You May Be Your Patient's Best Hope for Diagnosing a Rare, Yet Treatable, Disease[1-3]

Early-onset bilateral cataracts are a hallmark symptom in ~85% of these patients[4]

BEHIND THE BLUR
Early-Onset Bilateral Cataracts

Diagnosing Cerebrotendinous Xanthomatosis (CTX) can be challenging[3]

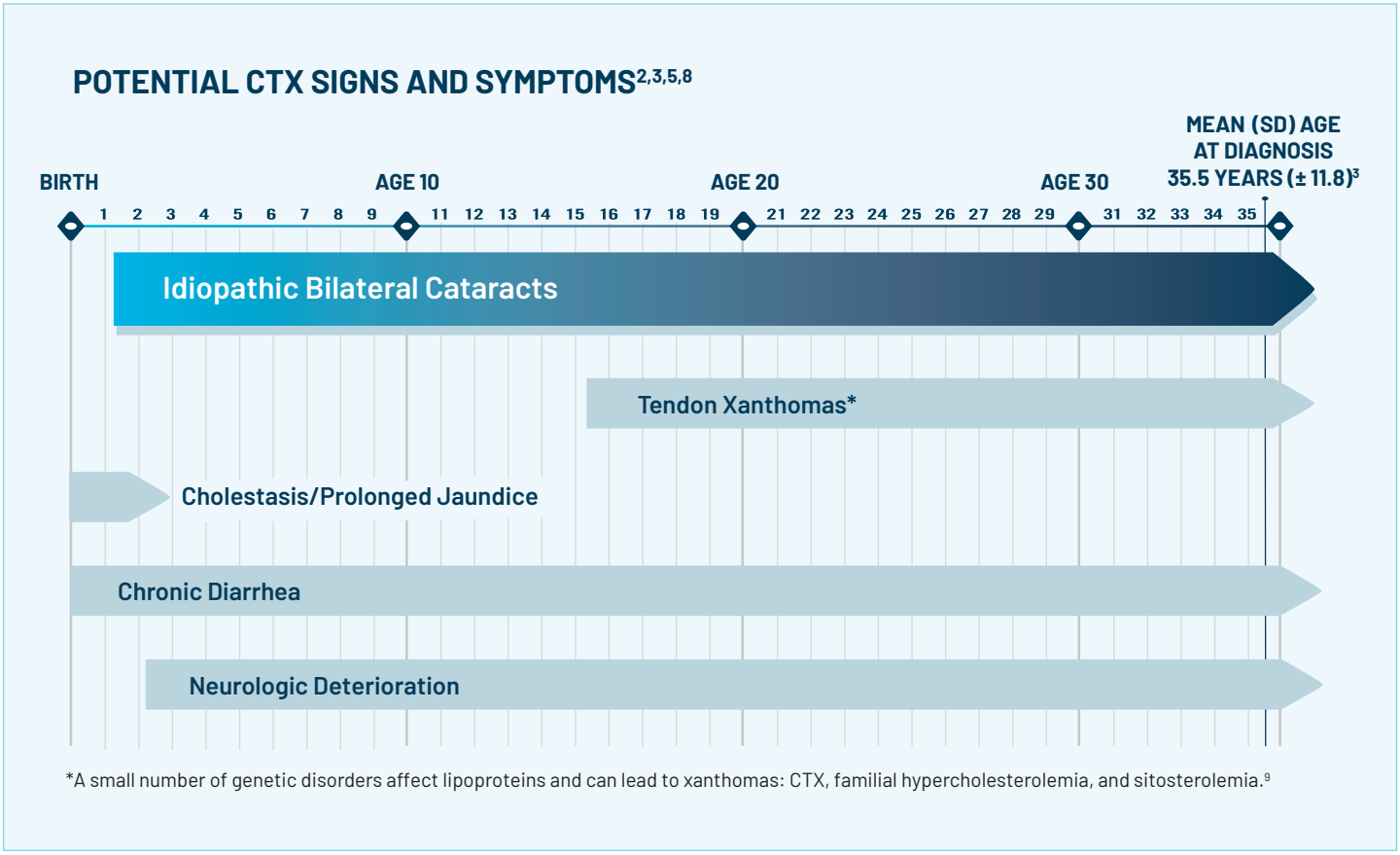
CTX diagnosis typically occurs 20-25 years after onset of signs and symptoms[3]

- CTX is a rare, genetic lipid storage disorder[3]
  - Excess bile acid precursors, such as cholestanol, accumulate in areas such as the lens of the eye, brain, and tendons[3,5,6]
  - Cataract morphology is often described as posterior subcapsular with fleck deposits[6]

Early-onset bilateral cataracts are a hallmark CTX symptom that may appear as early as childhood[3]

Yet mean age at CTX diagnosis is 35.5 years (± 11.8 years)[3]

Other CTX signs and symptoms are either nonspecific or most often occur after the first decade of life[2,3,5,7,8]



*A small number of genetic disorders affect lipoproteins and can lead to xanthomas: CTX, familial hypercholesterolemia, and sitosterolemia.[9]

Early-onset bilateral cataracts may be an important marker for identifying CTX in patients[10]

Up to a 500-fold higher CTX prevalence than in the general population[10,*]

~2 of every 100 patients with early-onset bilateral cataracts were diagnosed with CTX[10,*]

*Findings from a 26-site CTX prevalence study in a patient population diagnosed with early-onset idiopathic bilateral cataracts[10]

BEHIND THE BLUR

Early-Onset Bilateral Cataracts

A no-cost to patient genetic test is available to identify up to 66 causes of early-onset bilateral cataracts[11]

Genes included on the Early-Onset Bilateral Cataracts Genetic Panel*							
ABHD12	*ADAMTSL4*	*ALDH18A1*	*BCOR*	*BEST1*	*BFSP1*	*BFSP2*	*CHMP4B*
COL11A1	*COL18A1*	*COL2A1*	*COL4A1*	*CRYAA*	*CRYAB*	*CRYBA1*	*CRYBA2*
CRYBA4	*CRYBB1*	*CRYBB2*	*CRYGC*	*CRYGD*	*CRYGS*	***CYP27A1***	*DYNC1H1*
EPHA2	*ERCC2*	*FAM126A*	*FOXE3*	*FTL*	*FYCO1*	*FZD4*	*GALE*
GALK1	*GALT*	*GCNT2*	*GJA3*	*GJA8*	*GLA*	*HSF4*	*LEMD2*
LIM2	*LONP1*	*MAF*	*MIP*	*MIR184*	*MYH9*	*NACC1*	*NDP*
NF2	*NHS*	*OPA3*	*PAX6*	*PITX3*	*P3H2*	*RAB3GAP1*	*RDH11*
RECQL4	*SC5D*	*SIL1*	*SLC16A12*	*TFAP2A*	*TGM3*	*UNC45B*	*VIM*
WRN	*XYLT2*						

CTX is treatable. If positive for pathogenic mutations in CYP27A1, then refer patient for CTX management

- Specialties that manage CTX include neurologists and metabolic geneticists

***For a complete list of the defect/disorder/syndrome for all 66 genes, please refer to the accompanying insert.**

Behind the Blur

No-cost to patient genetic testing program for early-onset bilateral cataracts

BEHIND THE BLUR
Early-Onset Bilateral Cataracts

PROGRAM OVERVIEW

In partnership with PreventionGenetics, Retrophin offers a no-cost genetic testing program for qualifying patients to help identify the genetic cause of early-onset, often bilateral, cataracts through a 66-gene panel.

If you have a patient you suspect to have a genetic form of cataracts, they may be eligible for the no-cost genetic test.

HGNC APPROVED GENE SYMBOL	PHENOTYPE/DEFECT/DISORDER/SYNDROME
ABHD12	Polyneuropathy, hearing loss, ataxia, retinitis pigmentosa, and cataract
ADAMTSL4	Ectopia lentis et pupillae Ectopia lentis, isolated, autosomal recessive
ALDH18A1	Cutis laxa, autosomal dominant 3 Cutis laxa, autosomal recessive, type IIIA Spastic paraplegia 9A, autosomal dominant Spastic paraplegia 9B, autosomal recessive
BCOR	Microphthalmia, syndromic 2
BEST1	Bestrophinopathy, autosomal recessive Macular dystrophy, vitelliform Microcornea, rod-cone dystrophy, cataract, and posterior staphyloma Retinitis pigmentosa-50 Retinitis pigmentosa, concentric Vitreoretinochoroidopathy
BFSP1	Cataract 33, multiple types
BFSP2	Cataract 12, multiple types
CHMP4B	Cataract 31, multiple types
COL11A1	Deafness, autosomal dominant 37 {Lumbar disc herniation, susceptibility to} Fibrochondrogenesis 1 Marshall syndrome Stickler syndrome, type II
COL18A1	Glaucoma, primary closed-angle Knobloch syndrome, type 1
COL2A1	Epiphyseal dysplasia, multiple, with myopia and deafness Achondrogenesis, type II or hypochondrogenesis Avascular necrosis of the femoral head Czech dysplasia Kniest dysplasia Legg-Calve-Perthes disease Osteoarthritis with mild chondrodysplasia Platyspondylic skeletal dysplasia, Torrance type SED congenita SMED Strudwick type Spondyloepiphyseal dysplasia, Stanescu type Spondyloperipheral dysplasia Stickler sydrome, type I, nonsyndromic ocular Stickler syndrome, type I Vitreoretinopathy with phalangeal epiphyseal dysplasia

HGNC APPROVED GENE SYMBOL	PHENOTYPE/DEFECT/DISORDER/SYNDROME
COL4A1	Retinal arteries, tortuosity of {Hemorrhage, intracerebral, susceptibility to} Angiopathy, hereditary, with nephropathy, aneurysms, and muscle cramps Brain small vessel disease with or without ocular anomalies Microangiopathy and leukoencephalopathy, pontine, autosomal dominant
CRYAA	Cataract 9, multiple types
CRYAB	Cardiomyopathy, dilated, 1II Cataract 16, multiple types Myopathy, myofibrillar, 2 Myopathy, myofibrillar, fatal infantile hypertonic, alpha-B crystallin-related
CRYBA1	Cataract 10, multiple types
CRYBA2	Cataract 42
CRYBA4	Cataract 23
CRYBB1	Cataract 17, multiple types
CRYBB2	Cataract 3, multiple types
CRYGC	Cataract 2, multiple types
CRYGD	Cataract 4, multiple types
CRYGS	Cataract 20, multiple types
CYP27A1	Cerebrotendinous xanthomatosis
DYNC1H1	Charcot-Marie-Tooth disease, axonal, type 20 Mental retardation, autosomal dominant 13 Spinal muscular atrophy, lower extremity-predominant 1, AD
EPHA2	Cataract 6, multiple types
ERCC2	Cerebrooculofacioskeletal syndrome 2 Trichothiodystrophy 1, photosensitive Xeroderma pigmentosum, group D
FAM126A	Leukodystrophy, hypomyelinating, 5
FOXE3	{Aortic aneurysm, familial thoracic 11, susceptibility to} Anterior segment dysgenesis 2, multiple subtypes Cataract 34, multiple types

HGNC APPROVED GENE SYMBOL	PHENOTYPE/DEFECT/DISORDER/SYNDROME
FTL	Hyperferritinemia-cataract syndrome L-ferritin deficiency, dominant and recessive Neurodegeneration with brain iron accumulation 3
FYCO1	Cataract 18, autosomal recessive
FZD4	Exudative vitreoretinopathy 1 Retinopathy of prematurity
GALE	Galactose epimerase deficiency
GALK1	Galactokinase deficiency with cataracts
GALT	Galactosemia
GCNT2	[Blood group, Ii] Adult i phenotype without cataract Cataract 13 with adult i phenotype
GJA3	Cataract 14, multiple types
GJA8	Cataract 1, multiple types
GLA	Fabry disease Fabry disease, cardiac variant
HSF4	Cataract 5, multiple types
LEMD2	Cataract 46, juvenile-onset
LIM2	Cataract 19, multiple types
LONP1	CODAS syndrome
MAF	Ayme-Gripp syndrome Cataract 21, multiple types
MIP	Cataract 15, multiple types
MIR184	EDICT syndrome
MYH9	Deafness, autosomal dominant 17 Macrothrombocytopenia and granulocyte inclusions with or without nephritis or sensorineural hearing loss
NACC1	Neurodevelopmental disorder with epilepsy, cataracts, feeding difficulties, and delayed brain myelination
NDP	Exudative vitreoretinopathy 2, X-linked Norrie disease
NF2	Meningioma, NF2-related, somatic Neurofibromatosis, type 2 Schwannomatosis, somatic
NHS	Cataract 40, X-linked Nance-Horan syndrome
OPA3	3-methylglutaconic aciduria, type III Optic atrophy 3 with cataract
PAX6	Coloboma of optic nerve Coloboma, ocular Morning glory disc anomaly Aniridia Anterior segment dysgenesis 5, multiple subtypes Cataract with late-onset corneal dystrophy Foveal hypoplasia 1 Keratitis Optic nerve hypoplasia
PITX3	Anterior segment dysgenesis 1, multiple subtypes Cataract 11, multiple types Cataract 11, syndromic, autosomal recessive
P3H2	Myopia, high, with cataract and vitreoretinal degeneration
RAB3GAP1	Warburg micro syndrome 1
RDH11	Retinal dystrophy, juvenile cataracts, and short stature syndrome
RECQL4	Baller-Gerold syndrome RAPADILINO syndrome Rothmund-Thomson syndrome, type 2
SC5D	Lathosterolosis
SIL1	Marinesco-Sjogren syndrome
SLC16A12	Cataract 47, juvenile, with microcornea
TFAP2A	Branchiooculofacial syndrome
TGM3	Uncombable hair syndrome 2
UNC45B	Cataract 43
VIM	Cataract 30, pulverulent
WRN	Werner syndrome
XYLT2	{Pseudoxanthoma elasticum, modifier of severity of} Spondyloocular syndrome

Source: PreventionGenetics

For complete program details, please contact your Retrophin Clinical Account Manager or visit www.BehindTheBlur.com.

Retrophin®

You may be the key to diagnosing CTX earlier

Know the cause of early-onset bilateral cataracts so patients with CTX can be treated sooner[3,10]

- Earlier diagnosis and treatment of CTX can potentially lead to better outcomes[3,10]

Retrophin offers a no-cost Early-Onset Bilateral Cataracts Genetic Panel for qualified patients[11],*

- Retrophin, Inc. has partnered with PreventionGenetics, a College of American Pathologists–accredited laboratory†
- Flexibility of different genetic test samples: 1) Saliva, 2) Buccal swab, or 3) Blood
- Get results in ~3 weeks

To qualify, patients must meet all of the following criteria:

18 months to 35 years of age

+

Current or history of idiopathic bilateral cataracts ‡

+

Residence in United States

To order the no-cost to patient Early-Onset Bilateral Cataracts Genetic Panel, or for complete program details, please contact your Retrophin Clinical Account Manager or visit www.BehindTheBlur.com.

*Program may be cancelled or changed at any time.

†Note that Retrophin, Inc. cites the above-named external testing resource for information purposes only, and does not endorse or guarantee in any way the services or advice provided by them.

‡Not known to be due to infectious causes, trauma, etc.

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No actual patients are shown.

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