Orphanet a comprehensive information service for RD

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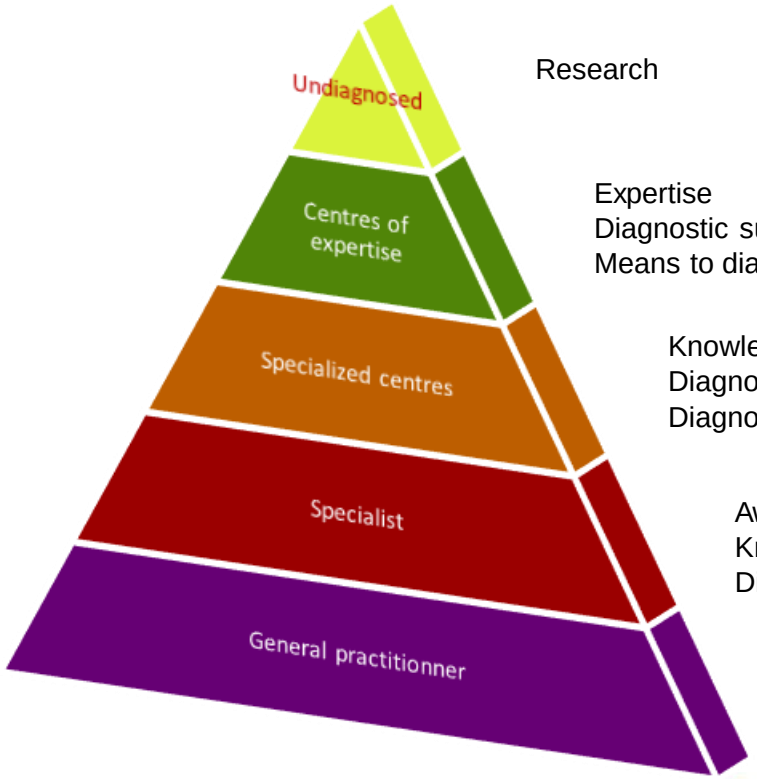
Inserm
La science pour la santé
From science to health

Objectives

- Have an overall knowledge on what Orphanet is
- Know how to search by disease, by gene
- Know how to find a centre of expertise, a patient organisation, information on research and drugs
- Know how to find a collection of texts for a given disease
- How to find expert services and research
- How to access Orphanet tutorials

The RD pyramid



Research

Integrated data for research

Expertise
Diagnostic suspicion
Means to diagnose: NGS…

Diagnostic tests

Knowledge
Diagnostic suspicion
Diagnosis

Best practice

Awareness
Knowledge
Diagnostic suspicion?

Find an expert

Awareness
Knowledge

Information

Orphanet's missions

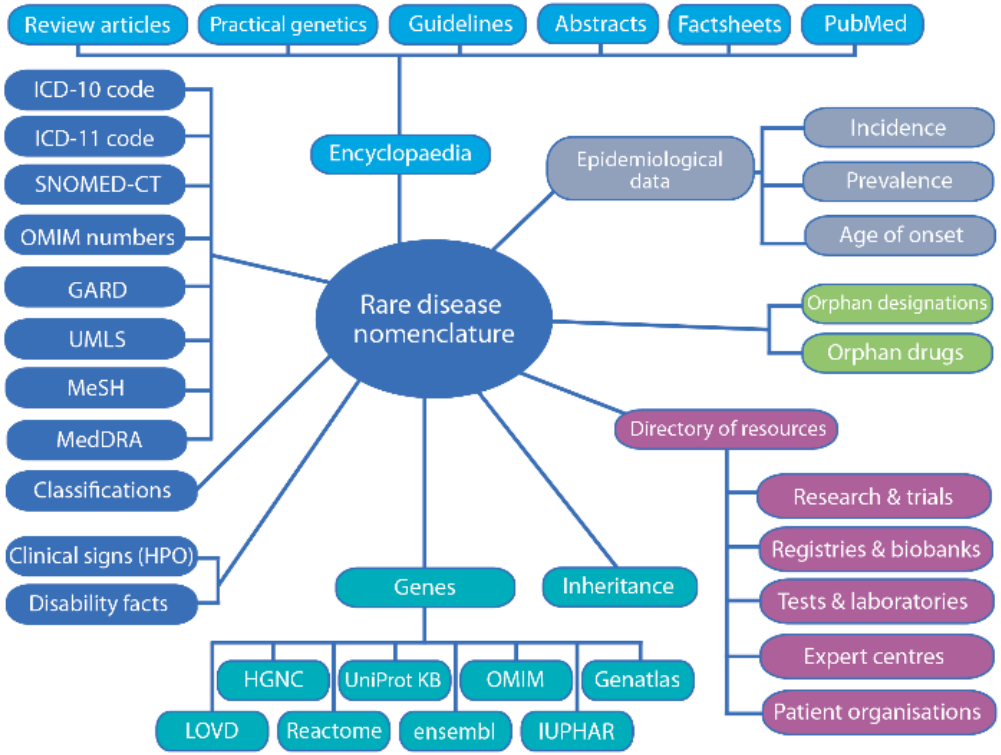
Improve the **visibility** of RD by providing **a common language** across healthcare and research systems (ORPHAcodes)

Provide **high-quality information** and **expertise** on RD

Contribute to **generating knowledge**

→ piecing together the parts of the puzzle for better understanding of RD

Orphanet, added-value knowledge base for health and research



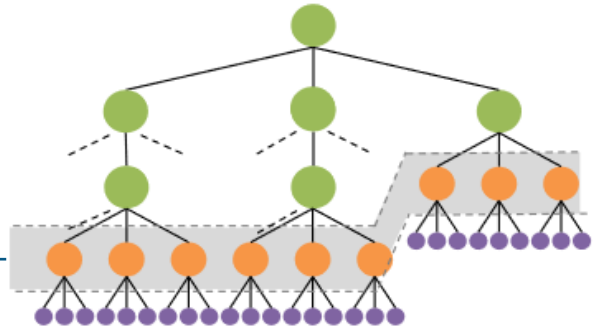
Reference rare disease nomenclature

WHAT IS THE ORPHANET NOMENCLATURE?

A MEDICAL TERMINOLOGY SPECIFIC TO RARE DISEASES (<1 in 2000 cases)

Clinical definition:

Disorders are clinically homogeneous entities described in at least two independent individuals, confirming that the clinical signs are not associated by fortuity.



Group

Disorder

Subtype

9,318 Clinical entities
- 2,175 Groups
- 6,162 Disorders
- 981 Subtypes

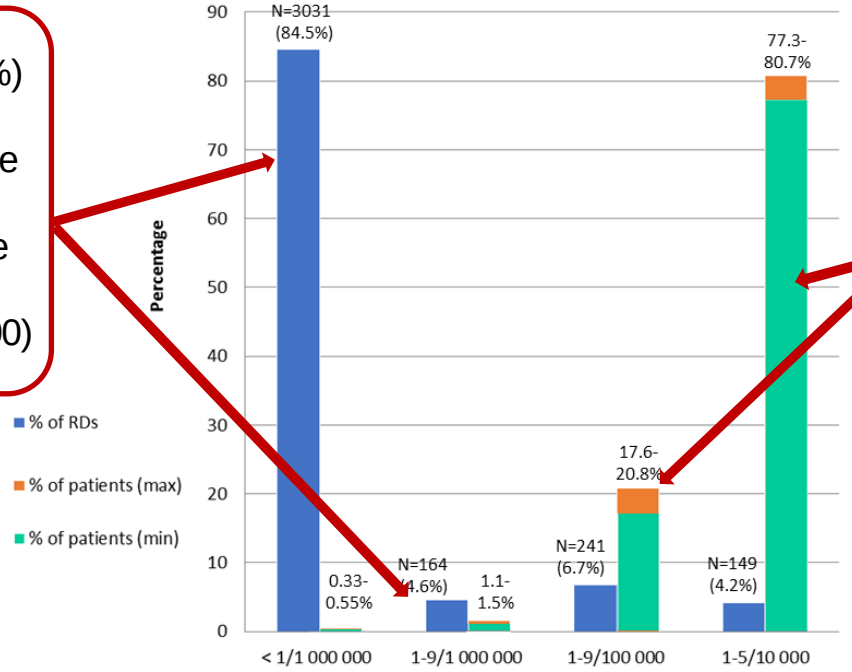
"Classification level"

ENG FR SP DE IT NL PG PL

Comprehensive, standardized, evidence-based, interoperable, versioned, computable and free (CC-BY 4.0)

How many patients suffering from RD?

Most (89.1%) of rare diseases are very rare (prevalence less than 1 per 100,000)



Almost all of the people with rare disease (>98%) have one of the 390 most prevalent diseases (more common than 1 per 100,000)

3.5 - 5.9% of the population (263 - 446 Million people) worldwide

*Based on 68% of prevalent RD based on EU definition (<50/100,000), data from literature.

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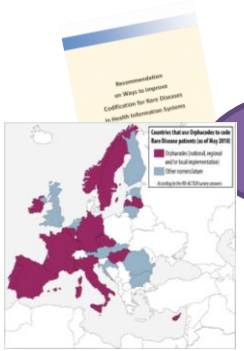
A common language across fields



Care
Health Information System (EHRs)

Research
Registries/Cohorts/Biobanks

Orphanet central nomenclature

Causality
Susceptibility
Modifier
...

E
NTBT
BTNT
...

Genes

Genes:
- HGNC
- OMIM
- ensembl
- Genatlas

Proteins:
- UniProt

Pathways:
- Reactome

Targets & compounds:
- IUPHAR

Phenotypes

Frequency
Dx criterion
Pathognomonic

Disabilities

Frequency
Severity
Temporality

Terminologies
- OMIM
- ICD10/11
- GARD
- UMLS
- MedDRA
- SNOMED

OD
ODrugs

IRDiRC RECOGNIZED RESOURCES

THE HUMAN VARIOME PROJECT
an NGO official partner of UNESCO
sharing data - reducing disease

elixir
Core Data Resource

hpo

HOOM

inserm

orphanet

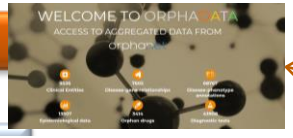
www.orpha.net

Different media for different users

Orphanet knowledge database

Orpha.net

Orphadata.org

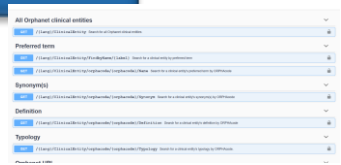


Ontologies

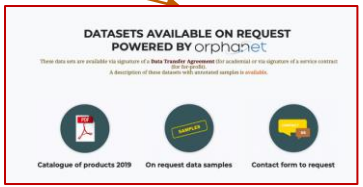
ordo
Orphanet Rare Disease Ontology

HOOM
HPO x ORDO Ontological Module

API



elixir Core Data Resource



www.orphadata.org

IRDiRC RECOGNIZED RESOURCES

THE HUMAN VARIOME PROJECT an NGO official partner of UNESCO sharing data - reducing disease

>RD-CODE

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Database content and website

- A network of **42 countries in Europe and beyond**
- A freely accessible website available in **8 languages**
- **45 million pages viewed** in 2020
- **6.8 million PDF documents** downloaded in 2020
- Orphanet & ORDO - **IRDiRC Recognized Resources** and **HVP Recommended Systems**
- **Orphadata** – An **ELIXIR Core Data Resource**

Diseases

6,171 **rare disorders with unique identifiers : ORPHA codes**
5,730 **genes linked to 3,795 rare disorders**
4,065 **disorders annotated with HPO terms**
5,822 **disorders annotated with point prevalence data**

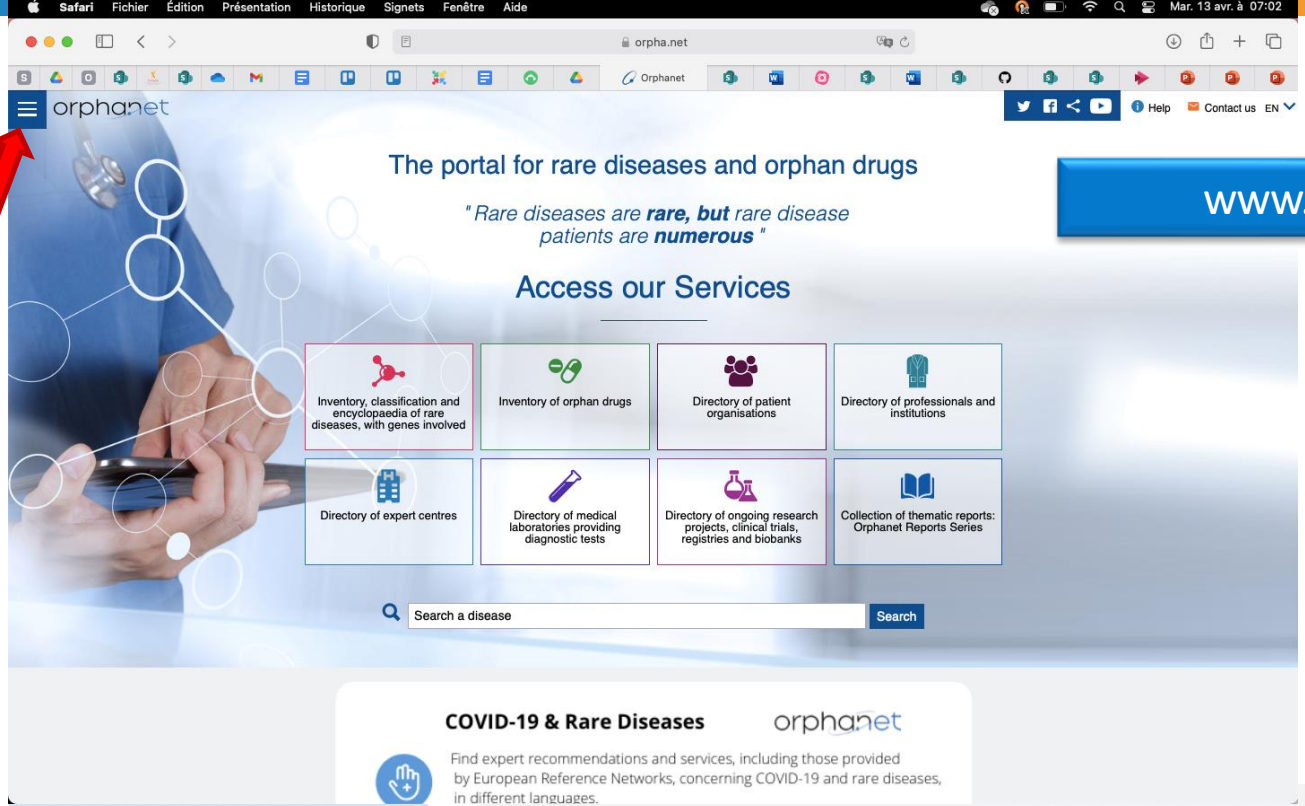
Rare disease summaries in 13 languages

6,603	English
4,079	French
5,358	Spanish
4,472	Italian
3,558	German
4,709	Dutch
1,160	Portuguese
1,248	Polish
420	Greek
253	Russian
166	Finnish
113	Japanese
103	Slovak

Directory of expert resources in the Orphanet network

28,460 Professionals referenced in the database
2,743 Patient organisations
8,249 Expert centres
1,621 Medical laboratories dedicated to diagnosis
44,356 Diagnostic tests
3,003 Ongoing research projects
4,602 Ongoing clinical trials
894 Patient registries
273 Mutation databases
185 Biobanks

Data unless stated otherwise from Orphanet 2019 Activity Report, database content in January 2020



www.orpha.net

ORPHANET IN NUMBERS

- 46 million pages viewed
- 10.4 million PDFs downloaded
- Visits from 236 countries

Around **1,5 million visitors per month** from **236 countries**

42 % health professionals
35 % patients, families and support groups
As well as **researchers, industry, policy makers, students**
Most appreciated products: **disease summaries, clinical signs, epidemiological data, classifications, and disability data***

* Annual Orphanet Users' Survey February 2020

Users

orphanet

Rare diseases

- Search
- Clinical Signs and Symptoms
- Classifications
- Genes
- Disability
- Encyclopaedia for patients
- Encyclopaedia for professionals
- Emergency guidelines

Orphan drugs

- Search

Expert centres and Networks

- Expert centres
- Networks of expert centre
- European reference networks

Diagnostic tests

- Laboratories
- Diagnostic tests

Research and trials

- Research projects
- Clinical trials
- Registries & biobanks
- Platforms

Patient organisations

- Patient organisation
- Federations/Alliances
- Helplines for personal queries

Professionals and institutions

- Institutions
- Professionals
- Network of experts
- Get in touch

Other information

- Quality charters
- About orphan drugs
- About Orphanet
- About rare diseases
- Orphanet Reports series
- Orphanet Tutorials
- Orphanet procedures

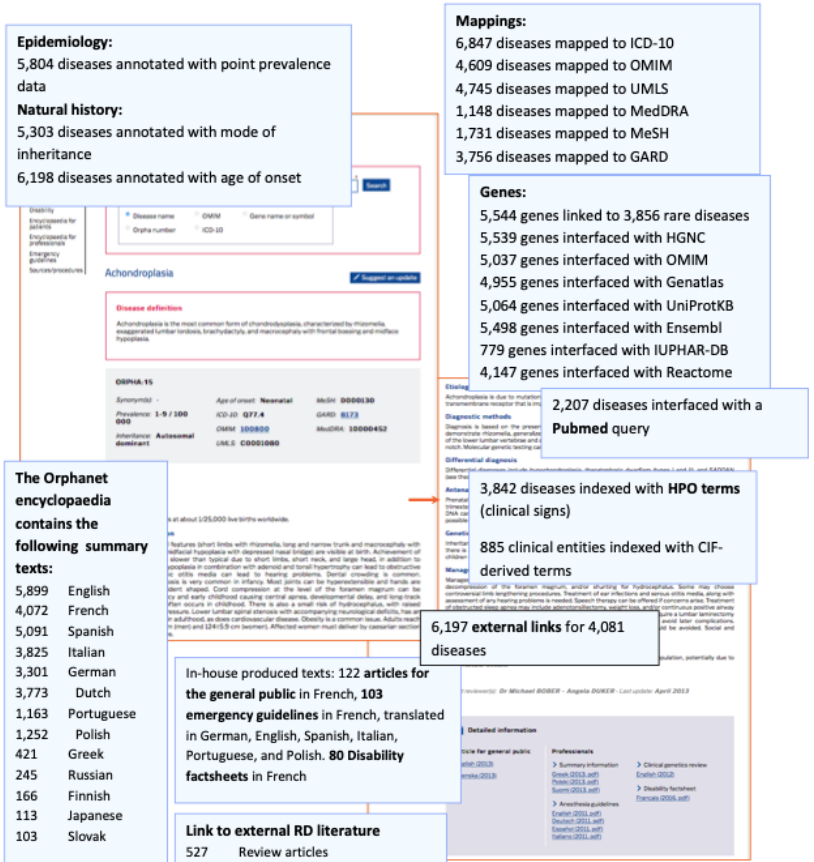


Figure 7 The disease database content as of January 2020

1.1 WHAT IS THE ORPHANET NOMENCLATURE?

A MEDICAL TERMINOLOGY SPECIFIC TO RARE DISEASES (<1 in 2000 cases)

PREFERRED TERM

Fanconi-Bickel syndrome

Suggest an update

DEFINITION

Disease definition

A rare glycogen storage disease due to a deficiency in solute carrier family 2, facilitated glucose transporter member 2 and characterized by hepatorenal glycogen accumulation leading to severe renal tubular dysfunction and impaired glucose and galactose metabolism.

ORPHAcode

ORPHA:2088

Classification level: Disorder

Synonym(s):

GSD due to GLUT2 deficiency

GSD type 11

GSD type XI

Glycogen storage disease due to GLUT2 deficiency

Glycogen storage disease type 11

Glycogen storage disease type XI

Glycogenosis due to GLUT2 deficiency

Prevalence: Unknown

Inheritance: Autosomal recessive

Age of onset: Infancy, Neonatal

ICD-10: E74.0

OMIM: 227810

UMLS: C3495427

MeSH: -

GARD: 2268

MedDRA: -

SYNONYMS

Rare diseases

Signs and symptoms

Help

Orphanet provides a clinical description of rare diseases using a set of clinical signs and symptoms (phenotypic abnormalities).

This description, based on cases published in biomedical literature, uses the phenotypic abnormalities referenced in the **Human Phenotype Ontology** (HPO).

Each phenotypic abnormalities are presented by order of frequency of occurrence in the patient population :

The frequency in the patients' population can be :

- always present: 100%
- very frequent: 99%-80%
- frequent: 79%-30%
- occasional: 29%-5%
- rare: 4%-1%

The phenotypic abnormality can be defined as one of the following :

- Pathognomonic sign : a sign whose presence indicates that a particular disease is present beyond any doubt. The absence of this sign does not exclude the possibility of the presence of the disease, but the presence of the pathognomonic sign affirms it with certainty.
- Diagnostic criterion : phenotypic abnormalities noted as « diagnostic criterion » are those included in established sets of criteria to establish the diagnosis of a particular disease having been published in a peer-reviewed journal.
- Exclusion criterion : phenotypic abnormalities noted as « exclusion criterion » are those that are always absent in a particular disease and therefore exclude its diagnosis.

HOOM human phenotype ontology

ORPHA:2331 Kawasaki disease

The phenotypic description of this disease is based on an analysis of the biomedical literature and uses the terms of the Human Phenotype Ontology (HPO). Phenotypic abnormalities are presented by order of frequency of occurrence in the patient population, then by alphabetical order inside each frequency group.

Diagnostic criterion *

Fever HP:0001945

Glossitis HP:0000206

Cervical lymphadenopathy HP:0025289

Cheilitis HP:0100825

Conjunctivitis HP:0000509

Palmoplantar erythema HP:0025493

Skin rash HP:0000988

* Phenotypic abnormalities noted as « diagnostic criterion » are those included in established sets of criteria to establish the diagnosis of a particular disease having been published in a peer-reviewed journal.

Clinical signs and symptoms

Very frequent

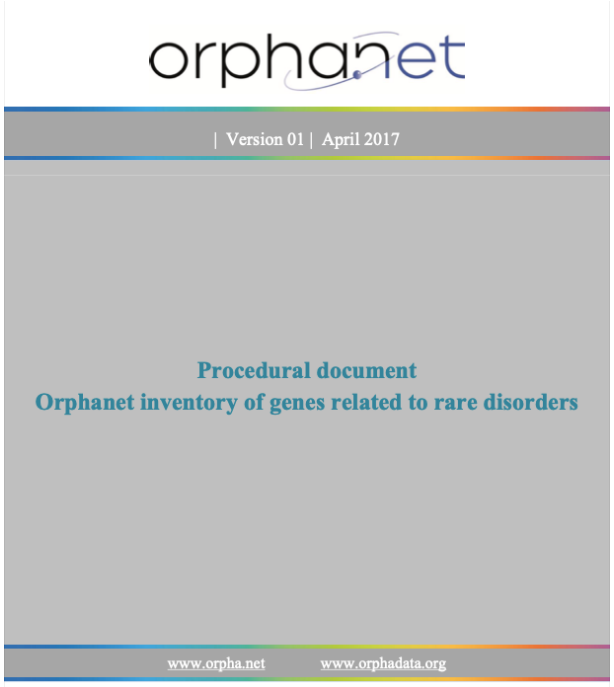
Cervical lymphadenopathy HP:0025289

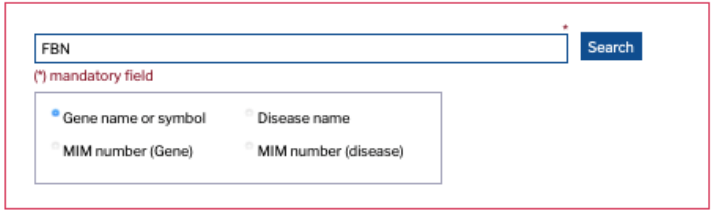
Cheilitis HP:0100825

Rare diseases

- Search
- Clinical Signs and Symptoms
- Classifications
- Genes
- Disability
- Encyclopaedia for patients
- Encyclopaedia for professionals
- Emergency guidelines
- Sources/procedures

Genetic information





FBN1 - fibrillin 1

Synonym(s) : **asprosin, Marfan syndrome, MASS, OCTD, SGS**

Previous symbols and names : **FBN, MFS1, WMS, fibrillin 1 (Marfan syndrome)**

Type : **gene with protein product**

Chromosomal location : **15q21.1**

OMIM: 134797

HGNC: 3603

UniProtKB: P35555

Genatlas: FBN1

Ensembl: ENSG00000166147

IUPHAR-DB: -

Reactome: P35555

LOVD: FBN1

Diseases list

- Disease-causing germline mutation(s) in Acromicric dysplasia ORPHA:969
- Disease-causing germline mutation(s) in Familial thoracic aortic aneurysm and aortic dissection ORPHA:91387
- Disease-causing germline mutation(s) in Geleophysic dysplasia ORPHA:2623
- Disease-causing germline mutation(s) in Isolated ectopia lentis ORPHA:1885
- Disease-causing germline mutation(s) in Marfan syndrome type 1 ORPHA:284963
- Disease-causing germline mutation(s) in Neonatal Marfan syndrome ORPHA:284979
- Disease-causing germline mutation(s) in Progeroid and marfanoid aspect-lipodystrophy syndrome ORPHA:300382
- Disease-causing germline mutation(s) in Stiff skin syndrome ORPHA:2833
- Disease-causing germline mutation(s) in Weill-Marchesani syndrome ORPHA:3449
- Candidate gene tested in Glaucoma-ectopia lentis-microspherophakia-stiff joints-short stature syndrome ORPHA:2084
- Candidate gene tested in Shprintzen-Goldberg syndrome ORPHA:2462

: Assessed

Functional consequences

Rare diseases

- Search
- Clinical Signs and Symptoms
- Classifications
- Genes
- Disability
- Encyclopaedia for patients
- Encyclopaedia for professionals
- Emergency guidelines
- Sources/procedures

Homepage > Rare diseases > **Disability**

Search for a disease and its functional consequences

Treacher Search

(*) mandatory field

Disease name
ORPHAcode

Orphanet Disability

ORPHA:861 Treacher-Collins syndrome

:: Activity limitation/participation restriction is described according to the Orphanet Functioning Thesaurus, derived and adapted from the International Classification of Functioning, Disability and Health – Children and Youth (ICF-CY, WHO 2007). The provided information is assessed from the whole patients' population affected by the disease, receiving standard care and management (specific and/or symptomatic management, prevention and prophylaxis, devices and aids, care and support). Functional consequences are organized by their frequency in the patients' population. This general information may not apply to specific cases. Some difficulties reported here can occur with a different temporality or severity degree, and others that are not listed can nevertheless arise.

Loss of an ability

Very frequent

Temporality	Severity	
Hearing/listening	Permanent limitation	Moderate
Hearing/listening	Acquisition delay	Severe
Acquiring language	Acquisition delay	Moderate
Learning to read	Permanent limitation	Low
Learning to read	Acquisition delay	Low
Learning to write	Permanent limitation	Low
Reading	Acquisition delay	Low
Writing	Acquisition delay	Low
Receiving spoken messages	Permanent limitation	Moderate
Receiving spoken messages	Acquisition delay	Severe
Receiving written messages	Acquisition delay	Low
Speaking	Permanent limitation	Low
Speaking	Acquisition delay	Severe
Writing messages	Acquisition delay	Low

Occasional

Temporality	Severity	
Seeing/watching	Permanent limitation	Unspecified
Hearing/listening	Permanent limitation	Severe
Hearing/listening	Acquisition delay	Low
Receiving spoken messages	Permanent limitation	Severe
Receiving spoken messages	Acquisition delay	Low
Motor skills	Acquisition delay	Low
Staying awake	Permanent limitation	Unspecified
Performing professional tasks	Permanent limitation	Moderate
Socializing	Permanent limitation	Unspecified
Practicing sports	Permanent limitation	Unspecified

Environmental factors

:: Following are the environmental factors that should be addressed in order to improve the functioning or limit the restrictions deriving from this disease.

Food
Sound intensity
Sound quality

Source: Pr Marie-Paule VAZQUEZ[Expert]_Pr David GENEVIEVE[Expert]_Pr Françoise DENOYELLE[Expert]_Association Coline[Patient organisation]
Last update: 02/06/2015

Additional information

Further information

- Disease(s)/group of diseases
- Article for general public
- Disability factsheet
- Clinical signs and symptoms

Specialised Social Services

- Eurordis directory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Encyclopédie Orphanet du handicap

Syndrome de Treacher-Collins

Syndrome de Franceschetti-Klein, dysostose mandibulo-faciale sans anomalies des extrémités

Cette fiche rassemble des informations susceptibles d'aider les professionnels du handicap dans leur travail d'évaluation et d'accompagnement des personnes atteintes de maladies rares. Elle ne se substitue pas à une évaluation individuelle.

Le syndrome de Treacher-Collins en bref

Extrait de l'Encyclopédie Orphanet pour les professionnels

- *Définition :* Le syndrome de Treacher-Collins est une **anomalie congénitale du développement cranio-facial** caractérisé par une **dysplasie oto-mandibulaire bilatérale et symétrique sans anomalies des extrémités**, associée à diverses **anomalies de la tête et du cou**.
- *Épidémiologie :* L'incidence annuelle à la naissance est estimée à 1/50 000.
- *Clinique :* Les enfants présentent une dysmorphie faciale caractéristique avec une hypoplasie bilatérale et symétrique des os malaires et de la margelle infra-orbitaire (80%) et de la mandibule (78%) (micrognathie, rétrognathie) qui entraîne une malocclusion dentaire souvent caractérisée par une béance antérieure. Une hypoplasie prédominante des tissus mous est observée au niveau du malaire, du rebord orbitaire inférieur et de la joue. Sont également observés des anomalies complexes de l'articulation temporo-mandibulaire responsables d'une limitation d'ouverture buccale de sévérité variable, une oblicité anti-mongoloïde des fentes palpébrales (89%) et un colobome des paupières inférieures à l'union 1/3 externe-1/3 moyen (69%) sans cils au 1/3 externe de la paupière inférieure. On observe un palais ogival et parfois une fente palatine (28%). Des anomalies de l'oreille externe selles qu'anxoie ou microtie, atrésie des conduits auditifs externes et anomalies de la chaîne des osselets sont souvent présentes (60%) et entraînent une surdité de transmission. L'intelligence est généralement normale. Des difficultés respiratoires et de nutrition peuvent se manifester durant les premières années du fait de l'étroitesse des voies respiratoires supérieures et de la limitation de l'ouverture buccale. Des signes moins constants sont les enchondromes et/ou fistules précragiens, des anomalies vertébrales et cardiaques, des fentes commissurales bilatérales.
- *Étiologie :* Le syndrome est dû à des mutations du gène TCOF1 (5q32-q33.1) codant pour la phosphoprotéine nucléolaire Treacle ou des gènes POLR1C (6p21.1) et POLR1D (13q12.2), codant pour des sous-unités des ARN polymérases I et III. La transmission est autosomique dominante avec une pénétrance de 90% et une expressivité variable, également chez des individus de la même famille.
- *Prise en charge et pronostic :* La prise en charge est pluridisciplinaire. En cas de détresse respiratoire postnatale, une trachéotomie, une ventilation non invasive (VNI) ou une distraction mandibulaire chirurgicale doivent être discutées. La chirurgie maxillo-faciale et plastique permet de corriger l'hypoplasie des tissus mous (lipostructure), l'hypoplasie osseuse (distraction chirurgicale, greffes osseuses), le colobome palpébral et la fente palatine. Le traitement de la limitation de l'ouverture buccale est très difficile. La chirurgie ORL spécialisée est requise pour les anomalies de l'oreille moyenne (chirurgie fonctionnelle)

Syndrome de Treacher-Collins – Encyclopédie Orphanet du Handicap
www.orpha.net/data/patho/Pub/fr/Handicap_TreacherCollins-FrFrPub293v01.pdf | 27 novembre 2013

1

Other selected texts

1- For professionals

- **Disease summary**
- **Emergency guidelines** (2007)…
- Anesthesia guidelines
- Clinical Practice Guidelines (AGREEII)
- Guidance for genetic testing
- GeneReviews …

2- For patients, families and general public

3- For medical-social sector

Disability Factsheets : (2013)…

Quality assessment

Multiple languages

Emergency guidelines

Numéros en cas d'urgence

Centre national de référence Maladies cardiaques héréditaires

Professeur Antoine Leenhardt

Unité de Rythmologie, service de Cardiologie - CHU Paris-Nord-Val-de-Seine
Hôpital Bichat-Claude-Bernard - 46, rue Henri-Huchard - 75018 PARIS
Tél. : **01 40 25 77 92**

Permanence USIC cardiologie
Tél. : 01 40 25 74 66

Centres de référence ou de compétence :
www.orpha.net

Centre de référence des troubles du rythme cardiaque génétiques
Service de Cardiologie
Professeur Vincent Probst
CHU de Nantes - Tél. : **02 40 16 57 14**

Centre de référence des troubles du rythme héréditaire
Service de Rythmologie
Professeur Philippe Chevalier
Hôpital Cardiologique de Lyon - Tél. : **04 72 35 76 89**

Filière de santé maladies rares :
Filière nationale de santé Maladies cardiaques héréditaires

Cardiogen
http://www.filiere-cardiogen.fr/
contact@filiere-cardiogen.fr

cardiogen
filière nationale de santé
maladies cardiaques héréditaires

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COVID-19 & Maladies Rares

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Des recommandations et des services d'expert, y compris ceux fournis par les Filières de Santé Maladies Rares (FSMR) et les Réseaux Européens de Référence (ERNs), concernant le COVID-19 et les maladies rares sont disponibles en plusieurs langues.

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Searc

European Union Institutions, Bodies, and Agencies

READ

European Reference Networks

READ

Learned Societies

READ

Patient organisations

READ

Expert networks outside of Europe

READ

COVID-19 et maladies rares en France

Le Gouvernement ouvre la vaccination aux patients vulnérables à très haut risque à compter du 18 janvier

READ

Filières de Santé Maladies Rares (France)

READ

Sociétes savantes (France)

READ

HAS

READ

BNDMR

READ

Fondations

READ

Associations

READ

Ressources (autres)

READ

Catalogue of expert services

Figure 9 Directory of expert services (January 2020)

FSMR

Centres experts et filières / réseaux

- Centres experts
- Filières / Réseaux
- Cartographie des filières
- Réseaux de référence européens

Accueil > Centres experts et filières / réseaux > **Cartographie des filières**

Cartographie des filières

Le Ministère de la Santé a labellisé 23 Filières de Santé Maladies Rares afin d'améliorer la coordination des structures concernées par un ensemble cohérent de maladies rares. Chaque filière regroupe des Centres de Référence Maladies Rares (CRMR) qui peuvent être mono-site et ce site unique est « site coordonnateur » ou multi-sites avec un « site coordonnateur » et un ou plusieurs « sites constitutifs » complémentaires. Le pilotage des filières est assuré par un « animateur » désigné en son sein.

Toutes régions | Toutes les Filières | Centres Experts | Tous les types de centres

Site constitutif | Site coordonnateur | Animateur filière

ERNs

Centres experts et filières / réseaux

- Centres experts
- Filières / Réseaux
- Cartographie des filières
- Réseaux de référence européens

Accueil > Centres experts et filières / réseaux > **Réseaux de référence européens**

Réseaux de référence européens

Les réseaux de référence européens aident les professionnels et les centres d'expertise nationaux à partager leurs connaissances.

Les réseaux de référence européens doivent :

- appliquer des critères définis par l'UE pour les maladies nécessitant des soins spécialisés
- servir de centres de recherche et de connaissances traitant des patients venus d'autres États membres
- garantir si nécessaire des possibilités de soins ultérieurs

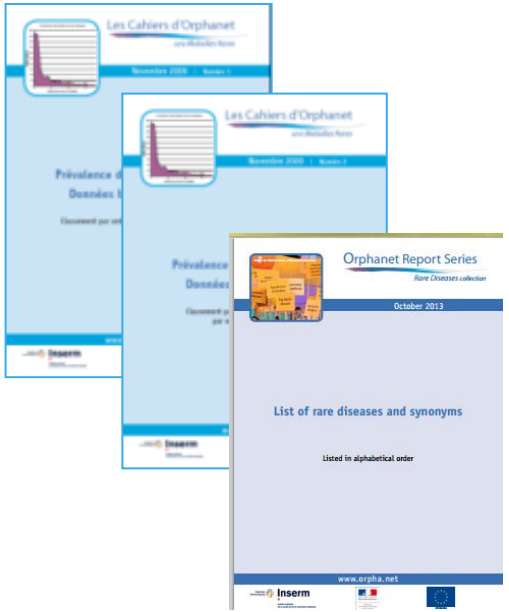
Informations complémentaires :

- Site web de la Commission Européenne : https://ec.europa.eu/health/rare_diseases/european_reference_networks_fr
- Site web RD-ACTION : http://www.rd-action.eu/european-reference-networks-erns/

Tous les ERN | Tous les Pays | Toutes institutions

Institution ERN | Coordonnateur ERN

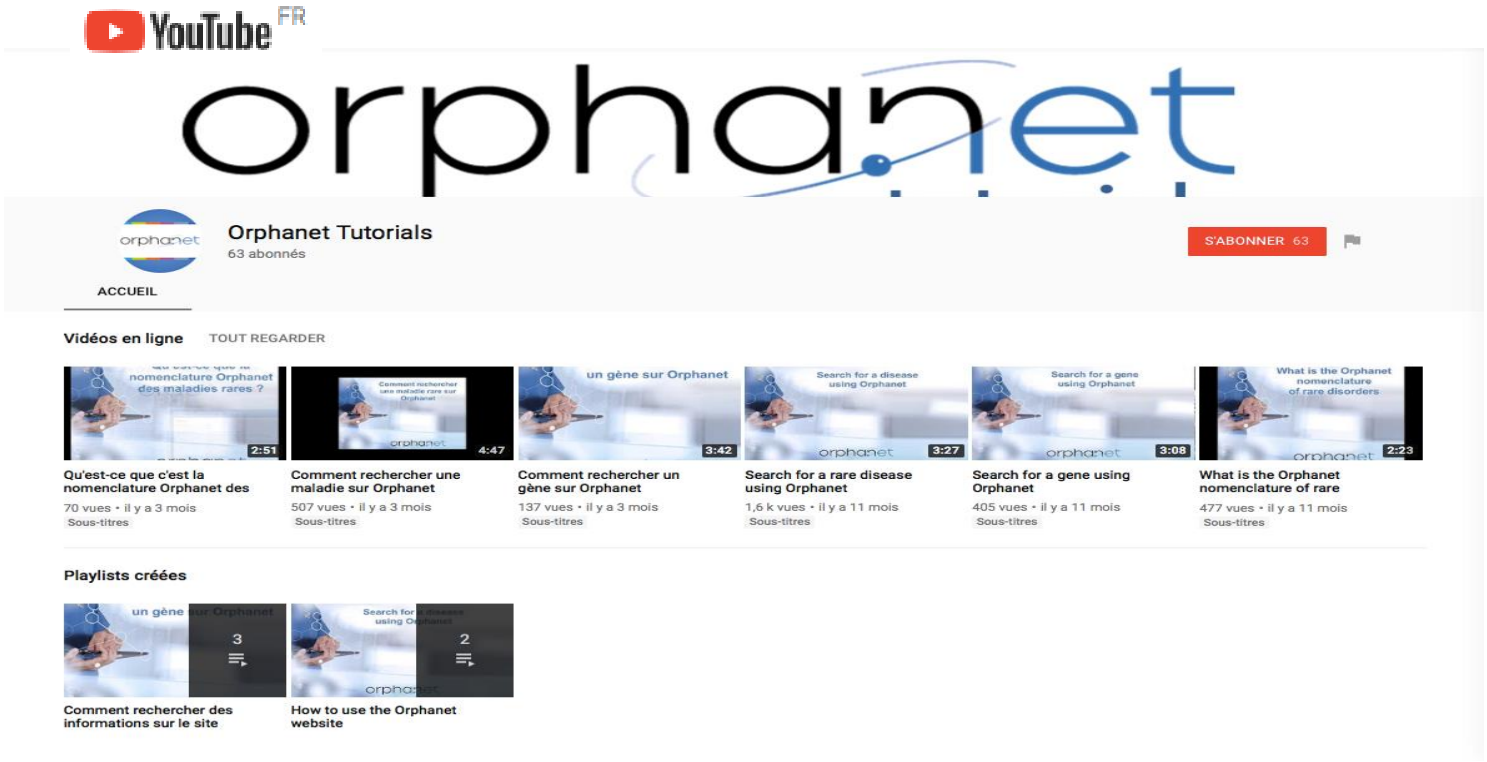
Vivre avec une maladie rare en France



https://www.orpha.net/orphacom/cahiers/docs/FR/Vivre_avec_une_maladie_rare_en_France.pdf

Scientific and political RD news

Tutorials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How to use the Orphanet website

ana.rath@inserm.fr

THANK YOU!