GENEReviews

Funded by the NIH · Developed at GeneTests (www.genetests.org), University of Washington, Seattle

Lenz Microphthalmia Syndrome

David Ng, MD
National Cancer Institute
National Institutes of Health
Bethesda

Initial Posting: June 4, 2002.
Last Revision: July 27, 2007.

Summary

Disease characteristics. Lenz microphthalmia syndrome (LMS) is characterized by unilateral or bilateral microphthalmia and/or anophthalmia with malformations of the ears, teeth, fingers, skeleton, or genitourinary system. Microphthalmia is often accompanied by microcornea and glaucoma. Coloboma is present in approximately 60% of microphthalmic eyes with severity ranging from isolated iris coloboma to coloboma of the ciliary body, choroid, and optic disk. Ears may be low set, anteverted, posteriorly rotated, simple, cup-shaped, or abnormally modeled. Hearing loss has been observed. Dental findings include irregularly shaped, missing, or widely spaced teeth. Duplicated thumbs, syndactyly, clinodactyly, camptodactyly, and microcephaly are common, as are narrow/sloping shoulders, underdeveloped clavicles, kyphoscoliosis, exaggerated lumbar lordosis, long cylindrical thorax, and webbed neck. Genitourinary anomalies include hypospadias, cryptorchidism, renal hypoplasia/aplasia, and hydroureter. Approximately 60% of affected males have mild-to-severe mental retardation or developmental delay.

Diagnosis/testing. The diagnosis of Lenz microphthalmia syndrome is based on clinical findings. Mild simple microphthalmia can be identified by measuring the axial length of the globe with A-scan ultrasonography. *BCOR* (MAA2 locus) is the only gene known to be associated with Lenz microphthalmia syndrome. One additional locus on the X chromosome (ANOP1) is known to be associated with LMS. Molecular genetic testing for *BCOR* is available on a research basis only.

Management. Treatment for individuals with anophthalmos or extreme microphthalmos includes regular evaluation by an ocularist for placement of serial enlarging orbital expanders, physical and occupational therapy, special education, and referral to services for the blind. Treatment for individuals with hearing loss and sleep disorders is dependent on the specific defect and similar to that used in the general population. Regular dental examinations and cleaning should be instituted, especially when cognitive developmental delay is present. Dental treatment is the same as for the general population. Surveillance includes annual ophthalmologic examination for those with residual vision, monitoring of renal function, developmental assessments, and lifelong case management to help affected individuals gain access to social services and assistive devices for the blind.

Genetic counseling. Lenz microphthalmia syndrome is inherited in an X-linked recessive manner. The risk to sibs depends upon the carrier status of the mother. If the mother is a carrier, the chance of transmitting the mutation is 50% in each pregnancy. Male sibs who inherit the mutation will be affected; female sibs who inherit the mutation will be carriers and will not be affected. The majority of males with Lenz microphthalmia syndrome do not reproduce. Prenatal testing may be available from laboratories offering custom prenatal testing for families in which the disease-causing mutation has been identified in an affected family member.

Prenatal ultrasound examination at 18 weeks' gestation can be offered to mothers of an affected male and to female sibs of a proband of indeterminate carrier status to evaluate fetal renal development.

Diagnosis

Clinical Diagnosis

Formal diagnostic criteria do not exist. The clinical findings of Lenz microphthalmia syndrome (LMS) include:

- Unilateral or bilateral microphthalmia and/or anophthalmia that may be symmetric or asymmetric
  - **Anophthalmia** refers to the histologic diagnosis of complete absence of the globe in the presence of ocular adnexae (eyelids, conjunctiva, and lacrimal apparatus). CT or MRI scan of the orbit shows absence of ocular tissue, optic nerve, and extraocular muscles. Note: The term "clinical anophthalmia" should be used for severe microphthalmia when the globe is not detectable on physical examination.
  - **"Simple microphthalmia" or "pure microphthalmia"** describes a globe that is reduced in total axial length (TAL), has all structural elements intact, and retains some vision. Mild simple microphthalmia can be identified by measuring the axial length of the globe with A-scan ultrasonography. Total axial length of the neonatal eye is normally near 17 mm; an age-adjusted total axial length below the fifth centile defines microphthalmia. The mean total axial length of the adult eye is 23.8 mm; a total axial length of less than 18.5 mm defines microphthalmia.
  - **Coloboma** is present in approximately 60% of microphthalmic eyes [Ng et al 2002], with severity ranging from isolated iris coloboma to coloboma of the ciliary body, choroid, and optic disk.
  - **Congenital cystic eye** has not been observed in LMS.
- Extraocular malformations that vary within and among families:
  - Hypospadias, cryptorchidism, renal aplasia/hypoplasia, hydroureter (77%)
  - Simple, anteverted, abnormally modeled ears (63%)
  - Abnormal shape of incisors, irregularly spaced teeth (48%)
  - Duplicated thumbs, syndactyly, clinodactyly, camptodactyly (44%)
  - Microcephaly (37%)
  - Narrow/sloping shoulders, underdeveloped clavicles, kyphoscoliosis, exaggerated lumbar lordosis, long cylindrical thorax, webbed neck (26%)
  - Cleft lip/palate (7%)
- Mental retardation, ranging from mild to severe, is seen in 63%
- Family history consistent with X-linked recessive inheritance

Testing

Karyotype is normal.

Molecular Genetic Testing

GeneReviews designates a molecular genetic test as clinically available only if the test is listed in the GeneTests Laboratory Directory *by either a US CLIA-licensed laboratory or a non-US clinical laboratory. GeneTests does not verify laboratory-submitted information or warrant any aspect of a laboratory's licensure or performance. Clinicians must communicate directly with the laboratories to verify information.*—ED.

Molecular Genetic Testing—Gene. *BCOR* (MAA2 locus) is the only gene known to be associated with Lenz microphthalmia syndrome [Ng et al 2004].

Other loci. One additional locus on the X chromosome (ANOP1) is known to be associated with LMS.

- Graham et al (1991) mapped the gene in a family with X-linked clinical anophthalmos to Xq27-q28. The authors reported extraocular features of preauricular skin tags and cleft palate; however, they considered the disorder present in this family to be distinct from LMS.
- Forrester et al (2001) mapped the gene in a family with the LMS phenotype (anophthalmia, moderate-to-severe mental retardation, delayed motor development, hypotonia, and ear, dental, digital, skeletal, cardiac, and renal abnormalities) to a 17.65-cM region inXq27-q28.

The linkage data demonstrating locus heterogeneity suggest that LMS, previously thought to be a single disorder, may actually be (1) two distinct disorders that are difficult to distinguish clinically or (2) a single disorder with a phenotypic spectrum caused by mutations in two different genes on the X chromosome.

Research testing

- **Sequencing of the entire coding region.** A missense mutation, 254C>T, resulting in a change of amino acid at position 85 from proline to leucine (p.Pro85Leu) in *BCOR*, was found in affected males of the family used to map the MAA2 locus [Ng et al 2002, Ng et al 2004]. Mutation at the MAA2 locus is rare for the Lenz microphthalmia syndrome phenotype, but mutation detection rate is unknown.
- **Mutation scanning**
  - Mutation detection rate for the Lenz microphthalmia syndrome phenotype is low.
  - The majority of individuals with oculofaciocardiodental syndrome (OFCD) analyzed thus far have detectable *BCOR* mutations [Ng et al 2004, Horn et al 2005].
- **FISH metaphase**
  - FISH analysis is not expected to be useful in analyzing families with the Lenz micropthalmia syndrome phenotype as they are not expected to have large deletions in *BCOR*.
  - FISH may be considered an adjunct in evaluating individuals with OFCD without detectable mutations by mutation scanning to determine if they have a submicroscopic chromosomal deletion.

Table 1 summarizes molecular genetic testing for this disorder.

Table 1. Molecular Genetic Testing Used in Lenz Microphthalmia Syndrome

Test Method	Mutations Detected	Mutation Detection Rate	Test Availability
Sequence analysis	*BCOR* sequence alterations	Unknown	Research only

Genetically Related (Allelic) Disorders

Oculofaciocardiodental syndrome is also associated with mutations in *BCOR* [Ng et al 2004, Horn et al 2005, Oberoi et al 2005].

OFCD is inherited in an X-linked dominant pattern with male lethality.

Females with OFCD may have congenital cataracts as the sole ocular manifestation or unilateral/bilateral microphthalmia with congenital cataracts. Microphthalmia is less severe in OFCD than in LMS.

Extraocular features include long narrow face, broad nasal tip with separated nasal cartilage, cleft palate, submucous cleft palate, cardiac anomalies (ventricular septal defect, atrial septal defect, floppy mitral valve) and dental anomalies (retained deciduous teeth, canine radiculomegaly, root dilacerations, and oligodontia).

Females with OFCD have normal intelligence, in contrast to males with LMS, who often have developmental delay/mental retardation, microcephaly, and structural CNS abnormalities.

Individuals with OFCD have mutations that are predicted to prematurely truncate the BCOR protein. In hemizygous males, truncating mutations are hypothesized to lead to a complete loss of *BCOR* function and are presumed to be lethal. Truncating *BCOR* mutations in females lead to haploinsufficiency and a milder phenotype. All families with OFCD have unique mutations.

Based on the known cases of OFCD scanned for BCOR mutations, penetrance is complete.

Other. Isolated (nonsyndromic) forms of microphthalmia have been mapped to the proximal p to q arm of the X chromosome [Lehman et al 2001].

Clinical Description

Natural History

The phenotype of Lenz microphthalmia syndrome linked to ANOP1 cannot be distinguished from the LMS phenotype linked to MAA2.

Lenz microphthalmia syndrome has a wide spectrum of ocular and extraocular abnormalities.

Eyes. The eyes may be asymmetrically affected. One globe can be of normal size while the other is microphthalmic. Severity can range from mild microphthalmia with retained vision to severe microphthalmia or clinical anophthalmia with blindness. Microphthalmia is often accompanied by microcornea and reduction in the size of the anterior segment of the eye, which predispose to the development of glaucoma.

Since mild microphthalmia may not be obvious on clinical examination, individuals with LMS with retained vision may not be identified until the first ophthalmologic examination when high hyperopia (+7 to +11 diopters) secondary to a foreshortened posterior segment of the globe is diagnosed.

Cataracts may be present.

Nystagmus may be present secondary to impaired vision.

Absence or diminished size of the globe may cause secondary underdevelopment of the bony orbits, shortened palpebral fissures, and fusion of the eyelid margins (ankyloblepharon).

Craniofacial. The occurrence of congenital microcephaly is variable. Affected individuals may be normocephalic or dolichocephalic.

Ears may be low set, anteverted, posteriorly rotated, simple, cup-shaped, or abnormally modeled. Preauricular tags may be present.

Hearing loss has been observed.

Cleft lip/palate or high arched palate is present in approximately 40% of individuals [Ng et al 2002].

Dental development may be delayed. Nonspecific dental findings include irregularly shaped, missing, or widely spaced teeth.

Genitourinary. Urogenital anomalies are the most frequent associated findings, reported in approximately 77% of individuals [Ng et al 2002]. These include hypospadias, cryptorchidism, renal hypoplasia/aplasia, and hydroureter.

Limbs. Hand findings include duplicated and/or proximally placed thumbs, cutaneous syndactyly, clinodactyly, and camptodactyly.

Skeletal. Long cylindrical thorax with sloping, narrow shoulders, underdeveloped clavicles, or thinning of the lateral third of the clavicles on x-ray as well as kyphoscoliosis and exaggerated lumbar lordosis have been seen in some families.

Cognitive/neurologic. Cognitive impairment varies within and among families. Approximately 60% of affected males have mild-to-severe mental retardation or developmental delay [Ng et al 2002].

Motor development may be delayed.

Seizures, behavioral disturbance, and self-mutilation may manifest in males with severe mental retardation. Sleep-wake cycles can be disturbed because of lack of normal diurnal variation.

Cranial MRI often reveals absent or hypoplastic optic nerves and optic chiasm. In addition, hypoplasia of the corpus callosum and cingulate gyrus have been noted. The latter is often clinically silent.

Genotype-Phenotype Correlations

No genotype-phenotype correlations are known.

Penetrance

An insufficient number of cases of BCOR-related Lenz microphthalmia exist to comment on penetrance.

Anticipation

Anticipation has not been reported.

Nomenclature

Lenz microphthalmia syndrome has been referred to as Lenz dysplasia, Lenz dysmorphogenetic syndrome [Goldberg & McKusick 1971], and microphthalmia with multiple associated anomalies (MAA[OMIM]). These terms were used to describe the extraocular developmental anomalies and mental retardation that co-occur with the microphthalmia in affected males. Although the consensus inheritance pattern is X-linked recessive, the term Lenz microphthalmia is used by clinicians for simplex cases (i.e., single occurrence in a family) with a Lenz-like phenotype.

Prevalence

Prevalence in ethnic groups is unknown. Most reported cases are Caucasian. An African-American family has been studied by several investigators [Ng et al 2002]. A Hispanic family with isolated X-linked colobomatous microphthalmia has been reported [Lehman et al 2001].

Differential Diagnosis

For current information on availability of genetic testing for disorders included in this section, see GeneTests Laboratory Directory. —ED.

See Anophthalmia/Microphthalmia Overview.

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease in an individual diagnosed with Lenz microphthalmia syndrome, the following evaluations are recommended:

- Physical examination for the presence of anomalies associated with the disorder
- Cranial MRI to estimate the size of the globes for prognosis regarding potential visual function and to detect concurrent CNS malformations such as hypoplastic corpus callosum and cingulate gyrus
- Visual evoked response testing and ophthalmologic examination to help determine visual acuity and/or the potential for vision
- Renal ultrasound examination to evaluate for renal aplasia, hypoplasia, and hydroureter
- Consideration of hearing evaluation during infancy if:
  - Head and neck examination reveals malformations of the auricle or ear canal, presence of skin tags or dimples around the ear, presence of cleft lip or palate, asymmetric facies, and microcephaly.
  - The parents have concerns that the child cannot hear (i.e., infant does not startle to loud noises, awakens to sound etc). The type of examination should be adjusted for the individual's cognitive level to allow for cooperation and maximize the chance of an informative test. (See Deafness and Hereditary Hearing Loss Overview.)
- Consideration of sleep evaluation if parents report excessive daytime somnolence, altered sleep-wake cycles, difficulty awakening the child or getting the child to fall asleep, apnea, loud snoring, and/or difficulty breathing while asleep

Treatment of Manifestations

- Individuals with anophthalmos or extreme microphthalmos benefit from regular evaluations by an ocularist for placement of serial enlarging orbital expanders to prevent deformation of facial structures and to encourage normal development of eye lashes and lid margins.
- Early intervention with physical therapy and occupational therapy helps to address disturbances of the sleep-wake cycle caused by lack of light perception and problems of delayed gross motor development often observed in children with visual impairment.
- Early intervention with special education maximizes cognitive development.
- Referral to services for the blind is recommended.
- Treatment for hearing loss and sleep disorders is dependent on the specific defect and similar to the general population.
- Referral to a sleep disorder specialist may be necessary depending on the individual's history and presentation to determine the appropriate tests.
- Dental examinations and cleaning should be instituted to monitor dental hygiene, especially when the affected individual has cognitive developmental delay. Missing and irregularly shaped teeth and wide spacing of teeth are common. Treatment is the same as for the general population in restoring masticatory function.

Prevention of Secondary Complications

If valvular abnormalities are present, antibiotic prophylaxis prior to dental care and specific medical procedures is necessary as for the general population.

Surveillance

- Annual ophthalmologic examination for those with residual vision given the predisposition to glaucoma and high hyperopia from foreshortening of the globe
- Monitoring of renal function (BUN, creatinine, and urine analysis) in those with known renal/ureteral anomalies
- Developmental assessments performed with each well-child visit as recommended by the American Academy of Pediatrics. More frequent and specialized assessments are tailored to each child if development is not on track.
- Lifelong case management to help affected individuals gain access to social services and assistive devices for the blind.

Agents/Circumstances to Avoid

In those with residual vision, dilating drops and medications that may dilate the pupils (i.e., antihistamines, decongestants, tricyclic antidepressants) should be used in consultation with an ophthalmologist, because of the narrow anterior chamber and risk for angle closure glaucoma.

Therapies Under Investigation

Search ClinicalTrials.gov for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Other

Genetics clinics, staffed by genetics professionals, provide information for individuals and families regarding the natural history, treatment, mode of inheritance, and genetic risks to other family members as well as information about available consumer-oriented resources. See the GeneTests Clinic Directory.

Support groups have been established for individuals and families to provide information, support, and contact with other affected individuals. The Resources section may include disease-specific and/or umbrella support organizations.

Genetics clinics are a source of information for individuals and families regarding the natural history, treatment, mode of inheritance, and genetic risks to other family members as well as information about available consumer-oriented resources. See the GeneTests Clinic Directory.

Support groups have been established for individuals and families to provide information, support, and contact with other affected individuals. The Resources section (below) may include disease-specific and/or umbrella support organizations.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members. This section is not meant to address all personal, cultural, or ethical issues that individuals may face or to substitute for consultation with a genetics professional. To find a genetics or prenatal diagnosis clinic, see the GeneTests Clinic Directory.

Mode of Inheritance

Lenz microphthalmia syndrome is inherited in an X-linked recessive manner.

Risk to Family Members

This section is written from the perspective that molecular genetic testing for this disorder is available on a research basis only and results should not be used for clinical purposes. This perspective may not apply to families using custom mutation analysis. —ED.

Parents of a proband

- The father of an affected male will not have the disease or be a carrier of the mutation.
- In a family with more than one affected male, the mother of an affected male is an obligate carrier.
- If only one male in the family is affected, the mother may be a carrier or the affected male may have a *de novo* gene mutation and, thus, the mother is not a carrier. The frequency of *de novo* mutations is not known.

Sibs of a proband

- The risk to sibs depends upon the carrier status of the mother.
- If the mother is a carrier, the chance of transmitting the mutation in each pregnancy is 50%. Male sibs who inherit the mutation will be affected; female sibs who inherit the mutation will be carriers and will not be affected.

- If the mother is not a carrier, the risk to sibs is low but greater than that of the general population because of the possibility of germline mosaicism.

Offspring of a proband. The majority of males with Lenz microphthalmia syndrome do not have children, possibly as a result of infertility or decreased reproductive fitness secondary to cognitive impairment. Males who are capable of reproducing pass the disease-causing mutation to all of their daughters and none of their sons.

Other family members. The proband's maternal aunts and their offspring may be at risk of being carriers or being affected (depending upon their gender, family relationship, and the carrier status of the proband's mother).

Carrier Detection

Carrier testing using molecular genetic techniques is not offered because it is not clinically available.

Related Genetic Counseling Issues

Family planning. The optimal time for discussion of genetic risk is before pregnancy.

DNA banking. DNA banking is the storage of DNA (typically extracted from white blood cells) for possible future use. Because it is likely that testing methodology and our understanding of genes, mutations, and diseases will improve in the future, consideration should be given to banking DNA of affected individuals. DNA banking is particularly relevant in situations in which molecular genetic testing is available on a research basis only. See DNA Banking for a list of laboratories offering this service.

Prenatal Testing

Ultrasound examination. Prenatal ultrasound examination at 18 weeks' gestation can be offered to mothers of an affected male and to female sibs of a proband of indeterminate carrier status to evaluate fetal renal development. No data exist regarding the effectiveness of screening for other malformations in fetuses at risk for LMS.

Note: Gestational age is expressed as menstrual weeks calculated either from the first day of the last normal menstrual period or by ultrasound measurements.

Molecular genetic testing. No laboratories offering molecular genetic testing for prenatal diagnosis of Lenz microphthalmia syndrome are listed in the GeneTests Laboratory Directory. However, prenatal testing may be available for families in which the disease-causing mutation has been identified. For laboratories offering custom prenatal testing, see Testing.

Preimplantation genetic diagnosis (PGD) may be available for families in which the disease-causing mutation has been identified. For laboratories offering PGD, see Testing.

Molecular Genetics

Information in the Molecular Genetics tables is current as of initial posting or most recent update. —ED.

Table A. Molecular Genetics of Lenz Microphthalmia Syndrome

Locus Name	Gene Symbol	Chromosomal Locus	Protein Name
ANOP1	Unknown	Xq27-q28	Unknown
MAA2	*BCOR*	Xp11.4	BCL-6 corepressor

Data are compiled from the following standard references: Gene symbol from HUGO; chromosomal locus, locus name, critical region, complementation group from OMIM; protein name from Swiss-Prot.

Table B. OMIM Entries for Lenz Microphthalmia Syndrome

300166	MICROPHTHALMIA, SYNDROMIC 2; MCOPS2
300485	BCL6 COREPRESSOR; BCOR
301590	MICROPHTHALMIA, SYNDROMIC 4; MCOPS4
309800	MICROPHTHALMIA, SYNDROMIC 1; MCOPS1

Table C. Genomic Databases for Lenz Microphthalmia Syndrome

Locus Name	Gene Symbol	Entrez Gene	HGMD
ANOP1	Unknown	289 (MIM No. 301590)	
MAA2	*BCOR*	54880 (MIM No. 300485)	BCOR

For a description of the genomic databases listed, click here.

Normal allelic variants: The *BCOR* gene extends over approximately 55 kb and includes 15 exons. The reference cDNA for BCOR isoform 1 is 6182 bp (NM 017745). The open reading frame is 5163 bp. BCOR isoform 2 is 3676 bp (NM 020926). BCOR long isoform, alternatively spliced is 5810 bp (AY316592.1).

Pathologic allelic variants: One mutation has been reported in individuals with LMS (MAA2) 254C>T (p.Pro85Leu) [Ng et al 2004].

Normal gene product: *BCOR* isoform 1 encodes a protein of 1,721 AA. *BCOR* isoform 2 encodes a protein of 1,004 AA. *BCOR* long isoform, alternatively spliced encodes a protein of 1755 AA.

Abnormal gene product: The p.Pro85Leu mutation is expressed and results in perturbation of ocular and extraocular organ development. Truncated and abnormally spiced variants of BCOR have not been detected in individuals with OFCD and are hypothesized to be eliminated by nonsense-mediated mRNA decay.

Resources

GeneReviews provides information about selected national organizations and resources for the benefit of the reader. GeneReviews is not responsible for information provided by other organizations. Information that appears in the Resources section of a GeneReview is current as of initial posting or most recent update of the GeneReview. Search GeneTests*for this disorder and select* Resources *for the most up-to-date Resources information.*—ED.

International Children's Anophthalmia Network (ICAN)
c/o Center for Developmental Medicine and Genetics
5501 Old York Road
Genetics Levy 2 West
Philadelphia PA 19141

Phone: 800-580-4226; 215-456-8722
Fax: 215-456-2356
Email: ican@anophthalmia.org
www.anophthalmia.org

National Eye Institute
Low Vision

National Federation of the Blind (NFB)
1800 Johnson Street
Baltimore MD 21230
Phone: 410-659-9314
Fax: 410-685-5653
Email: nfb@nfb.org
www.nfb.org

References

Medical Genetic Searches: A specialized PubMed search designed for clinicians that is located on the PubMed Clinical Queries page. PubMed

Published Statements and Policies Regarding Genetic Testing

No specific guidelines regarding genetic testing for this disorder have been developed.

Literature Cited

Forrester S, Kovach MJ, Reynolds NM, Urban R, Kimonis V. Manifestations in four males with and an obligate carrier of the Lenz microphthalmia syndrome. Am J Med Genet. 2001;98:92–100. [PubMed: 11426460]

Goldberg MF, McKusick VA. X-linked colobomatous microphthalmos and other congenital anomalies. A disorder resembling Lenz's dysmorphogenetic syndrome. Am J Ophthalmol. 1971;71:1128–33. [PubMed: 4998085]

Graham CA, Redmond RM, Nevin NC. X-linked clinical anophthalmos. Localization of the gene to Xq27-Xq28. Ophthalmic Paediatr Genet. 1991;12:43–8. [PubMed: 1679229]

Horn D, Chyrek M, Kleier S, Luttgen S, Bolz H, Hinkel GK, Korenke GC, Riess A, Schell-Apacik C, Tinschert S, Wieczorek D, Gillessen-Kaesbach G, Kutsche K. Novel mutations in BCOR in three patients with oculo-facio-cardio-dental syndrome, but none in Lenz microphthalmia syndrome. Eur J Hum Genet [Epub ahead of. 2005;13:563–9. [PubMed: 15770227]

Lehman DM, Sponsel WE, Stratton RF, Mensah J, Macdonald JC, Johnson-Pais TL, Coon H, Reveles XT, Cody JD, Leach RJ. Genetic mapping of a novel X-linked recessive colobomatous microphthalmia. Am J Med Genet. 2001;101:114–9. [PubMed: 11391653]

Ng D, Hadley DW, Tifft CJ, Biesecker LG. Genetic heterogeneity of syndromic X-linked recessive microphthalmia-anophthalmia: is Lenz microphthalmia a single disorder? Am J Med Genet. 2002;110:308–14. [PubMed: 12116202]

Ng D, Thakker N, Corcoran CM, Donnai D, Perveen R, Schneider A, Hadley DW, Tifft C, Zhang L, Wilkie AO, van der Smagt JJ, Gorlin RJ, Burgess SM, Bardwell VJ, Black GC, Biesecker LG. Oculofaciocardiodental and Lenz microphthalmia syndromes result from distinct classes of mutations in BCOR. Nat Genet. 2004;36:411–6. [PubMed: 15004558]

Oberoi S, Winder AE, Johnston J, Vargervik K, Slavotinek AM. Case reports of oculofaciocardiodental syndrome with unusual dental findings. Am J Med Genet A. 2005;136:275–7. [PubMed: 15957158]

Chapter Notes

Revision History

- 27 July 2007 (cd) Revision: clinical testing for *BCOR* mutations no longer available

- 6 September 2006 (cd) Revision: FISH, mutation scanning, linkage analysis, and X-chromosome inactivation studies no longer clinically available for *BCOR*
- 23 June 2006 (ca) Comprehensive update posted to live Web site
- 12 April 2005 (dn) Revision: *BCOR* testing clinically available
- 13 May 2004 (me) Comprehensive update posted to live Web site
- 5 February 2004 (dn) Revision: Molecular Genetics
- 4 June 2002 (me) Review posted to live Web site
- 8 February 2002 (dn) Original submission