

Bioinformatics

CS300

Crash course:

Mutations

Fall 2017

Oliver Bonham-Carter



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?

- Most mutations are neutral – no consequence
- Some mutations are beneficial – provides advantage in particular environment
- Some mutations are harmful





Chocolate Chip Cookies

Ingredients

2 $\frac{1}{4}$ cups all purpose flour
1 teaspoon baking soda
1 teaspoon salt
1 cup (2 sticks) butter, softened
 $\frac{3}{4}$ cup granulated sugar
 $\frac{3}{4}$ 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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2 $\frac{1}{4}$ cups all purpose flour
9 teaspoon baking soda
1 teaspoon salt
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Inversion

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2 cups butterscotch chips



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Substitution



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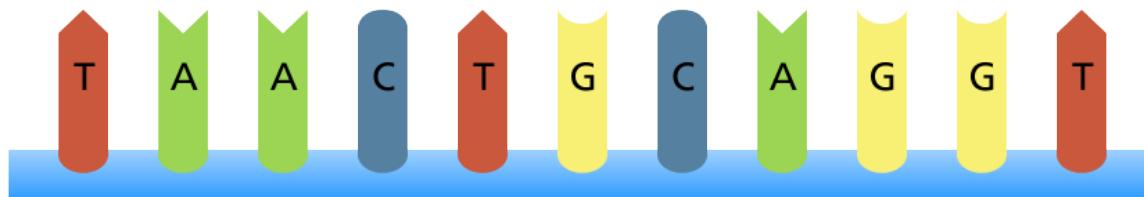
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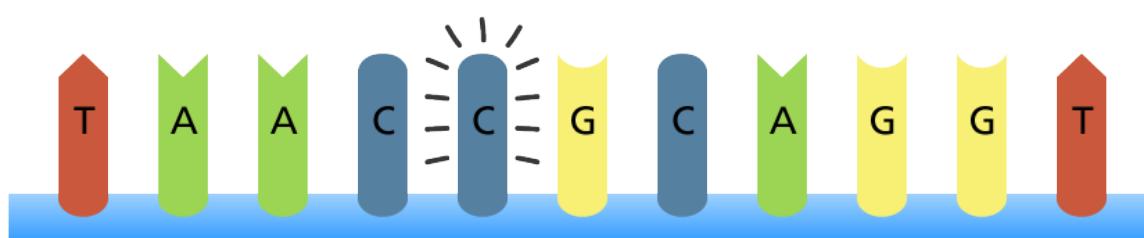
Mutation – Point Mutation

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

Original sequence



Point mutation

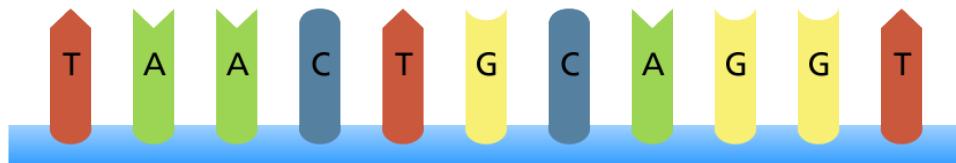




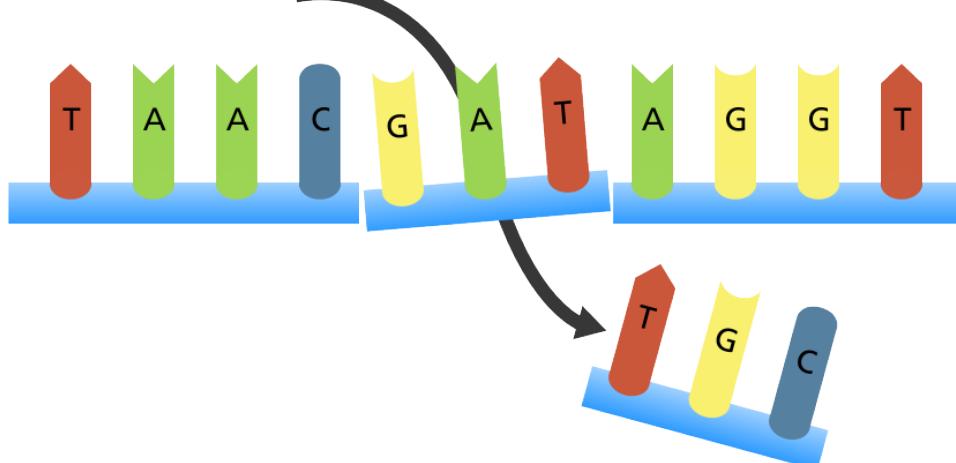
Mutation - Substitution

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

Original sequence



Substitution

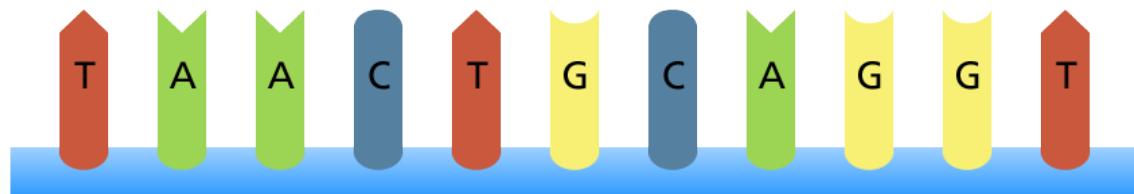




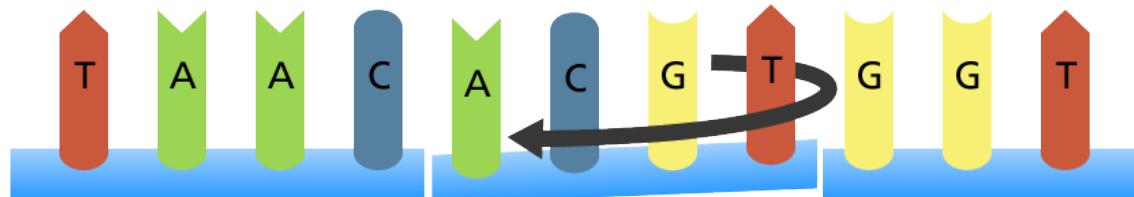
Mutation - Inversion

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

Original sequence



Inversion

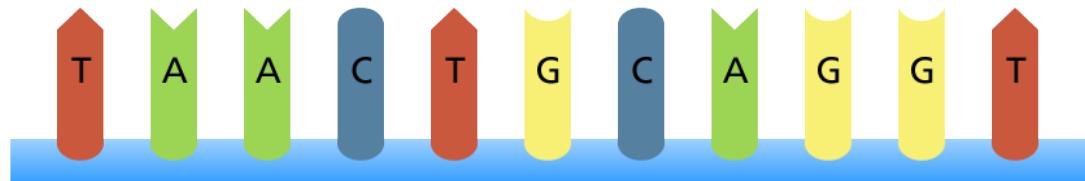




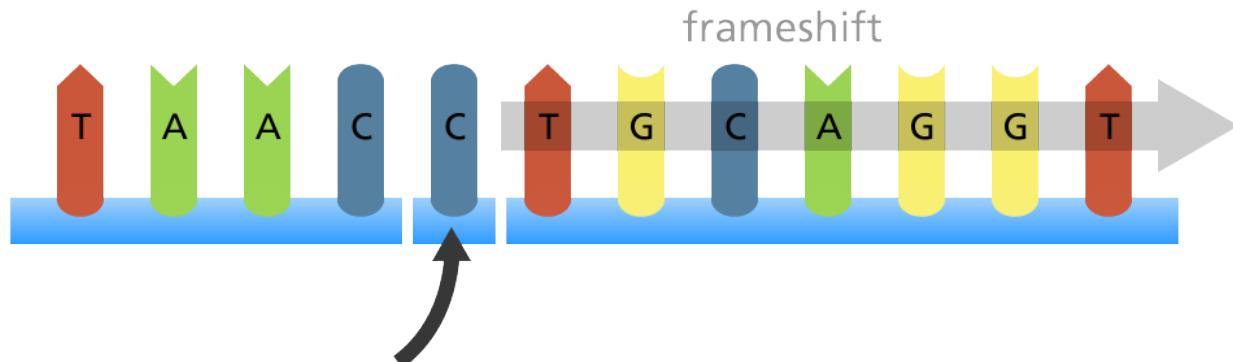
Mutation - Insertion

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

Original sequence



Insertion

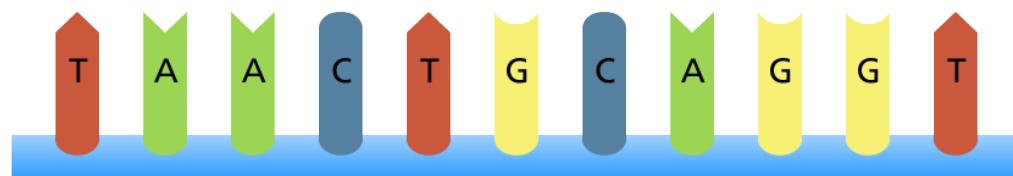




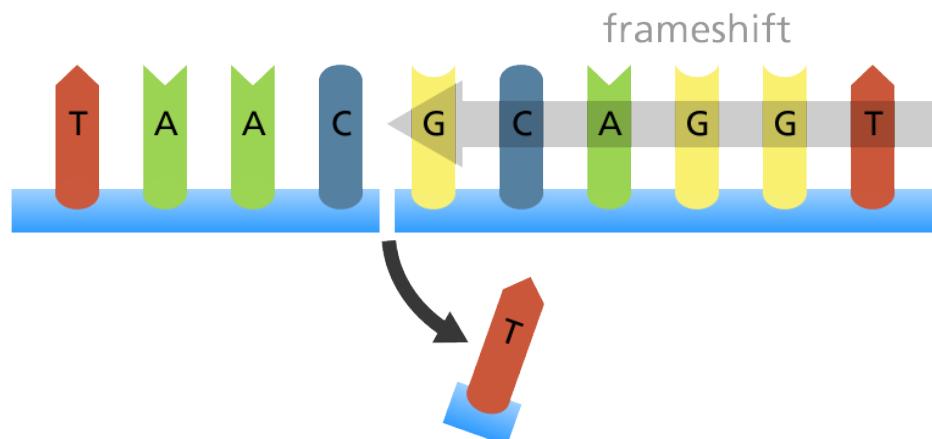
Mutation - Deletion

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

Original sequence



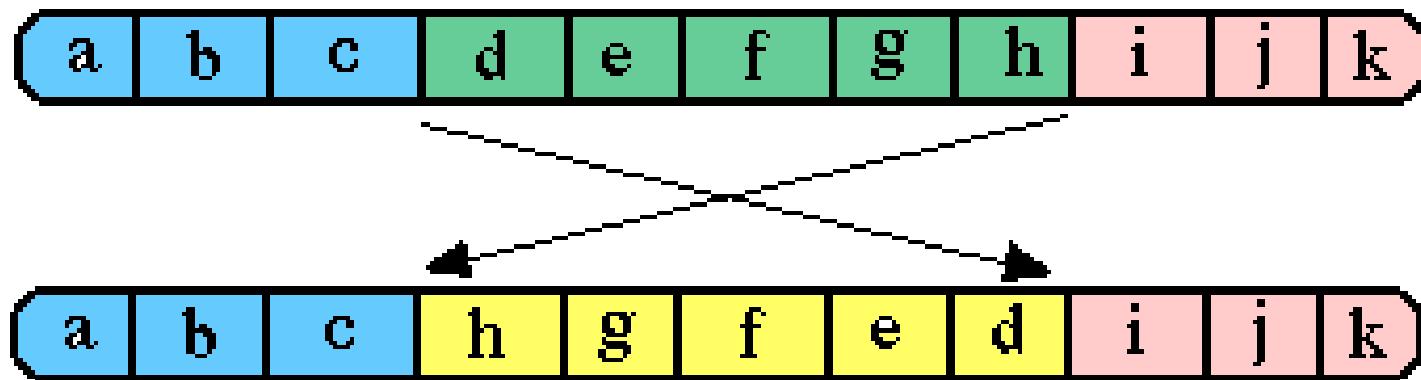
Deletion





Where do mutations come from?

- Cell division (meiosis)



- Usually okay as long as gene sequence is not interrupted



Where do mutations come from?

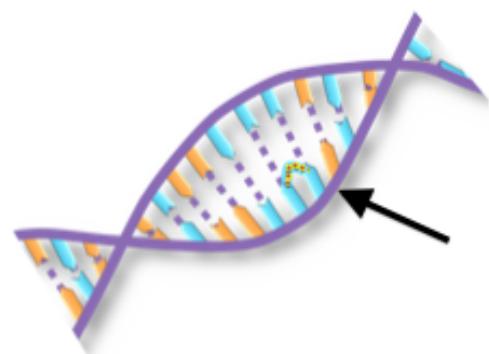
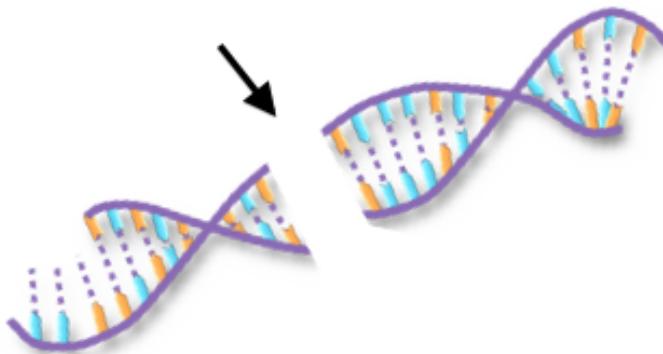
- Mistakes by the DNA polymerase during replication
 - Can be repaired by repair enzymes – not always perfect

A	C	T	G	C	G	T	A	C
T	G	A	T	G	C	A	T	G



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

Common Causes:

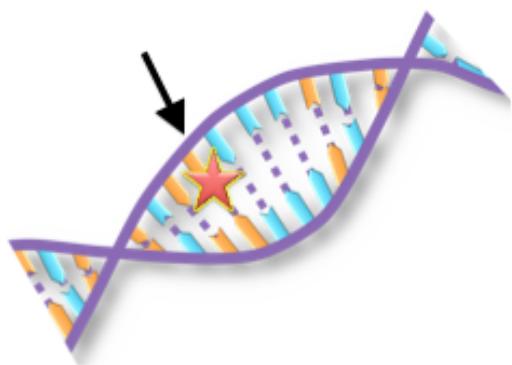
- Normal cellular activity
- Ionizing radiation (including X-rays)
- Chemotherapeutic drugs
- DNA repair of other types of damage

- Ultraviolet (UV) light



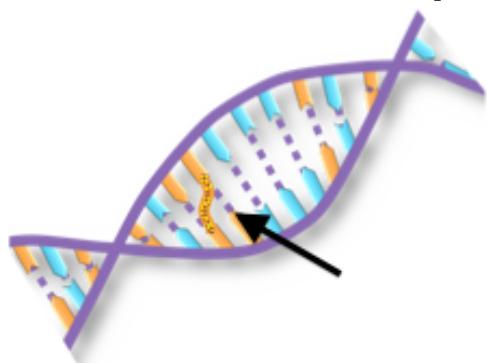
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Chemical modification
of a nucleotide

- Reactive oxygen species (ROS)
- Chemotherapeutic drugs
- Other cellular and environmental chemicals
- Normal modifications that regulate what genes are active



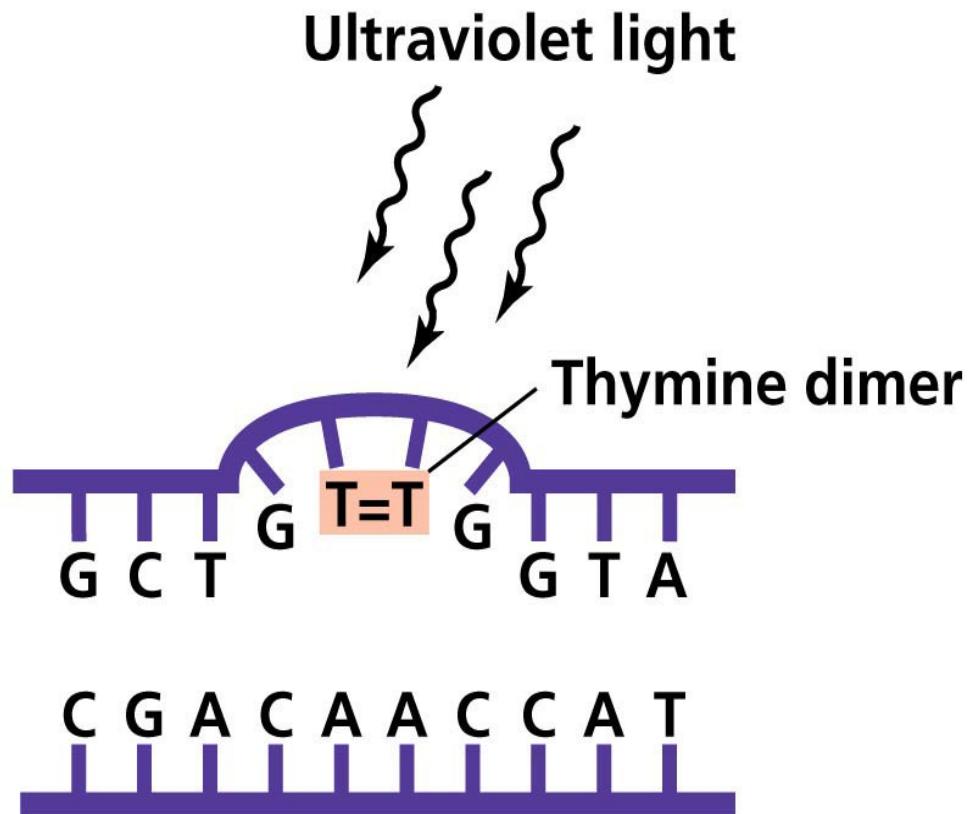
Chemical Linkage of
Two Strands

- Reactive oxygen species (ROS)
- Chemotherapeutic drugs
- Other cellular and environmental chemicals



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Where Do Mutations Come From?



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- 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?

- Sometimes nothing
 - “Silent mutations”
 - 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

TAT

Tyr

TAC

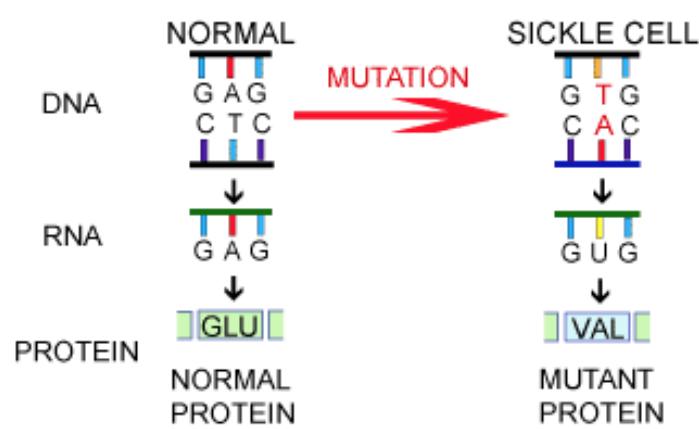
Tyr



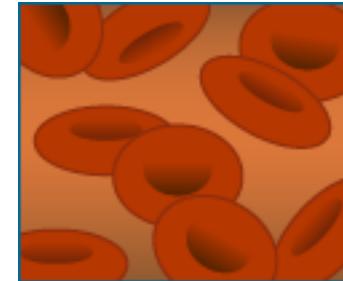
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Consequences of Mutation?

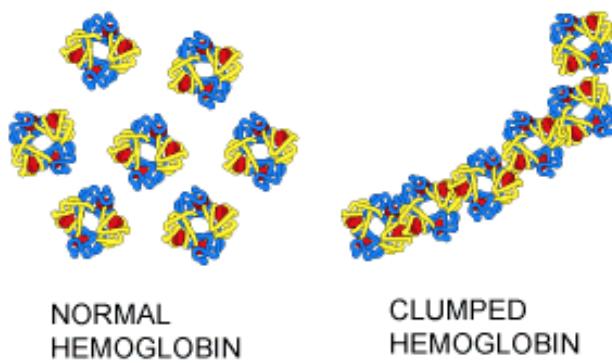
HBB gene - Sickle cell anemia - missense mutation



Normal RBC



Sickle RBC



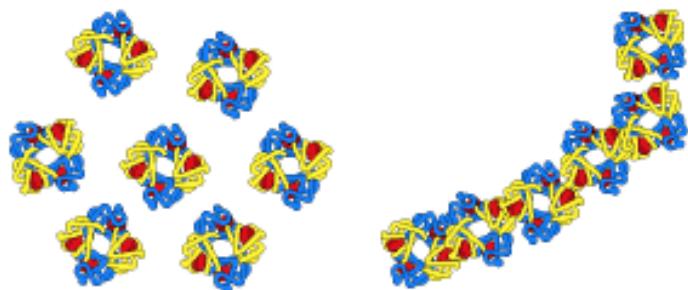
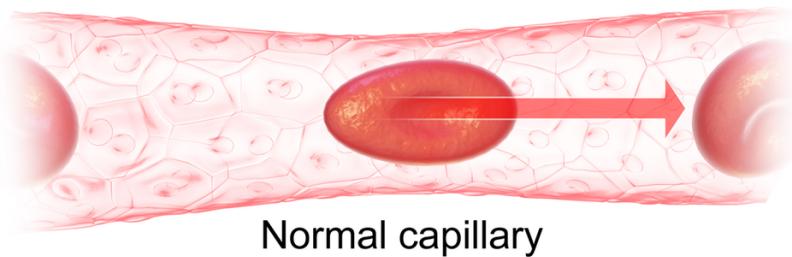
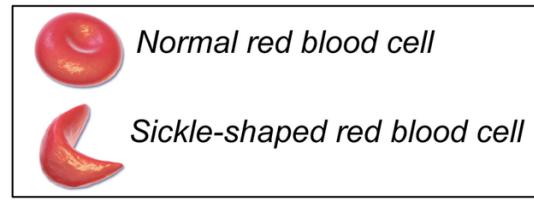
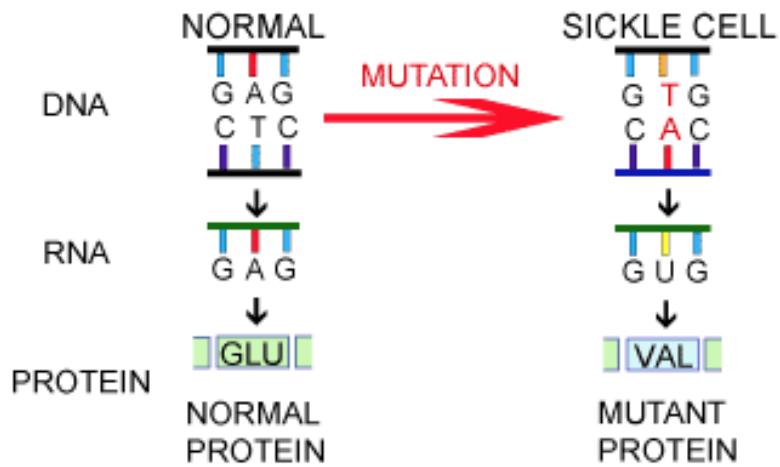
Sickled RBCs are abnormally shaped and rigid
Sickle shape can interrupt blood flow



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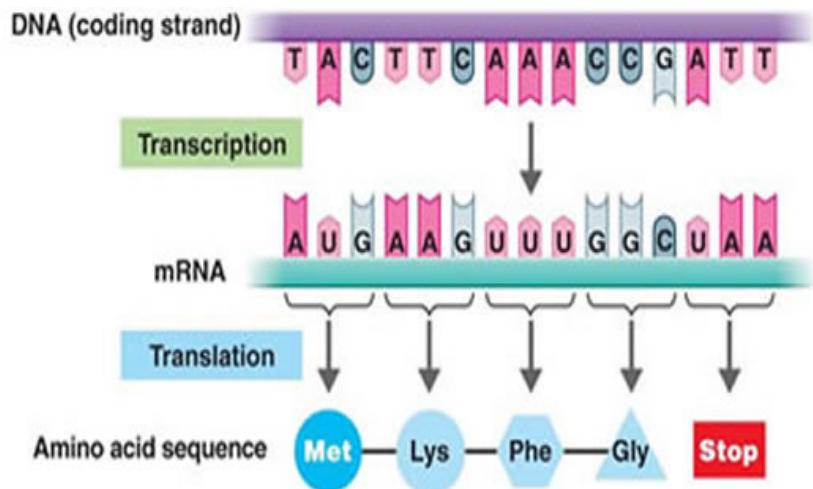
Consequences of Mutation?

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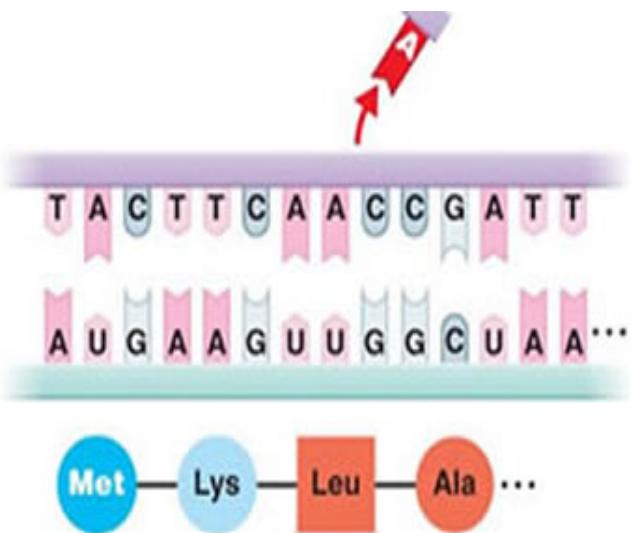




Frame shift mutation



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





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Python Programming

- Functions
- Syntax
- General coding

Follow along in
class and save
your notes in
a text file!!

