Genetics: Notes 3: Genetic Mutations

Bio 40S

Mr. Yeung

Our Unit so far…

Molecular Genetics

Structure of genetics
- Nucleotides
- Nitrogenous bases
- DNA
- RNA

DNA Replication
- Making more DNA
- Cell reproduction

Make proteins:
- Transcription
- Translation
- Amino acids to proteins

Errors in our DNA (Mutations):
- Types of mutations
- Benefits / ethics of genetics

Biotechnology:
- Technology with genetics

Mutations

- What is it?
  - Any change in DNA sequence
  - Caused by errors in **replication**, **transcription**, cell division or **external agents (radiation).**
- Result:
  - New phenotype – such as new traits, or a protein that won't function properly.
  - Or the mutation could be silent – such as nothing will happen.

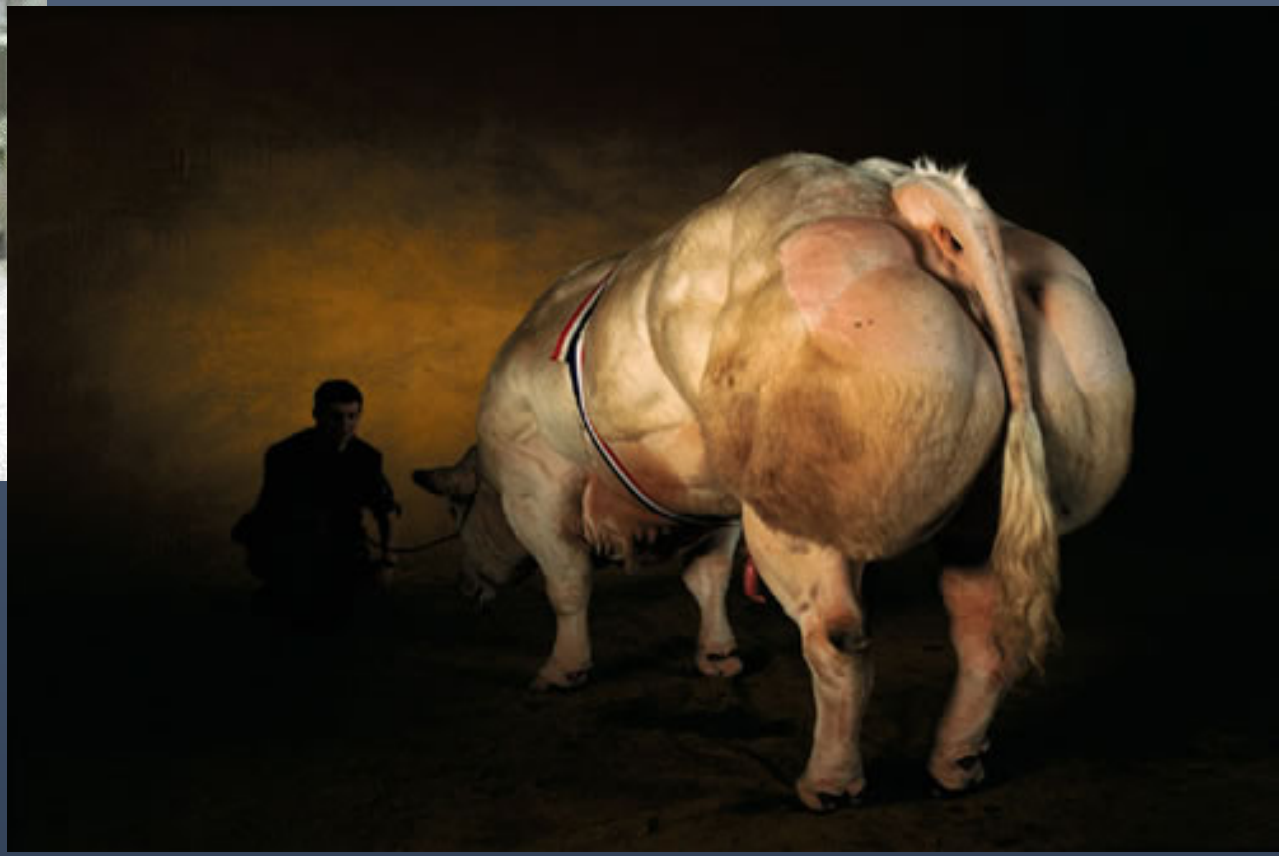
Sample DNA Sequence

DNA Sequence	3’ TAC	GCA	TGG	AAT	TAT	5’
mRNA	5’ AUG	CGU	ACC	UUA	AUA	3’
Amino acids	Met	Arg	Thr	Leu	Ile	

Mutations

- Some mutations can be carried on to offspring
- Or will simply stay within the individual.

Mutants



- ***Mighty muscles:*** *The image shows the difference between normal mice (left) and mice that lack myostatin and overproduce another protein, giving them four times as much muscle. Scientists are developing drugs that act through similar mechanisms to treat muscle-wasting diseases.*

Types of Mutations

- Small mutations
  - **Single** nucleotide change in DNA
  - Types of mutations
    1. Silent mutation
    2. Missense mutation
    3. Nonsense mutation

Which one would have a more damaging effect? Why?

- **Frameshift mutation:**
  - **Deletion** / **addition** of nucleotide in DNA

Sample DNA Sequence

DNA Sequence	3’ TAC	GCA	TGG	AAT	TAT	5’
mRNA	5’ AUG	CGU	ACC	UUA	AUA	3’
Amino acids	Met	Arg	Thr	Leu	Ile	

Types of Mutations
Type 1: Silent Mutation

Change 6th base to T

- DNA Sequence 3’ TAC GCT TGG AAT TAT 5’
- mRNA 5’ AUG CGA ACC UUA AUA 3’
- Amino acids Met Arg Thr Leu Ile

Silent mutation:

- a mutation that does not result in a change in amino acid.
- No new phenotype

Types of Mutations
Type 2: Missense Mutation

Change the 8th base to C

DNA Sequence	3’ TAC GCA TCG AAT TAT 5’
mRNA	5’ AUG CGU AGC UUA AUA 3’
Amino acids	Met Arg Ser Leu Ile

Missense mutation:

- 1 nucleotide is changed in the DNA sequence resulting in a change of amino acid.
- The result could vary depending on the protein that it forms.

Types of Mutations
Type 3: nonsense Mutation

Change the 11th base to C

- DNA Sequence 3’ TAC GCA TGG A**C**T TAT 5’
- mRNA 5’ AUG CGU ACC U**G**A AUA 3’
- Amino acids Met Arg Thr Stop Ile

Nonsense mutation: a mutation that converts a codon for an amino acid into a **termination** or codon

- The protein does not fully form
  - Digested by protease or malfunctioning protein

Types of Mutations
Addition / Deletion of nucleotides

Frameshift mutations involves a *shift* in reading the codons.

Addition and **deletion** of nucleotides will result in a frameshift mutation.

Amino acids after the addition/deletion are all affected. More damaging than point mutations.

Types of Mutations
Addition / Deletion of nucleotides

Frameshift mutations involves a *shift* in reading the codons.

Addition and **deletion** of nucleotides will result in a frameshift mutation.

Add here

- DNA Sequence 3’ TAC GCCA TGG AAT TAT 5’
- mRNA 5’ AUG CGGU ACC UUA AUA 3’
- Amino acids Met Arg Thr Leu Ile

- DNA Sequence 3’ TAC GCC ATG GAA TTA T 5’
- mRNA 5’ AUG CGG UAC CUU AAU A 3’
- Amino acids Met Arg Tyr Leu Asn

Types of Mutations
Addition / Deletion of nucleotides

What happens if we deleted one or more nucleotides are removed from the DNA sequence?

Delete C

• DNA Sequence	3’	TAC	G**C**A	TGG	AAT	TAT 5’
• mRNA	5’	AUG	C**G**U	ACC	UUA	AUA 3’
• Amino acids		Met	Arg	Thr	Leu	Ile

• DNA Sequence	3’	TAC	GAT	GGA	ATT	AT 5’
• mRNA	5’	AUG	CUA	CCU	UAA	UA 3’
• Amino acids		Met	Leu	Pro	**STOP**	Ile

- The Reading frame is shifted after the deletion and all the codons are different resulting in different amino acids

Sickle cell anemia

- Affects…
  - Red blood cells hemoglobin beta gene (HBB gene)
- Caused by…
  - Point mutation on the HBB gene changing **glutamic acid** to **valine** in the protein chain
- Hemoglobin is used for…
  - Carrying oxygen
- Abnormal hemoglobin protein causes…
  - Sickled shape of RBCs that become trapped within blood vessels producing pain and damaging organs

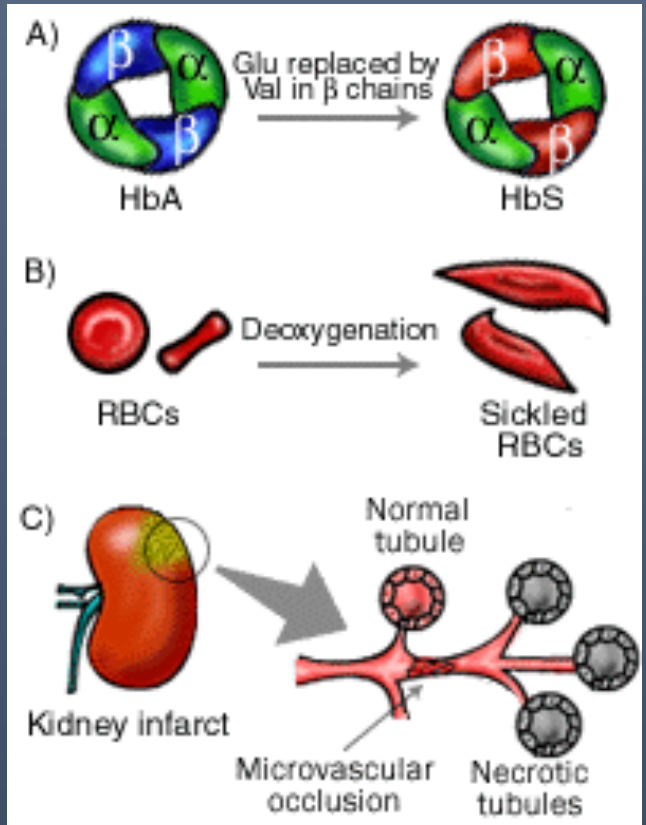
Sickle cell anemia

HBB Sequence in Normal Adult Hemoglobin (Hb A):

Nucleotide	CTG	ACT	CCT	GAG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Glu	Glu	Lys	Ser
	3			6			9

HBB Sequence in Mutant Adult Hemoglobin (Hb S):

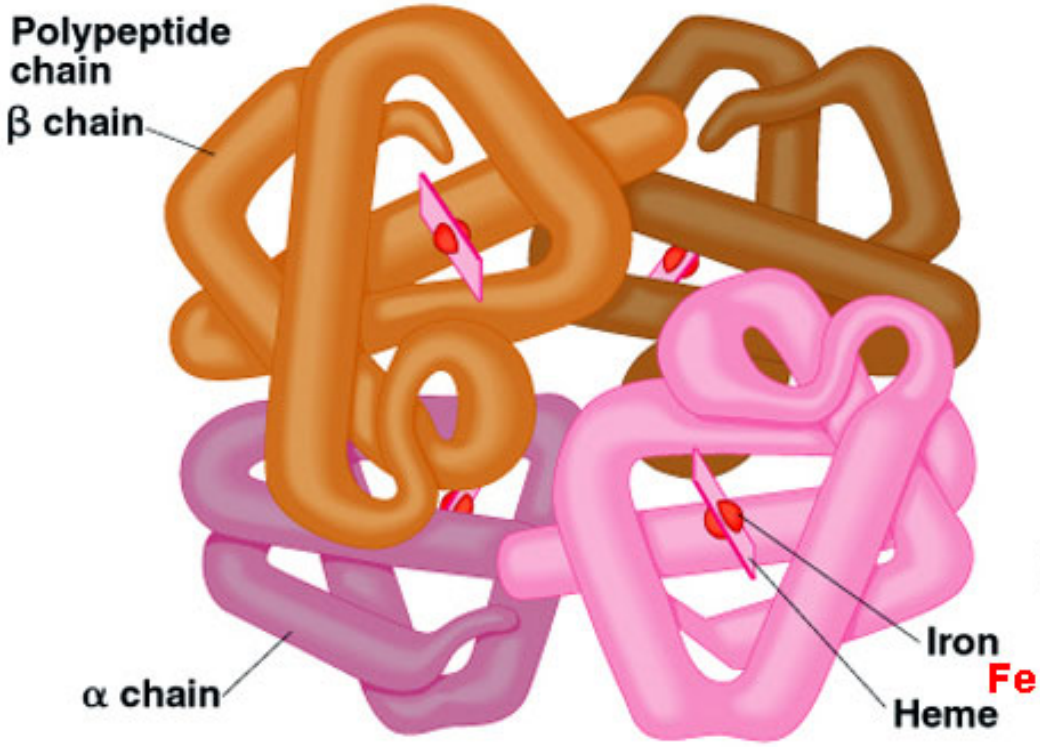
Nucleotide	CTG	ACT	CCT	GTG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Val	Glu	Lys	Ser
	3			6			9



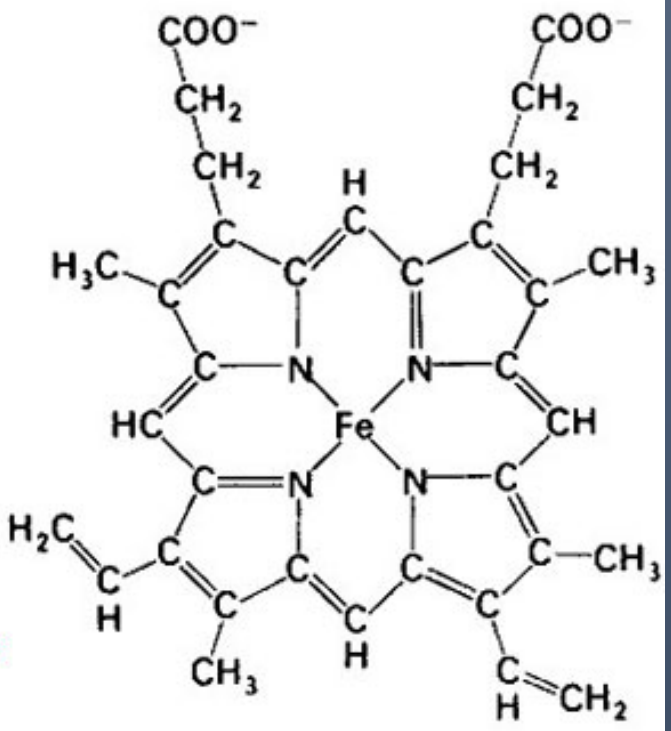
A) Hemoglobin is made up of 4 chanis: 2 α and 2 β. In SCA, a point mutation causes the amino acid glutamic acid (Glu) to be replaced by valine (Val) in the β chanis of HbA, resulting in the abnormal HbS. B) Under certain conditions, such as low oxygen levels, RBCs with HbS distort sickled shapes. C) These sickled cells can block small vessels producing microvascular occlusions which may cause necrosis (death) of the tissue.

B - thalassemia

- Affects…
  - β-globin chain in hemoglobin protein.
  - Reduces the production of hemoglobin.
- Beta thalassemia are caused by…
  - a mutation in the β-globin chain.
- Frameshift mutation and nonsense mutation usually result in…
  - The inability to produce any β-globin



Hemoglobin



Heme
(Fe-protoporphyrin IX)