

Mutations

Changes in DNA from the Original DNA Gene

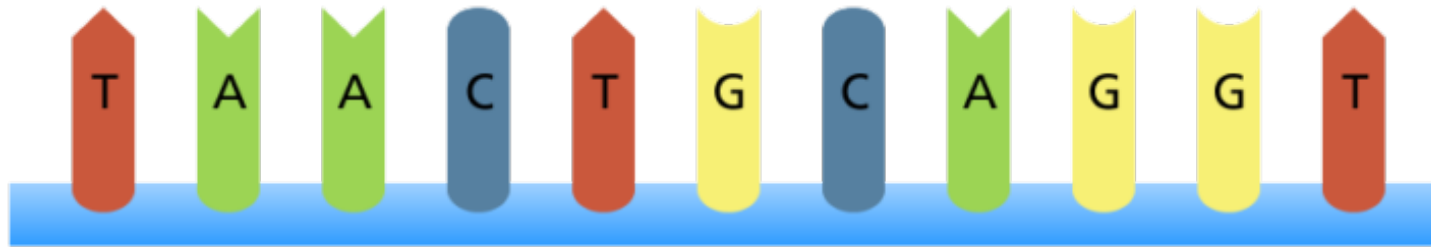


Point mutations

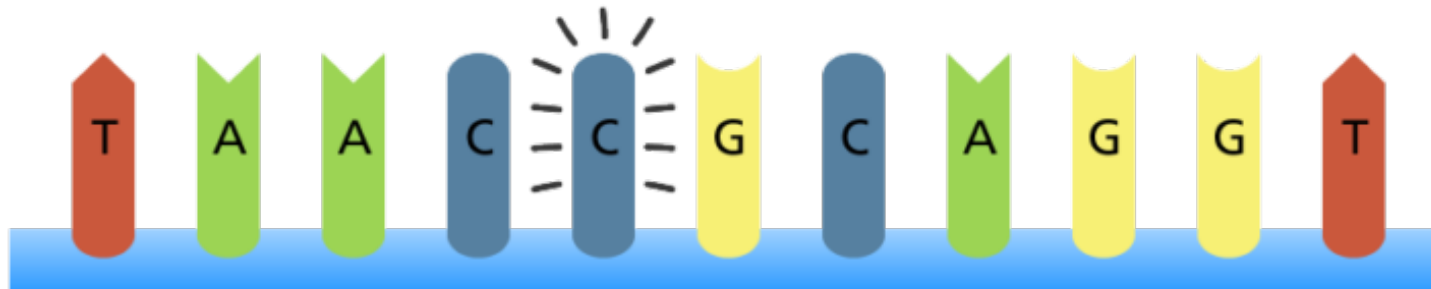
- A point mutation is a single change in a base from the original wild type DNA
 - Example: The original eye color in humans was brown. This is the “wild type” DNA/gene. Blue eye color would be called a “mutant” form of the gene.

Point mutations: Example...the T at base 5 changed into a C after the mutation

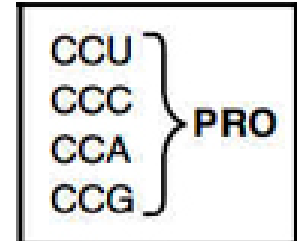
Original sequence



Point mutation



Types of Point Mutations



- **Silent Mutation: No Change in Amino Acid.**
 - Point Mutation that changes the 3rd base of a codon. This doesn't cause a change in an amino acid because of redundancy in the 3rd base. Look at the amino acid chart above. Many amino acids are coded for by several mRNA's thus for proline, only the first two letters (cc) matter.
- **Missense Mutation:** Changes a **single** base in the DNA, which in turn changes a **single** Amino Acid in the protein after transcription and translation
- **Nonsense Mutation:** Changes a letter, that would normally code for an amino acid, **into an early stop codon**. This terminates translation early and results in a non-functional protein.

Possible Outcomes of Point Mutations

No mutation

DNA

A T G

mRNA

U A C

tyrosine
(normal
protein)

Point mutations

A T **A**

U A U

tyrosine
(normal
protein)

A T **C**

U A G

stop
(incomplete
protein)

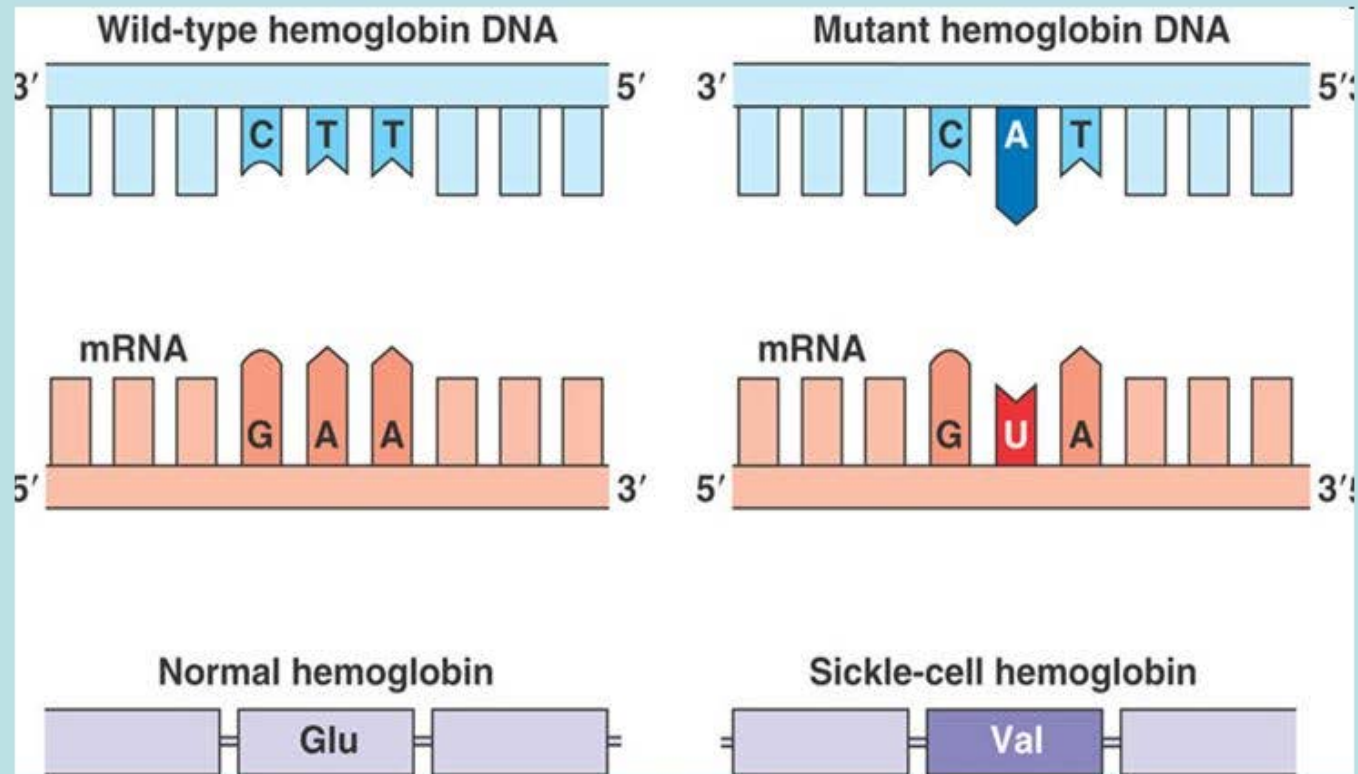
G T G

C A C

histidine
(faulty
protein)

Sickle Cell Anemia is caused by a Point Mutation. This point mutation changes a SINGLE amino acid out of 142 This causes proteins that carry oxygen in blood to “sickle”. This causes them to not carry oxygen well. See pic on next page

Point mutation



Sickled Red Blood Cell



Normal Red Blood Cell



Frameshift Mutations

- Insertions and Deletions, Typically a single letter of DNA is inserted or deleted
- This shifts the entire reading frame up 1 (deletion) or down 1 (insertion)
- The 3 letter words below are used to illustrate how adding or deleting a letter of DNA could cause different amino acids in a protein

CAT HAT BAT RAT MAT SAT CAT HAT BAT RAT MAT SAT

INSERT ↑ T

CAT HAT BAT RAT MAT SAT CAT **THA TBA TRA TMA TSA T**

(A similar result would happen if a letter was deleted and not inserted)

Wild-type

DNA template strand 3' T A C T T C A A A C C G A T T 5'
5' A T G A A G T T T G G C T A A 3'

mRNA 5' A U G A A G U U U G G C U A A 3'

Protein Met Lys Phe Gly Stop
Amino end Carboxyl end

Extra A
3' T A C A T T C A A A C C G A T T 5'
5' A T G T A A G T T T G G C T A A 3'

Extra U
5' A U G U A A G U U U G G C U A A 3'
Met Stop

Frameshift causing immediate nonsense (1 base-pair insertion)

n

n

n

n

Cystic Fibrosis is caused by a frameshift mutation, specifically a deletion of DNA.

- **Cystic fibrosis (CF)** is a genetic disorder that affects mostly the lungs.
- Long-term issues include difficulty breathing and coughing up mucus as a result of frequent lung infections.
- Other signs and symptoms may include sinus infections, poor growth, and infertility in most males. Different people may have different degrees of symptoms

The Cystic Fibrosis Disease

- CF is the most common lethal genetic disease among Caucasians
- The number of CF patients is estimated at 70,000 worldwide, about 30,000 of which are in the US
- In 2008, the median survival age of was ~37 years
- CF results in pathologies in multiple organs
 - ❖ Depressed lung function, lung infection, inflammation and advanced lung disease
- **Currently, there is no cure for CF and the only treatment is symptomatic**