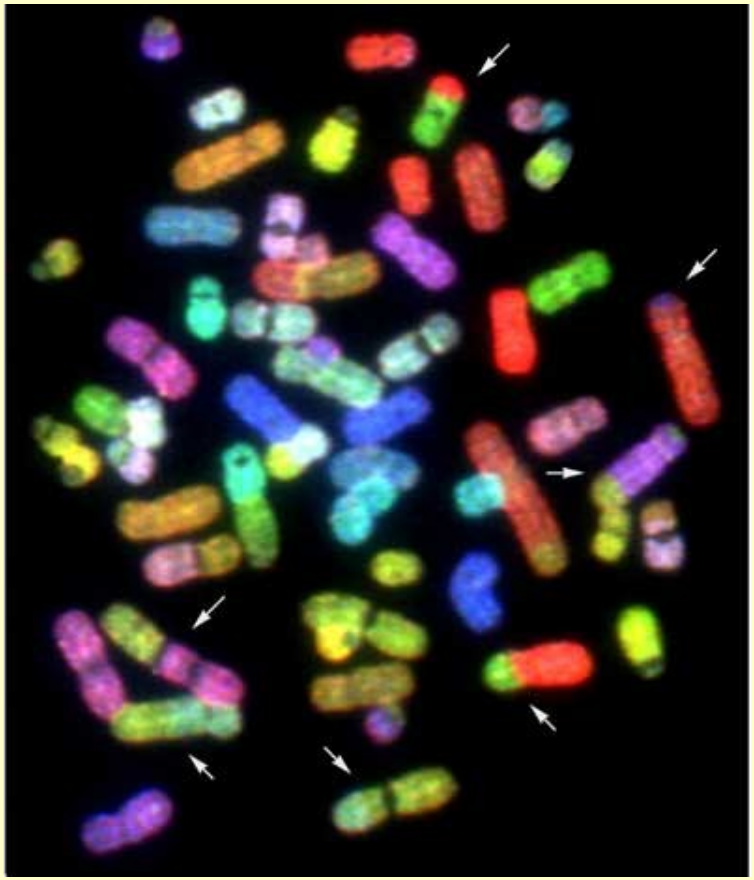
Diseases and Disease Databases

http://biochem118.stanford.edu/

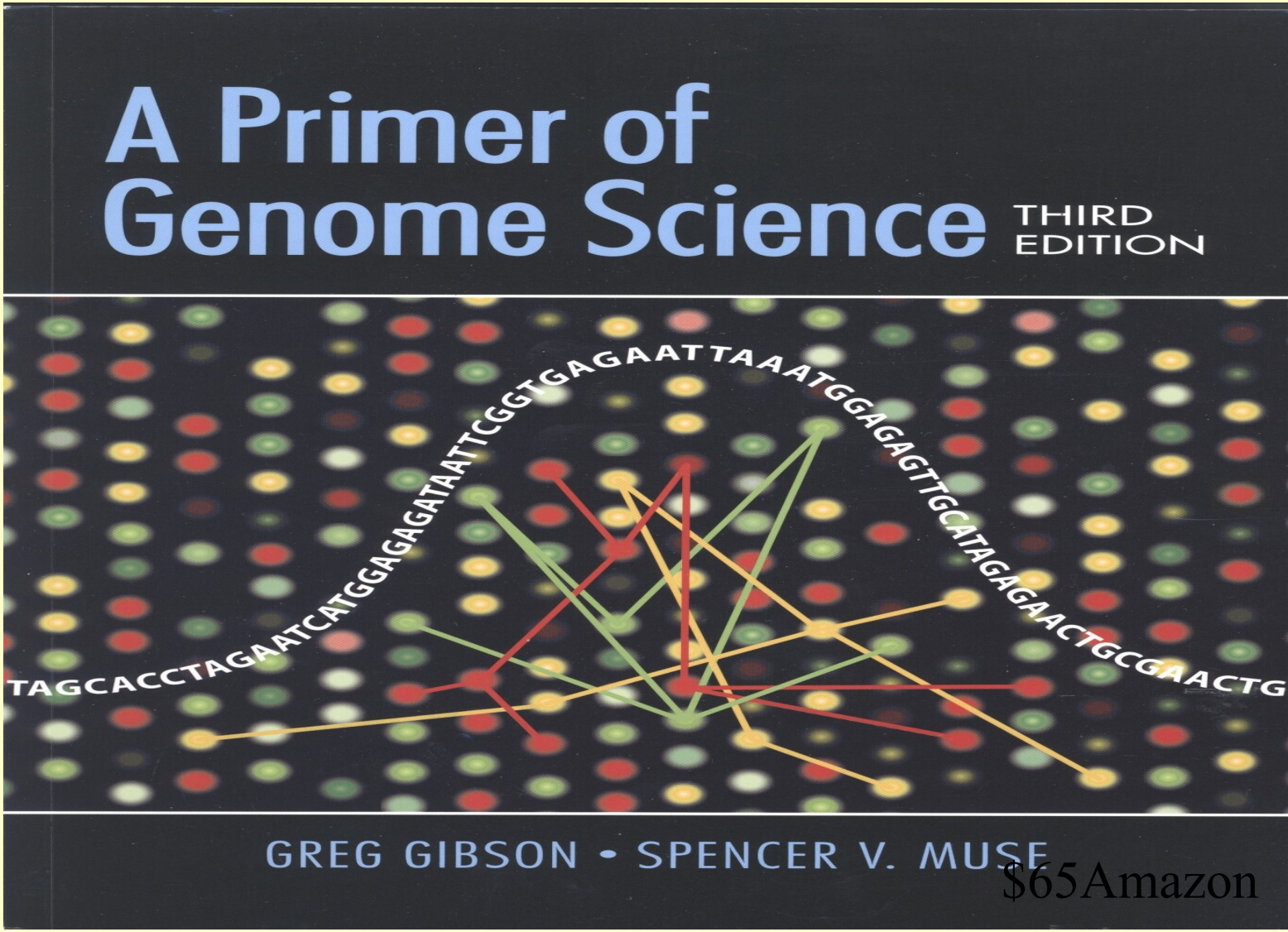


Doug Brutlag
Departments of Biochemistry & Medicine
Stanford University School of Medicine

Portrait of a Glitch

- Revere La Noue, MFA, Stanford, 2005
- What is this film about?
- What classes of glitches are mentioned?
- What do these glitches cause?
- Why did I show this film?

Greg Gibson & Spencer V. Muse
A Primer of Genome Science



$65 Amazon

Huntington's Disease

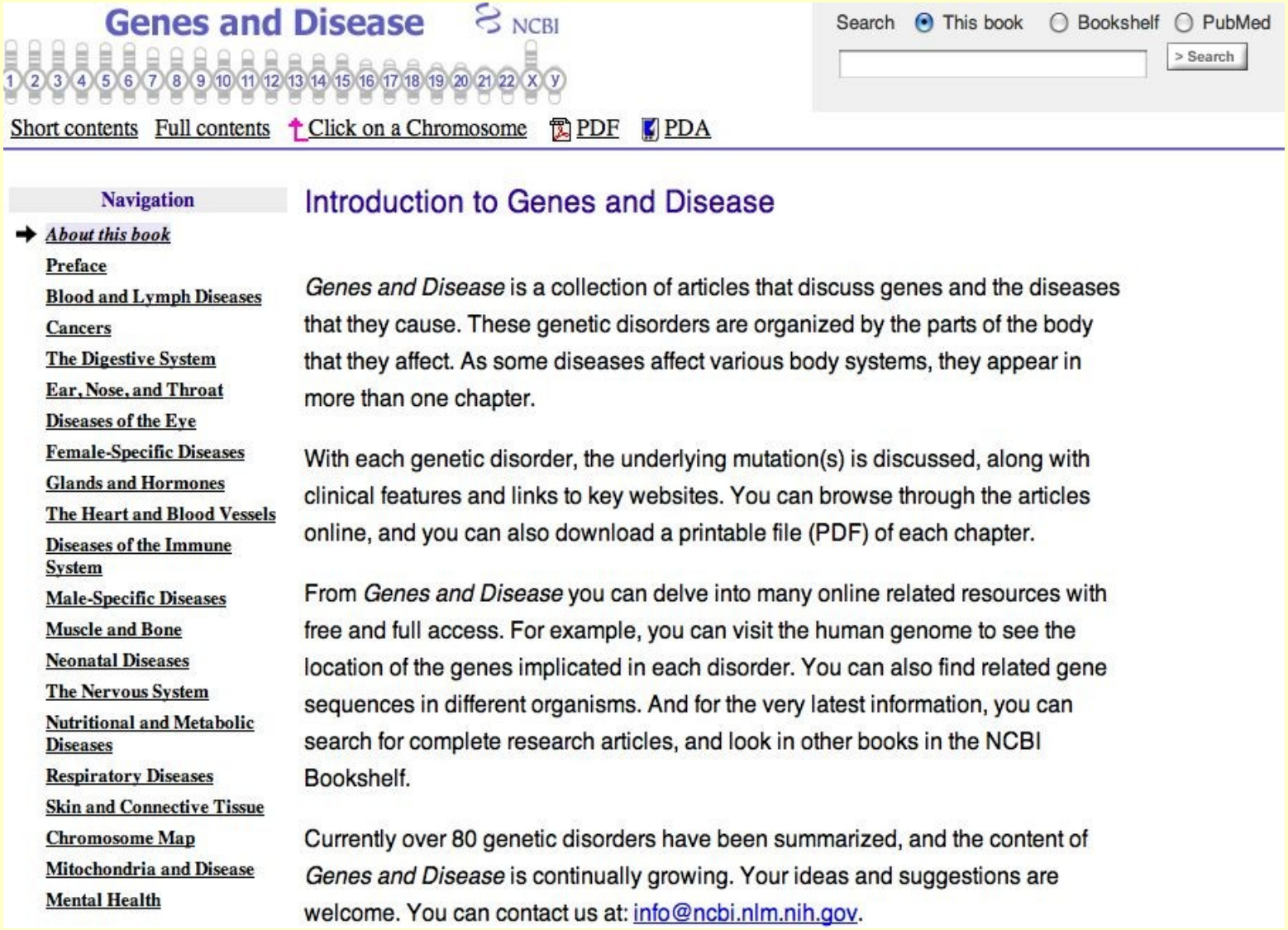
- Neurodegenerative disease
  - Loss of movement control
  - Loss of cognitive skills and hallucinations
  - Depression, hostility, aggression and loss of inhibitions
- Dyskinesias
  - Chorea: uncontrollable tics and involuntary movements of extremities, hyperkinesias
  - Dystonia uncontrollable muscle contractions
  - Dysphagia (difficulty in swallowing) and uncontrollable oral buccal dyskinesia
  - Bradykinesia, slow uncertain movements

The Inheritance

- You are 19 years old.
- Your father abandoned you and your mother when you only 2 years old.
- Your father died this year at 45 years of age and left you an inheritance.
- He died from an autosomal dominant disease known as Huntington's Chorea or Huntington Disease (HD).
- Since Huntington's is autosomal dominant, you have a 50% chance of inheriting this invariably fatal neurodegenerative disease.
- But there is a genetic test for this disease that can tell you not only if you have the disease, and if you do, at approximately what age you will suffer its symptoms.
- If you test positive, there is nothing medical that can be done to prevent the disease progression.
- Would you take the genetic test or not?
- Why?

Genes and Disease

http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?rid=gnd



Genes & Disease

http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?rid=gnd

Huntington's Disease

Genes and Disease NCBI

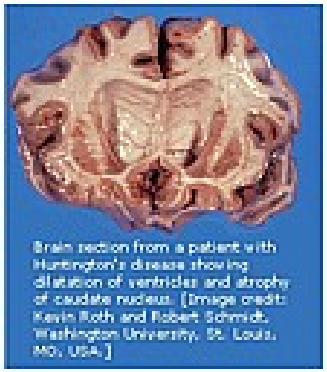
Search for Within This book All books PubMed Go

NCBI » Bookshelf » Genes and Disease » Huntington disease

Huntington disease

Huntington disease (HD) is an inherited, degenerative neurological disease that leads to dementia. About 30,000 Americans have HD and about 150,000 more are at risk of inheriting the disease from a parent.

The HD gene, whose mutation results in Huntington disease, was mapped to chromosome 4 in 1983 and cloned in 1993. The mutation is a characteristic expansion of a nucleotide triplet repeat in the DNA that codes for the protein huntingtin. As the number of repeated triplets - CAG (cytosine, adenine, guanine) - increases, the age of onset in the patient decreases. Furthermore, because the unstable trinucleotide repeat can lengthen when passed from parent to child, the age of onset can decrease from one generation to the next. Since people who have those repeats always suffer from Huntington disease, it suggests that the mutation causes a gain-of-function, in which the mRNA or protein takes on a new property or is expressed inappropriately.



Brain section from a patient with Huntington's disease showing dilatation of ventricles and atrophy of caudate nucleus. [Image credit: Kevin Roth and Robert Schmidt, Washington University, St. Louis, MO, USA.]

With the discovery of the HD gene, a new predictive test was developed that allows those at risk to find out whether or not they will develop the disease. Animal models have also been developed, and we know that mice have a gene that is similar to the human HD gene. Research on understanding the mechanism that causes the triplet repeat to increase is ongoing, since its discovery could be critical to the development of an effective treatment for this and other similar diseases.

Related diseases

See other Diseases of the Nervous System

Table of Contents

See Related

Records in Gene

Gene sequence

Genome view see gene locations

Entrez Gene collection of gene-related information

BLink related sequences in different organisms

The literature

Research articles online full text

Books online books section

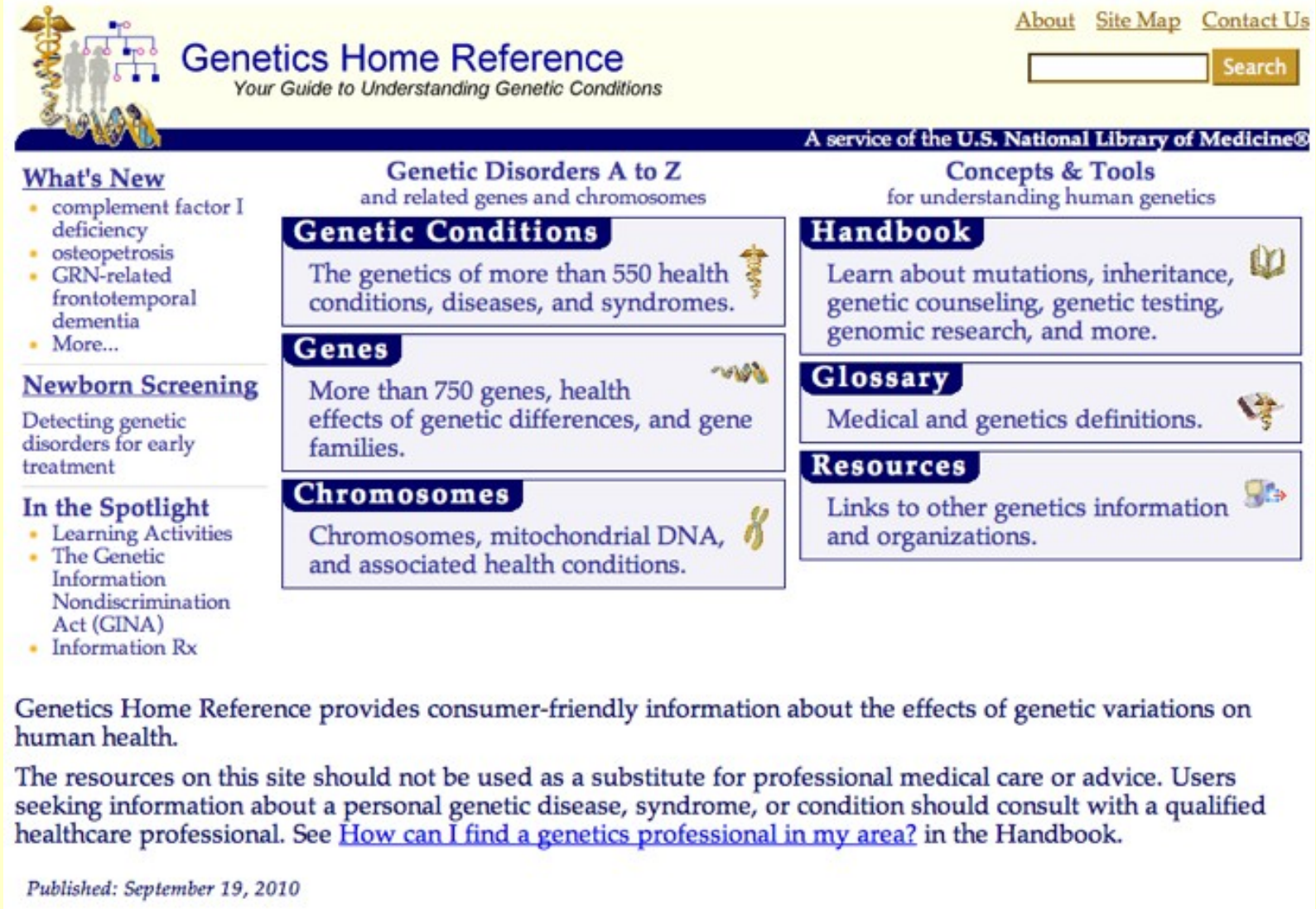
OMIM catalog of human genes and disorders

GeneReviews a medical genetics resource

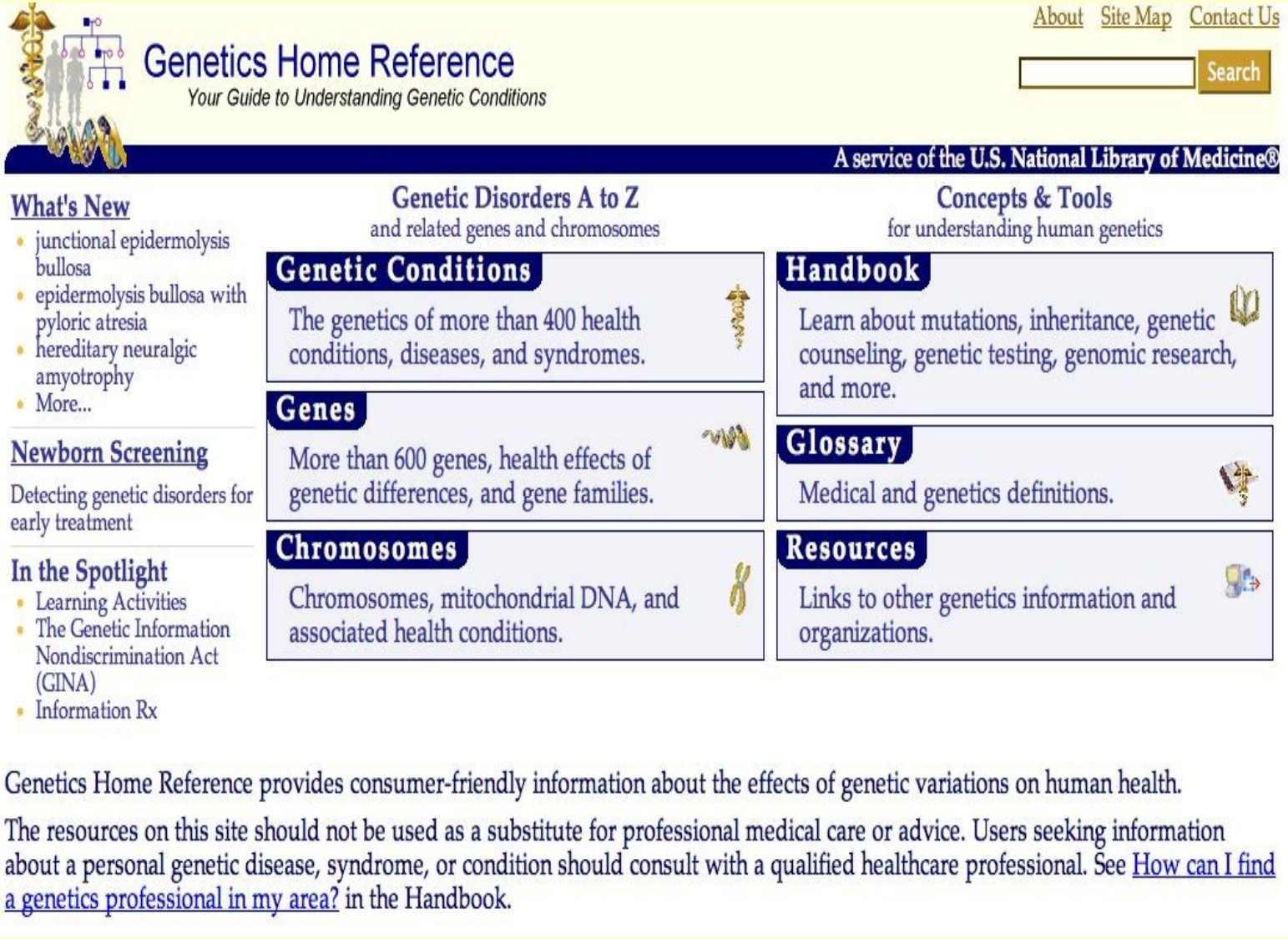
Websites

Huntington Disease Society of America information for patients and the public

Genetics Home Reference



Genetics Home Reference



Genetics Home Reference on HD

Genetics Home Reference
Your Guide to Understanding Genetic Conditions

About Site Map Contact Us

Search

A service of the U.S. National Library of Medicine®

Home | Conditions | Genes | Chromosomes | Handbook | Glossary | Resources

Genetic Conditions >

Huntington disease

Print version

- Related Gene(s)
- References
- Quick links to this topic

MedlinePlus
Health information

Genetic and Rare Diseases Information Center
Information about genetic conditions and rare diseases

Additional NIH Resources
National Institutes of Health

Educational resources
Information pages

Patient support
For patients and families

Gene Reviews
Clinical summary

Gene Tests
DNA test labs

Genetic Tools
Teaching cases

ClinicalTrials.gov
Research studies

PubMed
Recent literature

Online Books
Medical and science texts

OMIM
Genetic disorder catalog

On this page: Description Genetic changes Inheritance Treatment Additional information Other names Glossary definitions

Reviewed October 2008

What is Huntington disease?

Huntington disease is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of thinking ability (cognition).

Adult-onset Huntington disease, the most common form of this disorder, usually appears in a person's thirties or forties. Early signs and symptoms can include irritability, depression, small involuntary movements, poor coordination, and trouble learning new information or making decisions. Many people with Huntington disease develop involuntary jerking or twitching movements known as chorea. As the disease progresses, these movements become more pronounced. Affected individuals may have trouble walking, speaking, and swallowing. People with this disorder also experience changes in personality and a decline in thinking and reasoning abilities. Individuals with the adult-onset form of Huntington disease usually live about 15 to 20 years after signs and symptoms begin.

A less common, early-onset form of Huntington disease begins in childhood or adolescence. It also involves movement problems and mental and emotional changes. Additional signs of the early-onset form include slow movements, clumsiness, frequent falling, rigidity, slurred speech, and drooling. School performance often declines as thinking and reasoning abilities become impaired. Seizures occur in 30 percent to 50 percent of children with this condition. Early-onset Huntington disease tends to progress more quickly than the adult-onset form; affected individuals usually live 10 to 15 years after signs and symptoms appear.

How common is Huntington disease?

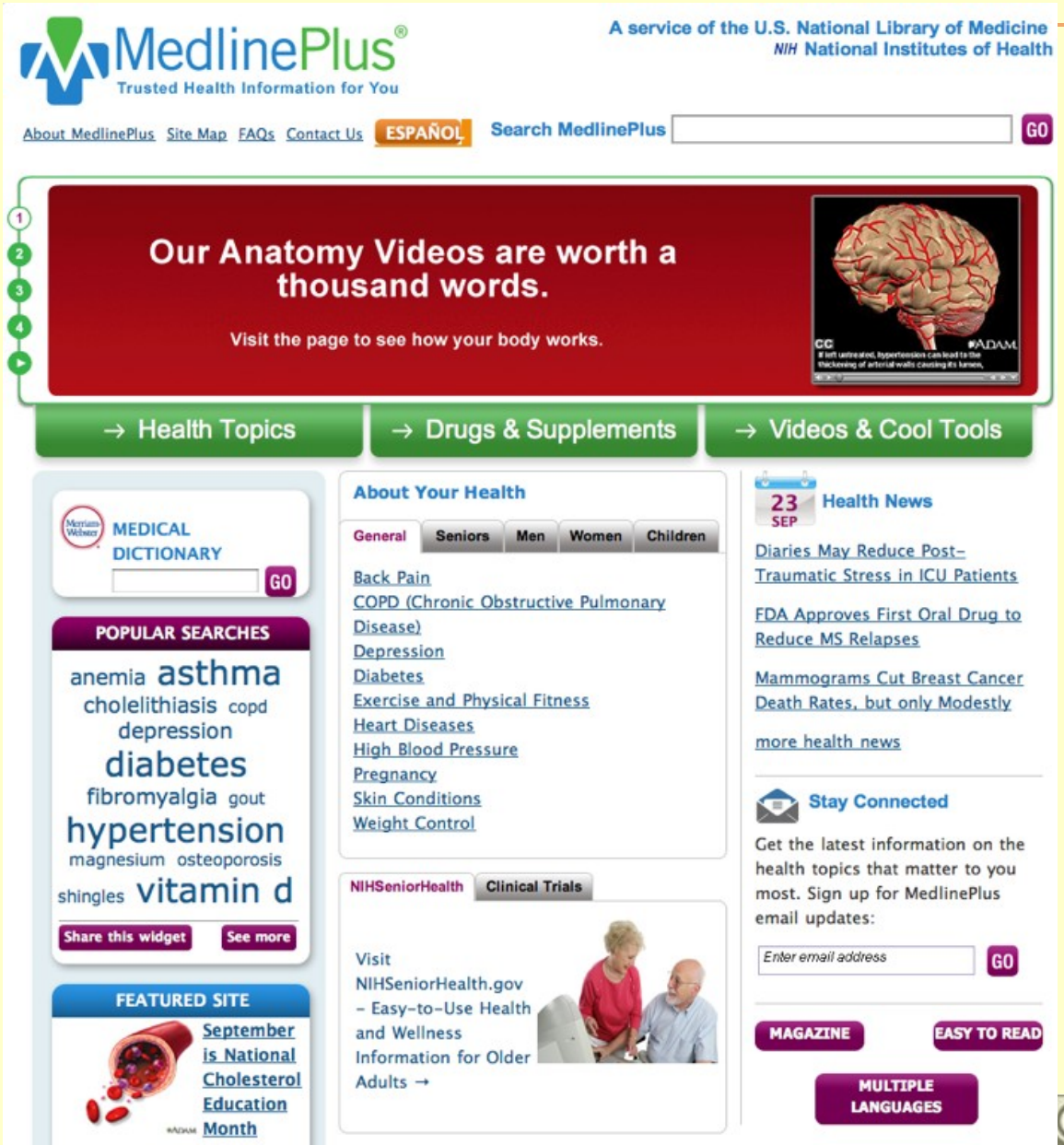
Huntington disease affects an estimated 3 to 7 per 100,000 people of European ancestry. The disorder appears to be less common in some other populations, including people of Japanese, Chinese, and African descent.

What genes are related to Huntington disease?

Mutations in the HTT gene cause Huntington disease. The HTT gene provides instructions for making a protein called huntingtin. Although the function of this protein is unknown, it appears to play an important role in nerve cells (neurons) in the brain.

Medline Plus (NLM)

http://www.nlm.nih.gov/medlineplus/medlineplus.html



Huntington's in Medline Plus

MedlinePlus
Trusted Health Information for You

A service of the U.S. National Library of Medicine
NIH National Institutes of Health

Home About MedlinePlus Site Map FAQs Contact Us

Search MedlinePlus Huntingtons GO

Health Topics | Drugs & Supplements | Videos & Cool Tools | ESPAÑOL

Refine by Type

- All Results (129)
- Health Topics (3)
- External Health Links (91)
- Drugs and Supplements (4)
- Medical Encyclopedia (13)
- Videos and Tutorials
- News (2)
- MedlinePlus Magazine (6)
- Other Resources (10)
- Multiple Languages

Refine by Keyword

All Results (129) remix

- Genetic (35)
- Brain (12)
- Research (12)
- Harvard School of Public Health (15)
- Chorea (8)
- America (8)
- Dementia (11)
- Multiple | Parkinson (7)
- Huntington Beach, CA (6)
- Nerve Diseases (5)

more

Huntington's Disease Search Help

Huntington's disease (HD) is an inherited disease that causes certain nerve cells in the brain to waste away. People are born with the defective gene, but symptoms usually don't appear until middle age. Early symptoms of HD may include uncontrolled movements, clumsiness or balance problems. Later, HD can take away the ability to walk, talk or swallow. Some people stop recognizing family members. Others are aware of their environment and are able to express emotions.

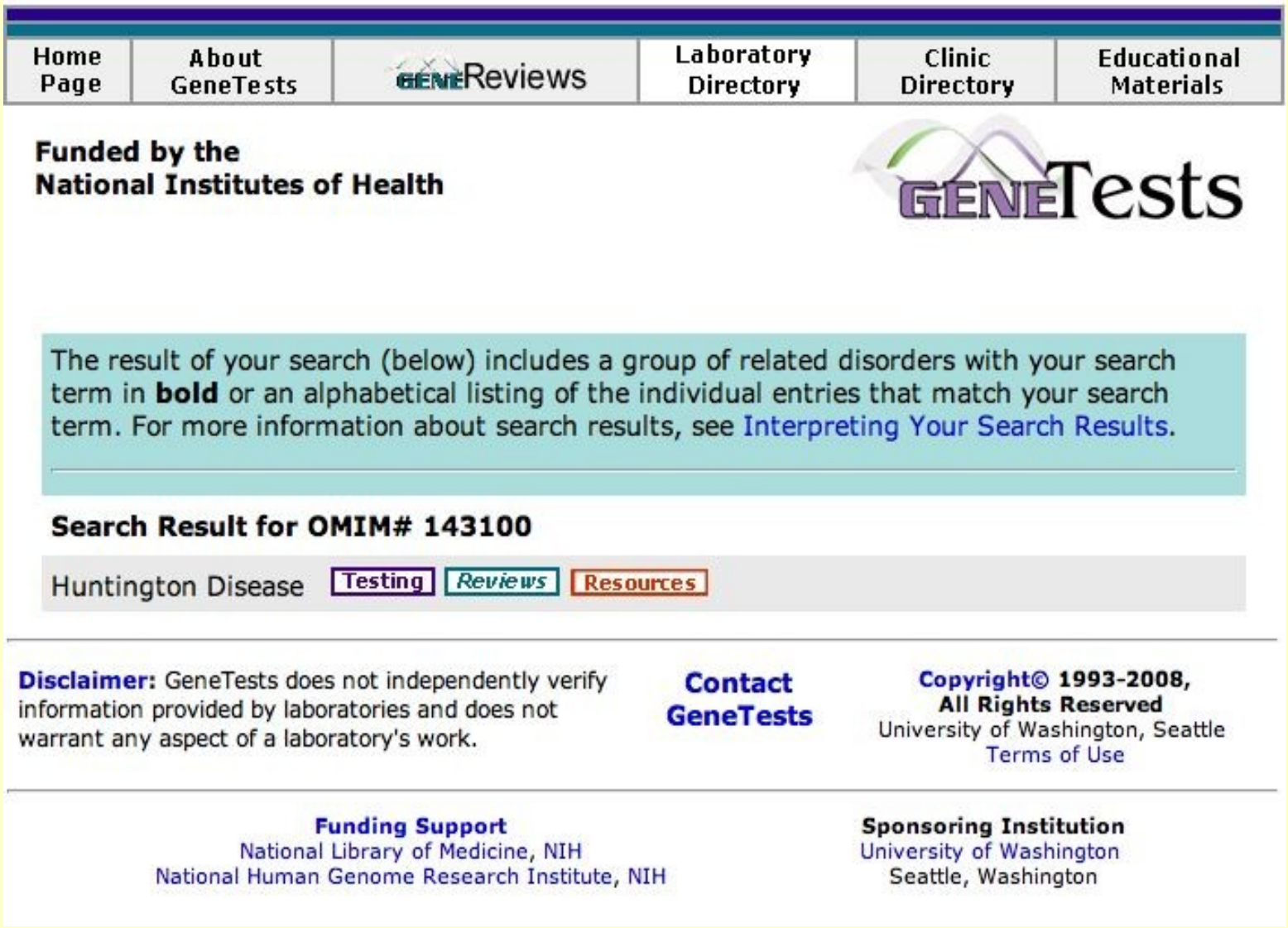
If one of your parents has Huntington's disease, you have a 50-50 chance of getting it. A blood test can tell if you have the HD gene and will develop the disease. Genetic counseling can help you weigh the risks and benefits of taking the test. (Read more)

Results 1 - 10 of 129 for **Huntingtons**

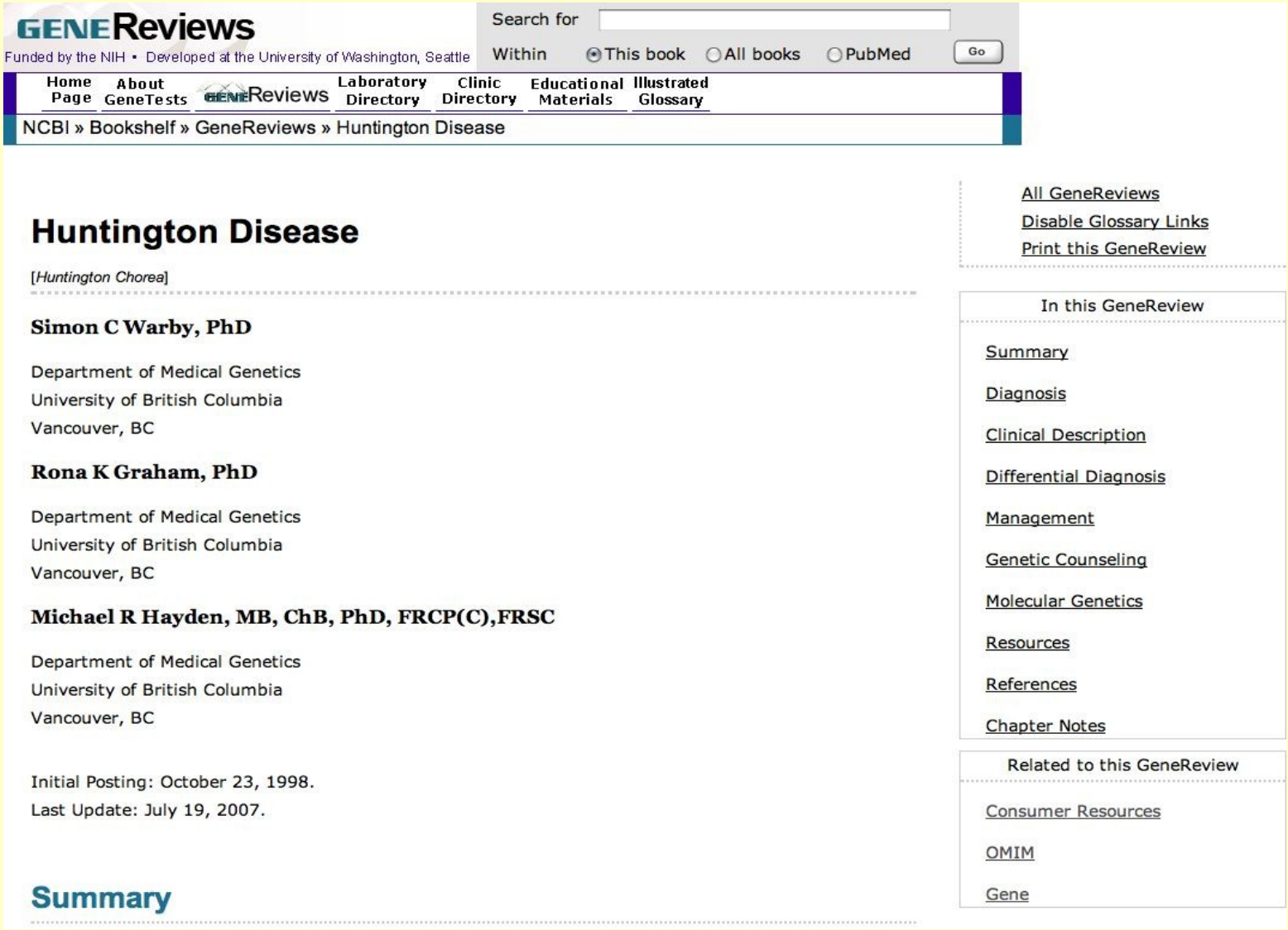
1. **Huntington's Disease** (National Library of Medicine)
   Huntington's disease (HD) is an inherited disease that causes certain nerve cells in the brain to waste ... express emotions. If one of your parents has **Huntington**'s disease, you have a 50-50 chance of ...
   www.nlm.nih.gov/medlineplus/huntingtonsdisease.html - Health Topics
2. **Huntington's disease**
   Huntington chorea ... American doctor George **Huntington** first described the disorder in 1872. **Huntington**'s disease is caused by a genetic defect on chromosome #4. The defect ...
   www.nlm.nih.gov/medlineplus/ency/article/000770.htm - Medical Encyclopedia
3. **Genetics Home Reference: Huntington disease** NIH (National Library of

GeneTests

http://www.genetests.org/



Gene Reviews of Huntington's



GENEReviews

Funded by the NIH • Developed at the University of Washington, Seattle

Search for

Within ◉ This book ○ All books ○ PubMed Go

Home Page | About GeneTests | GeneReviews | Laboratory Directory | Clinic Directory | Educational Materials | Illustrated Glossary

NCBI » Bookshelf » GeneReviews » Huntington Disease

All GeneReviews
Disable Glossary Links
Print this GeneReview

Huntington Disease

[*Huntington Chorea*]

Simon C Warby, PhD

Department of Medical Genetics
University of British Columbia
Vancouver, BC

Rona K Graham, PhD

Department of Medical Genetics
University of British Columbia
Vancouver, BC

Michael R Hayden, MB, ChB, PhD, FRCP(C),FRSC

Department of Medical Genetics
University of British Columbia
Vancouver, BC

Initial Posting: October 23, 1998.
Last Update: July 19, 2007.

In this GeneReview

Related to this GeneReview

Summary

Huntington Disease

[*Huntington Chorea*]

Simon C Warby, PhD

Department of Medical Genetics
University of British Columbia
Vancouver, BC

Rona K Graham, PhD

Department of Medical Genetics
University of British Columbia
Vancouver, BC

Michael R Hayden, MB, ChB, PhD, FRCP(C),FRSC

Department of Medical Genetics
University of British Columbia
Vancouver, BC

Initial Posting: October 23, 1998.
Last Update: July 19, 2007.

All GeneReviews
Disable Glossary Links
Print this GeneReview

In this GeneReview

Summary
Diagnosis
Clinical Description
Differential Diagnosis
Management
Genetic Counseling
Molecular Genetics
Resources
References
Chapter Notes

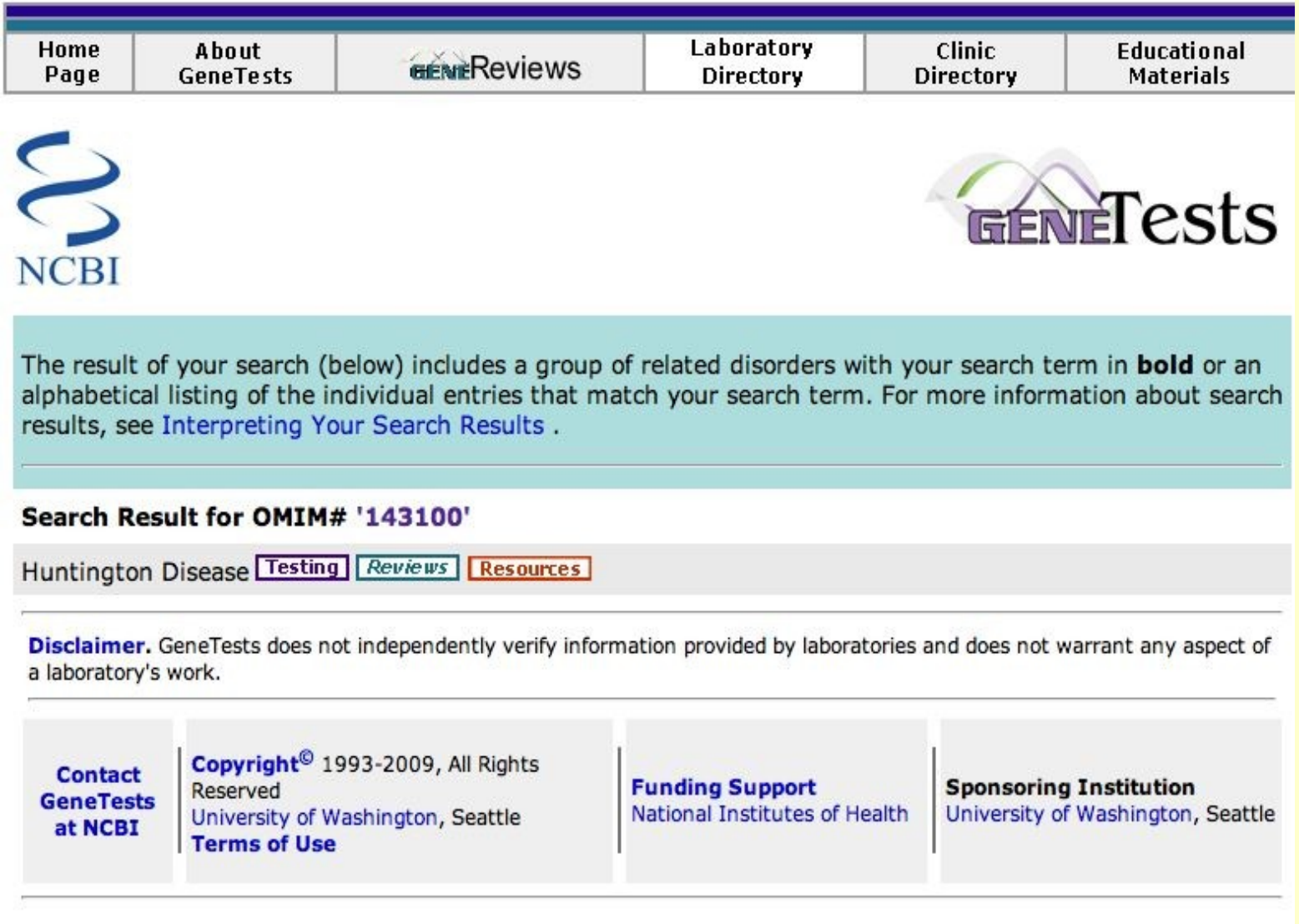
Related to this GeneRevie

Consumer Resources
OMIM
Gene

Summary

Disease characteristics. Huntington disease (HD) is a progressive disorder of motor, cognitive, and psychiatric disturbances. The mean age of onset is 35 to 44 years and the median survival time is 15 to 18 years after onset.

GeneTests, Gene Reviews & Resources



Home Page | About GeneTests | GeneReviews | Laboratory Directory | Clinic Directory | Educational Materials

NCBI

GeneTests

The result of your search (below) includes a group of related disorders with your search term in **bold** or an alphabetical listing of the individual entries that match your search term. For more information about search results, see Interpreting Your Search Results .

Search Result for OMIM# '143100'

Huntington Disease Testing Reviews Resources

Disclaimer. GeneTests does not independently verify information provided by laboratories and does not warrant any aspect of a laboratory's work.

Contact GeneTests at NCBI

Copyright© 1993-2009, All Rights Reserved
University of Washington, Seattle
Terms of Use

Funding Support
National Institutes of Health

Sponsoring Institution
University of Washington, Seattle

NCBI

GeneTe

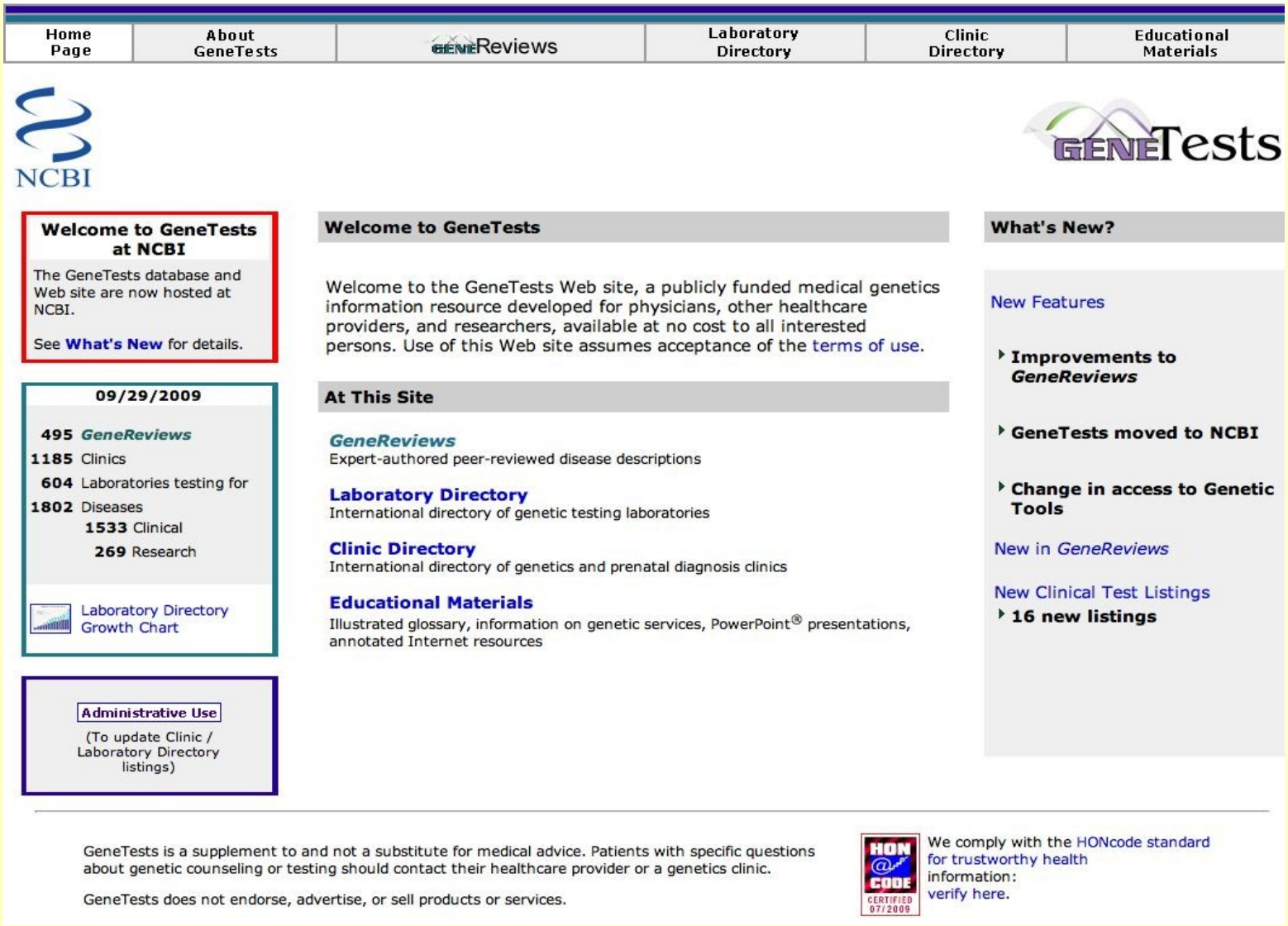
Huntington Disease | Huntington Chorea

Items 1 - 61 of 61

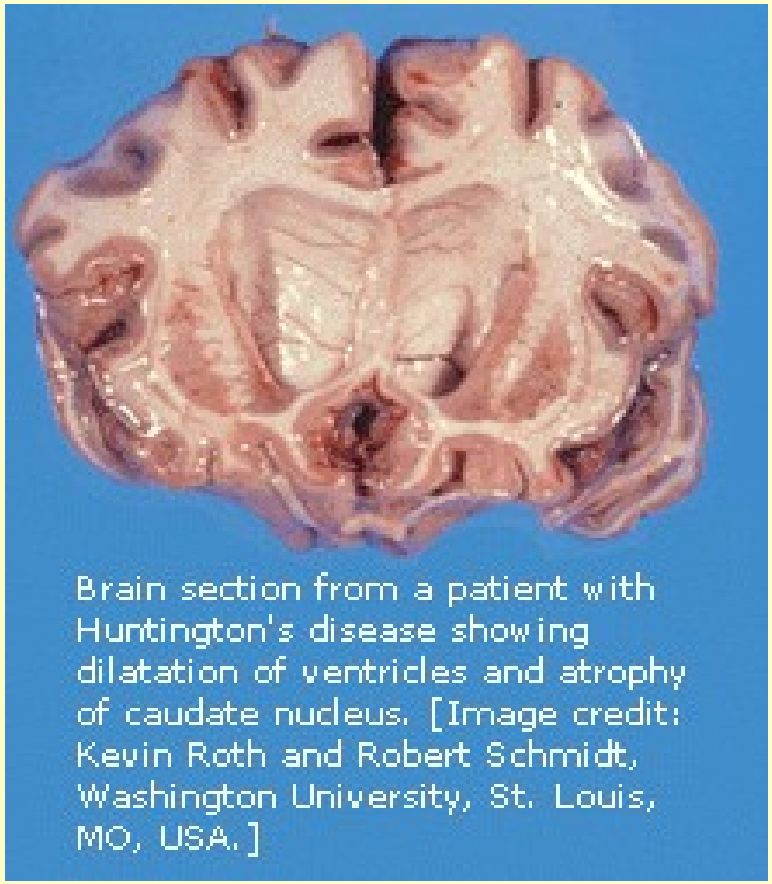
For this search term: **View details of clinical laboratories**

Laboratories offering clinical testing:	Targeted mutation analysis	Linkage analysis
All Children's Hospital Molecular Genetics Laboratory St. Petersburg, FL O Thomas Mueller, PhD, FACMG	•	
ARUP Laboratories Molecular Genetics Laboratory Salt Lake City, UT Elaine Lyon, PhD; Rong Mao, MD; Edward R Ashwood, MD; Pinar Bayrak-Toydemir, MD, PhD	•	
Athena Diagnostics Inc Reference Lab Worcester, MA Sat Dev Batish, PhD, FACMG; Masamichi Ito, PhD, FACMG; Christine M Stanley, PhD, FACMG	•	
Baylor College of Medicine Medical Genetics Laboratories Houston, TX Sau W. Cheung, PhD; Christine M Eng, MD, FACMG; William E O'Brien, PhD; Lee-Jun Wong, PhD	•	
Boston University School of Medicine Center for Human Genetics Boston, MA Aubrey Milunsky, MD, DSc; Jeff Mark Milunsky, MD	•	
Center for Genetic Testing at Saint Francis Genetics Laboratory Tulsa, OK Frederick V Schaefer, PhD, FACMG; Nancy J Carpenter, PhD, FACMG; Michael A Kayser, DO, FACMG	•	
Centogene GmbH Institute of Molecular Diagnostics Rostock, Germany Christoph Ehlers	•	
Centre for Cellular and Molecular Biology Molecular Diagnostics Division, Genome Research Group Hyderabad, India Giriraj Ratan Chandak, MD, PhD, DNB	•	

GeneTests



Huntington's Brain

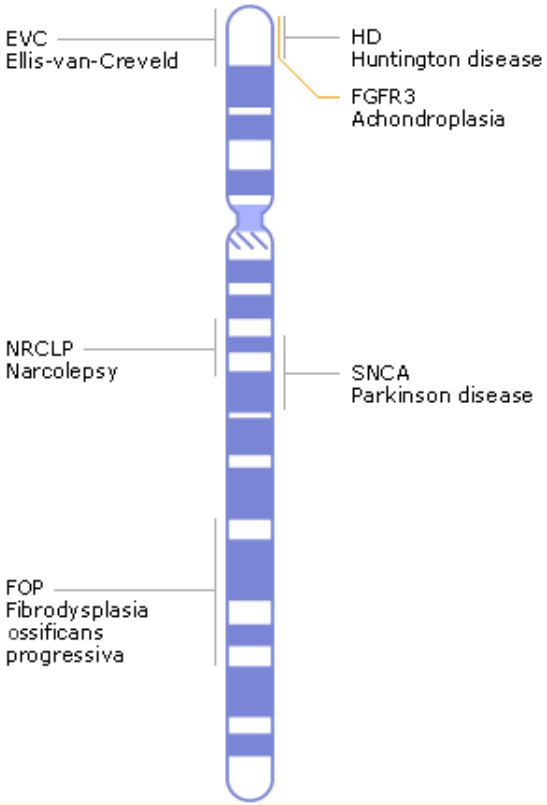


Brain section from a patient with Huntington's disease showing dilatation of ventricles and atrophy of caudate nucleus. [Image credit: Kevin Roth and Robert Schmidt, Washington University, St. Louis, MO, USA.]

Chromosome 4

Chromosome 4

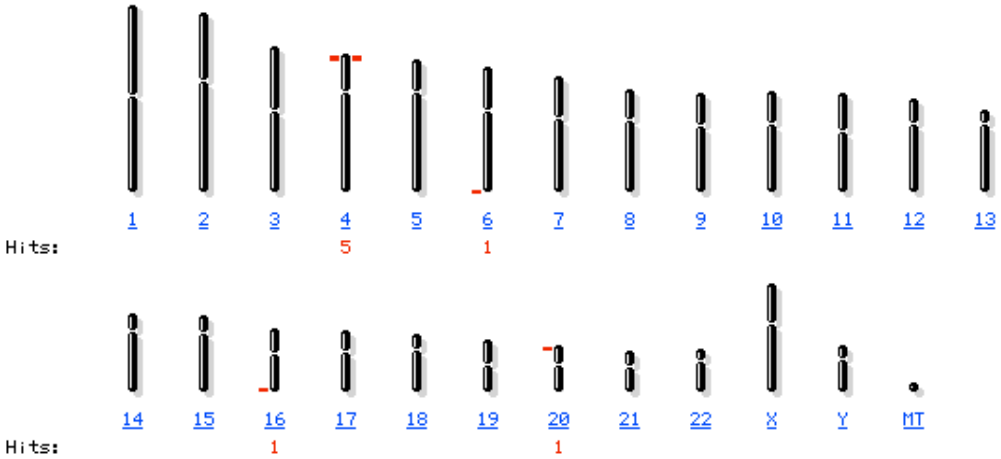
- Contains approximately 1600 genes
- Contains approximately 190 million base pairs, of which ~95% have been determined
- See the diseases associated with chromosome 4 in the MapViewer



Genome View

***Homo_sapiens* genome view**
Build 35.1 statistics

BLAST search the human genome



Search results for query "Huntington": 8 hits

Chr	Assembly	Match	Map element	Type	Maps
4	reference	all matches			
		Huntington disease-like 3	HLN2	MIM	Pheno | Morbid
		Huntington disease	HD	MIM	Pheno | Morbid
		huntingtin (Huntington disease)	HD	Gene	Genes_seq | Genes_cyto
4	Celera	all matches			
		Huntington disease-like 3	HLN2	MIM	Pheno
		huntingtin (Huntington disease)	HD	Gene	Genes_seq
6	reference	Spinocerebellar ataxia 17, 607136; Parkinson disease, 168600...	TBP	MIM	Pheno | Morbid
16	reference	Huntington disease-like 2, 606438	JPH3	MIM	Pheno | Morbid
20	reference	Creutzfeldt-Jakob disease, 123400; Gerstmann-Straussler disease...	176640	MIM	Morbid | Pheno

Gene Resources for Huntington

Jan 12 2009 14:16 PST

GeneTests
www.genetests.org

Huntington Disease Resources

- **Caring for People with Huntington's Disease**
  www.kumc.edu/hospital/huntingtons/index.html

- **High Q Foundation**
  350 Seventh Avenue Suite 601
  New York NY 10001
  Phone: 212-239-9300
  Fax: 212-239-2101
  Email: Please see the contacts page located at www.HighQFoundation.org/contacts
  www.highqfoundation.org

- **Huntington Society of Canada**
  151 Frederick Street Suite 400
  Kitchener ON N2H 2M2
  Canada
  Phone: 800-998-7398; 519-749-7063
  Fax: 519-749-8965
  Email: info@hsc-ca.org
  www.hsc-ca.org

- **Huntington's Disease Society of America (HDSA)**
  505 Eighth Avenue
  New York NY 10018
  Phone: 800-345-HDSA (800-3345-4372); 212-242-1968
  Fax: 212-239-3430
  Email: hdsainfo@hdsa.org
  www.hdsa.org

- **International Huntington Association**
  Email: iha@huntington-assoc.com
  www.huntington-assoc.com

- **National Library of Medicine Genetics Home Reference**
  Huntington disease

- **NCBI Genes and Disease**
  Huntington disease

- **Testing for Huntington Disease: Making an Informed Choice**
  Booklet providing information about Huntington disease and
  depts.washington.edu/neurogen/HuntingtonDis.pdf

#143100
HUNTINGTON DISEASE; HD

GeneTests, Links

Alternative titles; symbols

HUNTINGTON CHOREA

Gene map locus 4p16.3

TEXT

A number sign (#) is used with this entry because Huntington disease (HD) is caused by an expanded trinucleotide repeat in the gene encoding huntingtin (HTT; 613004) on chromosome 4p16.3.

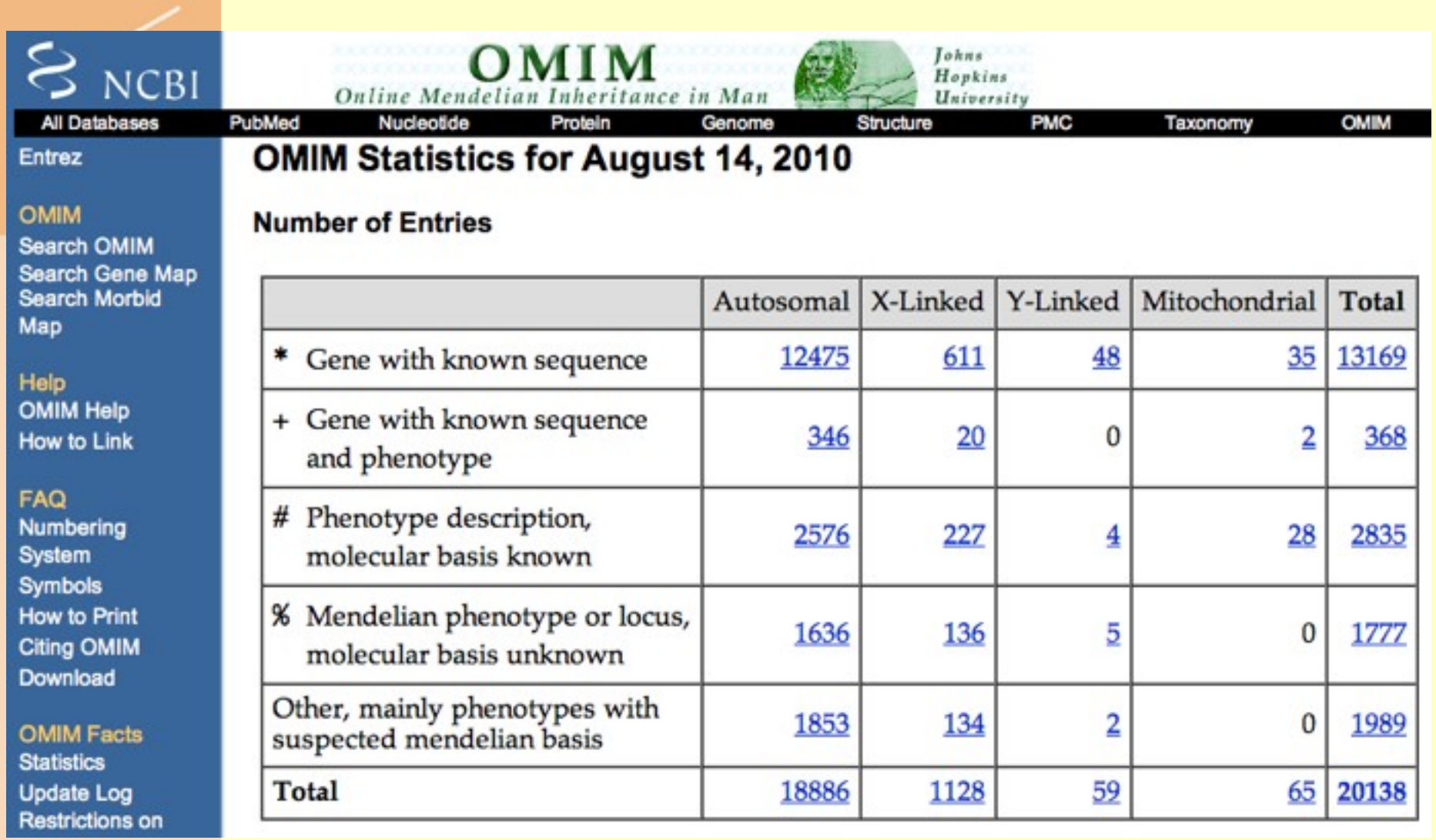
DESCRIPTION

Huntington disease (HD) is an autosomal dominant progressive neurodegenerative disorder with a distinct phenotype characterized by chorea, dystonia, incoordination, cognitive decline, and behavioral difficulties. There is progressive, selective neural cell loss and atrophy in the caudate and putamen. Walker (2007) provided a detailed review of Huntington disease, including clinical features, populatio genetics, molecular biology, and animal models.

CLINICAL FEATURES

The classic signs of Huntington disease are progressive chorea, rigidity, and dementia. A characteristi atrophy of the caudate nucleus is seen radiographically. Typically, there is a prodromal phase of mild psychotic and behavioral symptoms which precedes frank chorea by up to 10 years. Chandler et al. (1960) observed that the age of onset was between 30 and 40 years. In a study of 196 kindreds, Reed a

OMIM Statistics



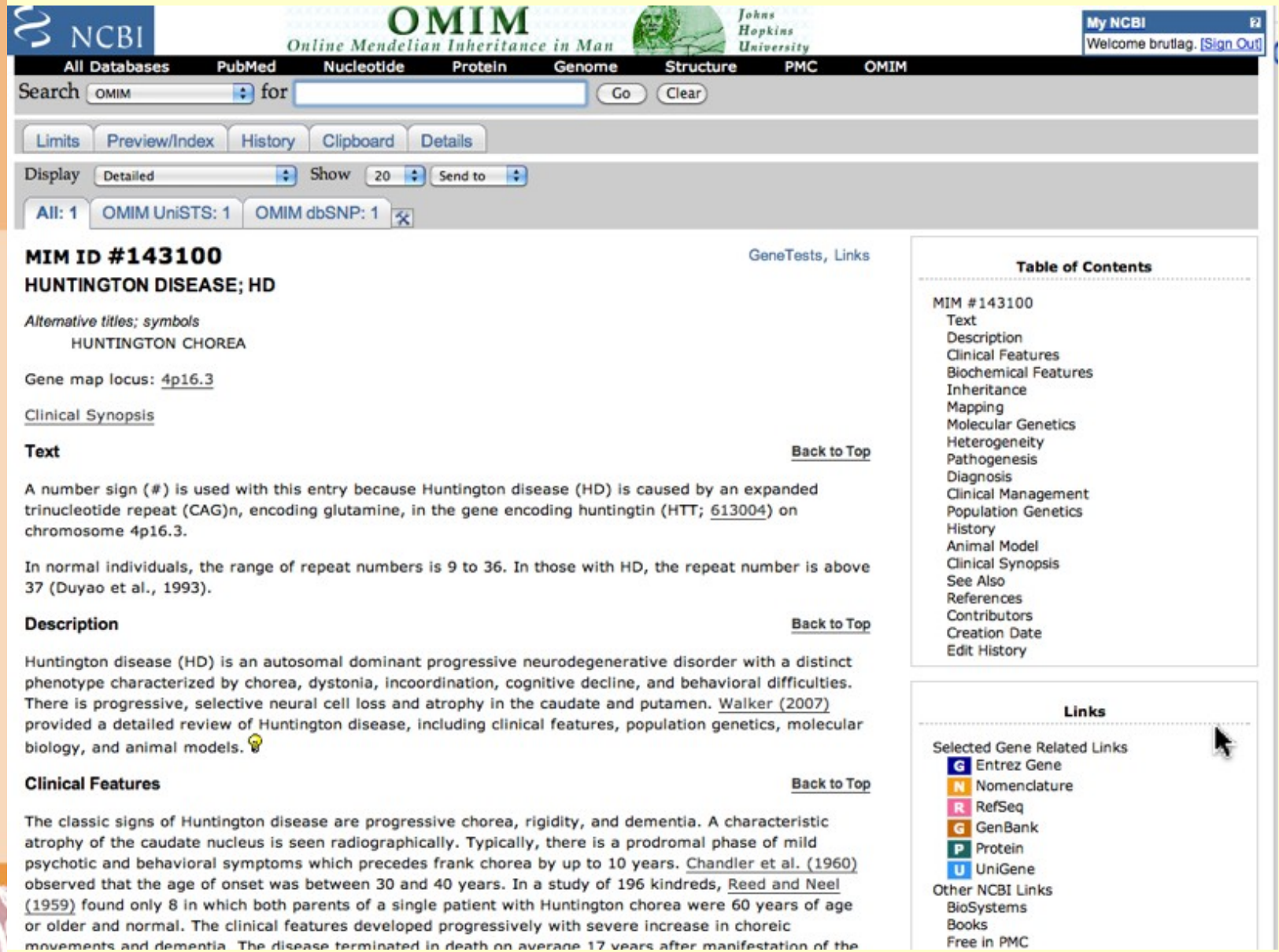
OMIM Statistics for August 14, 2010

Number of Entries

	Autosomal	X-Linked	Y-Linked	Mitochondrial	Total
* Gene with known sequence	12475	611	48	35	13169
+ Gene with known sequence and phenotype	346	20	0	2	368
# Phenotype description, molecular basis known	2576	227	4	28	2835
% Mendelian phenotype or locus, molecular basis unknown	1636	136	5	0	1777
Other, mainly phenotypes with suspected mendelian basis	1853	134	2	0	1989
Total	18886	1128	59	65	**20138**

OMIM
Online Mendelian Inheritance in Man

OMIM Links



Symbol Report: HTT

About HGNC | Gene Search | Guidelines | Gene Submission | Downloads | Home

Giving unique and meaningful names to every human gene

Quick Gene Search

Core Data	
Approved Symbol +	HTT
Approved Name +	huntingtin
HGNC ID +	HGNC:4851
Status +	Approved
Chromosome +	4p16.3
Previous Symbols +	HD
Previous Names +	"huntingtin (Huntington disease)"
Aliases +	IT15
Name Aliases +	
Locus Type +	gene with protein product

Gene Symbol Links

GENATLAS GeneCards GeneClinics/GeneTests GoPubmed

HCOP H-InvDB Treefam wikigenes

Specialist Database Links

COSMIC Orphanet:16190

Database Links				
RefSeq IDs +				
NM_002111	GenBank	EMBL	DDBJ	UCSC
Accession Numbers +				
L12392	GenBank	EMBL	DDBJ	UCSC
Mouse Genome Database ID +				
MGI:96067	MGD ID			
Rat Genome Database ID (mapped data supplied by RGD) +				
RGD:68337	RGD ID			
Entrez Gene ID +				
3064	Gene		Map Viewer	
CCDS IDs +				
CCDS43206.1	CCDS ID			
Pubmed IDs +				
8458085	PMID		CiteXplore	
Ensembl ID (mapped data supplied by Ensembl) +				
ENSG00000197386	Ensembl GeneView		UCSC	
OMIM ID (mapped data supplied by NCBI) +				
613004	OMIM			
UCSC ID (mapped data supplied by UCSC) +				
uc010icr.1	UCSC Index			
UniProt ID (mapped data supplied by UniProt) +				
P42858	UniProt		UCSC	

1: HTT huntingtin [*Homo sapiens*]

GeneID: 3064 updated 16-Sep-2009

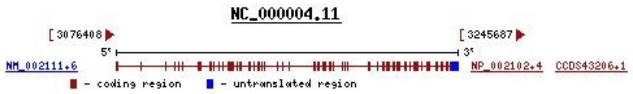
Summary

Official Symbol	HTT provided by HGNC
Official Full Name	huntingtin provided by HGNC
Primary source	HGNC:4851
See related	Ensembl:ENSG00000197386; HPRD:00883; MIM:613004
Gene type	protein coding
RefSeq status	REVIEWED
Organism	*Homo sapiens*
Lineage	*Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo*
Also known as	HD; IT15; HTT
Summary	Huntingtin is a disease gene linked to Huntington's disease, a neurodegenerative disorder characterized by loss of striatal neurons. This is thought to be caused by an expanded, unstable trinucleotide repeat in the huntingtin gene, which translates as a polyglutamine repeat in the protein product. A fairly broad range in the number of trinucleotide repeats has been identified in normal controls, and repeat numbers in excess of 40 have been described as pathological. The huntingtin locus is large, spanning 180 kb and consisting of 67 exons. The huntingtin gene is widely expressed and is required for normal development. It is expressed as 2 alternatively polyadenylated forms displaying different relative abundance in various fetal and adult tissues. The larger transcript is approximately 13.7 kb and is expressed predominantly in adult and fetal brain whereas the smaller transcript of approximately 10.3 kb is more widely expressed. The genetic defect leading to Huntington's disease may not necessarily eliminate transcription, but may confer a new property on the mRNA or alter the function of the protein. One candidate is the huntingtin-associated protein-1, highly expressed in brain, which has increased affinity for huntingtin protein with expanded polyglutamine repeats. This gene contains an upstream open reading frame in the 5' UTR that inhibits expression of the huntingtin gene product through translational repression. [provided by RefSeq]

Genomic regions, transcripts, and products

Go to reference sequence details

Try our new Sequence Viewer



Entrez Gene Home

Table Of Contents

Summary
Genomic regions, transcripts...
Genomic context
Bibliography
Interactions
General gene information
General protein information
Reference Sequences
Related Sequences
Additional Links

Links Explai

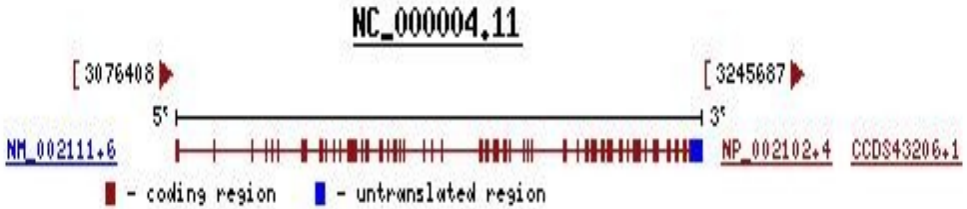
Order cDNA clone
BioSystems
Books
CCDS
Genome
GEO Profiles
HomoloGene
✓ Map Viewer
Nucleotide
OMIM
BioAssay, by Gene target
PubChem Compound
PubChem Substance
Full text in PMC
Probe
Protein
PubMed
PubMed (OMIM)
PubMed (GeneRIF)
SNP
SNP VarView
SNP: Genotype
SNP: GeneView
Taxonomy
UniSTS
AceView
Ensembl
Evidence Viewer
GeneTests for MIM: 143100
HGNC
HPRD

NCBI

Genomic regions, transcripts, and products

Go to reference sequence details

Try our new Sequence Viewer



Genomic context

chromosome: 4; Location: 4p16.3

See HTT in MapViewer

NCBI

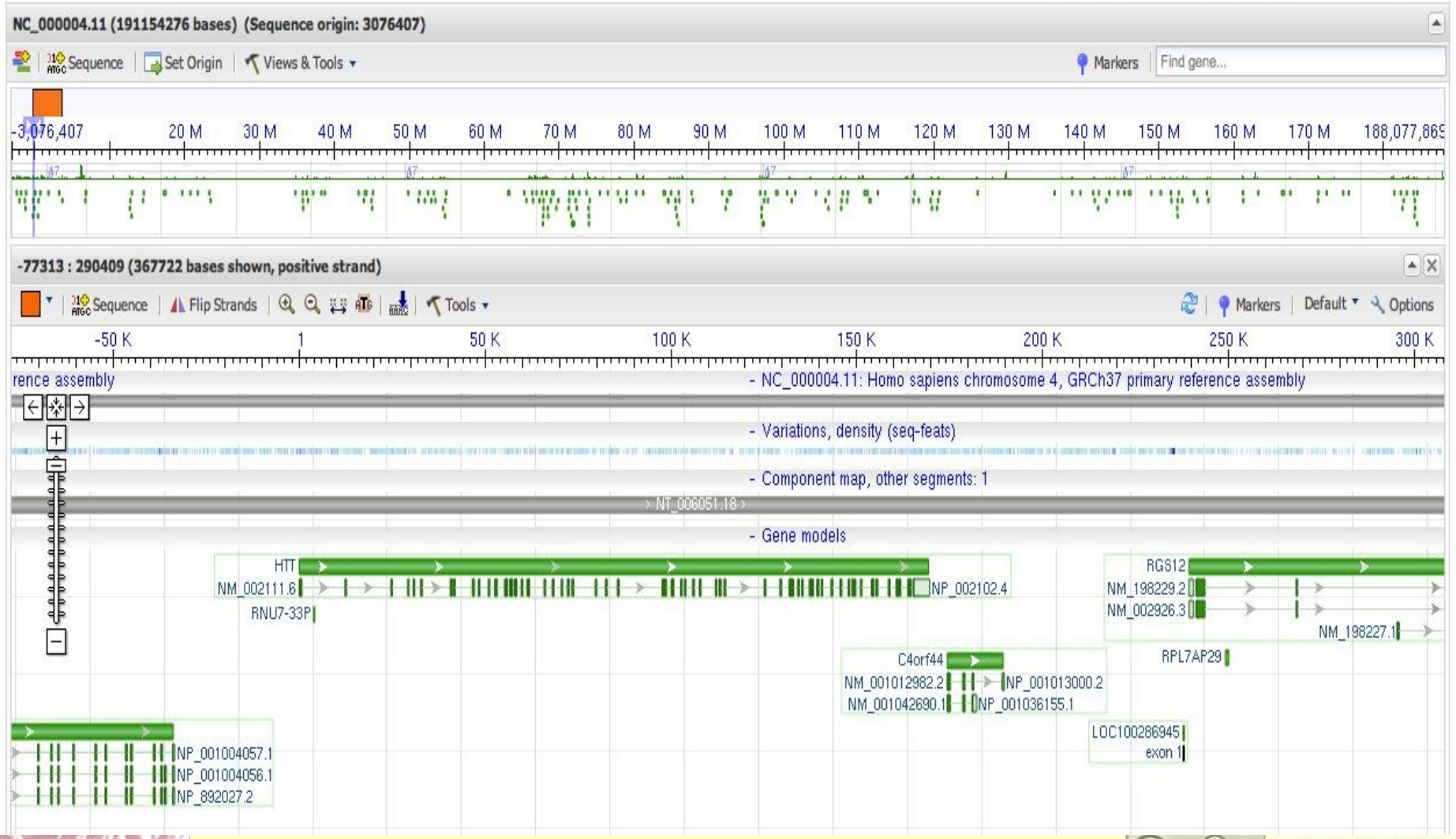
History | Clipboard | Details

Format: GenBank FASTA **Graphics** More Formats▼ Download▼ Save▼ Links▼

NCBI Reference Sequence: NC_000004.11

Homo sapiens chromosome 4, GRCh37 primary reference assembly

Link To This Page | Help | Feedback | Printer-Friendly Page



MapView of HTT Gene

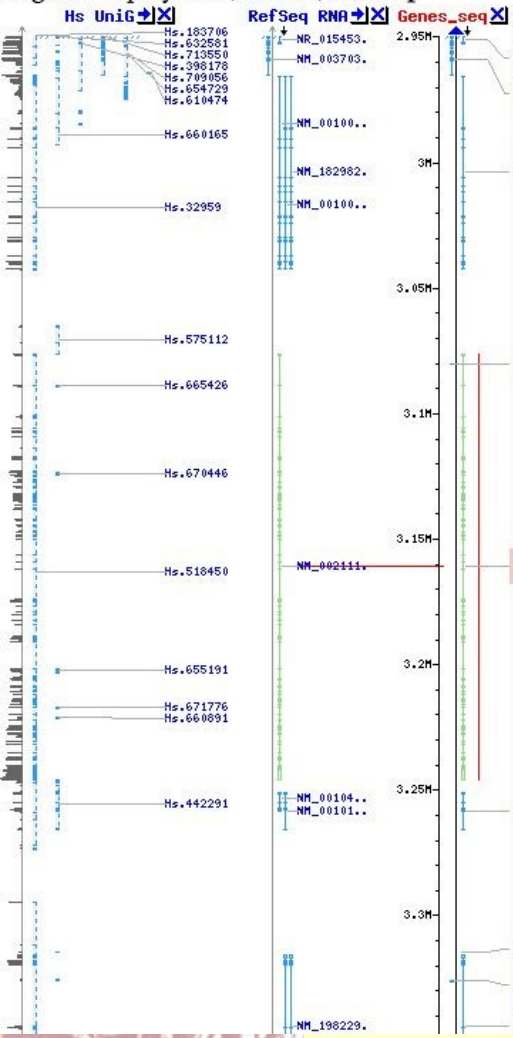
Homo sapiens (human) **Build 37.1 (Current)** BLAST The Human Genome

Chromosome: 1 2 3 [4] 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y MT

Query: 3064[gene_id] [clear]

Master Map: Genes On Sequence Summary of Maps Maps & Options

Region Displayed: **2,950K-3,370K bp** Download / View Sequence / Evidence



Symbol	O	Links	E	Cyto	Description
C4orf10	+	HGNC sv pr dlev mm sts	best RefSeq	4p16.3	chromosome 4 open reading frame 10
NOP14	+	OMIM HGNC sv pr dlev mm hm sts SNP	best RefSeq	4p16.3	NOP14 nucleolar protein homolog (yeast)
GRK4	+	OMIM HGNC sv pr dlev mm hm sts SNP	best RefSeq	4p16.3	G protein-coupled receptor kinase 4
RNU7-33P	+	HGNC sv dlev mm	best RefSeq	4p16.3	RNA, U7 small nuclear 33 pseudogene
HTT	+	OMIM HGNC sv pr dlev mm hm sts SNP	best RefSeq	4p16.3	huntingtin
C4orf44	+	HGNC sv pr dlev mm hm SNP	best RefSeq	4p16.3	chromosome 4 open reading frame 44
LOC100286945	+	sv dlev mm	protein	4p16.3	hypothetical LOC100286945
RPL7AP29	+	HGNC sv dlev mm	best RefSeq	4p16.2	ribosomal protein L7a pseudogene 29
RGS12	+	OMIM HGNC sv pr dlev mm hm sts SNP	best RefSeq	4p16.3	regulator of G-protein signaling 12

Huntingtin Protein

NCBI Reference Sequence: NP_002102.4

huntingtin [Homo sapiens]

Comment Features Sequence

```
LOCUS       NP_002102               3144 aa            linear   PRI 18-SEP-2009
DEFINITION  huntingtin [Homo sapiens].
ACCESSION   NP_002102
VERSION     NP_002102.4  GI:90903231
DBSOURCE    REFSEQ: accession NM_002111.6
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 3144)
  AUTHORS   Harper,S.Q.
  TITLE     Progress and challenges in RNA interference therapy for Huntington
            disease
  JOURNAL   Arch. Neurol. 66 (8), 933-938 (2009)
   PUBMED   19667213
  REMARK    GeneRIF: Reducing mutant huntingtin expression may offer a
            treatment for Huntington disease. RNA interference has emerged as a
            powerful method to silence dominant disease genes.
            Review article
REFERENCE   2  (residues 1 to 3144)
  AUTHORS   Morfini,G.A., You,Y.M., Pollema,S.L., Kaminska,A., Liu,K.,
            Yoshioka,K., Bjorkblom,B., Coffey,E.T., Bagnato,C., Han,D.,
            Huang,C.F., Banker,G., Pigino,G. and Brady,S.T.
  TITLE     Pathogenic huntingtin inhibits fast axonal transport by activating
            JNK3 and phosphorylating kinesin
  JOURNAL   Nat. Neurosci. 12 (7), 864-871 (2009)
   PUBMED   19525941
  REMARK    GeneRIF: data identify JNK3 as a critical mediator of pathogenic
            Htt (polyQ-Htt)toxicity and provide a molecular basis for
            polyQ-Htt-induced inhibition of fast axonal transport
```

NCBI

Hu TA)

NCBI Reference Sequence: NP_002102.4

huntingtin [Homo sapiens]

>gi|90903231|ref|NP_002102.4| huntingtin [Homo sapiens]

MATLEKLMKAFESLKSFQQQQQQQQQQQQQQQQQQQQQQQPPPPPPPPPPQLPQPPPQAQPLLPQPQPP
PPPPPPPPGPAVAEEPLHRPKKELSATKKDRVNHCLTICENIVAQSVRNSPEFQKLLGIAMELFLLCSDD
AESDVRMVADECLNKVIKALMDSNLPRLQLELYKEIKKNGAPRSLRAALWRFAELAHLVRPQKCRPYLVN
LLPCLTRTSKRPEESVQETLAAAVPKIMASFGNFANDNEIKVLLKAFIANLKSSSPTIRRTAAGSAVSIC
QHSRRTQYFYSWLLNVLLGLLVPVEDEHSTLLILGVLLTLRYLVPLLQQQVKDTSLKGSFGVTRKEMEVS
PSAEQLVQVYELTLHHTQHQDHNVVTGALELLQQLFRTPPPELLQTLTAVGGIGQLTAAKEESGGRSRSG
SIVELIAGGGSSCSPVLSRKQKGKVLLGEEEALEDDSESRSDVSSSALTASVKDEISGELAASSGVSTPG
SAGHDIITEQPRSQHTLQADSVDLASCDLTSSATDGDEEDILSHSSSQVSAVPSDPAMDLNDGTQASSPI
SDSSQTTTEGPDSAVTPSDSSEIVLDGTDNQYLGLQIGQPQDEDEEATGILPDEASEAFRNSSMALQQAH
LLKNMSHCRQPSDSSVDKFVLRDEATEPGDQENKPCRIKGDIGQSTDDDSAPLVHCVRLLSASFLLTGGK
NVLVPDRDVRVSVKALALSCVGAAVALHPESFFSKLYKVPLDTTEYPEEQYVSDILNYIDHGDPQVRGAT
AILCGTLICSILSRSRFHVGDWMGTIRTLTGNTFSLADCIPLLRKTLKDESSVTCKLACTAVRNCVMSLC
SSSYSELGLQLIIDVLTLRNSSYWLVRTELLETLAEIDFRLVSFLEAKAENLHRGAHHYTGLLKLQERVL
NNVVIHLLGDEDPRVRHVAAASLIRLVPKLFYKCDQGQADPVVAVARDQSSVYLKLLMHETQPPSHFSVS
TITRIYRGYNLLPSITDVTMENNLSRVIAAVSHELITSTTRALTFGCCEALCLLSTAFPVCIWSLGWHCG
VPPLSASDESRKSCTVGMATMILTLLSSAWFPLDLSAHQDALILAGNLLAASAPKSLRSSWASEEEANPA
ATKQEEVWPALGDRALVPMVEQLFSHLLKVINICAHVLDDVAPGPAIKAALPSLTNPPSLSPIRRKGKEK
EPGEQASVPLSPKKGSEASAASRQSDTSGPVTTSKSSSLGSFYHLPSYLKLHDVLKATHANYKVTLDLQN
STEKFGGFLRSALDVLSQILELATLQDIGKCVEEILGYLKSCFSREPMMATVCVQQLLKTLFGTNLASQF
DGLSSNPSKSQGRAQRLGSSSVRPGLYHYCFMAPYTHFTQALADASLRNMVQAEQENDTSGWFDVLQKVS
TQLKTNLTSVTKNRADKNAIHNHIRLFEPLVIKALKQYTTTTCVQLQKQVLDLLAQLVQLRVNYCLLDSD
QVFIGFVLKQFEYIEVGQFRESEAIIPNIFFFLVLLSYERYHSKQIIGIPKIIQLCDGIMASGRKAVTHA
IPALQPIVHDLFVLRGTNKADAGKELETQKEVVVSMLLRLIQYHQVLEMFILVLQQCHKENEDKWKRLSR
QIADIILPMLAKQQMHIDSHEALGVLNTLFEILAPSSLRPVDMLLRSMFVTPNTMASVSTVQLWISGILA
ILRVLISQSTEDIVLSRIQELSFSPYLISCTVINRLRDGDSTSTLEEHSEGKQIKNLPEETFSRFLLQLV
GILLEDIVTKQLKVEMSEQQHTFYCQELGTLLMCLIHIFKSGMFRRITAAATRLFRSDGCGGSFYTLDSL
NLRARSMITTHPALVLLWCQILLLVNHTDYRWWAEVQQTPKRHSLSSTKLLSPQMSGEEEDSDLAAKLGM
CNREIVRRGALILFCDYVCQNLHDSEHLTWLIVNHIQDLISLSHEPPVQDFISAVHRNSAASGLFIQAIQ
SRCENLSTPTMLKKTLQCLEGIHLSQSGAVLTLYVDRLLCTPFRVLARMVDILACRRVEMLLAANLQSSM
AQLPMEELNRIQEYLQSSGLAQRHQRLYSLLDRFRLSTMQDSLSPSPPVSSHPLDGDGHVSLETVSPDKD
WYVHLVKSQCWTRSDSALLEGAELVNRIPAEDMNAFMMNSEFNLSLLAPCLSLGMSEISGGQKSALFEAA
REVTLARVSGTVQQLPAVHHVFQPELPAEPAAYWSKLNDLFGDAALYQSLPTLARALAQYLVVVSKLPSH
LHLPPEKEKDIVKFVVATLEALSWHLIHEQIPLSLDLQAGLDCCCLALQLPGLWSVVSSTEFVTHACSLI
YCVHFILEAVAVQPGEQLLSPERRTNTPKAISEEEEEVDPNTQNPKYITAACEMVAEMVESLQSVLALGH
KRNSGVPAFLTPLLRNIIISLARLPLVNSYTRVPPLVWKLGWSPKPGGDFGTAFPEIPVEFLQEKEVFKE
FIYRINTLGWTSRTQFEETWATLLGVLVTQPLVMEQEESPPEEDTERTQINVLAVQAITSLVLSAMTVPV
AGNPAVSCLEQQPRNKPLKALDTRFGRKLSIIRGIVEQEIQAMVSKRENIATHHLYQAWDPVPSLSPATT
GALISHEKLLLQINPERELGSMSYKLGQVSIHSVWLGNSITPLREEEWDEEEEEEADAPAPSSPPTSPVN
SRKHRAGVDIHSCSQFLLELYSRWILPSSSARRTPAILISEVVRSLLVVSDLFTERNQFELMYVTLTELR
RVHPSEDEILAQYLVPATCKAAAVLGMDKAVAEPVSRLLESTLRSSHLPSRVGALHGVLYVLECDLLDDT
AKQLIPVISDYLLSNLKGIAHCVNIHSQQHVLVMCATAFYLIENYPLDVGPEFSASIIQMCGVMLSGSEE
STPSIIYHCALRGLERLLLSEQLSRLDAESLVKLSVDRVNVHSPHRAMAALGLMLTCMYTGKEKVSPGRT
SDPNPAAPDSESVIVAMERVSVLFDRIRKGFPCEARVVARILPQFLDDFFPPQDIMNKVIGEFLSNQQPY
PQFMATVVYKVFQTLHSTGQSSMVRDWVMLSLSNFTQRAPVAMATWSLSCFFVSASTSPWVAAILPHVIS
RMGKLEQVDVNLFCLVATDFYRHQIEEELDRRAFQSVLEVVAAPGSPYHRLLTCLRNVHKVTTC

SNP Viewer for Huntington

http://www.ncbi.nlm.nih.gov/SNP/snp_ref.cgi?locusId=3064

SNP linked to Gene HTT(geneID:3064) Via Contig Annotation

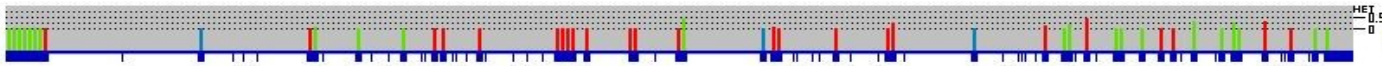
Send rs# on all gene models to Batch Query | Download all rs# to file. | Genotype

Gene Model (mRNA alignment) information from genome sequence

Total gene model (contig mRNA transcript):				3		
mrna	transcript	protein	mrna orientation	Contig	Contig Label	List SNP
NM_002111.6	plus strand	NP_002102.4	forward	NT_006081.18	reference	<- currently shown
NM_002111.6	plus strand	NP_002102.4	forward	NW_921918.1	Celera	View snp on GeneModel
NM_002111.6	minus strand	NP_002102.4	reverse	NW_001838896.2	HuRef	View snp on GeneModel

Include clinically associated | in gene region | cSNP | has frequency | double hit | refresh

gene model (contig mRNA transcript):	Contig Label	Contig	mrna	protein	mrna orientation	transcript	snp count
	reference	NT_006081.18	NM_002111.6	NP_002102.4	forward	plus strand	49, coding



Color Legend

Region	Contig position	mRNA pos	dbSNP rs# cluster id	Hetero-zygosity	Validation	3D	Clinically Associated	Function	dbSNP allele	Protein residue	Codon pos	Amino acid pos	PubMed
exon_1	1582205	146						start codon				1	
exon_1	1582232	173	rs10701858	N.D.				synonymous	CCG		1	10	
								contig reference	-		1	10	
	1582255	196	rs10618869	N.D.				synonymous	CAG		3	17	
								contig reference	-		3	17	
	1582309	250	rs9993357	N.D.				synonymous	A	Gln [Q]	3	35	
								contig reference	G	Gln [Q]	3	35	
	1582315	256	rs473915	N.D.				synonymous	G	Gln [Q]	3	37	
								contig reference	A	Gln [Q]	3	37	
	1582345	286	rs9993367	N.D.				synonymous	T	Pro [P]	3	47	
								contig reference	G	Pro [P]	3	47	

Predictive Testing for Huntington's: Adverse Psychological Events

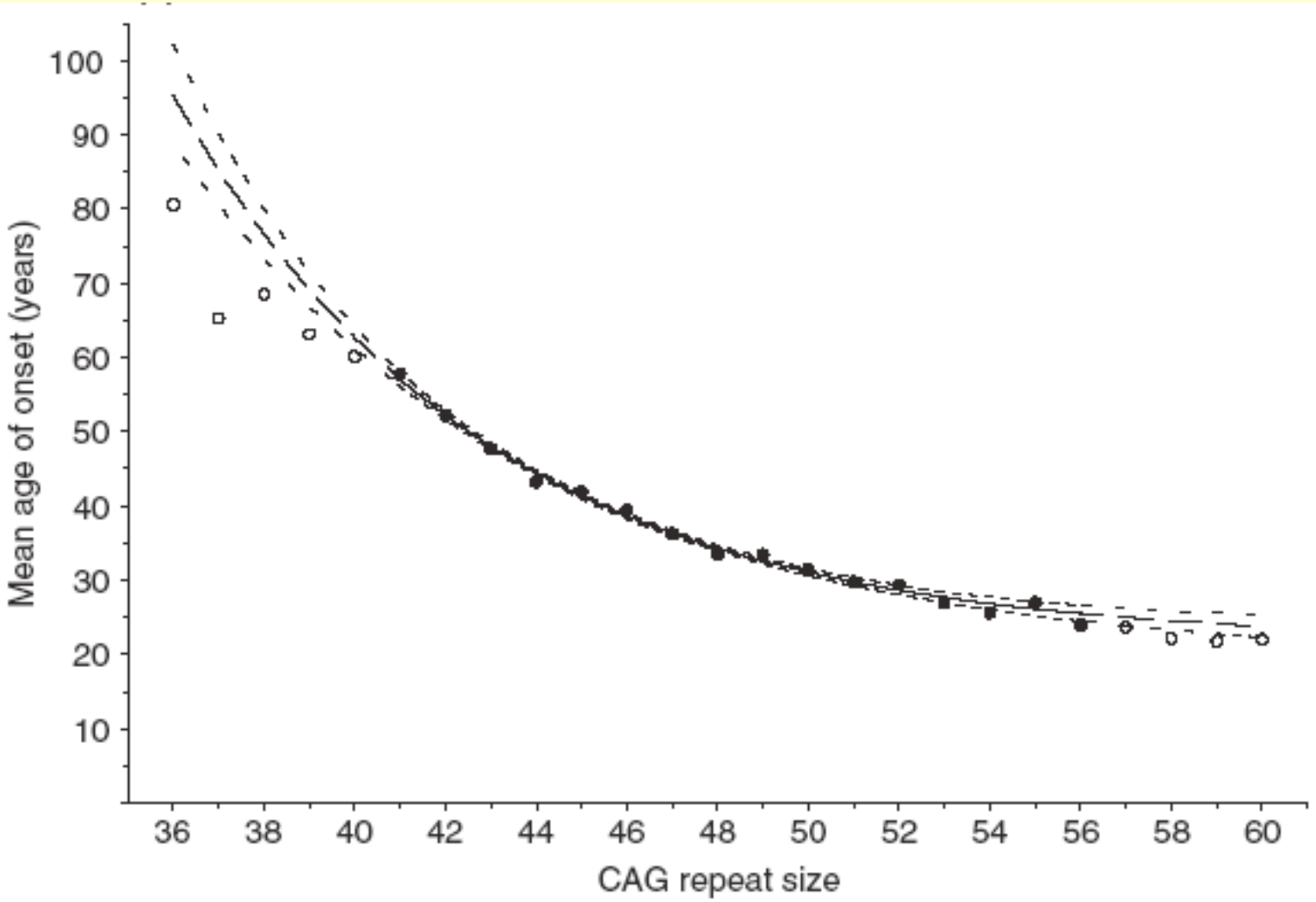
Adverse psychological events occurring in the first year after predictive testing for Huntington's disease. The Canadian Collaborative Study Predictive Testing.

Lawson K, Wiggins S, Green T, Adam S, Bloch M, Hayden MR.

Department of Medical Genetics, University of British Columbia, Vancouver, Canada.

A total of 135 participants in the Canadian predictive testing programme for HD were followed for at least one year in one of four study groups: increased risk (n = 37), decreased risk (n = 58), uninformative (n = 17), or not tested (n = 23). Clinical criteria for an adverse event were a suicide attempt or formulation of a suicide attempt plan, psychiatric hospitalisation, depression lasting longer than two months, a marked increase in substance abuse, and the breakdown of important relationships. Quantitative criteria, as measured by changes on the General Severity Index of the Symptom Checklist 90-R and the Beck Depression Inventory, were also used to identify people who had adverse events. Twenty of the 135 participants (14.8%) had an adverse event. There were no significant differences between those with or without an adverse event with respect to age, sex, marital status, education, psychiatric history, general psychiatric distress, or social supports at baseline. However, evidence for depression was associated with an increased frequency of adverse events ($p < 0.04$). The adverse events were similar and seen with equivalent frequency in those receiving an increased risk or decreased risk and persons at risk who did not receive a modification of risk. However, a significant difference was found in the timing of adverse events for the increased and decreased risk groups ($p < 0.0002$). In the increased risk group all of the adverse events occurred within 10 days after results whereas, in the decreased risk group, all of the adverse events occurred six months or later after reviewing test results. These results suggest that people entering into predictive testing with some evidence of clinical depression warrant special vigilance and also suggest that counselling and support should be available for all participants in predictive testing irrespective of the direction of test results.

Age of Onset and Repeat Length



Case Presentations

- Choose an inherited disease of interest
  - Send disease name in email to brutlag@stanford.edu
- Case Presentation
  - Describe disease and classical symptoms and diagnosis
  - Describe classical treatments if any
  - Describe molecular genetics
    - Mendelian, familial, complex, predisposition?
    - Penetrance
  - Does genetics lead to better diagnostics?
  - Does genetics lead to better therapies?

Fileservers

- Course Web Page
  - http://biochem118.stanford.edu/
- File Repository
  - http://wherever.stanford.edu/biochem118/