

DATABASE CENTER FOR LIFE SCIENCE,
JOINT SUPPORT-CENTER FOR DATA SCIENCE RESEARCH,
RESEARCH ORGANIZATION OF INFORMATION AND SYSTEMS



About PubCaseFinder

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OVERVIEW

PubCaseFinder is a search system for medical professionals to search genetic diseases, rare diseases, causative genes, and published cases in order of relevance by using symptoms and signs as queries.

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1. DISCLAIMER

The PubCaseFinder is intended to be used by qualified and licensed physicians to assist in the research about rare and genetic diseases and for use as a teaching aid. The PubCaseFinder should not be used to make medical decisions without the advice of a physician. PubCaseFinder provides data in good faith as an investigative tool, but without verifying the accuracy, clinical validity or utility of the data. PubCaseFinder makes no warranty, express or implied, nor assumes any legal liability or responsibility for any purpose for which the data are used. DBCLS shall bear no liability concerning damages incurred by the change, discontinuation or termination of the Service.

2. HOW TO SEARCH DISEASES

1) Inputting signs and symptoms

You can search for the appropriate HPO terms by typing part of the name or HPO ID into the search box. This search box provides autocompletion functionality: Possible matches are shown below, while the query is typed in (Figure 1). If you click the box including a sign or symptom, its detailed information appears on the modal dialog (Figure 2).

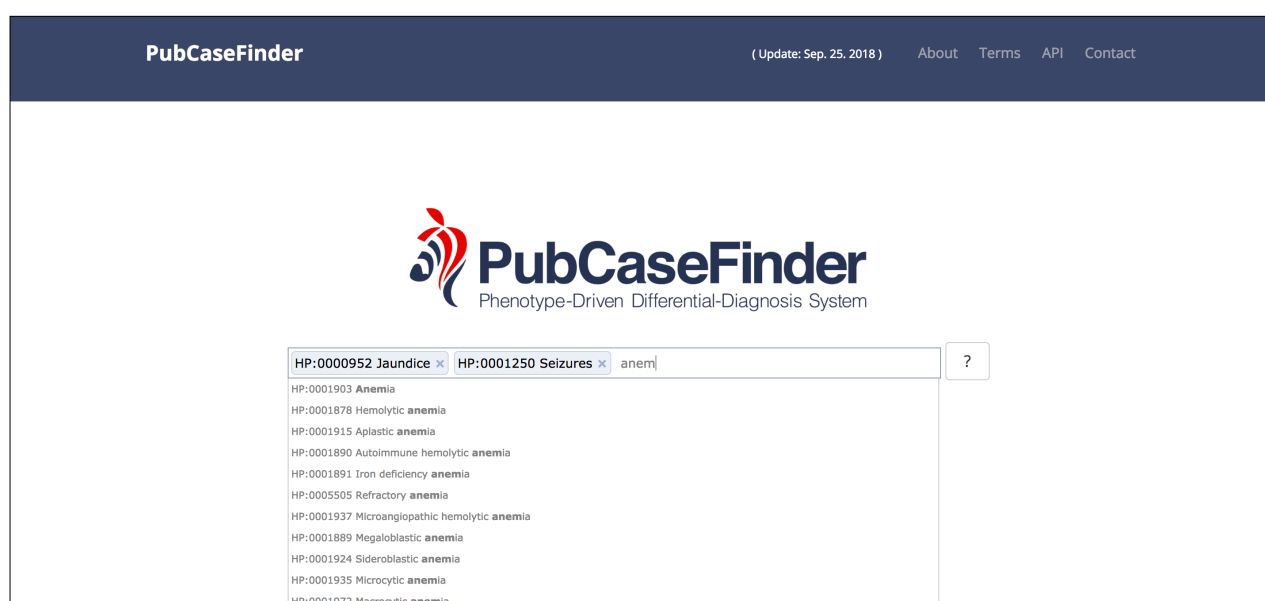


Figure 1

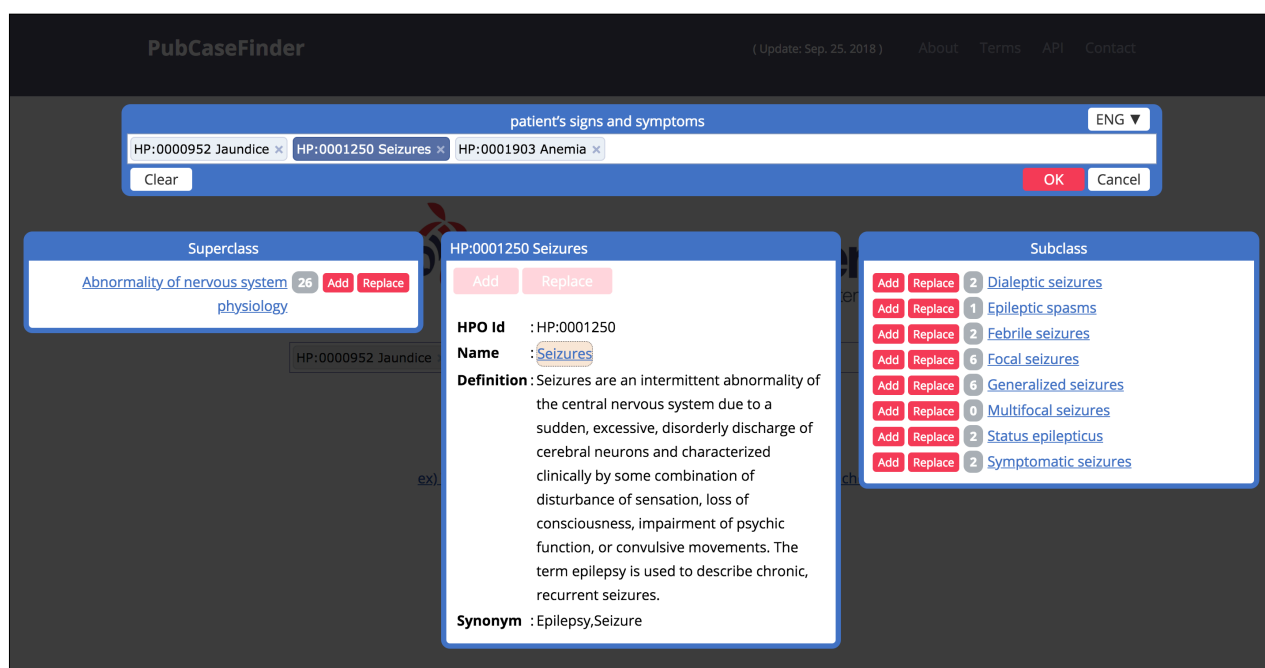
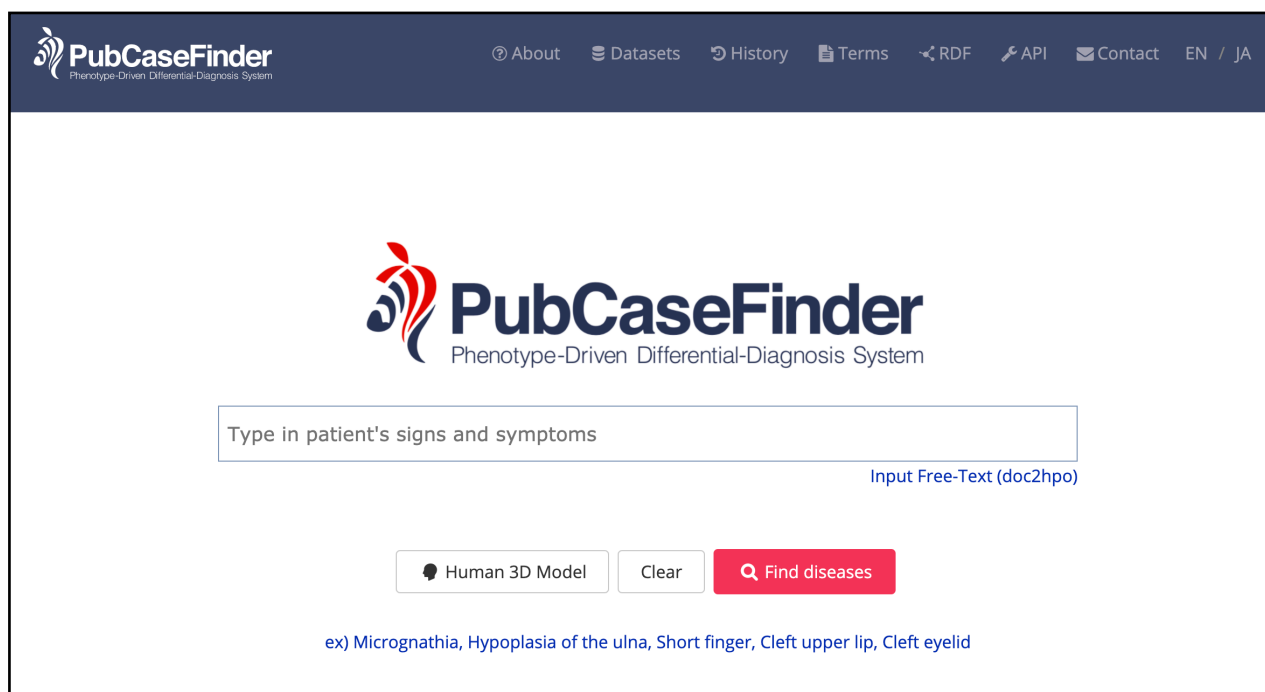


Figure 2

2) Searching rare and genetic diseases

After inputting signs and symptoms, you can get a ranked list of rare and genetic diseases by clicking the 'Find diseases' button (Figure 3). You can get a ranked list of rare diseases defined in Orphanet (Figure 4A) and genetic diseases defined in OMIM (Figure 4B) by comparing signs and symptoms of an affected individual against those of diseases defined in Orphanet and OMIM. The matched phenotypes and causative genes are shown in each row. The matched phenotypes mean that those phenotypes are the best matches for the query phenotypes base on the semantic similarity. You can download the summary of results which includes top 10 diseases of both Orphanet and OMIM by clicking the "Download Summary of Results" button. If you click the box including a phenotype in each row (Figure 4), you can confirm the detailed contextual information which includes both the phenotype and disease in published case reports (Figure 5).



The screenshot shows the PubCaseFinder web application interface. At the top, there is a dark blue header with the PubCaseFinder logo and navigation links: About, Datasets, History, Terms, RDF, API, Contact, and language options (EN / JA). The main content area features the PubCaseFinder logo and a search input field with the placeholder text "Type in patient's signs and symptoms". Below the input field, there is a link "Input Free-Text (doc2hpo)". At the bottom of the search area, there are three buttons: "Human 3D Model", "Clear", and "Find diseases". Below these buttons, there is an example text: "ex) Micrognathia, Hypoplasia of the ulna, Short finger, Cleft upper lip, Cleft eyelid".

Figure 3

USER GUIDE

PubCaseFinder

AboutTermsAPIContact

Input patient's **signs and symptoms**

+ Upload File (HPO ID):

HP:0000952 Jaundice x HP:0001903 Anemia x HP:0001744 Splenomegaly x HP:0100507 Folate deficiency x HP:0004444 Spherocytosis x

Narrow down the diseases

+ Upload File (Entrez Gene ID):

Download Summary of Results

Find diseases

Clear

Rare Diseases (Orphanet) 4,066 results

Genetic Diseases (OMIM) 6,969 results

Total: 4,066 results

123...407»

10 (per page)

Download Results

Rank (Similarity)	Disease Name (Disease ID)	Matched Phenotype	Causative Gene
1 (100.0%)	Hereditary spherocytosis (ORDO:822)	Folate deficiency Splenomegaly	Hemolytic anemia Jaundice Spherocytosis
		ANK1 EPB42 SLC4A1 SPTA1 SPTB	
		Hereditary spherocytosis is a congenital hemolytic anemia with a wide clinical spectrum (from symptom-free carriers to severe hemolysis) characterized by anemia, variable jaundice, splenomegaly and cholelithiasis. Find images (Google) Find case reports	
2 (95.4%)	Neuroblastoma (ORDO:635)	Hemolytic anemia Splenomegaly	Jaundice Methylmalonic acidemia Spherocytosis
		ALK HACET1 LIN28B LMO1 MYCN PHOX2B TOP2A	
		Neuroblastoma is a malignant tumor of neural crest cells, the cells that give rise to the sympathetic nervous system, which is observed in children. Find images (Google) Find case reports	
3 (95.4%)	Paroxysmal nocturnal hemoglobinuria (ORDO:447)	Hemolytic anemia Jaundice Vitamin B12 deficiency	Microspherocytosis Splenomegaly
		PIGA	
		Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired clonal hematopoietic stem cell disorder characterized by corpuscular hemolytic anemia, bone marrow failure and frequent thrombotic events. Find images (Google) Find case reports	
4 (93.0%)	Sickle cell anemia (ORDO:232)	Hemolytic anemia Jaundice Vitamin D deficiency	Spherocytosis Splenomegaly
		HBB	
		Sickle cell anemias are chronic hemolytic diseases that may induce three types of acute accidents: severe anemia, severe bacterial infections, and ischemic vasoocclusive accidents (VOA) caused by sickle-shaped red blood cells obstructing small blood vessels and capillaries. Many diverse complications can occur. Find images (Google) Find case reports	
5 (90.9%)	Graft versus host disease (ORDO:39812)	Anemia Jaundice Vitamin A deficiency	Schistocytosis Splenomegaly
		Acute graft-versus-host disease (GVHD) occurs after allogeneic hematopoietic stem cell transplant and is a reaction of donor immune cells against host tissues. Activated donor T cells damage host epithelial cells after an inflammatory cascade that begins with the preparative regimen. Find images (Google) Find case reports	

Figure 4A

PubCaseFinder

AboutTermsAPIContact

Input patient's **signs and symptoms**

+ Upload File (HPO ID):

HP:0000952 Jaundice x HP:0001903 Anemia x HP:0001744 Splenomegaly x HP:0100507 Folate deficiency x HP:0004444 Spherocytosis x

Narrow down the diseases

+ Upload File (Entrez Gene ID):

Download Summary of Results

Find diseases

Clear

Rare Diseases (Orphanet) 4,066 results

Genetic Diseases (OMIM) 6,969 results

Total: 6969 results

123...697»

10 (per page)

Download Results

Rank (Similarity)	Disease Name (Disease ID)	Matched Phenotype	Causative Gene
1 (82.0%)	hereditary spherocytosis type 2 (OMIM:616649)	Hemolytic anemia Splenomegaly	Hyperbilirubinemia Jaundice Spherocytosis
		SPTB	
		A hereditary spherocytosis that has_material_basis_in an autosomal dominant mutation of SPTB on chromosome 14q23.3. Find images (Google)	
1 (82.0%)	hereditary spherocytosis type 4 (OMIM:612653)	Hemolytic anemia Splenomegaly	Hyperbilirubinemia Jaundice Spherocytosis
		SLC4A1	
		A hereditary spherocytosis that has_material_basis_in an autosomal dominant mutation of SLC4A1 on chromosome 17q21.31. Find images (Google)	
1 (82.0%)	hereditary spherocytosis type 1 (OMIM:182900)	Hemolytic anemia Splenomegaly	Hyperbilirubinemia Jaundice Spherocytosis
		ANK1	
		A hereditary spherocytosis that has_material_basis_in an autosomal dominant mutation of ANK1 on chromosome 8p11.21. Find images (Google)	
4 (79.9%)	overhydrated hereditary stomatocytosis (OMIM:185000)	Hemolytic anemia Stomatocytosis	Hyperbilirubinemia Jaundice Splenomegaly
		RHAG STOM	
		Overhydrated hereditary stomatocytosis (OHS) is a disorder of red cell membrane permeability to monovalent cations and is characterized clinically by hemolytic anemia. Find images (Google)	
4 (79.9%)	anemia, congenital dyserythropoietic, type Ia (OMIM:224120)	Hydrops fetalis Prolonged neonatal jaundice Splenomegaly	Macrocytic dyserythropoietic anemia Poikilocytosis
		CDAN1	
		Find images (Google)	
6 (79.9%)	Dehydrated hereditary stomatocytosis 2; DHS2 (OMIM:616689)	Acanthocytosis Splenomegaly	Hemolytic anemia Hyperbilirubinemia Jaundice
		KCNN4	
		Find images (Google)	
7	cystic fibrosis-gastritis-	Biliary cirrhosis Exocrine pancreatic insufficiency Folate deficiency	

Figure 4B

PubCaseFinder

[About](#)
[Terms](#)
[API](#)
[Contact](#)

Hereditary spherocytosis

Hereditary spherocytosis is a congenital hemolytic anemia with a wide clinical spectrum (from symptom-free carriers to severe hemolysis) characterized by anemia, variable jaundice, splenomegaly and cholelithiasis.

Hemolytic anemia

A type of anemia caused by premature destruction of red blood cells (hemolysis).

Total: 13

1

20 (per page)

PMID (PMCID)		
27108201	MIXED_SAMPLE	Adult
<p>Disease-modifying influences of coexistent G6PD-deficiency, Gilbert syndrome and deletional alpha thalassemia in hereditary spherocytosis: A report of three cases.</p> <p>Jamwal M, Aggarwal A, Kumar V, Sharma P, Sachdeva MU, Bansal D, Malhotra P, Das R. Clin Chim Acta. 2016;458:51-4.</p> <p>Hereditary spherocytosis (HS) is a common inherited hemolytic anemia characterized by heterogeneous clinical presentations with variable degrees of anemia, jaundice, splenomegaly and gallstones.</p>		
27566068	MALE	Middle Aged
<p>Open-heart surgery using a centrifugal pump: a case of hereditary spherocytosis.</p> <p>Matsuzaki Y, Tomioka H, Saso M, Azuma T, Saito S, Aomi S, Yamazaki K. J Cardiothorac Surg. 2016;11(1):138.</p> <p>Hereditary spherocytosis is a genetic, frequently familial hemolytic blood disease characterized by varying degrees of hemolytic anemia, splenomegaly, and jaundice.</p>		
26711368	MALE	
<p>Pyoderma Gangrenosum in a Patient with Hereditary Spherocytosis.</p> <p>Kwon HI, Paek JO, Kim JE, Ro YS, Ko JY. Int J Low Extrem Wounds. 2016;15(1):92-5.</p> <p>However, there have been no previous reports of PG in a patient with hereditary spherocytosis, a common inherited hemolytic anemia.</p>		
23724634	MALE	
<p>A case of hereditary spherocytosis misdiagnosed as pyruvate kinase deficient hemolytic anemia.</p> <p>Vercellati C, Marcello AP, Fermo E, Barcellini W, Zanella A, Bianchi P. Clin Lab. 2013;59(3-4):421-4.</p> <p>A case of hereditary spherocytosis misdiagnosed as pyruvate kinase deficient hemolytic anemia.</p>		
20618221	MALE	Child
<p>Orthotopic heart transplantation in a child with hereditary spherocytosis.</p> <p>Johnson CE, Schmitz ML, McKamie WA, Edens RE, Imamura M, Jaquiss RD. Artif Organs. 2010;34(12):1154-6.</p> <p>Hereditary spherocytosis (HS) is a genetic, frequently familial hemolytic blood disease that presents with varying degrees of hemolytic anemia, splenomegaly, and jaundice. The disease arises as a result of defects in any of a number of proteins responsible for maintaining the shape and flexibility of the red blood cell, resulting in an osmotically fragile and characteristically spherical red blood cell.</p>		

Figure 5

USER GUIDE

3) Narrowing down rare and genetic diseases

By inputting gene symbols into the search box, you can narrow down the 4,066 rare diseases and 6,969 genetic diseases to the diseases whose causative genes are the user-specified genes. This search box also provides autocompletion functionality: Possible matches are shown below, while the query is typed in (Figure 6). After inputting gene symbols, you can narrow down the ranked list of rare diseases by clicking the 'Find diseases' button (Figure 7). Figure 7 shows that 4,066 rare diseases have narrowed down to 3 diseases, and 6,969 genetic diseases have narrowed down to 2 diseases.

PubCaseFinder

AboutTermsAPIContact

Input patient's **signs** and **symptoms** [+ Upload File \(HPO ID\) :](#)

HP:0000952 Jaundice

HP:0001903 Anemia

HP:0001744 Splenomegaly

HP:0100507 Folate deficiency

HP:0004444 Spherocytosis

Narrow down the diseases [+ Upload File \(Entrez Gene ID\) :](#)

ENT:286 ANK1 (SPH1)

ENT:2038 EPB42 (MGC116735 | MGC116737 | PA)

TOP

ENT:10210 **TOPORS** (LUN | TP53BPL)
ENT:65057 ACD (Pip1 | **Ptop** | Tint1 | Tpp1)
ENT:7153 **TOP2A**
ENT:8492 PRSS12 (BSSP-3 | MRT1 | **motopsin**)

Rare Diseases (Orphanet) 4,066 results

Genetic Diseases (OMIM) 6,969 results

Total: **4,066** results

1

2

3

...

407

»

10

 (per page)

Download Results

Rank (Similarity)	Disease Name (Disease ID)	Matched Phenotype	Causative Gene
1 (100.0%)	Hereditary spherocytosis (ORDO:822)	<div>Folate deficiency</div> <div>Hemolytic anemia</div> <div>Jaundice</div> <div>Spherocytosis</div> <div>Splenomegaly</div>	<div>ANK1</div> <div>EPB42</div> <div>SLC4A1</div> <div>SPTA1</div> <div>SPTB</div>
<div>Hereditary spherocytosis is a congenital hemolytic anemia with a wide clinical spectrum (from symptom-free carriers to severe hemolysis) characterized by anemia, variable jaundice, splenomegaly and cholelithiasis.</div> <div>Find images (Google) Find case reports</div>			

Figure 6

USER GUIDE

PubCaseFinder

AboutTermsAPIContact

Input patient's **signs** and **symptoms** [+ Upload File \(HPO ID\) :](#)

HP:0000952 Jaundice x

HP:0001903 Anemia x

HP:0001744 Splenomegaly x

HP:0100507 Folate deficiency x

HP:0004444 Spherocytosis x

Narrow down the diseases [+ Upload File \(Entrez Gene ID\) :](#)

ENT:286 ANK1 (SPH1) x

ENT:2038 EPB42 (MGC116735 | MGC116737 | PA) x

ENT:7153 TOP2A x

Download Summary of Results

Find diseases

Clear

Rare Diseases (Orphanet) 3 results

Genetic Diseases (OMIM) 2 results

Total: 3 results

1

10 (per page)

Download Results

Rank (Similarity)	Disease Name (Disease ID)	Matched Phenotype	Causative Gene
1 (100.0%)	Hereditary spherocytosis (ORDO:822)	<div>Folate deficiency Hemolytic anemia Jaundice Splenomegaly</div>	<div>ANK1 EPB42 SLC4A1 SPTA1 SPTB</div> <div>Hereditary spherocytosis is a congenital hemolytic anemia with a wide clinical spectrum (from symptom-free carriers to severe hemolysis) characterized by anemia, variable jaundice, splenomegaly and cholelithiasis.</div> <div>Find images (Google) Find case reports</div>
2 (95.4%)	Neuroblastoma (ORDO:635)	<div>Hemolytic anemia Jaundice Methylmalonic acidemia Splenomegaly</div>	<div>ALK HACE1 LIN28B LMO1 MYCN PHOX2B TOP2A</div> <div>Neuroblastoma is a malignant tumor of neural crest cells, the cells that give rise to the sympathetic nervous system, which is observed in children.</div> <div>Find images (Google) Find case reports</div>
3 (68.6%)	8p11.2 deletion syndrome (ORDO:251066)	<div>Azoospermia Hemolytic anemia Sacral dimple Splenomegaly</div>	<div>ANK1</div> <div>8p11.2 deletion syndrome is a contiguous gene syndrome characterized by the association of congenital spherocytosis, dysmorphic features, growth delay and hypogonadotropic hypogonadism.</div> <div>Find images (Google) Find case reports</div>

Figure 7

4) Uploading a list of phenotypes or genes

By using the uploading function, you can quickly input a list of phenotypes (HPO ID) or genes (Entrez Gene ID). In Figure 8, there are two links of “Upload File (HPO ID List)” and “Upload File (Entrez Gene ID List).” You can upload a file including a list of phenotypes (Figure 9) or genes (Figure 10) by clicking them. The comma-separated values format is supported.

PubCaseFinder About Terms API Contact

Input patient's **signs** and **symptoms** + Upload File (HPO ID) :

HP:0000952 Jaundice x HP:0001903 Anemia x HP:0001744 Splenomegaly x HP:0100507 Iron deficiency x
HP:0004444 Spherocytosis x

Narrow down the diseases + Upload File (Entrez Gene ID) :

ENT:286 ANK1 (SPH1) x ENT:2038 EPB42 (MGC116737) x MGC116737 | PA x ENT:7153 TOP2A x

Download Summary of Results Find diseases Clear

Figure 8

```
HP:0001009,HP:0001249,HP:0001250,HP:0002072,HP:0002315,HP:0001297,
HP:0100026,HP:0002637,HP:0030746,HP:0002138
```

Figure 9

```
59,57674,343035,145226,6121,57096,80184,23746,7287,23418,130557,9221
1,79947,24148,4117,5949,157657,9742,79797,23568,4751,26160,7275,5585
7,57709,9128,60509,92840,23370
```

Figure 10

5. HOW TO SEARCH CASE REPORTS

After getting a ranked list of rare and genetic diseases, you can check the link for getting a ranked list of published case reports in each row (Figure 7). By clicking the link, a ranked list of published case reports related to the rare disease are shown by comparing signs and symptoms of an affected individual against those included in published case reports (Figure 11). The matched phenotypes, genes, and mutations included in the published case report are shown in each row. Also, MeSH terms are shown in each row, and you can narrow down published case reports by inputting MeSH term in the box "Narrow down the case reports." You can download the results by clicking the "Download Results" button. If you click the tabs of

Case Reports (10)
Phenotypes
Causative Genes

Input patient's **signs** and **symptoms**

HP:0000952 Jaundice
HP:0001903 Anemia
HP:0001744 Splenomegaly
HP:0100507 Folate deficiency
HP:0001889 Megaloblastic anemia

Narrow down the case reports

MSH:D009154 Mutation

Search Clear

Total: **10** (papers)

1

20 (per page)

Matched PhenotypeGeneMutationMeSH

Similarity	PMID (PMCID)	
64.73%	27108201	Disease-modifying influences of coexistent G6PD-deficiency, Gilbert syndrome and deletional alpha thalassemia in hereditary spherocytosis: A report of three cases. Jamwal M, Aggarwal A, Kumar V, Sharma P, Sachdeva MU, Bansal D, Malhotra P, Das R. Clin Chim Acta. 2016;458:51-4. <div> JaundiceSplenomegalyHemolytic anemia </div> <div>G6PD</div> <div> AdultFemalesHomo sapiensMaleMutationSequence Deletionalpha-Thalassemia </div>
64.47%	20924216 (3304593)	A case of concomitant Gilbert's syndrome and hereditary spherocytosis. Lee HJ, Moon HS, Lee ES, Kim SH, Sung JK, Lee BS, Jeong HY, Lee HY, Eu YJ. Korean J Hepatol. 2010;16(3):321-4. <div> SplenomegalyAnemiaHyperbilirubinemia </div> <div>UGT1A1</div> <div> c SUB G 211 Ac SUB T -3279 G </div> <div> AdultAllelesAnkyrinsGlucuronosyltransferaseHeterozygoteHomo sapiensMaleMutationPolyacrylamide Gel ElectrophoresisSequence Analysis, DNASplenomegalyTertiary Protein Structure </div>

Figure 11

“Phenotypes” or “Causative Genes,” you can check the phenotypes or causative genes related to the rare disease (Figure 11).