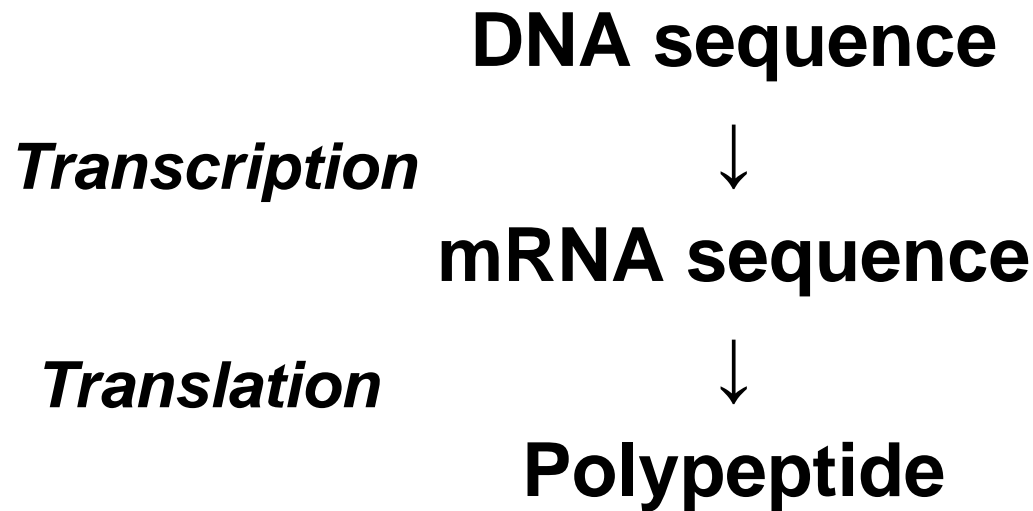




GENE MUTATIONS

aka point mutations

Gene mutations which affect only one gene



DNA (antisense strand)

Normal gene

GGTCTCCTCACGCCA

mRNA

CCAGAGGAGUGCGGU

Codons

Polypeptide

Pro-Glu-Glu-Cys-Gly

Amino acids

The **antisense strand** is the DNA strand which acts as the template for mRNA transcription

Mutations: Substitutions

Normal gene

GGTCTCCTCACGCCA



CCAGAGGAGUGCGGU
Codons



Pro-Glu-Glu-Cys-Gly

Amino acids

Substitution mutation

GGTCA**A**CCTCACGCCA



CCAG**U**GGAGUGCGGU



Pro-**Arg**-Glu-Cys-Gly

Substitutions will only affect a single codon

Their effects may not be serious unless they affect an amino acid that is essential for the structure and function of the finished protein molecule (e.g. sickle cell anaemia)



The genetic code is degenerate

A mutation to have **no** effect on the phenotype

Changes in the third base of a codon often have no effect

No change

Normal gene

GGTCTCCTCACGCCA



CCAGAGGAGUGCGGU
Codons



Pro-Glu-Glu-Cys-Gly
Amino acids

Substitution mutation

GGTCT**T**CTCACGCCA



CCAG**A**GAGUGCGGU



Pro-**Glu**-Glu-Cys-Gly

Disaster

Normal gene

GGTCTCCTCACGCCA



CCAGAGGAGUGCGGU

Codons



Pro-Glu-Glu-Cys-Gly

Amino acids

Substitution mutation

GGTCTCCTCACTCCA



CCAGAAGAGUGAGGU



Pro-Glu-Glu-STOP

Mutations: Inversion

Inversion mutations, also, only affect a small part of the gene

Normal gene

GGTCTCCTCACGCCA



CCAGAGGAGUGCGGU

Codons



Pro-Glu-Glu-Cys-Gly

Amino acids

Inversion mutation

GGTCTCTCACGCCA



CCAGGAGAGUGCGGU



Pro-Gly-Glu-Cys-Gly

Mutations: Additions

A frame shift mutation

Normal gene

GGTCTCCTCACGCCA



CCAGAGGAGUGCGGU

Codons



Pro-Glu-Glu-Cys-Gly

Amino acids

Addition mutation

GGT**G**CTCCTCACGCCA



CCA**C**GAGGAGUGCGGU



Pro-**Arg-Gly-Val-Arg**

Mutations: Deletions

A frame shift mutation

Normal gene

GGTCTCCTCACGCCA



CCAGAGGAGUGCGGU
Codons



Pro-Glu-Glu-Cys-Gly
Amino acids

Deletion mutation

GGT**C/C**CTCACGCCA



CCA**GG**GAGUGCGGU



Pro-**Gly-Ser-Ala-Val**

Mutations of haemoglobin

- Haemoglobin is a tetramer = 2 α and 2 β -chains
- The genes for these polypeptides are found on different chromosomes
- The β -chain gene is found on chromosome 11
- The α -chain gene is found on chromosome 16
- The nucleotide sequences have been worked out
- Several inherited diseases occur on the β -chain, which contains 146 amino acids

β haemoglobin sense strand cDNA sequence

- cDNA (**complementary DNA**) is obtained by back-transcribing the mRNA used to translate the polypeptide
- So cDNA has no introns
- This is done using **reverse transcriptase** enzyme

Methionine initiator

ATG GTG CAT CTG ACT CCT **GAG GAG** AAG TCT GCC
GTT ACT GCC CTG TGG GGC AAG GTG AAC GTG GAT
GAA GTT GGT GGT **GAG** GCC CTG GGC AGG CTG CTG
GTG GTC TAC CCT TGG ACC CAG AGG TTC TTT GAG
TCC TTT GGG GAT CTG TCC ACT CCT GAT GCT GTT
ATG GGC AAC CCT AAG GTG AAG GCT **CAT** GGC AAG
AAA **GTG** CTC GGT GCC TTT AGT GAT GGC CTG GCT
CAC CTG GAC AAC CTC AAG GGC ACC TTT GCC ACA
CTG AGT GAG CTG CAC TGT GAC AAG CTG CAC GTG
GAT CCT GAG AAC TTC AGG CTC CTG GGC AAC GTG
CTG GTC TGT GTG CTG GCC CAT CAC TTT GGC AAA
GAA TTC ACC CCA CCA GTG CAG GCT GCC TAT CAG
AAA GTG GTG GCT GGT GTG GCT AAT GCC CTG GCC
CAC AAG TAT CAC **TAA**

Nonsense terminator

Mutation	Codon	Change to DNA sense strand	Change in Amino Acid
S (sickle cell anaemia)	6	GAG to GTG	Glu to Val
C (cooley's syndrome)	6	GAG to AAG	Glu to Lys
G _{San Jose}	7	GAG to GGG	Glu to Gly
E	26	GAG to AAG	Glu to Lys
M _{Saskatoon}	63	CAT to TAT	His to Tyr
M _{Milwauki}	67	GTG to GAG	Val to Glu
O _{Arabia}	121	GAA to GTA	Glu to Val