We Are All Mutants

BIO*300/CMPSC*300 – SPRING 2016

CRASH COURSE IN MOLECULAR BIOLOGY

What is Mutation?

- a natural process that changes the DNA sequence
- a common process
  - during replication of the human genome a “typo” occurs every 100,000 or so nucleotides
  - that’s about 120,000 typos each time one of our cells divides
  - most are repaired

What is Mutation?

- a natural process that changes the DNA sequence
- most mutations are neutral – no consequence
- some mutations are beneficial – provides advantage in particular environment
- some mutations are harmful

Chocolate Chip Cookies

Ingredients

2 ¼ cups all purpose flour
1 teaspoon baking soda
1 teaspoon salt
1 cup (2 sticks) butter, softened
¾ cup granulated sugar
¾ cup packed brown sugar
1 teaspoon vanilla extract
2 large eggs
2 cups chocolate chips

PREHEAT over to 375°F

COMBINE flour, baking soda, and salt in a small bowl. Beat butter, sugars, and vanilla extract in a larger mixer bowl until creamy. Add eggs, one at a time, beating well after each addition. Gradually beat in flower mixture. Stir in chocolate chips. Drop by rounded tablespoons onto ungreased baking sheets.

BAKE for 9 to 11 minutes or until golden brown. Cool on baking sheet for 2 minutes; remove to wire rack to cool completely

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Point Mutation

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Inversion

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Chocolate Chip Cookies

Ingredients

Substitution

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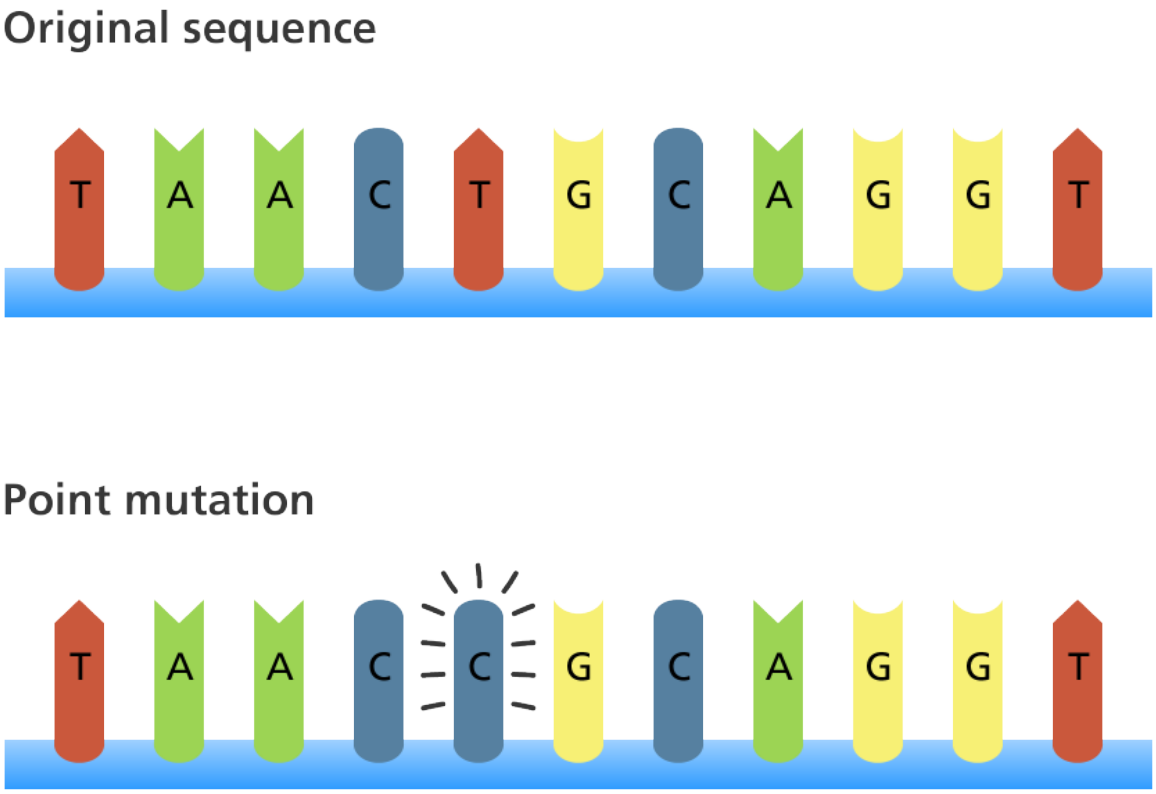
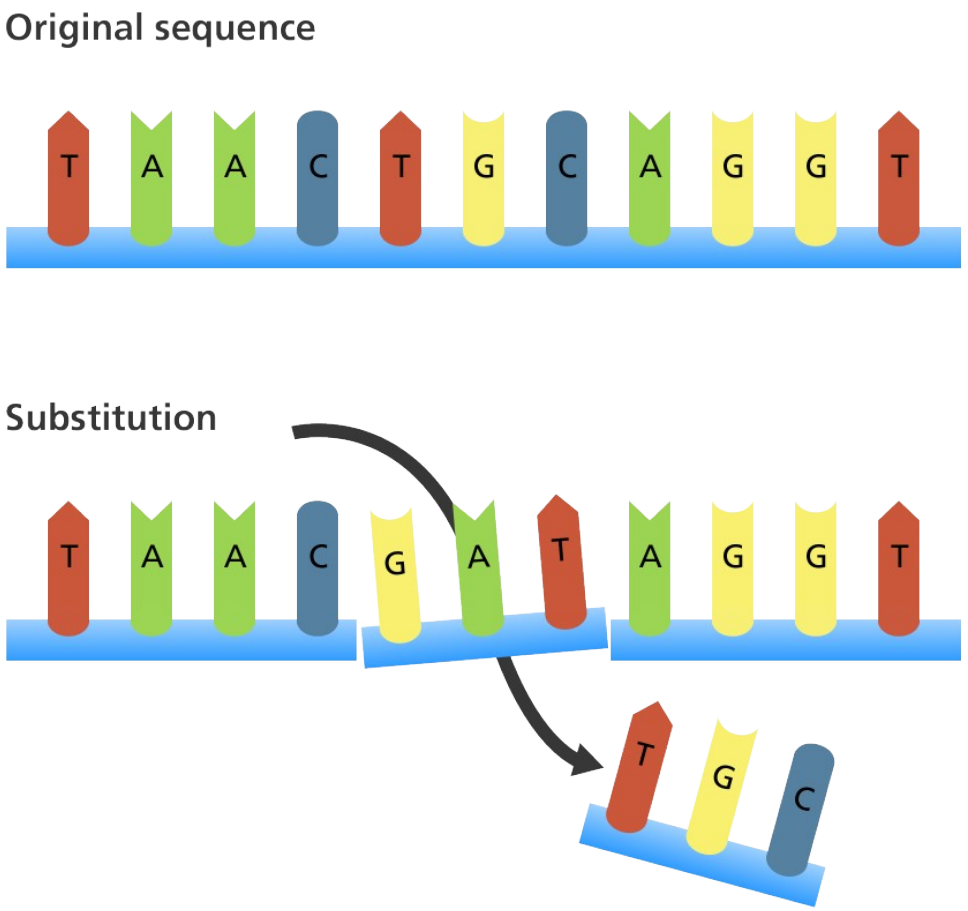
Mutation – Point Mutation

- A point mutation is a mutation that exchanges one base for another



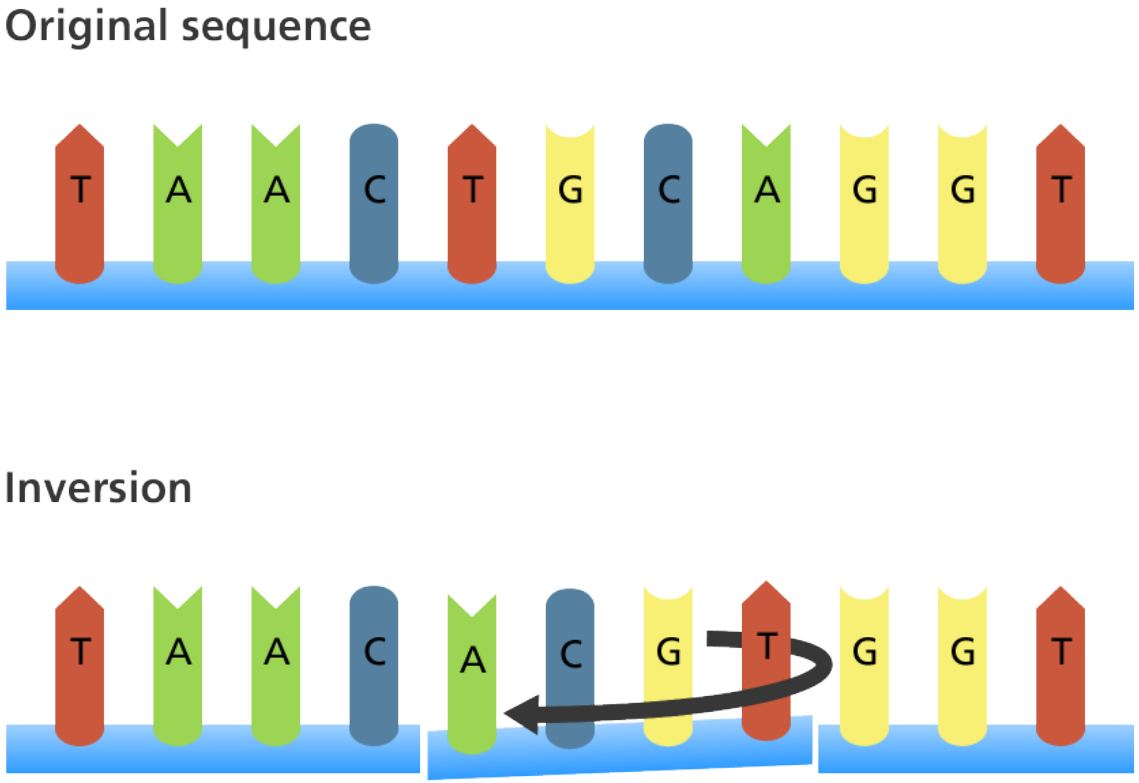
Mutation - Substitution

- A substitution is a mutation where one or more bases in the sequence is replaced by the same number of bases



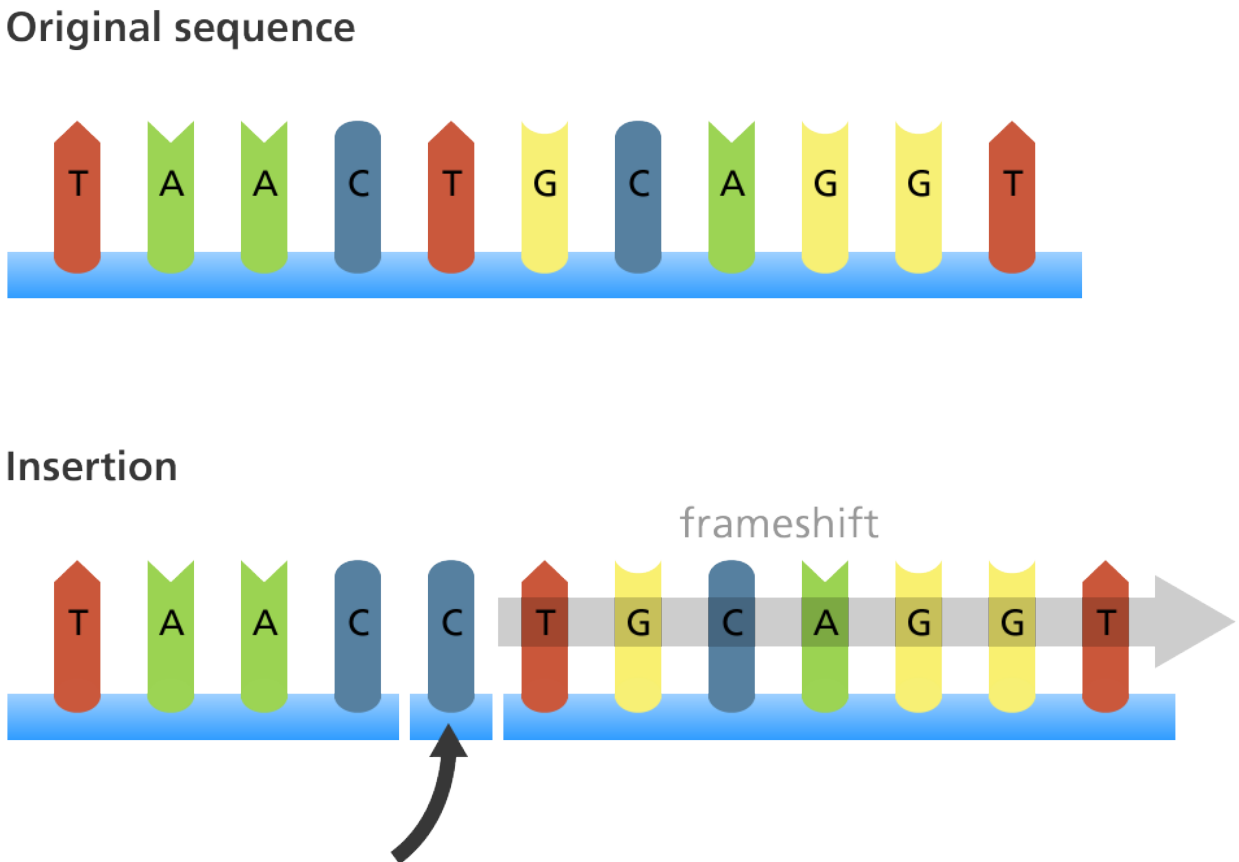
Mutation - Inversion

- An inversion is a mutation where a segment of DNA is reversed



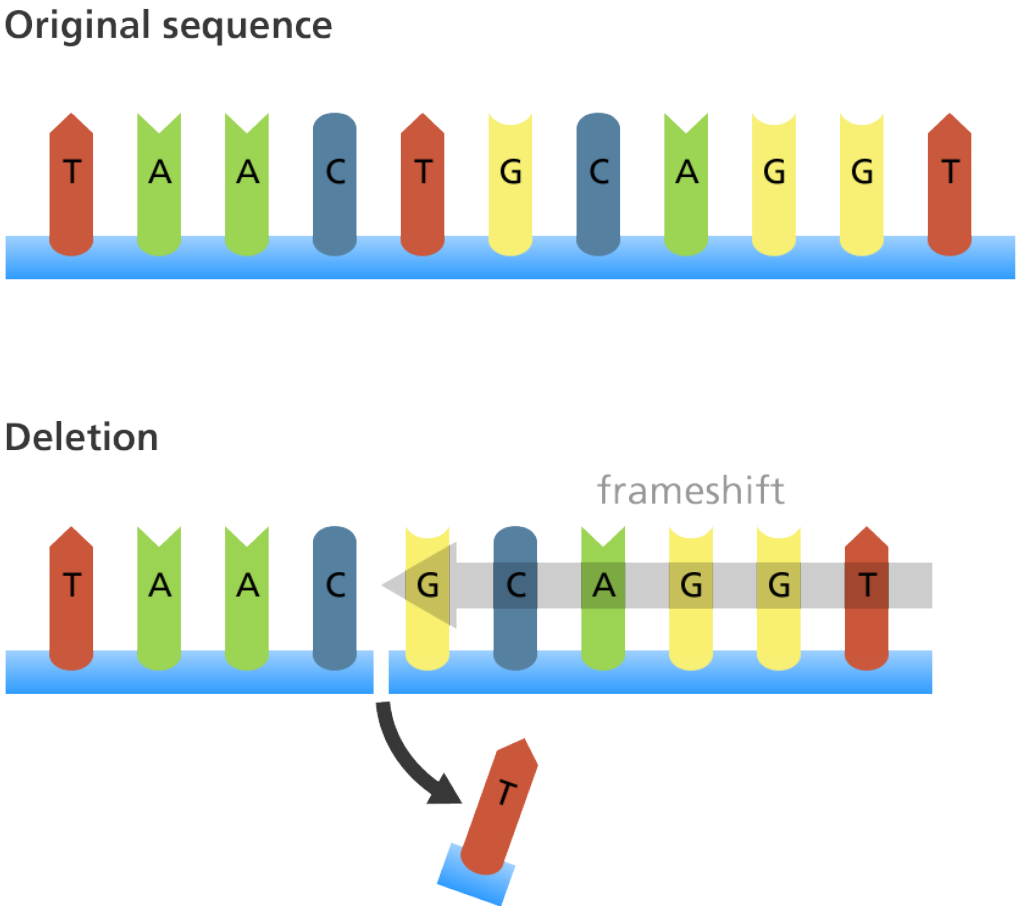
Mutation - Insertion

- An insertion is a mutation in which one or more nucleotides are added into the DNA



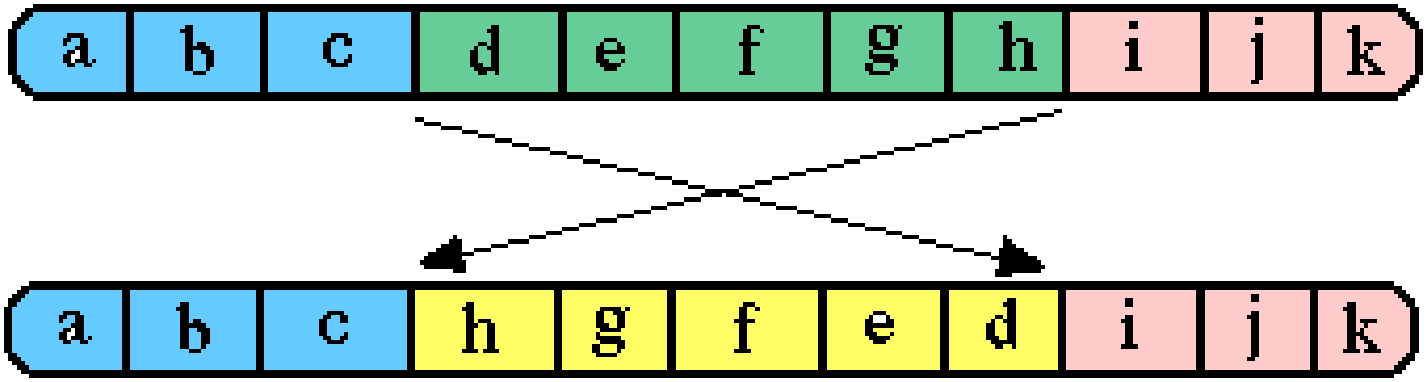
Mutation - Deletion

- A deletion is a mutation in which one or more nucleotides are removed from the DNA sequence



Where do mutations come from?

- Cell division (meiosis)



- Usually okay as long as gene sequence is not interrupted

Where do mutations come from?

- Mistakes by the DNA polymerase during replication
  - Can be repaired by repair enzymes – not always perfect

```
A C T G C G T A C
| | | | | | | | |
 T G A T G C A T G
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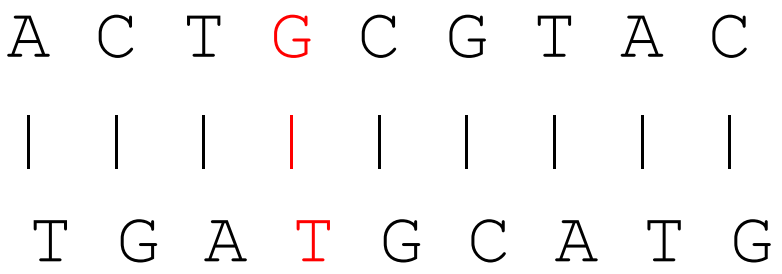
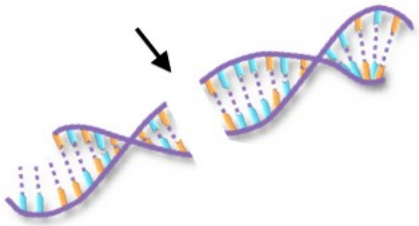
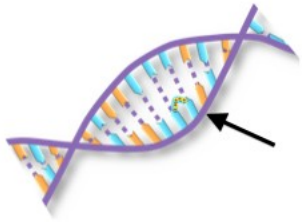
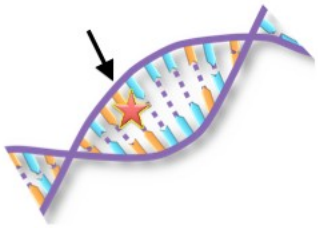


Where do mutations come from?

- DNA damage and imperfect repair
  - Cell can still divide but DNA sequence has changed

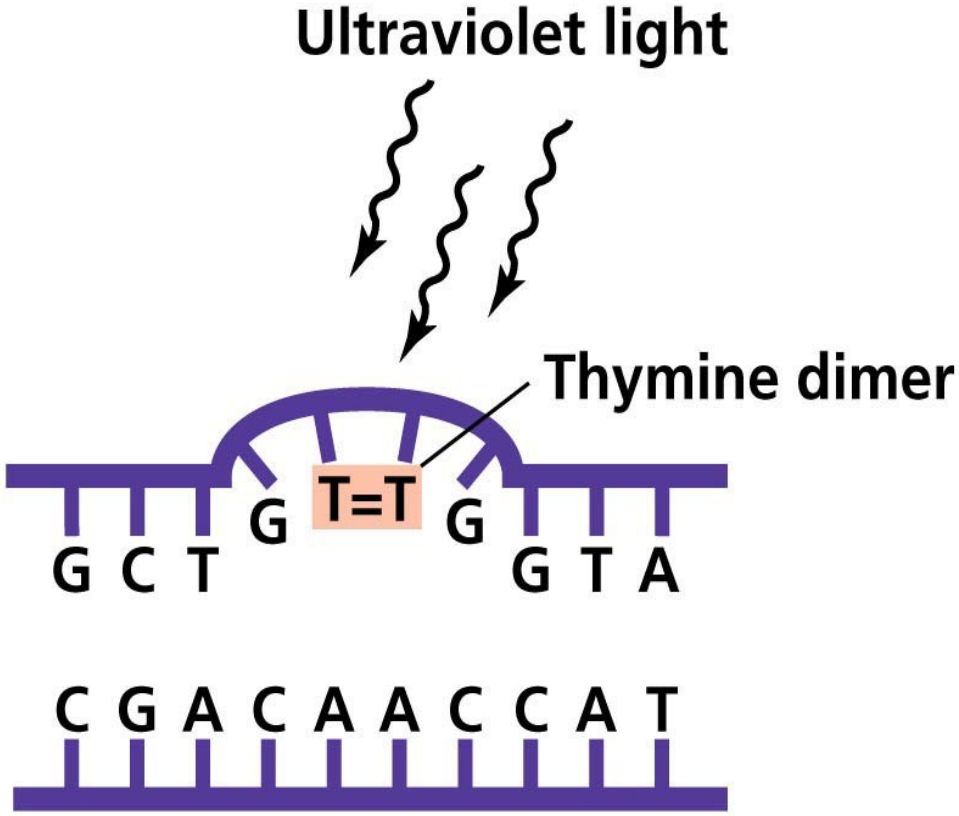






Type of Damage:	Double-strand break	Chemical bond between neighboring nucleotides	Chemical modification of a nucleotide	Chemical Linkage of Two Strands
Common Causes:	• Normal cellular activity • Ionizing radiation (including X-rays) • Chemotherapeutic drugs • DNA repair of other types of damage	• Ultraviolet (UV) light	• Reactive oxygen species (ROS) • Chemotherapeutic drugs • Other cellular and environmental chemicals • Normal modifications that regulate what genes are active	• Reactive oxygen species (ROS) • Chemotherapeutic drugs • Other cellular and environmental chemicals

Where Do Mutations Come From?



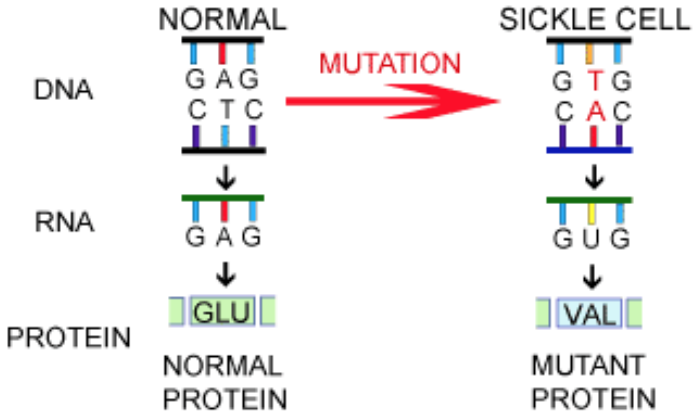
- UV light causes bond to form between adjacent Ts
- If left unrepaired, polymerase "guesses"
  - 25% chance per site
  - cell can still divide
  - hopefully not in a gene
- Chance of mistakes during repair process
  - polymerase isn't perfect
  - cell can still divide
  - hopefully not in a gene

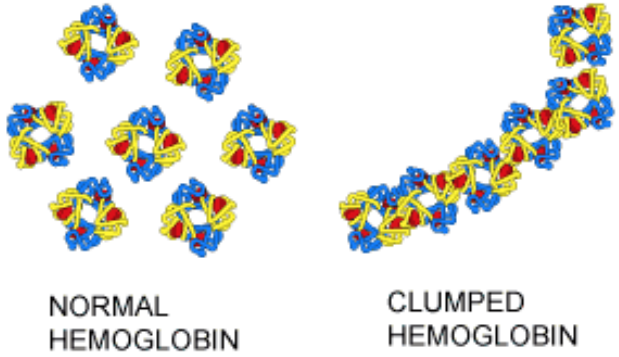
Consequences of Mutation?

- nothing
  - mutation does not occur in a gene
    - Humans, just 1.5% of the genome
  - silent change
    - occurs in gene, but does not change message
    - genetic code is redundant

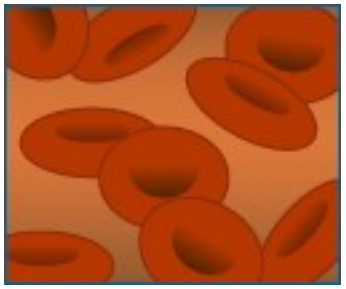
Consequences of Mutation?

HBB gene - Sickle cell anemia – missense mutation





Normal RBC

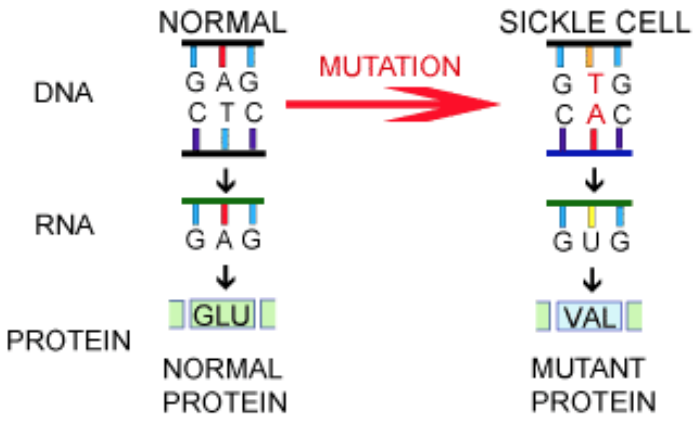


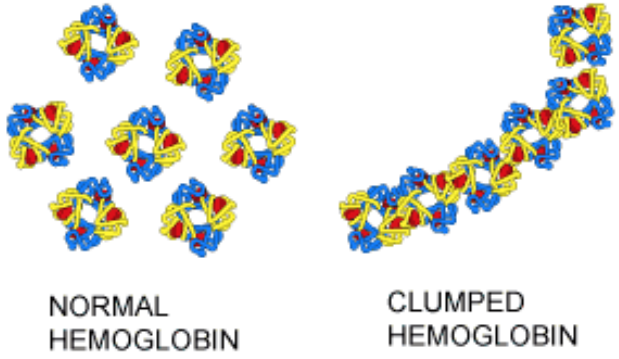
Sickle RBC

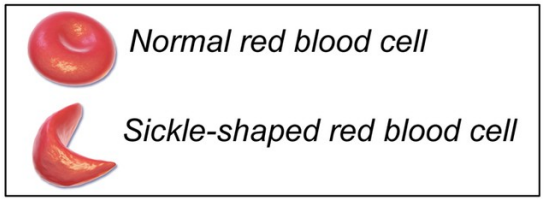
Sickled RBCs are abnormally shaped and ridgid
Sickle shape can interrupt blood flow

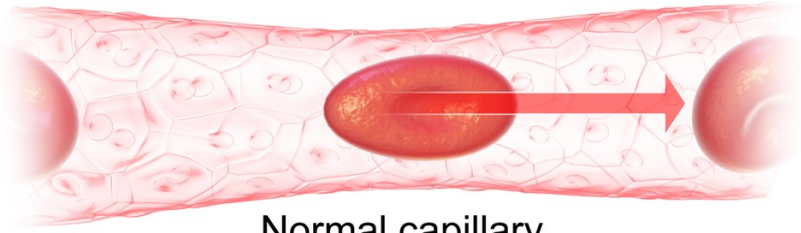
Consequences of Mutation?

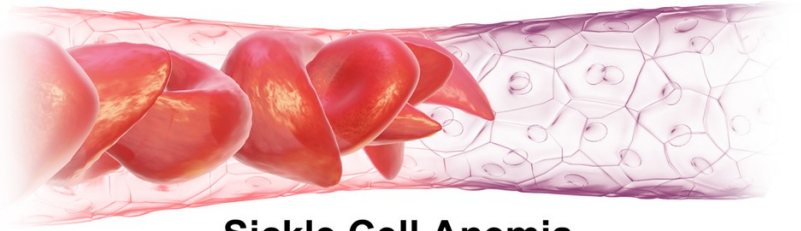
HBB gene - Sickle cell anemia – missense mutation








Normal capillary


Sickle Cell Anemia

Consequences of Mutation?

HBB gene – Thalassemia – Nonsense mutation

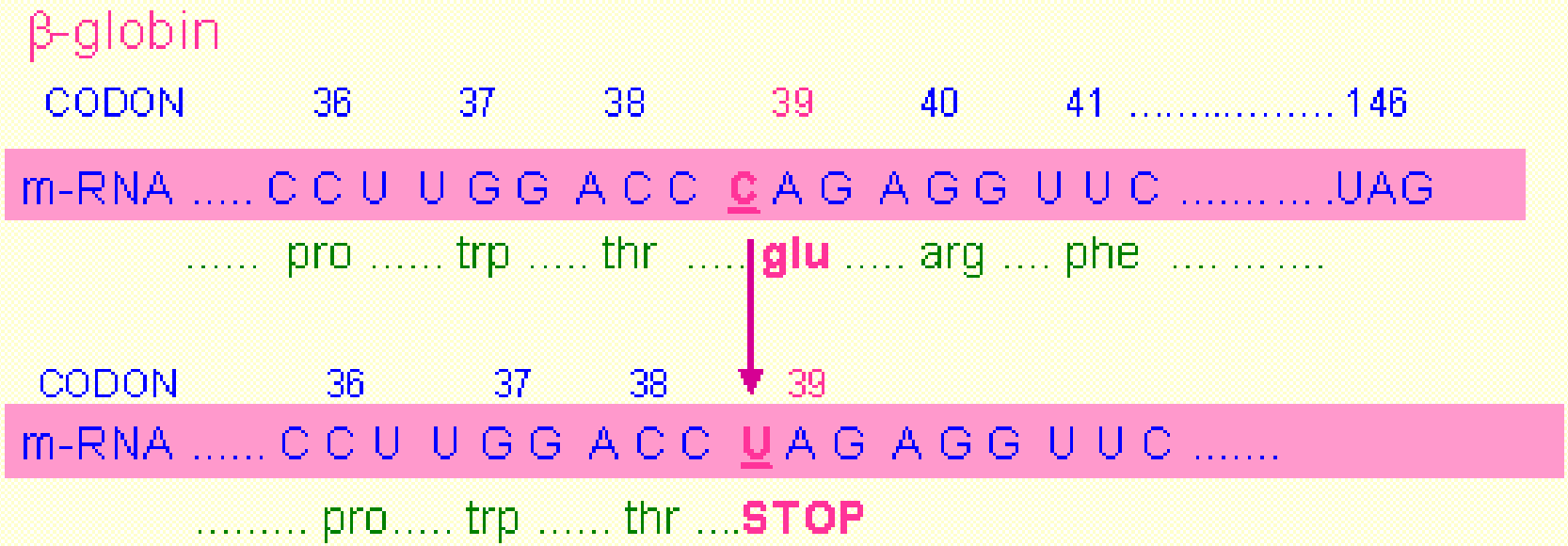
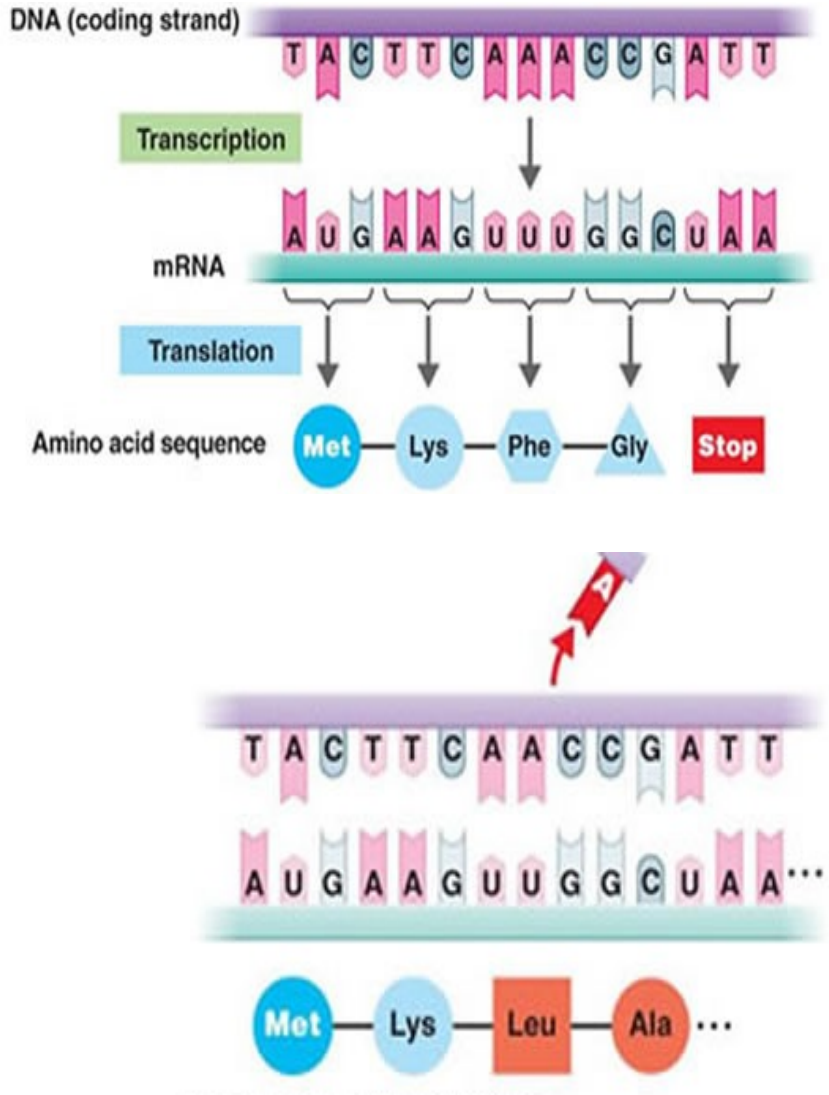


Fig 5.2. The mutation of C to U in codon 39 of the β-globin gene results in the substitution of the amino acid glutamine by a stop signal, resulting in a severely shortened β-globin protein chain.

Frame shift mutation



- Caused by an Insertion or a Deletion
- Changes codons and corresponding amino acids after mutation site