Changes in genotype can result in changes in phenotype. (3.C. 1)

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.
   - Heterozygous advantage. When individuals who are heterozygous at a particular locus have greater fitness than do both kinds of homozygous.
   - Individuals which are heterozygous for sickle-cell are protected against the most severe effects of malaria (although they are not resistant to malarial infection).
   - This protection is important in tropical regions where malaria is a major killer.

Changes in genotype can result in changes in phenotype. (3.C. 1)

Changes in genome can result in changes in phenotype. (3.C. 1)

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

1. Changes in chromosome number often result in new phenotypes, including sterility caused by triploidy and increased vigor of other polyploids.

Changes in genome can result in changes in phenotype. (3.C. 1)

2. Changes in chromosome number often result in human disorders with developmental limitations, including Trisomy 21 (Down syndrome) and XO (Turner syndrome).

Changes in genome can result in changes in phenotype. (3.C. 1)

### Alterations in a DNA sequence can lead to changes in the type or amount of the protein produced and the consequent phenotype.

- Wild-type hemoglobin (DNA): normal
- Mutant hemoglobin (DNA): sickle-cell
- In the DNA, the mutant template strand (top) has an A where the wild-type template has a T.
- The mutant mRNA has a U instead of an A in one codon.
- The mutant (sickle-cell) hemoglobin has a valine (Val) instead of a glutamic acid (Glu).

Sickle-cell anaemia. A point mutation in the b-globin chain of hemoglobin, causing the hydrophilic amino acid glutamic acid to be replaced with the hydrophobic amino acid valine. When oxygen concentration in the blood is reduced, the red blood cell sickles (3A1).

Changes in genome can result in changes in phenotype. (3.C. 1)

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.

- A number of physical and chemical agents, called mutagens, interact with DNA in ways that cause mutations.

Changes in genome can result in changes in phenotype. (3.C. 1)

- Hermann Joseph Muller was an American geneticist best remembered for his demonstration that mutations and hereditary changes can be caused by X rays striking the genes and chromosomes of living cell. His discovery of artificially induced mutation in genes that was reaching far reaching consequences, and he was awarded the Nobel Prize for Physiology or Medicine in 1946.

- Charlotte Auerbach, a German-Jewish zoologist and geneticist with AJ Clark and JM Robson discovered that mustard gas, a highly toxic substance that had been used in trench warfare, caused genetic mutation in fruit flies (Drosophila), and as doing so she founded the study of gene mutation by chemicals.

1. Whether or not a mutation is detrimental, beneficial or neutral depends on the environmental context.

2. Mutations are the primary source of genetic variation.

Changes in genome can result in changes in phenotype. (3.C. 1)

### Mutations

- Hermann Joseph Muller (1890-1967)
- Charlotte Auerbach (1899-1994)

- Mutations are the primary source of genetic variation.
Changes in genotype can result in changes in phenotype. (3.C. 1)

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.

1. Selection results in evolutionary change.
   - Antibiotic resistance mutations: Multidrug-resistant Tuberculosis (MDR-TB)
   - Pesticide resistance mutations:
     - England: rats in certain areas have developed such a strong resistance to rat poison that they can consume up to five times as much of it as normal rates without dying (http://www.sciencedaily.com/releases/2012/10/121018122837.htm).
   - Sickle cell disorder and heterozygote advantage (3A1 &3C1).

Bozeman Biology: Mechanisms that Increase Genetic Variation (12:00 min.)
http://www.bozemanscience.com/034-mechanisms-that-increase-genetic-variation

Bozeman Biology: Mutations (8:00 min.)
http://www.bozemanscience.com/mutations

Bozeman Biology: Natural Selection (9:00 min.)
http://www.bozemanscience.com/001-natural-selection