

AP Biology – Gene Mutations

Mutations

DNA → Transcription → mRNA → Translation → Protein

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

Val | His | Leu | Thr | Pro | Val | Glu | ...
1 2 3 4 5 6 7

Mutations

- Point mutations**
 - single base change
 - base-pair substitution
 - silent mutation**
 - no amino acid change
 - redundancy in code
 - missense**
 - change amino acid
 - nonsense**
 - change to stop codon

When do mutations affect the next generation?

Wild type
mRNA: 5' AUGAAGUUUUGUCCUUA 3'
Protein: Met-Lys-Phe-Gly-Stop

Base-pair substitution
No effect on amino acid sequence (U instead of C)
mRNA: 5' AUGAAGUUUUGUCCUUA 3'
Protein: Met-Lys-Phe-Gly-Stop

Missense
A instead of G
mRNA: 5' AUGAAGUUUUGUCCUUA 3'
Protein: Met-Lys-Phe-Ser-Stop

Nonsense
U instead of A
mRNA: 5' AUGAAGUUUUGUCCUUA 3'
Protein: Met-Stop

Point mutation leads to Sickle cell anemia

What kind of mutation?

Wild-type hemoglobin DNA: 3' ... GAG ... 5'
Mutant hemoglobin DNA: 3' ... GAG ... 5'

mRNA: 5' ... GAG ... 3' → Normal hemoglobin (Glu)
mRNA: 5' ... GAG ... 3' → Sickle-cell hemoglobin (Val)

Missense/

Sickle cell anemia

- Primarily Africans
 - recessive inheritance pattern
 - strikes 1 out of 400 African Americans

(a) Normal red blood structure of normal hydrophilic amino acid
(b) Sickled red blood structure of sickle hydrophobic amino acid

Mutations

- Frameshift**
 - shift in the **reading frame**
 - changes everything "downstream"
 - insertions**
 - adding base(s)
 - deletions**
 - losing base(s)

Wild type mRNA: 5' AUGAAGUUUUGUCCUUA 3' → Protein: Met-Lys-Phe-Gly-Stop

Base-pair insertion or deletion

Frameshift causing extensive missense
Missing base: Met-Lys-Leu-Ala-...

Frameshift causing immediate nonsense
Extra U: Met-Stop

Insertion or deletion of 3 nucleotides: no frameshift; extra or missing amino acid
Missing: Met-Phe-Gly-Stop

Where would this mutation cause the most change: beginning or end of gene?

Cystic fibrosis

- Primarily whites of European descent
 - strikes 1 in 2500 births
 - 1 in 25 whites is a carrier (Aa)
 - normal allele codes for a membrane protein that transports Cl⁻ across cell membrane
 - defective or absent channels limit transport of Cl⁻ (& H₂O) across cell membrane
 - thicker & stickier mucus coats around cells
 - mucus build-up in the pancreas, lungs, digestive tract & causes bacterial infections
 - without treatment children die before 5; with treatment can live past their late 20s

AP Biology

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Effect on Lungs

Chloride channel
 transports chloride through protein channel out of cell
 Osmotic effects: H_2O follows Cl^-

normal lungs airway

cells lining lungs

Cl^-

H_2O

Cl^- channel

cystic fibrosis

thickened mucus hard to secrete

bacteria & mucus build up

mucus secreting glands

Deletion leads to Cystic fibrosis

Chromosome 7

Sequence of nucleotides in *CFTR* gene

Amino acid sequence of *CFTR* protein

A — ISOLEUCINE 506

T — ISOLEUCINE 507

C — **delta F508**

T — PHENYLALANINE 508

F

G — GLYCINE 509

G

T

T — VALINE 510

CFTR GENE

DELETED IN MANY PATIENTS WITH CYSTIC FIBROSIS

loss of one amino acid

What's the value of mutations?