*Review Article*

Indian Journal of Genetics and Molecular Research
Volume 9 Number 1, January–June 2020
DOI: http://dx.doi.org/10.21088/ijgmr.2319.4782.9120.3

# Mutation, the Structural Genetic Change: A Short Review

**D K Sharma**

**How to cite this article:**
D K Sharma, Mutation, the Structural Genetic Change: A Short Review. Indian J Genet Mol Res. 2020;9(1):.23–27

**Abstract**

Mutation is an alteration that occurs in our DNA sequence, generally due to the error developed when the DNA is copied or as the result of environmental causes such as radiations like ultraviolet rays, cigarette smoke etc. On the whole, there are 3 kinds of DNA mutations, the base substitutions, the deletions and the additions. Mutation is the resource of newness and it creates new forms of species, potentially instantaneously in a sudden jump. This was envisaged as a pouring evolution and limited by the contribution of mutations. Mutationism is one of the alternatives to evolution by natural selection. It is continued living both before and after the publication of Charles Darwin's 1859 book, 'On the Origin of Species'. The whole human community is one species with the same genes. Mutation builds somewhat dissimilar translations of the similar genes, called alleles. Then meiosis and sexual reproduction combine different alleles in new ways to increase genetic variation. These little variations in the DNA series make each creature distinctive in its hair and skin color, dimension, form, figure, behavior and receptiveness of disease. These genetic dissimilarities are valuable in helping populations modify over time. Variations that help the living being go on to survive and to reproduce pass on to the subsequent generations. The variations which obstruct the survival and the reproduction are abolished from that population. This progression of normal selection can lead to major changes in the form, appearance, activities, behavior or functioning of the individuals in that population, in just a few subsequent generations.

**Keywords:** Replication; Polymerization; Mutagen; Phenotype; Translocation.

## Introduction

During the replication of the DNA, in the polymerization of the second strand, sometimes errors occur. These errors are called mutations and they affect the phenotype of the organism. The frequency of these errors is usually very low about 1 mutation in every 10-100 million bases due to the proofreading ability of the DNA polymerases.[1] Mutations can also be caused by the contact to the specific chemicals and the radiations which cause the DNA to be broken down and the cell would be ending up with the DNA somewhat different from the original DNA. The mutagenic chemicals promote mutation due to interfering with the arrangement of the base-pairing while UV radiation induces it by damaging the DNA structure. It has also been claimed that during chromosomal crossover to exchange the DNA and recombine genes, errors in alignment during meiosis can also cause mutations. These types of errors generate large structural modifications in the DNA sequence like the duplications, the inversions, the deletions of whole regions; or the accidental replacement of the entire parts of series among different chromosomes called chromosomal translocation. So the radiation, the chemicals, the derivatives of cellular metabolism, the free radicals, the ultraviolet rays from the sun etc harm the thousands of nucleotides in the cells every day. They have an effect on the nucleotides themselves changing one base to another, hammering the base off its moral fiber and even developing a split in the DNA filament. At the majority of the time, the mutation is reversed by the natural DNA repair mechanism, constantly working in the cells, setting

**Author's Affiliation:** Additional Professor and Head, Department of Anatomy, All India Institute of Medical Sciences (AIIMS), Raipur, Chhattisgarh-492099, India.

**Corresponding Author: D K Sharma,** Additional Professor and Head, Department of Anatomy, All India Institute of Medical Sciences (AIIMS), Raipur, Chhattisgarh-492099, India.

**E-mail:** dhyanesh.sharma@gmail.com

up the mismatched nucleotides and fixing together the DNA strands back together. In spite of this, some DNA changes remain persisted and if a cell accumulates too many changes or the DNA is so damaged that repair mechanism cannot fix it then it either stops dividing or it destructs. If any of these processes go wrong, the cell can become cancerous.

Mutations may or may not make perceptible changes in the recognizable characteristics or phenotype of an organism and play roles in both the normal and the abnormal biological processes including evolution, malignancy, development of the immune system, junctional diversity etc. There is actually the alteration of the nucleotide sequence of the genome of an organism, virus or extrachromosomal DNA. Mutations result from errors during DNA replication, mitosis and meiosis or other types of damage to the DNA such as pyrimidine dimmers that may be produced by the exposure to the radiation or the carcinogens and then may undergo error-prone repair.[2] This error-prone procedure frequently results in the mutations. Mutations may result also from the insertion or the deletion of the fragment of the DNA due to mobile genetic elements.[3] The genomes of RNA viruses are based on RNA rather than the DNA. The RNA genome in a virus can be the double-stranded as in the DNA or the single-stranded. In some viruses, the replication occurs rapidly and so there are no methods to verify the genome for its accuracy.

### *Description*

Mutations cause various changes in the sequences and the genes can have either no effect to alter the product or avert the gene from its functioning properly. Mutations can be possible and occur in the nongenic regions. Organisms have mechanisms like the DNA repairing to stop or to correct the mutations by correcting the mutated series back to its normal situation. Mutations can involve the duplication of large sections of the DNA, usually through genetic recombination.[4] Novel genes are created by several methods, commonly in the course of the duplication and the mutation of an inherited gene, or by the recombining parts of the different genes to form the new arrangements with the new functions.[5] One benefit of copying a gene or even a complete genome is that this increases engineering redundancy which permits one gene in the pair to obtain a new role whereas the other copy executes the original earlier function.[6] Sequences of the DNA which can shift regarding the genome such as transposons make up the important fractions of the genetic materials of the plants and the animals and may have been significant in the development and evolution of genomes. For the example, about a million copies of the Alu sequence are present in the human genome and these series have been recruited now to carry out functions like regulating gene expression.[7] Another outcome of these itinerant DNA series is that when they shift within a genome, they can alter, mutate or delete the existing genes and so can produce genetic diversities.

Changes in chromosome number may engage even the larger mutations, where the segments of the DNA in chromosomes split and after that get rearranged. In the evolution, the most imperative function of such chromosomal reorganizations may be to hasten the divergence of the population into the new species by building populations less likely to interbreed, and so preserving the genetic variations among these populations.[8] The profusion of some genetic modifications within that gene pool can be lessened by the natural selection, while the other more favorable mutations can amass and result in the adaptive alterations. Nonlethal mutations accumulate within the gene pool and can increase the quantity of genetic dissimilarities.[9] Neutral mutations are defined as the mutations, where the special effects do not manipulate the fitness of the creature. These can be increased in the rate of recurrence over time by the genetic drift. It is assumed that the overwhelming bulk of mutations have no significant outcome on the fitness of an organism.[10] Also, the DNA repairing mechanisms are capable to mend most changes prior to the turn out to be permanent mutations and the organisms have mechanisms for eradicating otherwise everlastingly mutated somatic cells. The beneficial mutations can get better reproductive achievement. [11]

### *Causes and Types*

The causes distinguish the mutations as (i) Spontaneous mutations due to molecular decay (ii) Error-prone replication mutations also called error-prone translation synthesis mutations (iii) Errors introduction during the DNA repair mutations and (iv) Mutagens induced mutations at molecular level by chemicals and radiation. No doubt the scientists can also consciously introduce mutant sequences through the DNA manipulation for the sake of scientific experimentation.

One 2017 studies declared that 66% of cancer producing mutations are accidental, 29% are due to the surrounding atmosphere or environment and only 5% are inherited. It is also claimed that

the human beings on an average pass about 60 new mutations to their offspring but fathers go by more mutations according to their age with every year adding two fresh mutations to the child.[12] Spontaneous mutation can be categorized by the precise alteration as the Tautomerism, the Depurination, the Deamination, the Slipped strand mispairing and the Replication slippage[13].

Mutations may also be broadly classified as follows:

A. Mutation due to effect on the structure of genes: It can be subclassified into several types. In Small-scale mutations, one single or a few nucleotides in a gene on chromosome are affected. If only a single nucleotide is affected then it is called a point mutation. In large scale mutations include amplifications/gene duplications or repetition of a chromosomal segment or presence of an extra piece of a chromosome, deletions of large chromosomal regions, distinct fusion genes, chromosomal rearrangements (translocations, inversions, crossover etc), interstitial/intra-chromosomal deletion and loss of heterozygosity.

B. Mutation due to effect on function: Inactivating or amorphic mutation is resulted when the allele has no function (null allele or amorph). In contrast there is an activating-mutation due to gain in function. In dominant negative mutation also called antimorphic mutation, an altered gene creation takes action antagonistically to the natural type allele resulting in a changed molecular purpose often inactive and differentiated by a dominant or semi-dominant phenotype.[14] Lethal mutations are mutations which lead to the fatality of the organisms carrying the mutations. A reverse mutation or reversion is a point mutation that re-establishes the original series and consequently the original phenotype.

C. Mutation in respect to fitness: It is either may be harmful or may be beneficial applied genetics. A harmful or deleterious mutation declines the fitness of the organism whereas a beneficial or advantageous mutation enhances the fitness of the organism. A neutral mutation has no harmful or beneficial result and consequence on the organism. Such mutations take place at a stable rate, forming the foundation for the molecular clock. In the neutral hypothesis of the molecular evolution, the neutral mutations make available the genetic drift as the base for the most dissimilarity at the molecular stage. The DNA damage can cause an error when the DNA is replicated, and this error of replication can cause a gene mutation that in turn could cause a genetic disorder. The DNA damages are restored by the natural DNA repair scheme of the cell. The cell has a number of ways by which the enzymes recognize and then repair damages in the DNA. As the DNA can also be damaged in many other ways, the course of the DNA repair is a significant way by which the organism's body protects itself from the disease. Once the DNA injury has specified and given rise to the mutation then this mutation cannot be repairable.

D. Mutation by the impact on protein sequence: It includes a frameshift mutation caused by the insertion/addition or the deletion/removal of the nucleotides which is not evenly dividable by the three from a DNA series. The addition or the removal of nucleotides can interrupt the reading structure because of the triplet nature of the gene expression by the codons or the alliance of the codons, ensuing in a completely different translation from the original.[15] In contrast to it, any addition or deletion which is uniformly dividable by the three is called an in-frame mutation.

E. Mutation by the inheritance: It can be subdivided into the germline mutation passing on to the offspring by their reproductive cells and the somatic or the acquired mutation which involves the cells exterior to the dedicated reproductive grouping and that is not generally conveyed to the descendants. On the basis of the occurrence of mutation on every chromosome, the mutations may be classified into three categories. A heterozygous mutation, when it involves only one allele. A homozygous mutation, when it is an identical mutation of the paternal and maternal alleles both. The compound heterozygous mutations or a genetic compound includes the two different mutations in the paternal as well as the maternal alleles.[16] A wild type or the homozygous organism with non-mutated is one in which no allele is mutated.

F. Mutation under certain permissive environmental conditions: It results in mutant or altered phenotype under definite restrictive conditions like a temperature-responsive mutation can result the cell-death at a high temperature restrictive condition but has no injurious consequences at a low temperature permissive condition.[17] The team of the Human Genome Variation Society (HGVS) hasframed the standard human sequence variation

nomenclature.[18] Which should be utilized by the researchers and the DNA diagnostic centers to generate an unmistakable mutation descriptions. The nomenclature denotes the type of the mutation and the base or the amino acid alterations like the nucleotide substitution, the amino acid substitution and the amino acid deletion etc.

### *Beneficial or Harmful*

If the mutation is in a germ cell, it can give rise to the off spring carrying the mutation in all of its cells as in hereditary diseases. Particularly, if the mutation is in a germ cell with DNA repair gene, such germline mutation in the human may have an increased risk of cancer. A record of 34 such germline mutations has been expressed in the article DNA repair-deficiency disorder. The example of that is the albinism, in which a mutation occurs in the OCA1 or OCA2 gene. The persons with this type of disorder are more prone or likely to develop many types of the cancers; many other such disarrays have the damaged vision. On the other side, a mutation in a somatic cell of an organism is presented in all the offsprings of this cell in the same organism and some mutations may cause the cell to turn out to be malignant and thus cause cancer.

Mutation may be positive in a specified surroundings and environment. In this casing, the mutation may facilitate the mutant organism to survive in the particular environmental conditions and hassles better than the wild-type organisms or mimic more quickly. In such cases, the mutation will be inclined to become more regular in the inhabitants in the course of natural selection. Examples include the HIV resistance where a particular 32 base-pair removal or deletion in the human confers the HIV resistance to the homozygotes and delays the AIDS onset in the heterozygotes.[19] The Malaria resistance is one of the examples of the harmful mutation, in which the sickle cell disease, a blood disorder where the body generates an unusual type of the oxygen transporting substance hemoglobin in the red blood cells. In the sickle cell disease, those with just one of the two alleles are more defiant to malaria, since the invasion or infestation of the malaria plasmodium is brought to an end by the sickling of the red blood cells that it infests. The Lactase persistence is a mutation allowing the humans to digest the lactose, which is doubtlessly one of the most advantageous mutations in the recent human evolution.[20]

The Genetics is a branch of the bioscience that deals with the study of the genes, the genetic variation and the heredity in the organisms. Millennia Gregor Mendel, a scientist and Augustinian friar during the 19th century was the first to revise the genetics methodically and scientifically. Mendel deliberated the 'trait-inheritance' and observed that the organisms inherit traits by the way of discrete 'units of inheritance'. The trait inheritance and the molecular inheritance of the genes are still the primary principles of the genetics during 21st century however the modern genetics has lengthened some more steps beyond the inheritance towards revision of the function and the behavior of the genes. A number of subfields are now included in genetics like molecular genetics, the epigenetics and the population genetics etc.

Mutation generates variations in the protein-coding portions of the genes that can affect the protein itself. But still more frequently, it creates dissimilarities in the switches that manage whenever a protein is active anywhere and to a great extent the protein is made. The lactase is an enzyme helping the infants in breaking down the lactose in milk. Usually the gene coding for the lactase is active in the babies and then got turned off at about the age of four. When the inhabitants who don't construct the lactase consume the milk, they develop gas, nausea/vomiting and discomfort; but a few inhabitants have a difference in a genetic switch which maintains the lactase gene full active. This variation is called the lactase persistence and the people that have it can continue the milk in their habit even as the adults.

It's useful to think of the mutation as a process that creates genetic variation. We frequently refer the mutation as a thing, the genetic distinction itself. This movement can be constructive when it comes to a gene linked with a disease, then the disease allele transmits a mutation and a DNA change which cooperates with the protein function. On the other hand, this approach offers the mutation a bad name. Living the role of a gene doesn't always have an effect on health. For example, the majority of mammals have numerous genes coding for the olfactory receptors, proteins helping us smell. The losing one among these genes in all probability doesn't create all that much distinction. In compare to the distinctions that cause illness, there are numerous examples of the distinctions which are neither good nor terrible but just different like blood groups and eye colors. The development of mutation creates these more impartial variations just similar to disease alleles. With the neutral/impartial variations, it cannot be possible to inform that which allele are the normal one which existed first and which is the mutant and the variation is frequently insignificant.

### *Conclusion*

Mutation is an alteration that occurs in our DNA sequence, generally due to the error developed when the DNA is copied or as the result of environmental causes. It is the source of novelty; creating novel forms and species; potentially instantaneously in a sudden jump. This is envisaged as a driving evolution and one of the alternatives to evolution by natural selection. So, mutation is of central importance to all life forms, including human beings. Our human species would not have evolved over several billion years without mutations. It is an obvious truth that without mutations the mankind would not be faced with innumerable illnesses including spontaneous abortions, inherited disorders, congenital anomalies and cancers etc. Hence, we must comprehend and appreciate both, the nature of mutations and the possessions they produce.

### References


1. Freisinger E, Grollman AP, Miller H, Kisker C. Lesion (in) tolerance reveals insights into DNA replication fidelity. The EMBO Journal 2004;23(7):1494–505.
2. Sharma S, Javadekar SM, Pandey M,et. al. Homology and enzymatic requirements of microhomology dependent alternative end joining. Cell Death & Disease. March 2015;6(3):e1697.
3. Y T Aminetzach, J M Macpherson, D A Petrov. Pesticide resistance via transposition-mediated adaptive gene truncation in Drosophila. Science July 2005;309(5735):764–7.
4. P J Hastings, J R Lupski, S M Rosenberg, Ira G. Mechanisms of change in gene copy number. Nature Reviews. Genetics August 2009;10(8):551–64.
5. C A Orengo, J M Thornton. Protein families and their evolution-a structural perspective. Annual Review of Biochemistry July 2005;74:867–900.
6. Hurles M. Gene duplication: the genomic trade in spare parts. PLoS Biology. July 2004;2(7): E206.
7. Hasler J, Strub K. Alu elements as regulators of gene expression. Nucleic Acids Research November 2006;34(19):5491–7.
8. Ayala FJ, Coluzzi M. Chromosome speciation: humans, Drosophila and mosquitoes. Proceedings of the National Academy of Sciences of the United States of America May 2005;102(1):6535–42.
9. Eyre-Walker A, Keightley PD. The distribution of fitness effects of new mutations (PDF). Nature Reviews Genetics August 2007;8(8):610–8.
10. Bohidar HB. Fundamentals of Polymer Physics & Molecular Biophysics. Cambridge University Press January 2015. ISBN 978-1-316-09302-3.
11. Tibayrenc Michel. Genetics and Evolution of Infectious Diseases. Elsevier. 12 January 2017. ISBN 9780128001530.
12. Jha Alok. Older fathers pass on more genetic mutations: study shows. the Guardian. 22 August 2012.
13. Montelone BA. Mutation, Mutagens and DNA Repair. www-personal.ksu.edu. 1998. Archived from the original on 26 September 2015. Retrieved 2 October 2015.
14. Goh AM, Coffill CR, Lane DP. The role of mutant p53 in human cancer. The Journal of Pathology January 2011;223(2):116–26.
15. Hogan C Michael. Mutation. In Monosson, Emily (ed.) Encyclopedia of Earth. Washington DC. Environmental Information Coalition, National Council of Science and the Environment. 12 October 2010. Archived from the original on 14 November 2015.
16. Compound heterozygote. MedTerms. New York: Web MD. 14 June 2012. Archived from the original on 4 March 2016. Retrieved 9 October 2015.
17. Alberts. Molecular Biology of the Cell (6 ed.). Garland Science. 2014;487.
18. Den Dunnen J T, Antonarakis S E. Mutation nomenclature extensions and suggestions to describe complex mutations: a discussion. Human Mutation. January 2000;15(1):7–12.
19. Sullivan AD, Wigginton J, Kirschner D. The coreceptor mutation CCR 5 Delta 32 influences the dynamics of HIV epidemics and is selected for by HIV. Proceedings of the National Academy of Sciences of the United States of America. August 2001;98(18):10214–9.
20. Segurel L, Bon C. On the Evolution of Lactase Persistence in Humans. Annual Review of Genomics and Human Genetics. August 2017;18:297–319.