

WEBLEM 6

Introduction to Specialized Databases

Specialized Databases:

Specialized databases are a collection of focused information on one or more specific fields of study. This information or data is arranged or indexed so that the user can locate and retrieve it quickly and easily.

Features of specialized databases:

- Guaranteed Authoritative information
 - Specialized databases often have strict guidelines on the types of articles and journal sources that are accepted. By searching a database, the articles you find are more likely to be both accurate and reliable.
- They're Tailored to specific subjects and fields of study
 - The databases outlined in this module are geared towards specific subjects (i.e) medicine, nursing, etc.). When you use these for your research, the articles you find are more likely to be relevant towards your area of study.
- They Provide Full-text and diagrammatic access
 - When accessing these databases you get full text and diagrammatic representation of data available in simple and easy to chunks.

KEGG:

While the genome sequencing projects rapidly determine gene catalogs for an increasing number of organisms, functional annotation of individual genes is still largely incomplete. KEGG (Kyoto Encyclopedia of Genes and Genomes) is an effort to link genomic information with higher order functional information by computerizing current knowledge on cellular processes and by standardizing gene annotations.

Generally speaking, the biological function of the living cell is a result of many interacting molecules; it cannot be attributed to just a single gene or a single molecule. The functional assignment in KEGG is a process of linking a set of genes in the genome with a network of interacting molecules in the cell, such as a pathway or a complex, representing a higher order biological function.

OMIM:

Online Mendelian Inheritance in Man (OMIM), a continuation of Dr Victor A. McKusick's Mendelian Inheritance in Man (MIM) (1), is the primary repository of comprehensive, curated information on genes and genetic phenotypes and the relationships between them. MIM was published through 12 editions between 1966 and 1998, and OMIM has been online and searchable since 1987.

With the advent of new sequencing technologies, there is a rapid increase in the reports of presumed gene-phenotype relationships. OMIM.org was created to provide a user-friendly and easily searchable portal to a curated compilation of the literature to aid in clinical and molecular genetic research.

References:

1. Hamosh, A. (2004). Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders. *Nucleic Acids Research*, 33(Database issue), D514–D517. <https://doi.org/10.1093/nar/gki033>
2. Kanehisa, M. (2000). KEGG: Kyoto Encyclopedia of Genes and Genomes. *Nucleic Acids Research*, 28(1), 27–30. <https://doi.org/10.1093/nar/28.1.27>

WEBLEM 6a

(url: <https://www.genome.jp/kegg/>)

Aim:

To study the AKT Pathway using KEGG Database:

Introduction:

The KEGG database project was initiated in 1995 under the Japanese Human Genome Project, foreseeing the need for a reference resource that would enable understanding of the biological systems, such as the cell and the organism, from genome sequence data. Major efforts have been undertaken to represent the biological systems in terms of molecular networks (molecular wiring diagrams), especially in the form of KEGG pathway maps that are manually created by capturing knowledge from published literature. Continuous efforts have also been made to develop and improve the KO (KEGG Orthology) system for representation of gene/protein functional orthologs in molecular networks.

- **KEGG PATHWAY** is a collection of manually drawn pathway maps representing our knowledge of the molecular interaction, reaction and relation networks for:
- **KEGG BRITE** is a collection of hierarchical classification systems capturing functional hierarchies of various biological objects, especially those represented as KEGG objects. They are represented as BRITE hierarchy files, also called hierarchical text (htext) files, supplemented with BRITE table files using html tables.
- The **KEGG MODULE** database consists of KEGG modules identified by M numbers and KEGG reaction modules identified by RM numbers, which are manually defined functional units of gene sets and reaction sets, respectively. KEGG modules are further divided into pathway modules and signature modules as shown below.
 - Pathway modules – functional units of gene sets in metabolic pathways, including molecular complexes.
 - Signature modules – functional units of gene sets that characterize phenotypic features.
 - Reaction modules – functional units of successive reaction steps in metabolic pathways.


Protein kinase B (Akt), similar to many other protein kinases, is at the crossroads of cell death and survival, playing a pivotal role in multiple interconnected cell signaling mechanisms implicated in cell metabolism, growth and division, apoptosis suppression and angiogenesis. Akt protein kinase displays important metabolic effects, among which are glucose uptake in muscle and fat cells or the suppression of neuronal cell death.

Disruptions in the Akt-regulated pathways are associated with cancer, diabetes, cardiovascular and neurological diseases. The regulation of the Akt signaling pathway renders Akt a valuable therapeutic target. The discovery process of Akt inhibitors using various strategies has led to the identification of inhibitors with great selectivity, low side-effects and toxicity. The usefulness of Akt emerges beyond cancer therapy and extends to other major diseases, such as diabetes, heart diseases, or neurodegeneration.

Methodology:

- Open the homepage of KEGG.
- Enter the pathway in search bar.
- Interpret the result.

[KEGG](#) [Databases](#) [Mapper](#) [Auto annotation](#) [Kanehisa Lab](#)



KEGG

AKT Pathway

Search

Help

[» Japanese](#)

KEGG Home
[Release notes](#)
[Current statistics](#)

KEGG Database
[KEGG overview](#)
[Searching KEGG](#)
[KEGG mapping](#)
[Color codes](#)

KEGG Objects
[Pathway maps](#)
[Brite hierarchies](#)
[KEGG DB links](#)

KEGG Software
[KEGG API](#)
[KGML](#)

KEGG FTP
[Subscription](#)
[Background info](#)

[GenomeNet](#)
[DBGET/LinkDB](#)
[Feedback](#)

KEGG: Kyoto Encyclopedia of Genes and Genomes

KEGG is a database resource for understanding high-level functions and utilities of the biological system, such as the cell, the organism and the ecosystem, from molecular-level information, especially large-scale molecular datasets generated by genome sequencing and other high-throughput experimental technologies. See [Release notes](#) (October 1, 2021) for new and updated features.

New article [KEGG mapping tools for uncovering hidden features in biological data](#)

Announcement [Field name changes in KEGG Database Entry Format](#)

● **Main entry point to the KEGG web service**

[KEGG2](#) [KEGG Table of Contents](#) [\[Update notes | Release history\]](#)

● **Data-oriented entry points**

KEGG PATHWAY	KEGG pathway maps	Pathway Brite Brite table Module Network KO (Function) Organism Virus Compound Disease (ICD) Drug (ATC) Drug (Target) Antimicrobials
KEGG BRITE	BRITE hierarchies and tables	
KEGG MODULE	KEGG modules	
KEGG ORTHOLOGY	KO functional orthologs [Annotation]	
KEGG GENES	Genes and proteins [SeqData]	
KEGG GENOME	Genomes [KEGG Virus Taxonomy]	
KEGG COMPOUND	Small molecules	
KEGG GLYCAN	Glycans	
KEGG REACTION	Biochemical reactions [RModule]	
KEGG ENZYME	Enzyme nomenclature	
KEGG NETWORK	Disease-related network variations	
KEGG DISEASE	Human diseases	

Fig1. Homepage of Kegg with query AKT Pathway

Search for

Database: KEGG - Search term: AKT Pathway

KEGG PATHWAY

map04151
PI3K-Akt signaling pathway

KEGG NETWORK

- N00154 CXCR-GNB/G-PI3K-AKT signaling pathway
- N00158 KSHV vGPCR to GNB/G-PI3K-AKT signaling pathway
- N00220 PTEN-PIP3-AKT signaling pathway
- N00353 HPV E6 to PTEN-PIP3-AKT signaling pathway
- N00354 HPV E6 to PTEN-PIP3-AKT signaling pathway
- ... » display all

Fig2. Hit page of query AKT Pathway



PATHWAY: map04151

[Help](#)

Entry	map04151	Pathway
Name	PI3K-Akt signaling pathway	
Description	<p>The phosphatidylinositol 3'-kinase (PI3K)-Akt signaling pathway is activated by many types of cellular stimuli or toxic insults and regulates fundamental cellular functions such as transcription, translation, proliferation, growth, and survival. The binding of growth factors to their receptor tyrosine kinase (RTK) or G protein-coupled receptors (GPCR) stimulates class Ia and Ib PI3K isoforms, respectively. PI3K catalyzes the production of phosphatidylinositol-3,4,5-triphosphate (PIP3) at the cell membrane. PIP3 in turn serves as a second messenger that helps to activate Akt. Once active, Akt can control key cellular processes by phosphorylating substrates involved in apoptosis, protein synthesis, metabolism, and cell cycle.</p>	
Class	Environmental Information Processing; Signal transduction BRITE hierarchy	
Pathway map	map04151 PI3K-Akt signaling pathway	

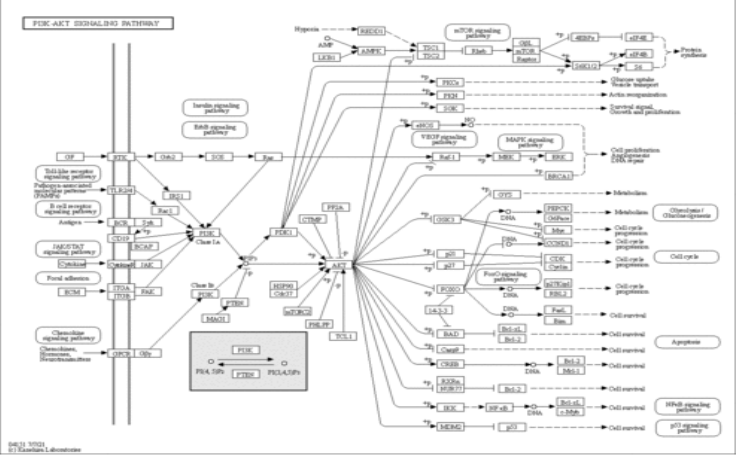


Diagram illustrating the PI3K-Akt signaling pathway. The pathway starts with the activation of PI3K (Phosphoinositide 3-kinase) by various receptors (RTK, GPCR) and other stimuli. Activated PI3K produces PIP3 (Phosphatidylinositol (3,4,5)-trisphosphate), which recruits and activates Akt (Protein Kinase B). Activated Akt then phosphorylates various substrates, leading to different cellular outcomes such as proliferation, survival, and metabolism. Key components include PI3K, PIP3, Akt, and various downstream effectors like FOXO, S6, and GSK3.

[Ortholog table](#)

All links

Disease (1)
KEGG DISEASE (1)
Chemical substance (4)
KEGG COMPOUND (4)
Gene (594784)
KEGG ORTHOLOGY (263)
RefGene (594521)
Literature (19)
PubMed (19)
All databases (594808)
[Download RDF](#)

Fig3. Result page for Pathway: map04151

KECC PI3K-Akt signaling pathway - Reference pathway

[Pathway menu | Pathway entry | Show description | Image (png) file | Help]

Change pathway type

Option

Scale: 100%

Search

ID search

Color

Network

☐ nt06214 PI3K signaling
 ☐ N00033 EGF-EGFR-PI3K signa
 ☐ N00390 EGF-EGFR-PI3K-NFKE
 ☐ N00220 PTEN-PI3K-AKT signa
 ☐ N00030 EGF-EGFR-RAS-PI3K
 ☐ nt06114 PI3K signaling (viruses)
 ☐ N00582 IGF-IGF1R-PI3K signa

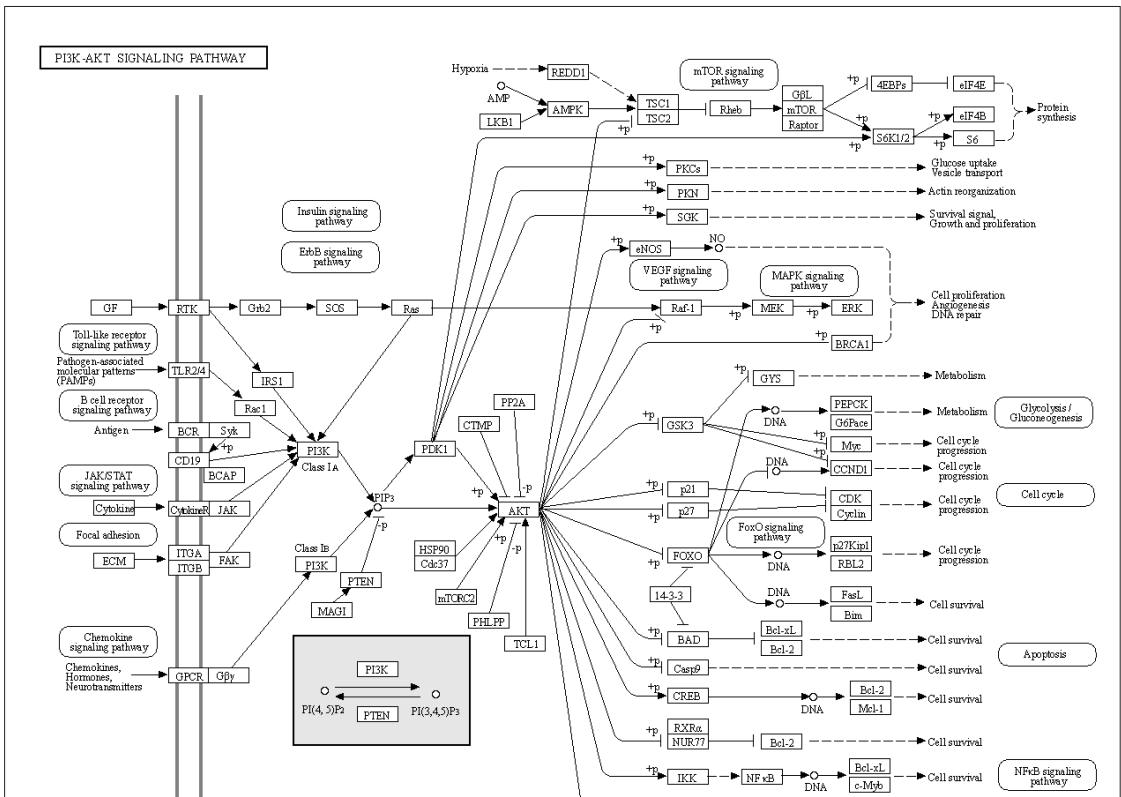


Fig4. AKT signalling pathway – Reference pathway.



NETWORK: N00154

[Help](#)

Entry	N00154	Network
Name	CXCR-GNB/G-PI3K-AKT signaling pathway	
Definition	CXCL8 -> CXCR2 -> GNB/G -> PI3Kgamma -> PIP3 -> AKT -> MTOR	
Expanded	3576 -> 3579 -> (2782,2783,2784,59345,10681,54331,2785,2786,2787,2788,94235,2790,2791,55970,51764,2792,2793) -> (5294,23533,146850) -> C05981 -> (207,208,10000) -> 2475	
Class	nt06224 CXCR signaling nt06124 Chemokine signaling (viruses) nt06150 Cytokine-cytokine receptor interaction (viruses) nt06167 Human cytomegalovirus (HCMV) nt06164 Kaposi sarcoma-associated herpesvirus (KSHV)	
Type	Reference	
Pathway	hsa04062 Chemokine signaling pathway	
Gene	3576 CXCL8; C-X-C motif chemokine ligand 8 3579 CXCR2; C-X-C motif chemokine receptor 2 2782 GNB1; G protein subunit beta 1 2783 GNB2; G protein subunit beta 2 2784 GNB3; G protein subunit beta 3 59345 GNB4; G protein subunit beta 4 10681 GNB5; G protein subunit beta 5 54331 GNG2; G protein subunit gamma 2 2785 GNG3; G protein subunit gamma 3 2786 GNG4; G protein subunit gamma 4 2787 GNG5; G protein subunit gamma 5 2788 GNG7; G protein subunit gamma 7 94235 GNG8; G protein subunit gamma 8 2790 GNG10; G protein subunit gamma 10 2791 GNG11; G protein subunit gamma 11 55970 GNG12; G protein subunit gamma 12 51764 GNG13; G protein subunit gamma 13 2792 GNGT1; G protein subunit gamma transducin 1 2793 GNGT2; G protein subunit gamma transducin 2 5294 PIK3CG; phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma 23533 PIK3R5; phosphoinositide-3-kinase regulatory subunit 5 146850 PIK3R6; phosphoinositide-3-kinase regulatory subunit 6 207 AKT1; AKT serine/threonine kinase 1 208 AKT2; AKT serine/threonine kinase 2 10000 AKT3; AKT serine/threonine kinase 3 2475 MTOR; mechanistic target of rapamycin	
Metabolite	C05981 Phosphatidylinositol-3,4,5-trisphosphate	

All links

Pathway (1)
KEGG PATHWAY (1)
Chemical substance (1)
KEGG COMPOUND (1)
Gene (26)
KEGG GENES (26)
Literature (3)
PubMed (3)
All databases (31)

[Download RDF](#)

Fig5. KEGG network: N00154

Option

Scale: 100%

Search

ID search

Color

Network

- ☐ nt06124 Chemokine signaling (v)
- ☐ N00401 CXCR4-GNAQ-PLCB/C
- ☐ N00546 CXCL12-CXCR4-PKC-I
- ☐ N00403 CX3CR1-GNAI-AC-PKC
- ☐ N00430 CXCR4-GNAI-PI3K-BAD
- ☐ N00399 CCR2-GNB/G-PI3K-NI
- ☐ N00153 CCR/CXCR-GNB/G-PI
- ☒ N00154 CXCR-GNB/G-PI3K-Akt
- ☐ N00413 CXCR4-GNB/G-PLCB-G
- ☐ N00428 CCR5-GNB/G-PLCB-G

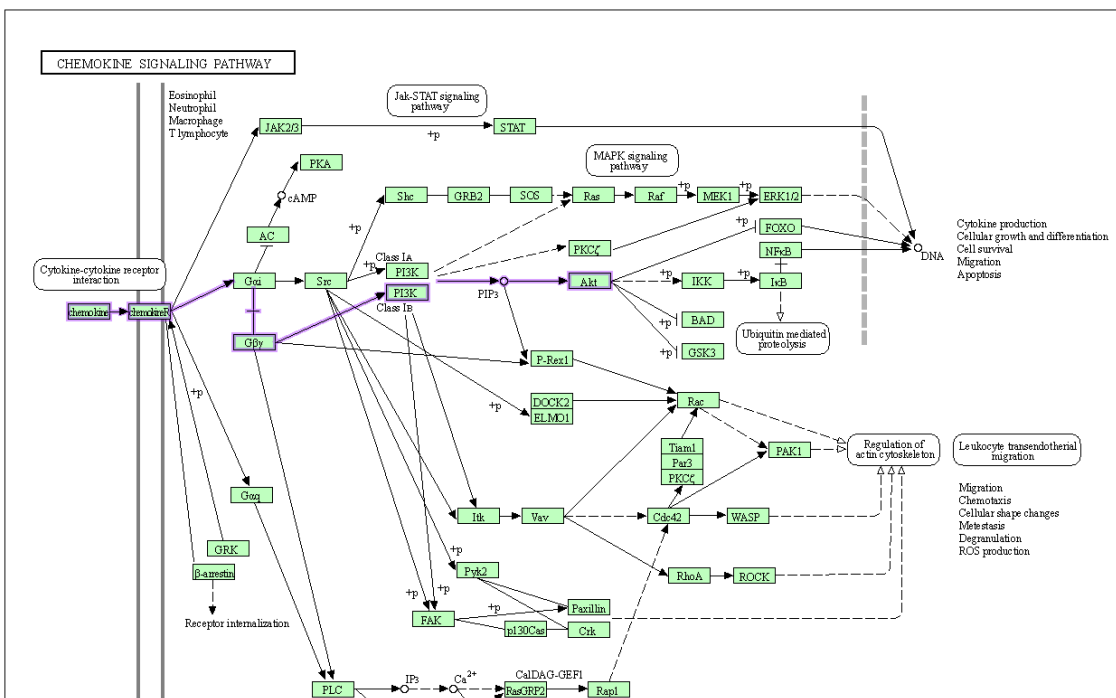


Fig6. KEGG chemokine signalling pathway homo sapiens

Results:

KEGG pathway is a great collection of manually drawn pathway maps representing our knowledge on the molecular interaction and reaction networks.

Conclusion:

KEGG is a great resource for the collection and cross checking of manually drawn pathways and information related to the same.

References:

1. The Akt Pathway in Oncology Therapy and Beyond (review) George Nitulescu-Maryna Van De Venter-Georgiana Nitulescu-Anca Ungurianu-Petras Juzenas-Qian Peng-Octavian Olaru-Daniela Grădinaru-Aristides Tsatsakis-Dimitris Tsoukalas-Demetrios Spandidos-Denisa Margina - <https://www.spandidos-publications.com/10.3892/ijo.2018.4597>
2. <https://www.genome.jp/kegg/pathway.html>
3. <https://www.genome.jp/kegg/brite.html>
4. <https://www.genome.jp/kegg/module.html>
5. <https://www.genome.jp/entry/map04151>
6. <https://www.genome.jp/pathway/map04151>
7. <https://www.genome.jp/entry/N00154>
8. <https://www.genome.jp/pathway/hsa04062+N00154>

WEBLEM 6b
(url: <https://www.omim.org/>)

Aim:

To study the disease Sickie Cell anemia using OMIM database.

Introduction:

Online Mendelian Inheritance in Man (OMIM), a continuation of Dr Victor A. McKusick's Mendelian Inheritance in Man (MIM) (1), is the primary repository of comprehensive, curated information on genes and genetic phenotypes and the relationships between them. MIM was published through 12 editions between 1966 and 1998, and OMIM has been online and searchable since 1987.

With the advent of new sequencing technologies, there is a rapid increase in the reports of presumed gene-phenotype relationships. OMIM.org was created to provide a user-friendly and easily searchable portal to a curated compilation of the literature to aid in clinical and molecular genetic research.

Advanced Search	:	In advanced search we can find history for our Entry.
Phenotype MIM Number	:	Main entry.
Genelocus MIM Number	:	Gene Information.

Symbols:

1. Phenotype Description , molecular basis known
2. Gene Discription
3. Phenotype & Gene Combine
4. No Symbol: Other , mainly phenotype with suspected mendelian basis.

Sickle cell anemia is one of a group of disorders known as sickle cell disease. Sickle cell anemia is an inherited red blood cell disorder in which there aren't enough healthy red blood cells to carry oxygen throughout your body. Normally, the flexible, round red blood cells move easily through blood vessels. In sickle cell anemia, the red blood cells are shaped like sickles or crescent moons. These rigid, sticky cells can get stuck in small blood vessels, which can slow or block blood flow and oxygen to parts of the body.

Methodology:

1. Open the homepage of OMIM.
2. Entry the query in search bar.
3. Open the Result page.
4. Interpret the Result.

Observation:

About

Statistics

Downloads

Contact Us

MIMmatch

Donate

Help

5 YEARS

OMIM

Human Genetics Knowledge for the World

OMIM®

Online Mendelian Inheritance in Man®

An Online Catalog of Human Genes and Genetic Disorders

Updated October 8, 2021

sickle cell anemia

Q

Advanced Search : OMIM, Clinical Synopses, Gene Map

Need help? : Example Searches, OMIM Search Help, OMIM Video Tutorials

Mirror site : <https://mirror.omim.org>

OMIM is supported by a grant from NHGRI, licensing fees, and generous contributions from people like you.

Make a donation!

WALSH & NATHANS

Department of Genetic Medicine

JOHNS HOPKINS

MEDICINE

Follow us on Twitter

IRDIRC

RESEARCH

RECOMMENDATION

Fig1. Homepage of OMIM with query Sickle cell anemia

Downloads

Contact Us

MIMmatch

Donate

Help

sickle cell anemia

Q

Options

View Results as: [Gene Map Table](#) [Clinical Synopsis](#)

Display: ☒ Highlights

Search: 'sickle cell anemia'

Results: 18,840 entries.

Show 100 | Download As | « First | < Previous | Next > | Last »

1: # 603903. SICKLE CELL ANEMIA

Cytogenetic location: 11p15.4

Matching terms: (anaemia | anemia), cell, sickle

Phenotype-Gene Relationships ICD+ Links

2: 143020. HPA I RECOGNITION POLYMORPHISM, BETA-GLOBIN-RELATED; HPA1

Matching terms: (anaemia | anemia), cell, sickle

Links

3: * 141900. HEMOGLOBIN--BETA LOCUS; HBB

Cytogenetic location: 11p15.4, Genomic coordinates (GRCh38): 11:5,225,463-5,227,070

Matching terms: (anaemia | anemia), cell, sickle

Gene-Phenotype Relationships ICD+ Links

4: # 141749. FETAL HEMOGLOBIN QUANTITATIVE TRAIT LOCUS 1; HBFQTL1

DELTA-BETA THALASSEMIA, INCLUDED

Cytogenetic locations: 11p15.4, 11p15.4, 11p15.4

Matching terms: (anaemia | anemia), cell, sickle

Phenotype-Gene Relationships ICD+ Links

5: * 142250. HEMOGLOBIN, GAMMA G; HBG2

Cytogenetic location: 11p15.4, Genomic coordinates (GRCh38): 11:5,253,187-5,254,780

Matching terms: (anaemia | anemia), cell, sickle

Gene-Phenotype Relationships ICD+ Links

6: % 142470. FETAL HEMOGLOBIN QUANTITATIVE TRAIT LOCUS 2; HBFQTL2

Cytogenetic location: 6q22.3-q23.1, Genomic coordinates (GRCh38): 6:126,800,000-130,900,000

Matching terms: (anaemia | anemia), cell, sickle

Gene-Phenotype Relationships ICD+ Links

7: * 141800. HEMOGLOBIN--ALPHA LOCUS 1; HBA1

Cytogenetic location: 16p13.3, Genomic coordinates (GRCh38): 16:176,679-177,521

Matching terms: (anaemia | anemia), cell, sickle

Gene-Phenotype Relationships ICD+ Links

8: # 613985. BETA-THALASSEMIA

Cytogenetic locations: 11p15.4, 11p15.4

Matching terms: (anaemia | anemia), cell, sickle

Phenotype-Gene Relationships ICD+ Links

9: % 305435. FETAL HEMOGLOBIN QUANTITATIVE TRAIT LOCUS 3; HBFQTL3

Cytogenetic location: Xp22.2, Genomic coordinates (GRCh38): X:9,600,000-17,400,000

Matching terms: (anaemia | anemia), cell, sickle

Fig2. Hit page for query Sickle cell anemia showing 18,840 entries

#603903

Table of Contents

Title

Phenotype-Gene Relationships

Clinical Synopsis

Text

Description

Clinical Features

Diagnosis

Clinical Management

Pathogenesis

Molecular Genetics

Population Genetics

Animal Model

History

References

Contributors

Creation Date

Edit History

603903

SICKLE CELL ANEMIA

Phenotype-Gene Relationships

Location	Phenotype	Phenotype MIM number	Inheritance	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
11p15.4	Sickle cell anemia	603903	AR	3	HBB	141900

Clinical Synopsis

PheneGene Graphics

TEXT

A number sign (#) is used with this entry because **sickle cell anemia** is the result of mutant beta globin (HBB; 141900) in which the mutation causes sickling of hemoglobin.

Description

Sickle cell anemia is a multisystem disease associated with episodes of acute illness and progressive organ damage. Hemoglobin polymerization, leading to erythrocyte rigidity and vasoocclusion, is central to the pathophysiology of the disease, but the importance of chronic **anemia**, hemolysis, and vasculopathy has been established. The most common cause of **sickle cell anemia** is the HbS variant (141900.0243), with hemoglobin SS disease being most prevalent in Africans (review by Rees et al., 2010).

See review of infection in **sickle cell** disease by Booth et al. (2010).

Piel et al. (2017) reviewed the genetic and nongenetic modifiers of the severity of **sickle cell** disease.

Clinical Features

Scriver and Waugh (1930) reported detailed studies of a 7-year-old child with **sickle cell anemia**. Her main complaints were cough, night sweats, vague pains in the legs and joints, occasional abdominal pain, poor appetite, and increasing fatigue. In a series of clever experiments that involved taking venous blood from the arm under different circumstances, the authors showed a correlation between oxygen tension and sickling of the red blood cells in vivo. Increased sickling was observed when

External Links

Protein

Clinical Resources

Clinical Trials

EuroGentest

Gene Reviews

Genetic Alliance

Genetics Home Reference

GTR

Newborn Screening

GARD

OrphaNet

Animal Models

Cell Lines

Fig3. Result page for Sickle cell anemia

#603903

Table of Contents

MIM Entry

603903

SICKLE CELL ANEMIA

INHERITANCE

- Autosomal recessive

CARDIOVASCULAR

Vascular

- Vasculopathy
- Microcirculatory occlusion
- Pulmonary hypertension
- Hyperemia

RESPIRATORY

Lung

- Acute chest syndrome

ABDOMEN

- Abdominal pain

Spleen

- Functional asplenia

GENITOURINARY

External Genitalia (Male)

- Priapism

Kidneys

- Renal failure

SKELETAL

Limbs

- Avascular joint necrosis
- Joint and leg pain

NEUROLOGIC

Central Nervous System

- Pain, secondary to vasoocclusion
- Stroke

HEMATOLOGY

- Sickle cell anemia
- Anemia, chronic
- Hemolysis
- Hypoxemia
- Leukocytosis

External Links

Clinical Resources

Clinical Trials

EuroGentest

Gene Reviews

Genetic Alliance

Genetics Home Reference

GTR

Newborn Screening

GARD

OrphaNet

Fig4. Clinical synopsis for sickle cell anemia

Graphical representation of phenotype/gene relationship(s) associated with this entry. Phenotypic Series (when available) are displayed with the relevant genes and subsequent phenotypes to a depth of 4 nodes. [A quick reference overview and guide \(PDF\)](#). **No hierarchy is implied.** [Feedback](#)



Graphical representation of phenotype/gene relationship(s) associated with this entry. Phenotypic Series (when available) are displayed with the relevant genes and subsequent phenotypes to a depth of 4 nodes. A quick reference overview and guide (PDF). **No hierarchy is implied.** [Feedback](#)



#603903
Table of Contents

- Title
- Phenotype-Gene Relationships
- Clinical Synopsis
- Text
 - Description
 - Clinical Features
 - Diagnosis
 - Clinical Management
 - Pathogenesis
 - Molecular Genetics
 - Population Genetics
 - Animal Model
 - History
- References
- Contributors
- Creation Date
- Edit History

Clinical Synopsis Phenotype Graphics

TEXT

Description

Sickle cell anemia is a multisystem disease associated with episodes of acute illness and progressive organ damage. Hemoglobin polymerization, leading to erythrocyte rigidity and vasoocclusion, is central to the pathophysiology of the disease, but the importance of chronic anemia, hemolysis, and vasculopathy has been established. The most common cause of **sickle cell anemia** is the HbS variant (141900.0243), with hemoglobin SS disease being most prevalent in Africans (review by [Rees et al., 2010](#)).

See review of infection in **sickle cell** disease by [Booth et al. \(2010\)](#).

[Piel et al. \(2017\)](#) reviewed the genetic and nongenetic modifiers of the severity of **sickle cell** disease.

Clinical Features

[Scriver and Waugh \(1930\)](#) reported detailed studies of a 7-year-old child with **sickle cell anemia**. Her main complaints were cough, night sweats, vague pains in the legs and joints, occasional abdominal pain, poor appetite, and increasing fatigue. In a series of clever experiments that involved taking venous blood from the arm under different circumstances, the authors showed a correlation between oxygen tension and sickling of the red blood **cells** in vivo. Increased sickling was observed when oxygen pressure fell below 40 to 45 mm Hg. [Scriver and Waugh \(1930\)](#) concluded that large aggregations of **sickle cells** seen in sinuses, vessels, and organs of **sickle cell** patients at autopsy reflected lowered oxygen tension resulting from death.

In many children with **sickle cell anemia**, functional asplenia develops during the first year of life and septicemia is the leading cause of death in childhood. The risk of septicemia in **sickle cell anemia** is greatest during the first 3 years of life and is reduced markedly by prophylactic penicillin therapy. Less is known about splenic dysfunction and the risk of overwhelming sepsis in children with **sickle cell-hemoglobin C** disease (see HbC; 141900.0038), although functional asplenia has been documented by radionuclide liver-spleen scans in some adult patients ([Ballas et al., 1982](#)) and an elevated erythrocyte pit count, a finding that indicates functional asplenia in children with **sickle cell anemia**, also has been found in some children with SC disease ([Pearson et al., 1985](#)). [Lane et al. \(1994\)](#) reported 7 fatal cases of pneumococcal septicemia in children with SC disease. The earliest death occurred in a 1-year-old child who had cyanotic congenital heart; the other children were aged 3.5 to 15 years. Only 1 child had received pneumococcal vaccine or prophylactic penicillin therapy. All 7 children had an acute febrile illness and rapid deterioration despite parenterally administered

External Links

- Protein
- Clinical Resources
 - Clinical Trials
 - EuroGentest
 - Gene Reviews
 - Genetic Alliance
 - Genetics Home Reference
 - GTR
 - Newborn Screening
 - GARD
 - OrphaNet
- Animal Models
- Cell Lines

Fig7. Description for query sickle cell anemia

#603903
Table of Contents

- Title
- Phenotype-Gene Relationships
- Clinical Synopsis
- Text
 - Description
 - Clinical Features
 - Diagnosis
 - Clinical Management
 - Pathogenesis
 - Molecular Genetics
 - Population Genetics
 - Animal Model
 - History
- References
- Contributors
- Creation Date
- Edit History

[Piel et al. \(2017\)](#) reviewed the genetic and nongenetic modifiers of the severity of **sickle cell** disease.

Clinical Features

[Scriver and Waugh \(1930\)](#) reported detailed studies of a 7-year-old child with **sickle cell anemia**. Her main complaints were cough, night sweats, vague pains in the legs and joints, occasional abdominal pain, poor appetite, and increasing fatigue. In a series of clever experiments that involved taking venous blood from the arm under different circumstances, the authors showed a correlation between oxygen tension and sickling of the red blood **cells** in vivo. Increased sickling was observed when oxygen pressure fell below 40 to 45 mm Hg. [Scriver and Waugh \(1930\)](#) concluded that large aggregations of **sickle cells** seen in sinuses, vessels, and organs of **sickle cell** patients at autopsy reflected lowered oxygen tension resulting from death.

In many children with **sickle cell anemia**, functional asplenia develops during the first year of life and septicemia is the leading cause of death in childhood. The risk of septicemia in **sickle cell anemia** is greatest during the first 3 years of life and is reduced markedly by prophylactic penicillin therapy. Less is known about splenic dysfunction and the risk of overwhelming sepsis in children with **sickle cell-hemoglobin C** disease (see HbC; 141900.0038), although functional asplenia has been documented by radionuclide liver-spleen scans in some adult patients ([Ballas et al., 1982](#)) and an elevated erythrocyte pit count, a finding that indicates functional asplenia in children with **sickle cell anemia**, also has been found in some children with SC disease ([Pearson et al., 1985](#)). [Lane et al. \(1994\)](#) reported 7 fatal cases of pneumococcal septicemia in children with SC disease. The earliest death occurred in a 1-year-old child who had cyanotic congenital heart; the other children were aged 3.5 to 15 years. Only 1 child had received pneumococcal vaccine or prophylactic penicillin therapy. All 7 children had an acute febrile illness and rapid deterioration despite parenterally administered antibiotic therapy and intensive medical support. Erythrocyte pit counts in 2 patients were 40.3 and 41.7%, respectively (normal, less than 3.6%). Autopsy findings in 5 cases included splenic congestion without infarction in 5, splenomegaly in 4, and bilateral adrenal hemorrhage in 3. [Lane et al. \(1994\)](#) concluded that pneumococcal vaccine should be administered in all children with SC disease. The routine use of prophylactic penicillin therapy in infants and children with SC disease remained controversial.

[Morris et al. \(1991\)](#) reported hematologic findings in 181 patients, aged 40 to 73 years, with hemoglobin SS disease. The studies showed a downward age-related trend in hemoglobin and platelets and falling reticulocyte count consistent with progressive bone marrow failure which could not be explained by renal impairment. [Kodish et al. \(1991\)](#) concluded that despite current rates of mortality and morbidity with bone marrow transplantation, a substantial minority of parents of children with **sickle cell** disease would consent to bone marrow transplantation for their children.

External Links

- Protein
- Clinical Resources
 - Clinical Trials
 - EuroGentest
 - Gene Reviews
 - Genetic Alliance
 - Genetics Home Reference
 - GTR
 - Newborn Screening
 - GARD
 - OrphaNet
- Animal Models
- Cell Lines

Fig8. Clinical Features for query sickle cell anemia

#603903
Table of Contents

Title

Phenotype-Genes
Relationships

Clinical Synopsis

Text

Description

Clinical Features

Diagnosis

Clinical Management

Pathogenesis

Molecular Genetics

Population Genetics

Animal Model

History

References

Contributors

Creation Date

Edit History

acute events (63.3%). The study showed that the first 24 hours after presentation for medical care is an especially perilous time for patients with sickle cell disease and an acute event.

Diagnosis

Prenatal Diagnosis

As a preliminary step to preimplantation diagnosis of sickle cell disease in unfertilized eggs or 8-cell embryos of heterozygous parents, Monk et al. (1993) established quality control by detection of the mutant and normal alleles of the HBB gene using single buccal cells. Efficient PCR amplification of a 680-bp sequence of the HBB gene spanning the site of the HbS mutation was obtained for 79% of single heterozygous cells. In 71% of cases, both alleles were detected. Monk et al. (1993) predicted that with that level of efficiency, a clinical preimplantation diagnosis at the 8-cell embryo stage could be carried out safely and reliably for a couple at risk of transmitting sickle cell disease to their children.

As a substitute for obtaining fetal cells for genetic diagnosis by the invasive procedures of amniocentesis, chorionic villus sampling, and fetal blood sampling, Cheung et al. (1996) reported a method for detecting point mutations in single gene disorders by enriching fetal cells from maternal blood by magnetic cell sorting followed by isolation of pure fetal cells by microdissection. In 2 pregnancies at risk for sickle cell anemia and beta-thalassemia, they successfully identified the fetal genotypes.

Xu et al. (1999) performed preimplantation genetic diagnosis (PGD) for sickle cell anemia on 7 embryos produced by in vitro fertilization for a couple who were both carriers of the sickle cell gene. PGD indicated that 4 were normal and 2 were carriers; diagnosis was not possible in 1. The embryos were transferred to the uterus on the fourth day after oocyte retrieval. A twin pregnancy was confirmed by ultrasonography, and subsequent amniocentesis showed that both fetuses were unaffected and were not carriers of the sickle cell mutation. The patient delivered healthy twins at 39 weeks' gestation.

Clinical Management

Yawn et al. (2014) summarized evidence-based recommendations for the management of sickle cell disease based on a review by an expert panel of 34 years of published studies.

Trompeter and Roberts (2008) provided a review of agents that increase fetal hemoglobin production and of the therapeutic use of such agents, including hydroxycarbamide, decitabine, and butyrate, in children with sickle cell disease.

In a report on a sickle cell workshop, Luzzatto and Goodfellow (1989) reviewed current treatment of

External Links

Protein

Clinical Resources

Clinical Trials
EuroGentest
Gene Reviews
Genetic Alliance
Genetics Home
Reference
GTR
Newborn Screening
GARD
OrphaNet

Animal Models

Cell Lines

Fig9. Diagnosis for query sickle cell anemia

#603903
Table of Contents

Title

Phenotype-Genes
Relationships

Clinical Synopsis

Text

Description

Clinical Features

Diagnosis

Clinical Management

Pathogenesis

Molecular Genetics

Population Genetics

Animal Model

History

References

Contributors

Creation Date

Edit History

unaffected and were not carriers of the sickle cell mutation. The patient delivered healthy twins at 39 weeks' gestation.

Clinical Management

Yawn et al. (2014) summarized evidence-based recommendations for the management of sickle cell disease based on a review by an expert panel of 34 years of published studies.

Trompeter and Roberts (2008) provided a review of agents that increase fetal hemoglobin production and of the therapeutic use of such agents, including hydroxycarbamide, decitabine, and butyrate, in children with sickle cell disease.

In a report on a sickle cell workshop, Luzzatto and Goodfellow (1989) reviewed current treatment of this disease. The lessons learned from sickle cell anemia will be applicable in other genetic diseases.

Stimulating fetal hemoglobin by increasing gamma-globin synthesis in patients with sickle cell disease would be expected, if the production of sickle hemoglobin is decreased concomitantly, to reduce the formation of intracellular S polymer and improve the acute and chronic hemolytic and vasoocclusive complications of the disease. Azacytidine and hydroxyurea have been shown to increase fetal hemoglobin levels in some patients with sickle cell disease (Charache et al., 1983; Dover et al., 1986). Rodgers et al. (1993) found that administration of intravenous recombinant erythropoietin with iron supplementation alternating with hydroxyurea elevated fetal hemoglobin levels more than hydroxyurea alone. The increases reduced intracellular polymerization of hemoglobin S. The program reduced the myelotoxic effects of hydroxyurea and was beneficial in patients who had not been helped by hydroxyurea alone. Not only does fetal hemoglobin inhibit the polymerization of hemoglobin S but it also can function as a substitute for the beta-globin chains that are defective or absent in patients with the beta-thalassemias. Butyrate has also been tried for the stimulation of fetal hemoglobin synthesis (Perrine et al., 1993). The trial with butyrate was based on the observation by Perrine et al. (1985) that infants who have high plasma levels of alpha-amino-n-butyric acid in the presence of maternal diabetes do not undergo the normal developmental gene switch from the production of predominantly gamma-globin to that of beta-globin before birth. Since other developmental processes were not delayed, the use of butyric acid as a safe and fairly specific agent was suggested. Butyrate may act through sequences near the transcriptional start site to stimulate the activity of the promoter of the gamma-globin genes. Perrine et al. (1993) showed that butyrate can significantly and rapidly increase fetal globin production to levels that can ameliorate beta-globin disorders.

On the basis of a double-blind, randomized clinical trial, Charache et al. (1995) reported that hydroxyurea therapy can ameliorate the clinical course of sickle cell anemia in adults with 3 or more

External Links

Protein

Clinical Resources

Clinical Trials
EuroGentest
Gene Reviews
Genetic Alliance
Genetics Home
Reference
GTR
Newborn Screening
GARD
OrphaNet

Animal Models

Cell Lines

Fig10. Clinical Management for query sickle cell anemia

Results:

In OMIM database the query sickle cell anemia shows 18,841 entries. It gives information regarding Human Genes & Genetic Disorders

Conclusions:

OMIM is a very easy to use and accessible database of human genes and genetic disorders compiled to support human genetics research and education and the practice of clinical genetics.

References:

1. <https://www.mayoclinic.org/diseases-conditions/sickle-cell-anemia/symptoms-causes/syc-20355876#:~:text=Sickle%20cell%20anemia%20is%20one,move%20easily%20through%20blood%20vessels.>
2. <https://www.omim.org/>
3. <https://www.omim.org/search?index=entry&sort=score+desc%2C+prefix%20sort+desc&start=1&limit=10&search=Sickle+cell+anemia>
4. <https://www.omim.org/entry/603903?search=sickle%20cell%20anemia&highlight=%28anaemia%7Canemia%29%20cell%20sickle>
5. [https://www.omim.org/clinicalSynopsis/603903?highlight=\(anaemia|anemia\)%20cell%20sickle](https://www.omim.org/clinicalSynopsis/603903?highlight=(anaemia|anemia)%20cell%20sickle)
6. <https://www.omim.org/graph/linear/603903>
7. <https://www.omim.org/graph/radial/603903>
8. <https://www.omim.org/entry/603903?search=sickle%20cell%20anemia&highlight=%28anaemia%7Canemia%29%20cell%20sickle#description>
9. <https://www.omim.org/entry/603903?search=sickle%20cell%20anemia&highlight=%28anaemia%7Canemia%29%20cell%20sickle#diagnosis>
10. <https://www.omim.org/entry/603903?search=sickle%20cell%20anemia&highlight=%28anaemia%7Canemia%29%20cell%20sickle#clinicalFeatures>
11. <https://www.omim.org/entry/603903?search=sickle%20cell%20anemia&highlight=%28anaemia%7Canemia%29%20cell%20sickle#clinicalManagement>