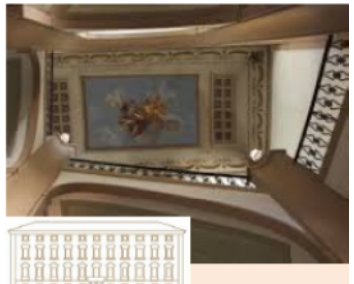
XVII Corso residenziale

REGISTRO TOSCANO DI FETTI CONGENITI

Malformazioni Congenite dalla Diagnosi Prenatale alla Terapia Postnatale

Le Mucopolisaccaridosi
La Trisomia 21

18-19 ottobre 2018



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BGENETICA GENETIC CARE

# LA GENETICA

# DELLA TRISOMIA 21


Sebastiano Bianca
Chiara Barone

Genetica Medica

geneticamedica@arnasgaribaldi.it – genetica@bgenetica.it

## Down syndrome in Down House: trisomy 21, *GATA1* mutations, and Charles Darwin

At the outer edge of the leafy southeastern London suburbs lies the small village of Downe, nestled in the rolling hills of Kent just 16 miles from the city. The chief attraction of Downe for nonresidents is Down House (the customary spelling for the estate is different from that of the village), the family home of the man who was arguably England's most important contribution to the biological sciences: the great naturalist Charles Robert Darwin (1809-1882). In recent years, Down House has been extensively restored, and the property is now maintained in the public trust by English Heritage. The site is an increasingly popular pilgrimage destination for biologists and others with an interest in the history of the natural sciences.

During a recent visit to Downe, my daughter and I were fascinated by the Darwin family photos scattered about the 19th-century rooms on the ground floor of Down House. I was prompted to read the sensitive and engaging account of Darwin's family life published by his great-great-grandson, Randal Keynes.[1] By all accounts, Darwin and his wife (and first cousin) Emma Wedgewood enjoyed a close, warm, and generally happy domestic existence, limited by Charles' poorly defined chronic ailments—possibly sequelae of Chagas disease contracted during the voyage of the *Beagle*—and broken by the premature deaths of 3 of their 10 children.



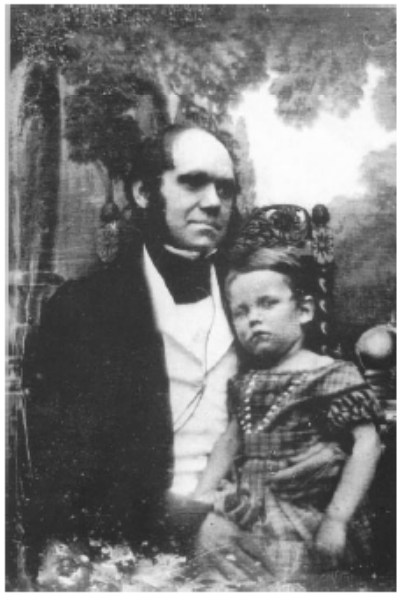


**Figure 2. An 1842 daguerrotype of Charles Darwin and his oldest son, William.** Copyright NMR/English Heritage, used with permission.

**Figure 1. An 1857 photograph of 48-year-old Emma Darwin and her youngest child, Charles Waring, taken by 17-year-old William with a camera he received for his birthday.** Although not diagnostic, the baby's facial features are consistent with a diagnosis of Down syndrome, and advanced maternal age and the notes taken by Charles also support this diagnosis. Copyright English Heritage, used with permission.

# LA SINDROME DI DOWN

Descritta da:

John Langdon Down

(1866)

Jerome Lejeune

(1959)

## OBSERVATIONS ON AN ETHNIC CLASSIFICATION OF IDIOTS.

By J. LANGDON H. DOWN, M.D., Lond.

---

Those who have given any attention to congenital mental lesions, must have been frequently puzzled how to arrange, in any satisfactory way, the different classes of this defect which may have come under their observation. Nor will the difficulty be lessened by an appeal to what has been written on the subject. The systems of classification are generally so vague and artificial, that, not only do they assist but feebly, in any mental arrangement of the phenomena which are presented, but they completely fail in exerting any practical influence on the subject.

The medical practitioner who may be consulted in any given case, has, perhaps in a very early condition of the child's life, to give an opinion on points of vital importance as to the present condition and probable future of the little one. Moreover, he may be pressed as to the question, whether the supposed defect dates from any cause subsequent to the birth or not. Has the nurse dosed the child with opium? Has the little one met with any accident? Has the instrumental interference which maternal safety demanded, been the cause of what seems to the anxious parents, a vacant future? Can it be that when away from the family attendant the calomel powders were judiciously prescribed? Can, in fact, the strange anomalies which the child presents, be attributed to the numerous causes which maternal solicitude conjures to the imagination, in order to account for a condition, for which any cause is sought, rather than hereditary

s 2



Dans ces nouvelles conditions expérimentales, la présence de la *m*-phénylènediamine comme catalyseur est indispensable : en son absence, il n'apparaît aucune formation d'urée.

Dans ce milieu hydroalcoolique, la présence des accepteurs d'oxygène exerce un effet inhibiteur analogue à celui qu'elle manifeste en milieu organique (tableau III) :

Tableau III.

| Poids d'hydroquinone ajouté au milieu hydroalcoolique irradié (mg). | Poids d'urée radioformée (mg). |
|---|---|
| 100 | 77,6 |
| 250 | 47,5 |

Le rendement élevé obtenu, en l'absence d'accepteurs d'oxygène, dans cette radiosynthèse de l'urée, est à souligner.

(1) *Comptes rendus*, 240, 1955, p. 1026.

GÉNÉTIQUE. — *Étude des chromosomes somatiques de neuf enfants mongoliens.* Note de M. Jérôme Lejeune, Mlle Marthe Gautier et M. Raymond Turpin, présentée par M. Léon Binet.

La culture de fibroblastes de neuf enfants mongoliens révèle la présence de 47 chromosomes, le chromosome surnuméraire étant un petit télocentrique. L'hypothèse du déterminisme chromosomique du mongolisme est envisagée.

Chez neuf enfants mongoliens l'étude des mitoses de fibroblastes en culture récente (1) nous a permis de constater régulièrement la présence de 47 chromosomes. Les observations faites dans ces neuf cas (cinq garçons et quatre filles) sont consignées dans le tableau ci-après.

Le nombre de cellules comptées dans chaque cas peut sembler relativement faible. Ceci tient au fait que seules ont été retenues dans ce tableau les images ne prêtant qu'à un minimum d'interprétation.

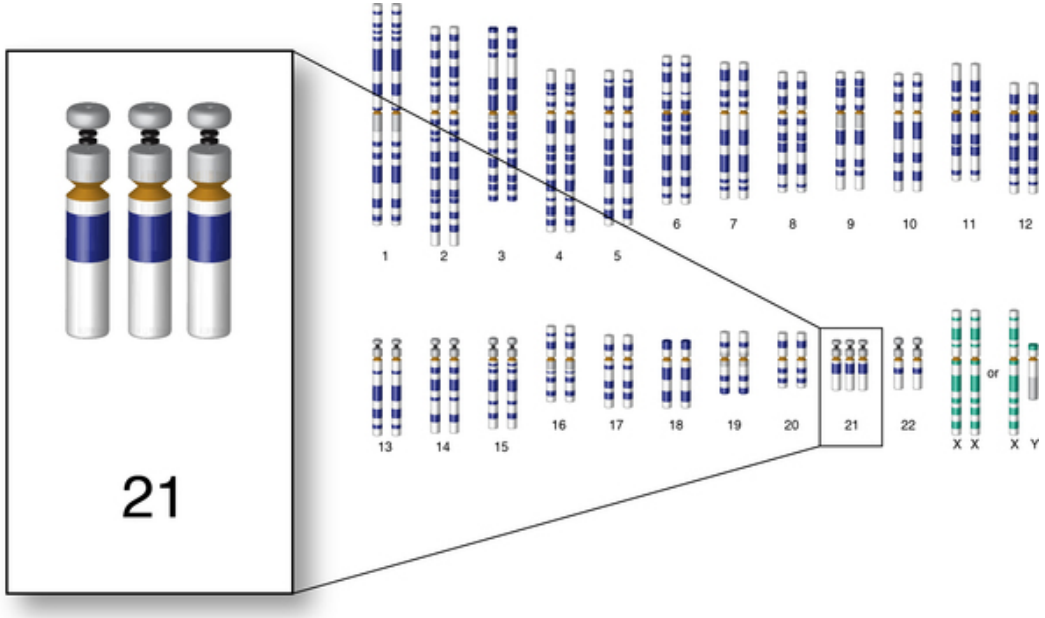
L'apparente variation du nombre chromosomique dans les cellules « douteuses », c'est-à-dire celles dont chaque chromosome ne peut être individualisé avec une absolue certitude est signalée par de nombreux auteurs (2). Ce phénomène ne nous semble pas correspondre à une réalité cytologique, mais reflète simplement les difficultés d'une technique délicate.

Il nous semble donc logique de préférer un petit nombre de dénombrements absolument certains (cellules « parfaites » du tableau) à une accumulation d'observations douteuses dont la variance statistique ne dépend que de l'imprécision des observations.

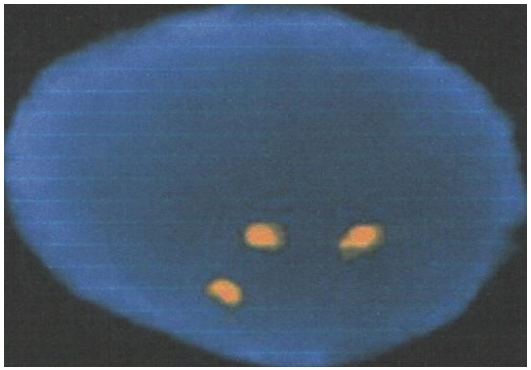
L'analyse de la garniture chromosomique des cellules « parfaites »

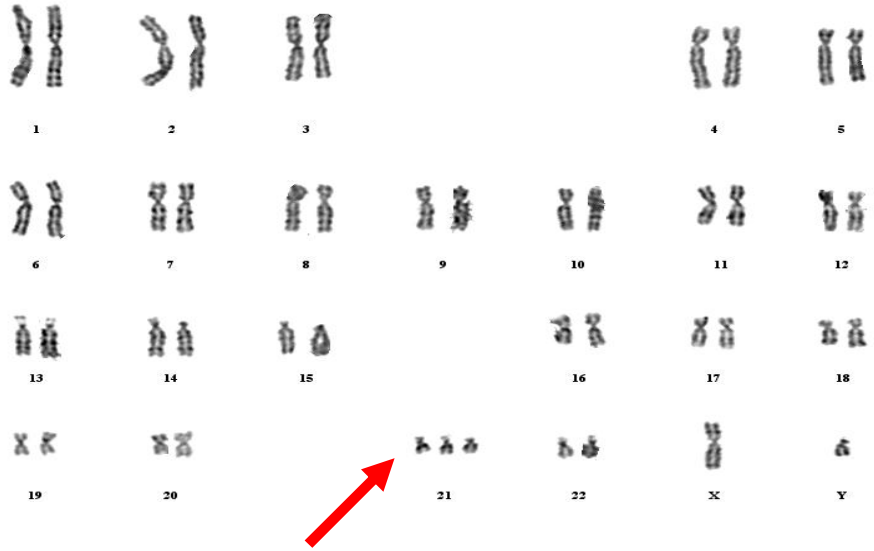
Source gallica.bnf.fr / Bibliothèque nationale de France

- Esistono tre tipi di anomalie cromosomiche nella sindrome di Down, il loro effetto finale è comunque identico: nelle cellule dei vari organi i geni del cromosoma 21 sono in triplice dose.

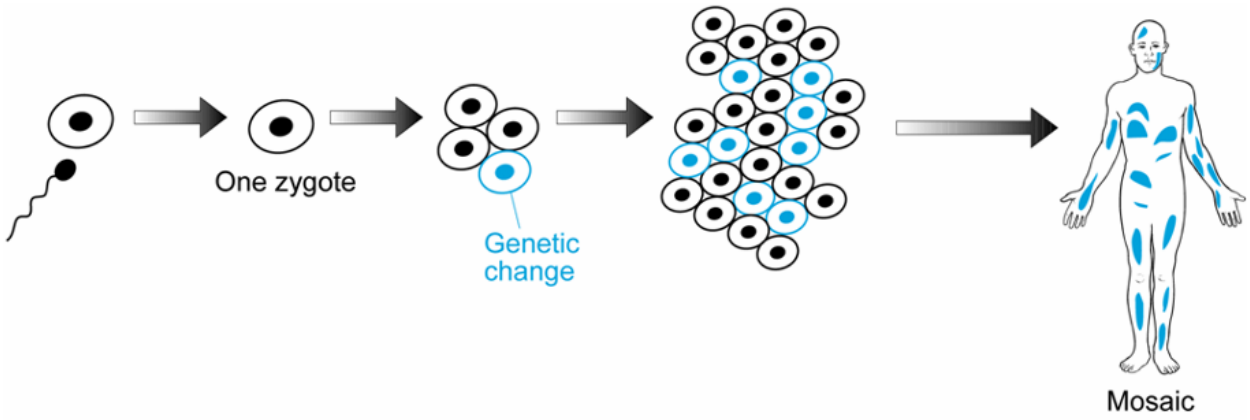


- L'anomalia più frequente è la **Trisomia 21 libera completa** (95% dei casi): in tutte le cellule dell'organismo vi sono tre cromosomi 21 invece di due; ciò è dovuto al fatto che durante le meiosi delle cellule germinali la coppia dei 21 non si è disgiunta come avrebbe dovuto (90% dei casi durante la meiosi della cellula uovo materna, 10% durante la meiosi degli spermatozoi paterni).





- Più raramente si riscontra la **Trisomia 21 libera in mosaicismo** (2% dei casi): nell'organismo della persona con la sindrome sono presenti sia cellule normali con 46 cromosomi che cellule con 47 cromosomi (la non disgiunzione della coppia 21 in questo caso si è verificata alle prime divisioni della cellula uovo fecondata).



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European Journal of Medical Genetics 48 (2005) 75–76
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## Letter to the editor

### Double aneuploidy mosaicism with Down–Klinefelter's syndrome

We read with interest the report of Iliopoulos et al. [4], on a double trisomy with Klinefelter and Down syndrome aneuploidy.

Recently, we observed a double aneuploidy mosaicism with Down–Klinefelter's syndrome in a 33 years old patient who required genetic counseling for sterility. He was born from healthy and non-consanguineous parents (32 years old mother and 35 years old the father). The cytogenetic study performed on peripheral blood lymphocytes culture showed a 47,XXY/47,XY+21 (52%/48%) mosaicism on 100 metaphases while the skin fibroblasts culture, a mosaicism 60%/40% on 55 metaphases that was also confirmed by FISH. Seminal evaluation showed a severe oligospermia with 20,000 spermatozoa/ml. Clinical examination showed mild facial dysmorphism with epicanthus, flat nasal bridge and large neck. He showed a mild mental retardation frequenting up to secondary school with support and actually work as male nurse in a hospital. No genitalia anomalies and no KS typical physical phenotype features were observed. Patient does not give permission to take clinical picture. For the primary infertility and the high risk of aneuploidy in the children, the assisted reproduction was not recommended.

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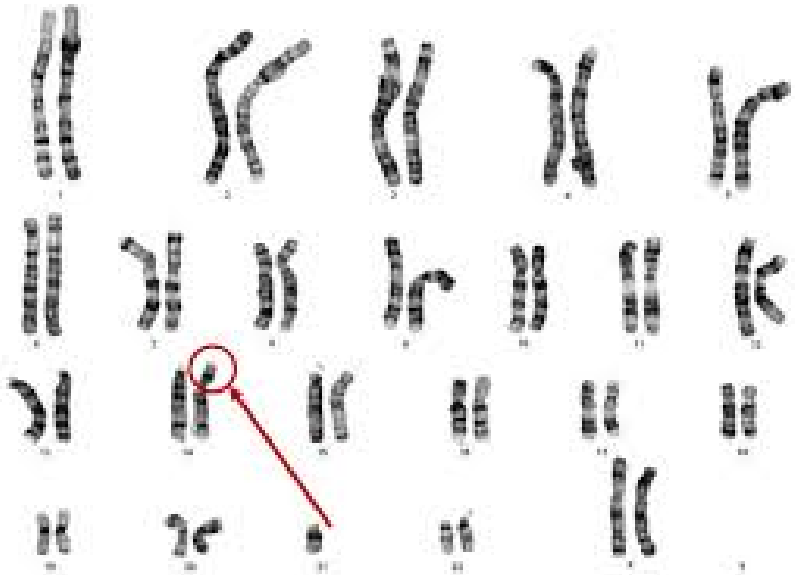
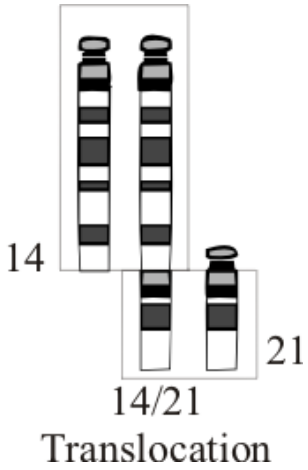
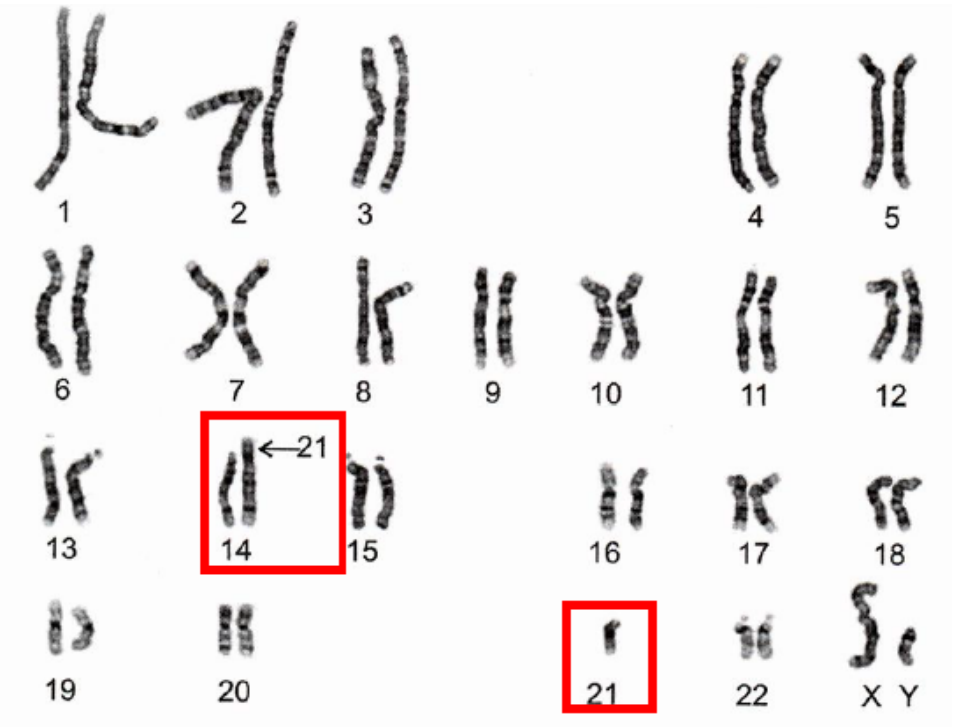
- Infine, il terzo tipo di anomalia, anch'essa rara, è la **Trisomia 21 da traslocazione** (3% dei casi): il cromosoma 21 in più (o meglio una parte di esso, almeno il segmento terminale) è attaccato ad un altro cromosoma di solito il numero 14, 21, o 22.

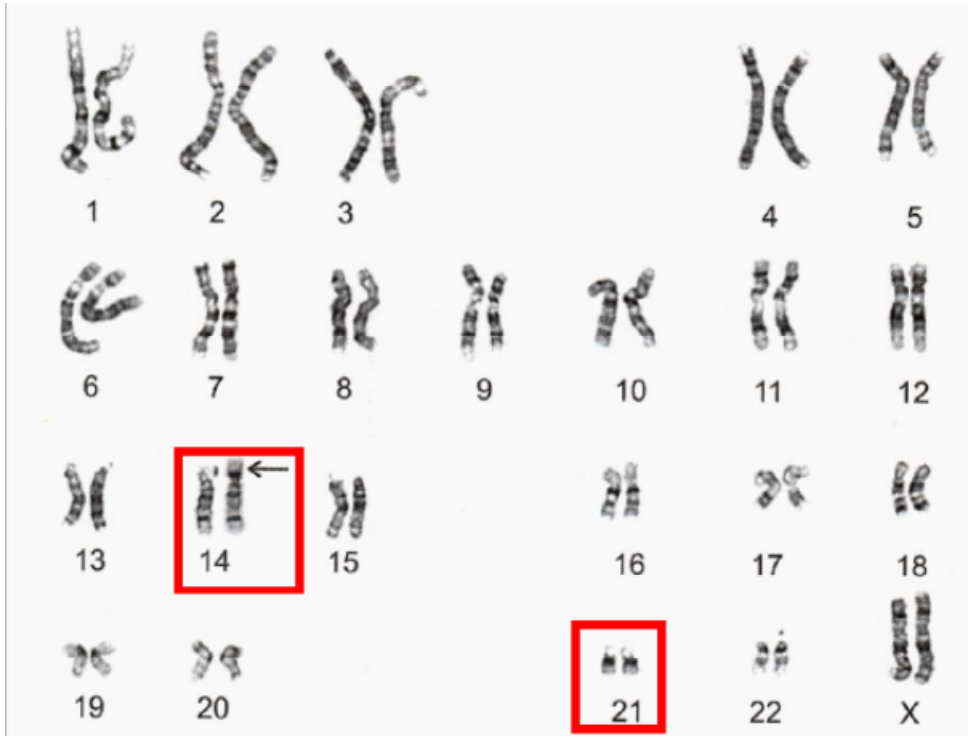




# Trisomia 21 da traslocazione

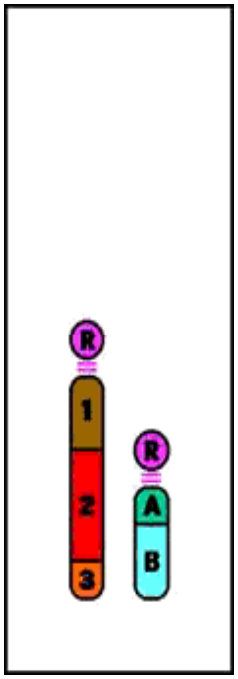



Penrose LS, et al. *Chromosomal translocations in mongolism and in normal relatives*. Lancet, 2, 409, 1960




Polani PE, et al. *A mongol girl with 46 chromosomes*. Lancet 1, 121, 1960

# traslocazioni robertsoniane (rob)




rob

- coinvolgono i cromosomi acrocentrici 13, 14, 15, 21 e 22
- nessuna regione cromosomica è assente, perché questi contengono un braccio corto privo di geni che può risultare perduto con la fusione dei bracci q di due cromosomi acrocentrici
- La più frequente traslocazione Robertsoniana è la rob(13q14q) che rappresenta il 75% di tutte le rob
- segue poi la rob(14q21q) e la rob(21q21q)
- si formano in genere durante la meiosi femminile e comportano infertilità maschile o abortività ripetuta.

## Percentuale alla nascita di figli con cariotipo sbilanciato da genitori con traslocazione robertsoniana

- t(13;14) M=F  1%
- t(14;21) F 15%  M 2%
- t(21;22) F 10%  M 5%
- t(21;21) M=F  100%

International Journal of Reproduction, Contraception, Obstetrics and Gynecology
*Vikraman SK et al. Int J Reprod Contracept Obstet Gynecol. 2015 Apr;4(2):514-517*
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: 10.5455/2320-1770.ijrcog20150451

**Case Report**

# A rare balanced parental t (21q; 21q) Robertsonian translocation that results in Down syndrome in all viable pregnancies

**Seneesh Kumar Vikraman*, Vipin Chandra, Bijoy Balakrishanan, Meenu Batra, Rekha Kuriakose, Gopinathan Kannoly**

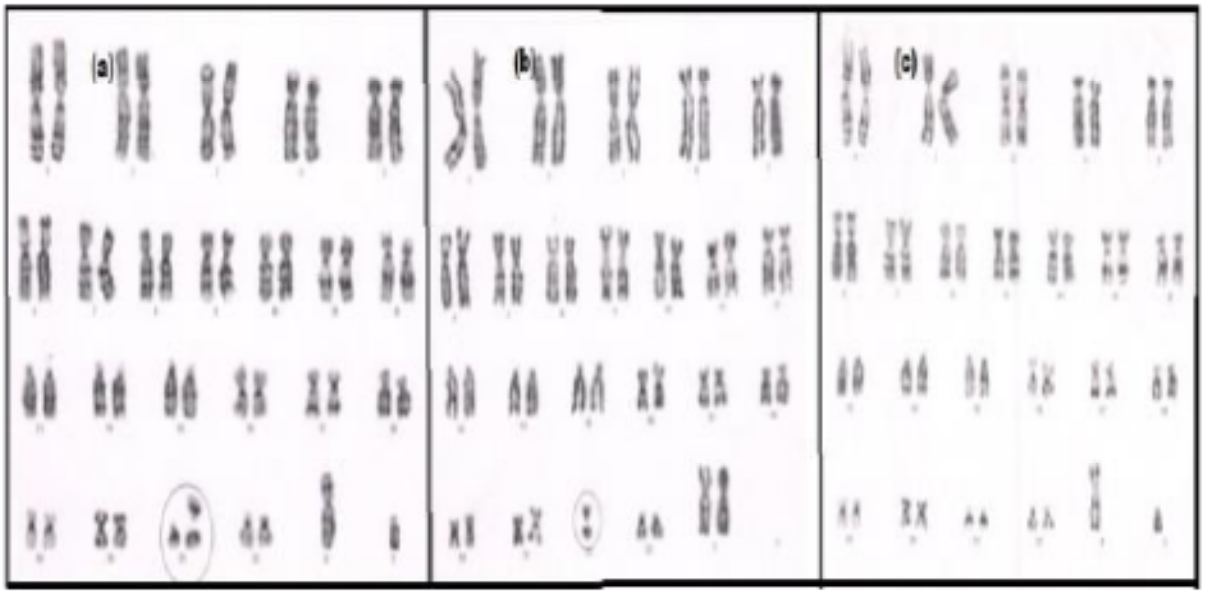
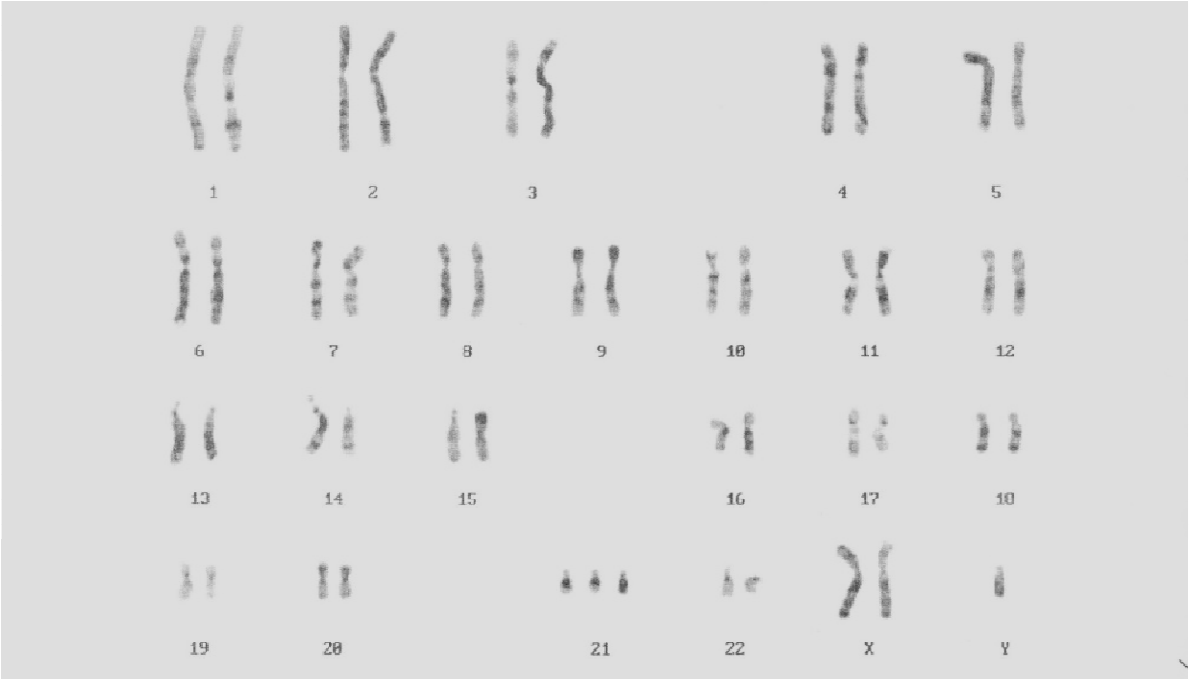



**Figure 1: a) Karyotype of the child affected with translocation Down syndrome -46, XY, -21, +t (21q; 21q); b) Karyotype of mother, shows isochromosome 21 in circle; c) Father's karyotype , normal 46XY. All**

## Traslocazione sbilanciata

- maggiori sono le dimensioni cromosomiche, minore è la possibilità di una gravidanza a termine
- minori sono le dimensioni, maggiore è il rischio di un feto malformato
- Sesso del genitore donna>uomo (gli spermatozoi hanno il 7.5% di difetti contro l'1% degli oociti, ma sono selezionati)

**L'esame del <u>cariotipo</u> evidenziava un assetto cromosomico 48,XXY+21.**




**Il riscontro di una doppia aneuploidia, ovvero la presenza di due anomalie cromosomiche numeriche in uno stesso individuo, è un fenomeno relativamente raro che origina da due eventi di non disgiunzione meiotica.**

# Doppia aneuploidia 48,XXY+21 con CAV

**La sindrome di Down e la sindrome di Klinefelter sono delle patologie cromosomiche piuttosto comuni che si presentano rispettivamente in 1/700 e 1/1000 nuovi nati.**
**La contemporanea presenza di entrambe le aneuploidie, secondo studi recenti, si presenterebbe con un'incidenza di circa $0,7 \times 10^{-5}$.**

**in caso di doppia aneuploidia Down-Klinefelter, le manifestazioni cliniche derivanti dalla presenza dell'autosoma accessorio tendono a prevalere su quelle determinate dal cromosoma sessuale accessorio essendo infatti il CAV la cardiopatia congenita più frequente nei soggetti Down**

# Inheritance of balanced translocation t(17; 22) from a Down syndrome mother to a phenotypically normal daughter

**X.Y. Liu, Y.T. Jiang, R.X. Wang, L.L. Luo, Y.H. Liu and R.Z. Liu**

Center for Reproductive Medicine, Center for Prenatal Diagnosis, First Hospital, Jilin University, Changchun, China

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DOI http://dx.doi.org/10.4238/2015.August.28.11

**ABSTRACT.** We report that a 30-year-old woman with mental retardation was referred for prenatal diagnoses during pregnancy. An ultrasound scan showed that the heart structure and function of the fetus were normal. Cytogenetic analysis showed that the female karyotype was 47,XX, t(17; 22) (q21; q11), +21. The woman's husband had a normal male karyotype and was phenotypically normal. During this first pregnancy, an amniocentesis, which was done at 19 weeks, revealed that the fetal karyotype was 46,XX, t(17; 22) (q21; q11). Fluorescence *in situ* hybridization testing of amniotic fluid gave a normal result for chromosome 21. The child was a phenotypically normal female baby.

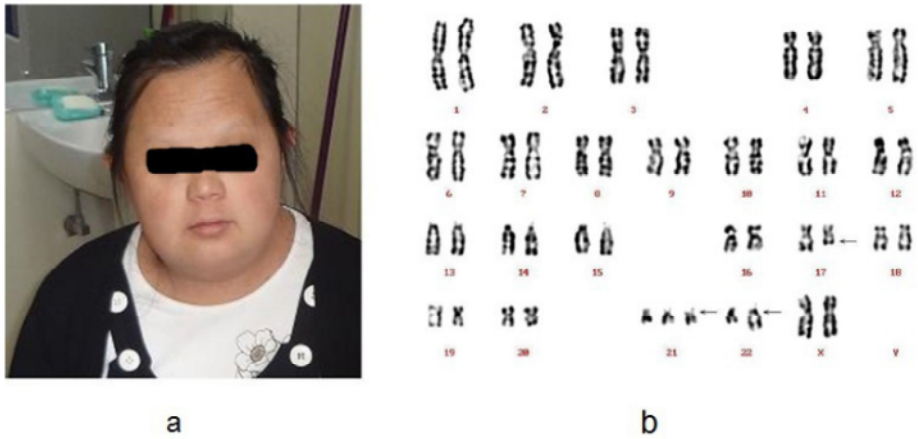


**Figure 1.** Facial features and chromosomal karyotype of the proband. **a.** Facial features of the female proband; **b.** abnormal karyotype of the female: 47,XX, t(17; 22) (q21; q11), +21.

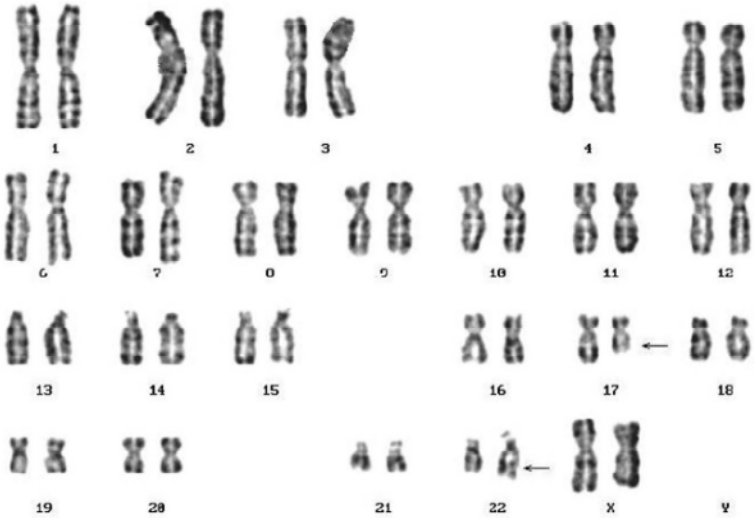


**Figure 2.** Karyotype of amniotic fluid cells: 46,XX, t(17; 22) (q21; q11) mat.

Bol Med Hosp Infant Mex 2011;68(3):206-210

CLINICAL CASE

# Down's syndrome associated with a balanced Robertsonian translocation 13;14 maternally transmitted in the product of a twin diamniotic pregnancy

Luis Gómez-Valencia,[1,2] Miriam Margot Rivera-Angles,[2,3] Anastasia Morales-Hernández,[2,3] and María de los Remedios Briceño-González[2,3]

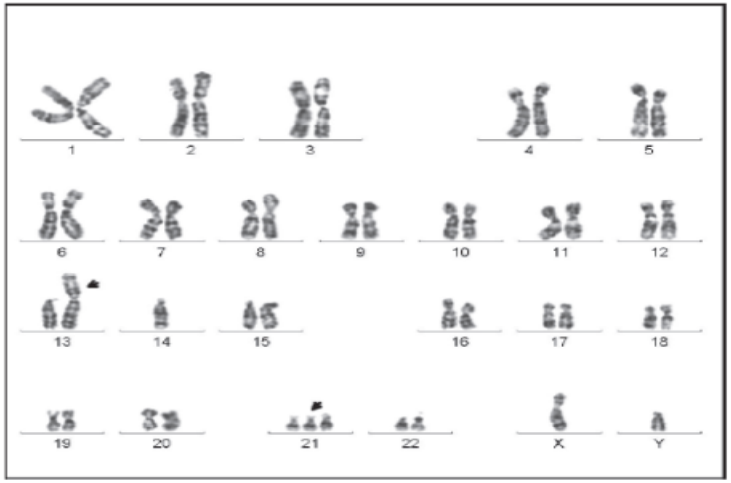


**Figure 3.** Metaphase and karyotype of the propositus showing the chromosome complement 46,XY, t(13-14) (q10,q10), +21.

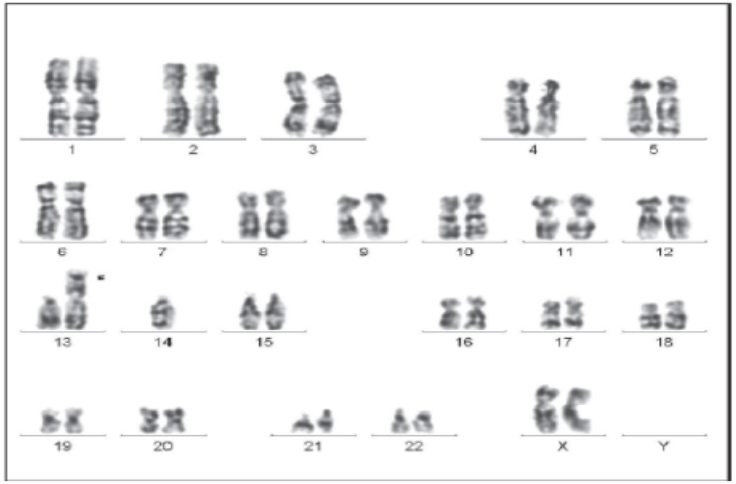


**Figure 4.** Metaphase and karyotype of the mother of the propositus who is a carrier of a balanced Robertsonian translocation 13,14.

# Sindrome di Down con 46 cromosomi: duplicazione regione critica

# Segni clinici

ductus arteriosus
constipation
celiac disease
inheritance
risk factor
hyperactivity
examination
diagnosis
father
maternal
heart disease
indicate
nuchal translucency test
mosaic
dementia
genetics
apnea
recurrence risk
infantile spasms
physical therapy
gonadotropin
brain
cardiac
amniocentesis
autism
ear
memory
down syndrome
human chorionic
analysis
acute
tetralogy of fallot
epicanthal fold
atresia
dysfunction
infant
cerebellum
fistula
hypotonia
depression
obesity
trisomy
chorionic villus sampling
hippocampus
adhd
tongue
nose
intervention
therapy
chromosome
ultrasound
sterosis
psychiatric
genes
speech therapy
pregnancy
serious disease
advanced maternal age
prenatal diagnosis
sleep apnea
cognitive
health problem

Asim et al. Journal of Biomedical Science (2015) 22:41
DOI 10.1186/s12929-015-0138-v

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REVIEW Open Access

# "Down syndrome: an insight of the disease"

Ambreen Asim, Ashok Kumar, Srinivasan Muthuswamy, Shalu Jain and Sarita Agarwal*

**Table 1 Some common gene present in chromosome 21**

| S. no. | Genes | Abbreviation |
|---|---|---|
| 1. | APP | Amyloid beta (A4) precursor protein |
| 2. | C21 or f59: | Chromosome 21 open reading frame 59 |
| 3. | CBS | Cystathionine-beta-synthase |
| 4. | CLDN14 | Claudin 14 |
| 5. | HLCS | Holocarboxylase synthetase (biotin-(proprionyl-coenzyme a-carboxylase (ATP-hydrolysing)) ligase) |
| 6. | KCNE1 | Potassium voltage-gated channel, isk-related family, member 1 |
| 7. | KCNE 2 | Potassium voltage-gated channel, isk-related family, member 2 |
| 8. | LAD | Leukocyte adhesion deficiency |
| 9. | SOD 1 | Superoxide dismutase 1 |
| 10. | TMPRSS3 | Transmembrane protease, serine 3 |
| 11. | PCNT | Centrosomal pericentrin |
| 12. | DSCR1 | Down Syndrome critical region 1 |
| 13. | DYRK1A | Dual specificity tyrosine-(Y)-phosphorylation regulated kinase 1A |
| 14. | RRPB1 | Ribosomal RNA processing 1 homolog B |
| 15. | S100B | Calcium binding protein |

Asim et al. Journal of Biomedical Science (2015) 22:41
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# "Down syndrome: an insight of the disease"

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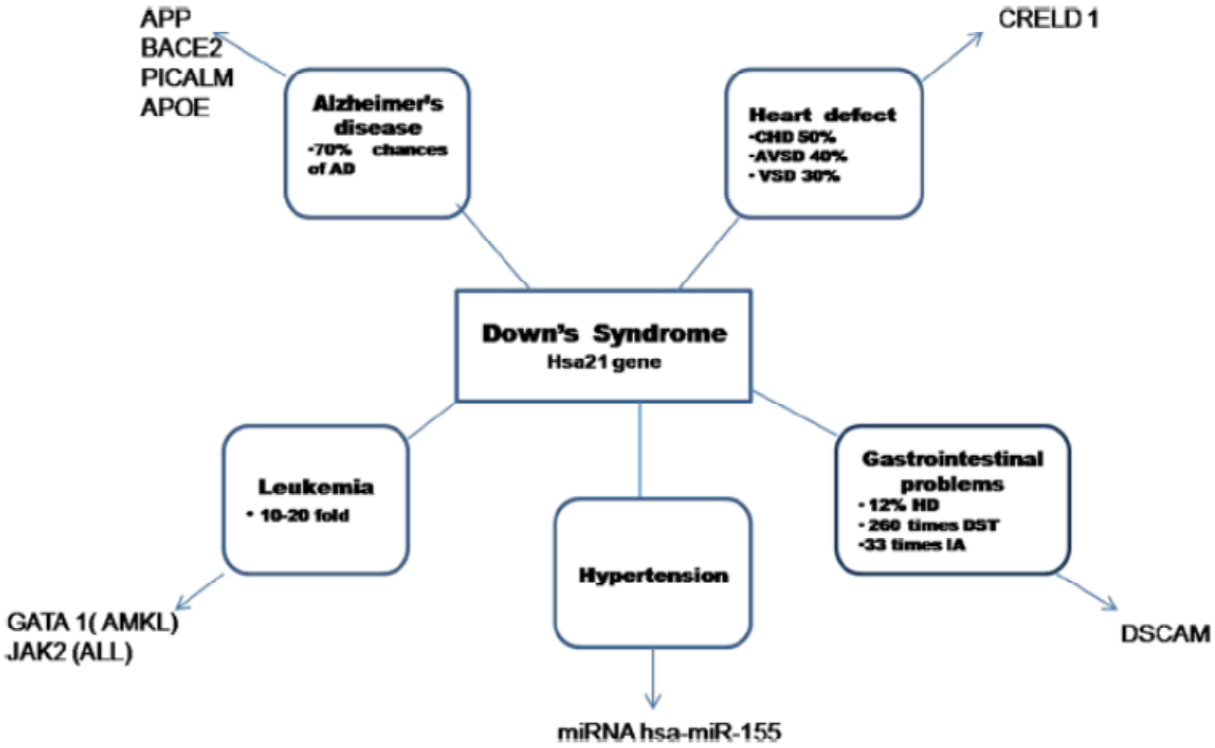


**Figure 1** Various conditions associated with Downs's syndrome with its causative genes.

OXFORD

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Advance Access Publication Date: 15 September 2015
Original Article

ORIGINAL ARTICLE

# Genetic dissection of the Down syndrome critical region

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## Abstract

Down syndrome (DS), caused by trisomy 21, is the most common chromosomal disorder associated with developmental cognitive deficits. Despite intensive efforts, the genetic mechanisms underlying developmental cognitive deficits remain poorly understood, and no treatment has been proven effective. The previous mouse-based experiments suggest that the so-called Down syndrome critical region of human chromosome 21 is an important region for this phenotype, which is demarcated by *Setd4/Cbr1* and *Fam3b/Mx2*. We first confirmed the importance of the *Cbr1-Fam3b* region using compound mutant mice, which carry a duplication spanning the entire human chromosome 21 orthologous region on mouse chromosome 16 [*Dp(16)1Yey*] and *Ms1Rhr*. By dividing the *Setd4-Mx2* region into complementary *Setd4-Kcnj6* and *Kcnj15-Mx2* intervals, we started an unbiased dissection through generating and analyzing *Dp(16)1Yey/Df(16Setd4-Kcnj6)Yey* and *Dp(16)1Yey/Df(16Kcnj15-Mx2)Yey* mice. Surprisingly, the *Dp(16)1Yey*-associated cognitive phenotypes were not rescued by either deletion in the compound mutants, suggesting the possible presence of at least one causative gene in each of the two regions. The partial rescue by a *Dyrk1a* mutation in a compound mutant carrying *Dp(16)1Yey* and the *Dyrk1a* mutation confirmed the causative role of *Dyrk1a*, whereas the absence of a similar rescue by *Df(16Dyrk1a-Kcnj6)Yey* in *Dp(16)1Yey/Df(16Dyrk1a-Kcnj6)Yey* mice demonstrated the importance of *Kcnj6*. Our results revealed the high levels of complexities of gene actions and interactions associated with the *Setd4/Cbr1-Fam3b/Mx2* region as well as their relationship with developmental cognitive deficits in DS.

Pediatric Surgery International
November 2018, Volume 34, Issue 11, pp 1127–1137 | Cite as

# Advances in understanding the association between Down syndrome and Hirschsprung disease (DS–HSCR)

Authors Authors and affiliations

S. W. Moore

## Abstract

The clinical association between Trisomy 21 (Down syndrome) and aganglionosis (Hirschsprung disease; DS–HSCR) is well-established, being of the order of 5% and remains the most common congenital association with Hirschsprung disease. However, little consensus exists as to the possible etiologic and genetic factors influencing this association. Recent research has identified a number of levels at which development of the enteric nervous system is potentially affected in Trisomy 21. These include a decreased central pool of available neuroblasts for migration into the enteric nervous system, abnormal neuroblast type, poor synaptic nerve function and early germline gene-related influences on the migrating neuroblasts due to genetic mutations of a number of important developmental genes, and possible somatic mutations resulting from alterations in the local tissue microenvironment. In this paper, we review available evidence for this association. In addition, we provide evidence of both germline and somatic gene mutations suggesting causation. Although the picture is complex, recent associations between specific RET proto-oncogene variations have been shown to be significant in Down syndrome patients with Hirschsprung disease, as they probably interfere with vital RET functions in the development of the autonomic and enteric nervous systems, increasing the risk of disturbed normal function. In addition, we explore potential role of other facilitatory influence of other susceptibility genes as well as potential other chromosome 21 gene actions and the microenvironment on the Down syndrome gastro-intestinal tract. The various ways in which trisomy of chromosome influences the enteric nervous system are becoming clearer. The sum of these effects influences the outcome of surgery in Down syndrome patients with Hirschsprung Disease.

Pediatric Cardiology
pp 1–5 | Cite as

# Targeted Next-Generation Sequencing of 406 Genes Identified Genetic Defects Underlying Congenital Heart Disease in Down Syndrome Patients

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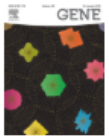
## Abstract

Down syndrome (DS) is the most common autosomal chromosome anomaly. DS is frequently associated with congenital heart disease (CHD). Patients with DS have 40–60% chance of having CHD. It means that CHD in DS is not only due to trisomy 21 and there are some other genetic factors underlying CHD in DS children. In this study, a total of 240 DNA samples from patients were analyzed including 100 patients with CHD only, 110 patients having CHD along with DS and 30 patients with isolated DS. A cardiovascular gene panel consisting of probes for 406 genes was used to screen DNA samples of all 240 patients for mutation identification. All variants were annotated and common variants were obtained. Briefly, 28 common variants (variants common in two or more than two individuals) were obtained in a group of samples containing DNA from DS patients having CHD as well, 63 variants were found to be unique to DS group of samples and 73 variants have been identified in patients with CHD only. In order to identify genomic variations determining the risk for CHD in DS, only those variants present in DS-CHD group and absent in isolated CHD and/or isolated DS group were considered for further analysis. Variants specific to DS-CHD group were further evaluated based on expression and function data and pathogenicity of the variant of interest. We have implicated mutations in *GATA3, KCNH2, ENG, FLNA*, and *GUSB* genes as an underlying risk factor for CHD in DS patients.

ELSEVIER

Gene

Volume 641, 30 January 2018, Pages 180-185




Research paper

# *CRELD1* gene variants and atrioventricular septal defects in Down syndrome ☆

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https://doi.org/10.1016/j.gene.2017.10.044

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## Highlights

- Sanger sequencing was done for detection of *CRELD1* gene variants in Down syndrome (DS) patients with AVSD
- 22 variants, 16 of which were novel were identified in DS with AVSD cases (Total n = 40)
- The E325 K variant in *CRELD1* gene was found in 3 DS with AVSD patients
- The same variant was also detected in one non-DS case with sporadic AVSD
- Bioinformatic analysis identified the variant to be possibly causative of the AVSD phenotype.
- *CRELD1* gene mutations appear to be a major factor in causation of AVSD in DS patients

*Nat Rev Neurosci*. 2015 September ; 16(9): 564–574. doi:10.1038/nrn3983.

# A genetic cause of Alzheimer disease: mechanistic insights from Down syndrome

Down syndrome, which arises in individuals carrying an extra copy of chromosome 21, is associated with a greatly increased risk of early-onset Alzheimer disease. It is thought that this risk is conferred by the presence of three copies of the gene encoding amyloid precursor protein (APP) — an Alzheimer disease risk factor — although the possession of extra copies of other chromosome 21 genes may also play a part. Further study of the mechanisms underlying the development of Alzheimer disease in people with Down syndrome could provide insights into the mechanisms that cause dementia in the general population.

*J Alzheimers Dis.* 2017 ; 56(2): 459–470. doi:10.3233/JAD-160836.

# Down Syndrome, Partial Trisomy 21, and Absence of Alzheimer's Disease: The role of APP

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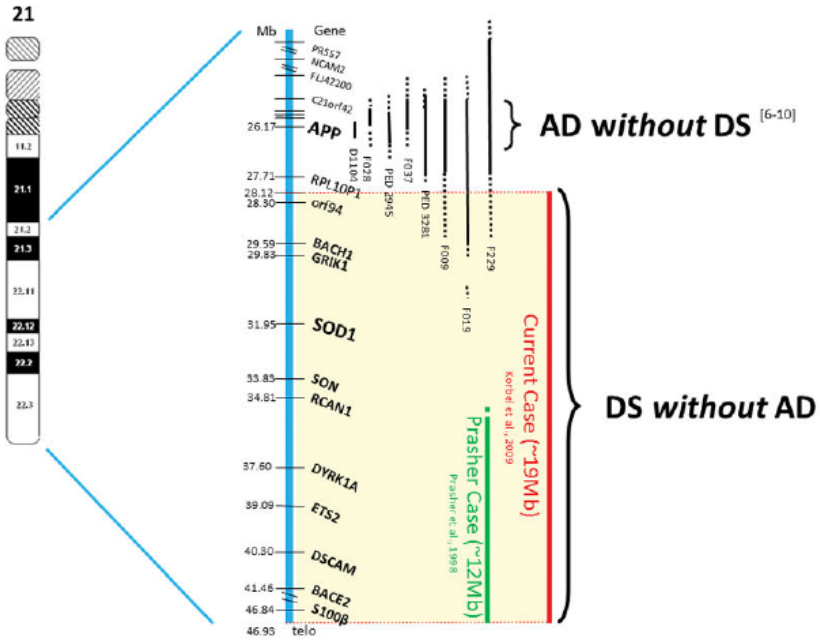


**Figure 1.**

Cases of AD without DS and of DS without AD. On the left side of the figure – chromosome 21. The vertical thick blue bar adjacent to the chromosome, indicates the distal ~25Mb of chromosome 21 genes and markers with their position in Mb. The first 6 vertical thin black bars indicate six families with APP locus duplication with AD but without DS [6–10]. The next vertical green bar represents a 78-year-old partial trisomy 21 individual with DS without AD [20]. The right red bar represents the current case. Vertical solid bars – duplicated regions. Vertical dotted bars – regions of uncertainty.

*Neurobiol Aging*. 2017 August ; 56: 150–158. doi:10.1016/j.neurobiolaging.2017.04.018.

# Candidate gene analysis for Alzheimer's disease in adults with Down syndrome

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## Abstract

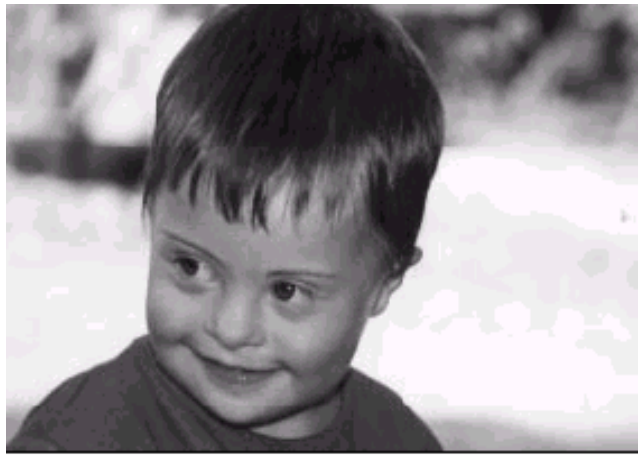
Individuals with Down syndrome (DS) overexpress many genes on chromosome 21 due to trisomy and have high risk of dementia due to the Alzheimer's disease (AD) neuropathology. However, there is a wide range of phenotypic differences (e.g., age at onset of AD, amyloid β levels) among adults with DS, suggesting the importance of factors that modify risk within this particularly vulnerable population, including genotypic variability. Previous genetic studies in the general population have identified multiple genes that are associated with AD. This study examined the contribution of polymorphisms in these genes to the risk of AD in adults with DS ranging from 30 to 78 years of age at study entry (N = 320). We used multiple logistic regressions to estimate the likelihood of AD using single-nucleotide polymorphisms (SNPs) in candidate genes, adjusting for age, sex, race/ethnicity, level of intellectual disability and *APOE* genotype. This study identified multiple SNPs in *APP* and *CST3* that were associated with AD at a gene-wise level empirical *p*-value of 0.05, with odds ratios in the range of 1.5–2. SNPs in *MARK4* were marginally associated with AD. *CST3* and *MARK4* may contribute to our understanding of potential mechanisms where *CST3* may contribute to the amyloid pathway by inhibiting plaque formation, and *MARK4* may contribute to the regulation of the transition between stable and dynamic microtubules.

# La comunicazione della diagnosi

*Concediti*
*la serenità di accettare le cose*
*che non puoi cambiare,*
*di cambiare ciò che puoi*
*e la saggezza*
*di riconoscerne la*
*differenza…*

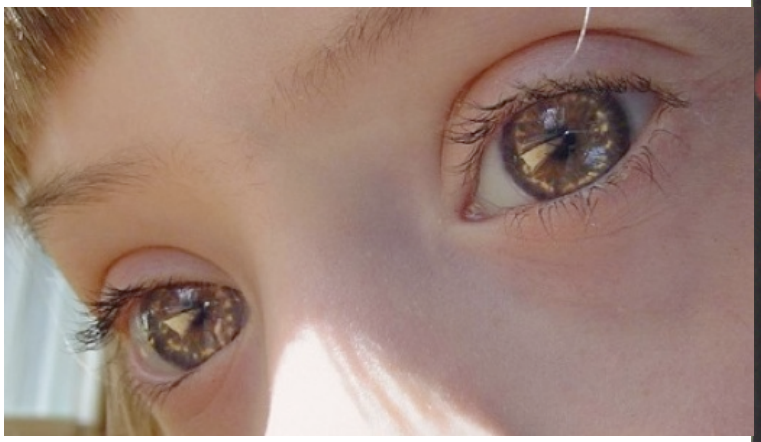
*San Francesco d'Assisi* "

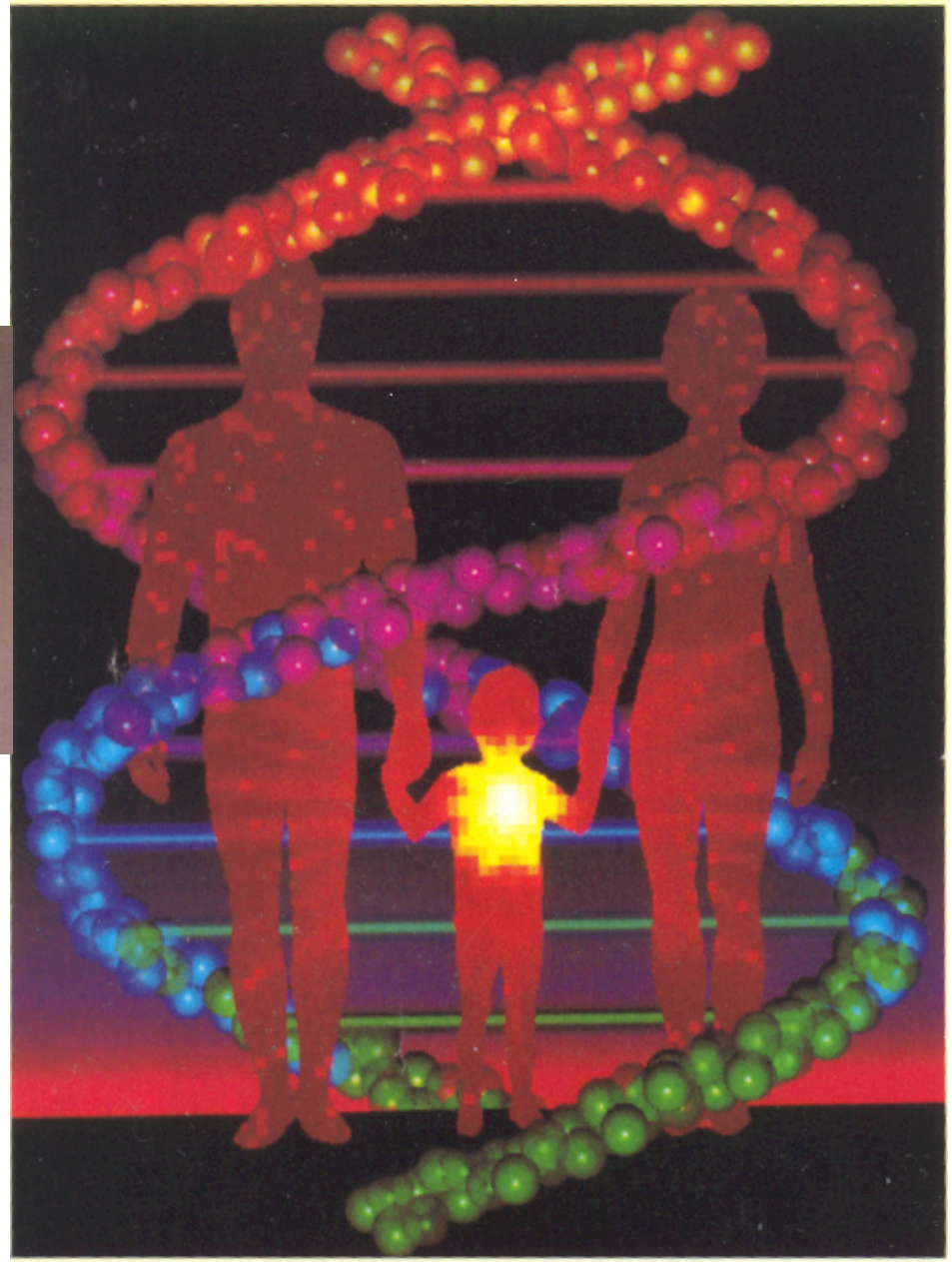
*Luigi è in incubatrice, lontano da me, e io ancora... non vivo davvero la mia maternità. E' un bambino Down, ma io non lo so. Nessuno dei familiari lo sa.....*
*Luigi ha quasi due mesi e io non l'ho ancora toccato. Una sera verso la fine di gennaio la verità mi arriva in questi termini per bocca di un parente, che non "sa" quello che mi sta dicendo: "Niente di speciale. Il dottore ha detto che Luigi ha un po' di mongolismo ..". Tipo "un po' di raffreddore". La disperazione, l'incredulità, la speranza dell'errore.*



*Verso le nove entrò il primario di pediatria e chiese chi fosse la signora che occupava il letto numero .... Mi avvicinai e lui disse che gli dispiaceva dovermi comunicare che mio figlio aveva dei problemi.*
*Subito mi afferrò un senso di paura "Che tipo di problemi ?" chiesi. "Suo figlio è affetto da sindrome di Down". "Cosa vuol dire ?" "Suo figlio è mongoloide" e uscì.*
*Rimasi impietrita.....Non era*

Madonna con bambino Down
Mantegna





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