the development of form-deprivation myopia in the chicken. Optom Vis Sci 2004; 81:148-55. [PMID: 15127934].

240. Qian YS, Chu RY, Hu M, Hoffman MR. Sonic hedgehog expression and its role in form-deprivation myopia in mice. Curr Eye Res 2009; 34:623-35. [PMID: 19899989].

241. Schippert R, Burkhardt E, Feldkaemper M, Schaeffel F. Relative axial myopia in Egr-1 (ZENK) knockout mice. Invest Ophthalmol Vis Sci 2007; 48:11-7. [PMID: 17197510].

242. Seko Y, Shimokawa H, Tokoro T. In vivo and in vitro association of retinoic acid with form-deprivation myopia in the chick. Exp Eye Res 1996; 63:443-52. [PMID: 8944551].

243. Siegwart JT Jr, Norton TT. Selective regulation of MMP and TIMP mRNA levels in tree shrew sclera during minus lens compensation and recovery. Invest Ophthalmol Vis Sci 2005; 46:3484-92. [PMID: 16186323].

244. Veth KN, Willer JR, Collery RF, Gray MP, Willer GB, Wagner DS, Mullins MC, Udvadia AJ, Smith RS, John SW, Gregg RG, Link BA. Mutations in zebrafish lrp2 result in adult-onset ocular pathogenesis that models myopia and other risk factors for glaucoma. PLoS Genet 2011; 7:e1001310-[PMID: 21379331].

245. Wang S, Liu S, Mao J, Wen D. Effect of retinoic acid on the tight junctions of the retinal pigment epithelium-choroid complex of guinea pigs with lens-induced myopia in vivo. Int J Mol Med 2014; 33:825-32. [PMID: 24535401].

246. Zhong XW, Ge J, Deng WG, Chen XL, Huang J. Expression of pax-6 in rhesus monkey of optical defocus induced myopia and form deprivation myopia. Chin Med J (Engl) 2004; 117:722-6. [PMID: 15161541].

247. Aberfeld DC, Hinterbuchner LP, Schneider M. Myotonia, dwarfism, diffuse bone disease and unusual ocular and facial

abnormalities (a new syndrome). Brain 1965; 88:313-22. [PMID: 4953364].

248. Ahmad N, Richards AJ, Murfett HC, Shapiro L, Scott JD, Yates JR, Norton J, Snead MP. Prevalence of mitral valve prolapse in Stickler syndrome. Am J Med Genet A 2003; 116a:234-7. [PMID: 12503098].

249. Aldahmesh MA, Mohamed JY, Alkuraya HS, Verma IC, Puri RD, Alaiya AA, Rizzo WB, Alkuraya FS. Recessive mutations in ELOVL4 cause ichthyosis, intellectual disability, and spastic quadriplegia. Am J Hum Genet 2011; 89:745-50. [PMID: 22100072].

250. Aldinger KA, Mosca SJ, Tetreault M, Dempsey JC, Ishak GE, Hartley T, Phelps IG, Lamont RE, O'Day DR, Basel D, Gripp KW, Baker L, Stephan MJ, Bernier FP, Boycott KM, Majewski J, Parboosingh JS, Innes AM, Doherty D. Mutations in LAMA1 cause cerebellar dysplasia and cysts with and without retinal dystrophy. Am J Hum Genet 2014; 95:227-34. [PMID: 25105227].

251. Alfaiz AA, Micale L, Mandriani B, Augello B, Pellico MT, Chrast J, Xenarios I, Zelante L, Merla G, Reymond A. TBC1D7 mutations are associated with intellectual disability, macrocrania, patellar dislocation, and celiac disease. Hum Mutat 2014; 35:447-51. [PMID: 24515783].

252. Alzahrani F, Al Hazzaa SA, Tayeb H, Alkuraya FS. LOXL3, encoding lysyl oxidase-like 3, is mutated in a family with autosomal recessive Stickler syndrome. Hum Genet 2015; 134:451-3. [PMID: 25663169].

253. Arno G, Hull S, Robson AG, Holder GE, Cheetham ME, Webster AR, Plagnol V, Moore AT. Lack of Interphotoreceptor Retinoid Binding Protein Caused by Homozygous Mutation of RBP3 Is Associated With High Myopia and Retinal Dystrophy. Invest Ophthalmol Vis Sci 2015; 56:2358-65. [PMID: 25766589].

254. Babcock D, Gasner C, Francke U, Maslen C. A single mutation that results in an Asp to His substitution and partial exon skipping in a family with congenital contractural arachnodactyly. Hum Genet 1998; 103:22-8. [PMID: 9737771].

255. Bach C, Maroteaux P, Schaeffer P, Bitan A, Crumiere C. Arch Fr Pediatr 1967; 24:23-33. Congenital spondylo-epiphysial dysplasia with multiple abnormalities[PMID: 6031460].

256. Bahuau M, Houdayer C, Tredano M, Soupre V, Couderc R, Vazquez MP. FOXC2 truncating mutation in distichiasis, lymphedema, and cleft palate. Clin Genet 2002; 62:470-3. [PMID: 12485195].

257. Baker S, Booth C, Fillman C, Shapiro M, Blair MP, Hyland JC, Ala-Kokko L. A loss of function mutation in the COL9A2 gene causes autosomal recessive Stickler syndrome. Am J Med Genet A 2011; 155a:1668-72. [PMID: 21671392].

258. Bakrania P, Efthymiou M, Klein JC, Salt A, Bunyan DJ, Wyatt A, Ponting CP, Martin A, Williams S, Lindley V, Gilmore J, Restori M, Robson AG, Neveu MM, Holder GE, Collin JR, Robinson DO, Farndon P, Johansen-Berg H, Gerrelli D, Ragge NK. Mutations in BMP4 cause eye, brain, and digit developmental anomalies: overlap between the BMP4 and hedgehog signaling pathways. Am J Hum Genet 2008; 82:304-19. [PMID: 18252212].

259. Ballo R, Beighton PH, Ramesar RS. Stickler-like syndrome due to a dominant negative mutation in the COL2A1 gene. Am J Med Genet 1998; 80:6-11. [PMID: 9800905].

260. Bandah-Rozenfeld D, Collin RW, Banin E, van den Born LI, Coene KL, Siemiatkowska AM, Zelinger L, Khan MI, Lefeber DJ, Erdinest I, Testa F, Simonelli F, Voesenek K, Blokland EA, Strom TM, Klaver CC, Qamar R, Banfi S, Cremers FP, Sharon D, den Hollander AI. Mutations in IMPG2, encoding interphotoreceptor matrix proteoglycan 2, cause autosomal-recessive retinitis pigmentosa. Am J Hum Genet 2010; 87:199-208. [PMID: 20673862].

261. Barker DF, Hostikka SL, Zhou J, Chow LT, Oliphant AR, Gerken SC, Gregory MC, Skolnick MH, Atkin CL, Tryggvason K. Identification of mutations in the COL4A5 collagen gene in Alport syndrome. Science 1990; 248:1224-7. [PMID: 2349482].

262. Barnes CS, Alexander KR, Fishman GA. A distinctive form of congenital stationary night blindness with cone ON-pathway dysfunction. Ophthalmology 2002; 109:575-83. [PMID: 11874764].

263. Bartsch O, Labonte J, Albrecht B, Wieczorek D, Lechno S, Zechner U, Haaf T. Two patients with EP300 mutations and facial dysmorphism different from the classic Rubinstein-Taybi syndrome. Am J Med Genet A 2010; 152a:181-4. [PMID: 20014264].

264. Baumann M, Giunta C, Krabichler B, Ruschendorf F, Zoppi N, Colombi M, Bittner RE, Quijano-Roy S, Muntoni F, Cirak S, Schreiber G, Zou Y, Hu Y, Romero NB, Carlier RY, Amberger A, Deutschmann A, Straub V, Rohrbach M, Steinmann B, Rostasy K, Karall D, Bonnemann CG, Zschocke J, Fauth C. Mutations in FKBP14 cause a variant of Ehlers-Danlos syndrome with progressive kyphoscoliosis, myopathy, and hearing loss. Am J Hum Genet 2012; 90:201-16. [PMID: 22265013].

265. Bech-Hansen NT, Naylor MJ, Maybaum TA, Sparkes RL, Koop B, Birch DG, Bergen AA, Prinsen CF, Polomeno RC, Gal A, Drack AV, Musarella MA, Jacobson SG, Young RS, Weleber RG. Mutations in NYX, encoding the leucine-rich proteoglycan nyctalopin, cause X-linked complete congenital stationary night blindness. Nat Genet 2000; 26:319-23. [PMID: 11062471].

266. Beighton P, Goldberg L, Hof JO. Dominant inheritance of multiple epiphyseal dysplasia, myopia and deafness. Clin Genet 1978; 14:173-7. [PMID: 699354].

267. Beltran-Valero de Bernabe D, Voit T, Longman C, Steinbrecher A, Straub V, Yuva Y, Herrmann R, Sperner J, Korenke C, Diesen C, Dobyns WB, Brunner HG, van Bokhoven H, Brockington M, Muntoni F. Mutations in the FKRP gene can cause muscle-eye-brain disease and Walker-Warburg syndrome. J Med Genet 2004; 41:e61-[PMID: 15121789].

268. Bergen AA, ten Brink JB, Riemslag F, Schuurman EJ, Tijmes N. Localization of a novel X-linked congenital stationary night blindness locus: close linkage to the RP3 type retinitis

pigmentosa gene region. Hum Mol Genet 1995; 4:931-5. [PMID: 7633454].

269. Bergia B, Sybers HD, Butler IJ. Familial lethal cardiomyopathy with mental retardation and scapuloperoneal muscular dystrophy. J Neurol Neurosurg Psychiatry 1986; 49:1423-6. [PMID: 3806120].

270. Bertelsen TI. Dysgenesis mesodermalis corneae et sclerae. Rupture of both corneae in a patient with blue sclerae. Acta Ophthalmol (Copenh) 1968; 46:486-91. [PMID: 5755738].

271. Bertoli-Avella AM, Gillis E, Morisaki H, Verhagen JM, de Graaf BM, van de Beek G, Gallo E, Kruithof BP, Venselaar H, Myers LA, Laga S, Doyle AJ, Oswald G, van Cappellen GW, Yamanaka I, van der Helm RM, Beverloo B, de Klein A, Pardo L, Lammens M, Evers C, Devriendt K, Dumoulein M, Timmermans J, Bruggenwirth HT, Verheijen F, Rodrigus I, Baynam G, Kempers M, Saenen J, Van Craenenbroeck EM, Minatoya K, Matsukawa R, Tsukube T, Kubo N, Hofstra R, Goumans MJ, Bekkers JA, Roos-Hesselink JW, van de Laar IM, Dietz HC, Van Laer L, Morisaki T, Wessels MW, Loeys BL. Mutations in a TGF-beta ligand, TGFB3, cause syndromic aortic aneurysms and dissections. J Am Coll Cardiol 2015; 65:1324-36. [PMID: 25835445].

272. Beryozkin A, Zelinger L, Bandah-Rozenfeld D, Shevach E, Harel A, Storm T, Sagi M, Eli D, Merin S, Banin E, Sharon D. Identification of mutations causing inherited retinal degenerations in the israeli and palestinian populations using homozygosity mapping. Invest Ophthalmol Vis Sci 2014; 55:1149-60. [PMID: 24474277].

273. Brody JA, Hussels I, Brink E, Torres J. Hereditary blindness among Pingelapese people of Eastern Caroline Islands. Lancet 1970; 1:1253-7. [PMID: 4192495].

274. Brunner HG, van Beersum SE, Warman ML, Olsen BR, Ropers HH, Mariman EC. A Stickler syndrome gene is linked to chromosome 6 near the COL11A2 gene. Hum Mol Genet 1994; 3:1561-4. [PMID: 7833911].

275. Burkitt Wright EM, Spencer HL, Daly SB, Manson FD, Zeef LA, Urquhart J, Zoppi N, Bonshek R, Tosounidis I, Mohan M, Madden C, Dodds A, Chandler KE, Banka S, Au L, Clayton-Smith J, Khan N, Biesecker LG, Wilson M, Rohrbach M, Colombi M, Giunta C, Black GC. Mutations in PRDM5 in brittle cornea syndrome identify a pathway regulating extracellular matrix development and maintenance. Am J Hum Genet 2011; 88:767-77. [PMID: 21664999].

276. Campeau PM, Kasperaviciute D, Lu JT, Burrage LC, Kim C, Hori M, Powell BR, Stewart F, Felix TM, van den Ende J, Wisniewska M, Kayserili H, Rump P, Nampoothiri S, Aftimos S, Mey A, Nair LD, Begleiter ML, De Bie I, Meenakshi G, Murray ML, Repetto GM, Golabi M, Blair E, Male A, Giuliano F, Kariminejad A, Newman WG, Bhaskar SS, Dickerson JE, Kerr B, Banka S, Giltay JC, Wieczorek D, Tostevin A, Wiszniewska J, Cheung SW, Hennekam RC, Gibbs RA, Lee BH, Sisodiya SM. The genetic basis of DOORS syndrome: an exome-sequencing study. Lancet Neurol 2014; 13:44-58. [PMID: 24291220].

277. Chassine T, Bocquet B, Daien V, Avila-Fernandez A, Ayuso C, Collin RW, Corton M, Hejtmancik JF, van den Born LI, Klevering BJ, Riazuddin SA, Sendon N, Lacroux A, Meunier I, Hamel CP. Autosomal recessive retinitis pigmentosa with RP1 mutations is associated with myopia. Br J Ophthalmol 2015; 99:1360-5. [PMID: 25883087].

278. Christensen AE, Knappskog PM, Midtbo M, Gjesdal CG, Mengel-From J, Morling N, Rodahl E, Boman H. Brittle cornea syndrome associated with a missense mutation in the zinc-finger 469 gene. Invest Ophthalmol Vis Sci 2010; 51:47-52. [PMID: 19661234].

279. Clement E, Mercuri E, Godfrey C, Smith J, Robb S, Kinali M, Straub V, Bushby K, Manzur A, Talim B, Cowan F, Quinlivan R, Klein A, Longman C, McWilliam R, Topaloglu H, Mein R, Abbs S, North K, Barkovich AJ, Rutherford M, Muntoni F. Brain involvement in muscular dystrophies with defective dystroglycan glycosylation. Ann Neurol 2008; 64:573-82. [PMID: 19067344].

280. Clement EM, Godfrey C, Tan J, Brockington M, Torelli S, Feng L, Brown SC, Jimenez-Mallebrera C, Sewry CA, Longman C, Mein R, Abbs S, Vajsar J, Schachter H, Muntoni F. Mild POMGnT1 mutations underlie a novel limb-girdle muscular dystrophy variant. Arch Neurol 2008; 65:137-41. [PMID: 18195152].

281. Coupry I, Sibon I, Mortemousque B, Rouanet F, Mine M, Goizet C. Ophthalmological features associated with COL4A1 mutations. Arch Ophthalmol 2010; 128:483-9. [PMID: 20385946].

282. Dahl N, Lagerstrom M, Erikson A, Pettersson U. Gaucher disease type III (Norrbottnian type) is caused by a single mutation in exon 10 of the glucocerebrosidase gene. Am J Hum Genet 1990; 47:275-8. [PMID: 2378352].

283. de Ligt J, Willemsen MH, van Bon BW, Kleefstra T, Yntema HG, Kroes T, Vulto-van Silfhout AT, Koolen DA, de Vries P, Gilissen C, del Rosario M, Hoischen A, Scheffer H, de Vries BB, Brunner HG, Veltman JA, Vissers LE. Diagnostic exome sequencing in persons with severe intellectual disability. N Engl J Med 2012; 367:1921-9. [PMID: 23033978].

284. Demirci FY, Rigatti BW, Wen G, Radak AL, Mah TS, Baic CL, Traboulsi EI, Alitalo T, Ramser J, Gorin MB. X-linked cone-rod dystrophy (locus COD1): identification of mutations in RPGR exon ORF15. Am J Hum Genet 2002; 70:1049-53. [PMID: 11857109].

285. den Hollander AI, ten Brink JB, de Kok YJ, van Soest S, van den Born LI, van Driel MA, van de Pol DJ, Payne AM, Bhattacharya SS, Kellner U, Hoyng CB, Westerveld A, Brunner HG, Bleeker-Wagemakers EM, Deutman AF, Heckenlively JR, Cremers FP, Bergen AA. Mutations in a human homologue of Drosophila crumbs cause retinitis pigmentosa (RP12). Nat Genet 1999; 23:217-21. [PMID: 10508521].

286. DeSanto C, D'Aco K, Araujo GC, Shannon N, Vernon H, Rahrig A, Monaghan KG, Niu Z, Vitazka P, Dodd J, Tang S, Manwaring L, Martir-Negron A, Schnur RE, Juusola J, Schroeder A, Pan V, Helbig KL, Friedman B, Shinawi M. WAC loss-of-function mutations cause a recognisable syndrome characterised by dysmorphic features, developmental delay and hypotonia and recapitulate 10p11.23

microdeletion syndrome. J Med Genet 2015; 52:754-61. [PMID: 26264232].

287. Devi RR, Vijayalakshmi P. Novel mutations in GJA8 associated with autosomal dominant congenital cataract and microcornea. Mol Vis 2006; 12:190-5. [PMID: 16604058].

288. Donnai D, Barrow M. Diaphragmatic hernia, exomphalos, absent corpus callosum, hypertelorism, myopia, and sensorineural deafness: a newly recognized autosomal recessive disorder? Am J Med Genet 1993; 47:679-82. [PMID: 8266995].

289. Douglas J, Cilliers D, Coleman K, Tatton-Brown K, Barker K, Bernhard B, Burn J, Huson S, Josifova D, Lacombe D, Malik M, Mansour S, Reid E, Cormier-Daire V, Cole T, Rahman N. Mutations in RNF135, a gene within the NF1 microdeletion region, cause phenotypic abnormalities including overgrowth. Nat Genet 2007; 39:963-5. [PMID: 17632510].

290. Doyle AJ, Doyle JJ, Bessling SL, Maragh S, Lindsay ME, Schepers D, Gillis E, Mortier G, Homfray T, Sauls K, Norris RA, Huso ND, Leahy D, Mohr DW, Caulfield MJ, Scott AF, Destree A, Hennekam RC, Arn PH, Curry CJ, Van Laer L, McCallion AS, Loeys BL, Dietz HC. Mutations in the TGF-beta repressor SKI cause Shprintzen-Goldberg syndrome with aortic aneurysm. Nat Genet 2012; 44:1249-54. [PMID: 23023332].

291. Dryja TP, McGee TL, Berson EL, Fishman GA, Sandberg MA, Alexander KR, Derlacki DJ, Rajagopalan AS. Night blindness and abnormal cone electroretinogram ON responses in patients with mutations in the GRM6 gene encoding mGluR6. Proc Natl Acad Sci USA 2005; 102:4884-9. [PMID: 15781871].

292. Erikson A, Wahlberg I. Gaucher disease–Norrbottnian type. Ocular abnormalities. Acta Ophthalmol (Copenh) 1985; 63:221-5. [PMID: 4003050].

293. Faivre L, Gorlin RJ, Wirtz MK, Godfrey M, Dagoneau N, Samples JR, Le Merrer M, Collod-Beroud G, Boileau C, Munnich A, Cormier-Daire V. In frame fibrillin-1 gene deletion in autosomal dominant Weill-Marchesani syndrome. J Med Genet 2003; 40:34-6. [PMID: 12525539].

294. Faletra F, D'Adamo AP, Bruno I, Athanasakis E, Biskup S, Esposito L, Gasparini P. Autosomal recessive Stickler syndrome due to a loss of function mutation in the COL9A3 gene. Am J Med Genet A 2014; 164a:42-7. [PMID: 24273071].

295. Forsius H, Eriksson AW. Klin Monatsbl Augenheilkd 1964; 144:447-57. A NEW EYE SYNDROME WITH X–CHROMOSOMAL TRANSMISSION. A FAMILY CLAN WITH FUNDUS ALBINISM, FOVEA HYPOPLASIA, NYSTAGMUS, MYOPIA, ASTIGMATISM AND DYSCHROMATOPSIA[PMID: 14230113].

296. Gardner JC, Michaelides M, Holder GE, Kanuga N, Webb TR, Mollon JD, Moore AT, Hardcastle AJ. Blue cone monochromacy: causative mutations and associated phenotypes. Mol Vis 2009; 15:876-84. [PMID: 19421413].

297. Geis T, Marquard K, Rodl T, Reihle C, Schirmer S, von Kalle T, Bornemann A, Hehr U, Blankenburg M. Homozygous dystroglycan mutation associated with a novel muscle-eye-brain disease-like phenotype with multicystic leucodystrophy. Neurogenetics 2013; 14:205-13. [PMID: 24052401].

298. Girirajan S, Elsas LJ 2nd, Devriendt K, Elsea SH. RAI1 variations in Smith-Magenis syndrome patients without 17p11.2 deletions. J Med Genet 2005; 42:820-8. [PMID: 15788730].

299. Godfrey C, Clement E, Mein R, Brockington M, Smith J, Talim B, Straub V, Robb S, Quinlivan R, Feng L, Jimenez-Mallebrera C, Mercuri E, Manzur AY, Kinali M, Torelli S, Brown SC, Sewry CA, Bushby K, Topaloglu H, North K, Abbs S, Muntoni F. Refining genotype phenotype correlations in muscular dystrophies with defective glycosylation of dystroglycan. Brain 2007; 130:2725-35. [PMID: 17878207].

300. Goldberg MF. Clinical manifestations of ectopia lentis et pupillae in 16 patients. Ophthalmology 1988; 95:1080-7. [PMID: 3266004].

301. Goyal S, Jager M, Robinson PN, Vanita V. Confirmation of TTC8 as a disease gene for nonsyndromic autosomal recessive retinitis pigmentosa (RP51). Clin Genet 2015; •••:1111- [PMID: 26195043].

302. Graul-Neumann LM, Kienitz T, Robinson PN, Baasanjav S, Karow B, Gillessen-Kaesbach G, Fahsold R, Schmidt H, Hoffmann K, Passarge E. Marfan syndrome with neonatal progeroid syndrome-like lipodystrophy associated with a novel frameshift mutation at the 3′ terminus of the FBN1-gene. Am J Med Genet A 2010; 152a:2749-55. [PMID: 20979188].

303. Gregory-Evans K, Kelsell RE, Gregory-Evans CY, Downes SM, Fitzke FW, Holder GE, Simunovic M, Mollon JD, Taylor R, Hunt DM, Bird AC, Moore AT. Autosomal dominant cone-rod retinal dystrophy (CORD6) from heterozygous mutation of GUCY2D, which encodes retinal guanylate cyclase. Ophthalmology 2000; 107:55-61. [PMID: 10647719].

304. Griffith AJ, Sprunger LK, Sirko-Osadsa DA, Tiller GE, Meisler MH, Warman ML. Marshall syndrome associated with a splicing defect at the COL11A1 locus. Am J Hum Genet 1998; 62:816-23. [PMID: 9529347].

305. Haim M, Fledelius HC. Skarsholm. X-linked myopia in Danish family. Acta Ophthalmol (Copenh) 1988; 66:450-6. [PMID: 3264103].

306. Haji-Seyed-Javadi R, Jelodari-Mamaghani S, Paylakhi SH, Yazdani S, Nilforushan N, Fan JB, Klotzle B, Mahmoudi MJ, Ebrahimian MJ, Chelich N, Taghiabadi E, Kamyab K, Boileau C, Paisan-Ruiz C, Ronaghi M, Elahi E. LTBP2 mutations cause Weill-Marchesani and Weill-Marchesani-like syndrome and affect disruptions in the extracellular matrix. Hum Mutat 2012; 33:1182-7. [PMID: 22539340].

307. Hamamy HA, Teebi AS, Oudjhane K, Shegem NN, Ajlouni KM. Severe hypertelorism, midface prominence, prominent/simple ears, severe myopia, borderline intelligence, and bone fragility in two brothers: new syndrome? Am J Med Genet A 2007; 143a:229-34. [PMID: 17230486].

308. Harel T, Yoon WH, Garone C, Gu S, Coban-Akdemir Z, Eldomery MK, Posey JE, Jhangiani SN, Rosenfeld JA, Cho MT, Fox S, Withers M, Brooks SM, Chiang T, Duraine L,

Erdin S, Yuan B, Shao Y, Moussallem E, Lamperti C, Donati MA, Smith JD, McLaughlin HM, Eng CM, Walkiewicz M, Xia F, Pippucci T, Magini P, Seri M, Zeviani M, Hirano M, Hunter JV, Srour M, Zanigni S, Lewis RA, Muzny DM, Lotze TE, Boerwinkle E, Gibbs RA, Hickey SE, Graham BH, Yang Y, Buhas D, Martin DM, Potocki L, Graziano C, Bellen HJ, Lupski JR. Recurrent De Novo and Biallelic Variation of ATAD3A, Encoding a Mitochondrial Membrane Protein, Results in Distinct Neurological Syndromes. Am J Hum Genet 2016; 99:831-45. [PMID: 27640307].

309. Hasselbacher K, Wiggins RC, Matejas V, Hinkes BG, Mucha B, Hoskins BE, Ozaltin F, Nurnberg G, Becker C, Hangan D, Pohl M, Kuwertz-Broking E, Griebel M, Schumacher V, Royer-Pokora B, Bakkaloglu A, Nurnberg P, Zenker M, Hildebrandt F. Recessive missense mutations in LAMB2 expand the clinical spectrum of LAMB2-associated disorders. Kidney Int 2006; 70:1008-12. [PMID: 16912710].

310. Hauke J, Schild A, Neugebauer A, Lappa A, Fricke J, Fauser S, Rosler S, Pannes A, Zarrinnam D, Altmuller J, Motameny S, Nurnberg G, Nurnberg P, Hahnen E, Beck BB. A novel large in-frame deletion within the CACNA1F gene associates with a cone-rod dystrophy 3-like phenotype. PLoS One 2013; 8:e76414-[PMID: 24124559].

311. Hoischen A, van Bon BW, Rodriguez-Santiago B, Gilissen C, Vissers LE, de Vries P, Janssen I, van Lier B, Hastings R, Smithson SF, Newbury-Ecob R, Kjaergaard S, Goodship J, McGowan R, Bartholdi D, Rauch A, Peippo M, Cobben JM, Wieczorek D, Gillessen-Kaesbach G, Veltman JA, Brunner HG, de Vries BB. De novo nonsense mutations in ASXL1 cause Bohring-Opitz syndrome. Nat Genet 2011; 43:729-31. [PMID: 21706002].

312. Hollstein R, Parry DA, Nalbach L, Logan CV, Strom TM, Hartill VL, Carr IM, Korenke GC, Uppal S, Ahmed M, Wieland T, Markham AF, Bennett CP, Gillessen-Kaesbach G, Sheridan EG, Kaiser FJ, Bonthron DT. HACE1 deficiency causes an autosomal recessive neurodevelopmental syndrome. J Med Genet 2015; 52:797-803. [PMID: 26424145].

313. Hoyer J, Ekici AB, Endele S, Popp B, Zweier C, Wiesener A, Wohlleber E, Dufke A, Rossier E, Petsch C, Zweier M, Gohring I, Zink AM, Rappold G, Schrock E, Wieczorek D, Riess O, Engels H, Rauch A, Reis A. Haploinsufficiency of ARID1B, a member of the SWI/SNF-a chromatin-remodeling complex, is a frequent cause of intellectual disability. Am J Hum Genet 2012; 90:565-72. [PMID: 22405089].

314. Iliff BW, Riazuddin SA, Gottsch JD. A single-base substitution in the seed region of miR-184 causes EDICT syndrome. Invest Ophthalmol Vis Sci 2012; 53:348-53. [PMID: 22131394].

315. Jacquinet A, Verloes A, Callewaert B, Coremans C, Coucke P, de Paepe A, Kornak U, Lebrun F, Lombet J, Pierard GE, Robinson PN, Symoens S, Van Maldergem L, Debray FG. Neonatal progeroid variant of Marfan syndrome with congenital lipodystrophy results from mutations at the 3′ end of FBN1 gene. Eur J Med Genet 2014; 57:230-4. [PMID: 24613577].

316. James AW, Miranda SG, Culver K, Hall BD, Golabi M. DOOR syndrome: clinical report, literature review and discussion of natural history. Am J Med Genet A 2007; 143a:2821-31. [PMID: 17994565].

317. Kantarci S, Al-Gazali L, Hill RS, Donnai D, Black GC, Bieth E, Chassaing N, Lacombe D, Devriendt K, Teebi A, Loscertales M, Robson C, Liu T, MacLaughlin DT, Noonan KM, Russell MK, Walsh CA, Donahoe PK, Pober BR. Mutations in LRP2, which encodes the multiligand receptor megalin, cause Donnai-Barrow and facio-oculo-acoustico-renal syndromes. Nat Genet 2007; 39:957-9. [PMID: 17632512].

318. Kaplan J, Bonneau D, Frezal J, Munnich A, Dufier JL. Clinical and genetic heterogeneity in retinitis pigmentosa. Hum Genet 1990; 85:635-42. [PMID: 2227956].

319. Kim HG, Kim HT, Leach NT, Lan F, Ullmann R, Silahtaroglu A, Kurth I, Nowka A, Seong IS, Shen Y, Talkowski ME, Ruderfer D, Lee JH, Glotzbach C, Ha K, Kjaergaard S, Levin AV, Romeike BF, Kleefstra T, Bartsch O, Elsea SH, Jabs EW, MacDonald ME, Harris DJ, Quade BJ, Ropers HH, Shaffer LG, Kutsche K, Layman LC, Tommerup N, Kalscheuer VM, Shi Y, Morton CC, Kim CH, Gusella JF. Translocations disrupting PHF21A in the Potocki-Shaffer-syndrome region are associated with intellectual disability and craniofacial anomalies. Am J Hum Genet 2012; 91:56-72. [PMID: 22770980].

320. Kloeckener-Gruissem B, Bartholdi D, Abdou MT, Zimmermann DR, Berger W. Identification of the genetic defect in the original Wagner syndrome family. Mol Vis 2006; 12:350-5. [PMID: 16636652].

321. Kolehmainen J, Black GC, Saarinen A, Chandler K, Clayton-Smith J, Traskelin AL, Perveen R, Kivitie-Kallio S, Norio R, Warburg M, Fryns JP, de la Chapelle A, Lehesjoki AE. Cohen syndrome is caused by mutations in a novel gene, COH1, encoding a transmembrane protein with a presumed role in vesicle-mediated sorting and intracellular protein transport. Am J Hum Genet 2003; 72:1359-69. [PMID: 12730828].

322. Konrad M, Schaller A, Seelow D, Pandey AV, Waldegger S, Lesslauer A, Vitzthum H, Suzuki Y, Luk JM, Becker C, Schlingmann KP, Schmid M, Rodriguez-Soriano J, Ariceta G, Cano F, Enriquez R, Juppner H, Bakkaloglu SA, Hediger MA, Gallati S, Neuhauss SC, Nurnberg P, Weber S. Mutations in the tight-junction gene claudin 19 (CLDN19) are associated with renal magnesium wasting, renal failure, and severe ocular involvement. Am J Hum Genet 2006; 79:949-57. [PMID: 17033971].

323. Kornak U, Reynders E, Dimopoulou A, van Reeuwijk J, Fischer B, Rajab A, Budde B, Nurnberg P, Foulquier F, Lefeber D, Urban Z, Gruenewald S, Annaert W, Brunner HG, van Bokhoven H, Wevers R, Morava E, Matthijs G, Van Maldergem L, Mundlos S. Impaired glycosylation and cutis laxa caused by mutations in the vesicular H+-ATPase subunit ATP6V0A2. Nat Genet 2008; 40:32-4. [PMID: 18157129].

324. Kumar A, Duvvari MR, Prabhakaran VC, Shetty JS, Murthy GJ, Blanton SH. A homozygous mutation in LTBP2 causes isolated microspherophakia. Hum Genet 2010; 128:365-71. [PMID: 20617341].

325. Landau D, Mishori-Dery A, Hershkovitz R, Narkis G, Elbedour K, Carmi R. A new autosomal recessive congenital contractural syndrome in an Israeli Bedouin kindred. Am J Med Genet A 2003; 117a:37-40. [PMID: 12548738].

326. Lee B, Vissing H, Ramirez F, Rogers D, Rimoin D. Identification of the molecular defect in a family with spondyloepiphyseal dysplasia. Science 1989; 244:978-80. [PMID: 2543071].

327. Leutelt J, Oehlmann R, Younus F, van den Born LI, Weber JL, Denton MJ, Mehdi SQ, Gal A. Autosomal recessive retinitis pigmentosa locus maps on chromosome 1q in a large consanguineous family from Pakistan. Clin Genet 1995; 47:122-4. [PMID: 7634534].

328. Levin AV, Seidman DJ, Nelson LB, Jackson LG. Ophthalmologic findings in the Cornelia de Lange syndrome. J Pediatr Ophthalmol Strabismus 1990; 27:94-102. [PMID: 2348318].

329. Li A, Jiao X, Munier FL, Schorderet DF, Yao W, Iwata F, Hayakawa M, Kanai A, Shy Chen M, Alan Lewis R, Heckenlively J, Weleber RG, Traboulsi EI, Zhang Q, Xiao X, Kaiser-Kupfer M, Sergeev YV, Hejtmancik JF. Bietti crystalline corneoretinal dystrophy is caused by mutations in the novel gene CYP4V2. Am J Hum Genet 2004; 74:817-26. [PMID: 15042513].

330. Malfait F, Syx D, Vlummens P, Symoens S, Nampoothiri S, Hermanns-Le T, Van Laer L, De Paepe A. Musculocontractural Ehlers-Danlos Syndrome (former EDS type VIB) and adducted thumb clubfoot syndrome (ATCS) represent a single clinical entity caused by mutations in the dermatan-4-sulfotransferase 1 encoding CHST14 gene. Hum Mutat 2010; 31:1233-9. [PMID: 20842734].

331. Manz F, Scharer K, Janka P, Lombeck J. Renal magnesium wasting, incomplete tubular acidosis, hypercalciuria and nephrocalcinosis in siblings. Eur J Pediatr 1978; 128:67-79. [PMID: 668721].

332. Martin JP, Zorab EC. Familial glaucoma. In nine generations of a South Hampshire family. Br J Ophthalmol 1974; 58:536-42. [PMID: 4421809].

333. Mataftsi A, Schorderet DF, Chachoua L, Boussalah M, Nouri MT, Barthelmes D, Borruat FX, Munier FL. Novel TULP1 mutation causing leber congenital amaurosis or early onset retinal degeneration. Invest Ophthalmol Vis Sci 2007; 48:5160-7. [PMID: 17962469].

334. McClements M, Davies WI, Michaelides M, Young T, Neitz M, MacLaren RE, Moore AT, Hunt DM. Variations in opsin coding sequences cause x–linked cone dysfunction syndrome with myopia and dichromacy. Invest Ophthalmol Vis Sci 2013; 54:1361-9. [PMID: 23322568].

335. McGuire RE, Sullivan LS, Blanton SH, Church MW, Heckenlively JR, Daiger SP. X-linked dominant cone-rod degeneration: linkage mapping of a new locus for retinitis pigmentosa (RP 15) to Xp22.13-p22.11. Am J Hum Genet 1995; 57:87-94. [PMID: 7611300].

336. Meier W, Blumberg A, Imahorn W, De Luca F, Wildberger H, Oetliker O. Idiopathic hypercalciuria with bilateral macular colobomata: a new variant of oculo-renal syndrome. Helv Paediatr Acta 1979; 34:257-69. [PMID: 500385].

337. Meindl A, Dry K, Herrmann K, Manson F, Ciccodicola A, Edgar A, Carvalho MR, Achatz H, Hellebrand H, Lennon A, Migliaccio C, Porter K, Zrenner E, Bird A, Jay M, Lorenz B, Wittwer B, D'Urso M, Meitinger T, Wright A. A gene (RPGR) with homology to the RCC1 guanine nucleotide exchange factor is mutated in X-linked retinitis pigmentosa (RP3). Nat Genet 1996; 13:35-42. [PMID: 8673101].

338. Mercuri E, Messina S, Bruno C, Mora M, Pegoraro E, Comi GP, D'Amico A, Aiello C, Biancheri R, Berardinelli A, Boffi P, Cassandrini D, Laverda A, Moggio M, Morandi L, Moroni I, Pane M, Pezzani R, Pichiecchio A, Pini A, Minetti C, Mongini T, Mottarelli E, Ricci E, Ruggieri A, Saredi S, Scuderi C, Tessa A, Toscano A, Tortorella G, Trevisan CP, Uggetti C, Vasco G, Santorelli FM, Bertini E. Congenital muscular dystrophies with defective glycosylation of dystroglycan: a population study. Neurology 2009; 72:1802-9. [PMID: 19299310].

339. Michaelides M, Holder GE, Webster AR, Hunt DM, Bird AC, Fitzke FW, Mollon JD, Moore AT. A detailed phenotypic study of "cone dystrophy with supernormal rod ERG". Br J Ophthalmol 2005; 89:332-9. [PMID: 15722315].

340. Mochida GH, Ganesh VS, de Michelena MI, Dias H, Atabay KD, Kathrein KL, Huang HT, Hill RS, Felie JM, Rakiec D, Gleason D, Hill AD, Malik AN, Barry BJ, Partlow JN, Tan WH, Glader LJ, Barkovich AJ, Dobyns WB, Zon LI, Walsh CA. CHMP1A encodes an essential regulator of BMI1–INK4A in cerebellar development. Nat Genet 2012; 44:1260-4. [PMID: 23023333].

341. Morales J, Al-Sharif L, Khalil DS, Shinwari JM, Bavi P, Al-Mahrouqi RA, Al-Rajhi A, Alkuraya FS, Meyer BF, Al Tassan N. Homozygous mutations in ADAMTS10 and ADAMTS17 cause lenticular myopia, ectopia lentis, glaucoma, spherophakia, and short stature. Am J Hum Genet 2009; 85:558-68. [PMID: 19836009].

342. Morava E, Lefeber DJ, Urban Z, de Meirleir L, Meinecke P, Gillessen Kaesbach G, Sykut-Cegielska J, Adamowicz M, Salafsky I, Ranells J, Lemyre E, van Reeuwijk J, Brunner HG, Wevers RA. Defining the phenotype in an autosomal recessive cutis laxa syndrome with a combined congenital defect of glycosylation. Eur J Hum Genet 2008; 16:28-35. [PMID: 17971833].

343. Narkis G, Ofir R, Manor E, Landau D, Elbedour K, Birk OS. Lethal congenital contractural syndrome type 2 (LCCS2) is caused by a mutation in ERBB3 (Her3), a modulator of the phosphatidylinositol-3-kinase/Akt pathway. Am J Hum Genet 2007; 81:589-95. [PMID: 17701904].

344. Nicole S, Davoine CS, Topaloglu H, Cattolico L, Barral D, Beighton P, Hamida CB, Hammouda H, Cruaud C, White PS, Samson D, Urtizberea JA, Lehmann-Horn F, Weissenbach J, Hentati F, Fontaine B. Perlecan, the major proteoglycan of basement membranes, is altered in patients with Schwartz-Jampel syndrome (chondrodystrophic myotonia). Nat Genet 2000; 26:480-3. [PMID: 11101850].

345. Nishimura DY, Swiderski RE, Alward WL, Searby CC, Patil SR, Bennet SR, Kanis AB, Gastier JM, Stone EM, Sheffield VC. The forkhead transcription factor gene FKHL7 is

responsible for glaucoma phenotypes which map to 6p25. Nat Genet 1998; 19:140-7. [PMID: 9620769].

346. Nishino I, Fu J, Tanji K, Yamada T, Shimojo S, Koori T, Mora M, Riggs JE, Oh SJ, Koga Y, Sue CM, Yamamoto A, Murakami N, Shanske S, Byrne E, Bonilla E, Nonaka I, DiMauro S, Hirano M. Primary LAMP-2 deficiency causes X-linked vacuolar cardiomyopathy and myopathy (Danon disease). Nature 2000; 406:906-10. [PMID: 10972294].

347. Norio R. Finnish Disease Heritage I: characteristics, causes, background. Hum Genet 2003; 112:441-56. [PMID: 12627295].

348. Ohkubo S, Takeda H, Higashide T, Ito M, Sakurai M, Shirao Y, Yanagida T, Oda Y, Sado Y. Immunohistochemical and molecular genetic evidence for type IV collagen alpha5 chain abnormality in the anterior lenticonus associated with Alport syndrome. Arch Ophthalmol 2003; 121:846-50. [PMID: 12796257].

349. Ohlsson L. CONGENITAL RENAL DISEASE, DEAFNESS AND MYOPIA IN ONE FAMILY. Acta Med Scand 1963; 174:77-84. [PMID: 14042467].

350. Passos-Bueno MR, Marie SK, Monteiro M, Neustein I, Whittle MR, Vainzof M, Zatz M. Knobloch syndrome in a large Brazilian consanguineous family: confirmation of autosomal recessive inheritance. Am J Med Genet 1994; 52:170-3. [PMID: 7802003].

351. Perez Y, Gradstein L, Flusser H, Markus B, Cohen I, Langer Y, Marcus M, Lifshitz T, Kadir R, Birk OS. Isolated foveal hypoplasia with secondary nystagmus and low vision is associated with a homozygous SLC38A8 mutation. Eur J Hum Genet 2014; 22:703-6. [PMID: 24045842].

352. Pihlajamaa T, Prockop DJ, Faber J, Winterpacht A, Zabel B, Giedion A, Wiesbauer P, Spranger J, Ala-Kokko L. Heterozygous glycine substitution in the COL11A2 gene in the original patient with the Weissenbacher-Zweymuller syndrome demonstrates its identity with heterozygous OSMED (nonocular Stickler syndrome). Am J Med Genet 1998; 80:115-20. [PMID: 9805126].

353. Pohl S, Encarnacao M, Castrichini M, Muller-Loennies S, Muschol N, Braulke T. Loss of N-acetylglucosamine-1-phosphotransferase gamma subunit due to intronic mutation in GNPTG causes mucolipidosis type III gamma: Implications for molecular and cellular diagnostics. Am J Med Genet A 2010; 152a:124-32. [PMID: 20034096].

354. Pomponio RJ, Reynolds TR, Cole H, Buck GA, Wolf B. Mutational hotspot in the human biotinidase gene causes profound biotinidase deficiency. Nat Genet 1995; 11:96-8. [PMID: 7550325].

355. Poulter JA, Davidson AE, Ali M, Gilmour DF, Parry DA, Mintz-Hittner HA, Carr IM, Bottomley HM, Long VW, Downey LM, Sergouniotis PI, Wright GA, MacLaren RE, Moore AT, Webster AR, Inglehearn CF, Toomes C. Recessive mutations in TSPAN12 cause retinal dysplasia and severe familial exudative vitreoretinopathy (FEVR). Invest Ophthalmol Vis Sci 2012; 53:2873-9. [PMID: 22427576].

356. Pyeritz RE, McKusick VA. The Marfan syndrome: diagnosis and management. N Engl J Med 1979; 300:772-7. [PMID: 370588].

357. Raitta C, Lamminen M, Santavuori P, Leisti J. Ophthalmological findings in a new syndrome with muscle, eye and brain involvement. Acta Ophthalmol (Copenh) 1978; 56:465-72. [PMID: 581135].

358. Ramer JC, Eggli K, Rogan PK, Ladda RL. Identical twins with Weissenbacher-Zweymuller syndrome and neural tube defect. Am J Med Genet 1993; 45:614-8. [PMID: 8456835].

359. Reish O, Townsend D, Berry SA, Tsai MY, King RA. Tyrosinase inhibition due to interaction of homocyst(e)ine with copper: the mechanism for reversible hypopigmentation in homocystinuria due to cystathionine beta-synthase deficiency. Am J Hum Genet 1995; 57:127-32. [PMID: 7611281].

360. Riazuddin SA, Shahzadi A, Zeitz C, Ahmed ZM, Ayyagari R, Chavali VR, Ponferrada VG, Audo I, Michiels C, Lancelot ME, Nasir IA, Zafar AU, Khan SN, Husnain T, Jiao X, MacDonald IM, Riazuddin S, Sieving PA, Katsanis N, Hejtmancik JF. A mutation in SLC24A1 implicated in autosomal-recessive congenital stationary night blindness. Am J Hum Genet 2010; 87:523-31. [PMID: 20850105].

361. Richards AJ, Yates JR, Williams R, Payne SJ, Pope FM, Scott JD, Snead MP. A family with Stickler syndrome type 2 has a mutation in the COL11A1 gene resulting in the substitution of glycine 97 by valine in alpha 1 (XI) collagen. Hum Mol Genet 1996; 5:1339-43. [PMID: 8872475].

362. Riveiro-Alvarez R, Xie YA, Lopez-Martinez MA, Gambin T, Perez-Carro R, Avila-Fernandez A, Lopez-Molina MI, Zernant J, Jhangiani S, Muzny D, Yuan B, Boerwinkle E, Gibbs R, Lupski JR, Ayuso C, Allikmets R. New mutations in the RAB28 gene in 2 Spanish families with cone-rod dystrophy. JAMA Ophthalmol 2015; 133:133-9. [PMID: 25356532].

363. Saitsu H, Osaka H, Sasaki M, Takanashi J, Hamada K, Yamashita A, Shibayama H, Shiina M, Kondo Y, Nishiyama K, Tsurusaki Y, Miyake N, Doi H, Ogata K, Inoue K, Matsumoto N. Mutations in POLR3A and POLR3B encoding RNA Polymerase III subunits cause an autosomal-recessive hypomyelinating leukoencephalopathy. Am J Hum Genet 2011; 89:644-51. [PMID: 22036171].

364. Salo AM, Cox H, Farndon P, Moss C, Grindulis H, Risteli M, Robins SP, Myllyla R. A connective tissue disorder caused by mutations of the lysyl hydroxylase 3 gene. Am J Hum Genet 2008; 83:495-503. [PMID: 18834968].

365. Sanyanusin P, Schimmenti LA, McNoe LA, Ward TA, Pierpont ME, Sullivan MJ, Dobyns WB, Eccles MR. Mutation of the PAX2 gene in a family with optic nerve colobomas, renal anomalies and vesicoureteral reflux. Nat Genet 1995; 9:358-64. [PMID: 7795640].

366. Schimmenti LA, Pierpont ME, Carpenter BL, Kashtan CE, Johnson MR, Dobyns WB. Autosomal dominant optic nerve colobomas, vesicoureteral reflux, and renal anomalies. Am J Med Genet 1995; 59:204-8. [PMID: 8588587].

367. Schwahn U, Lenzner S, Dong J, Feil S, Hinzmann B, van Duijnhoven G, Kirschner R, Hemberger M, Bergen AA, Rosenberg T, Pinckers AJ, Fundele R, Rosenthal A, Cremers FP, Ropers HH, Berger W. Positional cloning of the gene for X-linked retinitis pigmentosa 2. Nat Genet 1998; 19:327-32. [PMID: 9697692].

368. Siggers CD, Rimoin DL, Dorst JP, Doty SB, Williams BR, Hollister DW, Silberberg R, Cranley RE, Kaufman RL, McKusick VA. The Kniest syndrome. Birth Defects Orig Artic Ser 1974; 10:193-208. [PMID: 4214536].

369. Stevens E, Carss KJ, Cirak S, Foley AR, Torelli S, Willer T, Tambunan DE, Yau S, Brodd L, Sewry CA, Feng L, Haliloglu G, Orhan D, Dobyns WB, Enns GM, Manning M, Krause A, Salih MA, Walsh CA, Hurles M, Campbell KP, Manzini MC, Stemple D, Lin YY, Muntoni F. Mutations in B3GALNT2 cause congenital muscular dystrophy and hypoglycosylation of alpha-dystroglycan. Am J Hum Genet 2013; 92:354-65. [PMID: 23453667].

370. Stoll C. Shprintzen-Goldberg marfanoid syndrome: a case followed up for 24 years. Clin Dysmorphol 2002; 11:1-7. [PMID: 11822698].

371. Strom TM, Nyakatura G, Apfelstedt-Sylla E, Hellebrand H, Lorenz B, Weber BH, Wutz K, Gutwillinger N, Ruther K, Drescher B, Sauer C, Zrenner E, Meitinger T, Rosenthal A, Meindl A. An L-type calcium-channel gene mutated in incomplete X-linked congenital stationary night blindness. Nat Genet 1998; 19:260-3. [PMID: 9662399].

372. Sundin OH, Yang JM, Li Y, Zhu D, Hurd JN, Mitchell TN, Silva ED, Maumenee IH. Genetic basis of total colourblindness among the Pingelapese islanders. Nat Genet 2000; 25:289-93. [PMID: 10888875].

373. Swarr DT, Bloom D, Lewis RA, Elenberg E, Friedman EM, Glotzbach C, Wissman SD, Shaffer LG, Potocki L. Potocki-Shaffer syndrome: comprehensive clinical assessment, review of the literature, and proposals for medical management. Am J Med Genet A 2010; 152a:565-72. [PMID: 20140962].

374. Taitz LS, Green A, Strachan I, Bartlett K, Bennet M. Biotinidase deficiency and the eye and ear. Lancet 1983; 2:918- [PMID: 6137736].

375. Tekin M, Chioza BA, Matsumoto Y, Diaz-Horta O, Cross HE, Duman D, Kokotas H, Moore-Barton HL, Sakoori K, Ota M, Odaka YS, Foster J 2nd, Cengiz FB, Tokgoz-Yilmaz S, Tekeli O, Grigoriadou M, Petersen MB, Sreekantan-Nair A, Gurtz K, Xia XJ, Pandya A, Patton MA, Young JI, Aruga J, Crosby AH. SLITRK6 mutations cause myopia and deafness in humans and mice. J Clin Invest 2013; 123:2094-102. [PMID: 23543054].

376. Thiel C, Wilken M, Zenker M, Sticht H, Fahsold R, Gusek-Schneider GC, Rauch A. Independent NF1 and PTPN11 mutations in a family with neurofibromatosis-Noonan syndrome. Am J Med Genet A 2009; 149a:1263-7. [PMID: 19449407].

377. Thiffault I, Wolf NI, Forget D, Guerrero K, Tran LT, Choquet K, Lavallee-Adam M, Poitras C, Brais B, Yoon G, Sztriha L, Webster RI, Timmann D, van de Warrenburg BP, Seeger J, Zimmermann A, Mate A, Goizet C, Fung E, van der Knaap MS, Fribourg S, Vanderver A, Simons C, Taft RJ, Yates JR 3rd, Coulombe B, Bernard G. Recessive mutations in POLR1C cause a leukodystrophy by impairing biogenesis of RNA polymerase III. Nat Commun 2015; 6:7623-[PMID: 26151409].

378. Tompson SW, Faqeih EA, Ala-Kokko L, Hecht JT, Miki R, Funari T, Funari VA, Nevarez L, Krakow D, Cohn DH. Dominant and recessive forms of fibrochondrogenesis resulting from mutations at a second locus, COL11A2. Am J Med Genet A 2012; 158a:309-14. [PMID: 22246659].

379. Tonkin ET, Wang TJ, Lisgo S, Bamshad MJ, Strachan T. NIPBL, encoding a homolog of fungal Scc2-type sister chromatid cohesion proteins and fly Nipped-B, is mutated in Cornelia de Lange syndrome. Nat Genet 2004; 36:636-41. [PMID: 15146185].

380. Tsang SH, Woodruff ML, Jun L, Mahajan V, Yamashita CK, Pedersen R, Lin CS, Goff SP, Rosenberg T, Larsen M, Farber DB, Nusinowitz S. Transgenic mice carrying the H258N mutation in the gene encoding the beta-subunit of phosphodiesterase-6 (PDE6B) provide a model for human congenital stationary night blindness. Hum Mutat 2007; 28:243-54. [PMID: 17044014].

381. Van Camp G, Snoeckx RL, Hilgert N, van den Ende J, Fukuoka H, Wagatsuma M, Suzuki H, Smets RM, Vanhoenacker F, Declau F, Van de Heyning P, Usami S. A new autosomal recessive form of Stickler syndrome is caused by a mutation in the COL9A1 gene. Am J Hum Genet 2006; 79:449-57. [PMID: 16909383].

382. van Rahden VA, Fernandez-Vizarra E, Alawi M, Brand K, Fellmann F, Horn D, Zeviani M, Kutsche K. Mutations in NDUFB11, encoding a complex I component of the mitochondrial respiratory chain, cause microphthalmia with linear skin defects syndrome. Am J Hum Genet 2015; 96:640-50. [PMID: 25772934].

383. Villanova M, Mercuri E, Bertini E, Sabatelli P, Morandi L, Mora M, Sewry C, Brockington M, Brown SC, Ferreiro A, Maraldi NM, Toda T, Guicheney P, Merlini L, Muntoni F. Congenital muscular dystrophy associated with calf hypertrophy, microcephaly and severe mental retardation in three Italian families: evidence for a novel CMD syndrome. Neuromuscul Disord 2000; 10:541-7. [PMID: 11053679].

384. Vincent A, Audo I, Tavares E, Maynes JT, Tumber A, Wright T, Li S, Michiels C, Condroyer C, MacDonald H, Verdet R, Sahel JA, Hamel CP, Zeitz C, Heon E. Biallelic Mutations in GNB3 Cause a Unique Form of Autosomal-Recessive Congenital Stationary Night Blindness. Am J Hum Genet 2016; 98:1011-9. [PMID: 27063057].

385. Vincent A, Forster N, Maynes JT, Paton TA, Billingsley G, Roslin NM, Ali A, Sutherland J, Wright T, Westall CA, Paterson AD, Marshall CR, Heon E. OTX2 mutations cause autosomal dominant pattern dystrophy of the retinal pigment epithelium. J Med Genet 2014; 51:797-805. [PMID: 25293953].

386. Wang Y, Guo L, Cai SP, Dai M, Yang Q, Yu W, Yan N, Zhou X, Fu J, Guo X, Han P, Wang J, Liu X. Exome sequencing

identifies compound heterozygous mutations in CYP4V2 in a pedigree with retinitis pigmentosa. PLoS One 2012; 7:e33673-[PMID: 22693542].

387. Weber S, Hoffmann K, Jeck N, Saar K, Boeswald M, Kuwertz-Broeking E, Meij II, Knoers NV, Cochat P, Sulakova T, Bonzel KE, Soergel M, Manz F, Schaerer K, Seyberth HW, Reis A, Konrad M. Familial hypomagnesaemia with hypercalciuria and nephrocalcinosis maps to chromosome 3q27 and is associated with mutations in the PCLN-1 gene. Eur J Hum Genet 2000; 8:414-22. [PMID: 10878661].

388. Wenstrup RJ, Murad S, Pinnell SR. Ehlers-Danlos syndrome type VI: clinical manifestations of collagen lysyl hydroxylase deficiency. J Pediatr 1989; 115:405-9. [PMID: 2504907].

389. Whalen S, Heron D, Gaillon T, Moldovan O, Rossi M, Devillard F, Giuliano F, Soares G, Mathieu-Dramard M, Afenjar A, Charles P, Mignot C, Burglen L, Van Maldergem L, Piard J, Aftimos S, Mancini G, Dias P, Philip N, Goldenberg A, Le Merrer M, Rio M, Josifova D, Van Hagen JM, Lacombe D, Edery P, Dupuis-Girod S, Putoux A, Sanlaville D, Fischer R, Drevillon L, Briand-Suleau A, Metay C, Goossens M, Amiel J, Jacquette A, Giurgea I. Novel comprehensive diagnostic strategy in Pitt-Hopkins syndrome: clinical score and further delineation of the TCF4 mutational spectrum. Hum Mutat 2012; 33:64-72. [PMID: 22045651].

390. White J, Beck CR, Harel T, Posey JE, Jhangiani SN, Tang S, Farwell KD, Powis Z, Mendelsohn NJ, Baker JA, Pollack L, Mason KJ, Wierenga KJ, Arrington DK, Hall M, Psychogios A, Fairbrother L, Walkiewicz M, Person RE, Niu Z, Zhang J, Rosenfeld JA, Muzny DM, Eng C, Beaudet AL, Lupski JR, Boerwinkle E, Gibbs RA, Yang Y, Xia F, Sutton VR. POGZ truncating alleles cause syndromic intellectual disability. Genome Med 2016; 8:3-[PMID: 26739615].

391. Winterpacht A, Hilbert M, Schwarze U, Mundlos S, Spranger J, Zabel BU. Kniest and Stickler dysplasia phenotypes caused by collagen type II gene (COL2A1) defect. Nat Genet 1993; 3:323-6. [PMID: 7981752].

392. Wissinger B, Dangel S, Jagle H, Hansen L, Baumann B, Rudolph G, Wolf C, Bonin M, Koeppen K, Ladewig T, Kohl S, Zrenner E, Rosenberg T. Cone dystrophy with supernormal rod response is strictly associated with mutations in KCNV2. Invest Ophthalmol Vis Sci 2008; 49:751-7. [PMID: 18235024].

393. Xiao X, Zhang Q. Iris hyperpigmentation in a Chinese family with ocular albinism and the GPR143 mutation. Am J Med Genet A 2009; 149a:1786-8. [PMID: 19610097].

394. Yoshida A, Kobayashi K, Manya H, Taniguchi K, Kano H, Mizuno M, Inazu T, Mitsuhashi H, Takahashi S, Takeuchi M, Herrmann R, Straub V, Talim B, Voit T, Topaloglu H, Toda T, Endo T. Muscular dystrophy and neuronal migration disorder caused by mutations in a glycosyltransferase, POMGnT1. Dev Cell 2001; 1:717-24. [PMID: 11709191].

395. Zankl A, Zabel B, Hilbert K, Wildhardt G, Cuenot S, Xavier B, Ha-Vinh R, Bonafe L, Spranger J, Superti-Furga A. Spondyloperipheral dysplasia is caused by truncating mutations in the C-propeptide of COL2A1. Am J Med Genet A 2004; 129a:144-8. [PMID: 15316962].

396. Zeitz C, Jacobson SG, Hamel CP, Bujakowska K, Neuille M, Orhan E, Zanlonghi X, Lancelot ME, Michiels C, Schwartz SB, Bocquet B, Antonio A, Audier C, Letexier M, Saraiva JP, Luu TD, Sennlaub F, Nguyen H, Poch O, Dollfus H, Lecompte O, Kohl S, Sahel JA, Bhattacharya SS, Audo I. Whole-exome sequencing identifies LRIT3 mutations as a cause of autosomal-recessive complete congenital stationary night blindness. Am J Hum Genet 2013; 92:67-75. [PMID: 23246293].

397. Zhang Q, Guo X, Xiao X, Yi J, Jia X, Hejtmancik JF. Clinical description and genome wide linkage study of Y-sutural cataract and myopia in a Chinese family. Mol Vis 2004; 10:890-900. [PMID: 15570218].

398. Aldahmesh MA, Khan AO, Mohamed JY, Alkuraya H, Ahmed H, Bobis S, Al-Mesfer S, Alkuraya FS. Identification of ADAMTS18 as a gene mutated in Knobloch syndrome. J Med Genet 2011; 48:597-601. [PMID: 21862674].

399. van Trier DC, Vos AM, Draaijer RW, van der Burgt I, Draaisma JM, Cruysberg JR. Ocular Manifestations of Noonan Syndrome: A Prospective Clinical and Genetic Study of 25 Patients. Ophthalmology 2016; 123:2137-46. [PMID: 27521173].

400. Terhal PA, Nievelstein RJ, Verver EJ, Topsakal V, van Dommelen P, Hoornaert K, Le Merrer M, Zankl A, Simon ME, Smithson SF, Marcelis C, Kerr B, Clayton-Smith J, Kinning E, Mansour S, Elmslie F, Goodwin L, van der Hout AH, Veenstra-Knol HE, Herkert JC, Lund AM, Hennekam RC, Megarbane A, Lees MM, Wilson LC, Male A, Hurst J, Alanay Y, Anneren G, Betz RC, Bongers EM, Cormier-Daire V, Dieux A, David A, Elting MW, van den Ende J, Green A, van Hagen JM, Hertel NT, Holder-Espinasse M, den Hollander N, Homfray T, Hove HD, Price S, Raas-Rothschild A, Rohrbach M, Schroeter B, Suri M, Thompson EM, Tobias ES, Toutain A, Vreeburg M, Wakeling E, Knoers NV, Coucke P, Mortier GR. A study of the clinical and radiological features in a cohort of 93 patients with a COL2A1 mutation causing spondyloepiphyseal dysplasia congenita or a related phenotype. Am J Med Genet A 2015; 167A:461-75. [PMID: 25604898].

401. Buysse K, Riemersma M, Powell G, van Reeuwijk J, Chitayat D, Roscioli T, Kamsteeg EJ, van den Elzen C, van Beusekom E, Blaser S, Babul-Hirji R, Halliday W, Wright GJ, Stemple DL, Lin YY, Lefeber DJ, van Bokhoven H. Missense mutations in beta-1,3-N-acetylglucosaminyltransferase 1 (B3GNT1) cause Walker-Warburg syndrome. Hum Mol Genet 2013; 22:1746-54. [PMID: 23359570].

402. Chen S, Zhang Y, Wang Y, Li W, Huang S, Chu X, Wang L, Zhang M, Liu Z. A novel OPA1 mutation responsible for autosomal dominant optic atrophy with high frequency hearing loss in a Chinese family. Am J Ophthalmol 2007; 143:186-8. [PMID: 17188070].

403. Chitayat D, Toi A, Babul R, Levin A, Michaud J, Summers A, Rutka J, Blaser S, Becker LE. Prenatal diagnosis of retinal nonattachment in the Walker-Warburg syndrome. Am J Med Genet 1995; 56:351-8. [PMID: 7604843].

404. Fukuyama Y, Osawa M, Suzuki H. Congenital progressive muscular dystrophy of the Fukuyama type - clinical, genetic and pathological considerations. Brain Dev 1981; 3:1-29. [PMID: 7258547].

405. Helbling-Leclerc A, Zhang X, Topaloglu H, Cruaud C, Tesson F, Weissenbach J, Tome FM, Schwartz K, Fardeau M, Tryggvason K. Mutations in the laminin alpha 2-chain gene (LAMA2) cause merosin-deficient congenital muscular dystrophy. Nat Genet 1995; 11:216-8. [PMID: 7550355].

406. Jae LT, Raaben M, Riemersma M, van Beusekom E, Blomen VA, Velds A, Kerkhoven RM, Carette JE, Topaloglu H, Meinecke P, Wessels MW, Lefeber DJ, Whelan SP, van Bokhoven H, Brummelkamp TR. Deciphering the glycosylome of dystroglycanopathies using haploid screens for lassa virus entry. Science 2013; 340:479-83. [PMID: 23519211].

407. Kobayashi K, Nakahori Y, Miyake M, Matsumura K, Kondo-Iida E, Nomura Y, Segawa M, Yoshioka M, Saito K, Osawa M, Hamano K, Sakakihara Y, Nonaka I, Nakagome Y, Kanazawa I, Nakamura Y, Tokunaga K, Toda T. An ancient retrotransposal insertion causes Fukuyama-type congenital muscular dystrophy. Nature 1998; 394:388-92. [PMID: 9690476].

408. Manzini MC, Tambunan DE, Hill RS, Yu TW, Maynard TM, Heinzen EL, Shianna KV, Stevens CR, Partlow JN, Barry BJ, Rodriguez J, Gupta VA, Al-Qudah AK, Eyaid WM, Friedman JM, Salih MA, Clark R, Moroni I, Mora M, Beggs AH, Gabriel SB, Walsh CA. Exome sequencing and functional validation in zebrafish identify GTDC2 mutations as a cause of Walker-Warburg syndrome. Am J Hum Genet 2012; 91:541-7. [PMID: 22958903].

409. Naeem MA, Chavali VR, Ali S, Iqbal M, Riazuddin S, Khan SN, Husnain T, Sieving PA, Ayyagari R, Riazuddin S, Hejtmancik JF, Riazuddin SA. GNAT1 associated with autosomal recessive congenital stationary night blindness. Invest Ophthalmol Vis Sci 2012; 53:1353-61. [PMID: 22190596].

410. Schlingmann KP, Weber S, Peters M, Niemann Nejsum L, Vitzthum H, Klingel K, Kratz M, Haddad E, Ristoff E, Dinour D, Syrrou M, Nielsen S, Sassen M, Waldegger S, Seyberth HW, Konrad M. Hypomagnesemia with secondary hypocalcemia is caused by mutations in TRPM6, a new member of the TRPM gene family. Nat Genet 2002; 31:166-70. [PMID: 12032568].

411. Temtamy SA, Salam MA, Aboul-Ezz EH, Hussein HA, Helmy SA, Shalash BA. New autosomal recessive multiple congenital abnormalities/mental retardation syndrome with craniofacial dysmorphism absent corpus callosum, iris colobomas and connective tissue dysplasia. Clin Dysmorphol 1996; 5:231-40. [PMID: 8818452].

412. Tome FM, Evangelista T, Leclerc A, Sunada Y, Manole E, Estournet B, Barois A, Campbell KP, Fardeau M. Congenital muscular dystrophy with merosin deficiency. C R Acad Sci III 1994; 317:351-7. [PMID: 8000914].

413. Vainsel M, Vandevelde G, Smulders J, Vosters M, Hubain P, Loeb H. Tetany due to hypomagnesaemia with secondary hypocalcaemia. Arch Dis Child 1970; 45:254-8. [PMID: 5419995].

414. Vuillaumier-Barrot S, Bouchet-Seraphin C, Chelbi M, Devisme L, Quentin S, Gazal S, Laquerriere A, Fallet-Bianco C, Loget P, Odent S, Carles D, Bazin A, Aziza J, Clemenson A, Guimiot F, Bonniere M, Monnot S, Bole-Feysot C, Bernard JP, Loeuillet L, Gonzales M, Socha K, Grandchamp B, Attie-Bitach T, Encha-Razavi F, Seta N. Identification of mutations in TMEM5 and ISPD as a cause of severe cobblestone lissencephaly. Am J Hum Genet 2012; 91:1135-43. [PMID: 23217329].

415. Willer T, Lee H, Lommel M, Yoshida-Moriguchi T, de Bernabe DB, Venzke D, Cirak S, Schachter H, Vajsar J, Voit T, Muntoni F, Loder AS, Dobyns WB, Winder TL, Strahl S, Mathews KD, Nelson SF, Moore SA, Campbell KP. ISPD loss-of-function mutations disrupt dystroglycan O-mannosylation and cause Walker-Warburg syndrome. Nat Genet 2012; 44:575-80. [PMID: 22522420].

416. Zahrani F, Aldahmesh MA, Alshammari MJ, Al-Hazzaa SA, Alkuraya FS. Mutations in c12orf57 cause a syndromic form of colobomatous microphthalmia. Am J Hum Genet 2013; 92:387-91. [PMID: 23453665].

417. Logan NS, Gilmartin B, Marr JE, Stevenson MR, Ainsworth JR. Community-based study of the association of high myopia in children with ocular and systemic disease. Optom Vis Sci 2004; 81:11-3. [PMID: 14747755].

418. Marr JE, Halliwell-Ewen J, Fisher B, Soler L, Ainsworth JR. Associations of high myopia in childhood. Eye (Lond) 2001; 15:70-4. [PMID: 11318301].

419. Zhang Q, Xiao X, Li S, Jia X, Yang Z, Huang S, Caruso RC, Guan T, Sergeev Y, Guo X, Hejtmancik JF. Mutations in NYX of individuals with high myopia, but without night blindness. Mol Vis 2007; 13:330-6. [PMID: 17392683].

Articles are provided courtesy of Emory University and the Zhongshan Ophthalmic Center, Sun Yat-sen University, P.R. China. The print version of this article was created on 31 December 2017. This reflects all typographical corrections and errata to the article through that date. Details of any changes may be found in the online version of the article.