Mutation

A **mutation** is a permanent alteration in the **DNA sequence** of a gene, chromosome, or genome. Mutations can affect a single nucleotide or involve large segments of DNA, and they are fundamental drivers of genetic diversity, evolution, and many diseases, including cancer.

Types of Mutations

- **Point mutation** – A change in a single nucleotide.
  - *Missense*: Changes the amino acid.
  - *Nonsense*: Introduces a premature stop codon.
  - *Silent*: Does not change the amino acid.
- **Frameshift mutation** – Insertion or deletion (indel) of nucleotides that disrupts the reading frame.
- **Splice-site mutation** – Alters the normal splicing of exons and introns.
- **Insertion/Deletion (indel)** – Addition or loss of nucleotides.
- **Copy number variation (CNV)** – Duplication or deletion of gene regions.
- **Chromosomal rearrangement** – Inversions, translocations, or duplications of chromosomal segments.

Functional Consequences

- **Loss of function** – Common in tumor suppressor genes (e.g., *TP53*, *NF2*).
- **Gain of function** – Leads to new or increased activity (e.g., *EGFR* mutations).
- **Dominant-negative** – Mutated protein interferes with the normal version.
- **Neutral** – No significant impact on protein function.

Detection Methods

- **Sanger sequencing**
- **Next-Generation Sequencing (NGS)**
- **qPCR or digital PCR**
- **FISH (for large rearrangements)**

Related Concepts

- gene
- genetic_variation
- somatic_mutation
- germline_mutation
- dna_repair