# 유전학적 검사의 기초 및 관련 생물정보학

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# 발표내용

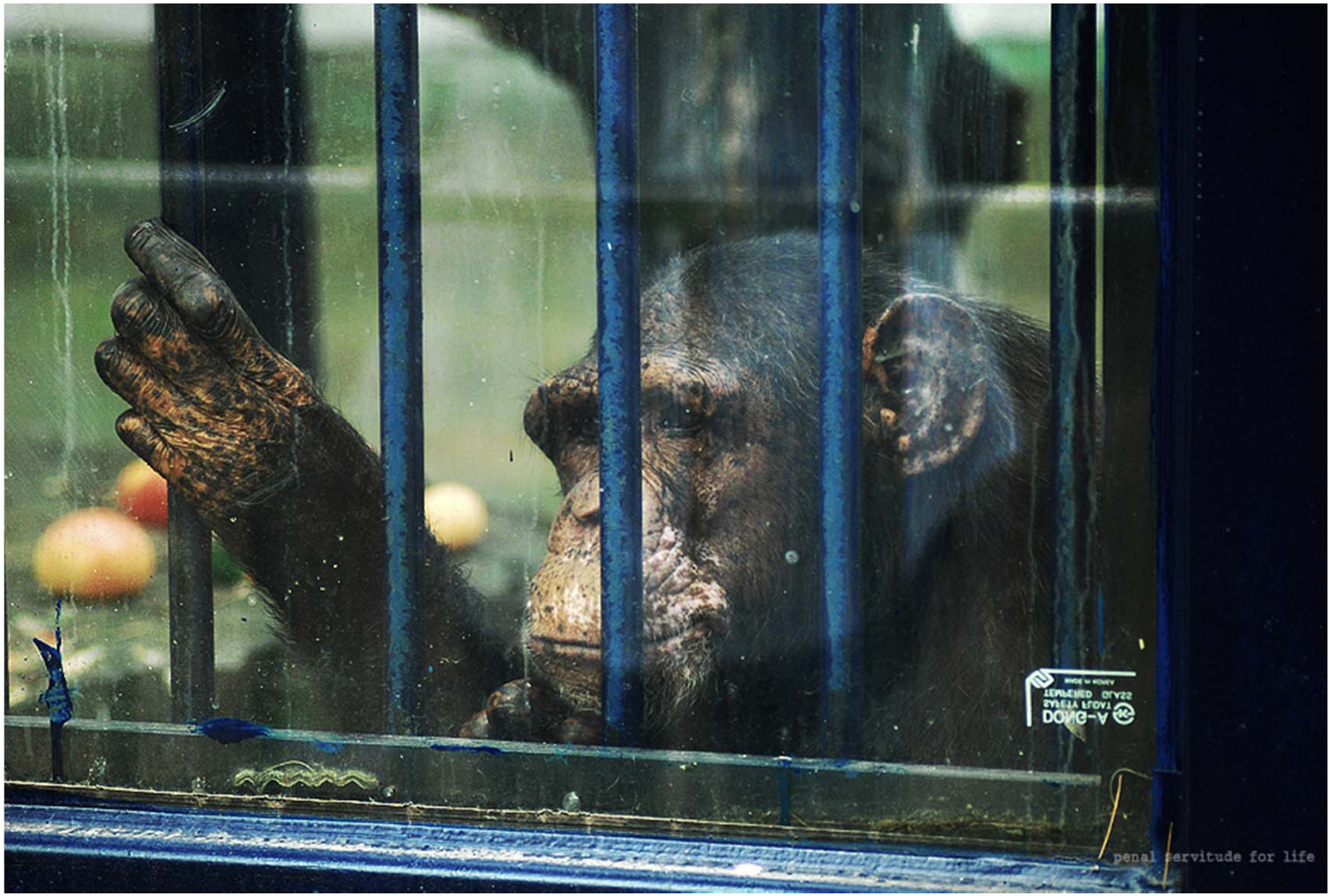
- 인간 유전체와 유전자
  - Genome sizes, genome statistics, gene statistics
- 유전학적 검사
  - 유전학적 검사의 분류
  - 분자유전검사의 이용
  - 유전학적 검사에서 고려사항
- 유전학적 검사에서 자주 이용하는 생물정보학
- 심혈관계 질환의 유전질환과 유전학적 연구

# Genome

- the entirety of an organism´s hereditary information
- Encoded in DNA (in RNA for many types of virus)
- Includes both the genes and the non-coding sequences of the DNA
- a blend of the words **gen**e and chromos**ome**
- In Greek, the word genome (γίνομαι) means *I become, I am born, to come into being*.

# Genome sizes

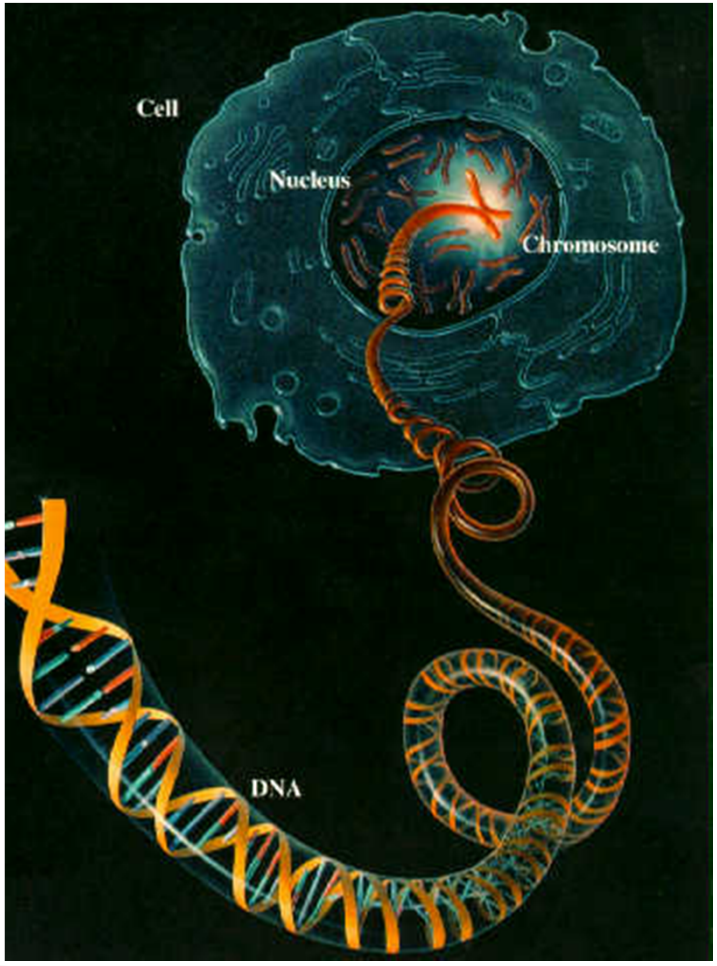
| Type | Organism | Genome size (bp) | Chrom.No | Remark |
|---|---|---|---|---|
| Bacterium | *E. coli* | 4,600,000 | 1 | Sequenced (1997) |
| Yeast | *Saccharomyces cerevisiae* | 12,100,000 | 16 | Sequenced (1996) |
| Plant | *Arabidopsis thaliana* | 157,000,000 | 10 | 애기장대(유채과) 1st plant genome sequenced |
| Nematode | *Caenorhabditis elegans* | 100,300,000 | 12 | First multicellular animal genome (1998) |
| Insect | *Drosophila melanogaster* | 130,000,000 | 8 | 초파리<br>Sequenced (2000) |
| Mammal | *Mus musculus* | 2.700,000,000 | 40 | Mouse<br>Sequenced (2002) |
| Mammal | *Canis familiaris* | 2,500,000,000 | 78 | Dog |
| Mammal | *Pan troglodytes* | 2.900,000,000 | 48 | Chimpanzee<br>Sequenced (2005) |
| Mammal | *Homo sapiens* | 3,100,000,000 | 46 | Sequenced (2003) |



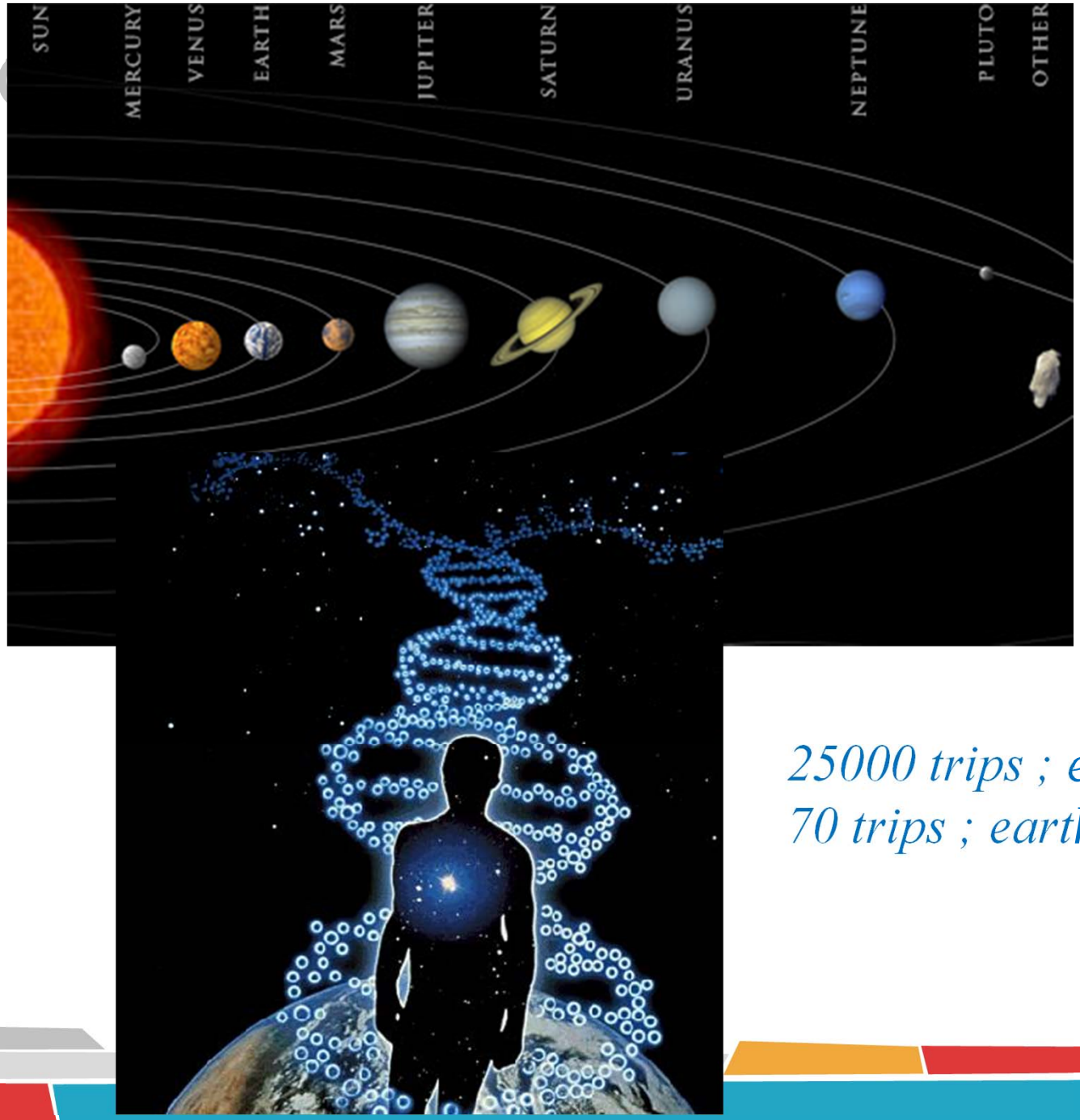

"종신형"
인간 유전자와 2% 다른 죄.. 인간 유전자와 98% 같은 죄..

네이버포토

# Human genome : size, length

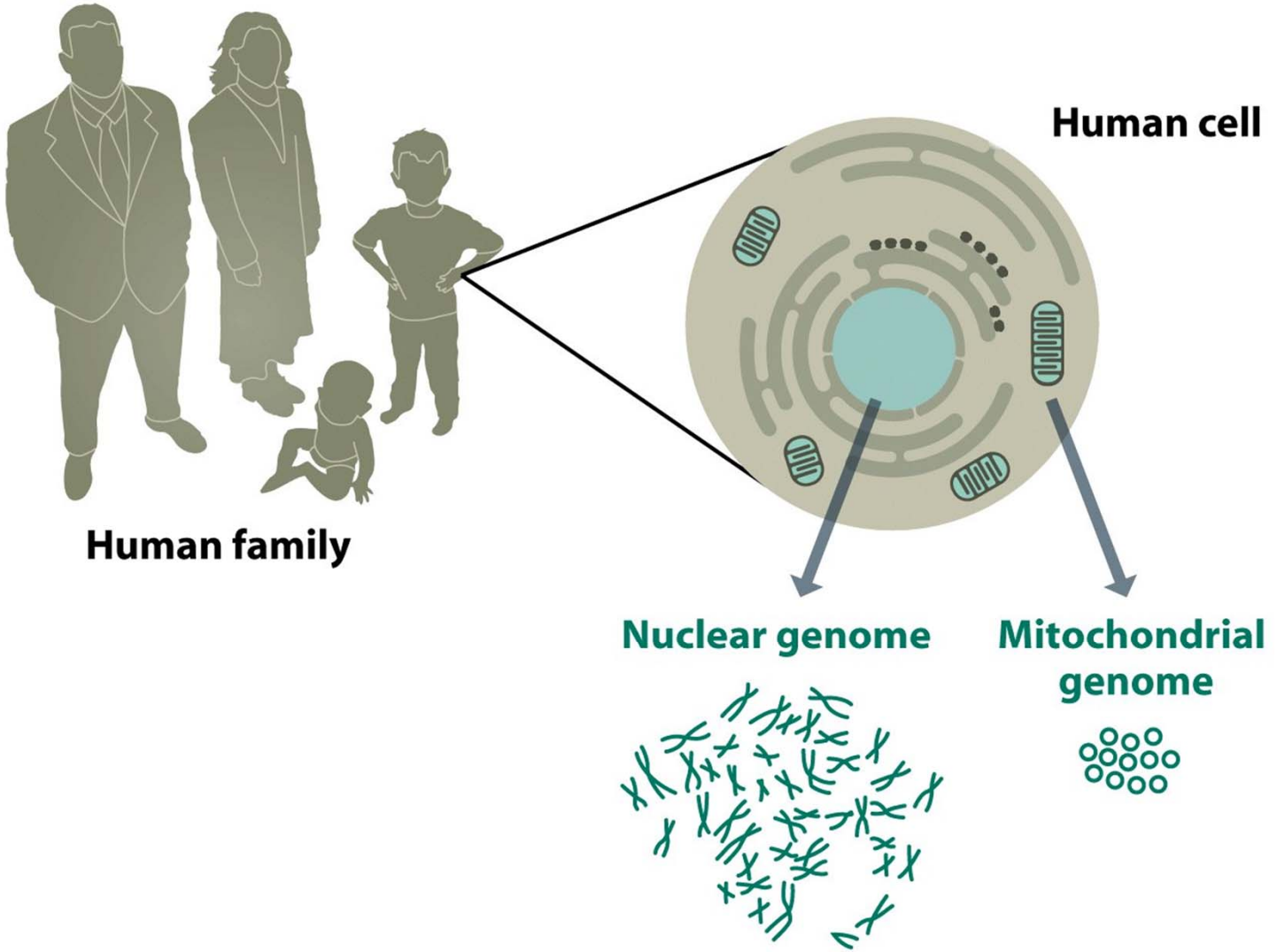



- One cell
  - $3 \times 10^9$ base pairs/haploid
  - $(3.4 \times 10^{-10}$ m/bp$)(6 \times 10^9$ bp$) = 2$ m
- DNA fiber length
  - $10^{13}$ cells x 2 m = $2 \times 10^{13}$ m




*25000 trips ; earth~moon*
*70 trips ; earth~sun*

# Human genome



# Nuclear genome

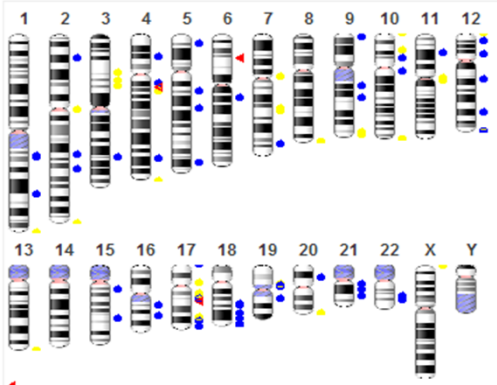
## Genome Reference Consortium

GRC Home | Data | Help | Report an Issue | Contact Us | Credits | Curators Only

Human Overview | Human Issues under Review | Human Assembly Data | Report a problem

### Human Genome Overview

*Information concerning the continuing improvement of the human genome.*




Regions containing alternate-loci
Regions containing fix patches
Regions containing novel patches

An ideogram representation of the latest human assembly, GRCh37.p4 (not showing unplaced or unlocalized sequences).

The GRC is working hard to provide the best possible reference assembly for human. We do this by both generating multiple representations ( alternate loci ) for regions that are too complex to be represented by a single path. Additionally, we are releasing regional fixes known as patches . This allows users who are interested in a specific locus to get an improved representation without affecting users who need chromosome coordinate stability.

#### Getting Data

GRCh37 (Latest Major Release): FTP
GRCh37 patch release 4 (Latest Minor Release): FTP
Information on regions under review: FTP

**GRC News and Updates**

23 Mar 2011

**Updating the genome: the CCL3L1 region of chr17q21**

13 Oct 2010

**Zebrafish genome joins GRC**

see all

**Recently Resolved Human Issues**

**Human (HG-486)** *Apr13, 2011*

AJ271736 located on the end of HschrX_ctg16 contains 1340bp of telomeric repeat, no further accessions are required in this region.

**Human (HG-1126)** *Apr13, 2011*

Made redundant by RP11-423O2 (chr.1).

*see all*

**References**

**Whole Genome Papers**
The HGP Reference Assembly
The Venter Genome Assembly

**Human Chromosome Papers**
Chr1 Chr2 Chr3 Chr4 Chr5 Chr6 Chr7 Chr8 Chr9 Chr10 Chr11 Chr12 Chr13 Chr14 Chr15 Chr16 Chr17 Chr18 Chr19 Chr20 Chr21 Chr22 ChrX ChrY

**Next assembly update**
The next assembly update (patch release 5) will be a minor update (only patches) and will happen in Jun 2011

Patch Release 4 | Patch Release 3 | Patch Release 2 | Patch Release 1 | GRCh37

### GRCh37 Patch Release 4 (GRCh7.p4)

**Release data:** April 12, 2011
**Release type:** minor
**Release notes:** In this release, 10 patches were added, 8 were of type Fix and 1 was of type novel. One patch from a previous release was updated. There were 13 issues resolved in this release.

## Assembly Statistics for GRCh37.p4

Choose another assembly GRCh37.p4

Chromosome Lengths | Total Lengths | Ungapped Lengths | N50s | Gaps | Counts

Chromosome lengths are calculated by summing the length of the placed scaffolds and estimated gaps.

Primary Assembly

| chr | total length | GenBank Accession | RefSeq Accession |
|---|---|---|---|
| 1 | 249,250,621 | CM000663.1 | NC_000001.10 |
| 2 | 243,199,373 | CM000664.1 | NC_000002.11 |
| 3 | 198,022,430 | CM000665.1 | NC_000003.11 |
| 4 | 191,154,276 | CM000666.1 | NC_000004.11 |
| 5 | 180,915,260 | CM000667.1 | NC_000005.9 |
| 6 | 171,115,067 | CM000668.1 | NC_000006.11 |
| 7 | 159,138,663 | CM000669.1 | NC_000007.13 |
| 8 | 146,364,022 | CM000670.1 | NC_000008.10 |
| 9 | 141,213,431 | CM000671.1 | NC_000009.11 |
| 10 | 135,534,747 | CM000672.1 | NC_000010.10 |
| 11 | 135,006,516 | CM000673.1 | NC_000011.9 |
| 12 | 133,851,895 | CM000674.1 | NC_000012.11 |
| 13 | 115,169,878 | CM000675.1 | NC_000013.10 |
| 14 | 107,349,540 | CM000676.1 | NC_000014.8 |
| 15 | 102,531,392 | CM000677.1 | NC_000015.9 |
| 16 | 90,354,753 | CM000678.1 | NC_000016.9 |
| 17 | 81,195,210 | CM000679.1 | NC_000017.10 |
| 18 | 78,077,248 | CM000680.1 | NC_000018.9 |
| 19 | 59,128,983 | CM000681.1 | NC_000019.9 |
| 20 | 63,025,520 | CM000682.1 | NC_000020.10 |
| 21 | 48,129,895 | CM000683.1 | NC_000021.8 |
| 22 | 51,304,566 | CM000684.1 | NC_000022.10 |
| X | 155,270,560 | CM000685.1 | NC_000023.10 |
| Y | 59,373,566 | CM000686.1 | NC_000024.9 |

- 3100 Mb (3.1 Gb)
- 200 Mb heterochromatin
- 1, 9, 16, acrocentric, Y

# Genome statistics

| Genome components | |
|---|---|
| Nuclear genome | 3.1 Gb |
| Euchromatic component | 2.9 Gb (~93%) |
| Highly conserved fraction | ~150 Mb (~5%) |
| Protein-coding DNA sequences | ~35 Mb (~1.1%) |
| Segmentally duplicated DNA | ~160 Mb (~5.5%) |
| Constitutive heterochromatin | ~200 Mb (~6.5%) |
| Transposon-based repeats | ~1.4 Gb (~45%) |

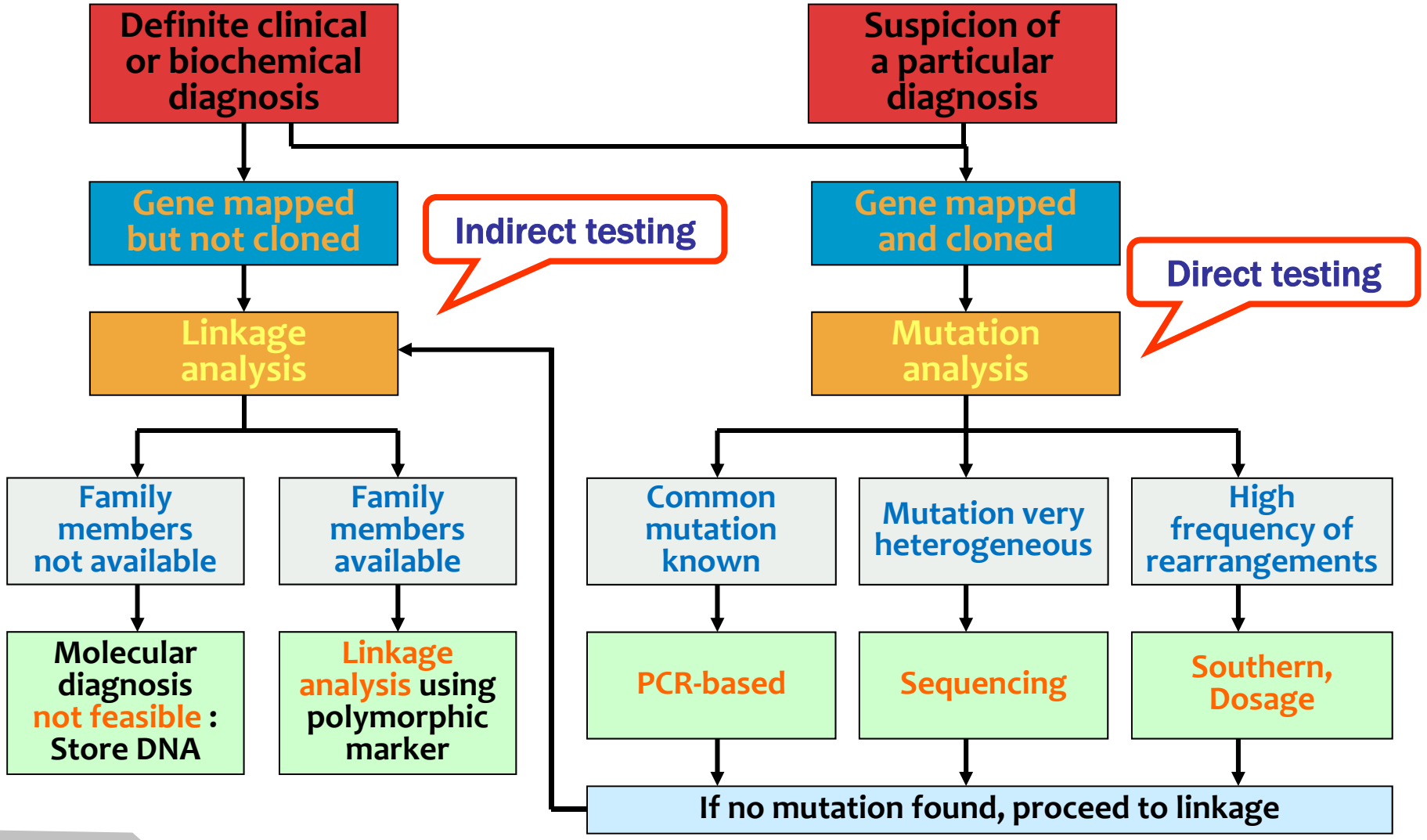
# Gene statistics

| Gene components | |
|---|---|
| Protein-coding genes | 20,000-21,000 |
| RNA genes | > 6,000 |
| Pseudogenes | > 12,000 |
| Gene density | > 1 per 120 kb |
| Protein-coding genes | |
| Average length | 53.6 kb (100s bp ~ 2.4 Mb) |
| Average number of exons | 9.8 (1 ~ 363, titin) |
| Average exon size | 288 bp (<10 bp ~18.2 kb) |
| RNA size | |
| Average mRNA size | 2kb |
| Largest mRNA | >103 kb (titin, NF2A) |
| Smallest & largest noncoding RNA | < 20 bp - 1 Mb |

# 유전학적 검사의 종류

| | |
|---|---|
| DNA testing<br>Molecular genetic testing | Single gene /Mitochondrial disorders<br>Multifactorial, Susceptibility gene<br>Genetic polymorphism<br>Cancer genetics |
| Cytogenetic analysis | Chromosomal disorders<br>Numerical & structural abnormalities<br>Cancer cytogenetics |
| Molecular cytogenetic analysis | Genomic disorders :<br>microdeletion/microduplicaiton<br>Cancer genetics |
| Biochemical genetic analysis | Inherited metabolic disorders<br>Maternal serum biochemical markers |

# Scheme for molecular genetic diagnosis



# Polymerase Chain Reaction (PCR)

- Principles
  - Denaturation : 94-95℃
  - Annealing : 55-66 ℃
  - Extension : 72℃
  - * Cycles : 28-35 cycles → $10^5$
- Advantages
  - Very small amounts of DNA
  - Fast, safe
  - Mutation detection
- Disadvantages
  - Primer design
  - Contamination
  - Limit of amplification

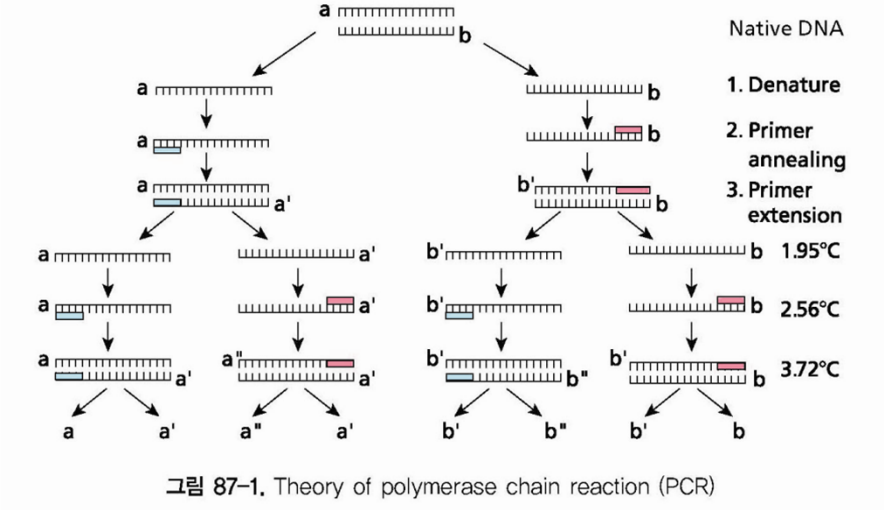



그림 87-1. Theory of polymerase chain reaction (PCR)

Kary Mullis accepting the Nobel Prize

Reverse transcriptase PCR (RT-PCR)
PCR-RFLP
Allele-specific PCR, Amplification refractory mutation system (ARMS)
Nested PCR
Multiplex PCR
Real-time PCR
DOP-PCR

# DNA sequence analysis

- Sanger dideoxynucleotide technique

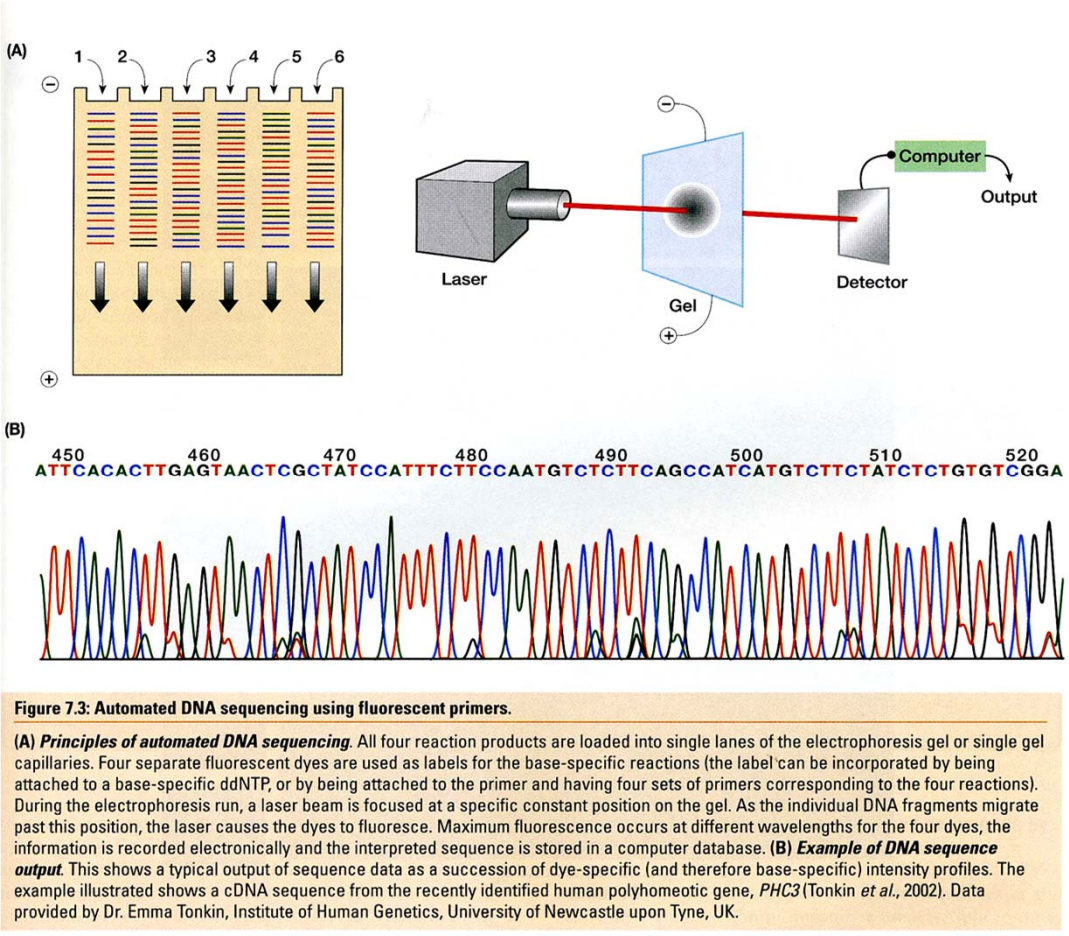
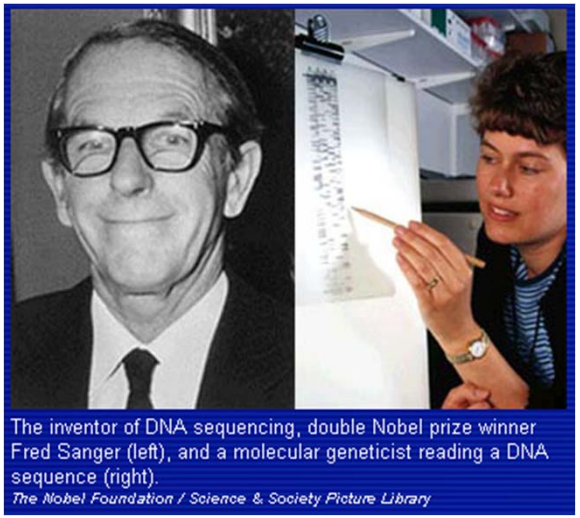



**Figure 7.3: Automated DNA sequencing using fluorescent primers.**

**(A)** ***Principles of automated DNA sequencing.*** All four reaction products are loaded into single lanes of the electrophoresis gel or single gel capillaries. Four separate fluorescent dyes are used as labels for the base-specific reactions (the label can be incorporated by being attached to a base-specific ddNTP, or by being attached to the primer and having four sets of primers corresponding to the four reactions). During the electrophoresis run, a laser beam is focused at a specific constant position on the gel. As the individual DNA fragments migrate past this position, the laser causes the dyes to fluoresce. Maximum fluorescence occurs at different wavelengths for the four dyes, the information is recorded electronically and the interpreted sequence is stored in a computer database. **(B)** ***Example of DNA sequence output.*** This shows a typical output of sequence data as a succession of dye-specific (and therefore base-specific) intensity profiles. The example illustrated shows a cDNA sequence from the recently identified human polyhomeotic gene, *PHC3* (Tonkin *et al.*, 2002). Data provided by Dr. Emma Tonkin, Institute of Human Genetics, University of Newcastle upon Tyne, UK.



The inventor of DNA sequencing, double Nobel prize winner Fred Sanger (left), and a molecular geneticist reading a DNA sequence (right).
*The Nobel Foundation / Science & Society Picture Library*

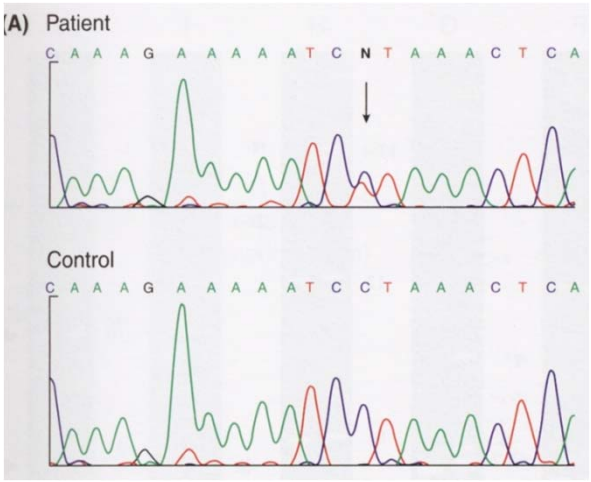
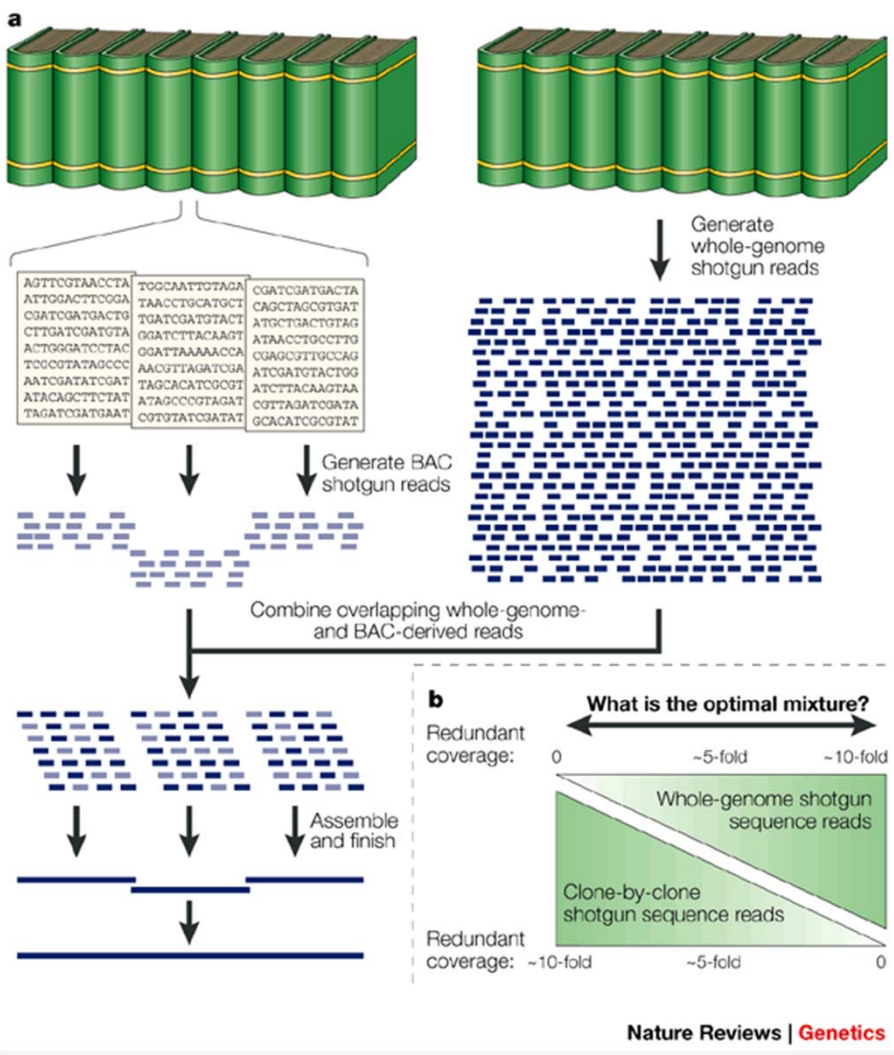



**Fig. CFTR gene sequencing (A) exon 3, c.332C>T (p.P67L)**

# Human Genome Project




Friday, June 01, 2007

## The $2 Million Genome

**James Watson, codiscoverer of the structure of DNA, now has a copy of his very own genome. Will you be next?**

By Emily Singer

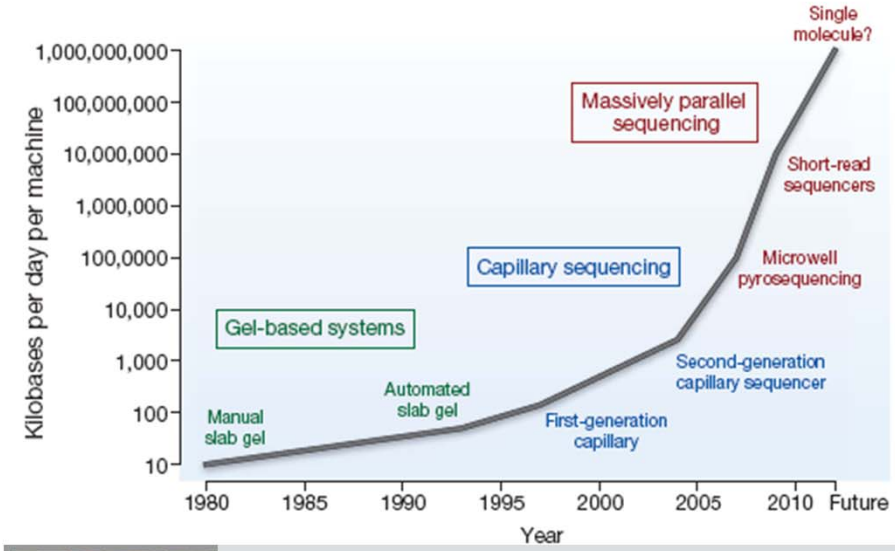
Audio » | Share » | Favorite | Print | E-mail

**DNA's daddy:** James Watson, pictured above, predicted the structure of DNA more than 50 years ago. On Thursday, he received a copy of his own genome as part of a landmark gene-sequencing project. Credit: National Library of Medicine

On Thursday, James Watson was handed a DVD containing his entire genome, sequenced in the past few months by 454, a company based in Branford, CT, that's developing next-generation technologies for efficiently reading the genome. At a cost of $2 million, 454 sequenced Watson's genome for roughly an order of magnitude less than it would have cost using traditional machines. While this is still too expensive for the average Joe, experts say that the advance marks a major milestone toward personal-genome sequencing--and more-personalized medicine--for all.

"We've heard people talking about personalized medicine for the last year or two, but this is the first concrete incarnation of that whole era," says George Weinstock, codirector of the Human Genome Sequencing Center at Baylor College of Medicine, in Houston. Scientists at Baylor collaborated on the genome project.

The $2 million and two months that it took to sequence Watson's genome is a far cry from the more than ten years and $3 billion required for the Human Genome Project's reference genome, released in 2003. Scientists ultimately hope to bring the cost down to less than $10,000, a target price that many believe will be the turning point in genomic medicine. At that price, many people could afford to have their genomes sequenced, and doctors could then use that data to give their patients more-personalized medical advice.



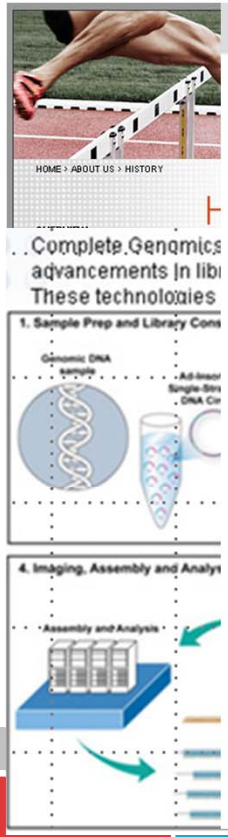

**ABI 3730XL**
(Applied Biosystems/Sanger)

up to 1.100 bases/read
96 reads/run
approx. 1 MB/day and machine

**First choice for finishing projects; full length cDNA sequencing; single sample sequencing.**

**GS FLX/454**
(Roche Diagnostics)

up to 250 bases/read
up to 400.000 reads/run
up to 100 MB/run/7.5 hours




Vol 460|20 August 2009|doi:10.1038/nature08211 nature

LETTERS

# A highly annotated whole-genome sequence of a Korean individual

Jong-Il Kim[1,2,4,5]*, Young Seok Ju[1,2]*, Hansoo Park[1,5], Sheehyun Kim[4], Seonwook Lee[4], Jae-Hyuk Yi[1], Joann Mudge[6], Neil A. Miller[6], Dongwan Hong[1], Callum J. Bell[6], Hye-Sun Kim[4], In-Soon Chung[4], Woo-Chung Lee[4], Ji-Sun Lee[4], Seung-Hyun Seo[5], Ji-Young Yun[5], Hyun Nyun Woo[4], Heewook Lee[4], Dongwhan Suh[1,2,3], Seungbok Lee[1,2,3], Hyun-Jin Kim[1,3], Maryam Yavartanoo[1,2], Minhye Kwak[1,2], Ying Zheng[1,2], Mi Kyeong Lee[5], Hyunjun Park[1], Jeong Yeon Kim[1], Omer Gokcumen[7], Ryan E. Mills[7], Alexander Wait Zaranek[8], Joseph Thakuria[8], Xiaodi Wu[8], Ryan W. Kim[6], Jim J. Huntley[9], Shujun Luo[9], Gary P. Schroth[9], Thomas D. Wu[10], HyeRan Kim[4], Kap-Seok Yang[4], Woong-Yang Park[1,2,3], Hyungtae Kim[4], George M. Church[8], Charles Lee[7], Stephen F. Kingsmore[6] & Jeong-Sun Seo[1,2,3,4,5]

# ACCE evaluation process for genetic testing

- Analytical validity
  - The ability of a laboratory test to identify the targeted characteristics
  - Analytical sensitivity, specificity, laboratory QC, etc
- Clinical validity
  - A test's ability to predict a particular clinical outcome
  - Clinical sensitivity, specificity, prevalence, PPV, NPV, etc
- Clinical utility
  - A test's ability to provide information that leads to an improved health outcome
  - Benefits >> risks, economic
- ELSI
  - Stigmatization, discrimination, privacy/confidentiality, personal/family social issue
  - Consent, ownership of data and/or samples, etc

# Bioinformatics for molecular diagnosis

## 1) 유전질환 데이터베이스

① OMIM (http://www.ncbi.nlm.nih.gov/sites/entrez?db=omim)

② GeneTests, GeneReviews (http://www.ncbi.nlm.nih.gov/sites/GeneTests/)

## 2) 유전자/유전체/단백질 서열 데이터베이스

① NCBI Gene (http://www.ncbi.nlm.nih.gov/gene)

② UCSC Genome browser (http://genome.ucsc.edu/)

③ Ensemble genome browser (http://www.ensembl.org/Homo_sapiens/Info/Index)

④ NCBI Protein (http://www.ncbi.nlm.nih.gov/protein/)

⑤ UniProt (http://www.uniprot.org/uniprot/)

NCBI

OMIM
Online Mendelian Inheritance in Man

Johns Hopkins University

My NCBI [Sign In] [Register]

All Databases | PubMed | Nucleotide | Protein | Genome | Structure | PMC | OMIM

Search OMIM for [ ] Go Clear

Limits | Preview/Index | History | Clipboard | Details

Entrez

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Search OMIM
Search Gene Map
Search Morbid Map

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How to Link

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How to Print
Citing OMIM
Download

OMIM Facts
Statistics
Update Log
Restrictions on Use

Allied Resources
Genetic Alliance
Databases
HGMD
Locus-Specific
Model Organisms
MitoMap
Phenotype
Human/Mouse/Rat Homology Maps
Coriell
The Jackson Laboratory
Human Gene Nomenclature

Human Genome Resources

- Enter one or more search terms.
- Use **Limits** to restrict your search by search field, chromosome, and other criteria.
- Use **Index** to browse terms found in OMIM records.
- Use **History** to retrieve records from previous searches, or to combine searches.

NCBI has not been able to obtain OMIM updates from Johns Hopkins University (JHU) since February 22, 2011. On January 1, 2011, NHGRI assumed funding responsibility for OMIM at JHU and has been working to conclude an agreement with JHU to allow NIH to obtain OMIM updates. NCBI will resume updates to OMIM as soon as this agreement is finalized.

## OMIM® - Online Mendelian Inheritance in Man®

Welcome to OMIM®, Online Mendelian Inheritance in Man®. OMIM is a comprehensive, authoritative, and timely compendium of human genes and genetic phenotypes. The full-text, referenced overviews in OMIM contain information on all known mendelian disorders and over 12,000 genes. OMIM focuses on the relationship between phenotype and genotype. It is updated daily, and the entries contain copious links to other genetics resources.

This database was initiated in the early 1960s by Dr. Victor A. McKusick as a catalog of mendelian traits and disorders, entitled Mendelian Inheritance in Man (MIM). Twelve book editions of MIM were published between 1966 and 1998. The online version, OMIM, was created in 1985 by a collaboration between the National Library of Medicine and the William H. Welch Medical Library at Johns Hopkins. It was made generally available on the internet starting in 1987. In 1995, OMIM was developed for the World Wide Web by NCBI, the National Center for Biotechnology Information.

OMIM is authored and edited at the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medi… …osh.

NLM's Profiles in Science -- The McKusick Papers More...

NOTE: OMIM is intended for use primarily by physicians and other professionals concerned with genetic disorders, by genetics re… …cience and medicine. While the OMIM database is open to the public, users seeking information about a personal medical or genetic conditio… …sician for diagnosis and for answers to personal questions.

NCBI

GeneTests

**Welcome to GeneTests at NCBI**

The GeneTests database and Web site are now hosted at NCBI.

**We'd like your feedback!**

**04/15/2011**

| | |
|---|---|
| 531 | *GeneReviews* |
| 1178 | Clinics |
| 596 | Laboratories testing for |
| 2313 | Diseases |
| | **2051** Clinical |
| | **262** Research |

Laboratory Directory Growth Chart

**Administrative Use**

(To update Clinic / Laboratory Directory listings)

## Welcome to GeneTests

Welcome to the GeneTests Web site, a publicly funded medical genetics information resource developed for physicians, other healthcare providers, and researchers, available at no cost to all interested persons. Use of this Web site assumes acceptance of the terms of use.

## At This Site

***GeneReviews***
Expert-authored peer-reviewed disease descriptions

**Laboratory Directory**
International directory of genetic testing laboratories

**Clinic Directory**
International directory of genetics and prenatal diagnosis clinics

**Educational Materials**
Illustrated glossary, information on genetic services, PowerPoint® presentations, annotated Internet resources

## What's New?

**2-17-11 — NOTICE**

As of 3-1-11, hyperlinks beginning with **http://www.genetests.org/** will forward directly to the GeneTests home page at NCBI. Please update your bookmarks.

New Features

- Changes to the Management of Laboratory and Clinic Information Online
- *GeneReviews* Indexed in PubMed

New in *GeneReviews*

New Clinical Test Listings

- 31 new listings

Looking for **Genetic Tools** curriculum materials?

# Bioinformatics for molecular diagnosis

### 3) SNP/mutation 데이터베이스

① Entrez SNP Home (http://www.ncbi.nlm.nih.gov/snp)
② dbSNP (http://www.ncbi.nlm.nih.gov/projects/SNP/index.html)
③ Human Gene Mutation Database (HGMD) (http://www.hgmd.cf.ac.uk/ac/index.php)
④ Catalogue of Somatic Mutations in Cancer (COSMIC)
⑤ PolyPhen (http://genetics.bwh.harvard.edu/pph/)
⑥ SIFT (http://sift.jcvi.org/)

### 4) 기타 생물정보학 웹사이트

① HUGO Gene Nomenclature (http://www.genenames.org/cgi-bin/hgnc_search.pl)
② Human Genome Variation Society (HGVS) (http://www.hgvs.org/)
③ NAR Database Categories list

### 5) 생물정보학 분석관련 소프트웨어

① NCBI Primer-BLAST (http://www.ncbi.nlm.nih.gov/tools/primer-blast/)
② Primer3 (http://frodo.wi.mit.edu/primer3/)
③ NCBI BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi)
④ 돌연변이 SW : SeqScape, Sequencher, Mutation Surveyor

# 심혈관계 질환의 유전질환과 유전학적 연구

1) Congenital heart disease
   (1) Chromosomal disorders : aneuploidy, tetrasomy 22p, tetrasomy 12p
   (2) Genomic disorders : DiGeorge, Williams
   (3) Single gene disorders : syndromic (Noonan, Holt-Oram, CHARGE, FBN1, TGFBR1, TGFBR2), non-syndromic (ELN, ZIC3, JAG1, NKX2.5, GATA4, CRELD1)
2) Inherited cardiomyopathies
   (1) Hypertrophic cardiomyopathy : sarcomere genes (MYH7, MYBPC3, TNNT2, TNNI3, TPM1, ACTC)
   (2) Inherited left ventricular hypertrophy : PRKAG2, LAMP2, CRP3
   (3) Dilated cardiomyopathy : sarcomere (ACTC, MYH7, TNNT2, TPM1), intermediate filament (DES, SGCD, VCL, ACTN, CSRP3, TCAP, DMD, LMNA), energy production (mitochondria), inctracellular calcium cycling (PLN)
3) Primary pulmonary hypertension : BMPR2
4) Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome) : ENG, ACVRL1

# 심혈관계 질환의 유전질환과 유전학적 연구

5) Hereditary disorder of the lymphatic and venous systems

(1) Inherited venous malformation : TIE2, GLMN

(2) Cerebral cavernous malformation : KRIT1, CCM2, PDCD10

(3) Hereditary lymphedema : FLT4 (VEGFR3)

6) Familial dysrhythmias and conduction disorders

(1) Ventricular arrhythmias : KCNQ1, KCNH2, SCN5A, ANK2, KCNE1, KCNE2, KCNJ2, CACNA1C, RYR2

(2) Supraventricular arrhythmias : KCNQ1, KCNE1, KCNE2, PRKAG2

(3) Conduction abnormalities : SCN5A

(4) Neurologic disorders with dysrhythmias : DMD, sarcoglycan, EMD, LMNA, FXN, mitochondria

# 심혈관계 질환의 유전질환과 유전학적 연구

## 7) Human hypertension

(1) Monogenic forms :

- Glucocorticoid-suppressible hypertension (CYP11B1, CYP11B2)
- Liddle syndrome (SCNN1B)
- Apparent mineralocorticoid excess (HSD11B2)
- Pseudohypoaldosteronism (WNK1, WNK4)

(2) Candidate genes in essential hypertension : SNP study, genome-wide association study

- Renin-Angiotensin system (REN, ACE, AGT, AT1R, ENPEP, ANPEP)
- Adrenergic system (ADRA, ADRB, BARK1, DRD, NPY, NPYY1, PNMT)
- Kallikrein-Kinin system (KNG1, KLK1, BDKRB1/2)
- Steroid associated (CYP11B1/2, CYP17, CYP21, CYP27, GRL, HSD11B1/2)
- Vascular tone (EDN1/2/3, EDNRA, EDNRB, ECE1/2, NOS1/2A/3, CACNA)
- Salt-water homeostasis (AVP, AVPR1A/1B/2, NPPA/B/C)
- Metabolism (INSRA/B, IRS1, LEP, LEPR, PTHRP)

# 심혈관계 질환의 유전질환과 유전학적 연구

8) Coagulation and fibrinolysis : SNP study
   (1) Venous thrombosis : PROC, PROS1, SERPINC1(AT3), FV, prothrombin
   (2) Arterial thrombosis : FVII, fibrinogen, FXIII, PAI-1 tPA

9) Atherosclerotic diseases : SNP study
   (1) Lipid : LDL-R, apo B-100, PCSK9, Lp(a), apo E, USF-1, LPL, PON-1
   (2) Acute phase : CRP, SAA
   (3) Adhesion-chemokine : P-selectin, E-selectin, ICAM-1 VCAM-1, CXC3L1, CCR2
   (4) Leukocyte/cytokine/macrophage related : TLR4, TNF-a, TNF-b, IL-1, IL-6, IL-10
   (5) Lymphocyte related : IL-4, IL-12, CD40L
   (6) Metabolic : Adiponectin, Leptin, Resistin, PPAR-r, UCP-2
   (7) Vascular/endothelial/matrix : MGP, OPG, OPN, ACE, eNOS, Connexin37, ATM
   (8) Thrombosis : MTHFR, Fibrinogen, PAI-1, Prothrombin, FVII, FV, GPIIIa, TM

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OMIM
Online Mendelian Inheritance in Man

Johns Hopkins University

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Search OMIM for Marfan syndrome | Go | Clear | Save Search

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1: #154700. MARFAN SYNDROME; MFS — GeneTests, Links
Gene map locus 15q21.1

2: *134797. FIBRILLIN 1; FBN1 — MGI, GeneTests, Links
Gene map locus 15q21.1

3: #194050. WILLIAMS-BEUREN SYNDROME; WBS — GeneTests, Links
Gene map locus 7q11.23

4: #130050. EHLERS-DANLOS SYNDROME, TYPE IV, AUTOSOMAL DOMINANT — GeneTests, Links
Gene map locus 2q31

5: #108300. STICKLER SYNDROME, TYPE I; STL1 — GeneTests, Links
Gene map locus 12q13.11-q13.2

6: #610380. LOEYS-DIETZ SYNDROME, TYPE 2B; LDS2B — GeneTests, Links
Gene map locus 3p22

7: #175100. ADENOMATOUS POLYPOSIS OF THE COLON; APC — GeneTests, Links
GARDNER SYNDROME, INCLUDED; GS, INCLUDED
Gene map locus 5q21-q22

8: #130000. EHLERS-DANLOS SYNDROME, TYPE I — GeneTests, Links
Gene map locus 9q34.2-q34.3, 2q31, 17q21.31-q22

9: #609192. LOEYS-DIETZ SYNDROME, TYPE 1A; LDS1A — GeneTests, Links
Gene map locus 9q22

# MIM ID #154700

## MARFAN SYNDROME; MFS

GeneTests, Links

*Alternative titles; symbols*

MARFAN SYNDROME, TYPE I; MFS1

Gene map locus: 15q21.1

Clinical Synopsis

### Text

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A number sign (#) is used with this entry because all cases of the true Marfan syndrome appear to be due to mutation in the fibrillin-1 gene (FBN1; 134797), which is located on chromosome 15q21.1.

### Description

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A heritable disorder of fibrous connective tissue, Marfan syndrome shows striking pleiotropism and clinical variability. The cardinal features occur in 3 systems--skeletal, ocular, and cardiovascular (McKusick, 1972; Pyeritz and McKusick, 1979; Pyeritz, 1993). It shares overlapping features with congenital contractural arachnodactyly (121050), which is caused by mutation in the FBN2 gene (612570).

Gray and Davies (1996) gave a general review. They published Kaplan-Meier survival curves for a cohort of British Marfan syndrome patients demonstrating greater survivorship in females than in males; a similar result had been reported by Murdoch et al. (1972) and by Silverman et al. (1995). Gray and Davies (1996) also proposed a grading scale for clinical comparison of the Marfan syndrome patients. The authors provided criteria for each grade and suggested uniform use of these scales may facilitate clinicomolecular correlations.

### Clinical Features

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Increased height, disproportionately long limbs and digits, anterior chest deformity, mild to moderate joint laxity, vertebral column deformity (scoliosis and thoracic lordosis), and a narrow, highly arched palate with crowding of the teeth are frequent skeletal features. Sponseller et al. (1995) evaluated spinal deformity in 113 patients with Marfan syndrome, 82 of whom were skeletally immature. Scoliosis was found in 52 of the 82 patients, with equal prevalence for the sexes. The thoracic portion of the curve was convex to the right in all but 2 patients.

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Gene Genotype
GeneTests

# MIM ID *134797

## FIBRILLIN 1; FBN1

MGI, GeneTests, Links

*Alternative titles; symbols*

FIBRILLIN; FBN

Gene map locus: 15q21.1

### Description

Back to Top

Fibrillin is the major constitutive element of extracellular microfibrils and has widespread distribution in both elastic and nonelastic connective tissue throughout the body. The cDNA was identified in 1991 and was mapped coincident with the locus for Marfan syndrome. Subsequent studies confirmed that mutations in the FBN1 gene are the major cause of Marfan syndrome (MFS; 154700).

### Cloning

Back to Top

The connective tissue protein fibrillin was isolated from the medium of human fibroblast cell cultures and was characterized and named by Sakai et al. (1986). Using monoclonal antibodies specific for fibrillin, they demonstrated its widespread distribution in the connective tissue matrices of skin, lung, kidney, vasculature, cartilage, tendon, muscle, cornea, and ciliary zonule. The molecular weight of fibrillin is about 350,000 Da. Sakai et al. (1991) pointed out that fibrillin contains approximately 14% cysteine, of which one-third appears to be in the free reactive sulfhydryl form.

Maslen et al. (1991) isolated cDNA clones for the fibrillin gene. Corson et al. (1993) and Pereira et al. (1993) completed characterization of the fibrillin cDNA, elucidated the exon/intron organization of the gene, and derived a physical map of the locus. The profibrillin sequence encodes a 2,871-amino acid protein which, excluding the signal peptide, is arranged into 5 structurally distinct regions. The largest of these regions, comprising about 75% of the protein, are the 46 EGF-like repeats, cysteine-rich domains originally found in human epidermal growth factor (131530). Forty-three of these repeats satisfy the consensus for calcium binding, an event that may mediate protein-protein interactions, and are called calcium-binding EGF-like repeats (cbEGFs). A mutation in one of these EGF-like repeats was identified in a Marfan syndrome patient; see 134797.0001. The tandem repetition of EGF-like domains is interrupted by 8 cysteine motifs that have homology to a domain first recognized in transforming growth factor beta-1-binding protein (TGFBR1; 190181), called a TB domain. Almost all of the EGF-like repeats are encoded by single exons. The other 4 regions include a unique amino-terminal stretch of basic residues, an adjacent second cysteine-rich region, a proline-rich domain, and the carboxy terminus.

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- Gene
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- GeneTests
- GeneView in dbSNP
- HomoloGene
- Map Viewer
- PubMed (calculated)

# FBN1 fibrillin 1 [ *Homo sapiens* ]

Gene ID: 2200, updated on 3-Apr-2011

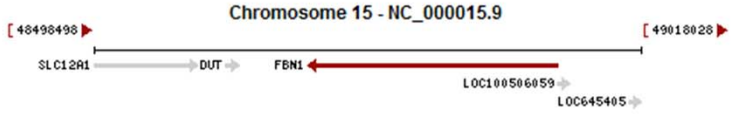
## Summary

| | |
|---|---|
| **Official Symbol** | FBN1 provided by HGNC |
| **Official Full Name** | fibrillin 1 provided by HGNC |
| **Primary source** | HGNC:3603 |
| **See related** | Ensembl:ENSG00000166147; HPRD:00618; MIM:134797 |
| **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** | FBN; SGS; WMS; MASS; MFS1; OCTD; SSKS; FBN1 |
| **Summary** | This gene encodes a member of the fibrillin family. The encoded protein is a large, extracellular matrix glycoprotein that serve as a structural component of 10-12 nm calcium-binding microfibrils. These microfibrils provide force bearing structural support in elastic and nonelastic connective tissue throughout the body. Mutations in this gene are associated with Marfan syndrome, isolated ectopia lentis, autosomal dominant Weill-Marchesani syndrome, MASS syndrome, and Shprintzen-Goldberg craniosynostosis syndrome. [provided by RefSeq] |

## Genomic context

**chromosome:** 15; **Location:** 15q21.1

See FBN1 in MapViewer

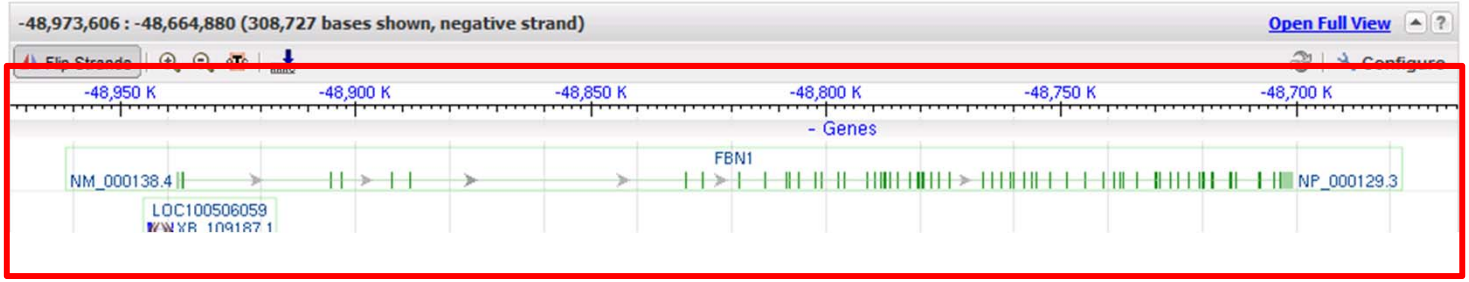



## Genomic regions, transcripts, and products

Go to reference sequence details

Genomic Sequence NC_000015 chromosome

Go to nucleotide Graphics FASTA GenBank

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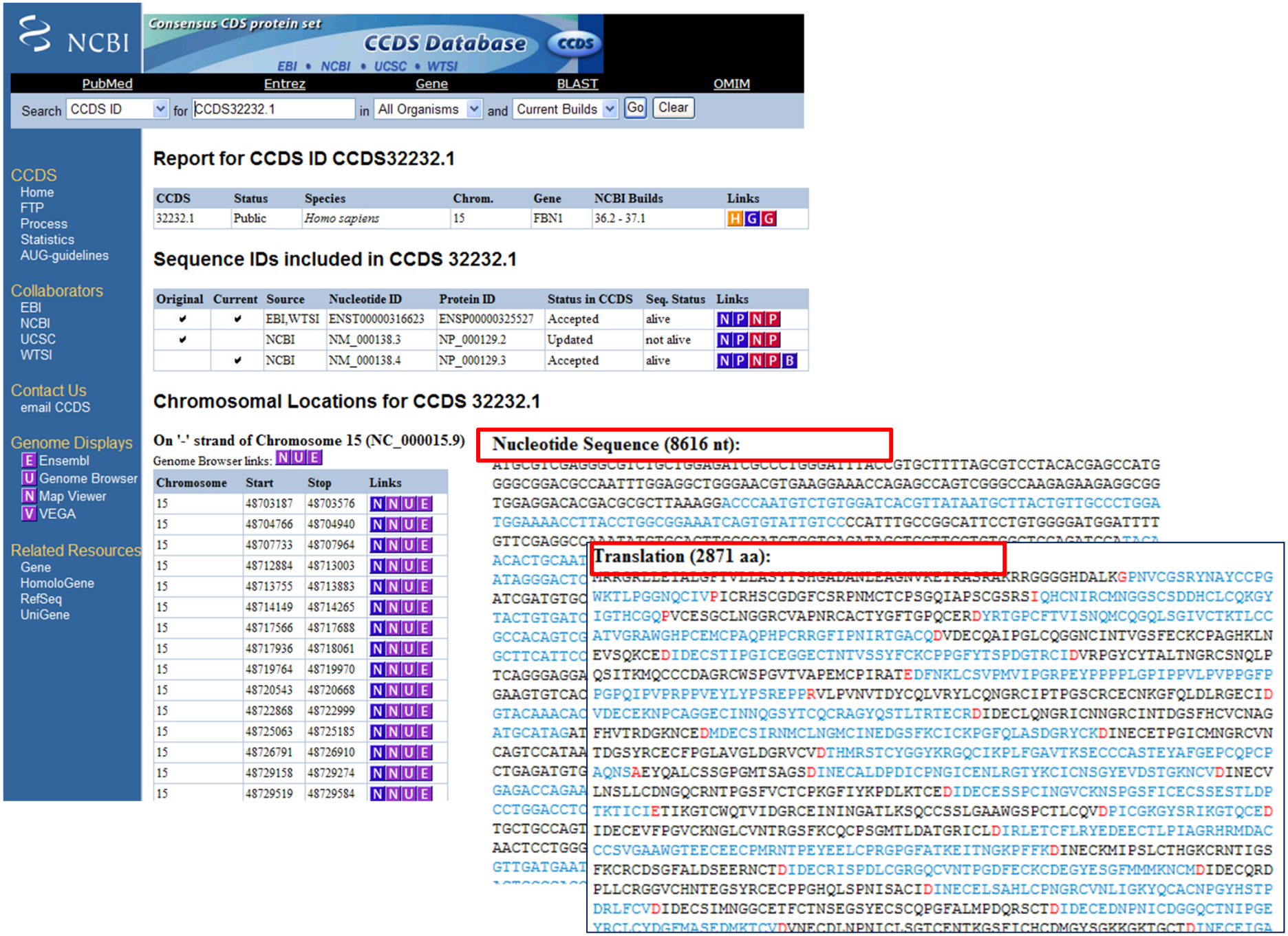

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Consensus CDS protein set

CCDS Database

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Search CCDS ID for CCDS32232.1 in All Organisms and Current Builds Go Clear

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NCBI
UCSC
WTSI

Contact Us
email CCDS

Genome Displays
E Ensembl
U Genome Browser
N Map Viewer
V VEGA

Related Resources
Gene
HomoloGene
RefSeq
UniGene

## Report for CCDS ID CCDS32232.1

| CCDS | Status | Species | Chrom. | Gene | NCBI Builds | Links |
|---|---|---|---|---|---|---|
| 32232.1 | Public | *Homo sapiens* | 15 | FBN1 | 36.2 - 37.1 | H G G |

## Sequence IDs included in CCDS 32232.1

| Original | Current | Source | Nucleotide ID | Protein ID | Status in CCDS | Seq. Status | Links |
|---|---|---|---|---|---|---|---|
| ✔ | ✔ | EBI,WTSI | ENST00000316623 | ENSP00000325527 | Accepted | alive | N P N P |
| ✔ | | NCBI | NM_000138.3 | NP_000129.2 | Updated | not alive | N P N P |
| | ✔ | NCBI | NM_000138.4 | NP_000129.3 | Accepted | alive | N P N P B |

## Chromosomal Locations for CCDS 32232.1

**On '-' strand of Chromosome 15 (NC_000015.9)**

Genome Browser links: N U E

| Chromosome | Start | Stop | Links |
|---|---|---|---|
| 15 | 48703187 | 48703576 | N N U E |
| 15 | 48704766 | 48704940 | N N U E |
| 15 | 48707733 | 48707964 | N N U E |
| 15 | 48712884 | 48713003 | N N U E |
| 15 | 48713755 | 48713883 | N N U E |
| 15 | 48714149 | 48714265 | N N U E |
| 15 | 48717566 | 48717688 | N N U E |
| 15 | 48717936 | 48718061 | N N U E |
| 15 | 48719764 | 48719970 | N N U E |
| 15 | 48720543 | 48720668 | N N U E |
| 15 | 48722868 | 48722999 | N N U E |
| 15 | 48725063 | 48725185 | N N U E |
| 15 | 48726791 | 48726910 | N N U E |
| 15 | 48729158 | 48729274 | N N U E |
| 15 | 48729519 | 48729584 | N N U E |

**Nucleotide Sequence (8616 nt):**

ATGCGTCGAGGGCGTCTGCTGGAGATCGCCCTGGGATTTACCGTGCTTTTAGCGTCCTACACGAGCCATG
GGGCGGACGCCAATTTGGAGGCTGGGAACGTGAAGGAAACCAGAGCCAGTCGGGCCAAGAGAAGAGGCGG
TGGAGGACACGACGCGCTTAAAGGACCCAATGTCTGTGGATCACGTTATAATGCTTACTGTTGCCCTGGA
TGGAAAACCTTACCTGGCGGAAATCAGTGTATTGTCCCCATTTGCCGGCATTCCTGTGGGGATGGATTTT
GTTCGAGGCC
ACACTGCAAT
ATAGGGACTC
ATCGATGTGC
TACTGTGATC
GCCACAGTCG
GCTTCATTCC
TCAGGGAGGA
GAAGTGTCAC
GTACAAACAC
ATGCATAGAT
CAGTCCATAA
CTGAGATGTG
GAGACCAGAA
CCTGGACCTC
TGCTGCCAGT
AACTCCTGGG
GTTGATGAAT

**Translation (2871 aa):**

MRRGRLLETALGFTVLLASYTSHGADANLEAGNVKETRASRAKRRGGGGHDALKGPNVCGSRYNAYCCPG
WKTLPGGNQCIVPICRHSCGDGFCSRPNMCTCPSGQIAPSCGSRSIQHCNIRCMNGGSCSDDHCLCQKGY
IGTHCGQPVCESGCLNGGRCVAPNRCACTYGFTGPQCERDYRTGPCFTVISNQMCQGGLSGIVCTKTLCC
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EVSQKCEDIDECSTIPGICEGGECTNTVSSYFCKCPPGFYTSPDGTRCIDVRPGYCYTALTNGRCSNQLP
QSITKMQCCCDAGRCWSPGVTVAPEMCPIRATEDFNKLCSVPMVIPGRPEYPPPPLGPIPPVLPVPPGFP
PGPQIPVPRPPVEYLYPSREPPPRVLPVNVTDYCQLVRYLCQNGRCIPTPGSCRCECNKGFQLDLRGECID
VDECEKNPCAGGECINNQGSYTCQCRAGYQSTLTRTECRDIDECLQNGRICNNGRCINTDGSFHCVCNAG
FHVTRDGKNCEDMDECSIRNMCLNGMCINEDGSFKCICKPGFQLASDGRYCKDINECETPGICMNGRCVN
TDGSYRCECFPGLAVGLDGRVCVDTHMRSTCYGGYKRGQCIKPLFGAVTKSECCCASTEYAFGEPCQPCP
AQNSAEYQALCSSGPGMTSAGSDINECALDPDICPNGICENLRGTYKCICNSGYEVDSTGKNCVDINECV
LNSLLCDNGQCRNTPGSFVCTCPKGFIYKPDLKTCEDIDECESSPCINGVCKNSPGSFICECSSESTLDP
TKTICIETIKGTCWQTVIDGRCEININGATLKSQCCSSLGAAWGSPCTLCQVDPICGKGYSRIKGTQCED
IDECEVFPGVCKNGLCVNTRGSFKCQCPSGMTLDATGRICLDIRLETCFLRYEDEECTLPIAGRHRMDAC
CCSVGAAWGTEECEECPMRNTPEYEELCPRGPGFATKEITNGKPFFKDINECKMIPSLCTHGKCRNTIGS
FKCRCDSGFALDSEERNCTDIDECRISPDLCGRGQCVNTPGDFECKCDEGYESGFMMMKNCMDIDECQRD
PLLCRGGVCHNTEGSYRCECPPGHQLSPNISACIDINECELSAHLCPNGRCVNLIGKYQCACNPGYHSTP
DRLFCVDIDECSIMNGGCETFCTNSEGSYECSCQPGFALMPDQRSCTDIDECEDNPNICDGGQCTNIPGE
YRCLCYDGFMASEDMKTCVDVNECDLNPNICLSGTCENTKGSFICHCDMGYSGKKGKTGCTDINECEIGA

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# Marfan Syndrome

Harry C Dietz, MD
Victor A McKusick Professor, Pediatrics, Medicine, and Molecular Biology & Genetics
Institute of Genetic Medicine
Johns Hopkins University School of Medicine
Baltimore, Maryland
hdietz@jhmi.edu

Initial Posting: April 18, 2001; Last Update: June 30, 2009.

## Summary

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**Disease characteristics.** Marfan syndrome is a systemic disorder of connective tissue with a high degree of clinical variability. Cardinal manifestations involve the ocular, skeletal, and cardiovascular systems. *FBN1* mutations associate with a broad phenotypic continuum, ranging from isolated features of Marfan syndrome to neonatal presentation of severe and rapidly progressive disease in multiple organ systems. Myopia is the most common ocular feature; displacement of the lens from the center of the pupil, seen in approximately 60% of affected individuals, is a hallmark feature. People with Marfan syndrome are at increased risk for retinal detachment, glaucoma, and early cataract formation. The skeletal system involvement is characterized by bone overgrowth and joint laxity. The extremities are disproportionately long for the size of the trunk (dolichostenomelia). Overgrowth of the ribs can push the sternum in (pectus excavatum) or out (pectus carinatum). Scoliosis is common and can be mild or severe and progressive. The major sources of morbidity and early mortality in the Marfan syndrome relate to the cardiovascular system. Cardiovascular manifestations include dilatation of the aorta at the level of the sinuses of Valsalva, a predisposition for aortic tear and rupture, mitral valve prolapse with or without regurgitation, tricuspid valve prolapse, and enlargement of the proximal pulmonary artery. With proper management, the life expectancy of someone with Marfan syndrome approximates that of the general population.

**Diagnosis/testing.** Marfan syndrome is a clinical diagnosis based on family history and the observation of characteristic findings in multiple organ systems. The four major diagnostic findings include dilatation or dissection of the aorta at the level of the sinuses of Valsalva, ectopia lentis, dural ectasia, and four of eight specific skeletal features. Molecular genetic testing of *FBN1* is available in clinical laboratories. It remains unclear whether the lack of full sensitivity of this test relates to an atypical location or character of *FBN1* mutations in some individuals (e.g., large deletions or promoter mutations) or to locus heterogeneity.

**Management.** *Treatment of manifestations:* Comprehensive management requires a team approach, including a geneticist, cardiologist, ophthalmologist, orthopedist, and cardiothoracic surgeon. Eyeglasses for most eye problems; rare need for surgical removal of a dislocated lens with implantation of an artificial lens (preferably after growth is complete). Surgical stabilization of the spine for scoliosis and repair of pectus deformity (largely for cosmetic indications. Orthotics and arch supports can lessen leg fatigue and muscle cramps associated with *pes planus*. Surgical repair of the aorta when the maximal measurement exceeds 5.0 cm in adults or older children, the rate of increase of the aortic diameter approaches 1.0 cm per year, or progressive aortic regurgitation occurs. Afterload-reducing agents can improve cardiovascular function when congestive heart failure is present.

*Prevention of primary manifestations:* Medications that reduce hemodynamic stress on the aortic wall, such as beta blockers, are generally initiated at diagnosis or for progressive aortic dilatation; verapamil or other antihypertensive agents can be used if beta blockers are not tolerated.


GeneReviews [Internet].
Pagon RA, Bird TD, Dolan CR, et al., editors.
Seattle (WA): University of Washington, Seattle; 1993-.
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Table 2. Summary of Molecular Genetic Testing Used in Marfan Syndrome

| Gene Symbol | Test Method | Mutations Detected | Mutation Detection Frequency by Test Method [1] | Test Availability |
|---|---|---|---|---|
| *FBN1* | Mutation scanning/ sequence analysis | Sequence variants [2] | ~70%-93% | Clinical Testing |
| | Complementary DNA sequence analysis | | | |
| | Deletion/duplication analysis [3] | Exonic and whole-gene deletions | Unknown | |

## Molecular Genetics

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*Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information.* —ED.

Table A. Marfan Syndrome: Genes and Databases

| Gene Symbol | Chromosomal Locus | Protein Name | Locus Specific | HGMD |
|---|---|---|---|---|
| *FBN1* | 15q21.1 | Fibrillin-1 | The FBN1 Gene Mutations Database<br>The FBN1 mutations database | FBN1 |

Data are compiled from the following standard references: gene symbol from HGNC; chromosomal locus, locus name, critical region, complementation group from OMIM; protein name from UniProt. For a description of databases (Locus Specific, HGMD) linked to, click here.

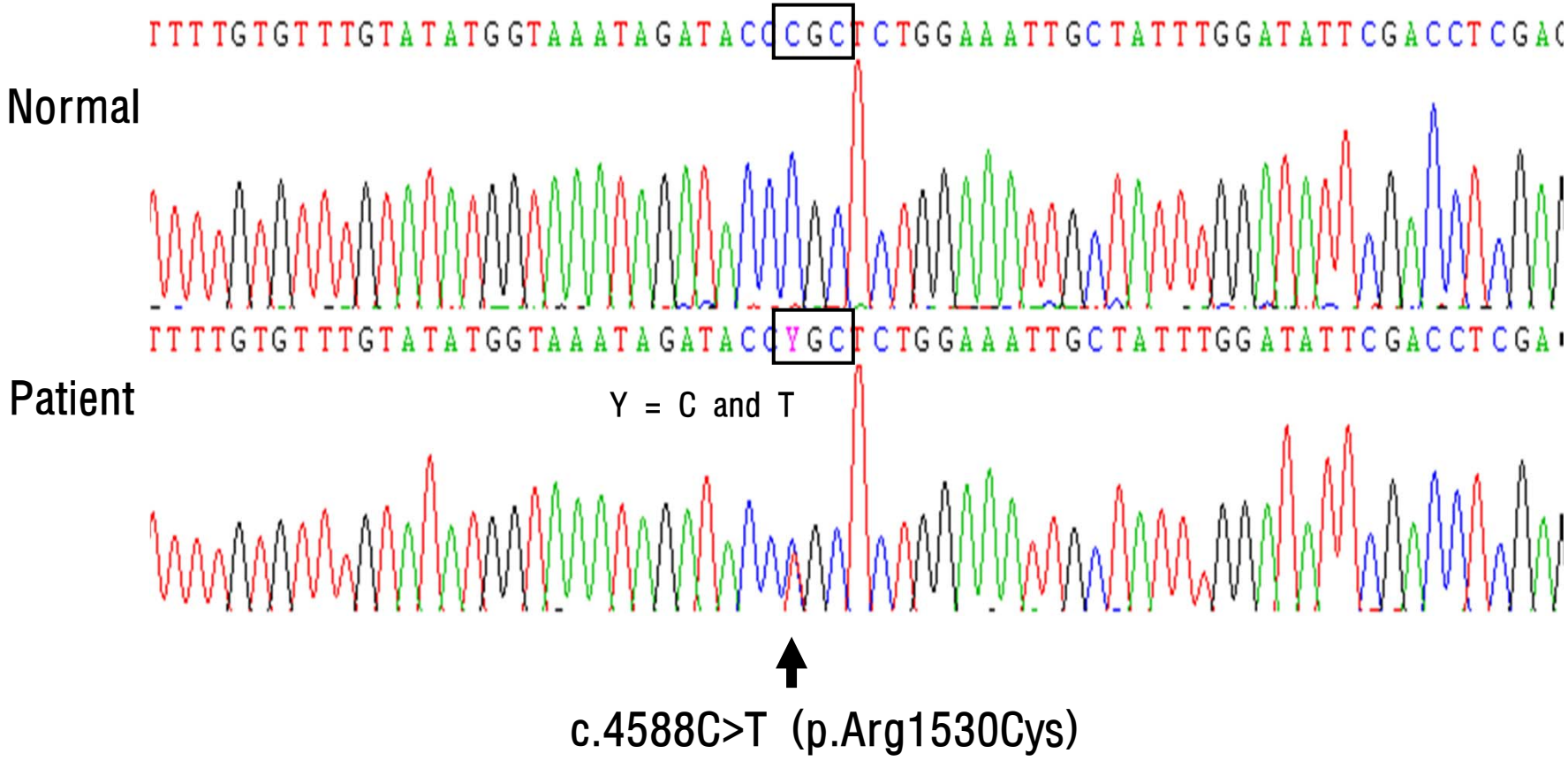
Table B. OMIM Entries for Marfan Syndrome (View All in OMIM)

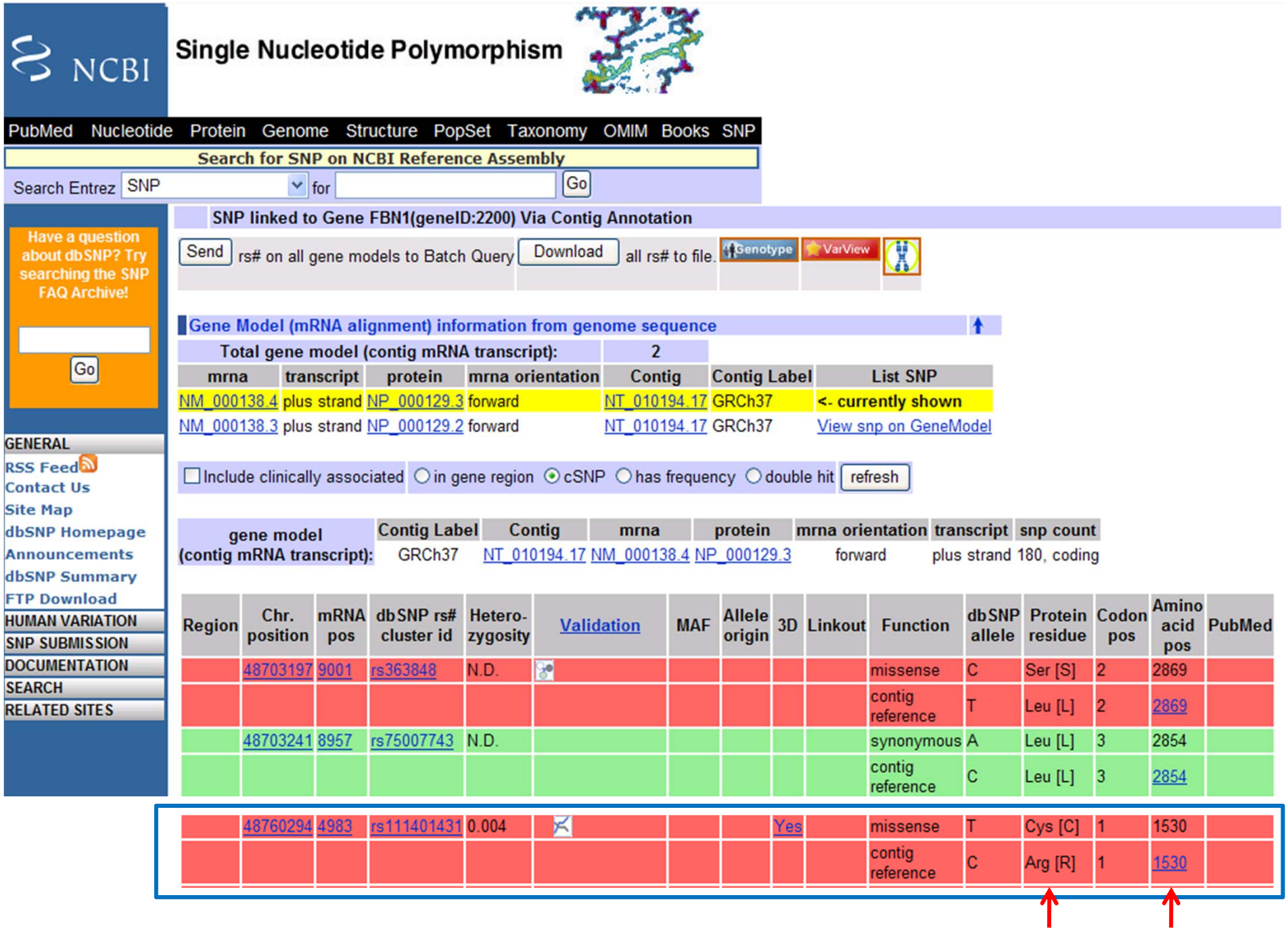
| | |
|---|---|
| 134797 | FIBRILLIN 1; FBN1 |
| 154700 | MARFAN SYNDROME; MFS |

**Normal allelic variants.** *FBN1* is large (>600 kb) and the coding sequence is highly fragmented (65 exons). The promoter region is large and poorly characterized. High evolutionary conservation of intronic sequence at the 5' end of the gene suggests the presence of intronic regulatory elements. Three exons at the extreme 5' end of the gene are alternatively utilized and do not appear to contribute to the coding sequence.

**Pathologic allelic variants.** More than 200 *FBN1* mutations that cause Marfan syndrome or related phenotypes have been described [Vollbrandt et al 2004]. No common mutation exists in any population. (For more information, see Table A.)

Partial sequence of *FBN1* gene





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Single Nucleotide Polymorphism

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SNP linked to Gene FBN1(geneID:2200) Via Contig Annotation

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

Gene Model (mRNA alignment) information from genome sequence

| Total gene model (contig mRNA transcript): | | | | 2 | | |
|---|---|---|---|---|---|---|
| mrna | transcript | protein | mrna orientation | Contig | Contig Label | List SNP |
| NM_000138.4 | plus strand | NP_000129.3 | forward | NT_010194.17 | GRCh37 | <- currently shown |
| NM_000138.3 | plus strand | NP_000129.2 | forward | NT_010194.17 | GRCh37 | View snp on GeneModel |

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

| gene model (contig mRNA transcript): | Contig Label | Contig | mrna | protein | mrna orientation | transcript | snp count |
|---|---|---|---|---|---|---|---|
| | GRCh37 | NT_010194.17 | NM_000138.4 | NP_000129.3 | forward | plus strand | 180, coding |

| Region | Chr. position | mRNA pos | dbSNP rs# cluster id | Hetero-zygosity | Validation | MAF | Allele origin | 3D | Linkout | Function | dbSNP allele | Protein residue | Codon pos | Amino acid pos | PubMed |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 48703197 | 9001 | rs363848 | N.D. | | | | | | missense | C | Ser [S] | 2 | 2869 | |
| | | | | | | | | | | contig reference | T | Leu [L] | 2 | 2869 | |
| | 48703241 | 8957 | rs75007743 | N.D. | | | | | | synonymous | A | Leu [L] | 3 | 2854 | |
| | | | | | | | | | | contig reference | C | Leu [L] | 3 | 2854 | |
| | 48760294 | 4983 | rs111401431 | 0.004 | | | | Yes | | missense | T | Cys [C] | 1 | 1530 | |
| | | | | | | | | | | contig reference | C | Arg [R] | 1 | 1530 | |


# The Human Gene Mutation Database at the Institute of Medical Genetics in Cardiff

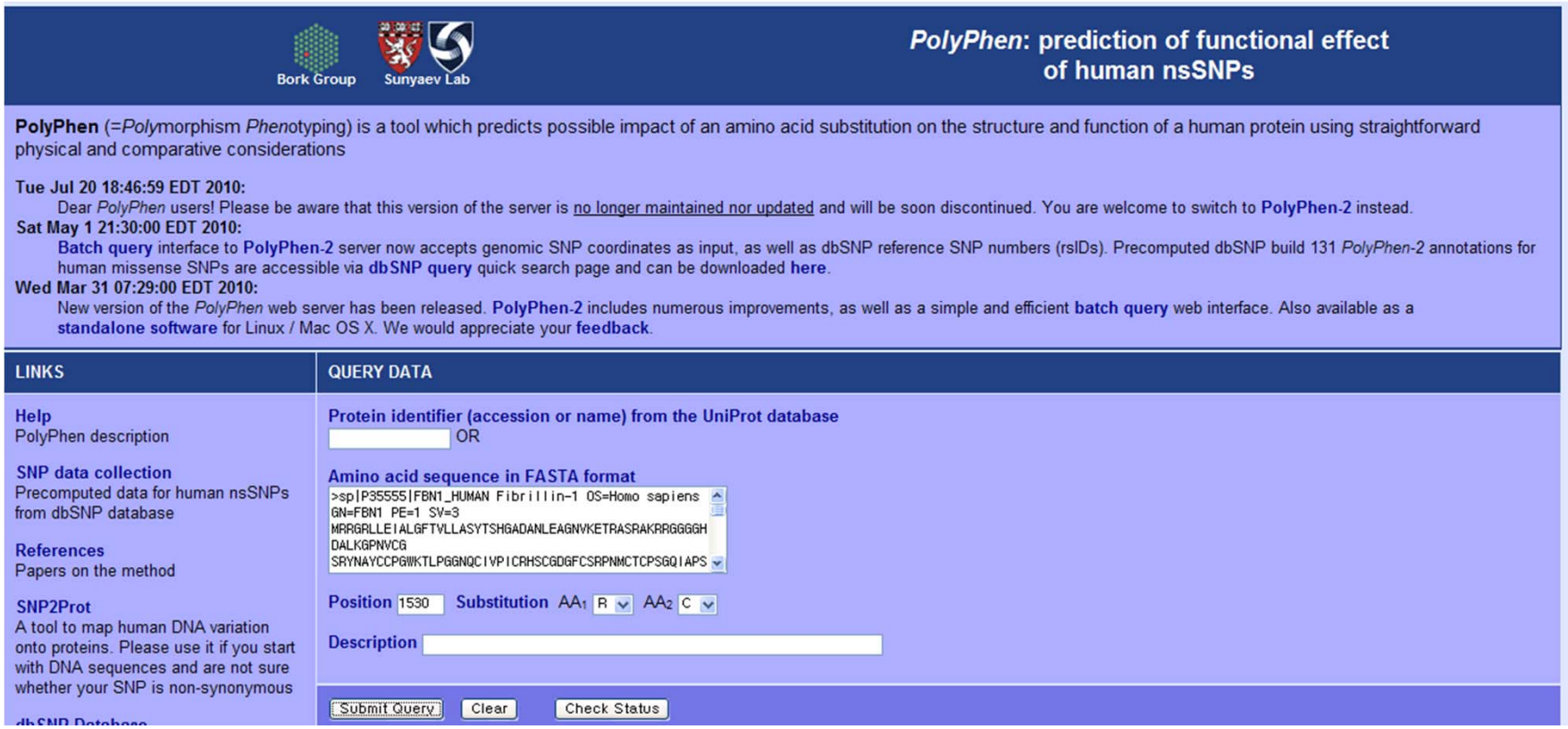







| Gene Symbol | Chromosomal location | Gene name | cDNA sequence | Extended cDNA | Splice junctions | Mutation viewer |
|---|---|---|---|---|---|---|
| FBN1 (Aliases: available to subscribers) | 15q21.1 | Fibrillin 1 (Aliases: available to subscribers) | NM_000138.3 | Not available | Splice junctions | BIOBASE Feature available to subscribers |

| | | | | | |
|---|---|---|---|---|---|
| CM020690 | TGT-TAT | Cys-Tyr | 1470 | Marfan syndrome | Matyas (2002) Hum Mutat **19**, 443 |
| CM055242 | aGGC-AGC | Gly-Ser | 1475 | Marfan syndrome | Rommel (2005) Hum Mutat **26**, 529 |
| CM972810 | cGAA-TAA | Glu-Term | 1477 | Marfan syndrome | Liu (1997) Genet Test **1**, 237 |
| CM074814 | cTGC-CGC | Cys-Arg | 1485 | Marfan syndrome | Comeglio (2007) Hum Mutat **28**, 928 |
| CM074842 | TGC-TAC | Cys-Tyr | 1497 | Aortic aneurysm | Waldmuller (2007) Eur J Cardiothorac Surg **31**, 970 |
| CM980730 | TGC-TCC | Cys-Ser | 1497 | Marfan syndrome | Perez (1998) Hum Mutat **13**, 84 |
| CM062705 | cAGT-TGT | Ser-Cys | 1499 | Marfan syndrome | Sakai (2006) Am J Med Genet A **140A**, 1719 |
| CM065181 | TGT-TAT | Cys-Tyr | 1502 | Marfan syndrome | Ganesh (2006) Arch Ophthalmol **124**, 205 |
| CM940766 | cTGC-CGC | Cys-Arg | 1513 | Marfan syndrome | Kainulainen (1994) Nat Genet **6**, 64 |
| CM065178 | TGCc-TGG | Cys-Trp | 1513 | Marfan syndrome | Ganesh (2006) Arch Ophthalmol **124**, 205 |
| CM001687 | tCGA-TGA | Arg-Term | 1523 | Marfan syndrome | Youil (2000) Hum Mutat **16**, 92 |
| CM074841 | tGAT-TAT | Asp-Tyr | 1528 | Marfan syndrome | Comeglio (2007) Hum Mutat **28**, 928 |
| CM013928 | cCGC-TGC | Arg-Cys | 1530 | Ectopia lentis | Loeys (2001) Arch Intern Med **161**, 2447<br>Additional phenotype report available to subscribers |
| CM010044 | tCGA-TGA | Arg-Term | 1539 | Marfan syndrome | Tiecke (2001) Eur J Hum Genet **9**, 13 |
| CM993159 | tCGA-TGA | Arg-Term | 1541 | Marfan syndrome | Halliday (1999) Hum Genet **105**, 587 |
| CM054721 | TGT-TTT | Cys-Phe | 1564 | Marfan syndrome | Arbustini (2005) Hum Mutat **26**, 494 |
| CM040040 | TGT-TAT | Cys-Tyr | 1564 | Marfan syndrome | Biggin (2004) Hum Mutat **23**, 99 |
| CM055243 | ATG-ACG | Met-Thr | 1576 | Marfan syndrome | Rommel (2005) Hum Mutat **26**, 529 |




## Query

| Acc number | Position | $AA_1$ | $AA_2$ | Description |
|---|---|---|---|---|
| P35555 | 1530 | R | C | RecName: Full=Fibrillin-1; Flags: Precursor; LENGTH: 2871 AA |

## Prediction

**This variant is predicted to be benign**

| Prediction | Available data | Prediction basis | Substitution effect | Prediction data |
|---|---|---|---|---|
| **benign** | alignment structure | alignment | N/A | PSIC score difference: 0.357 |

# HGNC Search

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

*Giving unique and meaningful names to every human gene*

This public copy of the database was last updated Friday April 15 04:20:51 2011
There are now 30495 approved gene symbols, of which 19345 are for protein-coding genes; further statistics are available from our downloads page.

# Quick Search

FBN1 ○ equals ○ begins ◉ contains
Display 20 Hits Quick Gene Search

# Advanced Search

| | | | | | |
|---|---|---|---|---|---|
| Approved Symbols | that | do | begin with | | AND |
| Approved Gene Names | that | do | contain | | AND |
| All Records | that | do | contain | | AND |
| Chromosomes | that | do | begin with | | |

Display Options:- Show 50 records in HTML format, sorted by Symbol

원래대로 Submit search

# Symbol Report: FBN1



*Giving unique and meaningful names to every human gene*

Quick Gene Search

| Core Data | |
|---|---|
| Approved Symbol + | FBN1 |
| Approved Name + | fibrillin 1 |
| HGNC ID + | HGNC:3603 |
| Status + | Approved |
| Chromosome + | 15q21.1 |
| Previous Symbols + | FBN, MFS1, WMS |
| Previous Names + | "fibrillin 1 (Marfan syndrome)" |
| Aliases + | MASS, OCTD, SGS |
| Name Aliases + | "Marfan syndrome" |
| Locus Type + | gene with protein product |

**Gene Symbol Links**

GENATLAS GeneCards GeneClinics/GeneTests GoPubmed

HCOP H-InvDB Treefam wikigenes

**Specialist Database Links**

COSMIC Orphanet

**Locus Specific Database Links**

UMD Locus Specific Databases

**Database Links**

| | | | | |
|---|---|---|---|---|
| **Accession Numbers +** | | | | |
| X63556 | GenBank | EMBL | DDBJ | UCSC |
| **Mouse Genome Database ID +** | | | | |
| MGI:95489 | MGD ID | | | |
| **Rat Genome Database ID (mapped data supplied by RGD) +** | | | | |
| RGD:620908 | RGD ID | | | |
| **CCDS IDs +** | | | | |
| CCDS32232.1 | CCDS ID | | | |
| **Pubmed IDs +** | | | | |
| 10036187, 12525539 | PMID | | CiteXplore | |
| **Ensembl ID (mapped data supplied by Ensembl) +** | | | | |
| ENSG00000166147 | Ensembl GeneView | | UCSC | |
| **Entrez Gene ID (mapped data supplied by NCBI) +** | | | | |
| 2200 | Gene | | Map Viewer | |
| **RefSeq (mapped data supplied by NCBI) +** | | | | |
| NM_000138 | GenBank | EMBL | DDBJ | UCSC |
| **OMIM ID (mapped data supplied by NCBI) +** | | | | |
| 134797 | OMIM | | | |
| **UCSC ID (mapped data supplied by UCSC) +** | | | | |
| uc001zwx.1 | UCSC Index | | | |
| **UniProt ID (mapped data supplied by UniProt) +** | | | | |
| P35555 | UniProt | | UCSC | |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