Your Genes and Your Health

http://bio84.stanford.edu/

Diseases and Disease Databases

Doug Brutlag, Professor Emeritus
Biochemistry & Medicine
Stanford University School of Medicine
Preventive Medicine

“Superior Doctors Prevent the Disease. Mediocre Doctors Treat the Disease Before Evident. Inferior Doctors Treat the Full Blown Disease.”

-Huang Dee: Nai - Ching (2600 B.C. 1st Chinese Medical Text)
The Molecular Mechanism of Disease

• If we know the gene that causes disease
• And we know the molecular function of that gene
• Then we understand the disease at the molecular level,
• And we know the cause of the disease at the molecular level.
• This knowledge permits development of better treatments, drugs, therapies and interventions to cure the cause of the disease.
NCBI: National Center for Biotechnology Information

Welcome to NCBI

The National Center for Biotechnology Information advances science and health by providing access to biomedical and genomic information.

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Get Started
- Tools: Analyze data using NCBI software
- Downloads: Get NCBI data or software
- How-To's: Learn how to accomplish specific tasks at NCBI
- Submissions: Submit data to GenBank or other NCBI databases

Genotypes and Phenotypes
Data from Genome Wide Association studies that link genes and diseases. See study variables, protocols, and analysis.

NCBI News
NAR's 2011 Database Issue is out with 9 NCBI-Authorved Papers
05 Jan 2011

New articles are available describing the new

New NCBI News Issue
29 Nov 2010

Information about the RefSeqGene Project and
Genes and Disease

http://www.ncbi.nlm.nih.gov/books/NBK22183/

Genes and Disease

National Center for Biotechnology Information (US)
Bethesda (MD): National Center for Biotechnology Information (US); 1998.-

Contents

Introduction to Genes and Disease

Copyright notice.

Genes and Disease is a collection of articles that discuss genes and the diseases that they cause. These genetic disorders are organized by the parts of the body that they affect. As some diseases affect various body systems, they appear in more than one chapter.

With each genetic disorder, the underlying mutation(s) is discussed, along with clinical features and links to key websites.
Contents

Introduction to Genes and Disease
Blood and Lymph Diseases
Cancers
The Digestive System
Ear, Nose, and Throat
Diseases of the Eye
Female-Specific Diseases
Glands and Hormones
The Heart and Blood Vessels
Diseases of the Immune System
Male-Specific Diseases
Muscle and Bone
Neonatal Diseases
The Nervous System
Nutritional and Metabolic Diseases
Respiratory Diseases
Skin and Connective Tissue
Chromosome Map

Copyright notice.
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.

Related diseases

See other Diseases of the Nervous System
Huntington Disease Gene

HTT huntingtin [Homo sapiens]
Gene ID: 3064, updated on 3-Jan-2011

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]
Huntingtin Protein

Huntingtin [Homo sapiens]
NCBI Reference Sequence: NP_002102.4

LOCUS NP_002102
DEFINITION huntingtin [Homo sapiens].
ACCESSION NP_002102
VERSION NP_002102.4 GI:90903231
DATABASE REFSEQ: accession NM_002111.6
KEYWORDS .
ORIGIN Homo sapiens (human)
ORGANISM Homo sapiens

REFERENCE AUTHORS
and
Zhang, B.
TITLES
Essential sequence of the N-terminal cytoplasmic localization-related domain of huntingtin and its effect on huntingtin aggregates
PUBLISHED 21509658
REMARK GeneRIF: Data demonstrate that huntingtin(4-17) is the essential sequence for huntingtin cytoplasmic localization.
REFERENCE AUTHORS
TITLES
Mutant huntingtin binds the mitochondrial fission GTPase dynamin-related protein-1 and increases its enzymatic activity
PUBLISHED 21336284
REMARK GeneRIF: Mutant huntingtin abnormally interacts with the mitochondrial fission GTPase dynamin-related protein-1 (DRP1) in
RecName: Full=Huntingtin; AltName: Full=Huntington disease protein; Short=HD protein

Swiss-Prot: P42858.2
GenPept

>g!296434520|sp1P42858.2|HD_HUMAN

Huntington Disease Protein Sequence
Huntington Disease can Arise from Unequal Crossing Over During Meiosis

- Crossing over between maternal and paternal chromosomes

- Unequal crossing over between maternal and paternal chromosomes
Age of Onset and Repeat Length

The resources on this site should not be used as a substitute for professional medical care or advice. Users seeking information about a personal genetic disease, syndrome, or condition should consult with a qualified healthcare professional. See How can I find a genetics professional in my area? in the Handbook.

Published: September 19, 2010
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.
Huntington Disease

Huntington Chorea

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Michael R Hayden, MB, ChB, PhD, FRCP(C), FRSC
Department of Medical Genetics
University of British Columbia
Vancouver, BC
mrh@cmnt.ubc.ca


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.

Diagnosis/testing. The diagnosis of HD rests on positive family history, characteristic clinical findings, and the detection of an expansion of 36 or more CAG trinucleotide repeats in HTT.

Management. Treatment of manifestations: pharmacologic therapy including typical neuroleptics (haloperidol), atypical neuroleptics, anticholinergic drugs, and benzodiazepines. Transplantation of fetal striatal tissue in HD was initially promising, but these results are not confirmed in subsequent trials. Neuroprotection trials are ongoing and may have an impact on the natural history of the disease.
GeneTests & GeneReviews for Huntington's Disease

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 Disease Name Containing 'huntington disease'

Genetic Prion Diseases
- Prion Disease Testing
- Prion Disease Reviews
- Prion Disease Resources
- Prion Disease OMIM
- Prion Disease Locus-Specific
- Prion Disease HGMD
- Prion Disease More Links

Familial Creutzfeldt-Jakob Disease
- Creutzfeldt-Jakob Disease Testing
- Creutzfeldt-Jakob Disease Reviews
- Creutzfeldt-Jakob Disease Resources
- Creutzfeldt-Jakob Disease OMIM
- Creutzfeldt-Jakob Disease Locus-Specific
- Creutzfeldt-Jakob Disease HGMD
- Creutzfeldt-Jakob Disease More Links

Familial Insomnia
- Familial Insomnia Testing
- Familial Insomnia Reviews
- Familial Insomnia Resources
- Familial Insomnia OMIM
- Familial Insomnia Locus-Specific
- Familial Insomnia HGMD
- Familial Insomnia More Links

Gerstmann-Straussler-Scheinker Disease
- Gerstmann-Straussler-Scheinker Disease Testing
- Gerstmann-Straussler-Scheinker Disease Reviews
- Gerstmann-Straussler-Scheinker Disease Resources
- Gerstmann-Straussler-Scheinker Disease OMIM
- Gerstmann-Straussler-Scheinker Disease Locus-Specific
- Gerstmann-Straussler-Scheinker Disease HGMD
- Gerstmann-Straussler-Scheinker Disease More Links

Huntington Disease
- Huntington Disease Testing
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Huntington Disease-Like 1
- Huntington Disease-Like 1 Testing
- Huntington Disease-Like 1 Reviews
- Huntington Disease-Like 1 Resources
- Huntington Disease-Like 1 OMIM
- Huntington Disease-Like 1 Locus-Specific
- Huntington Disease-Like 1 HGMD
- Huntington Disease-Like 1 More Links

Huntington Disease-Like 2
- Huntington Disease-Like 2 Testing
- Huntington Disease-Like 2 Reviews
- Huntington Disease-Like 2 Resources
- Huntington Disease-Like 2 OMIM
- Huntington Disease-Like 2 Locus-Specific
- Huntington Disease-Like 2 HGMD
- Huntington Disease-Like 2 More Links

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

<table>
<thead>
<tr>
<th>Laboratories offering clinical testing:</th>
<th>Targeted mutation analysis</th>
<th>Linkage analysis</th>
<th>Prenatal diagnosis</th>
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<td>Cambridge, United Kingdom</td>
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<td>Rebecca Treacy, FRCPath; Joanne Whittaker, FRCPath</td>
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Huntington Disease Resources

- **Caring for People with Huntington's Disease**
  Kansas University Medical Center, Department of Neurology
  KS
  [www.kumc.edu/hospital/huntingtons/index.html](http://www.kumc.edu/hospital/huntingtons/index.html)

- **Huntington Society of Canada**
  151 Frederick Street
  Suite 400
  Kitchener Ontario N2H 2M2
  Canada
  **Phone:** 800-998-7398 (toll-free); 519-749-7063
  **Fax:** 519-749-8965
  **Email:** info@huntingtonsociety.ca
  [www.huntingtonsociety.ca](http://www.huntingtonsociety.ca)

- **Huntington's Disease Society of America (HDSA)**
  505 Eighth Avenue
  Suite 902
  New York NY 10018
  **Phone:** 800-345-4372 (toll-free); 212-242-1968
  **Fax:** 212-239-3430
  **Email:** hdsainfo@hdsa.org
  [www.hdsa.org](http://www.hdsa.org)

- **International Huntington Association**
  Callunahof 8
  Harfsen 7217 ST
  Netherlands
  **Phone:** +31 573 431 595
  **Fax:** +31 573 431 719
  **Email:** iha@huntington-assoc.com
  [www.huntington-assoc.com](http://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 genetic testing*
  University of Washington Medical Center
  Seattle WA
  [Testing for Huntington Disease: Making an Informed Choice](http://www.ncbi.nlm.nih.gov/books/NBK8235/)

Jan 6 2011 16:44 EST
Entrez Gene for Huntington

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]
Huntington Disease Gene
**Homo sapiens (human) Build 36.3 (Current)**

**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**
Region Displayed: 2,920K-3,340K bp

**Summary of Maps**

- **NOL14**
  - OMIM HGNC sy pr dl ev run hm st CDSS SNP
  - best RefSeq 4p16.3 nuclear protein 14

- **GRK4**
  - OMIM HGNC sy pr dl ev run hm st CDSS SNP
  - mRNA 4p16.3 G protein-coupled receptor kinase 4

- **HTT**
  - OMIM HGNC sy pr dl ev run hm st CDSS SNP
  - best RefSeq 4p16.3 huntingtin

- **LOC345222**
  - sy pr dl ev run hm CDSS SNP
  - best RefSeq 4p16.2 hypothetical gene supported by BC0435
MedlinePlus
http://www.nlm.nih.gov/medlineplus/
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)
### OMIM Entry Statistics


#### Number of Entries in OMIM (11 January 2012):

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<tr>
<th>Prefix</th>
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# OMIM Gene Map Statistics

**OMIM Morbid Map Scorecard (11 January 2012):**

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<td>Number of disorders for which the molecular basis is known</td>
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**OMIM Synopsis of the Human Gene Map (11 January 2012):**

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Huntington Disease Search in OMIM

http://omim.org/search?index=entry&sort=score+desc+prefix_sort+desc&start=1&limit=10&search=Hunttings

1: # 143100. HUNTINGTON DISEASE; HD
   Cytogenetic location: 4p16.3

2: # 603218. HUNTINGTON DISEASE-LIKE 1; HDL1
   Cytogenetic location: 20p13

3: % 604802. HUNTINGTON DISEASE-LIKE 3; HDL3
   Cytogenetic location: 4p13.3, Genomic coordinates (GRCh37): 4:11,300,000 - 21,300,000

4: * 613004. HUNTINGTIN; HTT

5: # 606438. HUNTINGTON DISEASE-LIKE 2; HDL2
   Cytogenetic location: 16q24.2

6: # 607136. SPINOCEREBELLAR ATAXIA 17; SCA17
   Cytogenetic location: 6q27

7: # 125370. DENTATORUBRAL-PALLIDOLUYSIAN ATROPHY; DRPLA
   Cytogenetic location: 12p13.31

8: * 600947. HUNTINGTIN-ASSOCIATED PROTEIN 1; HAP1
   Cytogenetic location: 17q21.2, Genomic coordinates (GRCh37): 17:39,878,890 - 39,890,897
Huntington Disease Entry in OMIM
http://omim.org/entry/143100?search=Huntingtons&highlight=huntington

#143100

HUNTINGTON DISEASE; HD

Alternative titles; symbols
HUNTINGTON CHOREA

Phenotype Gene Relationships

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<thead>
<tr>
<th>Location</th>
<th>Phenotype</th>
<th>Phenotype MIM number</th>
<th>Gene/Locus</th>
<th>Gene/Locus MIM number</th>
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Clinical Synopsis

TEXT

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

In normal individuals, the range of repeat numbers is 9 to 36. In those with HD, the repeat number is above 37 (Duyao et al., 1993).

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
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.
Cystic Fibrosis is a hereditary disorder characterized by lung congestion and infection and malabsorption of nutrients by the pancreas.
Cystic Fibrosis

- Autosomal (chromosome 7q31.2) recessive.
- Inhibits many bodily secretions
  - Pancreatic digestive enzymes
  - Sweat glands
  - Lung mucosa in alveoli and bronchi
  - Infertility in males (>97%)
  - Cirrhosis of the liver
  - Hepatic steatosis
- Caused by mutations in the CFTR gene that encodes a chloride ion channel that pumps Chloride ion and water out of cells.
Cystic Fibrosis Transmembrane Conductance Regulator
### Mutations Causing Cystic Fibrosis

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Relative Frequency</th>
<th>Mutation Functional Class ¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔF508</td>
<td>66.0%</td>
<td>II</td>
</tr>
<tr>
<td>G542X</td>
<td>2.4%</td>
<td>I</td>
</tr>
<tr>
<td>G551D</td>
<td>1.6%</td>
<td>III</td>
</tr>
<tr>
<td>N1303Lys</td>
<td>1.3%</td>
<td>II</td>
</tr>
<tr>
<td>W1282X</td>
<td>1.2%</td>
<td>I</td>
</tr>
<tr>
<td>R553X</td>
<td>0.7%</td>
<td>I</td>
</tr>
<tr>
<td>621+1G&gt;T</td>
<td>0.7%</td>
<td>I</td>
</tr>
<tr>
<td>1717-1G&gt;A</td>
<td>0.6%</td>
<td>I</td>
</tr>
<tr>
<td>R117H</td>
<td>0.3%</td>
<td>IV</td>
</tr>
<tr>
<td>R1162X</td>
<td>0.3%</td>
<td>Not clear ⁴</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Population Group</th>
<th>Approximate Carrier Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>1:29</td>
</tr>
<tr>
<td>North American Caucasian</td>
<td>1:28</td>
</tr>
<tr>
<td>African American</td>
<td>1:61</td>
</tr>
</tbody>
</table>
Portrait of a Glitch
Revere La Noue, MFA, Stanford, 2005
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?