Big Idea 3: Living systems store, retrieve, transmit and respond to information essential to life processes.

Enduring understanding 3.C: The processing of genetic information is imperfect and is a source of genetic variation.

Essential knowledge 3.C.1: Changes in genotype can result in changes in phenotype.

a. Alterations in a DNA sequence can lead to changes in the type or amount of the protein produced and the consequent phenotype. [See also 3.A.1]

Evidence of student learning is a demonstrated understanding of the following:

1. DNA mutations can be positive, negative or neutral based on the effect or the lack of effect they have on the resulting nucleic acid or protein and the phenotypes that are conferred by the protein.

Mutations...gotta have them!

- **Any and all new alleles (genes) arise from mutations.**
- **Mutations- are change in nucleotide sequence in an organisms DNA**
- **Mutations are random**
  - ***Only mutations that occur in gametes (sperm/eggs) can be inherited and passed generation after generation***
  - ***Somatic (body cells) mutations can not be inherited and thus die with the individual.***

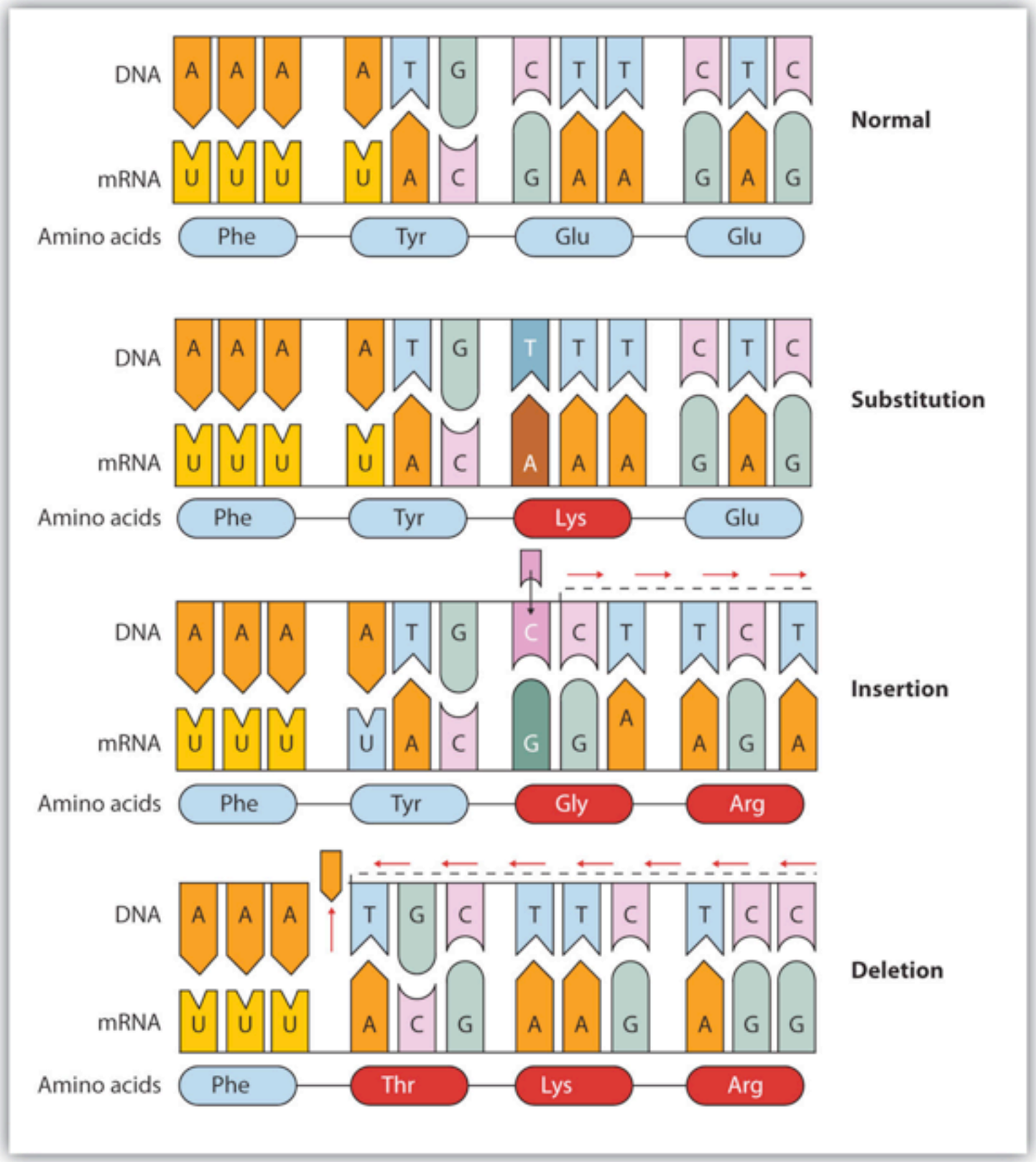
Effects of Mutations

- **Mutations change nucleotide sequences, which in turn changes the protein product, which in turn alters the phenotype (trait).**
- **Most mutations are neutral or perhaps slightly harmful.**
- **On rare occasions a mutation results in a new trait that provides a selective advantage to the individual and should they reproduce to their offspring.**
  - **Over time this new gene becomes more common.**

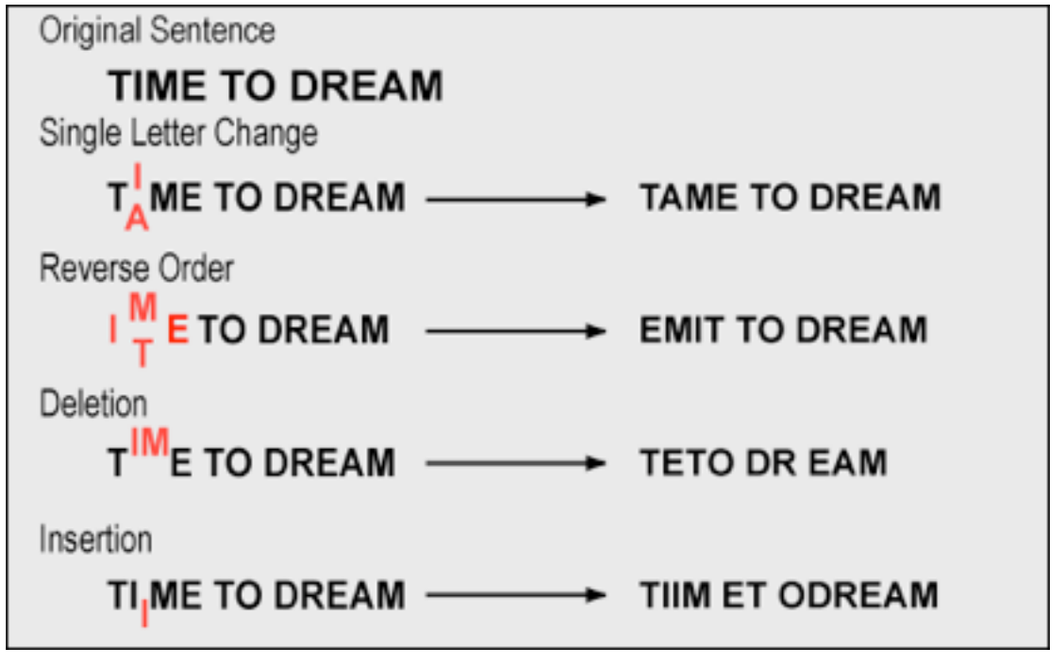
Mutations

- **Mutations can occur in any number of ways.**
  - **Gene Mutations (small scale)**
    - *substituting one nucleotide for another*
    - *adding or deleting a nucleotide*
  - **Chromosomal Mutations (large scale)**
    - *rearranging chromosomal pieces (moving an entire gene or genes) in a genome*
    - *deleting or duplicating chromosomal pieces (deleting or duplicating an entire gene or genes) in a genome*
    - *disrupting an entire gene or genes at one time*

Gene Mutations



The first two are called "point" mutations, it may or may not effect 1 amino acid

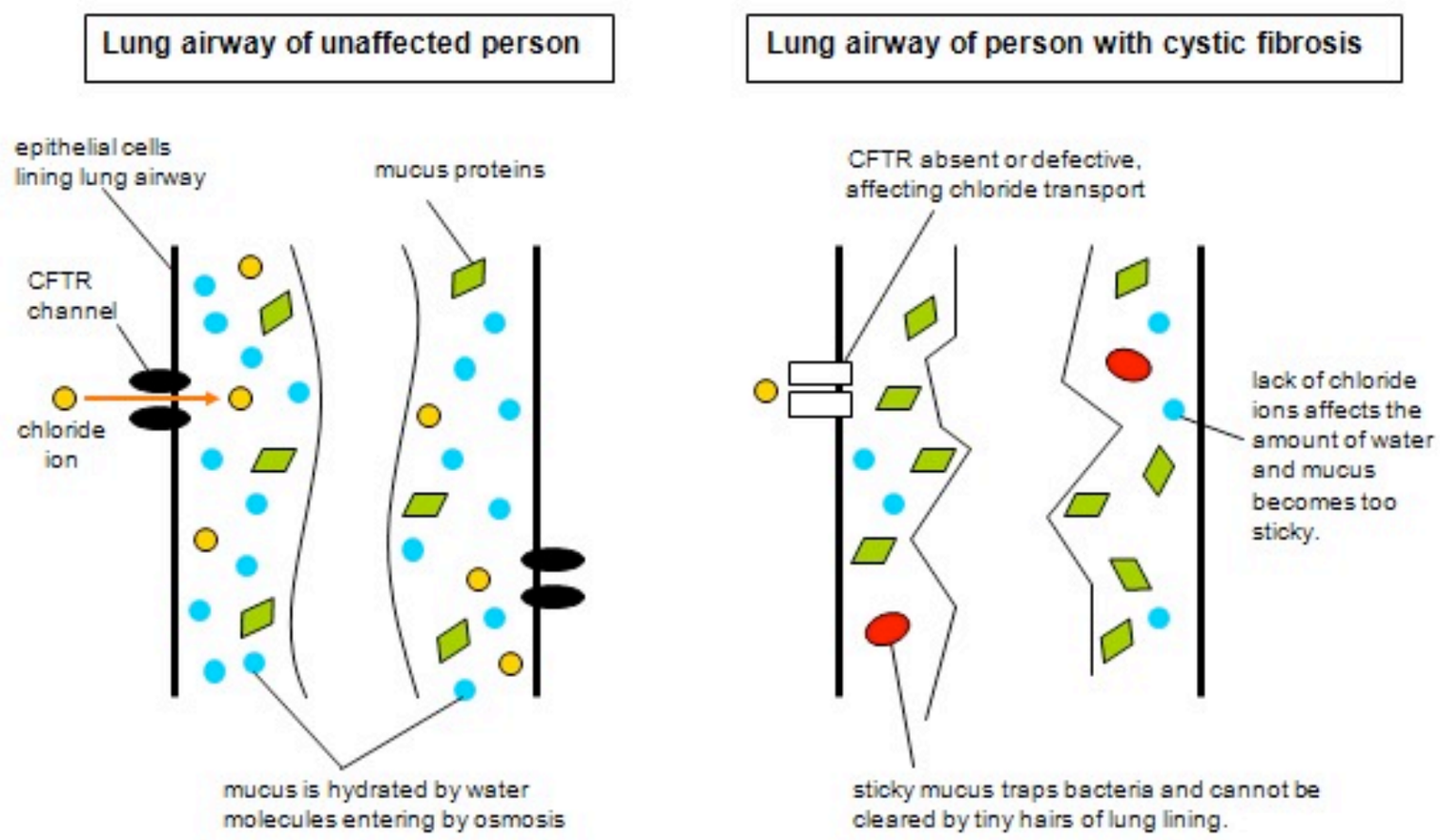


The last two are called "frameshift" mutations, it moves the entire reading frame, they have dramatic effects

Gene Mutations

Most mutations are neutral, have no effect on the fitness of the individual. Occasionally a mutation will provide a selective advantage and other rare times in results in a detrimental phenotype, reducing fitness. Here is an example of such a case

Cystic Fibrosis



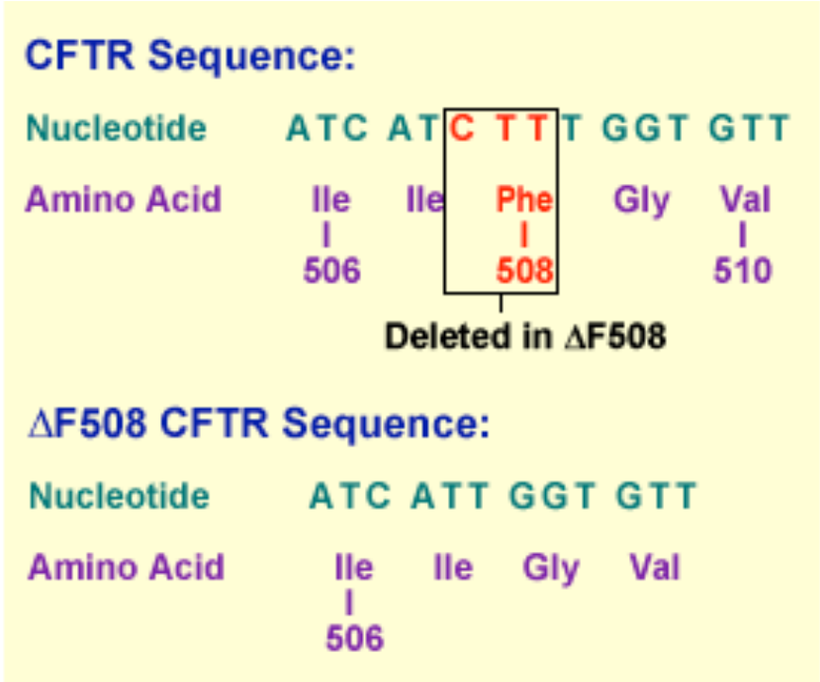
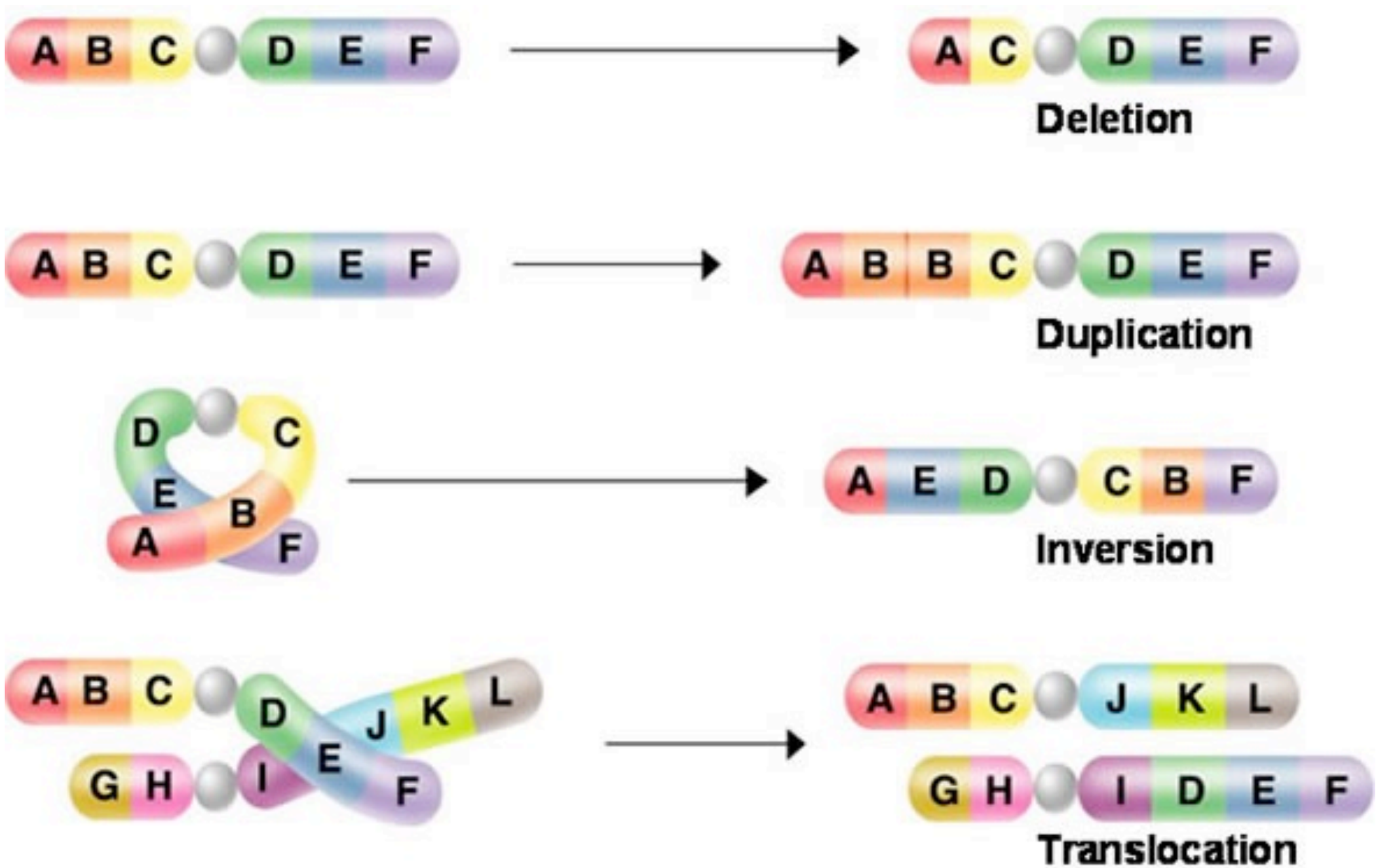


Figure 3: The deltaF508 deletion is the most common cause of cystic fibrosis. The isoleucine (Ile) at amino acid position 507 remains unchanged because both ATC and ATT code for isoleucine

1 amino acid is lost out 508 and this results in cystic fibrosis

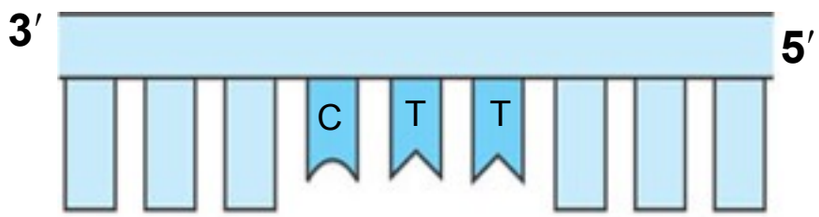
Chromosomal Mutations



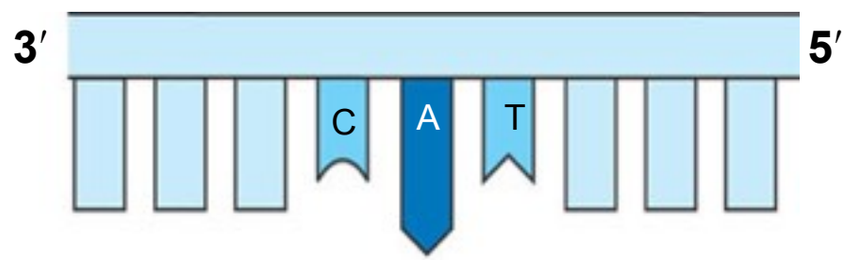
Point Mutations

Changes in one base pair of a gene.

Wild-type hemoglobin

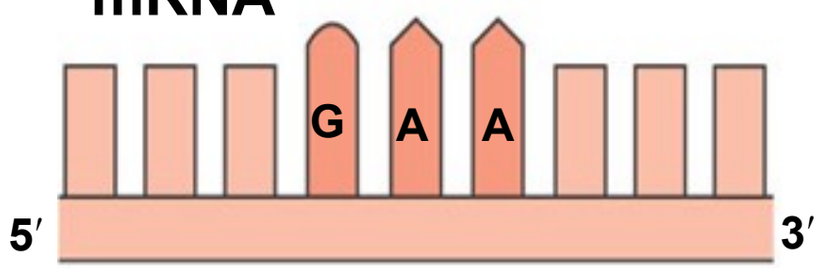


Mutant hemoglobin

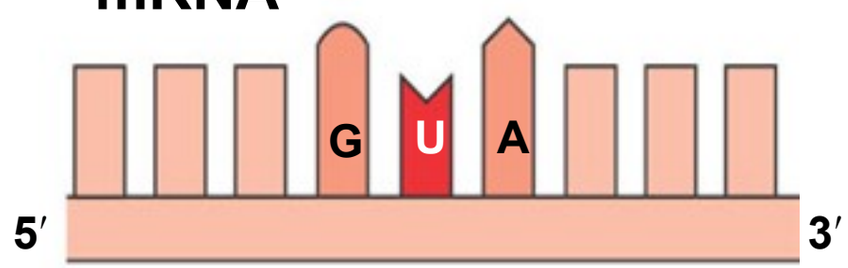


In the DNA, the mutant template strand has an A where the wild-type template has a T.

mRNA



mRNA



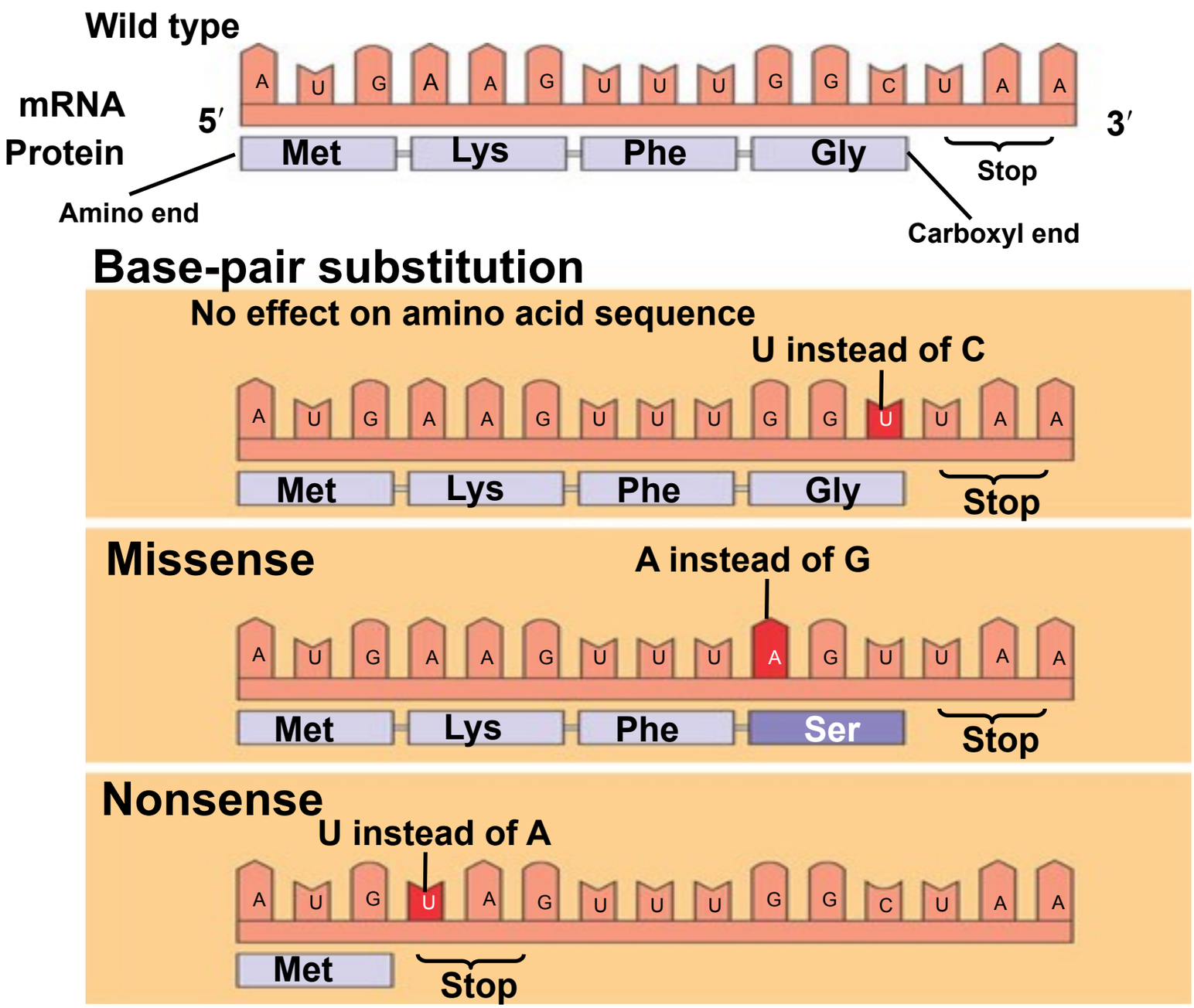
The mutant mRNA has a U instead of an A in one codon.

Normal hemoglobin

Sickle-cell hemoglobin

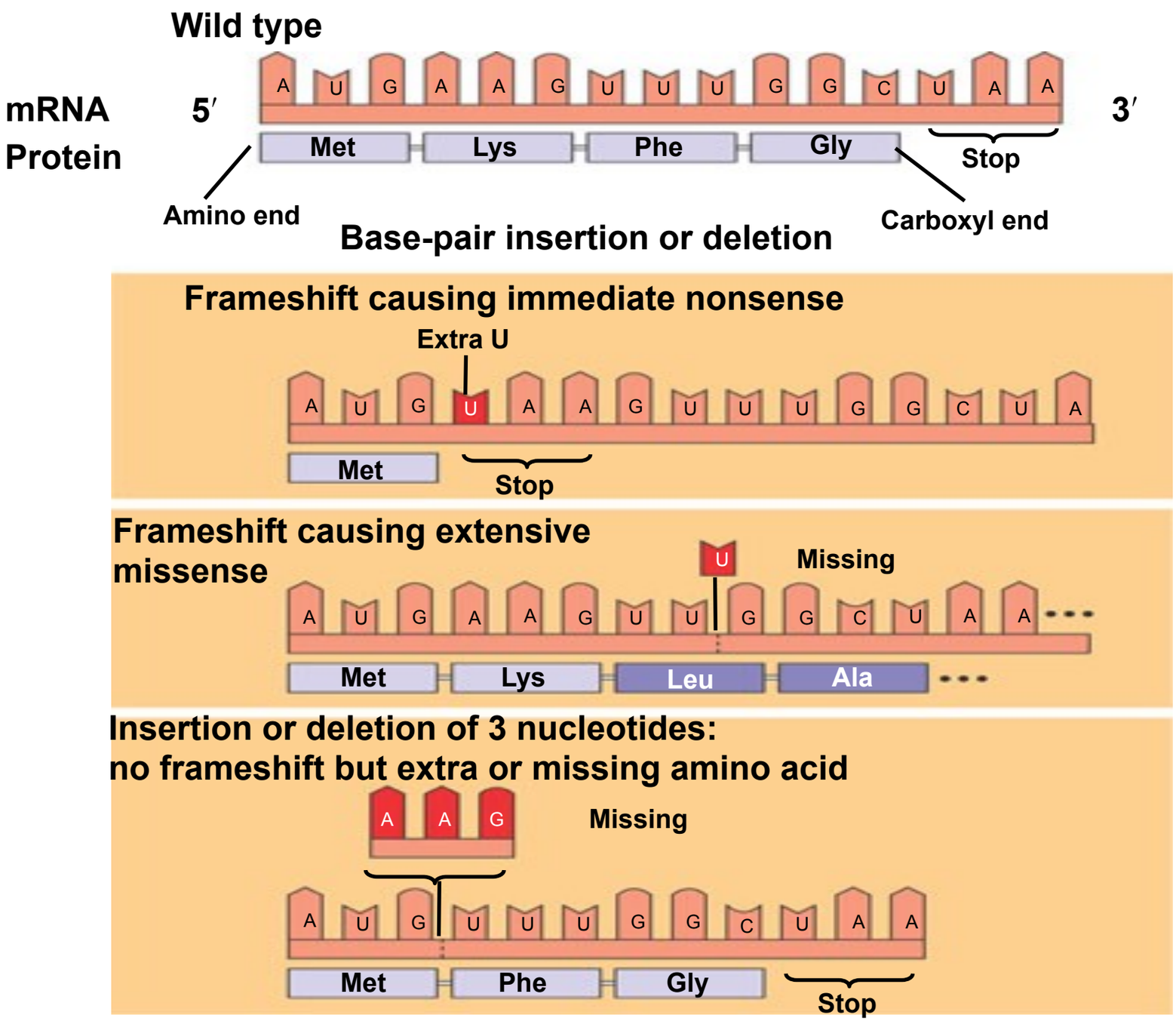
The mutant (sickle-cell) hemoglobin has a valine (Val) instead of a glutamic acid (Glu).

Point Mutations- Base Pair Substitutions



Replacement of one nucleotide and its partner with another pair of nucleotides, can result in missense or nonsense mutations

Point Mutations-
Base Insertions & Deletions



Additions and losses of nucleotide pairs in a gene, can cause frameshifts

Essential knowledge 3.C.1: Changes in genotype can result in changes in phenotype.

b. Errors in DNA replication or DNA repair mechanisms, and external factors, including radiation and reactive chemicals, can cause random changes, e.g., mutations in the DNA.

Evidence of student learning is a demonstrated understanding of the following:

1. Whether or not a mutation is detrimental, beneficial or neutral depends on the environmental context. Mutations are the primary source of genetic variation.

Mutations...gotta have them!

- **Any and all new alleles (genes) arise from mutations.**
- **Mutations- are change in nucleotide sequence in an organisms DNA**
- **Mutations are random**
  - ***Only mutations that occur in gametes (sperm/eggs) can be inherited and passed generation after generation***
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Effects of Mutations

- **Mutations change nucleotide sequences, which in turn changes the protein product, which in turn alters the phenotype (trait).**
- **Most mutations are neutral or perhaps slightly harmful.**
- **On rare occasions a mutation results in a new trait that provides a selective advantage to the individual and should they reproduce to their offspring.**
  - **Over time this new gene becomes more common.**

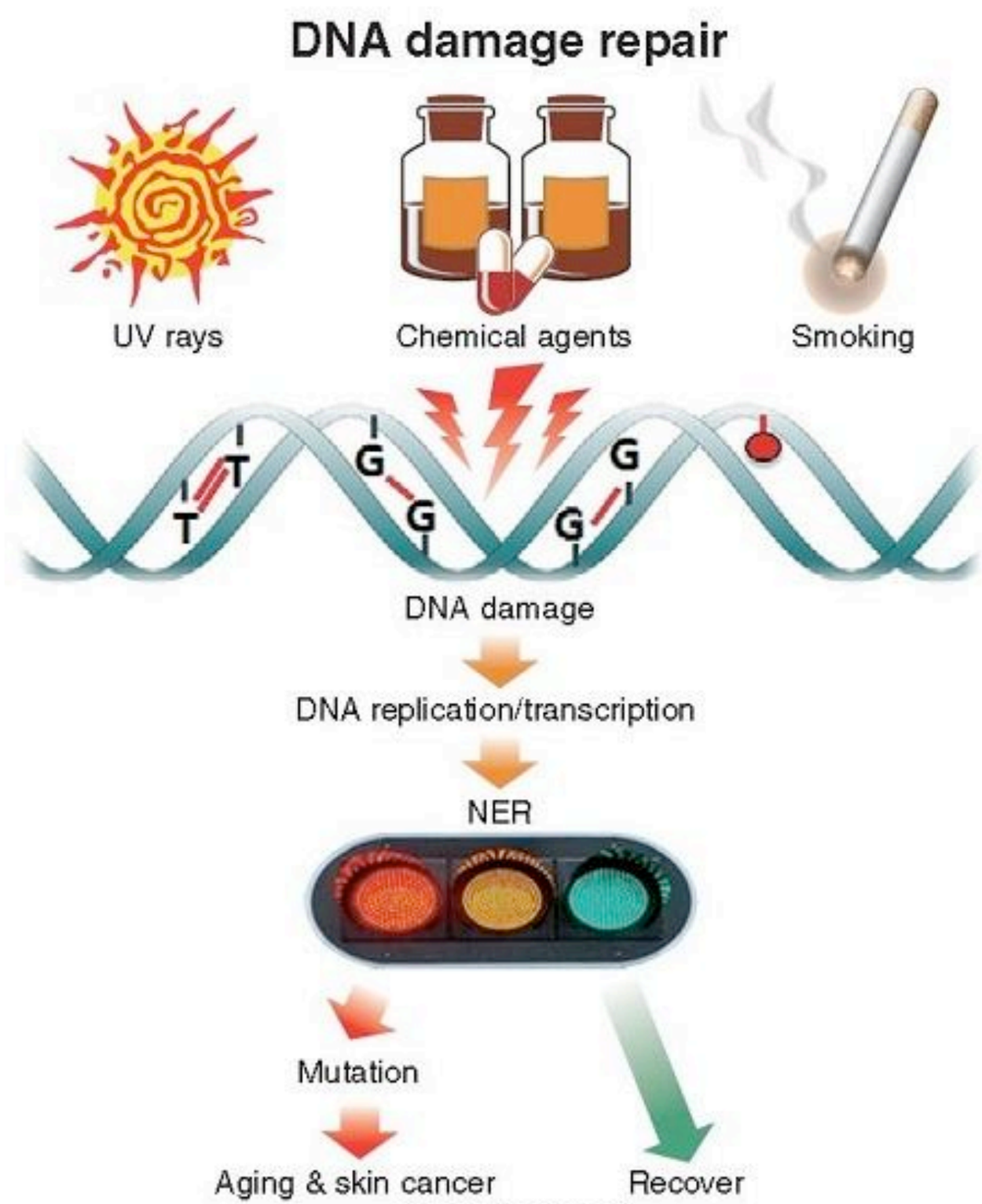
Proofreading & Repairing DNA

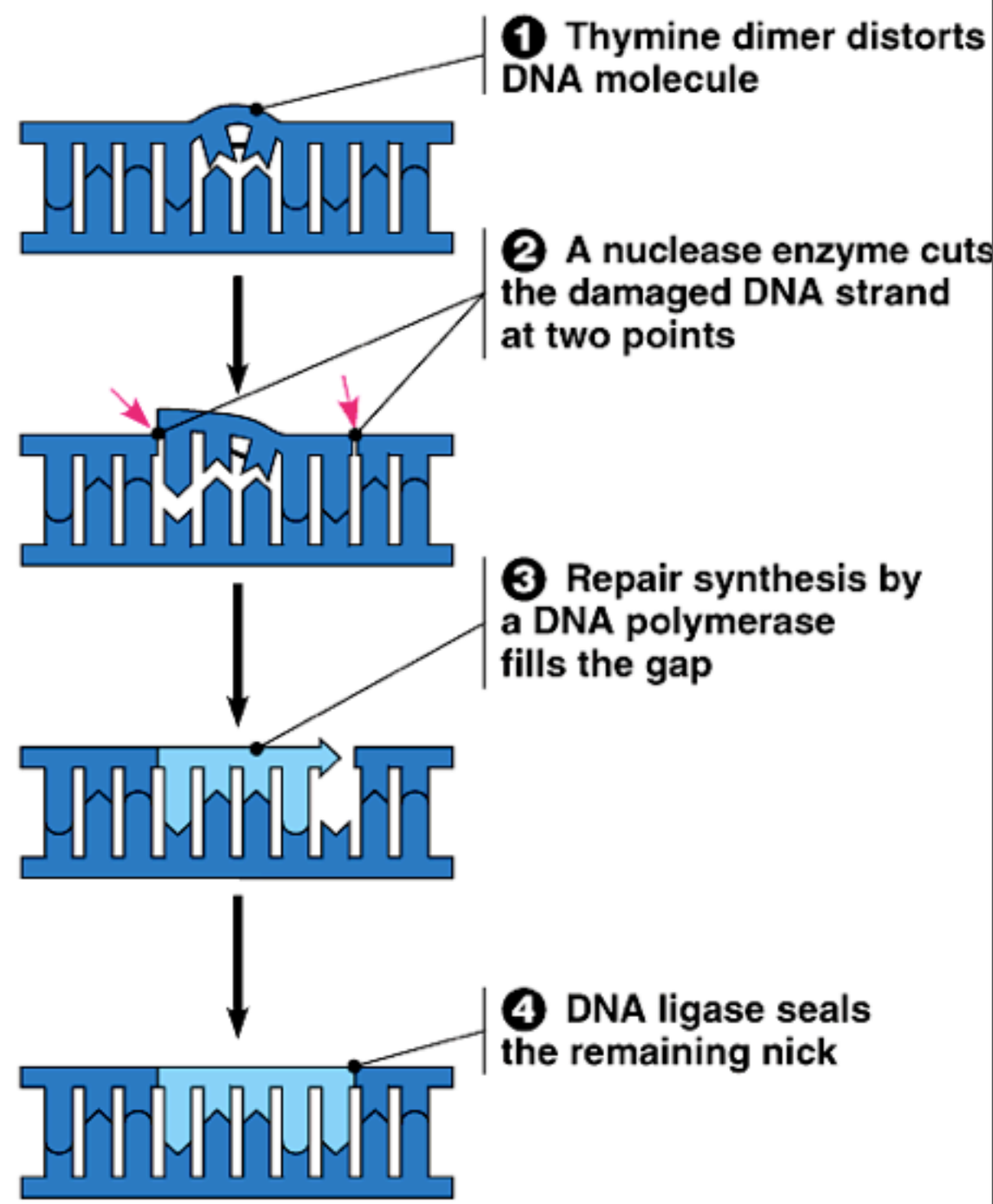
- DNA replication is extremely accurate, but because of the base pairing rules alone.
- The rate of base pairing errors is ~ 1 in 10,000
- Additional DNA polymerases and other proofreading enzymes search out and repair most of these mismatches resulting in a final error rate of ~ 1 in 10 billion!
  - As you might expect errors in the genes that produce these proofreading enzymes might have serious consequences.
  - *For example lack of the necessary proofreading enzymes in colon cells have been implicated in a particular type of colon cancer .*

Proofreading & Repairing DNA

- Alterations and errors in DNA can also after replication.
- **Mutagens**, chemical or physical agents such as cigarette smoke or x-rays increase the rate of DNA alterations
- Over 130 repair enzymes that correct these mutations have been identified in humans.
  - *Unfortunately these enzymes are not infallible, as result some of these mutations may develop into cancer. Mutagens that increase the rate of cancer are called* ***carcinogens****.*

Proofreading & Repairing DNA





Essential knowledge 3.C.1: Changes in genotype can result in changes in phenotype.

c. Errors in mitosis or meiosis can result in changes in phenotype.

Evidence of student learning is a demonstrated understanding of each of the following:

1. Changes in chromosome number often result in new phenotypes, including sterility caused by triploidy and increased vigor of other polyploids. [See also 3.A.2]
2. Changes in chromosome number often result in human disorders with developmental limitations, including Trisomy 21 (Down syndrome) and XO (Turner syndrome). [See also 3.A.2, 3.A.3]

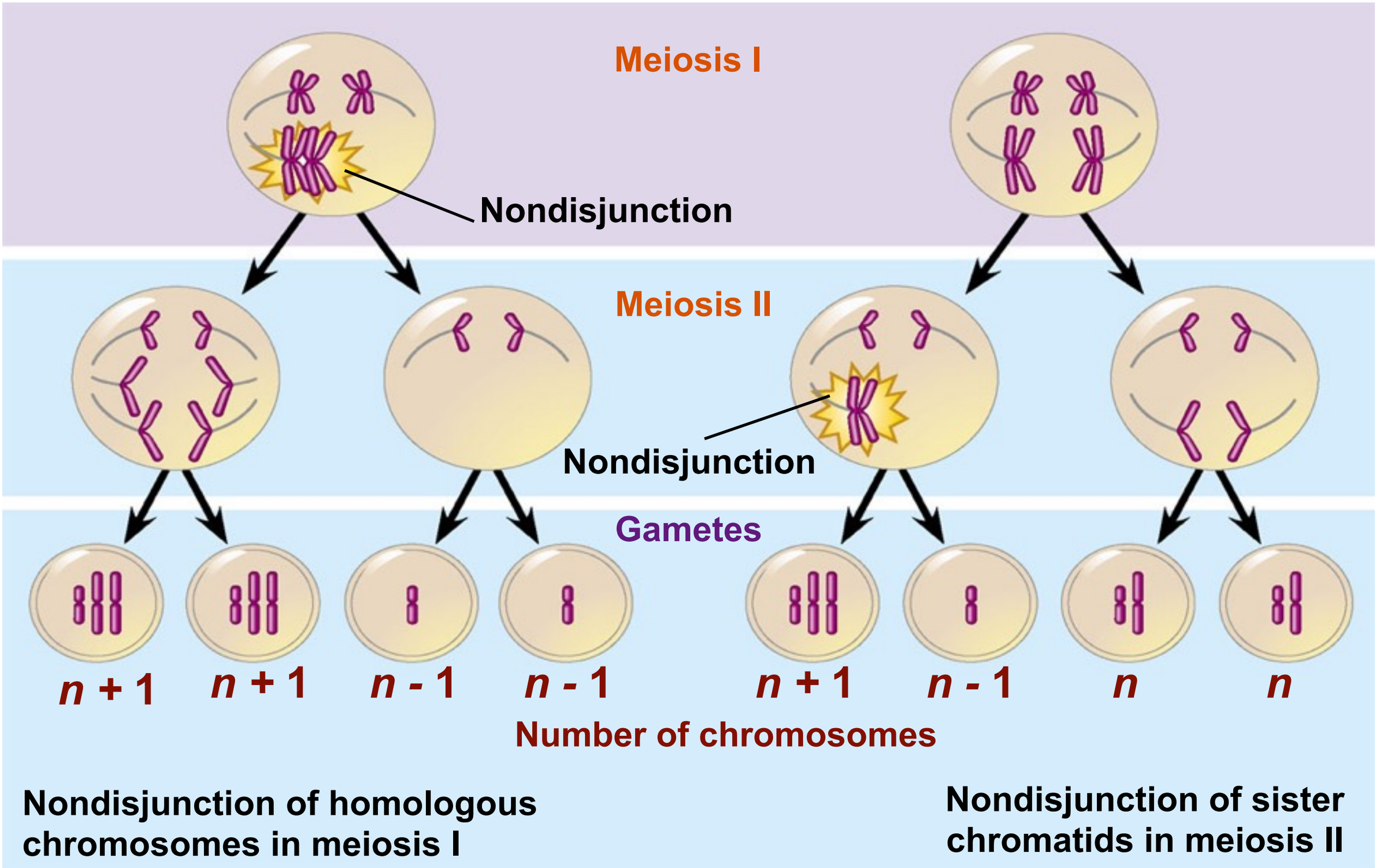
Chromosomal Disorders

- Large scale chromosomal changes can also effect an organisms phenotype and result in genetic disorders.
  - Errors in cell division can result in cells have too many chromosomes or too few chromosomes.
  - Physical and chemical disturbances can alter chromosome structure and function as well.
- These changes to the chromosome number or integrity result in genetic disorders.
- The disorders can vary in severity and plants tend to deal with these alterations better than animals.

Alteration in Chromosome Numbers

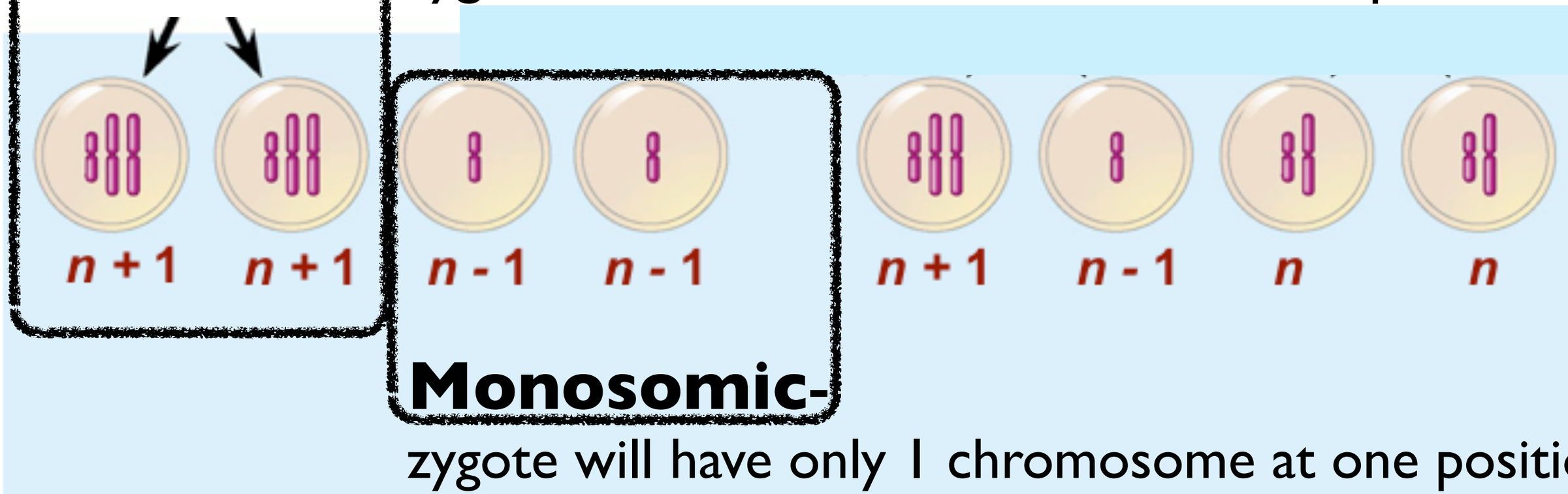
- Ideally chromosomes are distributed evenly and without error amongst daughter cells during meiosis.
- Occasionally errors occur, when, members of a pair of homologous chromosomes fail to separate during meiosis I or sister chromatids fail to separate during meiosis II it is called **nondisjunction**.
  - These errors in cell division result in some cells having too many chromosomes, while the other cells have too few chromosomes.
- Should any of these gametes fuse with a normal gamete the resulting zygote will also have an abnormal number of chromosomes

Nondisjunction



Nondisjunction can also occur in mitosis, during embryological development.

Trisomic- zygote will have 3 chromosomes at one position



Monosomic- zygote will have only 1 chromosome at one position

Aneuploidy- a condition where an individual has an abnormal number of chromosomes and it may involve more than one chromosome.

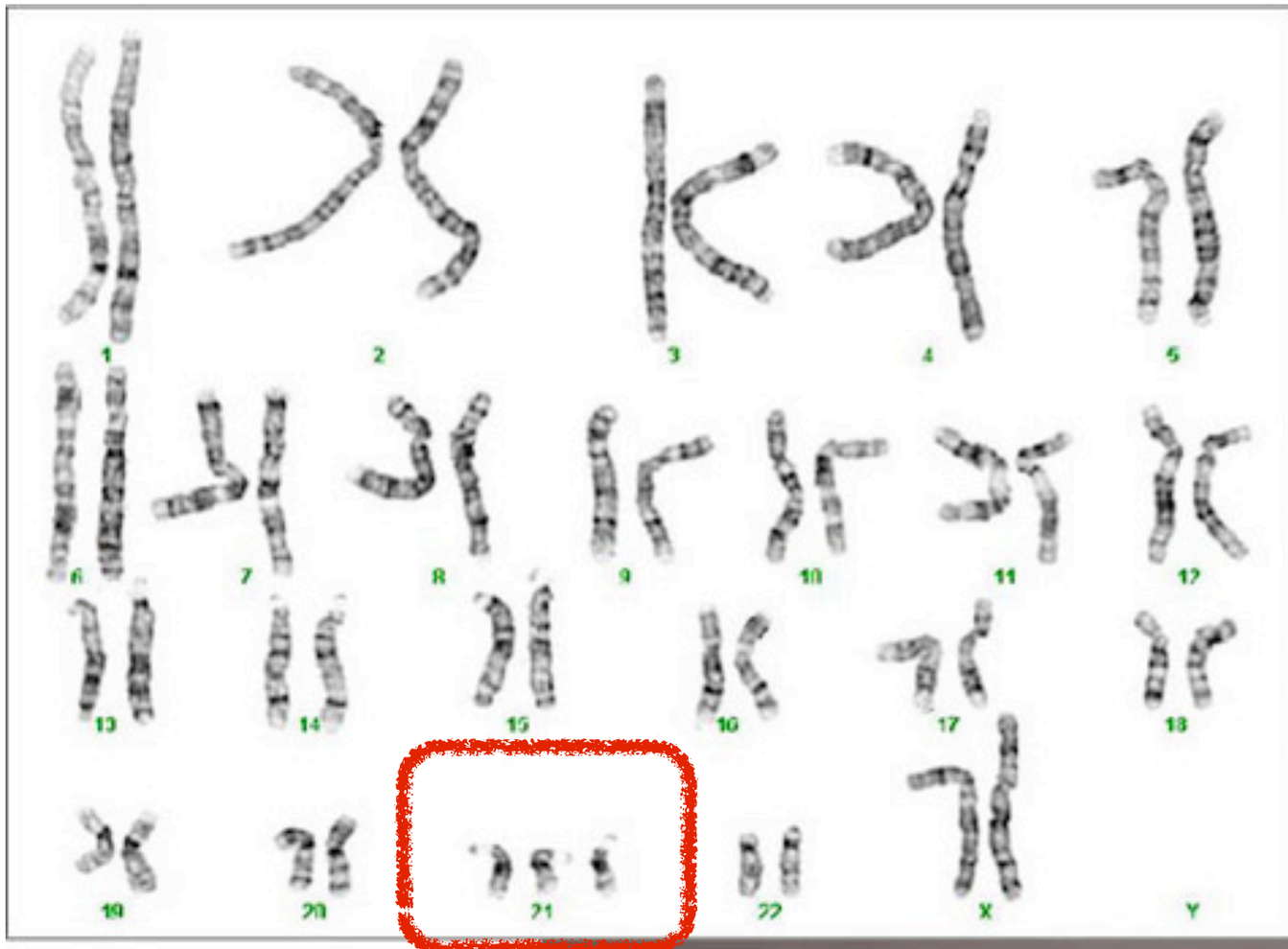
- Mitosis will consequently pass the anomaly to each and every cell of the body during development.

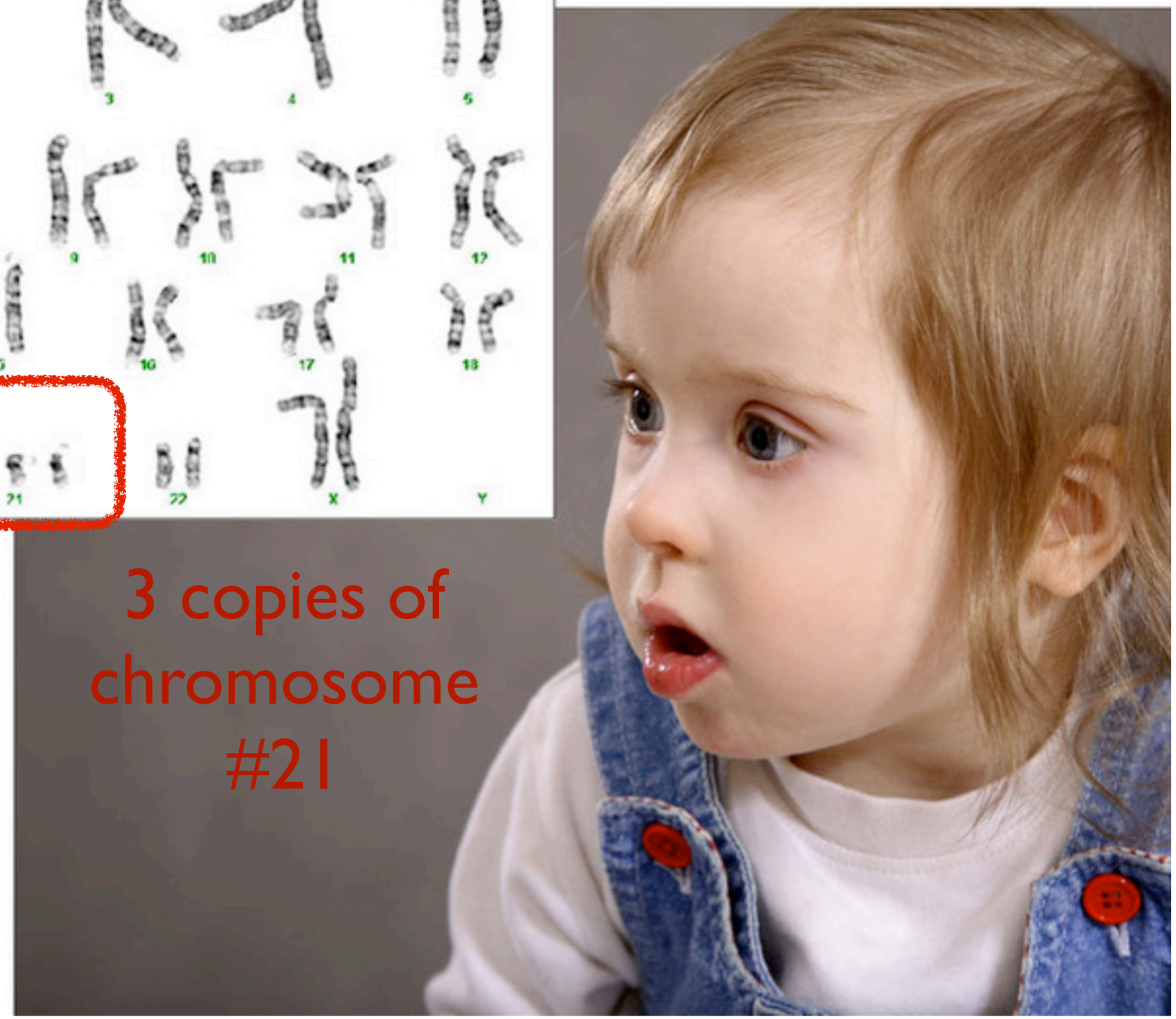
Alteration in Chromosome Number

- These alterations may be quite common but most of the time we never see the results of such alterations because the embryos spontaneously abort well before birth.
- When the embryo survives it results in a **syndrome**, a set of certain traits associated with that specific type of aneuploidy.
  - ex. Downs syndrome, Klinefelters, Turners

Downs Syndrome

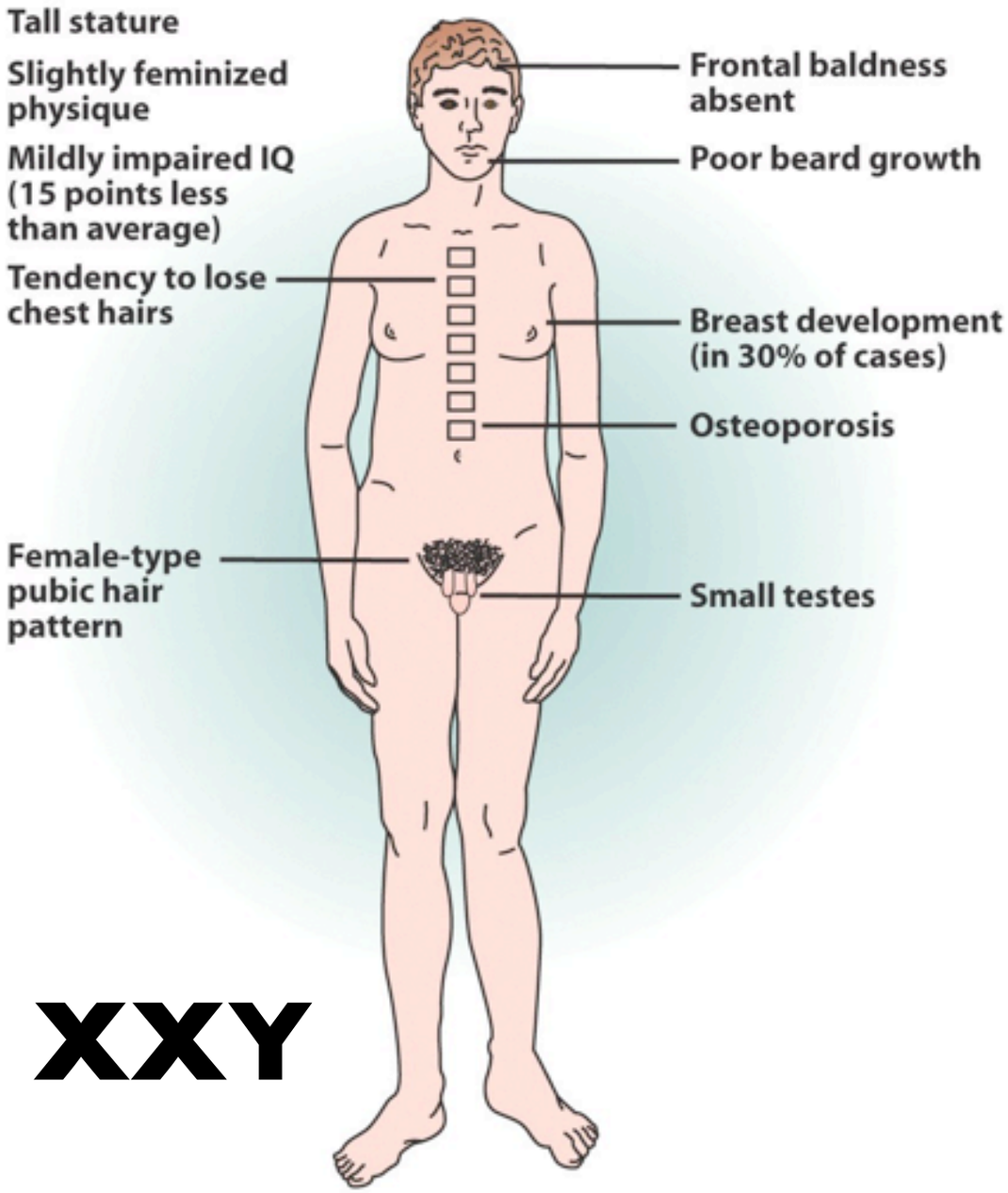
1 in 700
births in U.S.





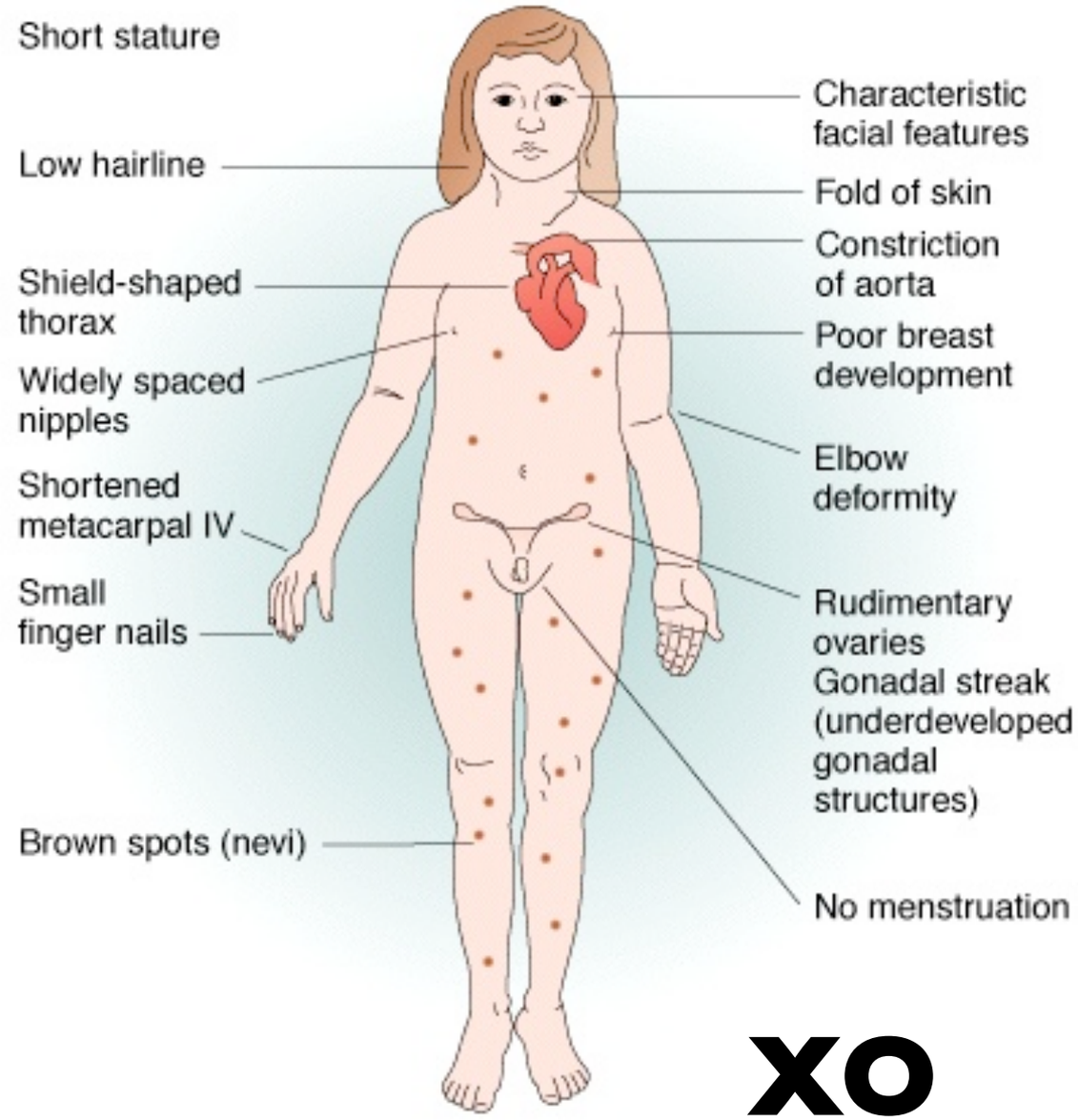
3 copies of
chromosome
#21

Two or the more common sex chromosome aneuploidy conditions



XXY

Klinefelter Syndrome



XO

Turner Syndrome

Aneuploidy in Sex Chromosomes

Table 1. Main features of numerical sex chromosome anomalies

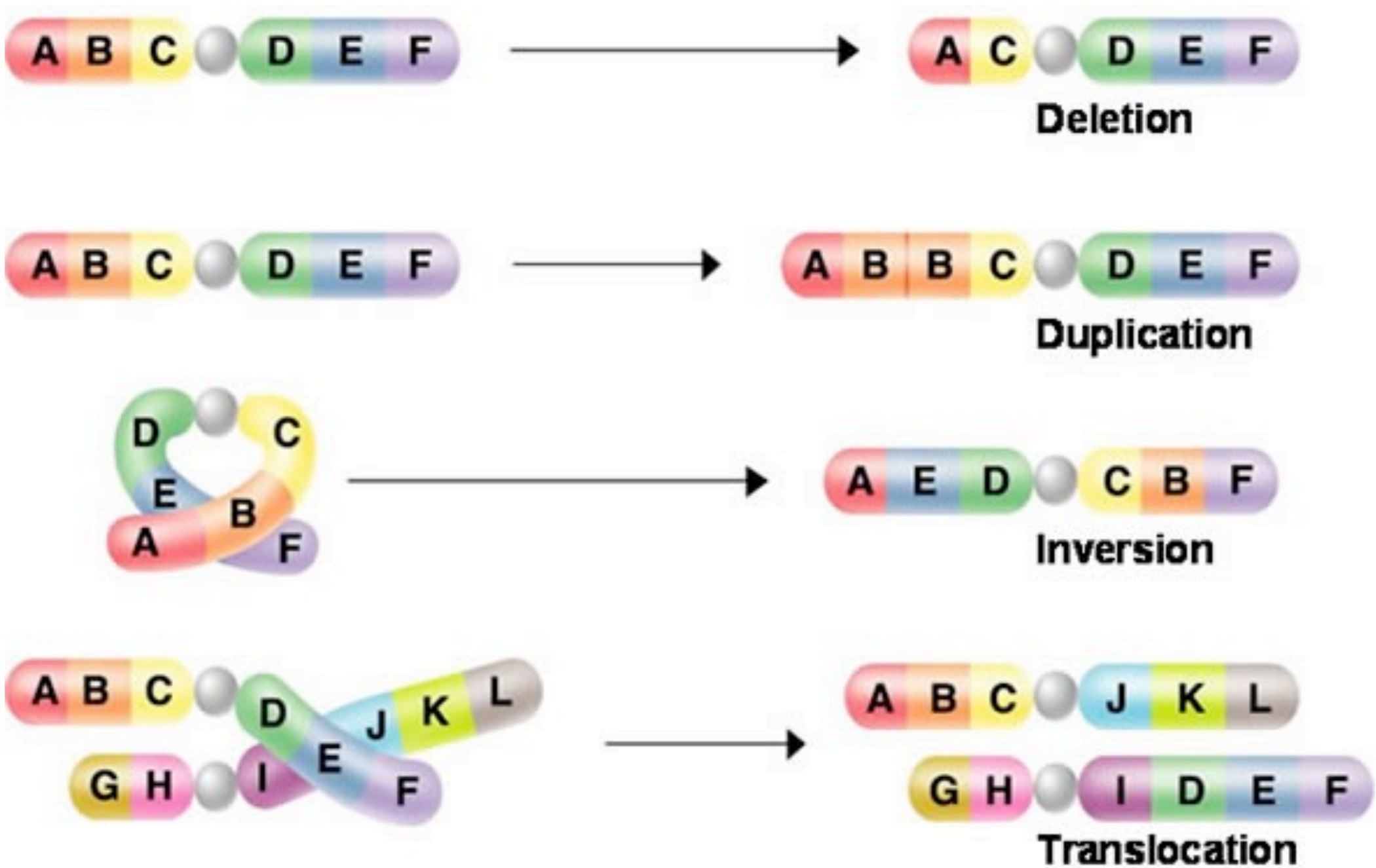
Karyotype	Incidence	Mental retardation	Behavioral disorders	Stature	Gonadal function	Congenital anomalies/ Additional medical problems	Ref.
45,X	1:2,130 F	-	-	Short	Hypergonadotropic hypogonadism	Dysmorphic picture, CV and renal anomalies, autoimmune disorders	1,2
47,XXY	1:576 M	Greater frequency when compared with normal men	Greater frequency when compared with normal men	Tall	Hypergonadotropic hypogonadism	Minor physical findings, varicose veins, DVT, *diabetes mellitus*, autoimmune disorders	1, 2,6
47,XYY	1:851 M	Greater frequency when compared with normal men	Greater frequency when compared with normal men	Tall	Usually normal	Minor physical findings	1,2,6
47,XXX	1:897 F	Greater frequency when compared with normal women	Greater frequency when compared with normal women	Tall	Usually normal Unknown frequency of premature ovarian failure	Minor physical findings, low frequency of genitourinary anomalies and seizures	1,2,6
48,XXXX 49,XXXXX	?	+	Variable	Short	Hypergonadotropic hypogonadism	Dysmorphic picture, CV anomalies	6,16
48,XXYY	1:18,000-1:40,000 M	+	+	Tall	Hypergonadotropic hypogonadism	Dysmorphic picture, CV and renal anomalies, type II diabetes, seizures, DVT	3,6,7
48,XXXY	1:50,000 M	+	+	Tall	Hypergonadotropic hypogonadism	Dysmorphic picture, CV and renal anomalies, type II diabetes, seizures, DVT	4,6,7
49,XXXXY	1:85,000-1:100,000 M	+	+	Short	Hypergonadotropic hypogonadism	Dysmorphic picture, CV and renal anomalies, type II diabetes, seizures, DVT	4,6,7

+ = present; - = absent; CV = cardiovascular; DVT = deep vein thrombosis; F = females; M = males.

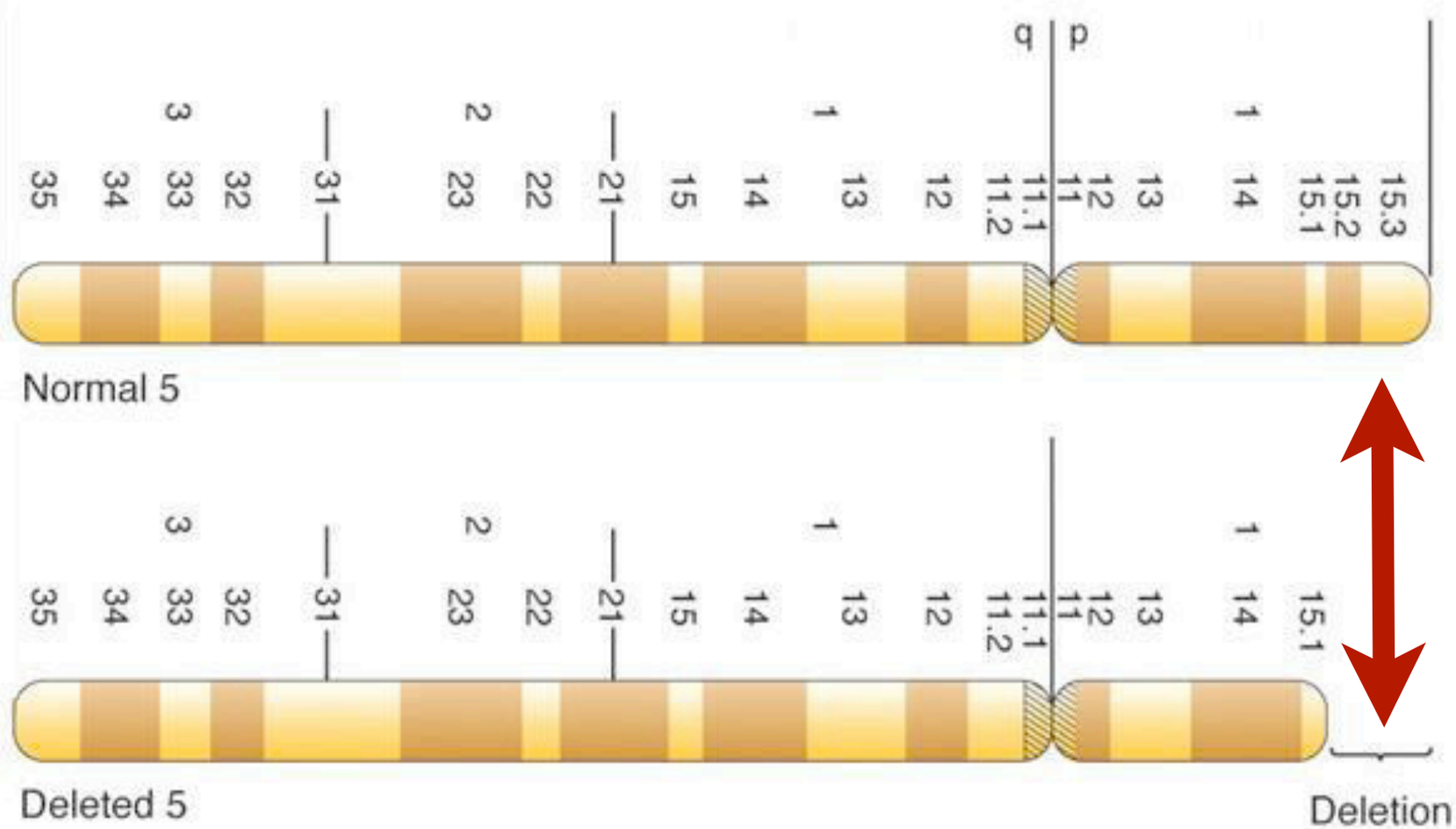
Alteration in Chromosome Structure

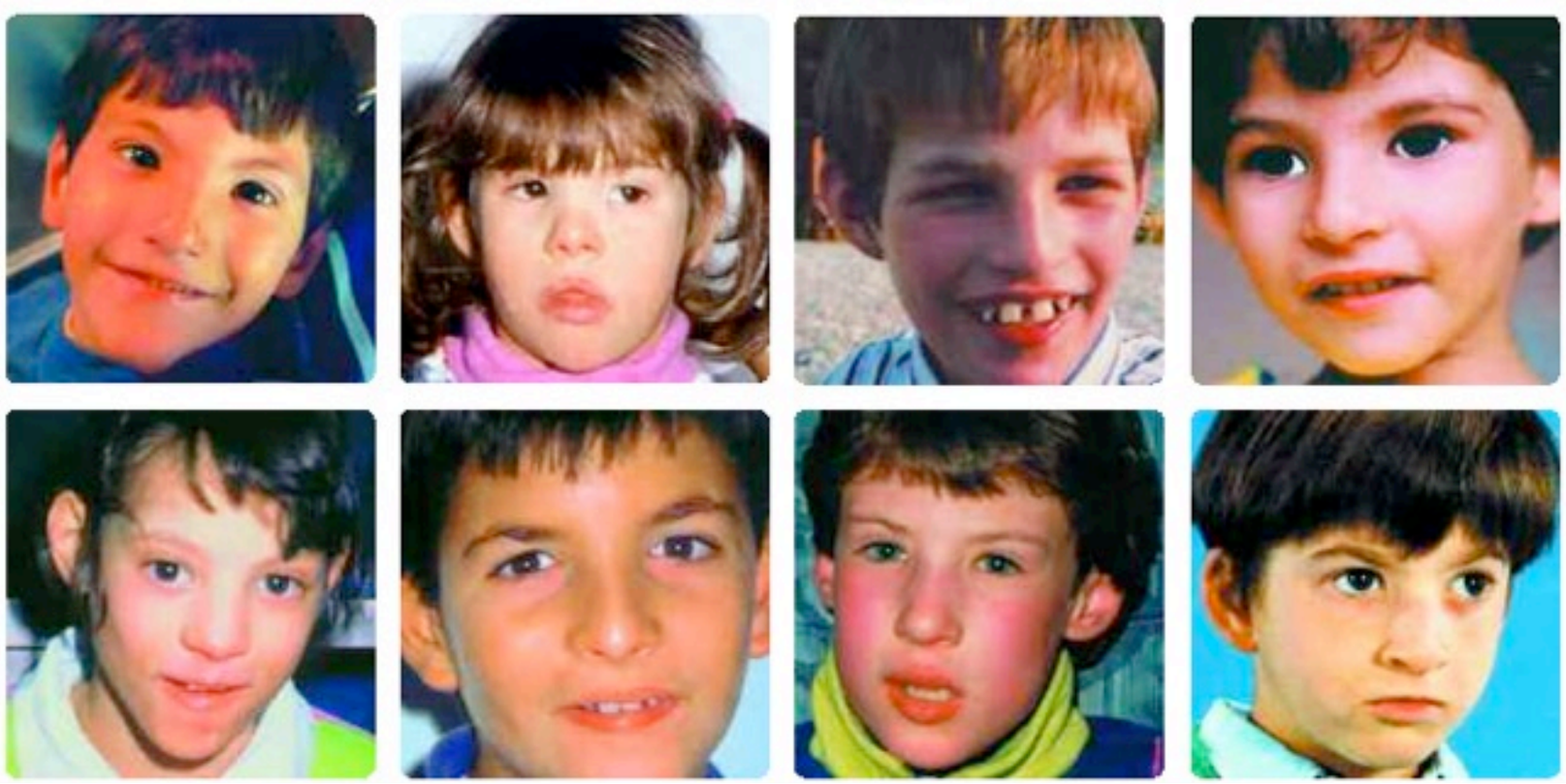
- Errors in meiosis or damaging agents can alter chromosome structure in 1 of 4 ways. (illustrated on next slide)
  - *deletions, duplications, inversions & translocations*
- These alterations may cause severe problems.
  - Cri du Chat, Chronic Myelogenous Leukemia, Burkitt's Lymphoma

Chromosomal Mutations



THE CRI DU CHAT SYNDROME





Essential knowledge 3.C.1: Changes in genotype can result in changes in phenotype.

d. Changes in genotype may affect phenotypes that are subject to natural selection. Genetic changes that enhance survival and reproduction can be selected by environmental conditions. [See also 1.A.2, 1.C.3]

To foster student understanding of this concept, instructors can choose an illustrative example such as:

- Antibiotic resistance mutations
- Pesticide resistance mutations
- Sickle cell disorder and heterozygote advantage

Evidence of student learning is a demonstrated understanding of the following:

1. Selection results in evolutionary change.

Darwin's Argument

- **Variation exists among individuals in a population!**

Darwin's Argument

- **Populations produce more offspring than the environment can support, thus some will fail to survive and/or reproduce!**

Darwin's Argument

- **Individuals with inherited traits that give them a better chance of surviving and reproducing in a particular environment tend to leave more offspring!**

Darwin's Argument

- **The unequal ability of individuals to survive and reproduce will lead to accumulation of favorable traits and less favorable traits will diminish in the population over *time!**

*Darwin noted that if artificial selection could produce dramatic changes in a relatively short time frame then given enough time nature could fashion the same dramatic changes

Darwin's Mechanism

- **NATURAL SELECTION- differential reproductive success!**

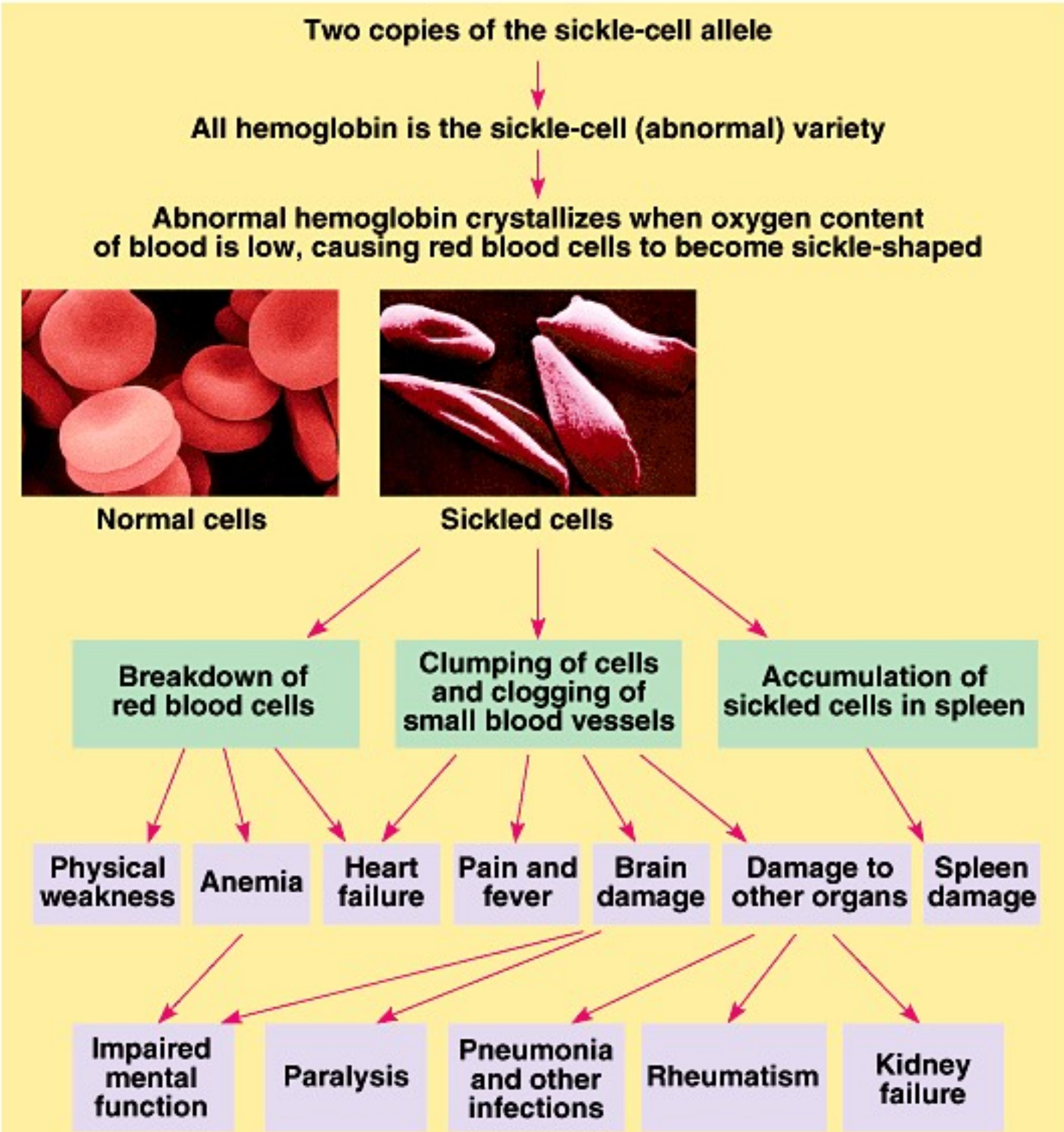
- Beneficial traits are subject to the environment, a beneficial trait for one may be deleterious to another.
  (should the environment change so to might the beneficial traits)

- Natural selections can only amplify or diminish the traits that differ in a population.
  (no variation = no selection)

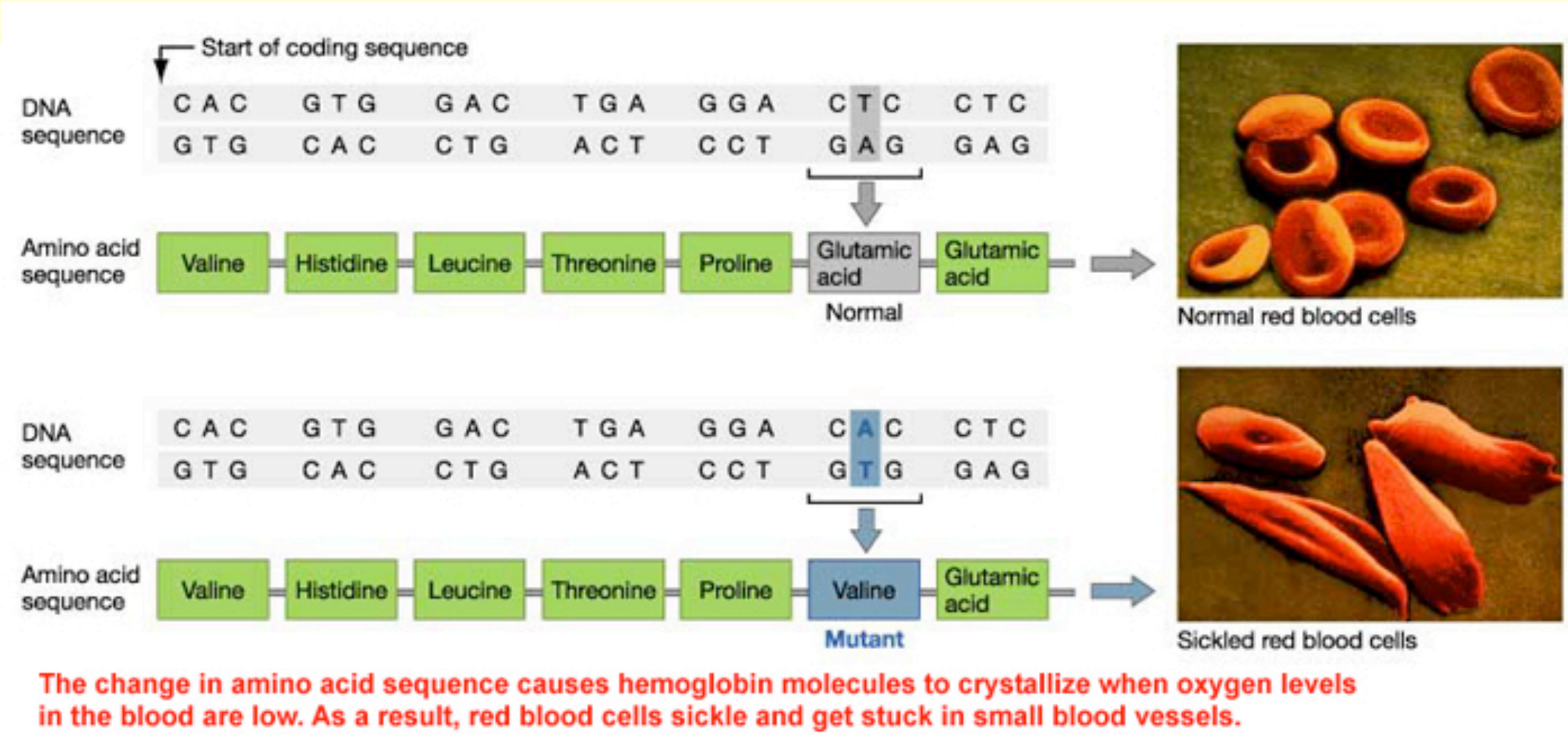
- Populations evolve not individuals.

Sickle Cell Anemia

- The most common genetic disease in people of African descent, strikes 1 in 400 people.
- About 1 in 10 African-Americans carry the trait.
- The high incidence stems from the partial resistance to malaria conferred by carrying the sickle cell trait thus being selected for in Africa where malaria is common.
- Regular blood transfusions can ward off brain damage in children and new drugs can help prevent and treat the disease other related problems but there is no cure.


Two copies of the sickle-cell allele
All hemoglobin is the sickle-cell (abnormal) variety
Abnormal hemoglobin crystallizes when oxygen content of blood is low, causing red blood cells to become sickle-shaped
Normal cells
Sickled cells
Breakdown of red blood cells
Clumping of cells and clogging of small blood vessels
Accumulation of sickled cells in spleen
Physical weakness
Anemia
Heart failure
Pain and fever
Brain damage
Damage to other organs
Spleen damage
Impaired mental function
Paralysis
Pneumonia and other infections
Rheumatism
Kidney failure

Sickle Cell Trait & Malaria

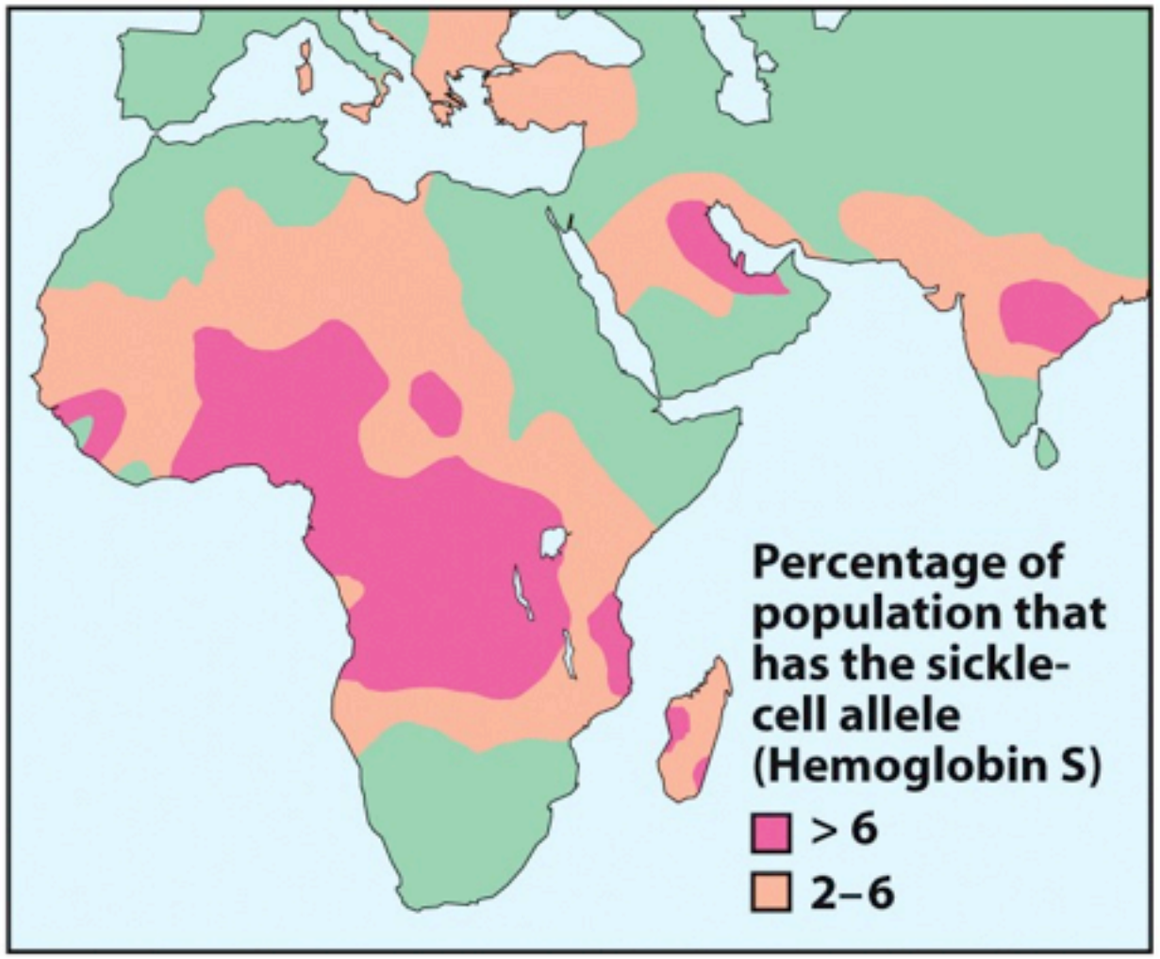


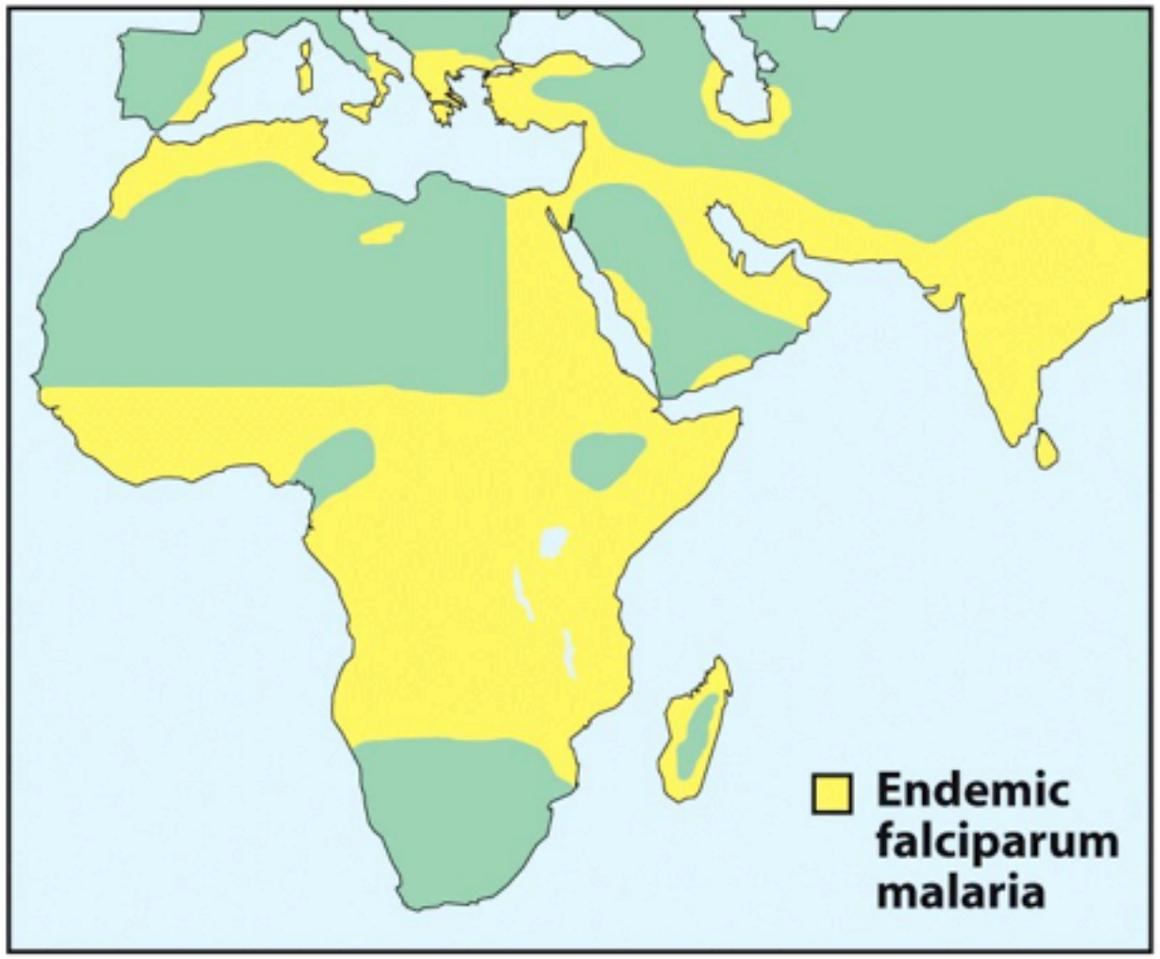
This is a "substitution" mutation notice the thymine was switched with alanine.

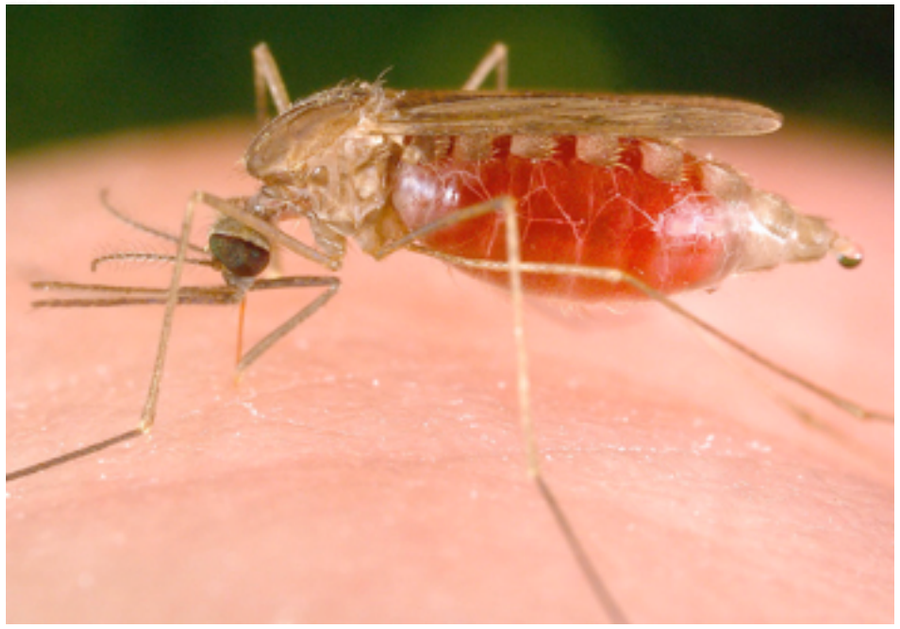
The normal beta subunit consists of 438 nucleotides and 146 amino acids.

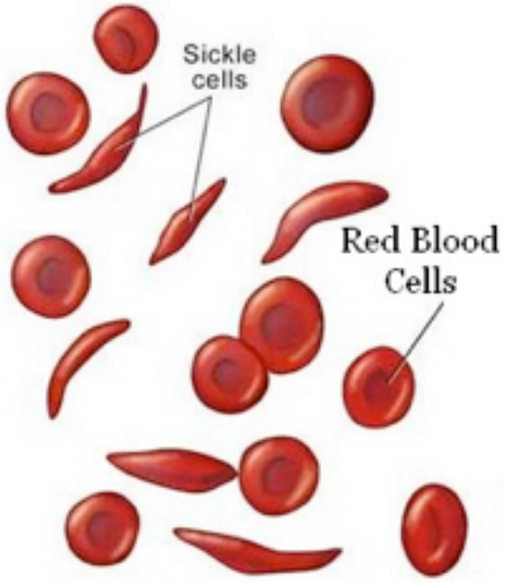
A change in 1 nucleotide, changes 1 amino acid resulting in sickle cell disease

Sickle Cell Trait & Malaria









	A	a
A	AA	Aa Carrier
a	Aa Carrier	aa Child has Sickle Cell Anemia

a — Sickle cell allele

Darwin's Mechanism

- **NATURAL SELECTION- differential reproductive success!**

- Beneficial traits are subject to the environment, a beneficial trait for one may be deleterious to another.
  (should the environment change so to might the beneficial traits)

- Natural selections can only amplify or diminish the traits that differ in a population.
  (no variation = no selection)

- Populations evolve not individuals.

*Pesticide Resistance

Variation exists in Populations
(mutation and/or sex maintain variation)

By chance **no** individual is resistant to the pesticide

Pest population is eliminated

Pesticide is effective

By chance an individual **is** resistant to the pesticide

Non resistant individuals die and leave less offspring

Resistant individuals more likely to survive and reproduce

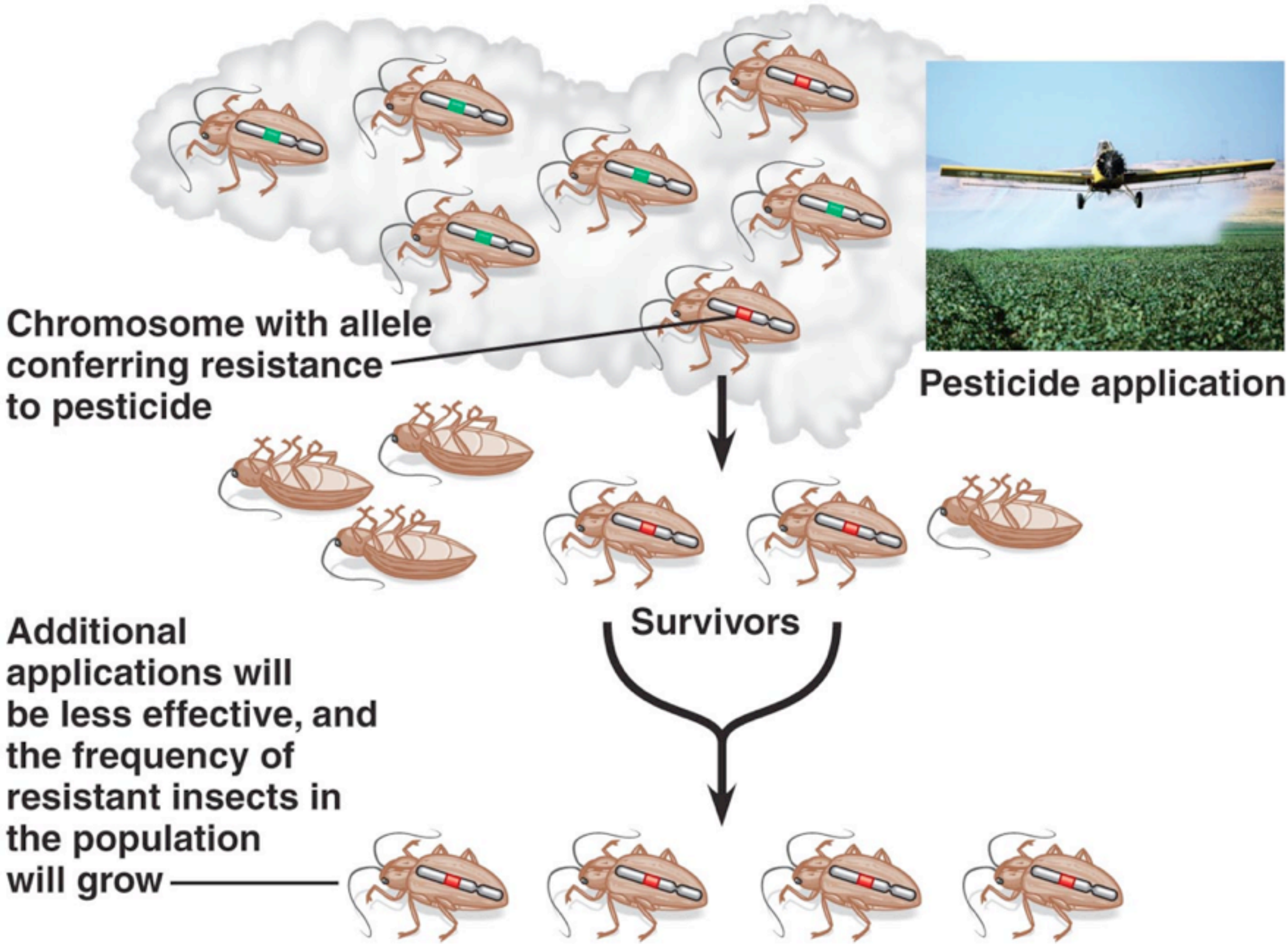
Number of non resistant individuals becomes small or zero

Number of Resistant individuals increase

Pesticide is **not** effective

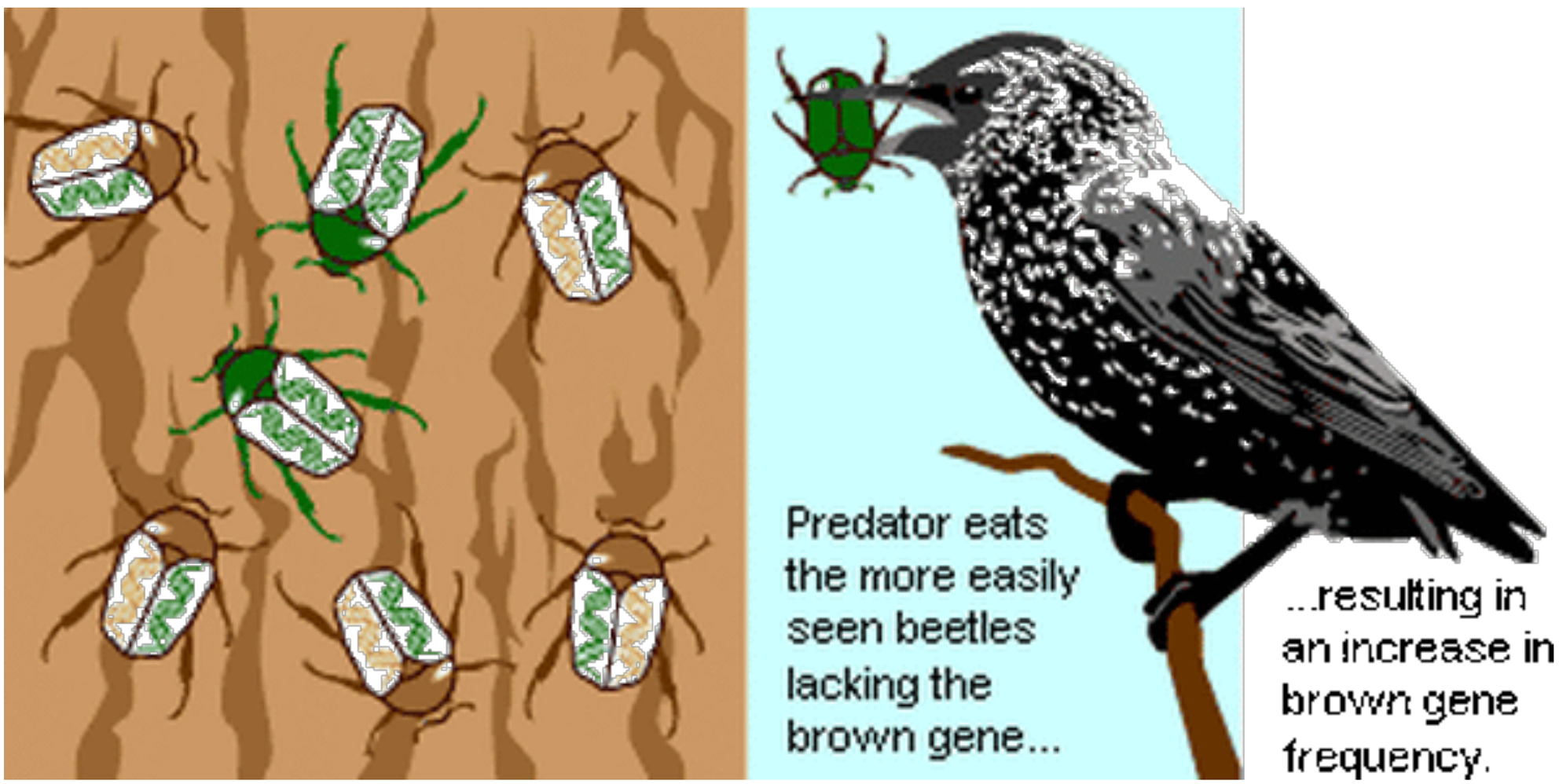
*Resistance can be found on insecticides, fungicides, herbicides, antibiotics, antiviral drugs the mechanism is no different

*Pesticide Resistance



Natural Selection

- **Natural Selection- differential reproductive success.**
  - **Certain favorable traits become more frequent, non favorable traits become less frequent and the population becomes better suited to its environment over time.**



Learning Objectives:

LO 3.24 The student is able to predict how a change in genotype, when expressed as a phenotype, provides a variation that can be subject to natural selection. [See SP 6.4, 7.2]

LO 3.25 The student can create a visual representation to illustrate how changes in a DNA nucleotide sequence can result in a change in the polypeptide produced. [See SP 1.1]

LO 3.26 The student is able to explain the connection between genetic variation in organisms and phenotypic variation in populations. [See SP 7.2]