LA CONSULENZA GENETICA E I TEST GENETICI NELLA PRATICA CLINICA

Siena 24 settembre 2009

Malformazioni congenite dell'occhio e sindromi correlate

Prof Marco Seri
Genetica Medica
Bologna

PATOLOGIE OCULARI CONGENITE presenti in diversi quadri sindromici

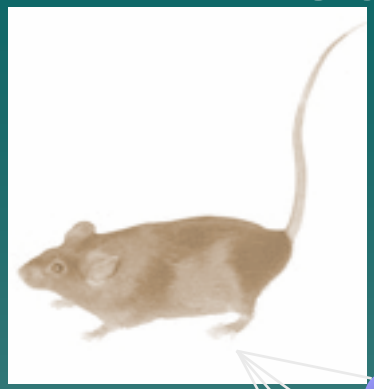
1. ANIRIDIA
    i. ISOLATA
    ii. SINDROMICA (WAGR E GILLESPIE)
2. COLOBOMA
    i. CHARGE SYNDROME
    ii. PAPILLORENAL
    iii. CAT EYE
3. Retinite pigmentosa
    i. USH 1 E 2
    ii. BBS

SINDROMI CORRELATE


PRESIDENT OF THE UNITED

Comparative Genomics

disease models



mouse

medicine

human

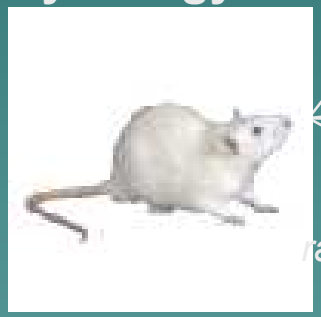
behavior

Drosophila

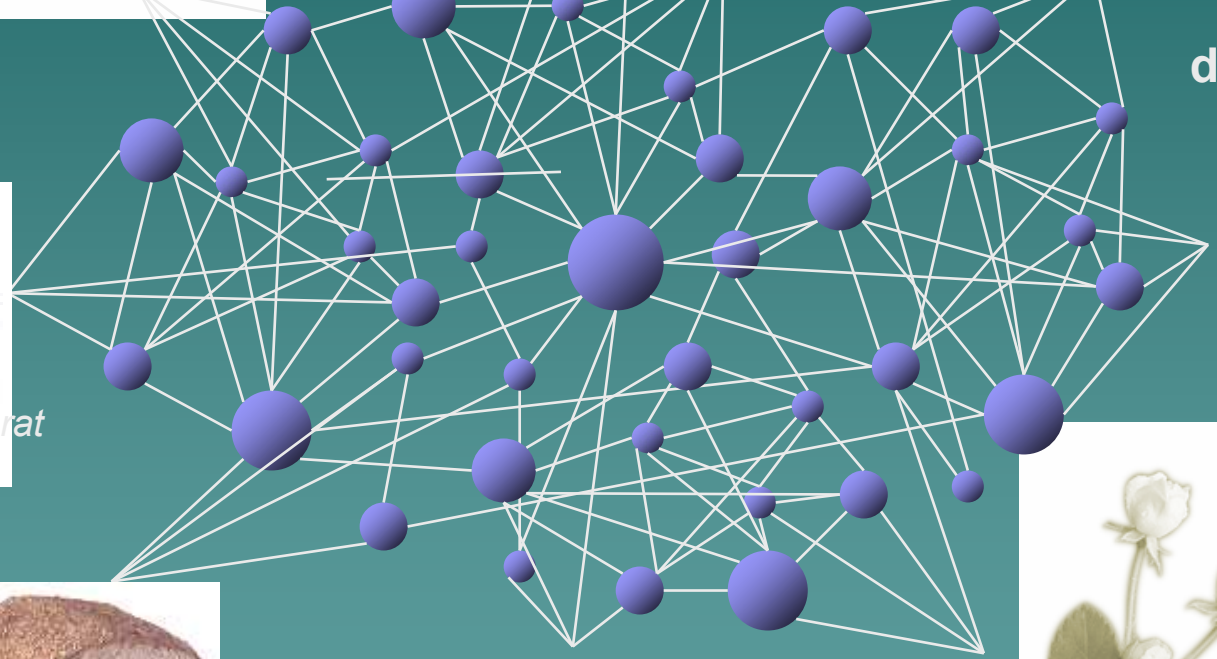
development

C. elegans

physiology



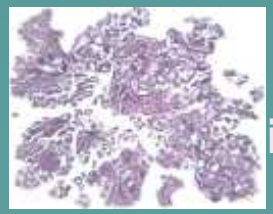
rat



genetics

yeast

biochemistry



infectious disease

microbes

crop yield

Arabidopsis

Power of Comparative Genomics

Mutations in the **Pax-6** gene of *Drosophila* cause an eyeless phenotype

Mutations in the **Pax-6** gene of humans causes Aniridia “no iris” phenotype

- Understanding the human genome through comparative genomics
- Evolution preserves function between species
- Genome comparisons increase the interpretative capability

1) ANIRIDIA

- ipoplasia dell'iride completa o parziale
  - Ipoplasia foveale associata
  - Ridotta acuità visiva
  - nistagmo

Frequentemente associata ad altre anomalie ad insorgenza più tardiva:

- ✓ Cataratta
- ✓ Glaucoma
- ✓ Opacità corneali

- ❖ Isolata → familiare 70%
  → sporadica 30%
- ❖ sindromica
  - ➢ (Wilms tumor, aniridia, genital anomalies, retardation: WAGR syndrome)
  - ➢ *Gillespie*

Mutazioni in PAX6: forme alleliche

- *Aploinsufficienza: aniridia classica*
- *Missenso: forme atipiche*

- ***Aniridia isolata***: mutazioni/delezioni **PAX6**
  mutazioni in più del 60%;
  Delezioni in circa 17%
- ***Aniridia sindromica***
  - ***Gillespie syndrome***

Caso clinico: Aniridia atassia e ritardo mentale

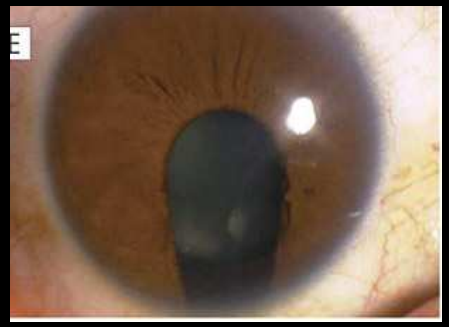
- **GILLESPIE syndrome**
  - Ipoplasia parziale dell'iride: *configurazione dell'iride caratteristica*
  - Atassia cerebellare
  - Ritardo mentale
- Caso clinico
  - Assenza dell'iride bilaterale, cristallino e cornea trasparenti
  - Atassia cerebellare
  - Ritardo mentale moderato

Mutazione (c.1133G) W257X in PAX6

AMPIO SPETTRO FENOTIPICO ASSOCIATO

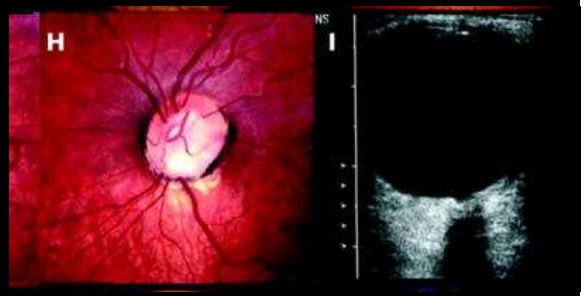
FIG. 1. **Panels A** and **B**: Frontal and lateral view of the patient's face showing round and asymmetric face, high forehead; depressed nasal bridge with anteverted nostrils; thin upper lip; folded up ears with hypoplastic antihelix. **Panel C**: Full view of the patient. It is possible to note arachnodactyly and genu valgum.

2) COLOBOMA



Iris coloboma

- Iride
- retina
- Disco ottico

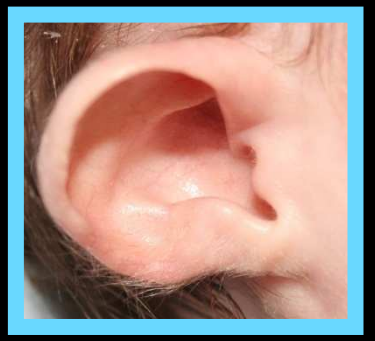


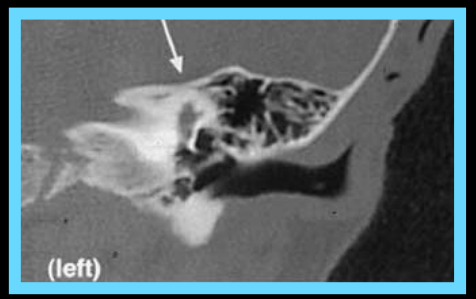
Left inferior disc coloboma

- Isolato
- Sindromico
  - CHARGE SYNDROME
  - COLOBOMA-RENAL (PAPILLORENAL) SYNDROME
  - CAT EYE SYNDROME

2) COLOBOMA

CHARGE SYNDROME

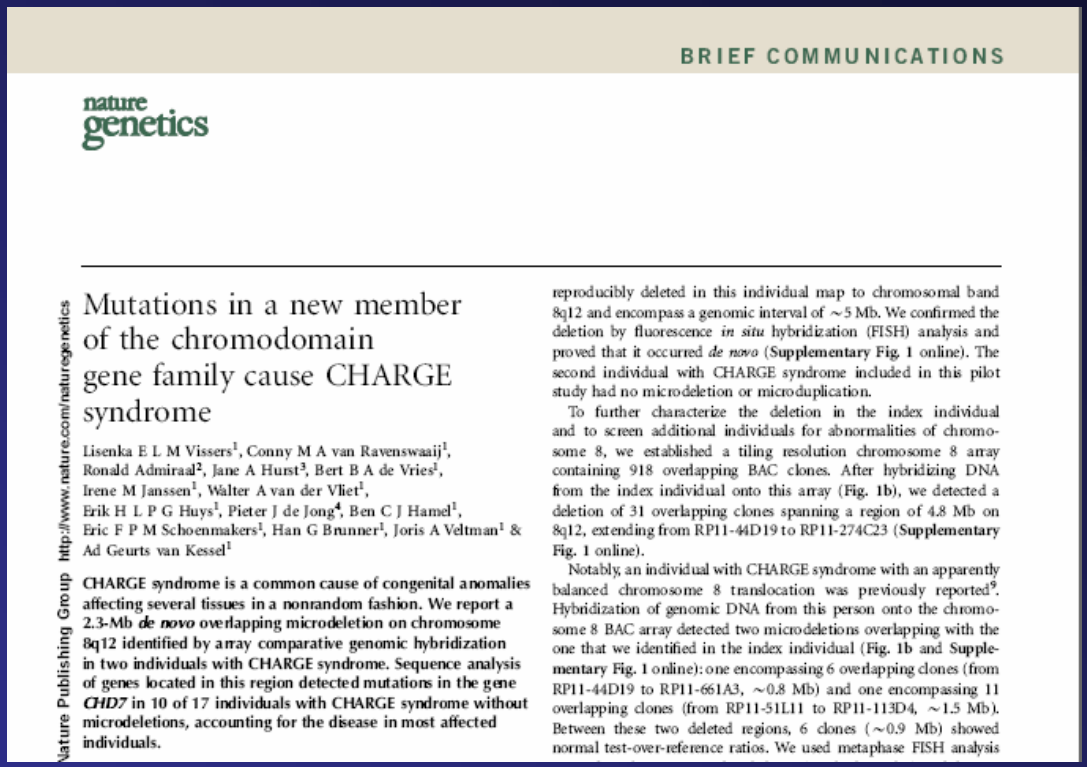




- Coloboma
- Heart defects
- Choanal Atresia,
- Retarded growth and development
- Genital abnormalities
- Ear anomalies.

Descritta per la prima volta da Hall 1979 e Pagon 1981

- Si tratta di una sindrome rara (incidenza compresa tra 0,1-1,2/100.000 nati vivi).
- Il coloboma può essere monolaterale o bilaterale e può coinvolgere solo l'iride o estendersi alla retina.
- Le cardiopatie congenite (la più frequente è la tetralogia di Fallot) sono presenti nel 75-80% dei pazienti.
- L'atresia delle coane può essere membranosa o ossea, bilaterale o monolaterale. Sono presenti poi anche altre anomalie delle vie aeree superiori (laringomalacia) che possono necessitare di tracheotomia.
- Il ritardo mentale è variabile con un QI che varia dalla quasi normalità al ritardo grave.
- Le anomalie dei genitali esterni, che possono presentare difetti dello sviluppo oppure sono ipoplasici, accomunano i maschi e le femmine.
- Le anomalie delle orecchie comprendono dismorfismi caratteristici, ipoacusia conduttiva e/o nervosa, con lieve o grave sordità.



nature genetics

Mutations in a new member of the chromodomain gene family cause CHARGE syndrome

Lisenka E L M Vissers[1], Conny M A van Ravenswaaij[1], Ronald Admiraal[2], Jane A Hurst[3], Bert B A de Vries[1], Irene M Janssen[1], Walter A van der Vliet[1], Erik H L P G Huys[1], Pieter J de Jong[4], Ben C J Hamel[1], Eric F P M Schoenmakers[1], Han G Brunner[1], Joris A Veltman[1] & Ad Geurts van Kessel[1]

CHARGE syndrome is a common cause of congenital anomalies affecting several tissues in a nonrandom fashion. We report a 2.3-Mb *de novo* overlapping microdeletion on chromosome 8q12 identified by array comparative genomic hybridization in two individuals with CHARGE syndrome. Sequence analysis of genes located in this region detected mutations in the gene *CHD7* in 10 of 17 individuals with CHARGE syndrome without microdeletions, accounting for the disease in most affected individuals.

reproducibly deleted in this individual map to chromosomal band 8q12 and encompass a genomic interval of ~5 Mb. We confirmed the deletion by fluorescence *in situ* hybridization (FISH) analysis and proved that it occurred *de novo* (**Supplementary Fig. 1** online). The second individual with CHARGE syndrome included in this pilot study had no microdeletion or microduplication.

To further characterize the deletion in the index individual and to screen additional individuals for abnormalities of chromosome 8, we established a tiling resolution chromosome 8 array containing 918 overlapping BAC clones. After hybridizing DNA from the index individual onto this array (**Fig. 1b**), we detected a deletion of 31 overlapping clones spanning a region of 4.8 Mb on 8q12, extending from RP11-44D19 to RP11-274C23 (**Supplementary Fig. 1** online).

Notably, an individual with CHARGE syndrome with an apparently balanced chromosome 8 translocation was previously reported[9]. Hybridization of genomic DNA from this person onto the chromosome 8 BAC array detected two microdeletions overlapping with the one that we identified in the index individual (**Fig. 1b** and **Supplementary Fig. 1** online): one encompassing 6 overlapping clones (from RP11-44D19 to RP11-661A3, ~0.8 Mb) and one encompassing 11 overlapping clones (from RP11-51L11 to RP11-113D4, ~1.5 Mb). Between these two deleted regions, 6 clones (~0.9 Mb) showed normal test-over-reference ratios. We used metaphase FISH analysis

- **mutazioni nel gene CHD7, un gene di grosse dimensioni, sono presenti nei 2/3 della popolazione esaminata.**
- **Il CHD7 codifica per un nuovo membro di una famiglia proteica, in particolare per il cromodominio di una elicasi.**
- **Si tratta di un gene essenziale per le fasi iniziali dello sviluppo embrionale, che interessa diversi organi, compreso il cuore, l'orecchio interno e la retina.**

CHD7 -*gene*-

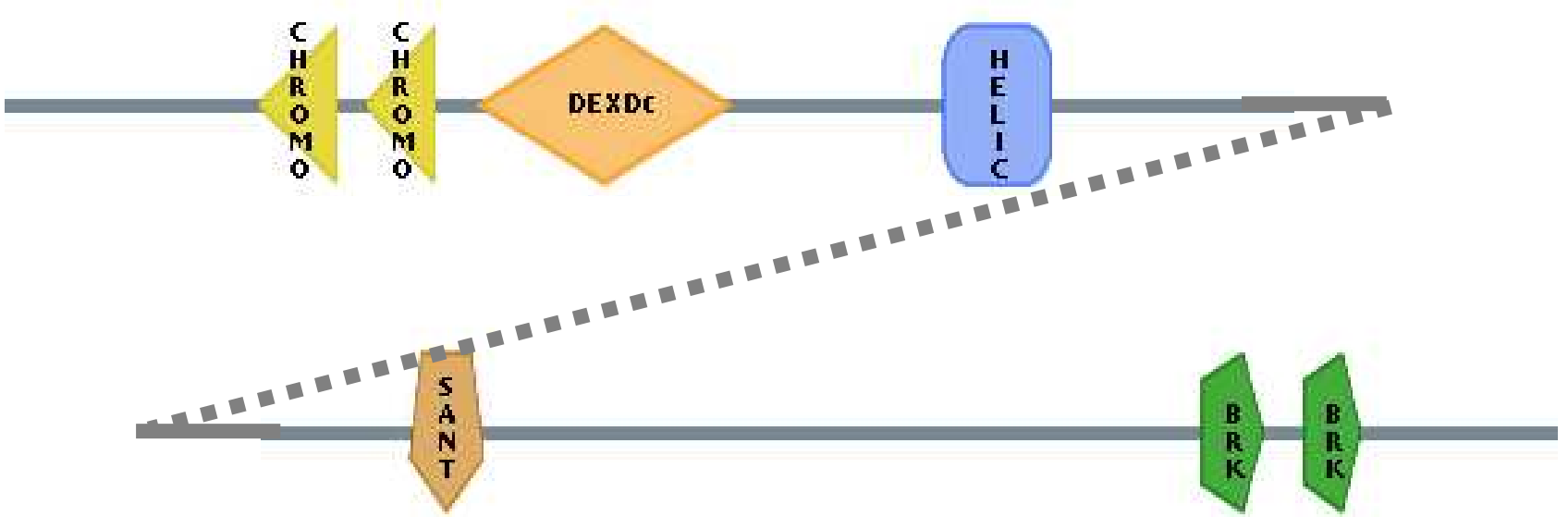
Chromodomain helicase DNA binding protein 7

Genomic Position: 8q12.2 *size:* 188 Kb

Complex gene: 38 exons (37 coding)

Large protein: 2997 amino acids, 336 kDa, nuclear localization

CHD7 *contains several domains conserved in proteins that modify chromatin organization.*



CHROMO	799 - 864 and 880 - 937
DEXDc	964 - 1165
HELIC	1320 - 1404
SANT	1962 - 2021
BRK	2564 - 2613 and 2642 - 2686

Table 2 Clinical criteria

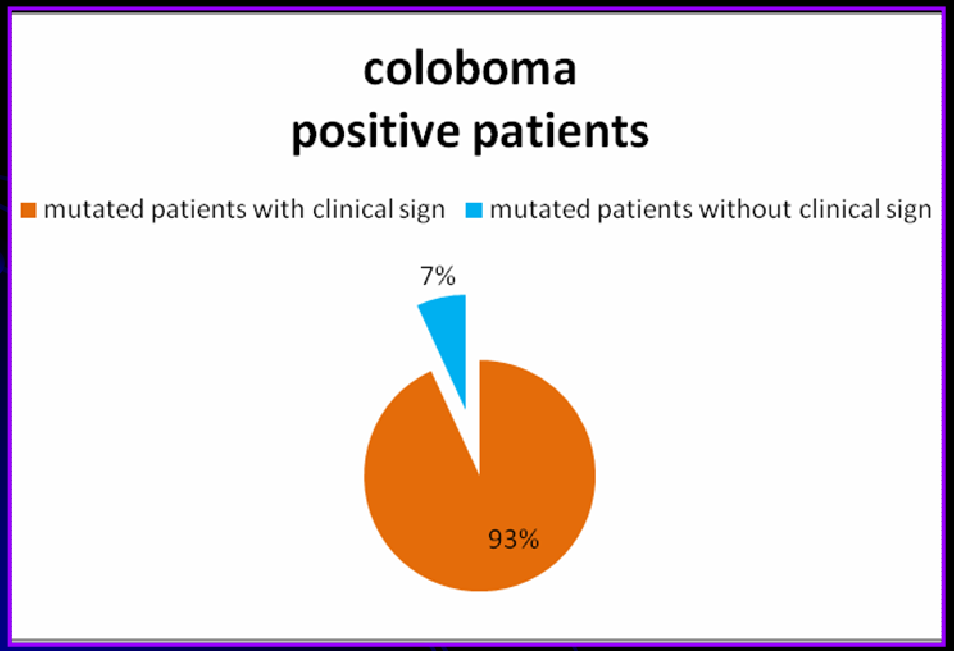
	Major criteria	*Minor criteria*	*Inclusion rule*
Pagon	1. Choanal atresia 2. Ocular coloboma	1. Heart defects of any type 2. Retardation (of growth and/or of development), 3. Genital anomalies 4. Ear anomalies (abnormal pinnae or hearing loss)	Four criteria out of six, and at least one major
Blake	1. Coloboma – of iris, retina, choroid, disc; microphthalmia 2. Choanal atresia – unilateral/bilateral, membranous/bony, stenosis/atresia 3. Characteristic ear abnormalities – external ear (lop or cup-shaped), middle ear (ossicular malformations, chronic serous otitis), mixed deafness, cochlear defects 4. Cranial nerve dysfunction – facial palsy (unilateral or bilateral), sensorineural deafness and/or swallowing problems	1. Genital hypoplasia – males: micropenis, cryptorchidism; females: hypoplastic labia; both males and females: delayed, incomplete pubertal development 2. Developmental delay – delayed motor milestones, language delay, mental retardation 3. Cardiovascular malformations – all types, especially conotruncal defects (eg, tetralogy of Fallot), AV canal defects, and aortic arch anomalies 4. Growth deficiencies – short stature, growth hormone deficiency 5. Orofacial cleft – cleft lip and/or palate 6. Tracheoesophageal-fistula – tracheoesophageal defects of all types 7. Characteristic face – sloping forehead, flattened tip of nose	Four majors OR three majors +three minors
Verloes	1. Ocular coloboma 2. Choanal atresia 3. Hypoplasia of semicircular canals	1. Rhombecephalic dysfunction (brainstem and cranial nerve III to XII anomalies, including sensorineural deafness) 2. Hypothalamo-hypophyseal dysfunction (including GH and gonadotrophin defects) 3. Malformation of the ear (internal or external) 4. Malformation of mediastinal organs (heart, esophagus,) 5. Mental retardation	Typical CHARGE: three majors OR two majors + two minors Partial CHARGE : two majors +one minor Atypical CHARGE: two majors but no minors OR one major + two minors

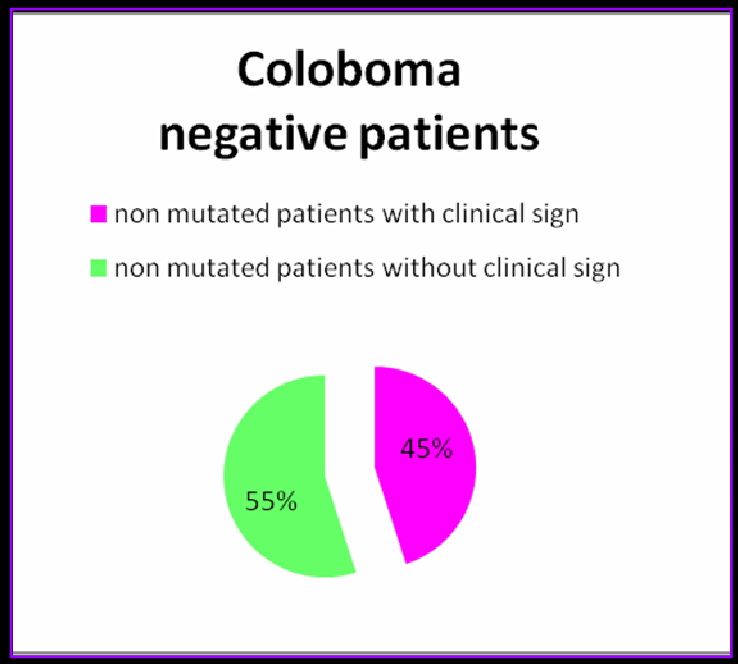
Diagnosi molecolare della casistica raccolta

- 33 pazienti (33/54; 61%):
- 25/ 52 pazienti dei quali era disponibile documentazione (57%) avevano una diagnosi definitiva secondo i criteri di Blake mentre 17 pazienti presentano una probabile/possibile diagnosi di Sindrome di CHARGE.
- Tra i 33 pazienti con mutazione, 18 hanno una diagnosi definitiva (4 criteri maggiori o 3 criteri maggiori e 3 minori) mentre 10 presentano una probabile/possibile diagnosi di Sindrome di CHARGE.

Coloboma e test genetico per CHARGE (positivi vs negativi al test)

- 54 PAZIENTI
- 33 CON MUTAZIONE
- 27/33 presentano COLOBOMA





3) RP: FORME SINDROMICHE

USHER	68 casi su 87
BARDET BIEDL	4 casi su 87

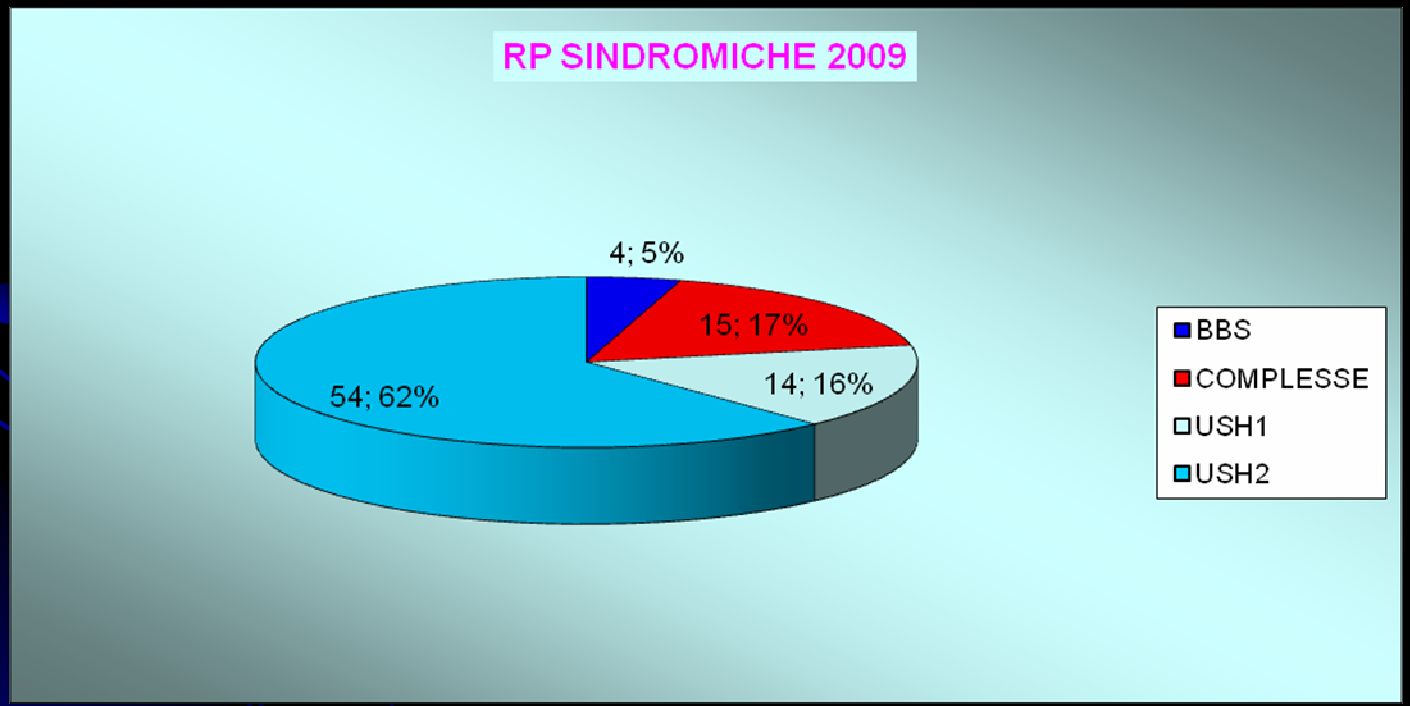


Table 1

Digenic Inheritance in Human Disease

Effect and Phenotype	Gene 1		Gene 2		Reference
	Mutation	Phenotype	Mutation	Phenotype	
Synergistic:					
RP	*ROM1*$^{+/G80insG}$	Normal	*RDS*$^{+/L185P}$	Normal	Kajiwara et al. 1994
RP	*ROM1*$^{+/L114insG}$	Normal	*RDS*$^{+/L185P}$	Normal	Kajiwara et al. 1994
Bardet-Biedl	*BBS2*$^{Y24X/Q59X}$	Normal	*BBS6*$^{+/Q147X}$	Normal	Katsanis et al. 2001
Deafness	*GJB2*$^{+/35delG}$	Normal	*GJB6*$^{+/-}$	Normal	Lerer et al. 2001
Deafness	*GJB2*$^{+/167delT}$	Normal	*GJB6*$^{+/-}$	Normal	del Castillo et al. 2002
Hirschsprung	*RET*$^{+/I647I}$	Normal	*EDNRB*$^{+/S305N}$	Normal	Auricchio et al. 1999
Severe insulin resistance	*PPARG*$^{+/A553delAAAiT}$	Normal	*PPP1R3A*$^{+/C1984delAG}$	Normal	Savage et al. 2002
Modifier:					
Juvenile-onset glaucoma	*MYOC*$^{+/G399V}$	Adult-onset glaucoma	*CYP1B1*$^{+/R368H}$	Normal	Vincent et al. 2002
Usher 1	*USH3*$^{mut/mut}$	Usher 3	*MYO7A*$^{+/delG\ (exon\ 25)}$	Normal	Adato et al. 1999
Congenital nonlethal JEB	*COL17A1*$^{R1226X/L855X}$	Juvenile JEB	*LAMB3*$^{+/R635X}$	Normal	Floeth et al. 1999
More severe ADPKD	*PKD1*$^{+/mut}$	Less severe ADPKD	*PKD2*$^{+/2152delA}$	Less severe ADPKD	Pei et al. 2001
More severe hearing loss	*DFNA1*	Mild hearing loss	*DFNA2*	Mild hearing loss	Balciuniene et al. 1998
WS2/OA	*MITF*$^{+/944delA}$	?WS2	*TYR*$^{+/R402Q}$	Normal	Morell et al. 1997
More severe WS2/OA	*MITF*$^{+/944delA}$	?WS2	*TYR*$^{R402Q/R402Q}$	Normal	

Note.—The phenotypic description applies to the family reported in the reference only. mut = haplotype consistent with mutation in the gene; + = wild type; − = partial deletion of gene.

3a) sindrome di USHER

La più comune causa genetica di sordità e cecità tra i bambini in età scolare.

Trasmissione autosomica recessiva

USH TIPO 1

- RP
- IPOACUSIA PROFONDA CONGENITA BILATERALE
- ALTERAZIONI VESTIBOLARI

Dalla nascita

  - 3 al 6% di tutte le sordità infantili
  - circa il 50%dei casi di sordità associata a cecità

GENI:
MYO7A(60% dei casi) o
CDH23 (10% dei casi)

USH TIPO 2

- RP a insorgenza più tardiva
- IPOACUSIA(meno severa)
- NO alterazioni vestibolari

GENI:
USH2A: 80% dei casi

SINDROME DI USHER TIPO 1

- SU 10 CASI ANALIZZATI 7 PRESENTANO MUTAZIONE nel gene MYO7A. (70%)

I

II

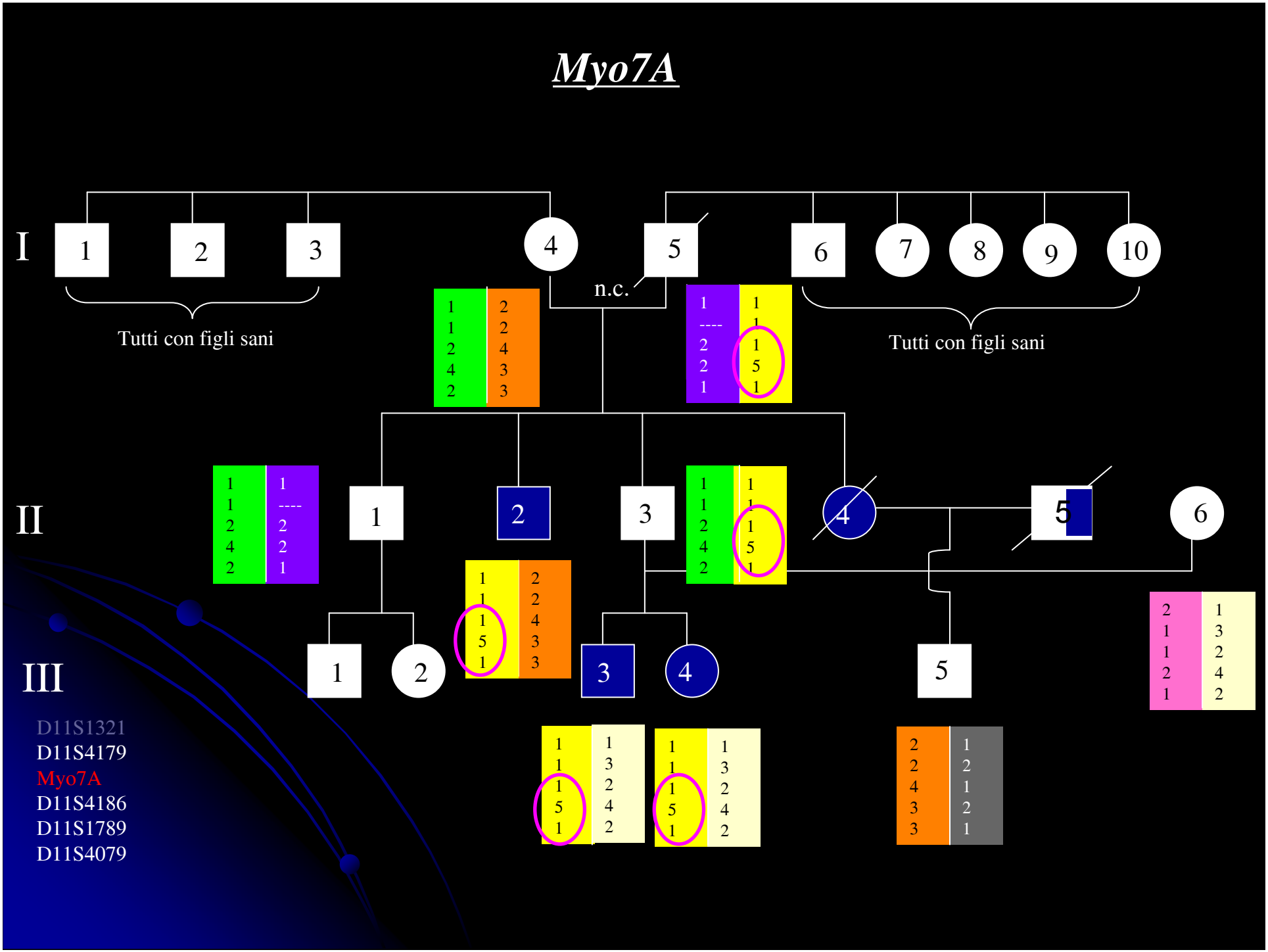
III

D11S1321
D11S4179
Myo7A
D11S4186
D11S1789
D11S4079

GENOTIPO/FAMIGLIA	MUTAZIONE 1	MUTAZIONE 2
OMOZIGOTI		
	c.5835-5838delCTTT (p.F1946SfsX23)	c.5835-5838delCTTT (p.F1946SfsX23)
	p.I1045T/P.L1836P	p.I1045T/P.L1836P
	p.R241G	p.R241G
ETEROZIGOTI COMPOSTI		
	p.A26E	p.L366P
	c.986dupG(p.N330QfsX5)	p.R1240Q
	p.R241G	c.6025delG(p.A2009PfsX32)
	p.R241G	p.G1218R
ETEROZIGOTI		
	p.R241G	N

RICORRENTE IN FAMIGLIE PUGLIESI. EFFETTO FONDATORE?

Myo7A


I
1
2
3
4
5
6
7
8
9
10
n.c.
Tutti con figli sani
Tutti con figli sani
II
1
2
3
4
5
6
III
1
2
3
4
5
D11S1321
D11S4179
Myo7A
D11S4186
D11S1789
D11S4079

USH2A: mutazioni

GENOTIPO O FAMIGLIA	MUTAZIONE 1	MUTAZIONE 2
ETEROZIGOTI		
	Y384X esone 7	N
	E478D (G>C nt1821 esone 8)	N
	E478D (G>C nt1821 esone 8)	N
	P1059L(C>T nt 3563 esone 16)	N
	C664F(G>T nt2376 esone12)	N
	G713R	N
	G713R	N
	L178R(T>G nt 917 esone 3)	N
	V230M(G>A nt1075 esone 4)	N
	C766R (G>A nt 2684 esone 16) in 2 casi	N
	G713R	N
	V218E(T>A nt1040 esone 4)	N
	R283S (G>C nt 1236 esone 6)	N
	Y1123C(A>G nt 3755 esone 17)	N
	C766R T>C nt2683 esone 16	N
	11864G>A	N
	P1059L NON CHIARO SIGNIF	N
	G268R	N

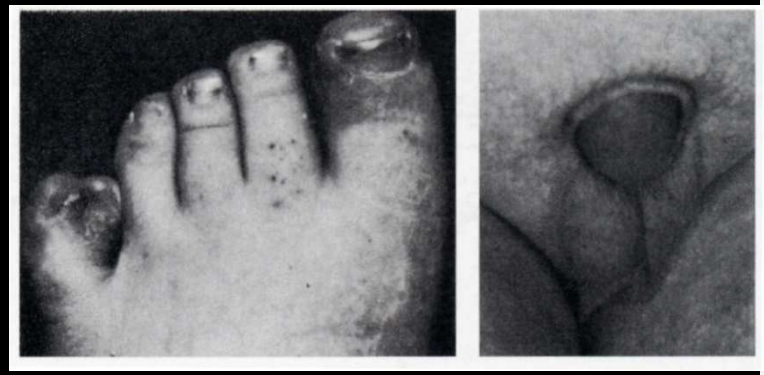
GENOTIPO O FAMIGLIA	MUTAZIONE 1	MUTAZIONE 2
	ins CAGC H308fs"	N
	T352I *mai descritta	N
ETEROZIGOTI COMPOSTI		
	E181FS	2299delG
	E478D (G>C nt1821 esone 8)	W1382R (G>C nt4532 esone19)
	C577R(T>C nt 2116 esone 10)	C870X(C>A nt 2996 esone 13)
	V230M (G>A nt 1076 esone 4)	V218E(T>A nt1040 esone 4)
OMOZIGOTI		
	Thr352Ile	Thr352Ile

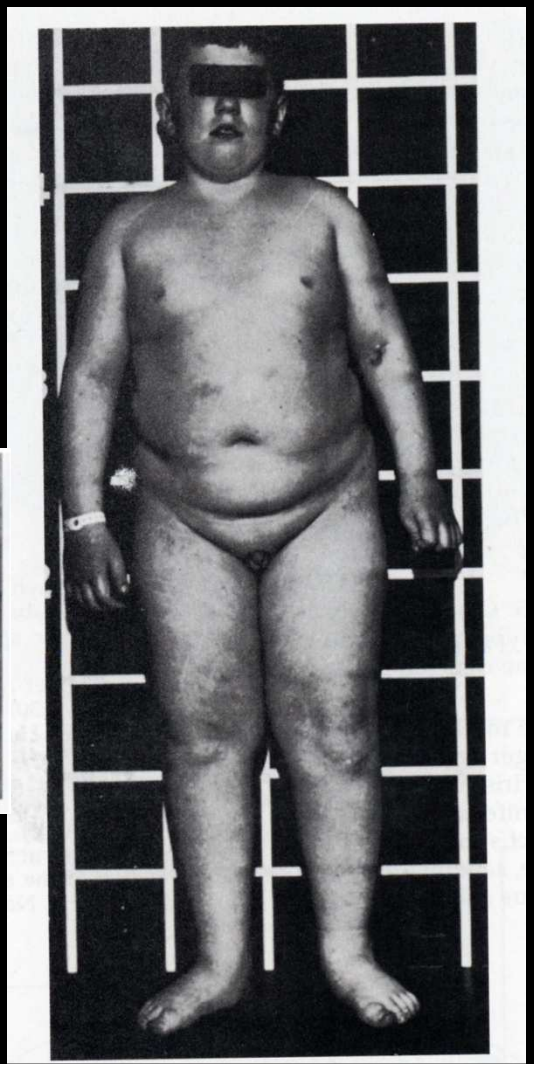
3b) BARDET BIEDL SYNDROME

prevalenza in Nord Europa e in America: da 1 su 100000 a 1 su 160000.

- Cone-rod dystrophy
- Polidattilia post assiale
- Obesità truncale
- Problemi d'apprendimento
- Ipogonadismo/anomalie genitali
- Anomalie renali

la cecità notturna è evidente già a 7 anni d'età





Trasmissione complessa

AR

multiallelica

Katsanis N, Ansley SJ, Badano JL, Eichers ER, Lewis RA, Hoskins BE, Scambler PJ, Davidson WS, Beales PL, Lupski JR.
Triallelic inheritance in Bardet-Biedl syndrome, a Mendelian recessive disorder.
Science. 2001; 293: 2256–9. [PubMed]

- Triallelica o digenica
  - Non è sufficiente l'omozigosi o l'eterozigosi composta per mutazioni in un gene BBS, occorre una terza mutazione in un altro gene BBS perché si manifesti la malattia

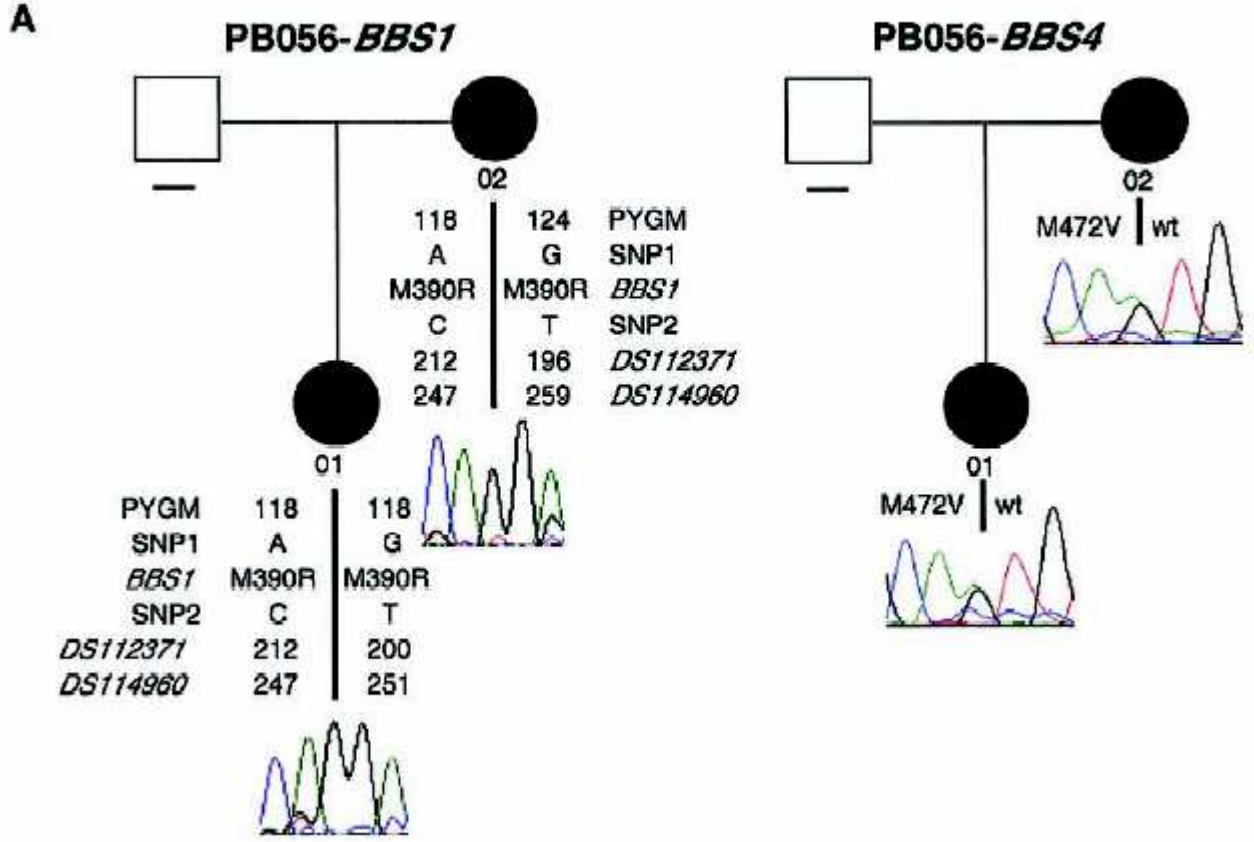
Am. J. Hum. Genet. 72:1187–1199, 2003

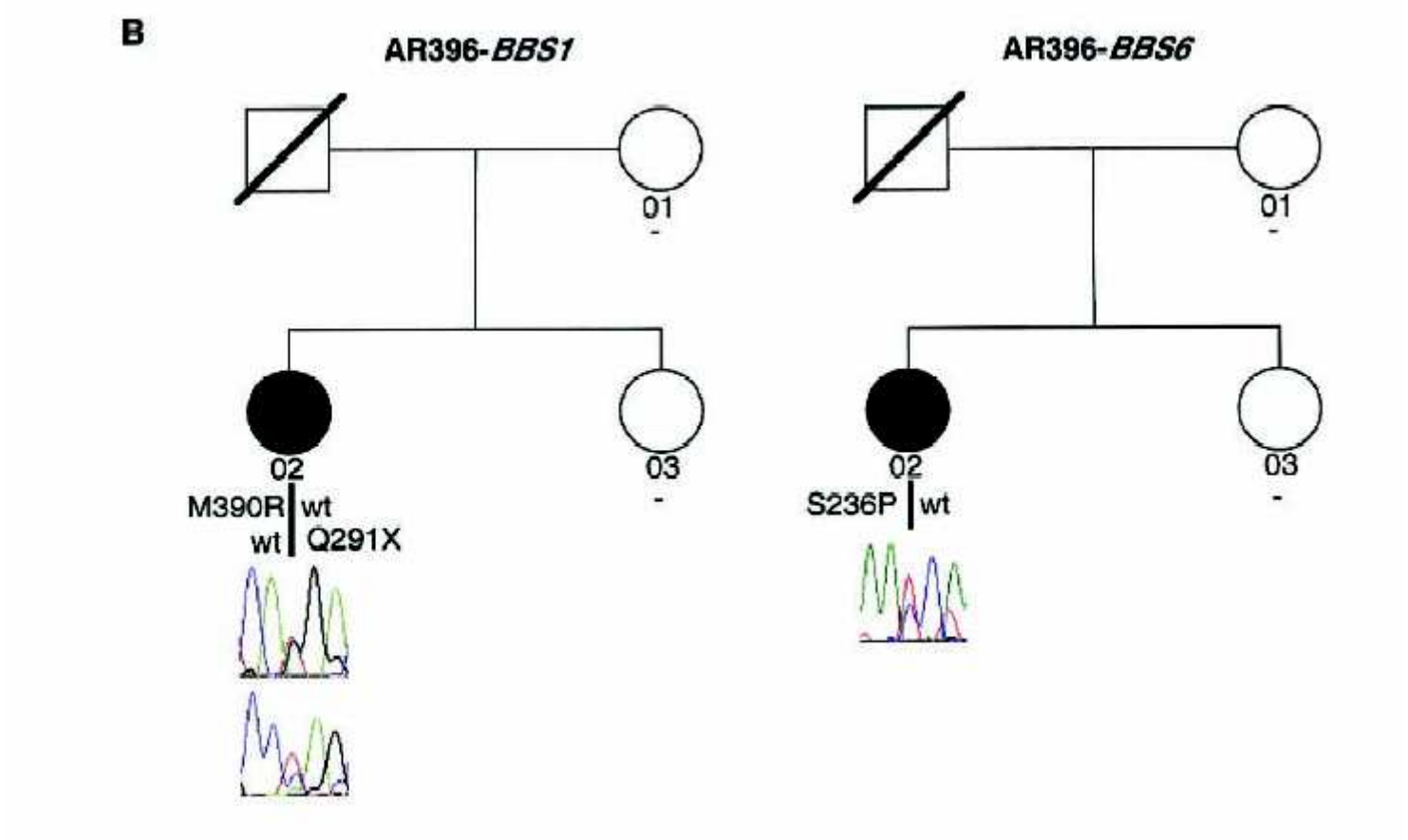
Genetic Interaction of *BBS1* Mutations with Alleles at Other *BBS* Loci Can Result in Non-Mendelian Bardet-Biedl Syndrome

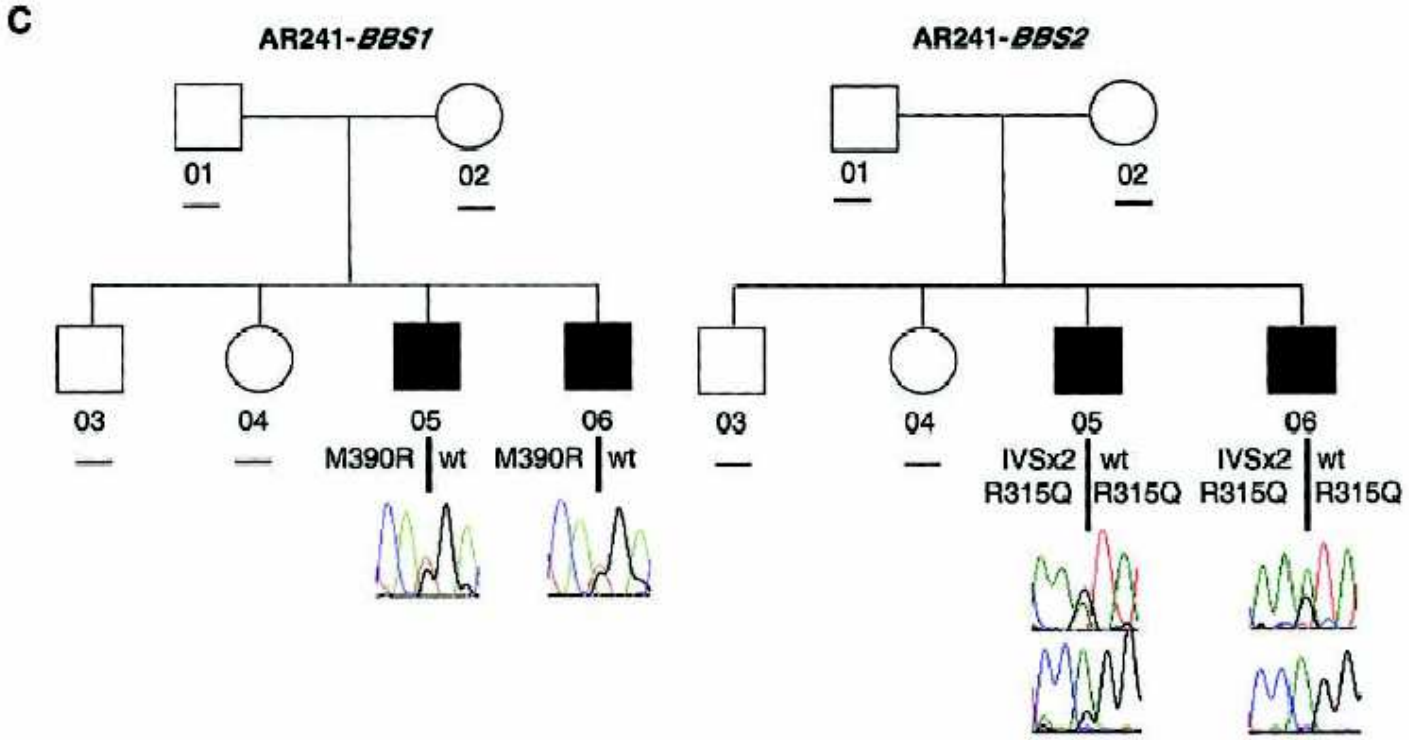
Philip L. Beales,[1,*] Jose L. Badano,[3,*] Alison J. Ross,[1] Stephen J. Ansley,[3] Bethan E. Hoskins,[1] Brigitta Kirsten,[2] Charles A. Mein,[2] Philippe Froguel,[2,5] Peter J. Scambler,[1] Richard Alan Lewis,[6,7,8,9] James R. Lupski,[6,8] and Nicholas Katsanis[3,4]

[1]Molecular Medicine Unit, Institute of Child Health, University College London, [2]Genome Centre, Barts and the London, Queen Mary's School of Medicine and Dentistry, London; [3]Institute of Genetic Medicine and [4]Wilmer Eye Institute, Johns Hopkins University, Baltimore; [5]CNR-Institute of Biology, Pasteur Institute, Lille, France; and Departments of [6]Molecular and Human Genetics, [7]Ophthalmology, [8]Pediatrics, and [9]Medicine, Baylor College of Medicine, Houston

Bardet-Biedl syndrome is a genetically and clinically heterogeneous disorder caused by mutations in at least seven loci (*BBS1–7*), five of which are cloned (*BBS1, BBS2, BBS4, BBS6,* and *BBS7*). Genetic and mutational analyses have indicated that, in some families, a combination of three mutant alleles at two loci (triallelic inheritance) is necessary for pathogenesis. To date, four of the five known *BBS* loci have been implicated in this mode of oligogenic disease transmission. We present a comprehensive analysis of the spectrum, distribution, and involvement in non-Mendelian trait transmission of mutant alleles in *BBS1*, the most common *BBS* locus. Analyses of 259 independent families segregating a BBS phenotype indicate that *BBS1* participates in complex inheritance and that, in different families, mutations in *BBS1* can interact genetically with mutations at each of the other known *BBS* genes, as well as at unknown loci, to cause the phenotype. Consistent with this model, we identified homozygous M390R alleles, the most frequent *BBS1* mutation, in asymptomatic individuals in two families. Moreover, our statistical analyses indicate that the prevalence of the M390R allele in the general population is consistent with an oligogenic rather than a recessive model of disease transmission. The distribution of BBS oligogenic alleles also indicates that all BBS loci might interact genetically with each other, but some genes, especially *BBS2* and *BBS6*, are more likely to participate in triallelic inheritance, suggesting a variable ability of the BBS proteins to interact genetically with each other.


A
PB056-BBS1
02
118 124 PYGM
A G SNP1
M390R M390R BBS1
C T SNP2
212 196 DS112371
247 259 DS114960
01
PYGM 118 118
SNP1 A G
BBS1 M390R M390R
SNP2 C T
DS112371 212 200
DS114960 247 251
PB056-BBS4
02
M472V wt
01
M472V wt


B
AR396-BBS1
01
-
02
M390R | wt
wt | Q291X
03
-
AR396-BBS6
01
-
02
S236P | wt
03
-


C
AR241-BBS1
01
02
03
04
05
06
M390R | wt
M390R | wt
AR241-BBS2
01
02
03
04
05
06
IVSx2 R315Q | wt R315Q
IVSx2 R315Q | wt R315Q

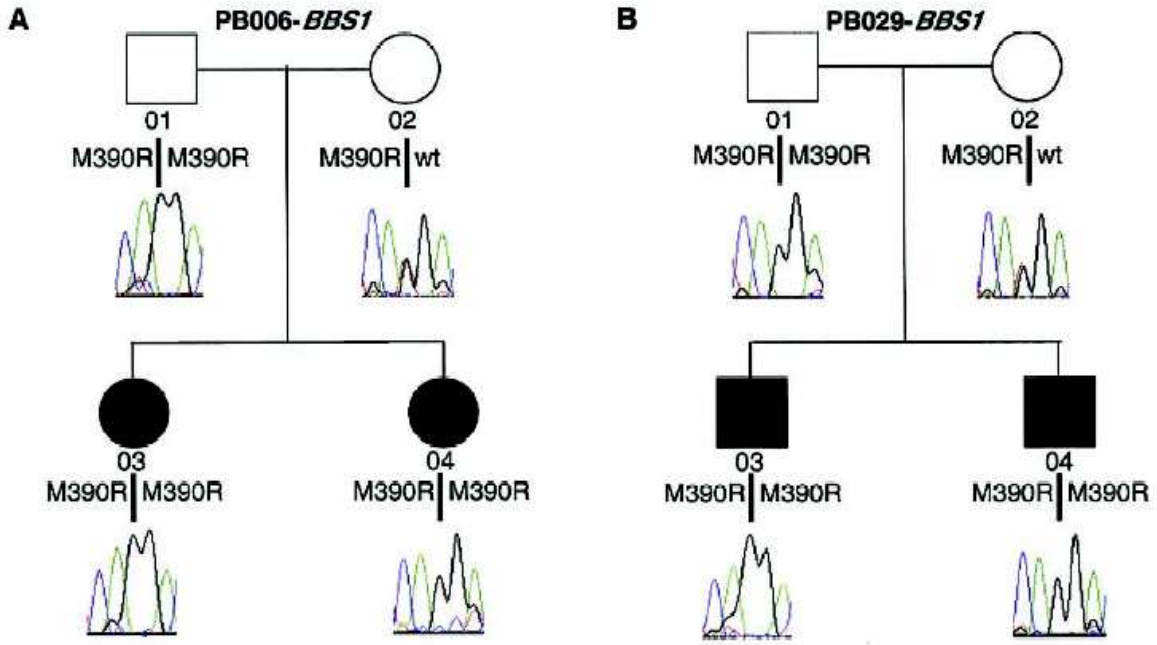
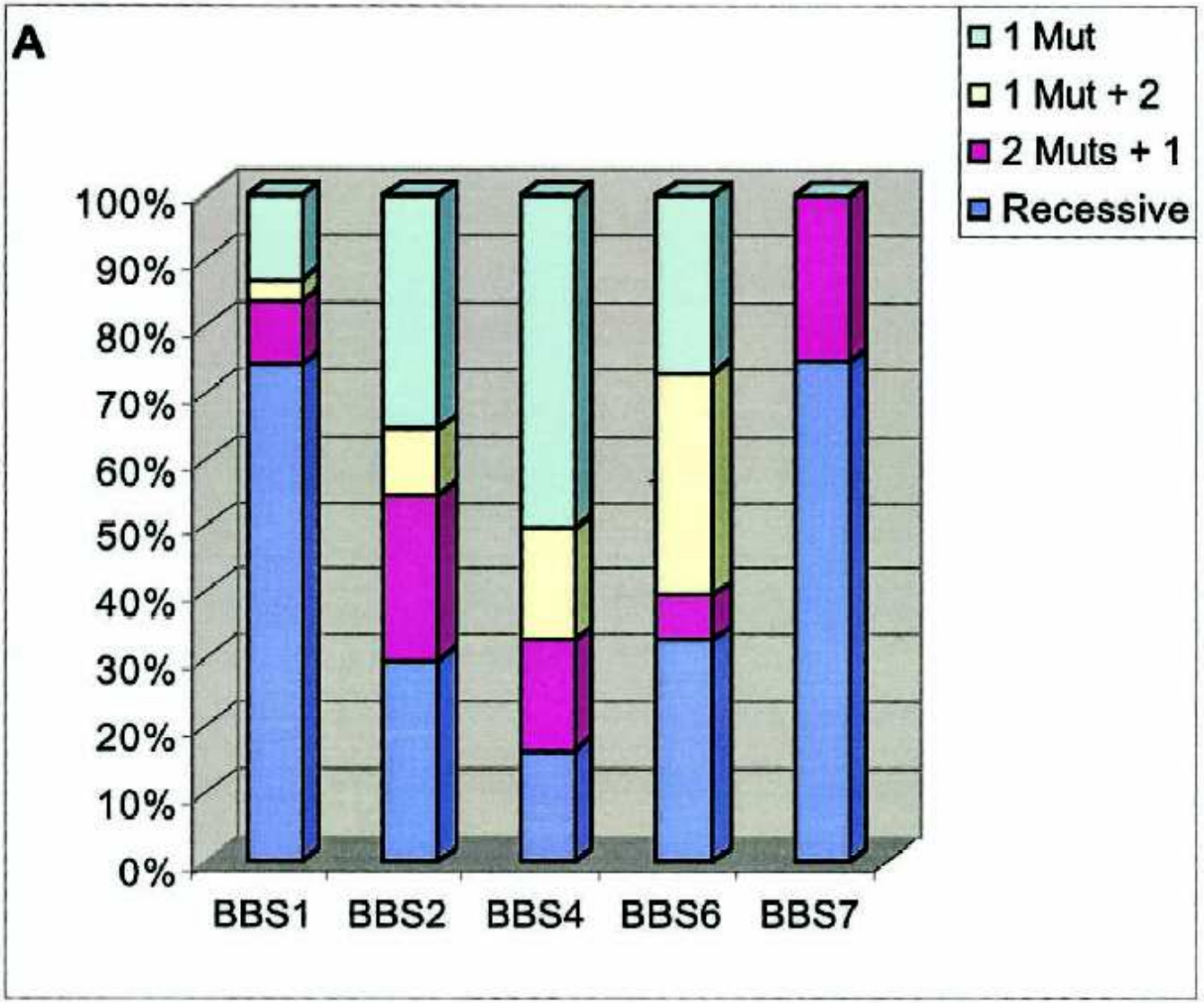


Figure 3 Two M390R mutations are not sufficient for pathogenesis. In pedigrees PB006 (*A*) and PB029 (*B*), the unaffected father is homozygous for the common M390R allele, as are all affected individuals. A third mutation has not yet been found in these two families.


A
1 Mut
1 Mut + 2
2 Muts + 1
Recessive
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
BBS1
BBS2
BBS4
BBS6
BBS7

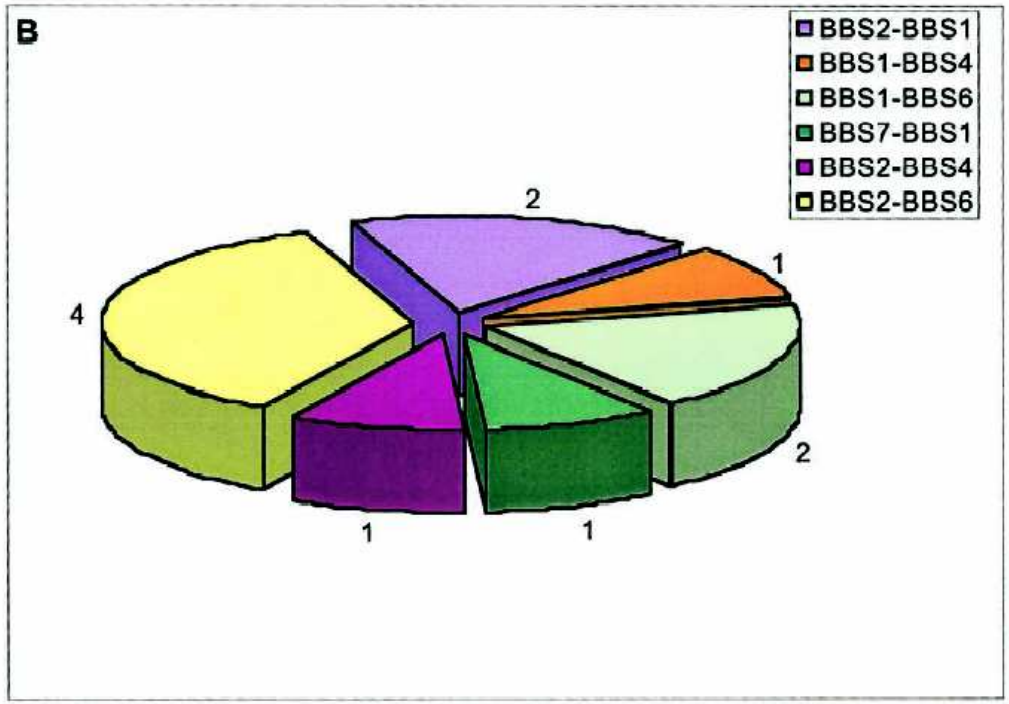


Figure 4 Analysis of triallelism. *A*, Bar graph demonstrating the distribution of recessive and complex alleles in each of the five cloned *BBS* genes. The relative contribution of one or two alleles is also indicated. *B*, Pie chart depicting the prevalence of locus combinations in families with complex BBS. Combinations were scored irrespective of the number of alleles provided by each locus. Numbers outside each slice indicate how many families exhibit each locus combination.

Human Molecular Genetics, 2003, Vol. 12, No. 14 **1651–1659**
DOI: 10.1093/hmg/ddg188

Heterozygous mutations in *BBS1*, *BBS2* and *BBS6* have a potential epistatic effect on Bardet–Biedl patients with two mutations at a second BBS locus

Jose L. Badano[1], Jun Chul Kim[2], Bethan E. Hoskins[3], Richard Alan Lewis[4], Stephen J. Ansley[1], David J. Cutler[1], Claudio Castellan[5], Philip L. Beales[3], Michel R. Leroux[2] and Nicholas Katsanis[1,5,6,*]

[1]Institute of Genetic Medicine, Johns Hopkins University, 600 North Wolfe Street, Baltimore, MD 21287, USA, [2]Department of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, BC, Canada V5A 1S6, [3]Molecular Medicine Unit, Institute of Child Health, University College London, London WC1N 1EH, UK, [4]Departments of Molecular and Human Genetics, Ophthalmology, Pediatrics, and Medicine, Baylor College of Medicine, One Baylor Plaza, Houston TX 77030, USA, [5]The Clinical Genetics Service, Bolzano General Hospital, Bolzano 39100, Italy and [6]Wilmer Eye Institute, Johns Hopkins University, 600 North Wolfe Street, Baltimore, MD 21287, USA

Received March 3, 2003; Revised and Accepted May 19, 2003

Bardet–Biedl syndrome (BBS) is a pleiotropic genetic disorder with substantial inter- and intrafamilial variability, that also exhibits remarkable genetic heterogeneity, with seven mapped BBS loci in the human genome. Recent data have demonstrated that BBS may be inherited either as a simple Mendelian recessive or as an oligogenic trait, since mutations at two loci are sometimes required for pathogenesis. This observation suggests that genetic interactions between the different BBS loci may modulate the phenotype, thus contributing to the clinical variability of BBS. We present three families with two mutations in either *BBS1* or *BBS2*, in which some but not all patients carry a third mutation in BBS1, BBS2 or the putative chaperonin BBS6. In each example, the presence of three mutant alleles correlates with a more severe phenotype. For one of the missense alleles, we also demonstrate that the introduction of the mutation in mammalian cells causes a dramatic mislocalization of the protein compared with the wild-type. These data suggest that triallelic mutations are not always necessary for disease manifestation, but might potentiate a phenotype that is caused by two recessive mutations at an independent locus, thus introducing an additional layer of complexity on the genetic modeling of oligogenicity.

Associazione CHARGE

Il nome CHARGE trae origine dall'acronimo delle iniziali dei difetti più comuni presenti in questi casi:

- C: Coloboma (difetto visivo);
- H: Heart defects (difetti cardiaci);
- A: Atresia delle coane;
- R: Ritardo mentale,di crescita e/o sviluppo;
- G: Genital and urinary abnormalities (malformazioni dell'apparato genitale ed urinario);
- E: ear (orecchio: malformazioni dell'orecchio interno ed esterno).