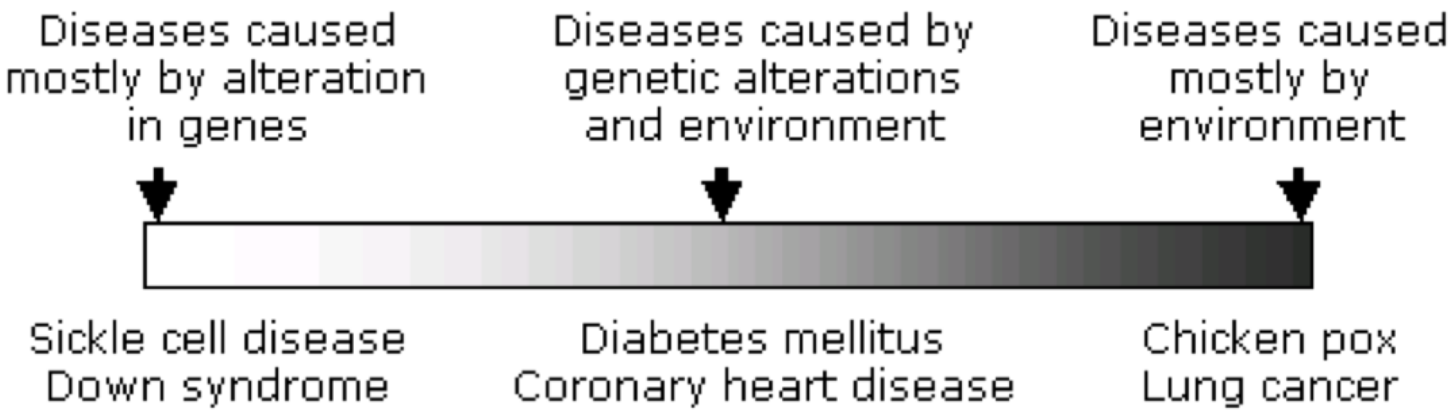
Diseases and Disease Databases

http://biochem118.stanford.edu/

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

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.

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

Huntington Disease Video

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.

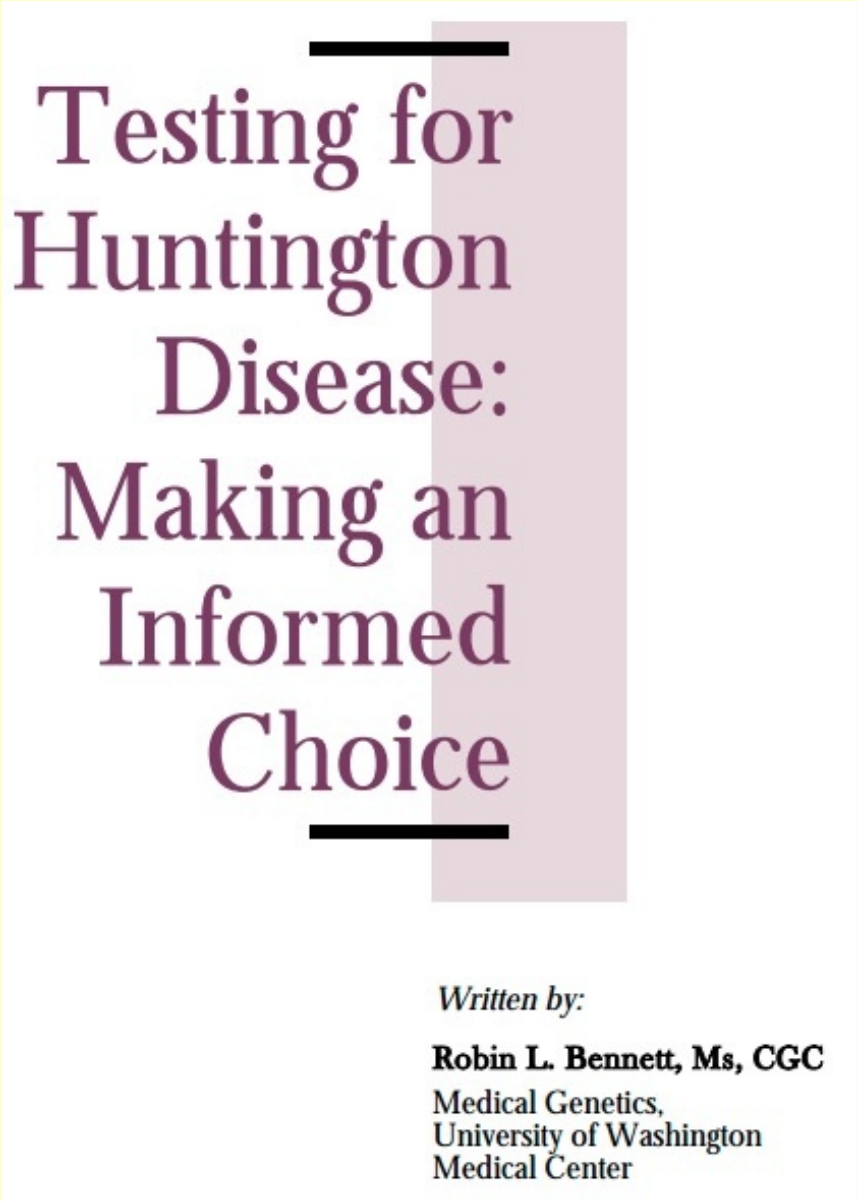
Adverse Events of Huntington's Test

- 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



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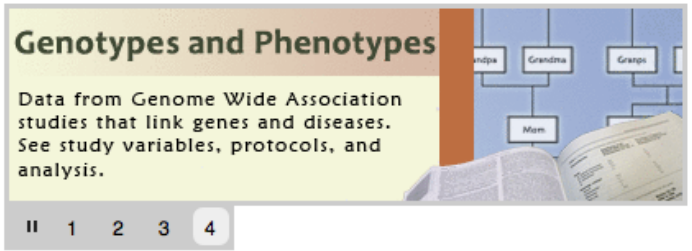

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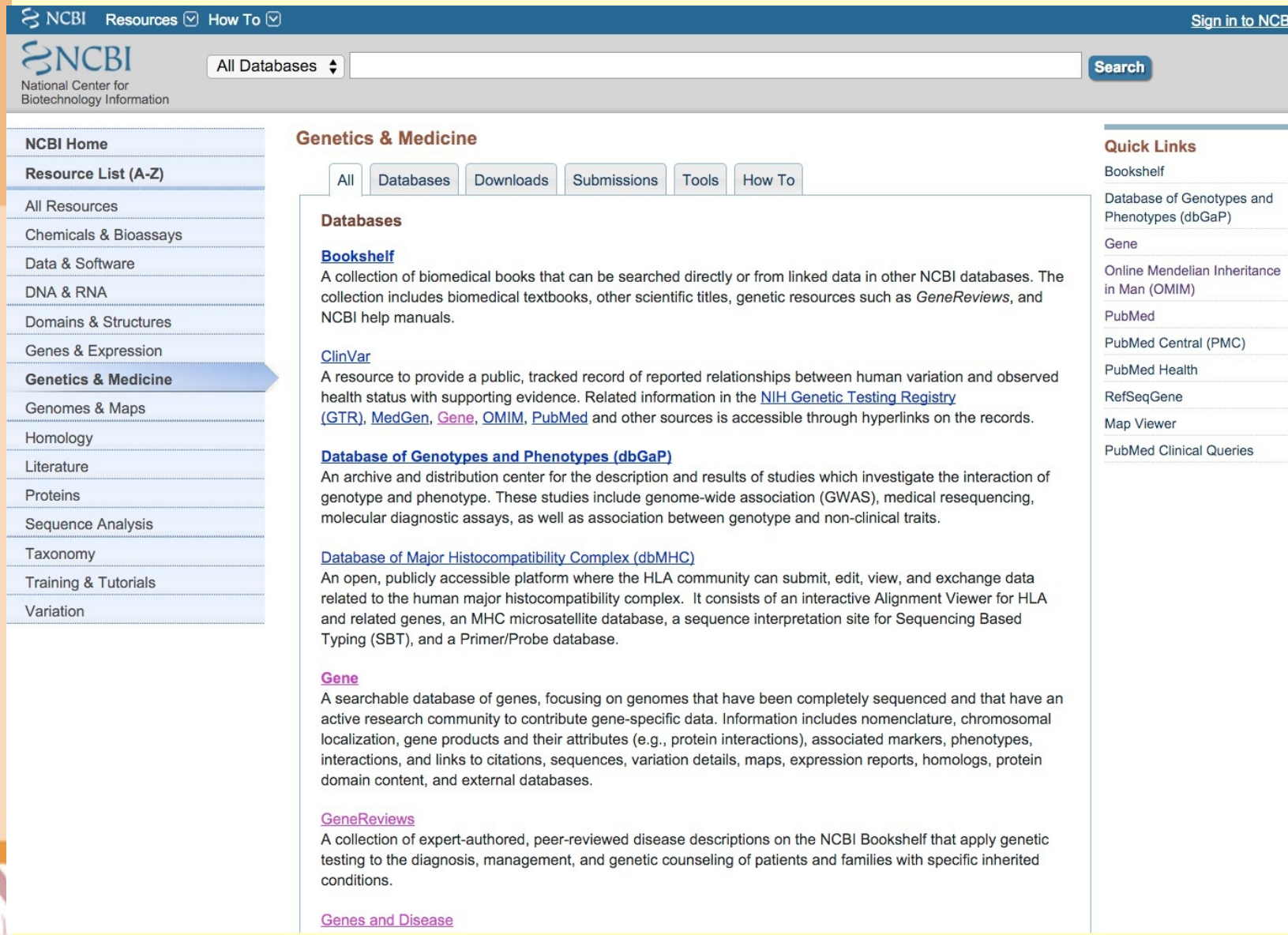
New NCBI News Issue
29 Nov 2010
Information about the RefSeqGene Project and

NCBI: Genetics and Medicinehttp://www.ncbi.nlm.nih.gov/guide/genetics-medicine/



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National Center for Biotechnology Information (US)

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

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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

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Blood and Lymph Diseases

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Contents

- Introduction to Genes and Disease
- Blood and Lymph Diseases
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- Glands and Hormones
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Contents

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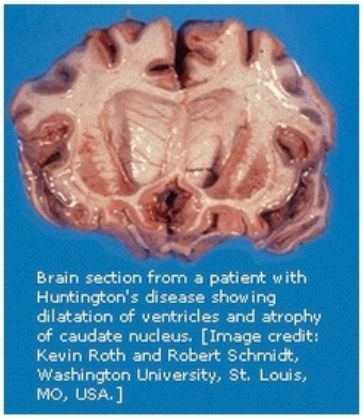

Brain section from a patient with Huntington's disease showing dilatation of ventricles and atrophy of caudate nucleus. [Image credit: Kevin Roth and Robert Schmidt, Washington University, St. Louis, MO, USA.]

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

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GeneReviews a medical genetics resource

Websites

Huntington Disease Society of America information for patients and the public

Genetics Home Reference

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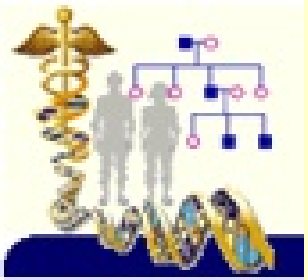

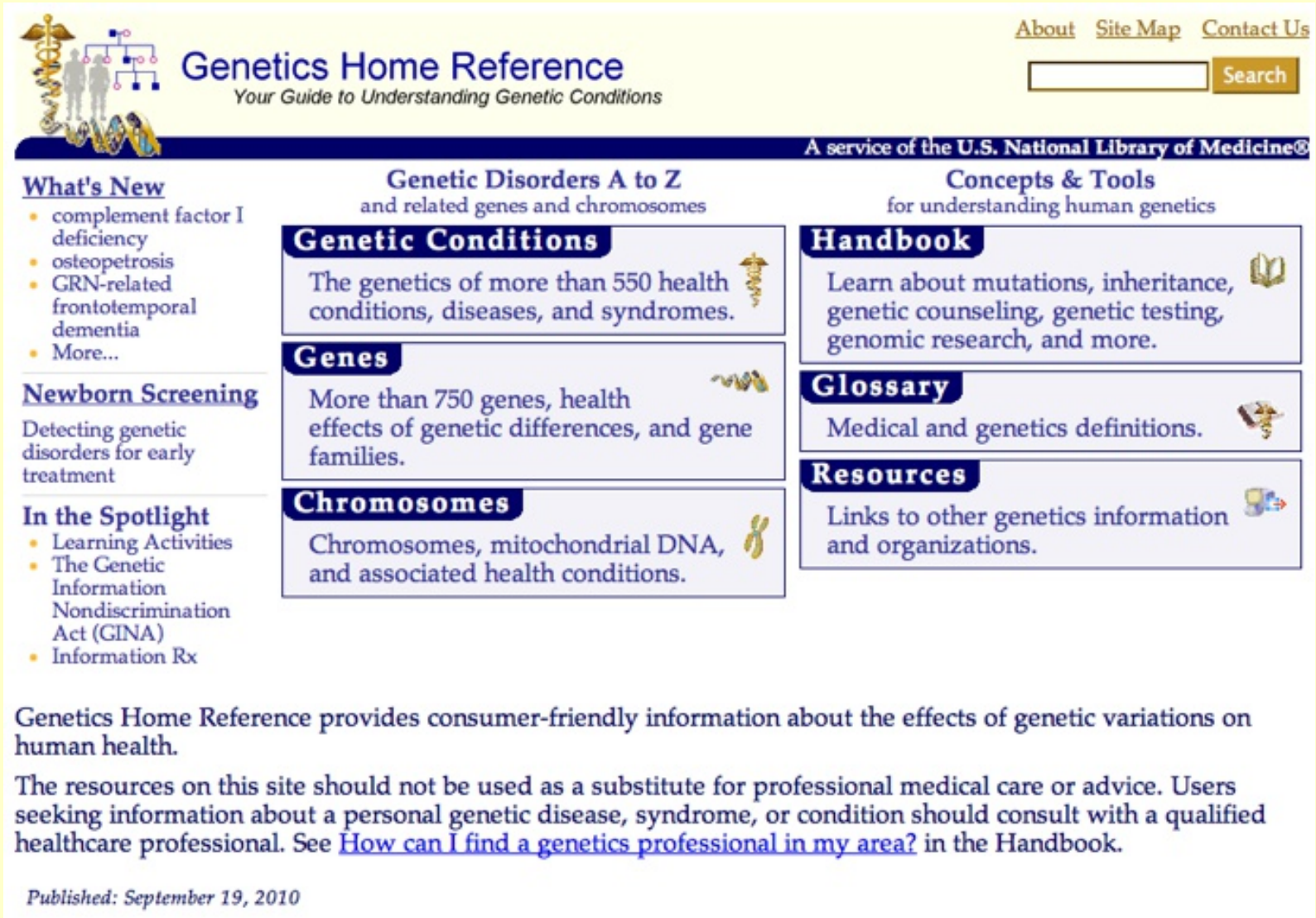

Huntington Disease in Genetics Home Reference

http://ghr.nlm.nih.gov/condition/huntington-disease

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

Reviewed October 2008

What is Huntington disease?

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

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

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

How common is Huntington disease?

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

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1 2 3 4 ▶

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Home → Health Topics → Huntington's Disease

Huntington's Disease

Also called: HD, Huntington's chorea

On this page

Basics
- Summary
- Start Here

Learn More
- Related Issues
- Genetics

See, Play and Learn
- Tutorials

Research
- Statistics and Research
- Clinical Trials
- Journal Articles

Resources
- Reference Desk
- Find an Expert

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- Teenagers
- Patient Handouts

A.D.A.M.

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.

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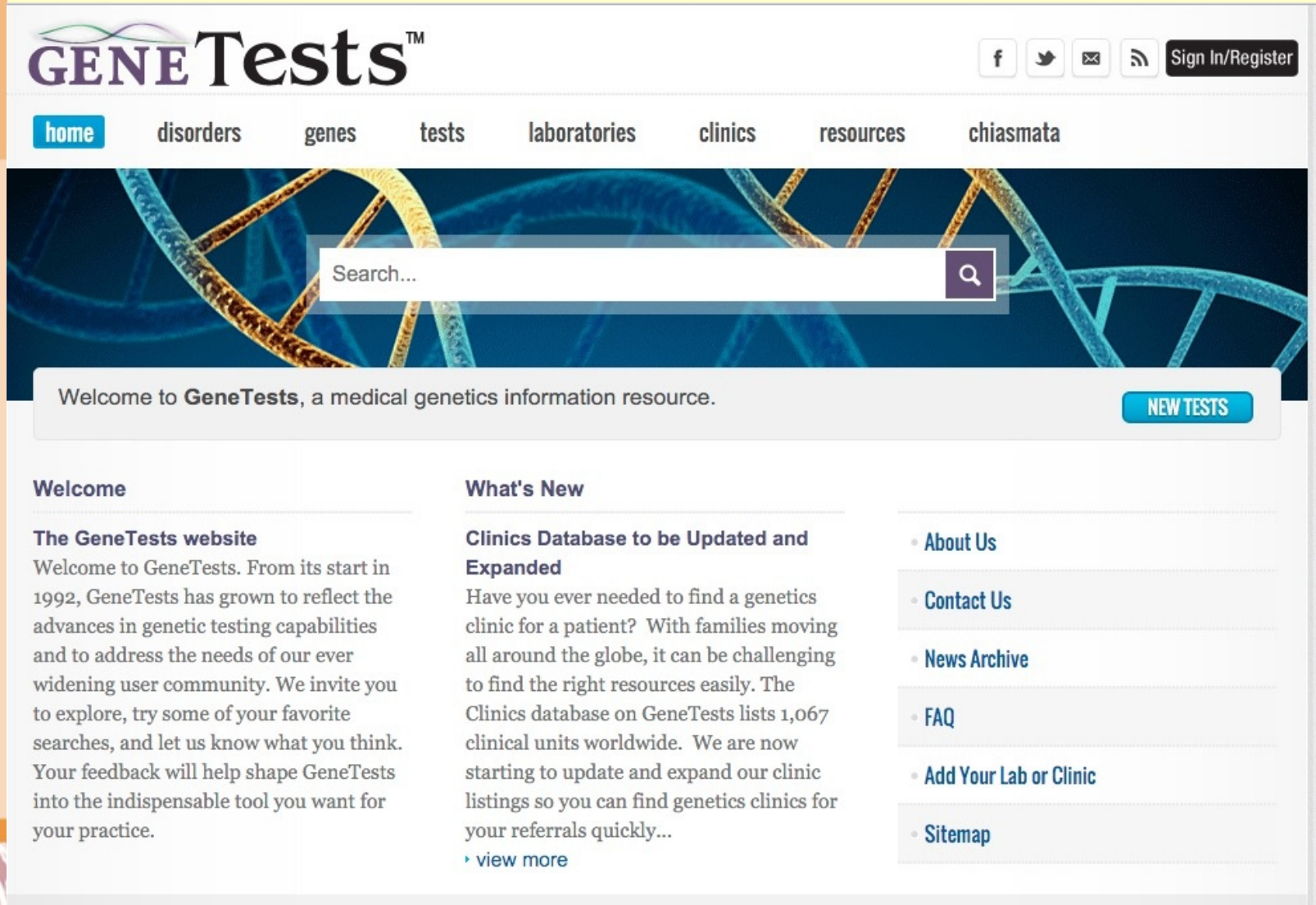
GeneTests & GeneReviews for Huntington's

https://www.genetests.org/



Huntington Disease Gene Review

http://www.ncbi.nlm.nih.gov/books/NBK1305/

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 *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.

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Test

Huntington Disease
TAT: 1-2 weeks
price: contact lab
gene(s): HTT
disorder(s): Huntington Disease
method(s): ◦ Repeat Expansion / Contraction
Stanford Clinical Laboratories, Molecular Pathology Laboratory - *Palo Alto, CA, USA*

Huntington Disease (HD) Mutation by PCR
TAT: 7-10 days
price: contact lab
gene(s): HTT
disorder(s): Huntington Disease
method(s): ◦ Genotyping (Microarray, Beads, etc.)
ARUP Laboratories, Molecular Genetics Laboratory - *Salt Lake City, UT, USA*

Huntington Disease Test
TAT: contact lab
price: contact lab
gene(s): HTT
disorder(s): Huntington Disease
method(s): ◦ Repeat Expansion / Contraction
All Children's Hospital, Johns Hopkins Medicine, Clinical Molecular Genetics Laboratory - *St. Petersburg, FL, USA*

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GENETests

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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

- **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

- **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

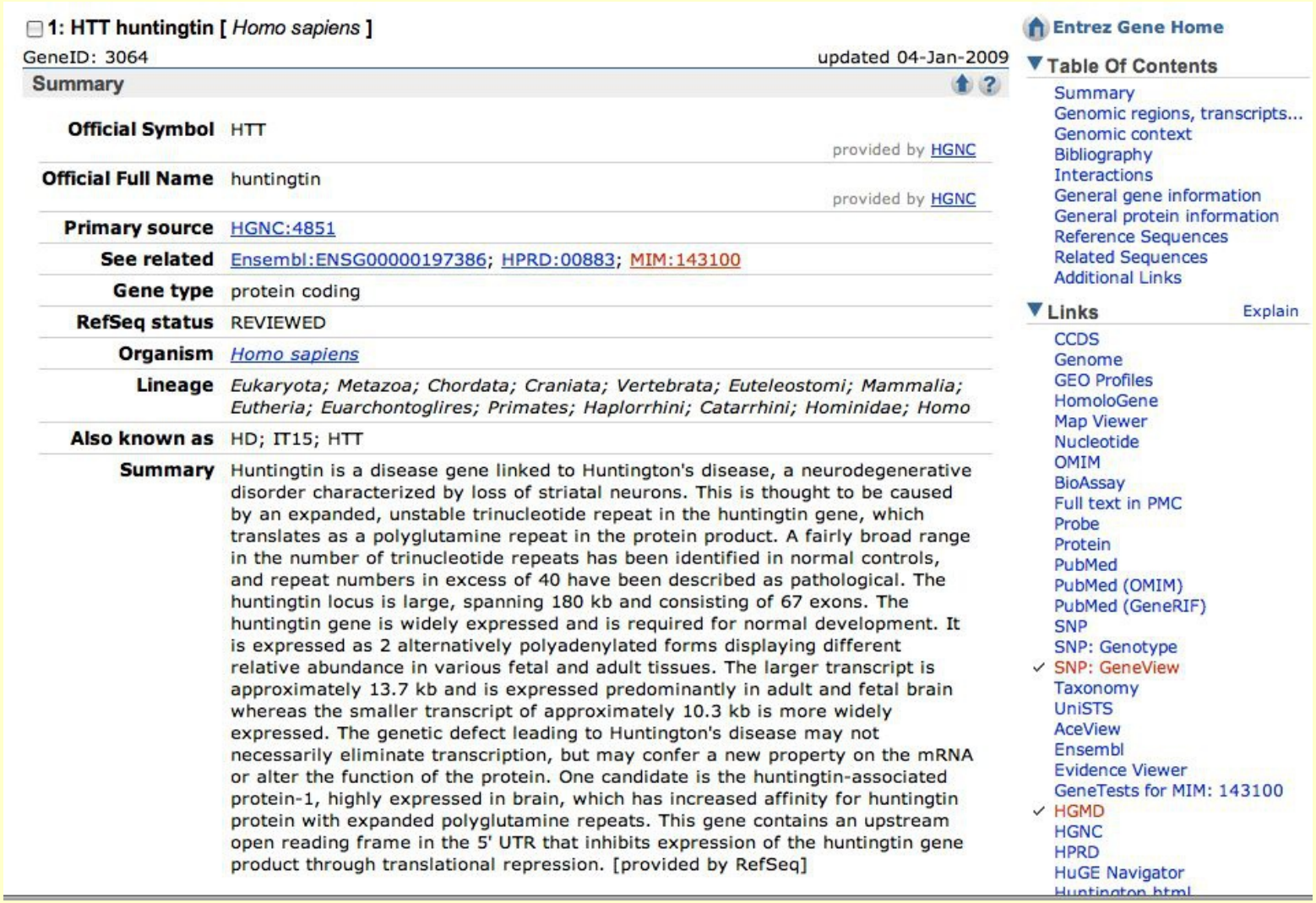
- **International Huntington Association**
  Callunahof 8
  Harfsen 7217 ST
  Netherlands
  Phone: +31 573 431 595
  Fax: +31 573 431 719
  Email: iha@huntington-assoc.com
  www.huntington-assoc.com

- **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

Entrez Gene for Huntington



1: HTT huntingtin [*Homo sapiens*]

GeneID: 3064 updated 04-Jan-2009

Summary

Official Symbol	HTT provided by HGNC
Official Full Name	huntingtin provided by HGNC
Primary source	HGNC:4851
See related	Ensembl:ENSG00000197386; HPRD:00883; MIM:143100
Gene type	protein coding
RefSeq status	REVIEWED
Organism	*Homo sapiens*
Lineage	*Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo*
Also known as	HD; IT15; HTT
Summary	Huntingtin is a disease gene linked to Huntington's disease, a neurodegenerative disorder characterized by loss of striatal neurons. This is thought to be caused by an expanded, unstable trinucleotide repeat in the huntingtin gene, which translates as a polyglutamine repeat in the protein product. A fairly broad range in the number of trinucleotide repeats has been identified in normal controls, and repeat numbers in excess of 40 have been described as pathological. The huntingtin locus is large, spanning 180 kb and consisting of 67 exons. The huntingtin gene is widely expressed and is required for normal development. It is expressed as 2 alternatively polyadenylated forms displaying different relative abundance in various fetal and adult tissues. The larger transcript is approximately 13.7 kb and is expressed predominantly in adult and fetal brain whereas the smaller transcript of approximately 10.3 kb is more widely expressed. The genetic defect leading to Huntington's disease may not necessarily eliminate transcription, but may confer a new property on the mRNA or alter the function of the protein. One candidate is the huntingtin-associated protein-1, highly expressed in brain, which has increased affinity for huntingtin protein with expanded polyglutamine repeats. This gene contains an upstream open reading frame in the 5' UTR that inhibits expression of the huntingtin gene product through translational repression. [provided by RefSeq]

Entrez Gene Home

Table Of Contents

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

Links Explain

- CCDS
- Genome
- GEO Profiles
- HomoloGene
- Map Viewer
- Nucleotide
- OMIM
- BioAssay
- Full text in PMC
- Probe
- Protein
- PubMed
- PubMed (OMIM)
- PubMed (GeneRIF)
- SNP
- SNP: Genotype
- ✓ SNP: GeneView
- Taxonomy
- UniSTS
- AceView
- Ensembl
- Evidence Viewer
- GeneTests for MIM: 143100
- ✓ HGMD
- HGNC
- HPRD
- HuGE Navigator
- Huntington.html

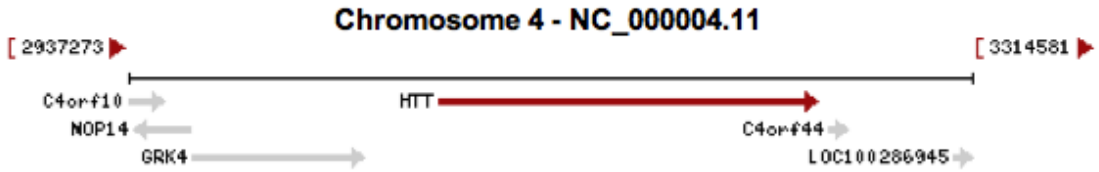
Huntington Disease Gene

http://www.ncbi.nlm.nih.gov/gene/3064

Genomic context

Location : 4p16.3
Sequence : Chromosome: 4; NC_000004.11 (3076408..3245687)

See HTT in MapViewer



Genomic regions, transcripts, and products

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Genomic Sequence NC_000004 chromosome 4 reference GRCh37.p5 Primary Assembly

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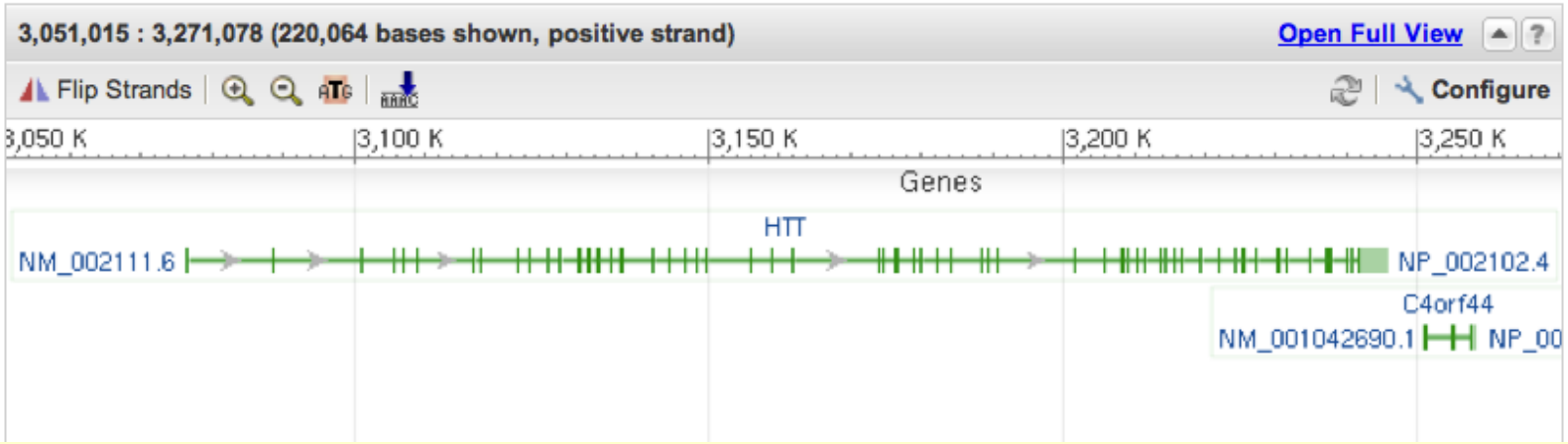

Huntington Disease Gene

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HTT huntingtin [*Homo sapiens*]

Gene ID: 3064, updated on 3-Jan-2011

Summary

Official Symbol	HTT provided by HGNC
Official Full Name	huntingtin provided by HGNC
Primary source	HGNC:4851
See related	Ensembl:ENSG00000197386; HPRD:00883; MIM:613004
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Homo sapiens
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo
Also known as	HD; IT15; HTT
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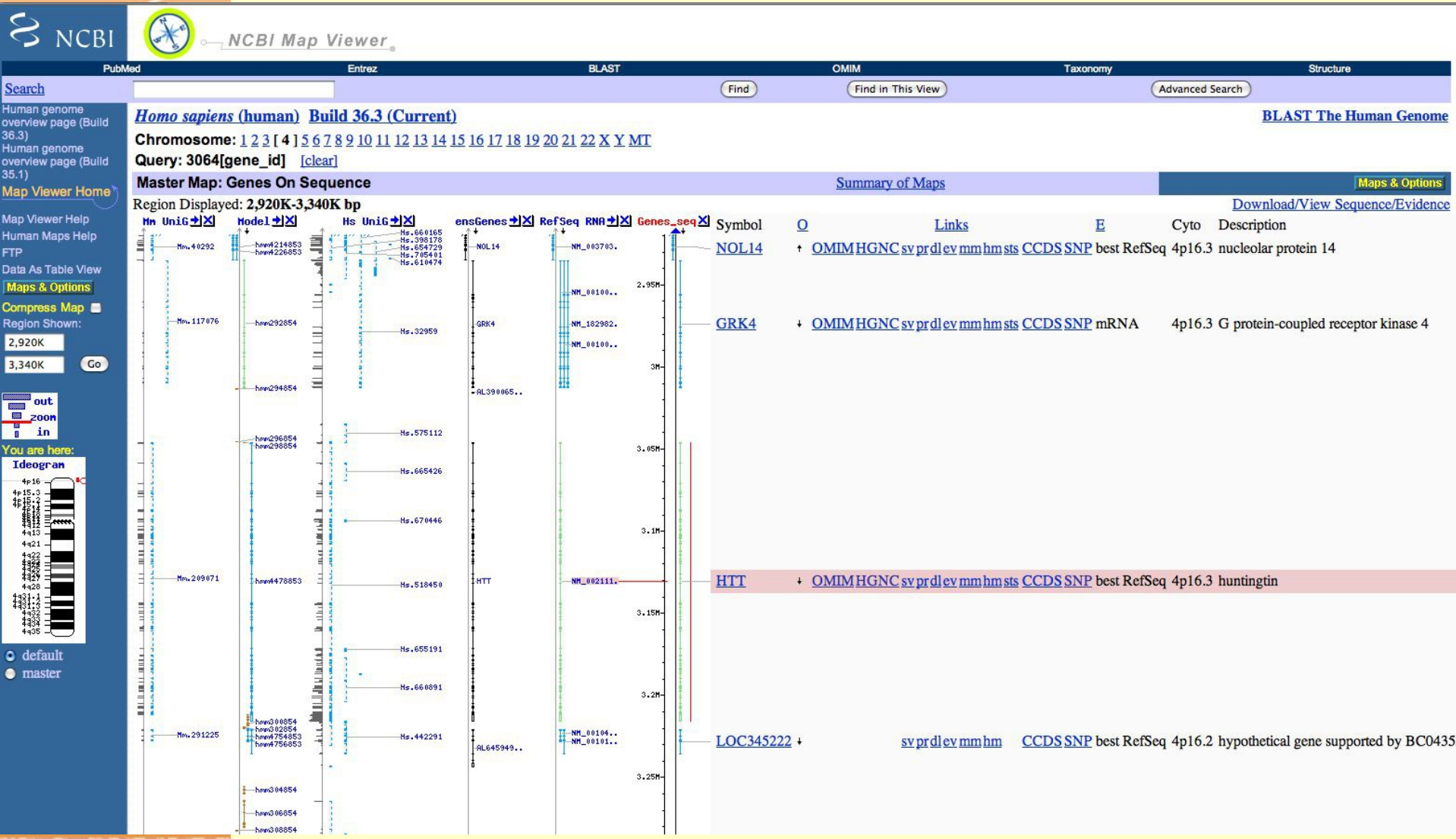
Table of contents

- Summary
- Genomic regions, transcripts, and products
- Genomic context
- Bibliography
- Phenotypes
- Interactions
- General gene info
- General protein info
- Reference sequences
- Related sequences
- Additional links

Links

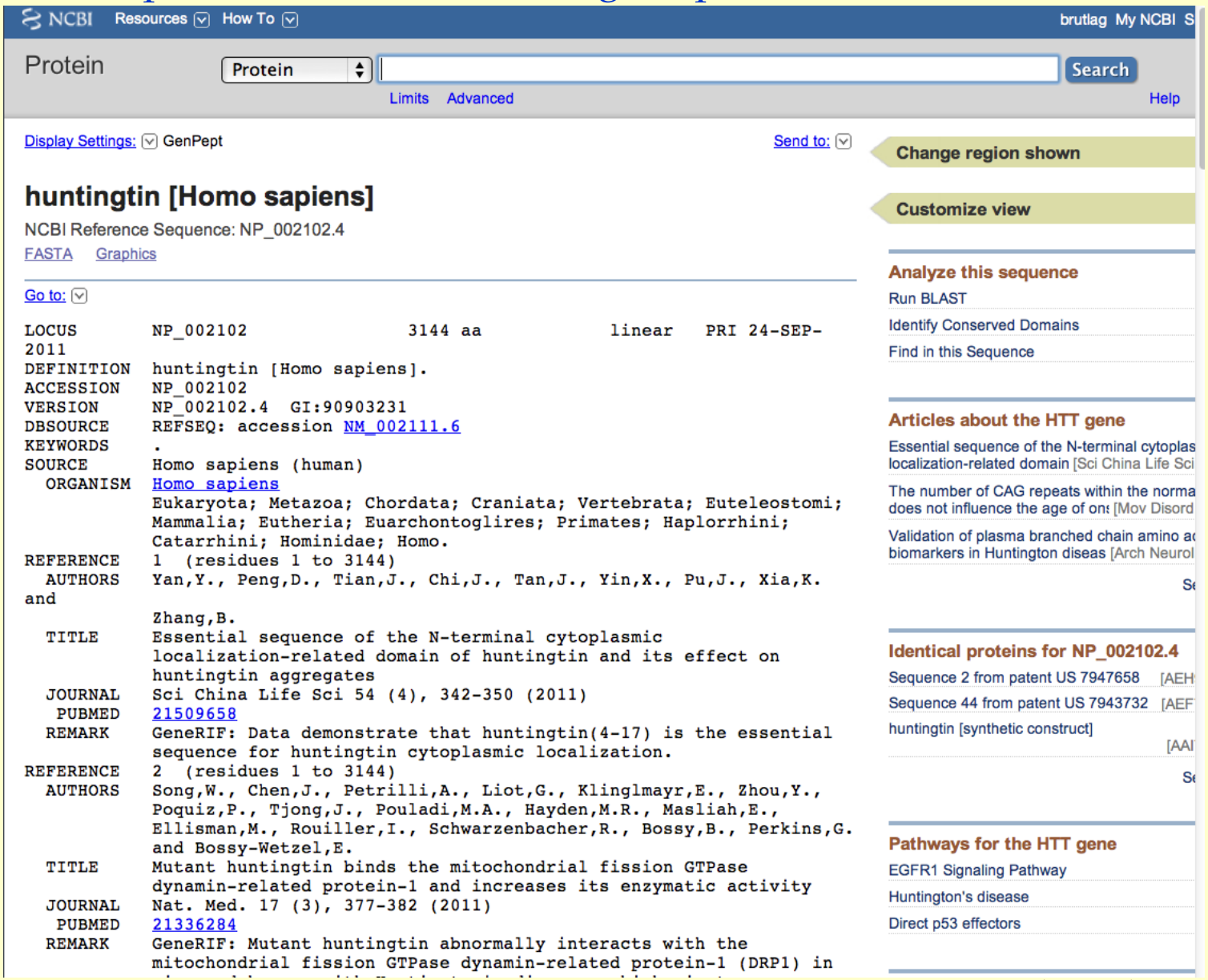
- Order cDNA clone
- BioAssay, by Gene target
- BioSystems
- Books
- CCDS
- Conserved Domains
- Full text in PMC
- GEO Profiles
- Genome
- HomoloGene
- Map Viewer
- Nucleotide

MapViewer for Huntington



Huntingtin Protein

http://www.ncbi.nlm.nih.gov/protein/NP_002102.4



NCBI Resources How To brutlag My NCBI S

Protein Protein Search

Limits Advanced Help

Display Settings: GenPept Send to:

Change region shown

Customize view

huntingtin [Homo sapiens]

NCBI Reference Sequence: NP_002102.4

FASTA Graphics

Go to:

```
LOCUS       NP_002102               3144 aa            linear   PRI 24-SEP-
2011
DEFINITION  huntingtin [Homo sapiens].
ACCESSION   NP_002102
VERSION     NP_002102.4  GI:90903231
DBSOURCE    REFSEQ: accession NM_002111.6
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 3144)
  AUTHORS   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
  JOURNAL   Sci China Life Sci 54 (4), 342-350 (2011)
   PUBMED   21509658
  REMARK    GeneRIF: Data demonstrate that huntingtin(4-17) is the essential
            sequence for huntingtin cytoplasmic localization.
REFERENCE   2  (residues 1 to 3144)
  AUTHORS   Song,W., Chen,J., Petrilli,A., Liot,G., Klinglmayr,E., Zhou,Y.,
            Poquiz,P., Tjong,J., Pouladi,M.A., Hayden,M.R., Masliah,E.,
            Ellisman,M., Rouiller,I., Schwarzenbacher,R., Bossy,B., Perkins,G.
and Bossy-Wetzel,E.
  TITLE     Mutant huntingtin binds the mitochondrial fission GTPase
            dynamin-related protein-1 and increases its enzymatic activity
  JOURNAL   Nat. Med. 17 (3), 377-382 (2011)
   PUBMED   21336284
  REMARK    GeneRIF: Mutant huntingtin abnormally interacts with the
            mitochondrial fission GTPase dynamin-related protein-1 (DRP1) in
```

Analyze this sequence

Run BLAST

Identify Conserved Domains

Find in this Sequence

Articles about the HTT gene

Essential sequence of the N-terminal cytoplas
localization-related domain [Sci China Life Sci

The number of CAG repeats within the norma
does not influence the age of ons [Mov Disord

Validation of plasma branched chain amino ac
biomarkers in Huntington diseas [Arch Neurol

Identical proteins for NP_002102.4

Sequence 2 from patent US 7947658 [AEH

Sequence 44 from patent US 7943732 [AEF

huntingtin [synthetic construct]
[AAI

Pathways for the HTT gene

EGFR1 Signaling Pathway

Huntington's disease

Direct p53 effectors

```
ORIGIN
        1 matleklmka feslksfqqq qqqqqqqqqq qqqqqqqqqq pppppppppp pqlpqpppqa
       61 qpllpqpqpp pppppppgp avaeeplhrp kkelsatkkd rvnhcltice nivaqsvrns
      121 pefqkllgia melfllcsdd aesdvrmvad eclnkvikal mdsnlprlql elykeikkng
      181 aprslraalw rfaelahlvr pqkcrpylvn llpcltrtsk rpeesvqetl aaavpkimas
      241 fgnfandnei kvllkafian lkssptirr taagsavsic qhsrrtqyfy swllnvllgl
      301 lvpvedehst llilgvlltl rylvpllqqq vkdtslkgsf gvtrkemevs psaeqlvqvy
      361 eltlhhtqhq dhnvvtgale llqqlfrtpp pellqtltav ggigqltaak eesggrsrsg
      421 siveliaggg sscspvlsrk qkgkvllgee ealeddsesr sdvsssalta svkdeisgel
      481 aassgvstpg saghdiiteq prsqhtlqad svdlascdlt ssatdgdeed ilshsssqvs
      541 avpsdpamdl ndgtqasspi sdssqttteg pdsavtpsds seivldgtdn qylglqigqp
      601 qdedeeatgi lpdeaseafr nssmalqqah llknmshcrq psdssvdkfv lrdeatepgd
      661 qenkpcrikg digqstddds aplvhcvrll sasflltggk nvlvpdrdvr vsvkalalsc
      721 vgaavalhpe sffsklykvp ldtteypeeq yvsdilnyid hgdpqvrgat ailcgtlics
      781 ilsrsrfhvg dwmgtirtlt gntfsladci pllrktlkde ssvtcklact avrncvmslc
      841 sssyselglq liidvltlrn ssywlvrtel letlaeidfr lvsfleakae nlhrgahhyt
      901 gllklqervl nnvvihllgd edprvrhvaa aslirlvpkl fykcdqgqad pvvavardqs
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     1021 raltfgccea lcllstafpv ciwslgwhcg vpplsasdes rksctvgmat miltllssaw
     1081 fpldlsahqd alilagnlla asapkslrss waseeeanpa atkqeevwpa lgdralvpmv
     1141 eqlfshllkv inicahvldd vapgpaikaa lpsltnppsl spirrkgkek epgeqasvpl
     1201 spkkgseasa asrqsdtsgp vttsksssig sfyhlpsylk lhdvlkatha nykvtldlqn
     1261 stekfggflr saldvlsqil elatlqdigk cveeilgylk scfsrepmma tvcvqqllkt
     1321 lfgtnlasqf dglssnpsks qgraqrlgss svrpglyhyc fmapythftq aladaslrnm
     1381 vqaeqendts gwfdvlqkvs tqlktnltsv tknradknai hnhirlfepl vikalkqytt
     1441 ttcvqlqkqv ldllaqlvql rvnyclldsd qvfigfvlkq feyievgqfr eseaiipnif
     1501 fflvllsyer yhskqiigip kiiqlcdgim asgrkavtha ipalqpivhd lfvlrgtnka
     1561 dagkeletqk evvvsmllrl iqyhqvlemf ilvlqqchke nedkwkrlsr qiadiilpml
     1621 akqqmhidsh ealgvlntlf eilapsslrp vdmllrsmfv tpntmasvst vqlwisgila
     1681 ilrvlisqst edivlsriqe lsfspylisc tvinrlrdgd ststleehse gkqiknlpee
     1741 tfsrfllqlv gilledivtk qlkvemseqq htfycqelgt llmclihifk sgmfrritaa
     1801 atrlfrsdgc ggsfytldsl nlrarsmitt hpalvllwcq illlvnhtdy rwwaevqqtp
     1861 krhslsstkl lspqmsgeee dsdlaaklgm cnreivrrga lilfcdyvcq nlhdsehltw
     1921 livnhiqdli slsheppvqd fisavhrnsa asglfiqaiq srcenlstpt mlkktlqcle
     1981 gihlsqsgav ltlyvdrllc tpfrvlarmv dilacrrvem llaanlqssm aqlpmeelnr
     2041 iqeylqssgl aqrhqrlysl ldrfrlstmq dslspsppvs shpldgdghv sletvspdkd
     2101 wyvhlvksqc wtrsdsalle gaelvnripa edmnafmmns efnlsllapc lslgmseisg
     2161 gqksalfeaa revtlarvsg tvqqlpavhh vfqpelpaep aaywsklndl fgdaalyqsl
     2221 ptlaralaqy lvvvsklpsh lhlppekekd ivkfvvatle alswhliheq iplsldlqag
     2281 ldccclalql pglwsvvsst efvthacsli ycvhfileav avqpgeqlls perrtntpka
     2341 iseeeeevdp ntqnpkyita acemvaemve slqsvlalgh krnsgvpafl tpllrniiis
     2401 larlplvnsy trvpplvwkl gwspkpggdf gtafpeipve flqekevfke fiyrintlgw
     2461 tsrtqfeetw atllgvlvtq plvmeqeesp peedtertqi nvlavqaits lvlsamtvpv
     2521 agnpavscle qqprnkplka ldtrfgrkls iirgiveqei qamvskreni athhlyqawd
     2581 pvpslspatt galishekll lqinperelg smsyklgqvs ihsvwlgnsi tplreeewde
     2641 eeeeeadapa pssppptspvn srkhragvdi hscsqfllel ysrwilpsss arrtpailis
     2701 evvrsllvvs dlfternqfe lmyvtltelr rvhpsedeil aqylvpatck aaavlgmdka
     2761 vaepvsrlle stlrsshlps rvgalhgvly vlecdllddt akqlipvisd yllsnlkgia
     2821 hcvnihsqqh vlvmcatafy lienypldvg pefsasiiqm cgvmlsgsee stpsiiyhca
     2881 lrglerllls eqlsrldaes lvklsvdrvn vhsphramaa lglmltcmyt gkekvspgrt
     2941 sdpnpaapds esvivamerv svlfdrirkg fpcearvvar ilpqflddff ppqdimnkvi
     3001 geflsnqqpy pqfmatvvyk vfqtlhstgq ssmvrdwvml slsnftqrap vamatwslsc
     3061 ffvsastspw vaailphvis rmgkleqvdv nlfclvatdf yrhqieeeld rrafqsvlev
     3121 vaapgspyhr lltclrnvhk vttc
//
```
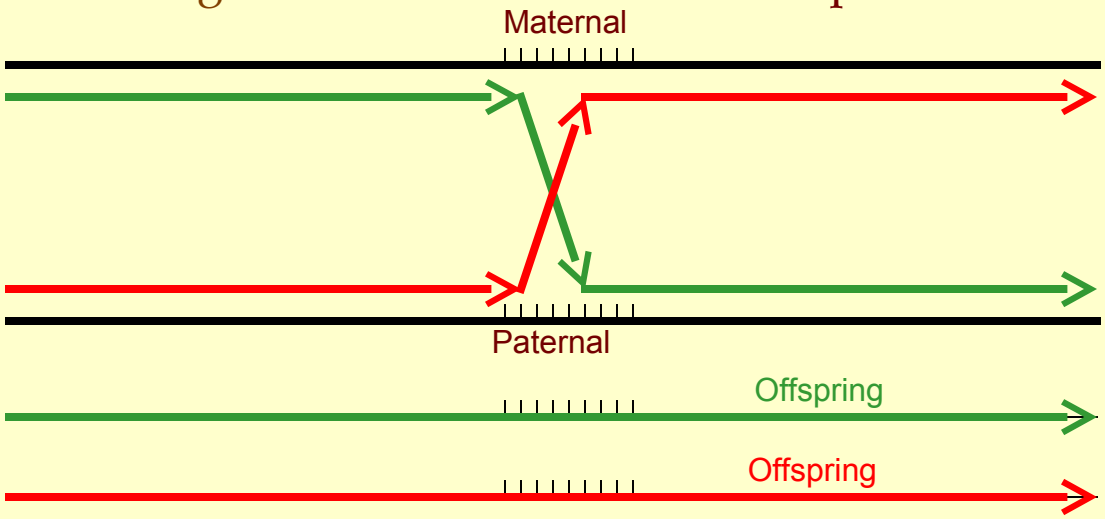
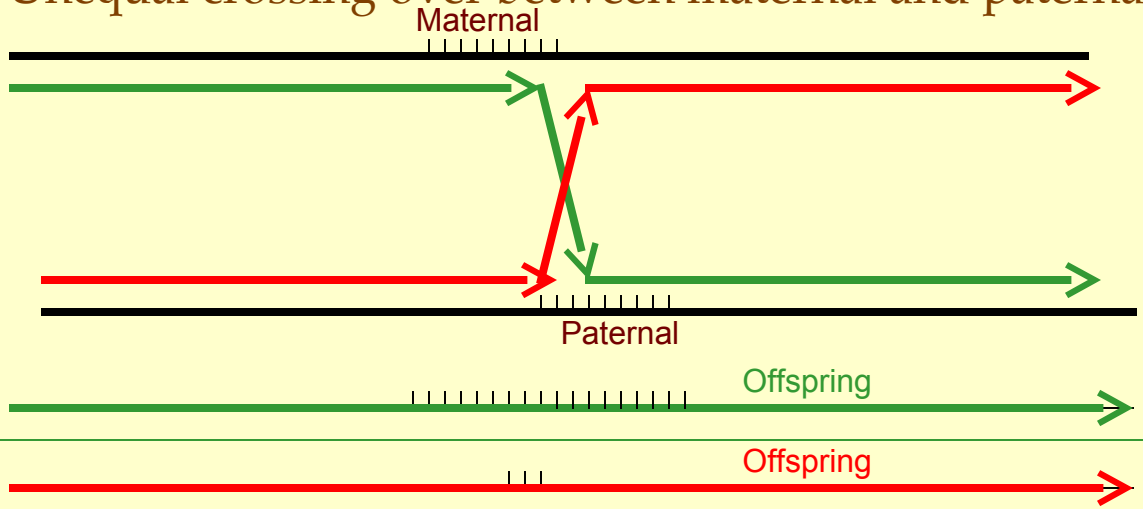

Huntington Disease can Arise from Unequal Crossing Over During Meiosis

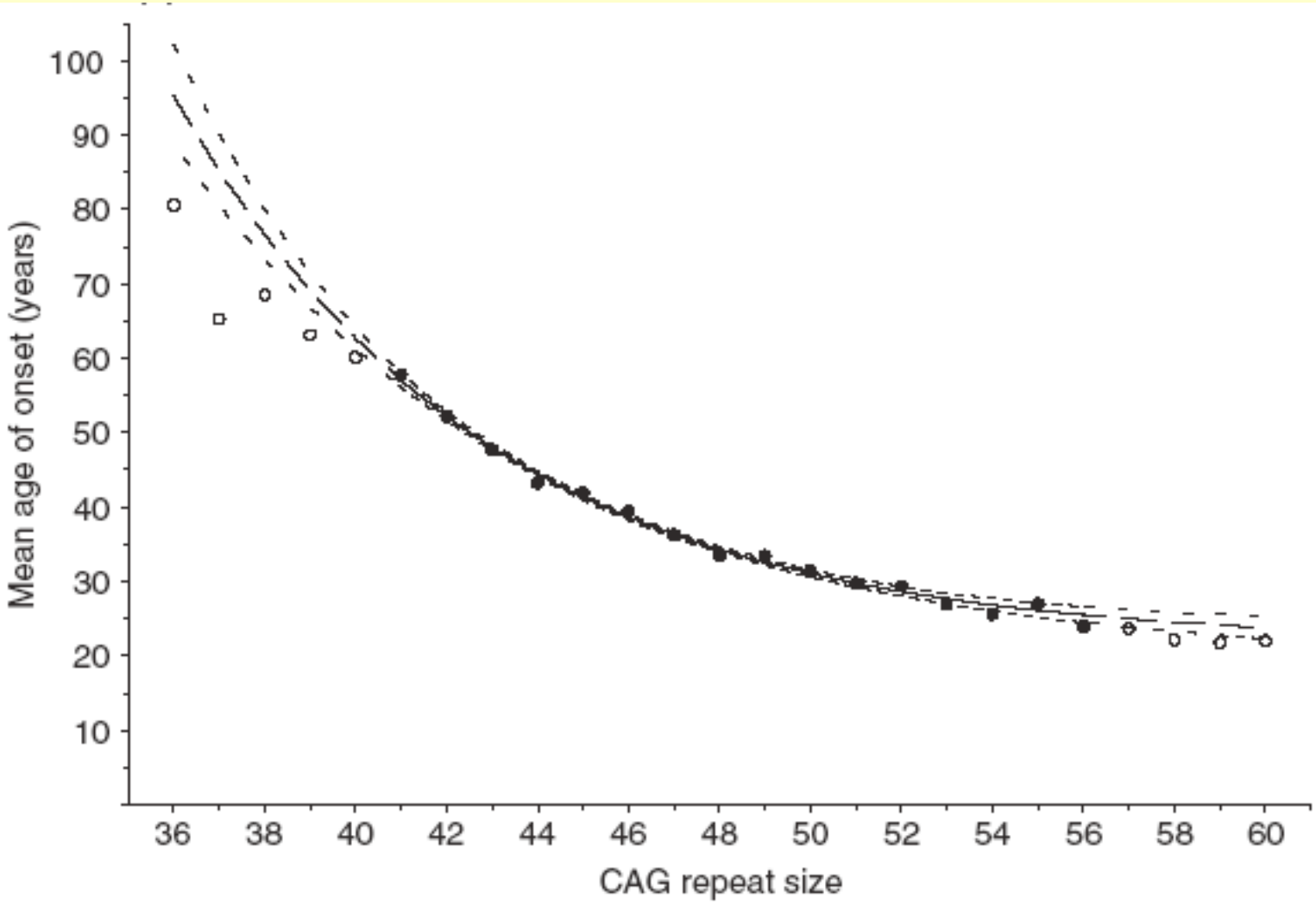
- Crossing over between maternal and paternal chromosomes



- Unequal crossing over between maternal and paternal chromosomes

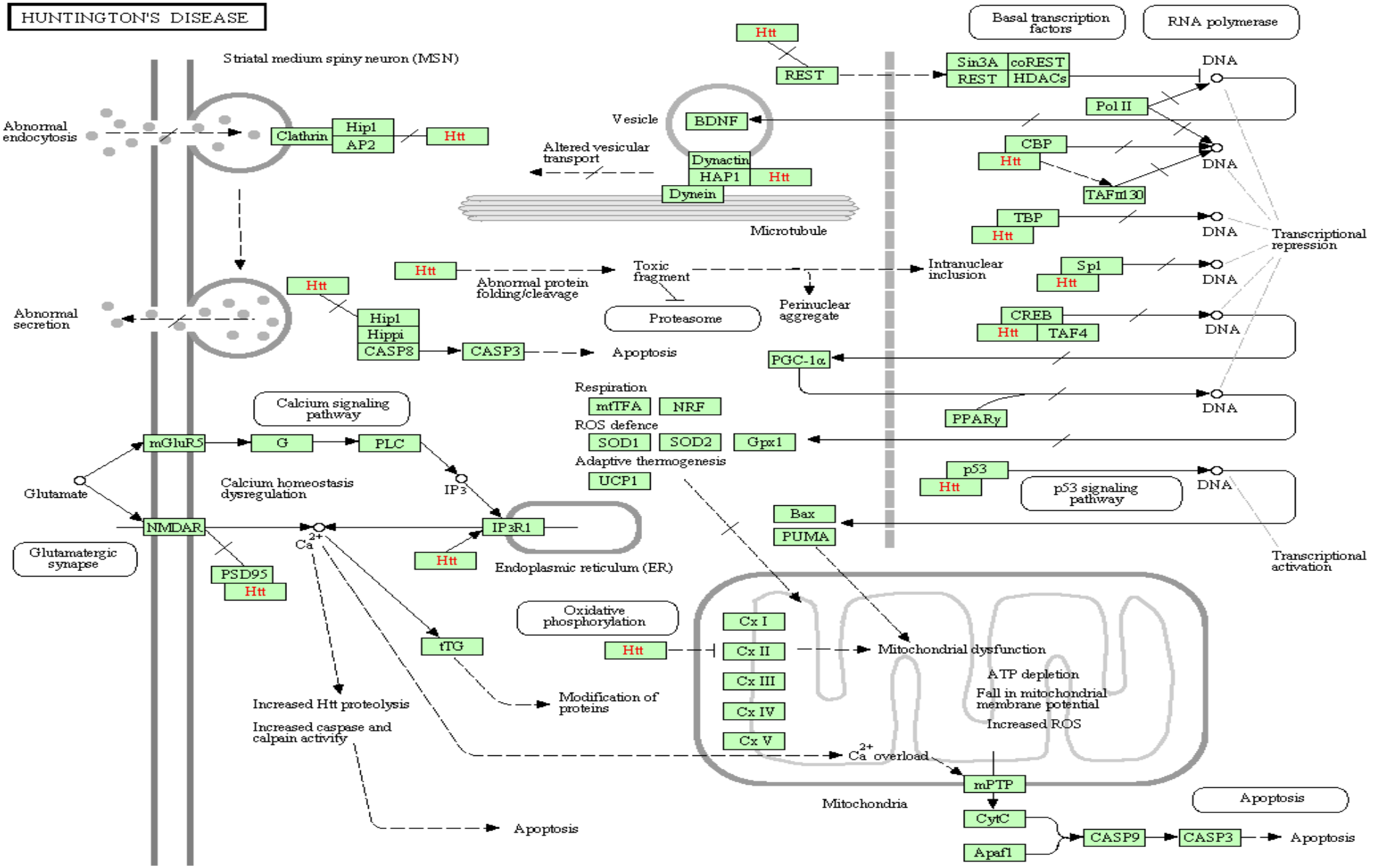


Age of Onset and Repeat Length



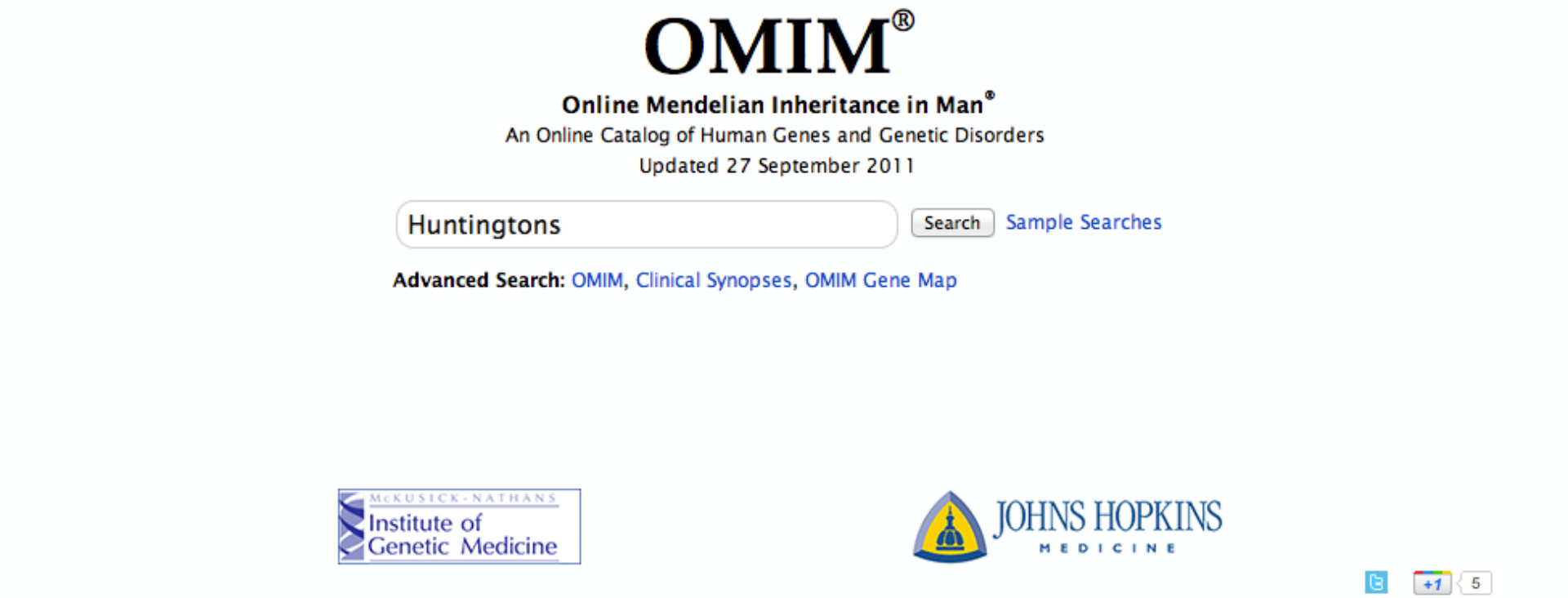
Huntington Disease Biosystem

http://www.ncbi.nlm.nih.gov/gene/3064



OMIM Home Page

http://omim.org/



Huntington Disease Search in OMIM

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

Huntingtons | Search | Sort by: Relevance | Date updated

Advanced Search: OMIM, Clinical Synopses, OMIM Gene Map **Display:** Toggle highlight
Search History: View, Clear

Retrieve corresponding: gene map | clinical synopses

Search: 'Huntingtons'

Results: 1 - 10 of 134 | Show top 100 | 1 2 3 4 5 6 7 8 9 10 Next Last

1 : # 143100. HUNTINGTON DISEASE; HD — Gene Tests, ICD+, Links
Cytogenetic location: 4p16.3

2 : # 603218. HUNTINGTON DISEASE-LIKE 1; HDL1 — Gene Tests, Links
Cytogenetic location: 20p13

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

4 : * 613004. HUNTINGTIN; HTT — Gene Tests, Links
Cytogenetic location: 4p16.3 , Genomic coordinates (GRCh37): 4:3,076,407 - 3,245,686

5 : # 606438. HUNTINGTON DISEASE-LIKE 2; HDL2 — Gene Tests, Links
Cytogenetic location: 16q24.2

6 : # 607136. SPINOCEREBELLAR ATAXIA 17; SCA17 — Gene Tests, Links
Cytogenetic location: 6q27

7 : # 125370. DENTATORUBRAL-PALLIDOLUYSIAN ATROPHY; DRPLA — Gene Tests, Links
Cytogenetic location: 12p13.31

8 : * 600947. HUNTINGTIN-ASSOCIATED PROTEIN 1; HAP1 — Links
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=huntingto

#143100

ICD+

HUNTINGTON DISEASE; HD

Alternative titles; symbols

HUNTINGTON CHOREA

Phenotype Gene Relationships

Location	Phenotype	Phenotype MIM number	Gene/Locus	Gene/Locus MIM number
4p16.3	Huntington disease	143100	HTT	613004

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

Table of Contents - #143100

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

External Links:

- Clinical Resources
- Animal Models
- Cell Lines
- Cellular Pathways

OMIM Coverage

http://www.ncbi.nlm.nih.gov/Omim/mimstats.html

OMIM Entry Statistics

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

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

OMIM Coverage

http://www.ncbi.nlm.nih.gov/Omim/mimstats.html

OMIM Gene Map Statistics:

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

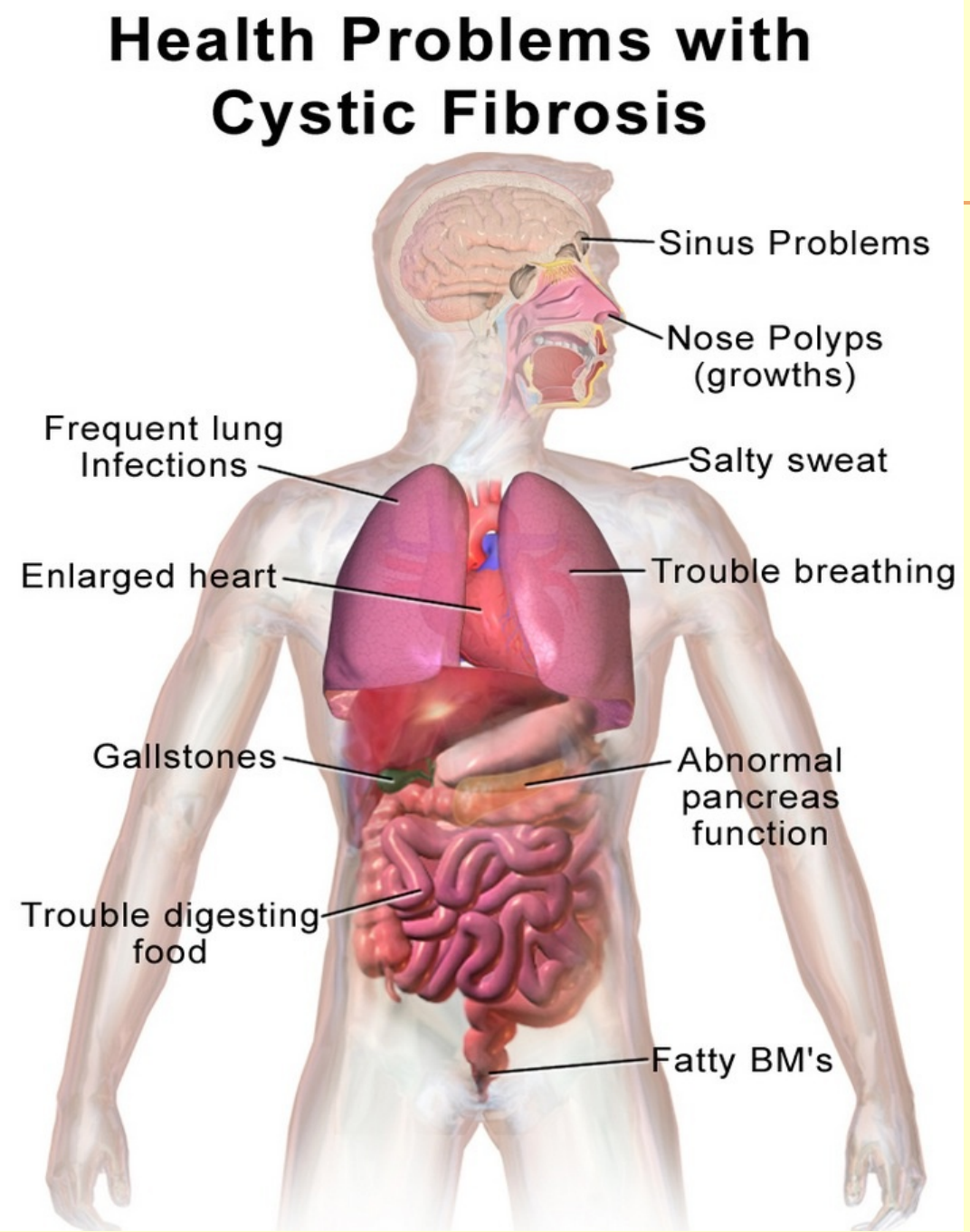
Number of phenotypes* for which the molecular basis is known	5,329
Number of genes with phenotype-causing mutation	3,289

* 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) :

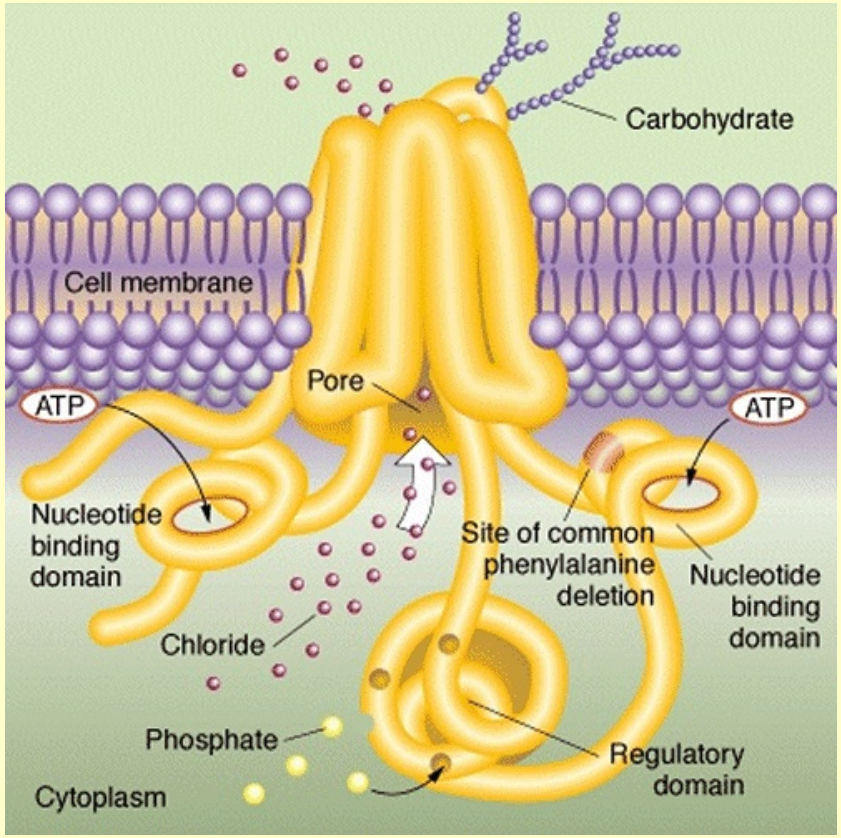
Chromosome	Count	Chromosome	Count
1	1,475	13	280
2	941	14	486
3	808	15	442
4	572	16	612
5	682	17	858
6	881	18	220
7	707	19	929
8	528	20	381
9	569	21	155
10	549	22	359
11	908	X	814
12	787	Y	53

Health Problems with Cystic Fibrosis



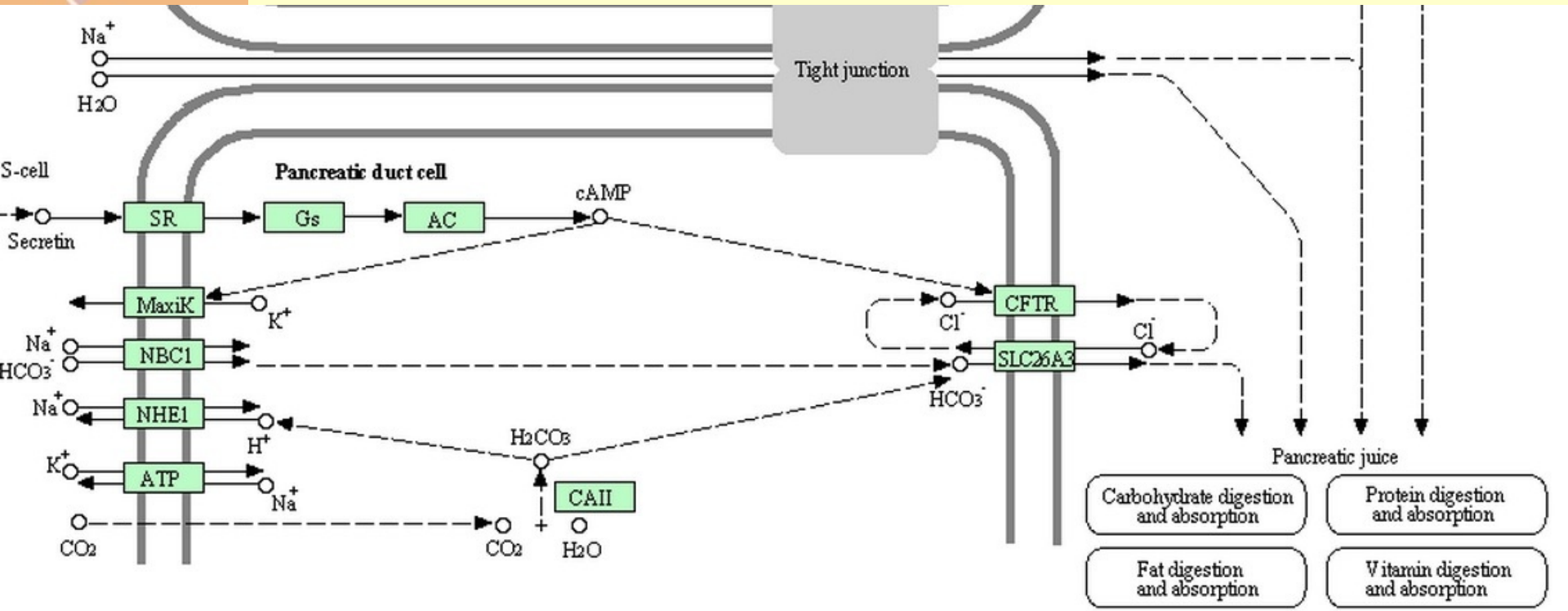
https://en.wikiversity.org/wiki/Blausen_gallery_2014

Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)



Role of CFTR in Pancreatic Secretion

http://www.ncbi.nlm.nih.gov/biosystems/169306



Mutations Causing Cystic Fibrosis

Mutation	Relative Frequency	Mutation Functional Class [1]
ΔF508	66.0%	II
G542X	2.4%	I
G551D	1.6%	III
N1303Lys	1.3%	II
W1282X	1.2%	I
R553X	0.7%	I
621+1G>T	0.7%	I
1717-1G>A	0.6%	I
R117H	0.3%	IV
R1162X	0.3%	Not clear [4]

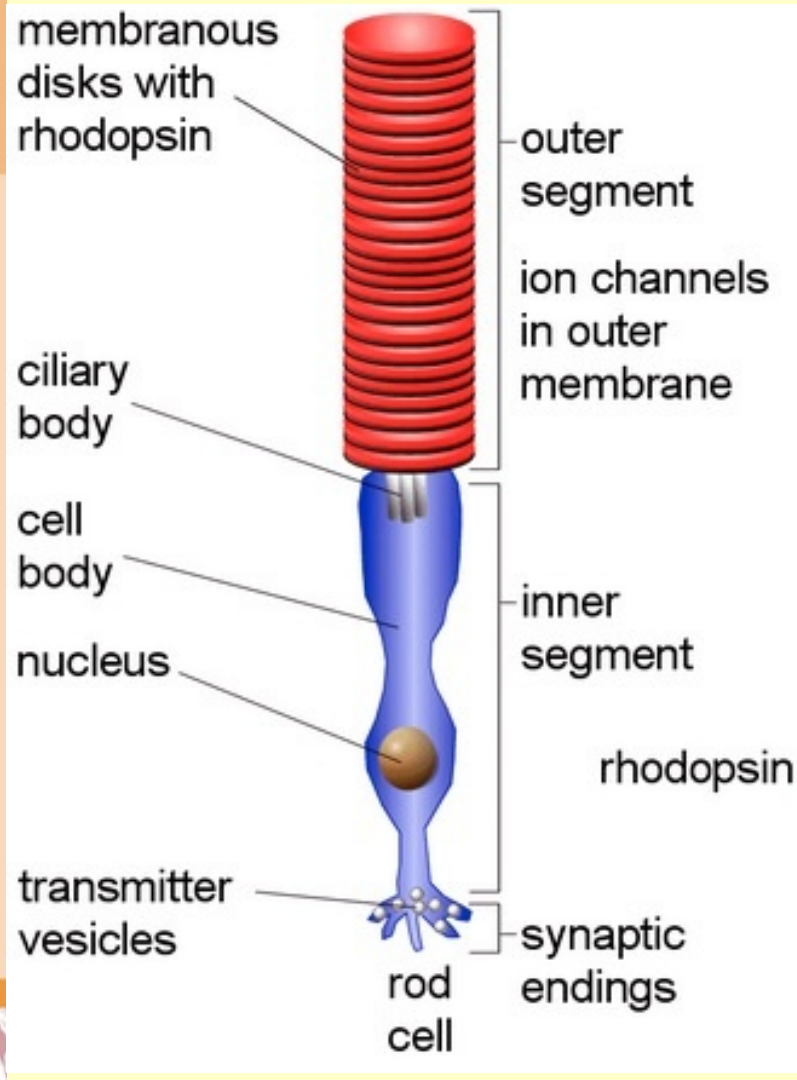
Population Group	Approximate Carrier Frequency
Ashkenazi Jewish	1:29
North American Caucasian	1:28
African American	1:61

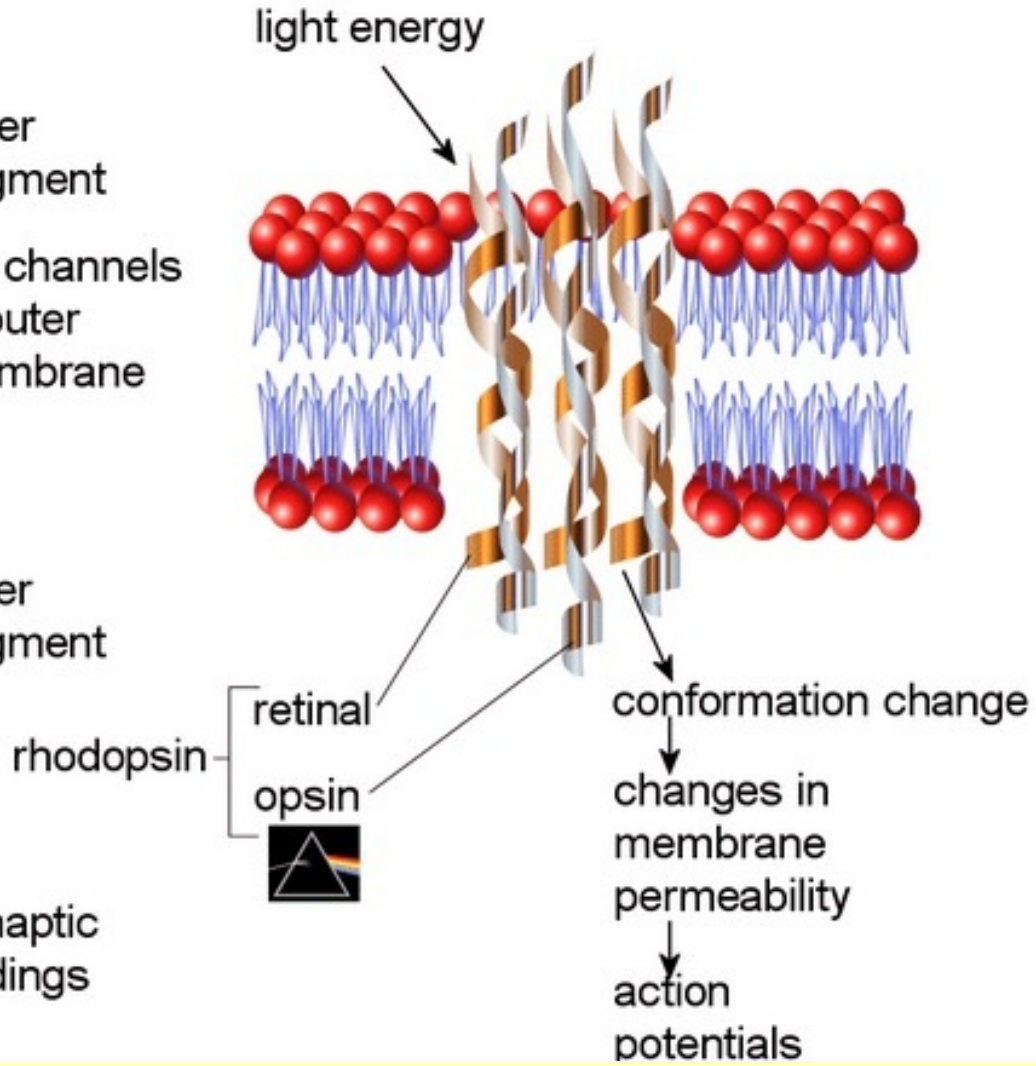
Cystic Fibrosis Mutation database http://www.genet.sickkids.on.ca/app

Gene Reviews http://www.ncbi.nlm.nih.gov/books/NBK1250

Rhodopsin and Colorblindnes

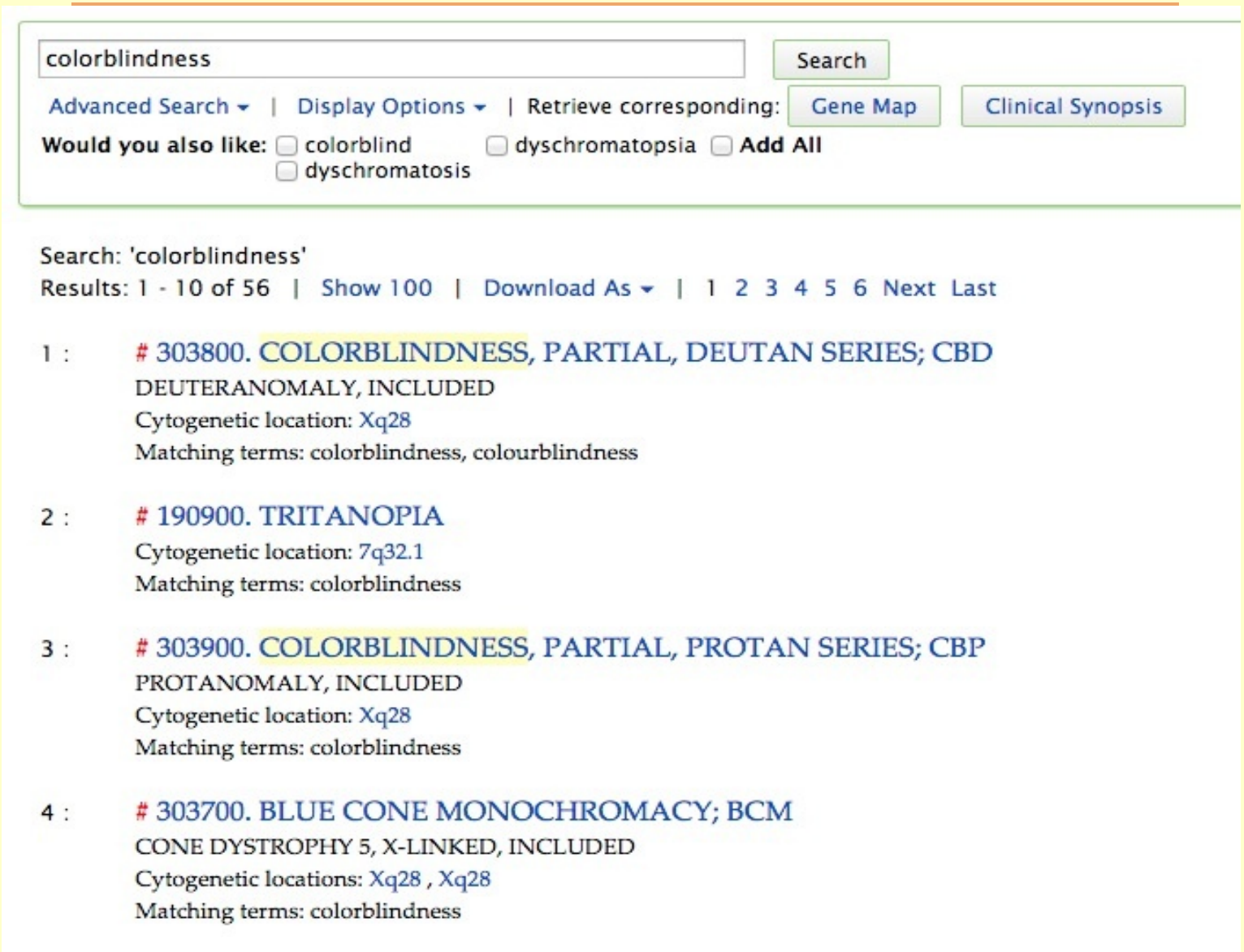
http://justinpamute.files.wordpress.com/2010/06/rhodopsin1.gifs





Colorblindness in OMIM

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



Colorblindness in OMIM

http://omim.org/entry/303800

#303800

COLORBLINDNESS, PARTIAL, DEUTAN SERIES; CBD

Alternative titles; symbols

DEUTAN COLORBLINDNESS; DCB
DEUTERANOPIA
GREEN COLORBLINDNESS

Other entities represented in this entry:

DEUTERANOMALY, INCLUDED

Table of Contents - #303800
Title
Phenotype Gene Relationships
Text
Description
Clinical Features
Mapping
Population Genetics
Inheritance
Evolution
Molecular Genetics
History
Clinical Synopsis
See Also
References
Contributors
Creation Date
Edit History
External Links:
Clinical Resources
Variation
Animal Models
Cellular Pathways

Phenotype Gene Relationships

Location	Phenotype	Phenotype MIM number	Gene/Locus	Gene/Locus MIM number
Xq28	Colorblindness, deutan	303800	OPN1MW	300821

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 303900) or blue plus red (deuteranopia). Anomalous trichromacy is trichromatic color vision based on a blue, green, and an anomalous red-like

Opsin1 Gene in OMIM

http://omim.org/entry/300821

*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* (from NCBI)

Table of Contents - *300821
External Links:
Genome
DNA
Protein
Gene Info
BioGPS
Ensembl
NCBI Gene
GeneCards
KEGG
PharmGKB
UCSC
Clinical Resources
Variation
Animal Models
Cellular Pathways

Gene Phenotype Relationships

Location	Phenotype	Phenotype MIM number
Xq28	Blue cone monochromacy	303700
	Colorblindness, deutan	303800

TEXT

Description

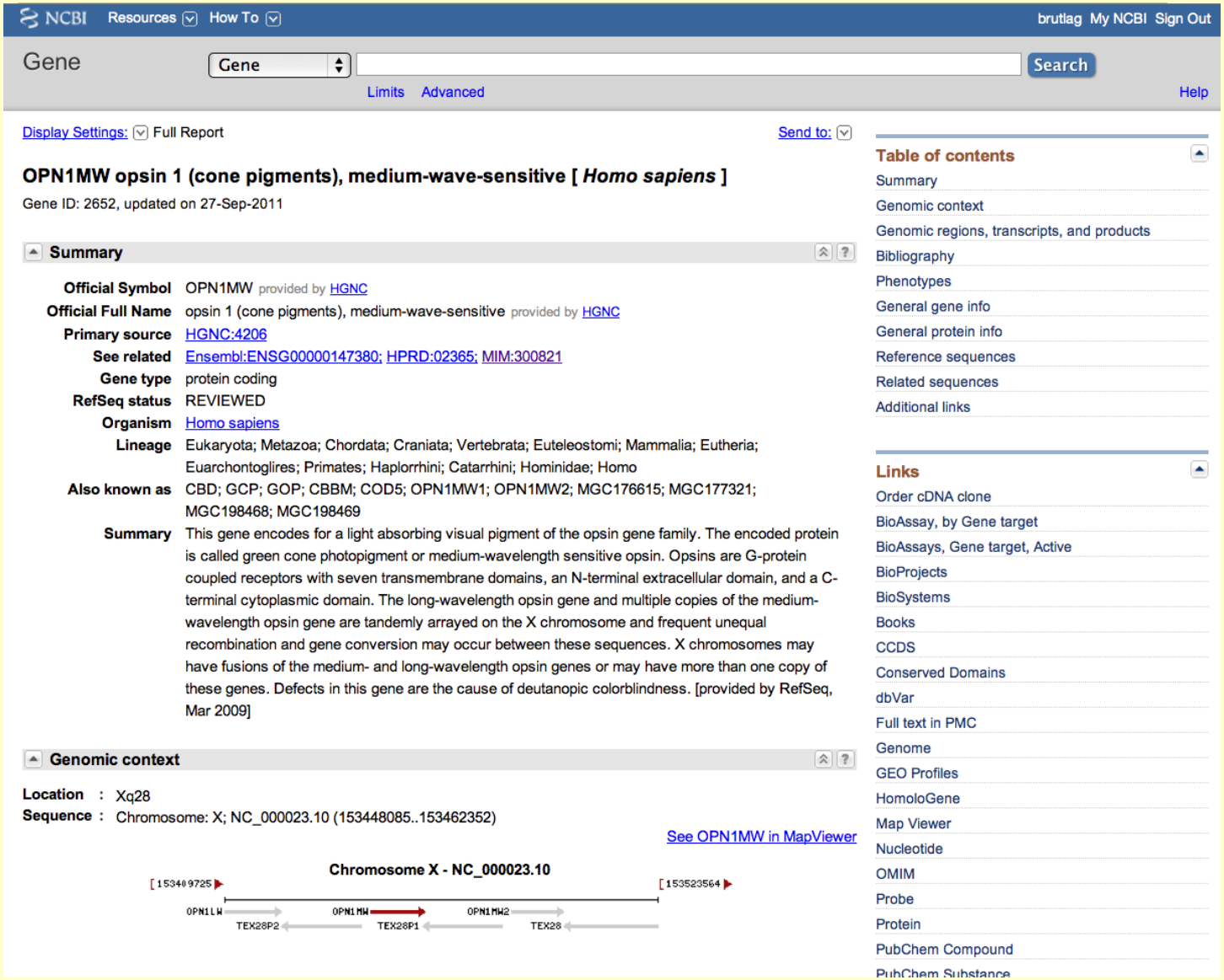
The medium-wave-sensitive opsin-1 gene (OPN1MW) encodes green cone pigment, 1 of 3 light-sensitive pigments that mediate human color vision. The green-sensitive and the red-sensitive (OPN1LW; 300822) opsins comprise a family of repeated genes on the X chromosome. Whereas there is a single red pigment 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

http://www.ncbi.nlm.nih.gov/gene/2652



NCBI Resources How To brutlag My NCBI Sign Out

Gene Gene Search

Limits Advanced Help

Display Settings: Full Report Send to:

OPN1MW opsin 1 (cone pigments), medium-wave-sensitive [*Homo sapiens*]

Gene ID: 2652, updated on 27-Sep-2011

Summary

Official Symbol	OPN1MW provided by HGNC
Official Full Name	opsin 1 (cone pigments), medium-wave-sensitive provided by HGNC
Primary source	HGNC:4206
See related	Ensembl:ENSG00000147380; 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; CBBM; COD5; OPN1MW1; OPN1MW2; MGC176615; MGC177321; MGC198468; MGC198469
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. 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

Location : Xq28
Sequence : Chromosome: X; NC_000023.10 (153448085..153462352)

See OPN1MW in MapViewer

Chromosome X - NC_000023.10

[153409725 [153523564

OPN1LW OPN1MW OPN1MW2

TEX28P2 TEX28P1 TEX28

Table of contents

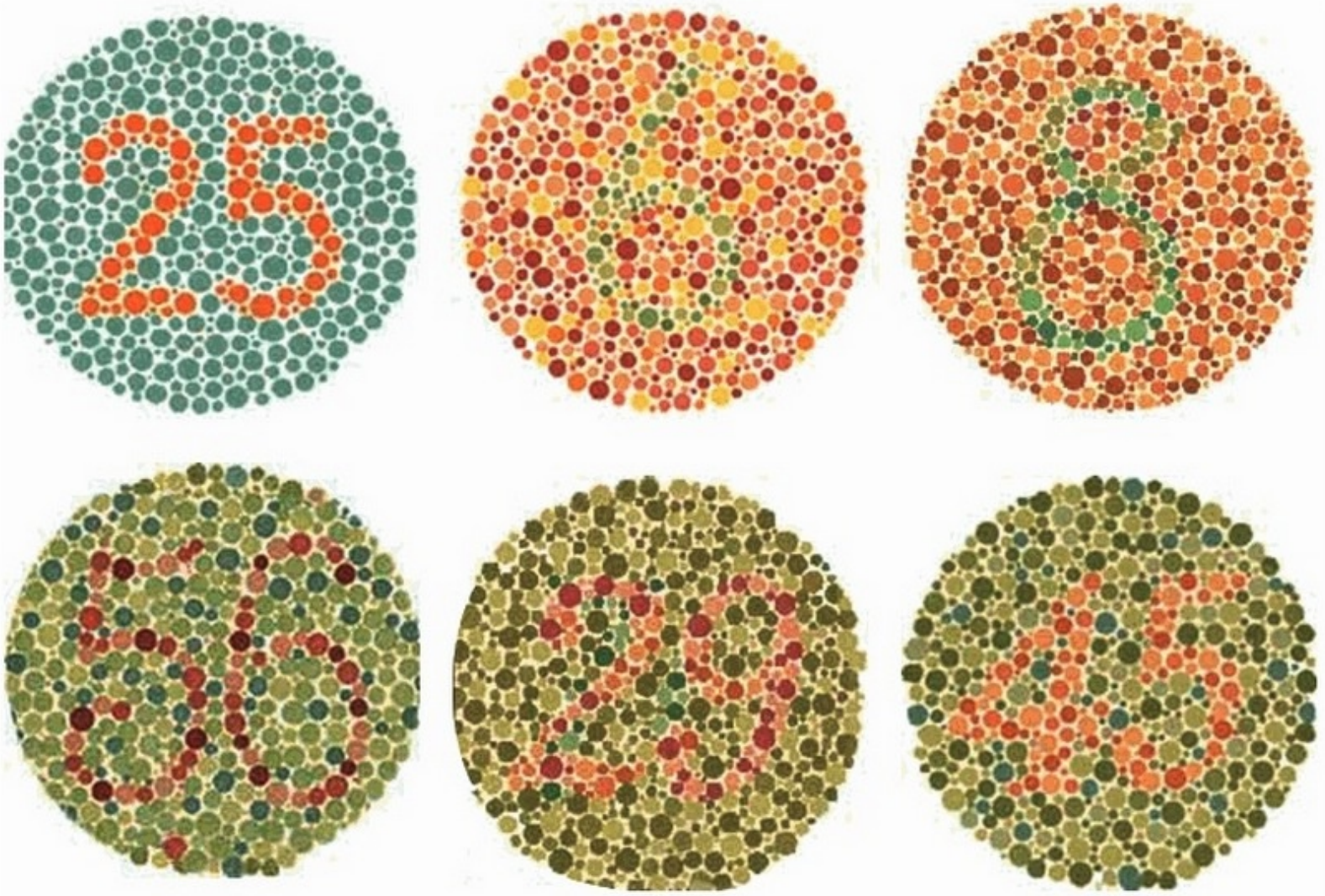
Summary
Genomic context
Genomic regions, transcripts, and products
Bibliography
Phenotypes
General gene info
General protein info
Reference sequences
Related sequences
Additional links

Links

Order cDNA clone
BioAssay, by Gene target
BioAssays, Gene target, Active
BioProjects
BioSystems
Books
CCDS
Conserved Domains
dbVar
Full text in PMC
Genome
GEO Profiles
HomoloGene
Map Viewer
Nucleotide
OMIM
Probe
Protein
PubChem Compound
PubChem Substance

Ishihara Test for Red-Green Color Blindness

http://www.ncbi.nlm.nih.gov/books/NBK1301/figure/rgcb.F3/?report=objectonly



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.