Diseases and Disease Databases
http://biochem118.stanford.edu/

Doug Brutlag, Professor Emeritus
Biochemistry and Medicine (by courtesy)
brutlag@stanford.edu
Genetic Penetrance

- Diseases caused mostly by alteration in genes:
  - Sickle cell disease
  - Down syndrome

- Diseases caused by genetic alterations and environment:
  - Diabetes mellitus
  - Coronary heart disease

- Diseases caused mostly by environment:
  - Chicken pox
  - Lung cancer

Genetic diseases, at the left of the spectrum, are categorized as single gene or chromosomal disorders, depending on the specific genetic cause.

Diseases in the middle of the spectrum — including most common diseases — are multifactorial, and result from the interaction or additive effect of genetic and non-genetic factors.
Huntington Disease

• **Autosomal Dominant**
  - On the tip of the short arm of chromosome 4
  - One bad gene causes disease (dominant)
  - Brain degeneration over 10-15 year period until death

• **Neurodegenerative disease**
  - Loss of movement control
  - Loss of cognitive skills (dementia) and hallucinations
  - Depression, hostility, aggression and loss of inhibitions

• **Dyskinesias**
  - Chorea: uncontrollable tics and involuntary movements of extremities, hyperkinesias
  - Dysphagia (difficulty in swallowing) and uncontrollable oral buccal dyskinesia
  - Dystonia uncontrollable muscle contractions
  - Bradykinesia, slow uncertain movements
The Inheritance

• You are 18 years old.
• Your father abandoned you and your mother when you only one year old.
• Your father died this year and left you an inheritance.
• He died from an autosomal dominant disease known as Huntington’s Chorea or Huntington’s Disease.
• 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, when you will get symptoms and when you will die from it.
• Would you take the genetic test or not?
• Why?
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.
Adverse Events of Huntington’s Test

- After 1 year, 15% and after 2 years 22% of those with a positive test had an adverse event.
  - Suicide, suicide attempt or suicide plan
  - Psychiatric hospitalization
  - Depression lasting > two months
  - Breakdown of important personal relations
- No incidence of increased substance abuse
- Those with a negative test result often suffered from guilt complex.
Scenario Two

• You are a physician and one of your patients, a 17 year old male has Huntington’s in his family
• His grandfather died of the disease at 65 and his older uncle also acquired the disease at 50.
• His father is 40 and is symptom free so far and has specifically told you he does not want the Huntington’s test himself.
• The patient comes to you asking for the genetic test to determine if he has the Huntington’s gene.
• Would you test the young patient?
• How would you evaluate your young patient about his reaction to both a positive and a negative diagnosis prior to taking the test?
Huntington Testing: Making an Informed Choice

Testing for Huntington Disease: Making an Informed Choice

Written by:
Robin L. Bennett, Ms, CGC
Medical Genetics,
University of Washington Medical Center
NCBI: Genetics and Medicine
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.

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The Nervous System
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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...
Genetics Home Reference

Genetics Home Reference provides consumer-friendly information about the effects of genetic variations on human health. 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

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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.
Huntington’s Disease
Also called: HD, Huntington’s chorea

Summary

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, and balance problems. Later, HD can take away the ability to walk, talk, and swallow. Some people stop recognizing family members. Others are aware of their environment and are able to express emotions.
GeneTests & GeneReviews for Huntington's

https://www.genetests.org/

Welcome

The GeneTests website
Welcome to GeneTests. From its start in 1992, GeneTests has grown to reflect the advances in genetic testing capabilities and to address the needs of our ever-widening user community. We invite you to explore, try some of your favorite searches, and let us know what you think. Your feedback will help shape GeneTests into the indispensable tool you want for your practice.

What's New

Clinics Database to be Updated and Expanded
Have you ever needed to find a genetics clinic for a patient? With families moving all around the globe, it can be challenging to find the right resources easily. The Clinics database on GeneTests lists 1,067 clinical units worldwide. We are now starting to update and expand our clinic listings so you can find genetics clinics for your referrals quickly...

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Huntington Disease
Synonym: Huntington Chorea

Warby SC, Graham RK, Hayden MR.

Publication Details

Summary
Clinical 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 \textit{HTT}.
Management. Treatment of manifestations: Pharmacologic therapy including typical neuroleptics (haloperidol), atypical neuroleptics (olanzapine), benzodiazepines, or the monoamine depleting agent tetrabenazine for choreic movements; anti-parkinsonian agents for hypokinesia and rigidity; psychotropic drugs or some types of antiepileptic drugs for psychiatric disturbances (depression, psychotic symptoms, outbursts of aggression); valproic acid for myoclonic hyperkinesia. Supportive care with attention to nursing needs, dietary intake, special equipment, and eligibility for state and federal benefits.

Prevention of secondary complications: Attention to the usual potential complications in persons requiring long-term supportive care and the side effects associated with pharmacologic treatments.

Surveillance: Regular evaluations of the appearance and severity of chorea, rigidity, gait problems, depression, behavioral changes, and cognitive decline; routine assessment of functional abilities using the Behavior Observation Scale Huntington (BOSH) and the Unified HD rating scale (UHDRS).

Agents/circumstances to avoid: L-dopa-containing compounds (may increase chorea), alcohol consumption, smoking.

Other: Children and adolescents with a parent with HD may benefit from referral to a local HD support group for educational materials and psychological support.

Genetic counseling. HD is inherited in an autosomal dominant manner. Offspring of an individual with a pathogenic variant have a 50% chance of inheriting the disease-causing allele. Predictive testing in asymptomatic adults at risk is available but requires careful thought (including pre- and post-test genetic counseling) as there is currently no cure for the disorder. However, asymptomatic individuals at risk may be eligible to participate in clinical trials. Predictive testing is not considered appropriate for asymptomatic at-risk individuals younger than age 18 years. Prenatal testing by molecular genetic testing is possible.

Diagnosis

Clinical Diagnosis

The diagnosis of Huntington disease (HD) is suspected clinically in the presence of the following:

- Progressive motor disability featuring chorea. Voluntary movement may also be affected.
### Results for HUNTINGTON

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<td>Huntington Disease Test</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:** hdsainsf@hdsa.org
  [www.hdsa.org](http://www.hdsa.org)

- **International Huntington Association**
  Callunahof 8
  Harfsten 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
Entrez Gene for Huntington

HTT huntingtin [Homo sapiens]

GeneID: 3064

Summary

Official Symbol
HTT

Official Full Name
huntingtin

Primary source
HGNC:4851

See related
Ensembl:ENSG00000197396; HPRD:00883; MIM:143100

Gene type
protein coding

RefSeq status
REVIEWED

Organism
Homo sapiens

Lineage
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominoidea; 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]
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]
MapViewer for Huntington
Huntingtinin Protein

LOCUS NP_002102
DEFINITION huntingtin [Homo sapiens].
ACCESSION NP_002102
VERSION NP_002102.4 GI:90903231
DBSOURCE RefSeq: accession NM_002111.6
ORGANISM Homo sapiens (human)
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Buiuochontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.
REFERENCE AUTHORS and
    1 (residues 1 to 3144)
        Yan,Y., Peng,D., Tian,J., Chi,J., Tan,J., Yin,X., Pu,J., Xia,K. and
        Zhang,B.
        TITLE Essential sequence of the N-terminal cytoplasmic localization-related domain of huntingtin and its effect on huntingtin aggregates
        PUBMED 21509658
        REMARK GeneRIF: Data demonstrate that huntingtin(4-17) is the essential sequence for huntingtin cytoplasmic localization.
        REFERENCE AUTHORS 2 (residues 1 to 3144)
            TITLE Mutant huntingtin binds the mitochondrial fission GTPase dynamin-related protein-1 and increases its enzymatic activity
            PUBMED 21336284
            REMARK GeneRIF: Mutant huntingtin abnormally interacts with the mitochondrial fission GTPase dynamin-related protein-1 (DRP1) in Huntingtin knockout neurons leading to mitochondrial dysfunction and cell death.
| 1  | matsu6lmlka feasiksvgfqqqq qqqqqqqqq qqqqqqqqq ppppppppp pqlppqppqpa  
| 2  | qplllppqppppp pppppppppp avafeplprf srkxstakkk rhvneltcor nivaugvrs  
| 3  | pefgklqgla melfilicadd aaeasvmmvad eclnivklga mdnsnlrlgl ylykeikkg  
| 4  | aprsraalw rfelaalhvr pkgcprylkyn lpclytrtsk rpeevesqelt aaavpkimas  
| 5  | fngfandnei kkkkafian lkssstprir taasavigsl qxsrrtgyp swllnvlgl  
| 6  | rvpvedehtsk lllilgylilt ptyllpplllqq qdkslkgasfl gtvkrmeves psaqelvgyv  
| 7  | elthhtqghq dhnnvghtgale llqlqflrrtpp pelgitltav gqigqtleakes eesgrsrsg  
| 8  | siveliagsg ssscpvlskk kqgkqkvilo eaeledsesr ssvssaatn ksvdeisng  
| 9  | aassgyksgp saqhditeq prsghltqad svldasclt stadsgeet ilshsssvgs  
| 10 | avpsdpamdi ndtgqasspl ssdsstgtq pdsavtptsd seilvdgtdn qyglghost  
| 11 | qdedeaetgq lpdeaseafrr nssmalqqah lknkmscrrq psssdsvdfv lrdatpeqd  
| 12 | qnepcrrlkg dqqgstddds amlvphcvrl1 snfllrgtgyk nplyvprdrv vskvala  
| 13 | vgavaalhepe sfskslykvp ldtteypeeq ysvsdlnyld heqdpqcvrtg alactrics  
| 14 | ilersrfhvg dwmntrtt lntfsladci plrllrkkc ltsvvtckact avrncvmslc  
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| 19 | fpdlisahqgd allilaginila asapkxalrs saseeeanpa atkgcveepwpv lgdralvnmv  
| 20 | e3aflhiikv inicahvddl vappappaxk pasipnppal spirrgqkeek epgeqasvpl  
| 21 | spkgseaae asrqualgat vptksskxst syflplk y11hcvkatha nkyvlgdlnq  
| 22 | sktefgfllir saidvslqil elatldqigk cveeligyf scfrespmna tvcqvgkltk  
| 23 | lfgtnlasqf dlissnpks qgraarqcss sgrvpolykyc macytnfhkg aladasirnm  
| 24 | vqaeeqngts gwtfwvqvkvvl qtkltnltvs tnknarqdl hnhrlitfe pvlakgytlt  
| 25 | ttcvqlkqkv vldlilavql rynvvdldsd vqfivvnlk qefieyvqgrq essaelipnfi  
| 26 | ffmllsyeer yhsdqllgip kiiqroldpm asgavrkgona ipaelqplvhw lfvlqntkak  
| 27 | dagkeletqgq evvsvnmlrl qylqghvleemf ilvqghqchke nedkwklrsl qiadilipm  
| 28 | akqemhindhk ealgvnlclfl elapossrlp vdlmlrsfnv ptntmasvst vglwsilga  
| 29 | ilvlqeset edilairqe lafepylrcq tvnrlrdgq stasleleea gqklinpe  
| 30 | tfsrfrlgvy gilledtvk glkveemseq htqfycqelt lmelihfhf sgmmfritaa  
| 31 | atmrlfredgc ggfsylucsh dlrlrarssmmt hpavllwvcc illvnhtydr rwwaeqvttq  
| 32 | khrhlisstf1 ispcymageee daalanskq cmmrerqrrg ilfscyvcq vnhldeeltw  
| 33 | livnhgidi slheppqvd fiasavhcrsa asqigfiaq clrcnttqel mikkkglcgle  
| 34 | gikliqsegv iltyvdrilq tpprralvmm dlvkrcrmm lnastnqssm aclqmmemnr  
| 35 | ieqllqgqsl glnsdpgqppv vdfrrquddv dslqpppsv spxgllglkg slvstpdvk  
| 36 | wyyvhlksqga wttrsdaal gaelmvripa edmnfmmns enflslleac lslqnsesig  
| 37 | 1661 gqksalfeaa revrlyarsv tvgdpavvwh vfpqelpaepp aaaywskdlnl fdgadalyqg  
| 38 | 2222 22222 tflariarlg lvnvsvlplsh hllpeeked lvdvftvate alswlhiheq ipsldiqag  
| 39 | 2341 2341 2341 2341 ieseexyvpt dntnpkyita acemvaenm slqgsvlbh krnsypafvl tpprnilinii  
| 40 | 2461 larlpnlsv trypvlpwlk gwspkpqfdgt stafpeipe fgievskfek fliirtlygsw  
| 41 | 2461 2461 2461 2461 stxgtfeetw attlgvltyq plvmeqeesp peedertqq nlvagvagits lvslatmtpv  
| 42 | 2520 2520 2520 2520 agnpavcse gqprknplka ldtrfgklks iirgigvem gamevkrne athley gwad  
| 43 | 2580 2580 2580 2580 ppvpslpat galiishkll lgipenelg smaylqggs hveswlnpni trieeawde  
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| 45 | 2640 2640 2640 2640 evvrallvna dlterrtngf mlytiteer ruhpsedel acylpvepct accvinmdaka  
| 46 | 2760 2760 2760 2760 vaepvsrile stlrsahips rvqahglvy vlcclelddt akliupvaid yllsnlkqim  
| 47 | 2821 2821 2821 2821 hcvnihsqgh vlvmcatayf lienyiplvdv pefmassiqu czvmslgsee stpsiyhca  
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| 52 | 3120 3120 3120 3120 vaapspphyl tttlcrlnhvk vtct
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
Huntington Disease Search in OMIM

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

1:  #143100. HUNTINGTON DISEASE; HD
    Cytogenetic location: 4p15.3

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

3:  #604802. HUNTINGTON DISEASE-LIKE 3; HDL3
    Cytogenetic location: 4p15.3, 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. SPINOCEBELLAR 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
#143100

HUNTINGTON DISEASE; HD

Alternative titles; symbols
HUNTINGTON CHOREA

Phenotype Gene Relationships

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<td>Huntington disease</td>
<td>143100</td>
<td>HTT</td>
<td>613004</td>
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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
## OMIM Entry Statistics

**Number of Entries in OMIM (Updated September 29th, 2014):**

<table>
<thead>
<tr>
<th>Prefix</th>
<th>Autosomal</th>
<th>X Linked</th>
<th>Y Linked</th>
<th>Mitochondrial</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Gene description</td>
<td>13,898</td>
<td>679</td>
<td>48</td>
<td>35</td>
<td>14,660</td>
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<tr>
<td>+ Gene and phenotype, combined</td>
<td>98</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>102</td>
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<tr>
<td># Phenotype description, molecular basis known</td>
<td>3,855</td>
<td>287</td>
<td>4</td>
<td>28</td>
<td>4,174</td>
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<tr>
<td>% Phenotype description or locus, molecular basis unknown</td>
<td>1,555</td>
<td>133</td>
<td>5</td>
<td>0</td>
<td>1,693</td>
</tr>
<tr>
<td>Other, mainly phenotypes with suspected mendelian basis</td>
<td>1,735</td>
<td>114</td>
<td>2</td>
<td>0</td>
<td>1,851</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>21,141</td>
<td>1,215</td>
<td>59</td>
<td>65</td>
<td>22,480</td>
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</tbody>
</table>
OMIM Gene Map Statistics:

OMIM Morbid Map Scorecard (Updated September 29th, 2014):

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
<td>Number of phenotypes* for which the molecular basis is known</td>
<td>5,329</td>
</tr>
<tr>
<td>Number of genes with phenotype-causing mutation</td>
<td>3,289</td>
</tr>
</tbody>
</table>

* Phenotypes include single-gene mendelian disorders, traits, some susceptibilities to complex disease (e.g., CFH and macular degeneration, 134370.0008), and some somatic cell genetic disease (e.g., FGFR3 and bladder cancer, 134934.0013)

OMIM Synopsis of the Human Gene Map (Updated September 29th, 2014):

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,475</td>
</tr>
<tr>
<td>2</td>
<td>941</td>
</tr>
<tr>
<td>3</td>
<td>808</td>
</tr>
<tr>
<td>4</td>
<td>572</td>
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<td>5</td>
<td>682</td>
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<tr>
<td>6</td>
<td>881</td>
</tr>
<tr>
<td>7</td>
<td>707</td>
</tr>
<tr>
<td>8</td>
<td>528</td>
</tr>
<tr>
<td>9</td>
<td>569</td>
</tr>
<tr>
<td>10</td>
<td>549</td>
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<tr>
<td>11</td>
<td>908</td>
</tr>
<tr>
<td>12</td>
<td>787</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>280</td>
</tr>
<tr>
<td>14</td>
<td>486</td>
</tr>
<tr>
<td>15</td>
<td>442</td>
</tr>
<tr>
<td>16</td>
<td>612</td>
</tr>
<tr>
<td>17</td>
<td>858</td>
</tr>
<tr>
<td>18</td>
<td>220</td>
</tr>
<tr>
<td>19</td>
<td>929</td>
</tr>
<tr>
<td>20</td>
<td>381</td>
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<td>21</td>
<td>155</td>
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<tr>
<td>22</td>
<td>359</td>
</tr>
<tr>
<td>X</td>
<td>814</td>
</tr>
<tr>
<td>Y</td>
<td>53</td>
</tr>
</tbody>
</table>
Health Problems with Cystic Fibrosis

- Sinus Problems
- Nose Polyps (growths)
- Frequent lung Infections
- Salty sweat
- Enlarged heart
- Trouble breathing
- Gallstones
- Abnormal pancreas function
- Trouble digesting food
- Fatty BM's

Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)
Role of CFTR in Pancreatic Secretion

Mutations Causing Cystic Fibrosis

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Relative Frequency</th>
<th>Mutation Functional Class</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>R162X</td>
<td>0.3%</td>
<td>Not clear</td>
</tr>
</tbody>
</table>

Population Group |
- Ashkenazi Jewish |
- North American Caucasian |
- African American |

Approximate Carrier Frequency |
- 1:29                  |
- 1:28                  |
- 1:61                  |

Cystic Fibrosis Mutation database: [http://www.genet.sickkids.on.ca/app](http://www.genet.sickkids.on.ca/app)
Rhodopsin and Colorblindness

http://justinpamute.files.wordpress.com/2010/06/rhodopsin1.gifs
Colorblindness in OMIM

http://omim.org/search?index=entry&sort=score%2C+prefix_sort+desc&start=1&limit=10&search=colorblindness

Search: 'colorblindness'
Results: 1 - 10 of 56

1:  # 303800. COLORBLINDNESS, PARTIAL, DEUTAN SERIES; CBD
DEUTERANOMALY, INCLUDED
Cytogenetic location: Xq28
Matching terms: colorblindness, colourblindness

2:  # 190900. TRITANOPIA
Cytogenetic location: 7q32.1
Matching terms: colorblindness

3:  # 303900. COLORBLINDNESS, PARTIAL, PROTAN SERIES; CBP
PROTANOMALY, INCLUDED
Cytogenetic location: Xq28
Matching terms: colorblindness

4:  # 303700. BLUE CONE MONOCHROMACY; BCM
CONE DYSTROPHY 5, X-LINKED, INCLUDED
Cytogenetic locations: Xq28, Xq28
Matching terms: colorblindness
#303800

COLORBLINDNESS, PARTIAL, DEUTAN SERIES; CBD

Alternative titles; symbols
DEUTAN COLORBLINDNESS; DCB
DEUTERANOPAIA
GREEN COLORBLINDNESS

Other entities represented in this entry:
DEUTERANOMALY, INCLUDED

Phenotype Gene Relationships

<table>
<thead>
<tr>
<th>Location</th>
<th>Phenotype</th>
<th>Phenotype MIM number</th>
<th>Gene/Locus</th>
<th>Gene/Locus MIM number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xq28</td>
<td>Colorblindness, deutan</td>
<td>303800</td>
<td>OPN1MW</td>
<td>300821</td>
</tr>
</tbody>
</table>

Clinical Synopsis

TEXT
A number sign (#) is used with this entry because deutan colorblindness is caused by mutation in the OPN1MW gene (300821), which encodes green cone pigment.

Description
Normal color vision in humans is trichromatic, being based on 3 classes of cone that are maximally sensitive to light at approximately 420 nm (blue cones; 613522), 530 nm (green cones; 300821), and 560 nm (red cones; 300822). Comparison by neural circuits of light absorption by the 3 classes of cone photoreceptors allows perception of red, yellow, green, and blue colors individually or in various combinations. Dichromatic color vision is severely defective color vision based on the use of only 2 types of photoreceptors, blue plus green (protanopia; see 300900) or blue plus red (deuteranopia). Anomalous trichromacy is trichromatic color vision based on a blue, green, and an anomalous red-like color.
*300821

**OPSIN 1, MEDIUM-WAVE-SENSITIVE; OPN1MW**

Alternative titles: symbols
GREEN CONE PIGMENT; GCP

HGNC Approved Gene Symbol: OPN1MW

Cytogenetic location: **Xq28**  Genomic coordinates (GRCh37): **X:153,448,084 - 153,462,351**

Gene Phenotype Relationships

<table>
<thead>
<tr>
<th>Location</th>
<th>Phenotype</th>
<th>Phenotype MIM number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xq28</td>
<td>Blue cone monochromacy</td>
<td>303770</td>
</tr>
<tr>
<td></td>
<td>Colorblindness, deutan</td>
<td>303800</td>
</tr>
</tbody>
</table>

**TEXT**

**Description**

The medium-wave-sensitive opsin-1 gene (OPN1MW) encodes green cone pigment, 1 of 3 light-sensitive pigments that mediate human color vision. The green-sensitive and the red-sensitive (OPNILW; 300822) opsins comprise a family of repeated genes on the X chromosome. Whereas there is a single red pigment gene, green pigment genes vary in number among persons with normal color vision. The red pigment gene and the multiple green pigment genes are arranged in a head-to-tail tandem array. The maximal sensitivity of green cones is 530 nm (Nathans et al., (1986, 1986)).

A master switch for the genes of this locus, called the locus control region (LCR; 300824), is located between 3.1 kb and 3.7 kb 5-prime of the gene array and has been shown to be essential for expression of both the red and green pigment genes as well as cone-specific expression of the genes and their segregated expression in separate cones (summary by Deeb, 2005).

**Cloning**
Opsin1MW Gene Entry

**Summary**

**Official Symbol**  OPN1MW provided by HUGO

**Official Full Name**  opsin 1 (cone pigments), medium-wave-sensitive  provided by HUGO

**Primary source**  HGNC-4205

**See related**  Ensembl:ENSQ00000147380; HPRD:02365; MIM:300821

**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**  CBD; GCP; GOP; CBM; CODS; OPN1MV1; OPN1MW2; MGC176615; MGC177321; MGC195488; MGC190489

**Summary**  This gene encodes for a light absorbing visual pigment of the opsin gene family. The encoded protein is called green cone photopigment or medium-wavelength sensitive opsin. Oropsins are G-protein coupled receptors with seven transmembrane domains, an N-terminal extracellular domain, and a C-terminal cytoplasmic domain. The long-wavelength opsin gene and multiple copies of the medium-wavelength opsin gene are tandemly arranged on the X chromosome and frequent unequal recombination and gene conversion may occur between these sequences. X chromosomes may have fusions of the medium- and long-wavelength opsin genes or may have more than one copy of these genes. Defects in this gene are the cause of deuteranopic colorblindness, [provided by RefSeq, Mar 2009]
Ishihara Test for Red-Green Color Blindness

Mendelian Disease Case Presentation

Please choose a single gene, Mendelian disease from one of the Disease databases (Genes and Diseases, Genetics Home Reference, Gene Reviews. or Online Inheritance in Man (OMIM) and prepare an oral case presentation of the disease.

Please Include:
1. a URL pointer to OMIM or Gene Reviews entry for your disease
2. a basic description of the disease and its symptoms and prevalence
3. the classical (pre-genetic) differential diagnosis of the disease
4. the classical (pre-genetic) treatment of the disease
5. description of genetics of the disease including world and ethnic distribution of the disease gene
6. any novel diagnostics that have resulted from knowing the genetics
7. any novel understanding of the disease that has lead to novel therapy based on genetic knowledge.