

Mutations

(topic 3.1)

Mutations can be caused by

- Radiation (Sun, X-rays, microwaves, cell phones, etc)
- Chemicals (found in food, drugs, cigarettes, soaps, etc).
- Infectious Agents (ie. Bacteria or viruses)

*mutations must be present in sex cells to be passed down

Mutation

- change in the DNA or RNA code
- DNA/RNA Polymerase also proofread the DNA and RNA codes
 - making sure all the As are with Ts, and Gs with Cs
 - Errors occur $\sim 1/1000$ bases, but proofreading catches almost all of them
 - When errors occur early enough in development they get passed down.
 - Why early?
 - ↳ within first trimester $\rightarrow$ bc it can connect to other cells.

To be inherited, Mutations must

- Remain uncorrected by DNA Polymerase 1

AND

- Occur early enough in development (i.e. First trimester usually)

or

- Occur during meiosis (creating sperm or egg)

* Syndrome $\neq$ mutation

↳ Down syndrome: meiosis, 21st chromosome, non junction $\rightarrow$ chromosomes

↳ mutation: within the gene.

Mutation continued

- Not all mutations cause disease or are even harmful

 - Ex: blue eyes, lighter colored skin, etc.

- Most mutations commonly go unnoticed within our bodies?

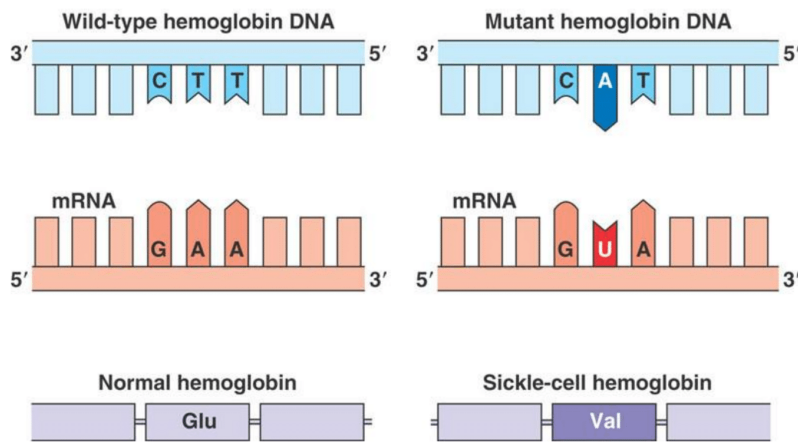
 - Why?, multiple codons w/ one amino acid.

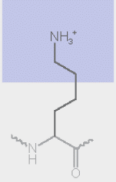
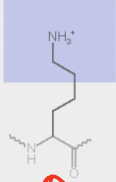
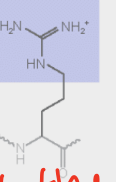
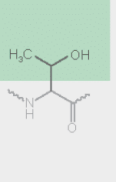
- Severe mutations result in death or deformity of the organism or protein, causing disorders and diseases

 - Severe does not always mean big changes, it can be as simple as a single base in the wrong gene

Types of Mutations: Point mutations

- Point mutation: a single change in one base
- Diseases such as sickle cell anemia are caused by this
- There are various types of point mutations
- Use the diagram to determine how they are different



	Point mutations				
	No mutation	Silent	Nonsense	Missense	
				conservative	non-conservative
DNA level	TTC	TTT	ATC	TCC	TGC
mRNA level	AAG	AAA	UAG	AGG	ACG
protein level	Lys	Lys	STOP	Arg	Thr
					

doesn't change protein (pointing to Silent mutation)
makes stop codon (pointing to Nonsense mutation)
stays the same charge / polarity (pointing to conservative missense mutation)
changes charges (pointing to non-conservative missense mutation)

basic polar

most detrimental? → probably non-conservative

Sickle Cell Disease

- caused by point mutation
- A single base substitution of the HBB gene
 - CTC → CAC
 - caused Glutamic acid → valine

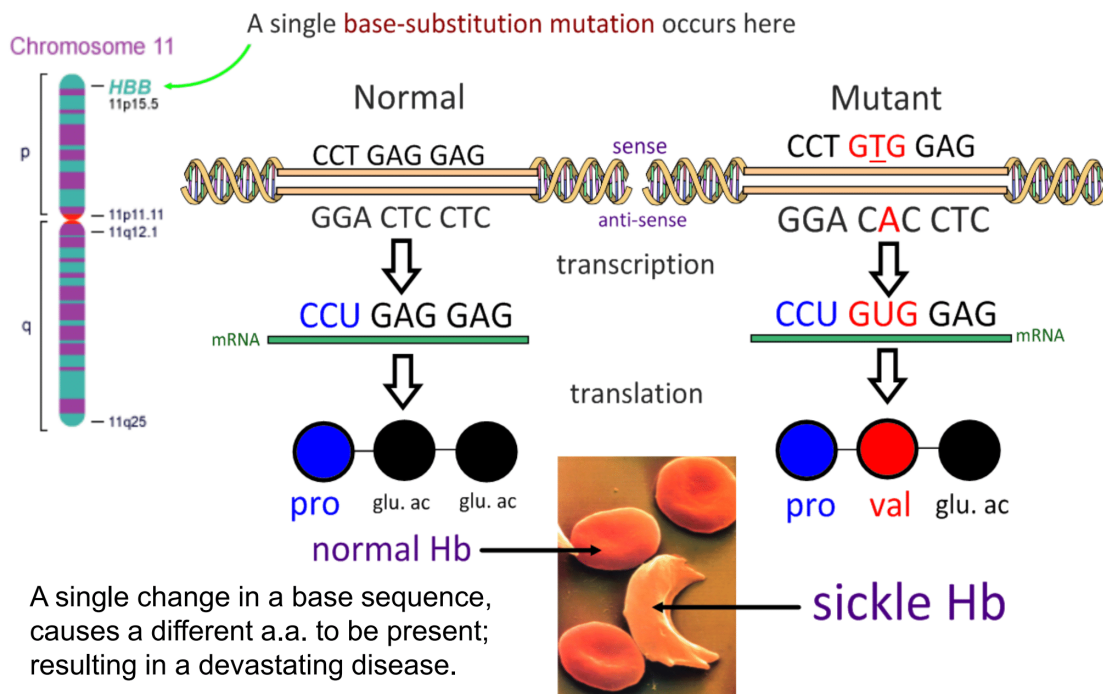
↳ changing from $\oplus$ to $\ominus$ which affects salt bridges/bonds & folding → can rip apart a protein making it unusable

- Results in the production of abnormal red blood cells

- Two copies (homozygous) → sickle shaped red blood cells

- One copy (heterozygous) → normal

Sickle Cell Disease



Consequences of Sick cell

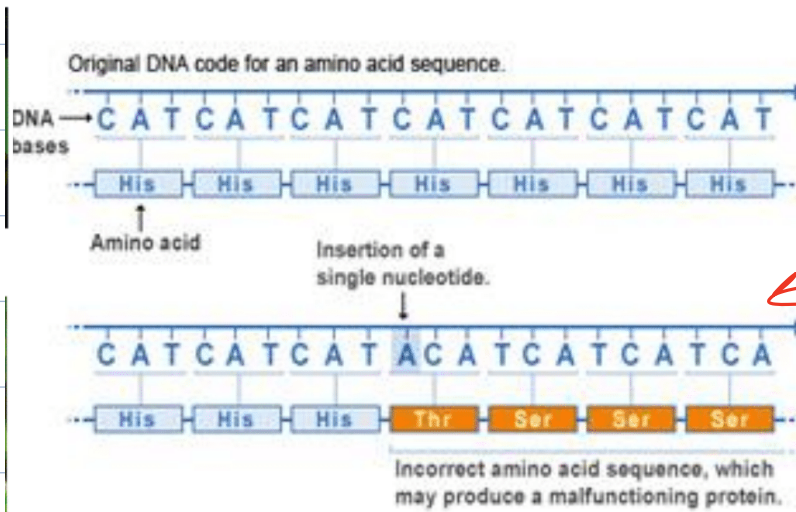
- Red blood cell
 - Weakened cell membrane
 - Rigid hemoglobin molecule bundles distort shape to sickle
 - Have a reduced life
 - Body cannot replace the red blood cell rapidly enough → anemia
 - Sickle shape blocks blood flow to normal capillaries
 - Results in lack of oxygen in tissues
 - Causes pain and eventual death of cells
- Severe anemia among other issues
- Heterozygotes immune to Malaria
 - May explain the high number of Africans with the disease

Types of mutations

- Insertions: A base or multiple bases are added to a gene
 - Huntington's Disease
 - Kennedy's Disease

- changes order! thus changing rest of amino acids / order

Insertion mutation

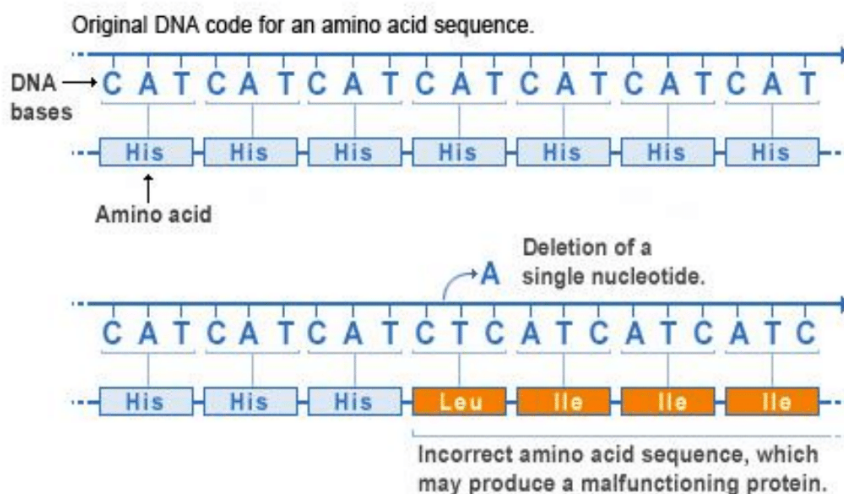


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Types of mutations continued

- Deletions: Bases or multiple bases are removed from a gene
- 2/3 of all Muscular Dystrophy cases are caused by deletions
- Cri du Chat

Deletion mutation



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Types of mutations: Translocation

- Translocations: pieces of DNA that are moved from one chromosome to a different chromosome

- Some cancers have been linked to translocations

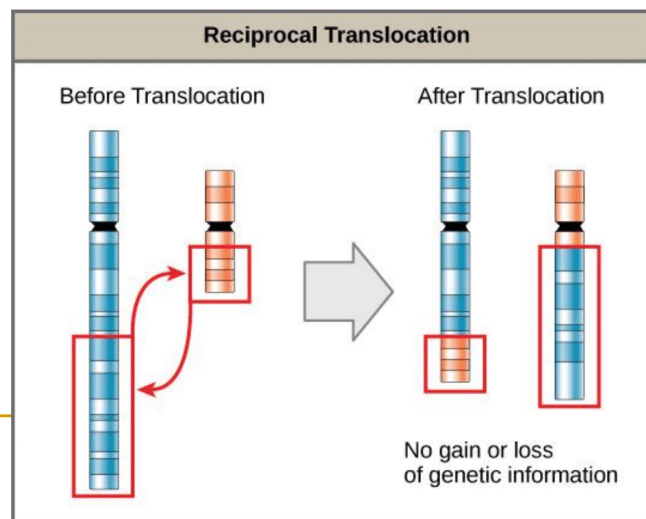
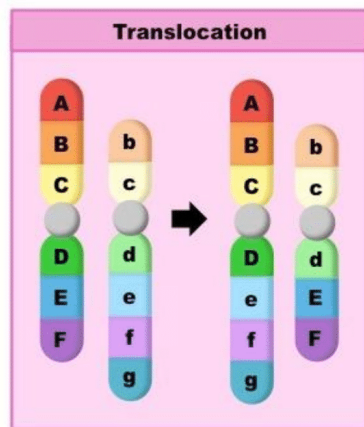
- Rare cases of Down's Syndrome

- Many cases of infertility

- Can be caused by faulty crossing over

part of chromosome break then cross over, but can sometimes move somewhere else.

any cases of infertility



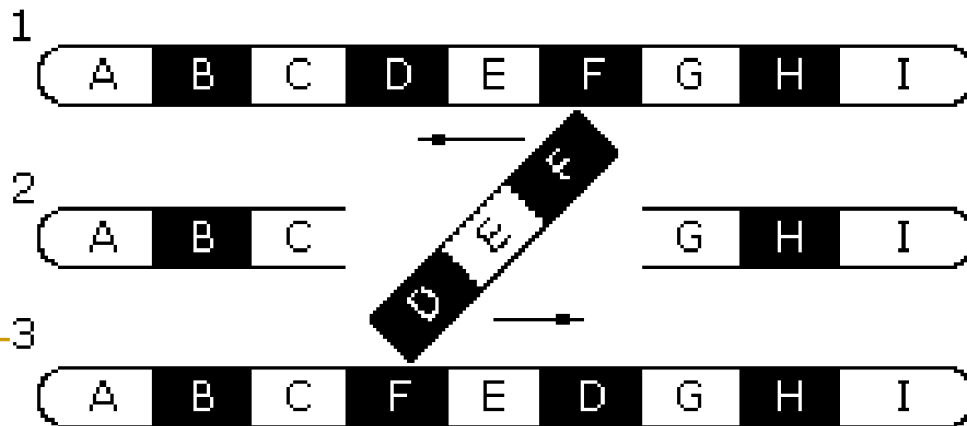
Types of mutations: Inversion

- Inversions: pieces of DNA are flipped around in the wrong direction on the same chromosome

- Inversion in chromosome 9 is one of

the more common ones.

- Growth retardation
- Recurring pregnancy loss/infertility
- Cancer



Disease by Mutation

Point mutations	Insertions	Deletions	Translocations	Inversion
Sickle Cell Anemia	Huntington's disease	Cri Du Chat	Infertility	Infertility
Cystic Fibrosis	Kennedy's Disease	Male infertility	Rare cases of Down's Syndrome	Growth retardation
Neurofibromatosis	Fragile X Syndrome	Williams Syndrome	Chronic Myelogenous Leukemia	Cancer (Leukemia)
Tay Sachs Disease	Smith-Magenis syndrome	Some cases of Muscular Dystrophy	Follicular Thyroid Cancer	Diabetes
Colorblindness	Crohn's disease	Spinal muscular atrophy	Schizophrenia	Optic nerve hypoplasia