AZIENDA OSPEDALIERA
UNIVERSITARIA SENESE
Santa Maria alle Scotte

D.A.I. Servizi
U.O.C. Genetica Medica

Programma formativo promosso dalla Regione Toscana

La consulenza genetica e i test genetici nella pratica clinica

Indicazioni, percorsi e interpretazioni

Siena, 24 settembre 2009

Anomalie della cornea isolate e sindromiche

Maria Antonietta Mencarelli
Genetica Medica, AOUS

Anomalie isolate:

DISTROFIE CORNEALI

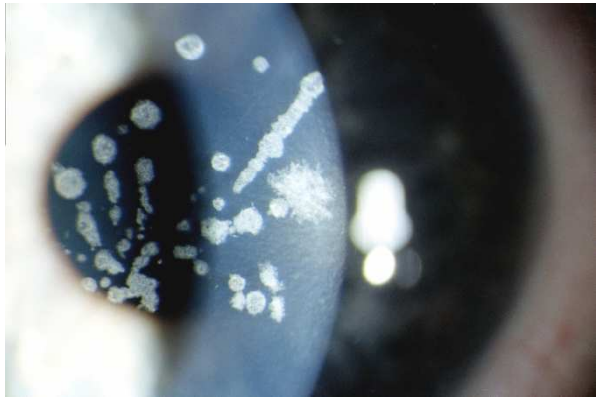
Classificazione:

International Committee for the Classification of Corneal Dystrophies

	Mode of inheritance	Gene locus	Gene	IC3D Category*
SUPERFICIAL CORNEAL DYSTROPHIES				
Meesmann dystrophy	AD	12q13	*KRT3*	1
Meesmann dystrophy	AD	17q12	*KRT12*	1
Stocker-Holt dystrophy	AD	17q12	*KRT12*	1
Granular corneal dystrophy type III (Reis-Bücklers dystrophy)	AD	5q31	*TGFBI*	1
Thiel-Behnke dystrophy	AD	5q31	*TGFBI*	1
Thiel-Behnke dystrophy	AD	10q23–q24	Unknown	2
Gelatinous droplike corneal dystrophy (familial subepithelial corneal amyloidosis)	AR	1p32	*TACSTD2 (M1S1)*	1
Subepithelial mucinous corneal dystrophy	AD	Unknown	Unknown	4
Lisch epithelial dystrophy	XR	Xp22.3	Unknown	2
Epithelial recurrent erosion dystrophy	AD	Unknown	Unknown	3
CORNEAL STROMAL DYSTROPHIES				
Macular corneal dystrophy	AR	16q22	*CHST6*	1
Granular corneal dystrophy type I	AD	5q31	*TGFBI*	1
Granular corneal dystrophy type II (Avellino dystrophy, combined lattice-granular dystrophy)	AD	5q31	*TGFBI*	1
Lattice corneal dystrophy type I and variants	AD	5q31	*TGFBI*	1
Lattice corneal dystrophy type II	AD	9q34	*GSN*	1
Fleck dystrophy	AD	2q35	*PIP5K3*	1
Schnyder corneal dystrophy	AD	1p34.1–p36	*UBIAD1*	1
Posterior amorphous corneal dystrophy	AD	Unknown	Unknown	3
Congenital stromal dystrophy	AD	12q13.2	*DCN*	1
POSTERIOR DYSTROPHIES				
Fuchs dystrophy (early onset)	AD	1p34.3	*COL8A*	1
Fuchs dystrophy (late onset)	AD	13pTel-13q12.13	Unknown	2
Fuchs dystrophy (late onset)	AD	18q21.2–q21.32	Unknown	2
Fuchs dystrophy (late onset)	?	20p13-p12	*SLC4A11*	1
Fuchs dystrophy (late onset)	?	10p11.2	*TCF8*	1
Posterior polymorphous dystrophy type 1	AD	20p11.2	Unknown	2
Posterior polymorphous dystrophy type 2	AD	1p34.3-p32.3	*COL8A2#*	1
Posterior polymorphous dystrophy type 3	AD	10p11.2	*TCF8*	1
Congenital endothelial dystrophy type 1	AD	20p11.2-q11.2	Unknown	2
Congenital endothelial dystrophy type 2	AR	20p13-p12	*SLC4A11*	1
X-linked endothelial corneal dystrophy	XR	Unknown	Unknown	2

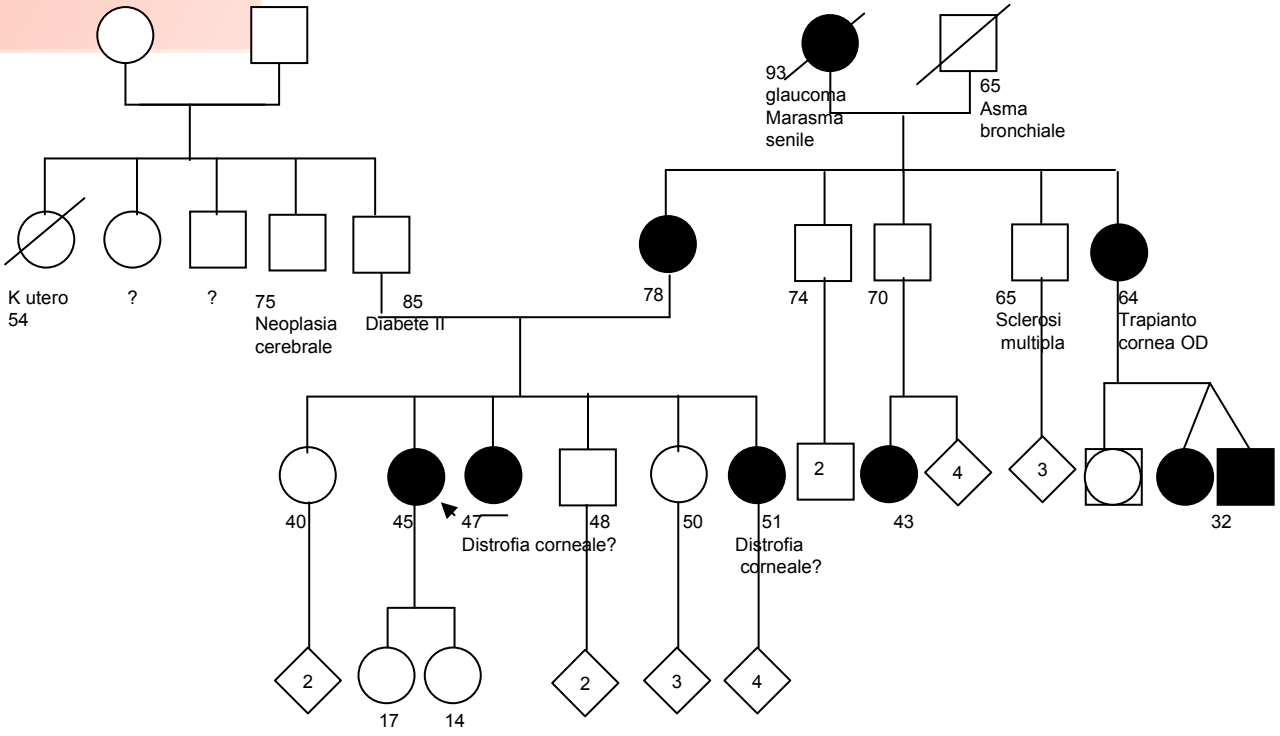
Distrofia Corneale Granulare Tipo II

42 anni
Asintomatica
Quadro corneale compatibile con distrofia corneale granulare di tipo II

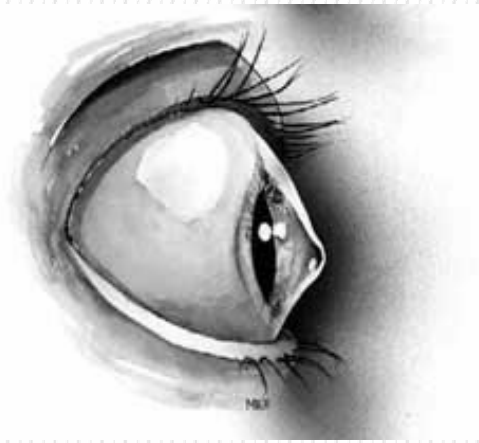


TGFBI

p.Arg124His
c.418G>A



Anomalie isolate:



CHERATOCONO

OMIM
Online Mendelian Inheritance in Man
Johns Hopkins University

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#148300
KERATOCONUS 1; KTCN1

GeneTests, Links

Gene map locus 20p11.2

TEXT

A number sign (#) is used with this entry because of evidence that one form of keratoconus (KTCN1) can be caused by mutation in the VSX1 gene (605020) on chromosome 20. Other loci for keratoconus have been mapped to chromosomes 16q22.3-q23.1 (KTCN2; 608932), 3p14-q13 (KTCN3; 608586), and 2p24 (KTCN4; 609271).

Keratoconus is a disorder in which the cornea thins and changes shape. Progressive thinning and protrusion of the cornea and loss of acuity are the clinical characteristics. It is a major indication for cornea transplantation in the Western world.

…ma anche sindromiche:

CHERATOCONO

- Trisomia 21
- S. Ehlers-Danlos
- S. Marfan
- S. Alport

Anomalie corneali associate a malattie sistemiche

DISORDINI DEL METABOLISMO

Malattie da deposito lisosomiale

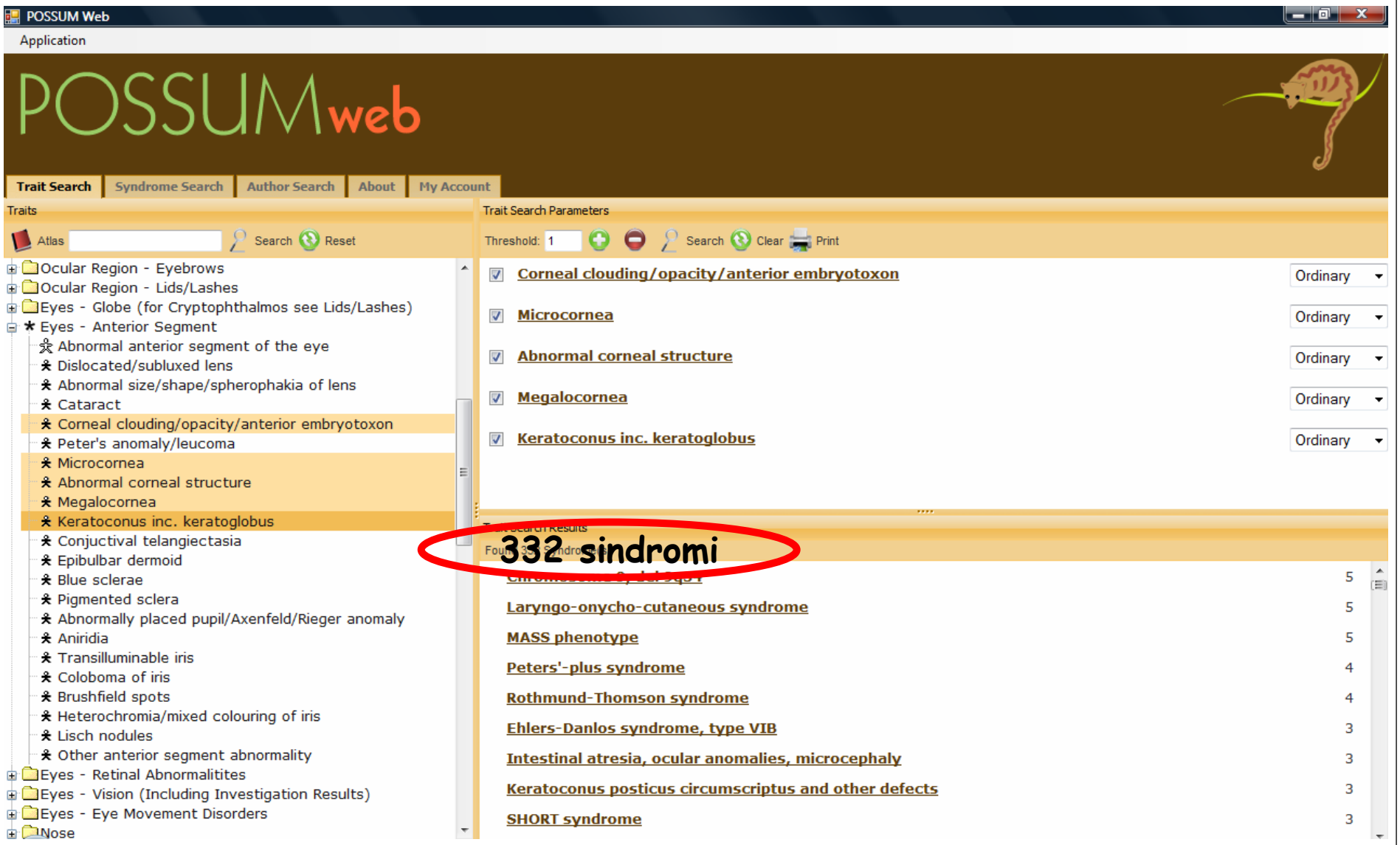
- Mucopolisaccaridosi
- Sfingolipidosi
- Mucolipidosi

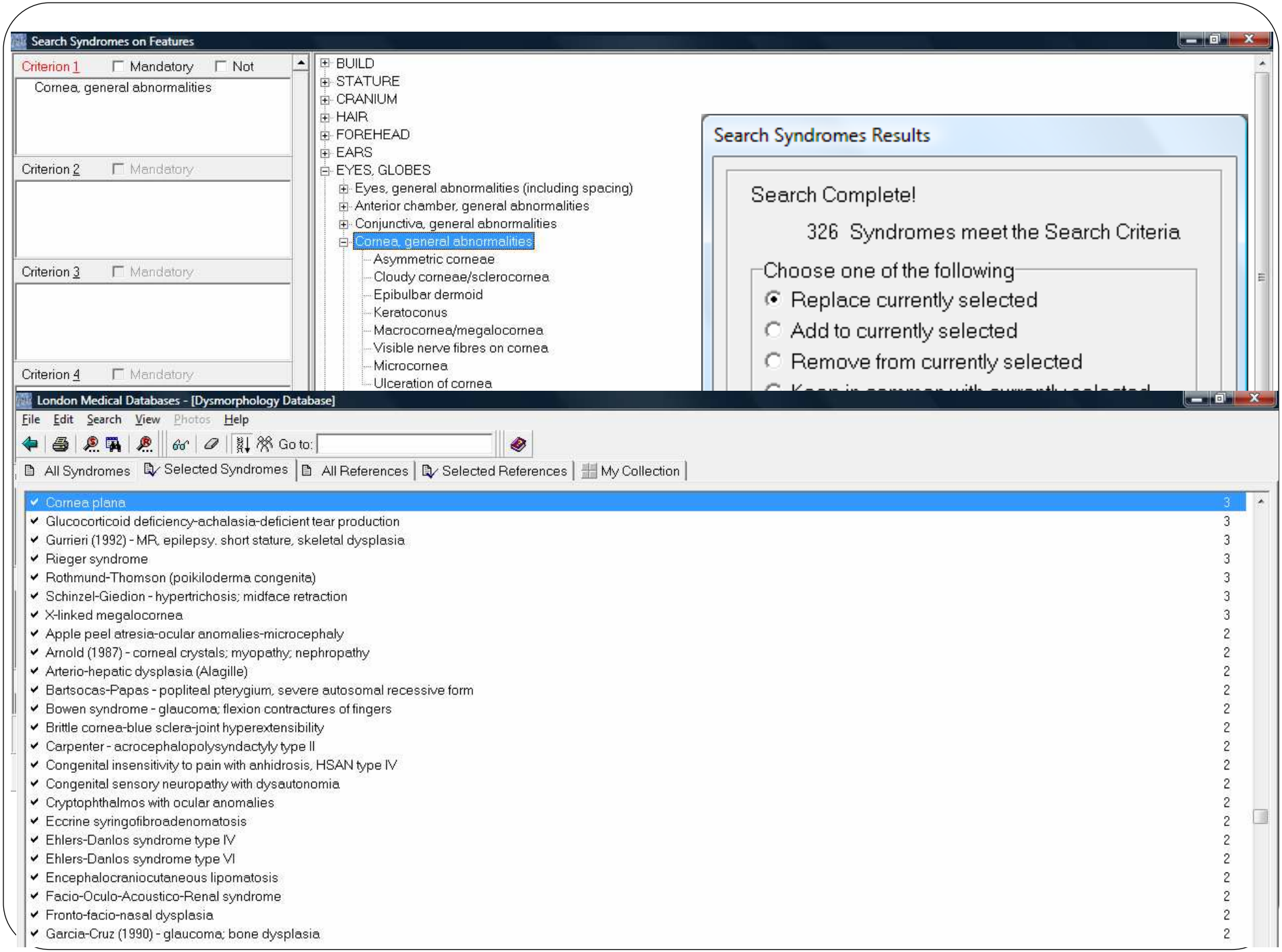
Difetti del metabolismo degli aminoacidi e delle proteine

- Cistinosi
- Tirosinemia
- M. Wilson

MALATTIE CON COINVOLGIMENTO DELLA CUTE

- Ittiosi
- Displasie ectodermiche
- Epidermolisi bullosa
- Xeroderma pigmentoso


POSSUM Web
Application
POSSUMweb
Trait Search
Syndrome Search
Author Search
About
My Account
Traits
Atlas
Search
Reset
Ocular Region - Eyebrows
Ocular Region - Lids/Lashes
Eyes - Globe (for Cryptophthalmos see Lids/Lashes)
Eyes - Anterior Segment
Abnormal anterior segment of the eye
Dislocated/subluxed lens
Abnormal size/shape/spherophakia of lens
Cataract
Corneal clouding/opacity/anterior embryotoxon
Peter's anomaly/leucoma
Microcornea
Abnormal corneal structure
Megalocornea
Keratoconus inc. keratoglobus
Conjuctival telangiectasia
Epibulbar dermoid
Blue sclerae
Pigmented sclera
Abnormally placed pupil/Axenfeld/Rieger anomaly
Aniridia
Transilluminable iris
Coloboma of iris
Brushfield spots
Heterochromia/mixed colouring of iris
Lisch nodules
Other anterior segment abnormality
Eyes - Retinal Abnormalitites
Eyes - Vision (Including Investigation Results)
Eyes - Eye Movement Disorders
Nose
Trait Search Parameters
Threshold: 1
Search
Clear
Print
Corneal clouding/opacity/anterior embryotoxon
Ordinary
Microcornea
Ordinary
Abnormal corneal structure
Ordinary
Megalocornea
Ordinary
Keratoconus inc. keratoglobus
Ordinary
332 sindromi
Laryngo-onycho-cutaneous syndrome 5
MASS phenotype 5
Peters'-plus syndrome 4
Rothmund-Thomson syndrome 4
Ehlers-Danlos syndrome, type VIB 3
Intestinal atresia, ocular anomalies, microcephaly 3
Keratoconus posticus circumscriptus and other defects 3
SHORT syndrome 3


Search Syndromes on Features
Criterion 1
Mandatory
Not
Cornea, general abnormalities
Criterion 2
Mandatory
Criterion 3
Mandatory
Criterion 4
Mandatory
BUILD
STATURE
CRANIUM
HAIR
FOREHEAD
EARS
EYES, GLOBES
Eyes, general abnormalities (including spacing)
Anterior chamber, general abnormalities
Conjunctiva, general abnormalities
Cornea, general abnormalities
Asymmetric corneae
Cloudy corneae/sclerocornea
Epibulbar dermoid
Keratoconus
Macrocornea/megalocornea
Visible nerve fibres on cornea
Microcornea
Ulceration of cornea
Search Syndromes Results
Search Complete!
326 Syndromes meet the Search Criteria
Choose one of the following
Replace currently selected
Add to currently selected
Remove from currently selected
London Medical Databases - [Dysmorphology Database]
File
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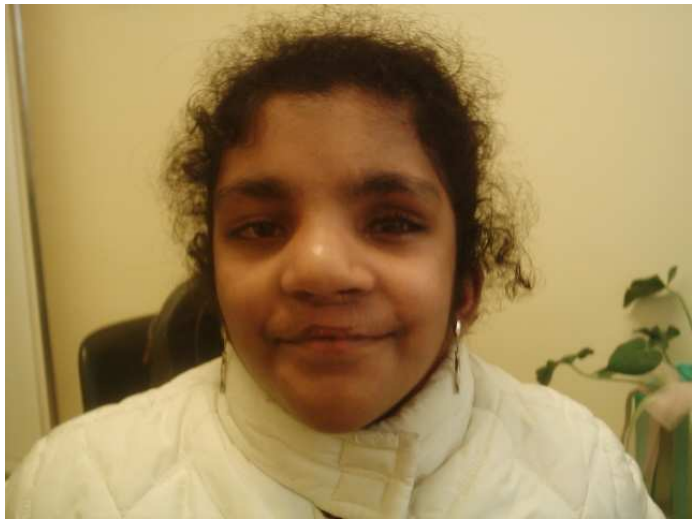
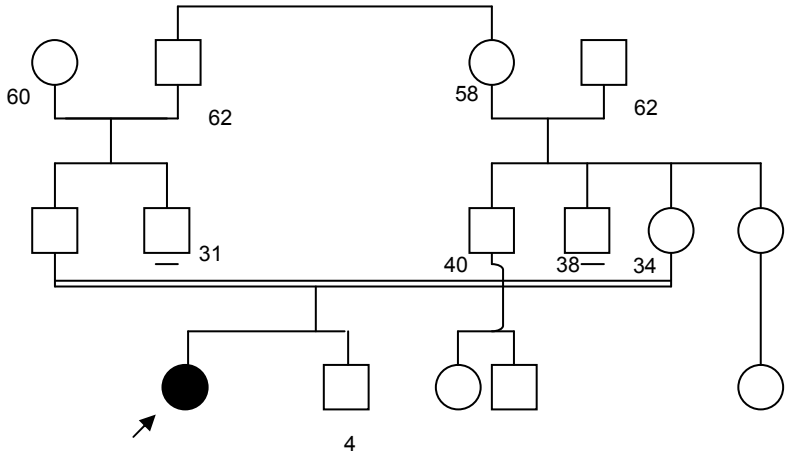
All Syndromes
Selected Syndromes
All References
Selected References
My Collection
Cornea plana 3
Glucocorticoid deficiency-achalasia-deficient tear production 3
Gurrieri (1992) - MR, epilepsy, short stature, skeletal dysplasia 3
Rieger syndrome 3
Rothmund-Thomson (poikiloderma congenita) 3
Schinzel-Giedion - hypertrichosis; midface retraction 3
X-linked megalocornea 3
Apple peel atresia-ocular anomalies-microcephaly 2
Arnold (1987) - corneal crystals; myopathy; nephropathy 2
Arterio-hepatic dysplasia (Alagille) 2
Bartsocas-Papas - popliteal pterygium, severe autosomal recessive form 2
Bowen syndrome - glaucoma; flexion contractures of fingers 2
Brittle cornea-blue sclera-joint hyperextensibility 2
Carpenter - acrocephalopolysyndactyly type II 2
Congenital insensitivity to pain with anhidrosis, HSAN type IV 2
Congenital sensory neuropathy with dysautonomia 2
Cryptophthalmos with ocular anomalies 2
Eccrine syringofibroadenomatosis 2
Ehlers-Danlos syndrome type IV 2
Ehlers-Danlos syndrome type VI 2
Encephalocraniocutaneous lipomatosis 2
Facio-Oculo-Acoustico-Renal syndrome 2
Fronto-facio-nasal dysplasia 2
Garcia-Cruz (1990) - glaucoma; bone dysplasia 2

Peters' Plus Syndrome



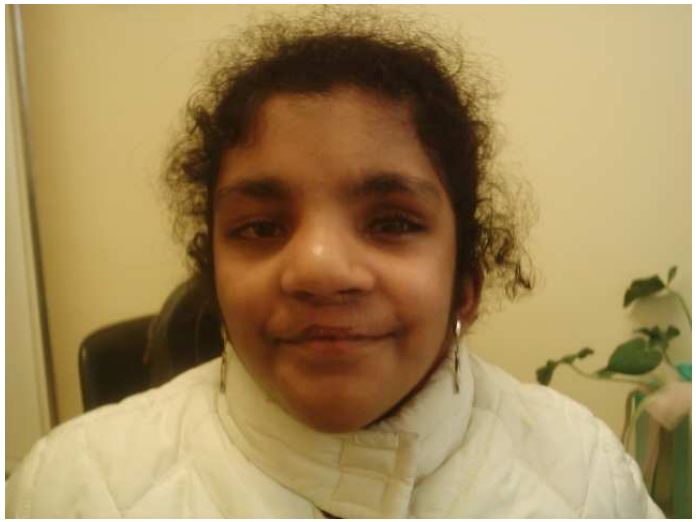
I incontro di consulenza genetica
Gennaio 2006: 11 anni 9 mesi

- Anomalie della camera anteriore con opacità corneali
- Labiopalatoschisi bilaterale
- Bassa statura
- Pervietà del forame ovale
- Caratteristiche cranio-facciali peculiari



MLPA 22q11.2	N
Array CGH 44K	N

Peters' Plus Syndrome



Follow up genetici: Gennaio 2007 e Luglio 2007

-> Lab. Molecolar Genetics
Leiden,The Netherlands

B3GALT

c.1052A>G; p.Asp351Gly
in omozigosi

REPORT

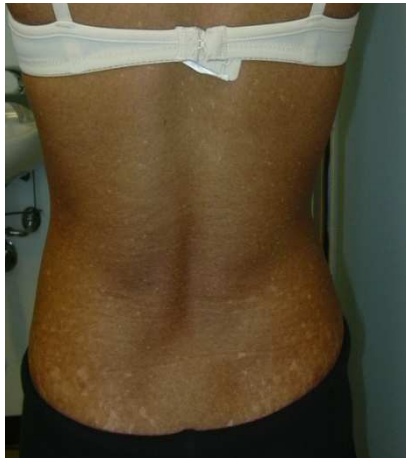
Peters Plus Syndrome Is Caused by Mutations in *B3GALTL*, a Putative Glycosyltransferase

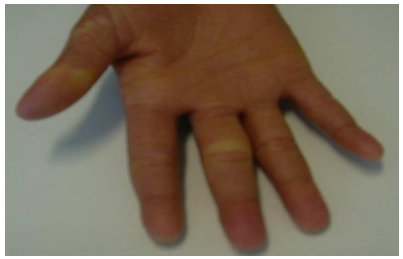
Saskia A. J. Lesnik Oberstein, Marjolein Kriek, Stefan J. White, Margot E. Kalf, Karoly Szuhai, Johan T. den Dunnen, Martijn H. Breuning, and Raoul C. M. Hennekam

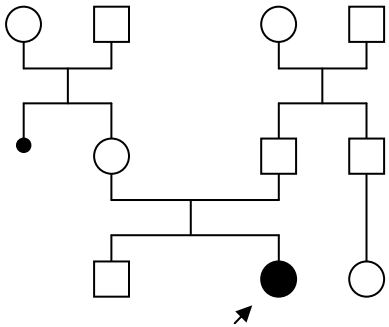
Peters Plus syndrome is an autosomal recessive disorder characterized by anterior eye-chamber abnormalities, disproportionate short stature, and developmental delay. After detection of a microdeletion by array-based comparative genomic hybridization, we identified biallelic truncating mutations in the β1,3-galactosyltransferase–like gene (*B3GALTL*) in all 20 tested patients, showing that Peters Plus is a monogenic, primarily single-mutation syndrome. This finding is expected to put Peters Plus syndrome on the growing list of congenital malformation syndromes caused by glycosylation defects.

The American Journal of Human Genetics September 2006

Rothmund-Thomson Syndrome







I incontro di consulenza genetica
Gennaio 1999: 14 anni 5 mesi

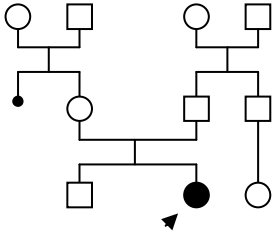
Follow up genetici: Settembre 2005, Dicembre 2008

- Cute marmorizzata con iperpigmentazione localizzata prevalentemente alle aree esposte
- Ipercheratosi palmo-plantare
- Persistenza dei canini decidui con agenesia di 12 elementi dentari
- Opacità corneali
- Sindrome mielodisplastica

RECQL4 (Marzo 2006)

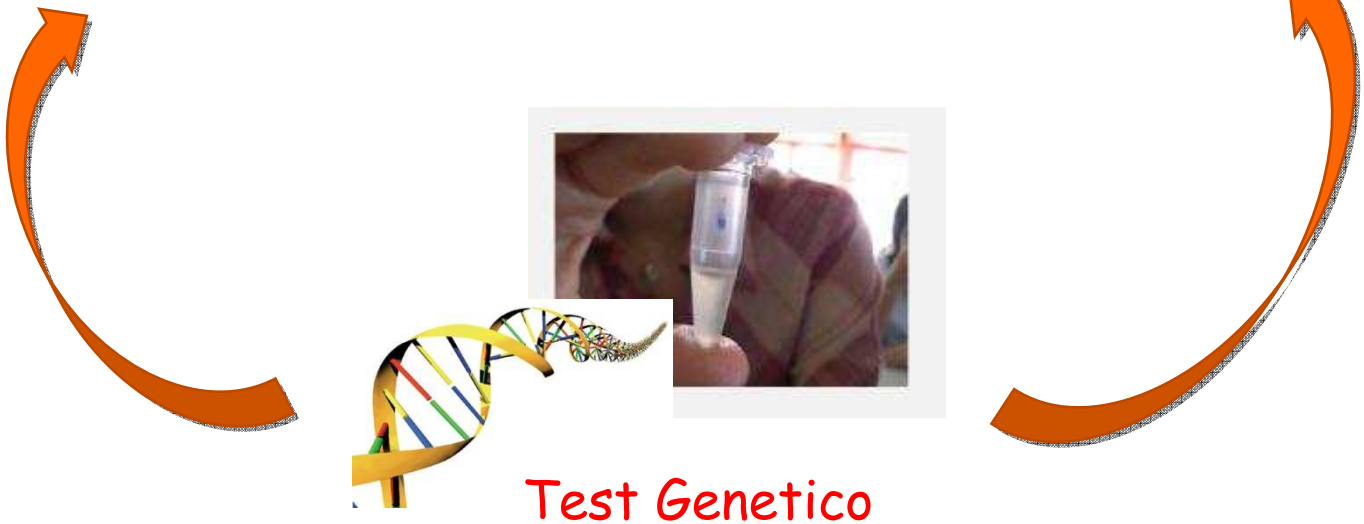
DD: Discheratosi Congenita *TERC* (Ottobre 2005)

Luglio 2009 identificata la presenza di due mutazioni in eterozigosi nel nuovo gene responsabile di RTS (Nature Genetics, in press)



Consulenza Genetica

Osservazione Clinica



Test Genetico