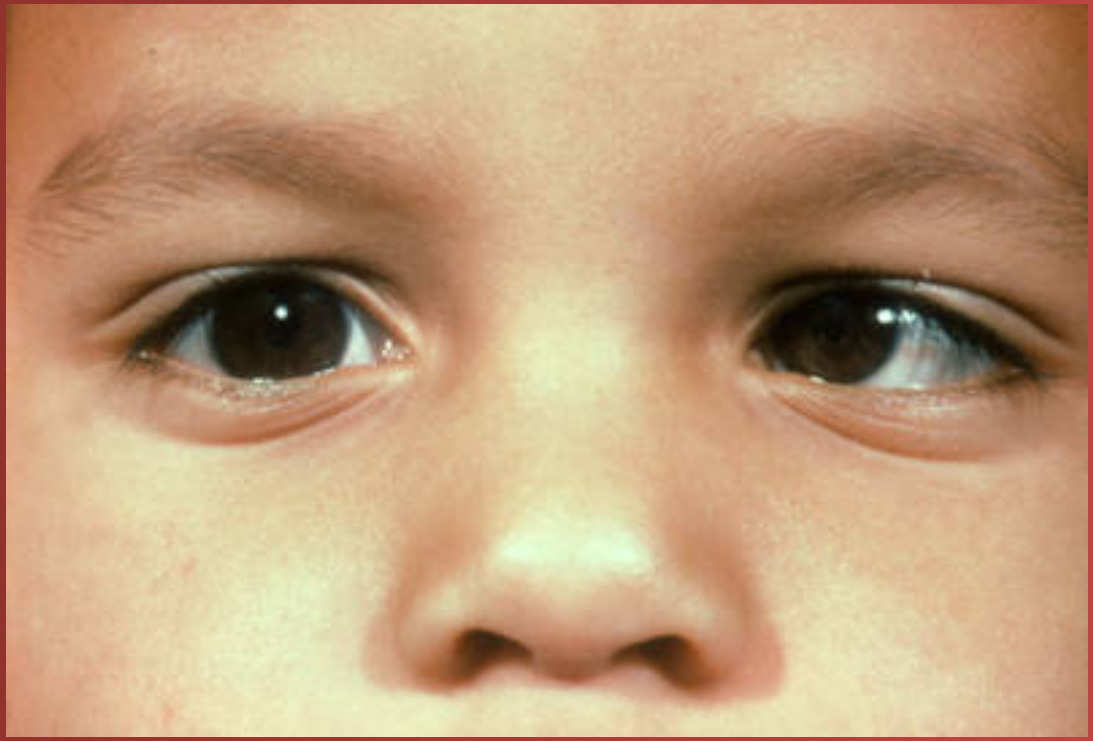
GENETICA Y ESTRABISMO



Optimized using
trial version
www.balesio.com

Importancia de la genética

- Conocimiento de la enfermedad (etiología, fisiopatogenia)
- Pronóstico
- Diagnóstico en casos dudosos
- Consejo genético
- Tratamiento

Optimized using
trial version
www.balesio.com

Table. Chromosomal Locations of Genes Associated With Glaucoma

Chromosome Location	Condition	Locus (Gene)	Inheritance Pattern
1q23	Early- and adult-onset POAG	*GLC1A* (*MYOC*)	Early-onset; AD Adult-onset; complex
1p36	Congenital glaucoma	*GLC3B*	AR
2p21	Congenital glaucoma	*GLC3A* (*CYP1B1*)	AR
2cen-2q13	Adult-onset POAG	*GLC1B*	AD
3q21-24	Adult-onset POAG	*GLC1C*	AD
4q25	Rieger syndrome	*RIEG1* (*PITX2*)	AD
5q22	Adult-onset POAG	*GLC1G* (*WDR36*)	AD; complex
6p25	Iridodysgenesis	*IRID1* (*FOXC1*)	AD
7q35	Adult-onset POAG	*GLC1F*	AD
7q35-q36	Pigment dispersion syndrome	*GPDS1*	AD
8q23	Adult-onset POAG	*GLC1D*	AD
9q22	Early-onset POAG	*GLC1J*	AD
9q34	Glaucoma associated with nail-patella syndrome	(*LMX1B*)	AD
10p15-p14	Adult-onset POAG; low-tension glaucoma	*GLC1E* (*OPTN*)	AD
11p	Nanophthalmos	*NNO1*	AD
11p13	Aniridia	*AN2* (*PAX6*)	AD
11q12	Nanophthalmos	*VMD2*	AD
11q23	Nanophthalmos	*MFRP*	AR
13q14	Rieger syndrome	*RIEG2*	AD
14q11	Adult-onset POAG	Locus pending	Complex
15q11-q13	Adult-onset POAG	*GLC1I*	Complex
[illegible]	Early-onset POAG	*GLC1K*	AD

autosomal dominant; AR, autosomal recessive; POAG, primary open-angle glaucoma.

Optimized using
trial version
www.balesio.com

Genetic etiologies of Glaucoma

Wiggs, J. L. Arch Ophthalmol 2007;125:30-37.

Table 1. Identified Myopia Loci as Approved by the HGNC

Myopia Locus	OMIM	Cytogenetic Location	Source	Myopia Severity Age at Onset
MYP1	310460	Xq28	84-86	High: −6.75 to −11.25 D Early: 1.5-5 y
MYP2	160700	18p11.31	87-89	High: −6 to −21 D Early: 6.8 y (average)
MYP3	603221	12q21-q23	80, 92	High: −6.25 to −15 D Early: 5.9 y (average)
MYP4	608367	7q36	94	High: −13.05 D (average)
MYP5	608474	17q21-q22	95	High: −5.5 to −50 D Early: 8.9 y (average)
MYP6	608908	22q12	101	Mild-moderate: −1.00 D or lower
MYP7	609256	11p13	9	−12.12 to +7.25 D
MYP8	609257	3q26	9	−12.12 to +7.25 D
MYP9	609258	4q12	9	−12.12 to +7.25 D
MYP10	609259	8p23	9, 102	−12.12 to +7.25 D
MYP11	609994	4q22-q27	98	High: −5 to −20 D Early: before school ag
MYP12	609995	2q37.1	96	High: −7.25 to −27 D Early: before 12 y
MYP13	300613	Xq23-q25	97	High: −6 to −20 D Early: before school ag

Abbreviations: D, diopters; HGNC, HUGO Gene Nomenclature Committee (http://www.gene.u /cgi-bin/nomenclature/searchgenes.pl); OMIM, Online Mendelian Inheritance in Man (http://ww .nih.gov/entrez/query.fcgi?db=OMIM).

Table 2. Identified Hyperopia/Nanophthalmos Loci or Genes as Approved by the HUGO Gene Nomenclature Committee

Cytogenetic Location	Source	Myopia Severity
11p	135	High: +7.75 to +22 D
11q23.3	136 137	
11q23.3	137	High: +8 to +25 D

MFRP, membrane-type frizzled-related protein; *NNO1*, autosomal dominant somal recessive nanophthalmos; OMIM, Online Mendelian Inheritance in n.gov/entrez/query.fcgi?db=OMIM).

Optimized using
trial version
www.balesio.com

Table 3. Identified Loci or Genes for Astigmatism/Keratoconus/Cornea Plana as Approved by the HUGO Gene Nomenclature Committee

Gene or Locus	OMIM	Cytogenetic Location	Source
VSX1	605020	20p11.2	144
KTCN2	608932	16q22.3-q23.1	145
KTCN3	608586	3p14-q13	146
KTCN4	609271	2p24	147
CNA1	121400	129	148, 152
CNA2	127300	12q22	152
KERA	603288	12q22	153-156

Abbreviations: *CNA*, cornea plana; *KERA*, keratocan; *KTCN*, keratoconus; OMIM, Online Mendelian Inheritance in Man (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM); *VSX1*, visual system homeobox 1.

Complex Trait Genetics of Refractive Error
Terri L. Young; Ravikanth Metlapally; Amanda E. Shay*c; Arh Ophthalmol.* 2007;125:38-48.

Table 1. Genes and Chromosomal Loci Associated With the Corneal Dystrophies

Corneal Dystrophy	Inheritance	Locus	Gene
Epithelial Dystrophies			
Epithelial basement membrane dystrophy (map-dot-fingerprint corneal dystrophy)	AD	Unknown	
Band-shaped, whorled microcystic corneal dystrophy (Lisch corneal dystrophy)	XL	Xp22.3	Unknown
Meesmann corneal dystrophy (Stocker-Holt dystrophy)	AD	12q13	*KRT3*
	AD	17q12	*KRT12*
Bowman Layer Dystrophies			
Corneal dystrophy of Bowman layer type I (Reis-Bücklers dystrophy)	AD	5q31	*TGFBI*
Corneal dystrophy of Bowman layer type II (Thiel-Behnke dystrophy [honeycomb-shaped dystrophy])	AD	5q31	*TGFBI*
	AD	10q23-10q24	Unknown
Grayson-Wilbrandt dystrophy	AD	Unknown	
Subepithelial mucinous corneal dystrophy	AD	Unknown	
Stromal Dystrophies			
Amyloidosis V (Lattice corneal dystrophy type II; Finnish-type amyloidosis [Meretoja syndrome])	AD	9q34	Gelsolin
Central cloudy dystrophy of François	AD	Unknown	
Central crystalline dystrophy of Schnyder	AD	1p34.1-1p36	Unknown
Central discoid corneal dystrophy	AD	Unknown	
Congenital hereditary stromal dystrophy	AD	12q22	Decorin
Fleck corneal dystrophy (François-Neetens speckled corneal dystrophy)	AD	2q35	*PIP5K3*
Gelatinous droplike corneal dystrophy	AR	1p32	*M1S1*
Lattice corneal dystrophy type III	AR	Unknown	
Macular corneal dystrophy type I	AR	16q22	*CHST6*
Macular corneal dystrophy type IA	AR	16q22	*CHST6*
Macular corneal dystrophy type II	AR	16q22	*CHST6*
Marginal crystalline corneoretinal dystrophy (Bietti dystrophy)	AR	4q35	*CYP4V2*
Posterior amorphous corneal dystrophy	AD	Unknown	
Pre-Descemet dystrophy with ichthyosis	XL	Xp22.32	*STS*
TGFBI dystrophies			
ttice corneal dystrophy	AD	5q31	*TGFBI*
strophy			
strophy type II			
ophy	AD	5q31	*TGFBI*
phy			
al dystrophy	AD	5q31	*TGFBI*
ystrophy type I			
dystrophy	AD	5q31	*TGFBI*
rophy type IIIA			
trophy type I/IIIA			
Lattice corneal dystrophy type IV			
Endothelial Dystrophies			
Classic Fuchs endothelial corneal dystrophy	AD	13q12	Unknown
	AD	18q21.2-18q21.32	Unknown
Variant Fuchs endothelial corneal dystrophy, early onset	AD	1p34.3-1p32	*COL8A2*
Congenital hereditary endothelial dystrophy type I	AD	20p13	Unknown
Congenital hereditary endothelial dystrophy type II	AR	20p11.2-20q11.2	*SLC4A11*
Posterior polymorphous corneal dystrophy	AD	20q11	Unknown
	AD	10p11-10q11	*TCF8*
X-linked endothelial corneal dystrophy	XL	Xq25	Unknown

Lattice corneal dystrophy type I/IIIA
Lattice corneal dystrophy type IV
Endothelial Dystrophies
Classic Fuchs endothelial corneal dystrophy AD 13q12 Unknown
AD 18q21.2-18q21.32 Unknown
Variant Fuchs endothelial corneal dystrophy, early onset AD 1p34.3-1p32 COL8A2
Congenital hereditary endothelial dystrophy type I AD 20p13 Unknown
Congenital hereditary endothelial dystrophy type II AR 20p11.2-20q11.2 SLC4A11
Posterior polymorphous corneal dystrophy AD 20q11 Unknown
AD 10p11-10q11 TCF8
X-linked endothelial corneal dystrophy XL Xq25 Unknown

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; TGFBI, transforming growth factor β–induced protein; XL, X-linked.

Elucidating the Molecular Genetic Basis of the Corneal Dystrophies: Are We There Yet?

Anthony J. Aldave; Baris Sonmez

Arch Ophthalmol. 2007;125:177-186.

Optimized using
trial version
www.balesio.com

Table. A Gene Map of Nonsyndromic Cataract

Chromosome	Locus/Gene (MIM)	DNA Change	Protein Change	Mode of Inheritance	Cataract Phenotype	Associated Phenotype
1p36	*CCV* (115665)			AD	Progressive lamellar	
	CTPP1 (116600)			AD	Posterior polar	
	[22]*			AD	Total	
1p32	*FOXE3* (601094)	c.943insC		AD	Anterior polar?	Anterior segment ocular dysgenesis
1p13.3	*GSTM1* (138350)	Null		C	Age-related (Japanese, Iranian)	
		None		C	Age-related cortical (Estonian)	
1q21.1	*GJA8* (600897)	c.G68C	p.R23T	AD	Nuclear	
		c.T131A	p.V44E	AD	Total	Microcornea, mild myopia
		c.G142A	p.E48K	AD	Zonular nuclear pulverulent	
		c.T191G	p.V64G	AD	Nuclear	
		c.C262T	p.P88S	AD	Zonular pulverulent	
		c.C262A	p.P88Q	AD	Lamellar pulverulent	
		c.G593A	p.R198Q	AD	Posterior subcapsular	Microcornea, mild myopia
		c.T741G	p.I247M	AD	Zonular pulverulent	
2p24-pter	[23]*			AD	Coralliform	
2p12	*CNNP* (607304)			AD	Nuclear	
2q33-q35	*CRYGC* (123680)	c.A13C	p.T5P	AD	Central zonular pulverulent	
		c.123-124ins5bp	p.C42fs	AD	Variable zonular pulverulent	
		c.C502T	p.R168W	AD	Lamellar	
	CRYGD (123690)	c.C43T	p.R14/15C	AD	Punctate	
				AD	Nuclear coralliform punctate	High myopia
		c.C70A	p.P23/24T	AD	Lamellar	
				AD	Cerulean	
				AD	Flaky silicalike nuclear	
				AD	Coral-like	
				AD	Fasciculiform	
		c.C109A	p.R36/37S	AD	Crystal-like	
				AD	Nuclear golden crystal	
		c.G176A	p.R58/59H	AD	Aculeiform	
		c.G470A	p.W156/157X	AD	Central nuclear	
	CCP (603212)			AD	Polymorphic	
3p21.3-p22.3	[24]*			AR	?	
3q21-q22	*BFSP2* (603212)	c.697_699delGAA	p.E233del	AD	Nuclear sutural stellate	
				AD	Y-sutural	Myopia
		c.859C>T	p.R287W	AD	Nuclear sutural lamellar	
3q25-qter	*CRYGS* (123730)	c.G53T	p.G18V	AD	Cortical progressive	
6p24	*GCNT2* (600429)	c.G983A	W328X	AR	?	Adult i blood group
6p12-q12	ARCC1 (609026)			C	Age-related cortical	
8q13.3	*EYA1* (601653)		p.R514G	AD	Nuclear type	Central corneal opacity, Peters anomaly
			p.G393S	AD	Nuclear type	BOR
9q13-q22	*CAAR* (605749)			AR	Adult-onset cortical pulverulent, progressive nuclear, and posterior subcapsular	
				AR	?Congenital	
10q25	*PITX3* (602669)	c.G38A	p.S13N	AD	Total	
		c.650delG		AD	Progressive posterior polar	
		c.656-657ins17bp		AD	Anterior cortical	ASMD, optic nerve defects
				AD	Posterior polar	ASMD
				AD	Posterior polar	ASMD
				AD	Progressive posterior polar	
				AD	Progressive posterior polar	
				AD	Posterior polar	
11p13	*PAX6* (607108)	c.C1058G	S353X	AD?	Lamellar anterior capsular, posterior subcapsular	Corneal dystrophy
		1a-3T>C		AD?	Cortical equatorial, progressive posterior polar	Peripheral corneal opacity, glaucoma, nystagmus
		8G	p.R120G	AD	"Discrete"	Myopathy
		8A	p.D140N	AD	Lamellar	
		delA	p.K150fs	AD	Posterior polar	
		1G	p.E134G	AD	Lamellar sutural	
		3G	p.T138R	AD	Progressive punctate polymorphic	
		delG	p.G213fs	AD	Punctate	
		A	p.V28M	AD	Variable total	
		A	p.F32L	AD	Nuclear pulverulent	
		4C	p.W45S	AD	Nuclear	
		6T	p.P59L	AD	Nuclear punctate	
		8G	p.N63S	AD	Variable pulverulent	
		c.G226A	p.R76H	AD	Nuclear lamellar pulverulent	
		c.C226G	p.R76G	AD	Total	
		c.C560T	p.P187L	AD	Zonular pulverulent	
		c.A563C	p.N188T	AD	Nuclear pulverulent	
		c.1137insC	p.S380fs	AD	Punctate	
14q24.3	*CHX10* (142993)	c.G599A/C	p.R200Q/P	AR	?	Microphthalmia, iris coloboma, dislocated lens
		c.C96A	p.F32L	AD	Nuclear pulverulent	
		c.G134C	p.W45S	AD	Nuclear	
		c.C176T	p.P59L	AD	Nuclear punctate	
		c.A188G	p.N63S	AD	Variable pulverulent	
		c.G226A	p.R76H	AD	Nuclear lamellar pulverulent	
		c.C226G	p.R76G	AD	Total	
		c.C560T	p.P187L	AD	Zonular pulverulent	
		c.A563C	p.N188T	AD	Nuclear pulverulent	
		c.1137insC	p.S380fs	AD	Punctate	
14q24.3	*CHX10* (142993)	c.G599A/C	p.R200Q/P	AR	?	Microphthalmia, iris coloboma, dislocated lens
15q21-q22	*CCSSO* (605728)			AD	Central saccular sutural	
16q22.12	*HSF4* (602438)	c.C59A	p.A20D	AD	?	
		c.A559G	p.I87V	AD	Cortical lamellar	
		c.T344C	p.L115P	AD	Lamellar	
		c.C358T	p.R120C	AD	Zonular stellate, anterior polar (Marner)	
		c.G524C	p.R175/176P	AR	Nuclear and cortical	
		c.595-599del5bp		AR	?	
		g.IVS12 + 4A>G		AR	Total	
16q22-q23	*MAF* (177075)	t(5;16)			Cortical pulverulent sutural, progressive posterior subcapsular	Peters anomaly
		c.G863C	p.R288P	AD	Cortical (lamellar) nuclear pulverulent	Microcornea, iris coloboma
17p13-p12	*CTAA2* (601202)			AD	Anterior polar	
17q11.2-q12	*CRYBA3/A1* (12361	g.IVS3 + 1G>A		AD	Zonular sutural	
				AD	Sutural nuclear cortical	
		g.IVS3 + 1G>C		AD	Pulverulent nuclear sutural	
		c.271-273del3bp	p.G91del	AD	Nuclear	
				AD	Nuclear suture-sparing	
				AD	Lamellar	
17q24	*GALK1* (604313)	c.C293T	p.A198V	?	Age-related (Asian)	
17q24	*CCA1* (115660)			AD	Cerulean	
19q13	[25]*			AR	Nuclear	
19q13.4	*FTL* (134790)	IRE†		AD	Nuclear cortical breadcrumblike	Hyperferritinemia-cataract syndrome
19q13.4	*LIM2* (154045)	c.T313G	p.F105V	AR	Pulverulent cortical sutural	
20p12-q12	*CTPP3* (605387)			AD	Posterior polar	
21q22.3	*CRYAA* (123580)	c.G27A	p.W9X	AR	?	
		c.C145T	p.R49C	AD	Central nuclear	
		c.C346T	p.R116C	AD	Zonular central nuclear, cortical, posterior subcapsular	Microcornea, microphthalmia
				AD	Fan-shaped	Microcornea
22q11.2	*CRYBB1* (600929)	c.G658T	p.G220X	AD	Central sutural pulverulent	
		c.T757C	p.X253R	AD	Nuclear cortical riders	Microcornea
	CRYBB (123620)	c.C463T	p.Q155X	AD	Cerulean	
				AD	Central zonular pulverulent	
				AD	Sutural cerulean	
				AD	Progressive polymorphic	
		c.G453T	p.W151C	AD	Central nuclear	
	CRYBB3 (123630)	c.G493C	p.G165R	AR	Nuclear cortical riders	
	CRYBA4 (123631)	c.T242C	p.L69P	AD	Congenital lamellar	Microphthalmia
Xp22	*CXN* (*NHS*?) (30045			XL	Fan-shaped nuclear	Cardiac anomalies

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; ASMD, anterior segment mesenchymal dysgenesis; BOR, branchiootorenal dysplasia syndrome; bp, base pair; C, complex; fs, frameshift; IRE, iron response element; MIM, Mendelian Inheritance in Man number; XL, X-linked; ?, morphology of the cataract is in doubt.

*This cataract is not listed in Online MIM and thus is independently referenced.

†Mutations located in the 5′ IRE.

Optimized using
trial version
www.balesio.com

Genetic Origins of Cataract

Alan Shiels; J. Fielding Hejtmancik

Arch Ophthalmol. 2007;125:165-173.

Table 2. Genes and Mapped Loci Causing Nonsyndromic, Nonsystemic Retinitis Pigmentosa*

Symbol	Location	Protein	Other Diseases
		Autosomal Dominant RP	
CA4	17q23.2	Carbonic anhydrase IV	None
CRX	19q13.32	Cone-rod homeobox	Recessive LCA, dominant LCA, dominant CORD
FSCN2	17q25.3	Fascin homolog 2, actin-bundling protein, retinal	None
GUCA1B	6p21.1	Guanylate cyclase activator 1B (retina)	Dominant MD
IMPDH1	7q32.1	IMP (inosine monophosphate) dehydrogenase 1	Dominant LCA
NRL	14q11.2	Neural retina leucine zipper	Recessive RP
PRPF3	1q21.2	PRP3 pre-mRNA processing factor 3 homolog (*Saccharomyces cerevisiae*)	None
PRPF8	17p13.3	PRP8 pre-mRNA processing factor 8 homolog (*S cerevisiae*)	None
PRPF31	19q13.42	PRP31 pre-mRNA processing factor 31 homolog (*S cerevisiae*)	None
RDS	6p21.2	Retinal degeneration, slow (peripherin 2)	Digenic RP with retinal outer segment membrane protein 1, dominant MD
RHO	3q22.1	Rhodopsin	Recessive RP, dominant CSNB
ROM1	11q12.3	Retinal outer segment membrane protein 1	Digenic RP with retinal degeneration, slow
RP1	8q12.1	RP-1 protein	Recessive RP
RP9	7p14.3	RP-9 (autosomal dominant)	None
RP31	9p22-p13	Unknown	None
RP33	2cen-q12.1	Unknown	None
SEMA4A	1q22	Sema domain, immunoglobulin domain (Ig), transmembrane domain (TM), and short cytoplasmic domain (semiphorin) 4A	Dominant CORD
		Autosomal Recessive RP	
ABCA4	1p22.1	ATP-binding cassette, subfamily A (ABC1), member 4	Recessive MD, recessive CORD
CERKL	2q31.3	Ceramide kinase–like protein	None
CNGA1	4p12	Cyclic nucleotide gated channel α1	None
CNGB1	16q13	Cyclic nucleotide gated channel β1	None
CRB1	1q31.3	Crumbs homolog 1	Recessive LCA
LRAT	4q32.1	Lecithin retinol acyltransferase	Recessive LCA
MERTK	2q13	C-mer proto-oncogene tyrosine kinase	None
NR2E3	15q23	Nuclear receptor subfamily 2, group E, member 3	Recessive enhanced S-cone syndrome
NRL	14q11.2	Neural retina leucine zipper	Dominant RP
PRCD	17q25.1	Progressive rod-cone degeneration gene	None
PDE6A	5q33.1	Phosphodiesterase 6A, cGMP-specific, rod, α	None
		Phosphodiesterase 6B, cGMP-specific, rod, β	Dominant CSNB
		Retinal G protein–coupled receptor	Dominant choroidal sclerosis
		Rhodopsin	Dominant RP
		Retinaldehyde-binding protein 1	Recessive Bothnia dystrophy
		RP-1 protein	Dominant RP
		Unknown	None
		Unknown	None
		Unknown	None
		Unknown	None
		Unknown	None
		RPE-specific 65-kd protein	Recessive LCA
		S-antigen; retina and pineal gland (arrestin)	Recessive Oguchi disease
TULP1	6p21.31	Tubby-like protein 1	Recessive LCA
USH2A	1q41	Usher syndrome 2A	Recessive Usher syndrome
		Autosomal Recessive LCA	
AIPL1	17p13.2	Arylhydrocarbon-interacting receptor protein-like 1	Dominant CORD
CEP290	12q21.32	Centrosomal 290-kd protein	Recessive Senior-Loken syndrome, recessive Joubert syndrome
CRB1	1q31.3	Crumbs homolog 1	Recessive RP
CRX	19q13.32	Cone-rod homeobox	Dominant CORD, dominant LCA, dominant RP
GUCY2D	17p13.1	Guanylate cyclase 2D, membrane (retina-specific)	Dominant CORD
LRAT	4q32.1	Lecithin retinol acyltransferase	Recessive RP
LCA3	14q24	Unknown	None
LCA5	6q11-q16	Unknown	None
LCA9	1p36	Unknown	None
RDH12	14q24.1	Retinol dehydrogenase 12	None
RPE65	1p31.2	RPE-specific 65-kd protein	Recessive RP
RPGRIP1	14q11.2	RP GTPase regulator interacting protein 1	None
TULP1	6p21.31	Tubby-like protein 1	Recessive RP
		Autosomal Dominant LCA	
CRX	19q13.32	Cone-rod homeobox	Dominant CORD, recessive LCA, dominant RP
IMPDH1	7q32.1	IMP (inosine monophosphate) dehydrogenase 1	Dominant RP
		X-Linked RP	
RP2	Xp11.23	RP-2 protein	None
RP6	Xp21.3-p21.2	Unknown	None
RP23	Xp22	Unknown	None
RP24	Xq26-q27	Unknown	None
RP34	Xq28-qter	Unknown	None
RPGR	Xp11.4	RP GTPase regulator	X-linked COD, X-linked CSNB

Abbreviations: ATP, adenosine triphosphate; cGMP, cyclic guanosine monophosphate; COD, cone dystrophy; CORD, cone-rod dystrophy; CSNB, congenital stationary night blindness; GTPase, guanosine triphosphatase; LCA, Leber congenital amaurosis; MD, macular dystrophy; mRNA, messenger RNA; RP, retinitis pigmentosa; RPE, retinal pigment epithelium.

*References are in RetNet (http://www.sph.uth.tmc.edu/RetNet/).

Optimized using
trial version
www.balesio.com

Retinosis pigmentaria no sindrómica

Daiger, S. P. et al. Arch Ophthalmol 2007;125:151-158.

Enfermedades retinianas

D.Sorsby	HAD	TIMP3
D.Stargardt	HAD, HAR	ELOVL4, ABCA4
Usher	HAR	USH1B
Retinoblastoma	HAD	RB1
D. En patrón	HAD	RDS
E.Norrie	Ligada a X	NDP
Malattia levetinese	HAD	EFEMP1
E.Best	HAD	VMD2
conos	HAD	CRX
det-Bield	HAR	BBS1-11
osquisis cong	Ligada a X	RS1

Optimized using
trial version
www.balesio.com

Otras

Atrofia óptica dominante	HAD	OPA1
Amaurosis cong de Leber	HAR	AIPL1,CRB1,CRX GUCY2D,RDH12, RPE65
Neuropatía óptica de Leber	Mitocondrial	ND1, 4 y 6
Facomatosis (NF..)		
iomas (Gorlin)	HAD	9q 22.3-q31
Hipple Lindau	HAD	VHL
omes sistémicos		

Optimized using
trial version
www.balesio.com

Patogenia del estrabismo

- Origen sensorial
  - Deprivación sensorial (catarata,etc)
  - Funcionales
    - Pérdida de fijación (nistagmus)
    - Refraccionales
    - Incomitancias lejos-cerca, etc
- Estrabismos concomitantes (origen motor)
- Origen motor
  - Miogénico (parálisis, fibrosis…)
  - Neurogénico (periférico o central)

Optimized using
trial version
www.balesio.com

Patogenia del estrabismo

- Origen sensorial
  - Deprivación sensorial (catarata,etc)
  - Funcionales
    - Pérdida de fijación (nistagmus)
    - Refraccionales
    - Incomitancias lejos-cerca, etc
- Estrabismos concomitantes (origen motor)
- Origen motor
  - Miogénico (parálisis, fibrosis…)
  - Neurogénico (periférico o central)

Optimized using
trial version
www.balesio.com

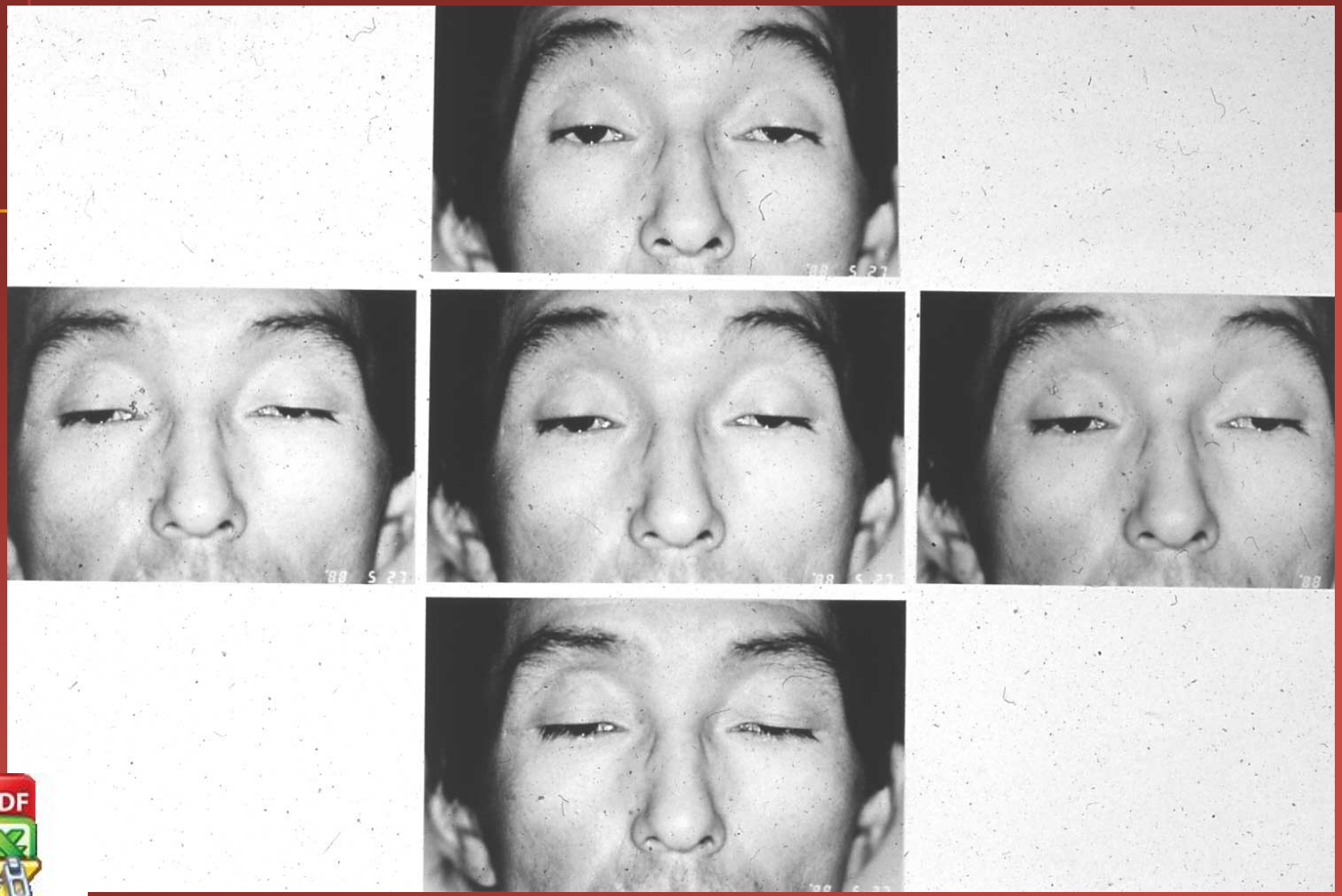
Estrabismos incomitantes

- OECP: delecciones (esporádica) o mutaciones puntuales en ADNmitocondrial

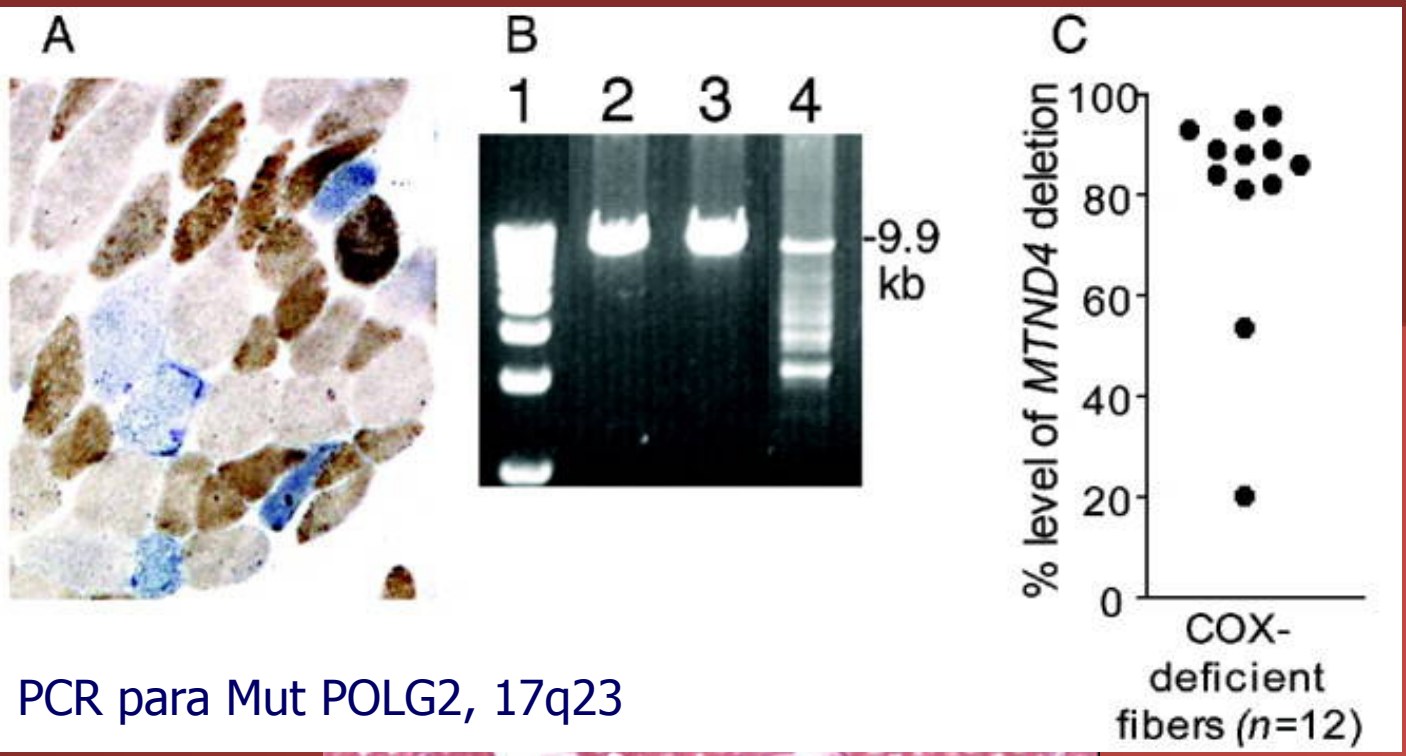
Gen	Proteína
ANT1	Translocador de adenina 1
POLG	Gamma polimerasa
C10orf2	Twinkle helicase

Optimized using
trial version
www.balesio.com

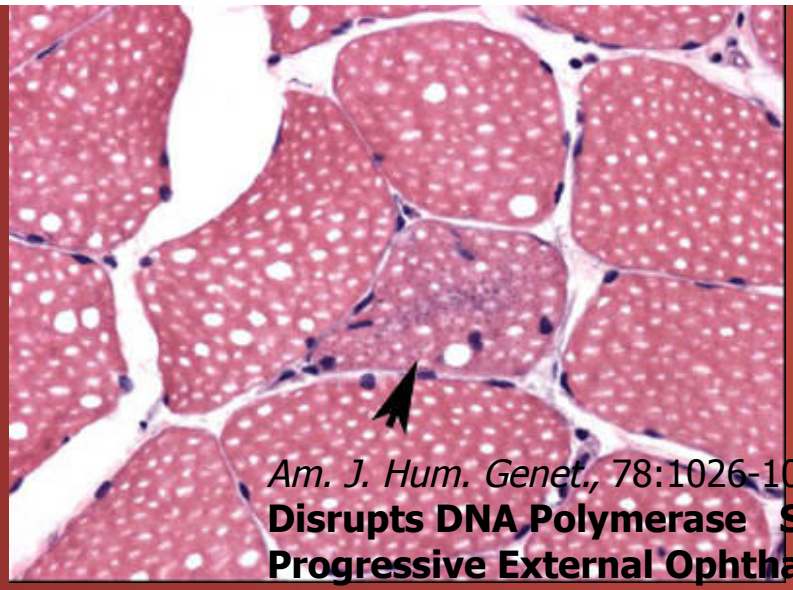
Michaelides M, Moore AT; The genetics of strabismus, Journal of Medical genetics, 2004; 41: 641-646



Optimized using
trial version
www.balesio.com



PCR para Mut POLG2, 17q23



Am. J. Hum. Genet., 78:1026-1034, 2006; **Mutant *POLG2* Disrupts DNA Polymerase Subunits and Causes Progressive External Ophthalmoplegia**; MJ. Longley, S Clark

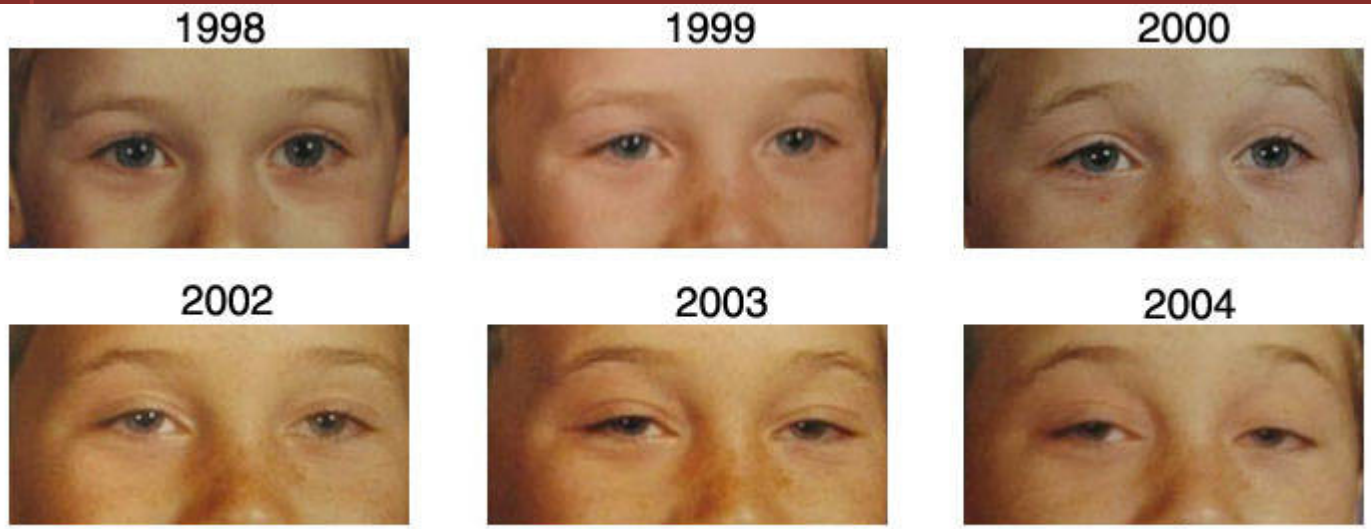
Optimized using
trial version
www.balesio.com

Estrabismos incomitantes

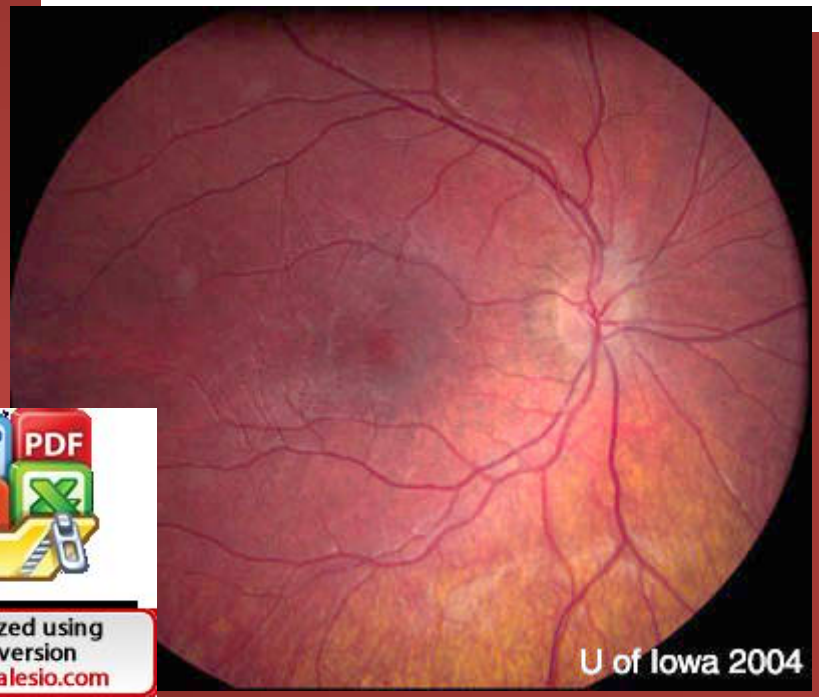
- Sd. Kearns-Sayre
  - RPigmentaria, Oftalmoplejia externa progresiva, Bloqueo cardíaco
  - Delecciones y mut.esporádicas
  - Mut. Puntuales (raras): A3243G (misma mut que en MELAS y MIDD)

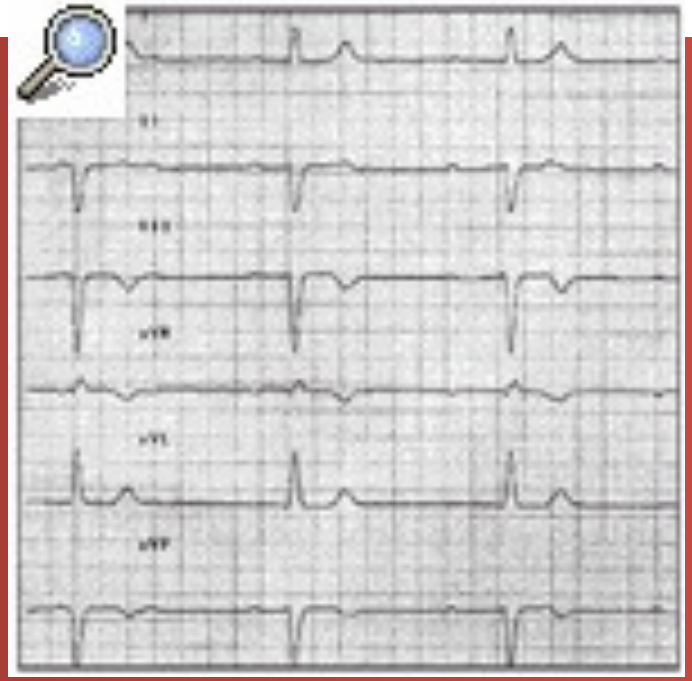
Optimized using
trial version
www.balesio.com

Michaelides M, Moore AT; The genetics of strabismus, Journal of Medical genetics, 2004; 41: 641-646



Erin O'Malley, MD





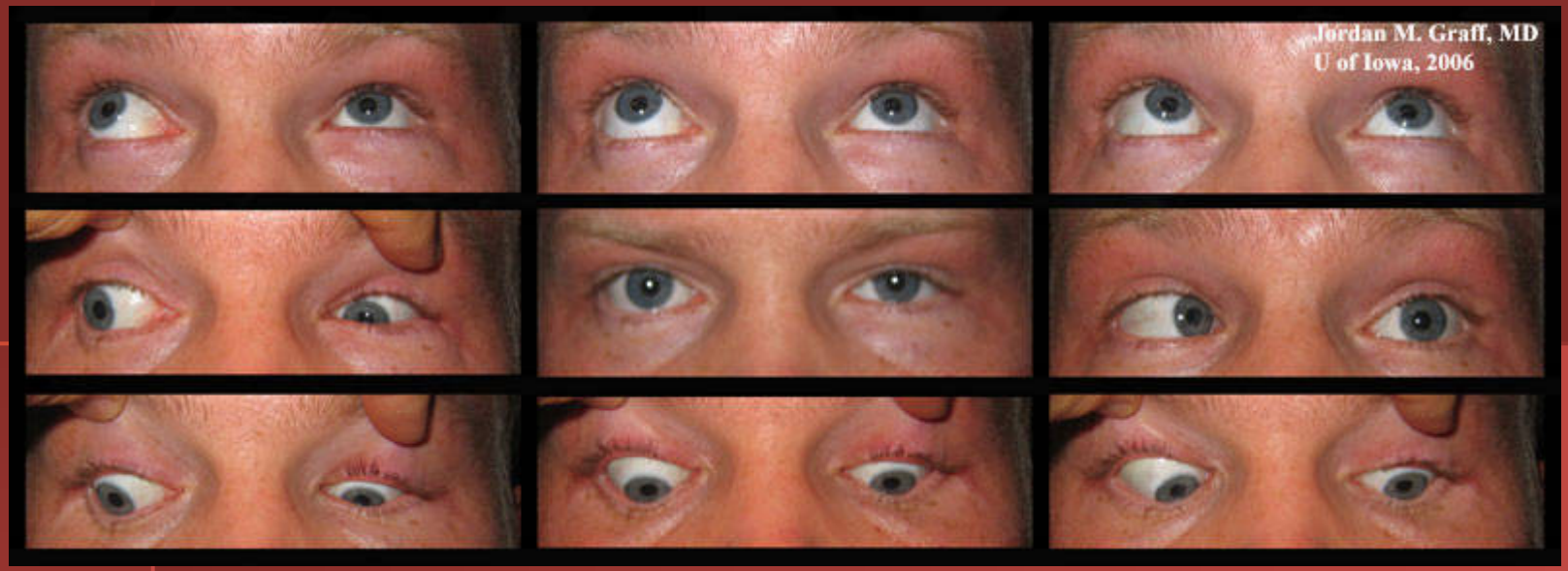
Optimized using
trial version
www.balesio.com

Duane

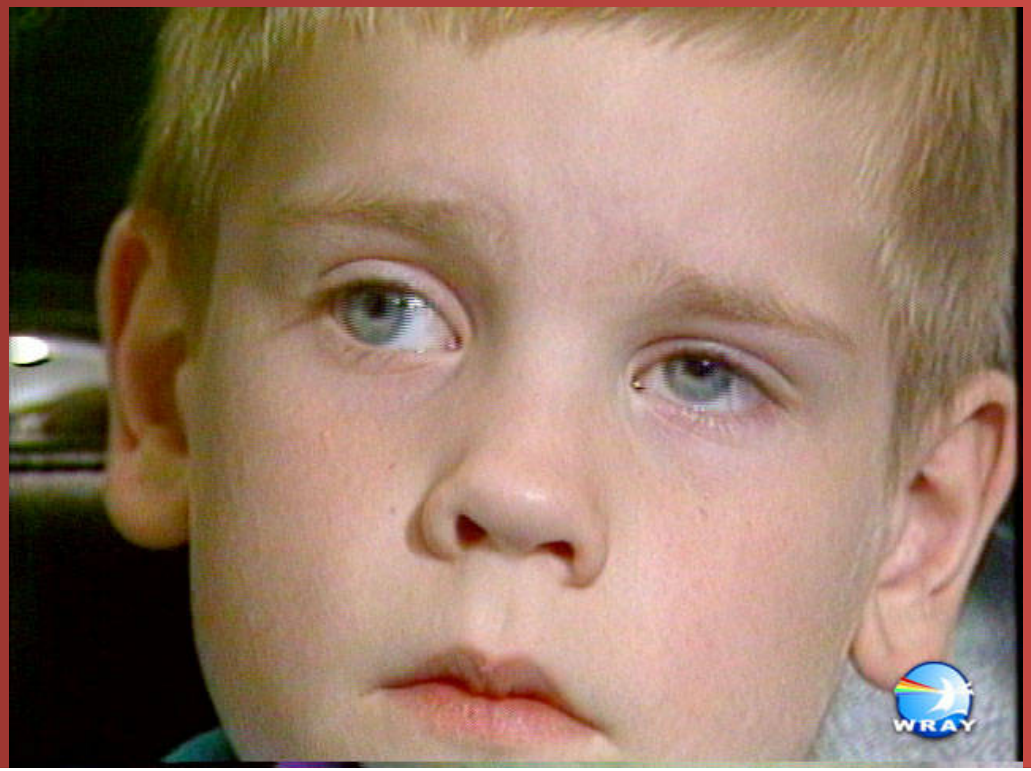
- 5% de estrabismos
- Varios tipos
- Aplasia/hipoplasia nerviosa implica atrofia y fibrosis del músculo denervado (2ª)
- Generalmente, núcleo del VI par (a veces incluso el nervio periférico)
- H.A.D. (crom 2q31, gen DURS1)
- En estudio: 8q13, 4q, 22q
- Sd. Okihiro (Duane+sordera+anomalías acrales): 20q13 (gen SALL4, metabolismo del Zn)

Optimized using
trial version
www.balesio.com

Hotchkiss MG, ;Miller NR; Arch Ophthalmol. 1980 May;98(5):870-4. Bilateral Duane's retraction syndrome. A clinical-pathologic case report.

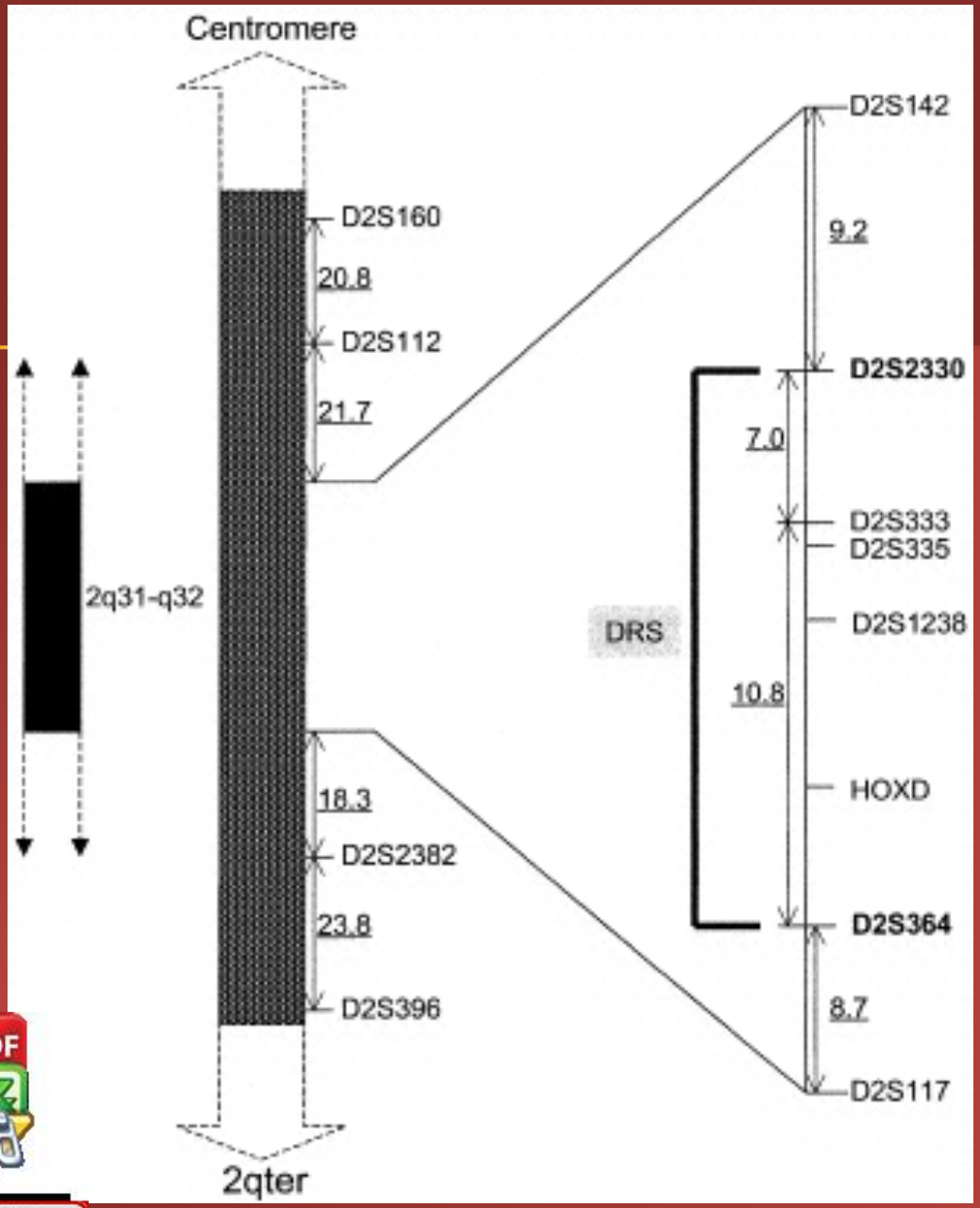


Tipo III



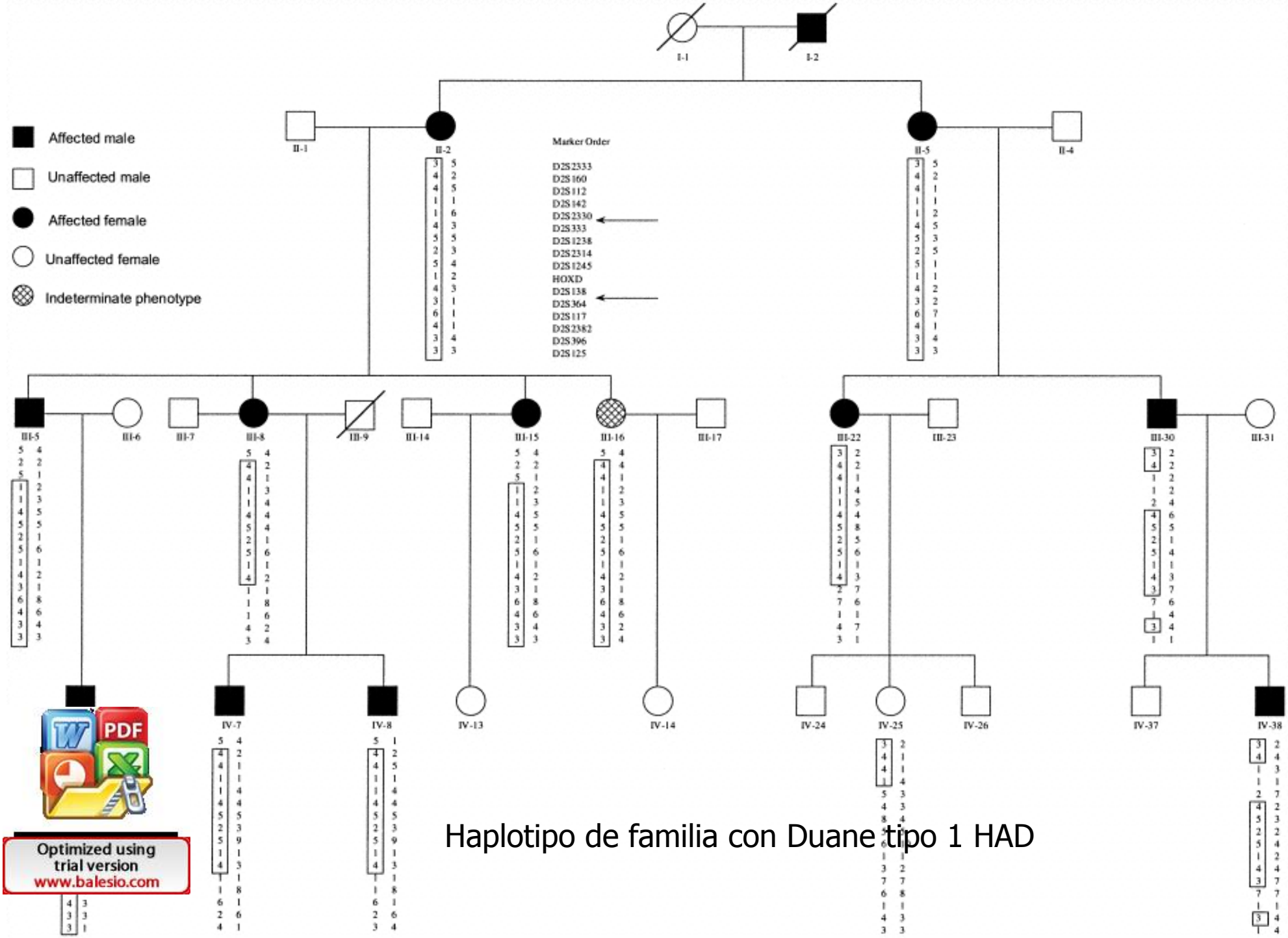
Tipo II

Optimized using
trial version
www.balesio.com



Optimized using
trial version
www.balesio.com

Am. J. Hum. Genet., 65:1639-1646, 1999; **Localization of a Gene for Duane Retraction Syndrome to Chromosome 2q31** Binoy Appukuttan, Elizabeth Gillanders

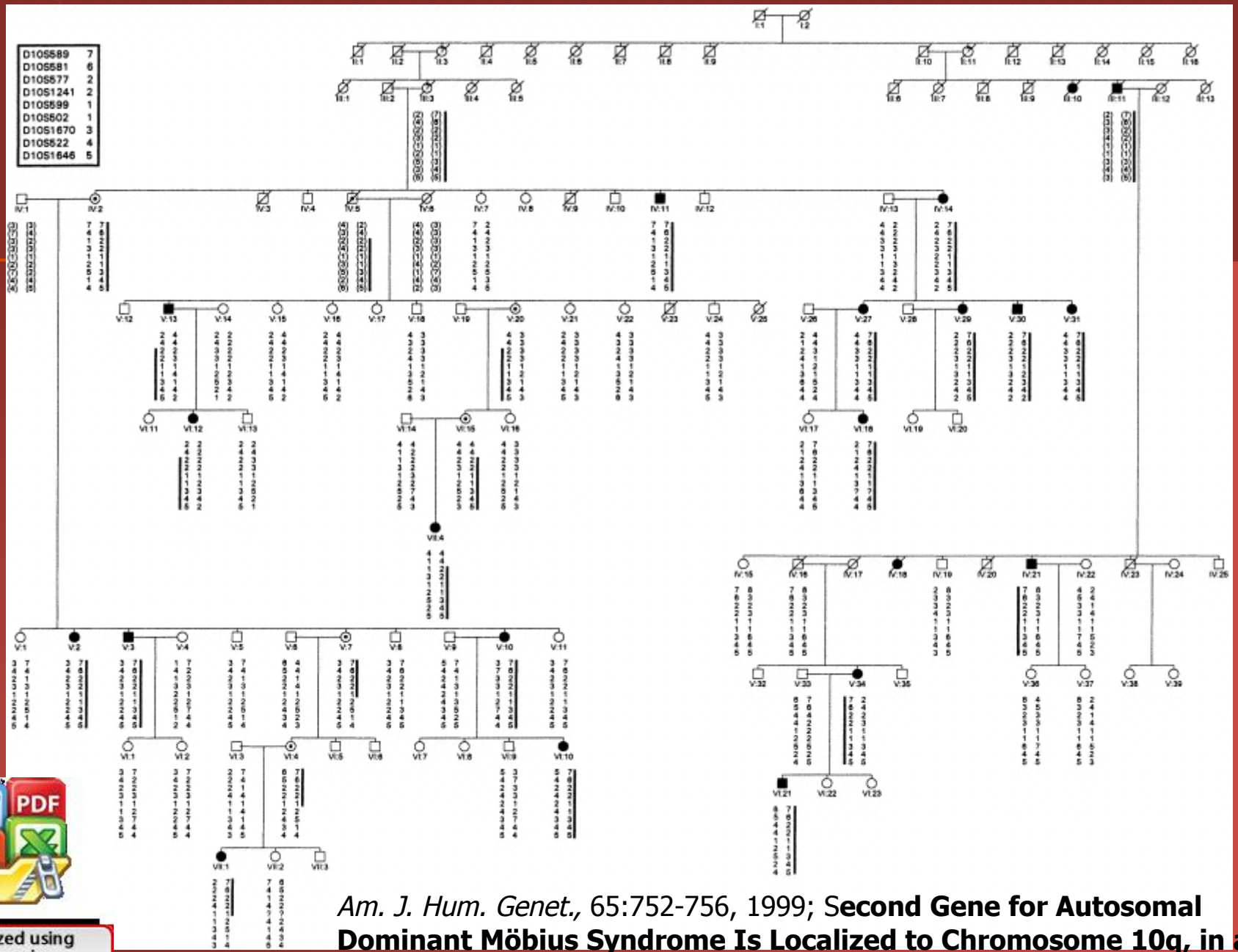


Haplotipo de familia con Duane tipo 1 HAD

- Moebius:
  - Esporádico generalmente
  - H.A.D.: 3q23 (gen SOX14)
  - Hipoplasia de núcleos/nervios VI, VII y XII

Optimized using
trial version
www.balesio.com

drome with Poland anomaly; Stritzke A, linger G Neonatal Intensive Care Unit, rau, Switzerland; December 2005; Swiss Society of Neonatology



Am. J. Hum. Genet., 65:752-756, 1999; S**econd Gene for Autosomal Dominant Möbius Syndrome Is Localized to Chromosome 10q, in a Dutch Family** H. T Verzijl, B. van den Helm

Optimized using
trial version
www.balesio.com

- Fibrosis congénita de músc extraoculares

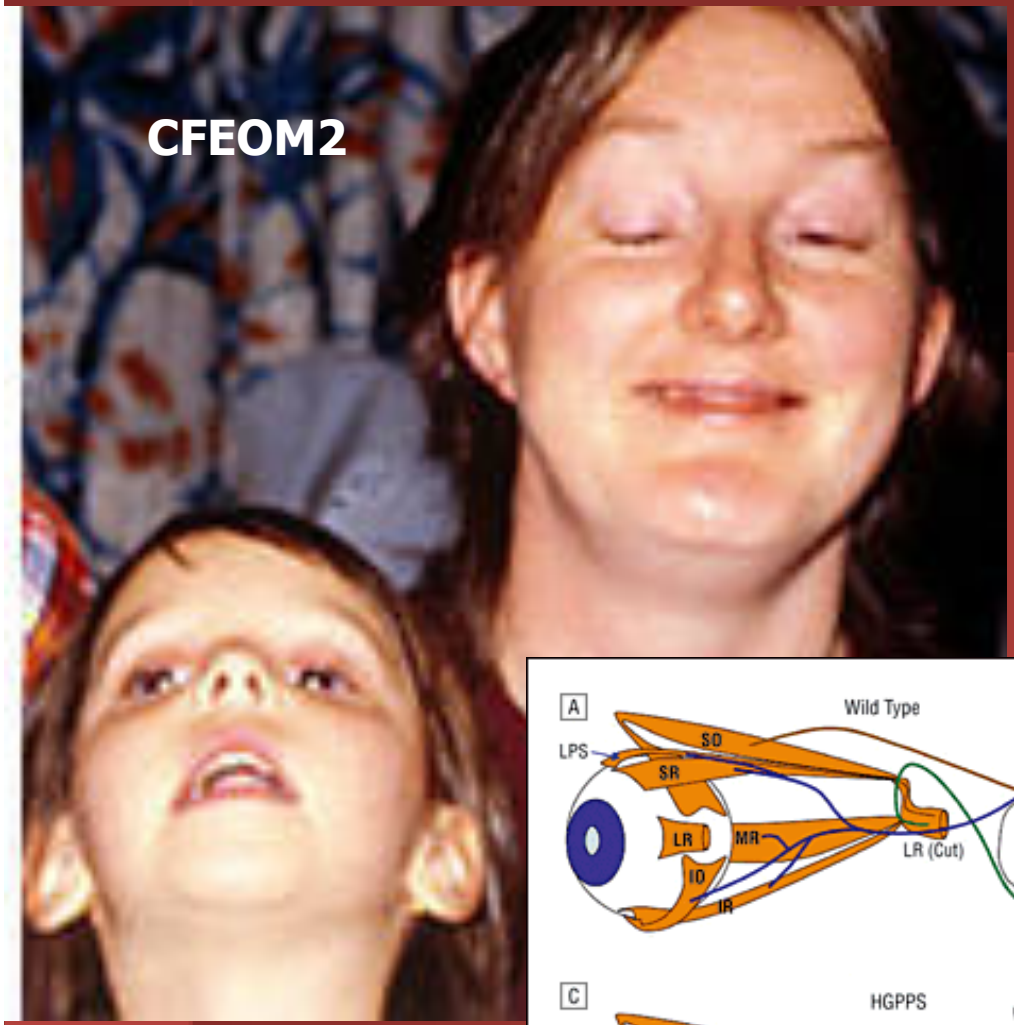
- Hipoplasia de nervios III, IV, VI

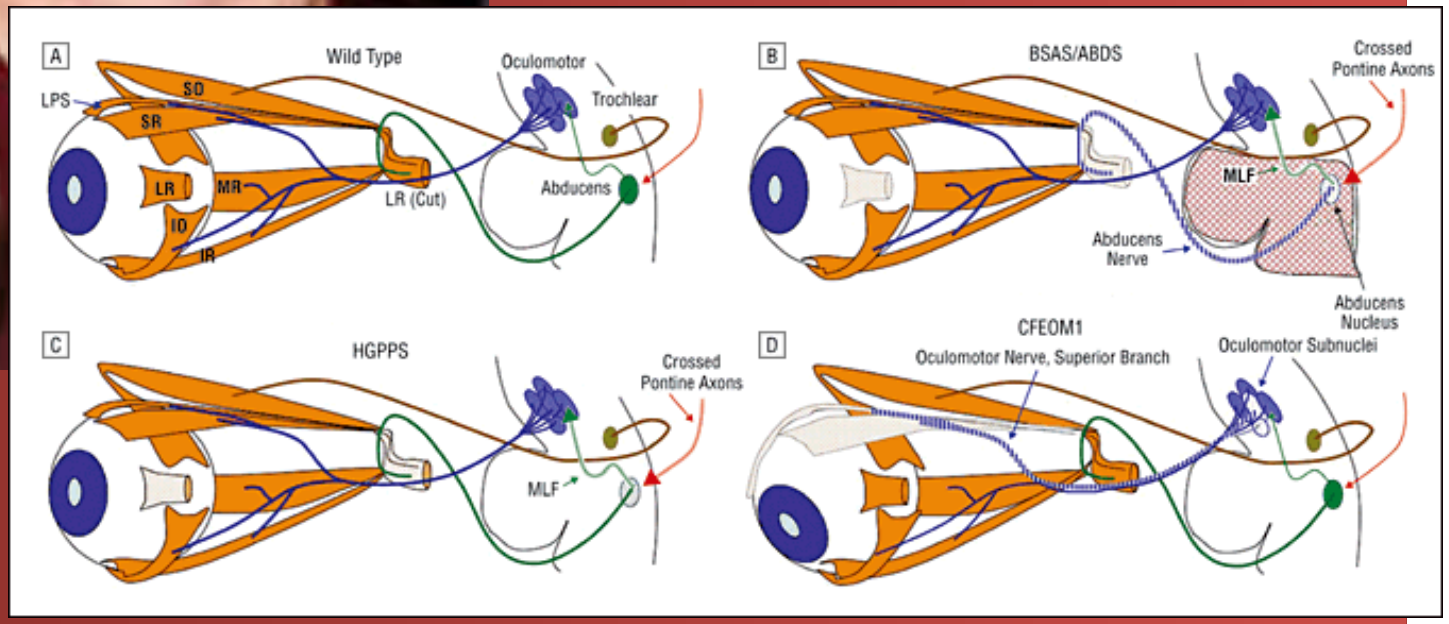
Tipo	Herencia	Clínica	Crom.	Gen	Proteína
1	HAD	Ptosis, oftalmoplejia	12p11.2	KF21A	Kinesina
2	HAR	+ exotropia	11q13	ARIX	Prot transcriptora motoneuronas α
3	HAD	Unilateral, upgaze normal	16q		

Optimized using
trial version
www.balesio.com

Michaelides M, Moore AT; The genetics of strabismus, Journal of Medical genetics, 2004; 41: 641-646

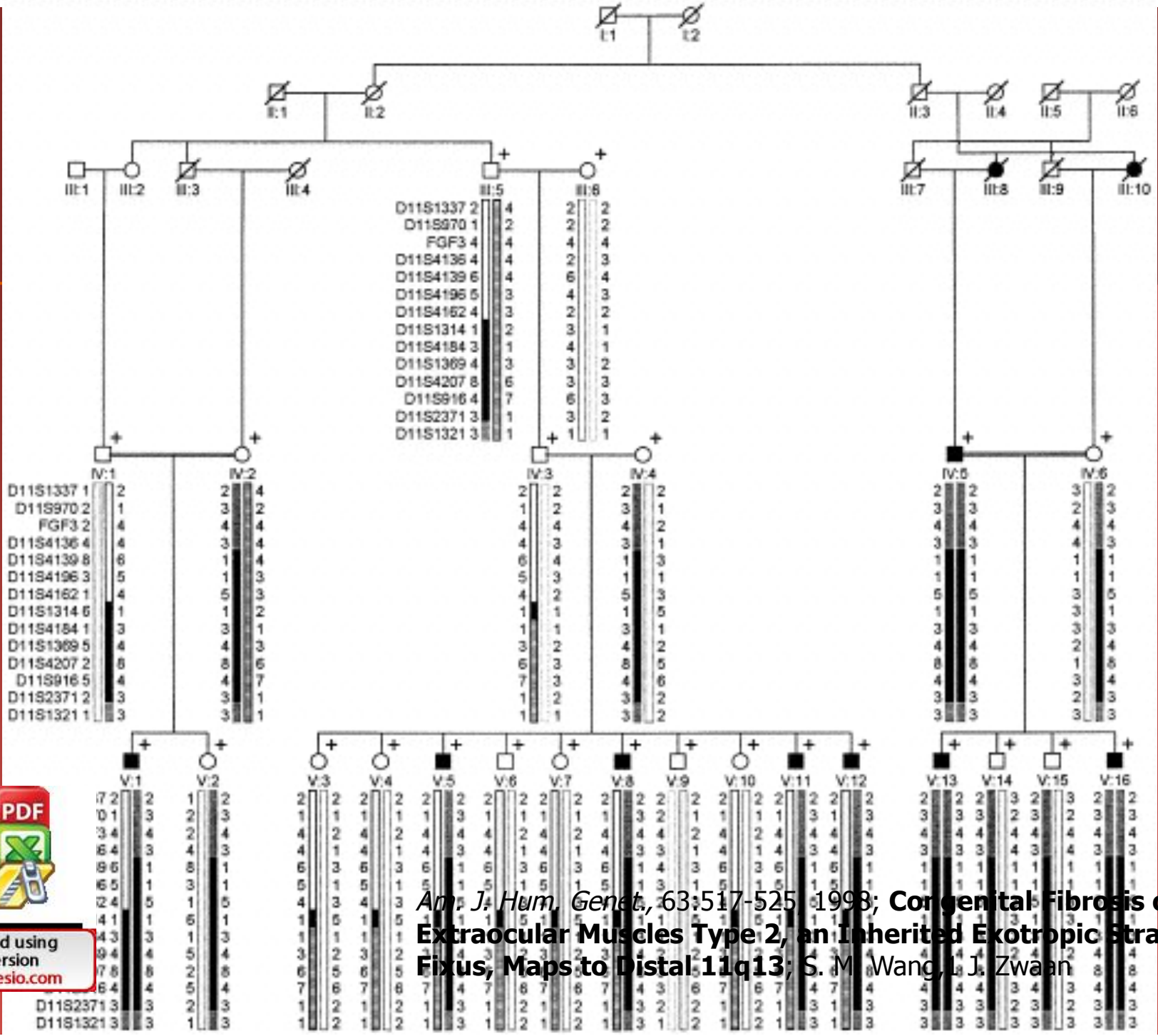
CFEOM2





Optimized using
trial version
www.balesio.com

Engle EC; Oculomotor nerve and muscle abnormalities in congenital fibrosis of the extraocular muscles; Ann Neurol 1997; 41; 314-25



Am. J. Hum. Genet., 63:517-525, 1998; **Congenital Fibrosis of the Extraocular Muscles Type 2, an Inherited Exotropic Strabismus Fixus, Maps to Distal 11q13**; S. M. Wang, L. J. Zwaan

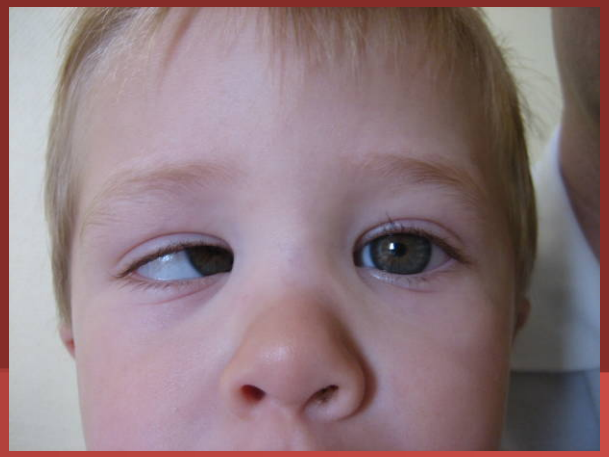
Optimized using
trial version
www.balesio.com

Estrabismos concomitantes

- 7100 pacientes
- 3-5 % de niños (ET = 3XT)
- 30% tiene Hª familiar
- 80% de concordancia entre monocigóticos (40% en dicigóticos)
- Riesgo Relativo en pariente de 1º grado: 3-5

Optimized using
trial version
www.balesio.com

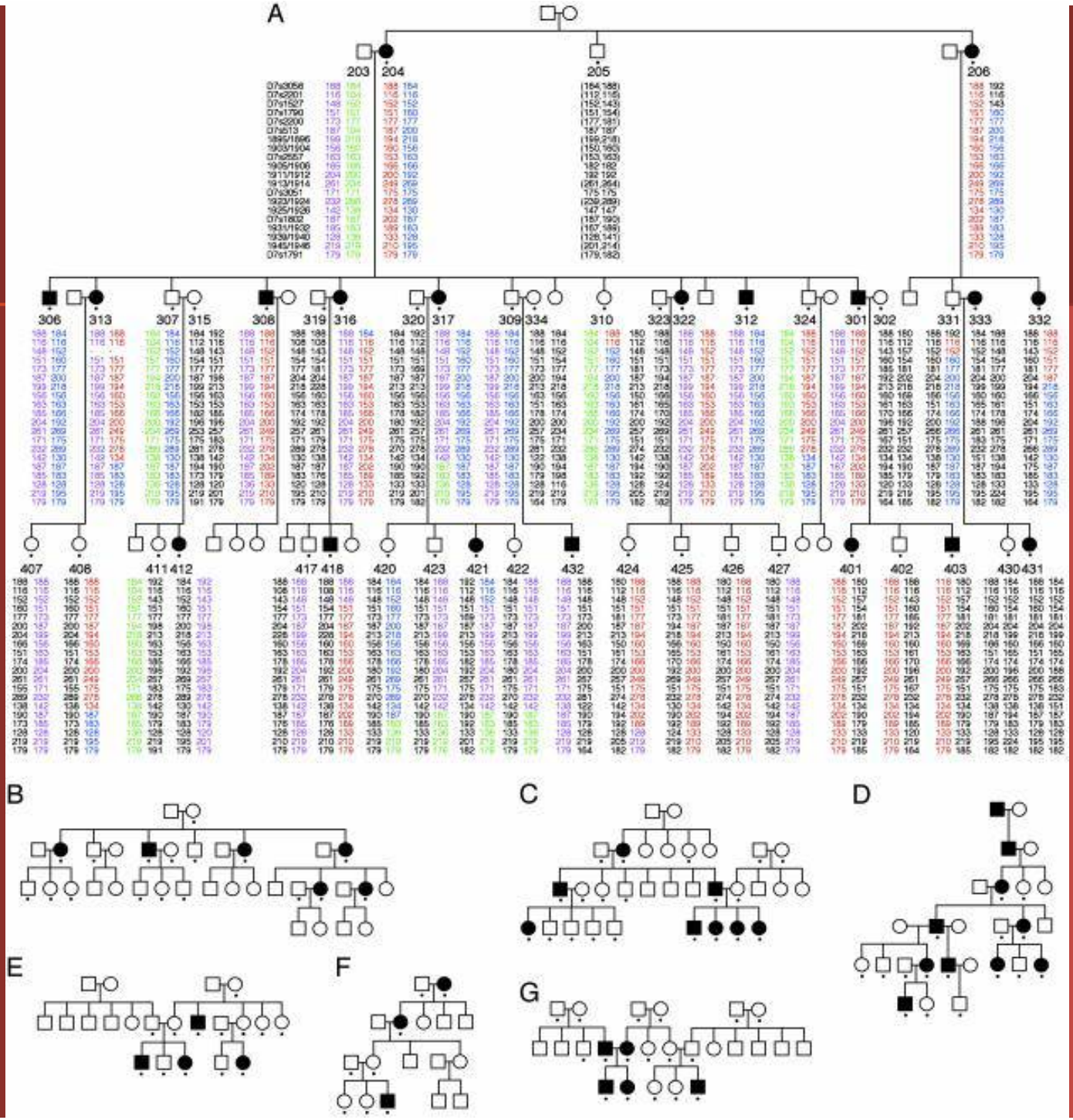
Engle E; Arch Ophthalmology, 2007; 125:189-195
Genetical Basis of Congenital Strabismus



- F.Riesgo:
  - hipermetropía
  - raza (XT en Asia-África, ET en caucásicos)
  - maternos: >35 años, tabaco
  - < 1500 g al nacer
  - Hidrocefalia, Down, parálisis cerebral
  - Hª familiar
  - H.A.R.: 7p22.1, gen STBMS1, penetrancia incompleta y expresividad variable

Proc Natl Acad Sci U S A. 2003 October 14; 100(21): 12283–12288. A **strabismus susceptibility locus on chromosome 7p;** V Parikh, YY Shugart

Optimized using
trial version
www.balesio.com



Optimized using
trial version
www.balesio.com