

Mutations

Superheroes



How did Cyclops from the X-Men get his superpowers?

- ❖ He was born with the mutation

How did the Hulk and Spiderman get their superpowers?

- ❖ The Hulk was exposed to gamma radiation and Spiderman was bitten by a radioactive spider

Learning about Mutations

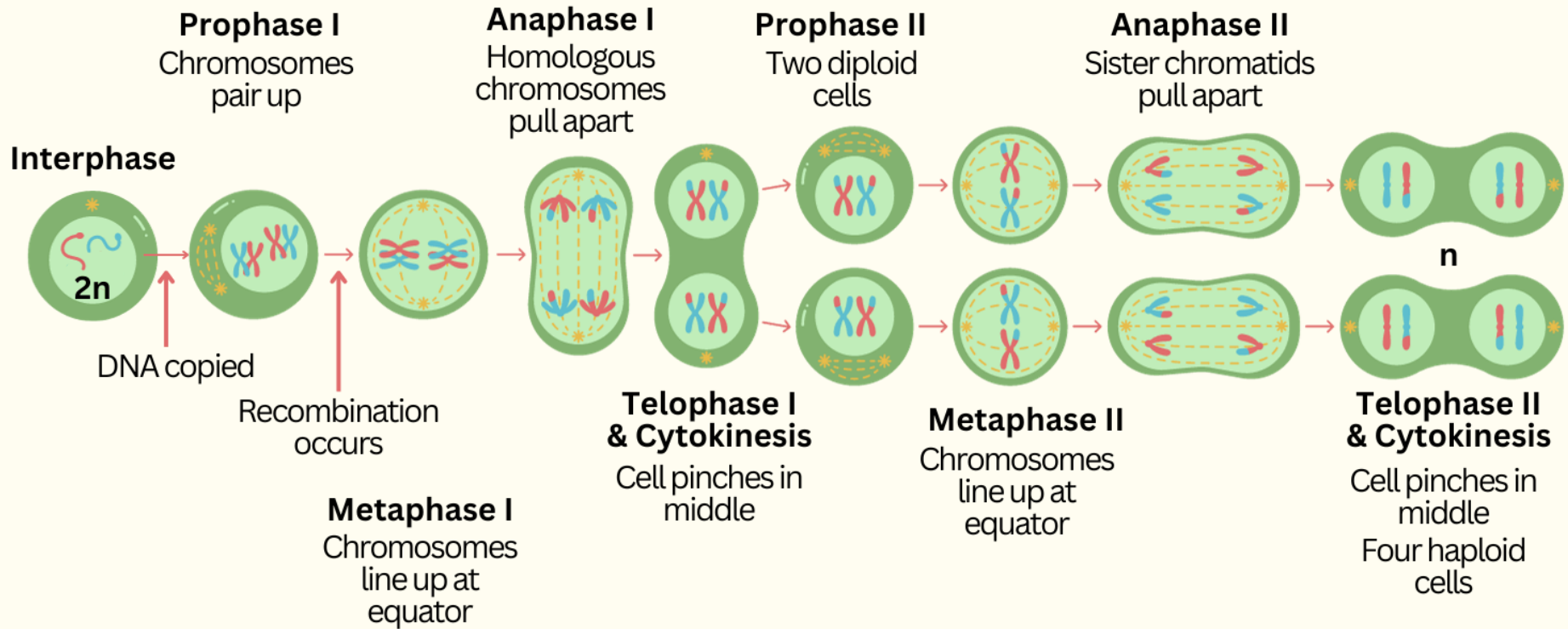
- ❑ Types of mutations and how they occur
- ❑ How environmental factors influence mutations
- ❑ Effects of mutations

Terminology

- ❓ Autosomes: Numbered Chromosomes (22 pairs in humans)
 - ❓ Autosomal Disorder: Occurs in genes on one of these chromosomes
 - ❓ Recessive: Passed by parents but not shown in parents
- ❓ Chromosomal Disorder: Occurs on the sex-chromosomes, usually from an error in cell division
- ❓ Diploid: Nucleus contains two complete sets (23 pairs) of chromosomes, one from each parent (2N)- Human somatic cells
- ❓ Haploid: Single set of chromosomes (half of diploid)- Only sperm and egg are haploid in humans

MEIOSIS

Meiosis is the process where a cell divides twice, forming four cells that each contain half the genetic information ($2n \rightarrow n$).

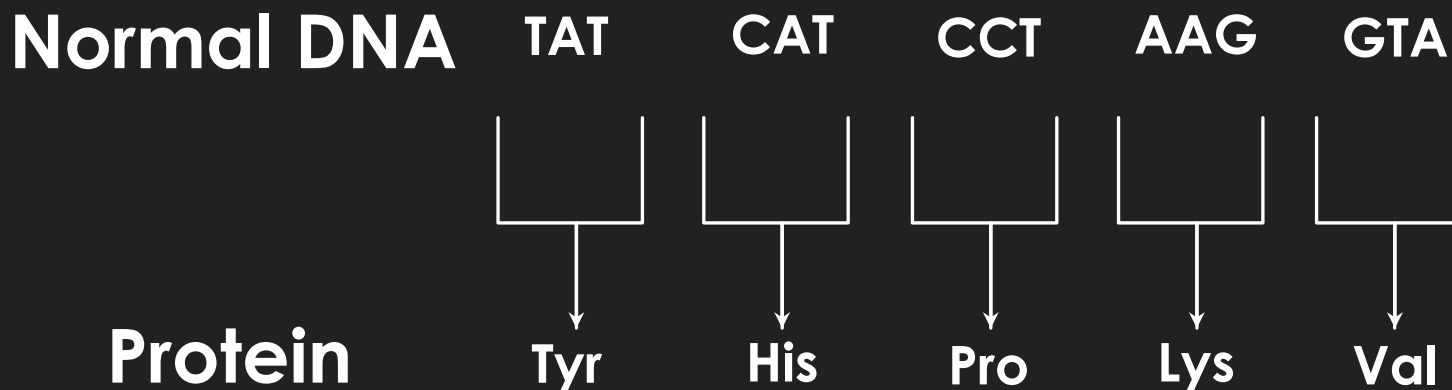


Meiosis forms sperm and egg (sex cells or gametes).

Types of Mutations

Small-scale mutations

- Affect DNA at the molecular level by changing the normal sequence of nucleotide base pairs
- Occur during the process of DNA replications (either meiosis or mitosis)

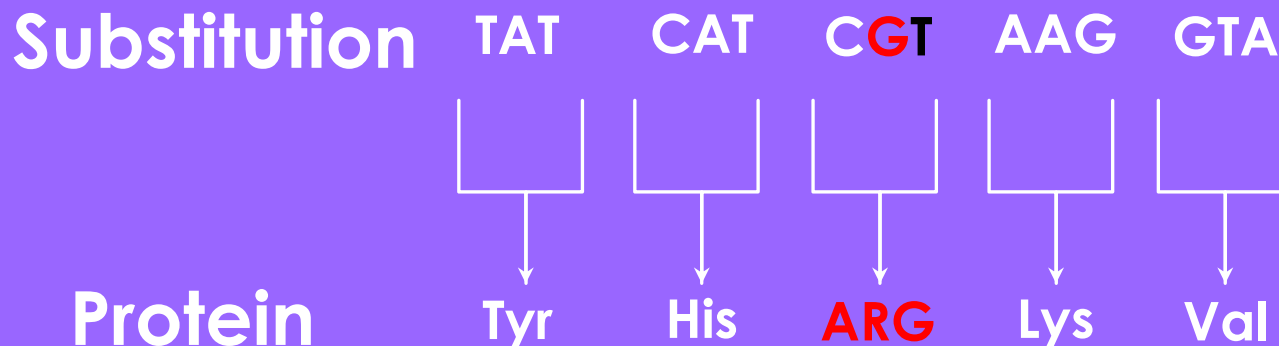


Small-Scale Mutations

1

1. Substitution (or a “point” mutation”)

- Substitutions occur when a nucleotide is replaced with a different nucleotide in the DNA sequence
- This type of mutation only affects the codon for a single amino acid

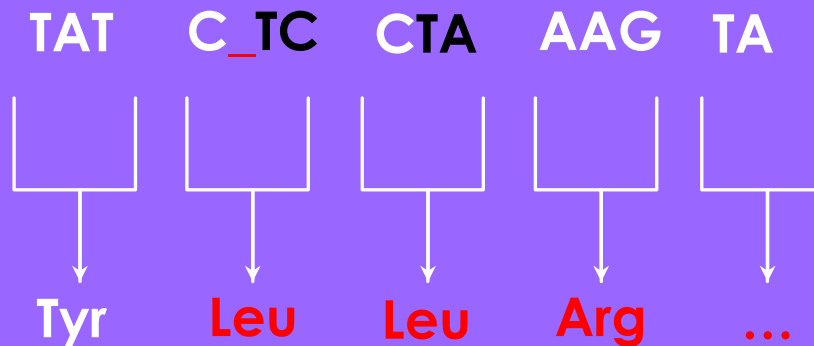


Small-Scale Mutations #2

2. Deletion (a “frameshift” mutation)

- Deletion is the removal of a nucleotide from the DNA sequence
- Removal of even a single nucleotide from a gene alters every codon after the mutation

Deletion



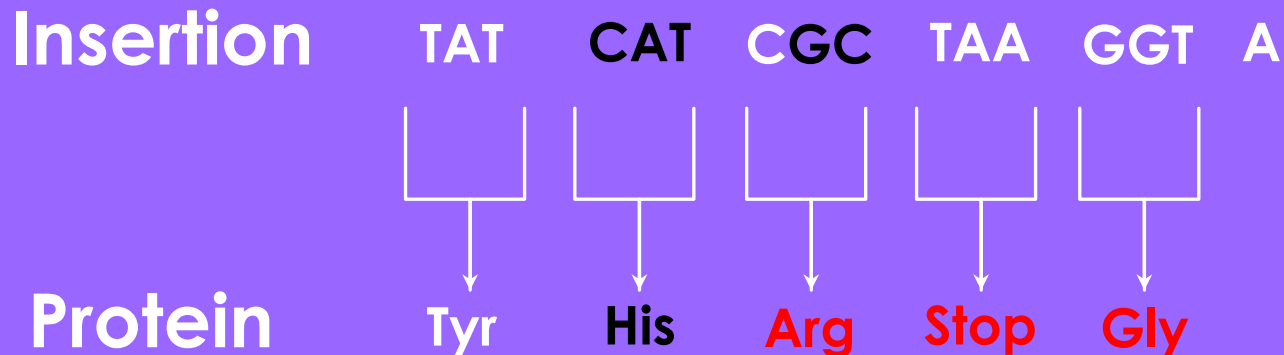
Protein

Small-Scale Mutations

#3

3. Insertion (a “frameshift” mutation)

- ❓ Addition of a nucleotide to the DNA sequence
- ❓ Addition of even a single nucleotide to a gene alters every codon after the mutation



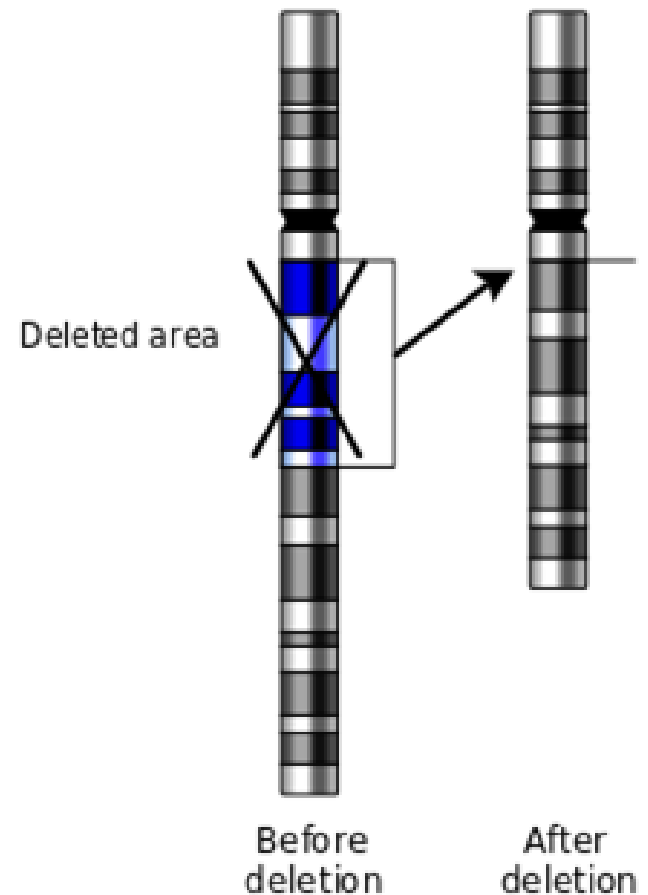
Large-Scale Mutations

- ❑ **Affect entire portions of the chromosome**
 - ❑ Some large-scale mutations affect only single chromosomes, others occur across nonhomologous pairs
 - ❑ Entire genes or sets of genes are altered rather than only single nucleotides of the DNA
 - ❑ Mutations involving multiple chromosomes are likely to occur in meiosis, during the prophase I

Large-Scale Mutations

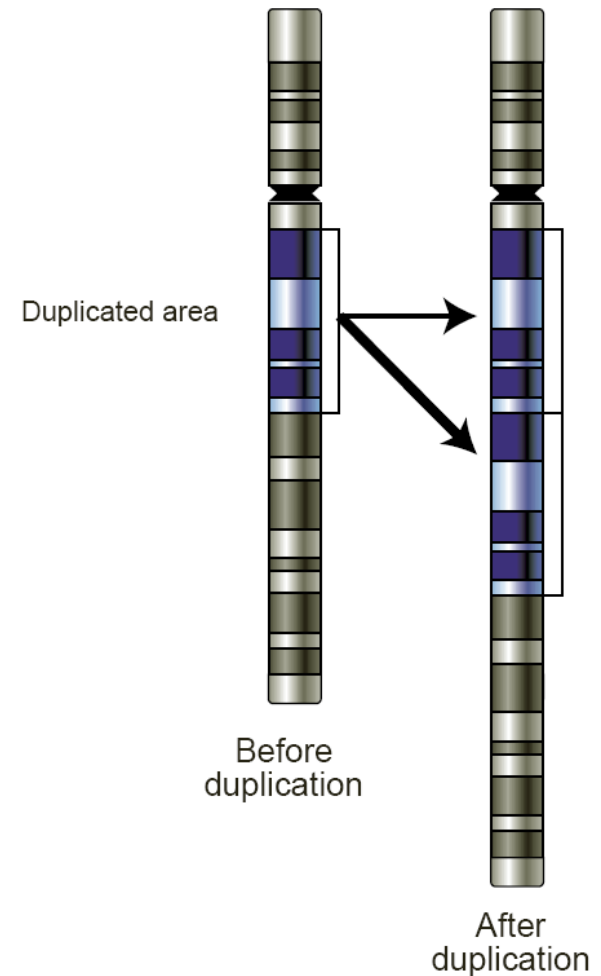
? Deletion

- ? Single chromosome mutation
- ? The loss of one or more gene(s) from the parent chromosome
- ? Ex: DiGeorge Syndrome (deletion of portion of c-22)
- ? Ex: Cri du Chat Syndrome (deletion of portion of c-5)



Large-Scale Mutations

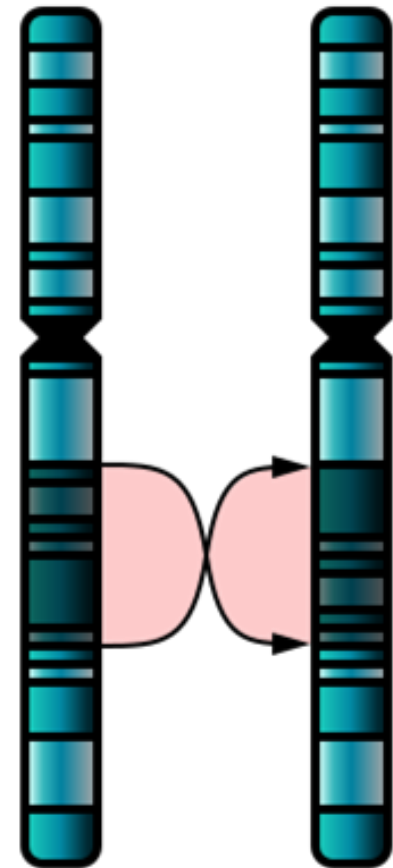
- ❑ Duplication (amplifications)
 - ❑ Single chromosome mutation
 - ❑ The addition of one or more gene(s) that are already present in the chromosome



Large-Scale Mutations

- ❑ Inversion (chromosomal inversions)
 - ❑ Single chromosome mutation
 - ❑ The complete reversal of one or more gene(s) within a chromosome; the genes are present, but the order is backwards from the parent chromosome

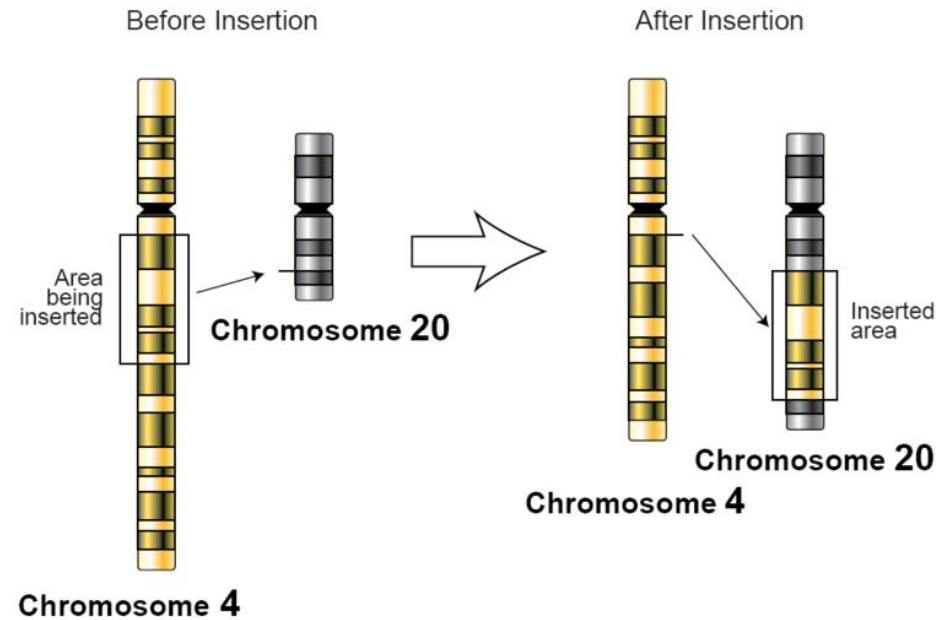
Inversion



Large-Scale Mutations

? Insertion

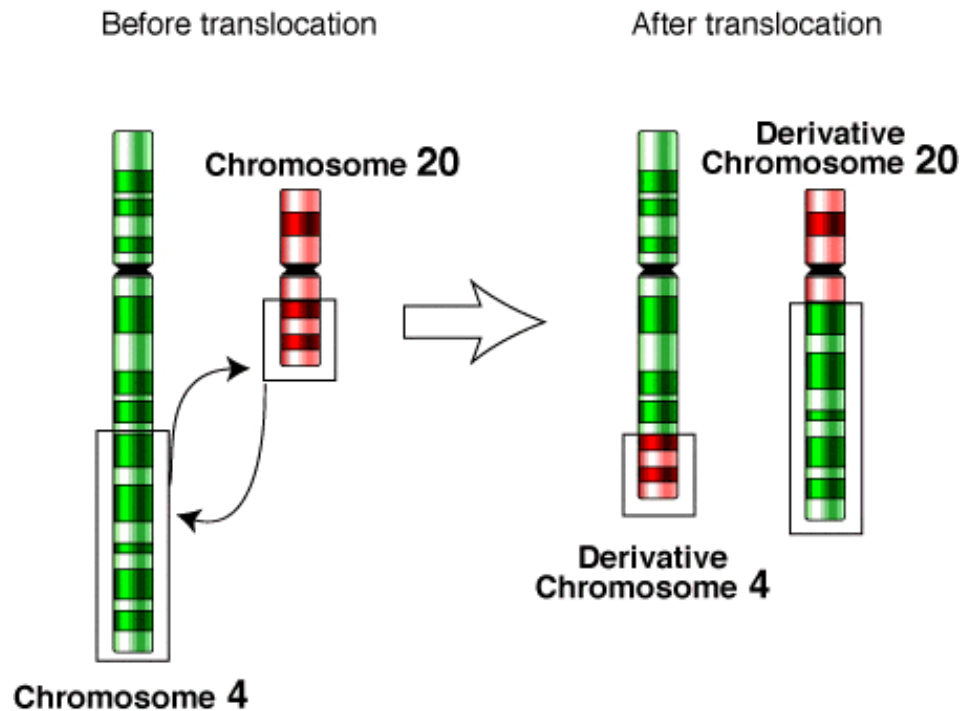
- ? Multiple chromosome mutation
- ? One or more gene(s) are removed from one chromosome and inserted into another nonhomologous chromosome
- ? Can occur by an error during the prophase I of meiosis when the chromosomes are swapping genes to increase diversity



Large-Scale Mutations

? Translocation

- ? Multiple nonhomologous chromosome mutation
- ? Chromosomes swap one or more gene(s) with another chromosome



Large-Scale Mutations

❑ Nondisjunction

- ❑ Does not involve any errors in DNA replication or crossing-over
- ❑ Mutations occur during the anaphase and telophase when the chromosomes are not separated correctly into the new cells
- ❑ Common nondisjunctions are missing or extra chromosomes

Effects of Mutations

- ❑ The effects of mutations may range from **nothing** to the **unviability of a cell**
- ❑ All mutations affect the proteins that are created during protein synthesis, but not all mutations have a significant impact

Small-Scale Mutation Effects

1. Silent

- ❑ The nucleotide is replaced, but the codon still produces the same amino acid

2. Missense

- ❑ The codon now results in a different amino acid, which may or may not significantly alter the protein's function

3. Nonsense

- ❑ The codon now results in a “stop” command, truncating the protein at the location where the mutated codon is read; this almost always leads to a loss of protein functionality

Large-Scale Mutation Effects

- ❑ Effects of large-scale mutations are more obvious than those of small-scale mutations
- ❑ Duplication of multiple genes causes those genes to be overexpressed while deletions result in missing or incomplete genes
- ❑ Mutations that change the order of the genes on the chromosome—such as deletions, inversions, insertions and translocations—result in genes that are close together

Large-Scale Mutation Effects

- ❑ When certain genes are positioned closely together, they may encode for a “fusion protein”
 - ❑ A fusion protein is a protein that would not normally exist but is created by a mutation in which two genes were combined
 - ❑ The new proteins give cells a growth advantage, leading to tumors and cancer

Large-Scale Mutation Effects

- ❑ Often, large-scale mutations lead to cells that are not viable
 - ❑ The cell dies due to the mutation

Mutation Influences

- ❑ Exposure to certain chemicals
 - ❑ Carcinogenic chemicals may cause cancer
- ❑ Exposure to radiation
- ❑ Retroviruses
 - ❑ Retroviruses such as HIV naturally experience mutations at a much higher rate than other organisms

Engineering Connection

- ❑ Humans have been genetically modifying plants and animals for thousands of years
 - ❑ **Example:** Breeding watermelons to be larger and have fewer seeds
 - ❑ **Example:** Breeding chickens to have more white meat and more breast meat

Engineering Connection

- ❑ Engineers can directly manipulate the genetic code of plants and animals (controversial)
 - ❑ **Examples:** Disease-resistant papaya, vitamin A-rich rice, and drought-tolerant corn
- ❑ Engineers and scientists are currently studying gene editing in the womb
 - ❑ May prevent the child from having diseases and disabilities

Mutations

ΔF508 deletion in cystic fibrosis

		2nd base			
		U	C	A	G
1st base	U	UUU (Phe/F) Phenylalanine	UCU (Ser/S) Serine	UAU (Tyr/Y) Tyrosine	UGU (Cys/C) Cysteine
		UUC (Phe/F) Phenylalanine	UCC (Ser/S) Serine	UAC (Tyr/Y) Tyrosine	UGC (Cys/C) Cysteine
		UUA (Leu/L) Leucine	UCA (Ser/S) Serine	UAA Ochre (Stop)	UGA Opal (Stop)
		UUG (Leu/L) Leucine	UCG (Ser/S) Serine	UAG Amber (Stop)	UGG (Trp/W) Tryptophan
	C	CUU (Leu/L) Leucine	CCU (Pro/P) Proline	CAU (His/H) Histidine	CGU (Arg/R) Arginine
		CUC (Leu/L) Leucine	CCC (Pro/P) Proline	CAC (His/H) Histidine	CGC (Arg/R) Arginine
		CUA (Leu/L) Leucine	OCA (Pro/P) Proline	CAA (Gln/Q) Glutamine	CGA (Arg/R) Arginine
		CUG (Leu/L) Leucine	CCG (Pro/P) Proline	CAG (Gln/Q) Glutamine	CGG (Arg/R) Arginine
	A	AUU (Ile/I) Isoleucine	ACU (Thr/T) Threonine	AAU (Asn/N) Asparagine	AGU (Ser/S) Serine
		AUC (Ile/I) Isoleucine	AOC (Thr/T) Threonine	AAC (Asn/N) Asparagine	AGC (Ser/S) Serine
		AUA (Ile/I) Isoleucine	ACA (Thr/T) Threonine	AAA (Lys/K) Lysine	AGA (Arg/R) Arginine
		AUG (Met/M) Methionine	ACG (Thr/T) Threonine	AAG (Lys/K) Lysine	AGG (Arg/R) Arginine
G	GUU (Val/V) Valine	GCU (Ala/A) Alanine	GAU (Asp/D) Aspartic acid	GGU (Gly/G) Glycine	
	GUC (Val/V) Valine	GCC (Ala/A) Alanine	GAC (Asp/D) Aspartic acid	GGC (Gly/G) Glycine	
	GUA (Val/V) Valine	GCA (Ala/A) Alanine	GAA (Glu/E) Glutamic acid	GGA (Gly/G) Glycine	
	GUG (Val/V) Valine	GCG (Ala/A) Alanine	GAG (Glu/E) Glutamic acid	GGG (Gly/G) Glycine	

Selection of notable mutations, ordered in a standard table of the genetic code of amino acids.

Clinically important missense mutations generally change the properties of the coded amino acid residue between being basic, acidic, polar or nonpolar, while nonsense mutations result in a stop codon.

Amino acids

- Basic
- Acidic
- Polar
- Nonpolar (hydrophobic)

Fragile X Syndrome

Polyglutamine (PolyQ) Diseases

- Huntington's disease
- Spinocerebellar ataxia (SCA) (most types)
- Spinobulbar muscular atrophy (Kennedy disease)
- Dentatorubral-pallidoluysian atrophy

Mutation type

- Trinucleotide repeat
- Deletion
- Missense
- Nonsense

β-Thalassemia

β-Thalassemia

McArdle's disease

- Myotonic dystrophy - SCA 8

Prostate Cancer

Colorectal cancer

Sickle-cell disease

Friedreich's ataxia

Examples of Notable Mutations