DIU Génétique et Reproduction

Introduction aux Banques de données biomédicales

18 Novembre 2022

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http://pdessen.free.fr/KB

Bases de données biomédicales

http://pdessen.free.fr/KB

Polymorphism

HGV HGVS Nomenclature HGV Guidelines Human Variome Project GME Variome LRG Locus Specific Mutation Databases HAPMAP DGV Variants DGV download dbVAR(NCBI) GnomAD browser TOPMED HLI Database of Genomic Variants Archive Singapore HumanMutation PennCNV Segmental Duplications GWA studies - NIH GWAS EBI Catalog GWAS Catalog GWA - Wellcome miRdSNP SM2PH Fast SNP ALFRED FrogKB dbGap LincSNP Mutanalyser Variant Annotation Tools Allele Frequencies dbSNFP ANNOVAR **ANNOVAR User Guide** **wANNOVAR(online)** Genetic variation databases VEP (Variants effect Predictor) UCSC Variant Integrator HGDP CRAVAT YHRD STR EUROFORGEN GAVIN dbMAE Haplotype Reference Consortium Michigan server NSTD37 1000GP GWASdb v2 INVITAE InterVar wInterVar 1000Genomes ISGR **Mutation Annotators** Variants Tools VCFv4.3 Varsome CancerGenomeInterpreter

Mutations

COSMIC CENSUS Fusions HGMD Mutation View MutDB HGSV BRCA IARC Db UMD IDbase PolyPhen-2 GERP MutPred DMDM SIFT(JCVI) SIFT(SG) MAPP snp3D PMut SAAP SNPeffect PolyDOMs I-Mutant.2.0 Align-GVGD ALAMUT MutoWeb-Roche CodonSuite MutationAssessor MutationTaster Condel IntOGen Align AGVGD FannsDB CONDEL GeneSplicer Human Splicing Finder MaxEntScan NNSplice Conjoined Genes IntOgen LOVD MutAnalyser VariantDB DoCM DGIdb dbNSFP CADD Mutation Aligner DriverDB BioMuta NCG mSignaturedb Oncogenic Mutations M-CAP

Diseases

OMIM Orphanet OrphaData BNDMR CRMR LORD GARD Huge Navigator IARC Publications IARC ICD-O3 International Classification of Diseases for Oncology Medical classification ICD10 Pathology ClinVar DISEASES PheGenITutorial DisGenet MalaCards Diseases Database SNPs3D UK10 Rare variants Disease Ontology BioPortal BioPortal Ontologies SNOMEDCT SNOMED CT(Wiki) ICD9CM HPO IRDiRC DNetDB Madeline EDAM(ontology for bioinformatics) EDAM (EBI) SIFR BioPortal eDGAR MatchMakerExchange eRAM digitalslide TCGA ONCOTREE PMKB EURACAN ERN-EURACAN EURACAN(European Rare Adult Cancers) DEPO Rare Cancers 2011PCT MDAnderson

Clinic and Drugs

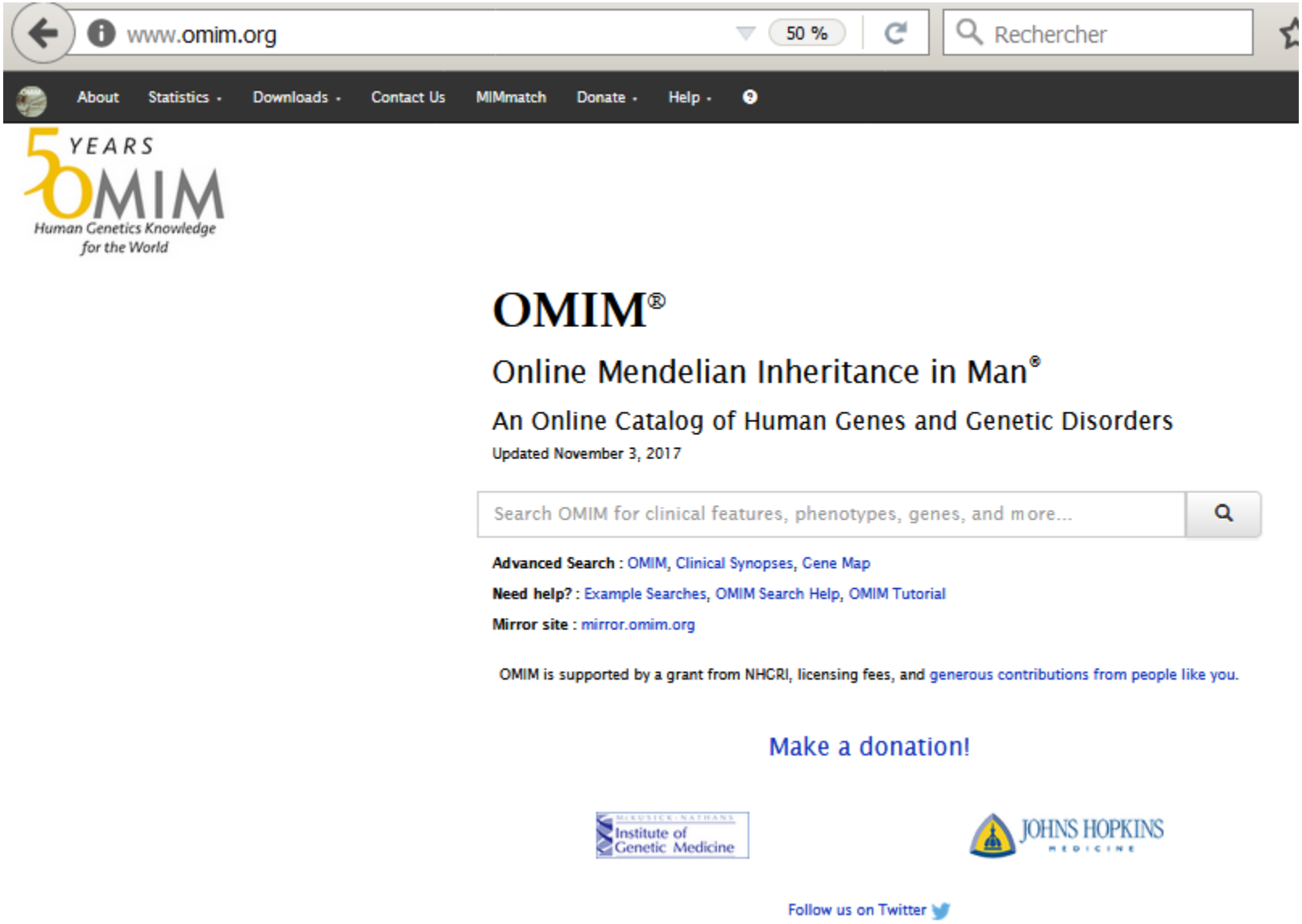
Medgen ClinVar Clinical Trials OrphaNet GeneReviews CTD DrugBank ClinicalTrials PharmGKB ddTargets (/Drug/Disease targets) cancerRxgene BioCentury PharmaGKB DGIdb CIViC DoCM MANTRA BioProfiling DRUGSURV Targeted therapies OncoTargets

http://pdessen.free.fr/links.html

OMIM

Online Mendelian Inheritance in Man

http://omim.org



http://www.omim.org/

OMIM Scope and History

Home | About | Statistics | Downloads/API | Help | External Links | Terms of Use | Contact Us | Select Language

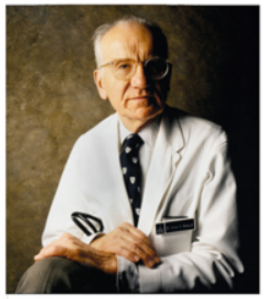
OMIM® - Online Mendelian Inheritance in Man®

Skip navigation

Profiles in Science National Library of Medicine

Home | Collection Home | Search | Browse | What's New | FAQ | About | Quick Search

The Victor A. McKusick Papers



- Biographical Information
- From "Musical Murmurs"
- The Bar Harbor Course a
- Beyond the Clinic: Geneti
- Medical Genetics, Molec
- Further Readings
- Glossary

All Documents

Victor McKusick (1921-2008) is widely considered to be the founding
educator, and researcher, he established the first medical genetics prog
Mendelian Inheritance in Man, an annually updated catalog of human
conducted landmark studies of hereditary disorders in the Amish. He w
involved in the early years of the Human Genome Project, and served
1997 in recognition of his lifelong contributions he received the Laske

NLM's Profiles in Science -- The McKusi

OMIM® and Online M

...nsive, authoritative compendium of
...e full-text, referenced overviews in
...s. OMIM focuses on the relationship
...us links to other genetics resources.

PERSPECTIVES IN HUMAN GENETICS

Mendelian Inheritance in Man and Its Online Version, OMIM

Victor A. McKusick

Last year marked the 40th anniversary of the publication of the first print edition of *Mendelian Inheritance in Man* (MIM).[1] This seems an appropriate juncture at which to review its origins, evolution, and present status, including and particularly those of its online version, OMIM (Online Mendelian Inheritance in Man). This is an opportunity, at the same time, to review in brief the rapid progress in an important part of medical genetics and genomics, as chronicled in MIM/OMIM over these 40 years, and to contemplate the future challenges of OMIM.

Description of MIM/OMIM

MIM[1,2] is a comprehensive knowledgebase of human genes and genetic
genes and g
is useful to

1963 as a resource for identifying both "old" and "new" recessive diseases in studies of the Old Order Amish.[8,9]

In the original three catalogs corresponding to the three major modes of Mendelian inheritance, the entries were arranged alphabetically according to the preferred title of the particular phenotype, and numbering was done consecutively. By the 11th book edition in 1994,[2] the X-linked catalog had been joined by two other chromosome-specific catalogs: those for the Y chromosome and for the mitochondrial chromosome. Entries in the original autosomal dominant, autosomal recessive, and X-linked catalogs had been assigned unique identification numbers, beginning with 1, 2, and 3, respectively. Entries in the two new chromosome-specific catalogs were given unique num-
...ndrial).
...66] and
...rs were

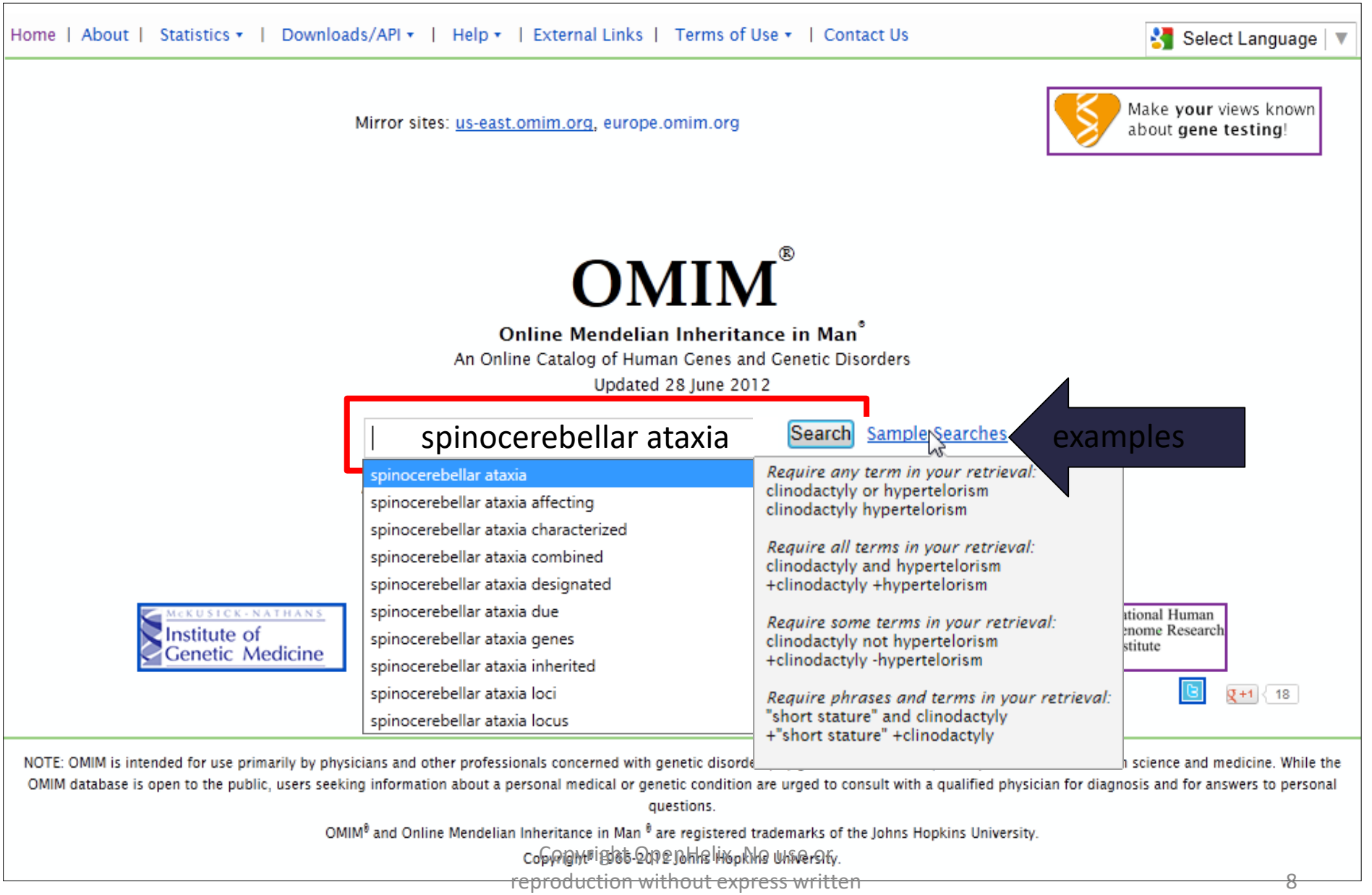
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1852721/

OMIM Content: Scope of Phenotypes

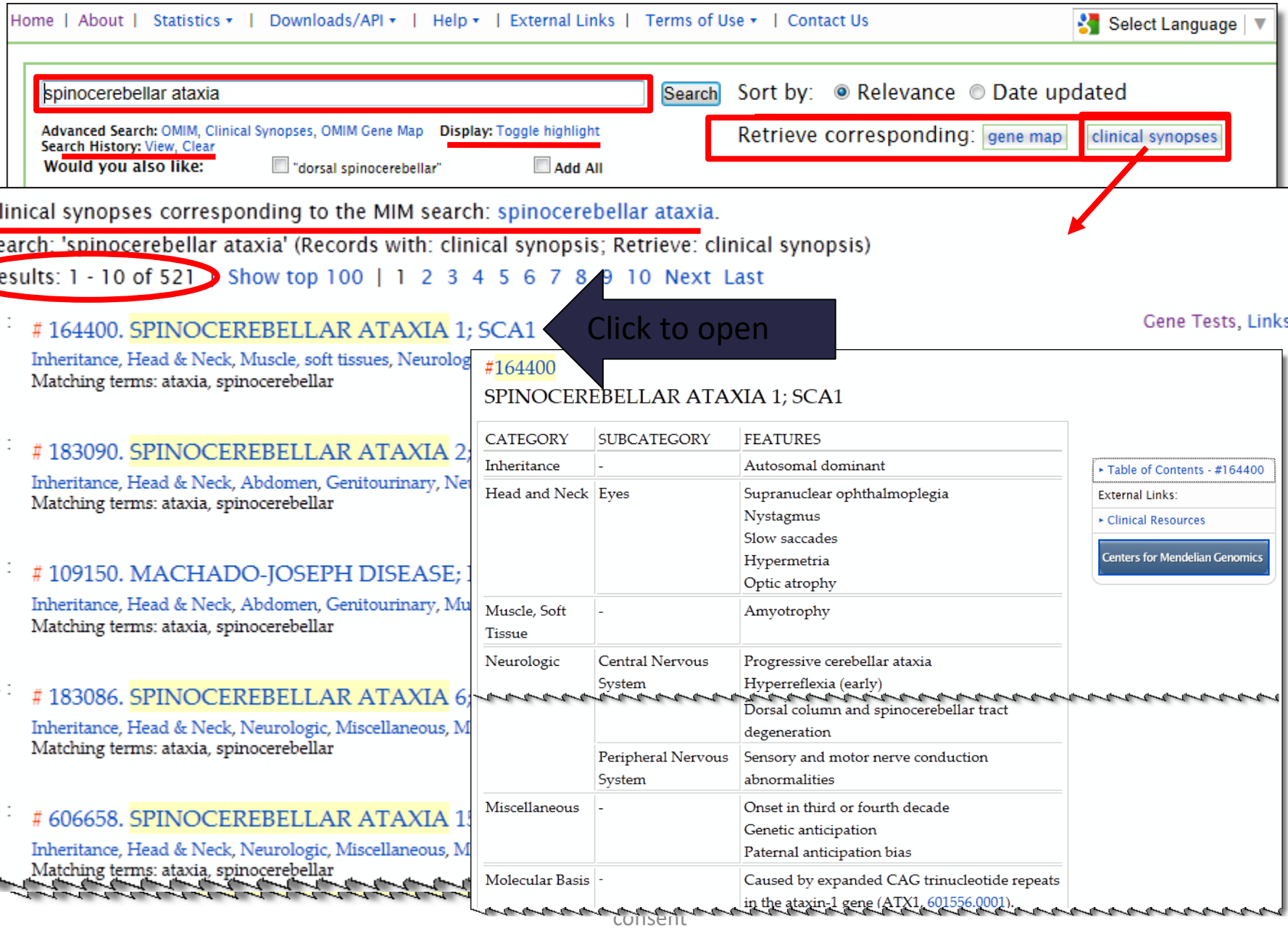
OMIM Focuses On:

- Single-gene mendelian disease/disorders/phenotypes (including: cystic fibrosis, sickle cell anemia, achondroplasia, phenotypic traits such as hair and eye color, susceptibility to drug reaction as in malignant hyperthermia and warfarin sensitivity, altered reaction to infection such as herpes simplex encephalitis and progression to AIDS in HIV infection, germline susceptibilities to cancer such as BRCA1 and breast/ovarian cancer, etc.)
- Complex diseases with significant single gene contribution (such as: complement factor H and age related macular degeneration)
- Descriptions of recurrent deletion and duplication syndromes (e.g., Potocki-Shaffer syndrome, and chromosome 10q26 deletion syndrome)

Basic Search

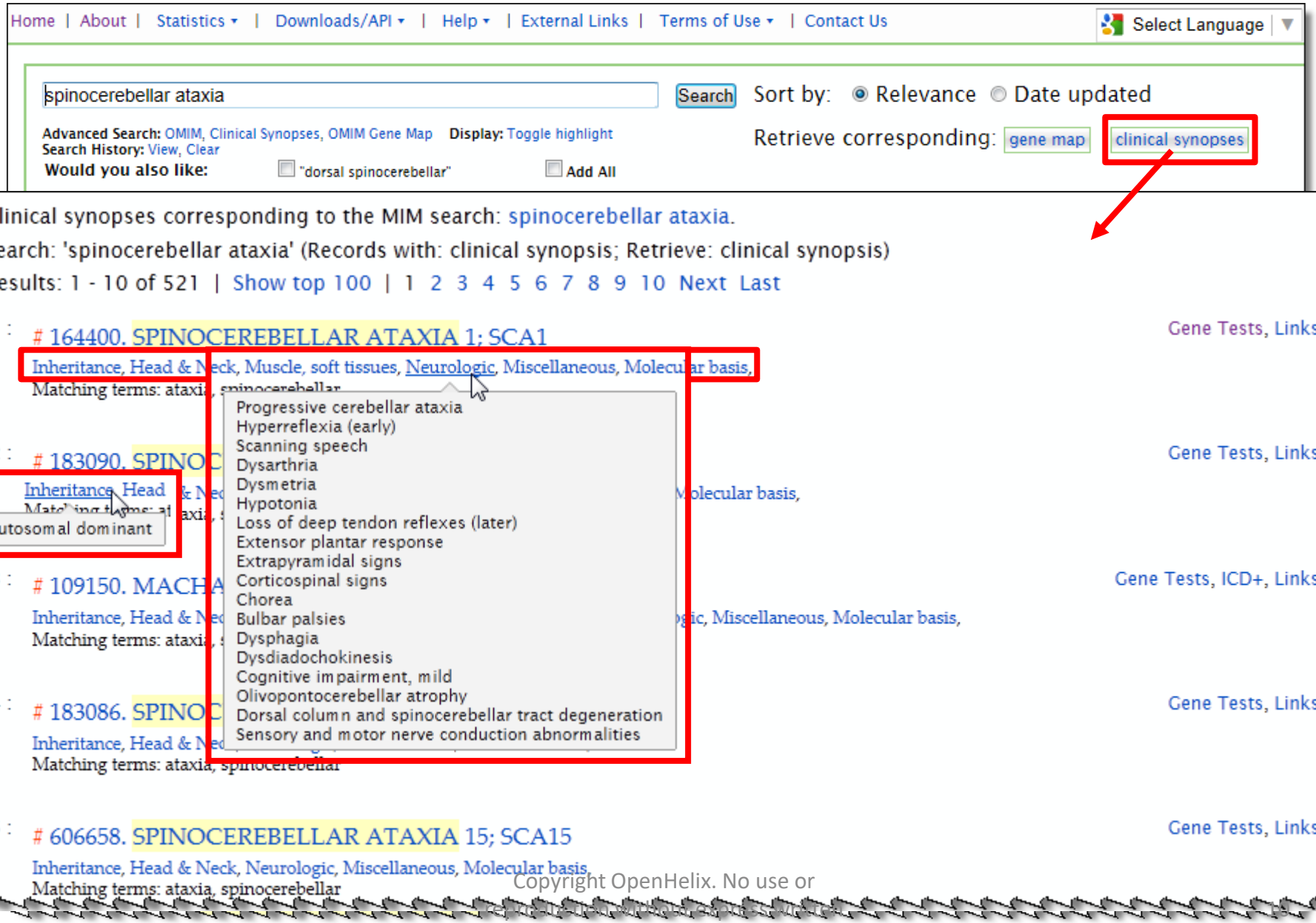


Basic Search Results



consent

Clinical Synopses Results



1.1 Basic Search

For basic searches, simply enter the terms in the search box and click the 'Search' button:

```
duchenne muscular dystrophy
```

The search engine will search for them in any order, ranking the entries containing all the terms higher than entries containing some o the terms.

Searches are case-insensitive, so a search for 'duchenne', 'Duchenne', or 'DUCHENNE' will return the same entries.

1.2 +/- Operators

Adding a '+' (plus) operator before specific terms will ensure that these appear in the entries returned:

```
+duchenne +muscular dystrophy
```

The returned entries will contain the terms 'duchenne' and 'muscular', but may or may not contain the term 'dystrophy'.

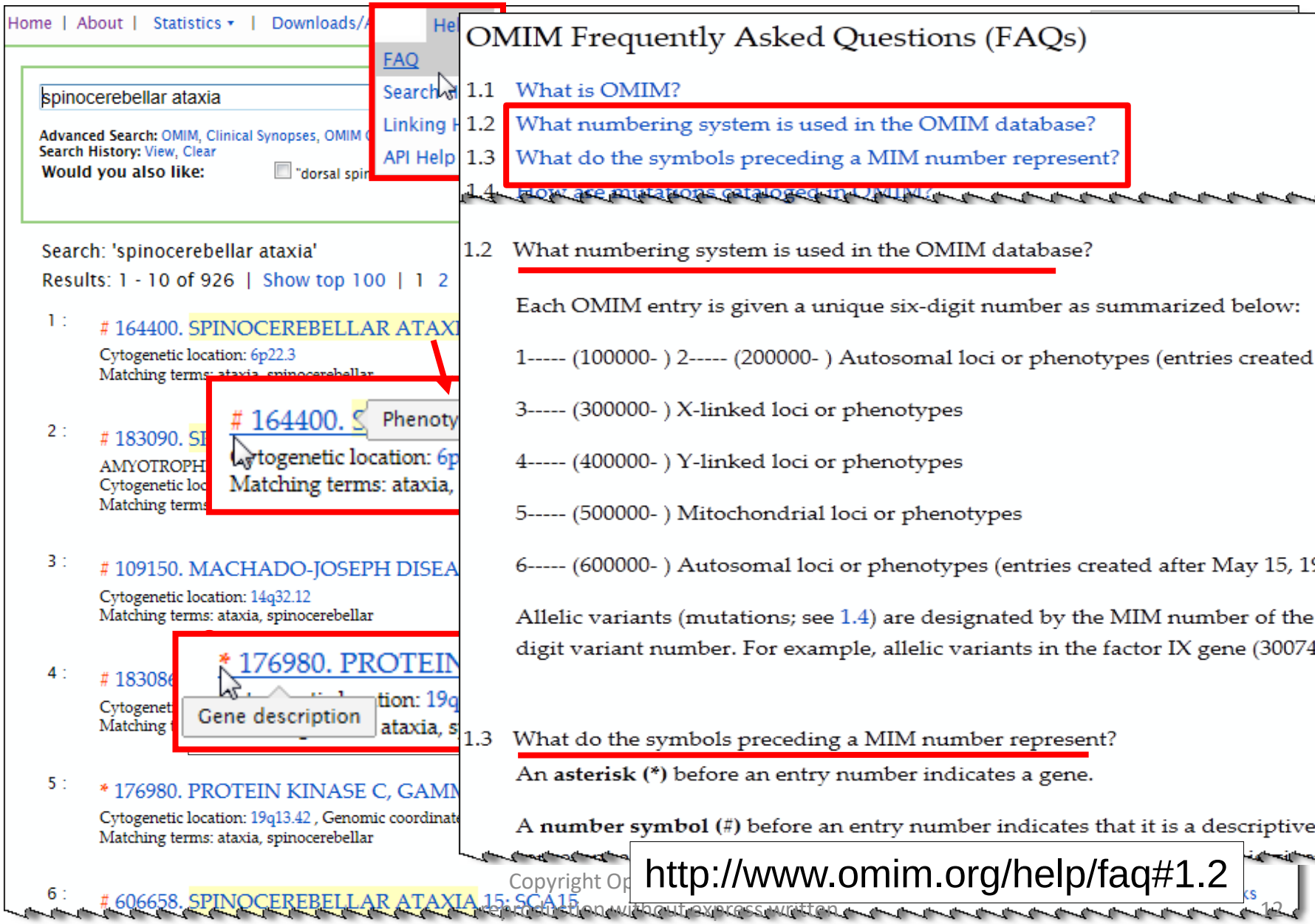
Conversely, you can affix a '-' (minus) operator to a term if you want to exclude entries that contain it:

```
+muscular +dystrophy -duchenne
```

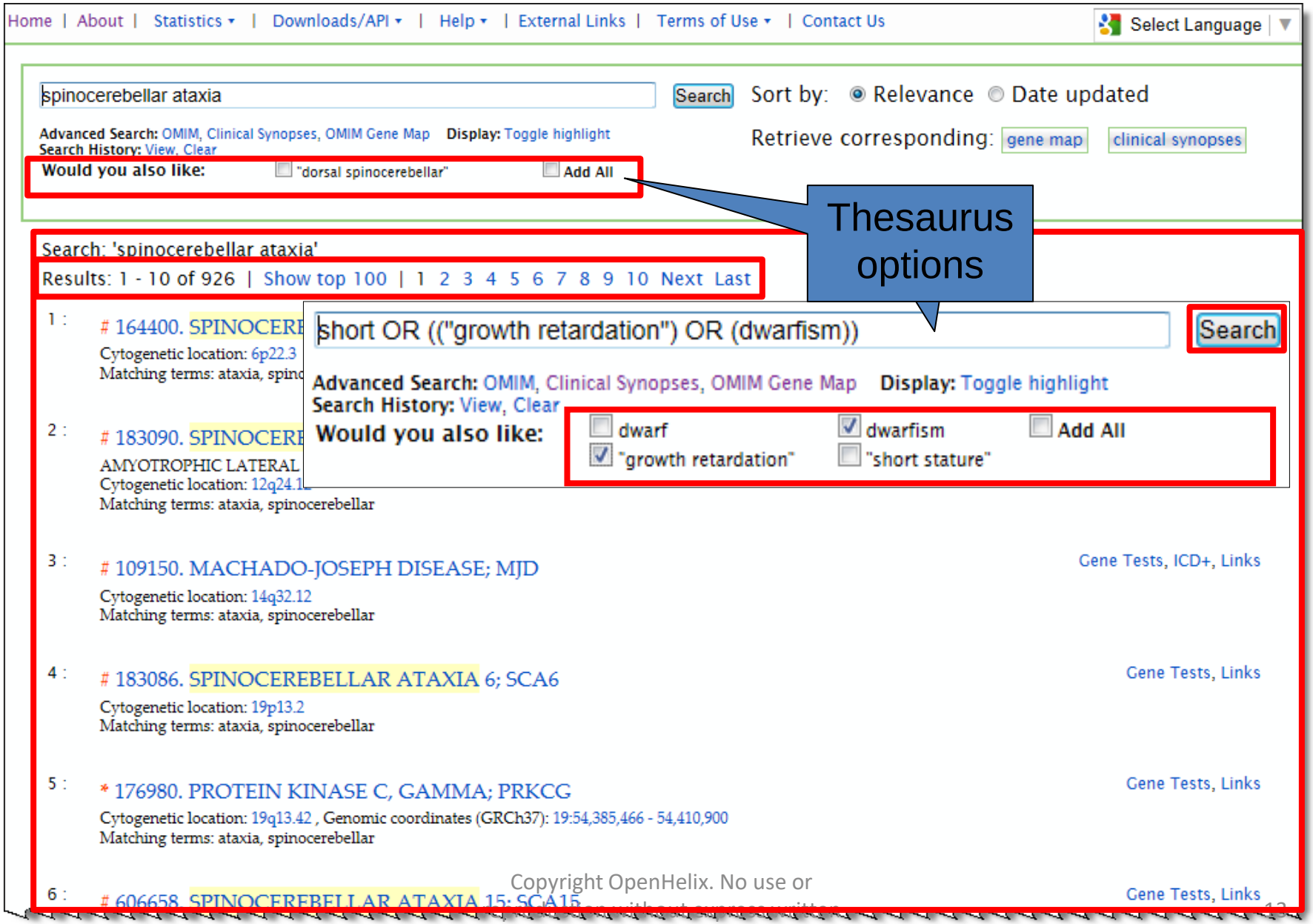
The returned entries will contain the terms 'muscular' and 'dystrophy', but will not contain the term 'duchenne'.

1.3 Phrase Search

Result Displays: MIM Numbers, etc.



Basic Search Results, cont.



Matching Terms

Basic Search Results: Links

Clinical Synopsis

#164400

SPINOCEREBELLAR ATAXIA 1; SC

Alternative titles; symbols

SPINOCEREBELLAR ATROPHY I
OLIVOPONTOCEREBELLAR ATROPHY I; OPCA
CEREBELLOPARENCHYMAL DISORDER I; CPD
MENZEL TYPE OPCA
OLIVOPONTOCEREBELLAR ATROPHY IV; OPC
SCHUT-HAYMAKER TYPE OPCA

Phenotype Gene Relationships

Location	Phenotype	Phenc MIM r
6p22.3	Spinocerebellar ataxia 1	164400

Phenotypic Series

Clinical Synopsis

click

TEXT

A number sign (#) is used with this entry because
(CAG)n trinucleotide repeat in the ataxin-1 gene (A

Description

The autosomal dominant cerebellar degener
'spinocerebellar ataxias' (SCAs) even though 'sp

#164400

SPINOCEREBELLAR ATAXIA 1; SCA1

CATEGORY	SUBCATEGORY	FEATURES
Inheritance	-	Autosomal dominant
Head and Neck	Eyes	Supranuclear ophthalmoplegia Nystagmus Slow saccades Hypermetria Optic atrophy
Muscle, Soft Tissue	-	Amyotrophy
Neurologic	Central Nervous System	Progressive cerebellar ataxia Hyperreflexia (early) Scanning speech Dysarthria Dysmetria Hypotonia Loss of deep tendon reflexes (later) Extensor plantar response Extrapyramidal signs Corticospinal signs Chorea Bulbar palsies Dysphagia Dysdiadochokinesis Cognitive impairment, mild Olivopontocerebellar atrophy Dorsal column and spinocerebellar trac degeneration
	Peripheral Nervous System	Sensory and motor nerve conduction abnormalities
Miscellaneous	-	Onset in third or fourth decade Genetic anticipation Paternal anticipation bias
Molecular Basis	-	Caused by expanded CAG trinucleotide repeats in the ataxin-1 gene (ATX1, 601556.0001).

Table of Contents - #164400
Title
Contributors
Creation Date
Edit History
External Links:
Clinical Resources
Centers for Mendelian Genomics

Clinical Synopsis

Provides an overview of the clinical features of a phenotype

Associated Gene/Locus

#164400

SPINOCEREBELLAR ATAXIA 1; SCA1

- Table of Contents - #164400

External Links:

- Clinical Resources
- Animal Models
- Cell Lines
- Cellular Pathways

Centers for Mendelian Genomics

Alternative titles; symbols

SPINOCEREBELLAR ATROPHY I
OLIVOPONTOCEREBELLAR ATROPHY I; OPCA I; OPCA1
CEREBELLOPARENCHYMAL DISORDER I; CPD1
MENZEL TYPE OPCA
OLIVOPONTOCEREBELLAR ATROPHY IV; OPCA IV; OPCA4
SCHUT-HAYMAKER TYPE OPCA

Phenotype Gene Relationships

Location	Phenotype	Phenotype MIM number	Gene/Locus	Gene/Locus MIM number
6p22.3	Spinocerebellar ataxia 1	164400	ATXN1	601556

click

Phenotypic Series

Clinical Synopsis

TEXT

A number sign (#) is used with this entry because spinocerebellar ataxia-1 is caused by an expanded (CAG)n trinucleotide repeat in the ataxin-1 gene (ATXN1; 601556).

Description

The autosomal dominant cerebellar degenerative disorders are generally referred to as 'spinocerebellar ataxias' (SCAs) even though 'spinocerebellar' is a hybrid term referring to both

OMIM Gene Entry

*601556

ATAXIN 1; ATXN1

HGNC Approved Gene Symbol: ATXN1

Cytogenetic location: 6p22.3 *Genomic coordinates (GRCh37): 6:16,299,342 - 16,761,720* (from NCBI)

Gene Phenotype Relationships

Location	Phenotype	Phenotype MIM number
6p22.3	Spinocerebellar ataxia 1	164400

TEXT

Description

ATXN1 and ATXN1L (614301) are chromatin-binding factors that suppress signaling within the Notch pathway (see 190198) in the absence of Notch activation (Tong et al., 2011).

Cloning

Using DNA fragments from a cosmid clone shown to contain the CAG trinucleotide repeat identified as the cause of spinocerebellar ataxia-1 (SCA1; 164400) by Orr et al. (1993), Banfi et al. (1994) screened 2 human fetal brain and 1 human adult cerebellar cDNA libraries to isolate the ATXN1 transcript. Banfi et al. (1994) demonstrated that the ATXN1 gene encodes an 816-amino acid protein with a molecular mass of 87 kD. The (CAG)n repeat, coding for a polyglutamine tract, lies within the coding region, and the protein is transcribed from both the wildtype and the CAG-expanded ATXN1 allele.

Mizutani et al. (2005) stated that the deduced 816-amino acid ATXN1 protein has an N-terminal BOAT (ATXN1L) and ataxin-1 (NBA) domain, followed by the polyglutamine tract, a self-association region (SAR), and a C-terminal ATXN1 and HBP1 (AXH) domain.

Expandable TOC

Full entry

consent

*602421

Gene CFTR's Table View

CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR; CFTR

Allelic Variants (Selected Examples):

Number	Phenotype	Mutation	dbSNP
.0001	CYSTIC FIBROSIS BRONCHIECTASIS WITH OR WITHOUT ELEVATED SWEAT CHLORIDE 1, MODIFIER OF, INCLUDED	CFTR, PHE508DEL	[rs113993960]
		ILE507DEL	-
		GLN493TER	[rs77101217]
		ASP110HIS	[rs113993958]
		ARG117HIS	[rs78655421]
		ARG347PRO	[rs77932196]
		ALA455GLU	[rs74551128]
		IVS10, G-A, -1	[rs76713772]
		GLY542TER	[rs113993959]
		SER549ASN	-
		SER549ILE	[rs121908755]
		SER549ARG	[rs121908757], [rs121909005]
		GLY551ASP	[rs75527207]
		ARG553TER	[rs74597325]
		ALA559THR	[rs75549581]

*601556

ATAXIN 1; ATXN1

1.4 How are mutations cataloged in OMIM?

Mutations are cataloged in OMIM in the Allelic Variants section of gene entries (see 1.2). For most genes, only selected mutations are included. Criteria for inclusion include the first mutation to be discovered, high population frequency, distinctive phenotype, historic significance, unusual mechanism of mutation, unusual pathogenetic mechanism, and distinctive inheritance (e.g., dominant with some mutations, recessive with other mutations in the same gene). Most of the allelic variants represent disease-causing mutations. A few polymorphisms are included, many of which show a positive c

http://www.omim.org/help/faq#1.4

Description

ATXN1 and ATXN1L (614301) are chromatin-binding factors that suppress signaling within the Notch pathway (see 190198) in the absence of Notch activation (Tong et al., 2011).

Cloning

Allelic Variants

Table View

References

Contributors

Creation Date

Edit History

*601556

Table View of Allelic Variants

ATAXIN 1; ATXN1

Allelic Variants (Selected Examples):

Number	Phenotype	Mutation	dbSNP
.0001	SPINOCEREBELLAR ATAXIA 1	ATXN1, (CAG)n EXPANSION	-

▸ Cellular Pathways

External Links for Genes: Genome

*601556

ATAXIN 1; ATXN1

HGNC Approved Gene Symbol: ATXN1

Cytogenetic location: 6p22.3 Genomic coordinates (GRCh37): 6:16,299,342 - 16,761,720 (from NCBI)

External Links

External Links:

- Table of Content
- Genome
  - Ensembl
  - NCBI Map Viewer
  - UCSC Genome Browser
- DNA
- Protein
- Gene Info
- Clinical Resources
- Variation
- Animal Models
- Cellular Pathways

Genomes | Genome Browser | Tools | Mirrors | Downloads | My Data | About Us | View | Help

UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly

move <<< << < > >> >>> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x

chr6:16,299,343-16,761,721 462,379 bp. enter position, gene symbol or search terms go

Click on a feature for details. Click or drag in the base position track to zoom in. Click side bars for track options. Drag side to new position.

track search | default tracks | default order | hide all | add custom tracks | track hubs | configure | reverse | resize | refresh

collapse all | Use drop-down controls below and press refresh to alter tracks displayed. Tracks with lots of items will automatically be displayed in more compact modes. | expand all

Mapping and Sequencing Tracks refresh

UCSC Genome Browser: An Introduction

by OpenHelix

Online Tutorial Suite

http://openhelix.com/catalog

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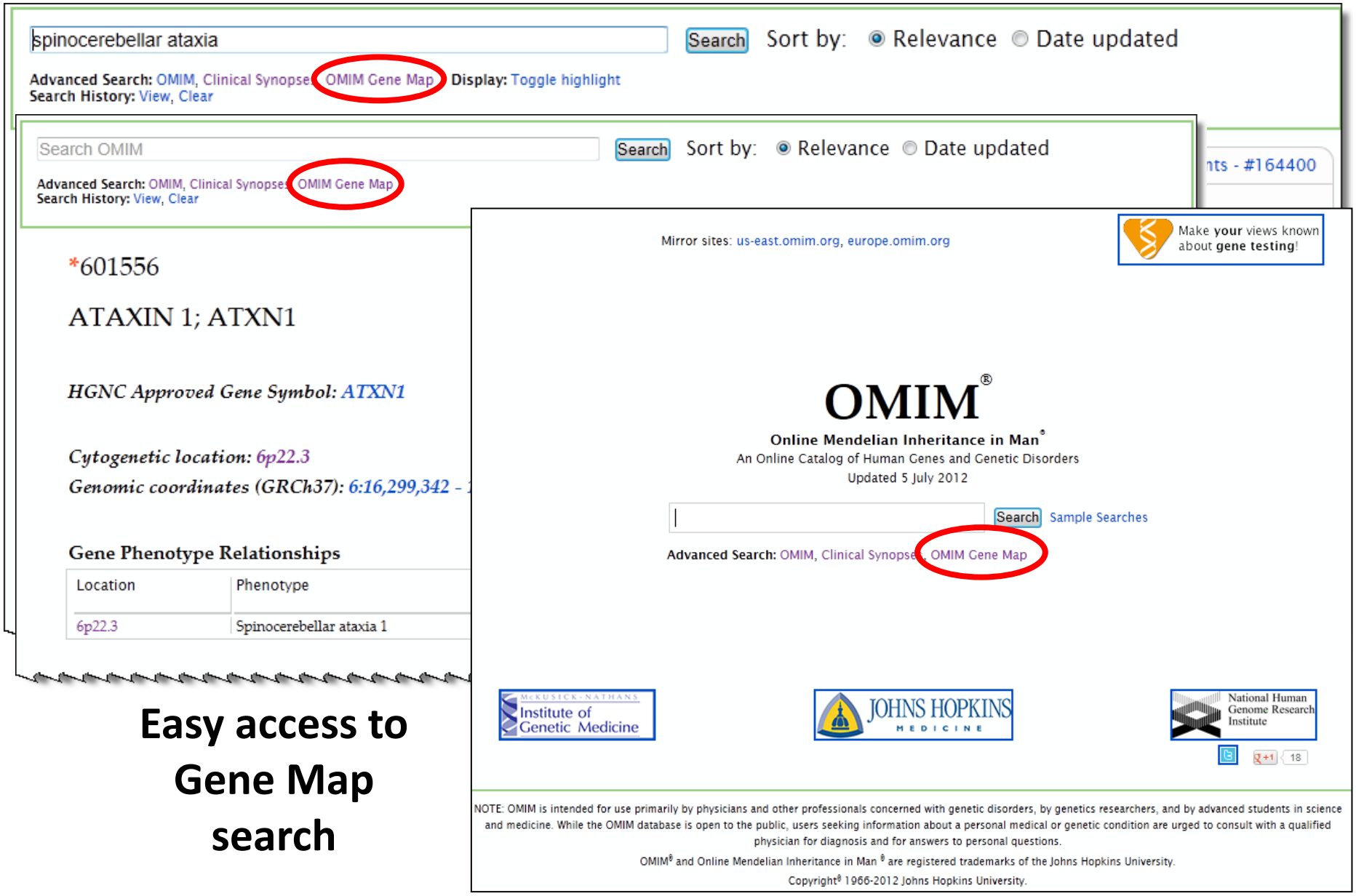
Gene Map Search



Easy access to Gene Map search

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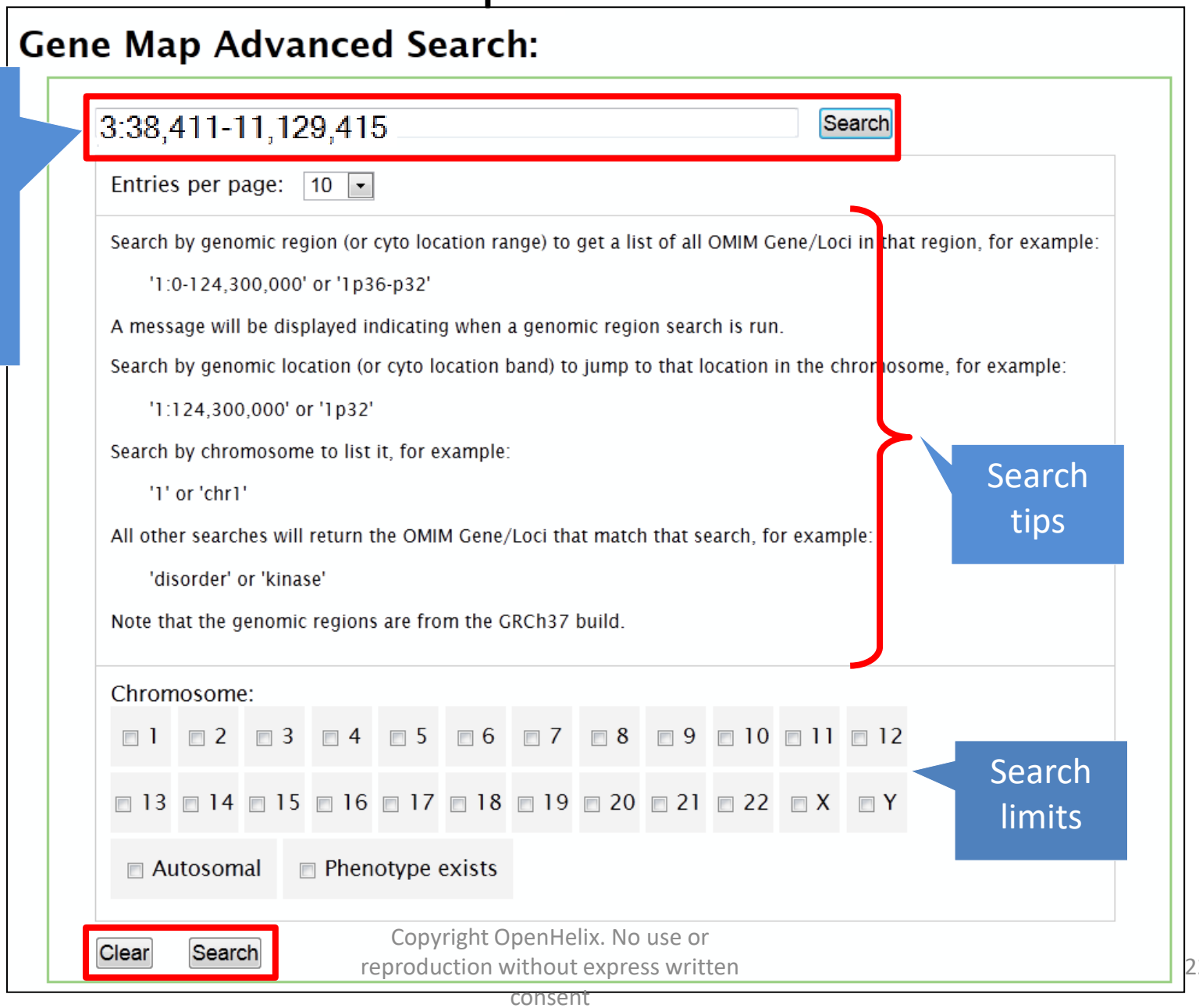
Gene Map Search Form



Example searches:
- 1p36
- kinase
- CFTR
- etc.

Search tips

Search limits

Gene Map Search Results

Gene Map

3:38,411-11,129,415

Search

Search: OMIM | **Advanced Search:** OMIM, Clinical Synopses, OMIM Gene Map **Toggle:** search terms highlighted

Search History: View, Clear

Phenotype Only Entries | All Entries

Start at lowest numbered chromosome (results)

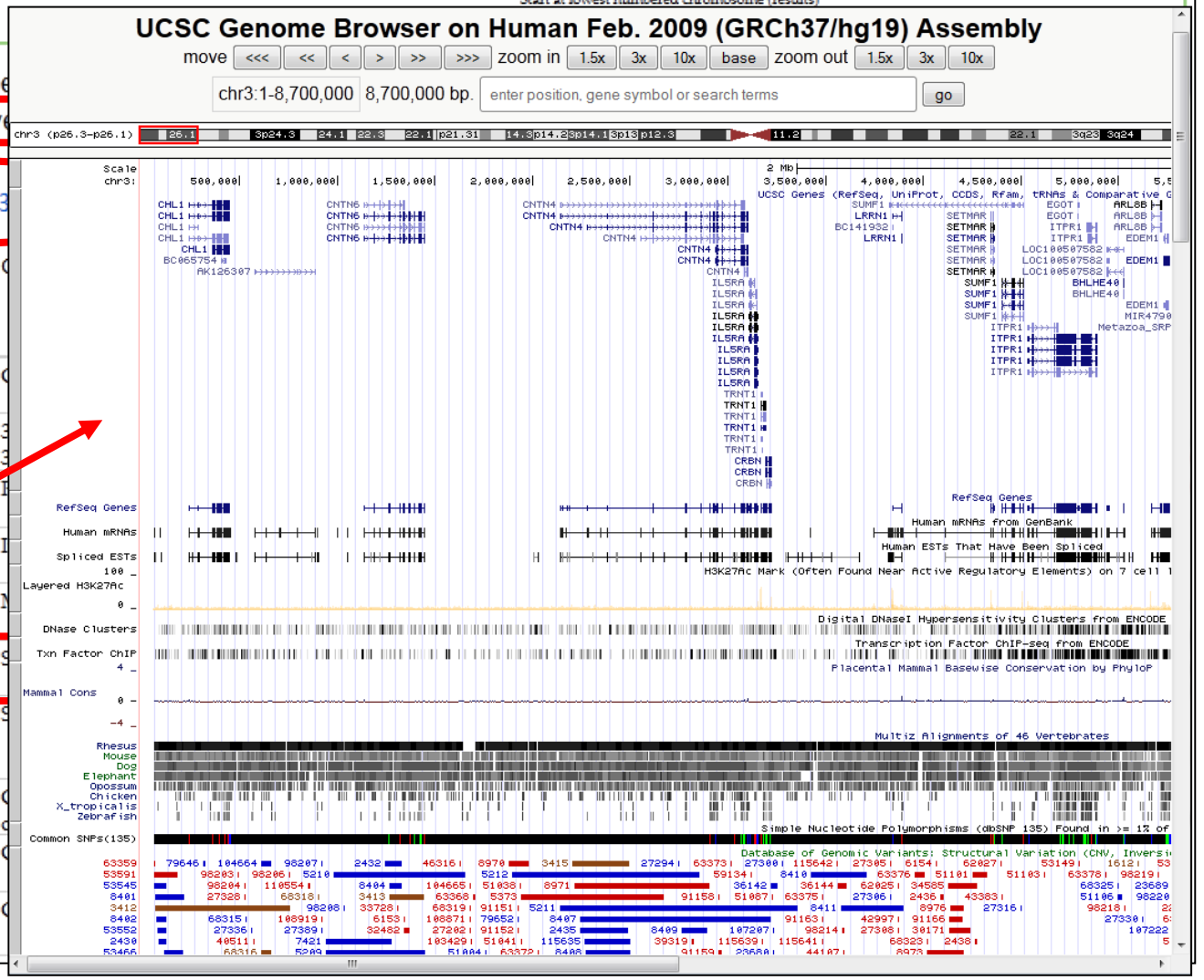
The search '3:38,411-11,129,415' mappe

retrieved entries that start, or end, or ove

Search: '3:38,411-11,129,415'

Results: 1 - 10 of 44 | Show all | 1 2 3

Genomic context table	Location (genomic start, cyto location) (from NCBI)	Gene/Locus
1 :	3:0 3p	CRCL
2 :	3:0 3pter-p25	DEL3pterp25, C3DELpterp25
3 :	3:0 3p26	HPC5
4 :	3:0 3p26	IBD9
5 :	3:0 3p26-p24	MYMY1, MYMY
6 :	3:0 3p26	SCA29
7 :	3:0 3p26	STQTL5
8 :	3:238,278 3p26.3	CHL1, CALL, L1CAM2
9 :	3:1,134,628 3p26.3	CNTN6, NB3
10 :	3:2,140,549 3p26.3-p26.2	CNTN4



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OMIM Summary: Gene, Variant & Phenotype Data

Detailed Entries

#164400

SPINOCEREBELLAR ATAXIA 1; SCA1

Alternative titles; symbols

SPINOCEREBELLAR ATROPHY I
OLIVOPONTOCEREBELLAR ATROPHY I; OPCA I; OPCA1
CEREBELLOPARENCHYMAL DISORDER I; CPD1
MENZEL TYPE OPCA
OLIVOPONTOCEREBELLAR ATROPHY IV; O
SCHUT-HAYMAKER TYPE OPCA

Phenotype Gene Relationships

Location	Phenotype	Ph M
6p22.3	Spinocerebellar ataxia 1	16

Phenotypic Series

Clinical Synopsis

TEXT

A number sign (#) is used with this entry beca
(CAG)n trinucleotide repeat in the ataxin-1 gen

Description

The autosomal dominant cerebellar degenerative disorders are generally referred to as 'spinocerebellar ataxias,' (SCAs) even though 'spinocerebellar' is a hybrid term, referring to both clinical signs and neuroanatomical regions (Margolis, 2003). Neuropathologists have defined SCAs as cerebellar ataxias with variable involvement of the brainstem and spinal cord, and the clinical features of the disorders are caused by degeneration of the cerebellum and its afferent and efferent connections, which involve the brainstem and spinal cord (Schols et al., 2004; Taroni and DiDonato, 2004).

ADCA III was a pure form of late-onset cerebellar ataxia without additional features. SCA1, SCA2 (183090), and SCA3, or Machado-Joseph disease (109150), are considered to be forms of ADCA I. These 3 disorders are characterized at the molecular level by CAG repeat expansions on 6p24-p23, 12q24.1, and 14q32.1, respectively. SCA7 (607640), caused by a CAG repeat expansion in the ATXN7 gene (607640) on chromosome 3p13-p12, is a form of ADCA II. SCA5 (600224), SCA31 (117210), SCA6 (183086), and SCA11 (600432) are associated with phenotypes most suggestive of ADCA III. However, Schelhaas et al. (2000) noted that there is significant phenotypic overlap between different forms of SCA as well as significant phenotypic variability within each subtype.

Gene Map

OMIM Gene/Loci: 68 - 77 of 784 on Chromosome 6 (All Entries) | Show 100

pter | Towards pter | Back 3 | Forward 3 | Towards qter | qter

Location (genomic start, cyto location) (from NCBI)	Gene/Locus	Gene/Locus name	Gene/Locus MIM number	Phenotype	Phenotype MIM number	Pheno map key	Comments	Mouse symbol (from MGI)
6:15,246,526 6p22.3	JMJ	Jumonji	601594					Jarid2
6:15,523,031 6p22.3	DTNBP1, HPS7	Dystrobrevin-binding protein 1 (dysbindin)	607145	Hermansky-Pudlak synd (Schi	614076	3		Dtnbp1

Phenotypic Series

Spinocerebellar ataxia - 164400

Location	Phenotype	Phenotype mapping	Phenotype MIM number	Gene/Locus	Gene/Locus MIM number
1p21-q21	Spinocerebellar ataxia 19				
2p21-p13	Spinocerebellar ataxia 25				
3p26	Spinocerebellar ataxia 29				
3p26.1	Spinocerebellar ataxia 15				
3p14.1	Spinocerebellar ataxia 7				
4q34.3-q35.1	?Spinocerebellar ataxia 30				
5q32	Spinocerebellar ataxia 12				
6p22.3	Spinocerebellar ataxia 1				
6p12.3-q16.2	Spinocerebellar ataxia 34				
6q27	Spinocerebellar ataxia 17				
7p21.3-p15.1	Spinocerebellar ataxia 21				
7q22-q32	Spinocerebellar ataxia 18				
7q32-q33	Spinocerebellar ataxia 32				

Clinical Synopsis

#164400

SPINOCEREBELLAR ATAXIA 1; SCA1

CATEGORY	SUBCATEGORY	FEATURES
Inheritance	-	Autosomal dominant
Head and Neck	Eyes	Supranuclear ophthalmoplegia Nystagmus Slow saccades Hypermetria Optic atrophy
Muscle, Soft Tissue	-	Amyotrophy
Neurologic	Central Nervous System	Progressive cerebellar ataxia Hyperreflexia (early) Scanning speech Dysarthria Dysmetria Hypotonia Dorsal column and spinocerebellar tract degeneration
	Peripheral Nervous System	Sensory and motor nerve conduction abnormalities
Miscellaneous	-	Onset in third or fourth decade Genetic anticipation Paternal anticipation bias
Molecular Basis	-	Caused by expanded CAG trinucleotide repeats in the ataxin-1 gene (ATX1, 601556.0001).

Contributors: Cassandra L. Kniffin - revised : 08/14/2002
Creation Date: John F. Jackson : 6/15/1995
Edit History: ckniffin : 08/14/2002

OMIM Summary: Data, cont.

219700. CYSTIC FIBROSIS; CF

Cytogenetic locations: 7q31.2 , 19q13.2

Gene Tests, Newborn Screening, ICD+, Links

Links to external sources

ICD+ for #219700 x

ICD10CM: E84.9,
ICD10CM: E84,
ICD9CM: 277.0,
SNOMEDCT: 190905008

Table of Allelic Variants

*602421

CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR; CFTR

Allelic Variants (Selected Examples):

Number	Phenotype	Mutation	dbSNP
.0001	CYSTIC FIBROSIS BRONCHIECTASIS WITH OR WITHOUT ELEVATED SWEAT CHLORIDE 1, MODIFIER OF, INCLUDED	CFTR, PHE508DEL	-
.0002	CYSTIC FIBROSIS	CFTR, ILE507DEL	-
.0003	CYSTIC FIBROSIS	CFTR, GLN493TER	[rs77101217]
.0004	CYSTIC FIBROSIS	CFTR, ASP110HIS	[rs113993958]
.0005	CYSTIC FIBROSIS VAS DEFERENS, CONGENITAL BILATERAL ABSENCE OF, INCLUDED	CFTR, ARG117HIS	[rs78655421]
.0006	CYSTIC FIBROSIS	CFTR, ARG347PRO	[rs77932196]
.0007	CYSTIC FIBROSIS	CFTR, ALA455GLU	[rs74551128]
.0008	CYSTIC FIBROSIS	CFTR, IVS10, G-A, -1	[rs76713772]
.0009	CYSTIC FIBROSIS	CFTR, GLY542TER	[rs113993959]
.0010	CYSTIC FIBROSIS	CFTR, SER549ASN	-
.0011	CYSTIC FIBROSIS	CFTR, SER549ILE	[rs121908755]
.0012	CYSTIC FIBROSIS	CFTR, SER549ARG	[rs121908757], [rs121909005]
.0013	CYSTIC FIBROSIS	CFTR, GLY551ASP	[rs75527207]
.0014	CYSTIC FIBROSIS	CFTR, ARG553TER	[rs74597325]
.0015	CYSTIC FIBROSIS	CFTR, ALA559THR	[rs75549581]

OMIM - Rich Source of Gene and Phenotype Data

OMIM database: http://omim.org

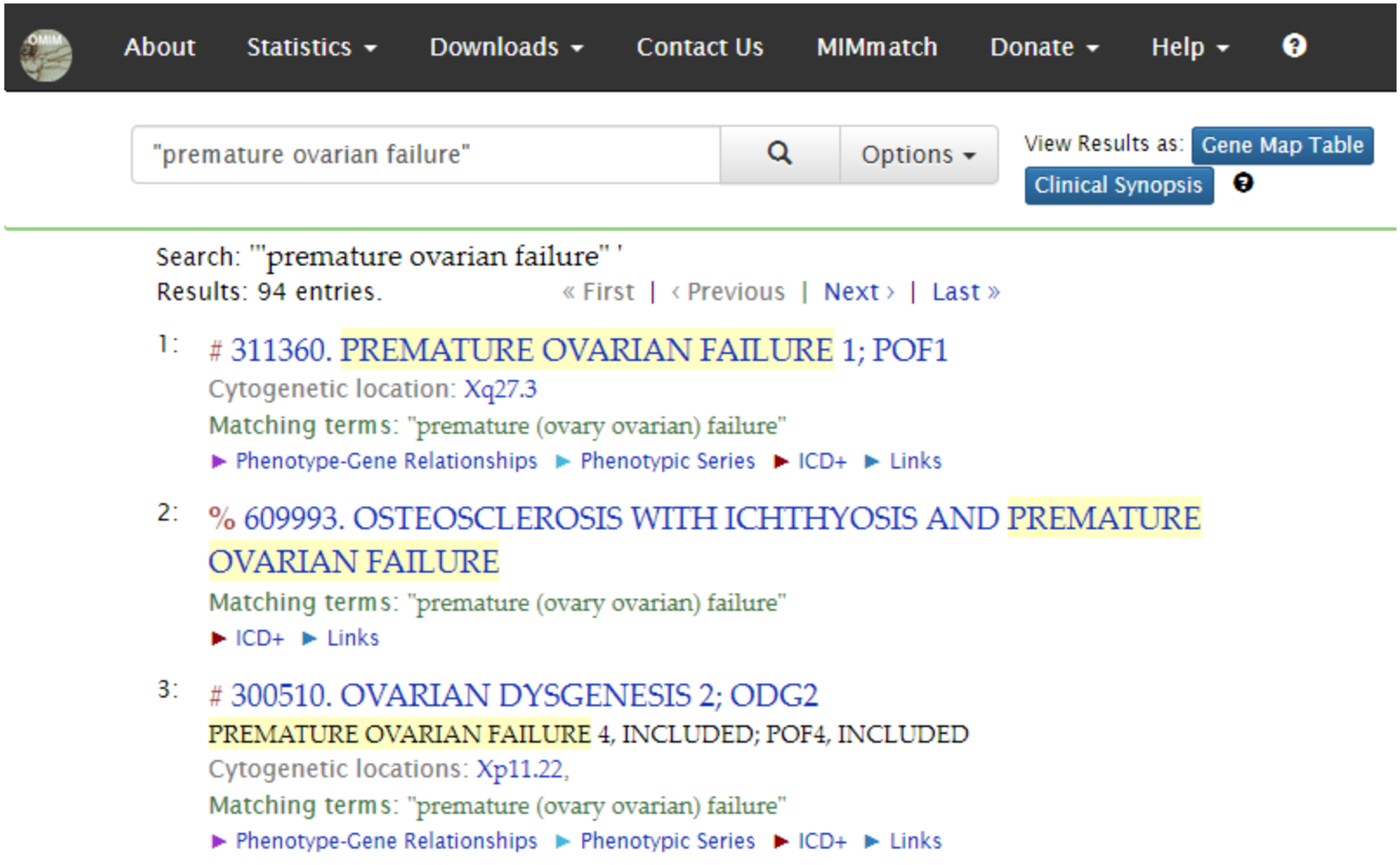
Exercices sur OMIM :

Explorer le syndromes de Perrault, de l'X fragile, de Turner, de Klinefelter,
de Leydig cell hypoplasia
Identifier les syndromes de hypogonadisme hypergonadotrope
ou de l' insuffisance ovarienne primitive (IOP) (premature ovarian failure)
ou de la diminution de réserve ovarienne DRO) (decreasing ovarian reserve)
Quels sont les phénotypes ?
Quels sont les gènes impliqués ?
Quels anomalies de caryotype ?
Quels variants ?

Pour chaque entrée :
Consulter le « Content » (à gauche) ou les « Links » (à droite)

Attention : queries in english !!

Insuffisance ovarienne précoce



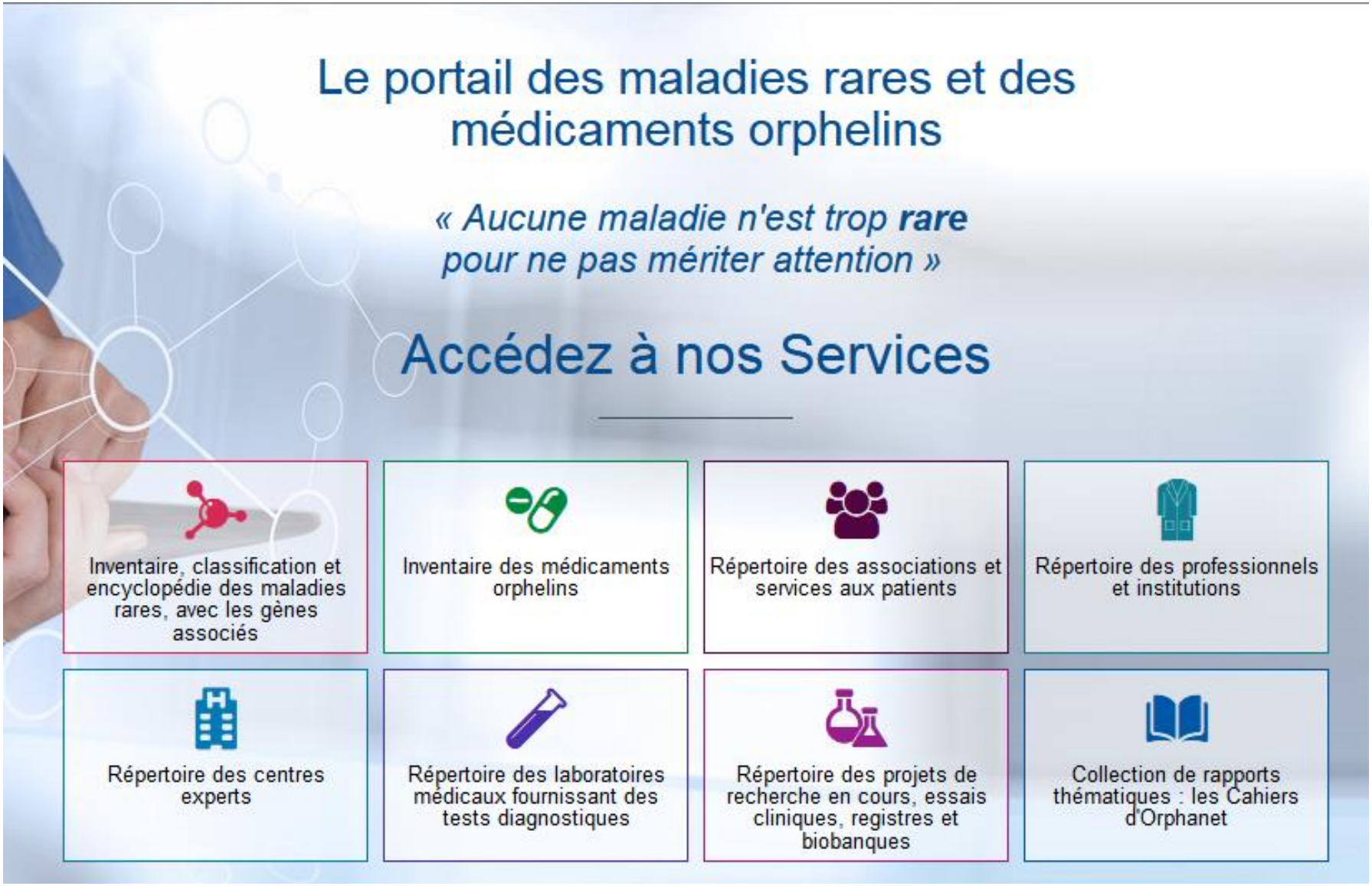
Et suite et links …

ORPHANET

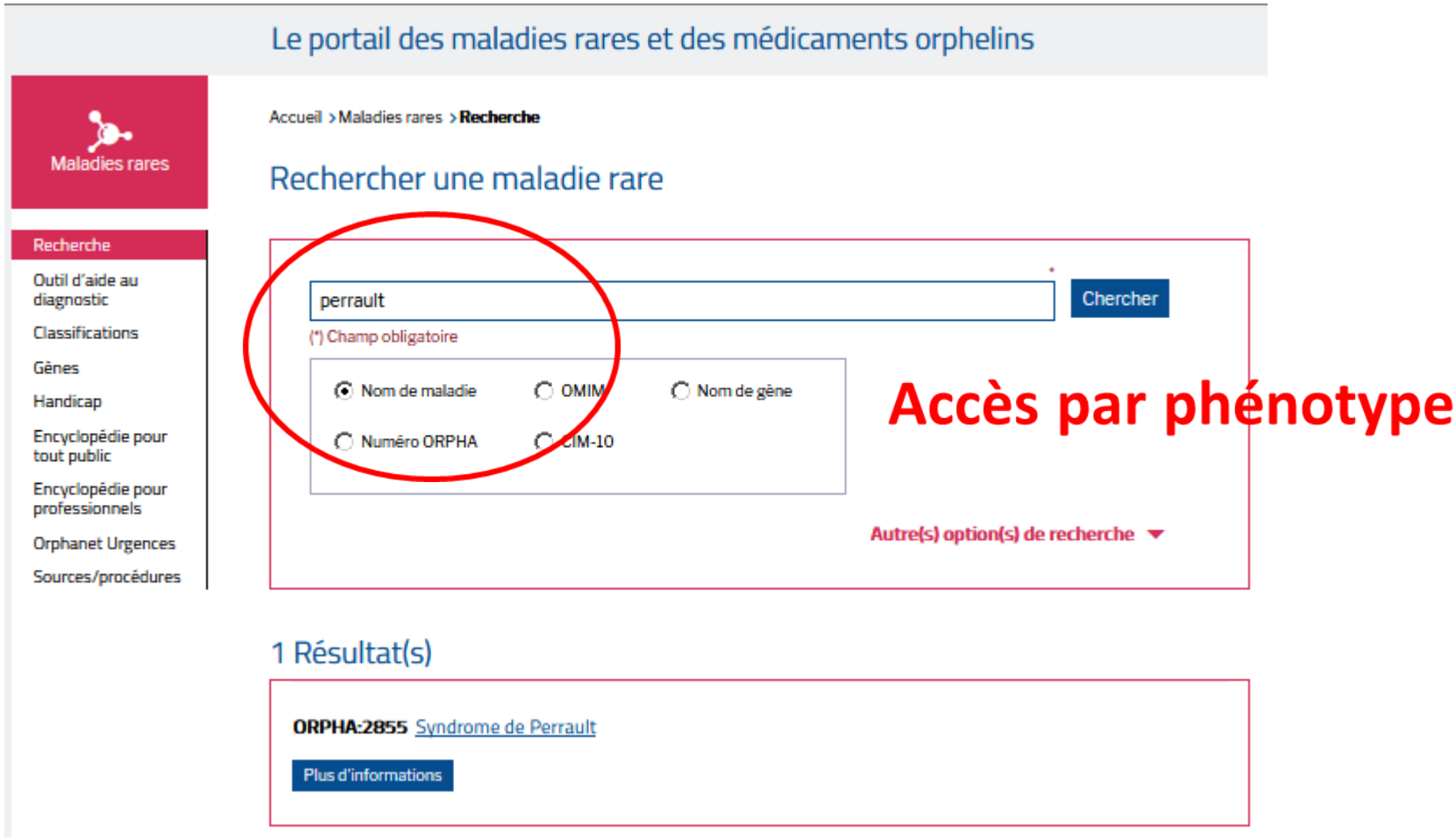
www.orpha.net

Portail des maladies rares

SC14 INSERM



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



Accès par phénotype

Perrault syndrome

ORPHA2855

		ICD-10:	Q87.8
Synonym(s):	XX gonodal dysgenesis-deafness syndrome	OMIM:	233400 [↗] 614129 [↗] 614926 [↗] 615300 [↗] 616138 [↗]
Prevalence:	<1 / 1 000 000		
Inheritance:	Autosomal recessive	UMLS:	C0685838
Age of onset:	Adolescent Childhood Adult	MeSH:	-
		MedDRA:	-

SUMMARY

Perrault syndrome (PS) is characterized by the association of ovarian dysgenesis in females with sensorineural hearing impairment. In more recent PS reports, some authors have described neurologic abnormalities, notably progressive cerebellar ataxia and intellectual deficit.

Prevalence is unknown but 34 patients with PS (28 females and 6 males) from 15 different families have been reported so far. However, the syndrome is probably underdiagnosed: hypogonadism is not a feature in males and in the absence of an affected sister the syndrome remains undetected.

Mean age at diagnosis is 22 years following presentation with delayed puberty in females with sensorineural deafness. Hearing defects were noted in all but one of the reported cases (mean age at diagnosis of 8 years). The hearing loss is always sensorineural and bilateral but the severity is variable (mild to profound), even in affected patients from the same family. Ovarian dysgenesis has been reported in all female cases but no gonad defects are detected in males. Amenorrhea is generally primary but secondary amenorrhea has also been reported. Delayed growth (height below the third percentile) was reported in half the documented cases. The exact frequency of the neurological abnormalities is unknown, but nine females and two males (16-37 years old) lacking neurological abnormalities have been reported. Neurological signs are progressive and generally appear later in life, however, walking delay or early frequent falls have been noted in young PS patients. Common neurological signs are ataxia, dyspraxia, limited extraocular movements, and polyneuropathy. Some cases with scoliosis have also been reported.

Mutations in the following genes have been excluded: *GJB2* (responsible for the most frequent form of isolated hearing loss), *FOXL2* (involved in premature ovarian failure) and *POLG*, *FRDA*, *AOA1* (implicated in ataxia or ophthalmoplegia). Karyotype is normal. The variability in the presence of the neurological symptoms may indicate that PS is a heterogeneous disease.

Additional information

Further information on this disease

> Classification(s) (8)
> Gene(s) (5)
> Other website(s) (1)

Health care resources for this disease

> Expert centres (391)
> Diagnostic tests (54)
> Patient organisations (60)
> Orphan drug(s) (1)

Research activities on this disease

> Research projects (54)
> Clinical trials (0)
> Registries/biobanks (29)
> Networks (29)

Specialised Social Services

> Eurordis directory [↗]

Orphanet Reports series

> Prevalence
> Orphan drugs in Europe

Mutations in the following genes have been excluded: *GJB2* (responsible for the most frequent form of isolated hearing loss), *FOXL2* (involved in premature ovarian failure) and *POLG*, *FRDA*, *AOA1* (implicated in ataxia or ophthalmoplegia). Karyotype is normal. The variability in the presence of the neurological symptoms may indicate that PS is a heterogeneous disease.

Diagnosis is made on the basis of the clinical signs and further investigations: CT scans revealing that the hearing loss is not associated with temporal bone malformations; hormonal tests revealing hypergonadotropic hypogonadism in females; pelvic examinations revealing absent ovaries or streak gonads, and a very hypoplasic uterus, and neurologic investigations revealing reduced nerve conduction velocities. Cerebral MRI may show a nonspecific white matter hypersignal or cerebellar atrophy.

Turner syndrome is the principle differential diagnosis (see this term).

Transmission of PS is probably autosomal recessive but no gene locus or mitochondrial mutations have been identified to date.

Treatment and follow-up should be multidisciplinary including audiologists, endocrinologists and neurologists. Hearing aids or cochlear implants may be of benefit for the hearing defect.

Life expectancy is normal. Outcome with treatment is very variable, depending on the association with other features, in particular the presence of neurologic disease.

Expert reviewer(s)

Dr Sandrine MARLIN

Last update: September 2008

Informations complémentaires

Plus d'information sur cette maladie

- Classification(s) (8)
- Gène(s) (6)
- Autre(s) site(s) Internet (2)

Ressources médicales pour cette maladie

- Centres experts (391)
- Tests diagnostiques (61)
- Associations (57)
- Médicament(s) orphelin(s) (1)

Activités de recherche sur cette maladie

- Projets de recherche (47)
- Essais cliniques (0)
- Registres/bases de données (29)
- Réseaux (32)

Services sociaux spécialisés

- Annuaire Eurordis

Rechercher une maladie rare

HARS2 *

Chercher

(*) Champ obligatoire

- Nom de maladie
- OMIM
- Nom de gène
- Numéro ORPHA
- CIM-10

Accès par gène

Autre(s) option(s) de recherche

1 Résultat(s)

> histidyl-tRNA synthetase 2, mitochondrial - HARS2

: : *HARS2* - histidyl-tRNA synthetase 2, mitochondrial

ORPHA268052

Synonyme(s) :	*HARSR, histidine tRNA ligase 2, mitochondrial (putative), HO3*	OMIM:	600783 [↗]
Anciens symbols et noms:	*HARSL, histidyl-tRNA synthetase-like*	HGNC:	4817 [↗]
Type:	gene with protein product	UniProtKB:	P49590 [↗]
Localisation chromosomique:	5q31.3	Genatlas:	HARS2 [↗]
		Ensembl:	ENSG00000112855 [↗]
		IUPHAR-DB:	-
		Reactome:	P49590 [↗]

Liste de maladies

- Mutation germinale causale dans Syndrome de Perrault ✓

✓ Vérifié

Informations complémentaires

Ressources médicales pour ce gène

> Tests diagnostiques (4)

Activités de recherche sur ce gène

> Projets de recherche (0)
> Registres/bases de données (0)

omim.org/entry/600783#0001

Rechercher

Search OMIM...

Search

Advanced Search | Search History | Display Options

Lien sur OMIM

*600783

HISTIDYL-tRNA SYNTHETASE 2; HARS2

Alternative titles; symbols

HISTIDYL-tRNA SYNTHETASE, MITOCHONDRIAL
MITOCHONDRIAL HISRS
HISTIDYL-tRNA SYNTHETASE-LIKE; HARSL
HARS-RELATED GENE; HARSR
HO3

HGNC Approved Gene Symbol: HARS2

Cytogenetic location: 5q31.3 Genomic coordinates (GRCh38):
5:140,691,425-140,699,317 (from NCBI)

Gene-Phenotype Relationships

Location	Phenotype	Phenotype MIM number	Inheritance (in progress)	Phenotype mapping key
5q31.3	?Perrault syndrome 2	614926	AR	3

TEXT

Description

The HARS2 gene encodes a histidyl tRNA synthetase, a highly conserved protein that functions in mitochondria (summary by Pierce et al., 2011).

Cloning and Expression

O'Hanlon et al. (1995) identified the HARS2 gene, which they called HO3, oriented head-to-head with the HARS gene (142810). The deduced 506-amino acid HO3 protein has a calculated molecular mass of 56.9 kD. HO3 shares 72% amino acid identity with HARS. Both proteins contain 3 motifs conserved among class II aminoacyl-tRNA synthetases and 2 signature regions of histidyl-tRNA synthetases. However, HARS and HARS2 have divergent N-terminal domains that

Une entrée OMIM en * correspond à un gène
Une entrée OMIM en # correspond à un phénotype

- Gene Info
- Clinical Resources
- Variation
- Animal Models
- Cellular Pathways

ALLELIC VARIANTS (2 Selected Examples):

Table View | ClinVar

.0001 PERRAULT SYNDROME 2 (1 family)

HARS2, LEU200VAL [dbSNP:rs397515410] [ClinVar]

In affected members of a family of European descent with Perrault syndrome-2 (PRLTS2; 614926), originally reported by Pallister and Opitz (1979), Pierce et al. (2011) identified compound heterozygosity for 2 mutations in the HARS2 gene: a paternally inherited 598C-G transversion in exon 6 resulting in a leu200-to-val (L200V) substitution at a highly conserved residue, and a maternally inherited 1102G-T transversion in exon 10 resulting in a val368-to-leu (V368L; 600783.0002) substitution at a highly conserved residue. The mutations were found by linkage analysis followed by candidate gene

.0002 PERRAULT SYNDROME 2 (1 family)

HARS2, VAL368LEU - [ClinVar]

For discussion of the val368-to-leu (V368L) mutation in the HARS2 gene that was found in compound heterozygous state in affected members of a family with Perrault syndrome-2 (PRLTS2; 614926) by Pierce et al. (2011), see 600783.0001.

OMIM apporte plus d'informations sur les variants

REFERENCES

1. Bonnefond, L., Fender, A., Rudinger-Thirion, J., Giege, R., Florentz,

Rechercher un centre expert

perrault *

Chercher

(*) Champ obligatoire

- (•) Consultation spécialisée
- ( ) Conseil Génétique
- ( ) Les deux types de consultation

- (•) Adultes
- ( ) Enfants
- ( ) Tout

France

☑ Centre officiellement désigné

Autre(s) option(s) de recherche

FRANCE
ILE-DE-FRANCE
PARIS

Centre national de ressources Robert Laplane

Centre de Ressources Expérimental Robert Laplane

Plus d'informations

FRANCE
AUVERGNE-RHONE-ALPES
CLERMONT-FERRAND

Centre de référence des anomalies du développement et syndromes malformatifs du Sud-Est - Site constitutif

CHU de Clermont-Ferrand - Hôpital d'Estaing

Plus d'informations

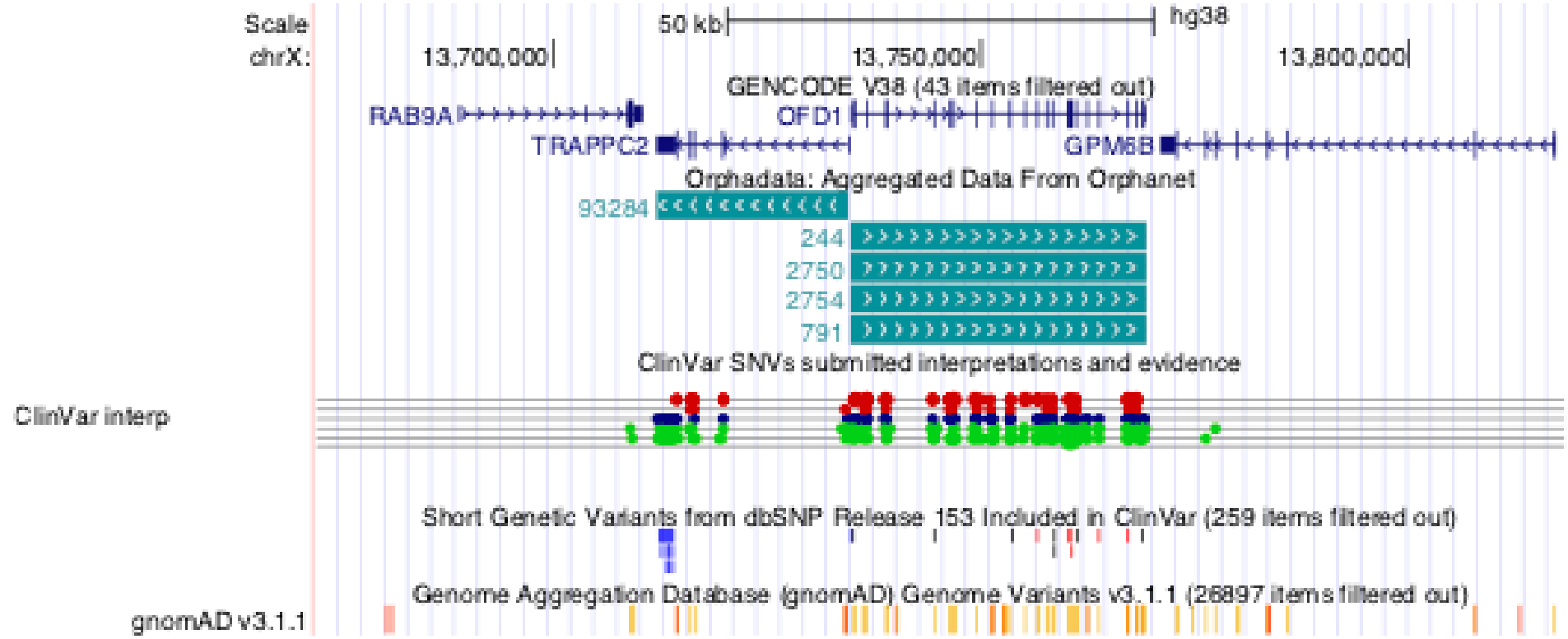
UCSC Browser et Orphanet

Hello Genome Browser enthusiasts,
We are happy to share another clinical resource for genetic disease analysis, the Orphadata track from the Orphanet consortium.

This track shows nearly 8000 gene-disease associations on hg19 and hg38. This data track includes information on human disorders and epidemiological information including Human Phenotype Ontology (HPO) disorder name, association type, modes of inheritance, age of first symptoms, and population disease prevalence (if available). For ease of use, we added mouseover information and a variety of filters. See our full announcement here:
https://genome.ucsc.edu/goldenPath/newsarch.html#111821

See this track along with a few other popular clinical tracks here:
https://genome.ucsc.edu/s/dschmelt/Orphadata.Orphanet.hg38

19.11.2021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hg38
chrX:
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13,750,000
13,800,000
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OFD1
TRAPPC2
GPM6B
Orphadata: Aggregated Data From Orphanet
93284
244
2750
2754
791
ClinVar SNVs submitted interpretations and evidence
ClinVar interp
Short Genetic Variants from dbSNP Release 153 Included in ClinVar (259 items filtered out)
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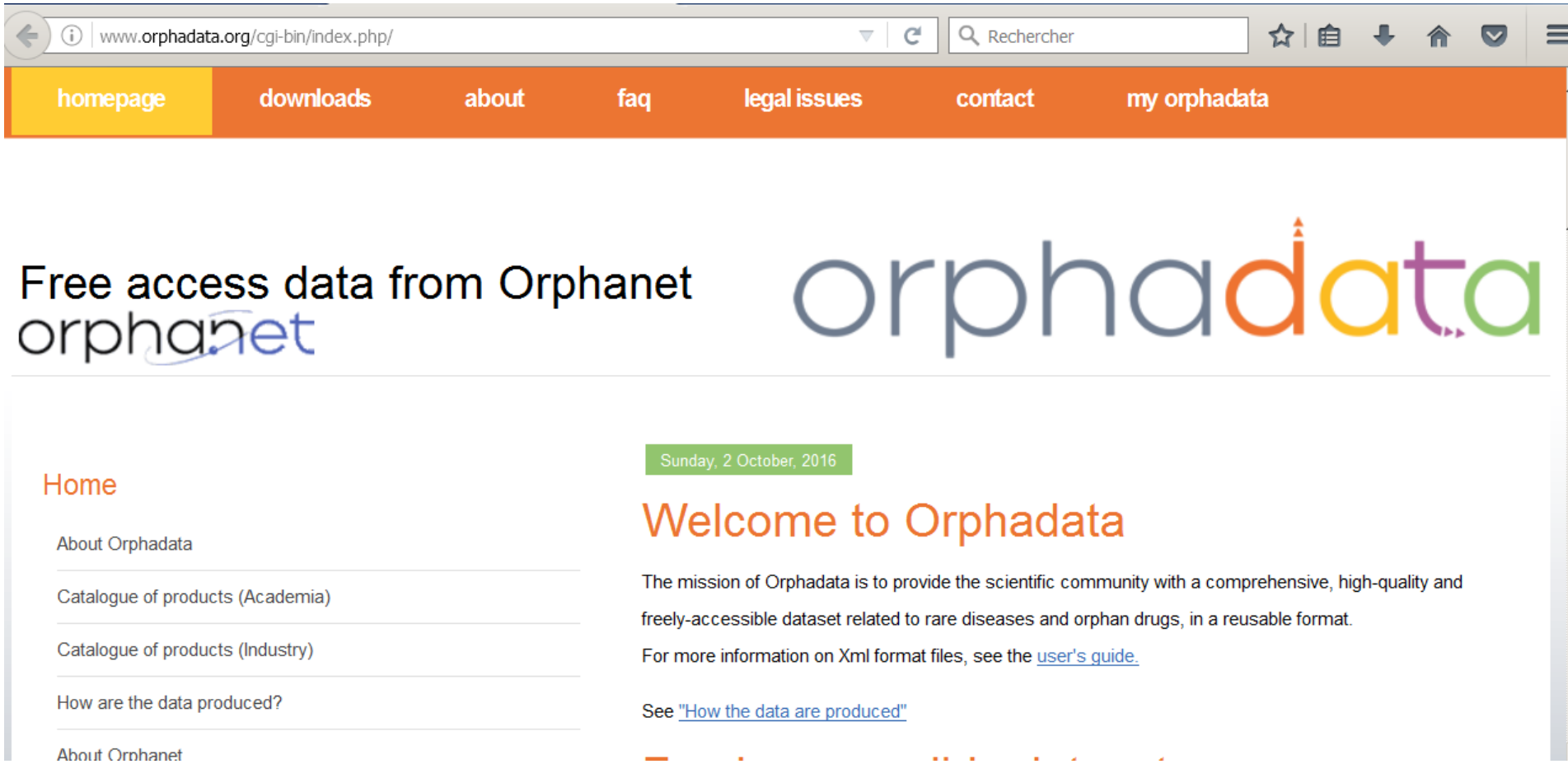
gnomAD v3.1.1


www.orphadata.org/cgi-bin/index.php/
Rechercher
homepage
downloads
about
faq
legal issues
contact
my orphadata
Free access data from Orphanet
orphanet
orphadata
Home
About Orphadata
Catalogue of products (Academia)
Catalogue of products (Industry)
How are the data produced?
About Orphanet
Sunday, 2 October, 2016
Welcome to Orphadata
The mission of Orphadata is to provide the scientific community with a comprehensive, high-quality and freely-accessible dataset related to rare diseases and orphan drugs, in a reusable format.
For more information on Xml format files, see the user's guide.
See "How the data are produced"

METHODOLOGY

Orphanet provides a comprehensive inventory of rare diseases in Europe, published biannually as a list. Rare diseases registered in Orphanet are defined according to two scopes:

- Every entity is defined by its clinical homogeneity, regardless of its etiology or the number of causing genes identified;

- The rarity is defined according to the European legislation defining a prevalence threshold of not more than 5 affected persons per 10'000 (Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, http://ec.europa.eu/health/files/eudralex/vol-1/reg_2000_141/reg_2000_141_en.pdf).

Data collection

As new scientific knowledge arises, the Orphanet rare diseases inventory is updated through the regular addition/update of diseases via two non-exclusive sources: documented sources and/or expert advice.

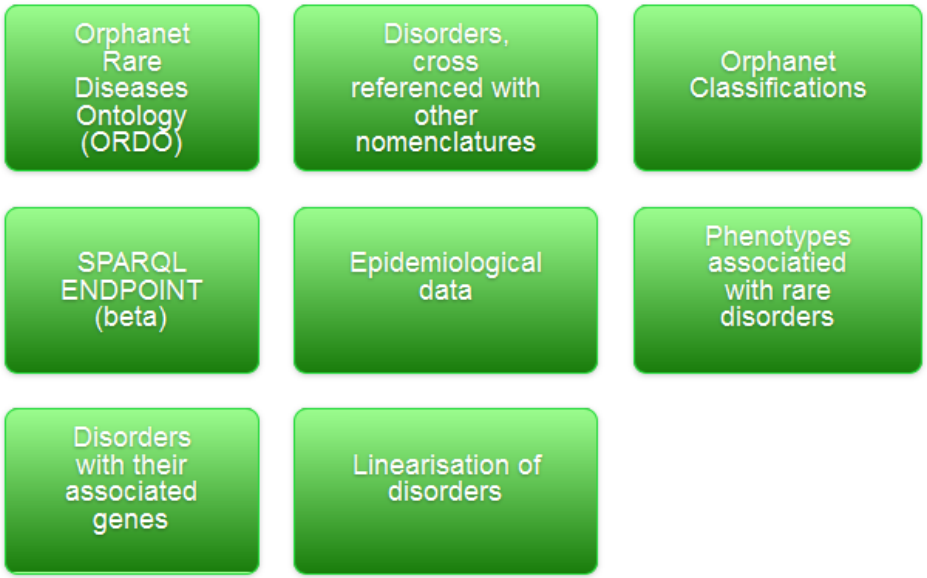
The scientific knowledge is monitored through:

- A bi-monthly analysis of a defined set of international peer-reviewed scientific journals covering the diversity of medical specialities represented in Orphanet;

- A monthly Medline search algorithm: (nosology[Title] OR classification[Title] OR nomenclature[Title] OR terminology[Title]) AND (rare disease* OR syndrome* OR disorder*);

Freely accessible datasets

Freely-accessible dataset



The dataset is a partial extraction of the data stored in Orphanet, which is also accessible at www.orpha.net for consultation purposes only.

Exercices sur Orphanet : www.orpha.net

Explorer le syndromes de Perrault, de l'X fragile, de Turner, de Klinefelter, de Leydig cell hypoplasia
Identifier les syndromes de hypogonadisme hypergonadotrope
ou de l' insuffisance ovarienne primitive
ou de la diminution de la réserve ovarienne

Quels sont les phénotypes ?
Quels sont les gènes impliqués ?
Quels anomalies de caryotype ?

A-t-on les mêmes renseignements que sur OMIM ?
Qu apporte de plus ORPHANET ?

Quels centres experts de références en région Bretagne ?

(manque la limitation à la localisation ….. Distance de domicile !!)

Rechercher une maladie rare

Insuffisance ovarienne précoce

(*) Champ obligatoire

Chercher

- (•) Nom de maladie
- ( ) Code ORPHA

7 Résultat(s)

ORPHA:243 (Pathologie) Dysgénésie gonadique 46,XX

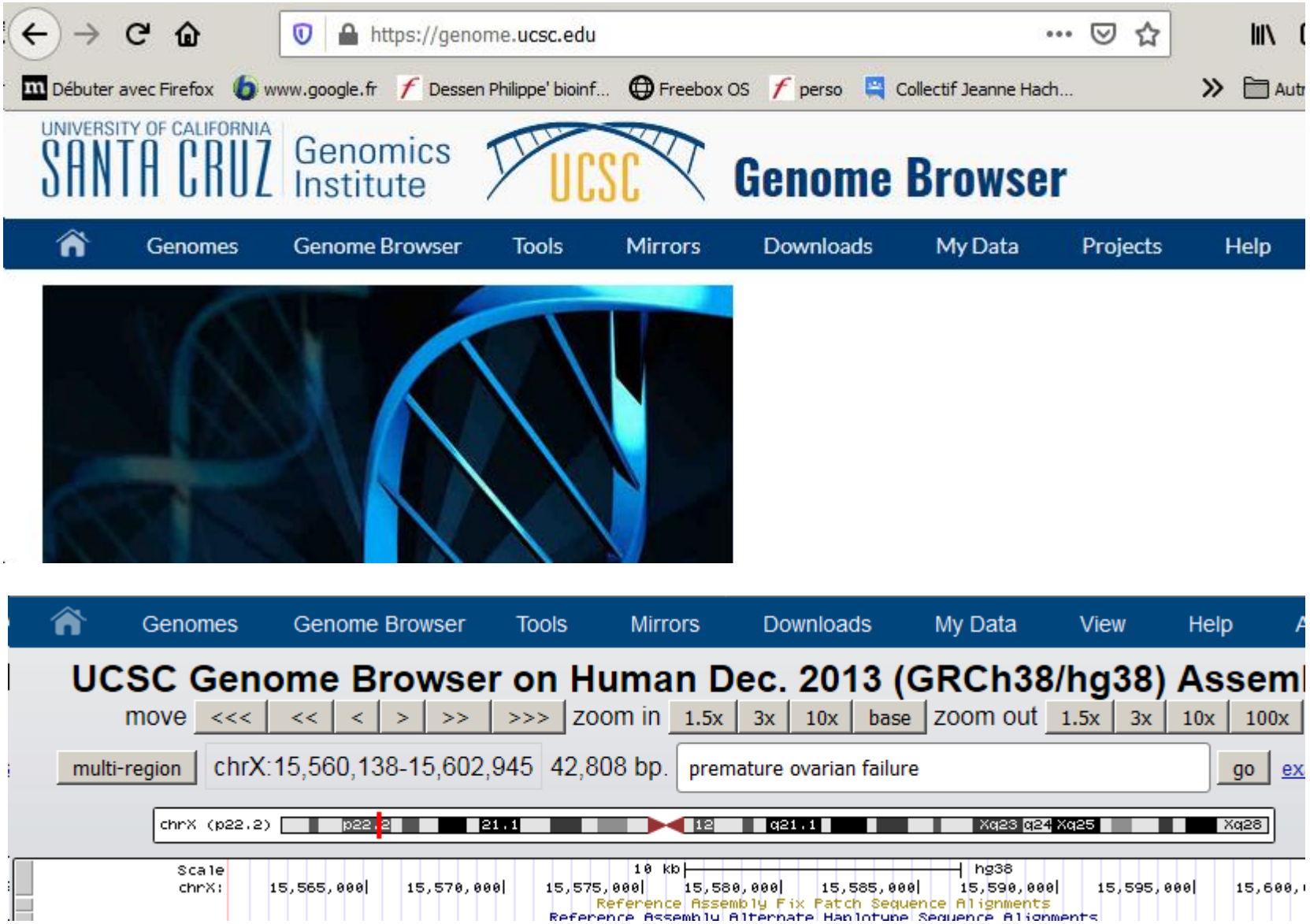
Plus d'informations

Mots-clés : Insuffisance ovarienne précoce

ORPHA:95709 (Groupe de pathologies) Insuffisance ovarienne précoce acquise

Plus d'informations

ORPHA:485382 (Groupe de pathologies) Insuffisance ovarienne précoce génétique non acquise



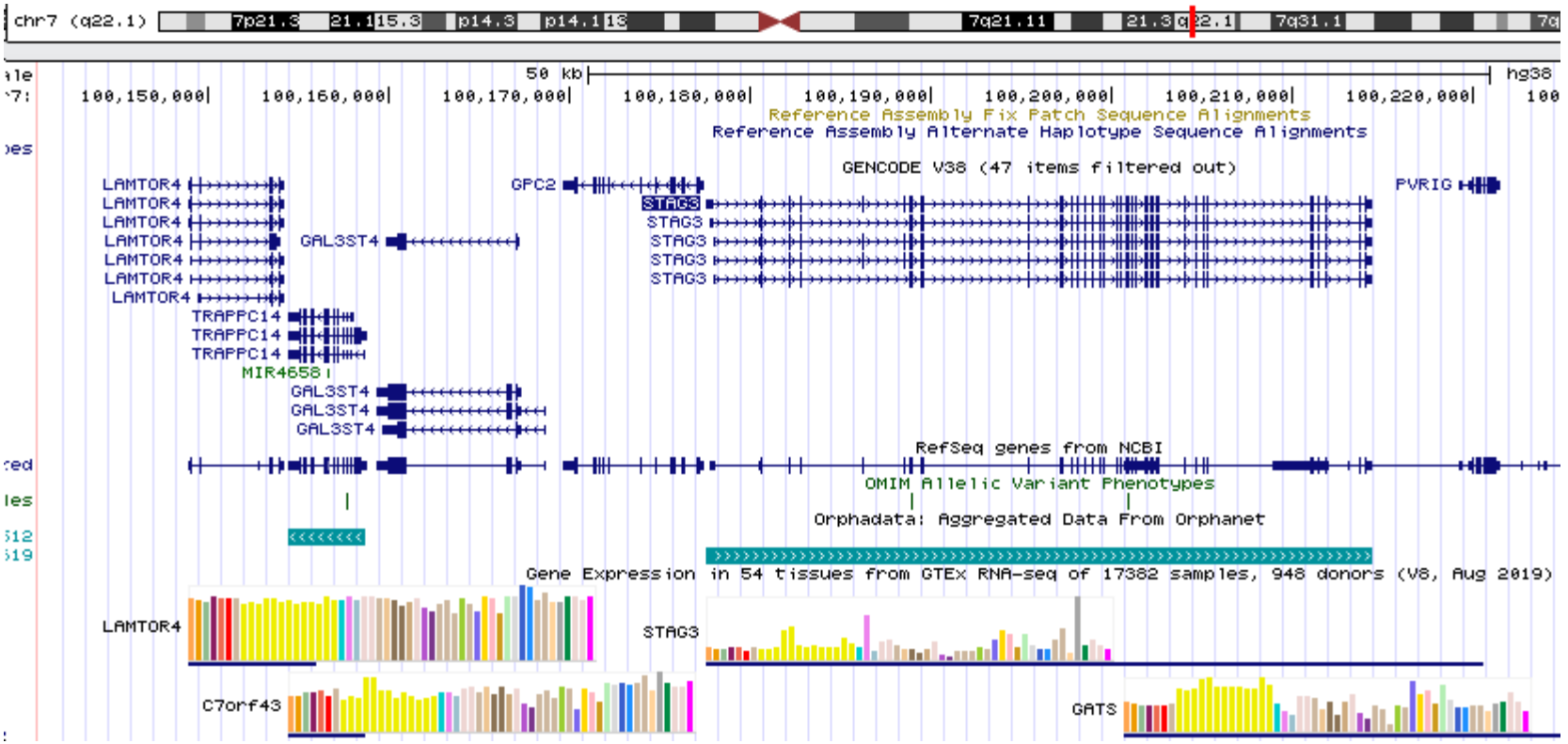
« Premature ovarian failure » comme critère de requête

Gènes associés au critère « **Premature ovarian failure** »

Your search resulted in multiple matches. Please select a position:

Gencode Genes

POF1B (ENST00000262753.9) at chrX:85277396-85379665 - Homo sapiens POF1B actin binding protein (POF1B), trans
NOBOX (ENST00000644387.2) at chr7_KZ208913v1_alt:446710-459685 - Homo sapiens NOBOX oogenesis homeobox (NOBOX
FOXL2 (ENST00000648323.1) at chr3:138944224-138947137 - Homo sapiens forkhead box L2 (FOXL2), mRNA. (from Ref
HFM1 (ENST00000370425.8) at chr1:91260766-91404837 - Homo sapiens helicase for meiosis 1 (HFM1), transcript v
STAG3 (ENST00000426455.5) at chr7:100177563-100214380 - Homo sapiens stromal antigen 3 (STAG3), transcript va
FIGLA (ENST00000332372.6) at chr2:70777310-70790643 - Homo sapiens folliculogenesis specific bHLH transcripti
DIAPH2 (ENST00000373049.8) at chrX:96684712-97469835 - Homo sapiens diaphanous related formin 2 (DIAPH2), tra
PABPC5 (ENST00000312600.4) at chrX:91434839-91438584 - Homo sapiens poly(A) binding protein cytoplasmic 5 (PA
INHA (ENST00000243786.3) at chr2:219572310-219575711 - Homo sapiens inhibin subunit alpha (INHA), mRNA. (from
MSH5 (ENST00000443040.5) at chr6_GL000253v2_alt:3045068-3052473 - Homo sapiens mutS homolog 5 (MSH5), transcr
MSH5 (ENST00000457917.6) at chr6_GL000255v2_alt:2995840-3017438 - Homo sapiens mutS homolog 5 (MSH5), transcr
FMR1 (ENST00000370475.9) at chrX:147911919-147951125 - Homo sapiens FMRP translational regulator 1 (FMR1), tr
SYCE1 (ENST00000303903.10) at chr10:133554290-133565583 - Homo sapiens synaptonemal complex central element p
MSH5 (ENST00000427735.5) at chr6_GL000252v2_alt:2987763-3010450 - Homo sapiens mutS homolog 5 (MSH5), transcr
MSH5 (ENST00000441395.5) at chr6_GL000254v2_alt:3081873-3104565 - Homo sapiens mutS homolog 5 (MSH5), transcr
PCMT1 (ENST00000464889.7) at chr6:149749741-149811419 - Homo sapiens protein-L-isoaspartate (D-aspartate) O-m
MSH5 (ENST00000375755.8) at chr6:31739948-31762676 - Homo sapiens mutS homolog 5 (MSH5), transcript variant 3
BMP15 (ENST00000252677.4) at chrX:50910735-50916641 - Homo sapiens bone morphogenetic protein 15 (BMP15), mRN
DACH2 (ENST00000373125.9) at chrX:86148451-86832602 - Homo sapiens dachshund family transcription factor 2 (D
GDF9 (ENST00000378673.2) at chr5:132861181-132866637 - Homo sapiens growth differentiation factor 9 (GDF9), t
NR5A1 (ENST00000373588.9) at chr9:124481236-124507399 - Homo sapiens nuclear receptor subfamily 5 group A mem



Phenotype and Literature

refresh

OMIM Alleles: dense	CADD: hide	Cancer Gene Expr: hide	ClinGen: hide	Deprecated ClinGen CNVs: hide	ClinVar Variants: hide
Coriell CNVs: hide	COSMIC Regions: hide	Development Delay: hide	Gene Interactions: hide	GeneReviews: hide	GWAS Catalog: hide
HGMD Variants: hide	LOVD Variants: hide	OMIM Cyto Loci: hide	OMIM Genes: hide	New Orphanet: full	New REVEL Scores: hide
SNPedia: hide	TCGA Pan-Cancer: hide	UniProt Variants: hide	Variants in Papers: hide		

Localisation de : Aggregated Data from Orphanet