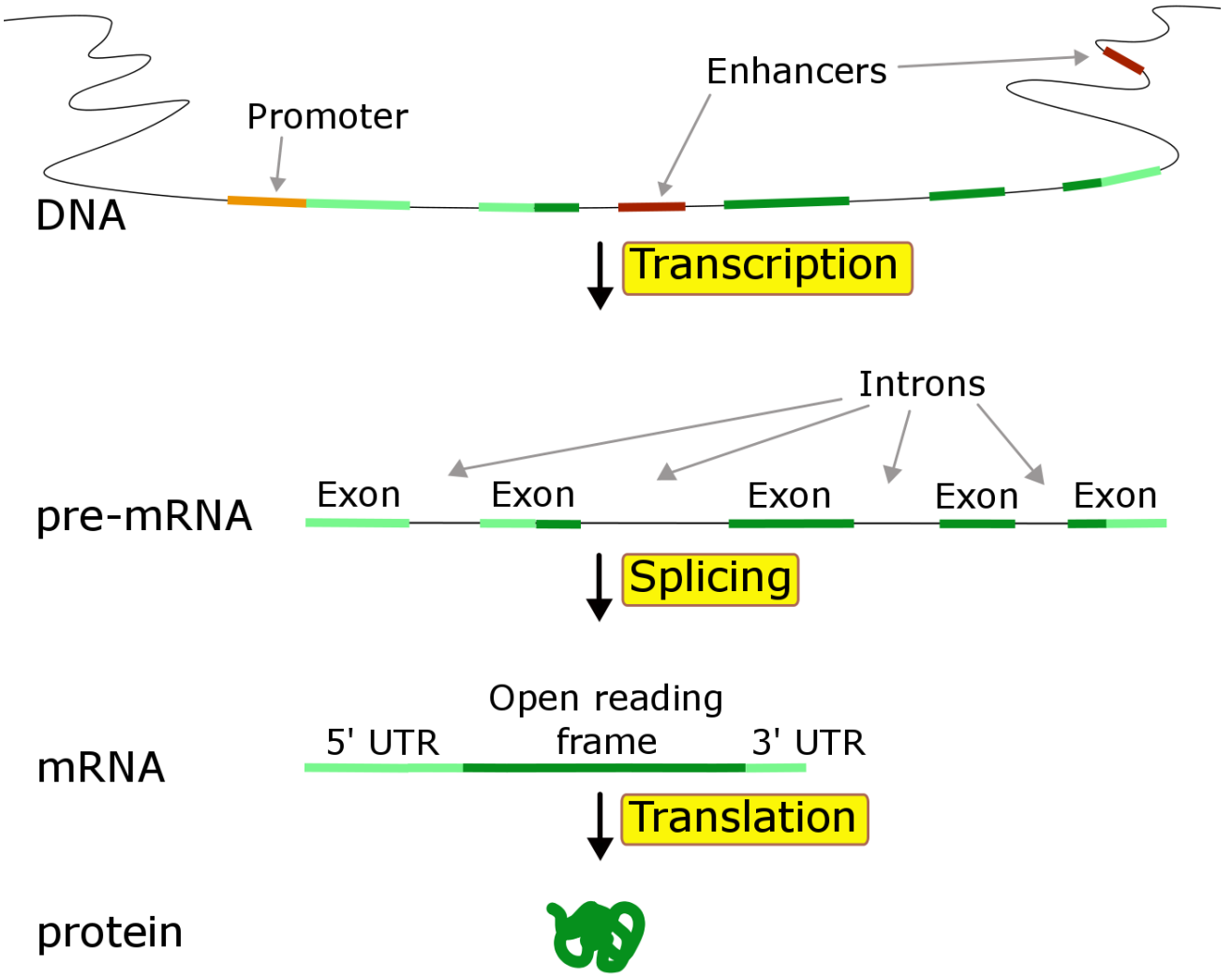
Biological Databases – Mutations

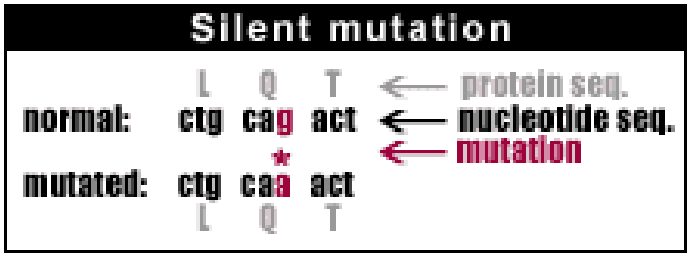
by Benjamin Drexler

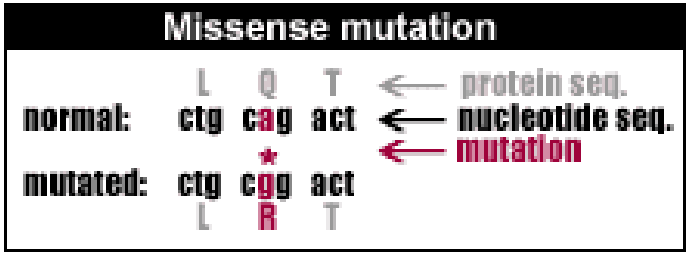
Eukaryotic Gene

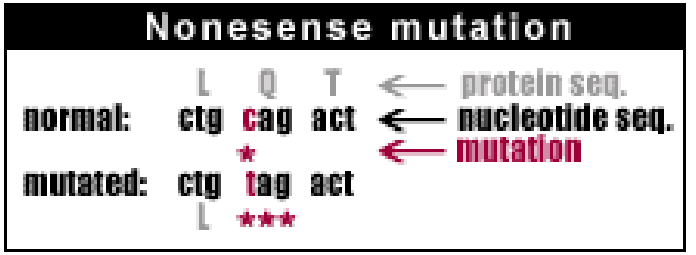


Mutations (1)

- Small-scale
  - Point mutations
    - Silent
    - Missense
    - Nonsense
  - Insertions
  - Deletions



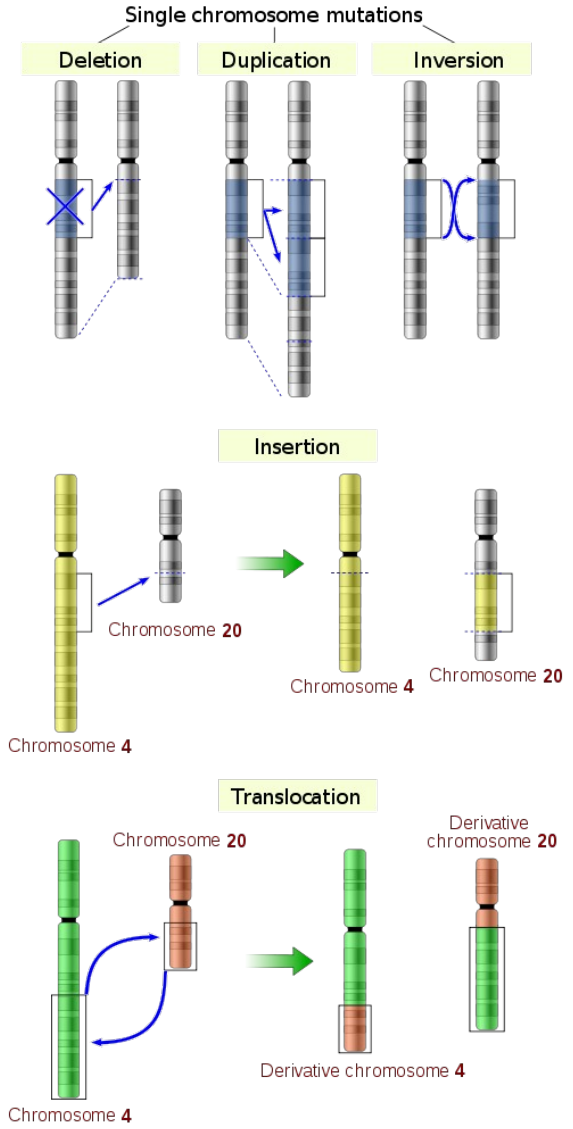




www.ebi.ac.uk

Mutations (2)

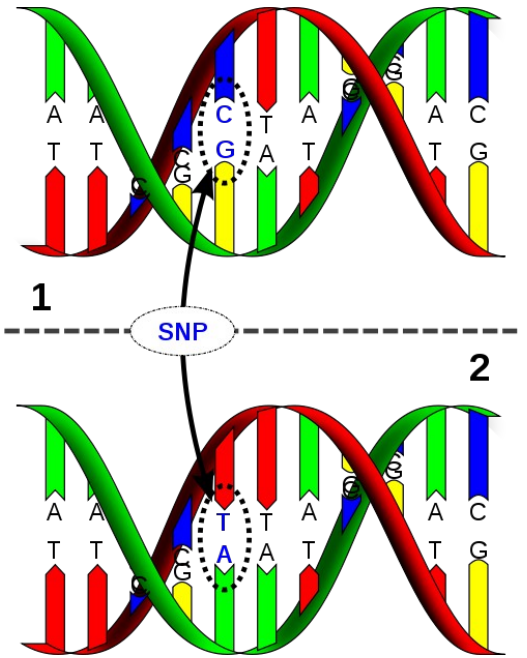
- Large-scale
  - Deletion
  - Duplication
  - Inversion
  - Insertion
  - Translocation



en.wikipedia.org

Single-nucleotide Polymorphism

- **S**ingle-**n**ucleotide **P**olymorphism (SNP)
- Applications
  - Genome wide association studies (GWAS)
  - Personalized medicine

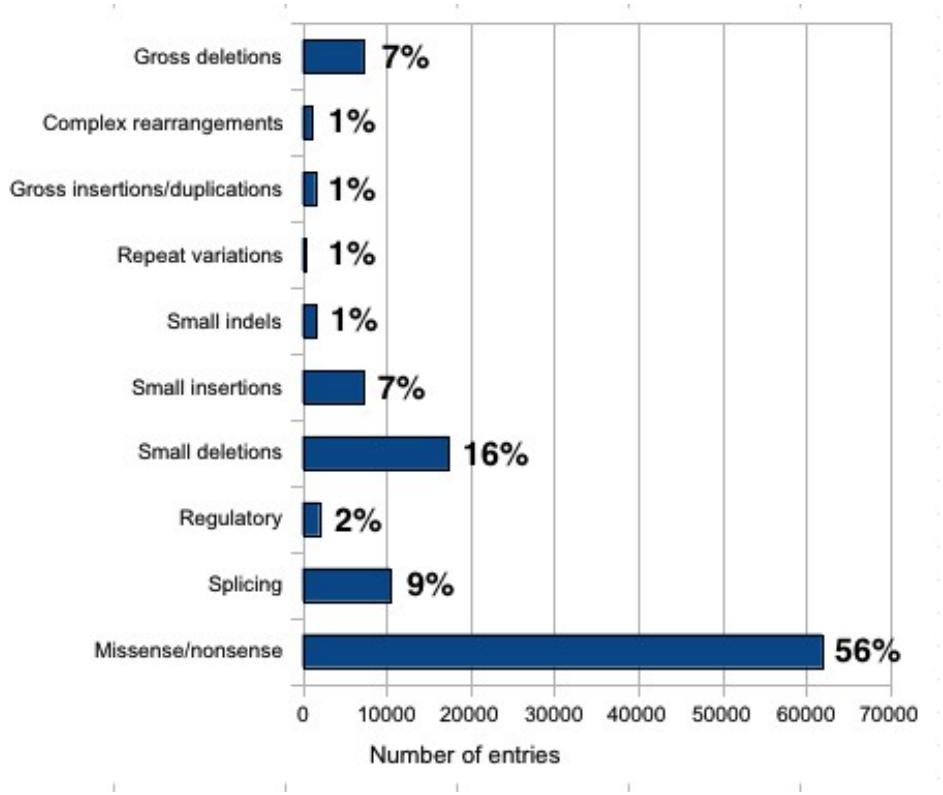


en.wikipedia.org

HGMD – Basics

- **H**uman **G**ene **M**utation **D**atabase (HGMD)
- Publicly available in 1996
- Records
  - Disease-causing mutations
  - Disease-associated polymorphism
- Data acquisition by computerized and manual search process

HGMD – Mutations



Small (<= 20 bp)

Gross (> 20 bp)

HGMD – Entries

- Only mutations with high confidence/quality
- No silent mutations
- SNPs generally in coding regions or promoter

HGMD – Professional Version

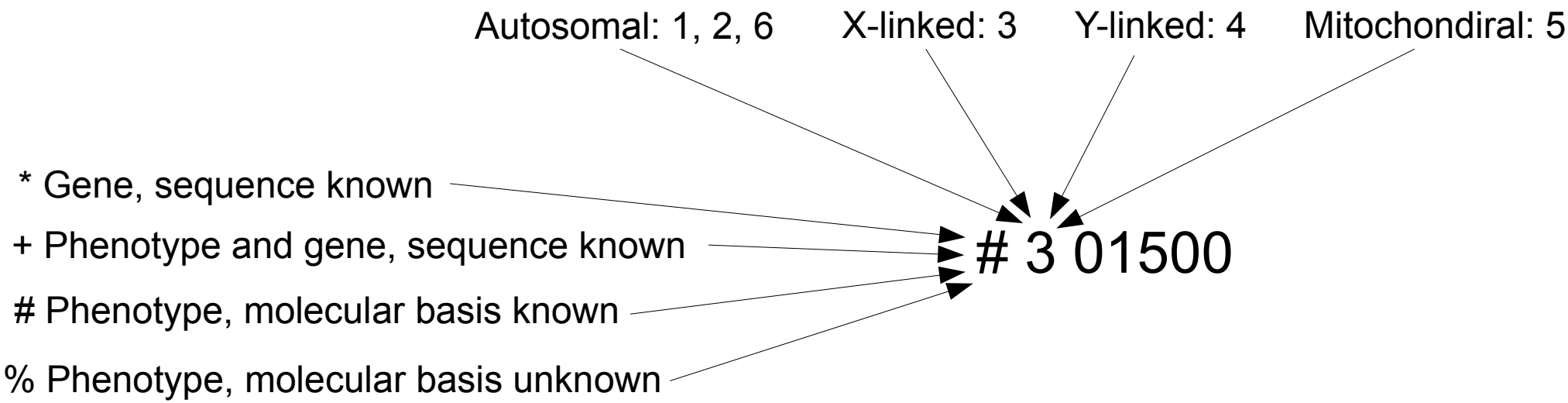
- Additional
  - Search tools
  - Information about mutations
  - Gene view with mutations
- Free version
  - mutation are atleast 2.5 years old

OMIM – Basics

- **O**nline **M**endelian **I**nheritance in **M**an (OMIM)
- Knowledgebase of human phenotypes and genes
- „Mendelian Inheritance in Man“ (MIM) by McKusick in 1966
- Data acquisition
  - Scanning biomedical literature
  - Manual review

OMIM – Entries (1)

- Unique six-digit number (MIM ID)
- First number indicates inheritance



- Prefix characterises entry type

OMIM – Entries (2)

MIM ID #301500

FABRY DISEASE

GeneTests, Links

Alternative titles; symbols

ANGIOKERATOMA CORPORIS DIFFUSUM
ANDERSON-FABRY DISEASE
HEREDITARY DYSTOPIC LIPIDOSIS
ALPHA-GALACTOSIDASE A DEFICIENCY
GLA DEFICIENCY
CERAMIDE TRIHEXOSIDASE DEFICIENCY

Other entities represented by this entry

FABRY DISEASE, CARDIAC VARIANT, INCLUDED

Gene map locus: Xq22

Clinical Synopsis

Text Back to Top

A number sign (#) is used with this entry because Fabry disease is caused by mutations in the gene encoding alpha-galactosidase A (GLA; 300644).

Description Back to Top

Fabry disease is an X-linked inborn error of glycosphingolipid catabolism resulting from deficient or absent activity of the lysosomal enzyme alpha-galactosidase A. This enzymatic defect leads to the systemic accumulation of globotriaoslyceramide (Gb3) and related glycosphingolipids in the plasma and cellular lysosomes of vessels, nerves, tissues, and organs throughout the body (Nance et al., 2006). The disorder is a systemic disease, manifest as progressive renal failure, cardiac disease, cerebrovascular disease, small-fiber peripheral neuropathy, and skin lesions, among other abnormalities (Schiffmann, 2009).

An atypical variant of Fabry disease has been reported in which cardiac disease, specifically left ventricular hypertrophy, with or without renal failure, develops in the sixth decade of life. These patients have residual GLA activity (Nakao et al., 1995; Nakao et al., 2003).

Although previously considered an X-linked recessive disorder, Wang et al. (2007) found that heterozygous women with Fabry disease experience significant life-threatening conditions requiring medical treatment and intervention. Thus, heterozygous Fabry women should not be called carriers, as this term underestimates the seriousness of the disease in these patients.

Clarke (2007) and Schiffmann (2009) provided detailed reviews of Fabry disease.

Clinical Features Back to Top

In his first paper on this subject, Fabry (1898) called the skin lesions 'purpura papulosa haemorrhagica Hebrae,' suggesting that they had previously been described by Hebra, the famous Austrian dermatologist. Affected individuals had painful crises in the extremities, thought to result from lipid changes in ganglion cells of the autonomic nervous system. Attacks of pain in the abdomen may have been misdiagnosed as appendicitis or other surgical emergencies. Vascular lesions of lipid nature occurred at other sites such as the ocular fundi and kidney. Renal failure was the usual cause of death.

Hamburger et al. (1964) described a familial nephropathy, manifested clinically by proteinuria and renal insufficiency. Renal biopsy showed that the epithelial cells of the glomerular tufts and to a lesser extent the tubular epithelial cells, glomerular endocapillary cells and arteriolar muscular cells were severely deformed with a large amount of cytoplasmic inclusion material appearing lipoid in nature. The mother's father died of uremia.

Skin lesion may be lacking even in patients with severe visceral manifestations (Johnston, 1967). Furthermore, identical angiokeratoma skin lesions occur in other lysosomal disorders: (see, e.g., Patel et al., 1972 and Loonen et al., 1974). Flynn et al. (1972) described a family without skin lesions. One affected male had severe enteropathy.

Franceschetti et al. (1969) reexamined a family with 'cornea verticillata' reported by Gruber (1946) and showed that Fabry disease was responsible for the corneal change. The extent of involvement of the cornea was about the same in males and females, thus allowing affected females to be identified. The corneal condition was formerly called Fleischer vortex

Table of Contents

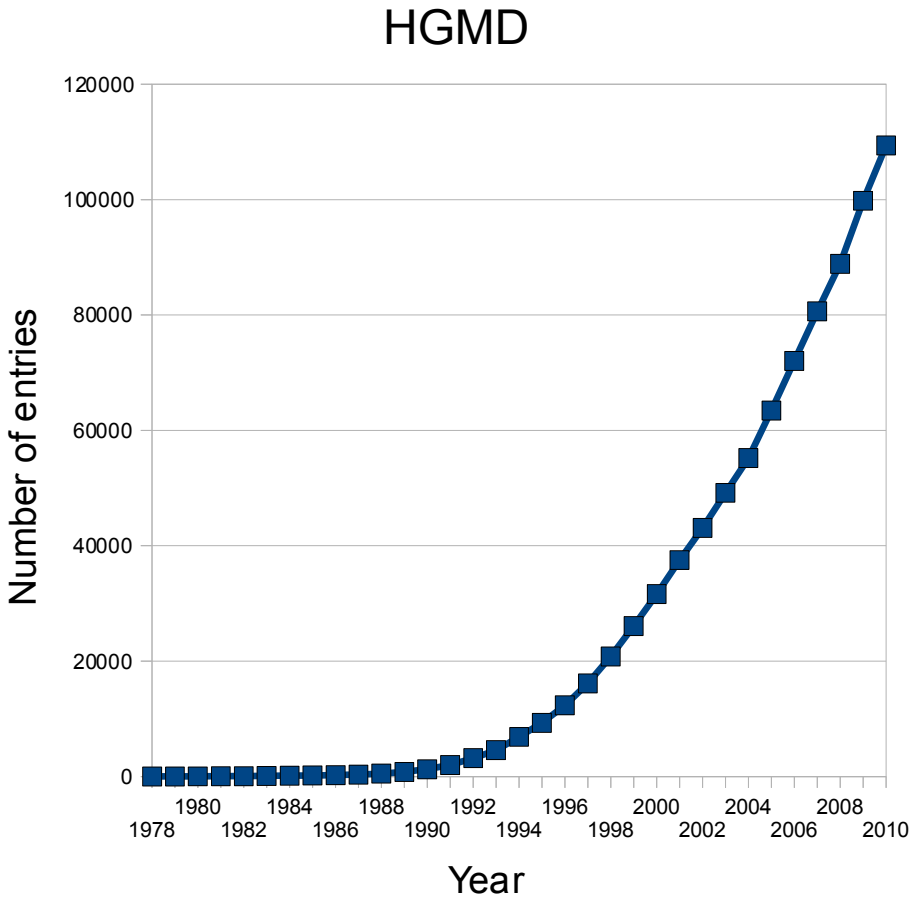
Links

Selected Gene Related Links
- G Entrez Gene
- N Nomenclature
- R RefSeq
- G GenBank
- P Protein
- U UniGene

Other NCBI Links
- BioSystems
- Books
- Free in PMC
- GEO Profiles
- Gene
- Gene Genotype
- GeneTests
- GeneView in dbSNP
- HomoloGene
- Map Viewer
- PubChem BioAssay
- PubMed (calculated)
- PubMed (cited)
- UniGene
- Related Entries
- EST
- Nucleotide
- Protein
- UniSTS

LinkOut
- UCSC Genome Browser
- KOMP Repository

HGMD & OMIM



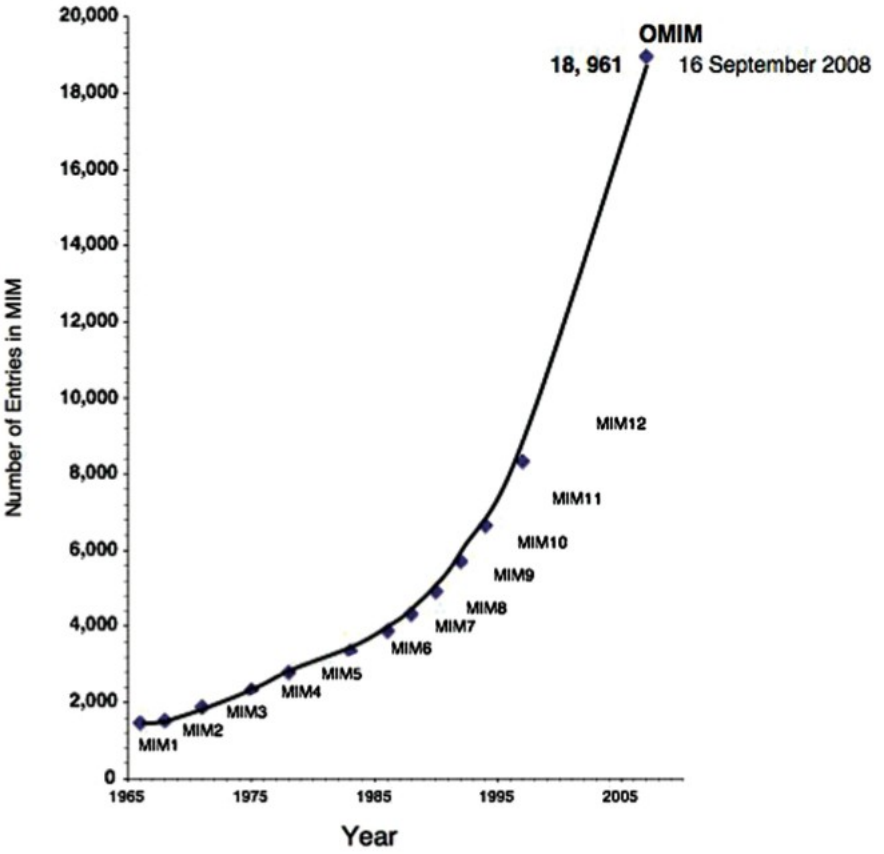


Figure 1. Number of entries in *Mendelian Inheritance in Man.*

Cooper et. al, 2009

Thanks for your attention!

References

- Cooper et. al, 'Human Gene Mutation Database – A Biomedical Information and Research Resource', Human Mutation, Volume 15, Issue 1
- Cooper et. al, 'The Human Gene Mutation Database: 2008 update', Genome Medicine 2009
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- OMIM website FAQ: http://www.ncbi.nlm.nih.gov/Omim/omimfaq.html
- Wikipedia website: http://en.wikipedia.org/wiki/Mutation
- EBI website: http://www.ebi.ac.uk/2can/disease/index.html