Genic and Genomic Mutations

Genic Mutations

Genic mutations are changes that occur within a single gene, altering the DNA sequence of that gene. Since genes code for proteins (or functional RNAs), such mutations can directly affect protein structure, function, or expression. They are among the most common and evolutionarily significant mutations studied in genetics, anthropology, and evolutionary biology.

1. Nature of Genic Mutations

A gene is made up of a specific sequence of nucleotides (A, T, G, C). Any permanent alteration in this sequence constitutes a genic mutation. Genic mutations differ from chromosomal mutations, which involve large segments of chromosomes, and genomic mutations, which involve changes in chromosome number.

2. Types of Genic Mutations

A. Base Substitution (Point Mutations)

A single nucleotide is replaced by another.

(i) Silent Mutation

Alters a codon but does not change the amino acid

(ii) Missense Mutation

Changes one amino acid in the protein

(iii) Nonsense Mutation

Converts a codon into a stop codon

B. Frameshift Mutations

Caused by insertion or deletion of one or more nucleotides not in multiples of three.

C. Insertion Mutations

Addition of one or more nucleotides

D. Deletion Mutations

Loss of one or more nucleotides

Why Do Genic Mutations Occur?

1. Errors During DNA Replication

Every time a cell divides, it must copy its entire DNA. Although cells have excellent proofreading systems, mistakes can still happen.

a. Base-pair mispairing

The wrong base is inserted during replication.

Example: Adenine (A) accidentally pairs with cytosine (C) instead of thymine (T). This single mistake may change the codon and alter the amino acid in the protein.

b. DNA slippage

During replication, the polymerase "slips" on repeated sequences, adding or missing bases.

Example: In diseases like **Huntington's disease**, repeated CAG sequences expand because of slippage.

Why it matters: Replication errors are the most common source of new mutations, occurring even in healthy cells

2. Spontaneous Chemical Changes in DNA

DNA is a chemical molecule, so it sometimes undergoes natural reactions even without external damage.

a. Deamination

A base loses an amino ($-NH_2$) group.

Standard example:
Cytosine (C) → Uracil (U).

Uracil pairs with adenine, so after replication the C–G pair may become a T–A pair.
This simple event can change an amino acid.

3. Mutagenic Agents (Environmental Causes of Mutation)

External physical or chemical agents can damage DNA, forcing the cell to repair it. Often the repair is imperfect, leading to mutation.

a. Radiation (UV, X-rays)

- **UV radiation** causes **thymine dimers**, linking two thymine bases together. During repair, incorrect bases may be inserted.
- **X-rays and gamma rays** cause DNA breaks, and rejoining can introduce small mutations.

b. Industrial chemicals and pollutants

Certain chemicals modify bases or insert themselves between DNA strands.

Example: Benzo[a]pyrene in cigarette smoke binds to guanine and distorts DNA, causing mispairing.

c. Reactive Oxygen Species (ROS)

These are highly reactive molecules produced during normal metabolism, inflammation, stress, or exposure to toxins.

Example: ROS can convert guanine → 8-oxoguanine, which incorrectly pairs with adenine. This leads to G→T mutations, common in aging and cancer.

1. Base Substitutions (Single Nucleotide Changes)

A base substitution occurs when **one nucleotide is replaced by another** (e.g., A → G). Depending on how this affects the protein-coding sequence, base substitutions may be:

- **Silent**
- **Missense**
- **Nonsense**

a. Silent Mutations

Silent mutations are a type of genic mutation in which a change occurs in the DNA sequence of a gene, but this change **does not alter the amino acid** sequence of the protein that is produced.

Because the protein remains the same, **the mutation usually has no visible effect on the organism's structure or function.** However, understanding silent mutations requires a clear grasp of how genetic information flows from DNA to protein.

First, it is important to understand **how proteins are made.** DNA carries genetic information in the form of nucleotide sequences. A gene is transcribed into messenger RNA (mRNA). During transcription, the DNA sequence is copied into **mRNA using complementary base pairing**. This mRNA then moves out of the nucleus to the cytoplasm, where it is translated into a protein by ribosomes.

Translation happens in groups of three nucleotides called **codons**. Each codon codes for one specific amino acid. For example, the codon GAA codes for the amino acid glutamic acid. The genetic code is said to be **degenerate**, meaning that most amino acids are coded by more than one codon. **Glutamic acid, for instance, is coded by both GAA and GAG**. This degeneracy is the central reason why silent mutations occur.

A silent mutation usually happens due to a base substitution. One nucleotide in the DNA is replaced by another. This change is carried into the mRNA during transcription. However, **because of the degeneracy of the genetic code, the altered codon may still code for the same amino acid**. As a result, the amino acid sequence of the protein remains unchanged, and the protein functions normally.

To understand the **mechanism step by step**, consider the following process. A gene has a DNA sequence that includes a codon such as CTT.

During transcription, this DNA codon produces an mRNA codon GAA.

During translation, the ribosome reads GAA and incorporates glutamic acid into the growing protein chain.

Now suppose a **mutation occurs in the DNA and CTT changes to CTC.**

During transcription, this produces the mRNA codon GAG instead of GAA. When the ribosome reads GAG, it still adds glutamic acid. Even though the DNA and mRNA sequences have changed, the final protein remains exactly the same.

This is a silent mutation.

Silent mutations most commonly occur at the third position of a codon. This position is often called the wobble position. Changes here are less likely to alter the amino acid because many codons differ only at this third base. For example, **the amino acid leucine is coded by UUA, UUG, CUU, CUC, CUA, and CUG.** A mutation changing CUU to CUC still results in leucine, making the mutation silent.

Another example involves the amino acid **glycine, which is coded by GGU, GGC, GGA, and GGG.** If a mutation changes GGU to GGC, the ribosome still inserts glycine. The DNA sequence has changed, but the protein is unaffected.

From an evolutionary perspective, silent mutations are very important. Since they usually do not affect fitness, **they can accumulate over generations.**

These neutral changes are widely used in molecular clocks to estimate evolutionary divergence between species. For example, comparisons of silent mutations in mitochondrial DNA are commonly used to trace human evolution and migration patterns.

b. Missense Mutations

Missense mutations are a type of genic mutation in which a change in the DNA sequence leads to the **replacement of one amino acid by another in a protein**. Unlike silent mutations, **missense mutations alter the amino acid sequence of the protein,** and this change can affect how the protein folds, behaves, or functions. The effect may be mild, severe, or sometimes even beneficial.

A missense mutation usually occurs because of a single base substitution in the DNA. One nucleotide is replaced by another. This altered DNA sequence is transcribed into mRNA, resulting in a changed codon.

When the ribosome reads this new codon during translation, it inserts a different amino acid into the protein at that position.

For example, consider a normal DNA sequence that includes the codon GAG. During transcription, this becomes the mRNA codon GAG, which codes for the amino acid glutamic acid.

If a mutation changes the DNA codon to GTG, the mRNA codon becomes GUG. GUG codes for valine instead of glutamic acid. This single amino acid change is a classic missense mutation.

The most well-known example of a missense mutation is **sickle cell anemia**. In this condition, a missense mutation occurs in the gene that codes for the beta chain of hemoglobin. **One nucleotide change leads to the substitution of glutamic acid with valine at the sixth position of the beta-globin protein**.

This small change alters the shape of hemoglobin, especially under low oxygen conditions, causing red blood cells to become sickle-shaped. These abnormal cells block blood vessels and lead to pain, anemia, and organ damage.

Not all missense mutations are harmful. Some cause only minor changes in protein function. For instance, a missense mutation might replace one amino acid with another that has similar properties, such as **substituting leucine with isoleucine. Both are nonpolar amino acids, so the overall structure of the protein may remain largely unchanged**. Such mutations are called conservative missense mutations.

In contrast, non-conservative missense mutations involve replacing an amino acid with one that has very different chemical properties. For example, **replacing a charged amino acid with a nonpolar one can disrupt protein folding or active sites**. The sickle cell mutation is a non-conservative missense mutation because a charged glutamic acid is replaced by a nonpolar valine.

c. Nonsense Mutations

Nonsense mutations are a type of genic mutation in which a change in the DNA sequence **converts a normal amino-acid–coding codon into a stop codon**. Because of this, protein synthesis stops earlier than it should, and the resulting protein is shorter and usually non-functional.

In the cytoplasm, the ribosome translates the mRNA into a protein. Translation occurs in sets of three nucleotides called codons. Each codon corresponds to a specific amino acid. **The ribosome starts translation at a start codon and continues adding amino acids one by one until it reaches a stop codon**.

Stop codons do not code for any amino acid. Instead, they signal the ribosome to stop translation. **In the genetic code, the stop codons are UAA, UAG, and UGA.**

A nonsense mutation occurs when a base substitution in the DNA changes a codon that normally codes for an amino acid into one of these **stop codons**. This mutation is copied into mRNA during transcription.

During translation, when the ribosome encounters this premature stop codon, it stops protein synthesis immediately. As a result, the protein produced is shorter than normal and often cannot perform its biological function.

For example, the codon CAG in DNA, which codes for glutamine. **A single base change can convert CAG into TAG**. During transcription, **TAG becomes UAG in mRNA**, **which is a stop codon.** This single change is enough to terminate protein synthesis prematurely. Translation stops at this point, and the protein chain is cut short.

In many cases, nonsense mutations trigger a protective cellular mechanism called **nonsense-mediated mRNA decay.** The cell recognizes that the mRNA contains a premature stop codon and destroys the mRNA before it can be translated. This prevents the production of faulty and potentially harmful truncated proteins. As a result, in such cases, no protein is produced at all.

Nonsense mutations are responsible for several genetic disorders. One example is **Duchenne muscular dystrophy**. In many patients, a nonsense mutation occurs in the **dystrophin gene.** This leads to the production of a very short and nonfunctional dystrophin protein or no protein at all. Without dystrophin, muscle fibers are easily damaged, leading to progressive muscle weakness.

Frameshift mutations

Frameshift mutations are a type of genic mutation in which the **reading frame of a gene is altered**. This happens when nucleotides are inserted into or deleted from the DNA sequence in numbers that are not multiples of three.

Because genetic information is read in groups of three nucleotides, **any such change shifts the entire reading frame**, leading to a completely different sequence of amino acids from the point of mutation onward. Frameshift mutations are usually very harmful because they drastically change the protein.

To understand frameshift mutations clearly, first understand that **the ribosome starts reading from a fixed start point and continues reading the sequence three bases at a time until it reaches a stop codon.**

In a normal gene, the sequence of codons is properly aligned, and the correct amino acids are added in the correct order. **This alignment is called the reading frame.** The reading frame depends on where translation begins and how the nucleotides are grouped into codons.

A frameshift mutation occurs when one or two nucleotides are inserted or deleted from the DNA sequence. Because the number of nucleotides added or removed is not divisible by three, **all the codons downstream of the mutation are regrouped.** As a result, the ribosome reads an entirely different set of codons after the mutation point.

For example, consider a **normal mRNA sequence: AUG UUU GCU ACA GGA UAA**

This sequence codes for a specific chain of amino acids. Now imagine that one nucleotide is deleted early in the sequence: **AUG UUG CUA CAG GAU AA**

After deletion, the grouping of codons changes completely. The ribosome now reads different codons, **resulting in different amino acids being added.**

The mechanism of a frameshift mutation begins at the DNA level. **During DNA replication, the DNA polymerase may accidentally skip a nucleotide or add an extra one.** This is more likely to occur in regions with repeated bases, such as AAA or CCC. Exposure to mutagens like certain chemicals or radiation can also cause insertions or deletions.

Once the altered DNA is transcribed into mRNA, the mRNA carries this shifted sequence to the ribosome. **The ribosome has no way of knowing that a mutation has occurred. It simply reads the mRNA in groups of three from the start codon.** Because the grouping is now wrong, **every codon after the mutation is incorrect.**

Frameshift mutations differ from base substitution mutations in their severity. A single base substitution affects only one codon, **while a frameshift mutation affects all downstream codons**. This is why frameshift mutations often result in nonfunctional proteins.

A classic example of a frameshift mutation is seen in **Tay–Sachs disease**. In many cases, a small insertion in the gene coding for the **enzyme hexosaminidase A** shifts the reading frame. As a result, the enzyme is not produced in a functional form. This leads to **the accumulation of toxic substances in nerve cells**, causing severe neurological damage.

2. Insertions and Deletions (Indels)

Insertion mutations

Insertion mutations are a type of genic mutation in which **one or more extra nucleotides are added** into the DNA sequence of a gene. This addition changes the original sequence of the gene and can affect how the genetic information is read and how the protein is made.

An insertion mutation begins at the DNA level. **During DNA replication, the enzyme DNA polymerase may accidentally add an extra nucleotide.** This error is more likely in regions where the same nucleotide is repeated many times, **such as AAAA or CCCC.** Insertions can also be caused by external factors like radiation, chemicals, or the movement of mobile genetic elements such as transposons.

Once the insertion has occurred in the DNA, it becomes a permanent part of the gene if it is not repaired. **This altered DNA is then transcribed into mRNA. The mRNA now carries the extra nucleotide or nucleotides.** During translation, the ribosome reads the mRNA from the start codon in groups of three bases, without skipping or correcting errors.

If the number of inserted nucleotides is not a multiple of three, the insertion causes a frameshift mutation. The reading frame changes, and every codon after the insertion is read incorrectly. This leads to a completely altered amino acid sequence and often introduces a premature stop codon. As a result, the protein is usually nonfunctional.

If the number of inserted nucleotides is a multiple of three, such as three or six, the reading frame is not shifted. In this case, **extra amino acids are added to the protein**, but the rest of the protein remains unchanged.

For example, if three nucleotides are inserted into a gene coding for an enzyme, **one extra amino acid will be added to the enzyme.** This extra amino acid may alter the shape of the active site and reduce or eliminate enzyme activity.

Insertion mutations are responsible for several genetic disorders. One example is **Huntington's disease,** which involves the insertion and expansion of repeated CAG codons in a gene. Each CAG codes for the amino acid glutamine. As the number of insertions increases, the resulting protein becomes toxic to nerve cells.

Deletion mutations

Deletion mutations are a type of genic mutation in which **one or more nucleotides are lost** from the DNA sequence of a gene. This loss changes the original genetic message and can strongly affect how a protein is made. **Deletion mutations are among the most disruptive genetic changes.**

A deletion mutation begins at the DNA level. **During DNA replication, the enzyme DNA polymerase may accidentally skip one or more**

nucleotides. This can happen especially in regions with repeated bases, such as AAAAA or CCCC, where the DNA strands can slip and misalign. Deletions can also be caused by external agents such as radiation, chemicals, or errors during DNA repair.

Once the deletion occurs and is not corrected by repair mechanisms, the altered DNA becomes permanent. This mutated DNA is transcribed into mRNA. The mRNA now lacks the nucleotide or nucleotides that were deleted in the DNA. When the ribosome reads this mRNA during translation, it reads the sequence exactly as it appears, without any correction.

If the number of deleted nucleotides is not a multiple of three, the deletion causes a frameshift mutation. The reading frame of the gene changes from the point of deletion onward. **As a result, all downstream codons are read incorrectly,** leading to a completely different amino acid sequence.

If the number of deleted nucleotides is a multiple of three, the reading frame remains intact. In this case, one or more amino acids are missing from the protein, but the rest of the protein is translated normally. Whether this affects protein function depends on the **importance of the missing amino acids.** If they are part of an active site or structural region, the protein may still be nonfunctional.

A well-known example of a deletion mutation is **cystic fibrosis** caused by the **deletion of three nucleotides in the CFTR gene.** This deletion removes a single amino acid, **phenylalanine**, from the protein. Although the reading frame is not shifted, the missing amino acid prevents proper folding of the protein, leading to its destruction inside the cell.

3. Splice-Site and Regulatory Mutations

Not all mutations occur within the protein-coding region. Mutations in **intron-exon boundaries** or **regulatory elements** can greatly alter gene expression.

a. Splice-Site Mutations

Genes in eukaryotes contain **introns (non-coding)** and **exons (coding)**. During RNA processing, introns are removed and exons joined.

Mutations at splice-site sequences can:

- Remove essential exons
- Include introns that should be removed
- Create entirely new splicing patterns (alternative splicing)

Example: A splice-site mutation in the **β-globin gene** can cause certain forms of β-thalassemia.

b. Regulatory Mutations

Mutations in **promoters, enhancers, silencers**, or **insulators** can alter *how much* and *when* a gene is expressed, even if the protein sequence is unchanged.

Effects:

- Increase gene expression
- Reduce gene expression
- Change tissue-specific expression
- Modify timing of development (heterochrony)

Examples in human adaptation:

1. **Lactase persistence** A regulatory mutation near the **LCT** gene allows adults to digest lactose.
   This is a classic gene–culture coevolution example.
2. **Brain development genes** Regulatory differences in genes such as **FOXP2** and **SRGAP2** contribute to neural and cognitive evolution.

Genomic Mutations

Genomic mutations are changes that **affect the number of chromosome**s in a cell rather than the structure of individual genes or chromosomes. In simple terms, they involve **gain or loss of whole chromosomes or entire sets of chromosomes.** These mutations arise mainly due to errors during cell division and have wide-ranging effects because they disturb the overall genetic balance of the organism.

To understand genomic mutations clearly, it is important to first recall **how chromosomes are normally maintained**. In sexually reproducing organisms, **body cells are diploid**, meaning they contain two sets of chromosomes. **Gametes are haploid** and contain one set. During meiosis, chromosomes must separate accurately so that each gamete receives the correct number. When this separation fails, genomic mutations occur.

Genomic mutations mainly arise due to a process called **nondisjunction. Nondisjunction is the failure of chromosomes or sister chromatids to separate properly during cell division.** This can occur during meiosis I, meiosis II, or even mitosis. As a result, some cells receive extra chromosomes while others lack them.

The effects of genomic mutations are usually severe because they disrupt the balance of gene expression. Each chromosome carries hundreds or thousands of genes. Adding or removing even one chromosome alters the dosage of many genes simultaneously, which affects development, metabolism, and overall viability.

Genomic mutations can be divided into two broad categories:

1. **Numerical changes (aneuploidy and polyploidy), and**
2. **Structural rearrangements (deletions, duplications, inversions, translocations).**

1. Numerical Chromosomal Changes

Numerical genomic mutations are **changes in the chromosome number of a cell.** In simple terms, they occur when cells gain or lose whole chromosomes or even entire sets of chromosomes. These mutations do not change the structure of chromosomes or individual genes, but **they disturb the total number of chromosomes present in a cell.** Because chromosomes carry many genes, numerical genomic mutations usually have strong effects on growth, development, and survival.

To understand numerical genomic mutations clearly, it is necessary to first understand how chromosome number is normally controlled. **In humans, body cells contain 46 chromosomes arranged in 23 pairs. This condition is called diploid.** Gametes such as sperm and eggs contain only one set of chromosomes, that is 23 chromosomes, and are called haploid. This reduction in chromosome number occurs through meiosis.

During meiosis, chromosomes must separate accurately so that each gamete receives exactly one chromosome from each pair. The same requirement exists during mitosis, where chromosomes must separate equally so that each daughter cell receives the same number of chromosomes. Numerical genomic mutations arise when this precise separation fails.

The main cause of numerical genomic mutations is nondisjunction. Nondisjunction is the failure of chromosomes or sister chromatids to separate properly during cell division. This can occur during meiosis I, meiosis II, or mitosis.

If nondisjunction occurs during meiosis I, homologous chromosomes fail to separate. Both chromosomes of a pair move into the same daughter cell. **As a result, some gametes receive an extra chromosome, while others**

receive none. When such abnormal gametes take part in fertilization, the resulting zygote has an abnormal chromosome number.

If nondisjunction occurs during meiosis II, sister chromatids fail to separate. This again leads to gametes with extra or missing chromosomes, although some gametes may remain normal.

Numerical genomic mutations can be broadly divided into two types: aneuploidy and polyploidy.

Aneuploidy involves the gain or loss of one or a few individual chromosomes, not entire sets. For example, trisomy means the presence of one extra chromosome, while monosomy means the absence of one chromosome. Aneuploidy is very common in humans and is responsible for many genetic disorders.

A classic example of aneuploidy is **Down syndrome**, where individuals have **three copies of chromosome 21**. Another example is Turner syndrome, where there is only one X chromosome. Klinefelter syndrome involves an extra X chromosome in males, resulting in an XXY condition. Trisomy 18 and trisomy 13 are other severe examples involving autosomes.

Polyploidy involves the presence of more than two complete sets of chromosomes. For example, triploid cells have three sets of chromosomes, and tetraploid cells have four sets. Polyploidy usually arises when cell division fails after DNA replication, or when unreduced gametes fuse during fertilization.

Polyploidy is rare and usually harmful in animals but very common and often beneficial in plants. Many crop plants are polyploid. Wheat is hexaploid, meaning it has six sets of chromosomes. Potatoes are tetraploid, and bananas are triploid. Polyploid plants often show larger size, increased vigor, and improved tolerance to environmental stress.

2. Structural Chromosomal Rearrangements

Structural genomic mutations are changes that involve the **physical structure of chromosomes.** In simple words, they occur when a part of a chromosome breaks, rearranges, or reattaches in an abnormal way. Unlike numerical genomic mutations, where the number of chromosomes changes, **structural genomic mutations alter the internal arrangement of genetic material** within chromosomes. These mutations can affect many genes at once and often have serious biological consequences.

To understand structural genomic mutations clearly, it is first important to understand the basic structure of chromosomes. **A chromosome is a long DNA molecule tightly packed with proteins.** Each chromosome has a **centromere, arms, and specific gene sequences arranged in a fixed order.** For normal functioning, this structure must remain stable. Structural mutations arise when chromosomes break and are incorrectly repaired.

The main cause of structural genomic mutations is breakage of DNA strands. Breaks can occur due to exposure to radiation, certain chemicals, viral infections, or errors during DNA replication. Sometimes, breaks also occur naturally during processes like crossing over in meiosis. Normally, the cell repairs these breaks accurately. However, if repair is faulty, structural mutations occur.

One common type of structural genomic mutation is deletion. In this case, **a segment of a chromosome is lost.** When a deletion occurs, all the genes present in that segment are missing. The severity of the effect depends on the size of the deleted segment and the importance of the genes involved.

A well-known example of deletion is **Cri-du-chat syndrome.** This condition occurs due to the **deletion of a part of the short arm of chromosome 5.** Affected infants have a characteristic cat-like cry, intellectual disability, and delayed development.

Another type of structural genomic mutation is duplication. In duplication, a segment of a chromosome is repeated, **resulting in extra copies**

of certain genes. This often occurs due to unequal crossing over during meiosis. Duplication increases gene dosage and can disturb normal development.

An example of duplication is seen in **Charcot–Marie–Tooth disease**, where duplication of a **segment on chromosome 17** affects nerve function and leads to muscle weakness and sensory problems.

Inversion is another form of structural mutation. In an inversion, a segment of a **chromosome breaks off, rotates 180 degrees, and reattaches** in the reverse direction. The total amount of genetic material remains the same, but the gene order is altered.

Inversions are of two types. If the inversion **does not include the centromere, it is called a paracentric inversion.** If it includes the centromere, it is called a **pericentric inversion**. In many cases, individuals with inversions are phenotypically normal. However, problems may arise during meiosis because proper pairing of chromosomes becomes difficult, leading to abnormal gametes.

Translocation is a structural mutation in which a segment of one chromosome is transferred to another chromosome. Translocations can be reciprocal, where two chromosomes exchange segments, or non-reciprocal, where a segment moves in one direction only.

A well-known example of translocation is the **Philadelphia chromosome**, seen in chronic myeloid leukemia. In this case, **a segment of chromosome 9 is translocated to chromosome 22**, creating a new abnormal gene that drives uncontrolled cell division.

Another important type of structural genomic mutation is **ring chromosome formation**. This occurs when both ends of a chromosome break and then join together to form a ring. Ring chromosomes are often unstable and can cause developmental problems.

Isochromosomes are another structural abnormality. In this case, a chromosome divides incorrectly, **resulting in two identical arms instead of one short and one long arm**. This leads to duplication of some genes and loss of others.

The mechanism behind all these structural mutations follows a common pattern.

First, the chromosome undergoes breakage.

Second, the broken ends are misrepaired or rejoined in an abnormal configuration.

Third, this altered chromosome is passed on during cell division, affecting gene expression and function.

In summary, structural genomic mutations involve rearrangements of chromosome segments caused by DNA breakage and faulty repair. They include deletions, duplications, inversions, translocations, ring chromosomes, and isochromosomes. These mutations affect many genes at once and are central to medical genetics, cancer biology, and evolutionary studies.

Structural Chromosomal Mutations in brief:

1. Deletions

A **deletion** occurs when a portion of a chromosome is lost. The size of the deletion determines how severe the effect is.

Small deletions remove a few genes; large deletions may remove hundreds.

Example: Cri-du-chat Syndrome

- Caused by deletion on the short arm of **chromosome 5**.
- Infants have a distinctive high-pitched cry (“cat-like”), facial features, and developmental delays.

2. Duplications

A **duplication** occurs when a segment of a chromosome is copied one or more times. This results in extra copies of genes, allowing evolution to "experiment."

Duplications are among the **most important sources of evolutionary innovation**.

Human evolutionary examples:

a. SRGAP2 duplications

- Slowed synapse maturation.
- Increased brain plasticity.
- Possibly linked to enhanced cognitive capacity in humans.

b. DUF1220 domain expansions

- Humans have far more copies than other primates.
- Strong correlation with brain size and neuron number.

c. AMY1 gene duplication

- Populations with high-starch diets (e.g., agricultural societies) have more copies of the **salivary amylase gene**, improving starch digestion.

3. Inversions

In an **inversion**, a chromosome segment breaks, flips 180°, and reinserts. No genetic material is gained or lost, but **gene order changes**.

Inversion heterozygotes (one inverted, one normal chromosome) often experience **reduced recombination** in the inverted region during meiosis.

Examples in human populations:

- A well-known inversion on **chromosome 17** has been linked to fertility differences and possible adaptive advantages in certain European groups.
- Some inversions correlate with climatic adaptation, immune resistance, or metabolic variation.

4. Translocations

A **translocation** occurs when a chromosome segment breaks and attaches to **another chromosome**.

Two main types:

1. **Reciprocal translocation** — segments are exchanged between chromosomes.
2. **Robertsonian translocation** — two acrocentric chromosomes fuse at their centromeres.

Example: Human chromosome 2

Humans have **46 chromosomes**, while chimpanzees and gorillas have **48**.
A **fusion (Robertsonian translocation)** created **human chromosome 2**.

This event:

- marks a key difference between humans and other apes
- is one of the strongest pieces of evidence for human–ape common ancestry
- may have influenced reproductive isolation and lineage separation