

**Clinica molecolare  
(molecular medicine): come  
utilizzare le informazioni del  
genoma per studiare le  
patologie genetiche**

# Dissezione del fenotipo (Fenomica)

- (1) Esame obiettivo (specialistico)
- (2) Consulenza Genetica (Genetica clinica, analisi del pedigree, valutazione componente genetica di un fenotipo, valutazione rischi empirici di ricorrenza, inquadramento genetico)
- (3) Esami strumentali specifici (EMG, TAC, RMN, etc.)
- (4) Esami biochimici (dosaggi enzimatici, dosaggi di metaboliti, ect)
- (5) Esami di proteomica (analisi delle proteine, Western blotting, immunoistochimica, etc.)
- (6) Valutazione interazione con fattori ambientali



# Allestire un percorso di medicina molecolare



- FENOMICA
- ANALISI DI LINKAGE (albero informativo)
  - Ricerca marcatori appropriati e loro designing
- ANALISI MOLECOLARE GENE CANDIDATO
  - Ricerca geni candidati (pubmed-OMIM-HGDB)
  - Valutazione anatomia genomica dei geni candidati
  - Valutazione espressione geni candidati
  - Sequenze annotate in HGMP
  - Gene Card
  - Strategie molecolari
  - Analisi dei dati molecolari (HGMP blast, HGDB, database specifici)
  - Validazione delle mutazioni identificate (ESE finder, etc)

**La bioinformatica come tool  
per la analisi di geni malattia**

# Human Genome Resources

## Browse Your Genome

Click on a chromosome to

show



## The NCBI Handbook



An online guide to the use of NCBI resources. Titles of selected chapters that refer to human genome resources are shown below.

 The Single Nucleotide Polymorphism Database (dbSNP) of Nucleotide

Search  for

A challenge facing researchers today is that of piecing together and analyzing the plethora of data currently being generated through the Human Genome Project and scores of smaller projects. NCBI's Web site serves as an integrated, one-stop, genomic information infrastructure for biomedical researchers from around the world so that they may use these data in their research efforts. [More...](#)

## GENES AND HUMAN HEALTH

### OMIM

A guide to genes and inherited disorders maintained by Johns Hopkins University and collaborators.

### RefSeq

Reference sequences of chromosomes, genomic contigs, mRNAs, and proteins for human and major model organisms.

### dbSNP

A database of single nucleotide polymorphisms (SNPs) and other nucleotide variations.

### Gene Database

A new database of genes and associated information is now available for searching in Entrez.

**Search for Genes**

from

with words

### LocusLink

A comprehensive catalog of genes and other genetic loci.

## THE GENOMIC SEQUENCE

 Five years after

 BLAST 4.0

http://www.ncbi.nlm.nih.gov/genome/guide/human/



HOME | SEARCH | SITE MAP | PubMed | All Databases | Human Genome | GenBank | Map Viewer | BLAST

Search across databases

cd38

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Help

3114		PubMed: biomedical literature citations and abstracts		37		Books: online books	
726		PubMed Central: free, full text journal articles		21		OMIM: online Mendelian Inheritance in Man	
none		Site Search: NCBI web and FTP sites		none		OMIA: Online Mendelian Inheritance in Animals	
1942		Nucleotide: sequence database (includes GenBank)		11		UniGene: gene-oriented clusters of transcript sequences	
199		Protein: sequence database		1		CDD: conserved protein domain database	
6		Genome: whole genome sequences		28		3D Domains: domains from Entrez Structure	
13		Structure: three-dimensional macromolecular structures		17		UniSTS: markers and mapping data	
none		Taxonomy: organisms in GenBank		15		PopSet: population study data sets	
549		SNP: single nucleotide polymorphism		46432		GEO Profiles: expression and molecular abundance profiles	
34		Gene: gene-centered information		23		GEO DataSets: experimental sets of GEO data	
13		HomoloGene: eukaryotic homology groups		53		Cancer Chromosomes: cytogenetic databases	
none		PubChem Compound: unique small molecule chemical structures		none		PubChem BioAssay: bioactivity screens of chemical substances	

<http://www.ncbi.nlm.nih.gov/omim/>



## **National Center for Biotechnology Information**

- OMIM: online mendelian inheritance in man
- Creato da Victor McKusick
- Continuamente aggiornato
- Punto chiave per acquisire informazione sui caratteri mendeliani umani, patologici e non
- A ogni carattere viene attribuito un numero a 6 cifre MIM

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Address <http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=143100> Go

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- NCBI
- MIM +143100
- Description
- Clinical Features
- Biochemical Features
- Other Features
- Inheritance
- Mapping
- Molecular Genetics
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- Edit History

- Clinical Synopsis
- Gene map

- Entrez Gene
- Nomenclature
- MIM +143100
- Description
- Clinical Features
- Biochemical Features
- Other Features
- Inheritance
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- Diagnosis
- Population Genetics
- Clinical Management



All Databases PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM

Search OMIM for

Limits Preview/Index History Clipboard Details

Display Detailed Show 20 Send to

All: 1

**+143100**  
**HUNTINGTON DISEASE; HD**

GeneTests, Links

*Alternative titles; symbols*

HUNTINGTON CHOREA  
HUNTINGTIN, INCLUDED; HD, INCLUDED  
HTT, INCLUDED  
IT15, INCLUDED

Gene map locus [4p16.3](#)

**TEXT**

**DESCRIPTION**

Huntington disease (HD) is inherited as an autosomal dominant disease that gives rise to progressive, selective (localized) neural cell death associated with choreic movements and dementia. The disease is associated with increases in the length of a CAG triplet repeat present in a gene called 'huntingtin' located on chromosome 4p16.3.

**CLINICAL FEATURES**

The classic signs of Huntington disease are progressive chorea, rigidity, and dementia, frequently associated with seizures. A characteristic atrophy of the caudate nucleus is seen radiographically. Typically, there is a prodromal phase of mild psychotic and behavioral symptoms which precedes frank chorea by up to 10 years. The results of a study by [Shwach and Norbury \(1994\)](#) clashed with the conventional wisdom that psychiatric symptoms are a frequent presentation of Huntington disease before the development of neurologic symptoms. They performed a control study of 93 neurologically healthy individuals at risk for Huntington disease. The 20 asymptomatic heterozygotes showed no increased incidence of psychiatric disease of any sort when compared to the 33 normal homozygotes in the same group. However, the whole group of heterozygous and homozygous normal at-risk individuals showed a significantly greater number of psychiatric episodes than did their 43 spouses, suggesting stress from the uncertainty associated with belonging to a family segregating this disorder. [Shwach and Norbury \(1994\)](#) concluded that neither depression nor psychiatric disorders are likely to be significant preneurologic indicators of heterozygous expression of the disease gene.





The OMIM Gene map presents the cytogenetic map location of disease genes and other expressed genes described in OMIM. See the [OMIM Morbid Map](#) for a list of disease genes organized by disease. For more refined maps of genes and DNA segments click on the **Location** to invoke NCBI Entrez [Map Viewer](#).

Search for:    (from the current location)

- Enter gene symbol, chromosomal location, or disorder keyword to search for, e.g. "CYP1", "5", "1pter", "Xq", or "alzheimer".
- You must capitalize X and Y to search for those chromosomes.

#### 4p16.3, HD to 4p16.1, HMX1

[<<Move Up](#) [Move Down>>](#)

Location	Symbol	Title	MIM #	Disorder	Comments	Method	Mouse
<a href="#">4p16.3</a>	HD, IT15	Huntingtin	<a href="#">143100</a>	Huntington disease (3)	distal to D4S10	Fd	<a href="#">5(Hdh)</a>
<a href="#">4p16.3</a>	IDUA, IDA	Iduronidase, alpha-L-	<a href="#">252800</a>	Mucopolysaccharidosis Ih, <a href="#">607014</a> (3); Mucopolysaccharidosis Is, <a href="#">607016</a> (3); Mucopolysaccharidosis Ih/s, <a href="#">607015</a> (3)		REa, A, S	<a href="#">5(Idua)</a>
<a href="#">4p16.3</a>	LETM1	Leucine zipper/EF-hand-containing transmembrane protein 1	<a href="#">604407</a>			A	
<a href="#">4p16.3</a>	LRPAP1, A2MRAP	Low density lipoprotein-related protein-associated protein 1 (alpha-2-macroglobulin receptor-associated protein 1)	<a href="#">104225</a>		?involved in Wolf-Hirschhorn syndrome	A, REa	
<a href="#">4p16.3</a>	MYL5	Myosin, light polypeptide-5, regulatory	<a href="#">160782</a>			RE	
<a href="#">4p16.3</a>	PDE6B, PDEB, CSNB3	Phosphodiesterase-6B, cGMP-specific, rod, beta	<a href="#">180072</a>	Night blindness, congenital stationary, type 3, <a href="#">163500</a> (3); Retinitis pigmentosa, autosomal recessive (3)		REa, A, Fd	<a href="#">5(Pdeb, rd)</a>

MM Morbid map - Microsoft Internet Explorer

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Address <http://www.ncbi.nlm.nih.gov/Omim/getmorbid.cgi?start=0&term=huntington>

Google omim Web Accelerator





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The OMIM Morbid Map presents the cytogenetic map location of disease genes described in OMIM. For a map organized by chromosome, see the [OMIM Gene Map](#). For more refined maps of genes and DNA segments, use NCBI Entrez [Map Viewer](#) and the [Genome Database](#).

Search for:    (from the current location)

- Enter gene symbol, chromosomal location, or disorder keyword to search for, e.g. "recessive", "CYP1", "5", "1pter", or "Xq".
- You must capitalize X and Y to search for those chromosomes.

[<<Move Up](#) [Move Down>>](#)

Disorder	Symbol(s)	OMIM	Location
Huntington disease (3)	HD, IT15	<a href="#">143100</a>	4p16.3
Huntington disease-like 1, <a href="#">603218</a> (3)	PRNP, PRIP	<a href="#">176640</a>	20pter-p12
Huntington disease-like 2, <a href="#">606438</a> (3)	JPH3, JP3, HDL2	<a href="#">605268</a>	16q24.3
Huntington disease-like 3 (2)	HDL3, HLN2	<a href="#">604802</a>	4p15.3
Huntington disease-like-4, <a href="#">607136</a> (3)	TBP, SCA17	<a href="#">600075</a>	6q27
Huriez syndrome (2)	TYS, HRZ	<a href="#">181600</a>	4q23
Hyalinosis, infantile systemic, <a href="#">236490</a> (3)	ANTXR2, CMG2, JHF, ISH	<a href="#">608041</a>	4q21
Hydatidiform mole, <a href="#">231090</a> (3)	NALP7, NOD12, PYPAF3, HYDM	<a href="#">609661</a>	19q13.4
Hydrocephalus due to aqueductal stenosis, <a href="#">307000</a> (3)	L1CAM, CAML1, HSAS1	<a href="#">308840</a>	Xq28
Hydrocephalus with Hirschsprung disease and cleft palate, <a href="#">142623</a> (3)	L1CAM, CAML1, HSAS1	<a href="#">308840</a>	Xq28
Hydrocephalus with congenital idiopathic intestinal pseudoobstruction, <a href="#">307000</a> (3)	L1CAM, CAML1, HSAS1	<a href="#">308840</a>	Xq28

The OMIM Morbid Map presents the cytogenetic map location of disease genes described in OMIM. For a map organized by chromosome, see the [OMIM Gene Map](#). For more refined maps of genes and DNA segments, use NCBI Entrez [Map Viewer](#) and the [Genome Database](#).

Search for:    (from the current location)

- Enter gene symbol, chromosomal location, or disorder keyword to search for, e.g. "recessive", "CYP1", "5", "1pter", or "Xq".
- You must capitalize X and Y to search for those chromosomes.

[<<Move Up](#) [Move Down>>](#)

Disorder	Symbol(s)	OMIM	Location
{Obesity, susceptibility to}, <a href="#">601665</a> (3)	ADRB2	<a href="#">109690</a>	5q32-q34
{Obesity, susceptibility to}, <a href="#">601665</a> (3)	ADRB3	<a href="#">109691</a>	8p12-p11.2
{Obesity, susceptibility to}, <a href="#">601665</a> (3)	CART	<a href="#">602606</a>	5q13.2
{Obesity, susceptibility to}, <a href="#">601665</a> (3)	ENPP1, PDNP1, NPPS, M6S1, PCA1	<a href="#">173335</a>	6q22-q23
{Obesity, susceptibility to}, <a href="#">601665</a> (3)	GHRL	<a href="#">605353</a>	3p26-p25
{Obesity, susceptibility to}, <a href="#">601665</a> (3)	UCP1	<a href="#">113730</a>	4q31
{Obesity, susceptibility to}, <a href="#">601665</a> (3)	UCP2	<a href="#">601693</a>	11q13
{Obesity/hyperinsulinism, susceptibility to} (2)	OQTL	<a href="#">602025</a>	20q13.11-q13.2
{Obsessive-compulsive disorder 1}, <a href="#">164230</a> (3)	SLC6A4, HTT, OCD1	<a href="#">182138</a>	17q11.1-q12
{Obsessive-compulsive disorder, protection against}, <a href="#">164230</a> (3)	BDNF	<a href="#">113505</a>	11p13
{Obsessive-compulsive disorder, susceptibility to}, <a href="#">164230</a> (3)	HTR2A	<a href="#">182135</a>	13q14-q21



PubMed Nucleotide Protein Genome Gene Structure PopSet Taxonomy Help

Search for  on chromosome(s)  assembly  All  Find

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- Map Viewer
  - Map Viewer Home
  - Map Viewer Help
  - Human Maps Help
  - Release Notes
- NCBI Resources
  - Genome Project
  - TaxPlot
  - Consensus CoDing Sequence (CCDS)
  - Human Genome Resources
  - NCBI Handbook
  - RefSeq
  - Whole Genome Association (WGA)
- Organism Data in

## Homo sapiens (human) genome view

[Build 36.1 statistics](#) [Switch to previous build](#)

[BLAST search the human genome](#)

**Lineage:** [Eukaryota](#); [Metazoa](#); [Chordata](#); [Craniata](#); [Vertebrata](#); [Euteleostomi](#); [Mammalia](#); [Eutheria](#); [Euarchontoglires](#); [Primates](#); [Haplorrhini](#); [Catarrhini](#); [Hominidae](#); [Homo](#); [Homo sapiens](#)

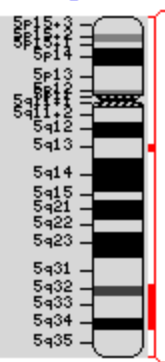
**March 2006:** NCBI released an update for the human genome (NCBI Build 36.1) that includes some changes to the reference genome assembly as well as updated annotation. This release includes a major change to the Map Viewer in that the previous build ([NCBI Build 35.1](#)) can still be accessed for Map Viewer display and for BLAST. For additional information about changes, statistics, and the status of the CCDS project please refer to:

- [Release Notes](#)
- [Statistics](#)
- [CCDS Project](#)

The NCBI Map Viewer provides graphical displays of features on the human genome sequence assembly as well as cytogenetic, genetic, physical, and radiation hybrid maps. Extensive [documentation](#) is provided to describe the resource features and methods used, tutorials, and statistics.

Map features that can be seen along the sequence include genes, transcripts, [NCBI contigs](#) (the 'Contig' map), the BAC tiling path (the 'Component' map), STSs, FISH mapped clones, ESTs and transcripts from several different organisms, [Gnomon](#) predicted gene models, and more.

You can find genes or markers of interest by submitting a query against the whole genome, or a chromosome at a time. Use the Advanced Search form for more complex



Region Displayed: 0-181M bp

Ideogram

Contig

Hs UniG

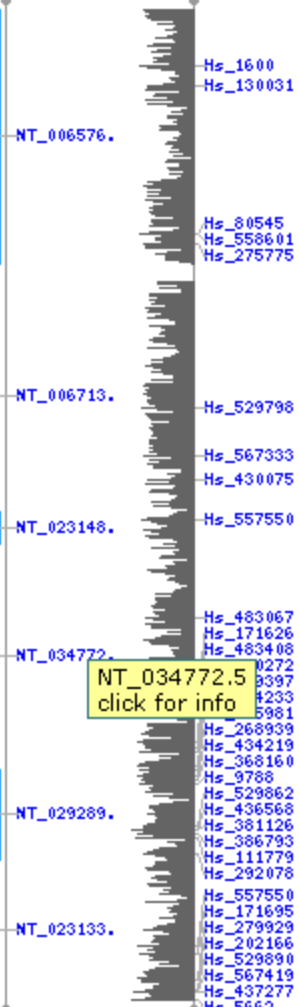
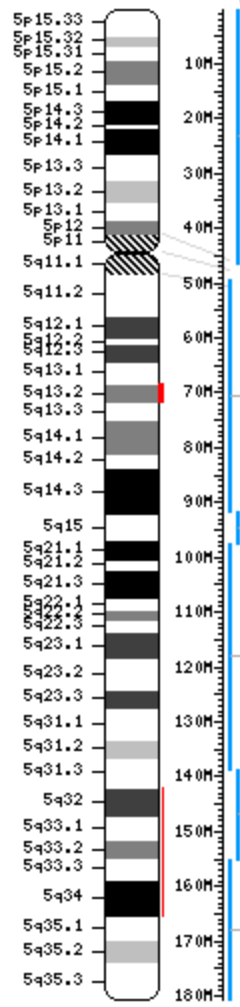
Genes\_seq

Symbol

○

Links

E



Symbol	○	Links	E
<a href="#">SRD5A1</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">LOC646126</a>	+	<a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a>	protein
<a href="#">C1QTNF3</a>	+	<a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">SEPP1</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a>	best RefSeq
<a href="#">IL6ST</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">MRPL49P1</a>	+	<a href="#">sv</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a>	best RefSeq
<a href="#">PRP2</a>	+	<a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">PAPD4</a>	+	<a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">LOC642488</a>	+	<a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a>	mRNA
<a href="#">FBXL17</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a>	best RefSeq
<a href="#">FLJ32921</a>	+	<a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">RAD50</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a>	best RefSeq
<a href="#">KIF20A</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">PCDHA6</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a>	best RefSeq
<a href="#">PCDHGC5</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">IL17B</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">LARP1</a>	+	<a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">PANK3</a>	+	<a href="#">OMIM</a> <a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq
<a href="#">HSPC111</a>	+	<a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a>	best RefSeq
<a href="#">COL23A1</a>	+	<a href="#">HGNC</a> <a href="#">sv</a> <a href="#">pr</a> <a href="#">dl</a> <a href="#">ev</a> <a href="#">mm</a> <a href="#">hm</a> <a href="#">sts</a> <a href="#">CCDS</a>	best RefSeq

NT\_034772.5  
click for info

How is genomics impacting on the practice of medicine?

...(genomics) catalogues only the birth of the genomic era and thus no more captures in detail the ultimate effect of genomic medicine than does the examination of a newborn foretell what the mature adult will be like...



CGCTGGGATAGAGCTTTCGCTAGAGGATCGGATCCCGGCATAGGCTAGAGGATGC  
CCATCAGCACTACTAGCTCGCATATCGGATATTTGATGAGGCTAGAGGATGC  
fdoI 275K 4500K 0 250K ushR

Entrez Genome

PubMed Nucleotide Protein Genome St

for **h5n1** Go Clear Save Search

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All: 16

Items 1 - 16 of 16

- 1: [NC 007362](#)  
Influenza A virus (A/Goose/Guangdong/1/96(H5N1)) segment 4, complete sequence  
ssRNA; linear; Length: 1,760 nt  
Replicon Type: viral segment  
Replicon Name: segment 4  
Created: 2005/08/26
- 2: [NC 004908](#)  
Influenza A virus (A/Hong Kong/1073/99(H9N2)) segment 4, complete sequence  
ssRNA; linear; Length: 1,714 nt  
Replicon Type: viral segment  
Replicon Name: segment 4  
Created: 2000/06/30
- 3: [NC 007358](#)  
Influenza A virus (A/Goose/Guangdong/1/96(H5N1)) segment 2, complete sequence  
ssRNA; linear; Length: 2,341 nt  
Replicon Type: viral segment



# NAVIGARE NEI GENE DATABASE

## Organismi Modello

L'obiettivo primario della biologia è lo studio e la comprensione degli organismi viventi. E' però praticamente impossibile studiarli tutti perchè ci sono milioni e milioni di specie diverse. E' quindi importante trovare degli organismi rappresentativi dei vari gruppi, che fungano da modello per l'intero gruppo e che siano i più semplici possibili.

Su questo principio molto semplice si basa il concetto degli organismi modello

Nei procarioti Escherichia coli rappresenta il batterio più studiato, anche se *Haemophilus influenzae* fu il primo batterio ad essere sequenziato nel 1995

Il lievito Saccharomyces cerevisiae (sequenziato nel 1996) permette di studiare diversi aspetti della biologia cellulare e della biologia di tutti gli organismi eucarioti

Arabidopsis thaliana (sequenziata nel 2000) è l'organismo modello per le piante; si tratta di una piccola crucifera che non ha alcuna applicazione pratica, ma rappresenta un ottimo organismo modello.

Caenorabditis elegans (sequenziato nel 1998) è un nematode è un animale, quindi il suo programma genetico è in grado di gestire i problemi del differenziamento delle cellule animali e dello sviluppo embrionale.

Drosophila melanogaster (sequenziata nel 2000) è un organismo modello molto utilizzato; oltre ad essere un modello di semplice animale, rappresenta anche un modello per tutti gli insetti.

I due pesci Zebrafish e Fugu rappresentano due ottimi modelli per lo studio dei vertebrati. Infine il topo e l'uomo sono i principali modelli per lo studio dei mammiferi.

# LINK A TAXONOMY

- Vediamo più in dettaglio alcuni dei campi ed in particolare i link agli altri database integrati in ENTREZ

LOCUS NM\_003673 963 bp mRNA Linear PRI 20-DEC-2003  
DEFINITION Homo sapiens titin-cap (teletonin) (TCAP), mRNA.  
ACCESSION NM\_003673  
VERSION NM\_003673.2 GI:19924299  
KEYWORDS .  
SOURCE Homo sapiens (human)  
ORGANISM [Homo sapiens](#)  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

NCBI Taxonomy Browser

Entrez PubMed Nucleotide Protein Genome Structure PMC Taxonomy Books

Search for [ ] as [complete name] [lock] [Go] [Clear]

Display [3] levels using filter: [none]

Nucleotide  Protein  Structure  Gene  Paper  SNP  
 3D Domains  Domains  GEO Datasets  GEO Expressions  UniGene  UniSTS  
 PubMed Central  Gene  MapView  LinkOut  BLAST  TRACE

Lineage (6/6): [root](#); [cellular organisms](#); [Eukaryota](#); [Fungi/Metazoa group](#); [Metazoa](#); [Eumetazoa](#); [Bilateria](#); [Coelomata](#); [Deuterostomia](#); [Chordata](#); [Craniata](#); [Vertebrata](#); [Gnathostomata](#); [Teleostomi](#); [Euteleostomi](#); [Sarcopterygii](#); [Tetrapoda](#); [Amniota](#); [Mammalia](#); [Theria](#); [Eutheria](#); [Primates](#); [Catarrhini](#); [Hominidae](#); [Homo/Pan/Gorilla group](#); [Homo](#)

• [Homo sapiens](#) (human) Click on organism name to get more information

- [Homo sapiens neanderthalensis](#)

**Disclaimer:** The NCBI taxonomy database is not an authoritative source for nomenclature or classification - please consult the relevant scientific literature for the most reliable information.

Comments and questions to [info@ncbi.nlm.nih.gov](mailto:info@ncbi.nlm.nih.gov)

Credits: Michail Donrachev, Scott Federhen, Carol Hottel, Detlef Leipe, Vladimir Sousoff, Richard Sternberg, Sean Turner.

## LINK AL GENE

*Vediamo ora più in dettaglio la parte di record relativa al gene*

FEATURES	Location/Qualifiers	
source	<code>1..963</code>	
	<code>/organism="Homo sapiens"</code>	
	<code>/mol_type="mRNA"</code>	tipo molecola (DNA, mRNA...)
	<code>/db_xref="taxon:9606"</code>	
	<code>/chromosome="17"</code>	
	<code>/map="17q12"</code>	cromosoma e posizione di mappa
<a href="#">gene</a>	<code>1..963</code>	
	<code>/gene="TCAP"</code>	nome ufficiale del gene e sinonimi
	<code>/note="synonyms: TELE, CHD1N, T-cap, LGMD2G, telethonin"</code>	
	<code>/db_xref="GeneID:8557"</code>	link al database dei geni Entrez Gene
	<code>/db_xref="LocusID:8557"</code>	
	<code>/db_xref="MIM:604488"</code>	link a malattie genetiche



All Databases   
  PubMed   
  Nucleotide   
  Protein   
  Genome   
  Structure   
  PMC   
  Taxonomy

Search:  for     current re

Display:  Show:  Send to:

**TCAP** **titin-cap (telethonin)** [*Homo sapiens*]  
 GeneID: 8557 Primary source: [HGNC:11610](#) updated 03-Feb-2006

**Summary** ? ↑

**Official Symbol:** TCAP and Name: titin-cap (telethonin) provided by [HUGO Gene Nomenclature Committee](#)  
**See related:** [HPRD:05133](#), [MIM:604489](#)  
**Gene type:** protein coding  
**Gene name:** TCAP  
**Gene description:** titin-cap (telethonin)  
**RefSeq status:** Reviewed  
**Organism:** [Homo sapiens](#)  
**Lineage:** *Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominoidea; Homo*  
**Gene aliases:** TELE; CMD1N; T-cap; LGMD2G; telethonin  
**Summary:** Sarcomere assembly is regulated by the muscle protein titin. Titin is a giant elastic protein with kinase activity that extends half the length of a sarcomere. It serves as a scaffold to which myofibrils and other muscle related proteins are attached. This gene encodes a protein found in striated and cardiac muscle that binds to the titin Z1-Z2 domains and is a substrate of titin kinase, interactions thought to be critical to sarcomere assembly. Mutations in this gene are associated with limb-girdle muscular dystrophy type 2G.

**Genomic regions, transcripts, and products** ? ↑



struttura gene, parte  
 trascritta, parte tradotta,  
 esoni/introni, UTR

**Genomic context** [See TCAP in Map Viewer](#) ? ↑



Contesto genomico

# RICERCA DI GENI

Proviamo a fare una ricerca complessa usando gli operatori booleani

## [Getting started](#)

Look for genes by name part and multiple species

Look for genes by chromosome and symbol

## Sample queries

[transporter AND \("Drosophila melanogaster"\[orgn\] OR "Mus musculus"\[orgn\]\)](#) [more...](#)

[\(II\[chr\] OR 2\[chr\]\) AND adh\\*\[sym\]](#) [more...](#)

**Cerchiamo uno dei geni della rubisco**

[http://www.rcsb.org/pdb/molecules/pdb11\\_1.html](http://www.rcsb.org/pdb/molecules/pdb11_1.html)

in *Arabidopsis thaliana*

The screenshot shows the NCBI Entrez search interface. At the top, there are tabs for different database types: Entrez, Pubmed, Medline, Protein, Genome, Structure, PDB, Taxonomy, Books, and CMI. Below these is a search bar with a dropdown menu set to 'Gene'. The search text is 'rubisco AND Arabidopsis thaliana [organism]'. There are 'Go' and 'Clear' buttons. A checkbox for 'current records only' is checked. Below the search bar are links for 'Limits', 'Preview/Index', 'History', 'Clipboard', and 'Details'. On the left side, there is a blue sidebar with 'Entrez' and 'SITE MAP' links. Below the search bar, there are options for 'Display' (set to 'Summary'), 'Show' (set to '5'), and 'Send to' (set to 'Text'). At the bottom, it shows 'Items 1-5 of 13' and 'Page 1 of 3 Next'.


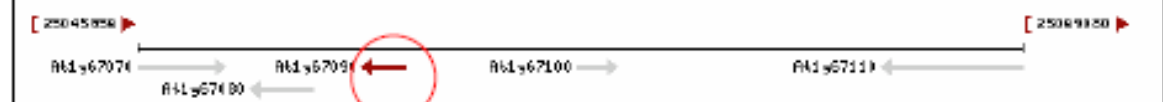
# RICERCA DI GENI

- Siamo interessati al gene “subunità 1A” di rubisco.

Database	Protein	Genome	Structure	PMC	Taxonomy	Books	ORF
for rubisco AND 1A AND Arabidopsis thaliana [org]		Go	Clear	<input checked="" type="checkbox"/> current records only			
Limits	Preview/Index	History	Clipboard	Details			
Display	Summary	Show: 5	Send to	Text			

1: [At1g67090](#) [Link](#)  
ribulose biphosphate carboxylase small chain 1A / RuBisCO small subunit 1A (RBCS-1A) (ATS1A) [*Arabidopsis thaliana*]  
**Other Aliases:** At1g67090, F1O19.14  
**Chromosome:** 1  
**GeneID:** 843029

struttura gene, parte trascritta (elica complementare!), parte tradotta, esoni/introni, UTR

Display	Graphics	Show: 5	Send to	Text
<input type="checkbox"/> 1: <a href="#">At1g67090</a> ribulose biphosphate carboxylase small chain 1A / RuBisCO small subunit 1A (RBCS-1A) (ATS1A) [ <i>Arabidopsis thaliana</i> ] <a href="#">Link</a>				
GeneID: 843029 Locus tag: <a href="#">At1g67090</a> updated 01-6-pr-2004				
Transcripts and products: (shown on reverse complement genome) <a href="#">RefSeq below</a>				
<b>NC_003070</b>				
				
Genomic context: chromosome: 1, map: unknown, clone: CHR1v01212004				
				
Gene type: protein coding				
RefSeq status: Provisional				
Organism: <i>Arabidopsis thaliana</i> (euphorbia: Columbia)				

## *LINK ALLE MALATTIE GENETICHE*

*Si possono esaminare le malattie genetiche associate a quella posizione di mappa (gene)*

```
FEATURES          Location/Qualifiers
  source          1..963
                  /organism="Homo sapiens"
                  /mol_type="mRNA"
                  /db_xref="taxon:9606"
                  /chromosome="17"
                  /map="17q12"
  gene           1..963
                  /gene="TCAP"
                  /note="synonyms: TELE, CMD1N, T-cap, LGMD2C, telethonin"
                  /db_xref="GeneID:8557"
                  /db_xref="LocusID:8557"
                  /db_xref="MIM:604488"
```



Mutazioni (alterazioni della sequenza nucleotidica di un gene) possono riflettersi in alterazioni della funzionalità della proteina da esso codificata. Queste mutazioni possono causare le cosiddette **malattie genetiche**.

Esempio: una mutazione a carico del gene della  $\beta$  globina fa sì che una particolare base del gene venga sostituita con un'altra, ciò altera il codone e nella proteina ciò si riflette nella sostituzione di un glutamato con una valina e in una ridotta funzionalità della proteina che causa una malattia genetica detta anemia a cellule falciformi (anemia falciforme).

Mutazioni a carico di geni differenti causano molte malattie genetiche diverse per questo è stato costituito il database OMIM.



## Database di malattie genetiche (umane)

Anche qui  
possiamo  
fare ricerche  
complesse

**NCBI**  
OMIM  
Online Mendelian Inheritance in Man  
Johns Hopkins University

All Databases: PubMed, Medline, Bookshelf, OMIM, Gene, Structure

Search: OMIM for [ ] Go Clear

Limits Preview/Index History Clipboard Details

Display: Detailed Show 20 Send to [ ]

All: 1 X

**\*604488**  
**TITIN-CAP: TCAP**

Alternative titles; symbols  
**TELETHONIN**

Gene map locus [17q12](#)

**TEXT**

**DESCRIPTION**

Telethonin is a sarcomeric protein of 19 kD found in cultured myocytes. Telethonin is a substrate of the other sarcomeric proteins. After activation by phorbol myristate.

**MAPPING**

[Valle et al. \(1997\)](#) mapped the telethonin gene to

**.0001 MUSCULAR DYSTROPHY, LIMB-GIRDLE, TYPE 2G [TCAP, GLN53TER]**

[Moxina et al. \(2000\)](#) observed 2 different mutations in the telethonin gene in 3 LGMD2G (601954) families. A 157C-to-T transition in exon 2 created a premature stop codon (glu53 to ter) and affected patients from 2 kindreds were homozygous for this mutation, whereas patients from a third kindred were heterozygous. The second mutation in the latter patient was a deletion of 2 guanine nucleotides within 4 guanines at the junction of exon 1 and intron 1 (604488.0002).

**.0002 MUSCULAR DYSTROPHY, LIMB-GIRDLE, TYPE 2G [TCAP, 2-BP DEL, 637GG]**

In a family with limb-girdle muscular dystrophy type 2G (601954), [Moxina et al. \(2000\)](#) found that affected members were compound heterozygotes for the Q53X mutation (604488.0001) and for deletion of 2 guanine nucleotides within a 4 guanine run (nucleotides 637-640 in the genomic sequence) at the junction of exon 1 and intron 1.

**.0003 CARDIOMYOPATHY, DILATED, 1N [TCAP, ARG87GLN ]**

[Knoll et al. \(2002\)](#) screened for mutations in the TCAP gene in 380 dilated cardiomyopathy patients (DCM) with 100 controls from the collected population at the University Hospital Benjamin Franklin in Berlin and identified a mutation, arg87 to gln (R87Q), in 1 patient. The resulting form of DCM was designated CMD1N (607497). The R87Q mutation was not found in any individual of the control population or in any of 400 control individuals in Japan.

**REFERENCES**

1. Knoll, R.; Hoshijima, M.; Hoffman, H. M.; Person, V.; Lorenzen-Schmidt, J.; Baug, M.-L.; Hayashi, T.; Sligo, N.;

Esempio di una query sul database OMIM: da notare l'estensiva descrizione di quanto noto sulla/e malattia/e determinate da mutazioni a carico del gene in esame

# LA REGIONE CODIFICANTE (CDS)

Consideriamo ora solo la parte codificante (tradotta in aminoacidi) della sequenza di RNA messaggero

gene

```
1..963 ← Il trascritto è lungo 963 nucleotidi
/gene="TCAD"
/note="synonyms: TELE, CMD1N, T-cap, LGMD2G, telethonin"
/db_xref="GeneID:8557"
/db_xref="LocusID:8557"
/db_xref="MIM:604488"
```

CDS

```
15..518 ← CDS: La parte tradotta va dalla base 15 alle 518
```

componente cellulare  
funzione

processo biologico

```
/gene="TCAD"
/note="19 kDa sarcomeric protein;"
go_component: cytoplasm [goid 0005737] [evidence NR];
go_function: structural constituent of muscle [goid 0008307] [evidence IAS] [pmid 9350988];
go_process: sarcomere alignment [goid 0006936] [evidence TAS] [pmid 9817759];
go_process: cell shape and cell size control [goid 0007146] [evidence E] [pmid 9817758];
go_process: protein complex assembly [goid 0006461] [evidence TAS] [pmid 9817758]"
```

GENE ONTOLOGY

<http://www.geneontology.org/>

```
/codon_start=1
/product="telethonin"
/protein_id="WP_003664.1" ← Link alla proteina
/db_xref="GI:4507435"
/db_xref="GeneID:8557"
/db_xref="LocusID:8557"
/db_xref="MIM:604488"
```

```
/translation="MATSELSCEVSEENCEDDEAFWAEWEDITLSTDPPECCSLHEED
TQRHETVHQGGCCQVLVQRSFVLMRRMGILGRGLQEQYQLPYQEVLPPIFTPAKMGAT
KEEREDTPIQLQELLALETALGGQCVDKQEVASITKQLPPVVFVSKPGALRRSLSRSM
SQAQDC"
```

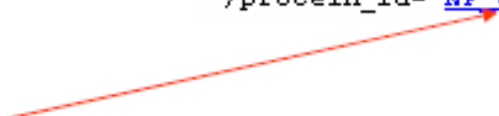
Sequenza Proteina

## LINK ALLA PROTEINA

Clickando sul link `protein_id` si arriva al record della proteina corrispondente

```
LOCUS       NP_003664                167 aa                linear    PRI 20-DEC-2003
DEFINITION telethonin; 19 kDa sarcomeric protein [Homo sapiens].
ACCESSION   NP_003664
VERSION     NP_003664.1  CI:4507435
DBSOURCE    EXFSQ: accession NM\_003673.2
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Cranista; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1 (residues 1 to 167)
  AUTHORS   Zou,P., Gautel,M., Geerlof,A., Wilmanns,M., Koch,H.H. and
            Svergun,D.I.
  TITLE     Solution scattering suggests cross-linking function of telethonin
            in the complex with titin
  JOURNAL   J. Biol. Chem. 278 (4), 2636-2644 (2003)
  PUBMED   12446666
  REMARK    GeneRIF: telethonin may play a role in linking titin filaments at
            the Z-disk periphery
  UNPROTEIN 2 (residues 1 to 167)
```

`/protein_id="`[NP\\_003664.1](#)`"`



# PROTEINA

Modalità grafica. Vedere il funzionamento delle opzioni

Display Graphics Show: 1 Send to File Get Subsequences

1: [NP\\_003664](#) telothronin, 19 kD ...[gi:4507435]

CDS with gene and mRNA  Other features  Hide sequence [Hide Toolbar](#) Refresh

Legend:  
— protein — other feature

Sequence:

```
1 HATSELSCEV SEENCERRR FAREUKILT L STRPEEGCSL HEEDDRHET YHGGGCDL → telothronin
61 VDRSPHLYNR IGDLCGLGE YQLPYRMLP LPIFTPNTG RTKEEREDTP IQLDQLLAE → telothronin
121 TALGGQVDK QEWREITKGL PPWPUSKPG ALRSLRSST SQEARD → telothronin
      ■ phosphorylation
```

[Home](#)
[Protein](#)
[Genome](#)
[Structure](#)
[PDB](#)
[Taxonomy](#)
[Tools](#)

[Limits](#)
[Preview/Index](#)
[History](#)
[Clipboard](#)
[Details](#)

Database: cdd.v.1.65

Click on boxes for multiple alignments

1: [P10795](#)  
 Ribulose b  
 gi|2773522

2: [NP\\_974099](#)  
 ribulose b  
 [thaliana]  
 gi|4257201

- 3: [NP\\_176880](#)  
 Ribulose biphosphate carboxylase small chain 1A / RuBisCO small subunit 1A (RBCS-1A) (ATS1A) [Arabidopsis  
 [thaliana]  
 gi|15219826|ref|NP\_176880.1|[15219826]
- [Link](#)
[Domains](#)
[Links](#)

Domini funzionali della proteina

Legend:

— protein

Sequence:

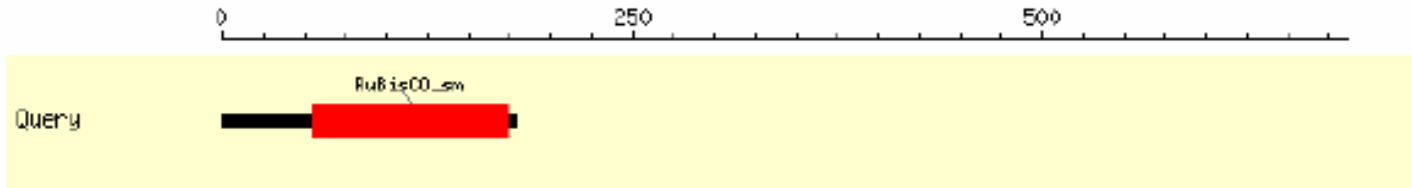
1 MRSSMLSEET IIVRSRQRTH VAFNCLKSS RAFPATIKAN NDITSITSHG GRVNCIDMMP → ribulose biphospha  
 61 PICKKKFETL SYLPDLTQSE LAKEVDYLIR NKHIPQVEFE LEHGFVYREH QNSFCYYDGR → ribulose biphospha  
 121 YVITNKLPLF GCTDSRDLK EVEECKEYF NAFIRLIGFD NTRQVDCISF IRYKPPSFTG → ribulose biphosphat

# PROTEINE CON GLI STESSI DOMINI

Sono immediatamente accessibili anche proteine aventi gli stessi domini



[Show](#) Domain Relatives      [Show](#) Domains in Entrez      [Show](#) Details



## Similar domain architectures



# How to build up a gene-specific molecular testing

## Gene cards

**National Center for Biotechnology Information**

National Library of Medicine

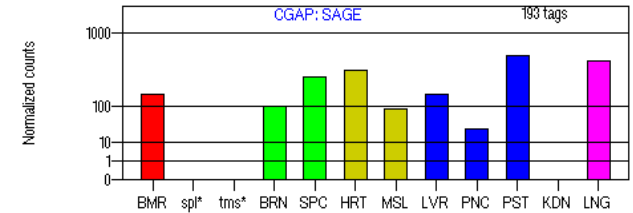
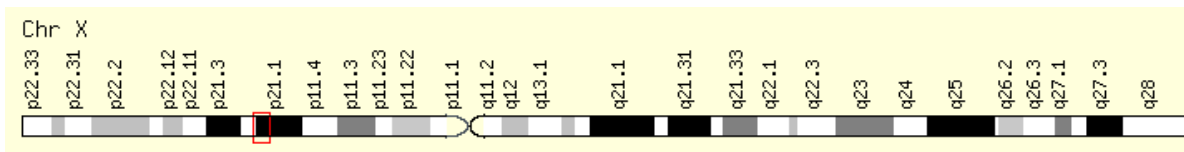
National Institutes of Health





agttatgtgacactttatctttcattgttatgaattgcctttttactttt  
 tgcagtcttgcggttgaatgtatcagaaactataatgtaaaaaaagctg  
 agtagaaatcttataaattaaaagttgtagcaagtcagaaaatggctcat  
 gcttttattgccattttgatgtttttgatggcaaaagtgttgagaaaaag  
 tctttagattcacgtgataagctgacagagtgaaacatcttaaggcttga  
 aagggcaagtagaagttataattattgtgtagattcacagtccttgtatt  
 gaattactcatctttgctctcatgctgcagGCCATAGAGCGAGAAAAAGC  
 TGAGAAGTTCAGAAAAC TGCAAGATGCCAGCAGATCAGCTCAGGCCCTGG  
 TGGAACAGATGGTGAATGgt aattacacgagttgatttagataatcttct  
 tagggatttgataaacacataggttcatatttatcagctgaattatatca  
 gacaagcacttgttaaatacaaatttaaattaaaaggtgtttgtatgttt  
 tttattattcttttttaatgctaaggaaattattaggagaaattcaact  
 ttgagttcattggaagaaaatgggatgtggtagaatattttatcagctctg  
 tagcagagaaataaattttaatgcaaactctgctagaatttatccaaataa  
 ttaagaaaataaggttaacagaaatttgaaaacattaacagtcatgtta

## Exon 44



[mRNA summary](#)

[cDNA clones](#)

[Gene summary](#)

[Protein  
annotation](#)

[mRNA structure](#)

[Sequences](#)

[Diagram](#)

[Phenotype](#)

[Function](#)

[Expression and  
regulation](#)

[Introns and exons](#)

# Gene card

# Tools bioinformatici in genetica medica

Esercizi effettuati su:

<https://www.ncbi.nlm.nih.gov/pubmed>

<https://www.ncbi.nlm.nih.gov/omim/>

<https://www.ncbi.nlm.nih.gov/gene/>

<https://www.ncbi.nlm.nih.gov/taxonomy/>

<http://www.orpha.net/consor/cgi-bin/index.php>