Diseases and Disease Databases

http://biochem158.stanford.edu/

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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 years 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
  - Dystonia uncontrollable muscle contractions
  - Bradykinesia, slow uncertain movements
  - Dysphagia (difficulty in swallowing) and uncontrollable oral buccal dyskinesia
Scenario 1: The Inheritance

- You are 20 years old.
- Your father abandoned you and your mother when you only 3 years old.
- Your father died this year and left you an inheritance.
- He died from an autosomal dominant disease known as Huntington Chorea or Huntington 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 die from it.
- Would you take the genetic test or not?
- Why?
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
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?
• What would you ask your young patient about his reaction to both a positive and a negative diagnosis prior to taking the test?
Please choose a single gene, Mendelian disease from one of the Disease databases (Genes and Disease, Genetics Home Reference, Gene Reviews or Online Inheritance in Man (OMIM)) and prepare a written case presentation of the disease (4 pages max) of double spaced text. Figures, Tables and References need not be included in this limit, just the written text.

Please Include:
1. A URL pointer to OMIM and/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. A 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.
Genetic Penetrance

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.
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: Genetics and Medicine

Genetics & Medicine

Databases

**Bookshelf**
A collection of biomedical books that can be searched directly or from linked data in other NCBI databases. The collection includes biomedical textbooks, other scientific titles, genetic resources such as GeneReviews, and NCBI help manuals.

**ClinVar**
A resource to provide a public, tracked record of reported relationships between human variation and observed health status with supporting evidence. Related information in the NIH Genetic Testing Registry (GTR), MedGen, Gene, OMIM, PubMed and other sources is accessible through hyperlinks on the records.

**Database of Genotypes and Phenotypes (dbGaP)**
An archive and distribution center for the description and results of studies which investigate the interaction of genotype and phenotype. These studies include genome-wide association (GWAS), medical resequencing, molecular diagnostic assays, as well as association between genotype and non-clinical traits.

**Database of Major Histocompatibility Complex (dbMHC)**
Gene
A searchable database of genes, focusing on genomes that have been completely sequenced and that have an active research community to contribute gene-specific data. Information includes nomenclature, chromosomal localization, gene products and their attributes (e.g., protein interactions), associated markers, phenotypes, interactions, and links to citations, sequences, variation details, maps, expression reports, homologs, protein domain content, and external databases.

GeneReviews
A collection of expert-authored, peer-reviewed disease descriptions on the NCBI Bookshelf that apply genetic testing to the diagnosis, management, and genetic counseling of patients and families with specific inherited conditions.

Genes and Disease
Summaries of information for selected genetic disorders with discussions of the underlying mutation(s) and clinical features, as well as links to related databases and organizations.

Genetic Testing Registry (GTR)
A voluntary registry of genetic tests and laboratories, with detailed information about the tests such as what is measured and analytic and clinical validity. GTR also is a nexus for information about genetic conditions and provides context-specific links to a variety of resources, including practice guidelines, published literature, and genetic data/information. The initial scope of GTR includes single gene tests for Mendelian disorders, as well as arrays, panels and pharmacogenetic tests.
NCBI: Genetics and Medicine

MedGen
A portal to information about medical genetics. MedGen includes term lists from multiple sources and organizes them into concept groupings and hierarchies. Links are also provided to information related to those concepts in the NIH Genetic Testing Registry (GTR), ClinVar, Gene, OMIM, PubMed, and other sources.

Online Mendelian Inheritance in Animals (OMIA)
A database of genes, inherited disorders and traits in animal species (other than human and mouse), with textual information and references, as well as links to relevant records from other NCBI databases, such as PubMed and Gene.

Online Mendelian Inheritance in Man (OMIM)
A database of human genes and genetic disorders. NCBI maintains current content and continues to support its searching and integration with other NCBI databases. However, OMIM now has a new home at omim.org, and users are directed to this site for full record displays.

PubMed
A database of citations and abstracts for biomedical literature from MEDLINE and additional life science journals. Links are provided when full text versions of the articles are available via PubMed Central (described below) or other websites.

PubMed Central (PMC)
A digital archive of full-text biomedical and life sciences journal literature, including clinical medicine and public health.

PubMed Health
A collection of clinical effectiveness reviews and other resources to help consumers and clinicians use and understand clinical research results. These are drawn from the NCBI Bookshelf and PubMed, including published systematic reviews from organizations such as the Agency for Health Care Research and Quality, The Cochrane Collaboration, and others (see complete listing). Links to full text articles are provided when available.
Genes and Disease

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

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
Contents

Introduction to Genes and Disease
Blood and Lymph Diseases
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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

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The brain and nervous system form an intricate network of electrical signals that are responsible for coordinating muscles, the senses, speech, memories, thought and emotion.

Several diseases that directly affect the nervous system have a genetic component: some are due to a mutation in a single gene, others are proving to have a more complex mode of inheritance. As our understanding of the pathogenesis of neurodegenerative disorders deepens, common themes begin to emerge: Alzheimer brain plaques and the inclusion bodies found in Parkinson disease contain at least one common component, while Huntington disease, fragile X syndrome and spinocerebellar atrophy are all 'dynamic mutation' diseases in which there is an expansion of a DNA repeat sequence. Apoptosis is emerging as one of the molecular mechanisms invoked in several neurodegenerative diseases, as are other, specific, intracellular signaling events. The biosynthesis of myelin and the regulation of cholesterol traffic also figure in Charcot-Marie-Tooth and Neimann-Pick disease, respectively.
<table>
<thead>
<tr>
<th>Diseases</th>
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<tr>
<td>Adrenoleukodystrophy</td>
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<tr>
<td>Alzheimer disease</td>
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<tr>
<td>Amyotrophic lateral sclerosis</td>
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<td>Angelman syndrome</td>
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<tr>
<td>Ataxia telangiectasia</td>
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<td>Charcot-Marie-Tooth syndrome</td>
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<tr>
<td>Cockayne syndrome</td>
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<td>Deafness</td>
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<td>Duchenne muscular dystrophy</td>
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<tr>
<td>Epilepsy</td>
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<tr>
<td>Essential tremor</td>
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<tr>
<td>Fragile X syndrome</td>
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<tr>
<td>Friedreich's ataxia</td>
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<td>Gaucher disease</td>
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<tr>
<td>Huntington disease</td>
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<tr>
<td>Lesch-Nyhan syndrome</td>
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<tr>
<td>Maple syrup urine disease</td>
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<tr>
<td>Menkes syndrome</td>
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<tr>
<td>Myotonic dystrophy</td>
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<tr>
<td>Narcolepsy</td>
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<tr>
<td>Neurofibromatosis</td>
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<tr>
<td>Niemann-Pick disease</td>
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<tr>
<td>Parkinson disease</td>
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<tr>
<td>Phenylketonuria</td>
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</tbody>
</table>
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.
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.
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

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 ...

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

   NIH (National Library of Medicine)
Huntington Disease

Huntington Chorea

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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 (risperidone, quetiapine), and psychosocial interventions. Genetic counseling: preconception genetic counseling and prenatal diagnosis are available options.
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](http://www.ncbi.nlm.nih.gov/sites/GeneTests/).

### Search Result for Disease Name Containing 'huntington disease'

<table>
<thead>
<tr>
<th>Genetic Prion Diseases</th>
<th>Testing</th>
<th>Reviews</th>
<th>Resources</th>
<th>OMIM</th>
<th>Locus-Specific</th>
<th>HGMD</th>
<th>More Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial Creutzfeldt-Jakob Disease</td>
<td>Locus-Specific</td>
<td>HGMD</td>
<td>More Links</td>
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<td></td>
<td></td>
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<tr>
<td>Fatal Familial Insomnia</td>
<td>Locus-Specific</td>
<td>HGMD</td>
<td>More Links</td>
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<tr>
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<td>Resources</td>
<td>OMIM</td>
<td>HGMD</td>
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Disclaimer. GeneTests does not independently verify information provided by laboratories and does not warrant any aspect of a laboratory's work.
### Genetic Testing Registry for Huntington


#### Showing 1 to 20 of 85 tests for 1 condition in 80 labs

<table>
<thead>
<tr>
<th>Condition</th>
<th>Test target</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Huntington disease</strong>&lt;br&gt;Lab: Molecular Diagnostic Laboratory Diagnostic Services of Manitoba, Health Sciences Centre site Winnipeg, Manitoba, Canada&lt;br&gt;Condition: Huntington's chorea&lt;br&gt;Test target: HTT&lt;br&gt;Methods: T Targeted variant analysis</td>
<td></td>
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<tr>
<td><strong>Huntington's Disease</strong>&lt;br&gt;Lab: Molecular Pathology Laboratory Ohio State University&lt;br&gt;Columbus, Ohio, United States&lt;br&gt;Condition: Huntington's chorea&lt;br&gt;Test target: HTT&lt;br&gt;Methods: T Targeted variant analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Huntington's Disease</strong>&lt;br&gt;Lab: Center for Human Genetics, Inc Cambridge, Massachusetts, United States&lt;br&gt;Condition: Huntington's chorea&lt;br&gt;Test target: HTT&lt;br&gt;Methods: T Targeted variant analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Huntington Disease</strong>&lt;br&gt;Lab: Knight Diagnostic Laboratories - Molecular Diagnostic Center Oregon Health and Science University&lt;br&gt;Portland, Oregon, United States&lt;br&gt;Condition: Huntington's chorea&lt;br&gt;Test target: HTT&lt;br&gt;Methods: T Targeted variant analysis</td>
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OMIM Coverage


January 5, 2015

OMIM Entry Statistics

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<tr>
<th>Prefix</th>
<th>Autosomal</th>
<th>X Linked</th>
<th>Y Linked</th>
<th>Mitochondrial</th>
<th>Totals</th>
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<tbody>
<tr>
<td>* Gene description</td>
<td>14,027</td>
<td>689</td>
<td>48</td>
<td>35</td>
<td>14,799</td>
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<tr>
<td>+ Gene and phenotype, combined</td>
<td>84</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>88</td>
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<tr>
<td># Phenotype description, molecular basis known</td>
<td>3,991</td>
<td>287</td>
<td>4</td>
<td>28</td>
<td>4,310</td>
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<tr>
<td>% Phenotype description or locus, molecular basis unknown</td>
<td>1,540</td>
<td>133</td>
<td>5</td>
<td>0</td>
<td>1,678</td>
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<tr>
<td>Other, mainly phenotypes with suspected mendelian basis</td>
<td>1,734</td>
<td>113</td>
<td>2</td>
<td>0</td>
<td>1,849</td>
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<tr>
<td>Totals</td>
<td>21,376</td>
<td>1,224</td>
<td>59</td>
<td>65</td>
<td>22,724</td>
</tr>
</tbody>
</table>

> 67% Genes

> 33% Phenotypes
Huntington Disease Search in OMIM

Search: 'Huntington Disease'
Results: 1 - 10 of 6,850 | Show top 100 | 1 2 3 4 5 6 7 8 9 10 Next Last

1: # 143100. HUNTINGTON DISEASE; HD
   Cytogenetic location: 4p16.3
   Matching terms: disease, huntington

2: * 613004. HUNTINGTIN; HIT
   Cytogenetic location: 4p16.3
   Genomic coordinates (GRCh37): 4:3,076,407 - 3,245,686
   Matching terms: disease, huntington

3: % 604802. HUNTINGTON DISEASE-LIKE 3; HDL3
   Cytogenetic location: 4p15.3
   Genomic coordinates (GRCh37): 4:11,300,000 - 21,300,000
   Matching terms: disease, huntington

4: # 606438. HUNTINGTON DISEASE-LIKE 2; HDL2
   Cytogenetic location: 16q24.2
   Matching terms: disease, huntington

5: # 603218. HUNTINGTON DISEASE-LIKE 1; HDL1
   Cytogenetic location: 20p13
   Matching terms: disease, huntington

6: # 607136. SPINOCEPHALIC ATAXIA 17; SCA17
   Cytogenetic location: 6q27
   Matching terms: disease, huntington

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Huntington Disease Entry in OMIM


#143100

HUNTINGTON DISEASE; HD

Alternative titles; symbols
HUNTINGTON CHOREA

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>4p16.3</td>
<td>Huntington disease</td>
<td>143100</td>
<td>HTT</td>
<td>613004</td>
</tr>
</tbody>
</table>

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 progressive, selective neural cell loss and atrophy in the caudate and putamen. Walker (2007) provided a detailed review of Huntington disease, including clinical features, population genetics, molecular biology, and animal models.
*613004

HUNTINGTIN; HTT

Alternative titles; symbols
IT15
HD GENE

HgNC Approved Gene Symbol: HTT

Cytogenetic location: 4p16.3   Genomic coordinates (GRCh37): 4;3,076,407 - 3,245,686   (from NCBI)

<table>
<thead>
<tr>
<th>Location</th>
<th>Phenotype</th>
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<tbody>
<tr>
<td>4p16.3</td>
<td>Huntington disease</td>
<td>143100</td>
</tr>
</tbody>
</table>

TEXT

Description
The HTT gene encodes huntingtin, a ubiquitously expressed nuclear protein that binds to a number of transcription factors to regulate transcription. Abnormal expansion of a polyglutamine tract in the N terminus of huntingtin causes Huntington disease (143100), a devastating autosomal dominant neurodegenerative disease characterized by motor, psychiatric, and cognitive dysfunction (summary by Futter et al., 2009).
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
MapViewer for Huntington

```plaintext
Symbol | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | polymerase (DNA directed) nu
HAUS5 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | HUA synthase-like complex, subunit 3
COX6B1P5 | HGN C sv dl ev stts | best RefSeq | 4p16.3 | cytochrome c oxidase subunit V1b polypeptide 1 (ubiquitous) pseudogene
MIR4800 | HGN C sv dl ev SNP | best RefSeq | 4p16.3 | microRNA 4800
MXD4 | HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | MAX dimerization protein 4
ZFYVE28 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | zinc finger, FYVE domain containing 28
RP11-503N18.1 | sv pr dl ev h m SNP | best RefSeq | 4p16.3 | uncharacterized LOC402160
RNF4 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | ring finger protein 4
FAM193A | HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | family with sequence similarity 193, member A
TNIP2 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | TNFAIP3 interacting protein 2
SH3BP2 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | SH3-domain binding protein 2
ADD1 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | aducin 1 (alpha)
MFS10 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | major facilitator superfamily domain containing 10
NOP4-AS1 | HGN C sv dl ev stts SNP | best RefSeq | 4p16.3 | NOP4 antisense RNA 1
NOP4 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | NOP4 nuclear protein
GRK4 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | G protein-coupled receptor kinase 4
HTT-A5 | HGN C sv dl ev SNP | best RefSeq | 4p16.3 | HTT antisense RNA (head to head)
HTT | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | huntingtin
MSANTD1 | HGN C sv pr dl ev h m CDSSNP | best RefSeq | 4p16.3 | Myb/SANT-like DNA-binding domain containing 1
RGS12 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | regulator of G-protein signaling 12
HGFAC | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16 | HGF activator
DOK7 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | docking protein 7
LRPAP1 | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16.3 | low density lipoprotein receptor-related protein associated protein 1
LINCO0955 | HGN C sv dl ev stts SNP | best RefSeq | 4p16.3 | long Intergenic non-protein coding RNA 955
BP3-513G18.2 | sv dl ev stts SNP | best RefSeq | uncharacterized LOC100133461
ADRA2C | OMIM HGN C sv pr dl ev h m ts CDSSNP | best RefSeq | 4p16 | adrenoreceptor alpha 2C
ALG117P | HGN C sv dl ev stts | best RefSeq | 4p16.3 | asparagine-linked glycosylation 1-like 7, pseudogene
FAM86TP | HGN C sv dl ev stts SNP | best RefSeq | 4p16.3 | family with sequence similarity 86, member A pseudogene
```
Huntingtin Protein

LOCUS  NP_002102
DEFINITION  huntingtin [Homo sapiens]
ACCESSION  NP_002102
VERSION  NP_002102.4  GI:90903231
DBSOURCE  REFSEQ: accession NM_002111.6
SOURCE  Homo sapiens (human)
ORGANISM  Homo sapiens
  Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Eutheromammalia; Primates; Haplorrhini; Catarrhini; Hominoidea; Homo.
REFERENCE AUTHORS  1 (residues 1 to 3144)
  Yan, Y., Peng, D., Tian, J., Chi, J., Tan, J., Yin, X., Pu, J., Xia, X., 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 vivo and in vitro.
Results: 4

1. **EGFR1 Signaling Pathway**
   - The androgen receptor is a member of the nuclear receptor family of ligand activated transcription factors. These receptors bind to steroid hormones, thyroid hormone, retinoids and vitamin D among others, dimerize and bind to DNA. Its ligands include testosterone, dehydroepiandrosterone...
   - Type: pathway  Taxonomic scope: organism-specific biosystem  Organism: *Homo sapiens*
   - Proteins  PubMed

2. **Huntington's disease**
   - Huntington disease (HD) is an autosomal-dominant neurodegenerative disorder that primarily affects medium spiny striatal neurons (MSN). The symptoms are choreiform, involuntary movements, personality changes and dementia. HD is caused by a CAG repeat expansion in the IT15gene, which...
   - Type: pathway  Taxonomic scope: organism-specific biosystem  Organism: *Homo sapiens*
   - Proteins  Genes  Compounds  PubMed

3. **Direct p53 effectors**
   - Type: pathway  Taxonomic scope: organism-specific biosystem  Organism: *Homo sapiens*
   - Proteins  PubMed

4. **Huntington's disease**
   - Huntington disease (HD) is an autosomal-dominant neurodegenerative disorder that primarily affects medium spiny striatal neurons (MSN). The symptoms are choreiform, involuntary movements, personality changes and dementia. HD is caused by a CAG repeat expansion in the IT15gene, which...
   - Type: pathway  Taxonomic scope: conserved biosystem
   - Proteins  Genes  Compounds  PubMed
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
Chi and Lam (2005) Structural roles of CTG repeats in slippage expansion during DNA replication
Nucleic acids Res. 33, 1604-1617.
Age of Onset and Repeat Length
Cystic Fibrosis

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

Mucus blocks air sacs (alveoli) in the lungs.

Mucus blocks pancreatic ducts.

Pancreatic duct

Stomach

Pancreas
Cystic Fibrosis

- Autosomal (chromosome 7q31.2) recessive
- 3% of North American Caucasians are carriers
- 1.5% of African Americans are carriers
- Inhibits many bodily secretions
  - Pancreatic digestive enzymes
  - Sweat glands
  - Lung mucosa in alveoli and bronchi
  - Infertility in males (>97%)
- 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>
<th>Population Group</th>
<th>Approximate Carrier Frequency</th>
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<tr>
<td>(\Delta F508)</td>
<td>66.0%</td>
<td>II</td>
<td>Ashkenazi Jewish</td>
<td>1:29</td>
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<td>G542X</td>
<td>2.4%</td>
<td>I</td>
<td>North American</td>
<td>1:28</td>
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<tr>
<td>G551D</td>
<td>1.6%</td>
<td>III</td>
<td>Caucasian</td>
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<tr>
<td>N1303Lys</td>
<td>1.3%</td>
<td>II</td>
<td>African American</td>
<td>1:61</td>
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<tr>
<td>W1282X</td>
<td>1.2%</td>
<td>I</td>
<td></td>
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<tr>
<td>R553X</td>
<td>0.7%</td>
<td>I</td>
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<tr>
<td>621+1G&gt;T</td>
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<td>I</td>
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<td>1717-1G&gt;A</td>
<td>0.6%</td>
<td>I</td>
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<td>R117H</td>
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<td>IV</td>
<td></td>
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<tr>
<td>R1162X</td>
<td>0.3%</td>
<td>Not clear (^4)</td>
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</tr>
</tbody>
</table>


© Doug Brutlag 2015
Role of CFTR in Pancreatic Secretion

Cone Cells in Retina Permit Color Vision

http://en.wikipedia.org/wiki/Opsin
Opsins are the visual pigments in the rod and cone cells.

http://en.wikipedia.org/wiki/Opsin
Opsins and Colorblindness

[Link to Wikipedia article on Opsin]

Rhodopsin (7TM, GPCR) and 11-cis retinal
Diagnosis of Colorblindness

Search: 'Colorblindness'
Results: 1 - 10 of 36 | Show all | 1 2 3 4 5 6 | Next | Last

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

5. # 262300. ACHROMATOPSIA 3; ACHM3
   Cytogenetic location: 8q21.3
   Matching terms: colorblindness, colourblindness

6. # 216900. ACHROMATOPSIA 2; ACHM2
   Cytogenetic location: 2q11.2
   Matching terms: colorblindness, colourblindness

7. * 605080. CYCLIC NUCLEOTIDE-GATED CHANNEL, BETA-3; CNGB3
   Cytogenetic location: 8q21.3, Genomic coordinates: GRCh37: 8:87,586,162 - 87,785,902
   Matching terms: colorblindness, colourblindness

8. * 300821. OPSIN 1, MEDIUM-WAVE-SENSITIVE; OPN1MW
   Cytogenetic location: Xq28, Genomic coordinates: GRCh37: X:153,448,084 - 153,462,351
   Matching terms: colorblindness
#303800

COLORBLINDNESS, PARTIAL, DEUTAN SERIES; CBD

Alternative titles; symbols
DEUTAN COLORBLINDNESS; DCB
DEUTERANOPIA
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>
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</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 anomalous red-like cone.
Opsin1 Gene in OMIM

http://omim.org/entry/300821

*300821

OPSN 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 (OPN1LW; 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**

This gene encodes a light absorbing visual pigment of the opsin gene family. The encoded protein is called green cone photopigment or medium-wavelength sensitive opsin. Opsins 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 arrayed 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 deutanopic colorblindness. [provided by RefSeq, Mar 2009]

### Genomic context

<table>
<thead>
<tr>
<th>Location</th>
<th>Xq28</th>
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<tbody>
<tr>
<td>Sequence</td>
<td>Chromosome: X; NC_000023.10 (153448095..153462352)</td>
</tr>
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</table>
Color Vision Post Gene Therapy

http://www.neitzvision.com/content/genetherapy.html#daltonvideo
Genetic and Medical Web Sites

• NLM and NCBI
  - Entrez Gene
    • Protein
    • Biosystems
  - GeneReviews
  - OMIM
  - Genetics Home Reference
  - Genes and Diseases
  - Genetic Testing Registry
  - MedGen
  - Medline Plus
Please choose a single gene, Mendelian disease from one of the Disease databases (Genes and Disease, Genetics Home Reference, Gene Reviews or Online Inheritance in Man (OMIM) and prepare a written case presentation of the disease (4 pages max) of double spaced text. Figures, Tables and References need not be included in this limit, just the written text.

Please Include:
1. A URL pointer to OMIM and/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. A 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.
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?
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?
Centers for Mendelian Genomics

http://mendelian.org/

Program Rationale

Announcements

January 3, 2013

CMG recently joined Twitter this past year! Follow us @solvemendelian for the latest news regarding the program, Mendelian conditions, and new publications.

Previous Announcements

Read more

Publications

Featured Publication:
Detection of clinically relevant copy number variants with whole-exome sequencing

Abstract:

Read more.